A simple and eco-friendly synthesis of 3-indolyl-3-hydroxy oxindoles and 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols in aqueous media

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Abstract
A simple and convenient method for the synthesis of 3-indolyl-3-hydroxy oxindoles and 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols catalyzed by K_2CO_3 in aqueous media is described.

Keywords: Isatin, K_2CO_3, oxindole derivatives, indenoquinoxalines, water mediated reaction

Introduction

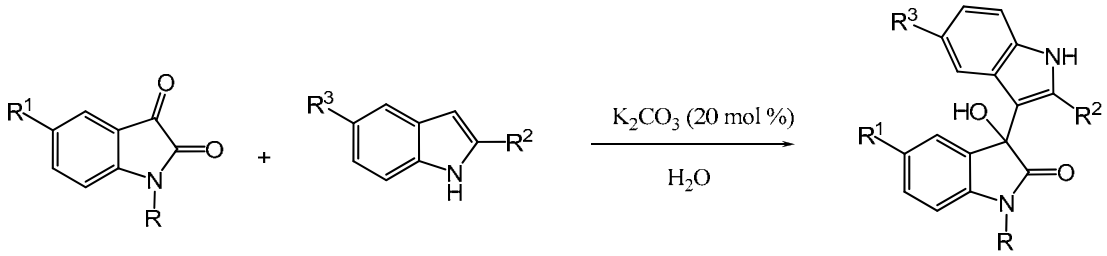
3-Substituted 3-hydroxyindolin-2-ones are important substrates for studies of biological activities as well as useful synthetic intermediates for drug candidates and alkaloids. The development of practical methods for their preparation is of interest. 3-Substituted 3-hydroxyoxindoles are encountered in a large variety of natural products with a wide spectrum of biological activities, such as convolutamydines,[1] donaxaridines,[2] maremycins,[3] dioxibrassinines,[4] celogentin K,[5] 3'-hydroxy glucoisatisin,[6] and TMC-95A.[7] 3-Alkenyl- and 3-aryl-substituted 3-hydroxyindoles,[8] and their derivatives [9] have been used in a number of recent pharmaceutical studies. The formation of quaternary carbon centers via addition of nucleophiles to ketone derivatives still constitutes a major challenge for synthetic chemistry. Recently, organic reactions in water have attracted great interest in organic synthesis because of its cost, safety and environmental concern.[10] Therefore, the development of an efficient synthetic methodology to form a carbon-carbon bond in water appears to be very important.

The synthesis of monosubstituted 3-indolyl-3-hydroxy oxindoles by Friedel-Crafts reaction of indoles with electron-deficient carbonyl compounds such as isatins will be one of the synthetically useful transformations.[11] Musabekova *et al.* have reported the condensation reaction of isatin with 2-methylindole in presence of acetic acid to afford 3-hydroxyindolines.[12a] Rama Rao *et al.*[12b] reported the synthesis of 3-indolyl-3-hydroxy oxindoles using β-cyclodextrin in good yields. The scope of the reaction was limited to isatin only and the reaction was carried

out at 50 ^{o}C. Thus, there is a need to develop a generally applicable, mild and environmentally benign practical methodology at ambient temperature.

Results and Discussion

As part of our current studies on the design of new routes for the preparation of biologically active heterocyclic compounds,[13] we herein disclose a simple and convenient method for the efficient synthesis of 3-indolyl-3-hydroxy oxindoles in water catalyzed by K_2CO_3 (Scheme 1).



Scheme 1

In order to study the scope and limitations of the reaction, various bases, including sodium acetate, potassium acetate, ammonium acetate, basic alumina, potassium carbonate and sodium carbonate and different solvent systems were investigated. The best overall yield (91%) was obtained with potassium carbonate in water. Optimal result was obtained using 20 mol % of K_2CO_3.

The experiment was conducted with isatin **1** and indole **2** in the presence of catalytic amount of K_2CO_3 (20 mol %) in water. The reaction proceeded spontaneously at ambient temperature and was completed within 1 h. The isolation of product was straightforward as the solid precipitated on completion of the reaction. The precipitated solid was filtered, dried and washed with 20 % ethyl acetate in petroleum ether to afford 3-indolyl-3-hydroxy oxindole **3**. The pure product **3** was isolated up to 91% yield without column chromatography. The result provided the incentive for further study of reactions with various other isatin derivatives and substituted indoles to furnish the corresponding 3-indolyl-3-hydroxy oxindoles.

