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Supporting information

Green synthesis and characterisation of novel [1,3,4]thiadiazolo/benzo[4,5]thiazolo[3,2a]pyrimidines via multicomponent reaction using vanadium oxide loaded on fluorapatite as a robust sustainable catalyst

Nagaraju Kerru, Lalitha Gummidi, Surya Narayana Maddila, Sandeep V H S Bhaskaruni, Suresh Maddila and Sreekantha B. Jonnalagadda*

*School of Chemistry & Physics, University of KwaZulu-Natal, Westville Campus, Chiltern Hills, Durban-4000, South Africa.

*Corresponding Author: Prof. Sreekantha B. Jonnalagadda School of Chemistry & Physics, University of KwaZulu-Natal, Durban 4000, South Africa. Tel.: +27 31 2607325, Fax: +27 31 2603091 E-mail: jonnalagaddas@ukzn.ac.za

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Figure S1: Recovered 2.5% V₂O₅/FAp catalyst of SEM (a), EDX (b) and FT-IR spectrum (c).

For illustration, 4-methoxy substituted derivative (4a) exhibited three sets of singlets in the ¹H NMR spectrum, the most prominent singlet was seemed at δ 8.30 ppm due to the one proton of pyrimidine moiety. Another two singlets were observed at δ 3.87 and 12.69 ppm, which belong to the OCH₃ and NH₂ groups, respectively. Additionally, one quartet at 4.29 ppm and triplet at 1.29 ppm corresponds to the –COOCH₂CH₃ group. The remaining aromatic protons appeared at the respective aromatic region. The most characteristic peak seemed at δ 168.74 ppm due to the ester moiety carbonyl carbon (C=O) in ¹³C NMR. Further, two vibrational bands found at 3146 cm⁻¹ and 1695 cm⁻¹ in the FT-IR spectrum belong to the NH₂ and C=O groups, respectively. The molecular-ion peak was found at m/z = 427.0618 in the HRMS spectrum, which was further confirmed the formation of compound 4a.

EXPERIMENTAL SECTION

General Remarks

All the chemicals and reagents used for the reaction were of analytical grade and utilized without any further purification. V₂O₅, Ca(NO₃)₃.4H₂O, Na₃PO₄.12H₂O and NaF were purchased from Alfa Aesar, Merck and Sigma–Aldrich. For the synthesized compounds, the structural elucidation was done by Bruker AMX 400 MHz NMR spectrometer and recording the spectral values of ¹H and ¹³C NMR spectrum. Chemical shift values are reported in δ (ppm), with TMS assisted as the internal standard and DMSO- d_6 as a solvent. TLC-aluminum plates coated with silica gel (Merck Kieselgel 60 F254) were used for the initial conforming of reaction completion. Bruker micro TOF-Q II ESI instrument functioning at ambient temperature was used for High-resolution mass data (HRMS). FT-IR spectrum was recorded at the 400 cm⁻¹ to 4000 cm⁻¹ range and using Perkin Elmer Precisely 100 FT-IR spectrometer. JEOL JSM-6100 microscopes and Jeol JEM-1010 electron microscope was employed for the SEM, EDX and TEM morphology data. X-ray diffraction data associated with the structural phases of the material was obtained by using the Bruker D8 Advance instrument (Cu K radiation source with a wavelength of 1.5406 Å). Materials were degassed by passing nitrogen overnight at 200 °C and BJH adsorption and desorption curves were attained at -196 °C. Surface area, pore size and pore volume of the material were established by using Micromeritics Tristar-II porosity and surface area analyzer.

V₂O₅/FAp catalyst preparation

Different weight percentages loading of vanadium oxide on fluorapatite (1, 2.5 and 5 wt%) were synthesized by the co-precipitation method according to the literature reported method [42]. 1.5 mmol of trisodium phosphate dodecahydrate (Na₃PO₄.12H₂O) was suspended in deionized water (25 mL) in a 50 mL of the beaker. Next, 0.5 mmol of sodium fluoride (NaF) was gradually added

to that solution under constant stirring for 30 min at room temperature. Then, 2.5 mmol of calcium nitrate tetrahydrate was added into this solution mixture and continue stirring for further 15 min. Finally, the necessary calculated volume of 99.9% vanadium oxide (0.5 mmol) was added slowly and the solution mixture was more stirring for 6 h. The subsequent suspensions were divided by centrifugation and the number of runs rinsed with deionized water. The afforded composite material systems were dried in the heating oven at 120 °C for 10h. Although, these catalyst materials were calcinated at 350°C for 4 h under continuous airflow, to get the vanadium oxide loaded fluorapatite (V₂O₅/FAp) catalyst materials.

