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for

Cellular Inhibition of Protein Tyrosine Phosphatase 1B by Uncharged Thioxothiazolidinone Derivatives

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Table S1: Sequence details of GST-PTP constructs and Michaelis constants (K_m) for *p*NPP.

Enzyme	Species[a]	K_m [mm]		Nucleotides[b]		Accession #
		pH 6.0	pH 7.0			
PTP1B	h	0.22	1.5	1-	963	NM_002827
TCPTP	h		0.74	1-	1064	NM_002828
HePTP	h		3.7	62-	1083	NM_002832
SHP1	h		3.8	728-	1785	NM_002831
MKPX	h		3.7	1-	525	AF165519
PTP-BAS	h		0.80	6505-	7458	NM_080683
LAR	h	0.43		3903-	4926	AB177857
PTP-σ	m	0.47		2631-	4494	BC083188

PEP	h	1.4	1-	969	NM_015967
PTP-μ	h	0.87	2457-	3720	X58288
PTP-α[c]	h		660-	1690	NM_080840

[a] h, human; m, mouse. [b] Numbering refers to the cloned nucleotide se-quence within the full-length open reading frame. [c] PTP-α activity was assayed using DIFMUP rather than *p*NPP. The K_m values of PTP-α and PTP1B for DIFMUP were 16 μM and 4 μM, respectively.

Synthesis of compound 1 and derivatives

General procedures. Chemicals were purchased from Aldrich Chemicals Company and Acros Chemicals. ^{1}H NMR spectra were recorded in $CDCl_3$ and [D_6]DMSO at 200 MHz, 300 Hz, 400 MHz and 500 MHz. Chemical shifts are reported in parts per million (*d*). Coupling constants, *J*, are reported in Hertz (Hz). HRMS-ESI analysis was performed at the McGill University Mass Spectrometry Unit. Flash column chromatography was performed over SORBENT silica gel 30-60 μm. All reagents were weighed and handled in air and backfilled under an inert atmosphere of nitrogen at room temperature.

Synthesis of 3-phenylrhodanine: To 115 mg (0.5 mmol) of di-(carboxymethyl)trithiocarbonate in 2 mL of water, 45 μl (0.5 mmol) of aniline was added. The test tube was sealed and heated at 100 °C overnight. The precipitate was then collected and washed with cold water giving 3-phenyl-rhodanine at 70% yield. ^{1}H NMR (CD_3Cl/TMS): 7.52(m, Ar-H 3H), 7.18(m, Ar-H 2H), 4.18 (s, 2H, CH_2).

Synthesis of 3-(m-chlorophenyl)rhodanine: To 690 mg (3 mmol) of di(carboxymethyl)trithiocarbonate in 12 mL of water, 390 mg (3 mmol) of *m*-chloroaniline was added. The solution, in a 25 mL round bottom flask, was heated at 100 °C overnight. The precipitate was collected, washed with cold water and gave 3-(*m*-chlorophenyl)rhodanine at 63% yield. ^{1}H NMR (CD_3Cl/TMS): 7.44-7.42(m, Ar-H 2H), 7.21-7.20(m, Ar-H 1H), 7.10-7.07(m, Ar-H 1H), 4.14(s, 2H CH_2).

*Synthesis of 3-(*p*-chlorophenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 64 mg (0.5 mmol) of *p*-chloro-aniline was added. The test tube was sealed and heated at 100 °C overnight. The next day, the precipitate was collected and washed with cold water, giving the crude 3-(*p*-chlorophenyl)-

rhodanine at 80% yield, then flash column chromatography (EtOAc/hexanes 1:2) was applied to give the desired product at 62% yield. mp: 116-118 °C (*Lit.* mp: 124-125 °C [1]).

*Synthesis of 3-(*p-*methoxyphenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 mg (0.5 mmol) of *p*-anisidine was added. The tube was sealed and heated at 100°C overnight. The precipitate was then collected and washed with cold water, giving 3-(*p*-methoxyphenyl)rhodanine at 76% yield. ^{1}H NMR (CD_3Cl/TMS): 7.08 (d, 2H, Ar-H, *J*=8.8Hz), 7.00 (d, 2H, Ar-H, *J*=8.8Hz), 4.12 (s, 2H, CH_2), 3.82(s, 3H, OCH_3).

