Supporting Information

One-Pot Selective Synthesis of Multisubstituted Quinoxalin-2(1H)-ones by a Ugi 4CR/Catalytic aza-Wittig Sequence

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General Methods:
Reactions were generally carried out in an appropriate round bottom flask with magnetic stirring. All reactions were performed in round-bottom flasks under air. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Toluene was distilled from Na, and stored over 4 Å molecular sieves. Column chromatography purifications were performed under “flash” conditions using 400–630 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F254 plates, which were visualized by exposure to ultraviolet light. Melting points were uncorrected. MS was measured on an Finnigan Trace MS spectrometer. NMR spectra were recorded in CDCl₃ on a Varian Mercury 400 or 600 spectrometer and resonances were relative to TMS. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ¹³C NMR spectra were recorded on a Varian Mercury 400/600 (100/150 MHz) with complete proton decoupling spectrophotometers (CDCl₃; 77.0 ppm).

Preparation of Ugi intermediates 5h and 5k
A mixture of 2-aminobenzoyl azide 1 (1 mmol), aldehyde 2 (1 mmol), keto acid 3 (1 mmol), and isocyanide 4 (1 mmol) was stirred in methanol (5 mL) at room temperature for 8-12 hr, after the reaction completed, the precipitate was filtered to give 5.

2-(N-(2-(tert-butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-2-oxo-2-phenylacetamido)-5-methylbenzoyl azide (5h): white solid (90%), mp 115-117 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 7.99-6.69 (m, 12H, Ar-H), 6.53-6.13 (m, 1H, NH), 6.04-5.97 (m, 1H, CH), 2.26-2.05 (m, 3H, CH₃), 1.38-1.36 (m, 9H, 3CH₃); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 189.3, 170.7, 168.6, 166.1, 139.2, 134.5, 134.2, 134.1, 133.6, 133.2, 132.3, 131.3, 130.9, 129.8, 129.6, 128.6, 128.4, 128.0, 65.1, 51.5, 28.2, 20.7; IR (KBr): 2142, 1707, 1690, 1675, 1638 cm⁻¹. Anal. Calcd for C₂₈H₂₆ClN₅O₂: C, 63.22; H, 4.93; N, 13.16; Found: C, 63.00; H, 4.98; N, 13.26.

2-(N-(2-(butylamino)-2-oxo-1-(4-(trifluoromethyl)phenyl)ethyl)-2-oxo-2-phenylacetamido)-5-methoxy benzoyl azide (5k): white solid (92%), mp 103-105 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.01-7.10 (m, 12H, Ar-H), 6.92-6.77 (m, 1H, NH), 6.25-6.20 (m, 1H, CH), 3.74-3.63 (m, 3H, OCH₃), 3.36-3.22 (m, 2H, CH₂), 1.46-1.27 (m, 4H, 2CH₂), 0.90-0.85 (m, 3H, CH₃); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 189.6, 170.6, 169.2, 166.7, 159.3, 136.3, 135.2, 134.3, 133.1, 131.6, 131.1, 130.7, 130.4, 129.8, 128.7, 128.6, 125.0, 124.7, 122.3, 118.8, 115.7, 65.1, 55.4, 39.7, 31.0, 19.8, 13.5; IR (KBr): 2183, 1700, 1681, 1642, 1635 cm⁻¹. Anal. Calcd for C₂₈H₂₆F₃N₅O₅: C, 59.89; H, 4.51; N, 12.04; Found: C, 59.90 ; H, 4.57; N, 12.00.

One-pot Synthesis of Quinoxalin-2(1H)-ones 7 Via Sequential Ugi and Catalytic aza-Wittig Reaction
A mixture of 2-aminobenzoyl azide 1 (1 mmol), aldehyde 2 (1 mmol), keto acid 3 (1 mmol), and isocyanide 4 (1 mmol) was stirred in methanol (5 mL) at room temperature for 8-12 hr, then the solvent was removed completely under reduced pressure at room temperature. Toluene (5 mL) and 3-methyl-1-phenyl-2-phospholene 1-oxide (0.01 g, 0.05 mmol) was added to the reaction system, and the reaction mixture was heated to 110 °C for 2-3 hr to form quinoxalin-2(1H)-ones 7. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1:4, V/V) to give 7.