General procedure for the synthesis of [1,3,4]thiadiazolo[3,2-*a*]pyrimidine and benzo[4,5]thiazolo[3,2-*a*]pyrimidine derivatives (4a-q)

A mixture of different substituted 1,3,4-thiadiazole-amine (1a-h, 1 mmol) or 2-aminobenzathiazole (5, 1 mmol), varieties of selected benzaldehydes (2a-f, 1 mmol), active methylene compounds (3a-c, 1 mmol) and 30 mg of heterogeneous catalyst (2.5% V₂O₅/FAp) in solvent ethanol (5 mL) were added in a round bottom flask. The reaction mixture was constantly stirred at room temperature for 25 to 30 min. The progress of the reaction monitored by TLC. After finishing the reaction mixture, the catalyst was separated from the reaction mixture by filtration through the addition of excess ethyl acetate. The recovered catalyst material was further reused for the next cycles. The filtrate was concentrated by rotatory evaporation with vacuum pressure. Then the furnished the solid products and which were recrystallized by using hot ethanol to facilitate the corresponding pure products. The structural elucidation of all the synthesized novel compounds were established and interpreted by different spectroscopic methods (FT-IR, HRMS, ¹H and ¹³C NMR). *Ethyl-7-amino-2-(3-fluorophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4a**)

White solid; m.p. 176-178 °C; IR cm⁻¹: 3146 (NH₂), 2906 (CH), 1695 (C=O), 1601 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.69 (s, 2H, NH₂), 8.30 (s, 1H, CH), 8.08 (d, J = 8.6 Hz, 2H, Ar-H), 7.98 (t, J = 10.3 Hz, 1H, Ar-H), 7.82 (d, J = 8.0 Hz, 1H, Ar-H), 7.57 (dd, J = 13.6, 7.5 Hz, 1H, Ar-H), 7.36 (t, J = 8.8 Hz, 1H, Ar-H), 7.15 (d, J = 8.6 Hz, 2H, Ar-H), 4.29 (q, J = 6.9 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 1.29 (t, J = 7.0 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 168.74, 163.52, 162.33, 161.12, 154.43, 133.48, 131.54, 131.46, 123.93, 123.26, 117.41, 117.20, 116.20, 114.94, 113.35, 113.11, 98.54, 62.04, 55.73, 22.38, 13.99; HRMS of [C₂₁H₁₉N₄O₃FS + H]⁺ (m/z) 427.0618; Calcd: 427.0621.

Ethyl-7-amino-2-(3-bromophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine -6-carboxylate (**4b**)

Cream white solid; m.p. 182-184 °C; IR cm⁻¹: 3147 (NH₂), 2906 (CH), 1695 (C=O), 1609 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 9.87 (s, 2H, NH₂), 8.29 (s, 1H, CH), 8.07 (d, J = 8.6 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.73 (d, J = 7.8 Hz, 1H, Ar-H), 7.61 (d, J = 7.8 Hz, 1H, Ar-H), 7.42 (t, J = 7.8 Hz, 1H, Ar-H), 7.14 (d, J = 8.5 Hz, 2H, Ar-H), 4.30 (q, J = 6.9 Hz, 2H, CH₂), 3.87 (s, 3H, OCH3), 1.30 (t, J = 7.0 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 164.02, 162.83, 154.89, 133.98, 133.64, 133.61, 132.58, 131.73, 128.68, 125.92, 124.43, 122.74, 116.68, 115.42, 115.34, 99.04, 62.53, 56.22, 14.48; HRMS of [C₂₁H₁₉N₄O₃BrS + H]⁺ (*m*/*z*) 487.9764; Calcd: 487.9777. *Ethyl-7-amino-2-(p-tolyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6carboxylate* (**4c**)

White solid; m.p. 189-181 °C; IR cm⁻¹: 3146 (NH₂), 2905 (CH), 1695 (C=O), 1609 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.59 (s, 2H, NH₂), 8.31 (s, 1H, CH), 8.09 (d, J = 9.0 Hz, 2H, Ar-

H), 7.82 (d, J = 8.0 Hz, 1H, Ar-H), 7.63 (d, J = 7.9 Hz, 1H, Ar-H), 7.34 (d, J = 8.0 Hz, 2H, Ar-H), 7.14 (d, J = 8.9 Hz, 2H, Ar-H), 4.30 (q, J = 7.1 Hz, 2H, CH₂), 3.87 (s, 3H, OCH3), 2.21 (s, 3H, CH3), 1.30 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 169.08, 164.03, 162.84, 154.93, 133.99, 133.71, 130.34, 127.27, 124.44, 116.71, 115.45, 115.38, 99.06, 62.54, 56.24, 22.89, 21.42, 14.50; HRMS of $[C_{22}H_{22}N_4O_3S + H]^+$ (*m/z*) 423.1623; Calcd: 423.1617.

