

SUPPLEMENTARY MATERIAL

All reactions were carried out under an atmosphere of argon, unless otherwise specified. Glassware was routinely oven-dried at 160 °C for a minimum of 4 h and then connected to a vacuum line before assembling under a dry argon stream. Anhydrous solvents were obtained by distillation immediately prior to use, from sodium benzophenone ketyl (tetrahydrofuran) or sodium (toluene). Melting points were determined using a Thomas Hoover capillary Melting Point Apparatus and are uncorrected. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Gemini-300 spectrometer using deuteriochloroform (CDCl_3) as solvent with TMS as the internal reference for ^1H NMR and the central line of CDCl_3 as the reference for ^{13}C NMR. The GC-MS instrument used in the optimization of the procedure was a Hewlett Packard 5890 Series II Gas Chromatograph coupled to a 5972 Mass Selective Detector. Elemental analyses were performed on a Carlo Erba-1106 instrument. Column chromatography was carried out on MCB silica gel (230-400 mesh).

General Procedure for the Preparation of Thiazolo[3,2-b]1,2,4-Triazoles 5a-f.

1-(Trimethylsilyl)-1*H*-1,2,4-triazole⁵ (11 mmol) was placed in a round-bottomed flask under Argon and thionyl chloride (6 mmol) was then added neat via syringe dropwise at room temperature. A yellow solid precipitated after the addition of the first drops. The mixture was stirred at room temperature under Argon for 15 min and the resulting solid was dried under vacuum. Dry toluene (10 mL) was then added followed by addition of the corresponding chalcone (5 mmol), the resulting mixture was heated at 90 °C overnight. The reaction mixture was then cooled to room temperature and concentrated in vacuo to afford a crude oil. Purification was achieved by column chromatography on silica gel (eluting with hexanes/ethyl acetate 1:1).

[6-(4-Methoxyphenyl)[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl](4-methylphenyl)

methanone (5a): yellow needles (22%), mp 140-141 °C; ¹H NMR (CDCl₃): δ 8.25 (s, 1H), 7.50 (t, 4H, J = 8.0 Hz), 7.00 (d, 2H, J = 7.7 Hz), 6.78 (d, 2H, J = 8.2 Hz), 3.76 (s, 3H), 2.30 (s, 3H); ¹³C NMR (CDCl₃): δ 188.3, 161.2, 157.1, 157.0, 143.9, 136.5, 133.4, 131.8, 129.6, 128.7, 126.0, 119.1, 113.8, 55.3, 21.5. Anal. Calcd. for C₁₉H₁₅N₃O₂S: N, 12.03. Found: N, 12.23. HRMS Calcd. for C₁₉H₁₆N₃O₂S: 350.0963 (M⁺+1); observed: 350.0977.

(4-Nitrophenyl)(6-phenyl[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl)methanone (5b):

yellow prisms (13%), mp 151-152 °C; ¹H NMR (CDCl₃): δ 8.29 (s, 1H), 8.13 (d, 2H, J = 8.5 Hz), 7.76 (d, 2H, J = 8.7 Hz), 7.63 (d, 2H, J = 7.2 Hz), 7.45 (t, 1H, J = 7.3 Hz), 7.26 (t, 2H, J = 7.5 Hz); ¹³C NMR (CDCl₃): δ 187.7, 157.5, 156.3, 148.4, 135.8, 133.9, 133.7, 132.8, 131.3, 129.4, 128.6, 128.5, 123.4. Anal. Calcd. for C₁₇H₁₀N₄O₃S: N, 15.99. Found: N, 16.03.

[6-(4-Chlorophenyl)[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl](4-methylphenyl)

methanone (5c): white needles (20%), mp 162-163 °C; ¹H NMR (CDCl₃): δ 8.25 (s, 1H), 7.50 (t, 4H, J = 7.4 Hz), 7.26 (d, 2H, J = 8.7 Hz), 7.03 (d, 2H, J = 7.8 Hz), 2.33 (s, 3H); ¹³C NMR (CDCl₃): δ 187.7, 157.2, 156.2, 144.6, 136.9, 135.0, 133.2, 131.4, 129.6, 129.0, 128.7, 125.3, 21.6. Anal. Calcd. for C₁₈H₁₂ClN₃OS: C, 61.10; H, 3.43; N, 11.88. Found: C, 60.79; H, 3.50; N, 11.74.

