Supporting Information

1-Benzyl-3-aryl-2-thiohydantoin derivatives as new anti-*Trypanosoma brucei* agents: SAR and in-vivo efficacy

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Mammalian cell growth inhibition assays

Compounds were screened against human lymphocytic cells as previously described (PMID: 22720744) with some modifications. CRL-8155 cells were grown in RPMI supplemented with 10% heat inactivated FBS, 2 mM L-glutamine, 0.4 mM sodium pyruvate, and 100 u/mL penicillin/100 µg/mL streptomycin at 37 ºC with 5% CO_2. Cells were added to 96-well plates with test compounds (quadruplicate serial three dilutions) and incubated for 48 hours. Plates were developed using AlamarBlue® (ThermoFisher Scientific) and percent inhibition was calculated by subtracting off the background (CRL-8155 cells with 50 µM Quinacrine purchased from MP Biomedicals, LLC) and comparing that to the high control (CRL-8155 cells without test compound). EC_{50} values were calculated by non-linear regression using software by the Collaborative Drug Database (Burlingame, CA. www.collaborativedrug.com).

Metabolic Stability

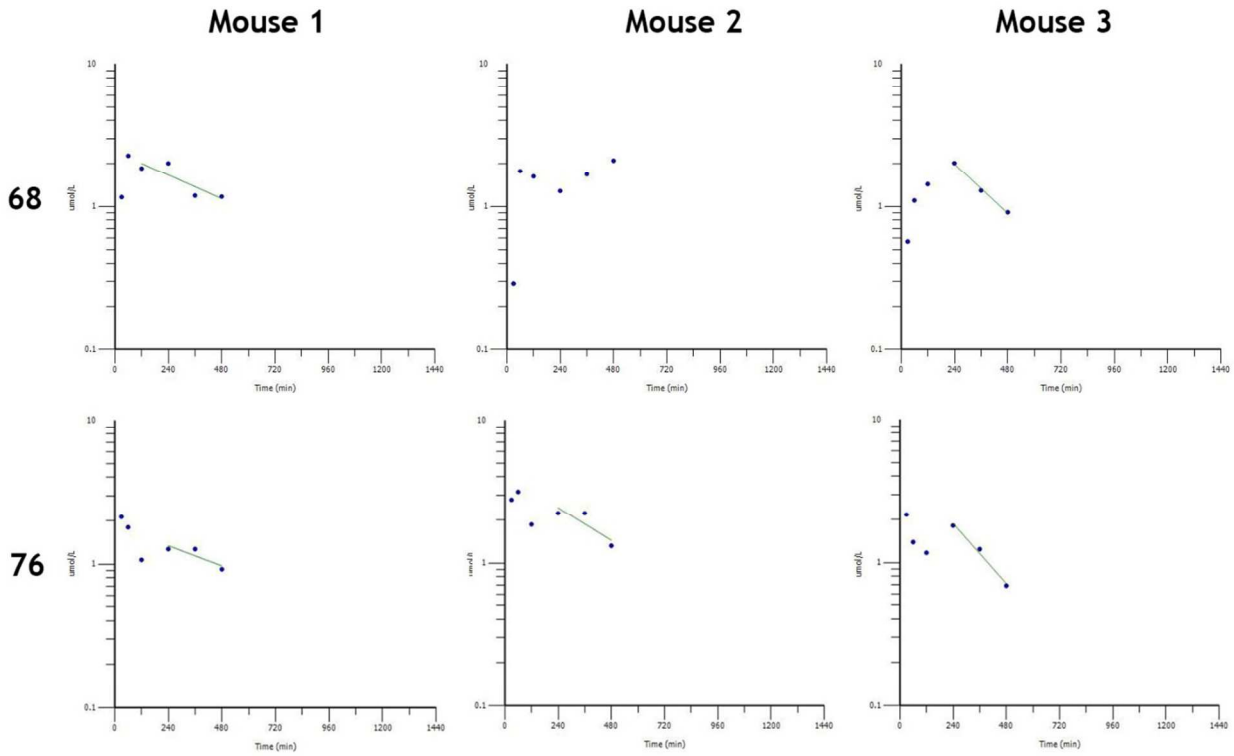
Compounds were tested in duplicate for stability against pooled mouse liver microsomes as previously described.[1] In brief, compounds were added to pooled mouse liver microsomes (BD Biosciences, San Jose, CA) to a final concentration of 1.5 µM of test compound and 0.5 mg/ml of mouse microsomes, and quenched at timepoints 0, 5, 10, 15, 30 and 60 minutes by addition of 4X volume of acetonitrile, then processed using liquid chromatography/tandem mass spectrometry. Control compounds testosterone and dextromethorphan (Sigma-Aldrich) were included as controls.

***T.brucei* toxicity assay**

Compounds were tested for antitrypanosomal activity against T.b.brucei (strain BF427) in HMI-9 media as previously described.[2] Compounds were assayed against *T.brucei* cells in triplicate against serial 3 dilutions of the compounds and quantified with Alamar Blue (ThermoFisher Scientific, Waltham, MA) at 48 h.[3] EC_{50} and EC_{90} values were calculated using nonlinear regression using software from the Collaborative Drug Database (Burlingame, CA. www.collaborativedrug.com). The control compound pentamidine isethionate (Sigma-Aldrich, St. Louis, MO.) was included in all assays.

Mouse Oral pharmacokinetics

Compounds were administered to mice orally at 50 mg/kg in a vehicle consisting of Phosal 53 MCT (Lipoid LLC, Newark, NJ) (60%), PEG400 (30%) and ethanol (10%), and blood was collected via tail-bleed into a heparinized capillary tube at timepoints 0.5, 1, 2, 4, 6, 8 and 24H post dose. This blood was spotted in a 15 µl volume onto Whatman FTA DMPK-C cards (GE Healthcare). A 3 mm disk was punched out of the dried blood spot, extracted with acetonitrile, then quantified by liquid chromatography/tandem mass spectrometry.



Brain-to-plasma concentration ratio determination
Compounds were administered to mice in a 400 ul volume at a concentration of 5 mg/kg via IP injection in a vehicle consisting of DMSO (5%), Tween80 (7%), and EtOH (3%) in a balance of 0.9% saline solution at t=0. A second set of mice (n=3) was also injected IP with vehicle. At 1 h post injection, mice were sacrificed, and blood was collected into heparinized capillary tubes, then briefly centrifuged to separate and collect plasma. Brains were removed at the same time and frozen to later be homogenized in water. The mouse plasma and brains from the vehicle group were used to generate standard curves, and levels of compound in the plasma and brain were determined via liquid chromatograph/tandem mass spectrometry. Calculations for brain concentrations accounted for the 3% volume/weight blood in the brain[4].

Solubility Assay
The solubility of select compounds was determined in a buffer of 1X phosphate buffered saline (PBS) that was pH adjusted to 7.4 to mimic the pH of blood. 50 µM solutions of the test compound were prepared. The 50 µM solutions were incubated at 37 ºC overnight while agitating on a plate shaker. After the incubation period, the solutions were centrifuged at 13500 rpm for 15 minutes at room temperature. Duplicate aliquots of each solutions' supernatant were isolated and analyzed using liquid chromatography/tandem mass spectrometry.