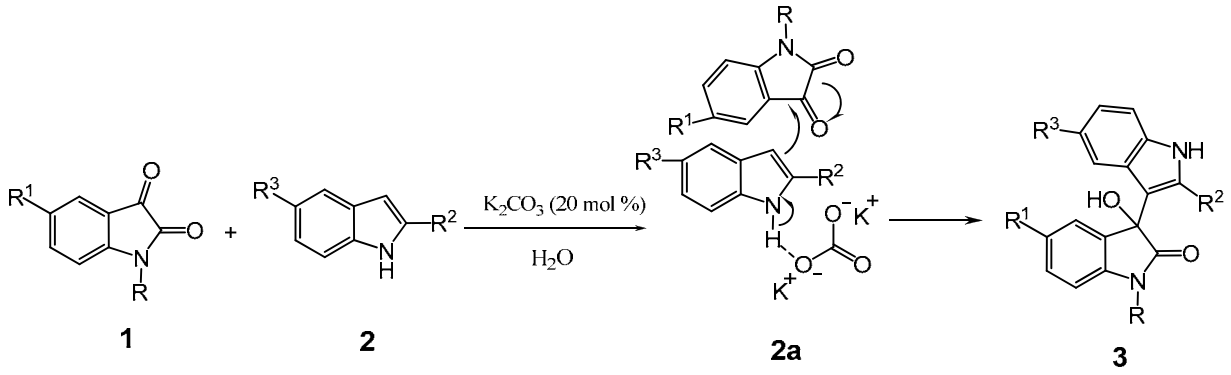
The structures of compounds **3a-n** were confirmed by IR, ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry and elemental analysis. The mass spectrum of **3c** displayed the molecular ion [M^{+}] peak at *m/z* 295. The ^{1}H NMR spectrum of **3c** exhibited broad singlets due to -OH and -NH protons at δ 6.32, 10.30 and 10.81 (D_2O exchangeable) respectively. Signals at δ 74.9 (quaternary carbon) and 178.4 (-C=O) in the ^{13}C spectrum confirmed the formation of the product.

Table 1. Synthesis of 3-indolyl-3-hydroxy oxindoles

R	R^1	R^2	R^3	Product (**3**)	Time(min.)	Yield(%)[a]
H	H	H	H	**3a**	60	91
H	H	methyl	H	**3b**	70	92
H	H	H	methoxy	**3c**	60	93
H	H	H	bromo	**3d**	120	85
Allyl	H	H	H	**3e**	90	90
Allyl	H	methyl	H	**3f**	80	92
Allyl	H	H	bromo	**3g**	140	83
Benzyl	H	H	H	**3h**	60	90
Benzyl	H	methyl	H	**3i**	70	92
Benzyl	H	H	methoxy	**3j**	60	91
Benzyl	H	H	bromo	**3k**	120	85
H	chloro	H	H	**3l**	90	89
H	chloro	methyl	H	**3m**	80	94
H	chloro	H	methoxy	**3n**	70	94

[a]Isolated yield confirmed through IR, NMR, mass spectrometry.

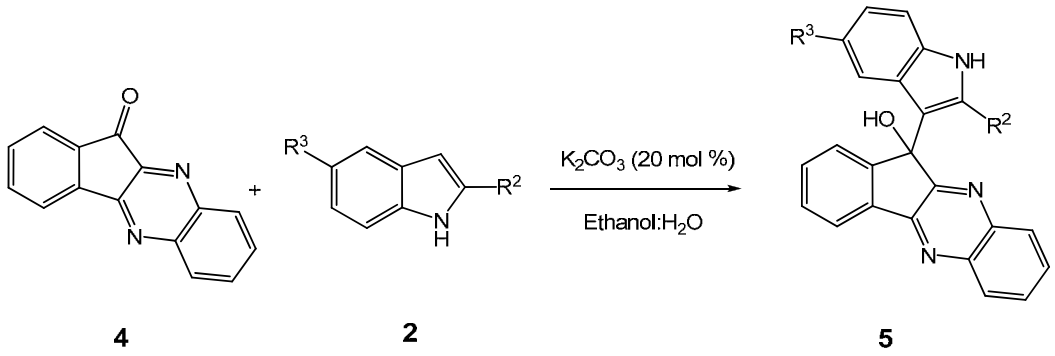
Based on the above results, we have proposed a plausible mechanism in Scheme 2. Initially isatin reacts with indole in presence of K_2CO_3 in water to give the transition state **2a** which leads to the formation of the product 3-indolyl-3-hydroxy oxindole **3**.



Scheme 2

Substituted quinoxaline derivatives are pharmacologically important compounds.[14a] Although rarely described in nature, various antibiotics such as echinomycin, levomycin and actinoleutin possessing a quinoxaline ring are known to inhibit the growth of gram-positive bacteria and are also active against various transplantable tumors.[14] Azizian *et al.*[15] have utilized the carbonyl group of the indenoquinoxaline in a reaction with 4-hydroxyproline for the

synthesis of pyrrolyl indenoquinoxaline derivatives. Azizian *et al.*[16] have synthesised new spiro indenoquinoxaline-pyrazolines from indenoquinoxaline and acetophenone. Recently, we reported the synthesis of spiroindenoquinoxaline by the three-component condensation of indenoquinoxaline, malononitrile and 1-phenyl-3-methyl pyrazolon-5-one.[13a] However, there have been no examples for the synthesis of 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols reported so far. Under similar conditions, we investigated the reaction of indenoquinoxaline **4** with indoles to synthesize the corresponding 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols **5**. The reaction was rather slow and the best overall yield (85%) was obtained when the reaction was carried out in water : ethanol (1:1) (Scheme 3).



