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Synthesis of thiazolidin-4-ones from α-enolic dithioesters

and α-halohydroxamates

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Table of Contents

1. General methods and materials .................................................................S2

2. General procedure for the preparation of thiazolidin-4-ones .........................S2

3. Characterization data of products .............................................................S2-S7

4. Copies of NMR spectra ..........................................................................S8-S32

5. Crystal Structure Information of Compound 3ab .......................................S33

6. References ...............................................................................................S34
1. General methods and materials

All isolated compounds were characterized on Bruker 400 or 500 MHz spectrometers at room temperature. Chemical shifts were reported as \( \delta \) values relative to internal CHCl\(_3\) (\( \delta \) 7.26 ppm for \(^1\)H NMR and 77.16 ppm for \(^{13}\)C NMR) and (CH\(_3\))\(_2\)CO (\( \delta \) 2.05 ppm for \(^1\)H NMR and 29.84 ppm for \(^{13}\)C NMR). \(^{19}\)F NMR chemical shifts were determined as \( \delta \) values relative to external standard PhCF\(_3\) at \(-63.50\) ppm. High-resolution mass spectra (HRMS) were obtained on a 4G mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QTof). All melting points were measured with the samples after column chromatography and uncorrected. Column chromatography was performed on silica gel. Solvents (analytical reagent) were used as obtained from commercial sources without further purification and dryness. \( \alpha \)-enolic dithioesters,\(^1\) \( \alpha \)-halohydroxamates\(^2\) were all known and prepared according to the literature.

2. General procedure for the preparation of thiazolidin-4-ones

To a mixture of \( \alpha \)-enolic dithioester \( 1 \) (0.2 mmol, 1.0 equiv.), \( \alpha \)-halohydroxamate \( 2 \) (0.24 mmol, 1.2 equiv.), and Na\(_2\)CO\(_3\) (0.4 mmol, 2.0 equiv.) in a sealed tube was added CH\(_3\)CN (2.0 mL). The reaction mixture was stirred at 80 °C or rt under air atmosphere. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (PE/EtOAc = 10:1 to 6:1) to afford the corresponding thiazolidin-4-ones.

**Gram-scale preparation of thiazolinone 3aa:** To a mixture of \( \alpha \)-enolic dithioester \( 1a \) (3.5 mmol, 1.0 equiv.), \( \alpha \)-halohydroxamate \( 2a \) (4.2 mmol, 1.2 equiv.), and Na\(_2\)CO\(_3\) (7.0 mmol, 2.0 equiv.) in a round bottom flask was added CH\(_3\)CN (35 mL). The reaction mixture was stirred at 80 °C under air atmosphere for 0.5 h. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (PE/EtOAc = 10:1 to 6:1) to afford the corresponding thiazolidin-4-one \( 3aa \) as a white solid (1.02 g, 85%).

**Preparation of \( \alpha \)-thioamide 4:** A solution of \( \alpha \)-enolic dithioester \( 1i \) (0.2 mmol, 1.0 equiv.), \( \alpha \)-halohydroxamate \( 2a \) (0.30 mmol, 1.5 equiv.), and Na\(_2\)CO\(_3\) (0.4 mmol, 2.0 equiv.) in CH\(_3\)CN (2.0 mL) was placed in a 10 mL sealed tube. The resulting mixture was stirred for 4 h at 80 °C under air atmosphere. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (PE/EtOAc = 15:1) to afford \( \alpha \)-thioamide 4 consisting of two configurational isomers.

**Preparation of thiazolinone 5:** A solution of 4 (0.074 mmol, 1.0 equiv.), Cs\(_2\)CO\(_3\) (0.15 mmol, 2.0
equiv.) in DMF (1.0 mL) was placed in a 10 mL sealed tube. Then, the reaction mixture was stirred at 100 °C under air atmosphere. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (PE/EtOAc = 15:1) to afford thiazolidin-4-one 5.

**Preparation of thiazolinone 6:** A solution of α-enolic dithioester 1j (0.2 mmol, 1.0 equiv.), α-halohydroxamate 2a (0.30 mmol, 1.5 equiv.), and Na₂CO₃ (0.4 mmol, 2.0 equiv.) in CH₃CN (2.0 mL) was placed in a 10 mL sealed tube. The resulting mixture was stirred for 30 min at 80 °C under air atmosphere. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting residue was redissolved in DMF (2.0 mL). Then, Cs₂CO₃ (0.4 mmol, 2.0 equiv.) was added and stirring continued for 30 min at 100 °C under air atmosphere. After completion of the reaction as monitored by TLC, water was added slowly to the reaction mixture. The mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (PE/EtOAc = 15:1) to give thiazolidin-4-one 6.