Phenyl(6-phenyl[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl)methanone (5d): white

microcrystals (30%), mp 148-149 °C; ¹H NMR (CDCl₃): δ 8.27 (s, 1H), 7.56 (d, 2H, J = 7.1 Hz), 7.49 (d, 2H, J = 6.8 Hz), 7.40-7.20 (m, 4H), 7.16 (t, 2H, J = 7.7 Hz); ¹³C NMR (CDCl₃): δ 188.8, 157.4, 137.0, 136.0, 133.0, 130.7, 130.3, 129.4, 128.7, 128.4, 128.1, 127.2, 126.8. Anal. Calcd. for C₁₇H₁₁N₃OS: C, 66.86; H, 3.64. Found: C, 67.26; H, 3.74.

(4-Methylphenyl)[6-(2-thienyl)[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl]methanone (5e):

glassy oil (18%); ¹H NMR (CDCl₃): δ 8.22 (s, 1H), 7.59 (d, 2H, J = 8.1 Hz), 7.54 (d, 1H, J =

4.3 Hz), 7.41 (d, 1H, J = 5.0 Hz), 7.05 (d, 2H, J = 8.1 Hz), 6.90 (t, 1H, J = 4.3 Hz), 2.29 (s, 3H); ^{13}C NMR (CDCl_3): δ 200.2, 184.7, 157.0, 144.7, 133.6, 132.8, 130.6, 129.0, 128.2, 127.2, 126.8, 126.6, 125.4, 21.7. HRMS Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_3\text{OS}_2$: 326.0422 (M^++1); observed: 326.0442.

(4-Chlorophenyl)(6-phenyl[1,3]thiazolo[3,2-b][1,2,4]triazol-5-yl)methanone (5f):

yellow needles (12%), mp 154-155 °C; ^1H NMR (CDCl_3): δ 8.26 (s, 1H), 7.58 (d, 2H, J = 7.7 Hz), 7.50-7.40 (m, 3H), 7.30-7.10 (m, 4H); ^{13}C NMR (CDCl_3): δ 188.4, 157.3, 137.0, 135.9, 133.2, 131.5, 129.3, 128.9, 128.6, 128.4, 128.2, 125.1. Anal. Calcd. for $\text{C}_{17}\text{H}_{10}\text{ClN}_3\text{OS}$: C, 60.08; H, 2.97; N, 12.37. Found: C, 60.11; H, 2.71; N, 12.04.

3-(4-Methoxyphenyl)-1-(4-methylphenyl)-3-(1H-1,2,4-triazol-1-yl)-1-propanone (6a):

⁶ yellow microcrystals (31%), mp 134-135 °C; ^1H NMR (CDCl_3): δ 8.07 (s, 1H), 7.98 (s, 1H), 7.74 (d, 2H, J = 8.2 Hz), 7.26 (d, 2H, J = 8.6 Hz), 7.13 (d, 2H, J = 8.1 Hz), 6.77 (d, 2H, J = 8.6 Hz), 6.04 (dd, 1H, J = 8.5 Hz, J = 5.0 Hz), 4.25 (dd, 1H, J = 17.7 Hz, J = 8.5 Hz), 3.67 (s, 3H), 3.51 (dd, 1H, J = 17.7 Hz, J = 5.0 Hz), 2.29 (s, 3H); ^{13}C NMR (CDCl_3): δ 195.3, 159.5, 151.6, 144.4, 143.2, 133.5, 130.6, 129.2, 128.2, 128.1, 114.1, 58.4, 55.1, 43.4, 21.5.

1-(4-Nitrophenyl)-3-phenyl-3-(1H-1,2,4-triazol-1-yl)-1-propanone (6b):

⁶ yellow microcrystals (25%), mp 110-111 °C; ^1H NMR (CDCl_3): δ 8.28 (s, 1H), 8.21 (d, 2H, J = 8.7 Hz), 8.00-7.90 (m, 3H), 7.70-7.50 (m, 3H), 7.50-7.40 (m, 2H), 6.35-6.30 (m, 1H), 4.50-4.30 (m, 1H), 3.80-3.60 (m, 1H); ^{13}C NMR (CDCl_3): δ 195.0, 152.3, 147.8, 145.7, 143.8, 135.7, 134.0, 128.8, 128.1, 124.2, 58.1, 43.7. Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}_3$: N, 17.39. Found: N, 17.32.

