Homo- and Cross-Annulation of sp$^3$ C–H bonds in Acetophenones for Divergent Synthesis of Thienothiazoles

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1) Materials and instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich, Acros and Merck, and were used as received without any further purification unless otherwise noted. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The GC yield was calculated using diphenyl ether as the internal standard. GC-MS analyses were analyzed on a Shimadzu GCMS-QP2010Ultra with a ZB-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). MS spectra were compared with the spectra gathered in the NIST library. The $^1$H NMR and $^{13}$C NMR were recorded on Bruker AV 500 spectrometers using residual solvent peak as a reference. HR-MS spectra were recorded by an Agilent HPLC 1200 Series coupled to Bruker microTOF-QII. Unless notice, molecular weight of sulfur used is 32 g per mol.
2) Optimization of reaction conditions


![Chemical structure diagram]

<table>
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<th>Entry</th>
<th>N source (mmol)</th>
<th>sulfur (mmol)</th>
<th>additive</th>
<th>solvent (µL)</th>
<th>yield&lt;sup&gt;b&lt;/sup&gt;</th>
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- Reaction conditions: 1a (0.2 mmol) at 120 °C under air for 12 h.
- Abbreviations: DABCO: 1,4-diazabicyclo[2.2.2]octane; DMSO: dimethyl sulfoxide.
- Yields are GC yields.
- Reaction carried out for 3 h.
- Reaction carried out for 2.5 h.
- Reaction carried out for 6 h.
- 140 °C.
- 150 °C.
- 110 °C.
(b) Synthesis of 2-(pyridin-4-yl)benzo[4,5]thieno[3,2-\textit{d}]thiazole from acetophenone and 4-picoline$^a$

![Reaction Diagram]

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<th>base (mmol)</th>
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Reaction conditions: 1a (0.1 mmol), in DMSO (1 mL) at 120 °C under air for 12 h.

Abbreviations: DABCO: 1,4-diazabicyclo[2.2.2]octane; DMSO: dimethyl sulfoxide.

Yields are GC yields.

3) General procedure for the synthesis of thieno[3,2-d]thiazole derivatives

(a) General procedure for the synthesis of compound 2a (General procedure A)

To an 8-mL screw-cap vial was added acetophenone (24 mg, 0.2 mmol), urea (36 mg, 0.6 mmol), elemental sulfur (10 mg, 0.31 mmol), and DMSO (0.2 mL). The vial was tightly capped and heated at 120 °C for 5 min, then pyridine (50 µL) was introduced into the vial, and the resulting mixture was stirred for additional 2.5 h. Upon completion of the reaction, the mixture was cooled to room temperature, and diphenyl ether (17.2 mg, 0.1 mmol) as an internal standard was added. The organic components were consequently extracted into ethyl acetate (2 mL), washed with NaHCO₃ solution (5% aqueous solution, 2 × 1 mL), dried over anhydrous Na₂SO₄, and analyzed by GC with reference to diphenyl ether. To isolate the corresponding product, the combined organic extracts were concentrated in vacuo and purified by column chromatography on silica gel with dichloromethane/hexane eluent to give the pure product. The product identity was further confirmed by GC-MS, ¹H NMR, and ¹³C NMR.
Gram-scale synthesis of compounds 2a and 2e

![Chemical Structures]

R = H, 1a (1.20 g, 10 mmol)  
R = Cl, 1e (1.55 g, 10 mmol)

R = H, 2a (1.05 g, 79%)  
R = Cl, 2e (0.974 g, 58%)

To a 50-mL round bottom flask was added acetophenone (1.20 g, 10 mmol) or 4’-chloroacetophenone (1.54 g, 10 mmol), urea (1.80 g, 30 mmol), elemental sulfur (500 mg, 16 mmol) and DMSO (10 mL). The reaction flask was sealed using septum and heated at 120 °C for 5 min in a sand bath, then pyridine (2.5 mL) was introduced into the reaction flask via syringe and the resulting mixture was stirred for an additional 2.5 hours. After disappearance of reactant as detected by TLC or GC, the mixture was diluted by ethyl acetate (50 mL). Organic phase was washed with NaHCO₃ solution (5% aqueous solution, 3 × 10 mL) and brine (3 × 10 mL), dried over anhydrous Na₂SO₄, and filtered through a short pad of silica gel. The combined organic extracts were concentrated in vacuo and purified by recrystallization in hot acetone to give the pure products.

Procedure for 1 mmol scale synthesis of 2a and 2e

For compound 2a: To an 8-mL screw-cap vial was added acetophenone (120 mg, 1.0 mmol), urea (180 mg, 3.0 mmol), elemental sulfur (50 mg, 1.55 mmol), and DMSO (1.0 mL). The vial was tightly capped and heated at 120 °C for 5 min, then pyridine (250 µL) was introduced into the vial, and the resulting mixture was stirred for an additional 2.5 h. Upon completion of the reaction, the reaction mixture was consequently diluted with ethyl acetate (10 mL), washed with NaHCO₃ solution (5% aqueous solution, 3 × 2 mL) and brine (3 × 2 mL). The aqueous phase was extracted with ethyl acetate (3 × 2 mL).
The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography (hexane/dichloromethane = 2:1) to afford the desired product 2a (112.6 mg, 84%) as a white solid.

For compound 2e: following the same procedure for synthesis of compound 2a, using 4’-chloroacetophenone (154 mg, 1 mmol) starting material. After column chromatography on silica gel (hexane/dichloromethane = 5:2), 109.3 mg (65%) of the desired product 2e as a white solid was obtained.

\textbf{(b) General procedure for the synthesis of compound 3a (General procedure B)}

\begin{center}
\begin{tikzpicture}
\node at (0,0) (a) {1a};
\node at (2,0) (b) {2};
\node at (4,0) (c) {3a};
\node at (2,0) (d) {DMSO/H$_2$O 120 °C, 6 h};
\node at (2,0) (e) {urea (0.75 equiv.)};
\node at (2,0) (f) {DABCO (0.5 equiv.)};
\node at (2,0) (g) {S$_8$ (3.5 equiv.)};
\draw[->] (a) -- (b);
\draw[->] (b) -- (c);
\end{tikzpicture}
\end{center}

To an 8-mL screw-cap vial was added acetophenone (24 mg, 0.2 mmol), urea (9 mg, 0.15 mmol), and DMSO (1.0 mL). The vial was tightly capped and heated at 80 °C for 30 min. After that, the mixture was cooled to room temperature. Subsequently, DABCO (11.2 mg, 0.1 mmol), elemental sulfur (22.4 mg, 0.7 mmol), and deionized water (50 µL) were added, and the resulting mixture was stirred at 120 °C for additional 6 h. Upon completion of the reaction, the mixture was cooled to room temperature. The organic components were consequently extracted into ethyl acetate (2 mL), washed with NaHCO$_3$ solution (5% aqueous solution, 2 × 1 mL), dried over anhydrous Na$_2$SO$_4$, and filtered. The combined organic extracts were concentrated \textit{in vacuo} and purified by column
chromatography on silica gel with dichloromethane/hexane eluent to give pure product. The product identity was further confirmed by $^1$H NMR and $^{13}$C NMR.

**Gram-scale synthesis of compound 3a**

To a 250-mL round bottom flask was added acetophenone (1.20 g, 10 mmol), urea (450 mg, 7.5 mmol), and DMSO (50 mL). The reaction flask was sealed using septum and heated at 80 °C for 30 min. The mixture was then cooled to room temperature and charged with DABCO (0.56 g, 5 mmol), elemental sulfur (1.12 g, 35 mmol, 32 g/mol), and deionized water (2.5 mL). The resulting mixture was stirred at 120 °C for an additional 6 hours. After completion of the reaction, the mixture was cooled to room temperature and poured onto water (20 mL). The organic components were extracted with ethyl acetate ($3 \times 30$ mL), washed with brine ($3 \times 10$ mL), dried over anhydrous Na$_2$SO$_4$, and filtered through a short pad of silica gel. The combined organic extracts were concentrated *in vacuo* and purified by recrystallization in hot acetone to give the pure product.

**Procedure for 1 mmol scale synthesis of 3a**

To a 25-mL Schlenk tube was added acetophenone (120 mg, 1.0 mmol), urea (45 mg, 0.75 mmol), and DMSO (5.0 mL). The tube was tightly capped and heated at 80 °C (oil bath temperature) for 30 min. After that, the mixture was cooled to room temperature and charged with DABCO (56 mg, 0.5 mmol), elemental sulfur (112 mg, 3.5 mmol), and
deionized water (0.25 mL). The resulting mixture was stirred at 120 °C (oil bath temperature) for an additional 6 h. Upon completion of the reaction, the reaction mixture was consequently diluted with ethyl acetate (25 mL), washed with NaHCO₃ solution (5% aqueous solution, 3 × 5 mL), and brine (3 × 5 mL). The aqueous phase was extracted with ethyl acetate (2 × 5 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/dichloromethane = 2:1) to afford the desired product 3a (107.4 mg, 73%) as a light yellow solid.
(c) General procedure for the reaction between acetophenone and methylhetarene derivatives (General procedure C)

\[
\begin{align*}
2 \text{acetophenone} & \quad + \quad 2 \text{equiv.} \text{methylhetarene} \\
& \quad \xrightarrow{S_8 (3 \text{ equiv.})} \\
& \quad \xrightarrow{\text{urea (2 equiv.) NaOAc (1 equiv.)}} \\
& \quad \xrightarrow{\text{DMSO, } 120^\circ\text{C, 12 h}} \\
& \quad \text{product}
\end{align*}
\]

To an 8-mL screw-cap vial was added acetophenone (12 mg, 0.1 mmol), 4-picoline (18.6 mg, 0.2 mmol), elemental sulfur (9.6 mg, 0.3 mmol), urea (12 mg, 0.15 mmol), NaOAc (8.2 mg, 0.1 mmol), and DMSO (1 mL). The vial was tightly capped and stirred at 120 °C for 12 h under air. Upon completion of the reaction, the mixture was cooled to room temperature. The organic components were consequently extracted with ethyl acetate (2 mL), washed with NaHCO₃ solution (5% aqueous solution, 2 × 1 mL), dried over anhydrous Na₂SO₄, and filtered. The combined organic extracts were concentrated \textit{in vacuo} and purified by column chromatography on silica gel with ethyl acetate/hexane solvent system to give the pure product. The product identity was further confirmed by GC-MS, \textsuperscript{1}H NMR, and \textsuperscript{13}C NMR.

