Supporting Information

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SI Text

Cell Assays and Biochemical Studies. ***Materials.*** Sulforaphane (SF) was from LKT laboratories and TP225 was a gift of M. B. Sporn (Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH). Biotin azide was prepared as described (1). Flag-Keap1 plasmid was a gift of M. Yamamoto (Tohoku University, Sendai, Miyagi, Japan).

Cell culture. All cell cultures were maintained in 5% CO_2 and 37 °C in the various media tailored for the specific cell line. Murine hepatoma (Hepa1c1c7) cells were maintained in α-MEM basal medium supplemented with 10% FBS (heated-inactivated at 55 °C for 90 min with 1% activated charcoal and sterile filtered). Human retina pigment epithelial (ARPE-19) cells were maintained in DMEM (1,000 mg/L glucose) and Hanks's F12 medium (1:1, vol/vol) supplemented with 10% FBS (heat-inactivated at 55 °C for 90 min with 1% activated charcoal and sterile-filtered), penicillin (100 U/mL) and streptomycin (100 μg/mL). PE murine keratinocytes were maintained in Eagle's minimal essential medium (Lonza) supplemented with 8% heat-inactivated FBS [treated with Chelex 100 resin (Bio-Rad) to remove Ca^{2+}, neutralized, and filtered], 0.05 mM $CaCl_2$, and 1% antibiotic mix (Gibco 15240-062). Macrophage-like RAW264.7 cells were maintained in DMEM (4,500 mg/L glucose) supplemented with 10% FBS (heat-inactivated at 55 °C for 30 min). The stable human mammary antioxidant response element (ARE)-reporter cell line, AREc32, was maintained in DMEM with glutamax, supplemented with 10% FBS, penicillin (100 U/mL), and streptomycin (100 μg/mL) (2). HEK293 cells were maintained in DMEM (4,500 mg/L glucose) supplemented with 10% FBS, penicillin (100 U/mL), and streptomycin (100 μg/mL). Mouse embryonic fibroblasts derived from day 13.5 embryos of wild-type, Nrf2-knockout, or Keap1/Nrf2-double knockout mice were maintained in plastic culture dishes coated for 30 min with 0.1% (wt/vol) gelatin prior to use. They were grown at 37 °C and 5% CO_2 in Iscoves Modified Dulbecco's Medium (with L-glutamine) supplemented with human recombinant epidermal growth factor (10 ng/mL), 1× insulin/transferring/selenium and 10% (vol/vol) heat-inactivated FBS.

Evaluation of NQO1 in mouse embryonic fibroblasts (MEF). Mouse embryonic fibroblasts were seeded on 6-well plates at a density of 150,000 cells per well. After 24 h, the culture media were replaced with fresh media containing inducers. After incubation for further 24 h, cells were washed three times with PBS and lysed with either (*i*) 0.08% digitonin for determination of NQO1 enzyme activity or (*ii*) radioimmunoprecipitation assay (RIPA) buffer supplemented with protease inhibitors (Roche) for immunoblotting. Clear supernatants were obtained after centrifugation at 13,000 rpm for 15 min. Protein concentrations were determined by the bicinchoninic acid assay.

NO inhibition assay. RAW264.7 cells (40,000 cells per well) were grown in 96-well plates for 24 h and then exposed to serial dilutions of compounds in the presence of lipopolysaccharide (10 ng/mL) for 48 h. Culture medium supernatants were assayed for nitrite concentrations by the Griess reaction (3): Culture medium (100 μL) was mixed with 100 μL Griess reagent [1% sulfanilamide in 5% phosphoric acid and 0.1% *N*-(1-naphthyl)ethylenediamine dihydrochloride in water (1:1, vol/vol)], and the absorbance was measured at 550 nm. Control cells were treated with lipopolysaccharide only.

ARE-driven luciferase reporter assay. AREc32 cells (12,000 cells per well) were seeded in 96-well plates. After 24 h, the culture media were replaced with fresh DMEM media containing compounds. At specific time points after exposure to inducers, cells were lysed, and the firefly luciferase activities were measured after addition of Luciferase Assay Reagent (Promega) as described (2) using a luminometer (Turner Designs Model TD-20/20, Promega). Control cells were treated with acetonitrile (final 0.1%) alone.

Transfection and compound treatment. HEK293 cells in 100-mm dishes with 70% confluency were washed with PBS and transiently transfected with pCMV-3 × FLAG-Keap1 plasmid with Polyethyleneimine MAX (Polysciences, Inc) (1:3, wt/wt) mixed in hybridoma medium. After incubation for 6 h at 37 °C, medium was changed to DMEM with 10% FBS, penicillin (100 U/mL), and streptomycin (100 μg/mL). After additional incubation for 42 h, cells were washed with PBS and incubated with **8f** (10 μM, 15 mL) dissolved in DMEM with 5% FBS, penicillin (100 U/mL), and streptomycin (100 μg/mL) for 30 min at 37 °C. For competition experiments, cells were incubated with different concentrations of **8a**, sulforaphane, or TP225 for 30 min. After washing with PBS, cells were incubated with **8f** (10 μM) for 30 min at 37 °C. Cells were then lysed with RIPA buffer (50 mM Tris, pH 7.4, 1% NP-40, 0.25% sodium deoxycholate, 150 mM sodium chloride, 1 mM EDTA) containing sodium fluoride (1 mM), sodium orthovanadate (1 mM), and protease inhibitors (Roche). Lysates were centrifuged at 13,000 rpm for 15 min, and supernatant was collected. Protein concentrations were measured with Bradford assay.

Probing proteins labeled by 8f in cell lysates. Cell lysates (0.2 mL, 2 mg/mL protein concentrations) were treated with stock solutions of biotin-azide (final 1 mM) and tris(2-carboxyethyl)phosphine (TCEP) (final 2 mM) prepared in water, N,N,N,N-tetramethyl-*O*-(benzotriazol-1-yl)uronium tetrafluoroborate (TBTU) (final 1 mM) prepared in t-butanol/DMSO (4/1, vol/vol), and $CuSO_4$ (final 2 mM) prepared in water. After incubation at 4 °C for 16 h, cell lysates proteins were diluted with loading buffer and separated on SDS-PAGE gel. Resolved proteins were then immunoblotted with streptavidin-HRP.

Probing Keap1 and target proteins labeled by 8f. Cell lysates (0.5 mL, 2 mg/mL protein concentrations) were immunoprecipitated with anti-FLAG antibody (Sigma) and Protein G agarose at 4 °C overnight. Bound proteins on beads were washed with Tris buffer saline with tween 20 (TBST) (50 mM Tris HCl, 150 mM NaCl, 0.1% tween, pH 7.4) three times with 5-min incubation, and subjected to click reaction in TBST with biotin azide (0.2 mM), TCEP (1 mM), TBTU (0.2 mM), and $CuSO_4$ (1 mM) at 4 °C for 16 h. After washing beads with TBST three times, FLAG-Keap1 was eluted with 3 × FLAG peptide (1 mg/mL, 4 volumes of beads) in TBST by incubating at room temperature (RT) for 1 h. Eluted samples were run on SDS-PAGE gel and immunoblotted with anti-FLAG antibody or streptavidin (Pierce) followed by antistreptavidin antibody (Abcam). For validation of selected target proteins, cell lysates were processed for immunoprecipitation and click reaction with protein specific antibody in the same procedure as above, but proteins were eluted with SDS loading buffer. Eluted samples were probed with protein specific antibody or streptavidin followed by antistreptavidin antibody.

Immunoblots. Resolved proteins on SDS-PAGE gel were transferred to PVDF membranes. For streptavidin-HRP, the membrane was blocked with 5% BSA in Tris buffered saline (TBS) buffer (50 mM Tris HCl, 150 mM NaCl, pH 7.4) for 1 h at RT. After twice washing with TBS for 10 min, the membrane was incubated with streptavidin-HRP (1 mg/mL, 1:1000 dilution, Pierce) in TBS buffer with 3% BSA at 4 °C overnight. Membranes were then washed with TBST (0.1% tween) five times for 30 min and visualized by chemiluminescence. For anti-FLAG (1:1,000 dilutions, 1 mg/mL, Sigma), anti-MIF (1:1,000 dilutions, 0.2 mg/mL, R&D systems), anti-AKAP149 (1:1,000 dilutions, 0.25 mg/mL, BD transduction laboratories), anti-Prx3 (1:2,000 dilutions, 1 mg/mL, Abcam), anti-KSRP (1:5,000 dilutions, 1 mg/mL, Abcam), anti-HAT1 (1:1,000 dilutions, 0.2 mg/mL, Santa Cruz Biotechnology), and anti-Trx (1:2,500 dilutions, 1 mg/mL, Abcam), membranes were blocked with 5% nonfat milk in TBS at RT for 1 h. After washing twice with TBS for 10 min, membranes were incubated with each antibody in TBS with 3% nonfat milk at 4 °C for overnight and washed five times with TBS for 30 min. Membranes were then incubated with anti-mouse IgG-HRP (1:2,000 dilutions, 1 mg/mL, Amersham Bioscience), anti-rabbit IgG-HRP (1:3,000 dilutions, 1 mg/mL, Amersham Bioscience), or antigoat IgG-HRP (1:2,500 dilutions, Abcam) in TBS with 3% nonfat milk for 1 h at RT. After washing five times with TBST for 30 min, proteins were visualized by chemiluminescence. For streptavidin, membrane was blocked with 5% BSA in TBS at RT for 1 h. After washing steps, membranes were incubated with streptavidin (1:5,000 dilutions, 10 mg/mL, Pierce) in TBS with 3% BSA for 1 h at RT and washed five times with TBS for 30 min. Membranes were further incubated with antistreptavidin from rabbit (1:40,000 dilution, 1 mg/mL, Abcam) in TBS with 3% BSA at 4 °C for overnight and washed five times with TBS for 30 min. Membranes were incubated with anti-rabbit IgG-HRP (1:5,000 dilutions) in TBS with 3% nonfat milk for 1 h at RT. After washing steps with TBST, proteins were visualized by chemiluminescence. Immunoblotting for NQO1 was performed as described previously using antisera against the rat protein at 1:1,000 dilution (4).

Keap1 trypsin digestion and avidin purification. 3 × FLAG-Keap1 (~3 μg) in TBST (0.8 mL) eluted from immunoprecipitation and click reaction after incubation of **8f** in HEK293 cells for 2.5 h was four times concentrated by Amicon filter [30,000 molecular weight (MW) cutoff, Millipore] with 20-min centrifugation at 3,200 rpm and 4 °C, and then dialyzed against Tris buffer (100 mM Tris HCl, pH 7.5) to remove 3 × FLAG peptide. The dialysate was reduced by DTT (2.5 mM) at 55 °C for 15 min, the cysteines were alkylated by iodoacetamide (10 mM) at 37 °C for 30 min, and the alkylation reaction was quenched by DTT (11.4 mM) at 37 °C for 30 min. The solution was then diluted twice with Tris buffer and acetonitrile (final 10%) and digested by trypsin (1 μg, three times with 4-h intervals) at 37 °C for 20 h. The digested mixture was lyophilized, reconstituted in water, and incubated with monomeric avidin-agarose (100-μL volume) (Pierce) for 1 h at RT. Beads were washed twice with wash buffer 1 (50 mM Tris HCl, pH 7.4, 150 mM NaCl), twice with wash buffer 2 (50 mM Tris HCl, pH 7.4, 500 mM NaCl), and finally twice with ddH_2O. Beads were then subjected to elution with 70% aqueous (aq.) acetonitrile containing 0.5% TFA. The eluted peptide solution was lyophilized and redissolved in 0.1% TFA in ddH_2O, further desalted by C18 ziptip, and finally eluted with 50% aq. acetonitrile with 0.1% TFA, and analyzed by either MALDI-TOF or liquid chromatography tandem mass spectrometry (LC-MS/MS).

Keap1 mutations. pCMV-3 × FLAG-Keap1 wild-type plasmid was used for single mutations of C151A, C273A, or C288A, following quick-change protocols. Double and triple mutants of cysteine 151, 273, and 288 in combinations were generated by quick-change mutagenesis with single and double mutant plasmids, respectively. The targeted mutagenesis was confirmed by DNA sequencing of the entire open reading frames.

Pull-down experiment of target proteins conjugated by 8f. HEK293 cells (95% confluency) were treated with **8f** (10 μM) for 2.5 h. Cell lysates were lysed with RIPA buffer as described above in compound treatment. Cell lysates (2 mg/mL, 2 mL) were subjected to click reaction with biotin azide (1 mM), TCEP (2 mM), TBTU (1 mM), and $CuSO_4$ (2 mM) at 4 °C for 16 h. Samples were subjected to three cycles of dilutions with Tris HCl (100 mM, pH 7.4, 12 mL) and concentration by Amicon membrane filter (10,000 MW cutoff, Millipore) with 30-min centrifugation at $3,000 \times g$ and 4 °C. Protein solutions was diluted to TBS (final 6 mL) with 0.2% SDS and incubated with Streptavidin beads (volume 50 μL, Pierce) for 1.5 h at RT. Beads were washed once with TBS (10 mL) containing 0.2% SDS, twice with TBS (10 mL), and three times with ddH_2O (10 mL). Protein-bound beads were suspended in PBS/6M urea (0.5 mL). Proteins on beads were reduced by adding TCEP (10 mM) and heating at 65 °C for 15 min, and alkylated by iodoacetamide (20 mM) at 37 °C for 30 min (5). Beads were washed with 100 mM NH_4CO_3 (0.5 mL) twice. Proteins on beads were digested by trypsin (5 μg) in 100 mM NH_4CO_3 (0.3 mL) for 16 h. Supernatants were collected and beads were further rinsed with ddH_2O (0.15 mL) and 70% aq. acetonitrile containing 0.5% TFA (0.3 mL). Eluted samples were lyophilized and analyzed by HPLC-MS/MS.

MALDI-mass spectrometry. Eluted peptides were cocrystallized in α-Cyano-4-hyrdoxycinnamic acid (10 mg/mL in 50% acetonitrile/0.1% TFA) and analyzed by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) on a Voyager DE STR (Applied Biosystems) using Voyager Instrument Control Panel (v 5.1) and Data Explorer (v 4.0). Data was acquired in reflector mode and masses were externally calibrated using a standard peptide mixture to better than 50 ppm error.

Liquid chromatography tandem mass spectrometry (LC-MS/MS). Eluted peptides were identified by LCMS/MS using an linear trap quadrupole ion trap MS (ThermoFisher Scientific) interfaced with a 2D nanoLC system (Eksigent) and an Agilent 1100 autosampler. Peptides were fractionated by reverse-phase HPLC on a 75 μm × 100 mm C18 column (YMC ODS-AQ 3 μm, 120) with a 10-μm emitter using 7–40–90% acetonitrile/0.1% formic acid gradient over 30 min at 300 nL/min. Peptide sequences were identified using Mascot or Bioworks (v3.3, ThermoFisher) to search raw MS data against the IPI Mouse v3.26 fasta database with using the following criteria: variable modifications of oxidation on Met, carboamidomethylation on Cys and +771.41 Da on Cys; peptide and fragment tolerances 1.5 Da and 0.8 Da, respectively; and trypsin protease with up to two missed cleavages.