Ethyl-7-amino-2-(3-nitrophenyl)-5-(4-methoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate (4d)

Pale yellow solid; m.p. 192-194 °C; IR cm⁻¹: 3146 (NH₂), 2912 (CH), 1697 (C=O), 1608 (C=C); ¹H NMR (400 MHz, DMSO- d_{δ}) δ 9.80 (s, 2H, NH₂), 8.49 (s, 1H, CH), 8.29 (s, 1H, Ar-H), 8.25 (d, *J* = 7.1 Hz, 1H, Ar-H), 8.15 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.08 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.75 (t, *J* = 7.9 Hz, 1H, Ar-H), 7.15 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.30 (dd, *J* = 13.8, 6.8 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 1.30 (t, *J* = 6.9 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_{δ}) δ 164.02, 162.83, 154.90, 148.70, 133.98, 132.99, 132.89, 131.55, 131.34, 124.43, 124.25, 120.53, 116.69, 115.43, 99.05, 62.54, 56.23, 22.89, 14.49; HRMS of [C₂₁H₁₉N₅O₅S+H]⁺ (*m/z*) 454.1720; Calcd: 454.1723. *Ethyl-7-amino-2-(3-fluorophenyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4e**)

Cream white solid; m.p. 174-176 °C; IR cm⁻¹: 3158 (NH₂), 2904 (CH), 1696 (C=O), 1610 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.70 (s, 2H, NH₂), 8.42 (s, 1H, CH), 8.16 (dd, J = 8.7, 5.6 Hz, 2H, Ar-H), 7.78 (d, J = 7.5 Hz, 2H, Ar-H), 7.60 (t, J = 4.6 Hz, 1H, Ar-H), 7.46 (t, J = 4.9 Hz, 1H, Ar-H), 7.36 (dd, J = 12.1, 8.2 Hz, 1H, Ar-H), 7.27 (t, J = 8.6 Hz, 1H, Ar-H), 4.32 (q, J = 7.1 Hz, 2H, CH₂), 1.31 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 169.25, 164.07, 162.24, 161.64, 159.32, 154.27, 134.22, 134.12, 132.05, 131.96, 128.59, 123.76, 117.91, 117.70, 117.21, 117.14, 116.99, 116.92, 113.86, 113.62, 113.13, 112.89, 102.72, 62.86, 22.89, 14.45; HRMS of [C₂₀H₁₆N₄O₂F₂S + H]⁺ (*m/z*) 415.1115; Calcd: 415.1109.

Ethyl-7-amino-2-(3-bromophenyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate (**4f**)

White solid; m.p. 202-204 °C; IR cm⁻¹: 3276 (NH₂), 2911 (CH), 1715 (C=O), 1610 (C=C); ¹H NMR (400 MHz, DMSO- d_{δ}) δ 12.70 (s, 2H, NH₂), 8.41 (s, 1H, CH), 8.15 (dd, J = 8.5, 5.6 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.73 (d, J = 7.8 Hz, 1H, Ar-H), 7.62 (d, J = 7.9 Hz, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.46 (t, J = 8.8 Hz, 2H, Ar-H), 4.32 (q, J = 7.1 Hz, 2H, CH₂), 1.31 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_{δ}) δ 166.40, 163.88, 162.23, 154.24, 134.21, 134.12, 133.61, 132.59, 131.74, 128.68, 128.58, 128.55, 125.93, 122.74, 117.20, 116.98, 116.02, 102.72, 102.70, 62.85, 22.86, 14.44; HRMS of [C₂₀H₁₆N₄O₂FBrS + H]⁺ (*m*/*z*) 475.9894; Calcd: 475.9892. *Ethyl-7-amino-2-(m-tolyl)-5-(4-fluorophenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (4g)

White solid; m.p. 194-196 °C; IR cm⁻¹: 3141 (NH₂), 2913 (CH), 1692 (C=O), 1611 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.78 (s, 2H, NH₂), 8.49 (s, 1H, Ar-H), 8.39 (s, 1H, CH), 8.24 (d, J = 7.9 Hz, 1H, Ar-H), 8.15 (d, J = 7.7 Hz, 2H, Ar-H), 7.75 (t, J = 8.0 Hz, 1H, Ar-H), 7.63 (s, 1H, Ar-H), 7.44 (t, J = 8.6 Hz, 2H, Ar-H), 4.32 (q, J = 7.0 Hz, 2H, CH₂), 2.24 (s, 3H, CH₃), 1.31 (t, J = 7.0 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 166.39, 163.87, 162.22, 154.22, 148.69, 134.20, 134.11, 132.97, 132.89, 131.32, 128.56, 128.53, 124.22, 120.51, 117.19, 116.97, 116.01, 102.69, 102.67, 62.85, 48.12, 22.87, 14.43; HRMS of [C₂₁H₁₉N₄O₂FS + H]⁺ (*m/z*) 411.0676; Calcd: 411.0671.

