Supporting Information for:

SELENIUM DIOXIDE MEDIATED SYNTHESIS OF FUSED 1,2,4-TRIAZOLES AS CYTOTOXIC AGENTS

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1. General Remarks

All the reagents and solvents for the synthesis and analysis were commercially available and used directly. Melting points were recorded on a YRT-3 melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were measured using a Bruker DRX 400 instrument [400 MHz for ^1H NMR and 100 MHz for the ^{13}C NMR (proton decoupled)] using $\text{DMSO}-d_6$ as solvent and TMS as internal standard, chemical shifts (δ scale) are reported in parts per million (ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz), integration. Mass spectra analyses of all the compounds were performed on a high-resolution q-TOF.

2. Procedures for the synthesis of hydrazones

Hydrazones **4b** and **4c** were prepared according to the literature procedure^[1]. The new hydrazones are prepared as follow: The hydrazine (15 mmol) was dissolved in a sufficient amount of boiling ethanol and the aldehyd (15 mmol), dissolved in 20 ml ethanol, was added dropwise. After that, the solution was stirred and heated under reflux for 1 h. The formed hydrazone was filtered from the cooled solution and used in the next reaction without any purification.

3. Procedures for the Synthesis of Fused 1,2,4-Triazoles

To a solution of hydrazone (10.0 mmol) in DMF (10 ml), selenium dioxide (2.20g, 20.0 mmol) was added while stirring. The mixture was stirred at 110°C and monitored by TLC. After the completion of the reaction, the reaction mixture was filtered, and the filtrate was evaporated in vacuum. The crude product was purified by recrystallization or by flash column chromatography to give the desired product.

4. In vitro Antiproliferative Activity Assay

The antiproliferative activity of the compounds was tested on HCT-116, A549 and Colo-205 cells. Cells were seeded in 96-well plates at a density of 5000 cells/well and incubated for 24 h. The cells were then incubated with serially diluted compounds for another 48 h. The final number of cells per well was assessed using the Sulforhodamine B dye (SRB, Sigma–Aldrich) following the standard procedure, and absorbance was measured using a microplate reader (SpectraMax M5) at a wavelength of 515 nm. The results were expressed as IC_{50} calculated using the Easy-fit software.

5. Analytical data of Hydrazones (1a-k, 1a-b, 3 and 4a)

(*E*)-4-methyl-2-(2-propylidenehydrazinyl)pyridine (**1a**): Yellow solid, m.p. 135-137° C; ^1H NMR (400 MHz,

DMSO-*d*₆): δ = 1.13 (t, J = 7.5 Hz, 3 H), 2.06 (s, 3 H), 2.63 (m, 2 H), 6.67 (dd, J = 1.4 Hz, 7.3 Hz, 1 H), 7.73 (d, J = 1.4 Hz, 1 H), 7.83 (t, J = 7.2 Hz, 1 H), 8.26 (d, J = 7.3 Hz, 1 H), 10.67 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₉H₁₄N₃, 164.1182; found, 164.1178.

(*E*)-4-methyl-2-(2-(3-methylbutylidene)hydrazinyl)pyridine (1b): Yellow solid. m.p. 152-154°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.90 (d, J = 6.8 Hz, 6 H), 1.95-2.07 (m, 1 H), 2.30 (s, 3 H), 2.92 (m, 2 H), 6.64 (dd, J = 1.2 Hz, 7.2 Hz, 1 H), 7.51 (d, J = 1.1 Hz, 1 H), 7.81 (t, J = 7.3 Hz, 1 H), 8.30 (d, J = 7.1 Hz, 1 H), 10.78 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₁H₁₈N₃, 192.1495; found, 192.1463.

(*E*)-2-(2-(2-(ethylthio)ethylidene)hydrazinyl)-4-methylpyridine (1c): Yellow solid. m.p. 146-148°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.10 (t, J = 7.5 Hz, 3 H), 2.33 (s, 3 H), 3.05 (q, J = 7.5 Hz, 2 H), 3.53 (d, J = 7.4 Hz, 2 H), 6.71 (dd, J = 1.1 Hz, 7.1 Hz, 1 H), 7.75 (d, J = 1.1 Hz, 1 H), 7.87 (d, J = 7.3 Hz, 1 H), 8.40 (d, J = 7.1 Hz, 1 H), 10.89 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₀H₁₆N₃S, 210.1059; found, 210.1042.

