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Supplementary information

Base-promoted regioselective synthesis of alkyl (2-tosyl/4ethylcarbonyl) thiazole-5-carboxylates employing dithioates and active methylene isocyanides

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General Procedure for the Synthesis of Alkyl 2-(Methylthio)-2-thioxoacetates (1a-s)



Reaction conditions: i. a (10 mmol, 1 equiv.), chloroacetyl chloride (10 mmol, 1 equiv.), Et₃N (20 mmol, 2 equiv.), DCM (10 mL). ii. S₈ (2.5 mmol, 0.25 equiv.), Et₃N (2 mmol, 2 equiv.), DMF (15 mL), 0 °C-RT, 6-8 h, Mel (1 mmol, 1 equiv.), 0 °C-RT, 0.5-1 h.

A solution of alcohols I (10.0 mmol, 1 equiv) in dichloromethane (10 mL) was cooled to 0 °C and added triethylamine (20.0 mmol, 2 equiv). After 10 minutes chloroacetyl chloride (10.0 mmol, 1 equiv) was added dropwise over a period. The completion of the reaction was monitored by TLC, which leads to the formation of alkyl 2-chloroacetate II. The excess DCM was removed under reduced pressure. The resulting alkyl 2-chloroacetates II and sulfur (2.5 mmol, 0.25 equiv) were stirred in DMF (15 mL) at 0 °C for 10 minutes. Later triethylamine (20.0 mmol, 2 equiv) was added slowly to the reaction mixture. The mixture was stirred at room temperature up to 8 h and concentrated under a vacuum to remove excess triethylamine. Then, methylation reaction was performed at 0 °C using iodomethane (10.0 mmol, 1 equiv) up to 60 minutes. The reaction was quenched with ice-cooled water and product was extracted with ethyl acetate and dried over Na₂SO₄. The solvent was evaporated, and the crude product was purified by column chromatography using hexane/ethyl acetate (10:90) as eluent to afford the precursors (**1a-s**).

Characterization Details of Compounds (1a-s)

4-Ethylbenzyl 2-(Methylthio)-2-thioxoacetate (1i): Wine red liquid; Yield 1.930 g (76%); IR:



 $u_{max}(cm^{-1})$ 735, 820, 1039, 1171, 1247, 1718, 2173, 3039; ¹H NMR (600 MHz, CDCl₃): δ 7.34 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.21 (d, *J* = 8.4 Hz, 2H, Ar-H), 5.31 (s, 2H, CH₂), 2.67 – 2.61 (m, 2H, CH₂), 2.65 (s, 3H, SMe), 1.23 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃): 217.0, 160.3, 145.0, 129.1, 128.7, 128.3, 68.9, 28.7, 19.7, 15.6;

HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₂H₁₅O₂S₂ 255.0508; found 255.0507.

3,4-Dimethoxybenzyl 2-(Methylthio)-2-thioxoacetate (1m): Wine red solid; Yield 2.178 g



(76%); IR: v_{max} (cm⁻¹) 745, 824, 1027, 1180, 1248, 1716, 2169, 3041; ¹H NMR (400 MHz, CDCl₃): δ 6.93 (dd, J = 8.1, 2.1 Hz, 1H, Ar-H), 6.89 (d, J = 2.1 Hz, 1H, Ar-H), 6.79 (d, J = 8.1 Hz, 1H, Ar-H), 5.22 (s, 2H, CH₂), 3.82 (s, 3H, OMe), 3.81 (s, 3H, OMe), 2.59 (s, 3H, SMe). ¹³C NMR (101 MHz, CDCl₃): ¹³C NMR (101 MHz, CDCl₃) δ

216.9, 160.3, 149.4, 149.0, 127.1, 121.6, 111.8, 111.0, 69.0, 55.9, 19.6; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{15}O_4S_2$ 287.0412; found 287.0407.

3-Fluorobenzyl 2-(Methylthio)-2-thioxoacetate (**1***n*): Wine red liquid; Yield 1.413 g (73%); IR: $\bigcirc_{max}(cm^{-1}) 717, 804, 1003, 1122, 1250, 1505, 1714, 2168, 2979; ^{1}H NMR (600 MHz, CDCl_3): 7.49 - 7.40 (m, 1H, Ar-H), 7.35 - 7.32 (m, 1H, Ar-H), 7.15 (td,$ *J*= 7.5, 1.2 Hz, 1H, Ar-H), 7.08 (ddd,*J* $= 9.7, 8.2, 1.1 Hz, 1H, Ar-H), 5.40 (s, 2H, CH₂), 2.66 (s, 3H, SMe). ¹³C NMR (151 MHz, CDCl_3): <math>\delta$ 216.20, 159.90, 130.37, 130.29, 123.63,

123.60, 115.69, 115.48, 115.13, 114.91, 62.8, 19.7; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{10}H_{10}FO_2S_2$ 245.0106; found 245.0100.

Furan-2-ylmethyl 2-(Methylthio)-2-thioxoacetate (10): Wine red liquid; Yield 1.771 g (82%);



IR: v_{max} (cm⁻¹) 723, 817, 1023, 1125, 1276, 1523, 1719, 2275, 2992; ¹H NMR (600 MHz, CDCl₃): δ 7.42 (ddd, J = 2.9, 1.8, 0.8 Hz, 1H, Het-H), 6.50 (ddd, J = 4.1, 3.4, 0.7 Hz, 1H, Het-H), 6.36 (dt, J = 4.5, 2.2 Hz, 1H, Het-H), 5.27 (s, 2H, CH₂), 2.64 (s, 3H, SMe). ¹³C NMR (151 MHz, CDCl₃): δ 216.4, 160.0, 143.9, 112.4, 112.0, 110.8, 60.6,

19.7; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₈H₉O₃S₂ 216.9993; found 216.9989

3-Methylbenzyl 2-(Methylthio)-2-thioxoacetate (1p): Wine red liquid; Yield 1.896 g (79%); IR:



 u_{max} (cm⁻¹) 743, 815, 1034, 1169, 1242, 1715, 2169, 3043; ¹H NMR (600 MHz, CDCl₃): δ 7.30 – 7.25 (m, 1H, Ar-H), 7.24 – 7.19 (m, 1H, Ar-H), 7.14 (dd, *J* = 12.1, 6.9 Hz, 1H, Ar-H), 5.28 (s, 2H, CH₂), 2.65 (s, 3H, SMe). ¹³C NMR (151 MHz, CDCl₃): 216.9, 160.3, 138.5, 134.7, 129.5, 129.2, 128.7, 125.6, 69.0, 21.5, 19.7; HRMS (ESI) m/z:

 $[M + H]^{+}$ calcd for C₁₁H₁₃O₂S₂ 241.0357; found 241.0349.