(d) General procedure for the reaction between acetophenone and phenylacetic acid derivatives (General procedure D)

\[
\begin{align*}
R^1 \text{acetophenone} & \quad + \quad R^2 \text{phenylacetic acid} \\
& \quad \xrightarrow{S_8 (3.5 \text{ equiv.}) NH_4OAc (2 \text{ equiv.) DABCO (1 equiv.)}} \\
& \quad \xrightarrow{\text{DMSO (0.2 M) } 120^\circ\text{C, 12 h}} \\
& \quad \text{product}
\end{align*}
\]

To an 8-mL screw-cap vial was added acetophenone (48 mg, 0.4 mmol), phenylacetic acid (27 mg, 0.2 mmol), NH₄OAc (30.8 mg, 0.4 mmol), elemental sulfur (22.4 mg, 0.7
mmol), DABCO (22.4 mg, 0.2 mmol), and DMSO (1 mL). The vial was tightly capped and heated at 120 °C for 12 h. Upon completion of the reaction, the mixture was cooled to room temperature. The organic components were consequently extracted with ethyl acetate (4 mL), washed with NaHCO₃ solution (5% aqueous solution, 2 × 2 mL), and dried over anhydrous Na₂SO₄. The organic extracts were concentrated in vacuo and purified by column chromatography on silica gel with dichloromethane/hexane solvent system to give the pure product. The product identity was further confirmed by GC-MS, ¹H NMR, and ¹³C NMR.

(e) General procedure for the reaction between acetophenone and benzaldehyde derivatives (General procedure E)

To an 8-mL screw-cap vial was added acetophenone (24 mg, 0.2 mmol), urea (12 mg, 0.2 mmol), and DMSO (0.5 mL). The vial was tightly capped and heated at 80 °C for 30 min. After that, the mixture was cooled to room temperature and 4-methylbenzaldehyde (12 mg, 0.1 mmol) and elemental sulfur (16 mg, 0.5 mmol) were subsequently added. The resulting mixture was stirred at 120 °C for 12 h. Upon completion of the reaction, the mixture was cooled to room temperature. The organic components were consequently extracted with ethyl acetate (2 mL), washed with NaHCO₃ solution (5% aqueous solution, 2 × 1 mL), dried over anhydrous Na₂SO₄, and filtered. The combined organic extracts were concentrated in vacuo and purified by column chromatography on silica gel.
with dichloromethane/hexane solvent system to give the pure products. The product identity was further confirmed by GC-MS, $^1$H NMR, and $^{13}$C NMR.

(f) General procedure for the synthesis of 4-aryl-5H-1,2,3-dithiazole-5-thione

(General procedure F)

![Chemical structure](image_url)

To an 8-mL screw-cap vial was added acetophenone ketoxime acetates (0.4 mmol), Li$_2$CO$_3$ (14.8 mg, 0.2 mmol), elemental sulfur (32 mg, 1 mmol), and DMSO (0.5 mL). The vial was tightly capped stirred at 120 °C for 12 h. Upon completion of the reaction, the mixture was cooled to room temperature, and NaHCO$_3$ solution (5% aqueous solution, 2 mL) was added. The organic components were consequently extracted with ethyl acetate (3 × 2.0 mL), washed with brine (2 × 1 mL), and dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with dichloromethane/hexane =1/10 solvent system to give the pure products. The product identities were further confirmed by GC-MS, $^1$H NMR, and $^{13}$C NMR.

4) Mechanistic studies

(a) Radical-trapping experiment

The reaction of acetophenone 1a (24 mg, 0.2 mmol) was performed under condition A or B. After stirring for 15 minutes at 120 °C, the corresponding radical scavenger (0.2 or 0.6 mmol) was injected into the reaction vial and the mixture was continuously stirred for an additional 2.25 h (condition A) or 5.75 h (condition B). Then, the vial was cooled to room
temperature and diphenyl ether internal standard (17.2 mg, 0.1 mmol) was added. From the solution aliquots was taken into ethyl acetate (2 mL), washed successively with NaHCO₃ solution (5% aqueous solution, 1 mL), and brine (1 mL), dried over anhydrous Na₂SO₄, filtered, and analyzed by GC-MS with reference to diphenyl ether.

(b) GC-MS analysis of reaction intermediates

The reaction of acetophenone 1a (24 mg, 0.2 mmol) was performed under condition A or B. After stirring for 30 minutes at 120 °C, the vial was cooled to room temperature and quenched with brine (1 mL). From the solution aliquots was taken into ethyl acetate (2 mL), washed successively with NaHCO₃ solution (5% aqueous solution, 1 mL) and brine (1 mL), dried over anhydrous Na₂SO₄, filtered, and analyzed by GC-MS.
MS spectrum of compound 4

MS spectrum of compound 5
(c) Benzoylformic acid 8, 2-oxothioamide 9 and phenylglyoxal 10, 11 as the reactants for thieno[3,2-\textit{d}]thiazole products formation
The reaction of 4-fluoroacetophenone 1h (13.8 mg, 0.1 mmol) with benzyloformic acid 8 (15.0 mg, 0.1 mmol)/thioamide 9 (23.5 mg, 0.1 mmol)/anhydrous phenylglyoxal 10 (13.4 mg, 0.1 mmol) or phenylglyoxal monohydrate 11 (15.2 mg, 0.1 mmol) was performed under condition A or B. Upon completion of the reaction, the mixture was cooled to room temperature and diphenyl ether internal standard (17.2 mg, 0.1 mmol) was added. From the solution aliquots was taken into ethyl acetate (2 mL), washed successively with NaHCO₃ solution (5% aqueous solution, 1 mL) and brine (1 mL), dried over anhydrous Na₂SO₄, filtered, and analyzed by GC-MS with reference to diphenyl ether.

\[
\begin{align*}
\text{(d) 2,4-Diphenylthiazole 12 and dithiazole 4 as the reactants for formation of thieno[3,2-\text{d}]thiazole products}
\end{align*}
\]

2,4-Diphenylthiazole 12 (23.8 mg, 0.1 mmol) or 4-phenyl-5H-1,2,3-dithiazole-5-thione 4 (42.3 mg, 0.2 mmol) was stirred under condition A. In another control experiment, 4-(4-fluorophenyl)-5H-1,2,3-dithiazole-5-thione 4-4F (22.9 mg, 0.1 mmol) and acetophenone 1a (12.0 mg, 0.1 mmol) were stirred under condition A. After 2.5 h, the mixture was
cooled to room temperature and diphenyl ether internal standard (17.2 mg, 0.1 mmol) was added. From the solution aliquots were added into ethyl acetate (2 mL), washed with NaHCO₃ solution (5% aqueous solution, 1 mL) and brine (1 mL), dried over anhydrous Na₂SO₄, filtered, and analyzed by GC-MS with reference to diphenyl ether.

(e) 3-Aminobenzothiophene 13 and 3-aminothiophene 14 as the reactants for thieno[3,2-d]thiazole products formation

A mixture of 3-aminobenzothiophene hydrochloride 5.HCl (18.6 mg, 0.1 mmol) or 3-aminothiophene hydrochloride 13 (13.6 mg, 0.1 mmol) and acetophenone 1a (12.0 mg, 0.1 mmol) was stirred under condition A or B. Upon completion of reaction, the mixture was cooled to room temperature and diluted with ethyl acetate (5 mL). The organic layer was washed successively with NaHCO₃ solution (5% aqueous solution, 2 × 2 mL) and brine (2 × 2 mL), dried over anhydrous Na₂SO₄, filtered, and purified by column chromatography on silica gel with hexane/dichloromethane:20/1.
(f) Intermolecular competition experiments

A mixture of acetophenone 1a (12.0 mg, 0.1 mmol) and 4'-methylacetophenone 1b (13.4 mg, 0.1 mmol) or 4'-fluoroacetophenone 1h (13.8 mg, 0.1 mmol) was stirred under condition A. Upon completion of reaction, the mixture was cooled to room temperature diluted with ethyl acetate (5 mL). The organic layer was washed successively with NaHCO₃ solution (5% aqueous solution, 2 × 2 mL), and brine (2 × 2 mL), dried over anhydrous Na₂SO₄, filtered, and purified by column chromatography on silica gel with hexane/dichloromethane:80/1.
(g) Plausible mechanism

[Chemical diagram with reaction steps and intermediates labeled A to L, including reactions with urea, base, and Willgerodt-Kindler conditions.]
(h) Unsuccessful substrates

\[
\begin{align*}
\text{X} & = \text{F or Cl} \\
\text{O} & \quad \text{sulfur (3.5 equiv)} \\
\text{X} & \quad \text{urea (0.75 equiv)} \\
\text{DABCO (0.5 equiv)} \\
\text{DMSO/H}_2\text{O (20:1)} \\
120 \degree \text{C, 12 h} \\
\rightarrow \text{complex mixtures}
\end{align*}
\]

\[
\begin{align*}
\text{NC} & \quad \text{sulfur, urea} \\
\text{O} & \quad \text{DABCO (0.5 equiv)} \\
\text{DMSO/H}_2\text{O (20:1)} \\
120 \degree \text{C, 12 h} \\
\rightarrow \text{no reaction}
\end{align*}
\]

5) Characterization data of products

\[
\begin{align*}
\text{2-Phenylbenzo[4,5]thieno[3,2-d]thiazole (2a)}
\end{align*}
\]

Prepared from acetophenone 1a (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 \(\mu\)m, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, \(R_f = 0.53\): White solid, 88\% yield (23.5 mg). This compound is known.\(^1\)

\(^1\)\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.28 (d, \(J = 7.5\) Hz, 1H), 8.28 (dd, \(J = 7.5\) Hz, 2.0 Hz, 2H), 7.84 (d, \(J = 8.5\) Hz, 1H), 7.52–7.44 (m, 4H), 7.41 (ddd, \(J = 8.0\) Hz, 7.5 Hz, 1.5 Hz).

