Supplemental Material

Synthesis and Biological Activity of Functionalized Indole-2-carboxylates, Triazino- and Pyridazino-indoles

Adel A. EL-Gendy[1], Mohamed M. Said[2], Nagat Ghareb[2], Yasser M. Mostafa[3], El Sayed H. El-Ashry[4,] *

Comp. No. M. p. / % yield / IR / NMR / CHN-Analyses

5: M. p. 87-88 °C, lit. [36] m. p. 90-91 °C (yield 70%). IR (cm^{-1}): 1618 (C=N), 1702 (C=O), 3211 (NH). Mass spectrum: m/z: 223.5 [M+] (100), 202.5 (3.7), 178.6 (4.3), 149.7 (50.2), 108.7 (97.6), 81.6 (73.7), 48.1 (8.6). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.24 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 2.03 (s, 3H, CH_3), 4.17 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.07-7.13 (dd, 2H, J = 8.9 Hz, J = 8.8 Hz), 7.22-7.26 (dd, 2H, J = 5.0 Hz, J = 2.8 Hz), 9.83 (s, 1H, NH).

6: M. p. 121-123 °C, lit. [38] m. p. 125 °C (yield 80%). IR (cm^{-1}): 1595 (C=N), 1701 (C=O), 3351 (NH). Mass spectrum: m/z: 274.1 [M+] (20.96), 200 (78.95), 159 (96.69), 132.9 (100), 97 (21.87), 63 (67.35). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.25 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 2.12 (s, 3H, CH_3), 4.21 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.38-7.41 (dd, 1H, J = 8.8 Hz, J = 2.2 Hz), 7.50 (d, 1H, J = 8.8 Hz), 7.58 (d, 1H, J = 2.3 Hz), 8.73 (s, 1H, NH).

7: M. p. 165 °C, lit. [21] m. p. 167-168 °C (yield 82.77%). IR (cm^{-1}): 1699 (C=O ester), 3317 (NH indole). Mass spectrum: m/z: 223.1 [M+] (42.14), 177.1 (100), 149 (31.4), 123 (46.3%), 87 (16.11), 63.1 (15.18). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.32 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.33 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.11 (s, 1H, H at C3 indole), 7.23-7.26 (dd, 1H, J = 8.8 Hz, J = 2.0 Hz), 7.60 (d, 1H, J = 8.8 Hz), 7.71 (d, 1H, J = 1.5 Hz), 12.06 (s, 1H, NH).

8: M. p. 150-152 °C, lit. [36] m. p. 148 °C (yield 75%). IR (cm^{-1}): 1694 (C=O ester), 3315 (NH indole). Mass spectrum: m/z: 207 [M+] (51.41), 161.1 (100), 133.1 (51.20), 107 (52.32%, 81 (9.43), 57 (13.31). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.32 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.32 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.08 (s, 1H, H at C3 indole), 7.44-7.46 (m, 3H,Ar-H), 11.97 (s, 1H, NH).

9: M. p. 157 °C, lit. [38] m. p. 159-160 °C (yield 65%). IR (cm^{-1}): 731 (C-Cl), 1704 (C=O ester), 3284 (NH indole). Mass spectrum: m/z: 257 [M+] (39.55), 210.9 (100), 184 (15.95), 156.9 (72.56), 114.1 (23.57), 87 (35.56), 62 (18.). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.33 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.33 (q, 2H, CH_2 ethyl, J = 7.2 Hz), 7.22 (s, 1H, H at C3 indole), 7.44 (d, 1H, J = 1.8 Hz), 7.74 (d, 1H, J = 1.8 Hz), 12.39 (s, 1H, NH).