Protein Binding Assay
The protein binding of select compounds was examined using a house-made microdialysis device (paper in submission process). For each compound, a 2 µM solution was prepared in 50% mouse plasma (lithium heparin, female pooled, Swiss Webster from BioreclamationIVT, Westbury, NY) and 10X PBS buffer. The compound propranolol was used as a control. Three dialysis chambers per compound were each charged with the 2 µM 50% plasma solution in the donor chamber and blank 10X PBS buffer in the acceptor chamber. Samples were covered with a CO_2-permeable film (Axyseal polyester sealing film with acrylic adhesive from Corning Inc., Corning, NY) and incubated at 37 $^{\circ}$C, 5% CO_2 overnight or for at least 8 hours while agitating on a plate shaker. Once samples had reached equilibrium, each 50% plasma donor solution and PBS acceptor solution was extracted from the microdialysis device and an 80 µL aliquot was taken. Each solution was diluted with 4x volume of acetonitrile and held over ice for 30 minutes to denature proteins and release the compound. Samples were centrifuged at 3000 rcf for 15 minutes and supernatants were isolated and then concentrated prior to analysis via liquid chromatography/tandem mass spectrometry.

***T.brucei* Acute Efficacy**
Mice were injected IP with 10^4 *T.rhodesiense* STIB900 trypomastigotes in IMDM media on day 0. 48 hours post infection, mice were dosed orally bid for 4 days with 50 mg/kg of test compound. Compound was administered by oral gavage in a 0.2 ml

volume of vehicle consisting of 5% DMSO, 7% Tween80, 3% EtOH in a balance of 0.9% saline. A vehicle control group was also included that contained vehicle with no compound[5]. Mice were monitors for recurrence of parasitemia via microscopic evaluation of blood tail blood 3 times per week for the first month, and then weekly until the conclusion of the experiment at 60 days post infection, at which point the mice were considered cured if no parasites had yet been detected. If at any point during the monitoring parasites were detected, that mouse was removed from the experiment. The vehicle control group had to be removed on the 3rd day of dosing due to extremely high parasitemia.

General

All starting materials were purchased from various chemical vendors and used without further purification unless noted. Thin-layer chromatography was performed on Merck Silica Gel 60 F254 pre-coated plates. Column chromatography was conducted under medium pressure on silica (Cleanert Silica (40-60 µm)) from Agela Technologies. ^{1}H NMR spectra were recorded on a Bruker AV-300 spectrometer. Chemical shifts were referenced with respect to the residual solvents signals. Electrospray (ESI) mass spectra were obtained on Bruker Esquire Ion Trap Mass Spectrometer. All target compounds were recrystallized from ethanol or purified by Varian semi-preparative HPLC (Varian PrepStar, model 218, column YMC ODS-A, 100x20 mm, 5µm, flow: 10 mL/min, UV detector at : 218 nm and 254 nm) with mobile phase water: methanol, gradient 50% to 80% methanol over 15 min. All final compounds are judged to be > 95% pure by HPLC (UV at 254 nm and 218 nm).

Synthesis of 68

Preparation of **4**.

A solution of 4-fluorobenzaldehyde 1.24 g (10 mmol), glycine hydrochloride methyl ester (1.88g, 15 mmol) and trimethylamine (1.5 g, 15 mmol) in $CHCl_3$ (30 ml) was stirred with molecular sieves 3Å at RT for 2h. $NaCNBH_3$ (0.768g, 12 mmol) was added and the reaction mixture stirred at RT overnight. Precipitate was removed by filtration. Filtrate was concentrated by rotary evaporator and residue loaded to FC column. Compound was eluted with Hexane: Ethyl acetate = 10:3, fractions containing compound were collected and combined. Solvent was removed, and the residue dried under vacuum. Obtained 0.95 g (yield 48%) of an oily product (**4**).

^{1} H NMR (300 MHz, $CDCl_3$): δ 7.32-7.25 (m, 2H), 7.04-6.96 (m, 2H), 3.76 (s, 2H), 3.73 (s, 3H), 3.40 (s, 2H).

Preparation of **6**

5.25 g (30 mmol) of 3-chloro-4-fluoro-nitrobenzene and 6.1 g (75 mmol) of dimethylamine hydrochloride were dissolved at room temperature in 30 ml of DMSO. To clear solution 20 g (150 mmol) of K_2CO_3 was added and reaction mixture was stirred at 80ºC. Reaction progress was monitored by TLC (DCM), (Hex:EtOAc=10:3). After 3h the reaction was complete. Reaction mixture cooled down to room temperature and poured in ice-water. Precipitate collected by filtration and dried at room temperature. Obtained 5.7 g of yellow solid (yield 95%). Product was used in next step without further purification.(**6**)

^{1} H NMR (300 MHz, $CDCl_3$): δ 8.21 (d, J=3Hz, 1H), 8.05 (dd, J=9Hz, J=3Hz, 1H), 6.96 (d, J=9Hz, 1H), 3.00 (s, 6H).

Preparation of 3-chloro-4-dimethylamino aniline

5.7 g (28.5 mmol) of compound **6** was dissolved in EtOAc (40 ml) and to the solution 19.7g (87 mmol) of $SnCl_2x2H_2O$ was added and the mixture stirred at 80ºC for 4 h. Reaction progress monitored by TLC (DCM: EtOAc = 10:3). Reaction mixture cooled to RT and poured into diluted aqueous potassium hydroxide solution (to basic reaction by pH paper). Compound extracted by EtOAc (3x60 ml), organic extracts collected together, washed with aq. $NaHCO_3$ and brine. Solvent removed and the residue purified by FC (DCM, 300 ml, then DCM:EtOAc = 10:3). Fractions containing product collected, solvent removed and residue dried in vacuum. Obtained 3.1 g (64%) of pure amine.

^{1} H NMR (300 MHz, $CDCl_3$): δ 6.92 (d, J=9Hz, 1H), 6.72 (d, J=3Hz, 1H), 6.54 (dd, J=9Hz, J=3Hz, 1H), 3.53 (bs, 2H), 2.70 (s, 6H).

Preparation of isothiocyanate **7**

To in ice bath cooled mixture of DCM (30 ml) and aq.$NaHCO_3$ (30 ml) a 0.9 ml (11.7 mmol) of thiophosgene was added. To vigorously stirred mixture a solution of 3-chloro-4-dimethylamino aniline 2.0 g (11.7 mmol) in DCM (6 ml) and additional 0.9 ml (11.7 mmol) of thiophosgene were added dropwise. After the completion of addition, reaction mixture stirred under cooling (ice bath) for additional 15 min, then at RT for 1h. The layers were separated and organic layer poured through the syringe containing Na_2SO_4 and small layer of silicagel. Solvent and excess of thiophosgene were removed in rotovap. To the residue a toluene was added and rotovaped, residue dried under vacuum. Obtained 2.1 g (84% yield) of isothiocyanate. It was used in next step without further purification.

Preparation of compound **68**

75 mg (0.38 mmol) of compound **4** and 80 mg (0.38 mmol) of isothiocyanate (7) were dissolved in 1 ml of ethanol. Within a few minutes a white precipitate formed. Reaction mixture stirred at RT for 2h. Product filtrated, dried in vacuum. Obtained 100 mg (70% yield) of compound **68** as white precipitate. Product purity was >95% by TLC (DCM: EtOAc =10:3) and HPLC.

Synthesis of 76

Preparation of **10**

To the cooled in ice bath solution of 2-chloro-4-fluoro benzylamine (8.78 g, 55 mmol) in dry THF (20 ml) was added solution of methyl bromoacetate (3.8 g, 25 mmol) in dry THF (15 ml). After complete addition, cooling was removed and the reaction mixture stirred at RT for 2 h. Formed precipitate was filtered off and the solvent was removed in rotovap. Residue was purified by FC (Hexane: EtOAc =10:3). Fraction containing product was collected and solvent was removed. Obtained 3.6 g (yield 62%) of pure product (**10**).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (dd, J=9Hz, J= 6H, 1H), 7.10(dd, J=9Hz, J=3Hz, 1H), 6.95 (dt, J=9Hz, J=2Hz , 1H), 3.86 (s, 2H), 3.72 (s, 3H), 3.42 (s, 2H).