Scheme 3

The structures of compounds **5a-c** were confirmed by spectroscopic and elemental data. The mass spectrum of **5a** displayed the molecular ion [M^+] peak at *m/z* 350. The ^{1}H NMR of **5a** displayed broad singlets at δ 6.61 and 11.03 due to –OH and –NH protons (D_2O exchangeable) respectively. A distinguishing signal at δ 77.1 (quaternary carbon) confirmed the formation of the product.

Table2. Synthesis of 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols

R^2	R^3	Product (**5**)	Time (min.)	Yield (%)[a]
H	H	**5a**	240	85
H	methoxy	**5b**	240	83
H	bromo	**5c**	280	78

[a]Isolated yield confirmed through IR, NMR, Mass spectrometry

Conclusions

In summary, we have developed a green approach to the synthesis of various 3-indolyl-3-hydroxy oxindoles and 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols. The present protocol

offers several advantages such as (a) clean and simple reaction procedure (b) isolation of products without employing purification methods like column chromatography (c) use of eco-friendly catalyst. Biological evaluation of these derivatives is underway.

Experimental Section

General Procedures. IR measurements were done as KBr pellets for solids using Perkin Elmer Spectrum RXI FT-IR. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 with JEOL 500MHz, Bruker 500MHz and Bruker 300MHz high resolution NMR spectrometer. DMSO-d_6 was used as the solvent for the NMR spectral measurements and spectra were recorded in ppm with TMS as internal standard. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). The mass spectra were analyzed by using a Electrospray Ionisation Method with Thermo Finnigan Mass spectrometer. Melting points were determined in capillary tubes and are uncorrected. Elemental analyses were recorded using a Thermo Finnigan FLASH EA 1112 CHN analyzer. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2mm thickness (Macherey-Nagel).

General procedure for the synthesis of 3-Indolyl-3-hydroxy oxindoles
To the reaction mixture containing isatin **1** (1 mmol) and indole **2** (1 mmol) in water (5 mL), catalytic amount of potassium carbonate (20 mol %) was added and stirred at room temperature for about 1 h. The precipitated solid was filtered, dried and washed with 20 % ethyl acetate in petroleum ether to afford the pure product in 91 % yield.

General procedure for the synthesis of 11-indolyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ols
To the reaction mixture containing indenoquinoxaline **4** (1 mmol) and indole **2** (1 mmol) in ethanol:water mixture (1:1), catalytic amount of potassium carbonate (20 mol %) was added and stirred at room temperature for about 4 h. The precipitated solid was filtered, dried and washed with 20 % ethyl acetate in petroleum ether to afford the pure product in 85 % yield.
3-Hydroxy-3-(1*H*-indol-3-yl)indolin-2-one (3a). White solid; mp: 294-296 ^{o} C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3401, 3054, 2926, 1706 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 6.34 (1 H, s, OH, D_2O exchangeable), 6.84-6.9 (3 H, m), 6.99 (1 H, t, *J* 7.65), 7.04 (1 H, d, *J* 2.3), 7.21 (2 H, t, *J* 8.4), 7.31 (2 H, t, *J* 9.1), 10.32 (1 H, s, NH), 10.96 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 75.4 (s), 110.1 (d), 112.0 (d), 115.9 (s), 118.9 (d), 120.8 (d), 121.5 (d), 122.2 (d), 124.0 (d), 125.2 (d), 125.4 (s), 129.5 (d), 133.9 (s), 137.3 (s), 142.1 (s), 178.9 (s); MS (EI): m/z = 265.08 [M^+]. Anal. Calcd for $C_{16}H_{12}N_2O_2$: C 72.72 H 4.58 N 10.60 . Found: C 72.68 H 4.53 N 10.55.
3-Hydroxy-3-(2-methyl-1*H*-indol-3-yl)indolin-2-one (3b). White solid; mp:176-178 ° C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3504, 3395, 3209, 1708, 1621, 1469, 755 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 2.36 (3 H, s), 6.24 (1 H, s, OH, D_2O exchangeable), 6.69 (1 H, t, *J*

7.65), 6.85-6.90 (4 H, m), 7.13-7.18 (3 H, m), 10.31 (1 H, s, NH), 10.84 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 13.7 (q), 76.3 (s), 109.9 (s), 110.1 (d), 110.7 (d), 118.6 (d), 119.3 (d), 119.7 (s), 120.3 (d), 122.2 (d), 125.4 (d), 127.1 (s), 129.5 (d), 134.6 (s), 135.3 (s), 142.0 (s), 179.1 (s); MS (EI): m/z = 279.11 [M^+]. Anal. Calcd for $C_{17}H_{14}N_2O_2$: C 73.37 H 5.07 N 10.07. Found: C 73.31 H 5.02 N 10.01.