(*E*)-4-methyl-2-(2-(2-phenylethylidene)hydrazinyl)pyridine (1d): Yellow solid. m.p. 220-222°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.34 (s, 3 H), 5.20 (d, J = 7.2 Hz, 2 H), 7.21 (dd, J = 1.1 Hz, 7.3 Hz, 1 H), 7.27-7.37 (m, 5 H), 7.72 (d, J = 0.9 Hz, 1 H), 7.90 (d, J = 7.2 Hz, 1 H), 8.32 (d, J = 7.3 Hz, 1 H), 10.85 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₄H₁₆N₃, 226.1339; found, 226.1312.

(*E*)-4-((2-(4-methylpyridin-2-yl)hydrazono)methyl)phenol (1e): Yellow solid. m.p. 207-208°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.30 (s, 3 H), 6.72 (dd, J = 1.3 Hz, 7.2 Hz, 1 H), 7.00 (d, J = 8.5 Hz, 2 H), 7.51 (d, J = 0.9 Hz, 1 H), 7.56 (d, J = 8.6 Hz, 2 H), 7.90 (s, 1 H), 8.37 (d, J = 7.2 Hz, 1 H), 10.05 (s, 1 H), 10.85 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₄N₃O, 228.1131; found, 228.1114.

(*E*)-2-(2-(4-methoxybenzylidene)hydrazinyl)-4-methylpyridine (1f): Yellow solid. m.p. 234-236°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.31 (s, 3 H), 3.95 (s, 3 H), 6.73 (dd, J = 1.3 Hz, 7.3 Hz, 1 H), 7.10 (d, J = 8.5 Hz, 2 H), 7.56 (d, J = 1.3 Hz, 1 H), 7.69 (d, J = 8.3 Hz, 2 H), 7.90 (s, 1 H), 8.38 (d, J = 7.1 Hz, 1 H), 10.90 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₄H₁₆N₃O, 242.1288; found, 242.1267.

(*E*)-4-methyl-2-(2-(3,4,5-trimethoxybenzylidene)hydrazinyl)pyridine (1g): white solid. m.p. 244-245°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.32 (s, 3 H), 3.78 (s, 3 H), 3.85 (s, 6 H), 6.80 (dd, J = 1.2 Hz, 7.3 Hz, 1 H), 7.05 (s, 2 H), 7.48 (s, 1 H), 7.89 (s, 1 H), 8.51 (d, J = 7.4 Hz, 1 H), 10.89 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₆H₂₀N₃O₃, 302.1499; found, 302.1473.

(*E*)-2-(2-(3,4-dichlorobenzylidene)hydrazinyl)-4-methylpyridine (1h): yellow solid. m.p. 227-229°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.31 (s, 3 H), 6.79 (d, J = 7.2 Hz, 1 H), 7.52 (s, 1 H), 7.79 (dd, J = 1.2 Hz, 8.3 Hz, 1 H), 7.85 (d, J = 8.4 Hz, 1 H), 8.01 (s, 1 H), 8.13 (d, J = 1.4 Hz, 1 H), 8.50 (d, J = 7.4 Hz, 1 H), 11.07 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₂Cl₂N₃, 280.0403; found, 280.0386.

(*E*)-4-methyl-2-(2-(3-nitrobenzylidene)hydrazinyl)pyridine (1i): yellow solid. m.p. 252-254°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.33 (s, 3 H), 6.75 (d, J = 7.2 Hz, 1 H), 7.57 (s, 1 H), 7.87 (t, J = 8.2 Hz, 1 H), 8.23 (s, 1 H), 8.30 (d, J = 8.2 Hz, 1 H), 8.40 (d, J = 8.3 Hz, 1 H), 8.47 (d, J = 7.1 Hz, 1 H), 8.66 (s, 1 H), 11.21 (s, 1 H) ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₃N₄O₂, 257.1033; found, 257.1018.

(E)-4-methyl-2-(2-(4-nitrobenzylidene)hydrazinyl)pyridine (1j): white solid. m.p. 255-256°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.33 (s, 3 H), 6.78 (dd, *J* = 1.2 Hz, 7.2 Hz, 1 H), 7.70 (d, *J* = 0.9 Hz, 1 H), 8.20 (s, 1 H), 8.33 (d, *J* = 8.7 Hz, 2 H), 8.42-8.45 (d, *J* = 8.7 Hz, 2 H), 8.63 (d, *J* = 7.2 Hz, 1 H), 11.19 (s, 1 H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₃H₁₃N₄O₂, 257.1033; found, 257.1011.

