Supplementary Material for:

Synergism of Fused Bicyclic 2-Aminothiazolyl compounds with polymyxin B against *Klebsiella pneumonia*

Rong Wang,[a] Shuang Hou,[a] Xiaojing Dong,[b] Daijie Chen,[b] * Lei Shao,[c] Liujia Qian, [c] Zhong Li[a, d] and Xiaoyong Xu[a, d*]

[a] *Shanghai Key Laboratory of Chemical Biology, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China;*
[b] *School of Pharmacy, Shanghai Jiaotong University*
[C]*Shanghai Institute of Pharmaceutical Industry*
[d]*Shanghai Collaborative Innovation Center for Biomanufacturing Technology, Shanghai 200237, China*

∗ Corresponding author. Tel.: +86-21-64252945; fax: +86-21-64252603. *E-mail:* xyxu@ecust.edu.cn.

Table of Contents

* Corresponding author. Tel: +86-21-64252945; fax: +86-21-64252603; e-mail: xyxu@ecust.edu.cn

Materials and General Methods

Unless otherwise noted, reagents and solvents were obtained from commercial sources and used without further purification. All reactions were carried out without nitrogen protection unless otherwise noted. Melting points (mp) were recorded on Büchi B540 apparatus (Büchi Labortechnik, Flawil, Switzerland) and are uncorrected. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on Bruker AM-400 spectrometer with DMSO-d_6 or $CDCl_3$ as solvent at ambient temperature and TMS as internal standard. Chemical shifts were reported in parts per million (δ). Coupling constants (J) were reported in hertz (Hz). High-resolution electron mass spectra (ESI-TOF) were performed on a Micromass LC-TOF spectrometer using ES ionization modes (positive or negative). Analytical thin-layer chromatography (TLC) was performed on precoated plates (silica gel 60 F254), and spots were visualized with ultraviolet (UV) light.

Minimum inhibitory concentration (MIC) and synergy testing

Acinetobacter baumanii strain (ATCC19606), *E. coli* strain (ATCC25922), *Pseudomonas aeruginosa* strain (ATCC27853) were obtained from the American Type Culture Collection (ATCC). Clinical isolates of *Acinetobacter baumanii* (4), *Klebsiella pneumonia* (3), *E. coli* (2), *Pseudomonas aeruginosa* (2) were obtained from the institute of Antibiotics at Shanghai Huashan Hospital, Shanghai, China. All these strains were grown in Mueller–Hinton cation-adjusted broth (pH 7.0) at 37°C with aeration. MICs of polymyxin B and tested compounds were determined by broth microdilution in MHB according to National Committee for Clinical Laboratory Standards guidelines (CLSI, M07-A9, 2012a). The checkerboard assay was performed to analyze the combination effect of the tested compounds with polymyxin B, a final inoculum of 0.25-0.5×10^6 CFU/ml of SIPI-KPN-1712 was added to 96 well plates containing a fixed concentration of one of the tested compounds (4μg ml^{-1}) and two-fold serial dilutions of polymyxin B. The FICI was calculated as:

$$FICI = \frac{\text{MIC of PB in combination}}{\text{MIC of PB alone}} + \frac{\text{MIC of compound in combination}}{\text{MIC of compound alone}}$$

The MICs of tested compounds cannot be determined because the bacteria can grow at the presence of 128 μg ml^{-1}, which is the highest concentration tested, so 128 μg ml^{-1} was considered to be the MIC of compound alone. Synergy was defined as an FICI of <0.5, partial synergy as an FICI of 0.5-0.75, additive effect as an FICI of 0.76-1, indifference as an FICI of 1-4, and antagonism as an FICI of >4.

Time-kill curves

Time-kill curves of monotherapy and combination therapy were performed in a culture containing 5×10^6 CFU/ml of SIPI-KPN-1712. For the monotherapy, compound **B1** or polymyxin B was added to yield a final concentration of 4 μg ml^{-1}, and for the combination therapy, compound **B1** and polymyxin B were added as follows: 4 μg ml^{-1} **B1**+0.5 μg ml^{-1} PB, 4 μg ml^{-1} **B1**+1μg ml^{-1} PB, 4 μg ml^{-1} **B1**+2 μg ml^{-1} PB, 4 μg ml^{-1} **B1** + 4 μg ml^{-1} PB, viable colony counts were performed at 0、1h、2h、4h、8h、24h.

General Procedure for the Synthesis of Intermediates

Synthesis of Intermediates 2

To a mixture of benzoyl chloride (1 mmol) and KSCN (1 mmol) were added in acetone (10 ml) at room temperature under inert atmosphere condition. The reaction mixture was stirred for one hour and then, precipitation was filtered and the filtrate was evaporated to adduct compound **2** without further purification.

Synthesis of Intermediates 5

A solution of intermediate **2** (1.2 mmol) in ethyl acetate (10 ml) with aniline derivatives **3** (1 mmol) was stirred under reflux condition and monitored with TLC. And then, the reaction mixture was evaporated to get intermediate **4**. Finally, the debenzoylation of **4** was gained by the mixture of EtOH (3 ml), NaOH (0.24 g) and H_2O (2 ml). The reaction mixture was warmed to reflux and stirred until the disappearance of the compounds **4** determined by TLC. Compounds **5** was filtered when the reactant solution was acidized with saturated aq.HCl until pH neutral.

General Procedure for the Synthesis of Target Compounds

To a microwave vial (2-5 mL) were added thiourea intermediate **5** (1 mmol), α,β-epoxy cycloketone **6** (1.1 mmol), and corresponding alcohol (2 mL). The sealed vial was heated in the Biotage Initiator Synthesizer for appropriate time. The mixture was then cooled to room temperature and the residue was obtained after evaporating under vacuum. The residue was subjected to purification over silica gel chromatography eluting with PE/EtOAc (9:1, v/v) to afford target compounds **A**.

The target compounds **B** was synthesized by the mixture of thiourea intermediate **5** (1 mmol) and α,β-epoxy cycloketone **6** (1.1 mmol) in H_2O (2 ml) under reflux condition. The reaction mixture was monitored with TLC and target compounds B were got by silica gel chromatography eluting with PE/EtOAc (10:1, v/v).

The synthesis of target compounds **C** were gained by a copper-catalyzed tandem reaction of 2-haloanilines **7** (1 mmol) with isothiocyanates **8** (1.1 mmol) using CuSO4 (1 mol %) as catalyst and Bu_3N (1.1 equiv.) as a base under ligand- and solvent-free conditions in air. The reaction was maintained at 80 ℃ and monitored with TLC. When the reaction was finished, the residue was washed with ethyl acetate and water (3x). Then, the combined organic phases were dried over $MgSO_4$, the solvent evaporated and target compounds **C** were purified by flash column chromatography (PE/EtOAc,

3:1, v/v).

N-(4-bromophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **compound 1108**: White solid, mp 132.8-133.0 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 4.36(t, *J* = 4.2 Hz, 1H), 3.31 (s, 2H), 2.63-2.45 (m, 2H), 1.87–1.71 (m, 4H); ^{13}C NMR(100 MHz, DMSO- d_6) δ 162.3, 148.8, 140.9, 132.0, 119.2, 118.5, 112.6, 72.6, 55.9, 28.7, 27.1, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{18}{}^{79}BrN_2OS$+ 339.0167, found: 339.0167; calcd for $C_{14}H_{16}{}^{81}BrN_2OS$+ 341.0146, found: 341.0148.

N-(4-chlorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A1**: White solid, mp 113.5-114.2 °C , yield: 93%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H),δ 7.65 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 4.37 (t, *J* = 4.2 Hz, 1H), 3.33 (s, 3H), 2.62-2.48 (m, 2H), 1.89-1.78(m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 148.8, 140.5, 129.2, 124.8, 118.7, 118.5, 72.6, 55.9, 28.7, 27.1, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{16}{}^{35}ClN_2OS$+: 295.0672, found: 295.0674; calcd for $C_{14}H_{16}{}^{37}ClN_2OS$+: 297.0642, found: 297.0642.