3-Hydroxy-5-methoxy-3-(1*H*-indol-3-yl)indolin-2-one (3c). White solid; mp: 196-198 ^{o} C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3326, 1721, 1619, 1472, 1177, 760 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 3.58 (3 H, s), 6.32 (1 H, s, OH, D_2O exchangeable), 6.67 (1 H, d, *J* 8.4), 6.81 (1 H, s,), 6.88 (1 H, d, *J* 8.4), 6.93-6.97 (2 H, m), 7.19-7.23 (3 H, m), 10.30 (1 H, s, NH), 10.81 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 55.1 (q), 74.9 (s), 102.7 (d), 109.5 (d), 110.8 (d), 112.0 (d), 115.0 (s), 121.7 (d), 124.2 (d), 124.8 (d), 125.3 (s), 129.0 (d), 132.0 (s), 133.3 (s), 141.7 (s), 152.7 (s), 178.4 (s); MS (EI): m/z = 295 [M^+]; Anal. Calcd for $C_{17}H_{14}N_2O_3$: C 69.38 H 4.79 N 9.52. Found: C 69.16 H 4.75 N 9.47.

3-(5-Bromo-1*H*-indol-3-yl)-3-hydroxyindolin-2-one (3d). White solid; mp: 314-316 ^{o} C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3411, 3310, 2924, 1723 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 6.25 (1 H, s, OH, D_2O exchangeable), 7.02-7.07 (3 H, m), 7.36-7.4 (4 H, m), 7.83 (1 H, d, *J* 2.22), 10.16 (1 H, s, NH), 10.93 (1 H, s); ^{13}C nnmr (125 MHz, DMSO-d_6): 75.1 (s), 110.2 (d), 111.6 (s), 114.0 (d), 115.7 (s), 122.3 (d), 123.6 (d), 124.1 (d), 125.2 (d), 125.6 (d), 127.4 (s), 129.7 (d), 133.3 (s), 136.0 (s), 142.1 (s), 178.7 (s); MS (EI): m/z = 343 [M^+], 345 [M^{+2}]. Anal. Calcd for $C_{16}H_{11}BrN_2O_2$: C 56.00 H 3.23 N 8.16. Found: C 56.27 H 3.34 N 8.08.

1-Allyl-3-hydroxy-3-(1*H*-indol-3-yl)indolin-2-one (3e). White solid; mp: 148-150°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3297, 1698, 1610, 1463, 1369, 742 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 4.23-4.35 (2 H, m), 5.13-5.2 (2 H, m) 5.8-5.86 (1 H, m) 6.49 (1 H, s, OH, D_2O exchangeable), 6.84 (1 H, t, *J* 6.9), 6.98-7.03 (4 H, m), 7.28-7.33 (4 H, m), 11.00 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 41.9 (t), 75.1 (s), 109.6 (d), 112.0 (t), 115.6 (s), 117.5 (d), 119.0 (d), 120.9 (d), 121.6 (d), 122.8 (d), 124.1 (d), 125.0 (d), 125.4 (s), 127.3 (d), 129.5 (d), 132.4 (s), 133.2 (s), 142.7 (s), 176.9 (s); MS (EI): m/z = 305.02 [M^+]; Anal. Calcd for $C_{19}H_{16}N_2O_2$: C 74.98 H 5.30 N 9.20. Found: C 74.92 H 5.24 N 9.15.

1-Allyl-3-hydroxy-3-(2-methyl-1*H*-indol-3-yl)indolin-2-one (3f). White solid; mp: 164-166°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3433, 3320, 1705, 1617, 1371, 1176, 744 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 3.03 (3 H, s) 4.24-4.36 (2 H, m), 5.14-5.2 (2 H, m), 5.80-5.84 (1 H, m), 6.40 (1 H, s, OH, D_2O exchangeable), 6.7 (1 H, t, *J* 6.9), 6.83-6.9 (2 H, m), 6.98 (2 H, t, *J* 7.7), 7.17 (1 H, d, *J* 8.45), 7.24 (1 H, d, *J* 6.9), 7.27 (1 H, t, *J* 10.7), 10.89 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 13.4 (q), 41.9 (t), 76.0 (s), 109.6 (d), 110.4 (t), 115.4 (d), 116.4 (s), 118.2 (d), 120.3 (d), 122.9 (d), 125.2 (d), 127.0 (s), 129.5 (d), 130.4 (d), 133.9 (s), 134.2 (s), 135.3 (s), 142.7 (s), 177.1 (s); MS (EI): m/z = 319 [M^+]. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C 75.45 H 5.70 N 8.80. Found: C 75.40 H 5.63 N 8.83.

1-Allyl-3-hydroxy-3-(5-bromo-1*H*-indol-3-yl)indolin-2-one (3g). White solid; mp: 136-138°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3287, 1697, 1610, 1465, 1370, 1104, 754 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 4.18-4.33 (2 H, m), 5.13 (2 H, t, *J* 10.7), 5.77-5.83 (1 H, m),

6.54 (1 H, s, OH, D_2O exchangeable), 6.93 (1 H, s), 6.99 (1 H, d, *J* 7.65), 7.05 (1 H, t, *J* 8.4), 7.14 (1 H, d, *J* 6.9), 7.28-7.32 (3 H, m), 7.70 (1 H, s), 11.19 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 41.9 (t), 74.9 (s), 109.7 (d), 110.9 (t), 114.5 (d), 115.5 (s), 117.5 (d), 122.9 (d), 123.7 (d), 124.2 (d), 125.0 (d), 125.6 (s), 127.4 (s), 129.8 (d), 132.3 (d), 132.6 (s), 136.0 (s), 142.6 (s), 176.6 (s); MS (EI): m/z = 383 [M^+], 385 [M^{+2}]. Anal. Calcd for $C_{19}H_{15}BrN_2O_2$: C 59.55 H 3.95 N 7.31. Found: C 59.50 H 3.91 N 7.27.

