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Synthesis of biologically important, fluorescence active 5-hydroxy benzo[*g*]indoles through four-component domino condensations and their fluorescence "Turn-off" sensing of Fe(III) ions

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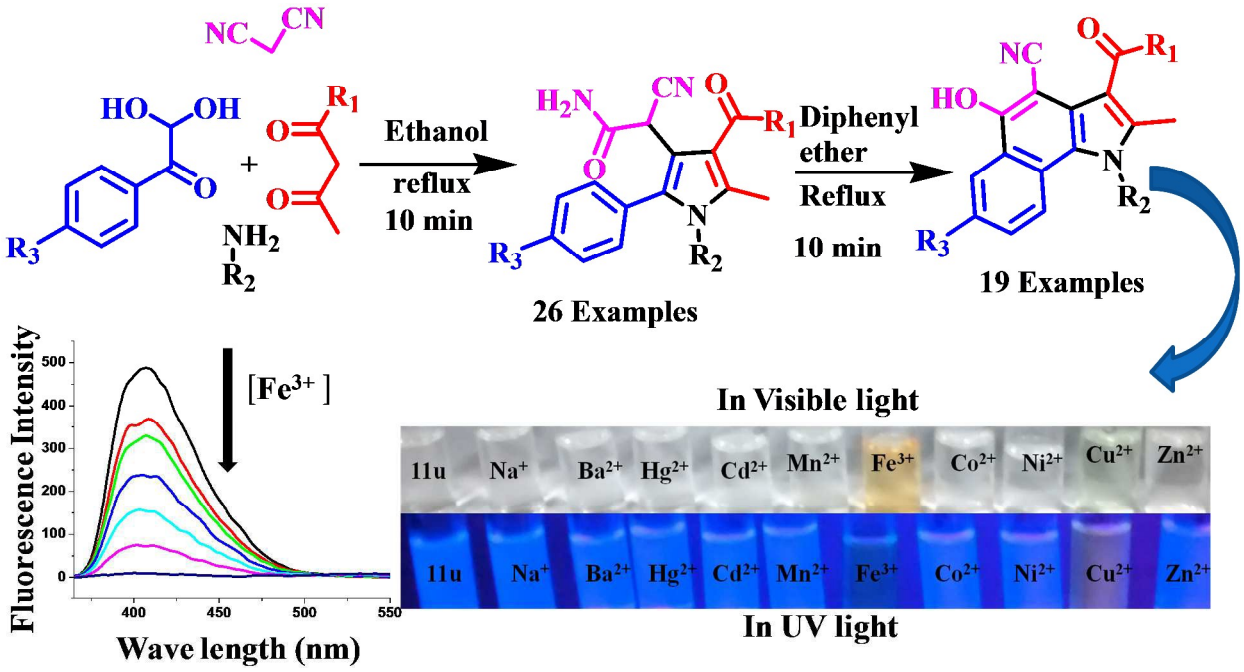


Abstract: Several highly substituted 2-pyrrolyl-2-cyanoacetamides were prepared through four-component domino condensation of various easily available 1,3-dicarbonyl compounds, amines, arylglyoxals and malononitrile. Subsequently these cyanoacetamide derivatives were converted to biologically important 5-hydroxy benzo[*g*]indoles through thermal cyclization under metal free condition. The synthesized 5-hydroxy benzo[*g*]indoles are fluorescence active

with good quantum yields (Φ_F = ~ 0.50). They also show excellent fluorescence "Turn-off" sensing of Fe^{3+} ions (detection limit = ~1.2 x 10^{-6} M). The interaction of 5-hydroxy benzo[*g*]indoles with Fe^{3+} ions can also be monitored through UV-Vis spectral change and naked-eye colour change in the presence and absence of UV radiation. The ^{1}H NMR titration unambiguously proves the formation of complex between 5-hydroxy benzo[*g*]indoles and Fe^{3+} ion through the coordination of –OH group with the metal. The Binding Constant of the complex (metal : ligand = 1:1) has been measured using Benesi-Hildebrand equation and found to be ~7.97 x 10^3 M^{-1}.

Introduction

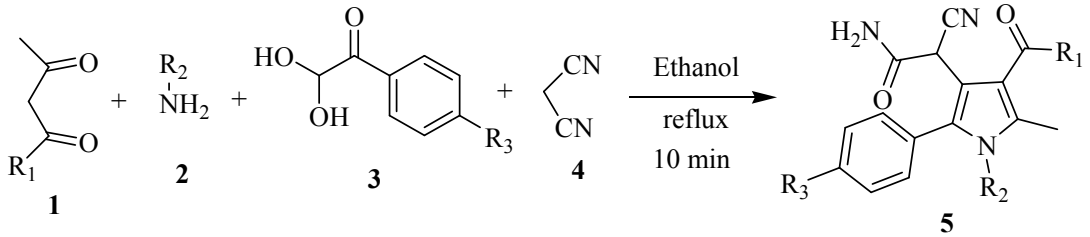
Nitrogen based heteocycles are important structural motifs for many natural products[1] and pharmaceuticals[2]. They are also useful building blocks for various biologically active molecules and functional materials.[3] As for example carbazoles, the fused indole based heterocycles, show important applications in materials science as organic light-emitting materials due to their wide band gap and high luminescent activity.[4] Fused indole based polycyclic frameworks with proper functionality can provide suitable ligand systems for diverse receptors.[5] This type of ligands with fluorescence activity can act as sensing agent for different metal ion through proper binding.[6] Form biological point of view sensing of metal ions shows significant demand in current research field.[7] More specifically detection of iron level have significant impact in biological research as iron regulates different biological processes such as electron transfer reactions, binding and transport of oxygen, and cell growth and differentiation.[8] To the best of our knowledge suitable benzo[*g*]indole based molecules with fluorescence sensing property have not been discovered as yet. So the development of new synthetic methodology for

construction of benzo[*g*]indole scaffolds is important in organic synthesis. Although there are number of methodologies for the synthesis of fused indole derivatives in literature[9], synthesis of substituted benzo[*g*]indoles are limited in number.[10] Therefore, a simple, efficient, metal-free, regiocontrolled, and diversified synthesis of substituted benzo[*g*]indole derivatives is still highly desirable. In continuation of our research interest in synthesis of various pyrrole and indole based heterocycles,[11] we wish to report herein an efficient synthetic strategy to access fluorescence active 5-hydroxy benzo[*g*]indoles from easily available starting materials. Since these compounds possess phenolic –OH group as potential binding site the effect of various metal ions on the fluorescence property has also been explored in solution phase. The selective ion sensitive fluorescence changes lead to the finding of fluorescence "Turn-off" sensor of Fe^{3+} ions.

Results and discussion

During our laboratory efforts on the development of multicomponent reactions for synthesis of biologically important heterocyclic compounds, we discovered that refluxing a mixture of acetylacetone **1** (R_1 = Me), aniline **2** (R_2 = Ph), phenyl glyoxal (**3**, R_3 = H) and malononitrile (**4**) in ethanol for 10 minutes produces a new compound 2-(4-acetyl-5-methyl-1,2-diphenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide **5a** in good yield, ~79% (Scheme 1). The reaction proceeds through a four-component domino condensation among the reactants. Interestingly, under the reaction conditions, one of the two cyano groups of malononitrile is selectively hydrolyzed to an amide group. Subsequently we examine the viability of this reaction in other solvents also such as acetonitrile, dioxane, DMF, THF and DCM for the formation of cyanoacetamide **5a**. However ethanol is found to be the best solvent in producing **5a** in highest yield (~79%) whereas acetonitrile produces **5a** only in moderate yield (~40%). The other

solvents including dioxane, DMF, THF and DCM produce very negligible amount of **5a**. By using the above methodology, a series of 2-pyrrolyl-2-cyanoacetamides **5a-z** were synthesized in ethanol medium by varying the 1,3-dicarbonyl compounds, amines as well as the arylglyoxal monohydrates (Scheme 1, Table 1). The results show that this four-component domino condensation reaction provides an elegant and rapid way to access various 2-pyrrolyl-2-cyanoacetamides in a single synthetic operation from simple building blocks.



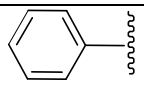
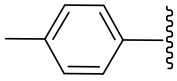
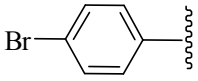
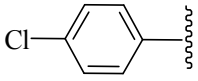
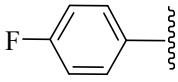
1 **2** **3** **4** **5**

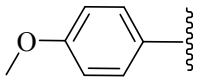
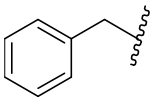
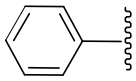
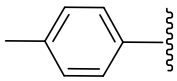
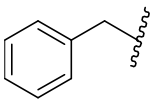
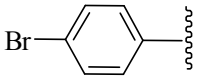
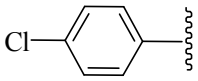
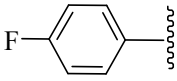
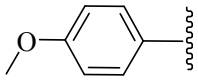
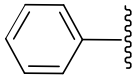
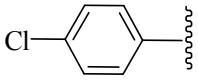
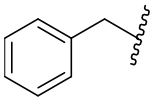
R_1 = Ph, Me, OEt
R_2 = Aryl, Benzyl, Alkyl
R_3 = H, Cl, OMe

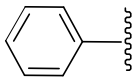
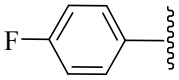
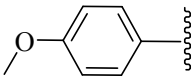
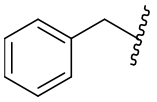
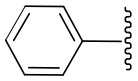
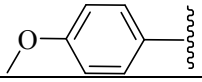
(71-82%)

Scheme 1 Synthesis of 2-pyrrolyl-2-cyanoacetamides **5** through domino condensation.

Table 1 Synthesis of 2-pyrrolyl-2-cyanoacetamides **5** in ethanol.

