**Supporting information**

**ULTRASOUND-ASSISTED GREEN SYNTHESIS OF NOVEL PYRIMIDINE DERIVATIVES AND THEIR COMPARISON WITH CONVENTIONAL METHODS**

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**CONVENTIONAL METHODS OF SYNTHESIS**

**Synthesis of compounds 3, 4 and 5**

A mixture of 0.01 mol of compound **2** and 0.01 mol of potassium 4-formylphenolate, potassium 4-(methoxycarbonyl)phenolate, or potassium 4-(hydrazinecarbonyl)phenolate in 20 mL of acetone was stirred at room temperature for 10 h until the isolation of trimethylamine ceased. The residue was filtered from salt, acetone was evaporated, then water was added and the reaction product was filtered off.

**4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzaldehyde (3).** 1H NMR, δ: 2.33 (s, 3H, SCH3); 2.43 (s, 3H, CH3-pyrim.); 6.54 (s, 1H, CH-pyrim.); 7.34 and 7.96 (m, 4H, C6H4); 9.98 (s, 1H, HC=O). 13C NMR, δ: 13.1, 23.3, 101.8, 121.5, 130.6, 133.1, 156.5, 167.6, 168.8, 170.9, 189.7. Anal.calc.: Found: C, 59.88; H, 4.59; N, 10.61. C13H12N2O2S. Calcul.: C, 59.98; H, 4.65; N, 10.76.

**Methyl 4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzoate (4).** 1H NMR, δ: 2.32 (s, 3H, SCH3); 2.42 (s, 3H, CH3-pyrim.); 3.89 (s, 3H, OCH3); 6.51 (s, 1H, CH-pyrim.); 7.23 and 8.04 (m, 4H, C6H4). 13C NMR, δ: 13.1, 23.2, 51.3, 101.6, 120.9, 126.5, 130.5, 155.5, 164.7, 167.7, 168.7, 170.9. Anal.calc.: Found: C, 57.81; H, 4.79; N, 9.49. C13H12N2O2S. C14H14N2O3S. Calcul.: C, 57.92; H, 4.86; N, 9.65.

**4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzohydrazide (5).** 1H NMR, δ: 2.06 (brs, 2H, NH2); 2.37 (s, 3H, SCH3); 2.42 (s, 3H, CH3-pyrim.); 6.50 (s, 1H, CH-pyrim.); 7.18 and 7.92 (m, 4H, C6H4); 10.31 (brs, 1H, NH). 13C NMR, δ: 13.2, 23.2, 101.6, 120.4, 120.5, 129.1, 131.0, 153.8, 168.0, 168.5, 170.8. Anal.calc.: Found: C, 53.69; H, 4.79; N, 19.18. C13H12N2O3S. Calcul.: C, 53.78; H, 4.86; N, 19.30.

**4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzaldehyde oxime (6).** To a solution of 0.015 mol NaOH, 0.015 mol of hydroxylamine in 10 mL of water, 0.01 mol of compound **3** was added at 0 °C, then 10 mL of ethanol for homogenization. The mixture was left overnight at room temperature, then heated for 2 h at 50-60 °C, the product was filtered off and dried in the air. 1H NMR, δ: 2.33 (s, 3H, SCH3); 2.40 (s, 3H, CH3-pyrim.); 6.44 (s, 1H, CH-pyrim.); 7.12 and 7.62 (m, 4H, C6H4); 8.04 (s, 1H, HC=N); 10.94 (s, 1H, OH). 13C NMR, δ: 13.1, 23.2, 101.4, 121.2, 127.1, 130.3, 146.3, 152.3, 168.2, 168.4, 170.9. Anal.calc.: Found: C, 56.66; H, 4.68; N, 15.02. C13H13N3O2S. Calcul.: C, 56.71; H, 4.76; N, 15.26.