10: M. p. 140 °C, (yield 60%). IR (cm^{-1}): 1708 (C=O ester), 3340 (NH indole). Mass spectrum: m/z: 321.7 [M+] (75.3), 292.7 (85.9), 263.8 (93.3), 235.8 (55.9), 220.8 (12.7), 189.8 (100), 161.8 (35.4), 126.9 (13.2), 82.9 (92.2). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.34 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 2.48 (t, 4H, J = 3.3 Hz, $N(CH_2)_2$), 3.51 (t, 4H, J = 4.1 Hz, O $(CH_2)_2$), 3.95 (s, 2H, CH_2), 4.34 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.23-7.26 (dd, 1H, J = 8.7

Hz, J = 1.9 Hz), 7.42 (d, 1H, J = 8.7 Hz), 7.87 (d, 1H, J = 1.7 Hz), 11.84 (s, 1H, NH). Anal.Calcd. for $C_{16}H_{19}ClN_2O_3$: C, 59.62; H, 5.90; N, 8.69. Found: C, 59.22; H, 5.65; N, 8.40.

11: M. p. 150 °C, (yield 60%). IR (cm^{-1}): 1708 (C=O ester), 3396 (NH indole). Mass spectrum: m/z: 306.7 [M+] (14.8), 276.7 (75.7), 247.8 (75.5), 219.8 (54.4), 173.8 (100), 145.9 (39.9), 125.9 (7.9), 99.9 (17.9), 86 (19.9), 57 (9.3). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.34 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 2.48 (t, 4H, J = 3.5 Hz, $N(CH_2)_2$), 3.51 (t, 4H, J = 4.4 Hz, O $(CH_2)_2$), 3.94 (s, 2H, CH_2), 4.33 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.11-7.58 (m, 3H, Ar-H), 11.74 (s, 1H, NH). Anal.Calcd. for $C_{16}H_{19}FN_2O_3$: C, 62.73; H, 6.25; N, 9.14. Found: C, 62.50; H, 6.00; N, 8.99.

12: M. p. 198 °C, (yield 50%). IR (cm^{-1}): 764 (C-Cl), 1709 (C=O ester), 3350 (NH indole). Mass spectrum: m/z: 356.1 [M+] (3.41), 327 (12.78), 284 (26.97), 256 (18.66), 223.9 (77.44), 200 (66.61), 161 (100), 132.9 (63.18), 86.1 (35.38), 56 (87.65). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.35 (t, 3H, CH_3 ethyl, J = 7.2 Hz), 2.38 (t, 4H, J = 3.2 Hz, $N(CH_2)_2$), 3.41 (t, 4H, J = 4.5 Hz, O $(CH_2)_2$), 3.88 (s, 2H, CH_2), 4.35 (q, 2H, CH_2 ethyl, J = 7.2 Hz), 7.44 (d, 1H, J = 2.5 Hz), 7.89 (d, 1H, J = 2.4 Hz), 12.06 (s, 1H, NH). Anal.Calcd. for $C_{16}H_{18}Cl_2N_2O_3$: C, 53.93; H, 5.05; N, 7.86. Found: C, 53.50; H, 4.78; N, 7.46.

13: M. p. 270 °C, (yield 88%). IR (cm^{-1}): 795 (C-Cl), 1662 (C=O amide), 3141 (NH), 3210-3224 (NH_2), 3303 (NH indole). Mass spectrum: m/z: 243 [M+] (21.74), 211.9 (89.44), 185.9 (20.77), 156.9 (100), 135.9 (3.04%, 114 (41.03), 97 (12.32), 87 (42.82), 69.1 (54.98). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 4.56 (s, 2H, NH_2), 7.12 (s, 1H, H at C3 indole), 7.35 (d, 1H, J = 1.6 Hz), 7.69 (d, 1H, J = 1.6 Hz), 9.85 (s, 1H, NH), 11.91 (s, 1H, NH indole).

14: M. p. > 300 °C, (yield 88%). IR (cm^{-1}): 752 (C-Cl), 1662 (C=O), 3113 (NH). Mass spectrum: m/z: 252.7 [M+] (100), 211.7 (25.1), 147.8 (15.8), 82.8 (30.9). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 7.45 (s, 1H, H at C4), 7.73 (d, 1H, J = 1.86 Hz), 8.00 (d, 1H, J = 1.83 Hz), 9.22 (s, 1H, H at C10), 12.16 (s, 1H, NH). Anal.Calcd. for $C_{10}H_5Cl_2N_3O$: C, 47.43; H, 1.98; N, 16.60. Found: C, 47.27; H, 1.87; N, 16.30.