1-Benzyl-3-hydroxy-3-(1*H*-indol-3-yl)indolin-2-one (3h). White solid; mp: 120-124°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3401, 1706, 1611, 1488, 1462, 1351, 1173, 746 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 4.89 (2 H, ABq, *J* 16.1), 6.57 (1 H, s, OH, D_2O exchangeable), 6.79 (1 H, t, *J* 7.65), 6.94-7.02 (3 H, m), 7.08 (1 H, s), 7.23-7.33 (9 H, m), 11.02 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 43.3 (t), 75.2 (s), 109.2 (d), 112.0 (d), 115.7 (s), 118.4 (d), 120.3 (d), 121.1 (d), 121.5 (d), 123.7 (d), 124.1 (d), 125.0 (d), 127.3 (s), 128.1 (d), 129.0 (d), 130.3 (s), 133.2 (d), 136.8 (s), 137.3 (s), 142.6 (s), 177.3 (s); MS (EI): m/z = 355 [M^+].Anal. Calcd for $C_{23}H_{18}N_2O_2$: C 77.95 H 5.12 N 7.90. Found: C 77.89 H 5.07 N 7.85.

1-Benzyl-3-hydroxy-3-(2-methyl-1*H*-indol-3-yl)indolin-2-one (3i). White solid; mp: 96-98°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3397, 2363, 1707, 1612, 1461, 1366, 1173, 747 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 2.35 (3 H, s), 4.89 (2 H, ABq, *J* 16.1) 6.47 (1 H, s, OH, D_2O exchangeable), 6.64 (1 H, t, *J* 7.65), 6.76 (1 H, d, *J* 8.4) 6.88 (1 H, t, *J* 7.6), 6.96 (2 H, t, *J* 8.4), 7.16-7.35 (8 H, m) 10.9 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 13.8 (q), 43.2 (t), 76.1 (s), 109.8 (d), 109.7 (d), 110.8 (s), 118.6 (d), 119.7 (d), 120.3 (d), 123.0 (s), 125.3 (d), 127.0 (d), 127.7 (d), 128.0 (d), 128.9 (d), 129.1 (d), 129.5 (d), 133.9 (s), 134.2 (s), 135.3 (s), 136.8 (s), 142.6 (s), 177.5 (s); MS (EI): m/z = 369 [M^+]. Anal. Calcd for $C_{24}H_{20}N_2O_2$: C 78.24 H 5.47 N 7.60. Found: C 78.20 H 5.42 N 7.53.

1-Benzyl-3-hydroxy-3-(5-methoxy-1*H*-indol-3-yl)indolin-2-one (3j). White solid; mp: 204-206°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3424, 1703, 1610, 1462, 1367, 1212, 1172, 1073, 802, 751 cm^{-1}; ^{1}H nmr (500 MHz, DMSO-d_6): δ 3.47 (3 H, s), 4.88 (2 H, ABq, *J* 16.0) 6.54 (1 H, s, OH, D_2O exchangeable), 6.67 (2 H, d, *J* 12.25) 6.94 (1 H, d, *J* 7.65), 7.01 (2 H, t, *J* 6.9), 7.2-7.3 (8 H, m), 10.86 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 43.1 (t), 55.4 (q), 75.2 (s), 102.6 (d), 109.6 (d), 111.7 (d), 112.6 (d), 115.1 (s), 123.1 (s), 124.8 (d), 125.1 (s), 125.7 (s), 127.8 (d), 127.9 (d), 129.0 (d), 129.6 (d), 132.4 (d), 133.1 (s), 136.8 (d), 142.6 (s), 153.2 (s), 177.3 (s); MS (EI): m/z = 385 [M^+]. Anal. Calcd for $C_{24}H_{20}N_2O_3$: C 74.98 H 5.24; N 7.29. Found: C 74.92 H 5.19 N 7.22.

1-Benzyl-3-hydroxy-3-(5-bromo-1*H*-indol-3-yl)indolin-2-one (3k). White solid; mp: 150-152°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3265, 1707, 1616, 1463, 1377, 744 cm^{-1}, ^{1}H nmr (500 MHz, DMSO-d_6): δ 4.84 (2 H, ABq, *J* 16.1), 6.63 (1 H, s, OH, D_2O exchangeable), 6.93 (2 H, d, *J* 8.4), 6.97 (1 H, d, *J* 2.25), 7.04 (1 H, t, *J* 7.65), 7.15 (1 H, d, *J* 6.9), 7.25-7.33 (7 H, m), 7.67 (1 H, d, *J* 2.3), 11.23 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 43.1 (t), 74.9 (s), 109.8 (d), 111.2 (s), 114.6 (d), 115.4 (s), 123.1 (s), 123.7 (d), 124.2 (d), 125.1 (d), 125.8 (d), 127.4 (s), 127.7 (d), 127.9 (d), 129.1 (d), 129.8 (d), 132.6 (s), 136.1 (s), 136.8 (d),

142.6 (s), 177.0 (s); MS (EI): m/z = 433 [M^+], 435 [M^{+2}]. Anal. Calcd for $C_{23}H_{17}BrN_2O_2$: C 63.75 H 3.95 N 6.47. Found: C 63.70; H 3.89 N 6.40.