6-Methyl-2-(p-tolyl)benzo[4,5]thieno[3,2-d]thiazole (2b)

Prepared from 4'-methylacetophenone 1b (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.48): White solid, 91% yield (26.8 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 8.13 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.31 (dd, J = 8.0 Hz, 0.5 Hz, 1H), 7.28 (d, J = 8.0, 2H), 2.51 (s, 3H), 2.41 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 170.6, 155.9, 143.1, 140.5, 135.1, 131.5, 129.7, 129.3, 128.3, 126.6, 126.4, 123.3, 121.4, 21.6, 21.4. HRMS (ESI) m/z calcd for C$_{17}$H$_{14}$NS$_2$$^+$(M+H)$^+$ 296.0562, found 296.0564.

6-Methoxy-2-(4-methoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (2c)

Prepared from 4'-methoxyacetophenone 1c (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 3:2 (v./v.), TLC silica gel 60 F254, Rf = 0.38): Light yellow solid, 92% yield (30.1 mg).
1H NMR (500 MHz, CDCl₃, ppm) δ 8.70 (dd, J = 7.0 Hz, 2.0 Hz, 2H), 8.183 (d, J = 9.0, 1H), 7.35 (d, J = 2.5 Hz, 1H), 7.13 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 7.05 (dt, J = 9.0 Hz, 2.5 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H).

13C NMR (125 MHz, CDCl₃, ppm) δ 170.1, 164.2, 158.6, 156.7, 144.7, 136.1, 133.6, 127.8, 124.2, 122.6, 114.5, 113.8, 106.8, 55.7, 55.5.

HRMS (ESI) m/z calcd for C₁₇H₁₄NO₂S₂⁺ (M+H)⁺ 328.0460, found 328.0457.

6-(Methylthio)-2-(4-(methylthio)phenyl)benzo[4,5]thieno[3,2-d]thiazole (2d)

Prepared from 4’-methylthioacetophenone 1d (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.41): Yellow solid, 84% yield (30.2 mg).

1H NMR (500 MHz, CDCl₃, ppm) δ 8.14 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 1.0 Hz, 1H), 7.41 (dd, J = 8.5 Hz, 1.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 2.58 (s, 3H), 2.54 (s, 3H). 13C NMR (125 MHz, CDCl₃, ppm) δ 170.3, 155.8, 143.7, 141.8, 135.7, 131.5, 130.6, 129.7, 128.1, 126.8, 126.2, 124.8, 124.7, 121.8, 120.9, 16.5, 15.3.

HRMS (ESI) m/z calcd for C₁₇H₁₄NS₂⁺ (M+H)⁺ 360.0004, found 360.0004.

6-Chloro-2-(4-chlorophenyl)benzo[4,5]thieno[3,2-d]thiazole (2e)
Prepared from 4'-chloroacetophenone 1e (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 5:2 (v./v.), TLC silica gel 60 F254, Rf = 0.36): White solid, 67% yield (22.5 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.09 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 2.0, 1H), 7.40 (td, J = 1.5 Hz, 7.5 Hz, 3H). 13C NMR (125 MHz, CDCl3, ppm) δ 169.6, 155.4, 143.7, 132.3, 131.2, 129.6, 129.3, 129.1, 128.5, 127.7, 126.0, 123.0, 122.5. HRMS (ESI) m/z calcd for C15H8(35Cl)2NS2+ (M+H)+ 335.9470, found 335.9472.

6-Bromo-2-(4-bromophenyl)benzo[4,5]thieno[3,2-d]thiazole (2f)

Prepared from 4'-bromoacetophenone 1f (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.45): Yellow solid, 55% yield (23.4 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.03 (d, J = 8.0, 1H), 7.92 (d, J = 1.5 Hz, 1H), 7.84 (dd, J = 6.5 Hz, 2.0 Hz, 2H), 7.56–7.54 (m, 3H). 13C NMR (125 MHz, CDCl3, ppm) δ 169.7, 155.5, 144.0, 132.7, 132.3, 131.3, 129.2, 128.6, 127.9, 125.9, 124.7, 122.8, 118.9. HRMS (ESI) m/z calcd for C15H8(79Br)2NS2+ (M+H)+ 423.8459, found 423.8462.
(2g)

Prepared from 4’-(trifluoromethyl)acetophenone 1g (0.2 mmol) as shown in the general 
experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, 
hexane/dichloromethane = 8:1 (v./v.), TLC silica gel 60 F254, Rf = 0.28): Brown solid, 
62% yield (25.0 mg).

1H NMR (500 MHz, DMSO-d6, ppm) δ 8.62 (s, 1H), 8.31 (d, J = 8.5 Hz, 1H), 8.24 (d, J 
= 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 7.82 (dd, J = 8.5 Hz, 1.0 Hz, 1H). 13C NMR 
(125 MHz, DMSO-d6, ppm) δ 169.5, 154.3, 143.4, 137.3, 137.1, 132.8, 130.7 (q, J = 31.8 
Hz), 129.5, 128.1, 127.3, 126.8 (q, J = 3.7 Hz), 126.1, 126.0, 125.9, 125.5, 124.8, 123.8, 
123.3, 122.3 (q, J = 3.4 Hz), 122.1 (q, J = 4.2 Hz), 122.0. HRMS (ESI) m/z calcd for 
C17H9F6NS2+ (M+H)+ 403.9997, found 403.9996.

6-Fluoro-2-(4-fluorophenyl)benzo[4,5]thieno[3,2-d]thiazole (2h)

Prepared from 4’-fluoroacetophenone 1h (0.2 mmol) as shown in the general 
experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, 
hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.43): White solid, 
94% yield (28.7 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.18 (dd, J = 9.0 Hz, 5.0 Hz, 1H), 8.02 (m, 2H), 7.54 
(dd, 8.5 Hz, 2.5 Hz, 1H), 7.27–7.23 (m, 1H), 7.18 (t, J = 8.5 Hz, 2H). 13C NMR (125 
MHz, CDCl3, ppm) δ 169.7, 164.0 (d, J = 251.4 Hz), 160.8 (d, J = 245.9 Hz),
155.3, 143.6 (d, $^3J_{CF} = 9.9$ Hz), 130.2 (d, $^4J_{CF} = 3.4$ Hz), 129.8 (d, $^4J_{CF} = 2.8$ Hz), 128.5 (d, $^3J_{CF} = 8.5$ Hz), 127.0, 122.6 (d, $^3J_{CF} = 9.2$ Hz), 116.2 (d, $^2J_{CF} = 22.3$ Hz), 113.8 (d, $^2J_{CF} = 23.9$ Hz), 110.0 (d, $^2J_{CF} = 25.9$ Hz). HRMS (ESI) m/z calcd for C$_{15}$H$_8$F$_2$NS$_2^+$ (M+H)$^+$ 304.0061, found 304.0063.

2-([1,1'-Biphenyl]-4-yl)-6-phenylbenzo[4,5]thieno[3,2-d]thiazole (2i)

Prepared from 4-acetyl biphenyl 1i (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v/v.), TLC silica gel 60 F254, R$_f$ = 0.44): Green solid, 54% yield (22.6 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 8.33 (d, $J = 8.5$ Hz, 1H), 8.13 (d, $J = 8.5$ Hz, 2H), 8.05 (d, $J = 1.0$ Hz, 1H), 7.75 (dd, $J = 8.5$ Hz, 1.5 Hz, 1H), 7.72 (d, $J = 8.5$ Hz, 2H), 7.69 (d, $J = 2.5$ Hz, 2H), 7.66 (d, $J = 2.5$ Hz, 2H), 7.48 (td, $J = 7.5$ Hz, 2.0 Hz, 4H), 7.41, 7.37 (m, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 170.4, 155.9, 143.6, 143.0, 140.7, 140.1, 138.5, 132.9, 131.1, 139.5, 128.9, 128.9, 127.8, 127.7, 127.3, 127.0, 127.0, 124.7, 122.0, 121.7. HRMS (ESI) m/z calcd for C$_{27}$H$_{18}$NS$_2^+$ (M+H)$^+$ 420.0875, found 420.0875.
6-Phenoxy-2-(4-phenoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (2j)

Prepared from 4’-phenoxyacetophenone 1j (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.41): Yellow solid, 48% yield (21.7 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.20 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 2.0 Hz, 1H), 7.41–7.35 (m, 5 H), 7.22 (dd, J = 9.0 Hz, 2.0 Hz, 1H), 7.10–7.06 (m, 7H).

13C NMR (125 MHz, CDCl3, ppm) δ 170.2, 157.3, 155.3, 143.9, 130.4, 129.96, 129.90, 128.2, 125.3, 124.0, 123.5, 122.5, 120.4, 119.5, 119.0, 118.7, 117.5, 113.0, 106.1. HRMS (ESI) m/z calcd for C27H18NO2S2+ (M+H)+ 452.0773, found 452.0777.