(E)-4-methyl-2-(2-(thiophen-2-ylmethylene)hydrazinyl)pyridine (1k): yellow solid. m.p. 155-156°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.30 (s, 3 H), 6.75 (dd, *J* = 1.3 Hz, 7.2 Hz, 1 H), 7.42 (dd, *J* = 3.9 Hz, 5.2 Hz, 1 H), 7.52 (d, *J* = 1.1 Hz, 1 H), 7.80 (dd, *J* = 1.0 Hz, 5.1 Hz, 1 H), 7.90 (dd, *J* = 1.0 Hz, 3.8 Hz, 1 H), 7.97 (s, 1 H), 8.52 (d, *J* = 7.1 Hz, 1 H), 11.00 (s, 1 H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₁H₁₂N₃S, 218.0746; found, 218.0726.

(E)-2-(2-(4-methoxybenzylidene)hydrazinyl)pyrimidine (2a): yellow solid. m.p. 192-193°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.83 (s, 3 H), 7.20 (d, *J* = 8.5 Hz, 2 H), 7.45 (t, *J* = 8.2 Hz, 1 H), 7.61 (d, *J* = 8.5 Hz, 2 H), 8.12 (d, *J* = 8.2 Hz, 2 H), 7.97 (s, 1H), 11.07 (s, 1 H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₂H₁₃N₄O, 229.1084; found, 229.1059.

(E)-2-(2-(2-nitrobenzylidene)hydrazinyl)pyrimidine (2b): yellow solid. m.p. 216-218°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 7.44 (t, *J* = 8.0 Hz, 1 H), 7.51 (td, *J* = 1.2 Hz, 7.7 Hz, 1 H), 7.74 (t, *J* = 7.6 Hz, 1 H), 7.95 (s, 1 H), 8.01 (d, *J* = 8.2 Hz, 1 H), 8.15 (d, *J* = 8.0 Hz, 2 H), 8.46-8.50 (m, 1H), 10.90 (s, 1 H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₁H₁₀N₅O₂, 244.0829; found, 244.0824.

(E)-2-(2-(2-nitrobenzylidene)hydrazinyl)quinoline (3): yellow solid. m.p. 227-229°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 7.13 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.1 Hz, 1 H), 7.57 (t, *J* = 7.3 Hz, 1 H), 7.73 (d, *J* = 8.6 Hz, 1 H), 7.87 (d, *J* = 8.6 Hz, 1 H), 8.01 (d, *J* = 8.0 Hz, 1 H), 8.07-8.11 (m, 3 H), 8.23 (s, 1 H), 8.36 (d, *J* = 7.3 Hz, 1 H), 10.56 (s, 1 H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₆H₁₃N₄O₂, 293.1033; found, 293.1028.

(E)-2-(2-propylidenehydrazinyl)quinoxaline (4a): yellow solid. m.p. 212-213°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.45 (t, *J* = 7.2 Hz, 3 H), 3.30 (m, 2 H), 7.68 (td, *J* = 1.0 Hz, 8.5 Hz, 1 H), 7.77 (td, *J* = 1.2 Hz, 8.5 Hz, 1 H), 7.95 (t, *J* = 7.2 Hz, 1 H), 8.06 (dd, *J* = 1.2 Hz, 8.0 Hz, 1 H), 8.06 (dd, *J* = 1.0 Hz, 8.0 Hz, 1 H), 8.46 (s, 1 H), 11.97 (s, 1H) ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₁H₁₃N₄, 201.1135; found, 201.1122.

6. Analytical data of the triazoles (5a-k, 6a-b, 7 and 8a-c)

3-Ethyl-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5a)²¹: yellow solid, m.p. 85-87° C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.33 (t, *J* = 7.5 Hz, 3 H), 2.33 (s, 3 H), 3.03 (q, *J* = 7.5 Hz, 2 H), 6.77 (dd, *J* = 1.3 Hz, 7.1 Hz, 1 H), 7.43 (d, *J* = 1.0 Hz, 1 H), 8.26 (d, *J* = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 11.3, 17.7, 21.2, 113.2, 116.2, 123.2, 138.1, 147.6, 149.9 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₉H₁₂N₃, 162.1026; found, 162.1042.