5-Chloro-3-hydroxy-3-(1*H*-indol-3-yl)indolin-2-one (3l). White solid; mp: 206-208°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3422, 3357, 1731, 1620, 1476, 1178, 749 cm^{-1}; ^1H nmr (500 MHz, DMSO-d_6): δ 6.51 (1 H, s, OH, D_2O exchangeable), 6.9-6.91 (2 H, m), 7.01 (1 H, t, *J* 8.4), 7.08 (1 H, d, *J* 3.1), 7.18 (1 H, d, *J* 3.1), 7.28 (1 H, d, *J* 8.4), 7.33 (2 H, t, *J* 6.85), 10.47 (1 H, s, NH,), 11.01 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 75.5 (s), 111.7 (d), 112.1 (d), 115.1(s), 119.1 (d), 120.5 (d), 121.7 (d), 124.1 (d), 125.08 (d) 125.2 (s), 126.2 (s), 129.4 (d), 135.9 (s), 137.3 (s), 141.0 (s), 178.5 (s); MS (EI): m/z = 298.90 [M^+], 300.85 [M^{+2}]. Anal. Calcd for $C_{16}H_{11}ClN_2O_2$: C 64.33 H 3.71 N 9.38. Found: C 64.26 H 3.65 N 9.32.

5-Chloro-3-hydroxy-3-(2-methyl-1*H*-indol-3-yl)indolin-2-one (3m). White solid; mp: 174-176°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3341, 1711, 1617, 1465, 1164, 749 cm^{-1}; ^1H nmr (500 MHz, DMSO-d_6): δ 2.39 (3 H, s), 6.44 (1 H, s, OH, D_2O exchangeable), 6.74 (1 H, t, *J* 7), 6.88-6.93 (3 H, m), 7.11 (1 H, d, *J* 1.5), 7.18 (1 H, d, *J* 8.4), 7.26 (1 H, d, *J* 6.1), 10.5 (1 H, s, NH), 10.9 (1 H, s, NH). ^{13}C nmr (125 MHz, DMSO-d_6): 13.7 (q), 76.4 (s), 109.1 (s), 110.9 (d), 111.7 (d), 118.9 (d), 119.3 (s), 120.4 (d), 125.2 (d), 126.2 (s), 126.9 (s), 129.3 (d), 134.1 (s), 135.3 (s), 136.6 (d), 140.9 (s), 178.7 (s); MS (EI): m/z = 312.82 [M^+], 314 [M^{+2}]. Anal. Calcd for $C_{17}H_{13}ClN_2O_2$: C 65.29 H 4.19 N 8.96. Found: C 65.23 H 4.12 N 8.91.

5-Chloro-3-hydroxy-3-(5-methoxy-1*H*-indol-3-yl)indolin-2-one (3n). White solid; mp: 208-210°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3301, 1712, 1622, 1476, 1216, 1170 cm^{-1}; ^1H nmr (500 MHz, DMSO-d_6): δ 3.61 (3 H, s), 6.5 (1 H, s, OH, D_2O exchangeable), 6.7 (1 H, d, *J* 8.4), 6.84 (1 H, d, J 2.3), 6.9 (1 H, d, *J* 8.4), 7.01 (1 H, d, *J* 2.3), 7.21 (2 H, t, *J* 8.4), 7.29 (1 H, d, *J* 8.4), 10.47 (1 H, s, NH), 10.87 (1 H, s, NH); ^{13}C nmr (125 MHz, DMSO-d_6): 55.7 (t), 75.5 (s), 102.9 (s), 111.4 (d), 111.6 (d), 112.7 (d), 114.7 (d), 124.8 (d), 125.2 (d), 125.6 (s), 126.2 (d), 129.3 (d), 132.5 (d), 135.8 (s), 141.0 (s), 153.3 (s), 178.5 (s); MS (EI): m/z = 328.93 [M^+], 330.82 [M^{+2}]. Anal. Calcd for $C_{17}H_{13}ClN_2O_3$: C 62.11 H 3.99 N 8.52. Found: C 62.07 H 3.92 N 8.46.