Preparation of **12**

2-Methoxy-4-nitroaniline (**11**) (3.36g, 20 mmol) and paraformaldehyde (5g, 163 mmol) were stirred in acetic acid (100 ml) at RT for 1h. $NaCNBH_3$ (5g, 80 mmol) was added to the solution and the reaction mixture stirred at RT overnight. Mixture poured into ice/water, basified with KOH to basic reaction by pH paper. Precipitate filtered, dried in vacuum. Obtained 3.7 g (yield 94%) of pure product **12**. Used in next step without further purification.

^{1}H NMR (300 MHz, CDCl3): δ 7.84 (dd, J=9Hz, J= 3H, 1H), 7.68(d, J=3Hz, 1H), 6.76 (d, J=9Hz, 1H), 3.93 (s, 3H), 2.97 (s, 6H).

Preparation of 3-methoxy-4-dimethylaniline

Compound **12** (3.6 g, 18.2 mmol) was dissolved in mixture of methanol (40 ml) and THF (20 ml). 360 mg of 10% Pd/C was added, reaction flask flushed with hydrogen gas, tightly closed and the excessive hydrogen pressure was set by balloon. Progress of the reaction was monitored by TLC (Hexane: EtOAc= 10:4). After stirring at RT for 12 h reaction was complete. Reaction mixture was filtrated trough Celite and solvent was removed. Obtained 2.7 g (89%) of pure product.

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.67 (d, J=9Hz, 1H), 6.63(d, J=3Hz, 1H), 6.28 (dd, J=9Hz, J=3Hz , 1H), 3.80 (s, 3H), 3.41 (bs, 2H), 2.75 (s, 6H).

Preparation of isothiocyanate **13**

To in ice bath cooled mixture of DCM (40 ml) and aq.$NaHCO_3$ (40 ml) a 0.9 ml (12 mmol) of thiophosgene was added. To vigorously stirred mixture a solution of 3-methoxy-4-dimethylaniline 2.0 g (12 mmol) in DCM (6 ml) and additional 0.9 ml (12 mmol) of thiophosgene were added dropwise. After the completion of additions, reaction mixture stirred under cooling (ice bath) for additional 15 min, then at RT for 1h. The layers were separated and organic layer poured through the syringe containing Na_2SO_4 and small layer of silicagel. Solvent and excess of thiophosgene were removed in rotovap. To the residue a toluene was added and rotovaped, residue dried under vacuum. Obtained 1.5 g (60% yield) of pure isothiocyanate (**13**).

Preparation of compound **76**

70 mg (0.30 mmol) of compound **10** and 63 mg (0.30 mmol) of isothiocyanate **13** were dissolved in 1 ml of ethanol. Within a few minutes a white precipitate formed. Reaction mixture stirred at RT for 2h. Product filtrated, dried in vacuum. Obtained 102 mg (yield 84%) of compound **76** as white precipitate. Product purity was >95% by TLC (DCM: EtOAc =10:3) and HPLC.

General procedure for the synthesis of 2-thiohydantoin derivatives.

0.13 mmol of corresponding N-benzylglycine methyl and 0.13 mmol of corresponding isothiocyanate were mixed and dissolved in 0.5 ml of ethanol. After stirring at RT precipitation of the product started within 1 min to 2h. Reaction mixture was kept at RT for 12h to complete precipitation. Product was filtrated, dried and if necessary recrystallized from ethanol. Purity of all compounds was >95%, confirmed by TLC, NMR and HPLC. Yields 0.11-0.06 mmol of pure product (85-46%).

NMR and MS spectra for compounds 1, 14-85. Yields for all final synthetic steps for all target compounds was >50% including purification. Individual yields for each compound are not given since yields after re-crystallzation will be highly variable and improved upon optimization of solvent amounts.

1-benzyl-3-(3-chloro-4-methoxyphenyl)-2-sulfanylideneimidazolidin-4-one (1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.35 (m, 6H), 7.22 (dd, J=3Hz, J=9Hz, 1H), 7.02 (d, J=9 Hz, 1H), 5.09 (s, 2H), 4.04 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 347.2 calculated for $[C_{17}H_{16}ClN_2O_2S]^+$: 347.1

1-benzyl-3-(4-methoxyphenyl)-2-sulfanylideneimidazolidin-4-one (14)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.35 (m, 4H), 7.24 (d , J= 9 Hz, 2H), 7.01 (d , J= 9 Hz, 2H), 5.10 (s, 2H), 4.04 (s, 2H), 3.84 (s, 3H); ESI MS m/z $(M+H)^+$: 313.4; $(M+Na)^+$: 335.4, calculated for $[C_{17}H_{17}N_2O_2S]^+$: 313.1 , $[C_{17}H_{16}N_2O_2SNa]^+$: 335.1

1-benzyl-3-(3-chlorophenyl)-2-sulfanylideneimidazolidin-4-one (15)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 7H), 7.28-7.22 (m, 2H), 5.09 (s, 2H), 4.06 (s, 2H); ESI MS m/z $(M+H)^+$: 317.4; $(M+Na)^+$: 339.2, calculated for $[C_{16}H_{14}ClN_2OS]^+$: 317.1, $[C_{16}H_{13}ClN_2OSNa]^+$: 339.0

1-benzyl-3-phenyl-2-sulfanylideneimidazolidin-4-one (16)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-7.29 (m, 10H), 5.11 (s, 2H), 4.06 (s, 2H); ESI MS m/z $(M+H)^+$: 283.4, calculated for $[C16H15N2OS]^+$: 283.1

1-benzyl-3-(3-methoxyphenyl)-2-sulfanylideneimidazolidin-4-one (17)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.34 (m, 6H), 7.00(dd, J=3Hz, J=9Hz, 1H), 6.92 (dd, J=3Hz, J=9Hz, 1H), 6.89-6.85 (m, 1H), 5.10 (s, 2H), 4.05 (s, 2H), 3.83 (s, 3H); ESI MS m/z $(M+H)^+$: 313.0, calculated for $[C17H17N2O2S]^+$: 313.1

1-benzyl-3-(4-chlorophenyl)-2-sulfanylideneimidazolidin-4-one (18)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50-7.25 (m, 9H), 5.09 (s, 2H), 4.06 (s, 2H); ESI MS m/z $(M+H)^+$: 317.4, calculated for $[C_{16}H_{14}ClN_2OS]^+$: 317.1

1-benzyl-3-(2-chlorophenyl)-2-sulfanylideneimidazolidin-4-one (19)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61-7.27 (m, 9H), 5.09 (q, J=15 Hz, 2H), 4.06 (d, J=6Hz, 2H); ESI MS m/z $(M+H)^+$: 317.3, calculated for $[C_{16}H_{14}ClN_2OS]^+$: 317.1

1-benzyl-3-(5-chloro-2-methoxyphenyl)-2-sulfanylideneimidazolidin-4-one (20)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.32 (m, 6H), 7.25(d, J=9Hz, 1H), 6.97 (d, J=9Hz, 1H), 5.18 (d, J=15Hz, 1H), 5.00 (d, J=15Hz, 1H), 4.05 (d, J=6Hz, 2H), 3.82 (s, 3H); ESI MS m/z $(M+H)^+$: 347.4, calculated for $[C_{17}H_{16}ClN_2O_2S]^+$: 347.1