N-(4-iodophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A2**: White solid, mp 162.9-169.9°C, yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 4.37 (t, *J* = 4.6 Hz, 1H), 3.42 (s, 3H), 2.75 – 2.61 (m, 1H), 2.55 (m, 1H), 1.96 (m, 3H), 1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.54, 148.90, 140.12, 138.21, 120.18, 118.61, 85.25, 73.04, 56.17, 28.66, 26.85, 19.13. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{16}IN_2OS$+ 387.0028, found: 387.0030.

7-methoxy-*N*-(4-(trifluoromethyl)phenyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A3**: White solid, mp 108.9-109.7 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 4.39(t, *J* = 4.8 Hz, 1H), 3.33 (s, 3H), 2.65-2.48 (m, 2H), 1.89–1.73 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 148.9, 144.9, 126.7 (q, *J* = 3.3 Hz), 125.1(q, *J*= 269.4 Hz), 121.2 (q, *J*= 31.9 Hz), 119.4,116.9, 72.6, 56.0, 28.7, 27.1, 19.3; ^{19}F NMR (376 MHz, DMSO-d_6) δ -58.82. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{16}F_3N_2OS$+: 329.0935, found: 329.0937.

7-methoxy-*N*-(4-nitrophenyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A4**: Dark yellow solid, mp 164.6-165.7 °C, yield: 93%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.94 (s, 1H), 8.21 (d, *J* = 9.2 Hz, 1H), 7.81 (d, *J* = 9.2 Hz, 1H), 4.41 (t, *J* = 4.2 Hz, 1H), 3.33 (s, 3H), 2.68-2.52 (m, 2H), 1.90–1.73 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 149.1, 147.4, 140.6, 126.0, 120.7, 116.6, 72.6, 56.0, 28.6, 27.1, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{16}N_3O_3S$+: 306.0912, found: 306.0912.

7-methoxy-N-(4-cyanophenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A5**: White solid, mp 143.7-144.3 °C, yield: 91%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 7.76 (m, 4H), 4.39 (t, *J* = 4.4 Hz, 1H), 3.32 (s, 3H), 2.55 (m, 3H), 1.88 -1.72 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.5, 149.0, 145.3, 133.9, 120.0, 117.1, 102.5, 72.6, 56.0, 28.6, 27.1 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{16}N_30S$+: 286.1014, found: 286.1014.

-(4-((7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)phenyl)acetamide **A6**: White solid, mp 169.3-170.5 °C, yield: 87%. ^{1}H NMR (400 MHz,DMSO-d_6) δ 9.98 (s, 1H), 9.81 (s, 1H), 7.66–7.38 (m, 4H), 4.34 (t, *J* = 4.2 Hz, 1H), 3.33 (s, 3H), 2.60-2.44 (m, 2H), 2.01 (s, 3H), 1.86 –1.72 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.2, 163.0, 148.8, 137.2, 133.6, 120.3, 117.8, 117.5, 72.7, 55.9, 28.8, 27.1, 24.3, 19.4. HRMS (ESI): m/z [M-H]- calcd for $C_{16}H_{18}N_3O_2S$+: 316.1120, found: 316.1123.

N-(3-chlorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A7**: White solid, mp 105.3-106.5 °C, yield: 91% . ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.32 (s, 1H), 7.85 (t, *J* = 2.0 Hz, 1H), 7.45 (m, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 6.95 (m, 1H), 4.37 (t, *J* = 4.4 Hz, 1H), 3.31 (s, 3H), 2.65-2.47 (m, 2H), 1.91–1.64 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.6, 148.3, 142.4, 133.2, 130.4, 120.4, 118.2, 115.9, 115.1, 72.1, 55.3, 28.1, 26.5, 18.8. HRMS (ESI): m/z [M+H]+ calcd for

$C_{14}H_{16}{}^{35}ClN_2OS$+: 295.0672, found: 295.0675; calcd for $C_{14}H_{16}{}^{37}ClN_2OS$+: 297.0642, found: 297.0642.

N-(3-bromophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A8**: White solid, mp 104.7-114.0°C, yield: 88%.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.4 Hz, 1H), 7.26 (s, 1H), 7.21 – 7.13 (m, 2H), 4.37 (t, *J* = 4.6 Hz, 1H), 3.43 (s, 3H), 2.69 (m, 1H), 2.56 (m, 1H), 2.11 – 1.88 (m, 3H), 1.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.46, 148.89, 141.70, 130.65, 125.70, 123.05, 121.01, 118.76, 116.61, 73.05, 56.16, 28.64, 26.87, 19.15. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{16}{}^{79}BrN_2OS$+ 339.0167, found: 339.0173; calcd for $C_{14}H_{16}{}^{81}BrN_2OS$+ 341.0146, found: 341.0154.

N-(3-fluorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A9**: White solid, mp 107.9-109.1°C, yield: 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 1H), 7.18 (m, 1H), 7.02 (dd, *J* = 2.0, 0.8 Hz, 1H), 6.72 (m, 1H), 4.38 (t, *J* = 4.4 Hz, 1H), 3.43 (s, 3H), 2.76 – 2.61 (m, 1H), 2.62 – 2.46 (m, 1H), 2.07 – 1.86 (m, 3H), 1.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.41 (d, *J* = 243.6 Hz), 163.72, 148.73, 142.08 (d, *J* = 10.6 Hz), 130.55, 118.53, 113.65, 109.47 (d, *J* = 21.3 Hz), 105.45, 73.04, 56.15, 28.65, 26.81, 19.13; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.93 – -111.43 (m,1F). HRMS (ESI): m/z [M-H]- calcd for $C_{14}H_{16}N_2OFS$+: 279.0967, found: 279.0968.

7-methoxy-*N*-(3-(trifluoromethyl)phenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A10**: White solid, mp 87.4-95.4°C, yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.53 (m, 2H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.29 (s, 1H), 4.38 (d, *J* = 4.4 Hz, 1H), 3.43 (s, 3H), 2.80 – 2.63 (m, 1H), 2.57 (m,1H), 2.13 – 1.88 (m, 3H), 1.91 – 1.70 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.56, 146.13, 141.69, 129.99, 129.65 (q, *J* = 33.2 Hz), 122.56, 121.85 (q, *J* = 170.6 Hz), 120.12, 118.82, 116.96 (q, *J* = 4.0 Hz), 116.18, 112.46 (q, *J* = 4.4 Hz), 26.29, 24.25, 23.36; ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.36 (s, 3F). HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{16}F_3N_2OS$+: 329.0935, found: 329.0936.

N-(2-chlorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A11**: White solid, mp 81.8-82.9 °C, yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.51 (s,1 H), 8.19 (d, *J* =8.1 Hz, 1 H), 7.44 (d, *J* =8. 0 Hz, 1 H), 7.31 (t, *J* =7. 8 Hz, 1 H), 7.03 (t, *J* =7.8 Hz, 1H), 4.34 (t, *J* =4.6 Hz, 1H), 3.30 (s, 3H), 2.57-2.43 (m, 2H), 1.85-1.68 (m, 4H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 163.4, 148.1, 138.3, 130.0, 128.1，124.0, 123.4, 122.1，119.2, 72.7, 55.9, 28.8, 26.9, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{16}{}^{35}ClN_2OS$+: 295.0672, found: 295.0674; calcd for $C_{14}H_{16}{}^{37}ClN_2OS$+: 297.0642, found: 297.0642.

7-methoxy-*N*-(2-(trifluoromethyl)phenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A12**: White solid, mp 93.5-101.1°C , yield: 92% . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.6 Hz 1H), 7.52 (t, *J* = 8.4 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 4.37 (d, *J* = 3.6 Hz, 1H), 3.42 (s, 3H), 2.82 – 2.65 (m, 1H), 2.65 – 2.48 (m, 1H), 2.15 – 1.90 (m, 3H), 1.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.31, 149.21, 138.55, 133.17, 126.70 (q, *J* = 5.2 Hz), 122.85, 123.74 (q, *J* = 271.2 Hz), 120.69, 119.65, 119.19 (q, *J* = 29.4 Hz), 73.05, 56.16, 28.65, 26.81, 19.11; ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.02(s, 3F).HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{16}F_3N_2OS$+: 329.0935, found: 329.0934.