Synthesis. ***Generals.*** All commercially available reagents were used as purchased without further purification. Unless otherwise noted, all chemical reagents were purchased from Sigma-Aldrich and Fisher. Analytical TLC was carried out on silica gel plates (Sigma) and visualized with UV light. Column chromatography was performed on 60-Å silica gel (200–400 mesh) (Sigma). NMR spectra were recorded on a Varian Mercury 400-MHz spectrometer. Chemical shifts are reported as δ in parts per million and coupling constants are reported as a J value in Hertz. Electrospray ionization (ESI)-high resolution mass spectrometry (HRMS) were obtained at the UC Riverside MS facility.

4-Methanesulfinyl-butan-1-ol (1). 4-(Methylthio)-1-butanol (1.07 mL, 8.84 mmol) was dissolved in methanol and H_2O (60 mL, 1:1 vol/vol) and sodium periodate (2.08 g, 9.72 mmol) was added at 0 °C. After stirring overnight, the reaction mixture was filtered to remove the precipitate. The filtrate was concentrated to dryness, redissolved in dichloromethane, and dried over magnesium sulfate. After removing magnesium sulfate, the filtrate was concentrated and purified by silica gel column chromatography eluting with methanol and ethyl acetate (1:9, vol/vol) to give **1** (1.10 g, 91%) as an oil. ^{1}H-NMR ($CDCl_3$) δ 3.61 (*q*, $J = 5.6$, 2H), 3.3 (*t*, $J = 5.2$, 1H), 2.72 (*m*, 2H), 2.54 (*s*, 3H), 1.84 (*p*, $J = 8$, 2H), 1.68 (*m*, 2H); ^{13}C-NMR ($CDCl_3$) δ 61.65, 54.28, 38.55, 31.66, 19.39. ESI-HRMS (M + H) calculated for $C_5H_{13}O_2S$ 137.0631, found m/z 137.0633.

Methanesulfonic acid 4-methanesulfinyl-butyl ester (2). Compound **1** (2.81 g, 20.63 mmol) was dissolved in dichloromethane (100 mL) and cooled to 0 °C. Triethylamine (3.15 mL, 22.7 mmol) was added slowly, followed by addition of methanesulfonyl chloride (1.76 mL, 22.7 mmol). After stirring for 2 h, the reaction mixture was diluted with dichloromethane and washed with ice-cold saturated (sat.) aq. sodium bicarbonate solution. The organic layer was dried over sodium sulfate, and the filtrate was concentrated and purified by column chromatography eluting with methanol and ethyl acetate (1:40, vol/vol) to give **2** (4.08 g, 92%) as an oil. ^{1}H-NMR ($CDCl_3$) δ 3.70 (*t*, $J = 6.0$, 2H), 2.89 (*s*, 3H), 2.88 (*m*, 2H), 2.67 (*s*, 3H), 1.91 (*m*, 2H), 1.74 (*m*, 2H); ^{13}C-NMR ($CDCl_3$) δ 61.88, 53.44, 39.59, 37.71, 31.33, 19.47. ESI-HRMS (M + H) calculated for $C_6H_{15}O_4S_2$ 215.0406, found m/z 215.0410.

S-Ethyl (4-methanesulfinyl-butyl)-methyl-thiocarbamate (3a). Compound **2** (260 mg, 1.21 mmol) and methylamine (2M in methanol, 1.82 mL, 3.64 mmol) were dissolved in ethanol (6 mL) in a heavy wall pressure vessel (Chemglass), and the cap was closed tightly. The reaction mixture was heated at 75 °C for 3 h. After completion of the reaction, the mixture was concentrated and dried under vacuum. This crude oil was dissolved in dichloromethane (15 mL) and cooled to 0 °C. *N*,*N*-diisopropylethylamine (2.9 mL, 16 mmol) was added slowly, followed by addition of ethyl chlorothioformate (1.04 mL, 10 mmol). After stirring for 1 h, the reaction mixture was diluted with dichloromethane (100 mL), washed with 1N aq. HCl, sat. aq. sodium bicarbonate, and sat. sodium chloride. The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated and purified by column chromatography eluting with methanol and ethyl acetate (1:30, vol/vol) to give **3a** (211 mg, 79%) as an oil. ^{1}H NMR ($CDCl_3$) δ 3.42 (*m*, 2H), 2.94 (*s*, 3H), 2.86 (*q*, $J = 7.6$, 2H), 2.72 (*m*, 2H), 2.54 (*s*, 3H), 1.75 (*m*, 4H), 1.25 (*t*, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 109.93, 54.09, 49.29, 48.36, 38.75, 34.85, 26.59, 24.92, 19.80, 15.55. ESI-HRMS (M + H) calculated for $C_9H_{20}NO_2S_2$ 238.0930, found m/z 238.0930.

S-Ethyl (4-methanesulfinyl-butyl)-propyl-thiocarbamate (3b). Compound (**3b**) was prepared in a similar procedure to that for **3a**, but with propylamine. Yield (77%), column chromatography eluting with methanol and ethyl acetate (1:10, vol/vol); ^{1}H NMR ($CDCl_3$) δ 3.24 (*m*, 4H), 2.79 (*q*, $J = 7.2$, 2H), 2.66 (*m*, 2H), 2.49 (*s*, 3H), 1.69 (*m*, 4H), 1.52 (*m*, 2H), 1.19 (*t*, $J = 7.2$, 3H), 0.82 (*m*, 3H); ^{13}C NMR ($CDCl_3$) δ 54.18, 49.82, 49.26, 47.48, 46.63, 38.76, 27.69, 27.11, 24.82, 21.76, 21.35, 20.04, 15.55, 11.41. ESI-HRMS (M + H) calculated for $C_{11}H_{24}NO_2S_2$ 266.1243, found m/z 266.1251.

S-Ethyl cyclopropyl-(4-methanesulfinyl-butyl)-thiocarbamate (3c). Compound (**3c**) was prepared in a similar procedure to that for **3a**, but with cyclopropylamine. Yield (47%), column chromatography eluting with methanol and ethyl acetate (1:10, vol/vol); ^{1}H NMR ($CDCl_3$) δ 3.42 (*m*, 2H), 2.85 (*q*, $J = 7.2$, 2H), 2.72 (*m*, 2H), 2.55 (*s*, 3H), 2.52 (*m*, 1H), 1.75 (*m*, 4H), 1.26 (*t*, $J = 7.2$, 3H), 0.88 (*m*, 2H), 0.78 (*m*, 2H); ^{13}C NMR ($CDCl_3$) δ 54.22, 47.14, 38.79, 28.70, 27.35, 24.76, 20.03, 15.41, 9.70. ESI-HRMS (M + H) calculated for $C_{11}H_{22}NO_2S_2$ 264.1086, found m/z 264.1093.

S-Ethyl cyclohexyl-(4-methanesulfinyl-butyl)-thiocarbamate (3d). Compound (**3d**) was prepared in a similar procedure to that for **3a**, but with cyclohexylamine. Yield (51%), column chromatography eluting with methanol and ethyl acetate (1:10, vol/vol); ^{1}H NMR ($CDCl_3$) δ 3.25 (*m*, 2H), 2.88 (*q*, $J = 7.2$, 2H), 2.72 (*m*, 2H), 2.56 (*s*, 3H), 1.60–1.82 (*m*, 10H), 1.34 (*m*, 4H), 1.27 (*t*, $J = 7.2$, 3H); ^{13}C NMR ($CDCl_3$) δ 168.07, 54.31, 38.80, 31.60, 26.07, 25.54, 24.82, 20.38, 15.48. ESI-HRMS (M + H) calculated for $C_{14}H_{28}NO_2S_2$ 306.1556, found m/z 306.1560.

S-Ethyl (4-methanesulfinyl-butyl)-phenyl-thiocarbamate (3e). Compound (**3e**) was prepared in a similar procedure to that for **3a**, but with aniline. Yield (36%), column chromatography eluting with methanol and ethyl acetate (1:20, vol/vol); ^{1}H NMR ($CDCl_3$) δ 7.20–7.43 (*m*, 5H), 3.76 (*t*, $J = 7.2$, 2H), 2.74 (*q*, $J = 7.2$, 2H), 2.70 (*t*, $J = 6.0$, 2H), 2.53 (*s*, 3H), 1.78 (*m*, 2H), 1.69 (*m*, 2H), 1.19 (*t*, $J = 7.6$, 3H) ; ^{13}C NMR ($CDCl_3$) δ 169.25, 140.39, 129.69, 129.57, 129.39, 128.91, 117.48, 112.81, 54.34, 54.06, 49.66, 43.42, 38.75, 38.69, 28.68, 27.17, 25.46, 20.47, 19.71, 15.20. ESI-HRMS (M + H) calculated for $C_{14}H_{22}NO_2S_2$ 300.1086, found m/z 300.1090.

S-Ethyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3f). Compound (**3f**) was prepared in a similar procedure to that for **3a**, but with benzylamine. Yield (54%), column chromatography eluting with methanol and ethyl acetate (1:30, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.21–7.11 (*m*, 5H), 4.45 (br, 2H), 3.24 (br, 2H), 2.83 (*q*, $J = 7.2$, 2H), 2.55 (*m*, 2H), 2.41 (*s*, 3H), 1.60 (br, 4H), 1.19 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.77, 137.24, 136.45, 128.88, 127.83, 127.44, 54.04, 51.41, 50.18, 46.82, 46.25, 38.72, 27.19, 26.73, 25.11, 19.98, 15.57. ESI-HRMS (M + H) calculated for $C_{19}H_{26}NO_2S_2$ 364.1399, found m/z 364.1402.

S-Ethyl (4-methanesulfinyl-butyl)-naphthalen-1-ylmethyl-thiocarbamate (3g). Compound (**3g**) was prepared in a similar procedure to that for **3a**, but with 1-naphthylmethylamine. Yield (56%), column chromatography eluting with methanol and ethyl acetate (1:50, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.97 (br, 1H), 7.82 (*d*, $J = 7.6$, 1H), 7.76 (*d*, $J = 7.6$, 1H), 7.52–7.44 (*m*, 2H), 7.39 (*t*, $J = 7.6$, 1H), 7.27 (*d*, $J = 7.2$, 1H), 5.03 (br, 2H), 3.28 (br, 2H), 2.94 (*q*, $J = 7.2$, 2H), 2.54 (*m*, 2H), 2.43 (*s*, 3H), 1.61 (*m*, 4H), 1.29 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.70, 133.99, 132.33, 131.59, 129.05, 128.79, 126.84, 126.28, 125.54, 124.67, 123.70, 122.89, 54.08, 49.35, 48.15, 46.36, 38.75, 27.07, 25.21, 20.04, 15.63. ESI-HRMS (M + H) calculated for $C_{19}H_{30}NO_2S_2$ 368.1718, found m/z 368.1715.

S-Ethyl (4-tert-butyl-benzyl)-(4-methanesulfinyl-butyl)-thiocarbamate (3h). Compound (**3h**) was prepared in a similar procedure to that for **3a**, but with 4-*tert*-butylbenzylamine. Yield (61%), column chromatography eluting with methanol and ethyl acetate (1:60, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.29 (*d*, $J = 7.6$, 2H), 7.11 (*d*, $J = 7.6$, 2H), 4.50 (br, 2H), 3.30 (br, 2H), 2.88 (*q*, $J = 7.2$, 2H), 2.62 (*m*, 2H), 2.47 (*s*, 3H), 1.66 (br, 4H), 1.24 (*t*, $J = 7.2$, 3H), 1.24 (*s*, 9H); ^{13}C-NMR ($CDCl_3$) δ 168.76, 150.86, 134.15, 133.27, 127.80, 127.19, 125.80, 54.16, 51.07, 49.75, 46.71, 46.06, 38.77, 34.71, 31.55, 27.21, 26.70, 25.14,

20.01, 15.61. ESI-HRMS (M + H) calculated for $C_{19}H_{32}NO_2S_2$ 370.1869, found m/z 370.1875.

S-Ethyl biphenyl-4-ylmethyl-(4-methanesulfinyl-butyl)-thiocarbamate (3i). Compound (**3i**) was prepared in a similar procedure to that for **3a**, but with 4-phenylbenzylamine. Yield (33%), column chromatography eluting with methanol and ethyl acetate (1:50, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.56–7.72 (*m*, 4H), 7.42–7.38 (*m*, 2H), 7.33–7.27 (*m*, 3H), 4.58 (br, 2H), 3.36 (br, 2H), 2.94 (*q*, $J = 7.2$, 2H), 2.66 (*m*, 2H), 2.49 (*s*, 3H), 1.72 (br, 4H), 1.30 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.96, 140.77, 136.27, 135.44, 129.05, 128.53, 127.92, 127.65, 127.26, 54.17, 51.22, 50.01, 46.97, 46.34, 38.79, 27.31, 26.81, 25.25, 20.10, 15.61. ESI-HRMS (M + H) calculated for $C_{21}H_{28}NO_2S_2$ 390.1556, found m/z 390.1566.

S-Ethyl (2,4-difluoro-benzyl)-(4-methanesulfinyl-butyl)-thiocarbamate (3j). Compound (**3j**) was prepared in a similar procedure to that for **3a**, but with 2,4-difluorobenzylamine. Yield (31%), column chromatography eluting with methanol and ethyl acetate (1:50, vol/vol); ^{1}H-NMR δ ($CDCl_3$) 7.26–7.20 (*m*, 1H), 6.84–6.74 (*m*, 2H), 4.54 (br, 2H), 3.30 (br, 2H), 2.89 (*q*, $J = 7.2$, 2H), 2.66 (*m*, 2H), 2.52 (*s*, 3H), 1.72 (br, 4H), 1.25 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.05, 163.87, 163.75, 162.25, 162.13, 161.39, 161.27, 159.75, 159.67, 131.66, 130.04, 120.17, 119.50, 112.02, 111.99, 111.81, 111.78, 104.32, 104.02, 103.82, 54.15, 47.19, 46.53, 44.32, 43.19, 38.81, 27.25, 25.18, 20.06, 15.47. ESI-HRMS (M + H) calculated for $C_{15}H_{22}NO_2F_2S_2$ 350.1055, found m/z 350.1061.

S-Benzyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3k). S-Benzyl chlorothioformate was prepared in one step from benzylmercaptan: Triphosgene (742 mg, 2.5 mmol) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. Benzylmercaptan (6.0 mmol) was added slowly, followed by addition of pyridine (0.5 mL, 6.2 mmol) dissolved in dichloromethane (4 mL). After stirring for 2 h at 0 °C, the reaction was quenched by addition of water (5 mL). The reaction mixture was diluted with dichloromethane (40 mL) and washed with ice-cold water (20 mL). The organic layer was dried over sodium sulfate, and the filtrate was concentrated and used immediately without further purification. Compound **2** (70 mg, 0.33 mmol) was dissolved in ethanol (5 mL). After addition of benzylamine (0.13 mL, 1.2 mmol), the reaction mixture was heated at 75 °C overnight. The reaction mixture was then concentrated and dried under vacuum. This crude oil was dissolved in dichloromethane (5 mL) and cooled to 0 °C. *N*, *N*-diisopropylethylamine (0.61 mL, 3.43 mmol) was added slowly, followed by addition of S-benzyl chlorothioformate (1 mmol) prepared as described above. After stirring for 1 h, the reaction mixture was diluted with dichloromethane (50 mL), washed with 1N aq. HCl, sat. aq. sodium bicarbonate, and sat. sodium chloride. The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated and purified by column chromatography eluting with methanol and ethyl acetate (1:25, vol/vol) to give **3k** (62 mg, 51%) as an oil. ^{1}H-NMR ($CDCl_3$) δ 7.37–7.20 (*m*, 10H), 4.58 (br, 2H), 4.21 (*s*, 2H), 3.33 (br, 2H), 2.67 (*m*, 2H), 2.52 (*s*, 3H), 1.71 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) δ 168.50, 138.15, 137.10, 136.35, 129.21, 128.99, 128.82, 128.04, 127.46, 54.15, 51.63, 50.52, 46.94, 46.52, 38.77, 35.26, 27.30, 26.75, 20.05. ESI-HRMS (M + H) calculated for $C_{20}H_{26}NO_2S_2$ 376.1405, found m/z 376.1402.