**Debenzyloxylation of 3aa:** To a solution of 3aa (0.1 mmol, 1.0 equiv.) in DMF (1.0 mL) was added Cs₂CO₃ (0.2 mmol, 2.0 equiv.). Then, the reaction mixture was stirred at 100 °C under air atmosphere. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (PE/EtOAc = 15:1) to afford debenzyloxylated thiazolidin-4-one 7.

3. Characterization data of products

**(Z)-3-(Benzyloxy)-5-methyl-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one.** Compound 3aa (61.7 mg, Yield = 91%, Rf = 0.2 (PE/EA = 7:1)) was isolated as a white solid; mp 140–141 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.91–7.82 (m, 2H), 7.56–7.49 (m, 3H), 7.48–7.43 (m, 2H), 7.43–7.38 (m, 3H), 6.86 (s, 1H), 5.20 (d, J = 10.0 Hz, 1H), 5.17 (d, J = 10.0 Hz, 1H), 3.83 (q, J = 7.3 Hz, 1H), 1.63 (d, J = 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 188.8, 169.8, 154.0, 138.2, 133.2, 132.5, 130.1, 129.9, 128.9, 128.6, 127.7, 94.7, 78.2, 37.6, 18.7; ESI-HRMS m/z calcd for C₁₉H₁₈NO₃S [M + H]⁺ 340.1002, found 340.1001.

**(Z)-3-(Benzyloxy)-2-(2-(4-fluorophenyl)-2-oxoethylidene)-5-methylthiazolidin-4-one.** Compound 3ab (54.5 mg, Yield = 77%, Rf = 0.3 (PE/EA = 5:1)) was isolated as a white solid; mp 140–141 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.00–7.79 (m, 2H), 7.59–7.48 (m, 2H), 7.47–7.37 (m, 3H), 7.19–7.06 (m, 2H), 6.76 (s, 1H), 5.20 (d, J = 10.0 Hz, 1H), 5.17 (d, J = 10.0 Hz, 1H), 3.82 (q, J = 7.2 Hz, 1H), 1.63 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 187.4, 169.9, 165.4, 154.0, 153.2, 152.5, 132.5, 130.1, 129.9, 129.0, 115.7 (d, J = 22.2
(Z)-3-(Benzyloxy)-2-(2-(4-chlorophenyl)-2-oxoethylidene)-5-methylthiazolidin-4-one. Compound 3ac (62.2 mg, Yield = 84%, Rf = 0.2 (PE/EA = 8:1)) was isolated as a white solid; mp 151–152 °C. 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82–7.72 (m, 2H), 7.52–7.47 (m, 2H), 7.45–7.42 (m, 2H), 7.41–7.38 (m, 3H), 6.76 (s, 1H), 5.20 (d, $J = 10.4$ Hz, 1H), 5.16 (d, $J = 10.0$ Hz, 1H), 3.83 (q, $J = 7.2$ Hz, 1H), 1.63 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 187.5, 169.8, 154.8, 138.8, 136.5, 133.2, 130.2, 130.0, 129.1, 129.0, 94.4, 78.4, 37.7, 18.7; ESI-HRMS m/z calcd for C$_{19}$H$_{17}$ClNO$_3$S [M + H]$^+$ 374.0612, found 374.0612.

(Z)-3-(Benzyloxy)-2-(2-(3-chlorophenyl)-2-oxoethylidene)-5-methylthiazolidin-4-one. Compound 3ad (63.6 mg, Yield = 85%, Rf = 0.2 (PE/EA = 8:1)) was isolated as a white solid; mp 124–125 °C. 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (t, $J = 1.9$ Hz, 1H), 7.70 (dt, $J = 7.7$, 1.4 Hz, 1H), 7.53–7.46 (m, 3H), 7.46–7.41 (m, 2H), 7.41–7.34 (m, 2H), 6.72 (s, 1H), 5.20 (d, $J = 10.0$ Hz, 1H), 5.16 (d, $J = 10.0$ Hz, 1H), 3.84 (q, $J = 7.2$ Hz, 1H), 1.63 (d, $J = 7.6$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 187.2, 169.8, 155.1, 139.8, 134.8, 133.2, 132.3, 130.2, 130.0, 129.0, 127.8, 125.7, 94.4, 78.4, 37.7, 18.6; ESI-HRMS m/z calcd for C$_{19}$H$_{17}$ClNO$_3$S [M + H]$^+$ 374.0612, found 374.0612.