1-benzyl-3-[4-chloro-3-(trifluoromethyl)phenyl]-2-sulfanylideneimidazolidin-4-one (21)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J=3Hz, 1H), 7.63 (d, J=9Hz, 1H), 7.51 (dd, J=3Hz, J=9Hz, 1H), 7.47-7.34 (m, 5H), 5.09 (s, 2H), 4.08 (s, 2H); ESI MS m/z $(M+H)^+$: 385.2 , calculated for $[C_{17}H_{13}ClF_3N_2OS]^+$: 385.0

1-benzyl-3-(3-chloro-4-fluorophenyl)-2-sulfanylideneimidazolidin-4-one (22)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.34 (m, 6H), 7.28-7.22 (m, 2H), 5.09 (s, 2H), 4.06 (s, 2H); ESI MS m/z $(M+H)^+$:335.2, calculated for $[C_{16}H_{13}ClFN_2OS]^+$: 335.0

1-benzyl-3-(5-chloro-2-fluorophenyl)-2-sulfanylideneimidazolidin-4-one (23)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48-7.32 (m, 6H), 7.20 (m, 2H), 5.14 (d, J=15 Hz, 1H), 5.03 (d, J=15Hz, 1H) 4.12 (d, J=18 Hz , 1H), 4.03 (d, J=18Hz, 1H); ESI MS m/z $(M+H)^+$: 335.3, calculated for $[C_{16}H_{13}ClFN_2OS]^+$: 335.0

1-benzyl-3-(4-fluorophenyl)-2-sulfanylideneimidazolidin-4-one (24)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.00 (m, 9H), 4.96 (s, 2H), 3.92 (s, 2H); ESI MS m/z $(M+H)^+$: 301.4; $(M+Na)^+$: 323.3, calculated for $[C_{16}H_{14}FN_2OS]^+$: 301.1, $[C_{16}H_{13}FN_2OSNa]^+$: 323.1

1-benzyl-3-[3,5-bis(trifluoromethyl)phenyl]-2-sulfanylideneimidazolidin-4-one (25)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.90 (s, 2H), 7.47-7.35 (m, 5H), 5.10 (s, 2H), 4.11 (s, 2H); ESI MS m/z $(M+H)^+$: 419.0, calculated for $[C_{18}H_{13}F_6N_2OS]^+$: 419.1

1-benzyl-3-[4-(dimethylamino)phenyl]-2-sulfanylideneimidazolidin-4-one (26)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 5H), 7.14 (d, J=9Hz, 2H), 6.77 (d, J=9Hz, 2H), 5.10 (s, 2H), 4.02 (s, 2H), 2.99 (s, 6H); ESI MS m/z $(M+H)^+$: 326.1, calculated for $[C_{18}H_{20}N_3OS]^+$: 326.1

1-benzyl-3-[4-(propan-2-yl)phenyl]-2-sulfanylideneimidazolidin-4-one (27)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 7H), 7.28-7.22 (m, 2H), 5.11 (s, 2H), 4.05 (s, 2H), 2.97 (q, 1H), 1.29 (s, 3H), 1.27 (s, 3H); ESI MS m/z $(M+H)^+$: 325.2, calculated for $[C_{19}H_{21}N_2OS]^+$: 325.1

1-benzyl-3-(4-hydroxyphenyl)-2-sulfanylideneimidazolidin-4-one (28)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.27 (m, 5H), 7.06 (d, J=9Hz, 2H), 6.88 (d, J=9Hz, 2H), 5.04 (s, 2H), 3.98 (s, 2H); ESI MS m/z $(M-H)^-$: 297.4, calculated for $[C_{16}H_{13}N_2O_2S]^-$: 297.1

3-(4-acetylphenyl)-1-benzyl-2-sulfanylideneimidazolidin-4-one (29)
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, J=9Hz, 2H), 7.49 (d, J=9Hz, 2H), 7.44-7.35 (m, 5H), 5.10 (s, 2H), 4.08 (s, 2H), 2.64 (s, 3H); ESI MS m/z $(M+H)^+$: 325.2, calculated for $[C_{18}H_{17}N_2O_2S]^+$: 325.1

4-(3-benzyl-5-oxo-2-sulfanylideneimidazolidin-1-yl)benzoic acid (30)
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, J=9Hz, 2H), 7.51 (d, J=9Hz, 2H), 7.47-7.34 (m, 5H), 5.11 (s, 2H), 4.09 (s, 2H); ESI MS m/z $(M+H)^+$: 327.1, $(M-H)^-$: 325.0, calculated for $[C_{17}H_{15}N_2O_3S]^+$: 327.1, $[C_{17}H_{13}N_2O_3S]^-$: 325.1

1-benzyl-3-(2,4-dimethoxyphenyl)-2-sulfanylideneimidazolidin-4-one (31)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 5H), 7.14(d, J=9Hz, 1H), 6.62-6.55 (m, 2H), 5.18 (d, J=15Hz, 1H), 5.03 (d, J=15Hz, 1H), 4.03 (d, J=6Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H); ESI MS m/z $(M+H)^+$: 343.1, calculated for $[C_{18}H_{19}N_2O_3S]^+$: 343.1

1-benzyl-3-(3,4-dimethoxyphenyl)-2-sulfanylideneimidazolidin-4-one (32)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.33 (m, 5H), 6.96 (d, J=9Hz, 1H), 6.89 (dd, J=3Hz, J=9Hz, 1H), 6.82 (d, J=3Hz, 1H), 5.10 (s, 2H), 4.04 (s, 2H), 3.91 (s, 3H), 3.89 (s, 3H); ESI MS m/z $(M+H)^+$: 343.7; $(M+Na)^+$: 365.4, calculated for $[C_{18}H_{19}N_2O_3S]^+$: 343.1, $[C_{18}H_{18}N_2O_3SNa]^+$: 365.1

1-benzyl-2-sulfanylidene-3-(3,4,5-trimethoxyphenyl)imidazolidin-4-one (33)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.34 (m, 5H), 6.54(s, 2H), 5.10 (s, 2H), 4.05 (s, 2H), 3.89 (s, 3H), 3.86 (s, 6H); ESI MS m/z $(M+H)^+$: 373.4, calculated for $[C_{19}H_{21}N_2O_4S]^+$: 373.1

1-benzyl-3-[3-chloro-4-(dimethylamino)phenyl]-2-sulfanylideneimidazolidin-4-one (34)
^{1}H NMR (300 MHz, CDCl3): δ 7.45-7.31 (m, 6H), 7.23-7.09 (m, 2H), 5.09 (s, 2H), 4.03 (s, 2H), 2.86 (s, 6H); ESI MS m/z $(M+H)^+$: 360.5, calculated for $[C_{18}H_{19}ClN_3OS]^+$: 360.1

1-benzyl-3-[4-(dimethylamino)-3-fluorophenyl]-2-sulfanylideneimidazolidin-4-one (35)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 5H), 7.05-6.89 (m, 3H), 5.09 (s, 2H), 4.03 (s, 2H), 2.90 (s, 6H); ESI MS m/z $(M+H)^+$: 344.1, calculated for [C18H19FN3OS]$^+$: 344.1

1-benzyl-3-[4-(dimethylamino)-3-methoxyphenyl]-2-sulfanylideneimidazolidin-4-one (36)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.35 (m, 5H), 7.00 (d, J=9Hz, 1H), 6.87 (dd, J=3Hz, J=9Hz, 1H), 6.78 (d, J=3Hz, 1H), 5.10 (s, 2H), 4.04 (s, 2H), 3.89 (s, 3H), 2.83 (s, 6H); ESI MS m/z $(M+H)^+$: 356.2 calculated for $[C_{19}H_{22}N_3O_2S]^+$: 356.1