3,4,5-Trimethoxybenzyl 2-(Methylthio)-2-thioxoacetate (**1***q*). Wine red solid; Yield 2.243 g (71%); IR: $\upsilon_{max}(cm^{-1})$ 743, 827, 1030, 1184, 1250, 1296, 1714, 2171, 2806, 3046; ¹H NMR (600 MHz, CDCl₃): δ 6.64 (s, 2H, Ar-H), 5.26 (s, 2H, CH₂), 3.85 (s, 6H, OMe), 3.82 (s, 3H, OMe), 2.66 (s, 3H, SMe).¹³C NMR (151 MHz, CDCl₃): δ 216.8, 160.3, 153.5, 138.3, 130.3, 105.6, 69.0, 60.9, 56.2, 19.7; HRMS (ESI) m/z: [M + H]⁺

calcd for $C_{13}H_{17}O_5S_2$ 317.0517; found 317.0509.

2-Chloro-6-fluorobenzyl 2-(Methylthio)-2-thioxoacetate (1r): Wine red liquid; Yield 2.096 g



(70%); IR: v_{max} (cm⁻¹) 711, 812, 1012, 1127,1262, 1499, 1716, 2172, 2960; ¹H NMR (400 MHz, CDCl₃): δ 7.27 (td, J = 8.0, 5.8 Hz, 1H, Ar-H), 7.13 – 7.05 (m, 1H, Ar-H), 6.99 – 6.91 (m, 1H, Ar-H), 5.25 (s, 2H, CH₂), 2.60 (s, 3H, SMe). ¹³C NMR (101 MHz, CDCl₃): δ 212.2, 164.1, 159.9, 137.1, 137.1, 130.4, 130.3, 123.6, 123.6, 115.7, 115.5,

115.1, 114.9, 67.8, 19.6; HRMS (ESI) m/z: $[M \ + \ H]^{*}$ calcd for $C_{10}H_9CIFO_2S_2$ 278.9717; found 278.9725

2-Chlorobenzyl 2-(Methylthio)-2-thioxoacetate (1s): Wine red solid; Yield 1.968 g (76%); IR:



 u_{max} (cm⁻¹) 716, 808, 1010, 1123, 1253, 1495, 1716, 2169, 2950; ¹H NMR (600 MHz, CDCl₃): δ 7.53 – 7.44 (m, 1H, Ar-H), 7.43 – 7.37 (m, 1H, Ar-H), 7.33 – 7.25 (m, 2H, Ar-H), 5.44 (s, 2H, CH₂), 2.67 (s, 3H, SMe). ¹³C NMR (151 MHz, CDCl₃): δ 216.3, 160.0, 133.7, 132.6, 130.0, 129.9, 129.7, 127.1, 66.1, 19.7; HRMS (ESI) m/z: [M + H]⁺

calcd for C₁₀H₁₀ClO₂S₂ 260.9811; found 260.9801.

General Procedure for the Synthesis of Alkyl 2-Tosylthiazole-5-carboxylate (3a-o)



Reaction condition: **1a-s** (1 mmol, 1 equiv.), **2a** (1 mmol, 1 equiv.), K₂CO₃ (2 mmol, 2 equiv.), THF (2 mL), 0 °C-RT, 30 min.

A solution of dithioates **1a-s** (1.0 mmol, 1 equiv.) and TosMIC **2a** (1.0 mmol, 1 equiv.) in tetrahydrofuran (2 mL) was added drop wise to a stirring suspension of K_2CO_3 (2 mmol, 2 equiv.) in THF (2 mL) at 0 °C. The resulting mixture was stirred at room temperature for 20-30 min. Upon completion of reaction as monitored by TLC, it was then quenched with ice-cold water and mixture was extracted with ethyl acetate (3 × 25 mL), washed with H₂O (2 × 50 mL), dried over Na₂SO₄ and evaporated. The crude product was subjected to column chromatography using hexane/ethyl acetate solvent system to give the desired compounds **3a-o**

Characterization Details of Alkyl 2-Tosylthiazole-5-carboxylate (3a-o)

Benzyl 2-Tosylthiazole-5-carboxylate (3a): White solid; Yield 0.331 q (89%); IR: umax(cm⁻¹) 879,



1047, 1388, 1712, 2972, 3351; ¹H NMR (400 MHz, CDCl₃): δ 8.46 (s, 1H, Het-H), 7.99 (d, J = 8.4 Hz, 2H, Ar-H), 7.41 (q, J =7.5, 6.0 Hz, 7H, Ar-H), 5.38 (s, 2H, CH₂), 2.47 (s, 3H, Me). ¹³C NMR (101 MHz, CDCl₃): δ 172.1, 159.9, 149.5, 146.3, 134.9, 134.8, 134.6, 130.3, 129.0, 128.8, 128.8, 128.5, 68.0, 21.8;

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{16}NO_4S_2$ 374.0521; found 374.0516

2-Methoxybenzyl 2-Tosylthiazole-5-carboxylate (3b): White solid; Yield 0.315 g (78%); IR:



 u_{max} (cm⁻¹) 873, 1039, 1360, 1397, 1713, 2976, 3347; ¹H NMR (600 MHz, CDCl₃): δ 8.41 (s, 1H, Het-H), 7.95 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.40 – 7.28 (m, 3H, Ar-H), 6.99 – 6.91 (m, 1H, Ar-H), 6.93 – 6.85 (m, 1H, Ar-H), 5.40 (s, 2H, CH₂), 3.84 (s, 3H, OMe), 2.42 (s, 3H, Me). ¹³C NMR (151 MHz, CDCl₃): δ 171.9, 161.2, 160.1,

149.4, 149.0, 146.3, 135.3, 130.4, 130.2, 130.0, 129.8, 129.1, 120.6, 110.8, 63.8, 55.6, 21.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}NO_5S_2$ 404.0626; found 404.0617

4-Methylbenzyl 2-Tosylthiazole-5-carboxylate (3c): White solid; Yield 0.321 g (83%); IR:



 $υ_{max}$ (cm⁻¹) 871, 1036, 1383, 1712, 2980, 3350; ¹H NMR (400 MHz, CDCl₃): δ 8.41 (s, 1H, Het-H), 7.96 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.37 (d, *J* = 7.9 Hz, 2H, Ar-H), 7.29 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.19 (d, *J* = 7.8 Hz, 2H, Ar-H), 5.31 (s, 2H, CH₂), 2.44 (s, 3H, Me), 2.36 (s, 3H, Me). ¹³C NMR (101 MHz, CDCl₃): δ 172.0,

160.1, 149.6, 146.3, 138.9, 135.0, 131.7, 130.4, 129.5, 129.1, 128.8, 126.3, 68.1, 21.9, 21.3; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}NO_4S_2$ 388.0677; found 388.0668

4-Ethylbenzyl 2-Tosylthiazole-5-carboxylate (3d): White solid; Yield 0.312g (78%); IR: Umax(cm⁻



¹) 867, 1033, 1379, 1710, 2977, 3343; ¹H NMR (600 MHz, CDCl₃): δ 8.40 (s, 1H, Het-H), 7.95 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.39 – 7.32 (m, 2H, Ar-H), 7.30 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.21 (dd, *J* = 8.2, 6.8 Hz, 2H, Ar-H), 5.30 (s, 2H, CH₂), 2.65 (q, *J* = 7.6, 4.4 Hz, 2H, CH₂), 2.42 (s, 3H, Me), 1.22 (t, *J* = 7.6 Hz, 3H,