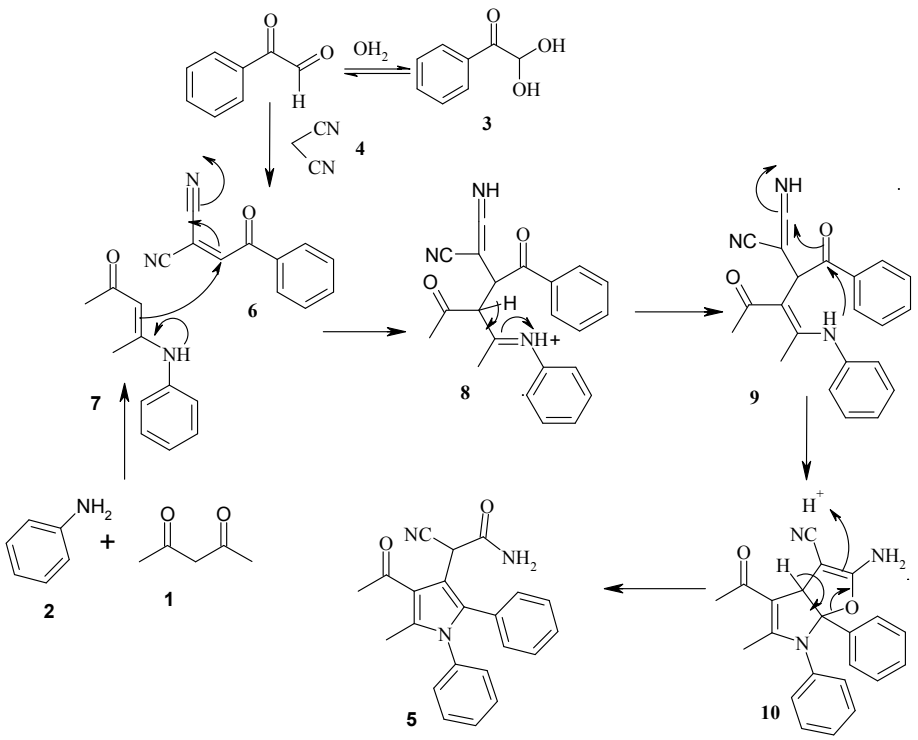
Entry	R_1	R_2	R_3	Product	Yield(%)[a]	M. p.
1	Me		H	**5a**	79	160-162
2	Me		H	**5b**	76	168-170
3	Me		H	**5c**	73	146-148
4	Me		H	**5d**	74	180-182
5	Me		H	**5e**	71	218-220

6	Me		H	**5f**	82	162-164
7	Me		H	**5g**	77	196-198
8	Me		H	**5h**	81	166-168
9	Me		Cl	**5i**	73	118-120
10	Me		Cl	**5j**	72	198-200
11	Me		Cl	**5k**	73	150-152
12	Me		Cl	**5l**	79	184-186
13	Me		Cl	**5m**	74	240-242
14	Me		Cl	**5n**	71	244-246
15	Me		Cl	**5o**	72	205-207
16	Me		Cl	**5p**	76	208-210
17	Me		OMe	**5q**	81	164-166
18	Me		OMe	**5r**	75	198-200
19	Me		OMe	**5s**	78	88-90
20	Me		OMe	**5t**	81	152-154

21	CO_2Et		H	**5u**	78	164-166
22	CO_2Et		H	**5v**	75	194-196
23	CO_2Et		H	**5w**	79	216-218
24	CO_2Et		H	**5x**	73	78-80
25	Ph		H	**5y**	impure[b]	--
26	Ph		H	**5z**	impure[b]	--

[a]Isolated Yield. [b]Compounds **5y** and **5z** were not possible to isolate because of closely spaced impurities. The crude masses were used for further reaction.

A proposed mechanism for the formation of compound **5** is shown in Scheme 2.[12] Initially, a Knoevenagel condensation between arylglyoxal monohydrate **3** and malononitrile produces α,β-unsaturated cyano intermediate **6**. Then enamine **7**, derived *in situ* from acetylacetone **1** and amines **2**, undergoes a Michael-type 1,4-addition with the intermediate **6** to produce imminium intermediate **8**, which subsequently tautomerizes to **9**. Then the intermediate **9** most probably produces a fused furano-pyrrole intermediate **10** through a tandem cyclization process. Finally, the 2-pyrrolyl-2-cyanoacetamides **5** are formed through a rearrangement of intermediate **10**. All the compounds **5a-x** were fully characterized by ^1H and ^{13}C NMR spectroscopy, and the X-ray crystal structure analysis of 2-[4-acetyl-2-(4-chlorophenyl)-5-methyl-p-tolyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (**5j**) further confirmed the structural assignment (Fig. 1).[13]



Scheme 2 Plausible mechanism for the formation of **5**.

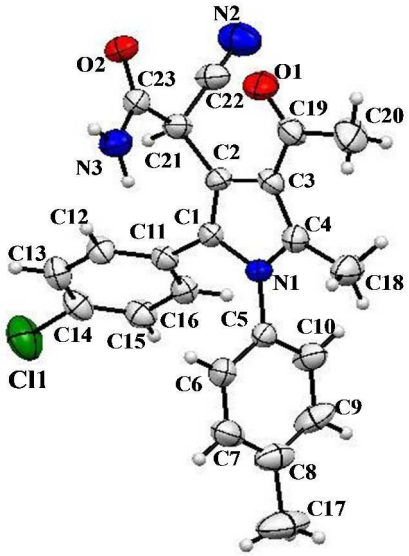
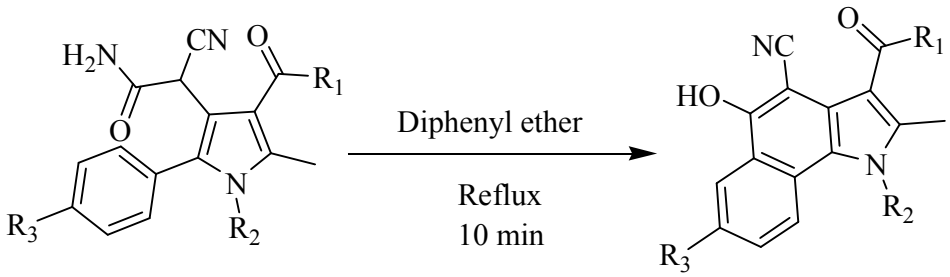


Fig. 1 ORTEP diagram of the X-ray crystal structure of compound **5j** with the atom numbering scheme; thermal ellipsoids are shown at the 50% probability.

After successful synthesis of 2-pyrrolyl-2-cyanoacetamides **5** we focussed our attention to explore the chemical property of this substance. Therefore, as a preliminary study, 2-(4′-acetyl-5-methyl-1,2-diphenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide **5a** was heated at reflux in diphenyl ether to examine the formation of any cyclic product. Interestingly, a cyclic product 3-acetyl-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile **11a** was formed in moderate yield (~61%) within 10 minutes through a thermal cyclization (Scheme 3). By employing this thermal method a series of biologically important 5-hydroxy benzo[*g*]indoles **11** were synthesized (Table 2). This novel thermal cyclization also provides an excellent opportunity to synthesise differently substituted 5-hydroxy benzo[*g*]indoles. Therefore we synthesized a series of cyanoacetamide derivatives **12** following a different reaction protocol[12] and converted them to the corresponding 5-hydroxy benzo[*g*]indoles **13** by refluxing in diphenyl ether for 10 minutes (Scheme 4, Table 3). All the compounds **11** and **13** were fully characterized by ^{1}H and ^{13}C NMR data. Further determination of X-ray crystal structure of 3-acetyl-5-hydroxy-1-cyclopropyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (**11h**) and 3-carboethoxy-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (**11u**) confirmed the product formation (Fig. 2).[13]



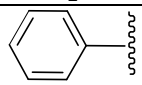
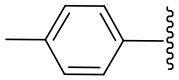
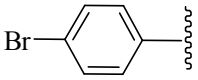
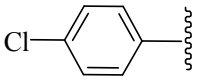
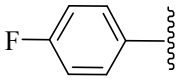
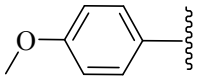
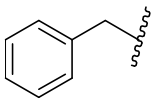
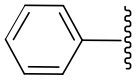
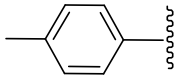
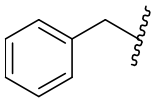
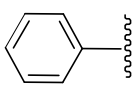
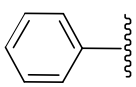
5

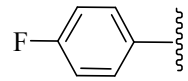
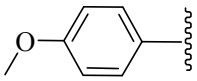
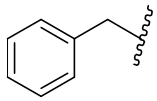
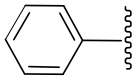
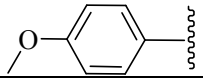
R_1 = Ph, Me, OEt
R_2 = Aryl, Benzyl, alkyl
R_3 = H, Cl, OMe

11

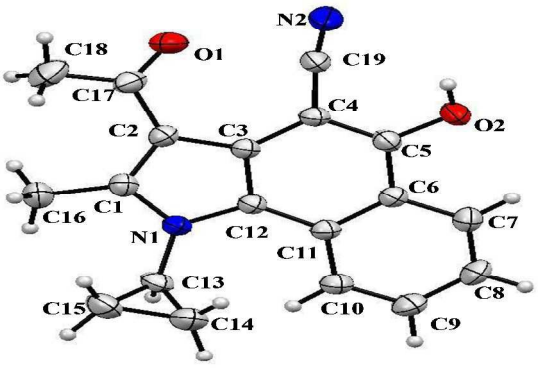
Scheme 3 Synthesis of benzo[*g*]jndole derivatives **11** through thermal cyclization.

Table 2 Synthesis of 5-hydroxy benzo[*g*]jndole derivatives **11**.

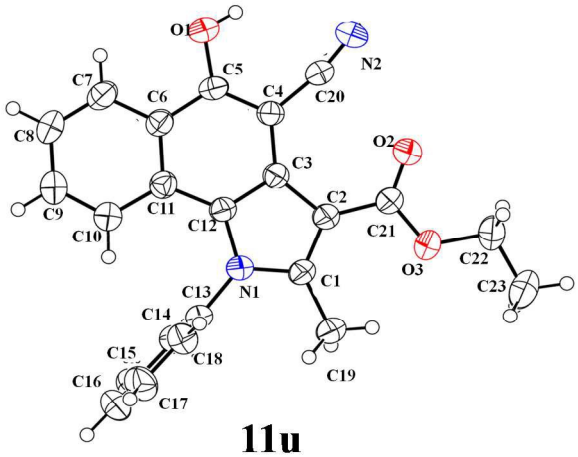
Entry	R_1	R_2	R_3	Starting	Product	Yield(%)[a]	M. p.
1	Me		H	**5a**	**11a**	61	228-230
2	Me		H	**5b**	**11b**	55	238-240
3	Me		H	**5c**	**11c**	52	212-214
4	Me		H	**5d**	**11d**	53	253-255
5	Me		H	**5e**	**11e**	51	247-249
6	Me		H	**5f**	**11f**	59	140-142
7	Me		H	**5g**	**11g**	60	202-204
8	Me		H	**5h**	**11h**	62	194-196
9	Me		Cl	**5i**	**11i**	53	270-272
10	Me		Cl	**5j**	**11j**	51	238-240
11	Me		Cl	**5k**	**11k**	56	178-180
12	Me		Cl	**5l**	**11l**	54	208-210
13	Me		OMe	**5q**	**11q**	52	188-190
14	CO_2Et		H	**5u**	**11u**	59	218-220

15	CO_2Et		H	**5v**	**11v**	56	246-248
16	CO_2Et		H	**5w**	**11w**	61	256-258
17	CO_2Et		H	**5x**	**11x**	55	192-194
18	Ph		H	**5y**	**11y**[b]	41	256-258
19	Ph		H	**5z**	**11z**[b]	43	248-250

[a]Isolated Yield. [b]For compound **11y** and **11z**, the yields are calculated with respect to starting material **1**

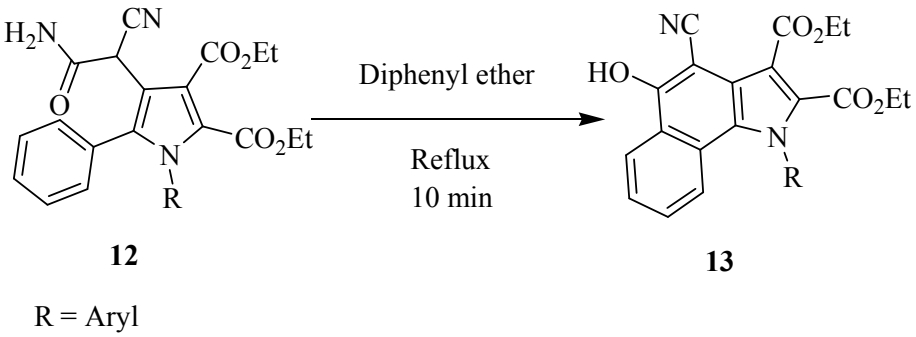


11h



11u

Fig. 2 ORTEP diagrams of the X-ray crystal structures of compounds **11h** and **11u** with the atom numbering scheme; thermal ellipsoids are shown at the 50% probability.