5-Chloro-2-(3-chlorophenyl)benzo[4,5]thieno[3,2-d]thiazole (2k)

7-Chloro-2-(3-chlorophenyl)benzo[4,5]thieno[3,2-d]thiazole (2k’)

Prepared from 3’-choloracetophenone 1k (0.4 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 8:1 (v./v.), TLC silica gel 60 F254) yielded 2k (24.8 mg, 37%, Rf = 0.17) and 2k’ (11.4 mg, 17%, Rf = 0.23) as light yellow solids.
(2k) $^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.16 (dd, $J = 8.0$ Hz, 1.0 Hz, 1H), 8.06 (d, $J = 2.0$ Hz, 1H), 7.88 (tt, $J = 4.5$ Hz, 1.5 Hz, 1H), 7.47 (t, $J = 8.0$ Hz, 1H), 7.44–7.40 (m, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 169.1, 156.2, 141.6, 135.3, 135.2, 132.0, 132.0, 130.3, 130.3, 128.2, 126.5, 126.5, 124.9, 124.7, 120.1.

(2k') $^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.25 (d, $J = 2.0$ Hz, 1H), 8.06 (d, $J = 2.0$ Hz, 1H), 7.89 (tt, $J = 4.0$ Hz, 2.0 Hz, 1H), 7.75 (d, $J = 8.5$ Hz, 1H), 7.45–7.40 (m, 2H), 7.39 (dd, $J = 9.0$ Hz, 2.0 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 169.0, 155.1, 140.7, 135.4, 135.2, 132.8, 131.7, 131.5, 130.4, 130.3, 126.5, 125.7, 124.6, 124.3, 121.7. HRMS (ESI) m/z calcd for C$_{13}$H$_8$($^{35}$Cl)$_2$NS$_2^+$ (M+H)$^+$ 335.9470, found 335.9467.

5-Bromo-2-(3-bromophenyl)benzo[4,5]thieno[3,2-d]thiazole (2l)

7-Bromo-2-(3-bromophenyl)benzo[4,5]thieno[3,2-d]thiazole (2l')

Prepared from 3'-bromoacetophenone 11 (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 3:1 (v./v.), TLC silica gel 60 F254, $R_f = 0.38$) yielded a mixture of 2l and 2l' (3:1) as a light yellow solid, 38% yield (16.4 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.41 (d, $J = 1.5$ Hz, 1H), 8.21 (s, 1H), 8.16 (s, 0.3H), 7.93 (d, $J = 8.0$ Hz, 1H), 7.90 (d, $J = 8.0$ Hz, 0.3H), 7.69 (d, $J = 8.5$ Hz, 1H), 7.59 (d, $J = 8.5$ Hz, 1H), 7.57 (d, $J = 8.5$ Hz, 0.3H), 7.53–7.48 (m, 1.6 H), 7.37–7.30 (m, 1.6H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 168.9, 155.0, 141.3, 135.6, 133.3, 133.0, 132.7, 131.9, 131.2, 130.6, 130.4, 130.3, 129.5, 129.43, 129.38, 128.3, 125.2, 125.1, 124.9, 124.7,
124.6, 123.3, 119.4, 114.1. HRMS (ESI) m/z calcd for C_{17}H_{14}NO_{2}S_{2}^{+} (M+H)^{+} 423.8459, found 423.8458.

5-Methoxy-2-(3-methoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (2m)

7-Methoxy-2-(3-methoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (2m’)

Prepared from 3’-methoxyacetophenone 1m (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 v/v.), TLC silica gel 60 F254, R_{f} = 0.43) yielded a mixture of 2m and 2m’ (15:1) as a light yellow solid, 87% yield (28.4 mg).

^1H NMR (500 MHz, CDCl_3, ppm) δ 7.83 (d, J = 7.5 Hz, 1H), 7.69 (d, J = 2.5 Hz, 0.06H), 7.62 (d, J = 8.5 Hz, 0.06H), 7.56 (d, J = 1.5 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 6.97 (dd, J = 8.5 Hz, 2.5 Hz, 0.06 Hz), 6.94 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 3.97 (s, 3H), 3.89 (s, 0.18H), 3.87 (s, 0.18H), 3.86 (s, 3H). ^13C NMR (125 MHz, CDCl_3, ppm) δ 170.4, 170.2, 160.1, 158.1, 156.4, 155.8, 154.4, 135.34, 135.30, 134.6, 132.1, 132.0, 131.5, 130.9, 130.14, 130.11, 126.5, 124.0, 119.2, 116.55, 116.52, 115.3, 114.5, 111.3, 105.4, 104.2, 55.8, 55.7, 55.5. HRMS (ESI) m/z calcd for C_{17}H_{14}NO_{2}S_{2}^{+} (M+H)^{+} 328.0460, found 328.0464.
5-(Trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)benzo[4,5]thieno[3,2-d]thiazole
(2n)

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{N} \\
\text{\text{-}} & \quad \text{\text{-}} \\
\text{\text{-}} & \quad \text{\text{-}} \\
\text{\text{-}} & \quad \text{\text{-}} \\
\text{\text{-}} & \quad \text{\text{-}} \\
\end{align*}
\]

7-(Trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)benzo[4,5]thieno[3,2-d]thiazole
(2n’)

Prepared from 3’-(trifluoromethyl)acetophenone (0.4 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 5:1 (v./v.), TLC silica gel 60 F254) yielded 2n (31.2 mg, 39%, Rf = 0.25) and 2n’ (36.4 mg, 45%, Rf = 0.36) as white solids.

(2n) \(^1\)H NMR (500 MHz, CDCl₃, ppm) \(\delta\) 8.37 (d, \(J = 8.0\) Hz, 1H), 8.25 (s, 1H), 8.10 (d, \(J = 8.0\) Hz, 1H), 7.65 (d, \(J = 8.0\) Hz, 2H), 7.54 (t, \(J = 7.5\) Hz, 2H). \(^{13}\)C NMR (125 MHz, CDCl₃, ppm) \(\delta\) 169.3, 155.6, 139.1, 134.4, 132.7 (q, \(J = 3.0\) Hz), 131.8 (q, \(J = 32.8\) Hz), 131.79, 129.7, 129.6, 126.9 (q, \(J = 3.6\) Hz), 125.6 (q, \(J = 33.3\) Hz), 125.3, 125.2, 124.9 (q, \(J = 31.7\) Hz), 123.3 (q, \(J = 3.9\) Hz), 123.1 (q, \(J = 4.5\) Hz), 122.8 (q, \(J = 31.3\) Hz).

(2n’) \(^1\)H NMR (500 MHz, CDCl₃, ppm) \(\delta\) 8.47 (s, 1H), 8.34 (s, 1H), 8.11 (d, \(J = 7.5\) Hz, 1H), 7.86 (d, \(J = 8.5\) Hz, 1H), 7.65 (d, \(J = 7.5\) Hz, 1H), 7.58 (dd, \(J = 8.5\) Hz, 1.0 Hz, 1H), 7.55 (t, \(J = 8.0\) Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl₃, ppm) \(\delta\) 169.3, 155.7, 145.8, 134.3, 132.9, 131.8 (q, \(J = 32.9\) Hz), 130.1, 129.7, 128.0 (q, \(J = 32.7\) Hz), 127.0 (q, \(J = 3.6\) Hz), 125.4, 124.8, 123.8, 123.3 (q, \(J = 3.7\) Hz), 123.2, 122.6, 121.7 (q, \(J = 3.4\) Hz), 121.1, 120.4, 119.1 (q, \(J = 4.1\) Hz). HRMS (ESI) m/z calcd for C\(_{17}\)H\(_8\)F\(_6\)NS\(_2\)\(^+\) (M+H\(^+\)) 403.9997, found 403.9996.
5-Methyl-2-\((m\text{-tolyl})\)benzo[4,5]thieno[3,2-\(d\)]thiazole (2\(o\))

7-Methyl-2-\((m\text{-tolyl})\)benzo[4,5]thieno[3,2-\(d\)]thiazole (2\(o'\))

Prepared from 3'-methylacetophenone (0.4 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 \(\mu\)m, hexane/dichloromethane = 5:1 (v./v.), TLC silica gel 60 F254) yielded 2\(o\) (36.5 mg, 62\%, \(R_f = 0.17\)) and 2\(o'\) (6.6 mg, 11\%, \(R_f = 0.27\)) as white solids.

(2\(o\)) \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.05 (d, \(J = 8.0\) Hz, 1H), 7.81 (s, 1H), 7.75 (d, \(J = 8.0\) Hz, 1H), 7.35 (t, \(J = 7.5\) Hz, 1H), 7.29 (t, \(J = 7.5\) Hz, 1H), 7.19 (d, \(J = 8.0\) Hz, 1H), 7.14 (d, \(J = 7.0\) Hz, 1H), 2.50 (s, 3H), 2.38 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 170.7, 156.7, 142.8, 138.9, 133.9, 132.5, 131.1, 130.4, 130.3, 128.9, 127.1, 125.6, 125.4, 123.8, 119.4, 21.4, 19.7.

(2\(o'\)) \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.03 (s, 1H), 7.81 (s, 1H), 7.75 (d, \(J = 8.0\) Hz, 1H), 7.63 (d, \(J = 8.0\) Hz, 1H), 7.29 (t, \(J = 7.5\) Hz, 1H), 7.19 (d, \(J = 8.0\) Hz, 1H), 7.16 (dd, \(J = 8.5\) Hz, 1.0 Hz, 1H), 2.46 (s, 3H), 2.38 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 170.7, 155.8, 139.9, 138.9, 135.0, 133.9, 131.1, 130.9, 130.7, 128.9, 127.0, 126.7, 123.8, 122.9, 122.0, 21.4, 21.4. HRMS (ESI) m/z calcd for \(C_{17}H_{14}NS_2^+\) (M+H)+ 296.0562, found 296.0564.
5-(Benzyloxy)-2-(3-(benzyloxy)phenyl)benzo[4,5]thieno[3,2-d]thiazole (2p)

7-(Benzyloxy)-2-(3-(benzyloxy)phenyl)benzo[4,5]thieno[3,2-d]thiazole (2p’)

Prepared from 3’-(benzyloxy)acetophenone 1p (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v/v.), TLC silica gel 60 F254, R_f = 0.34) yielded a mixture of 2p and 2p’ (18:1) as a light yellow solid, 44% yield (21.2 mg).