(Z)-3-(Benzyloxy)-2-(2-(2-chlorophenyl)-2-oxoethylidene)-5-methylthiazolidin-4-one. Compound 3ae (63 mg, Yield = 85%, Rf = 0.2 (PE/EA = 8:1)) was isolated as a white solid; mp 109–110 °C. 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.53–7.46 (m, 3H), 7.44–7.39 (m, 2H), 7.39–7.35 (m, 3H), 7.34–7.29 (m, 1H), 6.71 (s, 1H), 5.20 (d, $J = 9.6$ Hz, 1H), 5.16 (d, $J = 9.6$ Hz, 1H), 3.84 (q, $J = 7.2$ Hz, 1H), 1.63 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 190.0, 169.7, 153.8, 139.4, 132.8, 131.7, 131.2, 130.5, 130.2, 129.9, 129.8, 128.9, 127.1, 98.7, 78.2, 37.7, 18.6; ESI-HRMS m/z calcd for C$_{19}$H$_{17}$ClNO$_3$S [M + H]$^+$ 374.0612, found 374.0616.

(Z)-3-(Benzyloxy)-5-methyl-2-(2-(naphthalen-2-yl)-2-oxoethylidene) thiazolidin-4-one. Compound 3af (66.2 mg, Yield = 85%, Rf = 0.2 (PE/EA = 10:1)) was isolated as a white solid; mp 156–157 °C. 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36–8.32 (m, 1H), 8.00–7.93 (m, 2H), 7.93–7.86 (m, 2H), 7.63–7.57 (m, 2H), 7.57–7.53 (m, 2H), 7.50–7.41 (m, 3H), 7.00 (s, 1H), 5.25 (d, $J = 10.0$ Hz, 1H), 5.21 (d, $J = 10.0$ Hz, 1H), 3.86 (q, $J = 7.2$ Hz, 1H), 1.66 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 188.8, 169.9, 154.0, 135.5, 135.4, 133.3, 132.7, 130.2, 130.0, 129.6, 129.1, 128.9, 128.6, 128.3, 127.9, 126.8, 124.0, 95.0, 78.4, 37.7, 18.8; ESI-HRMS m/z calcd for C$_{23}$H$_{20}$NO$_3$S [M + H]$^+$ 390.1158, found 390.1161.

(Z)-3-(Benzyloxy)-5-methyl-2-(2-oxo-2-(thiophen-2-yl) ethylidene) thiazolidin-4-one. Compound 3ag (63.6 mg, Yield = 92%, Rf = 0.2 (PE/EA = 8:1)) was isolated as a white solid; mp 129–130 °C. 
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.61–7.54 (m, 2H), 7.54–7.46 (m, 2H), 7.46–7.36 (m, 3H), 7.11 (dd,
\[ J = 4.9, 3.8 \text{ Hz}, 1H \), 6.67 (s, 1H), 5.19 (d, \( J = 10.0 \text{ Hz}, 1H \)), 5.15 (d, \( J = 10.0 \text{ Hz}, 1H \)), 3.82 (q, \( J = 7.2 \text{ Hz}, 1H \)), 1.61 (d, \( J = 7.6 \text{ Hz}, 3H \)); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 181.4, 169.7, 153.3, 145.4, 133.1, 132.8, 129.9, 129.5, 129.0, 128.2, 94.9, 78.2, 37.7, 18.7 \]. ESI-HRMS m/z calcld for \( \text{C}_{17}\text{H}_{16}\text{NO}_3\text{S}_2 \left[ \text{M + H} \right]^+ \) 346.0566, found 346.0567.