S-cyclohexyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3l). Compound (**3l**) was prepared in a similar procedure to that for **3k**, but with S-cyclohexyl chlorothioformate prepared from cyclohexanethiol. Yield (15%), column chromatography eluting with methanol and ethyl acetate (1:30, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.28–7.15 (*m*, 5H), 4.48 (br, 2H), 3.39 (br, 2H), 3.26 (br, 1H), 2.61 (*m*, 3H), 1.96 (*m*, 2H), 1.65 (*m*, 6H), 1.36 (*m*, 6H); ^{13}C-NMR ($CDCl_3$) δ 168.85, 137.30, 136.50, 128.94, 128.21, 127.91, 127.59, 54.25, 51.58, 50.21, 46.87, 46.15, 44.45, 38.81, 33.96, 27.40, 26.75, 26.43, 25.84, 20.09. ESI-HRMS (M + H) calculated for $C_{19}H_{30}NO_2S_2$ 368.1718, found m/z 368.1715.

S-(2-methoxy-phenyl) benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3m). Compound (**3m**) was prepared in a similar procedure to that for **3k**, but with S-(2-methoxyphenyl) chlorothioformate prepared from 2-methoxythiophenol. Yield (61%), column chromatography eluting with methanol and ethyl acetate (1:25, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.43 (dd, $J = 1.6$, 7.6, 1H), 7.37–7.20 (*m*, 6H), 6.94-6.89 (*m*, 2H), 4.62 (br, 2H), 3.83 (*s*, 3H), 3.32 (br, 2H), 2.61 (*m*, 2H), 2.47 (*s*, 3H), 1.79 (*m*, br, 4H); ^{13}C-NMR ($CDCl_3$) δ 166.70, 160.05, 137.94, 137.14, 136.44, 131.78, 128.89, 127.99, 127.80, 127.60, 121.17, 116.96, 111.73, 56.20, 53.96, 51.98, 50.50, 47.35, 46.56, 38.65, 27.41, 26.64, 19.91. ESI-HRMS (M + H) calculated for $C_{20}H_{26}NO_3S_2$ 392.1349, found m/z 392.1359.

S-(Methoxycarbonylmethyl) benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3n). Compound (**3n**) was prepared in a similar procedure to that for **3k**, but with S-(methoxycarbonylmethyl) chlorothioformate prepared from methyl thioglycolate. Yield (41%), column chromatography eluting with methanol and ethyl acetate (1:25, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.33–7.25 (*m*, 5H), 4.58 (*d*, br, 2H), 3.76 (*s*, 2H and 3H), 3.33 (*d*, br, 2H), 2.66 (*m*, 2H), 2.54 (*s*, 3H), 1.76 (*m*, br, 4H); ^{13}C-NMR ($CDCl_3$) δ 169.93, 166.86, 136.74, 135.84, 128.92, 128.00, 127.80, 127.43, 53.90, 52.85, 51.63, 50.50, 47.06, 46.65, 38.66, 32.83, 27.20, 26.60, 19.89. ESI-HRMS (M + H) calculated for $C_{16}H_{24}NO_4S_2$ 358.1141, found m/z 358.1147.

S-Phenethyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3o). Compound (**3o**) was prepared in a similar procedure to that for **3k**, but with S-phenethyl chlorothioformate prepared from 2-phenylethanethiol. Yield (31%), column chromatography eluting with methanol and ethyl acetate (1:30, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.33–7.18 (*m*, 10H), 4.57 (*d*, br, 2H), 3.33 (*d*, br, 2H), 3.19 (*t*, $J = 7.2$, 2H), 2.94 (*t*, $J = 7.2$, 2H), 2.65 (*m*, 2H), 2.51 (*s*, 3H), 1.70 (*m*, br, 4H); ^{13}C-NMR ($CDCl_3$) δ 168.62, 140.48, 137.21, 136.37, 128.99, 128.95, 128.69, 128.03, 127.52, 126.65, 54.20, 51.58, 50.34, 46.91, 46.48, 38.84, 36.84, 32.16, 27.29, 26.81, 20.09. ESI-HRMS (M + H) calculated for $C_{21}H_{28}NO_2S_2$ 390.1561, found m/z 390.1557.

S-Pentyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3p). Compound (**3p**) was prepared in a similar procedure to that for **3k**, but with S-pentyl chlorothioformate prepared from 1-pentanethiol. Yield (51%), column chromatography eluting with methanol and ethyl acetate (1:30, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.26–7.16 (*m*, 5H), 4.51 (br, 2H), 3.28 (br, 2H), 2.87 (*t*, $J = 7.6$, 2H), 2.58 (*m*, 2H), 2.46 (*s*, 3H), 1.65 (br, 4H), 1.57 (*m*, 2H), 1.28 (*m*, 4H), 0.83 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.99, 137.14, 136.42, 128.90, 127.87, 127.48, 54.13, 51.50, 50.25, 46.84, 46.34, 38.76, 31.24, 30.79, 30.03, 27.24, 26.75, 22.44, 20.02, 14.23. ESI-HRMS (M + H) calculated for $C_{18}H_{30}NO_2S_2$ 356.1718, found m/z 356.1710.

S-Octyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3q). Compound (**3q**) was prepared in a similar procedure to that for **3k**, but with S-octyl chlorothioformate prepared from 1-octanethiol. Yield (48%), column chromatography eluting with methanol and ethyl acetate (1:50, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.33–7.22

(*m*, 5H), 4.57 (br, 2H), 3.34 (br, 2H), 2.93 (*t*, $J = 7.2$, 2H), 2.66 (*m*, 2H), 2.53 (*s*, 3H), 1.71 (br, 4H), 1.62 (*m*, 2H), 1.36 (*m*, 2H), 1.27 (*m*, 8H), 0.87 (*t*, $J = 6.8$, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.13, 137.30, 136, 50, 128.95, 127.94, 127.52, 54.24, 51.54, 50.32, 46.87, 46.42, 38.82, 32.04, 30.91, 30.37, 29.43, 29.38, 29.17, 27.40, 26.78, 22.88, 20.09, 14.36. ESI-HRMS (M + H) calculated for $C_{21}H_{36}NO_2S_2$ 398.2187, found m/z 398.2185.

S-Undecyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate (3r). Compound (**3r**) was prepared in a similar procedure to that for **3k**, but with S-undecyl chlorothioformate prepared from 1-undecanethiol. Yield (44%), column chromatography eluting with methanol and ethyl acetate (1:50, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.28–7.17 (*m*, 5H), 4.52 (br, 2H), 3.30 (br, 2H), 2.89 (*t*, $J = 7.2$, 2H), 2.62 (*m*, 2H), 2.48 (*s*, 3H), 1.67 (br, 4H), 1.58 (*m*, 2H), 1.34 (*m*, 2H), 1.21 (*m*, 14H), 0.83 (*t*, $J = 6.8$, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.00, 137.27, 136.44, 128.91, 127.89, 127.48, 54.17, 51.53, 50.28, 46.87, 46.32, 38.78, 32.11, 30.86, 30.37, 29.81, 29.74, 29.63, 29.55, 29.40, 29.14, 27.28, 26.77, 22.90, 20.04, 14.37. ESI-HRMS (M + H) calculated for $C_{24}H_{37}NO_2S_2$ 440.2647, found m/z 440.2654.

S-Ethyl (4-Methanesulfinyl-butyl)-methyl-thiocarbamate sulfoxide (4a). A solution of **3a** (100 mM in methanol) was added to Oxone® (200 mM in ddH_2O, 1.0 equivalent) on ice, kept for 2 h and diluted with ddH_2O 5 times in volume. The dilute was injected directly into preparative HPLC (a gradient of 0 to 100% acetonitrile in 30 min with a flow rate of 10 mL/ min monitoring UV absorbance at 214 nm). The peaks were collected and concentrated by lyophilization for further characterization. The yields are based upon the relative area percentage on preparative HPLC diagram. Yield (59%); ^{1}H NMR ($CDCl_3$) δ 3.80 (*m*, 1H), 3.49 (*m*, 1H), 3.21(*s*, 3H), 3.06 (*m*, 2H), 2.99 (*q*, $J = 7.6$, 2H), 2.97 (*s*, 3H), 1.81–1.91 (*m*, 4H), 1.39 (*t*, $J = 7.6$, 3H); ^{13}C NMR ($CDCl_3$) δ 168.58, 53.84, 53.77, 50.00, 50.02, 47.81, 47.76, 45.77, 45.74, 45.03, 38.84, 36.13, 36.09, 34.09, 34.05, 27.98, 27.86, 25.88, 25.80, 19.94, 19.88, 19.82, 7.25, 7.13; ESI-HRMS (M + H) calculated for $C_9H_{20}NO_3S_2$ 254.0879, found m/z 254.0874.

S-Ethyl (4-Methanesulfinyl-butyl)-propyl-thiocarbamate sulfoxide (4b). Compound (**4b**) was prepared in a similar procedure to that for **4a**. Yield (41%); ^{1}H NMR ($CDCl_3$) δ 3.30–3.62 (*m*, 4H), 3.01 (*m*, 2H), 2.74 (*m*, 2H), 2.58 (*s*, 3H), 1.78–1.86 (*m*, 4H), 1.65 (*m*, 2H), 1.38 (*m*, 3H), 0.95 (*m*, 3H); ^{13}C NMR ($CDCl_3$) δ 168.62, 53.95, 53.89, 50.60, 50.57, 48.27, 48.24, 47.72, 47.70, 45.81, 45.77, 45.66, 45.54, 38.90, 28.76, 28.67, 26.60, 26.56, 22.72, 20.84, 20.12, 20.05, 19.99, 19.89, 11.40, 11.11, 7.20, 7.16; ESI-HRMS (M + H) calculated for $C_{11}H_{24}NO_3S_2$ 282.1192, found m/z 282.1187.

S-Ethyl cyclopropyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4c). Compound (**4c**) was prepared in a similar procedure to that for **4a**. Yield (34%);^{1}H NMR ($CDCl_3$) δ 3.64 (*m*, 1H), 3.41 (*m*, 1H), 3.00 (*m*, 1H), 2.73 (*m*, 2H), 2.68 (*m*, 1H), 2.58 (*s*, 3H), 1.83 (*m*, 4H), 1.38 (*t*, $J = 7.6$, 3H), 1.04 (*m*, 2H), 1.00 (*m*, 1H), 0.83 (*m*, 1H); ^{13}C NMR ($CDCl_3$) δ 171.57, 53.96, 48.36, 48.27, 44.20, 39.00, 38.95, 28.96, 28.80, 26.93, 26.78, 20.12, 19.92, 10.99, 10.94, 9.31, 9.27, 7.15; ESI-HRMS (M + H) calculated for $C_{11}H_{22}NO_3S_2$ 280.1036, found m/z 280.1030.

S-Ethyl cyclohexyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4d). Compound (**4d**) was prepared in a similar procedure to that for **4a**. Yield (30%); ^{1}H NMR ($CDCl_3$) δ 3.91 (*m*, 1H), 3.36 (*m*, 1H), 2.92 (*q*, $J = 7.6$, 2H), 2.73 (*m*, 2H), 2.58 (*s*, 3H), 1.50–1.84 (*m*, 12H), 1.37 (*t*, $J = 7.6$, 3H), 1.33 (*m*, 2H); ^{13}C NMR ($CDCl_3$) δ 168.35, 167.54, 59.46, 56.28, 56.29, 54.03, 53.90, 45.96, 45.93, 45.44, 44.03, 43.99, 43.31, 43.19, 38.88, 32.25, 32.20, 31.74, 31.27, 31.20, 30.50, 28.31, 25.92, 25.73, 25.62, 25.39, 25.10, 20.38, 20.13, 20.04, 7.25, 7.14; ESI-HRMS (M + H) calculated for $C_{14}H_{28}NO_3S_2$ 322.1505, found m/z 322.1509.

S-Ethyl (4-methanesulfinyl-butyl)-phenyl-thiocarbamate sulfoxide (4e). Compound (**4e**) was prepared in a similar procedure to that for **4a**. Yield (19%); ^{1}H NMR ($CDCl_3$) δ 7.2-7.51 (*m*, 5H), 4.05 (*m*, 1H), 3.69 (*m*, 1H), 2.73 (*t*, $J = 7.2$, 2H), 2.65 (*t*, $J = 7.6$, 2H), 2.57 (*s*, 3H), 1.74–1.84 (*m*, 4H), 1.20 (*t*, $J = 7.6$, 3H); ^{13}C NMR ($CDCl_3$) δ 169.57, 137.79, 130.51, 129.94, 128.91, 53.94, 53.84, 51.48, 44.15, 38.89, 26.54, 26.47, 19.79, 6.97; ESI-HRMS (M + H) calculated for $C_{14}H_{22}NO_3S_2$ 316.1036, found m/z 316.1035.

S-Ethyl (4-methanesulfinyl-butyl)-benzyl-thiocarbamate sulfoxide (4f). Compound **3f** (270 mg, 0.86 mmol) was dissolved in dichloromethane (5 mL) and cooled to −78°C. A solution of 3-chloroperbenzoic acid (*m*-CPBA) (77%, 183 mg, 0.82 mmol) in dichloromethane (5 mL) was then added slowly. After stirring for 15 min, all the solvents were evaporated and the reaction mixture was purified by column chromatography eluting with acetone and ethyl acetate (2:1, vol/vol) to give **4f** (100 mg, 35%) as an oil. ^{1}H-NMR ($CDCl_3$) δ 7.37–7.21 (*m*, 5H), 4.73 (*m*, 2H), 3.52 (*m*, 2H), 3.00 (*m*, 2H), 2.64 (*m*, 2H), 2.53, 2.52 (two *s*, 3H), 1.73 (*m*, 4H), 1.35 (*m*, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.01, 169.02, 168.75, 168.71, 135.68, 135.11, 129.35, 129.20, 128.68, 128.56, 128.48, 127.62, 127.60, 53.88, 53.84, 53.79, 51.41, 51.38, 49.68, 49.64, 47.65, 47.57, 45.87, 45.85, 45.65, 44.96, 44.91, 38.89, 38.84, 28.14, 28.07, 26.18, 26.11, 20.04, 19.98, 19.95, 19.85, 7.24, 7.19. ESI-HRMS (M + H) calculated for $C_{15}H_{24}NO_3S_2$ 330.1198, found m/z 330.1193.