1H NMR (500 MHz, CDCl_3, ppm) δ 7.85 (d, J = 2.5 Hz, 1H), 7.72 (t, J = 1.5 Hz, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.51–7.48 (m, 3H), 7.44–7.39 (m, 5H), 7.37–7.32 (m, 3H), 7.12 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 7.07 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 5.22 (s, 2H), 5.18 (s, 2H).

13C NMR (125 MHz, CDCl_3, ppm) δ 170.1, 159.3, 157.3, 155.8, 136.8, 136.7, 135.3, 134.9, 132.1, 131.5, 130.2, 128.7, 128.6, 128.1, 128.0, 127.66, 127.62, 127.2, 124.0, 119.4, 117.1, 115.8, 112.6, 70.5, 70.3. (NMR signals of the major isomer 2p was given).

HRMS (ESI) m/z calcd for C_{29}H_{22}NO_{2}S_{2}^+ (M+H)^+ 480.1086, found 480.1087.

2-(2-Bromophenyl)benzo[4,5]thieno[3,2-d]thiazole (2q)

Prepared from 2’-bromoacetophenone 1q (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm,
hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, R_f = 0.33): yellow solid, 23% yield (7.9 mg).

^1H NMR (500 MHz, CDCl₃, ppm) δ 8.53 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.90 (td, J = 8.0 Hz, 1.0 Hz, 1H), 7.86 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H). ^13C NMR (125 MHz, CDCl₃, ppm) δ 168.7, 157.1, 143.2, 139.3, 136.5, 134.6, 133.6, 131.1, 130.3, 129.7, 129.3, 126.3, 125.6, 123.5, 122.2. HRMS (ESI) m/z calcd for C₁₅H₉BrNS₂⁺ (M+H)⁺ 345.9354, found 345.9914.

8-Methoxy-2-(2-methoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (2r)

Prepared from 2’-methoxyacetophenone 1r (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, R_f = 0.39): yellow solid, 64% yield (20.9 mg).

^1H NMR (500 MHz, CDCl₃, ppm) δ 8.30 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 7.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.51–7.46 (m, 2H), 7.23 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 4.15 (s, 3H), 3.94 (s, 3H). ^13C NMR (125 MHz, CDCl₃, ppm) δ 169.5, 159.6, 157.0, 143.2, 138.9, 136.1, 130.5, 129.6, 126.2, 125.6, 124.0, 123.5, 122.1, 120.5, 115.2, 55.6, 55.5. HRMS (ESI) m/z calcd for C₁₇H₁₄NO₂S₂⁺ (M+H)⁺ 328.0460, found 328.0464.
8-Methyl-2-(o-tolyl)benzo[4,5]thieno[3,2-d]thiazole (2s)

Prepared from 2’-methylacetophenone 1s (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.57): White solid, 48% yield (14.2 mg).

$^1$H NMR (500 MHz, CDCl₃, ppm) δ 7.70 (d, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.26 (d, $J = 4.0$ Hz, 2H), 7.25–7.16 (m, 3H), 2.92 (s, 3H), 2.66 (s, 3H). $^{13}$C NMR (125 MHz, CDCl₃, ppm) δ 169.2, 156.4, 142.7, 137.1, 133.7, 133.2, 131.8, 131.0, 129.8, 129.4, 129.4, 126.3, 126.2, 124.8, 120.6, 21.8, 19.6. HRMS (ESI) m/z calcd for C$_{17}$H$_{14}$NS$_2$+ (M+H)$^+$ 296.0562, found 296.0563.

8-(Benzyloxy)-2-(2-(benzyloxy)phenyl)benzo[4,5]thieno[3,2-d]thiazole (2t)

Prepared from 2’-benzyloxyacetophenone 1t (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.53): Light yellow solid, 77% yield (37.1 mg).

$^1$H NMR (500 MHz, CDCl₃, ppm) δ 8.62 (dd, $J = 8.0$ Hz, 1.5 Hz, 1H), 7.80 (d, $J = 7.5$ Hz, 2H), 7.47 (d, $J = 7.0$ Hz, 2H), 7.41–7.34 (m, 5H), 7.32–7.28 (m, 3H), 7.25 (t, $J = 8.0$ Hz, 2H), 7.20–7.12 (m, 5H), 7.08–7.00 (m, 3H), 6.89–6.80 (m, 3H), 6.78–6.70 (m, 3H), 6.67–6.59 (m, 3H), 5.11 (s, 3H), 4.03 (s, 3H).
Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 7.5 Hz, 1H), 5.34 (s, 2H), 5.27 (s, 2H). $^{13}$C NMR (125 MHz, CDCl, ppm) δ 164.6, 155.4, 154.1, 153.2, 144.6, 144.6, 137.5, 136.0, 131.9, 130.5, 130.4, 130.4, 128.9, 128.7, 128.4, 128.3, 128.0, 127.5, 127.5, 126.9, 125.8, 123.3, 121.3, 121.2, 116.3, 112.6, 107.9, 71.0, 70.3. HRMS (ESI) m/z calcd for C$_{29}$H$_{21}$N$_{4}$O$_{2}$S$_{2}$+ (M+Na)$^+$ 502.0906, found 502.0920.

![Chemical structure](image)


Prepared from 2-acetylthiophene 1u (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:3 (v./v.), TLC silica gel 60 F254, R$_f$ = 0.43): Yellow solid, 37% yield (10.5 mg).

$^1$H NMR (500 MHz, CDCl, ppm) δ 8.22 (dd, J = 3.5 Hz, 1.0 Hz, 1H), 7.84 (dd, J = 3.5 Hz, 1.0 Hz, 1H), 7.56 (d, J = 5.0 Hz, 1H), 7.35 (d, J = 5.0 Hz, 1H), 7.28 (t, J = 5.0 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl, ppm) δ 168.7, 152.9, 142.4, 139.8, 139.5, 137.0, 136.4, 129.5, 128.5, 128.0, 120.5. HRMS (ESI) m/z calcd for C$_{11}$H$_{6}$NS$_{4}$+ (M+H)$^+$ 279.9378, found 279.9385.

![Chemical structure](image)

2-(Pyridin-3-yl)thiazolo[4',5':4,5]thieno[2,3-b]pyridine (2v)

2-(Pyridin-3-yl)thiazolo[4',5':4,5]thieno[3,2-c]pyridine (2v’)

S36
Prepared from 3-acetylpyridine (0.2 mmol) as shown in the general experimental procedure A and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.28) yielded a mixture of 2v and 2v' (8:1) as a white solid, 83% yield (22.4 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) δ 9.80 (d, J = 2.0 Hz, 0.11H), 9.19 (d, J = 2.0 Hz, 1H), 9.11 (dd, J = 8.5 Hz, 1.5 Hz, 0.11H), 8.81 (dd, J = 5.0 Hz, 1.5 Hz, 0.11H), 8.72 (dd, J = 4.5 Hz, 1.5 Hz, 0.22H), 8.63 (dd, J = 4.5 Hz, 1.5 Hz, 1H), 8.58 (dd, J = 4.5 Hz, 1.5 Hz, 0.11H), 8.53 (4.5 Hz, 1.5 Hz, 1H), 8.46 (dd, J = 8.0 Hz, 1.5 Hz, 0.11H), 8.42 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 8.24 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.47–7.41 (m, 0.33H), 7.40–7.35 (m, 2H), 7.26 (dd, J = 8.0 Hz, 4.5 Hz, 0.11 H). \(^13\)C NMR (125 MHz, CDCl\(_3\), ppm) δ 166.5, 164.3, 153.8, 152.5, 152.2, 151.1, 150.6, 147.9, 147.6, 147.0, 138.1, 135.4, 133.7, 131.5, 130.7, 129.7, 129.7, 129.3, 128.3, 127.1, 124.9, 123.9, 123.4, 120.8, 120.6, 120.3. HRMS (ESI) m/z calcd for C\(_{13}\)H\(_8\)N\(_3\)S\(_2\)\(^+\) (M+H)\(^+\) 270.0154, found 270.0161.

**Benzo[4,5]thieno[3,2-d]thiazol-2-yl(phenyl)methanone (3a)**

Prepared from acetophenone 1a (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.42): Light yellow solid, 82% yield (24.3 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) δ 8.63 (dd, J = 8.5 Hz, 1.5 Hz, 2H), 8.31 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.68 (td, J = 8.0 Hz, 1.5 Hz, 1H), 7.58 (t, J = 7.5 Hz,
2H), 7.53 (td, $J = 7.5$ Hz, 1.0 Hz, 1H), 7.47 (td, $J = 7.5$ Hz, 1.5 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 183.7, 169.5, 157.0, 143.2, 138.8, 135.0, 133.7, 131.2, 130.5, 128.5, 126.2, 125.5, 123.5, 123.2. HRMS (ESI) m/z calcd for C$_{16}$H$_9$NNaOS$_2^+$ (M+Na)$^+$ 318.0018, found 318.0019.