15: M. p. 232 °C, lit. [38] m. p. 240-241 °C (yield 81%). IR (cm^{-1}): 1639 (C=O aldehyde), 1726 (C=O ester), 3135 (NH indole). Mass spectrum: m/z: 251.1 [M+] (33.64), 222 (100), 204 (82.47), 177.1 (24.85), 150 (23.23), 114.1 (43.57), 87 (16.27), 63.1 (10.26). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH3 ethyl, J = 7.1 Hz), 4.44 (q, 2H, CH2 ethyl, J = 7.1 Hz), 7.39-7.42 (dd, 1H, J = 8.7 Hz, J = 2.1 Hz), 7.57 (d, 1H, J = 8.7 Hz), 8.20 (d, 1H, J = 2.0 Hz), 10.54 (s, 1H, CHO), 13.00 (s, 1H, NH).

16: M. p. 230 °C (yield 85%). IR (cm^{-1}): 1641 (C=O aldehyde), 1724 (C=O ester), 3157 (NH indole). Mass spectrum: m/z: 235.1 [M+] (44.2), 206 (100), 188 (93.7), 161 (27.8), 133

(32.7), 107 (20.8), 82.9 (14.6). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.44 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.23-7.30 (ddd, 1H, J = 9.2 Hz, J = 6.6 Hz, J = 2.6 Hz), 7.56-7.59 (dd, 1H, J = 9.0 Hz, J = 4.6 Hz), 7.86-7.89 (dd, 1H, J = 9.5 Hz, J = 2.5 Hz), 10.55 (s, 1H, CHO), 12.94 (s, 1H, NH). High resolution mass spectrum: Calcd.mass = 235.0645: Found mass = 235.0639.

17: M. p. 190 °C (yield 70%). IR (cm^{-1}): 782 (C-Cl), 1643 (C=O aldehyde), 1720 (C=O ester), 3140 (NH indole). Mass spectrum: m/z: 284.1 [M+] (19.56), 240 (30.20), 212 (100), 171.9 (75.38), 144.9 (44.81), 109 (43.53), 75 (21.49). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.33 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.2 Hz), 7.50 (d, 1H, J = 1.8 Hz), 7.79 (d, 1H, J = 1.8 Hz), 10.52 (s, 1H, CHO), 12.38 (s, 1H, NH).

18: M. p. 170-172 °C (yield 60%).IR (cm^{-1}): 1693 (C=O), 1717 (C=O ester), 3291 (NH indole). Mass spectrum: m/z: 417 [M+] (3.18), 389 (5.24), 327 (9.59), 282 (24.85), 252 (51.30), 206 (100), 150 (16.87), 114 (8), 74 (8.19). ^{1}H-NMR (DMSO, 200 MHz): δ (ppm) = 1.39 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 3.29-3.48 (dd, 4H, J = 15.5 Hz, $(CH_2)_2$), 4.38 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 6.31 (s, 1H, CH), 7.30-7.35 (dd, 1H, J = 10.6 Hz, J = 1.8 Hz), 7.50 (d, 1H, J = 9.2 Hz), 7.97 (d, 1H, J = 2.0 Hz), 12.09 (s, 1H, NH), 13.10 (brs, 2H, $(COOH)_2$).

19: IR (cm^{-1}): 1614 (C = N imine), 1683 (C=Oester), 3296 (NH indole). Mass spectrum: m/z: 326 [M+] (29.29), 297 (88.1), 279.1 (37.45), 253 (14.01), 216.1 (16.58), 190.1 (16.86), 163.1 (4.39), 148 (19.34), 114 (14.28), 77 (100), 51 (49.95). High resolution mass spectrum: Calcd.mass = 326.0822: Found mass = 326.0793. ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.37 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.24-8.56 (m, 8H, Ar-H), 9.27 (s, 1H, CH = N), 12.65 (s, 1H, NH).