CH₃). ¹³C NMR (101 MHz, CDCl₃):) δ 172.1, 161.2, 160.0, 158.2, 149.5, 149.1, 146.3, 135.1, 130.4, 129.1, 128.8, 128.3, 68.1, 28.7, 21.8, 15.5; HRMS (ESI) m/z: [M + H]⁺ calcd for C₂₀H₂₀NO₄S₂ 402.0834; found 402.0827

4-Methoxybenzyl 2-Tosylthiazole-5-carboxylate (3e): White solid; Yield 0.318 g (79%); IR:



 u_{max} (cm⁻¹) 872, 1043, 1359, 1391, 1715, 2983, 3344; ¹H NMR (300 MHz, CDCl₃):) δ 8.41 (s, 1H, Het-H), 7.96 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.43 – 7.30 (m, 4H, Ar-H), 6.90 (d, *J* = 8.8 Hz, 2H, Ar-H), 5.28 (s, 2H, CH₂), 3.81 (s, 3H, OMe), 2.43 (s, 3H, Me). ¹³C NMR (75 MHz, CDCl₃): δ 172.9, 160.1, 150.4, 149.4, 146.5,

134.7, 130.5, 130.4, 129.1, 129.0, 126.7, 114.1, 68.0, 55.3, 21.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}NO_5S_2$ 404.0626; found 404.0611

4-Nitrobenzyl 2-Tosylthiazole-5-carboxylate (3f): White solid; Yield 0.359 g (86%); IR: vmax(cm⁻



¹) 692, 876, 1043, 1387, 1711, 2979, 3342; ¹H NMR (600 MHz, CDCl₃): δ 8.44 (s, 1H, Het-H), 8.23 (d, *J* = 7.0 Hz, 2H, Ar-H), 7.95 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.55 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.36 (d, *J* = 7.9 Hz, 2H, Ar-H), 5.43 (s, 2H, CH₂), 2.42 (s, 3H, Me). ¹³C NMR (151 MHz, CDCl₃): δ 172.8, 160.8, 159.7, 158.7,

149.9, 149.6, 142.5, 130.4, 129.1, 128.8, 128.7, 124.0, 66.4, 21.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₈H₁₅N₂O₆S₂ 419.0372; found 419.0361

3,4-Dimethoxybenzyl 2-Tosylthiazole-5-carboxylate (3g): White solid; Yield 0.320 g (74%); IR:



 υ_{max} (cm⁻¹) 867, 1038, 1353, 1387, 1711, 2979, 3339; ¹H NMR (600 MHz, CDCl₃): δ 8.40 (s, 1H, Het-H), 7.94 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.35 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.03 – 6.97 (m, 1H, Ar-H), 6.96 – 6.89 (m, 1H, Ar-H), 6.85 (t, *J* = 8.5 Hz, 1H, Ar-H), 5.26 (s, 2H, CH₂), 3.89 (s, 3H, OMe), 3.87 (s, 3H, OMe), 2.42 (s, 3H, Me).

¹³C NMR (151 MHz, CDCl₃): δ 172.1, 161.2, 160.1, 158.2, 149.5, 149.1, 146.3, 135.1, 130.4, 129.1, 121.9, 121.7, 112.1, 111.3, 68.3, 56.0, 21.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₂₀H₂₀NO₆S₂ 434.0732; found 434.0719

3-Fluorobenzyl 2-Tosylthiazole-5-carboxylate (3h): White solid; Yield 0.301 g (77%); IR:



 $υ_{max}$ (cm⁻¹) 871, 1048, 1368, 1709, 2972, 3351; ¹H NMR (300 MHz, CDCl₃): δ 8.43 (s, 1H, Het-H), 7.96 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.36 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.33 (dq, *J* = 8.7, 2.8 Hz, 1H, Ar-H), 7.21 – 7.14 (m, 1H, Ar-H), 7.10 (ddt, *J* = 23.5, 9.6, 2.2 Hz, 1H, Ar-H), 7.04 (tt, *J* = 8.5, 2.8 Hz, 1H, Ar-H), 5.32 (s, 2H, CH₂),

2.42 (s, 3H, Me). ¹³C NMR (75 MHz, CDCl₃):) δ 172.4, 161.0, 159.9, 158.5, 149.8, 149.4, 146.4, 130.4, 129.4, 129.1, 124.0, 123.8, 115.8, 115.5, 115.3, 66.5, 21.9; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₈H₁₅FNO₄S₂ 392.0427; found 392.0419

4-Fluorobenzyl 2-Tosylthiazole-5-carboxylate (3i): White solid; Yield 0.308 g (79%); IR: υ_{max}(cm⁻¹) 872, 1047, 1369, 1710, 2973, 3349; ¹H NMR (400 MHz, CDCl₃): δ 8.42 (s, 1H, Het-H), 8.02 – 7.91 (m, 2H, Ar-H), 7.46 - 7.30 (m, 4H, Ar-H), 7.07 (td, J = 8.7, 2.5 Hz, 2H, Ar-H),

5.31 (s, 2H, CH₂), 2.44 (s, 3H, Me). ¹³C NMR (101 MHz, CDCl₃): δ 172.1, 159.9, 158.3, 149.6, 149.2, 146.3, 134.8, 130.8, 130.6,

130.3, 129.0, 115.9, 115.6, 67.3, 21.8; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₈H₁₅FNO₄S₂ 392.0427; found 392.0413

4-Chlorobenzyl 2-Tosylthiazole-5-carboxylate (3j): White solid; Yield 0.325 g (80%); IR:



υ_{max}(cm⁻¹) 875, 1047, 1376, 1712, 2972, 3337; ¹H NMR (400 MHz, CDCl₃): δ 8.42 (s, 1H, Het-H), 7.96 (d, J = 8.4 Hz, 2H, Ar-H), 7.43 - 7.29 (m, 6H, Ar-H), 5.31 (s, 2H, CH₂), 2.44 (s, 3H, Me).¹³C NMR (101 MHz, CDCl₃): δ 172.3, 159.9, 149.7, 146.4, 135.0, 134.9, 134.7, 133.2, 132.1, 130.4, 130.1, 129.1, 67.3, 21.9;

HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₈H₁₅ClNO₄S₂ 408.0131; found 408.0120

4-Bromobenzyl 2-Tosylthiazole-5-carboxylate (3k): White solid; Yield 0.338 q (75%); IR:



υ_{max}(cm⁻¹) 879, 1047, 1384, 1711, 2972, 3326; ¹H NMR (400 MHz, CDCl₃): δ 8.42 (s, 1H, Het-H), 7.97 (d, J = 8.4 Hz, 2H, Ar-H), 7.52 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.38 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.28 (d, *J* = 7.0 Hz, 2H, Ar-H), 5.29 (s, 2H, CH₂), 2.44 (s, 3H, Me). ¹³C NMR (101 MHz, CDCl₃): δ 172.3, 159.9, 149.7, 146.4,