N-(2,6-dichlorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A13**: White solid, mp 141.4-142.4 °C , yield: 89%. ^{1}H NMR (400 MHz,DMSO-d_6) δ 9.98 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 6.95 (t, *J* = 8.2 Hz, 1H), 4.20 (t, *J* = 4.2 Hz, 1H), 3.81 (s, 3H), 3.25 (s, 3H), 2.46-2.28 (m, 2H), 1.81-1.66 (m, 4H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 164.6, 144.8, 138.8, 132.7, 129.4, 128.0, 115.5, 72.7, 56.0 , 28.6, 25.9, 19.0. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{15}{}^{35}Cl_2N_2OS$+: 329.0282, found: 329.0281; calcd for $C_{14}H_{15}{}^{35}Cl^{37}ClN_2OS$+: 331.0253, found:331.0253; calcd for $C_{14}H_{15}{}^{37}Cl_2N_2OS$+: 333.0223, found: 333.0224.

N-(2,6-difluorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A14**: White solid, 150.9-153.4 °C , yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.12 (m, 1H), 6.98 (t, *J* = 8.0 Hz,

2H), 4.29 (t, J =4.4 Hz, 1H), 3.36 (s, 3H), 2.57 (m, 1H), 2.46 (m, 1H), 1.92 (m, 3H), 1.73 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.55, 157.91（dd, ^1J = 249.4 Hz, ^3J = 4.6 Hz）, 148.27, 126.72, 118.69 (t, J = 15.8 Hz), 118.26, 112.22 (dd, ^2J = 18.0 Hz, ^3J = 5.4 Hz), 73.04, 56.07, 28.70, 26.45, 19.04; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.98 (s, 1F), -118.28 – -118.45 (m, 1F). HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{15}F_2N_2OS$+: 297.0873, found: 297.0874.

N-(2-chloro-4-(trifluoromethyl)phenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A15**: White solid, mp 106.0-106.6 °C, yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1 H), 8.62 (m, l H), 7. 82 (d, J = 2.0 Hz, 1 H), 7.68 (dd, J = 8.8, 2.2 Hz, 1 H), 4.40 (t, J =4.2 Hz, 1H), 3.33 (s, 1H), 2.53 (m, 2H), 1.88-1.72 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 128.2, 127.0, 125.5, 125.4, 122.8, 122.5, 122.2, 112.0, 72.6, 56.0, 28.6, 26.9, 19.3.1; ^{19}F NMR (376 MHz, DMSO-d6) δ -60.20. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{15}{}^{35}ClF_3N_2OS$+: 363.0467, found: 363.0467; calcd for $C_{15}H_{15}{}^{37}Cl$ F_3N_2OS+: 365.0438, found: 365.0438.

N-(2, 4-dichlorophenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A16**: White solid, mp 141.4-142.4 °C , yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.8 Hz, 1H), 7.38 (d, J = 2.4 Hz, 1H), 7.26 – 7.21 (dd, J = 2.6, 2.2 Hz 1H), 4.39 (t, J = 4.8 Hz, 1H), 3.43 (s, 3H), 2.73 (m, 1H), 2.60 (m, 1H), 2.11 – 1.88 (m, 3H), 1.88 – 1.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.92, 149.37, 135.68, 129.03, 127.95, 126.80, 122.04, 119.95, 118.63, 73.00, 56.18, 28.65, 26.90, 19.14. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{15}{}^{35}Cl_2N_2OS$+: 329.0282, found: 329.0281; calcd for $C_{14}H_{15}{}^{35}Cl{}^{37}ClN_2OS$+: 331.0253, found:331.0253; calcd for $C_{14}H_{15}{}^{37}Cl_2N_2OS$+: 333.0223, found: 333.0223

4-((7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)-2-(trifluoromethyl)benzonitrile **A17**: White solid, mp 33.5-134.2°C , yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1 H), 8.21(s, 1 H), $.0S (m, 2H), 4.42 (t, J = 4.6 Hz, 1H), 3.33 (s, 3H), 2.60 (m, 2H), 1.89-1.73 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 146.8, 145.4, 137.0, 132.4 (q, J = 31.2 Hz), 124.4, 123.0 (q, J =271.9 Hz), 119.5, 119.1, 119.0, 118.5, 116.8, 114.5 (q, J = 5.1 Hz), 98.5 (q, J =1.9 Hz), 49.0, 24.6, 23.8; ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.37. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{15}F_3N_3OS$+: 354.0810, found: 354.0810.

7-methoxy-*N*-phenyl-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A18**: White solid, mp 101.7-102.4 °C, yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6 δ 10.08 (s, 1H), 7.60 (d, J = 7.6 Hz,1H), 7.29 (m, 2H), 6.92 (m, 1H), 4.36 (t, J = 4.2 Hz, 1H), 3.32 (s, 3H), 2.62-2.45 (m, 2H), 1.93–1.61 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 148.8, 141.7, 129.4, 121.5, 117.9, 117.3, 72.7, 55.9, 28.8, 27.1, 19.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{17}N_2OS$+: 261.1062, found: 261.1062.

7-methoxy-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A19**: White solid, mp 112.1-112.7 °C, yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 4.34 (t, J = 4.8 Hz, 1H), 3.31 (s, 3H), 2.60-2.45 (m, 2H), 2.24 (s, 3H), 1.86-1.70 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 148.8, 139.3, 130.4, 129.8, 117.5, 72.7, 55.9, 28.8, 27.1, 20.8, 19.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{19}N_2OS$+: 275.1218, found: 275.1219.

N-(4-ethylphenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A20**: White solid, mp: 83.1-84.1°C, yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.98 (s, 1 H), 7.50 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 4.34 (t, J = 4.0 Hz, 1 H), 3.31 (s, 3H), 2.6I-2.40 (m, 2H), 1.93-1.66 (m, 4H), 1.15 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 148.8, 139.5, 137.0, 128.5, 117.6, 117.5, 72.7, 55.9, 28.8, 28.0, 27.1, 19.4, 16.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{21}N_2OS$+: 289.1375, found: 289.1364.

4-((7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)phenol **A21**: Bright yellow solid, mp

82.0-83.5 °C, yield: 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 9.82 (s, 1H), 7.45 (d, J = 8.8 Hz, 1H), 6.89 (d, J = 8.8 Hz, 1H), 4.36 (t, J = 4.2 Hz, 1H), 3.31 (s, 3H), 2.60-2.43 (m, 2H), 1.87–1.71 (m, 4H); ^{13}CNMR (100 MHz, DMSO-d_6) δ 164.0, 152.7, 148.8, 133.7, 126.6, 119.8, 115.8, 72.7, 55.8, 28.8, 27.1, 19.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{17}N_2O_2S$+: 277.1011, found: 277.1009.

7-methoxy-*N*-(4-methoxyphenyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A22**: White solid, mp 130.8-131.2 °C, yield: 83%. ^{1}H NMR (400 MHz,DMSO-d_6) δ 9.98 (s, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.25 (t, J = 8.2 Hz, 1H), 4.20 (t, J = 4.2 Hz, 1H), 3.25 (s, 3H), 2.62-2.45 (m, 2H), 1.82-1.66 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 154.5, 146.7.8, 135.1, 121.9, 119.2, 114.6, 72.7, 55.7, 49.1, 28.8, 27.1, 19.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{19}N_2O_2S$+: 291.1167, found: 291.1169.

N-(4-(tert-butyl)phenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A23**: Bright yellow solid, mp 137.2~145.1 °C, yield: 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 6.6 Hz, 2H), 7.24 (d, J = 6.4 Hz, 2H), 4.35 (t, J = 4.4 Hz, 1H), 3.41 (s, 3H), 2.67 m, 1H), 2.62 – 2.47 (m, 1H), 1.96 (m, 3H), 1.77 (m, 1H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.04, 148.79, 146.30, 137.74, 126.27, 118.67, 117.50, 73.10, 56.11, 34.34, 31.39, 28.79, 26.84, 19.15. HRMS (ESI): m/z [M+H]+ calcd for $C_{18}H_{25}N_2OS$+: 317.1688, found: 317.1688.