20: IR (cm^{-1}): 1611 (C = N imine), 1681 (C=Oester), 3301 (NH indole). Mass spectrum: m/z: 360 [M+] (61.3), 331 (100), 313 (31.4), 287 (13.8), 252 (9.5), 224 (6.6), 215 (8.7), 203.9 (10.9), 188 (4.2), 174 (3.1), 148 (11.5), 125 (4.2), 111 (25.1), 85 (4.1), 57 (14.1). High resolution mass spectrum: Calcd.mass = 360.0432: Found mass = 360.0437. ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.37 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 4.44 (q, 2H, CH_2 ethyl, J = 7.1 Hz), 7.26-8.52 (m, 7H, Ar-H), 9.24 (s, 1H, CH = N), 10.54 (s, 1H, NH).

21: IR (cm^{-1}): 1615 (C = N imine), 1689 (C=O ester), 3307 (NH indole). Mass spectrum: m/z: 344.2 [M+] (45.08), 315.1 (100), 297.1 (40.46), 271.1 (18.60), 234.1 (13.88), 204 (19.69), 177.1 (6.37), 148 (30.51), 114.1 (17.37), 95 (44.79), 75 (26.91). High resolution mass spectrum: Calcd.mass = 344.0728: Found mass = 344.0722. ^{1}H-NMR (DMSO, 300 MHz):δ (ppm) = 1.40 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.1 Hz), 7.22-8.55 (m, 7H, Ar-H), 9.25 (s, 1H, CH = N), 12.61 (s, 1H, NH).

22: IR (cm^{-1}): 1613 (C = N imine), 1687 (C=O ester), 3311 (NH indole). Mass spectrum: m/z: 356.2 [M+] (78.41), 327.1 (100), 309.1 (37.24), 284.1 (10.04), 269.1 (17.63), 239 (20.67), 204 (18.77), 177.1 (14.87), 148 (9.36), 114.1 (5.85), 92 (24.93), 77 (23.42). High resolution mass spectrum: Calcd.mass = 356.0928: Found mass = 356.0925. ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.45 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 3.83 (s, 3H, OCH_3), 4.47 (q, 2H, CH_2 ethyl, J = 7.1 Hz), 6.92-8.81 (m, 7H, Ar-H), 9.33 (s, 1H, CH = N), 11.50 (s, 1H, NH).

23: IR (cm^{-1}): 798 (C-Cl), 1614 (C = N imine), 1683 (C=O ester), 3307 (NH indole). Mass spectrum: m/z: 393 [M+] (51.8), 364.5 (100), 320.5 (8.6), 286.6 (8.8), 249.7 (5.6), 203.7 (16.5), 173.8 (3.5), 147.8 (17.7), 113.9 (5), 82.8 (31.9), 47.2 (3.9). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.43 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.29 (d, 1H, J = 8.5 Hz), 7.40-7.42 (dd, 1H, J = 8.7 Hz, J = 2.1 Hz), 7.47-7.50 (dd, 1H, J = 8.5 Hz, J = 2.3 Hz), 7.57 (d, 1H, J = 8.7 Hz), 7.71 (d, 1H, J = 2.3 Hz), 8.64 (d, 1H, J = 2.0 Hz), 9.24 (s, 1H, CH = N), 12.74 (s, 1H, NH).

24: IR (cm^{-1}): 1615 (C = N imine), 1685 (C=O ester), 3286 (NH, OH). Mass spectrum: m/z: 356 [M+] (65), 327 (80), 309 (100), 283 (22.3), 252 (22.7), 222 (26.8), 206 (48.2), 177 (17.3), 151 (19.5), 114 (17.7), 92 (19.1), 51 (24.5). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.33 (t, 3H, CH3 ethyl, J = 7.1 Hz), 2.32 (s, 3H, CH_3), 4.36 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.23-7.26 (dd, 2H, J = 8.7 Hz, J = 1.8 Hz), 7.43 (d, 2H, J = 8.8 Hz), 7.96 (d, 2H, J = 1.8 Hz), 8.30 (s, 1H, CH = N), 10.02 (s, 1H, OH), 11.91 (s, 1H, NH).