S-Ethyl (4-methanesulfinyl-butyl)-naphthalen-1-ylmethyl-thiocarbamate sulfoxide (4g). Compound (**4g**) was prepared in a similar procedure to that of **4f**. Yield (27%), column chromatography eluting with acetone and ethyl acetate (2:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.99–7.83 (*m*, 3H), 7.59–7.28 (*m*, 4H), 5.18 (*m*, 2H), 3.43 (*m*, 2H), 3.03 (*m*, 2H), 2.60 (*m*, 2H), 2.53, 2.52 (two *s*, 3H), 1.73 (*m*, 4H), 1.36 (*m*, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.53, 168.50, 168.48, 134.15, 134.05, 131.06, 131.02, 130.61, 130.47, 129.76, 129.37, 129.32, 129.23, 128.22, 127.27, 127.24, 126.68, 126.63, 125.54, 125.45, 124.62, 124.56, 123.51, 122.44, 53.87, 53.84, 53.76, 53.71, 49.14, 49.11, 48.04, 48.01, 47.62, 47.59, 45.90, 45.69, 44.14, 44.10, 38.86, 38.81, 28.11, 28.04, 26.46, 26.39, 20.04, 19.99, 19.94, 19.83, 7.25, 7.21. ESI-HRMS (M + Na) calculated for $C_{19}H_{25}NO_3NaS_2$ 402.1174, found m/z 402.1164.

S-Ethyl (4-tert-butyl-benzyl)-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4h). Compound (**4h**) was prepared in a similar procedure to that of **4f**. Yield (32%), column chromatography eluting with acetone and ethyl acetate (2:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.38 (*d*, $J = 8.0$, 1H), 7.35 (*d*, $J = 8.0$, 1H), 7.17 (*t*, $J = 8.0$, 2H), 4.67 (*m*, 2H), 3.56 (*m*, 2H), 2.99 (*m*, 2H), 2.68 (*m*, 2H), 2.55, 2.54 (two *s*, 3H), 1.75 (*m*, 4H), 1.36 (*m*, 3H), 1.30 (*s*, 9H); ^{13}C-NMR ($CDCl_3$) δ 169.08, 168.58, 168.55, 151.84, 151.54, 132.52, 131.95, 130.15, 129.81, 128.33, 127.32, 127.30, 126.27, 126.11, 53.91, 53.88, 53.83, 50.97, 50.95, 49.39, 49.35, 47.44, 47.41, 45.87, 45.84, 45.63, 44.76, 44.72, 38.87, 38.82, 34.84, 34.82, 31.51, 28.13, 28.04, 26.15, 26.09, 20.04, 19.98, 19.85, 7.28, 7.24. ESI-HRMS (M + Na) calculated for $C_{19}H_{31}NO_3NaS_2$ 408.1643, found m/z 408.1639.

S-Ethyl biphenyl-4-ylmethyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4i). Compound (**4i**) was prepared in a similar procedure to that of **4f**. Yield (33%), column chromatography eluting with

acetone and ethyl acetate (2:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.62–7.56 (*m*, 4H), 7.47–7.42 (*m*, 2H), 7.38–7.32 (*m*, 3H), 4.78 (*m*, 2H), 3.61 (*m*, 2H), 3.08 (*m*, 2H), 2.70 (*m*, 2H), 2.56, 2.55 (two *s*, 3H), 1.78 (*m*, 4H), 1.40 (*m*, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.00, 168.77, 168.74, 141.67, 141.44, 140.57, 140.42, 134.66, 134.08, 129.13, 129.10, 129.07, 128.12, 128.10, 128.04, 127.91, 127.82, 127.30, 53.92, 53.88, 53.83, 51.20, 51.18, 49.39, 49.36, 47.65, 47.62, 45.94, 45.91, 45.74, 45.05, 44.98, 38.91, 38.87, 28.23, 28.15, 26.21, 26.15, 20.10, 20.04, 20.02, 19.91, 7.30, 7.25. ESI-HRMS (M + Na) calculated for $C_{21}H_{27}NO_3NaS_2$ 428.1330, found m/z 428.1323.

S-Ethyl (2,4-difluoro-benzyl)-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4j). Compound (**4j**) was prepared in a similar procedure to that of **4f**. Yield (23%), column chromatography eluting with acetone and ethyl acetate (2:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.41–7.35 (*m*, 1H), 6.94–6.80 (*m*, 2H), 4.85 (*m*, 2H), 3.56 (*m*, 2H), 3.04 (*m*, 2H), 2.69 (*m*, 2H), 2.57, 2.56 (two *s*, 3H), 1.79 (*m*, 4H), 1.41, 1.36 (two *t*, $J = 7.6$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.93, 168.91, 168.69, 164.50, 164.38, 164.35, 164.23, 162.61, 162.59, 162.49, 162.47, 162.00, 161.87, 161.85, 161.73, 160.12, 160.00, 132.49, 132.44, 132.39, 132.34, 131.26, 131.21, 131.18, 131.13, 131.11, 118.86, 118.84, 118.72, 118.70, 118.57, 118.53, 118.43, 118.39, 115.40, 115.31, 112.53, 112.49, 112.45, 112.41, 112.32, 112.28, 112.23, 112.20, 104.86, 104.61, 104.33, 104.07, 53.88, 53.84, 53.79, 47.47, 45.92, 45.90, 45.87, 45.39, 45.36, 44.48, 42.65, 42.62, 38.92, 38.90, 38.88, 28.27, 28.19, 26.17, 26.12, 20.07, 20.01, 19.98, 19.88, 7.28, 7.09. ESI-HRMS (M + Na) calculated for $C_{15}H_{22}NO_3F_2S_2$ 366.1009, found m/z 366.1000.

S-Benzyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4k). Compound (**4k**) was prepared in a similar procedure to that of **4f**. Yield (22%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.33–7.13 (*m*, 9H), 6.93–6.90 (*m*, 1H), 4.27 (*m*, 4H), 3.00 (*m*, 2H), 2.56 (*m*, 2H), 2.49, 2.45 (two *s*, 3H), 1.48 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) δ 168.27, 168.24, 168.17, 168.13, 135.33, 135.00, 134.94, 130.72, 130.69, 129.20, 129.13, 129.10, 129.07, 128.99, 128.96, 128.89, 128.54, 128.52, 127.77, 58.14, 58.10, 57.94, 57.88, 54.04, 53.84, 53.79, 51.55, 49.14, 49.08, 47.82, 47.79, 44.07, 43.91, 38.95, 38.87, 38.81, 27.63, 27.60, 26.07, 26.06, 20.13, 19.76, 19.64. ESI-HRMS (M + Na) calculated for $C_{20}H_{25}NO_3NaS_2$ 414.1174, found m/z 414.1172.

S-Cyclohexyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4l). Compound (**4l**) was prepared in a similar procedure to that of **4f**. Yield (32%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.34–7.29 (*m*, 5H), 4.74 (*m*, 2H), 3.52 (*m*, 2H), 3.0 (*m*, 1H), 2.63 (*m*, 2H), 2.51, 2.50 (two *s*, 3H), 1.76 (*m*, 10H), 1.34 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) δ 168.60, 168.58, 168.52, 168.48, 135.82, 135.25, 135.22, 129.30, 129.18, 128.71, 128.64, 128.48, 127.79, 127.77, 60.61, 60.59, 60.19, 60.16, 53.87, 53.82, 51.51, 51.46, 49.58, 49.54, 47.57, 47.50, 44.72, 44.67, 38.84, 38.81, 38.78, 28.23, 28.15, 27.33, 27.28, 26.20, 26.15, 26.00, 25.97, 25.61, 25.32, 24.89, 24.70, 20.12, 20.06, 19.94, 19.84. ESI-HRMS (M + Na) calculated for $C_{19}H_{29}NO_3NaS_2$ 406.1487, found m/z 406.1491.

S-(2-Methoxy-phenyl) benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4m). Compound (**4m**) was prepared in a similar procedure to that of **4f**. Yield (7%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.90 (*m*, 1H), 7.15 (*m*, 8H), 4.54 (*m*, 2H), 3.76, 3.75, 3.65, 3.63 (4*s*, 3H), 3.25 (*m*, 2H), 2.52 (*m*, 2H), 2.57, 2.56, 2.50, 2.47 (4*s*, 3H), 1.62 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) 169.81, 169.77, 169.16, 169.12, 155.63, 135.79, 134.85, 133.56, 133.47, 129.14, 129.11, 129.02, 128.38, 128.36, 128.34, 128.29, 127.96, 127.89, 127.67, 127.09, 127.00, 122.55, 122.52, 122.48, 111.16, 111.07, 56.06, 55.94, 55.91, 54.00, 53.94, 53.87, 53.73, 51.03, 51.00, 49.81, 46.89, 46.75, 45.37, 39.00, 38.90, 38.70, 29.93, 28.04, 27.87, 25.90, 25.87, 20.15, 19.90, 19.75, 19.49. ESI-HRMS (M + Na) calculated for $C_{20}H_{25}NO_4NaS_2$ 430.1123, found m/z 430.1123.

S-(Methoxycarbonylmethyl) benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4n). Compound (**4n**) was prepared in a similar procedure to that of **4f**. Yield (15%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.41–7.24 (*m*, 5H), 4.82 (*m*, 2H), 4.10 (*m*, 2H), 3.79 (*s*, 2H), 3.73 (*s*, 3H), 2.68, 2.56 (two *s*, 3H), 3.46 (*m*, 2H), 1.79 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) δ 167.51, 167.38, 166.03, 165.94, 135.38, 135.03, 129.37, 129.20, 128.72, 128.57, 128.52, 127.88, 54.71, 53.93, 53.81, 53.78, 53.30, 53.24, 51.81, 51.79, 50.01, 49.96, 47.73, 45.37, 45.27, 38.80, 28.14, 28.08, 26.02, 25.98, 19.91, 19.85; ESI-HRMS (M + Na) calculated for $C_{16}H_{23}NO_5NaS_2$ 396.0915, found m/z 396.0919.

S-Phenethyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4o). Compound (**4o**) was prepared in a similar procedure to that of **4f**. Yield (26%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.31–7.09 (*m*, 10H), 4.61 (*m*, 2H), 3.32 (*m*, 2H), 3.17 (*m*, 2H), 3.03 (*m*, 2H), 2.60 (*m*, 2H), 2.48, 2.48, (two *s*, 3H), 1.67 (*m*, 4H); ^{13}C-NMR ($CDCl_3$) δ 169.26, 168.81, 138.55, 138.48, 135.63, 135.09, 129.40, 129.25, 129.07, 129.04, 128.96, 128.91, 128.72, 128.63, 128.55, 127.55, 127.53, 127.19, 127.14, 53.84, 53.73, 53.70, 53.28, 53.25, 53.06, 51.57, 51.54, 49.79, 49.74, 47.94, 47.91, 45.11, 45.05, 38.82, 38.78, 28.85, 28.16, 28.07, 26.22, 26.17, 20.07, 20.02, 19.93, 19.82. ESI-HRMS (M + Na) calculated for $C_{21}H_{27}NO_3NaS_2$ 428.1330, found m/z 428.1332.

S-Pentyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4p). Compound (**4p**) was prepared in a similar procedure to that of **4f**. Yield (36%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.38–7.21 (*m*, 5H), 4.70 (*m*, 2H), 3.54 (*m*, 2H), 2.92 (*m*, 2H), 2.65 (*m*, 2H), 2.53 (*s*, 3H), 1.74 (*m*, 6H), 1.32 (*m*, 4H), 0.87 (*q*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.53, 169.10, 169.07, 135.67, 135.13, 129.36, 129.19, 128.70, 128.58, 128.48, 127.55, 127.52, 53.84, 53.79, 53.75, 52.00, 51.94, 51.81, 51.40, 51.38, 49.78, 49.75, 47.73, 47.69, 45.03, 44.99, 38.84, 38.89, 30.96, 30.90, 28.13, 28.05, 26.18, 26.13, 22.49, 22.47, 22.45, 22.43, 20.05, 19.99, 19.89, 19.86, 14.04. ESI-HRMS (M + Na) calculated for $C_{18}H_{29}NO_3NaS_2$ 394.1487, found m/z 394.1486.

S-Octyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4q). Compound (**4q**) was prepared in a similar procedure to that of **4f**. Yield (36%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.37–7.21 (*m*, 5H), 4.69 (*m*, 2H), 3.53 (*m*, 2H), 2.91 (*m*, 2H), 2.65 (*m*, 2H), 2.53 (*s*, 3H), 1.75 (*m*, 6H), 1.39 (*m*, 2H), 1.23 (*m*, 8H), 0.84 (*m*, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.55, 169.14, 169.10, 135.69, 135.15, 129.35, 129.19, 128.68, 128.58, 128.58, 127.55, 127.52, 53.86, 53.82, 53.77, 52.02, 51.86, 51.40, 51.37, 49.77, 49.74, 47.74, 47.69, 45.01, 44.98, 38.86, 38.82, 31.93, 31.91, 29.36, 29.29, 29.25, 29.21, 28.89, 28.80, 28.14, 28.05, 26.19, 26.13, 22.81, 22.76, 22.73, 20.04, 19.99, 19.97, 19.86, 14.31. ESI-HRMS (M + Na) calculated for $C_{21}H_{35}NO_3NaS_2$ 436.1956, found m/z 436.1958.

S-Undecyl benzyl-(4-methanesulfinyl-butyl)-thiocarbamate sulfoxide (4r). Compound (**4r**) was prepared in a similar procedure to that

of **4f**. Yield (33%), column chromatography eluting with acetone and ethyl acetate (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.34–7.17 (*m*, 5H), 4.65 (*m*, 2H), 3.48 (*m*, 2H), 2.87 (*m*, 2H), 2.62 (*m*, 2H), 2.50 (*s*, 3H), 1.72 (*m*, 6H), 1.35 (*m*, 4H), 1.19 (*m*, 14H), 0.81 (*t*, $J = 6.8$, 3H); ^{13}C-NMR ($CDCl_3$) δ 169.56, 169.11, 169.08, 135.70, 135.15, 135.16, 129.36, 129.20, 128.70, 128.60, 128.48, 127.57, 127.54, 53.88, 53.84, 53.78, 52.04, 52.02, 51.88, 51.43, 51.40, 49.79, 49.76, 47.75, 47.70, 45.02, 44.97, 38.87, 32.12, 29.78, 29.74, 29.58, 29.54, 29.43, 29.36, 28.91, 28.83, 28.17, 28.07, 26.20, 26.14, 22.91, 22.79, 22.75, 20.06, 20.00, 19.98, 19.97, 14.37. ESI-HRMS (M + Na) calculated for $C_{24}H_{41}NO_3NaS_2$ 478.2426, found m/z 478.2422.

2-(4-Chloro-butyl)-2-methyl-[1,3]dioxolane (5). To a solution of 6-chloro-2-hexanone (1 mL, 7.58 mmol) in toluene (50 mL) was added ethylene glycol (0.85 mL, 15.2 mmol) and *p*-toluenesulfonic acid monohydrate (72 mg, 0.38 mmol). The reaction mixture was equipped with a Dean-stark trap and refluxed at 130 °C for 4 h. After cooling to RT, the mixture was diluted with ethyl acetate (200 mL) and washed with sat. aq. sodium bicarbonate (75 mL) and sat. sodium chloride (75 mL) twice. The organic layer was dried over sodium sulfate, and the filtrate was concentrated and dried under vacuum to give crude yellow oil (1.3 g, 96%). A small fraction (0.1 g) was purified by column chromatography eluting with ethyl acetate and hexane (1:30, vol/vol) for characterization, otherwise used without further purification. ^{1}H-NMR ($CDCl_3$) δ 3.94 (*m*, 4H), 3.54 (*t*, $J = 6.8$, 2H), 1.79 (pentet, $J = 7.2$, 2H), 1.66 (*m*, 2H), 1.55 (*m*, 2H), 1.32 (*s*, 3H); ^{13}C-NMR ($CDCl_3$) δ 110.08, 64.92, 45.20, 38.61, 32.94, 24.02, 21.71. ESI-HRMS (M + H) calculated for $C_8H_{16}O_2Cl$ 179.0833, found m/z 179.0830.