![Chemical Structure](image)

(6-Methylbenzo[4,5]thieno[3,2-d]thiazol-2-yl)(p-tolyl)methanone (3b)

Prepared from 4'-methylacetophenone 1b (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, $R_f = 0.41$): Light yellow solid, 84% yield (27.2 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.55 (d, $J = 8.0$ Hz, 2H), 8.18 (d, $J = 8.0$ Hz, 1H), 7.66 (s, 1H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 1H), 2.53 (s, 3H), 2.48 (s, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 183.3, 169.7, 157.0, 144.7, 143.5, 137.8, 136.4, 132.4, 131.3, 129.2, 128.2, 127.0, 123.4, 121.7, 21.8, 21.6. HRMS (ESI) m/z calcd for C$_{18}$H$_{13}$NNaOS$_2^+$ (M+Na)$^+$ 346.0331, found 346.0333.

![Chemical Structure](image)

(6-Methoxybenzo[4,5]thieno[3,2-d]thiazol-2-yl)(4-methoxyphenyl)methanone (3c)

Prepared from 4'-methoxyacetophenone 1c (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 µm,
hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, R_f = 0.33): Light yellow solid, 78% yield (27.8 mg).

^1^H NMR (500 MHz, CDCl_3, ppm) δ 8.70 (d, J = 9.0 Hz, 2H), 8.17 (d, J = 8.5 Hz, 1H), 7.34 (d, J = 2.0, 1H), 7.13 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 7.05 (d, J = 9.0 Hz, 2H), 3.93 (s, 3H), 3.91 (s, 3H). \(^1^3^C\) NMR (125 MHz, CDCl_3, ppm) δ 181.9, 170.1, 164.2, 158.6, 156.7, 144.7, 136.1, 133.6, 127.8, 124.2, 122.6, 114.5, 113.8, 106.8, 55.7, 55.5. HRMS (ESI) m/z calcd for C_{18}H_{14}NO_3S_2^+ (M+H)^+ 356.0410, found 356.0407.

![Image](image1.png)

(6-Chlorobenzo[4,5]thieno[3,2-d]thiazol-2-yl)(4-chlorophenyl)methanone (3e)

Prepared from 4'-chloroacetophenone 1e (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, R_f = 0.38): Light yellow solid, 61% yield (22.3 mg).

^1^H NMR (500 MHz, CDCl_3, ppm) δ 8.60 (d, J = 8.5 Hz, 2H), 8.21 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 1.5 Hz, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.52 (dd, J = 8.5 Hz, 1.5 Hz, 1H). \(^1^3^C\) NMR (125 MHz, CDCl_3, ppm) δ 182.3, 169.6, 156.2, 144.1, 140.6, 139.1, 133.1, 132.5, 132.3, 128.9, 128.8, 126.4, 123.2, 122.7. HRMS (ESI) m/z calcd for C_{16}H_{8}(^{35}Cl)_2NO_3S_2^+ (M+H)^+ 363.9419, found 363.9417.

![Image](image2.png)
(6-Bromobenzo[4,5]thieno[3,2-d]thiazol-2-yl)(4-bromophenyl)methanone (3f)

Prepared from 4'-bromoacetophenone 1f (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.36): Yellow solid, 54% yield (24.4 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 8.51 (d, J = 6.5 Hz, 2.0 Hz, 2H), 8.15 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 1.5 Hz, 1H), 7.72 (d, J = 9.0 Hz, 7.0 Hz, 2H), 7.66 (d, J = 8.5 Hz, 1.5 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 182.5, 169.6, 156.3, 144.4, 139.2, 133.5, 132.6, 131.9, 129.4, 129.2, 129.0, 126.1, 123.0, 120.0. HRMS (ESI) m/z calcd for C$_{16}$H$_8$(79Br)$_2$NO$_2$ (M+H)$^+$ 451.8409, found 451.8411.

![Chemical Structure](image)

(6-(Trifluoromethyl)benzo[4,5]thieno[3,2-d]thiazol-2-yl)(4-(Trifluoromethyl)phenyl)methanone (3g)

Prepared from 4'-(trifluoromethyl)acetophenone 1g (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.44): Light yellow solid, 87% yield (37.6 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) δ 8.73 (d, J = 8.0 Hz, 2H), 8.41 (d, J = 8.5 Hz, 1H), 8.18 (s, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.5 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) δ 182.8, 169.5, 156.1, 143.1, 141.5, 137.6, 135.0 (q, J = 32.8 Hz), 132.8, 131.4, 128.5 (q, J = 30.6 Hz), 125.5 (q, J = 3.8 Hz), 125.1, 124.8, 122.9, 122.6 (q, J =
3.5 Hz), 122.5, 121.0 (q, \( J = 4.1 \) Hz). HRMS (ESI) m/z calcd for C\(_{18}\)H\(_8\)F\(_6\)NOS\(_2\)\(^+\) (M+H)\(^+\) 431.9946, found 431.9943.

![Chemical Structure](image)


Prepared from 4’-fluoroacetophenone 1h (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 µm, hexane/dichloromethane = 2:1 (v/v.), TLC silica gel 60 F254, \( R_f = 0.47 \)): Light yellow solid, 88% yield (29.3 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \( \delta \) 8.73–8.70 (m, 2H), 8.24 (dd, \( J = 8.5 \) Hz, 5.5 Hz, 1H), 7.58 (ddd, \( J = 8.5 \) Hz, 2.5 Hz, 1H), 7.31–7.23 (m, 4H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \( \delta \) 181.9, 169.8, 166.3 (d, \( J_{CF} = 256.6 \) Hz), 161.3 (d, \( J_{CF} = 247.6 \) Hz), 156.2, 144.2 (d, \( J_{CF} = 9.9 \) Hz), 138.0 (d, \( J_{CF} = 2.2 \) Hz), 134.0 (d, \( J_{CF} = 9.4 \) Hz), 131.7, 131.1 (d, \( J_{CF} = 2.9 \) Hz), 128.5 (d, \( J_{CF} = 8.4 \) Hz), 126.9 (d, \( J_{CF} = 2.0 \) Hz), 125.4, 123.0 (d, \( J_{CF} = 9.3 \) Hz), 116.2 (d, \( J_{CF} = 22.1 \) Hz), 115.7 (d, \( J_{CF} = 21.7 \) Hz), 114.2 (d, \( J_{CF} = 23.9 \) Hz), 110.2 (d, \( J_{CF} = 26.0 \) Hz). HRMS (ESI) m/z calcd for C\(_{16}\)H\(_8\)F\(_2\)NOS\(_2\)\(^+\) (M+H)\(^+\) 332.0010, found 332.0016.

![Chemical Structure](image)

Prepared from 3’-methoxyacetophenone 1m (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.35): Light yellow solid, 71% yield (25.1 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.29 (d, J = 8.0 Hz, 1H), 8.15 (t, J = 2.0 Hz, 1H), 7.90 (d, J = 3.0 Hz, 1H), 7.49 (td, J = 8.0 Hz, 3.0 Hz, 2H), 7.23 (dd, J = 11.0 Hz, 1.0 Hz, 1H), 6.94 (d, J = 8.0Hz, 1H), 4.05 (s, 3H), 3.93 (s, 3H).

13C NMR (125 MHz, CDCl3, ppm) δ 183.4, 169.5, 159.5, 157.4, 154.4, 139.4, 136.1, 132.0, 129.4, 127.0, 124.0, 120.5, 115.1, 114.6, 106.4, 55.8, 55.5.

HRMS (ESI) m/z calcd for C18H14NO3S2+ (M+H)+ 356.0410, found 356.0409.

(5-Methylbenzo[4,5]thieno[3,2-d]thiazol-2-yl)(m-tolyl)methanone (3o)

(7-Methylbenzo[4,5]thieno[3,2-d]thiazol-2-yl)(m-tolyl)methanone (3o’)

Prepared from 3’-methylacetophenone 1o (0.4 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254) yielded a mixture of 3 and 3’ (7:1) as a pale yellow solid, 88% yield (56.7 mg).

1H NMR (500 MHz, CDCl3, ppm) δ 8.39 (d, J = 7.0 Hz, 1.33H), 8.27 (s, 1H), 8.24 (s, 0.33H), 8.05 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 8.00 (m, 0.33H), 7.63 (dd, J = 8.0 Hz, 4.5 Hz, 0.33H), 7.41–7.34 (m, 3.93H), 7.19–7.17 (m, 1.99H), 2.49 (s, 3H), 2.46 (0.99H), 2.41 (s, 0.99H), 2.40 (s, 3H).

13C NMR (125 MHz, CDCl3, ppm) δ 184.0, 169.5, 169.4, 157.7,
HRMS (ESI) m/z calcd for C_{18}H_{13}NNaO_{2}^+ (M+Na)^+ 346.0331, found 346.0332.


Prepared from 3’-(benzyloxy)acetophenone 1p (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, R_f = 0.47): Orange solid, 74% yield (37.6 mg).

^1H NMR (500 MHz, CDCl_3, ppm) δ 8.31 (dt, J = 8.0 Hz, 1.5 Hz, 1H), 8.22 (dt, J = 2.5 Hz, 1.5 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.52–7.33 (m, 12H), 7.29 (ddd, J = 8.0 Hz, 2.5 Hz, 1.5 Hz, 1H), 6.99 (d, J = 7.5 Hz, 1H), 5.33 (s, 2H), 5.20 (s, 2H). ^13C NMR (125 MHz, CDCl_3, ppm) δ 183.4, 169.5, 158.8, 157.4, 153.5, 139.5, 136.6, 136.3, 136.2, 132.1, 132.0, 129.5, 128.7, 128.6, 128.2, 128.1, 127.6, 127.2, 126.9, 124.3, 121.3, 116.1, 114.9, 108.0, 70.6, 70.2. HRMS (ESI) m/z calcd for C_{30}H_{22}NO_{3}S_{2}^+ (M+H)^+ 508.1036, found 508.1040.
Benzo[4,5]thieno[3,2-\textit{d}]thiazol-2-yl(2-bromophenyl)methanone (3q)

Prepared from 2'-bromoacetophenone 1q (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, R_f = 0.47): Light yellow solid, 34% yield (12.6 mg).