N^1-(7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)-N^4,N^4-dimethylbenzene-1,4-diamine **A24**: White solid, mp 149.0-149.8 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.66(s, 1H), 7.38 (d, J = 8.6 Hz, 1 H), 6.73 (d, J = 7.2 Hz, 1 H), 4.31 (t, J = 4.2 Hz, 1H), 3.29(s, 3H), 2.83 (s, 6H), 2.49 (m, 2H), 1.85-1.68 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.7, 148.3, 146.2, 131.6, 119.4, 115.9, 113.3, 72.3, 55.3, 40.7, 28.4, 26.6, 18.9. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{22}N_30S$+: 304.1484, found: 304.1484.

7-methoxy-*N*-(4-(o-tolyloxy)phenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A25**: White solid, mp 96.6-97.6 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1 H), 7.59 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.4 Hz, 1 H), 7.16 (t, J = 7.8 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1 H), 6.90 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.0 Hz, 1 H), 4.43 (t, J = 5.2 Hz, 1 H), 3.33 (s, 3H), 2.51 (m, 2H), 1.85-1.68 (m, 4H), 1.12 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 155.6, 151.3, 148.6, 137.3, 131.8, 128.7, 127.7, 123.7, 119.1, 119.0, 118.3, 118.1, 71.1，63 .4, 29.6, 27.1, I9.4, 16.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{21}H_{22}N_2O_2S$ +: 367.1402, found: 367.1400.

N-(4-(4-fluorophenoxy)phenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A26**: White solid, mp 92.1-93.6 °C, yield: 87% . ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.18 (t, J = 8.7 Hz, 2H), 7.02-6.96 (m, 4H), 4.35 (t, J = 4.0 Hz, 1H), 3.32 (s, 3H), 2.62-2.45 (m, 2H), 1.91-1.63 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 158.2 (d, J = 238.7 Hz), 154.3 (d, J = 2.2 Hz), 150.8, 148.8, 137.9, 120.1, 119.7 (d, J = 8.3 Hz), 119.0, 117.8, 116.8(d, J = 23.3 Hz), 72.7, 55.9, 28.8, 27.1, 19.4; ^{19}F NMR (376 MHz, DMSO-d_6) δ -121.05. HRMS (ESI): m/z [M+H]+ calcd for $C_{20}H_{20}FN_2O_2S$+: 371.1230, found: 371.1231.

1-(4-((7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)phenyl)ethan-1-one **A27**: White solid, mp 174.5-183.1 °C, yield: 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ10.51 (s, 1H), 7.91 (d, J = 8.7 Hz, 2H), 7.71 (d, J = 8.8 Hz, 2H), 5.28 (d, J = 6.3 Hz, 1H), 4.66 (dd, J = 6.6, 3.6 Hz, 1H), 3.33 (s, 1H), 2.52 (s, 2H), 1.93 (d, J = 10.7 Hz, 2H), 1.74 – 1.63 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.91, 160.86, 147.14, 145.33, 129.85, 129.39, 123.55, 115.67, 62.94, 33.01, 26.49, 26.22, 19.24. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{29}N_2O_2S$+: 303.1223, found: 303.1223.

7-methoxy-*N*-(o-tolyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A28**: White solid; yield, mp 85.8-86.4 °C, yield: 91%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.18 (m, 2H), 7.00 (m, 1H), 4.30 (t, J = 4.2 Hz, 1H), 3.29 (s, 3H), 2.55-2.38 (m, 2H), 2.24 (s, 3H), 1.90–1.60 (m,

4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.2, 148.6, 139.9, 131.0, 129.9, 126.9, 124.0, 122.2, 117.6, 72.7, 55.9, 28.9, 27.0, 19.3, 18.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{19}N_2OS$+: 275.1218, found: 275.1208.

7-methoxy-*N*-(m-tolyl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A29**: White solid, mp 95.4-96.1 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 7.45 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.35 (s, 1H), 7.17 (t, *J* = 8.2, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 4.34 (t, *J* = 4.0 Hz, 1H), 3.31 (s, 3H), 2.62-2.43 (m, 2H), 2.28 (s, 3H), 1.98–1.62 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 148.8, 141.6, 138.5, 129.2, 122.4, 117.9, 117.8, 114.6, 72.7, 55.9, 28.8, 27.1, 21.8, 19.4. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{19}N_2O_S$+: 275.1218, found: 275.1219.

N-(2,3-dimethylphenyl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A30**: White solid, mp 123.0-123.5 °C, yield: 94%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 7.39 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.07 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 4.27 (t, *J* = 3.6 Hz,1H), 3.27 (s, 3H), 2.47–2.41 (m, 2H), 2.26 (s, 3H), 2.12 (s, 3H), 1.83–1.67 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.4, 148.7, 139.8, 137.8, 130.2, 126.6, 126.2, 121.7, 117.1, 72.8, 55.9, 28.9, 27.0, 20.7, 19.3, 14.32. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{21}N_2OS$+: 289.1375; found: 289.1376.

7-methoxy-*N*-(3,4,5-trimethoxyphenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A31**: White solid, mp 130.8-131.2 0C, yield: 94%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 6.97 (s, 2H), 3.75 (s, 6H), 3.61 (s, 3H), 3.18 (s, 3H), 2.53 (m, 2H), 1.86 -1.68 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 153.5, 14$.8, 137.9, 132.5, 117.7, 95.6, 72.7, 60.6, 56.2, 55.9, 28.8, 27.1, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{17}H_{23}N_2O_4S$+: 351.1379, found: 351.1379.

N-(2-chloropyridin-4-yl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A32**: White solid, mp 142.4-143.3 °C, yield: 93%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.86 (s, 1H), 8.17 (d, *J* = 5.8 Hz, 1H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.41 (dd, *J* = 5.8, 2.0 Hz, 1H), 4.41 (t, *J* = 4.4 Hz, 1H), 3.33 (s, 3H), 2.69-2.53 (m, 2H), 1.89–1.73 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 151.5, 150.4, 149.7, 149.1, 120.9, 111.2, 110.3, 72.5, 56.0, 28.6, 27.0, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{15}{}^{35}ClN_3OS$+: 296.0624, found: 296.0628. calcd for $C_{13}H_{15}{}^{37}ClN_3OS$+: 298.0595, found: 298.0599.

N-(5-chloropyridin-2-yl)-7-methoxy-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A33**: White solid, mp 153.5-154.3 °C, yield: 96%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 1H), 8.32 (d, *J* = 2.4 Hz, 1H), 7.78 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 4.42 (t, *J* = 4.8 Hz, 1H), 3.34 (s, 3H), 2.64-2.45 (m, 2H), 1.87-1.71 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.7, 151.0, 147.2, 145.1, 138.2, 122.32, 120.7, 112.7, 72.7, 56.0, 28.8, 26.7, 19.4. HRMS (ESI): m/z [M-H]- calcd for $C_{13}H_{13}{}^{35}ClN_2OS$-: 294.0468, found: 294.0469; calcd for $C_{13}H_{13}{}^{37}ClN_2OS$-: 296.0438, found: 296.0441.

7-methoxy-*N*-(pyridin-3-yl)-4,5,6,7-tetrahydrobenzo[*d*]thiazol-2-amine **A34**: White solid, mp 146.3-147.4 °C, yield: 94%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 8.74 (d, *J* = 2.7 Hz, 1H), 8.18-8.16 (m, 1H), 8.16-8.12 (m, 1H), 7.34-7.30 (m, 1H), 4.37 (t, *J* = 4.2 Hz, 1H), 3.32 (s, 3H), 2.642.47 (m, 2H), 1.88 –1.71 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 148.9, 142.3, 139.3, 138.3, 124.1, 123.6, 118.9, 72.6, 55.9, 28.7, 27.1, 19.3. HRMS (ESI): m/z [M-H]- calcd for $C_{13}H_{14}N_3OS$: 260.0858, found: 260.08557.