134.9, 134.6, 133.7, 132.1, 130.4, 130.3, 129.1, 123.1, 67.3, 21.9; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₈H₁₅BrNO₄S₂ 451.9626; found 451.9610

Butyl 2-Tosylthiazole-5-carboxylate (31): Brown liquid; Yield 0.284 g (84%); IR: Umax(cm⁻¹) 877,



1042, 1379, 1713, 2980, 3339; ¹H NMR (300 MHz, CDCl₃): δ 8.41 (s, 1H, Het-H), 7.98 (d, J = 8.4 Hz, 2H, Ar-H), 7.39 (d, J = 7.2 Hz, 2H, Ar-H), 4.33 (t, J = 6.6 Hz, 2H, CH₂), 2.45 (s, 2H, Me), 1.72 (dt, J = 14.4, 7.1 Hz, 2H, CH₂), 1.43 (dq, J = 14.4, 7.3 Hz, 2H, CH₂), 0.96 (t, J = 7.4 Hz, 3H, CH₃). ¹³C NMR (75 MHz,

CDCl₃): δ 171.8, 160.1, 149.2, 146.2, 135.2, 134.9, 130.3, 129.0, 66.3, 30.5, 21.8, 19.1, 13.7; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₅H₁₈NO₄S₂ 340.0677; found 340.0669

3-Methylcyclohexyl 2-Tosylthiazole-5-carboxylate (3m): White gummy solid; Yield 0.310 g (82%); IR: υ_{max}(cm⁻¹) 878, 1047, 1384, 1712, 2972, 3328; ¹H NMR (400 MHz, CDCl₃): δ 8.39 (s, 1H, Het-H), 7.97 (d, J = 8.4 Hz, 2H, Ar-H), 7.38 (d, J = 9.3 Hz, 2H, Ar-H), 4.99 - 4.86 (m, 1H, CH), 2.44



(s, 3H, Me), 2.04 (dt, J = 12.2, 4.3 Hz, 2H, CH₂), 1.82 (dt, J = 9.9, 3.6 Hz, 1H, CH), 1.71 – 1.57 (m, 2H, CH₂), 1.45 – 1.36 (m, 2H, CH₂), 1.24 – 1.03 (m, 2H, CH₂), 0.95 (d, J = 6.5 Hz, 3H, Me). ¹³C NMR (101 MHz, CDCl₃): δ 171.6, 159.6, 149.2, 146.3, 135.9, 135.1, 130.4, 129.1, 76.1, 40.3, 33.8, 31.5, 31.4, 29.8, 23.9, 22.3,

21.9; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₈H₂₂NO₄S₂ 380.0990; found 380.0981

Thiophen-2-ylmethyl 2-Tosylthiazole-5-carboxylate (3n): White solid; Yield 0.301 g (80%); IR: $\bigcup_{max}(cm^{-1})$ 879, 1047, 1386, 1710, 2972, 3328; ¹H NMR (300 $\bigcup_{max}(cm^{-1})$ 879, 1047, 1386, 1710, 2972, 3328; ¹H NMR (300MHz, $CDCl_3$): δ 8.43 (s, 1H, Het-H), 7.96 (d, J = 8.4 Hz, 2H, Ar-H), 7.41 - 7.30 (m, 3H, Ar-H), 7.17 (d, J = 3.5 Hz, 1H, Het-H),7.00 (dd, J = 5.1, 3.5 Hz, 1H, Het-H), 5.50 (s, 2H, CH₂), 2.43 (s,3H, Me).¹³C NMR (75 MHz, CDCl₃): δ 172.2, 159.8, 149.7,

146.3, 136.3, 134.8, 134.7, 130.3, 129.3, 129.0, 127.7, 127.1, 62.1, 21.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₆H₁₄NO₄S₃ 380.0085; found 380.0078

Furan-2-ylmethyl 2-Tosylthiazole-5-carboxylate (30): Brown liquid; Yield 0.283 g (78%); IR:



 u_{max} (cm⁻¹) 876, 1046, 1388, 1709, 2973, 3330; ¹H NMR (600 MHz, CDCl₃): δ 8.40 (s, 1H, Het-H), 7.94 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.43 (ddd, *J* = 8.4, 1.9, 0.8 Hz, 1H, Het-H), 7.35 (d, *J* = 8.6 Hz, 2H, Ar-H), 6.48 (dd, *J* = 6.2, 3.3 Hz, 1H, Het-H), 6.40 – 6.33 (m, 1H, Het-H), 5.28 (s, 2H, CH₂), 2.41 (s, 3H, Me). ¹³C NMR

(151 MHz, CDCl₃): δ 172.2, 161.0, 149.7, 149.3, 148.8, 148.2, 146.4, 130.4, 129.4, 129.1, 111.5, 110.8, 59.6, 21.9; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₆H₁₄NO₅S₂ 364.0313; found 364.0302

X-Ray Crystallographic Information of Product (3i)

Single crystals of product **3i** with approximate dimensions 0.230 mm × 0.320 mm × 0.400 mm is obtained through slow evaporation (at room temperature) of a solution in hexane/ethyl acetate. The X-ray intensity data were collected on a Bruker Kappa Apex-II diffractometer having an X-rays tube containing Mo and Cu as a target. The graphite monochromator and CCD were used for recording the intensity peaks. APEX-II and SAINT software were used to carry-out for data collection and data reduction [1]. SHELXS97 was employed for structure solution [2] and SHELXL2018/3 was used for the structure refinement [3]. Anisotropic refinement was done for all the non-hydrogen atoms.

References

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3). Sheldrick, G. M. Crystal structure refinement with SHELXL. Acta Crystallogr., Sect. C: Struct. Chem. 2015, 71, 3–8.

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5). Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T.; McCabe, P.; Pidcock, E.; Platings, M.;

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Empirical formula Formula weight	C ₁₈ H ₁₄ FNO ₄ S ₂ 391.42
Temperature	150
Wavelength	0.71073 Å
Reflections for cell determination	6294
θ range for above	2.81° to 27.48°
Crystal system	Monoclinic
Space group	P 2 ₁ /c
Cell dimensions	<i>a</i> = 16.087(2) Å
	<i>b</i> = 11.8579(14) Å
	<i>c</i> = 9.1830(11) Å
	$\alpha = 90^{\circ}$
	$\beta = 94.929(4)^{\circ}$
	γ = 90°
Volume	1745.3(4) Å ³
Z	4
Density(calculated)	1.490 Mg m⁻³
Absorption coefficient	0.339 mm⁻¹
F ₀₀₀	808
Crystal size	0.230 mm × 0.320 mm × 0.400 mm
θ range for data collection	2.54° to 27.54°
Index ranges	$-20 \le h \le 20$
	-15 ≤ <i>k</i> ≤ 15

 $-11 \leq l \leq 11$

Multi-scan

3984 / 0 / 236

3984 [$R_{int} = 0.061$]

1.233; -0.386 e Å⁻³

full matrix least-squares on F^2

R1 = 0.0899, wR2 = 0.1862

R1 = 0.1060, wR2 = 0.1930

18748

1.232

The single crystal of the product **3i** was obtained by slow evaporation of the solvent when the compound was dissolved in minimum volume of hexane/ ethyl acetate mixture. The crystal data of product **3i** has already been deposited at Cambridge Crystallographic Data Centre. The CCDC reference number is 2263779.