N-(tert-butyl)-2-(6-chloro-2-oxo-3-phenylquinolizin-1(2H)-yl)-2-(o-tolyl)acetamide (7a): white solid (75%); mp: 220-223 °C; ¹H NMR (CDCl₃, 600 MHz) δ (ppm) 8.20-8.19 (m, 2H, Ar-H), 7.90 (s, 1H, Ar-H),
N-(tert-butyl)-2-(6-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-(2-fluorophenyl)acetamide (7b): yellow solid (78%); mp: 215-218 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.18-8.17 (m, 2H, Ar-H), 7.91 (d, J = 1.8 Hz, 1H, Ar-H), 7.60-7.32 (m, 7H, Ar-H), 7.21-7.09 (m, 2H, Ar-H), 6.95 (s, 1H, NH), 6.14 (s, 1H, CH), 1.31 (s, 9H, 3CH3); 13C NMR (CDCl3, 150 MHz) δ (ppm) 165.0, 161.5, 159.8, 155.0, 154.8, 135.4, 134.3, 131.1, 131.0, 130.7, 129.8, 129.5, 129.3, 128.1, 124.8, 121.6, 116.7, 116.1, 116.0, 57.1, 52.1, 28.4; MS (EI, 70eV) m/z (%) 463 (M+, 1), 390 (9), 364 (100), 335 (29). Anal. Calcd for C26H23ClFNO2: C, 70.50; H, 5.70; N, 9.14; Found: C, 70.58; H, 5.64; N, 9.20.

N-(tert-butyl)-2-(6-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-(thiophen-2-yl)acetamide (7c): white solid (76%); mp: 185-186 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.32 (d, J = 7.2 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.50-7.34 (m, 6H, Ar-H), 7.19 (s, 1H, Ar-H), 6.99-6.89 (m, 2H, Ar-H+NH), 5.93 (s, 1H, CH), 1.34 (s, 9H, 3CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 165.3, 154.8, 154.3, 135.2, 134.2, 130.8, 130.3, 129.8, 129.6, 129.3, 128.1, 127.9, 126.7, 116.2, 57.3, 52.2, 28.4; MS (EI, 70eV) m/z (%) 451 (M+, 10), 378 (78), 352 (28), 323 (21), 112 (27), 97 (100). Anal. Calcd for C24H22ClFNO2S: C, 63.78; H, 4.91; N, 9.30; Found: C, 63.80; H, 5.00; N, 9.18.

N-butyl-2-(4-(4-chlorobenzoyl)phenyl)-2-(6-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)acetamide (7d): yellow solid (83%); mp: 136-139 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.30 (d, J = 6.6 Hz, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 7.50-7.26 (m, 9H, Ar-H), 6.62 (s, 1H, NH), 6.08 (s, 1H, CH), 3.29-3.28 (t, J = 6 Hz, 2H, CH2), 1.46-0.87 (m, 16H, 4CH3+2CH2); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.9, 155.1, 154.8, 151.9, 153.4, 134.3, 131.1, 130.8, 130.3, 129.7, 129.2, 128.1, 127.8, 126.2, 117.1, 61.4, 39.8, 34.6, 31.3, 31.2, 20.0, 13.7; MS (EI, 70eV) m/z (%) 501 (M+, 6), 428 (100), 357 (14), 218 (38). Anal. Calcd for C30H22ClN2O2: C, 71.77; H, 6.42; N, 8.37; Found: C, 71.82; H, 6.45; N, 8.45.