3-(4-Chlorophenyl)-1-(4-methylphenyl)-3-(1H-1,2,4-triazol-1-yl)-1-propanone (6c):

⁶ yellow microcrystals (19%), mp 82-83 °C; ^1H NMR (CDCl_3): δ 8.20 (s, 1H), 7.91 (s, 1H), 7.83 (d, 2H, J = 8.1 Hz), 7.40-7.30 (m, 4H), 7.24 (d, 2H, J = 7.8 Hz), 6.20-6.15 (m, 1H), 4.33 (dd, 1H, J = 17.7 Hz, J = 8.7 Hz), 3.60 (dd, 1H, J = 17.7 Hz, J = 4.9 Hz), 2.39 (s, 3H); ^{13}C NMR (CDCl_3): δ 195.0, 151.8, 144.7, 143.5, 137.3, 134.4, 133.4, 129.3, 129.1, 128.4, 128.1, 58.2, 43.5, 21.6.

1,3-Diphenyl-3-(1*H*-1,2,4-triazol-1-yl)-1-propanone (6d):⁶ glassy oil (12%); ¹H NMR (CDCl₃): δ 8.10 (s, 1H), 7.90-7.80 (m, 3H), 7.50-7.20 (m, 8H), 6.15-6.10 (m, 1H), 4.35 (dd, 1H, J = 17.7 Hz, J = 8.7 Hz), 3.55 (dd, 1H, J = 17.7 Hz, J = 4.6 Hz); ¹³C NMR (CDCl₃): δ 195.8, 151.7, 143.5, 138.7, 136.1, 133.6, 129.0, 128.7, 128.6, 128.1, 126.9, 58.9, 43.7.

1-(4-Methylphenyl)-3-(2-thienyl)-3-(1*H*-1,2,4-triazol-1-yl)-1-propanone (6e): yellow needles (32%), mp 103-105 °C; ¹H NMR (CDCl₃): δ 8.24 (s, 1H), 7.91 (s, 1H), 7.84 (d, 2H, J = 8.2 Hz), 7.29-7.23 (m, 3H), 7.01 (d, 1H, J = 5.2 Hz), 6.95 (dd, 1H, J = 3.6 Hz, J = 5.2 Hz), 6.48 (q, 1H, J = 4.9 Hz), 4.34 (dd, 1H, J = 7.5 Hz, J = 17.7 Hz), 3.71 (dd, 1H, J = 4.9 Hz, J = 17.7 Hz), 2.39 (s, 3H); ¹³C NMR (CDCl₃): δ 194.8, 151.9, 144.7, 143.3, 141.1, 133.4, 129.4, 128.2, 126.9, 126.1, 54.6, 44.4, 21.6. Anal. Calcd. for C₁₆H₁₅N₃OS: C, 64.62; H, 5.08. Found: C, 64.57; H, 5.01.

1-(4-Chlorophenyl)-3-phenyl-3-(1*H*-1,2,4-triazol-1-yl)-1-propanone (6f):⁶ yellow needles (51%), mp 89-90 °C; ¹H NMR (CDCl₃): δ 8.21 (s, 1H), 8.00-7.90 (m, 3H), 7.60-7.30 (m, 7H), 6.20-6.10 (m, 1H), 4.38 (dd, 1H, J = 17.8 Hz, J = 8.5 Hz), 3.63 (dd, 1H, J = 17.7 Hz, J = 4.8 Hz); ¹³C NMR (CDCl₃): δ 195.5, 151.9, 143.5, 137.2, 135.9, 134.5, 133.7, 129.2, 128.7, 128.4, 128.1, 58.3, 43.7.

7-(4-Methoxyphenyl)-5-(4-methylphenyl)-7*H*-[1,2,4]triazolo[5,1-*b*][1,3] thiazine (8): yellow prisms (10%), mp 94-97 °C; ¹H NMR (CDCl₃): δ 7.95 (s, 1H), 7.42 (d, 2H, J = 8.1 Hz), 7.21-7.37 (m, 4H), 6.89 (d, 2H, J = 8.7 Hz), 6.25 (d, 1H, J = 4.7 Hz), 6.17 (d, 1H, J = 4.7 Hz), 3.79 (s, 3H), 2.38 (s, 3H). ¹³C NMR (CDCl₃): δ 160.0, 151.9, 139.8, 131.1, 130.1, 129.6, 129.5, 129.1, 128.6, 126.3, 116.6, 114.5, 61.7, 55.3, 21.2. HRMS Calcd. for C₁₉H₁₈N₃OS: 336.1120 (M⁺+1); observed: 336.1072.