Reflections collected

Data / restraints / parameters

Independent reflections

Absorption correction

Goodness-of-fit on F^2

R indices (all data)

Final *R* indices $[I > 2 \sigma(I)]$

Largest diff. peak and hole

Refinement method

ORTEP of the product (3i)





Figure S1. ORTEP (thermal ellipsoid plot) of Product 3i (drawn at 50% probability level)

General Procedure for the Synthesis of 5-Alkyl 4-Ethyl Thiazole-4,5-dicarboxylates (4a-r)



Reaction condition: **1a-s** (1 mmol, 1 equiv.), **2b** (1 mmol, 1 equiv.), K₂CO₃ (2 mmol, 2 equiv.), DMF (2 mL), 0 °C-RT, 30 min.

A solution of K_2CO_3 (2.0 mmol, 2 equiv.) in DMF was placed in an ice bath for 5 minutes. Dithioates **1a-s** (1.0 mmol, 1 equiv.) and ethyl isocyanoacetate **2b** (1.0 mmol, 1 equiv.) dissolved in DMF (2 mL) and added drop wise to a stirring suspension of K_2CO_3 in DMF at 0 °C and continue stirring for another 30 minutes. Upon completion of reaction as monitored by TLC, brine solution (50 mL) was added and reaction mixture was extracted with ethyl acetate (3 × 25 mL), washed with H₂O (2 × 50 mL), dried over Na₂SO₄ and evaporated. The crude product was subjected to column chromatography using hexane/ethyl acetate solvent system to give the desired compounds **4a-r**.

Characterization Details of 5-Alkyl 4-Ethyl Thiazole-4,5-dicarboxylates (4a-r)

5-Benzyl 4-Ethyl Thiazole-4,5-dicarboxylate (4a): Pale yellow gummy solid; Yield 0.267 g



(92%); IR: v_{max} (cm⁻¹) 879, 1047, 1378, 1713, 2972, 3331; ¹H NMR (400 MHz, CDCl₃): δ 8.87 (s, 1H, Het-H), 7.47 – 7.32 (m, 5H, Ar-H), 5.37 (s, 2H, CH₂), 4.36 (q, *J* = 7.2 Hz, 2H, CH₂), 1.34 (t, *J* = 7.2 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 162.5, 160.0, 155.9, 150.3, 134.8, 130.0, 128.8, 128.7, 128.5, 68.1, 62.4, 14.0; HRMS (ESI) m/z:

 $[M + H]^+$ calcd for C₁₄H₁₄NO₄S 292.0644; found 292.0637

4-Ethyl 5-(2-Methoxybenzyl) Thiazole-4,5-dicarboxylate (4b): Pale yellow gummy solid; Yield 0.285 g (89%); IR: v_{max} (cm⁻¹) 877, 1046, 1257, 1388, 1728, 2972, 3334; ¹H NMR (600 MHz, CDCl₃): δ 8.82 (s, 1H, Het-H), 7.38 – 7.29 (m, 2H, Ar-H), 6.95 (td, J = 7.4, 1.0 Hz, 1H, Ar-H), 6.91 – 6.87 (m, 1H, Ar-H), 5.39 (s, 2H, CH₂), 4.31 (q, J = 7.1 Hz, 2H, CH₂), 3.83 (s, 3H, OMe), 1.30 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (151 MHz,

CDCl₃): δ 162.6, 160.2, 157.8, 155.8, 150.2, 130.4, 130.2, 130.2, 123.2, 120.5, 110.6, 63.8, 62.4, 55.5, 14.0; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₅H₁₆NO₅S 322.0749; found 322.0737

4-Ethyl 5-(3-Methylbenzyl) Thiazole-4,5-dicarboxylate (7c): Pale yellow gummy solid; Yield



0.274 g (90%); IR: υ_{max} (cm⁻¹) 878, 1045, 1386, 1726, 2971, 3333; ¹H NMR (600 MHz, CDCl₃): δ 8.84 (s, 1H, Het-H), 7.26 (d, J = 7.3 Hz, 1H, Ar-H), 7.22 – 7.18 (m, 1H, Ar-H), 7.16 (d, J = 7.6 Hz, 1H, Ar-H), 5.30 (s, 2H, CH₂), 4.34 (q, J = 7.2 Hz, 2H, CH₂), 2.36 (s, 3H, Me), 1.31 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ

162.5, 160.1, 155.9, 150.3, 138.5, 134.7, 130.2, 129.5, 129.3, 128.7, 125.7, 68.3, 62.5, 21.4, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₅H₁₆NO₄S 306.0800; found 306.0793

4-Ethyl 5-(4-Methylbenzyl) Thiazole-4,5-dicarboxylate (4d): Pale yellow gummy solid; Yield 0.271 g (89%); IR: v_{max} (cm⁻¹) 877, 1046, 1387, 1728, 2972, 3331; ¹H NMR (400 MHz, CDCl₃): δ 8.86 (s, 1H, Ar-H), 7.32 (d, J = 8.1Hz, 2H, Ar-H), 7.21 (d, J = 7.9 Hz, 2H, Ar-H), 5.33 (s, 2H, CH₂), 4.37 (q, J = 7.2 Hz, 2H, CH₂), 2.38 (s, 3H, Me), 1.34 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 162.5, 160.0, 155.8, 150.2,

138.6, 131.8, 130.1, 129.3, 128.7, 68.1, 62.4, 21.2, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{16}NO_4S$ 306.0800; found 306.0791

4-Ethyl 5-(4-Ethylbenzyl) Thiazole-4,5-dicarboxylate (4e): Pale yellow gummy solid; Yield



0.277 g (87%); IR: υ_{max} (cm⁻¹) 876, 1046, 1385, 1727, 2973, 3335; ¹H NMR (600 MHz, CDCl₃): δ 8.83 (s, 1H, Het-H), 7.31 (d, J = 8.0 Hz, 2H, Ar-H), 7.20 (d, J = 8.1 Hz, 2H, Ar-H), 5.30 (s, 2H, CH₂), 4.32 (q, J = 7.2 Hz, 2H, CH₂), 2.64 (q, J = 7.6 Hz, 2H, CH₂), 1.30 (t, J = 7.2 Hz, 3H, CH₃), 1.22 (t, J = 7.6 Hz, 3H, CH₃). ¹³C NMR (151