3-Isobutyl-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5b): yellow solid. m.p. 102-104°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.89 (d, *J* = 6.7 Hz, 6 H), 2.05-2.17 (m, 1 H), 2.30 (s, 3 H), 2.92 (d, *J* = 7.2 Hz, 2 H), 6.74 (dd, *J* = 1.2 Hz, 7.1 Hz, 1 H), 7.41 (d, *J* = 0.8 Hz, 1 H), 8.32 (d, *J* = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.1, 22.5, 27.2, 32.6, 113.2, 116.2, 123.2, 137.9, 145.9, 149.9 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₁H₁₆N₃, 190.1339; found, 190.1363.

3-((Ethylthio)methyl)-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5c): yellow solid. m.p. 106-108°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.14 (s, 3 H), 2.53 (s, 3 H), 3.00 (t, *J* = 7.5 Hz, 2 H), 3.48 (t, *J* = 7.4 Hz, 2 H), 7.33 (dd, *J* = 1.1 Hz, 7.1 Hz, 1 H), 7.85 (s, 1 H), 8.80 (d, *J* = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 15.1, 21.7, 24.4, 29.9, 110.1, 119.6, 125.3, 145.8, 146.8, 147.5 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₀H₁₄N₃S, 208.0903; found, 208.0922.

3-Benzyl-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5d): White solid. m.p. 154-156°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.44 (s, 3 H), 4.60 (s, 2 H), 7.11 (dd, *J* = 1.2 Hz, 7.1 Hz, 1 H), 7.23-7.27 (m, 1 H), 7.31-7.36 (m, 4 H), 7.72 (d, *J* = 0.8 Hz, 1 H), 8.52 (d, *J* = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.5, 30.0, 111.4, 118.7, 124.2, 127.5, 129.1, 129.2, 135.3, 144.2, 146.4, 147.5 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₄H₁₄N₃, 224.1182; found, 224.1202.

4-(7-Methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenol (5e): white solid. m.p. 207-208°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.37 (s, 3 H), 6.82 (dd, *J* = 1.3 Hz, 7.2 Hz, 1 H), 6.97-7.00 (m, 2 H), 7.55 (s, 1 H), 7.68 (d, *J* = 8.6 Hz, 2 H), 8.37 (d, *J* = 7.2 Hz, 1 H), 10.01 (s, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 113.6, 116.5, 117.3, 117.7, 123.4, 130.0, 138.6, 146.2, 150.5, 159.3 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₃H₁₂N₃O, 226.0975; found, 226.0984.

3-(4-Methoxyphenyl)-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5f): White solid. m.p. 214-216°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.38 (s, 3 H), 3.85 (s, 3 H), 6.83 (dd, *J* = 1.4 Hz, 7.2 Hz, 1 H), 7.15-7.17 (m, 2 H), 7.56 (d, *J* = 0.8 Hz, 1 H), 7.79-7.81 (m, 2 H), 8.38 (d, *J* = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 55.8, 113.6, 115.1, 117.4, 119.4, 123.4, 129.9, 138.7, 145.9, 150.7, 160.8 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₄H₁₄N₃O, 240.1131; found, 240.1160.

7-Methyl-3-(3,4,5-trimethoxyphenyl)-[1,2,4]triazolo[4,3-a]pyridine (5g): white solid. m.p. 244-245°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.39 (s, 3 H), 3.76 (s, 3 H), 3.88 (s, 6 H), 6.85 (dd, *J* = 1.3 Hz, 7.2 Hz, 1 H), 7.12 (s, 2 H), 7.58 (s, 1 H), 8.51 (d, *J* = 7.2 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 56.6, 60.6, 106.0, 113.5, 117.5, 122.4, 123.8, 138.9, 139.1, 146.1, 150.8, 153.9 ppm. HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₆H₁₈N₃O₃, 300.1343; found, 300.1373.

3-(3,4-dichlorophenyl)-7-methyl-[1,2,4]triazolo[4,3-a]pyridine (5h): yellow solid. m.p. 232-234°C; ¹H NMR

(400 MHz, DMSO-*d*₆): δ = 2.41 (s, 3 H), 6.91 (d, J = 7.1 Hz, 1 H), 7.62 (s, 1 H), 7.84-7.91 (m, 2 H), 8.13 (d, J = 1.4 Hz, 1 H), 8.50 (d, J = 7.1 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 115.1, 115.9, 126.6, 127.0, 128.8, 129.7, 130.1, 133.3, 134.8, 135.3, 147.3, 150.7 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₀Cl₂N₃, 278.0246; found, 278.0256.