1-benzyl-3-[3-(dimethylamino)-4-methoxyphenyl]-2-sulfanylideneimidazolidin-4-one (37)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.35 (m, 5H), 6.93 (s, 2H), 6.85 (s, 1H), 5.10 (s, 2H), 4.04 (s, 2H), 3.92 (s, 3H), 2.81 (s, 6H); ESI MS m/z $(M+H)^+$: 356.2, calculated for $[C_{19}H_{22}N_3O_2S]^+$: 356.1

3-(3-chloro-4-methoxyphenyl)-1-[(4-chlorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (38)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.30 (m, 5H), 7.21 (dd, J=3Hz, J= 9Hz, 1H), 7.02 (d, J=9Hz, 1H), 5.06 (s, 2H), 4.04 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 381.8; $(M+Na)^+$: 403.5, calculated for $[C_{17}H_{15}Cl_2N_2O_2S]^+$: 381.1, $[C_{17}H_{14}Cl_2N_2O_2SNa]^+$: 403.0

3-(3-chloro-4-methoxyphenyl)-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (39)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.34 (m, 3H), 7.21 (dd, J=3Hz, J= 9Hz, 1H), 7.10 (t, J=9Hz, 2H), 7.02 (d, J= 9Hz, 1H), 5.06 (s, 2H), 4.04 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 365.6; $(M+Na)^+$: 387.2, calculated for $[C_{17}H_{15}ClFN_2O_2S]^+$: 365.1, $[C_{17}H_{14}ClFN_2O_2SNa]^+$: 387.0

3-(3-chloro-4-methoxyphenyl)-1-[(3-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (40)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.34 (m, 2H), 7.23 (dd, J=3Hz, J=9Hz, 1H), 7.16 (d, 9Hz, 1H), 7.13-7.06 (m, 2H), 7.03 (d, J=9Hz, 1H), 5.08 (s, 2H), 4.06 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 366.0; $(M+Na)^+$: 387.3, calculated for $[C_{17}H_{15}ClFN_2O_2S]^+$: 365.1, $[C_{17}H_{14}ClFN_2O_2SNa]^+$: 387.0

3-(3-chloro-4-methoxyphenyl)-1-[(4-methylphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (41)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, J=7Hz, 1H), 7.30-7.17 (m, 5H), 7.01 (d, J=9Hz, 1H), 5.04 (s, 2H), 4.02 (s, 2H), 3.94 (s, 3H), 2.37 (s, 3H); ESI MS m/z $(M+H)^+$: 361.6; $(M+Na)^+$: 383.2, calculated for $[C_{18}H_{18}ClN_2O_2S]^+$: 361.1, $[C_{18}H_{17}ClN_2O_2SNa]^+$: 383.1

3-(3-chloro-4-methoxyphenyl)-1-[(4-methoxyphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (42)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, J=3Hz, 1H), 7.32 (d, J=9Hz, 2H) 7.21 (d, J=3Hz, 1H), 7.02 (d, J=9Hz, 1H), 6.92 (d, J=9Hz, 2H), 5.02 (s, 2H), 4.02 (s, 2H), 3.94 (s, 3H), 3.83 (s, 3H); ESI MS m/z $(M+H)^+$: 377.2, calculated for $[C_{18}H_{18}ClN_2O_3S]^+$: 377.1

3-(3-chloro-4-methoxyphenyl)-2-sulfanylidene-1-{[4-(trifluoromethyl)phenyl]methyl}imidazolidin-4-one (43)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J=9Hz, 2H), 7.52 (d, J=9Hz, 2H), 7.37 (d, J=3Hz, 1H), 7.22 (dd, J=3Hz, J=9Hz, 1H), 7.03 (d, J=9Hz, 1H), 5.15 (s, 2H), 4.08 (s, 2H), 3.95 (s, 3H); ESI MS m/z $(M+H)^+$: 415.2 , calculated for $[C_{18}H_{15}ClF_3N_2O_2S]^+$: 415.0

4-{[3-(3-chloro-4-methoxyphenyl)-4-oxo-2-sulfanylideneimidazolidin-1-yl]methyl}benzonitrile (44)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J=9Hz, 2H), 7.50 (d, J=9Hz, 2H), 7.36 (d, J=3Hz, 1H), 7.22 (dd, J=9Hz, J=3Hz, 1H), 7.03 (d, J=9Hz, 1H), 5.14 (s, 2H), 4.09 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 372.2, calculated for $[C_{18}H_{15}ClN_3O_2S]^+$: 372.1

methyl 4-{[3-(3-chloro-4-methoxyphenyl)-4-oxo-2-sulfanylideneimidazolidin-1-yl]methyl}benzoate (45)
^{1}H NMR (300 MHz, CDCl3): δ 8.07 (d, J=6Hz, 2H), 7.44 (d, J=6Hz, 2H), 7.37 (bs, 1H), 7.29-7.18 (m, 1H), 7.02 (d, J=9Hz, 1H), 5.14 (s, 2H), 4.05 (s, 2H), 3.96 (bs, 6H); ESI MS m/z $(M+H)^+$: 405.2 , calculated for $[C_{19}H_{18}ClN_2O_4S]^+$: 405.1

3-(3-chloro-4-methoxyphenyl)-1-(pyridin-3-ylmethyl)-2-sulfanylideneimidazolidin-4-one (46)
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (bs, 2H), 7.80 (d, J=9Hz, 1H), 7.43-7.32 (m, 2H), 7.21 (dd, J=3Hz, J=9Hz, 1H), 7.03 (d, J=9Hz, 1H), 5.12 (s, 2H), 4.09 (s, 2H), 3.95 (s, 3H); ESI MS m/z (M+H)+: 348.2, calculated for $[C_{16}H_{15}ClN_3O_2S]^+$: 348.1

3-(3-chloro-4-methoxyphenyl)-1-[(2,4-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (47)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63-7.52 (m,,1H), 7.34 (d, J=3Hz, 1H), 7.19 (dd, J=3Hz, J=9Hz, 1H), 7.01(d, J=9Hz, 1H), 6.92 (d, J=9Hz, 2H), 5.09 (s, 2H), 4.16 (s, 2H), 3.94 (s, 3H); ESI MS m/z (M+H)+: 383.1, calculated for $[C_{17}H_{14}ClF_2N_2O_2S]^+$: 383.0

3-(3-chloro-4-methoxyphenyl)-1-[(2,6-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (48)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.32 (m, 2H), 7.20 (dd, J=3Hz, J=9Hz, 1H), 7.06-6.95 (m, 3H), 5.20 (s, 2H), 4.09 (s, 2H), 3.93 (s, 3H); ESI MS m/z (M+H)+: 383.1, calculated for $[C_{17}H_{14}ClF_2N_2O_2S]^+$: 383.0

3-(3-chloro-4-methoxyphenyl)-1-[(3,4-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (49)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, J=3Hz, 1H), 7.30-7.06 (m, 4H), 7.02 (d, J=9Hz, 1H), 5.04 (s, 2H), 4.07 (s, 2H), 3.94 (s, 3H); ESI MS m/z (M+H)+: 383.1, calculated for $[C_{17}H_{14}ClF_2N_2O_2S]^+$: 383.0

1-[(2-chloro-4-fluorophenyl)methyl]-3-(3-chloro-4-methoxyphenyl)-2-sulfanylideneimidazolidin-4-one (50)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (dd, J= 9Hz, J=6Hz, 1H), 7.35 (d, J=3Hz, 1H), 7.22 (dd, J=3Hz, J=1Hz, 1H), 7.21-7.18 (m, 1H), 7.09-6.99 (m, 2H), 5.20 (s, 2H), 4.13 (s, 2H), 3.94 (s, 3H); ESI MS m/z $(M+H)^+$: 399.1, calculated for $[C_{17}H_{14}Cl_2FN_2O_2S]^+$: 399.0