MHz, CDCl₃): δ 162.6, 160.2, 155.9, 150.3, 145.1, 132.0, 130.2, 128.9, 128.3, 68.3, 62.5, 28.7, 15.7, 14.0; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₆H₁₈NO₄S 320.0957; found 320.0948

4-Ethyl 5-(4-Methoxybenzyl) Thiazole-4,5-dicarboxylate (4f): Pale yellow gummy solid; Yield



0.269 g (84%); IR: υ_{max} (cm⁻¹) 876, 1046, 1257, 1383, 1727, 2973, 3335; ¹H NMR (300 MHz, CDCl₃): δ 8.84 (s, 1H, Het-H), 7.35 (d, *J* = 8.7 Hz, 2H, Ar-H), 6.91 (d, *J* = 8.7 Hz, 2H, Ar-H), 5.28 (s, 2H, CH₂), 4.35 (q, *J* = 7.2 Hz, 2H, CH₂), 3.81 (s, 3H, OMe), 1.33 (t, *J* = 7.2 Hz, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ 162.5, 160.1, 160.0,

155.8, 150.1, 130.5, 130.2, 126.8, 114.0, 68.0, 62.4, 55.3, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{16}NO_4S$ 322.0749; found 322.0745

5-(3,4-Dimethoxybenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4g): Pale yellow gummy solid;



Yield 0.291 g (83%); IR: υ_{max} (cm⁻¹) 877, 1046, 1264, 1386, 1722, 2971, 3334; ¹H NMR (600 MHz, CDCl₃): δ 8.83 (s, 1H, Het-H), 6.98 – 6.92 (m, 2H, Ar-H), 6.84 (d, *J* = 8.1 Hz, 1H, Ar-H), 5.26 (s, 2H, CH₂), 4.32 (q, *J* = 7.2 Hz, 2H, CH₂), 3.89 (s, 3H, OMe), 3.87 (s, 3H, OMe), 1.30 (t, *J* = 7.2 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ

162.5, 160.2, 155.9, 150.2, 149.5, 149.2, 130.4, 127.3, 121.7, 112.1, 111.1, 68.4, 62.5, 56.0, 14.1; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₆H₁₈NO₆S 352.0855; found 352.0850

4-Ethyl 5-(3,4,5-Trimethoxybenzyl) Thiazole-4,5-dicarboxylate (4h): Pale yellow gummy



solid; Yield 0.300 g (79%); IR: υ_{max} (cm⁻¹) 874, 1047, 1260, 1296, 1379, 1725, 2980, 3332; ¹H NMR (600 MHz, CDCl₃):) δ 8.85 (s, 1H, Het-H), 6.63 (s, 2H, Ar-H), 5.26 (s, 2H, CH₂), 4.33 (q, *J* = 7.2 Hz, 2H, CH₂), 3.86 (s, 6H, OMe), 3.83 (s, 3H, OMe), 1.30 (t, *J* = 7.1 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ 163.3, 162.5, 160.1,

156.0, 153.5, 150.2, 138.3, 130.6, 130.4, 130.3, 105.8, 68.5, 62.5, 60.9, 56.3, 14.1; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₇H₂₀FNO₇S 382.0960; found 382.0953

4-Ethyl 5-(4-Nitrobenzyl) Thiazole-4,5-dicarboxylate (4i): Pale yellow solid; Yield 0.305 g



(78%); IR: υ_{max} (cm⁻¹) 872, 1049, 1259, 1715, 2972, 3333; ¹H NMR (600 MHz, CDCl₃): δ 8.89 (s, 1H, Het-H), 8.23 (d, J = 8.8 Hz, 2H, Ar-H), 7.57 (d, J = 8.9 Hz, 2H, Ar-H), 5.42 (s, 2H, CH₂), 4.38 (q, J = 7.1 Hz, 2H, CH₂), 1.33 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ 162.3, 159.9, 156.3, 150.5, 142.0, 128.7, 127.1, 124.0,

123.8, 77.4, 77.2, 77.0, 66.6, 62.6, 14.1; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{13}N_2O_6S$ 337.0494; found 337.0488

4-Ethyl 5-(4-Fluorobenzyl) Thiazole-4,5-dicarboxylate (4j): Pale yellow gummy solid; Yield



0.268 g (87%); IR: υ_{max} (cm⁻¹) 878, 1047, 1387, 1717, 2971, 3324; ¹H NMR (300 MHz, CDCl₃): δ 8.86 (s, 1H, Het-H), 7.41 (dd, *J* = 8.9, 5.3 Hz, 2H, Ar-H), 7.08 (t, *J* = 8.8 Hz, 2H, Ar-H), 5.31 (s, 2H, CH₂), 4.36 (q, *J* = 7.2 Hz, 2H, CH₂), 1.33 (t, *J* = 7.2 Hz, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ 162.4, 160.0, 155.9, 150.3, 130.7, 130.6, 130.0,

115.8, 115.5, 67.4, 62.4, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₄H₁₃FNO₄S 310.0549; found 310.0557

5-(4-Chlorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4k): Pale yellow solid; Yield 0.286 g



(88%); IR: υ_{max} (cm⁻¹) 877, 1049, 1385, 1715, 2969, 3332; ¹H NMR (400 MHz, CDCl₃): δ 8.88 (s, 1H, Het-H), 7.53 (d, J = 8.4 Hz, 2H, Ar-H), 7.30 (d, J = 8.4 Hz, 2H, Ar-H), 5.31 (s, 2H, CH₂), 4.38 (q, J = 7.1 Hz, 2H, CH₂), 1.35 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 162.3, 159.9, 155.9, 150.3, 134.7, 133.3, 129.9, 128.9,

128.6, 67.3, 62.4, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{13}CINO_4S$ 326.0254; found 326.0239

5-(4-Bromobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (41): Pale yellow gummy solid; Yield



0.317 g (86%); IR: ν_{max} (cm⁻¹) 879, 1053, 1385, 1714, 2973, 3337; ¹H NMR (400 MHz, CDCl₃): δ 8.85 (s, 1H, Het-H), 7.34 (m, *J* = 1.5 Hz, 4H, Ar-H), 5.29 (s, 2H, CH₂), 4.36 (q, *J* = 7.2 Hz, 2H, CH₂), 1.32 (t, *J* = 7.2 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃): δ 162.3, 159.9, 156.0, 150.3, 133.8, 131.9, 130.1, 129.8, 122.8, 67.3, 62.4,

14.0; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₄H₁₃BrNO₄S 369.9749; found 369.9743

5-(2-Chloro-6-fluorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (**4m**): Pale yellow gummy solid; Yield 0.284 g (83%); IR: υ_{max}(cm⁻¹) 872, 1041, 1379, 1716, 2981, 3339; ¹H NMR (600 MHz, CDCl₃): δ 8.83 (s, 1H, Het-H), 7.32 (td, *J* = 8.3, 6.0 Hz, 1H, Ar-H), 7.24 (q, *J* = 1.1 Hz, 1H, Ar-H), 7.05



found 344.0169

(ddd, J = 9.3, 8.3, 1.2 Hz, 1H, Ar-H), 5.51 (s, 2H, CH₂), 4.32 (q, J = 7.1 Hz, 2H, CH₂), 1.31 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCI₃): δ 163.0, 162.4, 161.3, 159.8, 156.0, 156.0, 150.5, 136.7, 136.7, 131.4, 131.4, 129.6, 125.7, 125.7, 114.5, 114.4, 62.5, 14.0; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₄H₁₂CIFNO₄S 344.0160;