25: IR (cm^{-1}): 1611 (C = N imine), 1726 (C=O ester), 3138 (NH, OH). Mass spectrum: m/z: 342 [M+] (5.60), 313 (20.36), 295 (27.51), 269.2 (8.25), 252.1 (27.85), 222 (56.85), 206 (77.33), 177 (26.14), 150 (31.42), 114 (51.68), 92 (100), 74 (49.56), 51 (17.65). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.37 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.28-8.30 (m, 7H, Ar-H), 9.29 (s, 1H, CH = N), 10.45 (s, 1H, OH), 12.96 (s, 1H, NH).

26: IR (cm^{-1}): 1613 (C = N imine), 1687 (C=O ester), 3296 (NH indole). Mass spectrum: m/z: 310 [M+] (12.51), 281.1 (42.64), 263 (25.95), 236.1 (16.87), 208 (18.41), 158 (6.89), 132 (26.72), 107 (12.75), 77 (100), 51 (51.62). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.23-8.26 (m, 8H, Ar-H), 9.29 (s, 1H, CH = N), 12.54 (s, 1H, NH).

27: IR (cm^{-1}): 1617 (C = N imine), 1686 (C=O ester), 3316 (NH indole). Mass spectrum: m/z: 324 [M+] (2.76), 295 (15.32), 277 (8.08), 249.1 (7.60), 222 (7.25), 187 (13.92), 159 (7.95), 132 (22.26), 107 (11.25), 91 (78), 65 (100). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t,

3H, CH_3 ethyl, J = 7.0 Hz), 2.32 (s, 3H, CH_3), 4.41 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.16-8.27 (m, 7H, Ar-H), 9.29 (s, 1H, CH = N), 12.50 (s, 1H, NH).

28: IR (cm^{-1}): 1614 (C = N imine), 1687 (C=O ester), 3289 (NH indole). Mass spectrum: m/z: 355 [M+] (36.31), 326 (100), 308 (17.08), 282 (2.20), 234 (14.16), 208 (13.10), 188 (4.49), 90.1 (5.40), 76 (17.34). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.1 Hz), 7.29-8.31 (m, 7H, Ar-H), 9.30 (s, 1H, CH = N), 12.61 (s, 1H, NH).

29: IR (cm^{-1}): 1607 (C = N imine), 1684 (C=O ester), 3302 (NH indole). Mass spectrum: m/z: 378 [M+] (13.18), 349 (42.58), 305 (8.92), 270 (12.89), 234 (18.19), 186 (29.27), 132 (100), 109 (58.40), 75 (29.78). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.38 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.42 (q, 2H, CH_2 ethyl, J = 7.0 Hz), 7.27-8.33 (m, 6H, Ar-H), 9.25 (s, 1H, CH = N), 12.68 (s, 1H, NH).

30: M. p. 185 °C, (yield 50%), IR (cm^{-1}): 1688 (C=O thiazole), 1725 (C=O ester), 3307 (NH indole). Mass spectrum: m/z: 448 [M+] (5.98), 419 (2.40), 360 (46.87), 331 (100), 297 (0.71), 251 (23.01), 204 (46.58), 177 (8.79), 148 (20.39), 75 (15.19). ^{1}H-NMR (DMSO, 200 MHz): δ (ppm) = 1.42 (t, 3H, CH_3 ethyl, J = 7.2 Hz), 1.59 (d, 3H, CH_3 at thiazole ring, J = 7.0 Hz), 4.40 (q, 1H, CH of thiazole ring, J = 7.4 Hz), 4.47 (q, 2H, CH2 ethyl, J = 7.1 Hz), 6.58 (s, 1H, CH of thiazole ring), 7.28-8.08 (m, 7H, Ar-H), 12.67 (s, 1H, NH). Anal.Calcd. for $C_{21}H_{18}Cl_2N_2O_3S$: C, 56.45; H, 4.01; N, 6.25. Found: C, 55.97; H, 3.88; N, 5.97.