*Synthesis of 3-(*m-*methoxyphenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 µL (0.5 mmol) of *m*-anisidine was added. The test tube was sealed and heated at 100°C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*m*-methoxyphenyl)rhodanine at 76% yield. ^{1}H NMR (CD_3Cl/TMS): 7.44 (t, 1H, Ar-H, *J*=8.0Hz), 7.02 (ddd, 1H, Ar-H, *J*=8.0Hz, 2.4Hz, 0.8Hz), 6.78 (ddd, 1H, Ar-H, *J*=8.0Hz, 2.4Hz, 0.8Hz), 6.72 (t, 1H, Ar-H, 2.0Hz), 4.19 (s, 2H,CH_2), 3.82 (s, 3H, OCH_3).

*Synthesis of 3-(*p-*methylphenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 mg (0.5 mmol) of *p*-toluidine was added. The test tube was sealed and heated at 100°C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*p*-methylphenyl)rhodanine in 73% yield. ^{1}H NMR (CD_3Cl/TMS): 7.34 (d, 2H, Ar-H, *J*=8.0Hz), 7.08 (d, 2H, Ar-H, *J*=8.0Hz), 4.19 (s, 2H, CH_2), 2.42 (s, 3H, CH_3).

*Synthesis of 3-(*m-*methylphenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 mg (0.5 mmol) of *m*-toluidine was added. The test tube was sealed and heated at 100°C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*m*-methylphenyl)rhodanine in 91% yield. ^{1}H NMR (CD_3Cl/TMS): 7.42 (t, 1H, Ar-H, *J*=8.0Hz), 7.30 (d, 2H, Ar-H, *J*=8.0Hz), 7.05-6.99 (m, 2H, Ar-H), 4.18 (s, 2H, CH_2), 2.41 (s, 3H, CH_3).

*Synthesis of 3-(*p-*hydroxyphenyl)rhodanine*: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 mg (0.5 mmol) of *p*-aminophenol was added. The test tube was sealed and heated at 100 °C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*p*-hydroxyphenyl)-

rhodanine at 69% yield. ^{1}H NMR (CD_3Cl/TMS): 9.81 (s, 1H, OH), 7.07 (d, 2H, Ar-H, *J*=8.8Hz), 6.95 (d, 2H, Ar-H, *J*=8.8Hz), 4.32 (s, 2H, CH_2).

Synthesis of 3-(p-nitrophenyl)rhodanine: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 55 mg (0.5 mmol) of *p*-nitroaniline was added. The test tube was sealed and heated at 100 °C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*p*-nitrophenyl)rhodanine at 69% yield. ^{1}H NMR (CD_3Cl/TMS): 8.40 (d, 2H, Ar-H, *J*=8.4Hz), 7.44 (d, 2H, Ar-H, *J*=8.4Hz), 4.26 (s, 2H, CH_2).

Synthesis of 3-(3,4-dichlorophenyl)rhodanine: To 115 mg (0.5 mmol) of di(carboxymethyl)trithiocarbonate in 2 mL of water, 80 mg (0.5 mmol) of 3,4-dichloroaniline was added. The test tube was sealed and heated at 100^{o}C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(3,4-dichlorophenyl)-rhodanine at 43% yield. ^{1}H NMR (CD_3Cl/TMS): 7.60 (d, 1H, Ar-H, *J*=12.0Hz), 7.37 (d, 1H, Ar-H, *J*=3.2Hz), 7.08 (dd, 1H, Ar-H, *J*=12.0Hz, 3.2Hz), 4.20 (s, 2H,CH_2).