5-(2-Chlorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (**4n**): Pale yellow gummy solid; Yield 0.276 g (85%); IR: v_{max} (cm⁻¹) 876, 1049, 1387, 1715, 2969, 3333; ¹H NMR (600 MHz, CDCl₃):) δ 8.85 (s, 1H, Het-H), 7.49 – 7.43 (m, 1H, Ar-H), 7.43 – 7.38 (m, 1H, Ar-H), 7.33 – 7.25 (m, 2H, Ar-H), 5.45 (s, 2H, CH₂), 4.35 (q, J = 7.1 Hz, 2H, CH₂), 1.32 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ 162.5, 159.9, 156.0, 150.5,

134.1, 132.6, 130.4, 130.1, 129.8, 129.8, 127.1, 65.5, 62.5, 14.1; HRMS (ESI) m/z: $[M + H]^+$ calcd for C₁₄H₁₃CINO₄S 326.0254; found 326.0244

5-Butyl 4-Ethyl Thiazole-4,5-dicarboxylate (40): Pale yellow gummy solid; Yield 0.228 g



5-dicarboxylate (**40**): Pale yellow gummy solid; Yield 0.228 g (89%); IR: v_{max} (cm⁻¹) 878, 1046, 1386, 1713, 2972, 3325; ¹H NMR (400 MHz, CDCl₃): δ 8.86 (s, 1H, Het-H), 4.46 (q, J = 7.2 Hz, 2H, CH₂), 4.34 (t, J = 6.7 Hz, 2H, CH₂), 1.78 – 1.67 (m, 2H, CH₂), 1.42 (td, J = 7.3, 4.4 Hz, 5H, CH₂), 0.97 (t, J = 7.4 Hz, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ 162.5, 160.3, 155.6, 149.9, 130.5, 66.4, 62.4,

30.5, 19.1, 14.1, 13.7; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₁H₁₆NO₄S 258.0800; found 258.0793

4-Ethyl 5-(3-Methylcyclohexyl) Thiazole-4,5-dicarboxylate (4p): Pale yellow gummy solid;



Yield 0.261 g (88%); IR: υ_{max} (cm⁻¹) 872, 1050, 1389, 1714, 2969, 3332; ¹H NMR (600 MHz, CDCl₃): δ 8.81 (s, 1H, Het-H), 4.94 – 4.85 (m, 1H, CH), 4.43 (q, *J* = 7.1 Hz, 2H, CH₂), 2.11 – 2.00 (m, 2H, CH₂), 1.86 – 1.71 (m, 1H, CH), 1.66 – 1.53 (m, 2H, CH₂), 1.39 (t, *J* = 7.2 Hz, 3H, CH₂), 1.25 – 1.15 (m, 2H, CH₂), 1.12 – 1.01 (m, 2H, CH₂),

0.92 (d, J = 6.6 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ 162.7, 159.8, 155.5, 149.8, 131.0, 76.1, 62.4, 40.3, 33.9, 31.4, 31.4, 23.9, 22.3, 14.2; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₄H₂₀NO₄S 298.1113; found 298.1109

4-Ethyl 5-(Thiophen-2-ylmethyl) Thiazole-4,5-dicarboxylate (**4q**): Pale yellow gummy solid; Yield 0.243 g (82%); IR: υ_{max}(cm⁻¹) 876, 1047, 1389, 1717, 2970, 3332; ¹H NMR (300 MHz, CDCl₃): δ 8.85 (s, 1H, Het-H), 7.37 (dd, *J* = 5.1, 1.3 Hz, 1H, Het-H), 7.18 (dd, *J* = 3.6, 1.3 Hz, 1H, Het-H), 7.01 (dd, *J* = 5.1, 3.5 Hz, 1H, Het-H), 5.50 (s, 2H, CH₂), 4.38 (q, *J* = 7.2 Hz, 2H, CH₂), 1.35 (t, *J* = 7.2



Hz, 3H, CH₃). ¹³C NMR (75 MHz, CDCl₃): δ 162.3, 159.8, 156.0, 150.4, 136.4, 129.8, 129.1, 127.5, 127.0, 62.4, 62.2, 14.0; HRMS (ESI) m/z: [M + H]⁺ calcd for C₁₂H₁₂NO₄S₂ 298.0208; found 298.0199

4-Ethyl 5-(Furan-2-ylmethyl) Thiazole-4,5-dicarboxylate (4r): Brown liquid; Yield 0.224 g



(80%); IR: v_{max} (cm⁻¹) 877, 1047, 1390, 1716, 2971, 3334; ¹H NMR (600 MHz, CDCl₃): δ 8.84 (s, 1H, Het-H), 7.44 (dd, J = 1.8, 0.9 Hz, 1H, Het-H), 6.49 (dd, J = 3.3, 0.8 Hz, 1H, Het-H), 6.38 (dd, J = 3.3, 1.8 Hz, 1H, Het-H), 5.28 (s, 2H, CH₂), 4.38 (q, J = 7.2 Hz, 2H, CH₂), 1.35 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (151 MHz, CDCl₃): δ 162.3,

159.8, 156.0, 150.4, 136.4, 129.8, 129.1, 127.5, 127.0, 62.4, 62.2, 14.0; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{12}H_{12}NO_5S$ 282.0439; found 282.0428

X-Ray crystallographic information of products (4k)

Single crystals of product **4k** with approximate dimensions 0.232 × 0.363× 0.456 mm is obtained through slow evaporation (at room temperature) of a solution in hexane/ethyl acetate. The X-ray intensity data were collected on a Bruker Kappa Apex-II diffractometer having an X-rays tube containing Mo and Cu as a target. The graphite monochromator and CCD were used for recording the intensity peaks. APEX-II and SAINT software were used to carry-out for data collection and data reduction [1]. SHELXS97 was employed for structure solution [2] and SHELXL2018/3 was used for the structure refinement [3]. Anisotropic refinement was done for all the non-hydrogen atoms.

References

1). Bruker APEX2 (Version 1.22) and SAINT-Plus (Version 7.06a), 2009.

2). Sheldrick, G. M. A short history of SHELX. Acta Crystallogr., Sect. A: Found. Crystallogr.

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3). Sheldrick, G. M. Crystal structure refinement with SHELXL. Acta Crystallogr., Sect. C: Struct. Chem. 2015, 71, 3–8.

4). Spek, A. L. Single-crystal structure validation with the program PLATON. J. Appl.