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, ppm) δ 8.20 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.77 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.50–7.42 (m, 4H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, ppm) δ 186.6, 176.4, 167.7, 152.9, 142.4, 139.7, 138.1, 133.7, 132.1, 130.8, 130.2, 126.9, 126.3, 125.5, 123.5, 122.4, 120.7. HRMS (ESI) m/z calcd for C\textsubscript{16}H\textsubscript{9}BrN\textsubscript{2}O\textsubscript{2} + (M+H)	extsuperscript{+} 373.9303, found 373.9301.

Thieno[2',3':4,5]thieno[3,2-\textit{d}]thiazol-2-yl(thiophen-2-yl)methanone (3u)

Prepared from 2-acetylthiophene 1u (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, R_f = 0.47): Light yellow solid, 62% yield (19.1 mg).

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, ppm) δ 8.79 (dd, J = 3.5 Hz, 1.0 Hz, 1H), 7.84 (dd, J = 3.5 Hz, 1.0 Hz, 1H), 7.56 (d, J = 5.0 Hz, 1H), 7.35 (d, J = 5.0 Hz, 1H), 7.28 (t, J = 5.0 Hz, 1H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, ppm) δ 175.7, 168.7, 152.9, 142.4, 139.8, 139.6, 138.5.
137.0, 136.3, 129.5, 129.5, 128.5, 128.0, 120.5. HRMS (ESI) m/z calcd for C_{12}H_{6}NO_{4}S^{+} (M+H)^{+} 307.9327, found 307.9324.

\[
\text{2-(Pyridin-3-yl)thiazolo[4',5':4,5]thieno[2,3-b]pyridine (3v)}
\]

\[
\text{2-(Pyridin-3-yl)thiazolo[4',5':4,5]thieno[3,2-c]pyridine (3v')}
\]

Prepared from 3-acetylpyridine (0.2 mmol) as shown in the general experimental procedure B and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 1:1 (v./v.), TLC silica gel 60 F254, R_f = 0.28) yielded a mixture of 3 and 3' (7:1) as a white solid, 75% yield (22.2 mg).

\[
\text{1H NMR (500 MHz, CDCl}_3\text{, ppm)} \delta 9.81 (d, J = 1.5 Hz, 1H), 9.20 (d, J = 1.5 Hz, 0.12H), 8.82 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 8.75 (dt, J = 8.0 Hz, 1.5 Hz, 1H), 8.64 (dd, J = 5.0 Hz, 1.5 Hz, 0.12H), 8.59 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 8.54 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 8.48 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 8.44 (dd, J = 8.0 Hz, 1.5 Hz, 0.12H), 8.27 (dt, J = 8.0 Hz, 1.5 Hz, 0.12H).
\]

\[
\text{13C NMR (125 MHz, CDCl}_3\text{, ppm)} \delta 182.3, 168.2, 164.7, 153.7, 153.3, 152.1, 150.9, 147.9, 147.5, 147.0, 139.4, 138.2, 133.8, 130.7, 129.7, 129.3, 125.0, 123.9, 123.5, 120.7, 120.3. HRMS (ESI) m/z calcd for C_{14}H_{8}N_{3}OS_{2}^{+} (M+H)^{+} 298.0103, found 298.0105.
\]

\[
\text{2-(Pyridin-4-yl)benzo[4,5]thieno[3,2-d]thiazole (4a)}
\]
Prepared from acetophenone 1a (0.2 mmol) and 4-picoline (0.4 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.64): Yellow solid, 73% yield (39.3 mg). This compound is known.²

¹H NMR (500 MHz, DMSO-d₆, ppm) δ 8.76 (dd, J = 2.5 Hz, 1.5 Hz, 2H), 8.0 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.99 (dd, J = 2.5 Hz, 1.5 Hz, 2H), 7.57 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.51 (td, J = 7.5 Hz, 1.0 Hz, 1H). ¹³C NMR (125 MHz, DMSO-d₆, ppm) δ 167.8, 155.6, 151.3, 143.3, 140.3, 134.3, 130.1, 126.1, 125.9, 124.5, 121.6, 120.3.

2-(3-Methylpyridin-4-yl)benzo[4,5]thieno[3,2-d]thiazole (4b)

Prepared from acetophenone 1a (0.1 mmol) and 3,4-lutidine (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 1:1 (v./v.), TLC silica gel 60 F254, Rf = 0.57): Yellow solid, 51% yield (14.4 mg). This compound is known.²

¹H NMR (500 MHz, CDCl₃, ppm) δ 8.63 (s, 1H), 8.58 (d, J = 5.0 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 5.0 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 2.74 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm) δ 166.9, 156.2, 152.7, 147.5, 142.9, 139.6, 132.6, 130.7, 130.3, 125.6, 125.3, 123.4, 122.6, 121.9, 18.7.

2-(Pyridin-2-yl)benzo[4,5]thieno[3,2-d]thiazole (4c)

Prepared from acetophenone 1a (0.2 mmol) and 2-picoline (0.4 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 µm, hexane/ethyl acetate = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.63): Yellow solid, 74% yield (39.6 mg). This compound is known.\(^2\)

\(^1\)H NMR (500 MHz, DMSO-\(d_6\), ppm) \(\delta\) 8.69 (d, \(J = 4.0\) Hz, 1H), 8.27 (d, \(J = 8.0\) Hz, 1H), 8.19 (d, \(J = 8.0\) Hz, 1H), 8.12 (d, \(J = 8.0\) Hz, 1H), 8.03 (t, \(J = 6.5\) Hz, 1H), 7.58–7.48 (m, 3H). \(^13\)C NMR (125 MHz, DMSO-\(d_6\), ppm) \(\delta\) 171.8, 155.7, 151.0, 150.2, 143.2, 138.4, 134.5, 130.3, 125.9, 125.9, 125.8, 124.5, 121.4, 119.7.

2-(6-Methylpyridin-2-yl)benzo[4,5]thieno[3,2-d]thiazole (4d)

Prepared from acetophenone 1a (0.1 mmol) and 2,6-lutidine (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 µm, hexane/ethyl acetate = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.69): Yellow solid, 63% yield (17.6 mg). This compound is known.\(^2\)

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.26 (d, \(J = 8.0\) Hz, 1H), 8.11 (d, \(J = 8.0\) Hz, 1H), 7.84 (d, \(J = 8.5\) Hz, 1H), 7.71 (t, \(J = 7.5\) Hz, 1H), 7.50 (t, \(J = 7.0\) Hz, 1H), 7.41 (t, \(J = 8.5\) Hz, 1H), 7.19 (d, \(J = 7.5\) Hz, 1H), 2.63 (s, 3H). \(^13\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\)
2-(3-Methylpyridin-2-yl)benzo[4,5]thieno[3,2-d]thiazole (4e)

Prepared from acetophenone 1a (0.1 mmol) and 2,3-lutidine (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 2:1 (v./v.), TLC silica gel 60 F254, Rf = 0.72): Yellow solid, 42% yield (11.9 mg).

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.49 (dd, $J = 5.0$ Hz, 0.5 Hz, 1H), 8.23 (d, $J = 8.0$ Hz, 1H), 7.85 (dd, $J = 8.0$ Hz, 1H), 7.64 (dd, $J = 8.0$ Hz, 0.5 Hz, 1H), 7.50 (td, $J = 7.5$ Hz, 1.0 Hz, 1H), 7.40 (td, $J = 7.5$ Hz, 1.0 Hz, 1H), 7.23 (dd, $J = 7.5$ Hz, 5.0 Hz, 1H), 2.94 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 173.2, 156.5, 149.0, 146.6, 142.8, 140.0, 133.4, 132.0, 131.0, 125.0, 125.0, 123.6, 123.3, 121.6, 21.0. HRMS (ESI) m/z calcd for C$_{15}$H$_{11}$N$_2$S$_2$ $^+$ (M+H)$^+$ 283.0358, found 283.0361.

2-(Quinolin-2-yl)benzo[4,5]thieno[3,2-d]thiazole (4f)

Prepared from acetophenone 1a (0.1 mmol) and quinaldine (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 μm,
hexane/ethyl acetate = 2:1 (v./v.), TLC silica gel 60 F254, R_f = 0.38): Yellow solid, 34% yield (11.0 mg). This compound is known.\(^2\)

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.45 (d, \(J = 9.0\) Hz, 1H), 8.29 (t, \(J = 9.0\) Hz, 2H), 8.15 (d, \(J = 8.5\) Hz, 1H), 7.85 (t, \(J = 8.0\) Hz, 2H), 7.75 (td, \(J = 7.5\) Hz, 1.5 Hz, 1H), 7.57 (td, \(J = 7.5\) Hz, 1.0 Hz, 1H), 7.52 (td, \(J = 7.5\) Hz, 1.0 Hz, 1H), 7.43 (td, \(J = 7.5\) Hz, 1.0 Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 171.9, 156.5, 151.3, 147.8, 143.0, 137.0, 134.4, 130.6, 130.1, 129.4, 128.8, 127.7, 127.1, 125.2, 125.2, 123.4, 121.7, 117.8.