N-butyl-2-(6-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-(4-methoxyphenyl)acetamide (7e): yellow solid (80%); mp: 184-187 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.30-8.29 (m, 2H, Ar-H), 7.90 (d, J = 1.8 Hz, 1H, Ar-H), 7.51-7.26 (m, 7H, Ar-H), 6.89 (d, J = 9 Hz, 2H, Ar-H), 6.53 (s, 1H, NH), 6.09 (s, 1H, CH), 3.79 (s, 3H, OCH3), 3.32-3.22 (m, 2H, CH2), 1.47-1.43 (m, 2H, CH2), 1.31-1.24 (m, 2H, CH2), 0.89-0.87 (t, J = 7.2Hz, 3H, CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 167.0, 159.4, 154.6, 135.3, 134.0, 130.8, 130.5, 129.5, 129.4, 129.3, 128.9, 127.8, 125.3, 116.9, 114.3, 61.0, 55.0, 39.6, 31.0, 19.8, 13.5; MS (EI, 70eV) m/z (%) 475 (M+, 8), 402 (100), 347 (17), 220 (16), 192 (50). Anal. Calcd for C27H26ClN2O3: C, 68.13; H, 5.51; N, 8.83; Found: C, 68.32; H, 5.53; N, 8.68.

N-(tert-butyl)-2-(6-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-(p-tolyl)acetamide (7f): white solid (yield: 77%); mp: 167-169 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.27 (d, J = 6.6 Hz, 2H, Ar-H), 7.90 (d, J = 1.8 Hz, 1H, Ar-H), 7.52-7.47 (m, 3H, Ar-H), 7.34-7.17 (m, 6H, Ar-H), 6.68 (s, 1H, NH), 5.99 (s, 1H, CH), 2.34 (s, 3H, CH3), 1.34 (s, 9H, 3CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.2, 154.9, 154.8, 138.5, 135.5, 134.3, 131.0, 130.6, 129.8, 129.6, 129.4, 129.3, 128.0, 127.7, 117.7, 61.8, 52.0, 28.4, 21.1; MS (EI, 70 eV) m/z (%) 459 (M+, 6), 386 (33), 360 (50), 105 (100). Anal. Calcd for C27H26ClN2O2: C,
2-(7-chloro-2-oxo-3-phenylquinoxalin-1(2H)-yl)-N-cyclohexyl-2-phenylacetamide (7g): white solid (79%); mp: 236-237 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.27 (d, J = 6.6 Hz, 2H, Ar-H), 7.84 (d, J = 8.4 Hz, 1H, Ar-H), 7.49-7.25 (m, 10H, Ar-H), 6.59 (s, 1H, NH), 5.96 (d, J = 7.2 Hz, 1H, CH), 3.85-3.84 (m, 1H, NCH), 2.00-1.03 (m, 10H, 5CH2); 13C NMR (CDCl3, 100 MHz) δ (ppm) 165.6, 154.8, 154.0, 135.7, 135.5, 133.3, 132.3, 131.4, 130.6, 129.5, 129.3, 128.8, 128.1, 128.0, 124.4, 115.7, 62.0, 48.8, 32.5, 25.3, 24.6; MS (EI, 70eV) m/z (%) 471 (M+, 9), 372 (68), 346 (100), 317 (40), 239 (22). Anal. Calcd for C28H26ClN3O2: C, 71.25; H, 5.55; N, 8.90; Found: C, 71.18; H, 5.58; N, 8.93.

N-(tert-butyl)-2-(4-chlorophenyl)-2-(6-methyl-2-oxo-3-phenylquinoxalin-1(2H)-yl)acetamide (7h): yellow solid (88%); mp: 174-176 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.30-8.28 (m, 2H, Ar-H), 7.76 (s, 1H, Ar-H), 7.50-7.48 (m, 3H, Ar-H), 7.32-7.19 (m, 6H, Ar-H), 6.73 (s, 1H, NH), 5.97 (s, 1H, CH), 2.42 (s, 3H, CH3), 1.32 (s, 9H, 3CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.0, 155.1, 153.6, 135.8, 134.1, 134.0, 133.7, 132.5, 131.1, 130.4, 130.2, 129.6, 129.5, 129.2, 129.0, 128.0, 115.9, 60.7, 52.0, 28.4, 20.5; MS (EI, 70eV) m/z (%) 459 (M+, 9), 386 (48), 360 (100), 331 (37). Anal. Calcd for C27H24ClN3O2: C, 70.50; H, 5.70; N, 9.14; Found: C, 70.51; H, 5.64; N, 9.22.