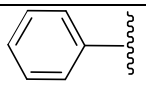
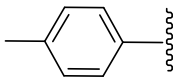
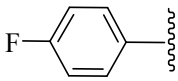
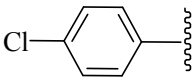
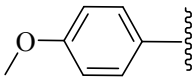
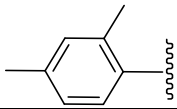


12 **13**

R = Aryl

Scheme 4 Synthesis of 2,3-dicarboethoxy-5-hydroxy-1-aryl-1*H*-benzo[*g*]indole-4-carbonitrile **13** through thermal cyclization.

Table 3 Synthesis of 2,3-dicarboethoxy-5-hydroxy-1-aryl-1*H*-benzo[*g*]indole-4-carbonitrile **13**.

Entry	R	Starting	Product	Yield(%)[a]	M. p.
1		**12a**	**13a**	64	180-182
2		**12b**	**13b**	52	168-170
3		**12c**	**13c**	61	238-240
4		**12d**	**13d**	60	194-196
5		**12e**	**13e**	63	180-182
6		**12f**	**13f**	55	176-178

[a] Isolated yield

After successful synthesis of various substituted 5-hydroxy benzo[*g*]indoles **11**/**13** we focussed our attention in exploring the photochemical property of this substance. Steady state absorption and emission spectra of some of the selective compounds **11u-w** have been taken in

different solvents with varying polarity such as CH_2Cl_2, CH_3CN and CH_3OH. The concentration of the compounds **11** was maintained at ~5 x 10^{-5} M. UV-Vis absorption spectrum shows structured band with peaks around 369 nm, 356 nm (Fig. 3a, Table 4). The emission spectrum shows a structure less band with maxima around 408 nm (Fig. 3b, Table 4). The shape and band position of the emission spectra are same regardless of excitation wavelength. Noticeably the molecules display significant Stokes shift (Table 4) which indicates that the structure of the emitting species and the ground state species are considerably different. The measured fluorescence quantum yields (Φ_F) of some of the representative compounds are found around ~0.5 which does not change much with the polarity of the solvent (Table 4).

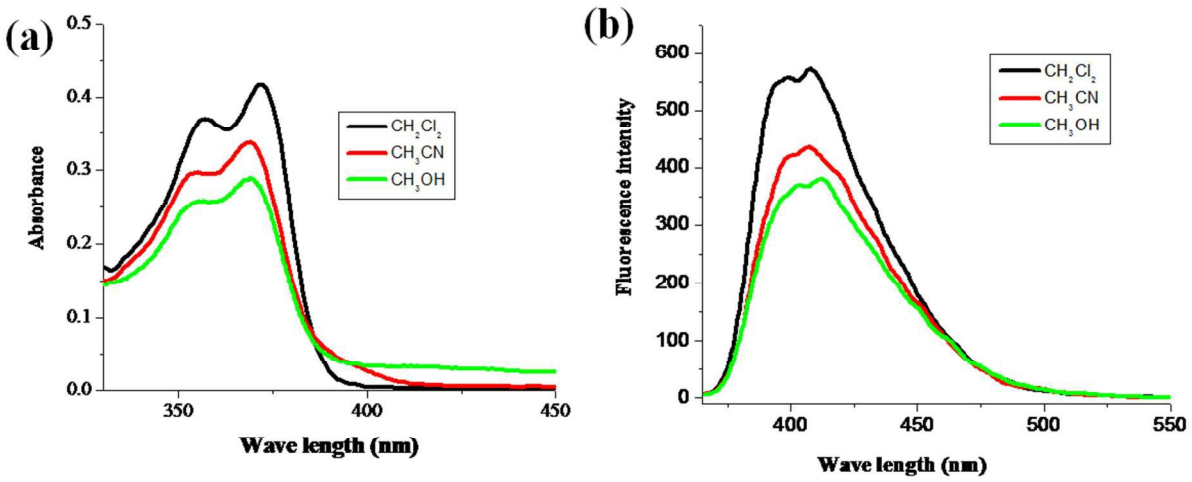


Fig. 3 (a) UV-Vis absorption spectra and (b) fluorescence emission spectra (λ in nm) of representative compound **11u** in different solvents ([**11u**] at ~5 x10^{-5} M conc.).

Table 4 Spectroscopic data of **11** in three solvents

Compounds	Solvents	λ_{abs}(nm)	λ_{em}(nm)	ε_{max}[a] (10^4 $cm^{-1}mol^{-1}$)	Φ_F[b]	Stokes shift[c] (10^4 cm^{-1})	ΔE (eV)[d]
11u	CH_2Cl_2	370	407	0.82	0.57	0.24	3.35
	CH_3CN	369	406	0.65	0.50	0.25	3.36
	CH_3OH	368	410	0.58	0.49	0.27	3.37
11v	CH_2Cl_2	371	404	0.94	0.51	0.22	3.34
	CH_3CN	368	408	0.68	0.49	0.26	3.37
	CH_3OH	369	407	0.59	0.48	0.25	3.36
11w	CH_2Cl_2	373	410	0.85	0.54	0.24	3.32
	CH_3CN	369	407	0.71	0.51	0.25	3.36
	CH_3OH	370	406	0.59	0.50	0.24	3.35

[a]ε_{max} is the extinction coefficient at λ_{max} of absorption.[b]Fluorescence quantum yields with reference to β-naphthol in methyl cyclohexane (Φ_F 0.53). [c]Stokes shift= ($1/\lambda_{abs}$-$1/\lambda_{em}$). [d]Determined from UV-Vis absorption maximum.

The photo-physical properties of the compound **11u** as a ligand have been explored in detail in presence of various metal ions Na^+, Ba^{2+}, Hg^{2+}, Cd^{2+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+} in acetonitrile. The complexation of ligand **11u** with Fe^{3+} ions in acetonitrile was accompanied by a change of colour of the solution from colourless to yellow which was easily observed by the naked-eye (Fig. 4A). On addition of Cu^{2+} ions a very light green colour was developed. The developing colour was more intense in case Fe^{3+} than in Cu^{2+} under similar conditions. The addition of 5 equiv. of other cations as their perchlorate salts resulted in no appreciable changes in colour under visible light (Fig. 4A). Interestingly, under UV light substantial fluorescence quenching is observed only in presence of Fe^{3+} ions (Fig. 4B). UV-Vis spectra of the ligand **11u**

in acetonitrile show no significant change on addition of metal perchlorate salts of Na^{+}, Ba^{2+}, Hg^{2+}, Cd^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+} (ESI, Fig. S5). However in presence of Fe^{3+} and Cu^{2+} the UV-Vis spectrum of **11u** shows appreciable change compared to that of free ligand hence indicating ligand-metal interaction. On gradual addition of Fe^{3+} salt an absorption band develops near 400 nm with simultaneous appearance of two isobestic points at 303 nm and 380 nm (Fig. 5). The emission spectra of ligand **11u** in acetonitrile shows no change in fluorescence intensity in presence of metal ions Na^{+}, Ba^{2+}, Hg^{2+}, Cd^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}(Fig. 6). On the other hand substantial quenching of ligand emission is observed in presence of Fe^{3+} and less extent of quenching is observed in presence of Cu^{2+} (Fig. 6). The result indicates that the extent of fluorescence quenching in Fe^{3+} is significantly higher compared to that of Cu^{2+} (Fig. 6). Further in fluorometric titration nearly complete fluorescence quenching is observed on addition of ~ 1.2 equivalent of Fe^{3+} ions (Fig. 7). The high selectivity of **11u** for Fe^{3+} may be due to the presence of more charges (3+) on iron ions compared to that of other metal ions (2+ or 1+), which probably causes strongest interaction with the phenolate anion. The detection limit of Fe^{3+} by probe **11u** has been estimated from fluorescence titration and found to be ~1.2 x 10^{-6} M (ESI, Fig. S6). From the same titration, the Binding Constant of probe **11u** with Fe^{3+} metal ion has been measured as ~7.97 x 10^{3} M^{-1} using Benesi-Hildebrand equation (see ESI, Fig. S7). The metal (Fe^{3+}) to ligand (**11u)** binding ratio has also been calculated by jobs plot method using UV titration and found to be in 1:1 ratio (see ESI, Fig. S8).

Subsequently the fluorescence "Turn-off" sensing of probe **11u** for Fe^{3+} ions has been examined in presence of other metal ions. When Fe^{3+} ions were added to various solutions of **11u** containing one of the different metal ions Co^{2+}, Ba^{2+}, Cd^{2+}, Cu^{2+}, Hg^{2+}, Mn^{2+}, Na^{+}, Ni^{2+}, Zn^{2+} in acetonitrile the binding of Fe^{3+} ions with **11u** was not significantly affected by the

presence of these other metal ions (Fig. 8). Therefore, the intensity of the fluorescence band of the complex [**11u**-Fe^{3+}] at 408 nm can be used to monitor the presence of Fe^{3+} ions alone as well as Fe^{3+} ions in presence of other metal ions.

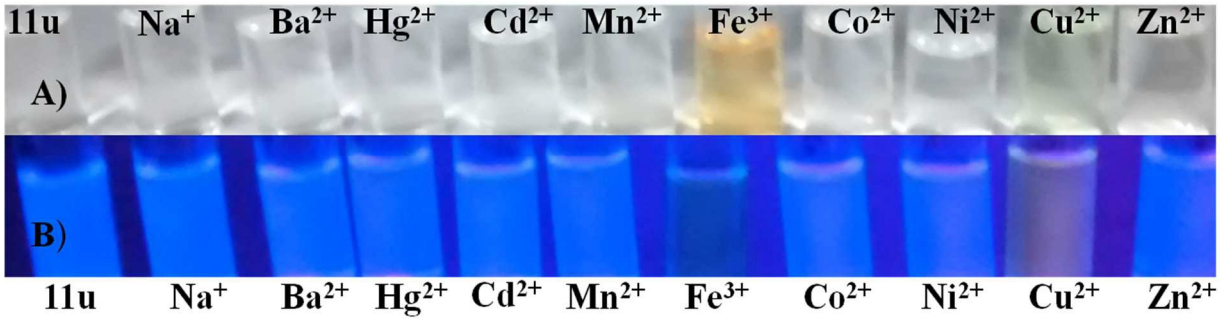


Fig. 4 Change in color of solution of **11u** in acetonitrile in presence of 5 equiv. of each metal ion (A) under visible light and (B) under UV light.

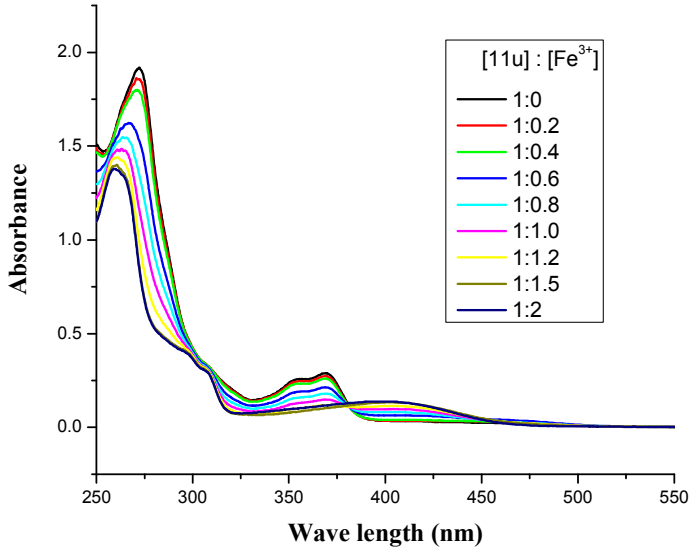


Fig. 5 Absorption spectra of **11u** ([**11u**] = ~5 x 10^{-5} M) on increasing concentration of Fe^{3+} ions in acetonitrile.