**4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzoic acid (7).** Compound **4** (0.01 mol) was added to an alcoholic solution of 0.02 mol KOH, left overnight at room temperature, then the alcohol was distilled off, water was added to the residue, the cloudy solution was filtered and neutralized with acetic acid, the reaction product was filtered off and dried. 1H NMR, δ: 2.32 (s, 3H, SCH3); 2.41 (s, 3H, CH3-pyrim.); 6.48 (s, 1H, CH-pyrim.); 7.20 and 8.03 (m, 4H, C6H4); 9.15 (brs, 1H, OH). 13C NMR, δ: 13.1, 23.2, 101.6, 120.6, 128.2, 130.6, 155.0, 166.2, 167.9, 168.6, 170.9. Anal.calc.: Found: C, 56.63; H, 4.44; N, 10.25. C13H12N2O3S. Calcul.: C, 56.51; H, 4.38; N, 10.14.

**4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzoyl azide (8).** To a mixture of 0.01 mol of compound **5** and 0.15 mol of NaNO2 in 10 mL of water, at -5 ‒ 0 °C 0.015 mol of acetic acid was added dropwise. The mixture was stirred at room temperature for 3 h and left overnight, then filtered off, washed with water and dried. IR ν (cm-1): 2137 and 2179 (N3). 1H NMR, δ: 2.33 (s, 3H, SCH3); 2.43 (s, 3H, CH3-pyrim.); 6.54 (s, 1H, CH-pyrim.); 7.28 and 8.05 (m, 4H, C6H4). IR 2137 and 2179 cm-1 13C NMR, δ:13.1, 23.3, 101.8, 121.3, 126.8, 130.5, 156.8, 167.5, 168.9, 170.1, 170.9. Anal.calc.: Found: C, 51.91; H, 3.75; N, 23.38. C13H11N5O2S. Calcul.: C, 51.82; H, 3.68; N, 23.24.

**2-(4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)phenyl)-1,3,4-oxadiazole (9).** A mixture of 0.01 mol of compound **5** and 8 mL of triethoxymethane was refluxed for 12 h, then the orthoester was distilled off, water was added and the reaction product was filtered off and dried. 1H NMR, δ: 2.33 (s, 3H, SCH3); 2.43 (s, 3H, CH3-pyrim.); 6.54 (s, 1H, CH-pyrim.); 7.35 and 8.11 (m, 4H, C6H4); 9.05 (s, 1H, CH-oxadiaz.). 13C NMR, δ: 13.1, 23.2, 101.7, 120.4, 121.9, 127.8, 153.3, 154.4, 162.8, 167.8, 168.8, 170.9. Anal.calc.: Found: C, 55.82; H, 3.92; N, 18.52. C14H12N4O2S. Calcul.: C, 55.99; H, 4.03; N, 18.66.

**(3,5-Dimethyl-1*H*-pyrazol-1-yl)(4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)phenyl)methanone (10).** A mixture of 0.01 mol of compound **5**, 4 ml of pentane-2,4-dione and 5-6 mL of acetic acid was left overnight at room temperature. The clear solution was evaporated, triturated with hexane and filtered off. 1H NMR, δ: 2.33 (s, 3H, SCH3); 2.36 (s, 3H, 3-CH3-pyraz.); 2.43 (s, 3H, CH3-pyrim.); 2.61 (s, 3H, 5-CH3-pyraz.); 6.09 (s, 1H, CH-pyraz.); 6.53 (s, 1H, CH-pyrim.); 7.25 and 8.08 (m, 4H, C6H4). 13C NMR, δ:13.2, 13.17, 13.19, 13.7, 23.3, 101.7, 110.4, 120.0, 129.6, 132.7, 144.1, 150.7, 154.9, 165.8, 167.8, 168.7, 171.0. Anal.calc.: Found: C, 61.11; H, 5.21; N, 15.99. C18H18N4O2S. Calcul.: C, 61.00; H, 5.12; N, 15.81.