Ethyl-7-amino-2-(4-chlorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate (**4h**) Cream white solid; m.p. 206-208 °C; IR cm⁻¹: 3138 (NH₂), 2914 (CH), 1692 (C=O), 1611 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.67 (s, 2H, NH₂), 8.29 (s, 1H, CH), 8.14 (d, J = 8.6 Hz, 1H, Ar-H), 7.96 (d, J = 8.6 Hz, 1H, Ar-H), 7.70 (d, J = 8.6 Hz, 2H, Ar-H), 7.58 (d, J = 8.6 Hz, 2H, Ar-H), 7.17 (d, J = 8.5 Hz, 1H, Ar-H), 4.30 (q, J = 7.1 Hz, 2H, CH₂), 3.88 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 1.30 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 169.24, 162.87, 155.28, 154.01, 149.19, 134.45, 129.85, 129.63, 129.03, 128.38, 124.47, 122.59, 113.44, 112.37, 98.98, 62.55, 56.39, 55.99, 22.88, 14.51; HRMS of [C₂₂H₂₁N₄O₄ClS + H]⁺ (m/z) 473.1340; Calcd: 473.1338.

Ethyl-7-amino-2-phenyl-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate (**4i**)

White solid; m.p. 176-178 °C; IR cm⁻¹: 3156 (NH₂), 2912 (CH), 1713 (C=O), 1589 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.63 (s, 2H, NH₂), 8.28 (s, 1H, CH), 8.02 – 7.86 (m, 2H, Ar-H), 7.80 – 7.70 (m, 2H, Ar-H), 7.63 – 7.38 (m, 3H, Ar-H), 7.17 (d, J = 8.5 Hz, 1H, Ar-H), 4.30 (q, J = 7.1 Hz, 2H, CH₂), 3.88 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 1.30 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 169.14, 162.86, 158.84, 155.26, 154.01, 149.19, 130.99, 130.69, 129.80, 127.35, 127.25, 126.77, 124.48, 116.85, 113.44, 112.36, 98.95, 62.53, 56.38, 55.98, 22.89, 14.50; HRMS of [C₂₂H₂₂N₄O₄S + H]⁺ (*m/z*) 439.0523; Calcd: 439.0511.

Ethyl-7-amino-2-(4-fluorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate (**4j**)

White solid; m.p. 191-193 °C; IR cm⁻¹: 3139 (NH₂), 2912 (CH), 1692 (C=O), 1589 (C=C); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.64 (s, 2H, NH₂), 8.30 (s, 1H, CH), 8.20 (dd, *J* = 8.5, 5.4 Hz, 2H, Ar-H), 8.00 (d, *J* = 3.0 Hz, 1H, Ar-H), 7.75 (t, *J* = 8.4 Hz, 2H, Ar-H), 7.49 (t, *J* = 8.8 Hz, 1H, Ar-H), 7.18 (d, *J* = 8.4 Hz, 1H, Ar-H), 4.31 (q, *J* = 7.1 Hz, 2H, CH₂), 3.88 (s, 3H, OCH₃), 3.81 (s, 3H,

OCH₃), 1.31 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 169.17, 162.87, 155.28, 154.02, 149.19, 129.95, 129.86, 129.72, 129.64, 127.23, 124.49, 120.50, 117.26, 117.04, 116.98, 116.76, 113.48, 112.39, 98.97, 62.53, 56.39, 55.99, 22.88, 14.51; HRMS of [C₂₂H₂₁N₄O₄FS + H]⁺ (*m/z*) 457.0515; Calcd: 457.0522.

Ethyl-7-amino-2-(3-fluorophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate (**4k**)

White solid; m.p. 184-186 °C; IR cm⁻¹: 3158 (NH₂), 2914 (CH), 1712 (C=O), 1588 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.64 (s, 2H, NH₂), 8.27 (s, 1H, CH), 7.74 (m, 3H, Ar-H), 7.53 (t, J = 12.6 Hz, 2H, Ar-H), 7.36 (t, J = 8.7 Hz, 1H, Ar-H), 7.16 (d, J = 7.9 Hz, 1H, Ar-H), 4.29 (q, J = 6.7 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 1.30 (d, J = 6.3 Hz, 3H, CH₃); ¹³C NMR (151 MHz, DMSO- d_6) δ 168.74, 165.47, 162.36, 161.25, 154.73, 153.55, 148.73, 131.50, 126.74, 124.00, 123.24, 117.33, 117.19, 116.32, 113.29, 113.13, 113.00, 111.89, 98.52, 62.02, 55.89, 55.51, 22.37, 13.99; HRMS of [C₂₂H₂₁N₄O₄FS + H]⁺ (*m/z*) 457.1714; Calcd: 457.1723. *Ethyl-7-amino-2-(3-bromophenyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a] pyrimidine-6-carboxylate* (**4**I)

