INSTRUMENTATION AND MATERIALS

Melting points were measured using Buchi apparatus in open capillaries and are uncorrected.

Infrared (IR) spectra were recorded on a PerkinElmer FT/IR version10.03.05 spectrophotometer (**υ,** expressed in cm^{-1})

NMR spectra were run on a JEOL AL300 FTNMR spectrometer; chemical shifts are given in δ ppm, relative to TMS as internal standard.

Elemental microanalysis was performed on Exeter Analytical Inc Model CE-440 CHN Analyzer.

XRD spectra were recorded on Scifert X-Ray Diffraction System.

TEM image were taken from TECNAI G2, FEI.

SEM image was recorded from Scanning Electron Microscope, QUANTA 200 F.

BET surface area analysis was carried by Smart Sorb-93 manufactured by Smart Instruments Pvt. Ltd.

Ball milling was carried out in a **ball mill** manufactured Shivam Instruments Pvt. Ltd. India, microwave assisted reactions are carried out in a **"MAS-II, Microwave Synthesis System"** manufactured by Sineo microwave chemistry technology co. Ltd.

Thin-layer Chromatography (TLC) was performed on glass plates (7.5 × 2.5 and 7.5 × 5.0) coated with silica gel GF 254 using various combinations of ethylacetate and n-hexane as eluent. Visualization of spots was accomplished either in iodine chamber or by exposure to UV light.

All the chemicals were procured from Aldrich, USA and E. Merck, Germany and were used as received. The solvents were purchased by CDH, Himedia and Merck, India and were purified prior to its use.

N-substituted Isatin derivatives were synthesized in laboratory by following methods.

General procedure for synthesis of *N*-alkylisatin/ 5-chloro *N*-alkylisatin derivatives (Chen et al, 2011)**:**

Isatin/ 5-chloroisatin (0.001mol) and alkylhalide (0.0012 mol) were dissolved in DMF (20 ml), and anhydrous K_2CO_3 (0.003 mol) was added. The mixture was stirred under room temperature until the disappearance of isatin, the completion of the reaction was monitored by TLC. The solvent was removed in vacuo and the residue was separated by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1), giving *N*-alkyl substituted isatin compound.

1-Ethylindoline-2, 3-dione

Dark-red solid, Mp 86 ^{0}C, **IR (KBr)υ**: 3064, 2987, 1738, 1727, 1610, 1469, 1354, 1289, 1158, 1162, 759, 701 cm^{-1}. **^{1}H-NMR (300 MHz, $CDCl_3$) δ**: 1.30 (t, 3H, *J*=6.9 Hz, CH_3), 3.86 (q, 2H, *J*=7.2 Hz, CH_2), 6.92- 7.65 (m, 4H, Ar-H) ppm. Anal. Calc. For ($C_{10}H_9NO_2$): C, 68.60; H, 5.21; N, 7.99; O, 18.20 (%). Found: C, 68.58; H, 5.22; N, 8.01; O, 18.19 (%).

5-Chloro-1-ethylindoline-2, 3-dione

Red solid, Mp 110 ^{0}C, **IR (KBr) υ**: 3049, 2956, 2845, 1722, 1710, 1614, 1569, 1463, 1350, 1248, 1135, 1090, 762, 723 cm^{-1}. **^{1}H-NMR (300 MHz, $CDCl_3$) δ**: 1.10 (t, 3H, *J*=7.2 Hz, CH_3), 3.52 (q, 2H, *J*=7.0 Hz, CH_2), 7.01- 7.89 (m, 3H, Ar-H) ppm. Anal. Calc. For ($C_{10}H_8ClNO_2$): C, 57.30; H, 3.85; N, 6.68; O, 15.26 (%). Found: C, 57.35; H, 3.84; N, 6.69; O, 15.25 (%).

Ethyl 2-(2, 3-dioxoindolin-1-yl)acetate

Yellow-brown solid, Mp 118 ^{0}C**, IR (KBr) υ**: 3054, 2986, 1746, 1730, 1715, 1615, 1470, 1347, 1341, 1277, 1213, 1176, 1096, 758, 715 cm^{-1}. **^{1}H-NMR (300 MHz, $CDCl_3$) δ**: 1.24 (t, 3H, *J*=7.2 Hz, CH_3), 4.18 (q, 2H, *J*=7.2 Hz, CH_2), 4.40 (s, 2H, CH_2), 7.70- 6.72 (m, 4H, Ar-H) ppm. Anal. Calc. For $C_{12}H_{11}NO_4$: C, 61.82; H, 4.74; N, 6.00; O, 27.44 (%). Found: C, 61.80; H, 4.75; N, 6.02; O, 27.43 (%).