7-methoxy-*N*-(thiazol-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A35**: White solid, mp 186.4-187.2 °C, yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 3.8 Hz, 1H), 6.80 (d, *J* = 3.8 Hz, 1H), 4.40 (t, *J* = 4.6 Hz, 1H), 3.45 (s, 3H), 2.85 – 2.70 (m, 1H), 2.71 – 2.55 (m, 1H), 2.20 – 1.88 (m, 3H), 1.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.54, 119.48, 110.52, 72.93, 56.22, 28.66, 26.48, 19.05. HRMS (ESI): m/z [M+H]+ calcd for $C_{11}H_{14}N_3OS_2$: 268.0578, found: 268.0580.

7-methoxy-*N*-(pyrimidin-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A36**: White solid, mp

144.3-151.7 °C, yield: 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (s, 1H), 8.66 (d, *J* = 4.8 Hz, 2H), 6.87 (t, *J* = 4.8 Hz, 1H), 4.48 (t, *J* = 4.6 Hz, 1H), 3.48 (s, 3H), 2.90 – 2.79 (m, 1H), 2.76 – 2.63 (m, 1H), 2.16 – 1.88 (m, 2H), 1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.34, 157.90, 157.29, 147.99, 121.76, 113.49, 73.11, 56.21, 28.95, 26.74, 19.29. HRMS (ESI): m/z [M+H]+ calcd for $C_{12}H_{15}N_4OS$: 263.0967, found: 263.0966.

7-methoxy-*N*-(quinolin-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A37**: White solid, mp 208.2-211.7 °C, yield: 69%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (s, 1H), 8.19 (d, *J* = 8.8 Hz, 1H), 7.83 (m, 2H), 7.66 (m, 1H), 7.39 (m, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 4.50 (t, *J* = 4.2 Hz, 1H), 3.39 (s, 3H), 2.64 (m, 1H), 2.58 – 2.41 (m, 1H), 1.99 – 1.84 (m, 3H), 1.84 – 1.61 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.05, 150.30, 146.61, 145.91, 137.68, 129.86, 127.75, 125.94, 123.97, 123.61, 120.73, 112.79, 72.24, 55.46, 28.28, 26.24, 18.92.. HRMS (ESI): m/z [M+H]+ calcd for $C_{17}H_{18}N_3OS$: 312.1171, found: 312.1172.

7-methoxy-*N*-(naphthalen-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A38**: White solid, mp 133.4-135.1 °C, yield: 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.4 Hz, 1H), 7.81 – 7.72 (m, 3H), 7.45 (m, 1H), 7.41 – 7.30 (m, 2H), 4.39 (t, *J* = 4.6 Hz, 1H), 3.43 (s, 3H), 2.78 – 2.64 (m, 1H), 2.66 – 2.50 (m, 1H), 2.12 – 1.86 (m, 3H), 1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.83, 148.74, 138.00, 134.19, 130.03, 129.35, 127.66, 127.14, 126.69, 124.58, 119.99, 117.83, 113.96, 73.13, 56.15, 28.73, 26.92, 19.20. HRMS (ESI): m/z [M+H]+ calcd for $C_{18}H_{19}N_2OS$+: 311.1218, found: 311.1216.

N-(7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)morpholin-4-amine **A39**: White solid, mp 125.4-125.8 °C, yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 (t, *J* = 4.4 Hz, 1H), 3.78 (t, *J* = 4.6 Hz, 4H), 3.43 (s, 3H), 2.89 (m, 4H), 2.71 – 2.57 (m, 1H), 2.57 – 2.45 (m, 1H), 2.06 – 1.86 (m, 3H), 1.83 – 1.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.94, 149.36, 118.56, 73.24, 67.04, 56.18, 28.65, 27.12, 19.14. HRMS (ESI): m/z [M+H]+ calcd for $C_{12}H_{20}N_3O_2S$+: 270.1276, found: 270.1275.

N-benzyl-7-methoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A40**: White solid, mp 72.3-73.5 °C, yield: 96%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (t, *J* = 4.8 Hz 1H), 7.33 (d, *J* = 4.2 Hz, 4H), 7.27-7.22 (m, 1H), 4.41 (d, *J* = 5.2 Hz, 2H), 4.23 (t, *J* = 4.2 Hz, 1H), 3.26 (s, 3H), 2.48-2.30 (m, 2H), 1.80-1.64 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.0, 148.7, 139.8, 128.7, 127.7, 127.3, 116.0, 72.9, 55.8, 47.9, 28.9, 27.1, 19.3. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{19}N_2OS$+: 275.1218, found: 275.1219.

7-ethoxy-*N*-(pyrimidin-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A41**: White solid, mp 192.3-195.3 °C, yield: 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.94 (s, 1H), 8.65 (d, *J* = 4.8 Hz, 2H), 6.87 (t, *J* = 4.8 Hz, 1H), 4.57 (t, *J* = 4.8 Hz, 1H), 3.67 (q, *J* = 7.0 Hz, 2H), 2.82 (m, 1H), 2.73 – 2.61 (m, 1H), 2.19 – 1.87 (m, 2H), 1.82 (m, 1H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.11, 157.90, 157.23, 147.78, 122.39, 113.52, 71.47, 63.98, 29.53, 26.72, 19.39, 15.70. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{17}N_4OS$+:277.1123, found: 277.1125.

7-ethoxy-*N*-(quinolin-2-yl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A42**: White solid, mp 177.8-179.7 °C, yield: 89%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.54 (s, 1H), 8.19 (d, *J* = 8.8 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 4.58 (t, *J* = 4.0 Hz, 1H), 3.62 (q, *J* = 6.8 Hz, 2H), 2.77 – 2.57 (m, 1H), 2.50 (m, 1H), 1.90 (m, 3H), 1.82 – 1.65 (m, 1H), 1.18 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.96, 150.32, 146.43, 145.91, 137.66, 129.85, 127.75, 125.94, 123.97, 123.60, 121.13, 112.79, 70.54, 63.00, 29.05, 26.24, 18.95, 15.61. HRMS (ESI): m/z [M+H]+ calcd for $C_{18}H_{20}N_3OS$+:326.1327, found: 326.1326.

N-(5-chloropyridin-2-yl)-7-ethoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A43**: White solid, mp 161.6-162.5°C, yield: 91%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 1 H), 8.32 (d, *J* = 2.4 Hz, 1 H),

7. 78 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.08 (d, *J* = 8.8 Hz, 1 H), 4.51 (t, *J* = 4.8 Hz, 1 H), 3 .57 (q, *J* = 8.2 Hz, 2H), 2.51 (m, 2H), 1.90-1.71 (m, 4H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 15 8.6, 151.0, 147.0, 145.2, 13 8.2, 122.3, 121.1, 112.7, 71.0, 63.5, 29.6, 26.7, 19.5,16.1. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{17}{}^{35}C1N_3OS$+: 310.0781;found: 310.0783; calcd for $C_{14}H_{17}{}^{37}C1N_3OS$+: 312.0751, found: 312.0754.

N-(4-bromophenyl)-7-ethoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A44**: White solid, mp 146.3-147.1°C, yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1 H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 4.45 (t, *J* = 4.2 Hz, 1H), 3.53 (m, 2H), 2.53 (m, 2H), 1.87-1.71 (m, 4H), 1.13 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 148.7, 141.0, 132.0, 119.2, 119.0, 112.6, 71.0, 63.5, 29.5, 27.1，19.4, 16.1. HRMS (ESI): m/z [M+HJ+ calcd for $C_{15}H_{18}{}^{79}BrN_2OS$+: 353.0323, found: 353.0320, calcd for $C_{15}H_{18}{}^{81}BrN_2OS$+:355.0303, found: 355.0300.