31: M. p. 160 °C (yield 40%). IR (cm^{-1}): 1683 (C=O thiazole), 1720 (C=O ester), 3161 (NH indole). Mass spectrum: m/z: 432 [M+] (16.5), 403 (26.8), 345 (20.1), 315 (23.5), 297 (16.2), 267 (12), 250 (33.2), 222 (100), 204 (41.3), 177 (11.8), 149 (21.7), 111 (14.9), 95 (11.2), 61 (17.8). ^{1}H-NMR (DMSO, 200 MHz):δ (ppm) = 1.39 (t, 3H, CH3 ethyl, J = 7.1 Hz), 1.42 (d, 3H, CH3 at thiazole ring, J = 7.2 Hz), 3.65 (q, 1H, CH of thiazole ring, J = 7.0 Hz), 4.40 (q, 2H, CH2 ethyl, J = 7.0 Hz), 6.44 (s, 1H, CH of thiazole ring), 7.0-7.88 (m, 7H, Ar-H), 11.63 (s, 1H, NH). Anal.Calcd. for $C_{21}H_{18}ClFN_2O_3S$: C, 58.33; H, 4.16; N, 6.47. Found: C, 57.95; H, 3.91; N, 6.04.

32: M. p. 100 °C (yield 30%), IR (cm^{-1}): 1683 (C=O thiazole), 1708 (C=O ester), 3321 (NH, OH). Mass spectrum: m/z: 444 [M+] (5.20), 415 (3.66), 371 (4.83), 339 (6.40), 309 (11.68), 266 (3.57), 252 (25.25), 222 (90.72), 204 (35.98), 177 (18.11), 134 (31.74), 114 (31.56), 61 (100). ^{1}H-NMR (DMSO, 200 MHz): δ (ppm) = 1.30 (t, 3H, CH3 ethyl, J = 6.8 Hz), 1.41 (d, 3H, CH3 at thiazole ring, J = 7.0 Hz), 2.50 (s, 3H, CH3), 3.71 (q, 1H, CH of thiazole ring, J = 7.1 Hz), 4.35 (q, 2H, CH_2 ethyl, J = 7.4 Hz), 6.50 (s, 1H, CH of thiazole ring), 7.02-8.01 (m,

6H, Ar-H), 10.12 (s, 1H, OH), 12.07 (s, 1H, NH). Anal.Calcd. for $C_{22}H_{21}ClN_2O_4S$: C, 59.45; H, 4.72; N, 6.30. Found: C, 59.10; H, 4.35; N, 6.04.

33: M. p. 115 °C (yield 20%), IR (cm^{-1}): 1689 (C=O thiazole), 1706 (C=O ester), 3230 (NH, OH). Mass spectrum: m/z: 430 [M+] (55.5), 401 (43.3), 357 (24.8), 313 (22.4), 295 (45.8), 268 (12.9), 252 (27.6), 221.9 (100), 205.9 (32.9), 190 (14.8), 177 (13.4), 120 (21.3), 61 (19.6). ^{1}H-NMR (DMSO, 200 MHz): δ (ppm) = 1.28 (t, 3H, CH3 ethyl, J = 7.0 Hz), 1.40 (d, 3H, CH3 at thiazole ring, J = 7.2 Hz), 3.82 (q, 1H, CH of thiazole ring, J = 7.0 Hz), 4.40 (q, 2H, CH_2 ethyl, J = 7.4 Hz), 6.28 (s, 1H, CH of thiazole ring), 6.91-8.13 (m, 7H, Ar-H), 10.02 (s, 1H, OH), 11.97 (s, 1H, NH). Anal.Calcd. for $C_{21}H_{19}ClN_2O_4S$: C, 58.60; H, 4.41; N, 6.50. Found: C, 58.33; H, 4.11; N, 6.20.