N-(tert-butyl)-2-(6-methyl-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-phenylacetamide (7i): white solid (yield: 86%); mp: 195-198 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.28-8.27 (t, J = 3.3 Hz, 2H, Ar-H), 7.74 (s, 1H, Ar-H), 7.48-7.26 (m, 9H, Ar-H), 7.18 (d, J = 9.0 Hz, 1H, Ar-H), 6.73 (s, 1H, NH), 5.99 (s, 1H, CH), 2.40 (s, 3H, CH3), 1.33 (s, 9H, 3CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.3, 155.0, 153.5, 135.9, 135.8, 134.3, 134.2, 133.6, 130.8, 130.1, 130.0, 129.9, 129.4, 128.8, 128.1, 127.9, 127.7, 116.1, 61.7, 51.7, 28.3, 20.4; MS (EI, 70 eV) m/z (%) 425 (M+, 14), 352 (39), 326 (100), 297 (41). Anal. Calcd for C27H25N3O2: C, 76.21; H, 6.40; N, 9.87. Found: C, 76.04; H, 6.45; N, 9.70.

N-(tert-butyl)-2-(3,6-dimethyl-2-oxoquinolin-1(2H)-yl)-2-phenylacetamide (7j): white solid (yield: 87%); mp: 188-189 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 7.59 (s, 1H, Ar-H), 7.35-7.13 (m, 7H, Ar-H), 6.60 (s, 1H, NH), 5.85 (s, 1H, CH), 2.63 (s, 3H, CH3), 2.38 (s, 3H, CH3), 1.33 (s, 9H, 3CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.1, 157.9, 155.3, 133.8, 133.6, 133.1, 130.2, 129.9, 129.2, 128.9, 128.3, 127.8, 115.7, 61.6, 51.9, 28.4, 21.6, 20.5; MS (EI, 70 eV) m/z (%) 363 (M+, 7), 290 (23), 264 (100), 235 (24), 158 (25). Anal. Calcd for C22H23N3O2: C, 72.70; H, 6.93; N, 11.56. Found: C, 72.78; H, 6.75; N, 11.40.

N-butyl-2-(6-methoxy-2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-(4-(trifluoromethyl)phenyl)acetamide (7k): yellow solid (90%); mp: 159-162 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.30 (d, J = 7.8 Hz, 2H, Ar-H), 7.60-7.42 (m, 8H, Ar-H), 7.26-7.24 (m, 1H, Ar-H), 7.00-6.95 (m, 2H, Ar-H+NH), 6.36 (s, 1H, CH), 3.87 (s, 3H, OCH3), 3.24-3.20 (m, 2H, CH2), 1.43-1.21 (m, 4H, 2CH2), 0.85-0.84 (t, J = 7.2 Hz, 3H, CH3); 13C NMR (CDCl3, 100 MHz) δ (ppm) 166.4, 156.3, 154.8, 153.7, 137.6, 153.6, 134.6, 130.5, 130.3, 130.0, 129.4, 128.0, 125.6, 125.5, 122.4, 119.1, 117.2, 111.7, 59.7, 55.5, 39.7, 31.0, 19.8, 13.4; MS (EI, 70eV) m/z (%) 509 (M+, 70), 436 (95), 410 (100), 381 (60), 251 (68), 235 (36), 120 (33). Anal. Calcd for C28H26F3N3O2: C, 66.00; H, 5.14; N, 8.25; Found: C, 66.03; H, 5.33; N, 8.20.

N-cyclohexyl-2-(2-oxo-3-phenylquinoxalin-1(2H)-yl)-2-phenylacetamide (7l): white solid (78%); mp: 152-154 °C. 1H NMR (CDCl3, 600 MHz) δ (ppm) 8.29-8.28 (t, J = 3.6 Hz, 2H, Ar-H), 7.93 (d, J = 7.8 Hz,
1H, Ar-H), 7.49-7.26 (m, 11H, Ar-H), 6.70 (s, 1H, NH), 5.99 (d, J = 7.8 Hz, 1H, CH), 3.86-3.84 (m, 1H, NCH), 1.99-0.83 (m, 10H, 5CH₂); 13C NMR (CDCl₃, 100 MHz) δ (ppm) 166.0, 155.1, 153.9, 135.8, 133.9, 133.7, 132.3, 130.3, 129.7, 129.5, 129.0, 128.4, 128.0, 127.9, 123.9, 116.0, 61.5, 48.7, 32.5, 32.4, 25.3, 24.5; MS (EI, 70 eV) m/z (%) 437 (M⁺, 1), 338 (26), 312 (30), 223 (32), 105 (100). Anal. Calcd for C₂₈H₉₂N₂O₂: C, 76.86; H, 6.22; N, 9.67. Found: C, 76.80; H, 6.23; N, 9.67.