S-Ethyl benzyl-[4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-thiocarbamate (6a). To a solution of benzylamine (0.25 mL, 2.24 mmol) in DMF (4 mL) was added potassium carbonate (0.31 g, 2.24 mmol), sodium iodide (0.33 g, 2.24 mmol), and a solution of compound (**5**) (0.33 g, 1.87 mmol) in DMF (2 mL). The mixture was heated at 90 °C for 6 h. After cooling to RT, the reaction mixture was diluted with ethyl acetate (80 mL) and washed with sat. sodium chloride (30 mL) four times. The organic layer was dried over sodium sulfate, and the filtrate was concentrated and dried under vacuum to give a yellow oil. This crude oil was dissolved in dichloromethane (15 mL) and cooled to 0 °C. *N*, *N*-diisopropylethylamine (0.97 mL, 5.6 mmol) was added slowly, followed by addition of ethyl chlorothioformate (0.46 mL, 4.5 mmol). After stirring for 1 h, the mixture was diluted with dichloromethane (80 mL) and washed with aq. 1N HCl, sat. aq. sodium bicarbonate, and sat. sodium chloride sequentially. The organic layer was dried over sodium sulfate and the filtrate was concentrated and purified by column chromatography eluting with ethyl acetate and hexane (1:15, vol/vol) to give **6a** as a clear oil (225 mg, 36%). ^{1}H-NMR ($CDCl_3$) δ 7.32–7.21 (*m*, 5H), 4.56 (br, 2H), 3.91 (*m*, 2H), 3.88 (*m*, 2H), 3.25 (br, 2H), 2.94 (*q*, $J = 7.6$, 2H), 1.59 (*m*, 4H), 1.35 (*m*, 2H), 1.30 (*t*, $J = 7.6$, 3H), 1.28 (*s*, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.86, 168.60, 137.49, 136.74, 128.86, 128.07, 127.63, 127.40, 110.09, 64.88, 51.42, 50.06, 47.34, 47.20, 38.96, 28.16, 27.79, 25.11, 24.00, 21.55, 15.61. ESI-HRMS (M + H) calculated for $C_{18}H_{28}NO_3S$ 338.1784, found m/z 338.1787.

S-Ethyl (3,4-dimethoxy-benzyl)-[4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-thiocarbamate (6b). Compound (**6b**) was prepared in a similar procedure to that of **6a**, but with 3,4-dimethoxybenzylamine. Yield (42%), column chromatography eluting with ethyl acetate and hexane (1:5, vol/vol), ^{1}H-NMR ($CDCl_3$) δ 6.74–6.67 (*m*, 3H), 4.42 (*d*, br, 2H), 3.83 (*m*, 4H), 3.77 (*s*, 6H), 3.20 (*d*, br, 2H), 2.86 (*q*, $J = 7.2$, 2H), 1.52 (*m*, 4H), 1.27 (*m*, 2H), 1.22 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.69, 168.26, 149.31, 148.59, 130.05, 129.09, 120.45, 119.73, 111.11, 110.47, 109.98, 64.80, 56.04, 56.00, 51.18, 49.79, 47.08, 46.90, 38.94, 28.12, 27.71, 25.00, 23.94, 21.50, 15.66.

S-Ethyl [4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-phenethyl-thiocarbamate (6c). Compound (**6c**) was prepared in a similar procedure to that of **6a**, but with phenethylamine. Yield (35%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol), ^{1}H-NMR ($CDCl_3$) δ 7.32–7.20 (*m*, 5H), 3.94 (*m*, 2H), 3.91 (*m*, 2H), 3.53 (*d*, br, 2H), 3.24 (*d*, br, 2H), 2.92 (*q*, $J = 7.2$, 2H), 2.88 (*m*, 2H), 1.64 (*m*, 2H), 1.56 (*m*, 2H), 1.36 (*m*, 2H), 1.30 (*s*, 3H), 1.29 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.05, 139.26, 138.59, 129.05, 128.80, 126.81, 126.61, 110.12, 64.89, 49.96, 48.81, 48.03, 39.00, 35.21, 34.52, 28.73, 28.29, 24.89, 23.99, 21.58, 15.66 ESI-HRMS (M + H) calculated for $C_{19}H_{30}NO_3S$ 352.1941, found m/z 352.1941.

S-Ethyl biphenyl-4-ylmethyl-[4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-thiocarbamate (6d). Compound (**6d**) was prepared in a similar procedure to that of **6a**, but with 4-phenylbenzylamine. Yield (58%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$)δ 7.59–7.54 (*m*, 4H), 7.44 (*t*, $J = 8.0$, 2H), 7.35 (*d*, $J = 7.6$, 1H), 7.30 (*d*, $J = 7.6$, 2H), 4.62 (br, 2H), 3.92 (*m*, 2H), 3.91 (*m*, 2H), 3.33 (br, 2H), 2.96 (*q*, $J = 7.2$, 2H), 1.61 (*m*, 4H), 1.38 (*m*, 2H), 1.32 (*t*, $J = 7.6$, 3H), 1.29 (*s*, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.93, 168.70, 140.96, 140.58, 136.55, 135.75, 129.02, 128.51, 127.81, 127.61, 127.30, 110.10, 64.89, 51.16, 49.84, 47.46, 47.25, 38.99, 28.21, 27.82, 25.12, 24.01, 21.58, 15.61. ESI-HRMS (M + H) calculated for $C_{24}H_{32}NO_3S$ 414.2097, found m/z 414.2105.

S-Ethyl (2,4-Difluoro-benzyl)-[4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-thiocarbamate (6e). Compound (**6e**) was prepared in a similar procedure to that of **6a**, but with 2,4-difluorobenzylamine. Yield (47%), column chromatography eluting with ethyl acetate and hexane (1:15, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.24–7.18 (*m*, 1H), 6.79–6.70 (*m*, 2H), 4.52 (br, 2H), 3.84 (*m*, 4H), 3.20 (br, 2H), 2.91 (*q*, $J = 7.2$, 2H), 1.55 (*m*, 4H), 1.31 (*m*, 2H), 1.22 (*t*, $J = 7.2$, 3H), 1.21 (*s*, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.93, 168.62, 163.71, 163.60, 162.22, 162.11, 161.24, 161.12, 159.73, 159.62, 131.44, 129.83, 120.40, 119.85, 111.84, 111.80, 111.63, 111.60, 109.96, 104.07, 103.82, 103.57, 64.80, 47.82, 47.40, 44.36, 43.12, 38.87, 28.23, 27.82, 25.01, 23.92, 21.44, 15.50. ESI-HRMS (M + H) calculated for $C_{18}H_{26}NO_3F_2S$ 374.1596, found m/z 374.1603.

S-Ethyl (4-hex-5-ynyloxy-benzyl)-[4-(2-methyl-[1,3]dioxolan-2-yl)-butyl]-thiocarbamate (6f). Compound (**6f**) was prepared in a similar procedure to that of **6a**, but with amine compound (**11**). Yield (40%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.10 (*d*, $J = 7.6$, 2H), 6.79 (*d*, $J = 7.6$, 2H), 4.45 (*d*, br, 2H), 3.91 (*t*, $J = 6.0$, 2H), 3.20 (*d*, br, 2H), 2.89 (*q*, $J = 7.2$, 2H), 2.21 (dt, $J = 2.4$, 6.8, 2H), 1.94 (*t*, $J = 2.4$, 1H), 1.84 (*m*, 2H), 1.66 (*m*, 2H), 1.54 (*m*, 4H), 1.29 (*m*, 2H), 1.25 (*t*, $J = 7.2$, 3H), 1.23 (*s*, 3H); ^{13}C-NMR ($CDCl_3$) δ 168.57, 168.20, 158.62, 129.47, 128.74, 114.71, 110.03, 84.23, 69.02, 67.42, 64.83, 50.83, 49.43, 47.03, 46.92, 38.93, 28.45, 28.11, 27.69, 25.23, 25.01, 23.98, 21.52, 18.34, 15.64. ESI-HRMS (M + H) calculated for $C_{24}H_{36}NO_4S$ 434.2460, found m/z 434.2354.

S-Ethyl benzyl-(5-oxo-hexyl)-thiocarbamate (7a). To compound **6a** (220 mg, 0.65 mmol) dissolved in THF (20 mL) was added 3N aq. HCl (2 mL). After stirring for 4 h at RT, the mixture was diluted with ethyl acetate (100 mL) and washed with water (40 mL), sat. aq. sodium bicarbonate (40 mL), and sat. sodium chloride (40 mL) sequentially. The organic layer was dried over sodium

sulfate. The filtrate was concentrated and purified by column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol) to give **7a** (175 mg, 92%) as a clear oil. ^{1}H-NMR ($CDCl_3$) δ 7.30–7.18 (*m*, 5H), 4.54 (*d*, br, 2H), 3.24 (*d*, br, 2H), 2.91 (*q*, $J = 7.2$, 2H), 2.38 (*t*, $J = 6.8$, 3H), 2.07 (*s*, 3H), 1.48 (*s*, br, 4H), 1.27 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.45, 168.73, 137.40, 136.60, 128.86, 128.06, 127.73, 127.44, 51.34, 50.04, 47.06, 46.63, 43.18, 30.14, 27.47, 27.01, 25.12, 20.99, 15.60. ESI-HRMS (M + H) calculated for $C_{16}H_{24}NO_2S$ 294.1522, found m/z 294.1526.

S-Ethyl (3,4-dimethoxy-benzyl)-(5-oxo-hexyl)-thiocarbamate (7b). Compound (**7b**) was prepared in a similar procedure to that of **7a**. Yield (79%), column chromatography eluting with ethyl acetate and hexane (1:4, vol/vol), ^{1}H-NMR ($CDCl_3$) δ 6.73–6.70 (*m*, 3H), 4.42 (*d*, br, 2H), 3.77 (*s*, 6H), 3.18 (*d*, br, 2H), 2.85 (*q*, $J = 7.2$, 2H), 2.34 (*t*, $J = 6.6$, 2H), 2.02 (*s*, 3H), 1.43 (*s*, br, 4H), 1.21 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.45, 168.56, 149.31, 148.63, 129.93, 128.96, 120.48, 119.79, 111.16, 110.50, 56.04, 56.01, 51.10, 49.75, 46.84, 46.39, 43.12, 30.10, 27.30, 26.94, 25.05, 20.95, 15.64. ESI-HRMS (M + H) calculated for $C_{18}H_{28}NO_4S$ 354.1734, found m/z 354.1736.

S-Ethyl (5-oxo-hexyl)-phenethyl-thiocarbamate (7c). Compound (**7c**) was prepared in a similar procedure to that of **7a**. Yield (89%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$) 7.34–7.29 (*m*, 5H), 3.50 (br, 2H), 3.22 (*d*, br, 2H), 2.92 (*q*, $J = 7.6$, 2H), 2.80 (br, 2H), 2.45 (*t*, $J = 6.0$, 2H), 2.13 (*s*, 3H), 1.53 (p, $J = 7.6$, 4H), 1.29 (*t*, $J = 7.6$, 3H); ^{13}C-NMR ($CDCl_3$) 208.80, 208.50, 168.18, 139.20, 138.54, 129.05, 128.83, 126.81, 126.65, 49.99, 48.58, 47.62, 43.29, 35.18, 34.51, 30.22, 28.07, 27.54, 24.92, 21.02, 15.64. ESI-HRMS (M + H) calculated for $C_{17}H_{26}NO_2S$ 308.1679, found m/z 308.1687.

S-Ethyl biphenyl-4-ylmethyl-(5-oxo-hexyl)-thiocarbamate (7d). Compound (**7d**) was prepared in a similar procedure to that of **7a**. Yield (93%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.58–7.54 (*m*, 4H), 7.42 (*t*, $J = 7.6$, 2H), 7.33 (*d*, $J = 8.0$, 1H), 7.30 (*d*, $J = 7.6$, 2H), 4.61 (*d*, br, 2H), 3.32 (*d*, br, 2H), 2.96 (*q*, $J = 7.2$, 2H), 2.42 (*t*, $J = 6.8$, 2H), 2.10 (*s*, 3H), 1.54 (br, 4H), 1.32 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.91, 208.61, 168.86, 140.86, 140.62, 136.49, 135.63, 129.05, 128.56, 127.89, 127.61, 127.27, 51.09, 49.84, 47.24, 46.72, 43.22, 30.19, 27.54, 27.06, 25.20, 21.03, 15.65. ESI-HRMS (M + H) calculated for $C_{22}H_{28}NO_2S$ 370.1835, found m/z 370.1843.

S-Ethyl (2,4-Difluoro-benzyl)- (5-oxo-hexyl)-thiocarbamate (7e). Compound (**7e**) was prepared in a similar procedure to that of **7a**. Yield (96%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$) 7.26–7.20 (*m*, 1H), 6.82-6.73 (*m*, 2H), 4.53 (br, 2H), 3.23 (br, 2H), 2.88 (*q*, $J = 7.6$, 2H), 2.41 (*t*, $J = 6.8$, 2H), 2.08 (*s*, 3H), 1.51 (br, 4H), 1.24 (*t*, $J = 7.6$, 3H); ^{13}C-NMR ($CDCl_3$) 208.49, 168.95, 163.79, 163.66, 162.25, 162.14, 161.31, 161.19, 161.31, 161.19, 159.76, 159.66, 131.55, 129.92, 120.30, 119.72, 111.92, 111.88, 111.70, 111.66, 104.14, 103.90, 103.64, 47.55, 46.91, 44.32, 43.13, 30.12, 27.54, 27.09, 25.10, 20.91, 15.47. ESI-HRMS (M + H) calculated for $C_{16}H_{22}NO_2F_2S$ 330.1334, found m/z 330.1337.

S-Ethyl (4-hex-5-ynyloxy-benzyl)- (5-oxo-hexyl)-thiocarbamate (7f). Compound (**7f**) was prepared in a similar procedure to that of **7a**. Yield (90%), column chromatography eluting with ethyl acetate and hexane (1:10, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.11 (*d*, $J = 7.6$, 2H), 6.79 (*d*, $J = 7.6$, 2H), 4.45 (br, 2H), 3.92 (*t*, $J = 6.0$, 2H), 3.21 (br, 2H), 2.89 (*q*, $J = 7.2$, 2H), 2.36 (br, 2H), 2.21 (dt, $J = 2.4$, 6.8, 2H), 2.05 (*s*, 3H), 1.93 (*t*, $J = 2.4$, 1H), 1.85 (*m*, 2H), 1.66 (*m*, 2H), 1.47 (br, 4H), 1.26 (*t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.51, 168.52, 158.67, 129.49, 128.81, 114.75, 84.25, 68.98, 67.45, 50.75, 49.41, 46.78, 46.31, 43.1930.14, 28.45, 27.40, 26.95, 25.23, 25.08, 21.00, 18.34, 15.61. ESI-HRMS (M + H) calculated for $C_{22}H_{32}NO_3S$ 390.2097, found m/z 390.2094.