*Synthesis of 3-(*m*-fluorophenyl)rhodanine*: To 226 mg (1.0 mmol) of di(carboxymethyl)trithiocarbonate in 4 mL of water, 111 mg (1.0 mmol) of *m*-fluoroaniline was added. The test tube was sealed and heated at 100 °C overnight. The next day, the precipitate was collected and washed with cold water, giving 3-(*m*-fluorophenyl)rhodanine at 82% yield. ^{1}H NMR (CD_3Cl/TMS): 7.52 (q, 1H, Ar-H, *J*=6.6Hz), 7.20 (tdd, 1H, Ar-H, *J*=8.4Hz, 2.2Hz, 0.6Hz), 7.04-6.93 (m, 2H, Ar-H), 4.14 (s, 2H, CH_2).

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(*m*-chlorophenyl)-2-thioxo-4-thiazolidinone (compound **1**)*: In a test tube, 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution *in vacuo* gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(*m*-chlorophenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR ([D_6]DMSO): 7.83 (s, 1H, =CHAr), 7.78 (d, 1H, Ar-H, *J*=2.0Hz), 7.62-7.57 (m, 3H, Ar-H), 7.51 (d, 1H, Ar-H, J=2.0Hz), 7.44-7.42 (m, 1H, Ar-H), 3.96 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{11}ClN_2O_5S_2\text{-}H]^-$: 420.9725; found: 420.9725.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-2-thioxo-4-thiazolidinone (compound **2**)*: Rhodanine (67 mg 0.50 mmol) and 5-nitrovanilline (100 mg

0.50 mmol) were combined in a test tube. AcONa/AcOH (2 mL 40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-2-thioxo-4-thiazolidinone product at 80% yield. ^{1}H NMR ([D$_6$]DMSO): 7.64 (s, 1H, =CHAr), 7.57 (s, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 3.92 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{11}H_8N_2O_5S_2\text{-}H]^-$: 310.9802; found: 310.800.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-phenyl-2-thioxo-4-thiazolidinone (compound **3**)*: In a test tube, 52 mg (0.25 mmol) of 3-phenylrhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined. AcONa/AcOH (1 mL 40 mg/mL) was then added. The tube was capped, and the mixture was stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-phenyl-2-thioxo-4-thiazolidinone product at 73% yield. ^{1}H NMR (CD_3Cl/TMS): 11.06 (s, 1H, OH) 7.93 (d, 1H, Ar-H *J*=2.0Hz), 7.69 (s, 1H, =CHAr), 7.61-7.53 (m, 3H, Ar-H), 7.28 (d, 2H, Ar-H, *J*=8.0Hz), 7.25(d, 1H, Ar-H, *J*=2.0Hz), 4.05(s, 3H, OCH_3). HRMS-ESI calcd for $[C_{17}H_{12}N_2O_5S_2\text{-}H]^-$: 387.0115; found: 387.0115.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(*p*-chlorophenyl)-2-thioxo-4-thiazolidinone (compound **4**)*: 60 mg (0.25 mmol) of 3-(*p*-chlorophenyl)rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The test tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution *in vacuo* gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-chlorophenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR ([D$_6$]-DMSO): 7.78 (s, 1H, Ar-H), 7.74 (s, 1H, =CHAr), 7.62 (d, 1H, Ar-H, *J*=8.0Hz), 7.44 (d, 1H, Ar-H, *J*=8.0Hz), 7.26 (s, 1H, Ar-H), 3.90 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{11}ClN_2O_5S_2\text{-}H]^-$: 420.9725; found: 420.9724.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(m-fluorophenyl)-2-thioxo-4-thiazolidinone (compound **5**)*: 57 mg (0.25 mmol) of 3-(*m*-fluorophenyl)rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL

AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(*m*-fluorophenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR ([D$_6$]DMSO): 11.50 (br s, , 1H, OH), 7.82 (s, 1H, =CHAr), 7.77 (d, 1H, Ar-H *J*=1.6Hz), 7.60 (q, 1H, Ar-H, *J*=7.6Hz), 7.50 (d, 1H, Ar-H, *J*=1.6Hz), 7.41-7.37 (m, 2H, Ar-H), 7.29 (d, 1H, Ar-H, *J*=8.4Hz), 3.96 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{11}FN_2O_5S_2H]^-$: 405.0021; found: 405.0021.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(m-methylphenyl) -2-thioxo-4-thiazolidinone (compound **6**)*: 56 mg (0.25 mmol) of 3-(*m*-methylphenyl)-rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(m-methylphenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR (CD_3Cl/TMS): 11.01 (s, 1H, OH), 7.91 (d, 1H, Ar-H, *J*=2.0Hz), 7.66 (s, 1H, =CHAr), 7.43 (t, 1H, Ar-H, *J*=8.0Hz), 7.31 (d, 1H, Ar-H, *J*=7.6Hz), 7.23 (d, 1H, Ar-H, *J*=2.0Hz), 7.07.05 (m, 2H, Ar-H), 4.04 (s, 3H, CH_3), 2.43 (s, 3H, CH_3); HRMS-ESI calcd for $[C_{18}H_{14}N_2O_5S_2\text{-}H]^-$: 401.0271; found: 401.0272.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(m-methoxyphenyl)-2-thioxo-4-thiazolidinone (compound **7**)*: 60 mg (0.25 mmol) of 3-(*m*-methoxyphenyl)rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(*m*-methoxyphenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR (CD_3Cl/TMS): 11.04 (br s, , 1H, OH), 7.94 (d, 1H, Ar-H, *J*=1.6Hz), 7.68 (s, 1H, =CHAr), 7.47 (t, 1H, Ar-H, *J*=7.8Hz), 7.26 (s, 1H, Ar-H), 7.05 (dd, 1H, Ar-H, *J*=8.0Hz,1.6Hz), 6.88-6.81 (m, 2H, Ar-H), 4.05 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-hydroxyphenyl)-2-thioxo-4-thiazolidinone (compound **8**)*: 56 mg (0.25 mmol) of 3-(*p*-hydroxyphenyl)-rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-hydroxyphenyl)-2-thioxo-4-thiazolidinone product at 86% yield. ^{1}H NMR ([D$_6$]DMSO): 11.04 (s, 1H, OH), 9.91 (s, 1H, OH), 7.78 (d, 1H, Ar-H, *J*=2.0Hz), 7.74 (s, 1H, =CHAr), 7.33 (s, 1H, OH), 7.12 (dd, 2H, Ar-H, *J*=8.0Hz, 1.6Hz), 6.88 (dd, 2H, Ar-H, *J*=8.0Hz, 1.6Hz), 3.90 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{12}N_2O_6S_2H]^-$ 403.0064; found: 403.0064.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-methylphenyl)-2-thioxo-4-thiazolidinone (compound **9**)*: 56 mg (0.25 mmol) of 3-(*p*-methylphenyl)-rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-methylphenyl)-2-thioxo-4-thiazolidinone product at 86% yield. ^{1}H NMR (CD_3Cl/TMS): 11.06 (s, 1H, OH), 7.93 (d, 1H, Ar-H, *J*=2.0Hz), 7.68 (s, 1H, =CHAr), 7.37 (d, 2H, Ar-H, *J*=8.0Hz), 7.24 (d, 1H, Ar-H, *J*=2.0Hz), 7.16 (d, 2H, Ar-H, *J*=8.0Hz), 4.05 (s, 3H, OCH_3), 2.45(s, 3H, CH_3); HRMS-ESI calcd for $[C_{18}H_{14}N_2O_5S_2$-$H]^-$: 401.0271; found: 401.0270.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-methoxyphenyl)-2-thioxo-4-thiazolidinone (compound **10**)*: 60 mg (0.25 mmol) of 3-(*p*-methoxyphenyl)rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-methoxyphenyl)-2-thioxo-4-thiazolidinone product at 82% yield. ^{1}H NMR (CD_3Cl/TMS): 11.01 (s, 1H, OH), 7.91 (d, 1H, Ar-H, *J*=2.0Hz), 7.66 (s, 1H, =CHAr), 7.24 (d, 1H, Ar-H, *J*=2.0Hz), 7.18 (d, 2H, Ar-H, *J*=8.8Hz), 7.05 (d, 2H, Ar-H,