7-ethoxy-*N*-(4-fluorophenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A45**: White solid, mp 105.5-106.2°C, yield: 86%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1 H),7.63 (dd, *J* = 8.8, 4.8 Hz, 2H), 7.14 (t, *J* = 8.8 Hz, 2H), 4.45 (t, *J* = 4.8 Hz, 1 H), 3 .54 (m, 2H), 2.53 (m, 2H), 1.86-1.70 (m, 4H), 1.13 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 157.2 (d, *J* = 237.4 Hz), 148.6, 138.2 (d, *J* = 1.4 Hz), 118.8 (d, *J* = 7.6 Hz), 118.4, 115.9 (d, *J* = 22.3 Hz), 71.0, 63.5, 29.6, 27.1, 19.4, 16.1; ^{19}F NMR (376 MHz, DMSO-d_6) δ -122.32. HRMS (ESI): m/z [M-H]- calcd for $C_{15}H_{16}FN_2OS$-: 291.0967; found: 291.0966.

N-(4-chlorophenyl)-7-ethoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A46**: White solid, mp 133.0-134.2 °C, yield:95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = Hz, 2H), 4.45 (t, *J* = 4.8 Hz, 1 H), 3.54 (q, *J* = 7.2 Hz, 2H), 2.62-2.47 (m, 2H), 1.87-1.71 (m, 4H), 1.13 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz,DMSO-d_6) δ 162.3, 148.6, 140.6, 129.2, 124.8, 118.9, 118.7, 71.0, 63.5, 29.5, 27.1, 19.4, 16.1. HRMS(ESI): m/z [M+H]+ calcd for $C_{15}H_{18}{}^{35}C1N_2OS$+: 309.0828, found: 309.0830; calcd for $C_{15}H_{18}{}^{37}C1N_2OS$+: 311.0799, found: 311.0802.

7-ethoxy-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A47**: White solid, mp 126.0-126.8 °C, yield: 91%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, 1 H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 4.44 (t, *J* = 4.8 Hz, 1H), 3.53 (q, *J* = 8.2 Hz, 2H), 2.52 (m, 2H), 2.24 (s, 3H), 1.86-1.70 (m, 4H), 1.13 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO--d_6) δ 162.9, 148.6, 139.3, 130.4, 129.8, 118.0, 117.5, 71.0, 63.4, 29.6, 27.1，20.8, I 9.4, 16.1. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{21}N_2OS$ +: 288.1375, found: 288.1364.

7-ethoxy-*N*-(4-(o-tolyloxy)phenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A48**: White solid, mp 100.8-101.8 °C, yield: 93%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.04 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 1 H), 7.16 (t, *J* = 7.8 Hz, 1 H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.43 (t, *J* = 5.2 Hz, 1 H), 3.52 (m, 2H), 2.51 (m, 2H), 2.21 (s, 3H), 1.85- 1.68 (m, 4H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 155.6, 151.3, 148.6, 137.3, 131.8, 128.7, 127.7, 123.7, 119.1, 119.0,118.3,118.1,71.1，63.4, 29.6, 27.1, 19.4, 16.4, 16.1. HRMS (ESI): m/z [M+H]+ calcd for $C_{22}H_{24}N_2O_2S$ +: 381.1637, found: 381.1635.

N-(4-fluorophenyl)-7-propoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A49**: White solid, mp 100.2-100.8 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1 H), 7.63 (dd, *J* = 8.8, 4.8 Hz, 2H), 7.13 (t, *J* = 8.8 Hz, 2H), 4.43 (t, *J* = 4.8 Hz, 1H), 3.44 (m, 2H), 2.53 (m, 2H), 1.86-1.66 (m, 4H), 1.51 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 157.2 (d, *J* = 237.4 Hz), 148.5, 138.2 (d, *J* = 1.4 Hz), 118.8 (d, *J* = 7.6 Hz), 118.5, 115.9 (d, *J* = 22.2 Hz), 71.3, 69.8, 29.5, 27.1, 23.3, 19.5, 11.1; ^{19}F NMR (376 MHz, DMSO-d_6) δ -122.3(m, 1F). HRMS (ESI): m/z [M-H]- calcd for $C_{16}H_{18}FN_2OS$-: 305.1124; found: 305.1122.

7-propoxy-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A50**: White solid, mp 118.9-119.8 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, 1 H), 7.48 (d, J = 7.8 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 4.42 (t, J = 4.8 Hz, 1 H), 3.45 (t, J = 7.2 Hz, 2H), 2.51 (m, 2H), 2.24 (s, 3H), 1.88-1.71 (m, 4H), 1.52 (m, 2H), 0.89 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 148.6, 139.3, 130.3, 129.8, 118.1, 117.5, 71.3, 69.8, 29.5, 27.1，23.3, 20.8, 19.5, 11.1. HRMS (ESI): m/z [M-H]- calcd for $C_{17}H_{21}N_2OS$-: 301.1375, found: 301.1376.

7-butoxy-*N*-(4-chlorophenyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A51**: White solid, mp 119.6-120.6 °C, yield: 82%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1 H), 7.65 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz 2H), 4.45 (t, J = 4.8 Hz, 1 H), 3.45 (t, J = 7.2 Hz, 2H), 2.61-2.46 (m, 2H), 1.87-1.71 (m, 4H), 1.52-1.45 (m, 2H), 1.39-1.30 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 148.6, 140.6, 129.2, 124.7, 119.0, 118.7, 71.3, 67.8, 32.1, 29.4, 27.1，19.4, 14.2. HRMS (ESI): m/z [M+H]+ calcd for $C_{17}H_{22}{}^{35}C1N_2OS$+: 337.1141, found: 349.1141;calcd for $C_{17}H_{22}{}^{37}C1N_2OS$ +: 339.1112, found: 339.1110.

7-butoxy-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A52**: White solid, mp 117.3-117.7 °C, yield: 87%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 4.42 (t, J = 4.8 Hz, 1H), 3.45 (t, J = 7.2 Hz, 2H), 2.51 (m, 2H), 2.24 (s, 3H), 1.87-1.71 (m, 4H),1.47 (m, 2H), 1.35 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 148.3, 139.3, 130.3, 129.8, 118.9, 117.5, 69.4, 68.8, 30.6, 27.0, 23.5, 23.1，20.8, 19.5. HRMS (ESI): m/z [M-H]- calcd for $C_{18}H_{23}N_2OS$-: 315.1531, found: 315.1530.

N-(4-chlorophenyl)-7-isopropoxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A53**: White solid, mp 123.9-124.7 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24(s, 1 H), 7.65 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H), 4.48 (t, J = 4.8 Hz, 1H), 3.80-3.70 (m, 1H), 2.60-2.45 (m, 2H), 1.88-1.72 (m, 4H), 1.12 (d, J = 5.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 148.3, 140.6, 129.2, 124.7, 119.9, 118.7, 69.5, 68.8, 30.6, 27.0, 23.5, 23.1, 19.5. HRMS (ESI): m/z [M+H]+ calcd for $C_{16}H_{20}{}^{35}C1N_2OS$+: 323.0985, found: 323.0988; calcd for $C_{16}H_{20}{}^{37}C1N_2OS$+: 325.0955, found: 325.0958.

7-isopropoxy-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A54**: White solid, mp 121.5-122.2 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.97 (s, I H), 7.48 (d, J = 7.8 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 4.42 (t, J = 4.8 Hz, 1 H), 3.75 (m, 1 H), 2.54 (m, 2H), 2.24 (s, 3H), 1.88-1.72 (m, 4H), 1.12 (d, J = 5.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 148.3, 139.3, 130.3, 129.8, 118.9, 117.5, 69.4, 68.8, 30.6, 27.0, 23.5, 23.1, 20.8, 19.5. HRMS (ESI): m/z [M-H]- :calcd for $C_{17}H_{21}N_2OS$-: 301.1375, found: 301.1374.

7-(2-methoxyethoxy)-*N*-(p-tolyl)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A55**: White solid, mp 85.2-85.9 °C, yield: 82%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.96 (s,1H), 7.47 (d, J = 8.2 Hz, 2H), 7.08 (d, J = 8.2 Hz, 2H), 4.47 (t, J = 4.0 Hz, 1H), 3.64-3.57 (m,2H), 3.48-3.41 (m, 2H), 3.26 (s, 3H), 2.61-2.39 (m, 2H), 2.23 (s, 3H), 1.88-1.66 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 148.3, 138.8, 129.9, 129.2, 117.2, 117.0, 71.6, 71.0, 67.1, 58.1, 28.9, 26.6, 20.3, 18.8. HRMS (ESI): m/z [M+H]+ calcd for $C_{17}H_{23}N_2O_2S$+: 315.1475, found: 315.1479.