S-Ethyl benzyl-(5-oxo-hexyl)-thiocarbamate sulfoxide (8a). Compound **7a** (170 mg, 0.58 mmol) was dissolved in dichloromethane (5 mL) and cooled to −78°C. A solution of *m*-CPBA (77%, 123 mg, 0.55 mmol) in dichloromethane (5 mL) was then added slowly. After stirring for 15 min, all solvents were evaporated to dryness. The reaction mixture was dissolved in ethyl acetate (100 mL) and washed with sat. aq. sodium bicarbonate (50 mL) and sat. sodium chloride (50 mL). The organic layer was dried over sodium sulfate and the filtrate was concentrated and purified by column chromatography eluting with ethyl acetate and hexane (1:1, vol/vol) to give **8a** (120 mg, 67%) as a clear oil, which turned slightly yellow after drying under vacuum. ^{1}H-NMR ($CDCl_3$) δ 7.39–7.23 (*m*, 5H), 4.72 (*m*, 2H), 3.46 (*m*, 2H), 2.99 (*m*, 2H), 2.43 (*m*, 2H), 2.11, 2.10 (two *s*, 3H), 1.57 (*m*, 4H), 1.37, 1.36 (two *t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.52, 208.36, 168.90, 168.80, 135.76, 135.28, 129.29, 129.14, 128.61, 128.56, 128.38, 127.60, 51.01, 49.35, 47.77, 45.74, 45.65, 45.22, 42.94, 42.81, 30.26, 30.23, 28.25, 26.36, 20.71, 20.55, 7.23, 7.20. ESI-HRMS (M + Na) calculated for $C_{16}H_{23}NO_3NaS$ 332.1296, found m/z 332.1302.

S-Ethyl (3,4-dimethoxy-benzyl)-(5-oxo-hexyl)-thiocarbamate sulfoxide (8b). Compound (**8b**) was prepared in a similar procedure to that of **8a**. Yield (59%), column chromatography eluting with ethyl acetate and hexane (2:1, vol/vol); ^{1}H-NMR ($CDCl_3$) 6.84–6.76 (*m*, 3H), 4.63 (*m*, 2H), 3.86 (*s*, 3H), 3.85 (*d*, $J = 9.2$, 3H), 3.43 (*m*, 2H), 3.00 (*m*, 2H), 2.44 (*m*, 2H), 2.12, 2.11 (two *s*, 3H), 1.57 (*m*, 4H), 1.37, 1.36 (two *t*, $J = 7.6$, 3H); ^{13}C-NMR ($CDCl_3$) 208.61, 208.42, 168.78, 168.54, 149.70, 149.56, 149.28, 149.18, 128.26, 127.50, 121.28, 120.14, 111.68, 111.40, 111.22, 110.66, 56.16, 56.14, 50.85, 49.18, 47.51, 45.66, 45.53, 45.00, 42.93, 42.80, 30.26, 28.23, 26.34, 20.72, 20.57, 7.21, 7.17. ESI-HRMS (M + Li) calculated for $C_{18}H_{27}LiNO_5S$ 376.1765, found m/z 376.1761.

S-Ethyl (5-oxo-hexyl)-phenethyl-thiocarbamate sulfoxide (8c). Compound (**8c**) was prepared in a similar procedure to that of **8a**. Yield (48%), column chromatography eluting with ethyl acetate and hexane (2:3, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.34–7.19 (*m*, 5H), 3.72 (*m*, 2H), 3.40 (*m*, 2H), 2.93 (*m*, 2H), 2.81 (*m*, 2H), 2.47 (*m*, 2H), 2.14, 2.13 (two *s*, 3H), 1.59 (*m*, 4H), 1.31 (*q*, $J = 7.6$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.55, 208.37, 168.52, 168.21, 138.131, 137.49, 129.23, 129.08, 129.05, 128.93, 127.28, 127.02, 50.11, 48.27, 48.08, 46.74, 45.59, 45.48, 43.01, 42.87, 35.87, 33.74, 30.29, 30.27, 28.76, 26.81, 20.80, 20.54, 7.28, 7.16. ESI-HRMS (M + H) calculated for $C_{17}H_{26}NO_3S$ 324.1628, found m/z 324.1633.

S-Ethyl biphenyl-4-ylmethyl-(5-oxo-hexyl)-thiocarbamate sulfoxide (8d). Compound (**8d**) was prepared in a similar procedure to that of **8a**. Yield (56%), column chromatography eluting with ethyl acetate and hexane (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.61–7.56 (*m*, 4H), 7.47–7.42 (*m*, 2H), 7.38–7.31 (*m*, 3H), 4.78 (*m*, 2H), 3.51 (*m*, 2H), 3.03 (*m*, 2H), 2.46 (*m*, 2H), 2.13, 2.12 (two *s*, 3H), 1.61 (*m*, 4H), 1.40, 1.39 (two *t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.56, 208.40, 168.94, 168.79, 141.55, 141.34, 140.63, 140.49, 134.75, 134.24, 129.11, 129.09, 128.07, 127.98, 127.85, 127.79, 127.30, 50.77, 49.05, 47.81, 45.77, 45.72, 45.31, 42.96, 42.84, 30.29, 30.28, 28.30, 26.38, 20.73, 20.57, 7.28, 7.25.

ESI-HRMS (M + Na) calculated for $C_{22}H_{27}NO_3NaS$ 408.1609, found m/z 408.1614.

S-Ethyl (2,4-Difluoro-benzyl)-(5-oxo-hexyl)-thiocarbamate sulfoxide (8e). Compound (**8e**) was prepared in a similar procedure to that of **8a**. Yield (37%), column chromatography eluting with ethyl acetate and hexane (2:3, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.41–7.33 (*m*, 1H), 6.94–6.80 (*m*, 2H), 4.85 (*m*, 2H), 3.44 (*m*, 2H), 3.04 (*m*, 2H), 2.46 (*m*, 2H), 2.13, 2.12 (two *s*, 3H), 1.60 (*m*, 2H), 1.40, 1.34 (two *t*, $J = 7.2$, 3H); ^{13}C-NMR ($CDCl_3$) 208.46, 208.33, 169.11, 168.46, 164.43, 164.30, 164.18, 162.59, 162.47, 161.93, 161.81, 161.68, 160.11, 159.99, 132.51, 132.45, 132.42, 132.36, 131.18, 131.13, 131.09, 131.03, 118.95, 118.91, 118.80, 118.76, 118.69, 118.66, 118.55, 118.51, 112.43, 112.39, 112.37, 112.33, 112.22, 112.18, 112.16, 112.12, 104.80, 104.55, 104.51, 104.29, 104.26, 104.01, 47.71, 45.90, 45.77, 45.72, 44.17, 44.14, 42.91, 42.79, 42.40, 42.37, 30.24, 28.38, 26.35, 20.68, 20.51, 7.25, 7.08. ESI-HRMS (M + H) calculated for $C_{16}H_{22}NO_3F_2S$ 346.1283, found m/z 346.1277.

S-Ethyl (4-hex-5-ynyloxy-benzyl)-(5-oxo-hexyl)-thiocarbamate sulfoxide (8f). Compound (**8f**) was prepared in a similar procedure to that of **8a**. Yield (67%), column chromatography eluting with ethyl acetate and hexane (1:1, vol/vol); ^{1}H-NMR ($CDCl_3$) δ 7.20–7.14 (*m*, 2H), 6.88–6.83 (*m*, 2H), 4.64 (*m*, 2H), 3.97 (two *t*, $J = 6.4$, 2H), 3.42 (*m*, 2H), 3.00 (*m*, 2H), 2.44 (*m*, 2H), 2.27 (two *t*, $J = 7.0$, 2H), 2.13, 2.12 (two *s*, 3H), 1.97 (*t*, $J = 2.8$, 1H), 1.89 (*m*, 2H), 1.70 (*m*, 2H), 1.58 (*m*, 4H), 1.37, 1.36 (two *t*, $J = 7.4$, 3H); ^{13}C-NMR ($CDCl_3$) δ 208.58, 208.41, 168.71, 168.64, 159.27, 159.13, 130.11, 129.07, 127.72, 126.97, 115.14, 114.99, 84.26, 68.92, 67.58, 67.53, 50.43, 48.86, 47.42, 45.72, 45.59, 44.87, 42.95, 42.84, 30.26, 28.43, 28.23, 26.33, 25.23, 20.72, 20.57, 18.37, 7.25, 7.20. ESI-HRMS (M + Na) calculated for $C_{22}H_{31}NO_4NaS$ 428.1866, found m/z 428.1856.

4-Hex-5-ynyloxy-benzaldehyde (9). To a solution of 4-hydroxybenzaldehyde (2 g, 16.37 mmol) in DMF (30 mL) was added potassium carbonate (4.52 g 32.7 mmol), potassium iodide (1.35 g, 8.2 mmol), and 6-chloro-hex-1-yne (2.98 mL, 24.6 mmol). The mixture was heated at 80 °C for 4 h. After cooling to RT, the mixture was diluted with ethyl acetate (150 mL) and washed with H_2O (70 mL) twice and sat. sodium chloride (50 mL) twice. The organic layer was dried over sodium sulfate. The filtrate was concentrated, solidified in diethyl ether and hexane, and filtered to give **9** (2.95 g, 89%). ^{1}H-NMR ($CDCl_3$) δ 9.87 (*s*, 1H), 7.82 (dd, $J = 1.6$, 6.4, 2H), 6.98 (dd, $J = 1.6$, 6.4, 2H), 4.07 (*t*, $J = 6.4$, 2H), 2.29 (dt, $J = 2.4$, 7.2, 2H), 1.98 (*t*, $J = 2.4$, 1H), 1.94 (*m*, 2H), 1.73 (*m*, 2H); ^{13}C-NMR ($CDCl_3$) δ 191.10, 164.30, 132.25, 130.06, 114.95, 84.10, 69.07, 67.92, 28.27, 25.12, 18.35. ESI-HRMS (M + H) calculated for $C_{13}H_{15}O_2$ 203.1067, found m/z 203.1069.

(4-Hex-5-ynyloxy-phenyl)-methanol (10). Compound **9** (2.83 g, 14.0 mmol) was dissolved in ethanol (100 mL) and cooled to 0 °C. Sodium borohydride (535 mg, 14.0 mmol) was then added. After stirring for 30 min, the mixture was diluted with ethyl acetate (200 mL) and washed with H_2O and sat. sodium chloride. The organic layer was dried over sodium sulfate. The filtrated was concentrated and purified by column chromatography eluting with ethyl acetate and hexane (1:3, vol/vol) to give **10** (2.30 g, 81%) as clear oil. ^{1}H-NMR ($CDCl_3$) δ 7.27 (*m*, 2H), 6.88 (*m*, 2H), 4.61 (*d*, $J = 6.4$, 2H), 3.98 (*t*, $J = 6.4$, 2H), 2.27 (dt, $J = 2.4$, 6.8, 2H), 1.97 (*t*, $J = 2.4$, 1H), 1.91 (*m*, 2H), 1.72 (*m*, 2H), 1.63 (*t*, $J = 6.4$, 1H); ^{13}C-NMR ($CDCl_3$) δ 158.86, 133.25, 128.90, 114.75, 84.34, 68.90, 67.54, 65.32, 28.49, 25.26, 18.39 ESI-HRMS $(M\text{-}OH)^+$ calculated for $C_{13}H_{15}O$ 187.1123, found m/z 187.1117, also $(M\text{-}H)^+$ calculated for $C_{13}H_{15}O_2$ 203.1067, found m/z 203.1064.

4-Hex-5-ynyloxy-benzylamine (11). Compound **10** (1.85 g, 9.1 mmol) was dissolved in dichloromethane (20 mL) and cooled to 0 °C. To the solution was added *N*, *N*-diisopropylethylamine (1.92 mL, 10.9 mmol) and methanesulfonyl chloride (0.81 mL, 10.4 mmol). After stirring for 1 h, the mixture was diluted with ethyl acetate (150 mL) and washed with ice-cold aq. 1N HCl (40 mL), sat. aq. sodium bicarbonate (40 mL) and sat. sodium chloride (40 mL) sequentially. The organic layer was dried over sodium sulfate. The filtrate was concentrated and quickly passed through silica gel (2 cm × 6 cm) eluting with hexane to give clear oil. This oil was dissolved in ethanol (10 mL) and cooled to 0 °C. After addition of 7N ammonia solution in methanol (15 mL), the mixture was stirred at RT overnight. All solvents were evaporated, and the mixture was diluted with dichloromethane (100 mL) and washed with 10% aq. sodium carbonate. The organic layer was dried over potassium carbonate. The filtrate was concentrated and purified by column chromatography eluting with methanol and dichloromethane (1:10, vol/vol) to give **11** (550 mg, 30%). ^{1}H-NMR ($CDCl_3$) δ 7.21 (*d*, $J = 8.4$, 2H), 6.86 (*d*, $J = 8.4$, 2H), 3.97 (*t*, $J = 6.4$, 2H), 3.80 (*s*, 2H), 2.27 (dt, $J = 2.4$, 6.8, 2H), 1.97 (*t*, $J = 2.4$, 1H), 1.90 (*m*, 2H), 1.72 (*m*, 2H), 1.68 (br, 2H); ^{13}C-NMR ($CDCl_3$) δ 158.17, 135.52, 128.53, 114.73, 84.36, 68.85, 67.52, 46.09, 28.52, 25.27, 18.39. ESI-HRMS $(M\text{-}NH_2)^+$ calculated for $C_{13}H_{15}O$ 187.1117, found m/z 187.1120.