J=8.8Hz), 4.04 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{18}H_{14}N_2O_6S_2\text{-}H]^-$: 417.0220; found: 417.0222.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-nitrophenyl)-2-thioxo-4-thiazolidinone (compound **11**)*: 56 mg (0.25 mmol) of 3-(*p*-nitroxyphenyl)-rhodanine and 50 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(p-nitrophenyl)-2-thioxo-4-thiazolidinone product at 86% yield. ^{1}H NMR ([D_6]DMSO): 8.40 (d, 2H, Ar-H, *J*=8.4Hz), 7.84 (s, 1H, =CHAr), 7.79-7.76 (m, 3H, Ar-H), 7.47 (s, 1H, Ar-H), 3.95 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{11}N_3O_7S_2\text{-}H]^-$: 431.9966; found: 431.9966.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(3,4-dichlorophenyl)-2-thioxo-4-thiazolidinone (compound **12**)*: 23 mg (0.25 mmol) of 3-(3,4-dichlorophenyl)rhodanine and 17 mg (0.25 mmol) of 5-nitrovanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-nitrophenyl)methylene]-3-(3,4-dichlorophenyl)-2-thioxo-4-thiazolidinone product at 72% yield. ^{1}H NMR (CD_3Cl/TMS): 11.04 (s, 1H, OH), 7.92 (d, 1H, Ar-H, *J*=2.8Hz), 7.69 (s, 1H, =CHAr), 7.63 (d, 1H, Ar-H, *J*=12.0Hz), 7.42 (d, 1H, Ar-H, *J*=3.2Hz), 7.23 (d, 1H, Ar-H, *J*=2.8Hz), 7.16 (dd, 1H, Ar-H, *J*=12.0Hz, 3.2Hz), 4.05 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{17}H_{10}Cl_2N_2O_5S_2\text{-}H]^-$: 454.9335; found: 454.9338.

*Synthesis of 5-[(4-hydroxy-5-nitrophenyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone (compound **13**)*: 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 42 mg (0.25 mmol) of 4-hydroxy-3-nitrobenzaldehyde were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-nitrophenyl)methylene]-3-(*m*-chlolrophenyl)-2-thioxo-4-thiazolidinone product at 78% yield. ^{1}H NMR

([D_6]DMSO): 8.25 (s, 1H, Ar-H), 7.84 (s, 1H, =CHAr), 7.81 (dd, 1H, Ar-H, *J*=9.2Hz, 1.6Hz), 7.62-7.58 (m, 3H, Ar-H), 7.44-7.39 (m, 1H, Ar-H), 7.29 (d, 1H, Ar-H *J*=9.2Hz); HRMS-ESI calcd for [$C_{16}H_9ClN_2O_4S_2$-H]$^-$: 390.9619; found: 390.9616.

*Synthesis of 5-[(4-hydroxy-3-methoxyphenyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone (compound **14**)*: 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 40 mg (0.25 mmol) of vanilline were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxyphenyl)methylene]-3-(*m*-chlolrophenyl)-2-thioxo-4-thiazolidinone product at 70% yield. ^{1}H NMR ([D_6]DMSO): 10.10 (br s, , 1H, OH), 7.75 (s, 1H, =CHAr), 7.58 (m, 3H, Ar-H), 7.41 (m, 1H, Ar-H), 7.23 (d, 1H, Ar-H, *J*=1.6Hz), 7.16 (dd, 1H, Ar-H, *J*=1.6Hz, 8.8Hz), 6.94 (d, 1H, Ar-H, *J*=8.8Hz), 3.84 (s, 3H, OCH_3); HRMS-ESI calcd for [$C_{16}H_{11}ClNO_3S_2$-H]$^-$: 375.9874; found: 375.9870.