Pale yellow solid; m.p. 183-185 °C; IR cm⁻¹: 3159 (NH₂), 2942 (CH), 1712 (C=O), 1588 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 12.69 (s, 2H, NH₂), 8.27 (s, 1H, CH), 8.23 (s, 1H, Ar-H), 8.10 (t, J = 1.7 Hz, 1H, Ar-H), 7.91 (dd, J = 4.4, 1.6 Hz, 1H, Ar-H), 7.74 (dd, J = 10.0, 1.9 Hz, 2H, Ar-H), 7.51 (t, J = 8.1 Hz, 1H, Ar-H), 7.16 (d, J = 8.5 Hz, 2H, Ar-H), 4.29 (q, J = 7.1 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 1.30 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 168.73, 162.36, 154.74, 153.50, 148.67, 133.10, 132.32, 131.43, 131.23, 126.74, 126.44, 123.96, 116.35, 112.90, 112.71, 111.84, 98.41, 62.02, 55.87, 55.45, 22.37, 14.00; HRMS of [C₂₂H₂₁N₄O₄BrS + H]⁺ (m/z) 517.9402; Calcd: 517.9399. *Ethyl-7-amino-2-(p-tolyl)-5-(3,4-dimethoxyphenyl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate* (**4m**)

White solid; m.p. 201-203 °C; IR cm⁻¹: 3160 (NH₂), 2942 (CH), 1698 (C=O), 1588 (C=C); ¹H NMR (400 MHz, DMSO- d_6) δ 13.02 (s, 2H, NH₂), 8.29 (s, 1H, CH), 8.05 (d, J = 8.1 Hz, 2H, Ar-H), 7.85 (d, J = 8.1 Hz, 2H, Ar-H), 7.73 (dd, J = 12.9, 4.4 Hz, 1H, Ar-H), 7.36 (dd, J = 8.0, 4.9 Hz, 2H, 1H, Ar-H), 7.17 (d, J = 8.5 Hz, 1H, Ar-H), 4.30 (q, J = 7.1 Hz, 2H, CH₂), 3.87 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 2.36 (s, 3H, CH₃), 1.29 (t, J = 7.1 Hz, 3H, CH₃); ¹³C NMR (151 MHz, DMSO- d_6) δ 168.57, 162.37, 154.77, 153.56, 148.75, 143.36, 140.48, 129.87, 128.43, 126.83, 124.02, 116.34, 113.08, 111.94, 98.56, 62.03, 55.92, 55.55, 21.09, 20.94, 14.02; HRMS of [C₂₃H₂₄N₄O₄S + H]⁺ (*m*/*z*) 453.0276; Calcd: 453.0282.

Ethyl-2-phenyl-5-(4-bromophenyl)-7-methyl-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carboxylate (**4n**)

White solid; m.p. 158-160 °C; ¹H NMR (400 MHz, DMSO- d_6) δ 7.67 (d, J = 7.7 Hz, 2H, Ar-H), 7.60-7.47 (m, 5H, Ar-H), 7.35 (d, J = 7.9 Hz, 2H, Ar-H), 6.61 (s, 1H, CH), 3.89 (q, J = 7.1 Hz, 2H, CH₂), 2.30 (s, 3H, CH₃), 1.07 (t, J = 7.2 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 166.04, 160.65, 151.39, 144.23, 140.69, 139.42, 132.22, 129.87, 129.79, 129.07, 126.60, 120.09, 109.65, 61.54, 55.37, 31.15, 22.06; HRMS of [C₂₁H₁₈N₃O₂SBr + Na]⁺ (*m*/*z*) 478.9894; Calcd: 478.9892.

1-(2-phenyl-5-(4-Bromophenyl)-7-methyl-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidin-6-yl)ethenone (40)

White solid; m.p. 164-166 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.30 (s, 1H, CH), 7.94 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.68 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.31 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.04 (dd, *J* = 38.2, 8.2 Hz, 3H, Ar-H), 3.24 (s, 3H, CH₃), 3.18 (s, 3H, CH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 192.52,

161.89, 153.84, 137.52, 136.10, 134.09, 133.57, 131.80, 129.78, 128.69, 122.77, 115.70, 104.80, 63.01, 21.65, 14.43; HRMS of [C₂₁H₁₆N₃O₂SBr + Na]⁺ (*m/z*) 448.0921; Calcd: 448.0920.