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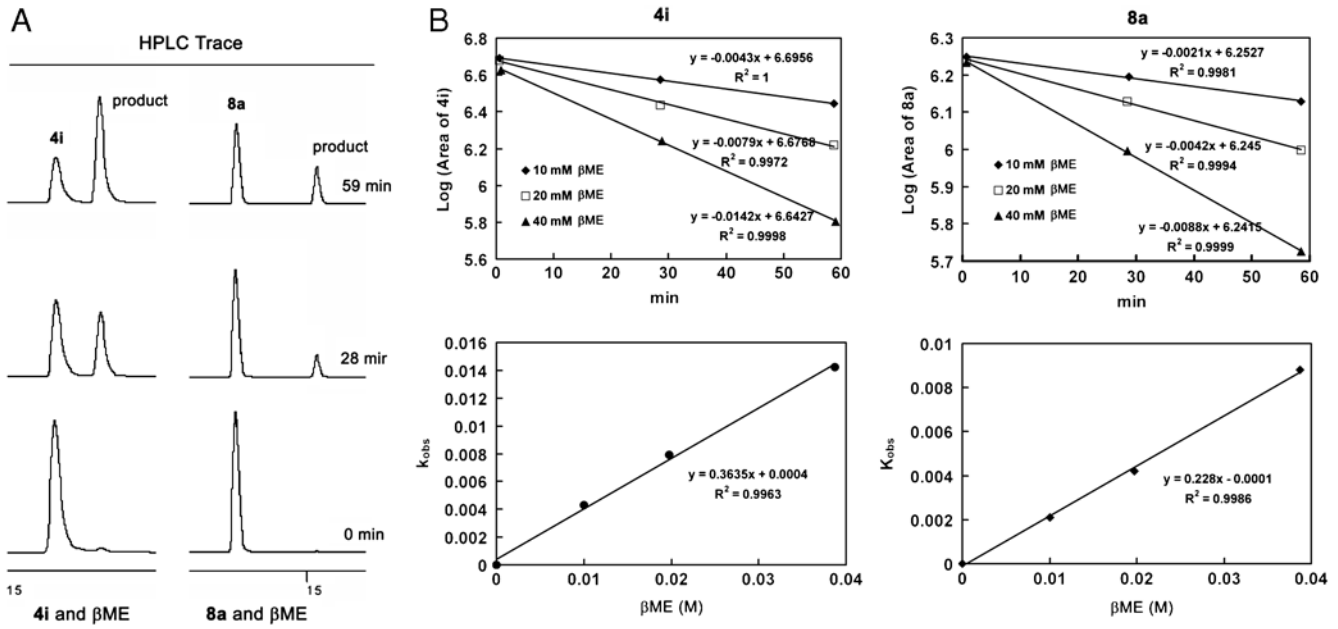

Fig. S1. Reactivity of sulfoxythiocarbamates with thiol. Reaction progress was monitored by HPLC. (*A*) HPLC traces of reaction of sulfoxythiocarbamates with β-mercaptoethanol (βME). To compound **4i** or **8a** (stock 40 mM in acetonitrile, final 1 mM) in phosphate buffer (100 mM pH 7.4) was added β-mercaptoethanol (stock 1 M in water with 0.1% TFA, final 10, 20, or 40 mM). Fractions were then injected at different time points for analysis by reversed phase (C-18) HPLC. HPLC traces with 20 mM βME are shown. (*B*) Logarithm values of area integrations of **4i** or **8a** peaks at different times were plotted for reaction rate (*Top*). Reactions were assumed to follow a pseudo-first order kinetic mechanism. Reaction rates were plotted as a function of βME concentrations (*Bottom*). The second order rate constant of **4i** with 0.36 M^{-1} min^{-1} and **8a** with 0.23 M^{-1} min^{-1}.

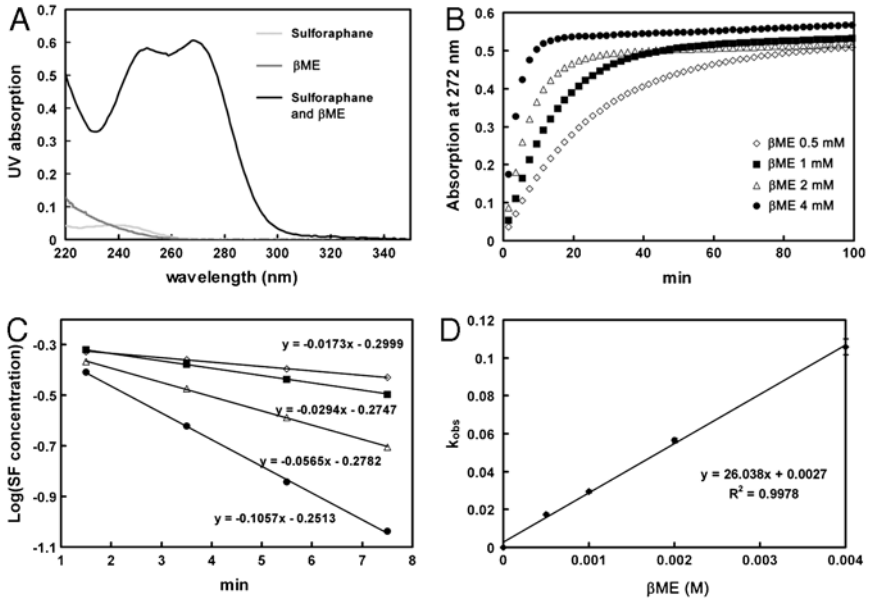

Fig. S2. Reactivity of sulforaphane with thiol. (*A*) UV spectra of sulforaphane or βME alone, and the reaction of sulforaphane and βME at 1.5 h. Sulforaphane (40 mM stock in acetonitrile, final 50 μM) was added to βME (stock 1 M in water with 0.1% TFA, final 500 μM) in phosphate buffer (100 mM, pH 7.4). (*B*) Reaction kinetics of sulforaphane with βME. Reaction was monitored by UV absorption at 272 nm, based on dithiocarbamate absorption (1). (*C*) Logarithm values of sulforaphane concentrations were plotted vs. time. (*D*) Plot of reaction rates of sulforaphane with βME as a function of βME concentration, which gives the second order rate constant with 26.04 M^{-1} min^{-1}.

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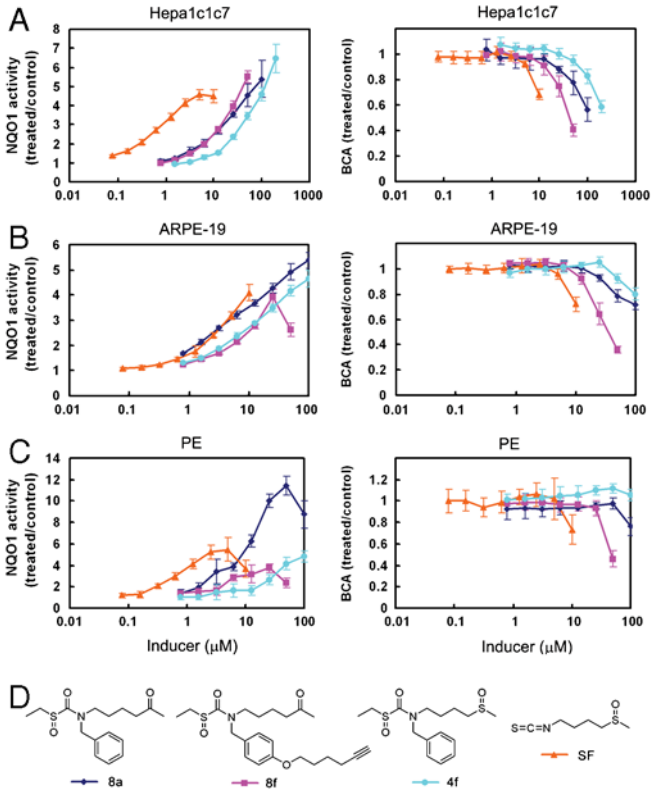


Fig. S3. NQO1 induction activities and toxicities of sulfoxythiocarbamate analogs and SF in three different cell lines including murine hepatoma cells (Hepa1c1c7), human retinal pigment epithelial cells (ARPE-19), and murine keratinocytes (PE). Results are shown as means ± SD ($n = 8$).

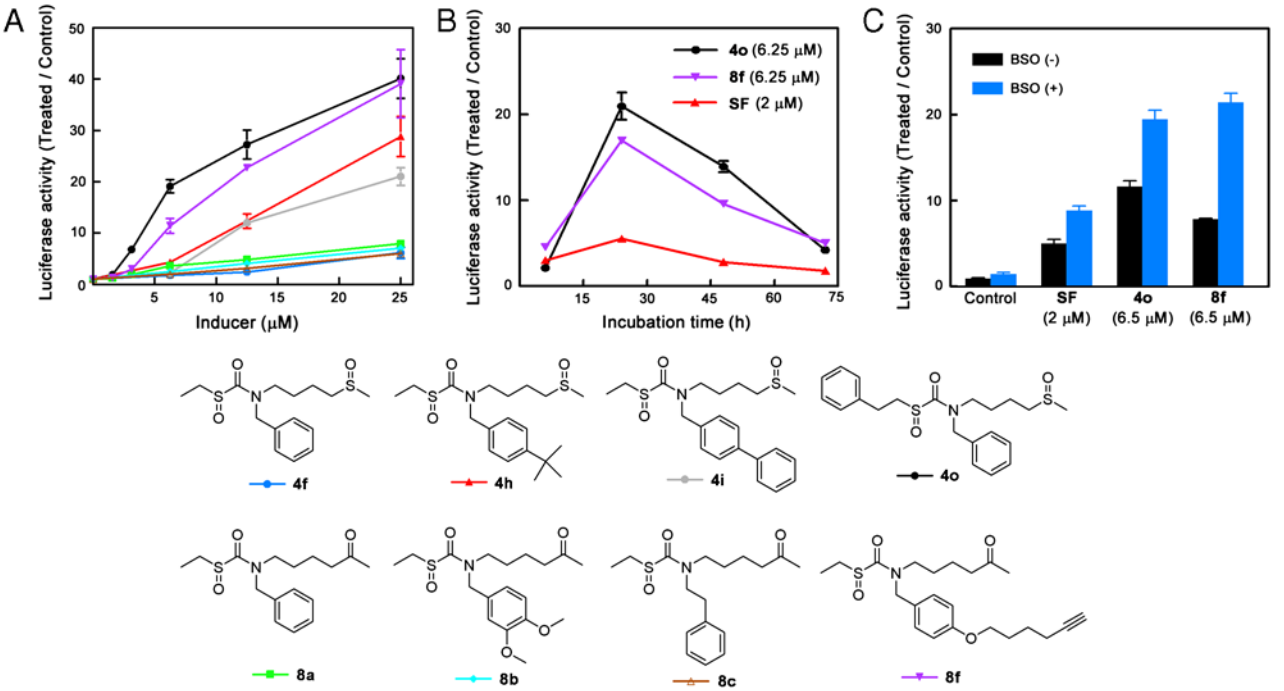


Fig. S4. Sulfoxythiocarbamate analogs induce ARE-driven gene expression in a concentration- and time-dependent manner. Glutathione depletion enhances inducer potency. (*A*) Induction of ARE-dependent gene expression. AREc32 cells expressing luciferase gene under the transcriptional control of eight tandemly arrayed copies of the ARE were seeded on 96-well plates. After 24 h, cells were exposed to increasing concentrations of compounds. The ARE-driven luciferase reporter activity was determined in cell lysates 24 h later. (*B*) Time course of ARE-dependent luciferase induction in response to compounds **4o**, **8f**, or sulforaphane. AREc32 cells were exposed to inducers and the luciferase activity was determined in cell lysates at 6, 24, 48, and 72 h. (*C*) Depletion of cellular glutathione enhances inducer potency. AREc32 cells were incubated with L-buthionine-sulfoximine (BSO) (20 μM), an inhibitor of glutamyl-cysteine ligase, for 24 h. The cells were then exposed to compounds **4o**, **8f**, or sulforaphane for further 24 h, and the luciferase activity was determined in cell lysates. The value of luciferase activity of cells treated with acetonitrile (control) was set to 1. Values are means ± SD.

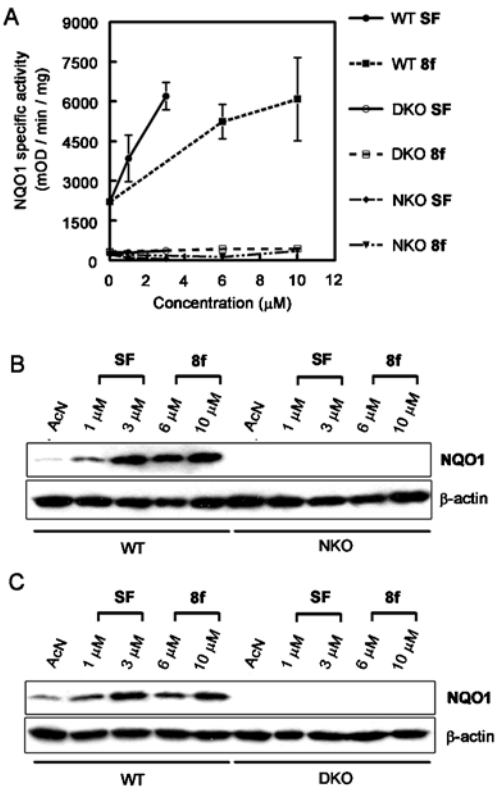


Fig. S5. Sulforaphane and its sulfoxythiocarbamate analog **8f** induce NQO1 gene expression in a Keap1/Nrf2-dependent manner. MEF derived from WT, Nrf2-knockout (NKO), or Keap1/Nrf2-double knockout (DKO) mice were seeded on 6-well plates at a density of 150,000 cells per well. After 24 h, cells were exposed to two different concentrations of sulforaphane (1 or 3 μM) or compound **8f** (6 or 10 μM). The NQO1 enzyme activity (*A*) and protein levels (*B* and *C*) were determined in cell lysates 24 h later.

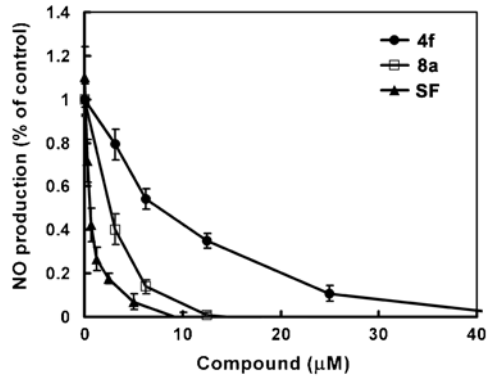


Fig. S6. Sulfoxythiocarbamate analogs suppress lipopolysaccharide (LPS)-induced nitric oxide (NO) generation in macrophage-like RAW264.7 cells. RAW264.7 cells (40,000 cells per well) were grown for 24 h in 96-well plates and treated with LPS (10 ng/mL) in the presence of serial dilutions of compounds for 48 h. NO production was then measured as nitrite accumulation in the medium. Control cells were treated with LPS only. Values are means ± SD ($n = 8$).