*Synthesis of 5-[(3, 4-dihydroxy--5-nitrophenyl)methylene]-3-(*m-*chlorophenyl)-2-thioxo-4-thiazolidinone (compound **15**)*: 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 45 mg (0.25 mmol) of 3,4-dihydroxy-5-nitrobenzaldehyde were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo furnished the desired 5-[(3,4-dihydroxy-5-nitrophenyl)-methylene]-3-(*m*-chlorophenyl)-2-thioxo-4-thiazolidinone product at 85% yield. ^{1}H NMR ([D_6]DMSO): 10.90 (br s, , 2H, OH), 7.79 (s, 1H, =CHAr), 7.75 (s, 1H, Ar-H), 7.60-7.56 (m, 3H, Ar-H), 7.42-7.38 (m, 1H, Ar-H), 7.28 (s, 1H, Ar-H); HRMS-ESI calcd for [$C_{16}H_9ClN_2O_5S_2$-H]$^-$: 406.9569; found: 406.9567.

Synthesis of 5-[(3,4-dimethoxyphenyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone (compound 16): 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 38 mg (0.25 mmol) of 3,4-dimethoxybenzaldehyde were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(3,4-dimethoxyphenyl)methylene]-3-(*m*-chlorophenyl)-2-thioxo-4-thiazolidinone product at 75% yield. ^{1}H NMR ([D_6]DMSO): 7.80 (s,

1H, =CHAr), 7.62-7.56 (m, 3H, Ar-H), 7.44-7.41 (m, 1H, Ar-H), 7.29-7.27 (m, 2H, Ar-H), 7.17 (d, 1H, Ar-H, *J*=8.0Hz), 3.85 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{18}H_{14}ClNO_3S_2+H]^+$: 392.0176; found: 392.0176.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5-carboxyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone (compound **17**)*: 60 mg (0.25 mmol) of 3-(*m*-chlorophenyl)rhodanine and 50 mg (0.25 mmol) of 5-formyl-2-hydroxy-3-methoxybenzoic acid were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The test was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was stopped and 5 mL water was added to the solution. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-carboxyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone product at 82% yield. ^{1}H NMR ([D_6]DMSO): 7.79 (s, 1H, =CHAr), 7.67 (d, 1H, Ar-H, *J*=2.0Hz), 7.61-7.56 (m, 3H, Ar-H), 7.44 (d, 1H, Ar-H, *J*=2.0Hz), 7.43-7.40 (m, 1H, Ar-H), 3.86 (s, 3H, OCH_3); HRMS-ESI calcd for $[C_{18}H_{12}ClNO_5S_2-H]^-$: 419.9773; found: 419.9783.

*Synthesis of 5-[(4-hydroxy-3-methoxy-5- phosphonomethyl)methylene]-3-(m-chlorophenyl) -2-thioxo-4-thiazolidinone (compound **18**)*: 25 mg (0.05 mmol) of 3-(*m*-chlorophenyl)rhodanine and 10 mg (0.05 mmol) of 5-formyl-2-hydroxy-3-methoxybenzylphosphonic acid were combined in a test tube. 1 mL AcONa/AcOH (40 mg/mL) was then added. The tube was capped and stirred at 120 °C for 2 h. At this point, the solution turned clear. Heating was then stopped and 5 mL water was added. Yellow precipitate was thus formed. Finally, filtration of the solution in vacuo gave the desired 5-[(4-hydroxy-3-methoxy-5-phosphonomethyl)methylene]-3-(m-chlorophenyl)-2-thioxo-4-thiazolidinone product at 62%yield. ^{1}H NMR ([D_6]DMSO): 7.67 (s, 1H, =CHAr), 7.59-7.54 (m, 3H, Ar-H), 7.41-7.38 (m, 2H, Ar-H), 7.02-6.98 (m, 2H, Ar-H), 3.79 (s, 3H, OCH_3), 2.83 (d, 2H, CH_2, *J*=18.8Hz); HRMS-ESI calcd for $[C_{18}H_{15}ClNO_6PS_2-H]^-$: 469.9694; found: 469.9692.

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[1] L. M. Werbel, N. Headen, E. F. Elslager, *J. Med. Chem.* **1968**, *11*, 364-365.