(Z)-3-(Benzyloxy)-5-methyl-2-(2-oxopropylidene) thiazolidin-4-one. Compound 3ah (38.5 mg, Yield = 70%, \( R_f = 0.3 \) (PE/EA = 5:1)) was isolated as a white solid; mp 75–76 \( ^{\circ} \text{C} \). \( ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.50–7.44 (m, 2H), 7.43–7.38 (m, 3H), 6.14 (s, 1H), 5.12 (d, \( J = 7.6 \text{ Hz}, 1H \)), 5.08 (d, \( J = 7.6 \text{ Hz}, 1H \)), 3.76 (q, \( J = 6.0 \text{ Hz}, 1H \)), 2.17 (s, 3H), 1.58 (d, \( J = 6.0 \text{ Hz}, 3H \)); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 196.2, 169.8, 151.5, 133.1, 130.0, 129.8, 128.9, 98.0, 77.9, 37.4, 30.3, 18.7; \] ESI-HRMS m/z calcld for \( \text{C}_{14}\text{H}_{16}\text{NO}_3\text{S} \left[ \text{M + H} \right]^+ \) 278.0845, found 278.0845.

(Z)-3-methoxy-5-methyl-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3ba (47.3 mg, Yield = 89%, \( R_f = 0.2 \) (PE/EA = 10:1)) was isolated as a white solid; mp 108–109 \( ^{\circ} \text{C} \). \( ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.99–7.91 (m, 2H), 7.58–7.50 (m, 1H), 7.49–7.43 (m, 2H), 6.93 (s, 1H), 4.02 (s, 3H), 3.83 (q, \( J = 7.2 \text{ Hz}, 1H \)), 1.64 (d, \( J = 7.2 \text{ Hz}, 3H \)); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 189.0, 169.4, 153.4, 138.2, 132.6, 128.7, 94.2, 63.5, 37.7, 18.6; \] ESI-HRMS m/z calcld for \( \text{C}_{13}\text{H}_{14}\text{NO}_3\text{S} \left[ \text{M + H} \right]^+ \) 264.0689, found 264.0689.

(Z)-3-ethoxy-5-methyl-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3bb (45.6 mg, Yield = 80%, \( R_f = 0.5 \) (PE/EA = 3:1)) was isolated as a white solid; mp 74–75 \( ^{\circ} \text{C} \). \( ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.94 (d, \( J = 7.7 \text{ Hz}, 2H \)), 7.62–7.39 (m, 3H), 6.92 (s, 1H), 4.27 (q, \( J = 6.0 \text{ Hz}, 2H \)), 3.83 (q, \( J = 6.0 \text{ Hz}, 1H \)), 1.65 (d, \( J = 6.0 \text{ Hz}, 3H \)), 1.44 (t, \( J = 5.6 \text{ Hz}, 3H \)); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 189.1, 169.8, 154.3, 138.4, 132.5, 128.7, 127.8, 94.4, 72.2, 37.7, 18.7, 13.7; \] ESI-HRMS m/z calcld for \( \text{C}_{14}\text{H}_{16}\text{NO}_3\text{S} \left[ \text{M + H} \right]^+ \) 278.0845, found 278.0845.

(Z)-3-(allyloxy)-5-methyl-2-(2-oxo-2-enylethylidene) thiazolidin-4-one. Compound 3bc (47.7 mg, Yield = 83%, \( R_f = 0.2 \) (PE/EA = 8:1)) was isolated as a white solid; mp 75–76 \( ^{\circ} \text{C} \). \( ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 8.00–7.89 (m, 2H), 7.55 (t, \( J = 6.0 \text{ Hz}, 1H \)), 7.48 (t, \( J = 6.0 \text{ Hz}, 2H \)), 6.94 (s, 1H), 6.23–6.01 (m, 1H), 5.52–5.40 (m, 2H), 4.79–4.67 (m, 2H), 3.83 (q, \( J = 6.0 \text{ Hz}, 1H \)), 1.64 (d, \( J = 5.6 \text{ Hz}, 3H \)); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 189.0, 169.9, 154.4, 138.3, 132.5, 130.4, 128.7, 127.8, 123.2, 94.6, 77.1, 37.7, 18.9; \] ESI-HRMS m/z calcld for \( \text{C}_{15}\text{H}_{16}\text{NO}_3\text{S} \left[ \text{M + H} \right]^+ \) 290.0845, found 290.0845.