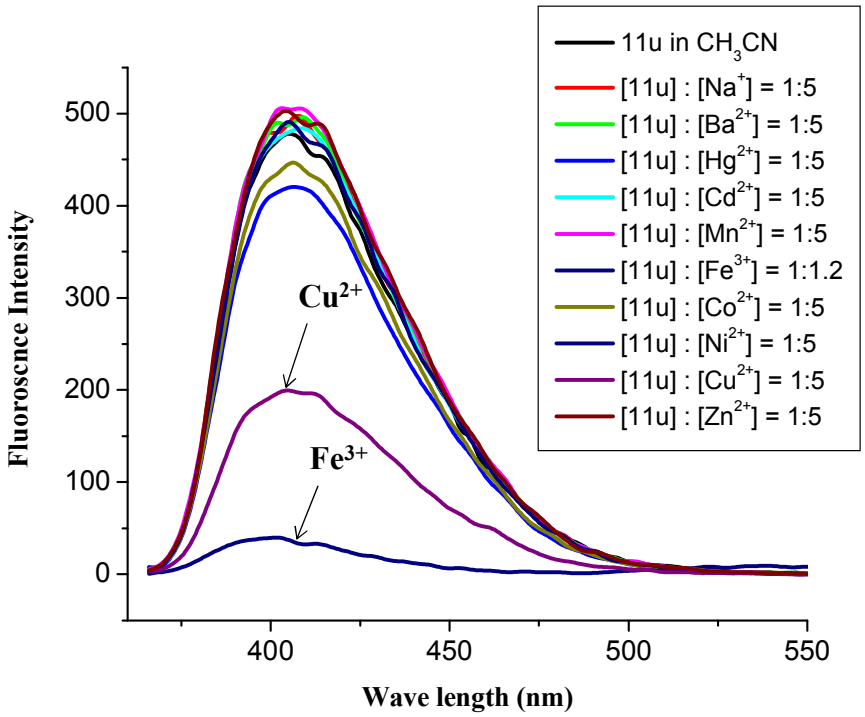


Fig. 6 Emission spectra of **11u** in acetonitrile in presence of various metal ions ([**11u**] at 5 x10^{-5} M conc.).

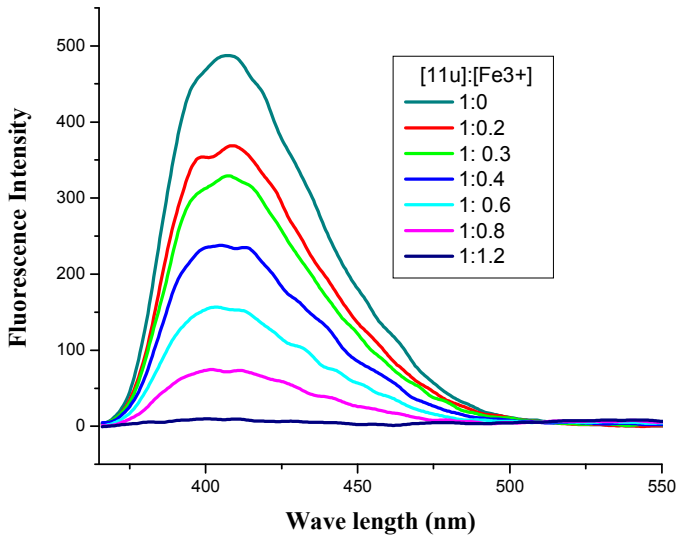


Fig. 7 Emission spectra of **11u** in acetonitrile on gradual addition of Fe $^{3+}$ ions ([**11u**] at 5 x10^{-5} M conc.).

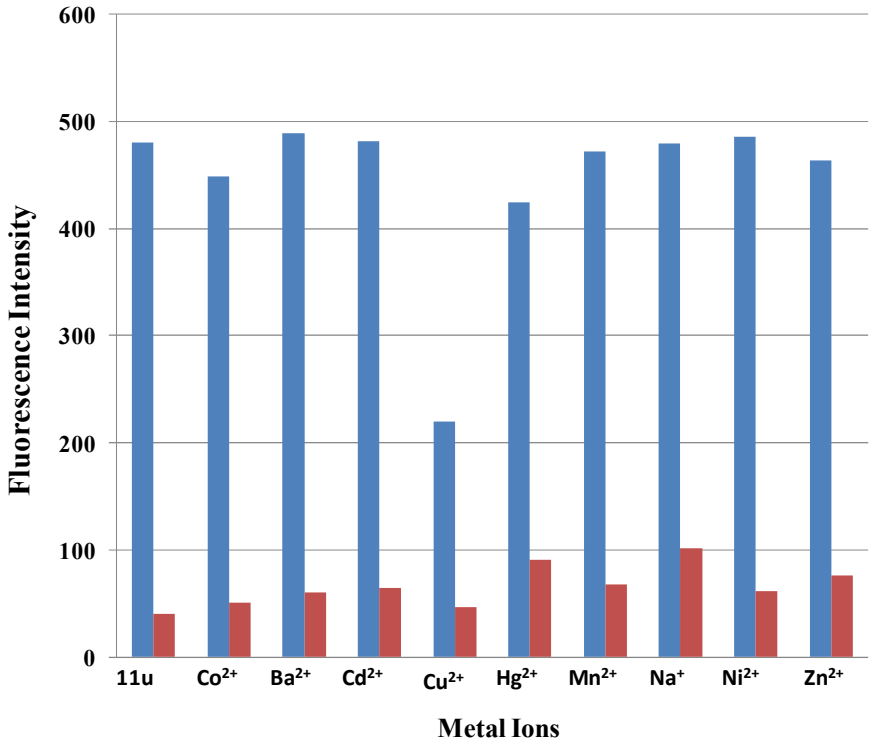


Fig. 8 The selectivity of **11u** ($5x10^{-5}$ M conc.) in the presence of various metal ions in acetonitrile. The blue bars represent the emission intensity of **11u** in the presence of other metal ions ($25x10^{-5}$ M conc.). The red bars represent the emission intensity that occurs upon the subsequent addition of Fe^{3+} ions ($5 x10^{-5}$ M conc.) to the above solution (λ_{em}=408 nm).

In order to get more insights about the nature of Fe^{3+} ligand interactions ^1H NMR titration was carried out. In this experiment the perchlorate salt of Fe^{3+} ions was gradually added to a DMSO-d_6 solution of **11u**. The results show that the intensity of the proton signal corresponding to 5-hydroxyl group (-OH) of **11u** at 10.86 ppm, which is the most probable binding site for Fe^{3+} ions, decreases significantly relative to that of other protons upon exposure to Fe^{3+} (Fig 9). This effect proves unambiguously the formation of complex between **11u** and Fe^{3+} ion. Additionally, a rapid broadening and finally disappearance of the proton signal at 10.86 ppm was observed

with gradual addition of Fe^{3+} ions which further confirms the fast exchange of hydroxyl (–OH) protons due to complexation with Fe^{3+} ion. Moreover during the NMR titration a light yellow colour was developed initially which gradually intensified with addition of more and more perchlorate salt of Fe^{3+} ions to the DMSO-d_6 solution of **11u** indicating complexation between Fe^{3+} ion and **11u**. The UV-Vis and NMR data clearly suggest that the phenolic hydroxyl groups (-OH) of **11u** are deprotonated due to complexation with Fe^{3+} ions which is probably responsible for strong fluorescence quenching.

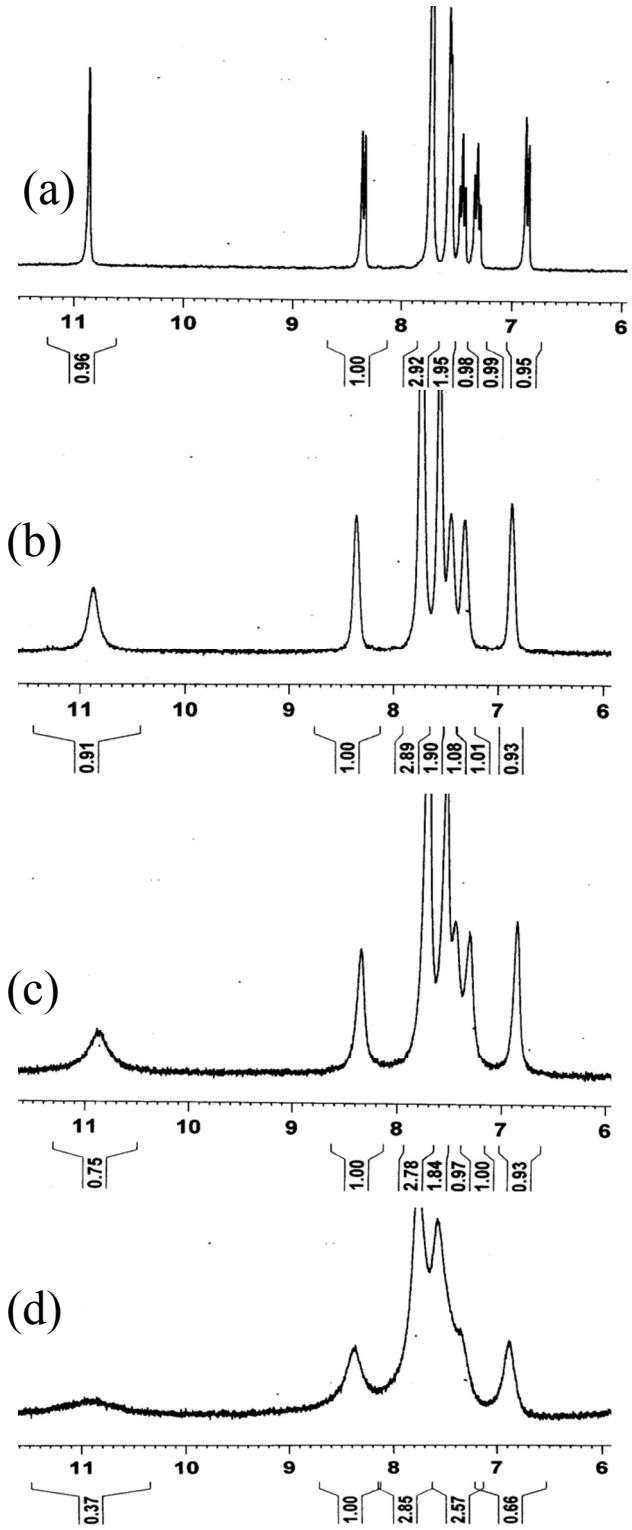


Fig. 9 Change in ^{1}H NMR spectra of **11u** upon addition of Fe^{3+} ions, (a)00 equiv., (b) 0.5 equiv., (c) 1.0 equiv., and (d) 2.0 equiv. in [d_6]-DMSO.