7-Methyl-3-(3-nitrophenyl)-[1,2,4]triazolo[4,3-a]pyridine (5i): yellow solid. m.p. 192-194°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.43 (s, 3 H), 6.95 (d, J = 7.1 Hz, 1 H), 7.67 (s, 1 H), 7.91 (t, J = 8.0 Hz, 1 H), 8.36 (d, J = 7.7 Hz, 1 H), 8.40 (d, J = 8.3 Hz, 1 H), 8.59 (d, J = 7.1 Hz, 1 H), 8.68 (s, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 114.8, 115.6, 122.9, 124.1, 124.4, 125.8, 128.4, 132.7, 133.6, 134.3, 144.4, 148.3, 150.3 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₁N₄O₂, 255.0877; found, 255.0881.

7-methyl-3-(4-nitrophenyl)-[1,2,4]triazolo[4,3-a]pyridine (5j): white solid. m.p. 185-186°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.43 (s, 3 H), 6.98 (dd, J = 1.4 Hz, 7.2 Hz, 1 H), 7.70 (s, 1 H), 8.23-8.25 (m, 2 H), 8.42-8.45 (m, 2 H), 8.63 (d, J = 7.2 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.3, 114.6, 115.7, 122.8, 124.2, 128.1, 130.0, 134.2, 144.5, 148.4, 150.8 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₃H₁₁N₄O₂, 255.0877; found, 255.0872.

7-Methyl-3-(thiophen-2-yl)-[1,2,4]triazolo[4,3-a]pyridine (5k): yellow solid. m.p. 155-156°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.40 (s, 3 H), 6.95 (dd, J = 1.5 Hz, 7.2 Hz, 1 H), 7.32 (dd, J = 3.8 Hz, 5.1 Hz, 1 H), 7.62 (d, J = 1.1 Hz, 1 H), 7.81 (dd, J = 1.0 Hz, 5.1 Hz, 1 H), 7.87 (dd, J = 1.0 Hz, 3.7 Hz, 1 H), 8.62 (d, J = 7.1 Hz, 1 H), ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 21.2, 113.7, 118.0, 123.8, 126.9, 128.2, 128.7, 128.8, 139.3, 141.5, 150.9 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₁H₁₀N₃S, 216.0590; found, 216.0580.

3-(4-Methoxyphenyl)-[1,2,4]triazolo[4,3-a]pyrimidine (6a): yellow solid. m.p. 152-153°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.91 (s, 3 H), 7.23 (d, J = 8.7 Hz, 2 H), 7.50 (dd, J = 1.0 Hz, 8.3 Hz, 1 H), 7.55 (td, J = 1.3 Hz, 8.4 Hz, 1 H), 7.72 (d, J = 10.0 Hz, 2 H), 8.11 (dd, J = 1.0 Hz, 8.0 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 55.9, 115.1, 116.2, 120.6, 126.6, 127.9, 129.8, 130.8, 132.0, 136.6, 144.5, 144.8, 149.4, 161.6 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₂H₁₁N₄O, 227.0927; found, 227.0939.

3-(2-Nitrophenyl)-[1,2,4]triazolo[4,3-a]pyrimidine (6b): yellow solid. m.p. 160-162°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 6.90-6.93 (m, 1 H), 7.56 (td, J = 1.2 Hz, 7.7 Hz, 1 H), 7.72 (t, J = 7.6 Hz, 1 H), 8.01 (d, J = 8.2 Hz, 1 H), 8.15 (d, J = 7.9 Hz, 1 H), 8.46-8.50 (m, 2H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 115.0, 125.9, 128.7, 130.7, 130.8, 134.7, 137.5, 148.9, 155.5, 159.7, 161.0 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₁H₈N₅O₂, 242.0673; found, 242.0664.