5-{[3-(3-chloro-4-methoxyphenyl)-4-oxo-2-sulfanylideneimidazolidin-1-yl]methyl}-2-fluorobenzonitrile (51)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74-7.64 (m, 2H), 7.36 (d, J=3Hz, 1H), 7.33 -7.18(m, 2H), 7.03 (d, J=9Hz, 1H), 5.09 (s, 2H), 4.10 (s, 2H), 3.95 (s, 3H); ESI MS m/z $(M+H)^+$: 390.4, calculated for $[C_{18}H_{14}ClFN_3O_2S]^+$: 390.0

3-(3-chloro-4-methoxyphenyl)-1-[(4-fluoro-2-methoxyphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (52)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (dd, J=9Hz, J=6Hz, 1H), 7.34 (d, J=3Hz, 1H), 7.19 (dd, J=9Hz, J=3Hz, 1H), 7.00 (d, J=9Hz, 1H), 6.73-6.62 (m, 2H), 5.02 (s, 2H), 4.14 (s, 2H), 3.93 (s, 3H), 3.88 (s, 3H); ESI MS m/z $(M+H)^+$: 395.1, calculated for $[C_{18}H_{17}ClFN_2O_3S]^+$: 395.1

3-(3-chloro-4-methoxyphenyl)-1-[(4-fluoro-2-nitrophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (53)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (dd, J=9Hz, J=3Hz, 1H), 7.72 (dd, J=9Hz, J=6Hz, 1H), 7.46-7.38 (m ,1H), 7.37 (d, J=3Hz, 1H), 7.22 (dd, J=9Hz, J=3Hz, 1H), 7.03 (d, J=9Hz, 1H), 5.41 (s, 2H), 4.24 (s, 2H), 3.95 (s, 3H); ESI MS m/z $(M+H)^+$: 410.2, calculated for $[C_{17}H_{14}ClFN_3O_4S]^+$: 410.0

3-(3-chloro-4-methoxyphenyl)-1-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-2-sulfanylideneimidazolidin-4-one (54)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (dd, J=9Hz, J=6Hz, 1H), 7.44 (dd, J=9Hz, J=3Hz, 1H), 7.37 (d, J=3Hz, 1H), 7.32 (dt, J=9Hz, J=3Hz, 1H), 7.23 (dd, J=9Hz, J=3Hz, 1H), 7.03 (d, J=9Hz ,1H), 5.28 (s, 2H), 4.04 (s, 2H), 3.95 (s, 3H); ESI MS m/z $(M+H)^+$: 433.2, calculated for $[C_{18}H_{14}ClF_4N_2O_2S]^+$: 433.0

3-(3-chloro-4-methoxyphenyl)-1-[(4-fluorophenyl)methyl]imidazolidine-2,4-dione (55)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (d, J=3Hz, 1H), 7.35-7.27 (m, 3H), 7.10 (d, J=9Hz, 1H), 7.07 (d, J=9Hz, 1H), 7.00 (d, J=9Hz, 1H), 4.61 (s, 2H), 3.93 (s, 3H), 3.89 (s, 2H); ESI MS m/z $(M+H)^+$: 349.1, calculated for $[C_{17}H_{15}ClFN_2O_3]^+$: 349.1

3-(3-chloro-4-methoxyphenyl)-5-ethoxy-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (56)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J=9Hz, 1H), 7.42 (d, J=9Hz, 1H), 7.32 (d, J=3Hz, 1H) 7.18 (dd, J=9Hz, J=3Hz, 1H), 7.08 (t, J=9Hz, 2H), 7.01 (d, J=9Hz, 1H), 5.51 (d, J=14Hz, 1H), 5.03 (s, 1H), 4.55 (d, J=14Hz, 1H), 3.94 (s, 3H), 3.75-3.64 (m ,1H), 3.63-3.50 (m, 1H), 1.25 (t, J=6Hz, 3H); ESI MS m/z $(M+H)^+$: 409.3, calculated for $[C_{19}H_{19}ClFN_2O_3S]^+$: 409.1

3-(3-chloro-4-methoxyphenyl)-1-[(4-fluorophenyl)methyl]-5-methyl-2-sulfanylideneimidazolidin-4-one (57)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.34 (m, 3H), 7.22 (dd, J=3Hz, J= 9Hz, 1H), 7.10 (d, J=9Hz, 1H), 7.07 (d, J=9Hz, 1H), 7.02 (d, J= 9Hz, 1H), 5.69 (d, J=15Hz, 1H), 4.52 (d, J=15Hz, 1H), 4.05 (q, J=7Hz, 1H), 3.94 (s, 3H), 1.53 (d, J=7Hz, 3H); ESI MS m/z (M+H)+: 379.2, calculated for $[C_{18}H_{17}ClFN_2O_2S]^+$: 379.1

1-benzyl-3-(3-chloro-4-methoxyphenyl)-2-sulfanylideneimidazolidine-4,5-dione (58)
1 H NMR (300 MHz, $CDCl_3$): δ 7.55-7.44 (m, 2H), 7.43-7.30 (m, 4H), 7.17 (dd, J=9Hz, J=3Hz, 1H), 7.02 (d, J=9Hz, 1H), 5.21 (s, 2H), 3.95 (s, 3H); ESI MS m/z $(M+H)^+$: 361.1, calculated for $[C_{17}H_{14}ClN_2O_3S]$: 361.0

3-(3-chloro-4-methoxyphenyl)-1-(1-phenylethyl)-2-sulfanylideneimidazolidin-4-one (59)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.31 (m, 6H), 7.21 (dd, J=3Hz, J=9Hz, 1H), 7.01 (d, J=9 Hz, 1H), 6.37 (q, J=7Hz,1H), 4.03 (d, J=19Hz, 1H), 3.94 (s, 3H), 3.73 (d, J=19Hz, 1H), 1.70 (d, J=7Hz, 3H); ESI MS m/z $(M+H)^+$: 361.1, calculated for $[C_{18}H_{18}ClN_2O_2S]^+$: 361.1

1-[(2-chloro-4-fluorophenyl)methyl]-3-(3,4-dimethoxyphenyl)-2-sulfanylideneimidazolidin-4-one (60)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (dd, J= 9Hz, J=6Hz, 1H), 7.21 (dd, J=9Hz, J=3Hz, 1H), 7.09-7.01 (m, 1H), 6.96 (d, J=9Hz, 1H), 6.88 (dd, J=9Hz, J=3Hz, 1H), 6.80 (d, J=9Hz, 1H), 5.21 (s, 2H), 4.14 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H); ESI MS m/z (M+H)+: 395.2, calculated for $[C_{18}H_{17}ClFN_2O_3S]^+$: 395.1

3-(3,4-dimethoxyphenyl)-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (61)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.33 (m, 2H), 7.15-7.05 (m, 2H), 6.96 (d, J=9Hz, 1H), 6.88 (dd, J=3Hz, J=9Hz, 1H), 6.81 (d, J=3Hz, 1H), 5.07 (s, 2H), 4.04 (s, 2H), 3.91 (s, 3H), 3.86 (s, 3H); ESI MS m/z $(M+H)^+$: 361.2, $(M+Na)^+$: 383.0, calculated for $[C_{18}H_{18}FN_2O_3S]^+$: 361.1, $[C_{18}H_{17}FN_2O_3SNa]^+$: 383.1