Ethyl 2-(5-chloro-2, 3-dioxoindolin-1-yl)acetate

Yellow solid, Mp 140 ^{0}C, **IR (KBr) υ**: 3155, 2969, 1735, 1722, 1702, 1620, 1560, 1472, 1365, 1311, 1263, 1199, 1127, 1089, 753, 739 cm^{-1}. **^{1}H-NMR (300 MHz,**

$CDCl_3$) δ: 1.62 (t, 3H, *J*=7.2 Hz, CH_3), 4.20 (q, 2H, *J*=7.2 Hz, CH_2), 4.51 (s, 2H, CH_2), 6.98- 7.84 (m, 3H, Ar-H) ppm. Anal. Calc. For ($C_{12}H_{10}ClNO_4$): C, 53.85; H, 3.77; N, 5.23; O, 23.91 (%). Found: C, 53.80; H, 3.80; N, 5.20; O, 23.94 (%).

1-Propylindoline-2, 3-dione

Red solid, Mp 107 ^{0}C, **IR (KBr) υ**: 3124, 3020, 2985, 2851, 1718, 1710, 1605, 1570, 1480, 1355, 1269, 1144, 1020, 759, 748 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 1.10-1.15 (t, *J*= 7.0 Hz , 3H), 1.66-1.76 (m, 2H), 3.25-3.31 (t, *J*=7.2 Hz, 2H), 7.11- 7.98 (m, 4H, aromatic protons) ppm. Anal. Calcd for: $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40; O, 16.91Found: C, 69.80; H, 5.90; N, 7.43; O, 16.87.

5-Chloro-1-propylindoline-2, 3-dione

Red solid, Mp 136^{0}C, **IR (KBr) υ**: 3189, 3055, 2950, 2844, 1727, 1716, 1621, 1565, 1473, 1360, 1250, 1161, 1012, 754, 749 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 1.09-1.13 (t, *J*= 6.9 Hz, 3H), 1.80-1.88 (m, 2H), 3.15-3.20 (t, *J*=7.0 Hz, 2H), 7.15- 7.72 (m, 3H, aromatic protons) ppm. Anal. Calcd for : $C_{11}H_{10}ClNO_2$: C, 59.07; H, 4.51; N, 6.26; O, 14.31Found: C, 59.00; H, 4.60; N, 6.20; O, 14.28.

1-Benzylindoline-2, 3-dione

Red solid, Mp 128 ^{0}C, **IR (KBr) υ**: 3200, 3078, 2980, 2848, 1725, 1713, 1612, 1567, 1481, 1345, 1263, 1141, 1051, 755 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 5.77 (s, 2H), 7.16- 8.00 (m, 9H, aromatic protons) ppm. Anal. Calcd for: $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90; O, 13.49 Found: C, 75.91; H, 4.70; N, 5.88; O, 13.50.

1-Benzyl-5-chloroindoline-2, 3-dione

Red solid, Mp 136^{0}C, **IR (KBr) υ**: 3184, 3100, 2991, 2868, 1729, 1717, 1616, 1568, 1480, 1353, 1280, 1150, 1033, 760 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 5.58 (s, 2H), 7.22- 8.05 (m, 8H, aromatic protons) ppm. Anal. Calcd for: $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71; N, 5.16; O, 11.78 Found: C, 66.30; H, 3.70; N, 5.20; O, 11.74.

1-(4-Bromobutyl) indoline-2, 3-dione

Reddish- yellow solid, Mp 186 ^{0}C,**IR (KBr) υ**: 3087, 2928, 1733, 1605, 1467, 1360,1341, 1189, 1162, 753, 735 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ**: 1.63 (m, 2H, CH_2), 1.97 (m, 2H, CH_2), 3.6 (t, 2H, *J*=7.2 Hz, CH_2), 4.19 (t, 2H, *J*=7.5 Hz, CH_2), 7.21-7.72 (m, 4H, Ar-H) ppm.Anal. Calcd. For $C_{12}H_{12}BrNO_2$: C, 51.09; H, 4.29; N, 4.96; O, 11.34 (%). Found: C, 51.10; H, 4.28; N, 4.97; O, 11.35 (%).