N-(4-chlorophenyl)-7-(nonan-5-yloxy)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A56**: White solid, mp 98.2-99.1 °C, yield: 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 7.65 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz 2H), 4.45 (t, J = 4.8 Hz, 1 H), 3 .43 (t, J = 5.6 Hz, 1H), 2.61-2.45 (m, 2H), 1.91-1.64 (m, 4H), 1.48-1.19 (m, 12H), 0.93-0.85 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 148.4, 140.6, 129.1, 124.7, 119.8, 118.7, 77.2, 69.5, 34.3, 34.1, 30.3, 27.8, 27.2, 27.1, 23.0, 22.8, 19.4, 14.5, 14.5. HRMS (ESI): m/z [M+H]+ calcd for $C_{22}H_{32}{}^{35}C1N_2OS$ +: 407.1924, found: 407.1923; calcd

for $C_{22}H_{32}{}^{37}C1N_2OS$ +: 409.1894 found: 409.1891.

N-(4-chlorophenyl)-7-(cyclopentyloxy)-4,5,6,7-tetrahydrobenzo[d]thiazol-2-amine **A57**: White solid, mp 108.8-109.5 °C, yield: 76%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1 H), 7.65 (d, J = 8.6 Hz, ZH), 7.34 (d, J = 8.6 Hz 2H), 4.45 (t, J = 4.8 Hz, 1 H), 4.10 (t, J = 4.8 Hz, 1H), 2.60-2.45 (m, 2H), 2.03-1.40 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 148.4, 140.6, 129.2, 124.7, 119.8, 11$.7, 79.0, 69.3, 33.1, 32.9, 30.1, 27.0, 23.6, 23.4, 19.5. HRMS (ESI): m/z [M+H]+ calcd for $C_{18}H_{22}{}^{35}C1N_2OS$ +: 349.1141, found: 349.1143; calcd for $C_{18}H_{22}{}^{37}C1N_2OS$ +: 351.1112, found: 351.1114.

2-((4-chlorophenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl 1*H*-imidazole-1-carboxylate **A58**: White solid, mp 206.8-207.2 °C, yield: 86%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 7.70 – 7.60 (m, 3H), 7.38 – 7.31 (m, 2H), 7.15 (d, J = 1.2 Hz, 1H), 6.90 (d, J = 1.2 Hz, 1H), 5.58 (t, J = 5.8 Hz, 1H), 2.79 – 2.66 (m, 1H), 2.65 – 2.55 (m, 1H), 2.18 (m, 1H), 2.05 – 1.92 (m, 1H), 1.91 – 1.71 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.24, 149.49, 139.83, 136.33, 128.71, 128.42, 124.52, 118.37, 118.10, 116.06, 50.80, 40.13, 31.97, 26.16, 19.47. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{16}{}^{35}ClN_4O_2S^+$: 375.0677, found: 375.0681; calcd for $C_{17}H_{16}{}^{37}ClN_4O_2S^+$: 377.0648, found: 377.0652.

2-((4-fluorophenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl 1*H*-imidazole-1-carboxylate **A59**: White solid, mp 201.8-202.8 °C, yield: 92%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.70 – 7.58 (m, 3H), 7.19 – 7.09 (m, 3H), 6.90 (d, J = 1.2 Hz, 1H), 5.56 (t, J = 5.8 Hz, 1H), 2.71 (m, 1H), 2.63 – 2.53 (m, 1H), 2.17 (m, 1H), 2.05 – 1.92 (m, 1H), 1.81 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.2, 157.3 (d, J= 236.2 Hz) 149.9, 138.0 (d, J = 1.8 Hz), 136.8, 128.9, 119.0 (q, J = 7.6 Hz), 118.6, 116.0, 115.9 (q, J = 22.2 Hz), 51.3, 32.5, 26.7, 20.0; ^{19}F NMR (376 MHz, DMSO-d_6) δ = -121.9 (m, 1F). HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{16}FN_4O_2S^+$: 359.0973, found: 359.0975.

2-((4-(trifluoromethyl)phenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl-1*H*-imidazole-1-carboxylate **A60**: White solid, mp 194.5-195.5 °C, yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 7.80 (d, J = 8.6 Hz, 2H), 7.71 – 7.59 (m, 3H), 7.17 (d, J = 1.2 Hz, 1H), 6.91 (s, 1H), 5.61 (t, J = 5.8 Hz, 1H), 2.75 (m, 1H), 2.63 (m, 1H), 2.19 (m, 1H), 2.07 – 1.94 (m, 1H), 1.92 – 1.71 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 150.1, 144.7, 136.9, 129.0, 126.7 (q, J = 3.8 Hz), 125.1 (q, J = 270.8 Hz), 121.4 (q, J = 31.8 Hz), 118.6, 117.5, 117.1, 55.4, 51.3, 32.4, 26.7, 20.0; ^{19}F NMR (376 MHz, DMSO-d_6) δ -59.87 (s, 3F). HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{18}H_{16}F_3N_4O_2S^+$: 409.0941, found: 409.0945.

2-((5-chloropyridin-2-yl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl 1*H*-imidazole-1-carboxylate **A61**: White solid, mp 208.9-209.7 °C, yield: 94%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.48 (s, 1H), 8.26 (d, J = 2.4 Hz, 1H), 7.78 (m, 1H), 7.70 (s, 1H), 7.15 (s, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.92 (s, 1H), 5.64 (t, J = 5.2 Hz, 1H), 2.78-2.55 (m, 2H), 2.19 (m 1H), 1.99 (m, 1H), 1.93-1.76 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.5, 150.3, 147.8, 144.6, 137.8, 136.4, 128.4, 122.0, 118.5, 118.1, 112.2, 51.0, 32.1, 25.7, 19.8. HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{16}H_{15}{}^{35}ClN_5O_2S^+$: 376.0629, found: 376.0633; calcd for $C_{16}H_{15}{}^{37}ClN_5O_2S^+$: 378.0600, found: 378.0604.

2-(phenylamino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl 1*H*-imidazole-1-carboxylate **A62**: White solid, mp 195.0-195.7 °C, yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.15 (s, 1H), 7.67 (d, J = 1.2 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.34 – 7.24 (m, 2H), 7.15 (d, J = 1.2 Hz, 1H), 6.94 (m, 2H), 5.57 (t, J = 5.8 Hz, 1H), 2.79 – 2.66 (m, 1H), 2.65 – 2.54 (m, 1H), 2.18 (m, 1H), 1.99 (m, 1H), 1.90 – 1.70 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.62, 149.47, 140.93, 136.31, 128.88, 128.41, 121.24, 118.10,

116.96, 115.51, 50.84, 32.01, 26.16, 19.49. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{17}N_4O_2S^+$: 341.1067, found: 341.1065.

2-(p-tolylamino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-yl 1*H*-imidazole-1-carboxylate **A63**: White solid, mp 200.2-201.8 °C °C, yield: 91%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 7.67 (s, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.15 (s,1H), 7.10 (d, J = 8.4 Hz, 2H), 6.90 (s, 1H), 5.55 (t, J = 5.4 Hz, 1H), 2.75-2.65 (m, 1H), 2.63-2.53 (m, 1H), 2.24 (s, 3H), 2.22-2.12 (m, 1H), 2.03-1.93 (m, 1H), 1.89-1.73 (m, 1H), 1.87-1.74 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.4, 150.0, 139.1, 136.8, 130.7, 129.8, 128.9, 118.6, 117.6, 115.6, 51.4, 32.5, 26.7, 20.8, 20.0. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{19}N_4O_2S^+$: 355.1223, found: 355.1225.