1-[(2,4-difluorophenyl)methyl]-3-(3,4-dimethoxyphenyl)-2-sulfanylideneimidazolidin-4-one (62)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.54 (m, 1H), 6.99-6.83 (m, 4H), 6.79 (d, J=3Hz, 1H), 5.10 (s, 2H), 4.16 (s, 2H), 3.91 (s, 3H), 3.87 (s, 3H); ESI MS m/z $(M+H)^+$: 379.1, calculated for $[C_{18}H_{17}F_2N_2O_3S]^+$: 379.1

3-(3,4-dimethoxyphenyl)-1-[(4-fluoro-2-methoxyphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (63)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (dd, J=9Hz, J=6Hz, 1H), 6.95 (d, J=9Hz, 1H), 6.86 (dd, J=9Hz, J=3Hz, 1H), 6.80 (d, J=3Hz ,1H), 6.73-6.64 (m, 2H), 5.03 (s, 2H), 4.15 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H); ESI MS m/z $(M+H)^+$: 391.0, calculated for $[C_{19}H_{20}FN_2O_4S]^+$: 391.1

1-[(3,4-difluorophenyl)methyl]-3-(3,4-dimethoxyphenyl)-2-sulfanylideneimidazolidin-4-one (64)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.07 (m, 3H), 6.96 (d, J=9Hz, 1H), 6.88 (dd, J=3Hz, J=9Hz, 1H), 6.81 (d, J=3Hz, 1H), 5.05 (s, 2H), 4.07 (s, 2H), 3.92 (s, 3H), 3.89 (s, 3H); ESI MS m/z $(M+H)^+$: 379.1, calculated for $[C_{18}H_{17}F_2N_2O_3S]^+$: 379.1

3-(3,4-dimethoxyphenyl)-1-[(4-fluoro-2-nitrophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (65)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (dd, J=9Hz, J=3Hz, 1H), 7.72 (dd, J=9Hz, J=6Hz, 1H), 7.46-7.37 (m, 1H), 6.97 (d, J=9Hz ,1H), 6.89 (dd, J=9Hz, J=3Hz, 1H), 6.81 (d, J=3Hz, 1H), 5.42 (s, 2H), 4.23 (s, 2H), 3.92 (s, 3H), 3.89 (s, 3H); ESI MS m/z $(M+H)^+$: 406.2, calculated for $[C_{18}H_{17}FN_3O_5S]^+$: 406.1

3-(3,4-dimethoxyphenyl)-1-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-2-sulfanylideneimidazolidin-4-one (66)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (dd, J=9Hz, J=6Hz, 1H), 7.44 (dd, J=9Hz, J=3Hz, 1H), 7.32 (dt, J=9Hz, J=3Hz, 1H), 6.97 (d, J=9Hz, 1H), 6.90 (dd, J=9Hz, J=3Hz, 1H), 6.82 (d, J=3Hz, 1H), 5.29 (s, 2H), 4.04 (s, 2H), 3.92 (s, 3H), 3.89 (s, 3H); ESI MS m/z $(M+H)^+$: 429.2, calculated for $[C_{19}H_{17}F_4N_2O_3S]^+$: 429.1

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(2-chloro-4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (67)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (dd, J= 9Hz, J=6Hz, 1H), 7.32 (d, J=3Hz, 1H), 7.21 (dd, J=9Hz, J=3Hz, 1H), 7.17-7.01 (m, 3H), 5.20 (s, 2H), 4.13 (s, 2H), 2.86 (s, 6H); ESI MS m/z $(M+H)^+$: 412.5, calculated for $[C_{18}H_{17}Cl_2FN_3OS]^+$: 412.0

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (68)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.32 (m, 3H), 7.21-7.15 (m, 1H), 7.18 (d, J=3Hz, 1H), 7.11 (d, J=9Hz, 1H), 7.08 (d, J=9Hz ,1H), 5.06 (s, 2H), 4.04 (s, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 183.1 (CO), 169.4 (CS), 151.1 (CF), 130.6 (CN), 130.4 (2CH), 130.3 (2CH), 127.7 (CCl), 127.3 (C), 119.7 (C), 116.3 (CH), 115.9 (2CH), 51.5 (CH_2), 50.1 (CH_2), 43.4 ($2NCH_3$) ESI MS m/z $(M+H)^+$: 378.3, calculated for $[C_{18}H_{18}ClFN_3OS]^+$: 378.1; HRMS m/z $(M+H)^+$: 378.0836, calculated for $[C_{18}H_{18}ClFN_3OS]^+$: 378.0838.

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(2,4-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (69)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.53 (m, 1H), 7.31 (d, J=3Hz, 1H), 7.19-7.06 (m, 2H), 6.98-6.84 (m, 2H), 5.10 (s, 2H), 4.16 (s, 2H), 2.86 (s, 6H); ESI MS m/z $(M+H)^+$: 396.3, calculated for $[C_{18}H_{17}ClF_2N_3OS]^+$: 396.1

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(4-fluoro-2-methoxyphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (70)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (dd, J=9Hz, J=6Hz, 1H), 7.31 (d, J=3Hz, 1H), 7.20-7.08 (m, 2H), 6.73-6.62 (m, 2H), 5.02 (s, 2H), 4.14 (s, 2H), 3.88 (s, 3H), 2.86 (s, 6H); ESI MS m/z $(M+H)^+$: 408.3, calculated for $[C_{19}H_{20}ClFN_3O_2S]^+$: 408.1

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(3,4-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (71)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.07 (m, 6H), 5.04 (s, 2H), 4.06 (s, 2H), 2.87 (s, 6H); ESI MS m/z $(M+H)^+$: 396.4, calculated for $[C_{18}H_{17}ClF_2N_3OS]^+$: 396.1

3-[3-chloro-4-(dimethylamino)phenyl]-1-[(4-fluoro-2-nitrophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (72)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (dd, J=9Hz, J=3Hz, 1H), 7.79 (dd, J=9Hz, J=6Hz, 1H), 7.54-7.45 (m, 1H), 7.43-7.40 (m, 1H), 7.35 -7.18 (m, 2H), 5.50 (s, 2H), 4.31 (s, 2H), 2.95 (s, 6H); ESI MS m/z $(M+H)^+$: 423.4, calculated for $[C_{18}H_{17}ClFN_4O_3S]^+$: 423.1

3-[3-chloro-4-(dimethylamino)phenyl]-1-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-2-sulfanylideneimidazolidin-4-one (73) ^{1}H NMR (300 MHz, CDCl3): δ 7.61 (1H, bs), 7.44 (d, J=6Hz, 1H), 7.37-7.28 (m, 2H), 7.23-7.08 (m, 2H), 5.29 (s, 2H), 4.03 (s ,2H), 2.87 (s, 6H); ESI MS m/z $(M+H)^+$: 446.3, calculated for $[C_{19}H_{17}ClF_4N_3OS]^+$: 446.1

1-[(2-chloro-4-fluorophenyl)methyl]-3-[4-(dimethylamino)-3-fluorophenyl]-2-sulfanylideneimidazolidin-4-one (74)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (dd, J=9Hz, J=7Hz, 1H), 7.21 (dd, J=9Hz, J=3Hz, 1H), 7.10-6.87 (m, 4H), 5.20 (s, 2H), 4.12 (s, 2H), 2.91 (s, 6H); ESI MS m/z $(M+H)^+$: 396.3, calculated for $[C_{18}H_{17}ClF_2N_3OS]^+$: 396.1