General Procedure for synthesis of *N*-acetylisatin and 5-Chloro *N*-acetylisatin (Popp and Piccirilli, 1971)

Isatin (0.003 mol) and acetic anhydride (3 ml) were refluxed until disappearance of isatin, the completion of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled. The product formed was dried at room temperature and recrystallized from ethanol.

1-Acetylindoline-2, 3-dione

Yellow crystals, Mp 144 ^{0}C, **IR (KBr)υ**: 3152, 3001, 2952, 2850, 1732, 1712, 1690, 1610, 1569, 1486, 1391, 1287, 756 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 2.12 (s, 3H, CH_3), 7.15- 7.77 (m, 4H, Ar-H) ppm. Anal. Calcd. For $C_{10}H_7NO_3$: C, 63.49; H, 3.73; N, 7.40; O, 25.37 (%). Found: C, 63.40; H, 3.78; N, 7.42; O, 25.39 (%).

1-Acetyl-5-chloroindoline-2, 3-dione

Yellow crystals, Mp 174 ^{0}C, **IR (KBr)υ**: 3200, 3040, 2955, 2863, 1725, 1709, 1703, 1612, 1569, 1485, 1380, 1283, 745 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ**: 2.10 (s, 3H, CH_3), 6.97- 7.63 (m, 3H, Ar-H) ppm. Anal. Calcd. For $C_{10}H_6ClNO_3$: C, 53.71; H, 2.70; N, 6.26; O, 21.46 (%). Found: C, 53.68; H, 2.77; N, 6.28; O, 21.44(%).

General Procedure for synthesis of 1-[(diphenylamino)methyl]indoline-2, 3-dione and 1-(diethylamino)methyl]indoline-2, 3-dione (Solomon et al, 2009)

Secondary amine (0.004 mol) in 10 ml of ethanol was added to slurry containing appropriate isatin (0.004 mol) and 0.3 ml of formaldehyde solution (37% v/v) in 10 ml of ethanol. The reaction mixture was stirred for 6h at room temperature and

the completion of the reaction was monitored by TLC. Reaction mixture was then refrigerated for 48h. The products were separated by suction filtration, vacuum dried and recrystallized from ethanol.

1-[(Diphenylamino)methyl]indoline-2, 3-dione

Light- red solid, Mp 138 ^{0}C, **IR (KBr) υ**: 3030, 2850, 1728, 1616, 1460, 1402, 1331, 770, 735 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ**: 4.98 (s, 2H, CH_2), 6.73-7.82 (m, 14H, Ar-H) ppm. Anal. Calcd. For $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.92; N, 8.53; O, 9.74 (%). Found: C, 76.80; H, 4.93; N, 8.51; O, 9.76 (%).

1-[(Diethylamino)methyl]indoline-2, 3-dione

Red solid, Mp 176 ^{0}C, **IR (KBr) υ**: 2963, 2873, 1732, 1610, 1471, 1352, 766, 755 cm^{-1}. ^{1}H **NMR (300 MHz, $CDCl_3$) δ**: 1.55 (t, 6H, *J*=6.9 Hz, CH_3), 2.68(q, 4H, *J*=7.0 Hz, CH_2), 4.41 (s, 2H, CH_2), 7.8-7.3 (m, 4H, Ar-H)ppm. Anal. Calcd. For $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06; O, 13.78 (%). Found: C, 67.23; H, 6.92; N, 12.06; O, 13.79 (%).

References

Chen,G., Wang, Y, Hao, X., Mu, S., Qianyun, S., Simple isatin derivatives as free radical scavengers: Synthesis, biological evaluation and structure-activity relationship*, Chemistry Central Journal,* 37, 1-5, 2011.

Popp, F. D., Piccirilli, M. The reaction of N-acetylisatin with amines. *J. Heterocycl. Chem.* 8**,** 473–475, 1971.

Solomon,V. R., Hu, C., Lee, H., Hybrid pharmacophore design and synthesis of isatin–benzothiazole analogs for their anti-breast cancer activity, *Bioorganic & Medicinal Chemistry*, 17, 7585-7592, 2009.