Ethyl-2-amino-4-(4-ethylphenyl)-4H-benzo[4,5]thiazolo[3,2-a]pyrimidine-3-carboxylate (4p)

White solid; m.p. 206-208 °C; ¹H NMR (400 MHz, DMSO- d_6) δ 12.35 (s, 2H, NH₂), 8.33 (s, 1H, CH), 7.99 – 7.93 (m, 2H, Ar-H), 7.73 (d, J = 7.9 Hz, 2H, Ar-H), 7.41 (d, J = 7.0 Hz, 2H, Ar-H), 7.28 (t, J = 7.4 Hz, 2H, Ar-H), 4.30 (q, J = 6.9 Hz, 2H, CH₂), 2.67 (q, J = 7.3 Hz, 2H, CH₂), 1.30 (t, J = 6.9 Hz, 3H, CH₃), 1.19 (t, J = 7.3 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 169.87, 162.47, 158.40, 155.42, 150.84, 148.98, 131.55, 129.24, 126.49, 123.88, 122.09, 120.93, 116.27, 101.66, 62.74, 28.79, 23.22, 15.46, 14.44; HRMS of [C₂₁H₂₁N₃O₂S + H]⁺ (*m*/*z*) 380.0484; Calcd: 380.0481.

Ethyl-2-amino-4-(2,4-dichlorophenyl)-4H-benzo[4,5]thiazolo[3,2-a]pyrimidine-3-carboxylate (4q)

White solid; m.p. 210-212 °C; ¹H NMR (400 MHz, DMSO- d_6) δ 10.15 (s, 2H, NH₂), 8.55 (s, 1H, Ar-H), 8.49 (s, 1H, CH), 8.19 (d, J = 8.5 Hz, 1H, Ar-H), 8.07 (d, J = 8.6 Hz, 1H, Ar-H), 8.01 (t, J = 7.4 Hz, 2H, Ar-H), 7.68 (d, J = 7.5 Hz, 1H, Ar-H), 7.64 (d, J = 7.4 Hz, 1H, Ar-H), 4.33 (q, J = 6.7 Hz, 2H, CH₂), 1.33 (t, J = 6.9 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO- d_6) δ 162.39, 155.34, 135.27, 134.92, 132.79, 129.76, 129.71, 129.60, 129.51, 129.43, 129.39, 128.30, 127.87, 124.97, 116.24, 102.74, 62.85, 55.35, 14.46; HRMS of [C₁₉H₁₅N₃O₂SCl₂ + Na]⁺ (*m/z*) 442.2028; Calcd: 442.2018.

Spectras



Figure S2. ¹H-NMR spectra of compound 4a



Figure S3. ¹³C-NMR spectra of compound 4a

Elemental Composition Report										
Single Ma Tolerance = Element pre Number of	ss Analysis 5.0 PPM / DBB ediction: Off isotope peaks use	E: min = -1 d for i-FIT	.5, max = 5 = 2	0.0						
Monoisotopie 29 formula(e Elements Us C: 20-25 PTS-8 2 (0.03 TOF MS ES+	c Mass, Even Electro) evaluated with 1 re ed: H: 15-20 N: 5-10 4) Cm (1:61)	on lons esults within) O: 0-5	limits (up to F: 1-1 S	20 closest re: : 0-1	sults for each	mass)				1 910+005
100- - - - - - - - - - - -					427.0618					1.810+005
- 410.03 0- (373 414.0552	4 <mark>1</mark> 7.1979	419.2364	424.0717		429.0664	433.06	59 435.3405	439.279	2 441.2415 m/z
410.0	412.5 415.0	417.5	420.0 4	425.	0 427.5	430.0	432.5	435.0	437.5	440.0
Minimum: Maximum:		5.0	5.0	-1.5 50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT	(Norm)	Formula		
427.0618	427.0621	-0.3	-0.7	15.5	37.2	0.0		C21 H19	N4 03	FS

Figure S4. HRMS-spectra of compound 4a



Figure S5. ¹H-NMR spectra of compound 4b



Figure S6. ¹³C-NMR spectra of compound 4b



Figure S7. HRMS-spectra of compound 4b



Figure S8. ¹H-NMR spectra of compound 4c



Figure S9. ¹³C-NMR spectra of compound 4c

Elemental Composition Report

Page 1 Single Mass Analysis Tolerance = 5.0 PPM / DBE: min = -1.5, max = 500.0 Element prediction: Off Number of isotope peaks used for i-FIT = 2 Monoisotopic Mass, Even Electron Ions 13 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 20-25 H: 20-25 N: 0-5 O: 0-5 S: 0-1 PTS-01 35 (1.146) Cm (1:61) TOF MS ES+ 3.28e+005 423.1623 100-%-424.1678 425.1652 417.2135 418.1401 431.2131 m/z 0-424.0 430.0 418.0 420.0 422.0 426.0 428.0 -1.5 500.0 Minimum: 5.0 5.0 Maximum: Calc. Mass i-FIT (Norm) Formula Mass mDa PPM DBE i-FIT 423.1623 40.5 C22 H22 N4 O3 S 423.1617 0.6 1.4 18.5 0.0