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5). Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T.; McCabe, P.; Pidcock, E.; Platings, M.;

Shields, G. P.; Stevens, J. S.; Towler, M. Mercury 4.0: from visualization to analysis,

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Empirical formula	C ₁₄ H ₁₂ CINO ₄ S		
Formula weight	329.24		
Temperature	293 К		
Wavelength	0.71073 Å		
Reflections for cell determination	3673		
θ range for above	2.74° to 27.88°		
Crystal system	Monoclinic		
Space group	P 21/c		
Cell dimensions	<i>a</i> = 13.7650(7) Å		
	<i>b</i> = 7.5431(4) Å		
	<i>c</i> = 15.3707(9) Å		
	α = 90°		
	$\beta = 104.898(2)^{\circ}$		
	$\gamma = 90^{\circ}$		
Volume	1542.30(15) Å ³		
Z	4		
Density(calculated)	1.418 Mg m⁻³		
Absorption coefficient	0.396 mm ⁻¹		
F_{000}	672		
Crystal size	0.232 mm × 0.363 mm × 0.456 mm		
θ range for data collection	2.74° to 27.88°		
Index ranges	-18 ≤ <i>h</i> ≤ 18		
	$-9 \leq k \leq 9$		
	$-20 \leq l \leq 20$		
Reflections collected	51308		
Independent reflections	3673 [<i>R</i> _{int} = 0.0634]		
Absorption correction	Multi-scan		
Refinement method	full matrix least-squares on <i>F</i> ²		
Data / restraints / parameters	3673 / 0 / 191		
Goodness-of-fit on F ²	1.129		
Final <i>R</i> indices $[l > 2 \sigma(l)]$	<i>R</i> 1 = 0.0634, <i>wR</i> 2 = 0.1764		
<i>R</i> indices (all data)	R1 = 0.0840, wR2 = 0.2114		
Largest diff. peak and hole	0.460; -0.293 e Å ⁻³		

Table S2: Crystal data and structure refinement details of 4k

The single crystal of the product **4k** was obtained by slow evaporation of the solvent when the compound was dissolved in minimum volume of hexane/ ethyl acetate mixture. The crystal data of product **4k** has already been deposited at Cambridge Crystallographic Data Centre. The CCDC reference number is 2324088.

ORTEP of the product (4k)



Figure S2. ORTEP (thermal ellipsoid plot) of Product 4k (drawn at 50% probability level)



4-Ethylbenzyl 2-(Methylthio)-2-thioxoacetate (11)





3,4-Dimethoxybenzyl 2-(Methylthio)-2-thioxoacetate (1m)





3-Fluorobenzyl 2-(Methylthio)-2-thioxoacetate (1n)









3-Methylbenzyl 2-(Methylthio)-2-thioxoacetate (1p)





3,4,5-Trimethoxybenzyl 2-(Methylthio)-2-thioxoacetate (1q)





2-Chloro-6-Fluorobenzyl 2-(Methylthio)-2-thioxoacetate (1r)





2-Chlorobenzyl 2-(Methylthio)-2-thioxoacetate (1s)











2-Methoxybenzyl 2-Tosylthiazole-5-carboxylate (3b)





4-Methylbenzyl 2-Tosylthiazole-5-carboxylate (3c)







4-Methoxybenzyl 2-Tosylthiazole-5-carboxylate (3e)





4-Nitrobenzyl 2-Tosylthiazole-5-carboxylate (3f)





3,4-Dimethoxybenzyl 2-Tosylthiazole-5-carboxylate (3g)




3-Fluorobenzyl 2-Tosylthiazole-5-carboxylate (3h)







4-Fluorobenzyl 2-Tosylthiazole-5-carboxylate (3i)





4-Chlorobenzyl 2-Tosylthiazole-5-carboxylate (3j)





4-Bromobenzyl 2-Tosylthiazole-5-carboxylate (3k)



SI39









3-Methylcyclohexyl 2-Tosylthiazole-5-carboxylate (3m)





Thiophen-2-ylmethyl 2-Tosylthiazole-5-carboxylate (3n)





Furan-2-ylmethyl 2-Tosylthiazole-5-carboxylate (30)





5-Benzyl 4-Ethyl Thiazole-4,5-dicarboxylate (4a)





4-Ethyl 5-(2-Methoxybenzyl) Thiazole-4,5-dicarboxylate (4b)





4-Ethyl 5-(3-Methylbenzyl) Thiazole-4,5-dicarboxylate (4c)





4-Ethyl 5-(4-Methylbenzyl) Thiazole-4,5-dicarboxylate (4d)





4-Ethyl 5-(4-Ethylbenzyl) Thiazole-4,5-dicarboxylate (4e)





4-Ethyl 5-(4-Methoxybenzyl) Thiazole-4,5-dicarboxylate (4f)





5-(3,4-Dimethoxybenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4g)





4-Ethyl 5-(3,4,5-Trimethoxybenzyl) Thiazole-4,5-dicarboxylate (4h)





4-Ethyl 5-(4-Nitrobenzyl) Thiazole-4,5-dicarboxylate (4i)





4-Ethyl 5-(4-Fluorobenzyl) Thiazole-4,5-dicarboxylate (4j)





5-(4-Chlorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4k)





5-(4-Bromobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4l)





5-(2-Chloro-6-fluorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4m)





5-(2-Chlorobenzyl) 4-Ethyl Thiazole-4,5-dicarboxylate (4n)





5-Butyl 4-Ethyl Thiazole-4,5-dicarboxylate (40)





4-Ethyl 5-(3-Methylcyclohexyl) Thiazole-4,5-dicarboxylate (4p)





4-Ethyl 5-(Thiophen-2-ylmethyl) Thiazole-4,5-dicarboxylate (4q)





4-Ethyl 5-(Furan-2-ylmethyl) Thiazole-4,5-dicarboxylate (4r)



Cartesian coordinates (Å) of the optimized structures of all intermediates and transition states at BP86/def2-SVP level of theory. E_e^s represents the absolute electronic energy in Hartree at M06/def2-TZVP level of theory.

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н	8.668743000	-6.501210000	-1.510054000	Н	-1.199037000	-5.438290000	2.757779000	
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S	3.699812000	-3.596756000	-4.613287000	н	6.522570000	-0.577218000	-4.800144000
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Figure S3. The free energies of optimized geometries of the reactants, intermediates, and product for the reaction mechanism of **2a** with **1**. Free energy values are the M06(SMD-THF)/def2-TZVP//BP86/def2-SVP level of theory. The all values are in kcal/mol.



Reaction Progress

Figure S4 Mechanistic energy profiles for formation of the benzyl 2-tosylthiazole-5carboxylate (3a)



Figure S5. The free energies of optimized geometries of the reactants, intermediates, and product for the reaction mechanism of **2b** with **1**. Free energy values are the M06(SMD-THF)/def2-TZVP//BP86/def2-SVP level of theory. The all values are in kcal/mol.


Reaction Progress

Figure S6 Mechanistic energy profiles for formation of the benzyl 2-tosylthiazole-5carboxylate (4a)