11-(1*H*-Indol-3-yl)-11*H*-indeno[1,2-*b*]quinoxalin-11-ol (5a). Yellow solid; mp: 250-252°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3246, 1335, 1097, 759 cm^{-1}; ^1H nmr (DMSO-d_6, 500 MHz): δ 6.61 (1 H, s, OH, D_2O exchangeable), 6.64 (1 H, t, *J* 7.65), 6.77 (1 H, d, *J* 7.65), 6.90 (1 H, t, *J* 7.65), 7.27 (1 H, d, *J* 8.45), 7.34 (1 H, d, *J* 2.3), 7.51-7.55 (3 H, m), 7.68 (1 H, t, *J* 8.4), 7.75 (1 H, t, *J* 8.4), 7.93 (1 H, d, *J* 8.4), 8.10 (2 H, t, *J* 8.4), 11.03 (1 H, s, NH,); ^{13}C nmr (DMSO-d_6, 75 MHz): 77.1 (s), 111.5 (s), 116.4 (s), 118.4 (d), 119.2 (d), 120.8 (d), 121.6 (s), 123.6 (d), 124.6 (s), 125.6 (s), 128.7 (d), 129.1 (s), 129.7 (d), 129.8 (d), 132.3 (d), 135.3 (d), 136.7 (s), 141.1 (d), 141.9 (d), 152.1 (d), 153.2 (s), 164.5 (s); MS (EI): m/z = 350 [M^+]; Anal. Calcd for $C_{23}H_{15}N_3O$: C 79.07 H 4.33 N 12.03. Found: C 79.25 H 4.29 N 11.97.

11-(5-Methoxy-1*H*-indol-3-yl)-11*H*-indeno[1,2-*b*]quinoxalin-11-ol (5b). Yellow solid; mp: 214-216°C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3265, 1356, 1123, 819 cm^{-1}; ^1H nmr (DMSO-d_6, 500 MHz): δ 3.48 (3 H, s), 6.48 (1 H, s, OH, D_2O exchangeable), 6.59-6.61 (2 H, m), 7.16-7.19 (2 H, m), 7.57-7.61 (2 H, m), 7.62-7.65 (1 H, m), 7.71 (1 H, t, J 7.45), 7.76 (1

H, t, J 7.45), 7.96 (1 H, d, J 7.45), 8.1-8.14 (2 H, m), 10.85 (1 H, s); ^{13}C nmr (125 MHz, DMSO-d_6): 55.5 (q), 77.8 (s), 102.5 (d), 111.3 (d), 112.1 (s), 113.1 (s), 116.6 (s), 122.1 (s), 124.52 (s), 125.7 (d), 126.2 (s), 129.2 (s), 129.7 (d), 129.9 (d), 130.3 (d), 132.4 (d), 133.1 (d), 136.1 (s), 141.5 (d), 142.6 (d), 152.5 (d), 153.1 (d), 153.7 (s), 165.10 (s); MS (EI): m/z = 380 [M^+]; Anal. Calcd for $C_{24}H_{17}N_3O_2$: C 75.97 H 4.52 N 11.08. Found: C 76.15 H 4.39 N 10.97.

11-(5-Bromo-1*H*-indol-3-yl)-11*H*-indeno[1,2-*b*]quinoxalin-11-ol (5c). Yellow solid; mp: 264-266^{o}C; R_f 0.25 (50% AcOEt/Petroleum ether); IR (neat): 3289, 1334, 1077, 754 cm^{-1}; ^{1}H nmr (DMSO-d_6, 500 MHz): δ 6.65 (1 H, s, OH, D_2O exchangeable), 6.70 (1 H, t, *J* 7.65), 6.8 (1 H, d, *J* 7.65), 7.32 (1 H, d, *J* 8.45), 7.38 (1 H, d, *J* 2.3), 7.58-7.62 (3 H, m), 7.72 (1 H, t, *J* 8.4), 7.82 (1 H, t, *J* 8.4), 8.1 (1 H, d, *J* 8.4), 8.18 (2 H, t, *J* 8.4), 11.06 (1 H, s, NH,); ^{13}C nmr (DMSO-d_6, 75 MHz): 77.7 (s), 111.8 (s), 115.8 (s), 118.1 (d), 119.8 (d), 121.5 (d), 121.6 (s), 124.2 (s), 125.3 (s), 125.6 (d), 127.6 (d), 128.7 (d), 129.4 (s), 129.7 (s), 131.3 (d), 134.7 (d), 135.8 (s), 141.6 (d), 142.2 (d), 152.1 (d), 153.8 (s), 165.5 (s); MS (EI): m/z = 429 [M^+], 431 [M^{+2}]; Anal. Calcd for $C_{23}H_{14}N_3O$: C 64.50 H 3.29 N 9.81. Found: C 64.61 H 3.23 N 9.76.