(Z)-3-(Benzyloxy)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3bd (41.5 mg, Yield = 64%, \( R_f = 0.2 \) (PE/EA = 5:1)) was isolated as a white solid; mp 134-135 \( ^{\circ} \text{C} \). \( ^1H \text{ NMR} (400 \text{ MHz, CDCl}_3) \delta 7.92–7.79 (m, 2H), 7.57–7.50 (m, 3H), 7.49–7.45 (d, 2H), 7.45–7.40 (m, 3H), 6.87 (s, 1H), 5.18 (s, 2H), 3.67 (s, 2H); \] 
\[ ^{13}C \text{ NMR} (100 \text{ MHz, CDCl}_3) \delta 188.9, 166.4, 155.1, 138.0, 133.2,
132.6, 130.1, 129.9, 129.0, 128.7, 127.8, 95.2, 78.4, 29.0; ESI-HRMS m/z calcd for C_{18}H_{16}NO_{3}S [M + H]^+ 326.0845, found 326.0848.

(Z)-3-(Benzyloxy)-5-ethyl-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3be (57.9 mg, Yield = 85%, R_f = 0.3 (PE/EA = 10:1)) was isolated as a white solid; mp 72–73 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.92–7.82 (m, 2H), 7.57–7.48 (m, 3H), 7.47–7.43 (m, 2H), 7.43–7.37 (m, 3H), 6.86 (s, 1H), 5.17 (s, 2H), 3.79 (dd, J = 8.2, 4.4 Hz, 1H), 2.19–2.06 (m, 1H), 1.91 (ddd, J = 14.0, 8.1, 7.0 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H); ^13C NMR (100 MHz, CDCl_3) δ 188.7, 169.0, 154.3, 138.1, 133.2, 132.4, 130.0, 129.8, 129.6, 127.7, 94.7, 78.2, 44.6, 26.2, 10.4; ESI-HRMS m/z calcd for C_{20}H_{20}NO_{3}S [M + H]^+ 354.1158, found 354.1160.

(Z)-3-(Benzyloxy)-2-(2-oxo-2-phenylethylidene)-5-phenylthiazolidin-4-one. Compound 3bf (53 mg, Yield = 66%, R_f = 0.2 (PE/EA = 10:1)) was isolated as a white solid; mp 150–151 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, J = 7.5 Hz, 2H), 7.59–7.53 (m, 1H), 7.53–7.49 (m, 2H), 7.49–7.45 (m, 2H), 7.44–7.40 (m, 3H), 7.40–7.34 (m, 5H), 6.94 (s, 1H), 5.24 (d, J = 8.0 Hz, 1H), 5.21 (d, J = 8.0 Hz, 1H), 4.92 (s, 1H); ^13C NMR (100 MHz, CDCl_3) δ 189.0, 167.6, 153.9, 138.1, 134.7, 133.2, 132.6, 130.3, 130.0, 129.3, 129.1, 129.0, 128.7, 128.6, 127.8, 95.2, 78.4, 47.5; ESI-HRMS m/z calcd for C_{24}H_{20}NO_{3}S [M + H]^+ 402.1158, found 402.1161.

(Z)-3-(Benzyloxy)-5-(2-fluorophenyl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3bg (57.1 mg, Yield = 69%, R_f = 0.3 (PE/EA = 3:1)) was isolated as a white solid; mp 128–129 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (dt, J = 7.2, 1.4 Hz, 2H), 7.59–7.52 (m, 3H), 7.52–7.45 (m, 2H), 7.45–7.40 (m, 3H), 7.36 (m 1H), 7.29 (td, J = 7.6, 1.8 Hz, 1H), 7.20–7.08 (m, 2H), 6.94 (s, 1H), 5.28 (d, J = 8.0 Hz, 1H), 5.23 (d, J = 8.0 Hz, 1H), 5.14 (s, 1H); ^13C NMR (100 MHz, CDCl_3) δ 189.1, 167.0, 161.0 (d, J = 249.2 Hz), 153.8, 138.0, 133.3, 132.6, 131.0 (d, J = 8.6 Hz), 130.4 (d, J = 2.8 Hz), 130.2, 129.9, 129.0, 128.7, 127.8, 124.9 (d, J = 3.6 Hz), 122.6 (d, J = 13.1 Hz), 116.4 (d, J = 21.0 Hz), 95.0, 78.4, 42.1 (d, J = 2.0 Hz); ^19F NMR (376 MHz, CDCl_3) δ -115.3; ESI-HRMS m/z calcd for C_{26}H_{19}FNO_{3}S [M + H]^+ 420.1064, found 420.1065.