Conclusions

In conclusion, a convenient two steps methodology has been developed for the synthesis of biologically important 5-hydroxy benzo[*g*]indoles from various easily available 1,3-dicarbonyl compounds, amines, arylglyoxals and malononitrile under metal free conditions. The present synthetic protocol is quite atom economical in nature since only two molecules of water and one molecule of ammonia are released during the course of the reactions. The synthesised 5-hydroxy benzo[*g*]indoles show fluorescence activity with good quantum yields (Φ_F = ~ 0.50) and ability to act as fluorescence "Turn-off" sensor for Fe^{3+} ions. The interaction of 5-hydroxy benzo[*g*]indoles with Fe^{3+} ions can also be monitored through UV-Vis spectral change and naked-eye colour change in the presence and absence of UV radiation. Thus, the sensing of 5-hydroxy benzo[*g*]indoles for iron at the low level (detection limit = ~1.2 x 10^{-6} M) may have potential applications in current biomedical and pathological research works. It is also worth mentioning that phenolics containing iron-binding motifs have also been identified in many bio-active plants such as grapes, tea and traditional Chinese medicine plants.

EXPERIMENTAL SECTION

General: Arylglyoxals **3** were prepared from corresponding acetophenones by oxidation with selenium dioxide in dioxane.[14] Solvents were purchased from commercial suppliers and used after distillation. Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded with a Perkin-Elmer 782 spectrophotometer. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in DMSO-d_6 with a Bruker 300 MHz instrument. Elemental analyses (C, H and N) were performed by using a Perkin-Elmer 240C elemental analyzer. The

X-ray diffraction study of crystallized compounds was performed with Bruker APEX-II CCD system.

2-pyrrolyl-2-cyanoacetamides5a-z; General Procedure: A mixture of 1,3-dicarbonyl compound **1** (1.0 mmol) and amine **2** (1.0 mmol) in ethanol (20 mL) was heated for 2 minutes. Then to the above hot mixture, arylglyoxal **3** (1.0 mmol) and malononitrile **4** (1.3 mmol) were added and the reaction mixture was heated at reflux for 10 minutes. After completion of the reaction (monitored by TLC analysis), the solvent was removed under reduced pressure. The resulting solid residues were purified by column chromatography (EtOAc–hexane) on silica gel to get the light yellow solid products **5**.

2-(4-Acetyl-5-methyl-1,2-diphenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5a). Light yellow solid; yield: 282 mg (79%); m.p.: 160-162 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.40-7.30 (m, 4H), 7.28-7.21 (m, 5H), 7.12-7.07 (m, 3H), 4.73 (s, 1H), 2.47 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ =193.8, 166.6, 137.3, 136.7, 135.3, 131.1, 130.0, 129.5, 129.3, 129.0, 128.6, 128.5, 120.4, 117.9, 111.8, 37.2, 31.1, 14.2 ppm; IR (KBr): 2378, 1705, 1650 cm^{-1}; Anal calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76% Found C, 73.85; H, 5.30; N, 11.69%.

2-(4-Acetyl-5-methyl-2-phenyl-1-*p*-**tolyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5b)**. Light yellow solid; yield: 281 mg (76%); m.p.: 168-170 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.37 (s, 1H), 7.31-7.24 (m, 3H), 7.22-7.12 (m, 6H), 7.06 (s, 1H), 4.73 (s, 1H), 2.47 (s, 3H), 2.32 (s, 3H), 2.25 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ =193.8, 166.6, 138.4, 136.8, 135.4, 134.7, 131.1, 130.1, 129.9, 128.9, 128.6, 128.5, 120.3, 117.9, 111.7, 37.2, 31.3, 21.0, 14.3 ppm; IR (KBr): 2376, 1708, 1647 cm^{-1}; Anal calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31% Found C, 74.30; H, 5.62; N, 11.23%.

2-[4-Acetyl-5-methyl-1-(4-bromophenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5c). Light yellow solid; yield: 317 mg (73%); m.p.: 146-148 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.58 (d, J = 5.4 Hz, 2H), 7.38 (s, 1H), 7.27-7.17(m, 5H), 7.13-7.10 (m, 2H), 7.05 (s, 1H), 4.69 (s, 1H), 2.47 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ =193.8, 166.5, 136.7, 135.2, 132.5, 131.4, 131.1, 129.8, 128.8, 128.7, 122.2, 120.6, 117.8, 112.0, 107.8, 37.1, 31.1, 14.2 ppm; IR (KBr): 2370, 1701, 1649 cm^{-1}; Anal calcd for $C_{22}H_{18}BrN_3O_2$: C, 60.56; H, 4.16; N, 9.63% Found C, 60.48; H, 4.10; N, 9.55%.

2-[4-Acetyl-5-methyl-1-(4-chlorophenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5d). Light yellow solid; yield: 289 mg (74%); m.p.: 180-182 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.46-7.40 (m, 4H), 7.28-7.21 (m, 4H), 7.16-7.14(m, 2H), 7.08 (s, 1H), 4.74 (s, 1H), 2.50 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ =193.8, 166.6, 136.7, 136.3, 135.3, 133.7, 131.2, 129.8, 129.5, 128.7, 120.6, 117.9, 112.0, 37.2, 31.2, 14.2 ppm; IR (KBr): 2372, 1704, 1647 cm^{-1}; Anal calcd for $C_{22}H_{18}ClN_3O_2$: C, 67.43; H, 4.63; N, 10.72% Found C, 67.34; H, 4.55; N, 10.65%.

2-[4-Acetyl-5-methyl-1-(4-fluorophenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5e). Light yellow solid; yield: 266 mg (71%); m.p.: 218-220 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.40-7.36 (m, 2H), 7.28-7.20 (m, 6H), 7.15-7.13(m, 2H), 7.07 (s, 1H), 4.73 (s, 1H), 2.49 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ =193.8, 166.6, 163.5, 160.3, 136.9, 135.5, 133.7, 133.6, 131.5, 131.2, 129.9, 128.8, 128.6, 120.4, 117.9, 116.5, 116.2, 111.8, 37.2, 31.1, 14.2 ppm; IR (KBr): 2371, 1701, 1652 cm^{-1}; Anal calcd for $C_{22}H_{18}FN_3O_2$: C, 70.39; H, 4.83; N, 11.19% Found C, 70.31; H, 4.76; N, 11.12%.

2-[4-Acetyl-5-methyl-1-(4-methoxyphenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5f). Light yellow solid; yield: 317 mg (82%); m.p.: 162-164 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.33 (s, 1H), 7.27-7.21 (m, 4H), 7.15-7.12 (m, 3H), 7.05 (s, 1H), 6.92(d, J = 8.7 Hz, 2H), 4.72 (s, 1H), 3.73 (s, 3H), 2.48 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.8, 166.6, 159.3, 137.0, 135.5, 131.2, 130.3, 130.2, 128.6, 128.5, 120.2, 118.0, 116.5, 114.6, 114.6, 111.6, 55.7, 37.2, 31.1, 14.2 ppm; IR (KBr): 2370, 1706, 1656 cm^{-1}; Anal calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85% Found C, 71.22; H, 5.38; N, 10.77%.

2-(4-Acetyl-5-methyl-1-benzyl-2-phenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5g). Light yellow solid; yield: 285 mg (77%); m.p.: 196-198 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.32-7.31 (m, 3H), 7.23-7.11 (m, 6H), 6.88-6.84 (m, 3H), 4.97 (s, 2H), 4.70 (s, 1H), 2.35 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.5, 137.6, 136.1, 135.0, 131.2, 129.8, 129.5, 129.1, 127.7, 126.1, 120.5, 118.1, 111.7, 47.7, 37.0, 31.3, 13.4 ppm; IR (KBr): 2375, 1703, 1646 cm^{-1}; Anal calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31% Found C, 74.30; H, 5.64; N, 11.24%.

2-(4-Acetyl-5-methyl-1-cyclopropyl-2-phenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5h). Light yellow solid; yield: 260 mg (81%); m.p.: 166-168 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.49-7.44 (m, 3H), 7.41-7.35 (m, 2H), 7.25 (s, 1H), 6.84 (s, 1H), 4.68 (s, 1H), 3.26-3.20 (m, 1H), 2.67 (s, 3H), 2.42 (s, 3H), 0.77-0.69 (m, 2H), 0.44-0.43 (m, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.5, 166.7, 138.7, 135.6, 130.9, 130.7, 128.8, 128.7, 119.7, 118.0, 110.7, 37.0, 31.2, 27.5, 14.2, 9.6, 9.5 ppm; IR (KBr): 2371, 1701, 1652 cm^{-1}; Anal calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08% Found C, 69.92; H, 5.90; N, 13.01%.

2-[4-Acetyl-5-methyl-1-phenyl-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5i). Light yellow solid; yield: 285 mg (73%); m.p.: 118-120 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.39-7.34 (m, 4H), 7.33-7.31 (m, 4H), 7.16-7.13(m, 3H), 4.90 (s, 1H), 2.49 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.1, 166.5, 137.1, 136.9, 133.9, 133.6, 133.0, 129.6, 129.2, 129.1, 128.6, 120.5, 117.9, 112.2, 36.9, 31.2, 14.2 ppm; IR (KBr): 2372, 1704, 1647 cm^{-1}; Anal calcd for $C_{22}H_{18}ClN_3O_2$: C, 67.43; H, 4.63; N, 10.72% Found C, 67.35; H, 4.54; N, 10.63%.

2-[4-Acetyl-5-methyl-1-*p*-tolyl-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5j). Light yellow solid; yield: 292 mg (72%); m.p.: 198-200 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.39 (s, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.22-7.13 (m, 7H), 4.88 (s, 1H), 2.48 (s, 3H), 2.33 (s, 3H), 2.30 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.5, 138.7, 137.0, 134.5, 133.9, 133.6, 133.0, 130.1, 129.1, 128.9, 128.6, 120.4, 112.1, 107.8, 36.9, 31.2, 21.0, 14.2 ppm; IR (KBr): 2376, 1707, 1649 cm^{-1}; Anal calcd for $C_{23}H_{20}ClN_3O_2$: C, 68.06; H, 4.97; N, 10.35% Found , 67.98; H, 4.91; N, 10.27%.

2-[4-Acetyl-5-methyl-1-benzyl-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5k). Light yellow solid; yield: 296 mg (73%); m.p.: 150-152 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.47 (d, J = 8.4 Hz, 2H), 7.31-7.24 (m, 6H), 7.07 (s, 1H), 6.93 (d, J = 7.2 Hz, 2H), 5.06 (s, 2H), 4.97 (s, 1H), 2.46 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.2, 166.4, 137.5, 136.3, 134.4, 133.5, 133.1, 129.1, 128.8, 127.7, 126.0, 120.6, 118.0, 112.2, 47.7, 36.6, 31.4, 13.4 ppm; IR (KBr): 2375, 1704, 1653 cm^{-1}; Anal calcd for $C_{23}H_{20}ClN_3O_2$: C, 68.06; H, 4.97; N, 10.35% Found , 67.95; H, 4.90; N, 10.28%.

2-[4-Acetyl-5-methyl-1-cyclopropyl-2-(4'-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5l). Light yellow solid; yield: 281 mg (79%); m.p.: 184-186 ºC; ^{1}H NMR (300 MHz, DMSO-

d_6): δ = 7.31 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.07 (s 1H), 6.70 (s, 1H), 4.61 (s, 1H), 3.05-3.02 (m, 1H), 2.46 (s, 3H), 2.21 (s, 3H), 0.62-0.58 (m, 2H), 0.25-0.23 (m, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.7, 166.6, 139.0, 134.3, 133.5, 132.6, 129.9, 128.8, 119.8, 117.9, 111.2, 36.7, 31.4, 27.5, 14.5, 14.2, 9.6 ppm; IR (KBr): 2370, 1702, 1657 cm^{-1}; Anal calcd for $C_{19}H_{18}ClN_3O_2$: C, 64.13; H, 5.10; N, 11.81% Found , C, 64.07; H, 5.04; N, 11.74%.