1-[(2,4-difluorophenyl)methyl]-3-[4-(dimethylamino)-3-fluorophenyl]-2-sulfanylideneimidazolidin-4-one (75)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-7.52 (m, 1H), 7.07-6.85 (m, 5H), 5.10 (s, 2H), 4.15 (s, 2H), 2.90 (s, 6H); ESI MS m/z $(M+H)^+$: 380.1, calculated for $[C_{18}H_{17}F_3N_3OS]^+$: 380.1

1-[(2-chloro-4-fluorophenyl)methyl]-3-[4-(dimethylamino)-3-methoxyphenyl]-2-sulfanylideneimidazolidin-4-one (76)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (dd, J= 9Hz, J=6Hz, 1H), 7.21 (dd, J=9Hz, J=3Hz, 1H), 7.09-7.01 (m, 1H), 6.96 (d, J=9Hz, 1H), 6.85 (dd, J=9Hz, J=3Hz, 1H), 6.76 (d, J=3Hz, 1H), 5.21 (s, 2H), 4.14 (s, 2H), 3.88 (s, 3H), 2.82 (s, 6H); ^{13}C NMR (75 MHz, CDCl3): δ 183. 7 (CO), 169.7 (CS), 152.2 (CF), 143.2 (COCH3), 134.7, 132.3, 132.2, 126.9, 120.6, 117.7, 117.4, 117.1, 115.1, 114.8, 55.6 (OCH_3), 52.1 (CH_2), 47.4 (CH_2), 42.9 ($2NCH_3$); ESI MS m/z $(M+H)^+$: 408.3, calculated for $[C_{19}H_{20}ClFN_3O_2S]^+$: 408.1; HRMS m/z $(M+H)^+$: 408.0940, calculated for $[C_{19}H_{20}ClFN_3O_2S]^+$: 408.0943

3-[4-(dimethylamino)-3-methoxyphenyl]-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (77)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.34 (m, 2H), 7.11 (d, J=9Hz, 1H), 7.08 (d, J=9Hz, 1H), 7.00 (d, J=9Hz, 1H), 6.86 (dd, J=3Hz, J=9Hz, 1H), 6.77 (d, J=3Hz, 1H), 5.07 (s, 2H), 4.04 (s, 2H), 3.88 (s, 3H), 2.83 (s, 6H); ESI MS m/z $(M+H)^+$: 374.1, calculated for $[C_{19}H_{21}FN_3O_2S]^+$: 374.1

1-[(2,4-difluorophenyl)methyl]-3-[4-(dimethylamino)-3-methoxyphenyl]-2-sulfanylideneimidazolidin-4-one (78)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.54 (m, 1H), 6.99 (d, J=9Hz, 1H), 6.97-6.94 (m, 1H), 6.92 (d, J=9Hz, 1H), 6.84 (dd, J=3Hz, J=9Hz, 1H), 6.75 (d, J=3Hz, 1H), 5.11 (s, 2H), 4.16 (s, 2H), 3.87 (s, 3H), 2.82 (s, 6H); ESI MS m/z $(M+H)^+$: 392.1, calculated for $[C_{19}H_{20}F_2N_3O_2S]^+$: 392.1

3-[4-(dimethylamino)-3-methoxyphenyl]-1-[(4-fluoro-2-methoxyphenyl)methyl]-2-sulfanylideneimidazolidin-4-one (79)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (dd, J=9Hz, J=6Hz, 1H), 7.00 (bs, 1H), 6.84 (dd, J=9Hz, J=3Hz, 1H), 6.75 (d, J=3Hz, 1H), 6.73-6.64 (m, 2H), 5.04 (s, 2H), 4.15 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 2.82 (s, 6H); ESI MS m/z $(M+H)^+$: 404.2, calculated for $[C_{20}H_{23}FN_3O_3S]^+$: 404.1

1-[(3,4-difluorophenyl)methyl]-3-[4-(dimethylamino)-3-methoxyphenyl]-2-sulfanylideneimidazolidin-4-one (80)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32-7.08 (m, 3H), 7.00 (d, J=9 Hz, 1H), 6.86 (dd, J=9Hz, J=3Hz, 1H), 6.77 (d, J=3Hz, 1H), 5.05 (s, 2H), 4.06 (s, 2H), 3.89 (s, 3H), 2.83 (s, 6H); ESI MS m/z $(M+H)^+$: 392.3, calculated for $[C_{19}H_{20}F_2N_3O_2S]^+$: 392.1

3-[4-(dimethylamino)-3-methoxyphenyl]-1-[(4-fluoro-2-nitrophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (81)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (dd, J=9Hz, J=3Hz, 1H), 7.73 (dd, J=9Hz, J=6Hz, 1H), 7.47-7.37 (m, 1H), 7.09-6.97 (bs ,1H), 6.88 (dd, J=9Hz, J=3Hz, 1H), 6.79 (d, J=3Hz, 1H), 5.43 (s, 2H), 4.24 (s, 2H), 3.89 (s, 3H), 2.84 (s, 6H); ESI MS m/z $(M+H)^+$: 419.3, calculated for $[C_{19}H_{20}FN_4O_4S]^+$: 419.1

3-[4-(dimethylamino)-3-methoxyphenyl]-1-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}-2-sulfanylideneimidazolidin-4-one (82) ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (dd, J=9Hz, J=6Hz, 1H), 7.44 (dd, J=9Hz, J=3Hz, 1H), 7.31 (dt, J=9Hz, J=3Hz, 1H), 7.01 (bs, 1H), 6.88 (dd, J=9Hz, J=3Hz, 1H), 6.78 (d, J=3Hz, 1H), 5.30 (s, 2H), 4.04 (s, 2H), 3.90 (s, 3H), 2.84 (s, 6H); ESI MS m/z $(M+H)^+$: 442.2, calculated for $[C_{20}H_{20}F_4N_3O_2S]^+$: 442.1

3-[3-chloro-4-(pyrrolidin-1-yl)phenyl]-1-[(2-chloro-4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (83)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (dd, J=9Hz, J=6Hz, 1H), 7.24-7.17 (m, 2H), 7.09-7.00 (m, 2H), 6.88 (d, J=9Hz, 1H), 5.20 (s, 2H), 4.11 (s, 2H), 3.46 (m, 4H), 1.94 (m, 4H); ESI MS m/z $(M+H)^+$: 438.7, calculated for $[C_{20}H_{19}Cl_2FN_3OS]^+$: 438.1

3-[3-chloro-4-(pyrrolidin-1-yl)phenyl]-1-[(4-fluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (84)
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41-7.33 (m, 2H), 7.24 (d, J=3Hz, 1H), 7.14-7.03 (m, 3H), 6.91 (d, J=9Hz, 1H), 5.06 (s, 2H), 4.02 (s, 2H), 3.47 (t, J=6Hz, 4H), 1.95 (t, J=6Hz, 4H); ESI MS m/z $(M+H)^+$: 404.3, calculated for $[C_{20}H_20ClFN_3OS]^+$: 404.1

3-[3-chloro-4-(pyrrolidin-1-yl)phenyl]-1-[(2,4-difluorophenyl)methyl]-2-sulfanylideneimidazolidin-4-one (85)
^{1} H NMR (300 MHz, $CDCl_3$): δ 7.62-7.53 (m, 1H),7. 21 (d, J=3Hz, 1H), 7.05 (dd, J=9Hz, J=3Hz, 1H), 6.97-6.84 (m, 3H), 5.09 (s, 2H), 4.14 (s, 2H), 3.46 (m, 4H), 1.94 (m, 4H); ESI MS m/z $(M+H)^+$: 422.7, calculated for $[C_{20}H_{19}ClF_2N_3OS]^+$: 422.1

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