2-(3-bromophenyl)-N-(tert-butyl)-2-(2-oxo-3-phenylquinazolin-1(2H)-yl)acetamide (7m): yellow solid (84%); mp: 180-181 °C. 1H NMR (CDCl₃, 600 MHz) δ (ppm) 8.30-8.29 (m, 2H, Ar-H), 7.96 (d, J = 7.8 Hz, 1H, Ar-H), 7.55-7.21 (m, 10H, Ar-H), 6.72 (s, 1H, NH), 5.98 (s, 1H, CH), 1.33 (s, 9H, 3CH₃); 13C NMR (CDCl₃, 100 MHz) δ (ppm) 165.7, 155.1, 153.7, 136.3, 135.6, 133.7, 131.9, 131.4, 130.8, 130.5, 130.3, 129.9, 129.5, 128.1, 126.4, 124.2, 122.9, 116.1, 60.9, 52.1, 28.4; MS (EI, 70 eV) m/z (%) 491 (M⁺, 4), 416 (16), 392 (100), 361 (35), 221 (36). Anal. Calcd for C₃₆H₃₂BrN₂O₂: C, 63.68; H, 4.93; N, 8.57; Found: C, 63.80; H, 5.00; N, 8.45.

N-(tert-butyl)-2-(3-methyl-2-oxoquinazolin-1(2H)-yl)-2-phenylacetamide(7n): white solid (yield: 79%); mp: 132-134 °C. 1H NMR (CDCl₃, 600 MHz) δ (ppm) 7.80 (d, J = 7.8 Hz, 1H, Ar-H), 7.35-7.27 (m, 8H, Ar-H), 6.57 (s, 1H, NH), 5.82 (s, 1H, CH), 2.64 (s, 3H, CH₃), 1.33 (s, 9H, 3CH₃); 13C NMR (CDCl₃, 100 MHz) δ (ppm) 166.1, 158.1, 155.5, 133.8, 133.3, 132.3, 129.5, 129.0, 128.5, 127.9, 123.9, 115.9, 62.0, 52.0, 28.4, 21.5; MS (EI, 70 eV) m/z (%) 349 (M⁺, 5), 276 (19), 250 (100). Anal. Calcd for C₂₆H₂₃BrN₂O₂: C, 72.18; H, 6.63; N, 12.03. Found: C, 72.01; H, 6.62; N, 12.10.

N-(tert-butyl)-2-(2-oxo-3-phenylquinazolin-1(2H)-yl)pentanamide (7o): white solid (yield: 85%); mp: 131-132 °C. 1H NMR (CDCl₃, 600 MHz) δ (ppm) 8.32-7.27 (m, 9H, Ar-H), 6.08 (s, 1H, NH), 5.60 (s, 1H, CH), 2.41-2.04 (m, 2H, CH₂), 1.35-1.15 (m, 11H, CH₂+3CH₃), 0.90-0.88 (t, J = 7.5 Hz, 3H, CH₃); 13C NMR (CDCl₃, 150 MHz) δ (ppm) 168.4, 155.5, 153.7, 133.6, 130.7, 130.5, 130.1, 129.5, 128.1, 124.3, 115.7, 115.6, 56.3, 51.7, 30.0, 28.4, 19.9, 13.7; MS (EI, 70 eV) m/z (%) 377 (M⁺, 29), 249 (93), 222 (100), 194 (24), 77 (20). Anal. Calcd for C₂₃H₂₇N₃O₂: C, 73.18; H, 7.21; N, 11.13. Found: C, 73.05; H, 7.02; N, 11.30.
$^1$H NMR and $^{13}$C NMR Spectrums for Compounds 5h, 5k and 7

![H NMR and 13C NMR Spectra for Compounds 5h, 5k and 7](image-url)