2-((4-chlorophenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B1**: White solid, mp 159.7-163.1 °C, yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 7.65 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H), 5.24 (d, J = 6.1 Hz, 1H), 4.64 (t, .J = 4.2 Hz- 1H), 2.58-2.45 (m, 2H), 1.96-1.$8 (m, 2H), 1.70-1.64 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.0, 147.5, 140.7, 129.1, 124.5, 122.9, 118.6, 63.4, 33.6, 27.0, 19.7. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{14}{}^{35}C1N_2OS$+: 281.0515, found: 281.0519; calcd for $C_{13}H_{14}{}^{37}C1N_2OS$ +: 283.0486, found: 283.0488.

2-((4-fluorophenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B2**: White solid, mp 140.5.7-141.6 °C, yield: 86%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 7.76-7.48 (m, 2H), 7.16-7.09 (m, 2H), 5.22 (d, J = 6.4 Hz, 1 H), 4.63 (t, J = 2.4 Hz, 1H), 2.58-2.39 (m, 2H), 1.95-1.86 (m, 2H), 1.81-1.60 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 157.1 (d, J = 235.6 Hz) 147.3, 138.3 (d, J = 1.7 Hz), 122.4, 118.6 (d, J = 7.5 Hz), 115.8 (d, J = 22.0 Hz), 63.4, 33.6, 27.0, 19.7; ^{19}F NMR (376 MHz, DMSO-d_6) δ -122.6 (m, 1F). HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{14}FN_2OS$+: 265.0805, found: 265.0805.

2-((4-(trifluoromethyl)phenyl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B3**: White solid, mp 155.4-155.9 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.47 (s, 1 H), 7.80 (d, J = 8.6 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H), 5.28 (s, 1 H), 4.66 (s, 1 H), 2.53 (m, 2H), 1.93 (dt, J = 10.5, 3.4 Hz, 2H), 1.69 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.5, 147.6, 145.0, 126.7 (q, J = 3.8 Hz), 125.2 (q, J = 269 Hz), 123.9, 121.0 (q, J = 31.7 Hz), 116.7, 63.4, 33.5, 27.0, 19.7; ^{19}F NMR (376 MHz, DMSO-d_6) δ -59.79 (s, 3F). HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{14}F_3N_2OS$+: 315.0773, found: 315.0771.

2-(phenylamino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B4**: White solid, mp 134.5-135.4 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 7.60 (d, J = 7.8 Hz, 2H), 7.29 (t, J = 8.0 Hz, 2H), 6.92 (t, J = 7.4 Hz, 1H), 5.24 (d, J = 6.1 Hz, 1 H), 4.64 (t, J = 4.2 Hz- 1 H), 2.58-2.45 (m, 2H), 1.96-1.88 (m, 2H), 1.70-1.64 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 148.8, 141.7, 129.4, 121.5, 117.9, 117.3, 63.4, 33.6, 27.0, 19.7. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{15}N_2OS$ +: 247.0900, found: 247.0901.

2-(p-tolylamino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B5**: White solid, mp 129.5-130.3 °C, yield: 89%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 5.20 (d, J = 6.4 Hz, 1 H), 4.66-4.60 (m, 1H), 2.57-2.38 (m, 2H), 2.33 (s, 3H),1.94-1.86 (m, 2H) , 1.70-1.64 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 147.4, 139.4, 130.1, 129.7, 121.9, 117.3, 63.4, 33.6, 27.0, 20.8, 19.7. HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{17}N_2OS$ +: 261.1056, found: 261.1056.

1-(4-((7-hydroxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)amino)phenyl)ethan-1-one **B6**: White solid, mp 174.5-183.1 °C, yield: 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.51 (s, 1H), 7.91 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.8 Hz, 2H), 5.28 (d, J = 6.4 Hz, 1H), 4.66 (d, J =4.6 Hz, 1H), 3.33 (s, 1H), 2.52 (s, 2H), 1.93 (m, 2H), 1.74 – 1.63 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.91, 160.86, 147.14,

145.33, 129.85, 129.39, 123.55, 115.67, 62.94, 33.01, 26.49, 26.22, 19.24. HRMS (ESI): m/z [M+H]+ calcd for $C_{15}H_{17}N_2O_2S$+: 289.1011, found: 289.1012.

2-((5-chloropyridin-2-yl)amino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B7**: White solid, mp 180.3-181.0 °C, yield: 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.23 (s, 1H), 8.29 (d, J = 2.6 Hz, 1 H), 7.77 (dd, J = 9.0, 2.6 Hz, 1 H), 7.08 (d, J = 8. 8 Hz, 1 H), 5.21 (s, 1H), 4.70 (s, 1H), 2.60-2.40 (m, 2H), 1.91 (m, 2H), 1.74-1.60 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.4, 151.1, 145.1, 138.1, 125.0, 122.2, 119.8, 112.6, 63.4, 33.6, 26.6, 19.8. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{14}{}^{35}C1N_2OS$+: 283.051, found: 283.05 19; calcd for $C_{13}H_{14}{}^{37}C1N_2OS$+: 285.0486, found: 285.0488.

2-(naphthalen-2-ylamino)-4,5,6,7-tetrahydrobenzo[d]thiazol-7-ol **B8**: White solid, mp 160.6-162.4 °C, yield: 86%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.28 (d, J = 2.2 Hz, 1H), 7.87 – 7.71 (m, 3H), 7.55 (dd, J = 8.8, 2.4 Hz, 1H), 7.43 (m, 1H), 7.32 (m, 1H), 5.26 (d, J = 6.4 Hz, 1H), 4.68 (m, 1H), 2.58 (m, 2H), 2.09 – 1.83 (m, 2H), 1.83 – 1.61 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.63, 147.06, 138.89, 133.90, 128.47, 127.42, 126.69, 126.38, 123.49, 122.30, 118.94, 110.99, 62.97, 33.11, 26.59, 19.28. HRMS (ESI): m/z [M+H]+ calcd for $C_{17}H_{17}N_2OS$+:297.1062, found: 297.1061.

N-(4-chlorophenyl)benzo[d]thiazol-2-amine **C1**: White solid, mp 208.8-209.9 °C, yield: 88%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 7.88 – 7.79 (m, 3H), 7.63 (d, J = 8.0 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.34 (m, 1H), 7.18 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.23, 151.87, 139.49, 129.95, 128.79, 125.90, 125.34, 122.46, 121.09, 119.32, 119.13. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_{10}{}^{35}ClN_2S$+: 261.0253, found: 261.0254; calcd for $C_{13}H_{10}{}^{37}ClN_2S$+: 263.0224, found: 263.0222.

6-chloro-N-(4-chlorophenyl)benzo[d]thiazol-2-amine **C2**: White solid, mp 225.3-226.8 °C , yield: 83%.^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 7.96 (d, J = 2.2 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.60 (d, J = 8.6 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.35 (dd, J = 8.6, 2.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.93, 150.79, 139.23, 131.68, 128.83, 126.27, 126.09, 125.64, 120.82, 120.27, 119.28. HRMS (ESI): m/z [M+H]+ calcd for $C_{13}H_9{}^{35}Cl_2N_2S$+: 294.9863, found: 294.9862; calcd for $C_{13}H_9{}^{35}Cl^{37}ClN_2S$+: 296.9884, found: 296.9838; calcd for $C_{13}H_9{}^{37}Cl_2N_2S$+: 298.9804, found: 298.9804.

N-phenyl-6-(trifluoromethyl)benzo[d]thiazol-2-amine **C3**: White solid, mp 179.4-181.0°C , yield: 93%.^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (s, 1H), 8.29 (s, 1H), 7.80 (d, J = 8.6 Hz, 2H), 7.74 (d, J = 8.4 Hz, 1H), 7.63 (dd, J = 8.6, 1.8 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.08 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.43, 155.00, 140.07, 130.67, 129.04, 123.29 (q, J = 269.2 Hz), 122.85 (q, J = 9.6 Hz), 122.69, 119.10, 118.84 (q, J = 4.2 Hz), 118.22; ^{19}F NMR (376 MHz, DMSO-d_6) δ -59.37 (s, 1F) HRMS (ESI): m/z [M+H]+ calcd for $C_{14}H_{10}F_3N_2S$+: 295.0517, found: 295.0518.