(Z)-3-(Benzyloxy)-5-(2-methoxyphenyl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 3bh (46.4 mg, Yield = 54%, R_f = 0.2 (PE/EA = 3:1)) was isolated as a white solid; mp 168–169 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, J = 7.5 Hz, 2H), 7.60–7.55 (m, 2H), 7.56–7.47 (m, 2H), 7.46 ( br s, 2H), 7.45–7.40 (m, 2H), 7.38–7.28 (m, 1H), 7.24–7.15 (m, 1H), 7.02–6.77 (m, 3H), 5.28 (d, J = 12.8 Hz, 1H), 5.23 (d, J = 13.2 Hz, 1H), 5.12 (s, 1H), 3.83 (s, 3H); ^13C NMR (100 MHz, CDCl_3) δ 188.9, 168.1, 157.4, 155.3, 138.3, 133.4, 132.4, 130.5, 130.2, 130.0, 129.8, 129.0, 128.7, 127.8, 123.2, 121.1, 111.5, 94.1, 78.2, 56.0, 43.8; ESI-HRMS m/z calcd for C_{25}H_{22}NO_{3}S [M + H]^+ 432.1264, found 432.1266.
(Z)-3-(Benzyloxy)-5-(3-methoxyphenyl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one.

Compound 3bi (55 mg, Yield = 64%, R<sub>f</sub> = 0.2 (PE/EA = 8:1)) was isolated as a white solid; mp 150–151 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.94–7.85 (m, 2H), 7.59–7.53 (m, 1H), 7.52–7.46 (m, 4H), 7.46–7.38 (m, 3H), 7.31 (t, J = 7.9 Hz, 1H), 7.00–6.93 (m, 2H), 6.93–6.87 (m, 2H), 5.24 (d, J = 13.2 Hz, 1H), 5.20 (d, J = 13.2 Hz, 1H), 4.90 (s, 1H), 3.82 (s, 3H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 189.0, 167.4, 160.3, 153.8, 138.1, 136.0, 133.2, 132.6, 130.4, 130.3, 130.0, 129.0, 128.7, 127.8, 120.8, 114.6, 114.3, 95.2, 78.4, 55.5, 47.4; ESI-HRMS m/z calcd for C<sub>25</sub>H<sub>22</sub>NO<sub>4</sub>S [M + H]<sup>+</sup> 432.1264, found 432.1266.

(Z)-3-(Benzyloxy)-5-(4-chlorophenyl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one.

Compound 3bj (55.2 mg, Yield = 64%, R<sub>f</sub> = 0.2 (PE/EA = 7:1)) was isolated as a white solid; mp 176–177 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (d, J = 7.6 Hz, 2H), 7.60–7.53 (m, 1H), 7.53–7.45 (m, 4H), 7.45–7.39 (m, 3H), 7.39–7.34 (m, 2H), 7.34–7.29 (m, 2H), 6.94 (s, 1H), 5.24 (d, J = 8.0 Hz, 1H), 5.20 (d, J = 8.0 Hz, 1H), 4.89 (s, 1H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 189.1, 167.2, 153.4, 138.0, 135.1, 133.1, 132.7, 130.3, 129.9, 129.5, 129.0, 128.8, 127.9, 95.4, 78.4, 53.6, 46.8; ESI-HRMS m/z calcd for C<sub>24</sub>H<sub>19</sub>ClNO<sub>3</sub>S [M + H]<sup>+</sup> 436.0769, found 436.0771.

(Z)-3-(Benzyloxy)-5-(2,4-dimethylphenyl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one.

Compound 3bk (52 mg, Yield = 61%, R<sub>f</sub> = 0.2 (PE/EA = 6:1)) was isolated as a white solid; mp 110–111 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (dt, J = 7.1, 1.4 Hz, 2H), 7.60–7.51 (m, 3H), 7.50–7.45 (m, 2H), 7.45–7.41 (m, 3H), 7.12 (d, J = 7.8 Hz, 1H), 7.07–6.99 (m, 2H), 6.94 (s, 1H), 5.24 (d, J = 8.0 Hz, 1H), 5.20 (d, J = 8.0 Hz, 1H), 4.89 (s, 1H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 189.0, 168.0, 154.2, 138.9, 138.2, 137.0, 133.3, 132.5, 132.1, 130.2, 130.0, 129.9, 129.0, 128.7, 128.5, 127.8, 127.6, 94.9, 78.4, 44.7, 21.2, 19.7; ESI-HRMS m/z calcd for C<sub>26</sub>H<sub>24</sub>NO<sub>3</sub>S [M + H]<sup>+</sup> 430.1471, found 430.1472.