2-[4-Acetyl-5-methyl-1-(4-bromophenyl)-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5m). Light yellow solid; yield: 347 mg (74%); m.p.: 240-242 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.64-7.61 (m, 2H), 7.41 (s, 1H), 7.37-7.35 (m, 2H), 7.30-7.22 (m, 2H), 7.17- 7.11 (m, 3H), 4.87 (s, 1H), 2.49 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.5, 136.9, 133.8, 133.0, 132.6, 131.4, 128.8, 122.4, 120.7, 117.8, 112.4, 36.9, 31.2, 14.2 ppm; IR (KBr): 2371, 1709, 1643 cm^{-1}; Anal calcd for $C_{22}H_{17}BrClN_3O_2$: C, 56.13; H, 3.64; N, 8.93% Found C, 56.06; H, 3.58; N, 8.85%.

2-[4-Acetyl-5-methyl-1,2-bis-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5n). Light yellow solid; yield: 302 mg (71%); m.p.: 244-246 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.47 (d, J = 8.7 Hz, 2H), 7.41 (s, 1H), 7.35-7.26 (m, 4H), 7.14-7.10 (m, 3H), 4.84 (s, 1H), 2.47 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.5, 137.0, 136.0, 133.9, 133.8, 133.0, 131.2, 131.1, 129.7, 128.8, 120.7, 117.8, 112.4, 36.9, 31.2, 14.2 ppm; IR (KBr): 2367, 1702, 1648 cm^{-1}; Anal calcd for $C_{22}H_{17}Cl_2N_3O_2$: C, 61.98; H, 4.02; N, 9.86% Found C, 61.91; H, 3.95; N, 9.80%.

2-[4-Acetyl-5-methyl-1-(4-fluorophenyl)-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5o). Light yellow solid; yield: 295 mg (72%); m.p.: 205-207 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.41-7.26 (m, 7H), 7.17-7.12 (m, 3H), 4.88 (s, 1H), 2.50 (s, 3H), 2.35

(s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.5, 137.1, 134.0, 133.7, 133.4, 133.0, 131.5, 128.9, 128.7, 120.5, 117.8, 116.7, 116.4, 112.2, 36.9, 31.2, 14.2 ppm; IR (KBr): 2371, 1709, 1643 cm^{-1}; Anal calcd for $C_{22}H_{17}ClFN_3O_2$: C, 64.47; H, 4.18; N, 10.25% Found C, 64.41; H, 4.12; N, 10.18%.

2-[4-Acetyl-5-methyl-1-(4-methoxyphenyl)-2-(4-chlorophenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5p). Light yellow solid; yield: 320 mg (76%); m.p.: 208-210 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.39-7.32 (m, 3H), 7.20-7.11 (m, 5H), 6.94 (d, J = 8.1 Hz, 2H), 4.88 (s, 1H), 3.74 (s, 3h), 2.48 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 194.0, 166.6, 159.4, 137.2, 134.1, 133.6, 133.0, 130.4, 130.3, 129.7, 129.2, 128.6, 120.3, 117.9, 114.7, 112.0, 55.7, 36.9, 31.2, 14.2 ppm; IR (KBr): 2375, 1702, 1640 cm^{-1}; Anal calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96% Found C, 65.41; H, 4.72; N, 9.89%.

2-[4-Acetyl-5-methyl-1-phenyl-2-(4-methoxyphenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5q). Light yellow solid; yield: 313 mg (81%); m.p.: 164-166 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.38-7.30 (m, 4H), 7.28-7.23 (m, 2H), 7.05-7.02 (m, 3H), 6.79(d, J = 8.7 Hz, 2H), 4.71 (s, 1H), 3.66 (s, 3H), 2.47 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.8, 166.7, 159.4, 137.4, 136.4, 135.2, 132.5, 129.5, 129.0, 122.0, 120.3, 118.0, 114.0, 111.6, 55.4, 37.2, 31.1, 14.2 ppm; IR (KBr): 2369, 1701, 1655 cm^{-1}; Anal calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85% Found C, 71.21; H, 5.36; N, 10.75%.

2-[4-Acetyl-5-methyl-1-(4-chlorophenyl)-2-(4-methoxyphenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5r). Light yellow solid; yield: 316 mg (75%); m.p.: 198-200 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.48-7.25 (m, 5H), 7.07-6.98 (m, 3H), 6.92-6.82 (m, 2H), 4.70 (s, 1H), 3.69 (s, 3H), 2.47 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.5, 166.4,

159.3, 136.2, 135.0, 133.4, 132.3, 130.9, 129.3, 128.6, 121.5, 120.2, 117.7, 113.9, 111.6, 55.2, 37.0, 30.9, 13.9 ppm; IR (KBr): 2371, 1704, 1643 cm^{-1}; Anal calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96% Found C, 65.40; H, 4.71; N, 9.87%.

2-[4-Acetyl-5-methyl-1-benzyl -2-(4-methoxyphenyl)-1*H*-3-pyrrolyl]-2-cyanoacetamide (5s). Light yellow solid; yield: 312 mg (78%); m.p.: 88-90 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.33-7.28 (m, 4H), 7.25-7.17 (m, 2H), 6.97-6.95 (m, 5H), 5.04 (s, 2H), 4.78 (s, 1H), 3.74 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.7, 166.4, 159.9, 137.5, 135.6, 134.7, 132.4, 128.9, 127.4, 125.9, 121.5, 120.2, 117.9, 114.3, 111.5, 55.3, 36.8, 31.1, 13.2 ppm; IR (KBr): 2374, 1705, 1657 cm^{-1}; Anal calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47% Found , C, 71.72; H, 5.71; N, 10.40%.

2-[4-Acetyl-5-methyl-1-cyclopropyl-2-(4-methoxyphenyl)-1*H*-3-pyrrolyl]-2-cyano acetamide (5t). Light yellow solid; yield: 284 mg (81%); m.p.: 152-154 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.68 (d, J = 8.1 Hz, 3H), 7.01 (d, J = 7.8 Hz, 2H), 6.82 (s, 1H), 4.65 (s, 1H), 3.78 (s, 3H), 3.20-3.10 (m, 1H), 2.65 (s, 3H), 2.40 (s, 3H), 0.92-0.90 (m, 2H), 0.46-0.44 (m, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 193.5, 166.7, 159.5, 138.4, 135.6, 132.1, 123.0, 119.6, 118.1, 114.2, 110.6, 55.5, 37.0, 31.2, 27.4, 14.1, 9.4 ppm; IR (KBr): 2368, 1704, 1652 cm^{-1}; Anal calcd for $C_{20}H_{21}N_3O_3$: C, 68.36; H, 6.02; N, 11.96% Found , C, 68.28; H, 5.94; N, 11.90%.

2-(4-Carboethoxy-5-methyl-1,2-diphenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5u). Light yellow solid; yield: 302 mg (78%); m.p.: 164-166 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.45 (s, 1H), 7.30-7.27 (bs, 4H), 7.18-7.17 (m, 4H), 7.09-7.05 (m, 3H), 4.57 (s, 1H), 4.18-4.11 (m, 2H), 2.41 (s, 3H), 1.25-1.20 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 161.0, 158.7, 132.3, 131.5, 129.3, 125.3, 124.2, 123.7, 123.2, 122.8, 122.5, 112.4, 105.8, 104.3, 53.9, 31.7, 9.2,

7.8 ppm; IR (KBr): 2251, 1701, 1690 cm^{-1}; Anal calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85% Found C, 71.22; H, 5.39; N, 10.78%.

2-[4-Carboethoxy-5-methyl-1-(4-fluorophenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5v). Light yellow solid; yield: 303 mg (75%); m.p.: 194-196 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.55 (s, 1H), 7.46 (s, 1H), 7.35-7.21 (m, 6H), 7.16-7.11 (m, 3H), 4.65 (s, 1H), 4.27-4.20 (m, 2H), 2.32 (s, 3H), 1.39-1.28 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 166.4, 164.0, 159.9, 138.0, 134.8, 133.3, 130.9, 130.7, 129.5, 128.4, 128.3, 117.8, 116.1, 115.8, 111.2, 109.8, 59.4, 37.1, 14.1, 12.4 ppm; IR (KBr): 2250, 1702, 1688 cm^{-1}; Anal calcd for $C_{23}H_{20}FN_3O_3$: C, 68.14; H, 4.97; N, 10.36% Found C, 68.07; H, 4.91; N, 10.30%.

2-[4-Carboethoxy-5-methyl-1-(4-methoxyphenyl)-2-phenyl-1*H*-3-pyrrolyl]-2-cyanoacetamide (5w). Light yellow solid; yield: 329 mg (79%); m.p.: 216-218 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.51 (s, 1H), 7.28-7.27 (m, 4H), 7.16-7.14 (m, 4H), 6.92-6.90 (m, 2H), 4.62 (s, 1H), 4.26-4.19 (m, 2H), 3.72 (s, 3H), 2.30 (s, 3H), 1.33-1.28 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 166.4, 164.1, 158.9, 138.1, 134.9, 130.7, 129.8, 129.5, 128.3, 117.8, 114.1, 110.9, 109.5, 59.3, 55.3, 37.1, 14.1, 12.5 ppm; IR (KBr): 2253, 1703, 1693 cm^{-1}; Anal calcd for $C_{24}H_{23}N_3O_4$: C, 69.05; H, 5.55; N, 10.07% Found C, 68.98; H, 5.49; N, 10.01%.

2-(4-Carboethoxy-5-methyl-1-benzyl-2-phenyl-1*H*-3-pyrrolyl)-2-cyanoacetamide (5x). Light yellow solid; yield: 293 mg (73%); m.p.: 78-80 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.51-7.43 (m, 4H), 7.33-7.23 (m, 5H), 7.05 (s, 1H), 7.95 (d, J = 7.2 Hz, 2H), 5.04 (s, 2H), 4.64 (s, 1H), 4.23-4.17 (m, 2H), 2.40 (s, 3H), 1.32-1.24 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 166.2, 164.1, 137.1, 134.3, 130.8, 129.5, 129.1, 128.8, 128.7, 127.2, 125.7, 117.9, 111.2, 109.7,

59.2, 47.3, 36.9, 14.0, 11.5 ppm; IR (KBr): 2248, 1701, 1688cm^{-1}; Anal calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47% Found C, 71.73; H, 5.72; N, 10.41%.

Benzo[*g*]jndole 11; General Procedure: The 2-pyrrolyl-2-cyanoacetamide **5** (0.5 mmol) in diphenyl ether (10 mL) was heated at reflux for 10 minutes. Upon completion of the reaction, the crude mass was purified by chromatography on a silica gel column (EtOAc/hexane, 1:1) to get pure compound **11** as brown solid.

3-Acetyl-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11a). Brown solid; yield: 103 mg (61%); m.p.: 228-230 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.91 (s, 1H), 8.35 (d, J = 8.4 Hz, 1H), 7.73-7.20 (m, 3H), 7.53 (t, J = 3.6 Hz, 2H), 7.44 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 8.7Hz, 1H), 2.62 (s, 3H), 2.28 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.9, 156.4, 140.5, 138.9, 131.0, 130.5, 129.2, 125.4, 124.8, 124.7, 123.2, 120.5, 119.4, 118.0, 117.1, 88.6, 32.6, 12.9 ppm; IR (KBr): 3330, 2214, 1647 cm^{-1}; Anal calcd for $C_{22}H_{16}N_2O_2$: C, 77.63; H, 4.74; N, 8.23% Found, C, 77.56; H, 4.67; N, 8.16%.