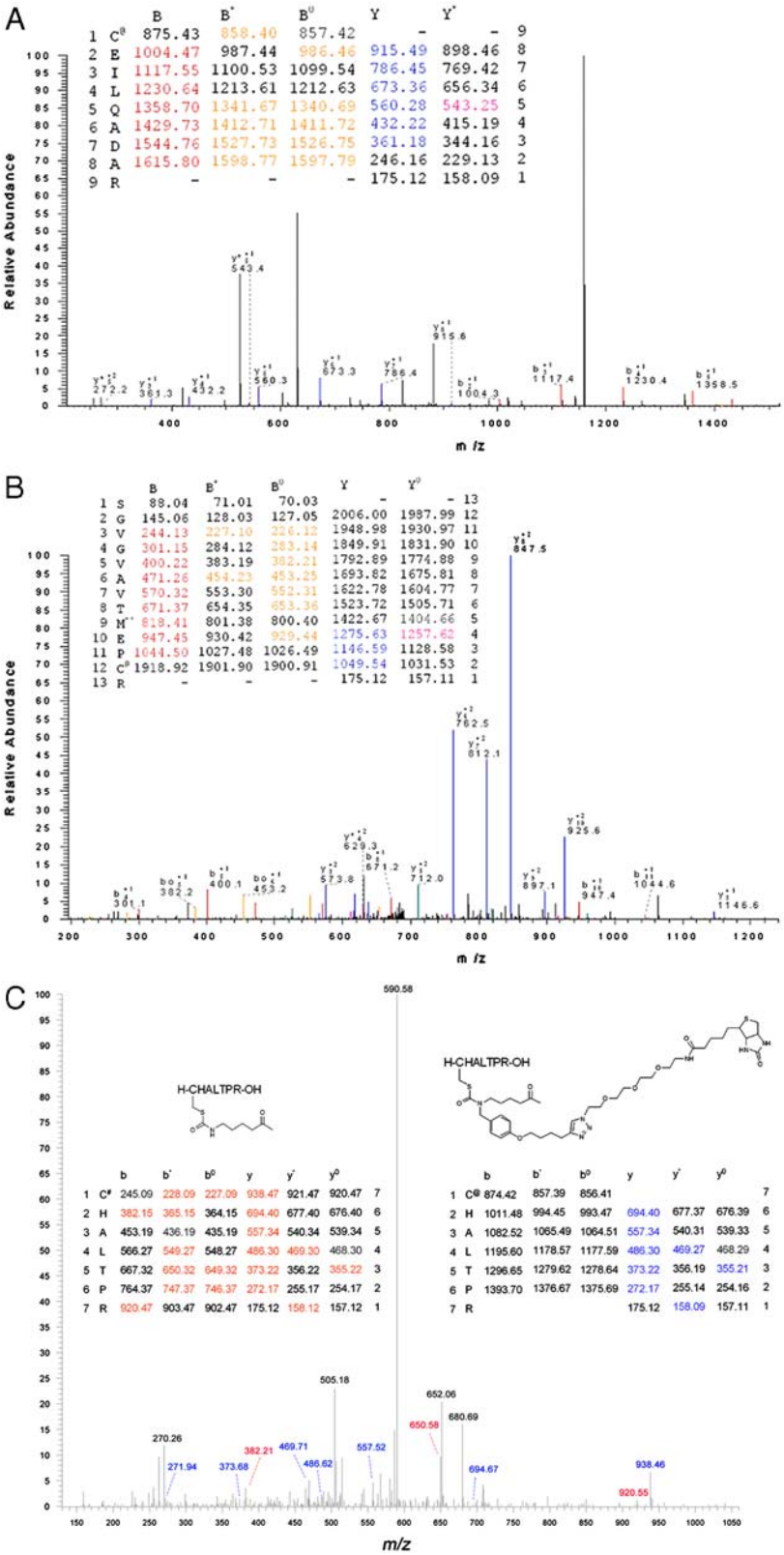
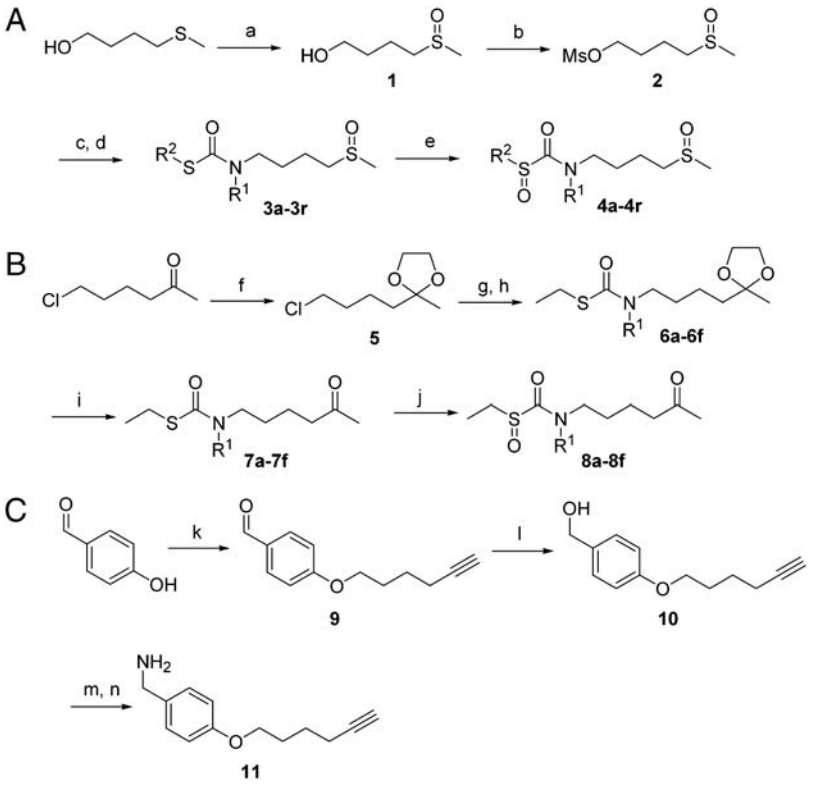


Fig. S7. HPLC-MS/MS spectra of Keap1 tryptic digest with Cys modification by **8f**. (*A*) Cys 288 modification. Peptide K.$\underline{C_{288}}$EILQADAR.C ($MH^+ = 1790$ Da) was found where Cys 288 is modified by **8f** with mass increase of +771.41 Da. (*B*) Cys 613 modification. Peptide R.SGVGVAVTM**EP$\underline{C_{613}}$R.K ($MH^+ = 2093$ Da) was found where Cys 613 is modified by **8f** with mass increase of +771.41 Da. (*C*) MS/MS spectra of m/z 523.60 and fragmentation table for peptide of R.C_{273}HALTPR.F with Cys 273 modification. *b* and *y* ion mass of R.C_{273}HALTPR.F modified by 771.41 Da (*Right*), and *b* and *y* ion mass of R.C_{273}HALTPR.F modified by 141.09 Da (*Left*) in case that ionization process breaks down the bond between benzyl group and amine. @, **, and # denotes the modification of +771.41 Da, oxidation of methionine, and a mass increase of 141.09 Da, respectively.



Scheme S1 Synthesis of sulfoxythiocarbamate sulforaphane analogs. (*A*) Synthesis of sulfoxide-containing analogs (**4a–4r**). Reagents and conditions: (*a*) sodium periodate, methanol/H_2O, 91%. (*b*) Methanesulfonyl chloride, triethylamine, DCM, 0 °C, 92%. (*c*) R^1NH_2, ethanol, 70 °C. (*d*) Alkyl (R^2) chlorothioformate, DIPEA, DCM, 0 °C, 15–61% over two steps. (*e*) *m*-CPBA, DCM, −78°C, 7–36% or Oxone, methanol/H_2O, 0 °C, 19–59%. (*B*) Synthesis of keto-analogs (**8a–8f**). Reagents and conditions: (*f*) ethylene glycol, p-toluenesulfonic acid monohydrate, toluene, 130 °C. (*g*) R^1NH_2, potassium carbonate, sodium iodide, *N*, *N* dimethylformamide. (*h*) Ethyl chlorothioformate, DIPEA, DCM, 0 °C. 34–56% over three steps. (*I*) 3N aq. hydrochloric acid, tetrahydrofuran, 79–96%. (*j*) *m*-CPBA, DCM, −78°C, 37–67%. (*C*) Synthesis of compound **11** for preparation of compound **6f**. Reagents and conditions: (*k*) 6-chloro-hex-1-yne, potassium carbonate, potassium iodide, DMF, 75 °C, 89%. (*l*) Sodium borohydride, ethanol, 0°C, 81%. (*m*) Methanesulfonyl chloride, triethylamine, dichloromethane, 0 °C. (*n*) 7N ammonia solution in methanol, 0 °C to RT, 30% two steps. Abbreviations: DCM, dichloromethane; DIPEA, *N, N*-diisopropylethylamine; *m*-CPBA, 3-chloroperbenzoic acid.

Table S1. List of proteins with 8f modification in HEK293 cells identified by HPLC MS/MS

*Protein	GI number	Peptide hit #	P (probability)
Abhydrolase domain containing 10	8923001	4	2.73E-08
Actin, beta	4501885	1	5.06E-07
Actin, beta-like 2	63055057	1	1.88E-04
Actin-like protein	62420916	1	4.41E-06
Acyl protein thioesterase 1	11513309	3	7.86E-08
ADP-ribosylation factor-like 1	4502227	1	1.05E-08
AF177343_1	10503986	1	8.14E-07
A-kinase anchor protein	4502015	1	1.83E-05
Annexin A2	4757756	1	9.62E-04
Apoptosis inhibitor 5 isoform b	5729730	1	1.78E-06
ASY	5821140	2	9.77E-07
Ataxin 10	7106299	1	7.94E-05
ATP synthase, H+ transporting, mitochondrial F1 complex	4757810	2	1.00E-09
ATPase, Ca++ transporting, fast twitch 1	27886529	2	3.63E-04
BCL2-associated X protein isoform alpha	20631958	1	7.49E-05
Brain creatine kinase	21536286	2	3.00E-07
Cathepsin A	189163485	1	3.13E-07
Cellular apoptosis susceptibility protein, CSE1L/CAS	29029559	2	7.27E-09
CGI-111	4929691	4	1.82E-07
Chaperonin	31542947	8	1.19E-06
Chaperonin containing TCP1, subunit 2	5453603	1	9.74E-07
Chaperonin containing TCP1, subunit 8 (theta)	48762932	1	5.60E-05
Chromosome 17 open reading frame 25, isoform CRA_e	119611054	2	7.23E-09
Cleavage stimulation factor, 3′ pre-RNA, subunit 2	14149675	1	9.10E-04
Cyclophilin A	1633054	1	7.65E-11
Cytochrome b5	2662291	4	6.09E-05
Cytoskeleton-associated protein 4	19920317	3	8.24E-05
DNA fragmentation factor, alpha	47132600	1	5.66E-06
Dynein light chain A variant	62896865	1	9.95E-09
Enolase 1	4503571	1	6.60E-04
Eukaryotic translation elongation factor 1 alpha	4503471	1	1.23E-04
Eukaryotic translation elongation factor 1 gamma	4503481	1	4.78E-06
Eukaryotic translation initiation factor 3	4503519	1	9.85E-04
Glutatione-S-transferase omega 1 (GSTO1)	4758484	1	4.05E-04
Glutatione-S-transferase pi (GSTP1)	4504183	2	1.19E-07
Glyoxalase-1	5020074	2	8.21E-11
hCG2008737	119612312	1	6.82E-04
Heme oxygenase 2	8051608	4	6.97E-11
Heterogeneous nuclear ribonucleoprotein F	4826760	1	6.77E-07
High mobility group box 1	4504425	1	2.07E-05
Histone acetyltransferase 1	4504341	2	1.75E-08
Hsp70-1B	167466173	1	3.18E-05
Hsp70B	34419635	1	1.12E-08
Hsp70-HOM	4529894	4	1.34E-09
Hsp90 1b	20149594	1	7.40E-04
Hydroxysteroid (17-beta) dehydrogenase 10	83715985	2	1.86E-05
Hypothetical protein	6807716	1	3.89E-04
Hypothetical protein LOC28971	34147384	2	1.28E-04
Isochorismatase domain containing 2 isoform 2	13376007	2	2.97E-08
Isochorismatase domain containing 2 isoform 2	13376007	1	2.28E-04
Karyopherin beta 1	19923142	1	1.80E-05
KH-type splicing regulatory protein (KSRP)	2055427	6	3.53E-08
KIAA0084	577299	1	4.97E-07
KIAA0830	4240149	3	2.64E-07
KIAA0896	71891755	1	9.42E-04
Klotho beta	28376633	1	6.04E-04
KM-102-derived reductase-like factor	1843434	1	1.09E-10
L-Lactate Dehydrogenase	13786849	2	5.75E-12
Lysophosphatidic acid acyltransferase zeta precursor	30520329	1	3.78E-04
MACRO domain containing 1	13569840	1	1.07E-06
Macrophage migration inhibitory factor	13399777	1	1.44E-04
Malate dehydrogenase 2	2906146	1	1.16E-05
Microtubule-associated protein 4	539639	1	5.23E-06
Mitochondrial trifunctional protein, beta subunit precursor	4504327	4	1.49E-05
MYB binding protein 1a	157694492	1	1.26E-07
5′-Nitrilase family, member 2	9910460	1	3.57E-06
Nogo-A protein	9408096	3	1.44E-11

*Protein	GI number	Peptide hit #	P (probability)
Nucleotidase, cytosolic II-like 1 protein	38570156	3	1.25E-13
Pallidin	6912574	1	9.25E-09
Paraneoplastic antigen MA2	11464969	2	6.56E-07
Peroxiredoxin 1	4505591	6	4.70E-06
Peroxiredoxin 2	32189392	1	1.32E-04
Peroxiredoxin 3	5802974	1	3.44E-08
Peroxiredoxin 5	6912238	1	7.18E-06
Peroxisomal acyl-CoA thioesterase 1 isoforma a	34577075	1	4.40E-06
Phosphoglycerate dehydrogenase	23308577	8	4.03E-08
Phosphotriesterase related	20070186	1	8.17E-06
Poly (ADP-ribose) polymerase family, member 1	156523968	1	1.40E-09
Poly(rC) binding protein 2 isoform b	14141166	1	2.38E-05
Polypyrimidine tract binding protein 2	10863997	1	4.45E-04
Polypyrimidine tract-binding protein 1 isoform a	4506243	1	1.71E-05
Polyubiquitin	2627129	1	1.10E-04
PRA1 domain family, member 2	6005794	1	1.37E-10
Profilin	5542165	1	5.57E-08
Prolyl oligopeptidase	558596	7	2.60E-11
Prostaglandin reductase 2	22748929	3	9.61E-07
Protease, serine, 1	4506145	2	4.67E-04
Pyruvate kinase	33286418	3	2.08E-10
Receptor accessory protein 5	115430112	1	2.00E-05
Reticulon 3	5174655	1	2.52E-05
Ribosomal protein L4	16579885	1	2.94E-05
Similar to actin alpha 1	169213772	1	7.88E-05
Similar to beta-actin	88942898	2	4.00E-10
Solute carrier family 25, member A6	156071462	1	2.12E-05
Tau-tubulin kinase	27451602	1	1.28E-04
Thioredoxin-1	119389938	5	1.52E-06
Thymopoietin isoform alpha	4507555	1	1.21E-04
Transgelin 2	4507357	1	1.28E-12
4-Trimethylaminobutyraldehyde dehydrogenase	62511242	1	2.92E-06
Tubulin alpha 6	14389309	7	7.47E-10
Tubulin alpha-1A chain	135435	1	4.35E-08
Tubulin beta 2	5174735	2	6.56E-09
Tubulin, beta	2119276	4	7.99E-08
Tubulin, beta 2	4507729	2	5.67E-05
Tubulin, beta 4	21361322	3	5.09E-08
Tubulin, beta 4	50592996	1	2.31E-04
Tumor necrosis factor type 1 receptor associated protein TRAP-1	1082886	1	7.40E-04
Tyrosine 3/tryptophan 5 -monooxygenase activation protein, zeta polypeptide	4507953	1	2.01E-10
Ubiquitin and ribosomal protein L40 precursor	4507761	1	1.10E-04
Ubiquitin carboxyl-terminal esterase L1	21361091	3	1.22E-04
Ubiquitin carboxyl-terminal esterase L3	5174741	1	7.47E-07
Ubiquitin-conjugating enzyme E2L 3 isoform 1	4507789	1	1.98E-06
Unnamed protein product	16554270	2	5.75E-12
Unnamed protein product	18676733	1	1.09E-06
Unnamed protein product	32486	2	1.51E-06
Unnamed protein product	194379998	2	4.81E-06
Unnamed protein product	34526448	1	2.78E-05
Unnamed protein product	7023808	1	7.83E-04
VDAC1	4507879	1	3.78E-05
VDAC2	48146045	3	3.14E-06
Zinc finger protein 652, isoform CRA_b	119615089	1	2.01E-04

*Proteins were identified with filter options of X_{corr} (1.5, 2.0, 2.5, 3.0) vs. charge state (1, 2, 3, 4), and probability ($p < 0.001$).