34: M. p. >300 °C, lit. (39) m. p. >300 °C. IR (cm^{-1}): 1662 (C=O amide), 3113 (NH indole). Mass spectrum: m/z: 219.1 [M+] (100), 190.1 (2.68), 163.1 (14.12), 128 (20.21), 99 (16.60), 74 (16.09), 55 (10.26). High resolution mass spectrum: Calcd.mass = 219.0199: Found mass = 219.0178. ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 7.48-7.51 (dd, 1H, J = 8.7 Hz, J = 2.1 Hz), 7.60 (d, 1H, J = 8.7 Hz), 8.29 (d, 1H, J = 1.92 Hz), 8.75 (s, 1H, H at C1 pyridazine), 12.86 (s, 2H, 2 (NH)).

35: M. p. >300 °C, IR (cm^{-1}): 1660 (C=O amide), 3126 (NH indole). Mass spectrum: m/z: 203 [M+] (100), 174 (4.27), 147 (21.76), 121 (19.79), 99 (7.09), 82.9 (13.87), 57 (4.67). 1H-NMR (DMSO, 300 MHz): δ (ppm) = 7.33-7.40 (ddd, 1H, J = 11.7 Hz, J = 9.1 Hz, J = 2.6 Hz), 7.58-7.62 (dd, 1H, J = 9.0 Hz, J = 4.4 Hz), 7.98-8.02 (dd, 1H, J = 9.3 Hz, J = 2.5 Hz), 8.72 (s, 1H, H at C1 pyridazine), 12.83 (s, 2H, 2 (NH)).

36: M. p. >300 °C, IR (cm^{-1}): 805 (C-Cl), 1668 (C=O amide), 3149 (NH indole). Mass spectrum: m/z: 253 [M+] (62.1), 212 (100), 184 (15.2), 157 (19.8), 109 (9.4). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 7.53 (d, 1H, J = 1.86 Hz), 7.98 (d, 1H, J = 1.83 Hz), 9.22 (s, 1H, H at C1 pyridazine), 12.16 (s, 2H, 2 (NH)).

37: M. p. 250 °C, IR (cm^{-1}): 791 (C-Cl), 1607 (C = N imine), 1684 (C=O ester), 3302 (NH), 3402 (NH indole). Mass spectrum: m/z: 393 [M+] (46.32), 347 (5.64), 312.1 (30.94), 285.1 (15.17), 258 (7.09), 205 (22.91), 187.1 (69.34), 159.9 (71.03), 132.9 (100), 107 (54.73), 63 (24.01). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.39 (t, 3H, CH_3 ethyl, J = 7.0 Hz), 4.44 (q, 2H, CH2 ethyl, J = 7.0 Hz), 7.23-8.04 (m, 6H, Ar-H), 9.11 (s, 1H, CH = N), 10.17 (s, 1H, NH), 12.12 (s, 1H, NH indole).

38: M. p. 140 °C, IR (cm^{-1}): 786 (C-Cl), 1614 (C = N imine), 1692 (C=O ester), 3299 (NH), 3410 (NH indole). Mass spectrum: m/z: 445 (M++2, 15.84), 364 (6.59), 336 (4.10), 273 (2.43), 237 (27.5), 211 (16.02), 184 (26.61), 162 (61.87), 133 (100), 109 (23.31), 63 (24.89).

^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 1.35 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 4.41 (q, 2H, CH2 ethyl, J = 7.1 Hz), 7.44-8.04 (m, 5H, Ar-H), 9.11 (s, 1H, CH = N), 10.17 (s, 1H, NH), 12.72 (s, 1H, NH indole).

39: M. p. >300 °C, IR (cm^{-1}): 883 (C-Cl), 3427 (NH indole). Mass spectrum: m/z: 221 [M+] (100), 185.8 (7.3), 158 (44.4), 131 (18), 106 (4.4), 81 (3.6), 57 (3.4). High resolution mass spectrum: Calcd.mass = 221.0156: Found mass = 221.0136. ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 7.63-7.70 (ddd, 1H, J = 11.7 Hz, J = 9.1 Hz, J = 2.5 Hz), 7.84-7.89 (dd, 1H, J = 9.0 Hz, J = 4.3 Hz), 8.30-8.34 (dd, 1H, J = 8.8 Hz, J = 2.4 Hz), 10.21 (s, 1H, H at C1 pyridazine), 13.51 (s, 1H, NH).