3-Acetyl-5-hydroxy-1-*p*-tolyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11b). Brown solid; yield: 97 mg (55%); m.p.: 238-240 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.89 (s, 1H), 8.35 (d, J = 8.1 Hz, 1H), 7.53-7.50 (m, 1H), 7.46-7.30 (m, 3H), 7.53 (t, J = 3.6 Hz, 2H), 6.96 (d, J = 8,4 Hz, 1H), 2.61 (s, 3H), 2.50 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.9, 156.4, 140.7, 140.1, 136.2, 131.4, 129.3, 128.9, 125.5, 124.7, 124.5, 123.2, 120.6, 119.3, 117.9, 117.1, 88.6, 32.6, 21.3, 12.9 ppm; IR (KBr): 3334, 2216, 1648 cm^{-1}; Anal calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90 Found , C, 77.88; H, 5.05; N, 7.83.

3-Acetyl-5-hydroxy-1-(4-bromophenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11c). Brown solid; yield: 109 mg (52%); m.p.: 212-214 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.96

(s, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.94-7.90 (m, 2H), 7.56-7.42 (m, 3H), 7.30-7.14 (m, 1H), 6.95 (d, *J* = 6.9 Hz, 1H), 2.61 (s, 3H), 2.27 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 196.0, 156.5, 140.5, 138.2, 134.0, 131.5, 130.4, 129.5, 125.3, 124.9, 123.7, 123.2, 120.5, 119.5, 119.0, 118.3, 117.0, 88.5, 32.7, 12.8 ppm; IR (KBr): 3335, 2216, 1645 cm^{-1}; Anal calcd for $C_{22}H_{15}BrN_2O_2$: C, 63.02; H, 3.61; N, 6.68% Found , C, 62.94; H, 3.53; N, 6.60%.

3-Acetyl-5-hydroxy-1-(4-chlorophenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11d). Brown solid; yield: 100 mg (53%); m.p.: 253-255 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.89 (s, 1H), 8.26 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H),7.40-7.17 (m, 2H), 6.85 (d, *J* = 8.1 Hz, 1H), 2.41 (s, 3H), 2.18 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 196.0, 156.5, 140.5, 137.8, 135.1, 131.2, 131.0, 129.5, 125.3, 124.8, 124.7, 124.3, 123.2, 120.4, 117.0, 88.6, 32.6, 12.8 ppm; IR (KBr): 3330, 2219, 1653 cm^{-1}; Anal calcd for $C_{22}H_{15}ClN_2O_2$: C, 70.50; H, 4.03; N, 7.47% Found , C, 70.44; H, 3.96; N, 7.41%.

3-Acetyl-5-hydroxy-1-(4-fluorophenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11e). Brown solid; yield: 91 mg (51%); m.p.: 247-249 ºC. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.82 (s, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 7.56-7.43 (m , 4H), 7.38-7.26 (m, 2H), 6.81 (d, *J* = 8.4 Hz, 1H), 2.51 (s, 3H), 2.17 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 196.0, 156.5, 140.7, 135.1, 131.6, 131.5, 129.5, 124.8, 124.7, 124.4, 123.2, 120.4, 119.4, 118.1, 117.8, 117.0, 88.5, 32.6, 12.8 ppm; IR (KBr): 3326, 2224, 1648 cm^{-1}; Anal calcd for $C_{22}H_{15}FN_2O_2$: C, 73.73; H, 4.22; N, 7.82% Found , C, 73.65; H, 4.16; N, 7.74%.

3-Acetyl-5-hydroxy-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11f). Brown solid; yield: 109 mg (59%); m.p.: 140-142 ºC;^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.87 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 7.45-7.33 (m, 4H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.4 Hz,

1H), 3.90 (s, 3H), 2.60 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.6, 160.2, 156.1, 140.8, 131.0, 130.1, 129.1, 125.4, 124.5, 124.4, 124.3, 122.9, 120.4, 119.0, 117.6, 116.9, 115.8, 88.4, 55.8, 32.4, 12.7 ppm; IR (KBr): 3330, 2223, 1649 cm^{-1}; Anal calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56% Found , C, 74.51; H, 4.84; N, 7.51%.

3-Acetyl-5-hydroxy-1-benzyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11g). Brown solid; yield: 106 mg (60%); m.p.: 202-204 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.94 (s, 1H), 8.37 (bs, 1H), 8.14-8.13 (m, 1H), 7.68-7.51(m, 2H), 7.33-7.27 (m, 3H), 7.05 (bs, 2H), 5.88 (s, 2H), 2.62 (s, 3H), 2.52 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 196.7, 156.1, 140.1, 137.1, 129.8, 129.5, 127.8, 125.9, 124.8, 124.5, 123.2, 121.4, 119.5, 118.0, 117.2, 88.4, 49.4, 33.0, 11.9 ppm; IR (KBr): 3336, 2216, 1647 cm^{-1}; Anal calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90 Found , C, 77.87; H, 5.04; N, 7.84.

3-Acetyl-5-hydroxy-1-cyclopropyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11h). Brown solid; yield: 94 mg (62%); m.p.: 194-196 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.79 (s, 1H), 8.89 (d, J = 8.7 Hz, 1H), 8.37 (d, J = 8.1 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 3.79 (m, 1H), 2.65 (s, 3H), 2.53 (s, 3H), 1.43-1.42 (m, 2H), 0.87 (bs , 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.7, 156.0, 142.5, 128.9, 126.0, 124.8, 124.4, 124.3, 123.5, 123.0, 118.8, 117.5, 117.2, 88.5, 32.6, 29.1, 14.4, 12.4 ppm; IR (KBr): 3331, 2218, 1653 cm^{-1}; Anal calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20 Found , C, 74.92; H, 5.23; N, 9.14.

3-Acetyl-7-chloro-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11i). Brown solid; yield: 99 mg (53%); m.p.: 270-272 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.09 (s, 1H), 8.31 (d, J = 2.1 Hz, 1H), 7.72-7.71 (m, 3H), 7.53-7.52 (m, 2H), 7.37-7.33 (dd, J_1= 9.0 Hz, J_2= 2.1Hz, 1H), 6.81 (d, J = 9.0 Hz, 1H), 2.59 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR (75 MHz,

DMSO-d_6): δ = 195.8, 155.4, 141.2, 138.5, 131.1, 130.7, 129.5, 129.4, 129.1, 125.2, 124.2, 123.7, 122.7, 122.6, 118.0, 116.6, 88.9, 32.6, 12.9 ppm; IR (KBr): 3327, 2223, 1648 cm^{-1}; Anal calcd for $C_{22}H_{15}ClN_2O_2$: C, 70.50; H, 4.03; N, 7.47% Found , C, 70.43; H, 3.97; N, 7.40%.

3-Acetyl-7-chloro-5-hydroxy-1-*p*-tolyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11j). Brown solid; yield: 98 mg (51%); m.p.: 238-240 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.31 (bs, 1H), 7.50 (d, J = 7.5 Hz, 2H), 7.39 (d, J = 7.8 Hz, 3H), 6.90 (d, J = 9.0 Hz, 1H), 2.58 (s, 3H), 2.48 (s, 3H), 2.24 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.8, 155.3, 141.4, 140.4, 135.9, 131.6, 129.5, 129.4, 128.8, 125.3, 124.2, 123.6, 122.7, 117.9, 116.6, 90.0, 32.5, 21.3, 12.9 ppm; IR (KBr): 3329, 2218, 1651 cm^{-1}; Anal calcd for $C_{23}H_{17}ClN_2O_2$: C, 71.04; H, 4.41; N, 7.20% Found , C, 70.97; H, 4.34; N, 7.14%.

3-Acetyl-7-chloro-5-hydroxy-1-benzyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11k). Brown solid; yield: 108 mg (56%); m.p.: 178-180 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ =11.18 (bs, 1H), 8.34 (d, J = 2.1 Hz, 1H), 8.13 (d, J = 9.0 Hz, 1H), 7.56-7.52 (J_1= 9.0 Hz, J_2= 2.1Hz, 1H), 7.36-7.25 (m, 4H), 7.02 (d, J = 7.2 Hz, 1H), 5.87 (s, 2H), 2.61 (s, 3H), 2.53 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 196.6, 155.1, 140.6, 136.8, 129.6, 129.5, 129.3, 127.9, 125.9, 124.4, 124.2, 123.8, 123.7, 122.7, 120.0, 118.0, 116.8, 89.7, 49.3, 33.0, 12.0 ppm; IR (KBr): 3329, 2218, 1651 cm^{-1}; Anal calcd for $C_{23}H_{17}ClN_2O_2$: C, 71.04; H, 4.41; N, 7.20% Found , C, 70.96; H, 4.32; N, 7.13%.

3-Acetyl-7-chloro-5-hydroxy-1-cyclopropyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11l). Brown solid; yield: 91 mg (54%); m.p.: 208-210 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ =10.94 (s, 1H), 8.90 (d, J = 9.3 Hz, 1H), 8.34 (bs, 1H), 7.73-7.70 (J_1= 9.0 Hz, J_2= 2.1Hz, 1H), 3.79 (m, 1H), 2.65 (s, 3H), 2.52 (s, 3H), 1.43-1.41 (m, 2H), 0.88 (bs, 2H) ppm; ^{13}C NMR (75

MHz, DMSO-d_6): δ =195.4, 154.7, 142.9, 129.0, 128.6, 125.6, 123.8, 123.0, 122.9, 119.0, 117.3, 116.5, 89.6, 32.3, 28.8, 14.2, 12.1 ppm; IR (KBr): 3338, 2221, 1653 cm^{-1}; Anal calcd for $C_{19}H_{15}ClN_2O_2$: C, 67.36; H, 4.46; N, 8.27% Found , C, 67.29; H, 4.40; N, 8.21%.

3-Acetyl-7-methoxy-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11q). Brown solid; yield: 96 mg (52%); m.p.: 188-190 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.79 (s, 1H), 7.72 (bs, 4H), 7.52 (bs, 2H), 6.99 (d, J = 8.1 Hz, 1H), 6.77 (d, J = 9.3 Hz, 1H), 3.83 (s, 3H), 2.68 (s, 3H), 2.25 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 195.8, 156.4, 155.4, 139.8, 138.9, 131.0, 130.5, 129.2, 124.5, 122.3, 120.2, 119.3, 117.7, 104.6, 89.0, 55.7, 32.6, 12.9 ppm; IR (KBr): 3330, 2223, 1649 cm^{-1}; Anal calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56% Found , C, 74.50; H, 4.83; N, 7.51%.

3-Carboethoxy-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11u). White solid; yield: 110 mg (59%); m.p.: 218-220 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.86 (s, 1H), 8.36 (d, J = 8.1 Hz, 1H), 7.73-7.71 (m, 3H), 7.56-7.53 (m, 2H), 7.44 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 4.41- 4.34 (m, 2H), 2.32 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.0, 150.7, 137.3, 133.0, 125.2, 124.7, 123.4, 123.3, 119.6, 118.9, 118.5, 117.3, 114.7, 113.6, 111.4, 101.2, 83.1, 54.1, 8.8, 6.7 ppm; IR (KBr): 3305, 2214, 1712 cm^{-1}; Anal calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56 Found , C, 74.51; H, 4.83; N, 7.50.