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References

1. Kamano, Y.; Zhang, H. P.; Ichihara Y.; Kizu, H.; Komiyama, K.; Pettit,G. R. *Tetrahedron Lett*. **1995**, *36*, 2783 .
2. Rasmussen, H. B.; MacLeod, J. K. *J. Nat. Prod*. **1997**, *60*, 1152.
3. Balk-Bindseil, W.; Helmke, E.; Weyland, H.; Laatsch, H.; *Liebigs Ann*. **1995**, 1291.
4. Monde, K.; Sasaki, K.; Shirata, A.; Tagusuki, M. *Phytochemistry* **1991**, *30*, 2915
5. Suzuki, H,; Morita, H.; Shiro, M.; Kobayashi, M. *Tetrahedron* **2004**, *60*, 2489
6. Frechard, A.; Fabre, N.; Pean, C.; S. Montaut, S.; Fauvel, M. T.; Rollin, P.; Fouraste, I. *Tetrahedron Lett*. **2001**, *42*, 9015.
7. Kohno, J.; Koguchi, Y.; Nishio, M.; Nakao, K.; Kuroda, M.; Shimizu, R.; Ohnuki, T.; Komatsubara, S. *J. Org. Chem*. **2000**, *65*, 990.
8. (a) Hewawasam, P.; Meanwell, N. A.; Gribkoff, V. K.; Dworetzky, S. I.; Biossard, C. G. *Bioorg. Med. Chem. Lett*. **1997**, *7*, 1255. (b) Hewawasam, P.; Erway, M.; Moon, S. L.; Knippe, J.; Weiner, H.; Biossard, C. G.; Post-Munson, D. J.; Gao, Q.; Huang, S.; Gribkoff, V. K.; Meanwell, N. A. *J. Med. Chem.* **2002**, *45*, 1487.
9. (a) Natarajan, A.; Fam, Y. H.; Chen, H.; Guo, Y.; Iyasere, J.; Harbinski, F.; Christ, W. J.; Aktas, H.; Halperin, J. A. *J. Med. Chem.* **2004**, *47*, 1882. (b) Cliffe, I. A.; Lien, E. L.;

Mansell, H. L.; Steiner, K. E.; Todd, R. S.; White, A. C.; Black, R. M. *J. Med. Chem.* **1992**, *35*, 1169.

10. (a) Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2005**, *44*, 3275. (b) Li, C -J. *Chem. Rev.* **2005**, *105*, 3095. (c) Kavala, V.; Samal. A. K.; Patel, B. K. *ARKIVOC* **2005,** *(i),* 20. (d) Hui, A.; Xu, X.; Zha, Z.; Zhou, C.; Wang, Z. *ARKIVOC* **2004**, *(ix),* 52. (e) Gupta, M.; Wakhloo, B. P. *ARKIVOC* **2007**, *(i),* 94. (f) Tohma, H.; Maegawa, T.; Kita, Y. *ARKIVOC* **2003,** (*vi*) 62. (g) Wang, G. W.; Cheng, B. *ARKIVOC* **2004**, *(ix),* 4. (h) Jin, T. S.; Zhao. R. Q.; Li, T. S.; *ARKIVOC* **2006**, *(xi),* 176. (i) Amantini, D.; Fringuelli, F.; Piermatti, O.; Tortoioli, S.; Vaccaro, L.; *ARKIVOC* **2002**, *(xi),* 293. (j) Naik, S.; Bhattacharjya, G.; Kavala, V. R.; Patel, B. K. *ARKIVOC* **2004**, *(i),* 55.
11. Wang, S. Y.; Ji, S. J. *Tetrahedron* **2006**, *62*, 1527.
12. (a) Musabekova, Z. R.; Gurevich, P. A.; Zykova, T.V.: *Zhurnal Obshchei Khimii* **1994**, *64*, 254. (b) Kumar, V. P.; Reddy, V.P.; Sridhar, R.; Srinivas, B.; Narender, M.; Rama Rao, K. *J. Org. Chem*., **2008**, *73*, 1646.
13. (a) Shanthi, G.; Subbulakshmi, G.; Perumal, P. T. *Tetrahedron* **2007**, *63*, 2057. (b) Shanthi, G.; Perumal, P. T. *Tetrahedron Lett.* **2007**, *48*, 6785. (c) Savitha, G.; Niveditha, S. K.; Muralidharan, D.; Perumal, P. T. *Tetrahedron Lett.* **2007**, *48*, 2943. (d) Selvam, N. P.; Shanthi, G.; Perumal, P. T. *Can. J. Chem.* **2007**, *85*, 989.
14. (a) Azizian, J.; Mohammadizadeh, M. R.; Zomorodbakhsh, S.; Mohammadi, A. A.; Karimi, A. R. *ARKIVOC* **2007**, *(xv),* 24. (b) Islami, M. R.; Hassani, Z. *ARKIVOC* **2008**, *(xv),* 280. (c) Hasaninejad, A.; Zare, A.; Mohammadizadeh, M. R.; Shekouhya, M. *ARKIVOC* **2008**, *(xiii)*, 28. (d) Heravi, M. M.; Bakhtiari, K.; Tehrani, M. H.; Javadi, N. M.; Oskooie, H. A. *ARKIVOC* **2006**, *(xvi),* 16.
15. Azizian, J.; Ali, R. K.; Zahra, K.; Ali, A. M.; Mohammad, R. M. *Tetrahedron Lett.* **2005**, *46*, 6155.
16. Azizian, J.; Shaabanzadeh, M.; Hatamjafari, F.; Mohammadizadeh, M. R. *ARKIVOC* **2006,** (*xi*), 47.