2-(Benzo[4,5]thieno[3,2-d]thiazol-2-yl)-5-methylbenzo[d]oxazole (4g)

Prepared from acetophenone 1a (0.1 mmol) and 2,5-dimethylbenzoxazole (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 \(\mu\)m, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, R_f = 0.64): Tan solid, 54% yield (17.2 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \(\delta\) 8.41 (d, \(J = 7.5\) Hz, 1H), 7.88 (d, \(J = 8.0\) Hz, 1H), 7.62 (s, 1H), 7.57–7.54 (m, 2H), 7.48 (t, \(J = 7.0\) Hz, 1H), 7.27–7.25 (m, 1H), 2.51 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \(\delta\) 171.9, 156.9, 156.0, 149.0, 143.2, 141.6, 153.4, 153.0, 130.0, 127.9, 126.0, 125.6, 123.5, 122.3, 120.4, 110.6, 21.5. HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{11}\)N\(_2\)O\(_5\)S\(_2\)\(^{\text{+}}\) (M+H\(^+\)) 323.0307, found 323.0309.
2-(Pyridin-4-yl)benzo[4,5]thieno[3,2-d]thiazole (4a)

Prepared from acetophenone 1a (0.1 mmol) and 4-ethylpyridine (0.2 mmol) as shown in the general experimental procedure C and purified on silica gel (230-400 mesh or 37-63 μm, hexane/ethyl acetate = 3:2 (v./v.), TLC silica gel 60 F254, Rf = 0.55): Yellow solid, 68% yield (16.4 mg).

![Structure 4a]

2-(p-Tolyl)benzo[4,5]thieno[3,2-d]thiazole (5a)

Prepared from acetophenone 1a (0.4 mmol) and p-tolylacetic acid (0.2 mmol) as shown in the general experimental procedure D and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 8:1 (v./v.), TLC silica gel 60 F254, Rf = 0.38 (Hexane/DCM:3/1): White solid, 47% yield (26.5 mg). This compound is known.¹

¹H NMR (500 MHz, CDCl₃, ppm) δ 8.26 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.49 (td, J = 8.0 Hz, 1.5 Hz, 1H), 7.40 (td, J = 8.0 Hz, 1.5 Hz, 1H), 7.28 (d, J = 8.5 Hz, 2H), 2.41 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm) δ 170.8, 156.0, 142.8, 140.6, 131.4, 130.6, 130.4, 129.8, 129.1, 126.6, 125.5, 125.16, 125.13, 125.0, 123.3, 121.8, 21.5.

![Structure 5a]

2-(3-Methoxyphenyl)benzo[4,5]thieno[3,2-d]thiazole (5b)
Prepared from acetophenone 1a (0.4 mmol) and 3-methoxyphenylacetic acid (0.2 mmol) as shown in the general experimental procedure D and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 5:1 (v./v.), TLC silica gel 60 F254, Rf = 0.23: White solid, 58% yield (34.3 mg). This compound is known.¹

¹H NMR (500 MHz, CDCl₃, ppm) δ 8.28 (d, J = 7.5 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 2.5 Hz, 1H), 7.60 (d, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.41 (td, J = 8.0 Hz, 1.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.01 (dd, J = 8.0 Hz, 2.5 Hz, 1H), 3.92 (s, 3H).¹³C NMR (125 MHz, CDCl₃, ppm) δ 170.4, 160.1, 156.0, 142.8, 135.3, 130.9, 130.5, 130.1, 125.16, 125.12, 123.3, 121.9, 119.1, 116.5, 111.3, 55.5.

2-(4-(Trifluoromethyl)phenyl)benzo[4,5]thieno[3,2-d]thiazole (5c)

Prepared from acetophenone 1a (0.4 mmol) and 2-(4-(trifluoromethyl)phenyl)acetic acid (0.2 mmol) as shown in the general experimental procedure D and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 15:1 (v./v.), TLC silica gel 60 F254, Rf = 0.46 (Hexane/DCM:2/1): White solid, 38% yield (25.5 mg). This compound is known.³

¹H NMR (500 MHz, CDCl₃, ppm) δ 8.28 (d, J = 8.0 Hz, 1H), 8.17 (d, J = 8.5 Hz, 2H), 7.86 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.52 (t, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃, ppm) δ 168.4, 156.5, 142.9, 137.1, 131.9,

130.5 (q, \( J = 276.9 \) Hz), 128.1, 126.7, 126.1 (q, \( J = 3.7 \) Hz), 125.5, 125.3, 124.9, 123.4, 122.8, 121.9.

![Diagram of 2-(p-Tolyl)benzo[4,5]thieno[3,2-d]thiazole (5a)](image)


Prepared from acetophenone 1a (0.2 mmol) and \( p \)-tolualdehyde (0.1 mmol) as shown in the general experimental procedure E and purified on silica gel (230-400 mesh or 37-63 \( \mu \)m, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, \( R_f = 0.56 \): White solid, 68\% yield (19.2 mg).

![Diagram of 2-(Benzo[d][1,3]dioxol-5-yl)benzo[4,5]thieno[3,2-d]thiazole (5d)](image)

**2-(Benzo[d][1,3]dioxol-5-yl)benzo[4,5]thieno[3,2-d]thiazole (5d)**

Prepared from acetophenone 1a (0.2 mmol) and piperonal (0.1 mmol) as shown in the general experimental procedure E and purified on silica gel (230-400 mesh or 37-63 \( \mu \)m, hexane/dichloromethane = 1:1 (v./v.), TLC silica gel 60 F254, \( R_f = 0.42 \): White solid, 48\% yield (14.9 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\), ppm) \( \delta \) 8.28 (d, \( J = 7.5 \) Hz, 1H), 7.86 (d, \( J = 8.0 \) Hz, 1H), 7.60 (s, 1H), 7.57 (d, \( J = 8.0 \) Hz, 1H), 7.52 (t, \( J = 7.5 \) Hz, 1H), 7.43 (t, \( J = 7.5 \) Hz, 1H), 6.92 (d, \( J = 8.0 \) Hz, 1H), 6.08 (s, 2H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\), ppm) \( \delta \) 170.2, 155.7, 159.5, 148.4, 142.7, 130.5, 130.0, 128.4, 125.1, 125.0, 123.3, 121.8, 121.2, 108.7, 106.9, 101.6. HRMS (ESI) m/z calcd for C\(_{16}\)H\(_{16}\)NO\(_2\)S\(_2\)\(^+\) (M+H)\(^+\) 312.0147, found 312.0149.
4-(4-Fluorophenyl)-5H-1,2,3-dithiazole-5-thione (4-4F)

Prepared from acetophenone ketoxime acetate (0.4 mmol) as shown in the general experimental procedure F and purified on silica gel (230-400 mesh or 37-63 μm, hexane/dichloromethane = 2:1 (v./v.), TLC silica gel 60 F254, RF = 0.72: Brown solid, 72% yield (65.8 mg). This compound is known.4

1H NMR (500 MHz, CDCl3, ppm) δ 7.98–7.95 (m, 2H), 7.16–7.12 (m, 2H). 13C NMR (125 MHz, CDCl3, ppm) δ 207.9, 166.7, 164.0 (d, 1JC_F = 251.9 Hz), 131.7 (d, 3JC_F = 8.5 Hz), 127.5 (d, 4JC_F = 3.5 Hz), 115.2 (d, 2JC_F = 21.7 Hz).

6) Copies of $^1$H and $^{13}$C NMR spectra of products

$^1$H and $^{13}$C NMR spectra of 2a
$^1$H and $^{13}$C NMR spectra of 2b
$^1$H and $^{13}$C NMR spectra of 2c
$^1$H and $^{13}$C NMR spectra of 2d
$^1$H and $^{13}$C NMR spectra of 2e
$^1$H and $^{13}$C NMR spectra of 2f
$^1$H and $^{13}$C NMR spectra of 2g
$^1$H and $^{13}$C NMR spectra of 2h
$^1$H and $^{13}$C NMR spectra of 2i
$^1$H and $^{13}$C NMR spectra of 2j
$^1$H and $^{13}$C NMR spectra of 2k
\(^1\)H and \(^{13}\)C NMR spectra of 2k*
$^1$H and $^{13}$C NMR spectra of 2l and 2l'}
$^1$H and $^{13}$C NMR spectra of 2m and 2m$'$
$^1$H and $^{13}$C NMR spectra of 2n
$^1$H and $^{13}$C NMR spectra of 2n$^*$
$^1$H and $^{13}$C NMR spectra of 2o
$^1$H and $^{13}$C NMR spectra of 2o
$^1$H and $^{13}$C NMR spectra of $2r$ and $2r'$
$^1$H and $^{13}$C NMR spectra of 2q
$^1$H and $^{13}$C NMR spectra of 2r
$^1$H and $^{13}$C NMR spectra of 2s
$^1$H and $^{13}$C NMR spectra of 2t
$^1$H and $^{13}$C NMR spectra of 2u
$^1$H and $^{13}$C NMR spectra of 2v + 2v′
$^1$H and $^{13}$C NMR spectra of 3a
$^1$H and $^{13}$C NMR spectra of 3b
$^1$H and $^{13}$C NMR spectra of $3e$
$^1$H and $^{13}$C NMR spectra of 3e
$^{1}$H and $^{13}$C NMR spectra of 3f
${}^{1}H$ and $^{13}C$ NMR spectra of 3g
$^1$H and $^{13}$C NMR spectra of $3h$
$^1$H and $^{13}$C NMR spectra of 3m
$^{1}$H and $^{13}$C NMR spectra of 3o and 3o'
$^1$H and $^{13}$C NMR spectra of 3p
$^1$H and $^{13}$C NMR spectra of 3q
$^1$H and $^{13}$C NMR spectra of 3u
$^1$H and $^{13}$C NMR spectra of 3v and 3v’
$^1$H and $^{13}$C NMR spectra of 4a
$^1$H and $^{13}$C NMR spectra of 4b
$^1$H and $^{13}$C NMR spectra of 4c
$^1$H and $^{13}$C NMR spectra of 4d
$^1$H and $^{13}$C NMR spectra of 4e
$^1$H and $^{13}$C NMR spectra of 4f
$^1$H and $^{13}$C NMR spectra of 4g
$^1$H and $^{13}$C NMR spectra of 5a
$^1$H and $^{13}$C NMR spectra of 5b
$^1$H and $^{13}$C NMR spectra of 5c

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$^1$H and $^{13}$C NMR spectra of 5d
$^1$H and $^{13}$C NMR spectra of 4-4F