(Z)-3-(Benzyloxy)-5-(naphthalen-1-yl)-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one.

Compound 3bl (39.3 mg, Yield = 44%, R<sub>f</sub> = 0.2 (PE/EA = 7:1)) was isolated as a white solid; mp 172–173 °C. 1H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.97–7.90 (m, 3H), 7.90–7.86 (m, 2H), 7.63–7.58 (m, 1H), 7.58–7.56 (m, 2H), 7.56–7.53 (m, 2H), 7.50–7.47 (m, 3H), 7.47–7.43 (m, 3H), 6.99 (s, 1H), 5.73 (s, 1H), 5.31 (d, J = 8.0 Hz, 1H), 5.29 (d, J = 8.0 Hz, 1H); 13C NMR (100 MHz, CDCl<sub>3</sub>) δ 189.0, 167.8, 154.0, 138.1, 134.3, 133.3, 132.6, 131.5, 130.8, 130.3, 130.0, 129.8, 129.4, 129.1, 128.8, 127.8, 127.3, 126.5, 126.4, 125.6, 122.9, 95.1, 78.5, 44.4; ESI-HRMS m/z calcd for C<sub>28</sub>H<sub>22</sub>NO<sub>3</sub>S [M + H]<sup>+</sup> 452.1315, found 452.1316.

N-(benzyloxy)-2-((2-methyl-1-(methylthio)-3-oxo-3-phenylprop-1-en-1-yl)thio)propanamide

Compound 4 (74.0 mg, Yield = 93%, R<sub>f</sub> = 0.2 (PE/EA = 5:1), Z/E = 1:1) was isolated as an oil. 1H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.58 (s, 1H), 8.76 (s, 1H), 7.84 (d, J = 7.5 Hz, 2H), 7.80 (d, J = 7.5 Hz, 2H), 7.63–7.53 (m, 2H), 7.50–7.46 (m, 2H), 7.56–7.43 (m, 3H), 7.43–7.39 (m, 3H), 7.39–7.35
(m, 3H), 7.35-7.31 (m, 3H), 5.03-4.89 (m, 2H), 3.77-3.70 (m, 1H), 3.70-3.63 (m, 1H), 2.34 (s, 3H), 2.20 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H), 1.35 (d, J = 7.0 Hz, 3H). 13C NMR (125 MHz, CDCl₃) δ 198.7, 197.1, 169.6, 168.9, 148.9, 146.1, 135.5, 135.2, 135.0, 134.1, 133.6, 131.4, 129.5, 129.3, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 78.5, 78.1, 44.0, 42.0, 20.4, 20.2, 17.4, 17.3, 17.0, 16.7; ESI-HRMS m/z calcd for C₂₁H₂₄NO₃S₂ [M+H]⁺ 402.1192, found 402.1194.

(Z)-5-methyl-2-(1-oxo-1-phenylpropan-2-ylidene)thiazolidin-4-one Compound 5 (11.6 mg, Yield = 64%, Rf = 0.2 (PE/EA = 15:1)) was isolated as a white solid. mp 106–108 °C. 1H NMR (500 MHz, CDCl₃) δ 11.88 (s, 1H), 7.49-7.43 (m, 3H), 7.43-7.39 (m, 2H), 4.0 (dd, J = 14.5, 7.5 Hz, 1H), 1.9 (s, 3H), 1.68 (d, J = 7.5 Hz, 3H). 13C NMR (125 MHz, CDCl₃) δ 194.9, 176.9, 155.7, 140.4, 130.7, 128.3, 127.4, 103.6, 42.2, 19.1, 16.7; ESI-HRMS m/z calcd for C₁₃H₁₄NO₂S [M+H]⁺ 248.0740, found 248.0740.