40: M. p. >300 °C, IR (cm^{-1}): 779 (C-Cl), 3400 (NH indole). Mass spectrum: m/z: 273 (M++2, 100), 253 (51.8), 237 (14.1), 208 (22.7), 172 (28.3), 91 (16), 57 (5). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 7.88 (d, 1H, J = 1.74 Hz), 8.69 (d, 1H, J = 1.62 Hz), 10.25 (s, 1H, H at C1 pyridazine), 10.84 (s, 1H, NH).

41: M. p. >300 °C, IR (cm^{-1}): 3427 (NH indole). Mass spectrum: m/z: 272 [M+] (33), 255 (13), 227 (42.1), 201 (28.6), 187 (100), 160 (29.6), 119 (13.7), 86 (18.5), 57 (15.6). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 2.08 (m, 4H, $N(CH_2)_2$), 3.22 (m, 4H, O (CH2)2), 7.37-7.42 (ddd, 1H, J = 10.8 Hz, J = 8.9 Hz, J = 3.0 Hz), 7.60-7.62 (dd, 1H, J = 8.9 Hz, J = 3.4 Hz), 7.90-8.02 (dd, 1H, J = 9.0 Hz, J = 2.1 Hz), 8.75 (s, 1H, H at C1 pyridazine), 12.83 (s, 1H, NH). Anal.Calcd. for $C_{14}H_{13}FN_4O$: C, 61.76; H, 4.77; N, 20.58. Found: C, 61.50; H, 4.55; N, 20.33.

42: M. p. >300 °C, IR (cm^{-1}): 798 (C-Cl), 3330 (NH indole). Mass spectrum: m/z: 322 [M+] (40.6), 293 (32.9), 265 (100), 237 (61.4), 212 (27.4), 197 (13.2), 174 (14), 149 (15.9), 86 (48.6), 57 (37.8). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 2.48 (m, 4H, $N(CH_2)_2$), 3.25 (m, 4H, O $(CH_2)_2$), 7.66 (d, 1H, J = 1.7 Hz), 8.00 (d, 1H, J = 1.6 Hz), 9.47 (s, 1H, H at C1 pyridazine), 10.57 (s, 1H, NH). Anal.Calcd. for $C_{14}H_{12}Cl_2N_4O$: C, 52.17; H, 3.74; N, 17.39. Found: C, 51.91; H, 3.55; N, 17.00.

43: M. p. 270 °C (yield 40%) IR (cm^{-1}): 1643 (C=O), 3141 (NH indole). Mass spectrum: m/z: 345.1 [M+] (2.17), 274.1 (2.49), 219 (91.54), 163.1 (7.22), 127.1 (100), 84.1 (36.93). ^{1}H-NMR (DMSO, 300 MHz): δ (ppm) = 0.90 (t, 3H, CH_3 ethyl, J = 7.1 Hz), 2.24 (q, 2H, CH2 ethyl, J = 7.0 Hz), 2.65-3.26 (m, 8H, N(CH2)4), 5.06 (s, 2H, CH_2), 7.49-7.52 (dd, 1H, J = 8.7 Hz, J = 2.1 Hz), 7.61 (d, 1H, J = 8.7 Hz), 8.31 (d, 1H, J = 1.6 Hz), 8.76 (s, 1H, H at C1 pyridazine), 12.86 (s, 1H, NH). High resolution mass spectrum: Calcd.mass = 345.1356: Found mass = 345.1340. Anal.Calcd. for $C_{17}H_{20}ClN_5O$: C, 59.13; H, 5.79; N, 20.28. Found: C, 59.00; H, 5.65; N, 20.00.