Figure S10. HRMS-spectra of compound 4c



Figure S11. ¹H-NMR spectra of compound 4d



Figure S12. ¹³C-NMR spectra of compound 4d



Figure S13. HRMS-spectra of compound 4d



Figure S14. ¹H-NMR spectra of compound 4e



Figure S15. ¹³C-NMR spectra of compound 4e

Elemental Composition	Report				Page 1
Single Mass Analysis Tolerance = 5.0 PPM / DB Element prediction: Off Number of isotope peaks use	E: min = -1.5, max ed for i-FIT = 2	= 50.0			
Monoisotopic Mass, Even Electi 61 formula(e) evaluated with 1 r Elements Used: C: 20-25 H: 15-20 N: 5-1 PTS-2 43 (1.416) Cm (1:61) TOF MS ES+	ron lons esults within limits (u 0 O: 0-5 F: 1-5	p to 20 closest re S: 0-1	esults for each	mass)	
100-				415.1115	2.59e+005
%-			413.1147	1104	
	409.0 410.0	110 4120	414.	0 415.0 416.0	417.2122 418.2333 419.2365 m/z
Minimum:	5.0 5.0	-1.5	415.0 414	.0 413.0 410.0	417.0 416.0 419.0
Mass Calc. Mass	mDa PPM	DBE	i-FTT	i-FIT (Norm)	Formula
415.1115 415.1109	0.6 1.5	14.5	8.7	0.0	C20 H16 N4 O2 F2 S

Figure S16. HRMS-spectra of compound 4e



Figure S17. ¹H-NMR spectra of compound 4f



Figure S18. ¹³C-NMR spectra of compound 4f







Figure S20. ¹H-NMR spectra of compound 4g



Figure S21. ¹³C-NMR spectra of compound 4g

Elemental Composition Report

Page 1 Single Mass Analysis Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 2 Monoisotopic Mass, Even Electron Ions 29 formula(e) evaluated with 1 results within limits (up to 20 closest results for each mass) Elements Used: C: 20-25 H: 15-20 N: 5-10 O: 0-5 F: 1-1 S: 0-1 PTS-4 7 (0.202) TOF MS ES+ 9.55e+002 411.0676 100-% 404.2126 405.2552 407.0863 412.0693 413.0994 415.0370 417.2003 418.3059 412.0 414.0 416.0 418.0 409.2871 421.0968 m/z 0-404.0 406.0 Т T 408.0 420.0 410.0 -1.5 50.0 Minimum: 5.0 5.0 Maximum: i-FIT (Norm) Formula Calc. Mass mDa PPM DBE i-FIT Mass 411.0671 35.1 C21 H19 N4 O2 F S 411.0676 0.5 1.2 15.5 0.0

Figure S22. HRMS-spectra of compound 4g



Figure S23. ¹H-NMR spectra of compound 4h



Figure S24. ¹³C-NMR spectra of compound 4h



Figure S25. HRMS-spectra of compound 4h



Figure S26. ¹H-NMR spectra of compound 4i



Figure S27. ¹³C-NMR spectra of compound 4i

Elemental Composition Report

Page 1 Single Mass Analysis Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0 Element prediction: Off Number of isotope peaks used for i-FIT = 3 Monoisotopic Mass, Even Electron Ions 8 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass) Elements Used: C: 20-25 H: 20-25 N: 0-5 O: 0-5 S: 0-1 PTS-10 2 (0.034) Cm (1:61) TOF MS ES+ 3.54e+005 439.0523 100-441.0678 442.0518 443.0676 440.3279 442.3281 444.0766 446.2813 m/z 445.0791 438.1711 0-438.00 440.00 441.00 445.00 446.00 442.00 443.00 444.00 439.00 -1.5 Minimum: Maximum: 5.0 50.0 DBE i-FIT (Norm) Formula Mass Calc. Mass mDa PPM i-FIT 439.0523 439.0511 1.2 2.7 18.5 74.0 0.0 C22 H22 N4 04 S