(Z)-5-methyl-2-(1-oxo-3,4-dihydronaphthalen-2(1H)-ylidene) thiazolidin-4-one. Compound 6 (16.0 mg, Yield = 31%, Rf = 0.2 (PE/EA = 15:1)) was isolated as a yellow solid. mp 108–110 °C. 1H NMR (400 MHz, CDCl₃) δ 12.13 (s, 1H), 8.03 (dd, J = 7.6, 1.6 Hz, 1H), 7.45 (td, J = 7.6, 1.6 Hz, 1H), 7.34 (td, J = 7.2, 1.2 Hz, 1H), 7.25–7.20 (m, 1H), 4.03 (q, J = 7.2 Hz, 1H), 2.95 (t, J = 6.4 Hz, 2H), 2.67–2.58 (m, 2H), 1.7 (d, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl₃) δ 184.9, 176.8, 152.8, 142.4, 133.9, 132.9, 128.1, 127.8, 127.2, 105.4, 42.3, 28.4, 26.0, 19.2; ESI-HRMS m/z calcd for C₁₄H₁₄NO₂S [M+H]⁺ 260.0740, found 260.0740.

(Z)-5-methyl-2-(2-oxo-2-phenylethylidene) thiazolidin-4-one. Compound 7 (12.6 mg, Yield = 54%, Rf = 0.2 (PE/EA = 6:1), Z/E = 5:1) was isolated as a white solid; mp 185–186 °C. 1H NMR of the major isomer (500 MHz, Acetone-d₆) δ 10.55 (s, 1H), 7.93-7.88 (m, 2H), 7.55–7.46 (m, 3H), 6.93 (s, 1H), 4.01 (q, J = 6.0 Hz, 1H), 1.57 (d, J = 6.0 Hz, 3H). 13C NMR of the major isomer (100 MHz, Acetone-d₆) δ 188.3, 177.6, 160.1, 139.6, 132.7, 129.5, 128.0, 95.3, 41.5, 18.7; ESI-HRMS m/z calcd for C₁₂H₁₂NO₂S [M + H]⁺ 234.0583, found 234.0583.
4. Copies of NMR spectra

3aa. CDCl₃, 400 MHz

3aa. CDCl₃, 100 MHz
3ac, CDCl₃, 100 MHz

3ad, CDCl₃, 400 MHz
$\delta_{(13C)}/$ ppm

18.56  37.72  63.48  76.84  77.16  77.48  94.16  127.79  128.70  132.57  138.17  153.39  169.43  189.05

$\delta_{(1H)}/$ ppm

3.12  2.87  1.00  2.11  1.03  3.06  2.03

$\delta_{(13C)}/$ ppm

189.05  169.43  153.39  138.17  132.57  128.70  127.79  94.16  77.48  77.16  76.84  63.48  37.72  18.56

$\delta_{(1H)}/$ ppm


3b, CDCl$_3$, 100 MHz

3b, CDCl$_3$, 400 MHz
$\delta$ (13C) / ppm

13.72 18.71 37.71 72.20 76.91 77.16 77.41 94.35 127.78 128.72 132.52 138.35 154.27 169.83 189.06

$\delta$ (1H) / ppm


3bb, CDCl$_3$, 100 MHz

3bc, CDCl$_3$, 400 MHz
$3b_{14}$, CDCl$_3$, 100 MHz

$\delta^{(13C)}/$ppm

29.03 76.84 77.16 77.48 78.37 95.18 127.76 128.70 129.02 129.90 130.08 132.57 133.21 138.03 155.08 166.44 188.92

$\delta^{(1H)}/$ppm

3.24 1.13 1.04 0.96 2.01 1.00 2.95 2.05 3.11 2.06

$3b_{16}$, CDCl$_3$, 400 MHz

$\delta^{(1H)}/$ppm

2.00 2.11 2.46 2.41 1.30 2.20 2.28 3.60 3.68 3.84 3.88 7.38 7.40 7.41 7.42 7.43 7.44 7.46 7.49 7.50 7.51 7.52 7.53 7.54 7.85 7.86 7.87 7.87 7.88
$\delta$ (1H) / ppm

$\delta$ (13C) / ppm

3Me, CDCl$_3$, 400 MHz

3Me, CDCl$_3$, 100 MHz
4. CDCl₃, 500 MHz  
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5. Crystal Structure Information of Compound 3ab

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6. References