***N'*-Benzoyl-4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzohydrazide (11).** To 0.01 mol of compound **5** in 10 mL of dioxane, 0.011mol of benzoyl chloride was added dropwise and the mixture was heated for 4 hours at reflux, then dioxane was distilled off, ice water was added and the product filtered off. 1H NMR, δ: 2.37 (s, 3H, SCH3); 2.43 (s, 3H, CH3-pyrim.); 6.52 (s, 1H, CH-pyrim.); 7.21-8.09 (m, 9H, C6H5 and C6H4); 10.38 (s, 1H, NH); 10.42 (s, 1H, NH). 13C NMR, δ: 13.2, 23.3, 101.7, 120.7, 127.4, 127.7, 129.1, 129.6, 130.9, 132.5, 154.4, 164.5, 165.3, 168.0, 168.6, 170.9. Anal.calc.: Found: C, 60.81; H, 4.55; N, 14.12. C20H18N4O3S. Calcul.: C, 60.90; H, 4.60; N, 14.20.

**(4-((4-Methyl-6-(methylthio)pyrimidin-2-yl)oxy)phenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)methanone (12).** A mixture of 0.01 mol of compound **11** in 5 mL of POCl3 was refluxed for 4 h at 100 °C. POCl3 was distilled off, 10 mL of ice water was added to the residue, neutralized with 25% NH4OH, and the reaction product was filtered off and dried. 1H NMR, δ: 2.34 (s, 3H, SCH3); 2.44 (s, 3H, CH3-pyrim.); 6.55 (s, 1H, CH-pyrim.); 7.34-8.21 (m, 9H, C6H5 and C6H4). 13C NMR, δ: 13.2, 23.3, 101.7, 120.5, 122.0, 123.4, 126.3, 127.7, 128.6, 131.1, 154.5, 163.0, 163.5, 167.8, 168.8, 171.0. Anal.calc.: Found: C, 62.28; H, 3.89; N, 13.72. C21H16N4O3S. Calcul.: C, 62.36; H, 3.99; N, 13.85.

**Synthesis of compounds 14 and 16**

A mixture of 0.01 mol of potassium salt of hydroxybenzoic acid (prepared from 0.01 mol of hydroxybenzoic acid and 0.005 mol of K2CO3), 0.01 mol of 1-chloro-4-(chloromethyl)benzene or methyl 2-chloroacetate in 10 mL of DMF was left overnight at room temperature. Then 0.01 mol of quaternary salt **2** in 20 mL of acetone was added and left overnight at room temperature until the isolation of trimethylamine was completed. The mixture was filtered from the salt, acetone was evaporated, water was added and the reaction product was filtered off.

**4-Chlorobenzyl 4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzoate (14).** 1H NMR, δ: 2.34 (s, 3H, SCH3); 2.42 (s, 3H, CH3-pyrim.); 5.33 (s, 2H, OCH2); 6.54 (s, 1H, CH-pyrim.); 7.24-8.13 (m, 8H, C6H4 and C6H4). 13C NMR, δ:13.1, 23.2, 65.0, 101.7, 121.0, 126.3, 128.1, 129.3, 130.6, 133.1, 134.3, 155.7, 164.1, 167.7, 168.7, 170.9. Anal.calc.: Found: C, 59.84; H, 4.21; N, 6.85. C20H17ClN2O3S. Calcul.: C, 59.92; H, 4.27; N, 6.99.

**2-Methoxy-2-oxoethyl 4-((4-methyl-6-(methylthio)pyrimidin-2-yl)oxy)benzoate (16).** 1H NMR, δ: 2.35 (s, 3H, SCH3); 2.43 (s, 3H, CH3-pyrim.); 3.77 (s, 3H, OCH3); 4.85 (s, 2H, OCH2); 6.54 (s, 1H, CH-pyrim.); 7.29 and 8.10 (m, 4H, C6H4). 13C NMR, δ: 13.2, 23.4, 51.4, 60.5, 101.8, 121.1, 125.7, 130.9, 155.9, 163.9, 167.1, 167.7, 168.9, 170.9.Anal.calc.: Found: C, 55.10; H, 4.70; N, 8.15. C16H16N2O5S. Calcul.: C, 55.16; H, 4.63; N, 8.04.