3-Carboethoxy-5-hydroxy-1-(4-fluorophenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11v). White solid; yield: 108 mg (56%); m.p.: 246-248 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.90 (s, 1H), 8.36 (d, J = 7.8 Hz, 1H), 7.67-7.53 (m, 4H), 7.48-7.36 (m, 2H), 6.91 (d, J = 8.1 Hz, 1H), 4.41- 4.34 (m, 2H), 2.33 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz,

DMSO-d_6): δ = 164.4, 164.2, 160.9, 156.2, 142.9, 134.7, 131.1, 129.0, 125.1, 124.4, 123.9, 122.8, 120.0, 119.1, 117.4, 116.5, 106.8, 88.5, 59.5, 14.2, 12.1 ppm; IR (KBr): 3302, 2216, 1715 cm^{-1}; Anal calcd for $C_{23}H_{17}FN_2O_3$: C, 71.13; H, 4.41; N, 7.21 Found , C, 71.06; H, 4.34; N, 7.14.

3-Carboethoxy-5-hydroxy-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11w). White solid; yield: 122 mg (61%); m.p.: 256-258 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.84 (s, 1H), 8.34 (d, J = 8.1 Hz, 1H), 7.47-7.36 (m, 4H), 7.24-7.20 (m, 2H), 7.00-6.97 (m, 1H), 4.40- 4.33 (m, 2H), 3.91 (s, 3H), 2.32 (s, 3H), 1.41-1.35 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 164.4, 160.0, 156.1, 143.2, 130.8, 129.8, 128.9, 125.2, 124.3, 124.1, 122.7, 120.1, 118.9, 116.6, 115.6, 106.4, 88.5, 59.4, 55.6, 14.2, 12.1 ppm; IR (KBr): 3301, 2213, 1711 cm^{-1}; Anal calcd for $C_{24}H_{20}N_2O_4$: C, 71.99; H, 5.03; N, 7.00 Found , C, 71.92; H, 4.97; N, 6.93.

3-Carboethoxy-5-hydroxy-1-benzyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11x). White solid; yield: 105 mg (55%); m.p.: 192-194 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.85 (s, 1H), 8.37 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.55-7.45 (m, 2H), 7.35-7.22 (m, 3H), 7.02 (d, J = 7.2 Hz, 2H), 5.87 (s, 2H), 4.41- 4.34 (m, 2H), 2.61 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 164.6, 155.9, 142.5, 136.8, 129.3, 129.1, 127.4, 125.5, 124.3, 124.2, 123.9, 122.7, 121.0, 119.4, 116.6, 106.5, 88.6, 59.6, 49.1, 14.2, 11.2 ppm; IR (KBr): 3302, 2217, 1710 cm^{-1}; Anal calcd for $C_{24}H_{20}N_2O_3$: C, 74.98; H, 5.24; N, 7.29 Found , C, 74.91; H, 5.18; N, 7.22.

3-Benzoyl-5-hydroxy-1-phenyl-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11y). Brown solid; yield: 82 mg (41%); m.p.: 256-258 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.78 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 7.2 Hz, 2H), 7.73-7.43 (m, 8H), 7.36 (t, J = 7.8 Hz, 1H), 7.25 (t, J = 6.9 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 1.91 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-

d_6): δ = 191.9, 155.8, 140.3, 139.9, 138.9, 133.4, 130.9, 130.4, 129.9, 129.1, 125.4, 124.8, 124.6, 124.5, 123.2, 120.4, 116.2, 115.1, 88.2, 12.8 ppm; IR (KBr): 3335, 2210, 1649 cm^{-1}; Anal calcd for $C_{27}H_{18}N_2O_2$: C, 80.58; H, 4.51; N, 6.96% Found, C, 80.51; H, 4.44; N, 6.90%.

3-Benzoyl-5-hydroxy-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*g*]indole-4-carbonitrile (11z). Brown solid; yield: 93 mg (43%); m.p.: 248-250 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.83 (s, 1H), 8.34 (d, J = 8.1 Hz, 1H), 7.87 (d, J = 8.1 Hz, 2H) 7.67-7.35 (m, 7H), 7.23 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H), 1.98 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 191.8, 160.3, 155.8, 140.7, 139.9, 133.4, 131.3, 130.2, 129.9, 125.5, 124.7, 124.5, 123.2, 120.5, 120.2, 116.3, 115.9, 114.9, 8.2, 55.9, 12.8 ppm; IR (KBr): 3336, 2225, 1647 cm^{-1}; Anal calcd for $C_{28}H_{20}N_2O_3$: C, 77.76; H, 4.66; N, 6.48% Found , C, 77.70; H, 4.59; N, 6.41%.

2,3-Dicarboethoxy-5-hydroxy-1-aryl-1*H*-benzo[*g*]indole-4-carbonitril 13; General Procedure: Dicarboethoxy substituted-2-cyanoacetamide **12** (0.5 mmol) in diphenyl ether (10 mL) was heated at reflux for 10 minutes. Upon completion of the reaction, the crude mass was purified by chromatography on a silica gel column (EtOAc/hexane, 1:1) to get pure compound **13** as white solid.

2,3-Dicarboethoxy-5-hydroxy-1-phenyl-1*H*-benzo[*g*]indole-4-carbonitrile (13a). White solid; yield: 137 mg (64%); m.p.: 180-182 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.32 (s, 1H), 8.31 (d, J = 8.4 Hz, 1H), 7.61-7.47 (m, 6H), 7.29 (t, J = 8.4 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 4.33-4.26 (m, 2H), 4.02- 3.95 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.6, 153.8, 151.5, 133.5, 124.7, 124.5, 124.1, 123.3, 122.8, 121.6, 120.8, 119.7, 119.5, 115.7, 111.7, 110.0, 109.7, 80.8, 55.7, 8.6, 8.1 ppm; IR (KBr): 3270,

2227, 1739, 1714 cm^{-1}; Anal calcd for $C_{25}H_{20}N_2O_5$: C, 70.08; H, 4.71; N, 6.54 Found , C, 70.01; H, 4.65; N, 6.45.

2,3-Dicarboethoxy-5-hydroxy-1-*p*-tolyl-1*H*-benzo[*g*]indole-4-carbonitrile (13b). White solid; yield: 115 mg (52%); m.p.: 168-170 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.38 (s, 1H), 8.40 (d, J = 8.1 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.44-7.39 (m, 5H), 6.98 (d, J = 8.4 Hz, 1H), 4.41-4.34 (m, 2H), 4.11- 4.04 (m, 2H), 2.49 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H), 1.06 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.6, 153.8, 151.4, 134.2, 130.8, 124.9, 124.1, 123.0, 121.6, 120.8, 119.6, 119.4, 119.1, 115.7, 111.7, 110.0, 109.5, 80.9, 55.7, 55.6, 15.6, 8.6, 8.2 ppm; IR (KBr): 3272, 2225, 1735, 1716 cm^{-1}; Anal calcd for $C_{26}H_{22}N_2O_5$: C, 70.58; H, 5.01; N, 6.33 Found , C, 70.51; H, 4.94; N, 6.26.

2,3-Dicarboethoxy-5-hydroxy-1-(4-fluorophenyl)-1*H*-benzo[*g*]indole-4-carbonitrile (13c). White solid; yield: 136 mg (61%); m.p.: 238-240 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.43 (s, 1H), 8.42 (d, J = 7.8 Hz, 1H),7.69-7.47 (m, 6H), 6.94 (d, J = 8.1 Hz, 1H), 4.42- 4.36 (m, 2H), 4.13- 4.01 (m, 2H), 1.37 (t, J = 7.2 Hz, 3H), 1.08 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.7, 153.7, 151.5, 129.8, 125.7, 125.6, 124.3, 122.4, 121.8, 120.9, 119.8, 119.5, 119.1, 115.6, 111.7, 111.2, 110.3, 110.0, 80.7, 55.7, 8.6, 8.2 ppm; IR (KBr): 3271, 2226, 1738, 1714 cm^{-1}; Anal calcd for $C_{25}H_{19}FN_2O_5$: C, 67.26; H, 4.29; N, 6.28 Found , C, 67.20; H, 4.22; N, 6.21.

2,3-Dicarboethoxy-5-hydroxy-1-(4-chlorophenyl)-1*H*-benzo[*g*]indole-4-carbonitrile (13d). White solid; yield: 138 mg (60%); m.p.: 194-196 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.45 (s, 1H), 8.42 (d, J = 8.1 Hz, 1H), 7.73-7.57 (m, 5H), 7.48 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 8.1 Hz, 1H), 4.43- 4.36 (m, 2H), 4.14- 4.07 (m, 2H), 1.37 (t, J = 7.2 Hz, 3H), 1.08 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.7, 153.6, 151.5, 132.5, 129.2, 125.3, 124.5, 122.1,

121.7, 120.9, 119.8, 119.5, 119.0, 115.6, 111.8, 110.6, 110.0, 80.7, 55.8, 8.6, 8.2 ppm; IR (KBr): 3274, 2221, 1739, 1716 cm^{-1}; Anal calcd for $C_{25}H_{19}ClN_2O_5$: C, 64.87; H, 4.14; N, 6.05 Found , C, 64.81; H, 4.06; N, 5.96.

2,3-Dicarboethoxy-5-hydroxy-1-(4-methoxyphenyl)-1*H*-benzo[*g*]indole-4-carbonitrile (13e). White solid; yield: 144 mg (63%); m.p.: 180-182 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.41 (s, 1H), 8.41 (d, J = 8.1 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H) 7.48-7.42 (m, 3H), 7.17 (d, J = 9.0 Hz, 2H), 7.02 (d, J = 8.1 Hz, 1H), 4.41- 4.34 (m, 2H), 4.12- 4.08 (m, 2H), 3.90 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H), 1.07 (t, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 164.3, 160.4, 159.5, 157.2, 131.5, 130.1, 129.8, 126.4, 125.1, 124.9, 121.4, 115.8, 115.2, 115.0, 86.8, 61.4, 61.3, 55.9, 14.3, 13.9 ppm; IR (KBr): 3276, 2223, 1735, 1719 cm^{-1}; Anal calcd for $C_{26}H_{22}N_2O_6$: C, 68.11; H, 4.84; N, 6.11 Found , C, 68.05; H, 4.76; N, 6.04.

2,3-Dicarboethoxy-5-hydroxy-1-(2,4 dimethyl phenyl)-1*H*-benzo[*g*]indole-4-carbonitrile (13f). White solid; yield: 125 mg (55%); m.p.: 176-178 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.42 (s, 1H), 8.42 (d, J = 7.8 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.35-7.23 (m, 3H), 6.94 (d, J = 8.4 Hz, 1H), 4.42- 4.34 (m, 2H), 4.12- 4.04 (m, 2H), 2.45 (s, 3H), 1.98 (s, 3H) 1.37 (t, J = 7.2 Hz, 3H), 1.07 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.6, 153.8, 151.5, 134.4, 130.6, 130.0, 126.3, 124.5, 122.9, 122.6, 120.9, 119.6, 119.2, 114.8, 111.8, 110.1, 109.5, 81.0, 55.8, 55.7, 15.5, 11.4, 8.6, 8.1 ppm; IR (KBr): 3273, 2224, 1737, 1714 cm^{-1}; Anal calcd for $C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14 Found , C, 70.97; H, 5.23; N, 6.07.

ASSOCIATED CONTENT

Supporting Information

Supplementary data (^{1}H, ^{13}C data of compounds **5**, **11** and **13** and crystallographic data for **5j**, **11h**, **11u**) is available free of charge *via* the Internet at--------

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13. CCDC 1025342 (for **5j**), CCDC 1025253 (for **11h**), CCDC 1042549 (**11u**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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