Figure S28. HRMS-spectra of compound 4i



Figure S29. ¹H-NMR spectra of compound 4j



Figure S30. ¹³C-NMR spectra of compound 4j



Figure S31. HRMS-spectra of compound 4j



Figure S32. ¹H-NMR spectra of compound 4k



Figure S33. ¹³C-NMR spectra of compound 4k



Figure S34. HRMS-spectra of compound 4k



Figure S35. ¹H-NMR spectra of compound 41







Figure S37. HRMS-spectra of compound 41



Figure S38. ¹H-NMR spectra of compound 4m



Figure S39. ¹³C-NMR spectra of compound 4m

Elemental Con	Elemental Composition Report										
Single Mass A Tolerance = 5.0 F Element predictio Number of isotop	n alysis PPM / DBE: mii n: Off e peaks used for	in = -1.5, max = 50 r i-FIT = 2	.0								
Monoisotopic Mass 61 formula(e) evalu Elements Used: C: 20-25 H: 20- PTS-6 51 (1.686) Cm TOF MS ES+	, Even Electron lor lated with 1 results 25 N: 0-5 O: (1:61)	ns s within limits (up to 2 0-5 S: 0-1	0 closest res	sults for each n	nass)		4 00 - 005				
100-						453.0276	4.33e+005				
				446.0325							
%			445.	0424							
- 433.0168	437.3588	441.2469 442	.8234	447.0444	0427 449.0443		455.3322 457.2405				
434.0	436.0 438.0	440.0 442.0	444.0	446.0 44	48.0 <mark>4</mark> 50.0	452.0 454.0	456.0				
Minimum: Maximum:	5.	.0 5.0	-1.5 50.0								
Mass Cal	c. Mass mD	Da PPM	DBE	i-FIT	i-FIT (Norm)	Formula					
453.0276 453	.0282 -0	0.6 -1.4	15.5	61.5	0.0	C23 H24 N4	4 04 S				

Figure S40. HRMS-spectra of compound 4m



Figure S41. ¹H-NMR spectra of compound 4n



Figure S42. ¹³C-NMR spectra of compound 4n



Figure S43. HRMS-spectra of compound 4n



Figure S44. ¹H-NMR spectra of compound 40



Figure S45. ¹³C-NMR spectra of compound 40

Elemental Composition Report										
Single Ma Tolerance = Element pr Number of	ass Analysis = 5.0 PPM / E ediction: Off isotope peaks u	BE: min = -1.	5, max = 5 = 2	0.0						
Monoisotopi 27 formula(e Elements Us C: 20-25 H F 4 4 (0.102 TOF MS ES+	c Mass, Even Ele e) evaluated with sed: H: 15-20 N: 0-5 cm (1:61)	ctron lons 1 results within O: 0-5 Na:	limits (up to 1-1 S: 0-	20 closest r 1 Br: 0-1	esults for eac	ch mass)		0.70 - 005		
100-	448.0921							6.70e+005		
						450.0986				
_			449.09	53						
-							451.104	2 m/z		
0	448.00	448.50	449.00	449.	50	450.00	450.50 451.00	451.50		
Minimum: Maximum:		5.0	5.0	-1.5 50.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (N	orm) Formula			
448.0921	448.0920	0.1	0.2	14.5	11.7	0.0	C21 H16 N3 C Br	2 Na S		

Figure S46. HRMS-spectra of compound 40



Figure S47. ¹H-NMR spectra of compound 4p











Figure S50. ¹H-NMR spectra of compound 4q



Figure S51. ¹³C-NMR spectra of compound 4q

Elementa	I Composition	Report						Page 1
Single Ma Tolerance = Element pro Number of	ass Analysis = 5.0 PPM / DI ediction: Off isotope peaks us	3E: min = -1 ed for i-FIT	.5, max = 50 = 3	0.0				
Monoisotopi 11 formula(e Elements Us C: 15-20 F 5 61 (2.023) TOF MS ES+	c Mass, Even Elec e) evaluated with 1 sed: H: 15-20 N: 0-{) Cm (1:61)	tron lons results within 5 O: 0-5	limits (all res Na: 1-1 S	ults (up to 1 : 0-1 CI:	000) for eac 0-2	th mass)		
100			442.202	3				3.10e+005
	75 434 2200	keshti muma		443.2063 444.209	8		458 1891	
0-4-0-	43	5.2356 439.11	75		446.1968	450.0	456.2047	463.1824 m/z
430.0	432.5 435.0	437.0 4	40.0 442.0	445.0	447.0	450.0 452.5	455.0 457.5 400.0	402.5
Minimum: Maximum:		5.0	5.0	-1.5 50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Nor	m) Formula	
442.2028	442.2018	1.0	2.3	15.5	16.9	0.0	C19 H15 N3 O2 C12	Na S

Figure S52. HRMS-spectra of compound 4q