1-(2-Nitrophenyl)-[1,2,4]triazolo[4,3-a]quinoline (7)^[3]: yellow solid. m.p. 210-212°C; ¹H NMR (400 MHz, DMSO-*d*₆): δ = 7.18 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 8.1 Hz, 1 H), 7.56 (t, J = 7.2 Hz, 1 H), 7.83 (d, J = 9.6 Hz, 1 H), 7.91 (d, J = 9.6 Hz, 1 H), 8.00 (d, J = 8.4 Hz, 1 H), 8.03-8.10 (m, 3 H), 8.46 (d, J = 7.5 Hz, 1 H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 114.9, 115.7, 124.5, 124.8, 126.1, 126.8, 130.2, 130.3, 130.8, 131.6, 133.2, 133.7, 135.5, 144.8, 148.6, 149.6 ppm. HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₆H₁₁N₄O₂, 291.0877; found, 291.0832.

1-Ethyl-[1,2,4]triazolo[4,3-a]quinoxaline (8a)^[4]: yellow solid. m.p. 151-153°C; ¹H NMR (400 MHz, DMSO-*d*₆):

δ = 1.50 (t, J = 7.3 Hz, 3 H), 3.48 (q, J = 7.3 Hz, 2 H), 7.68 (td, J = 1.1 Hz, 8.4 Hz, 1 H), 7.77 (td, J = 1.3 Hz, 8.4 Hz, 1 H), 8.06 (dd, J = 1.3 Hz, 8.1 Hz, 1 H), 8.06 (dd, J = 1.1 Hz, 8.1 Hz, 1 H), 9.26 (s, 1 H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): δ = 11.4, 22.0, 117.11, 126.65, 127.7, 130.3, 130.5, 136.3, 144.4, 150.0, 152.1 ppm. HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{11}\text{N}_4$, 199.0978; found, 199.0972.

1-(4-Methoxyphenyl)-[1,2,4]triazolo[4,3-a]quinoxaline (8b)^[5]: Yellow solid. m.p. 182-183°C; ^1H NMR (400 MHz, DMSO- d_6): δ = 3.91 (s, 3 H), 7.24 (d, J = 8.4 Hz, 2 H), 7.49-7.51 (m, 1 H), 7.55 (td, J = 1.4 Hz, 8.6 Hz, 1 H), 7.65 (td, J = 1.4 Hz, 8.0 Hz, 1 H), 7.71-7.73 (m, 2 H), 8.10 (dd, J = 1.2 Hz, 8.0 Hz, 1 H), 9.51 (s, 1 H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): δ = 55.9, 115.1, 116.2, 120.6, 126.6, 127.9, 129.8, 130.8, 132.0, 144.5, 144.8, 149.4, 152.5, 161.6 ppm. HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{N}_4\text{O}$, 277.1084; found, 277.1108.

1-(2-Nitrophenyl)-[1,2,4]triazolo[4,3-a]quinoxaline (8c)^[5]: yellow solid. m.p. 243-244°C; ^1H NMR (400 MHz, DMSO- d_6): δ = 7.31-7.38 (m, 4 H), 7.57 (t, J = 7.6 Hz, 2 H), 7.82 (d, J = 8.1 Hz, 1 H), 8.19 (m, 1 H), 9.31 (s, 1 H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): δ = 117.7, 124.5, 124.8, 126.7, 126.9, 130.2, 130.3, 130.9, 131.6, 133.3, 133.6, 135.7, 144.8, 149.6, 159.6 ppm. HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{10}\text{N}_5\text{O}_2$, 292.0829; found, 292.0842.

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7. ^1H NMR and ^{13}C NMR of the compounds (5a-k, 6a-b, 7 and 8a-c)

Figure 1. ^1H NMR spectrum (400 MHz, DMSO- d_6) of compound 5a

Figure 2. ^{13}C NMR spectrum (100 MHz, DMSO- d_6) of compound 5a

Figure 3. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5b**

Figure 4. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5b**

Figure 9. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5e**

Figure 10. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5e**

Figure 11. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5f**

Figure 12. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5f**

Figure 13. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5g**

Figure 14. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5g**

Figure 15. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound 5h

Figure 16. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound 5h

Figure 17. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5i**

Figure 18. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5i**

Figure 19. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5j**

Figure 20. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5j**

Figure 21. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **5k**

Figure 22. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **5k**

Figure 23. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound 6a

Figure 24. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound 6a

Figure 25. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **6b**

Figure 26. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **6b**

Figure 27. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound 7

Figure 28. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound 7

Figure 29. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **8a**

Figure 30. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **8a**

Figure 31. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of compound **8b**

Figure 32. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of compound **8b**

Figure 33. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of compound **8c**

Figure 34. ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) of compound **8c**