Synthesis of 3- Benzylidene, 5-Substituted 3-Benzylidene, 3-Hetarylmethylene and 5-Substituted Hetarylmethylene Derivatives of Indolin-2-ones

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Abstract: A wide variety of titled compounds, several of which have neuro-protecting properties has been prepared in yields ranging between 70 to 90%. The compounds were identified by ^{1}HNMR, ^{13}C NMR, 1D and 2D NOE analysis, and HRMS. An investigation of the effect of certain 5-substitutuents on the *E* to *Z* ratios in DMSO-d_6 was carried out. The 5-nitro and 5-acetyl substituents were not isomerized, whereas the 5-fluoro, 5-chloro and 5-bromo underwent significant isomerization. In the former cases resonance interaction of the lone pair electrons of NH group of the indolin-2-one with the 5-nitro or 5-acetyl of the indolin-2-one prevents rotation of the benzylidene C=C bond whereas in the case of the latter 5-halo substituent, the lone pair electrons on the NH group interacts with the benzylidene C=C bond giving rise to anionic C-C$^-$ bond in which rotation about this bond can occur.

Keywords: Synthesis, 3-benzylidenindolin-2-ones, 5-substituted-3-benzylidene-2-ones, 3-hetarylmethyleneindolin-2-ones, E/Z isomerism, spectral properties.

INTRODUCTION

Neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS), disrupt the quality of life for patients, put a tremendous burden on family caregivers, and cost society billions of dollars annually. The most consistent risk factor for developing neurodegenerative disease is aging. Because of the dramatic increase in life expectancy, the incidence of individuals afflicted with the aging-associated disorders is on the rise representing a major health problem. A commonality shared among this diverse set of disorders is the progressive and relentless loss of certain populations of neurons. Current medications for neurodegenerative diseases alleviate only the symptoms associated with these diseases but not affect the underlying cause – degeneration of neurons. Because neurolonal loss continues unabated, such palliative treatments have no effect on disease progression. The identification of small-molecule inhibitors of neuronal death is thus of urgent and critical importance (for more information see references [1, 2]).

Recently, we [3] have identified a class of 3 -substituted indolones that can protect neurons from degeneration. Furthermore, the group has conducted a structure-activity relationship study to identify substituent groups that are important for neuroprotective efficacy. The current study identifies several compounds that are more efficacious than the commercially available GW5074 (5-iodo-3-(3',5'-dibromo-'4'-hydroxybenzylidene)indolin-2-one) and display no cytotoxicity even when used at high doses. These 3'- substituted indolones are novel and promising candidates for therapeutic agents for pre-clinical testing against human neurodegenerative conditions. The synthesis, physical, spectral properties, and HRMS analyses of 45 indolin-2-ones that underwent biological testing [3] are reported herein.

Chemical Synthesis of 3-(benzylidene)indolin-2-ones

A wide variety of 3-benzylidenes (**1-6**) and 5-substituted (3-benzylidene)indolin-2-ones (**7-34**) were prepared according to Scheme **1** and the results are listed in Table **1**. Compounds **1, 7, 16, 21**, **30**, and **34** were prepared according to (Method A) of Andreani *et al.* [4], whereas compounds **2-6, 8-15, 17-20**, **22-29**, and **31-33** were synthesized by method (B) of Sun *et al.* [5]. In all cases, mixtures of Z and *E* isomers were obtained. The *Z:E* product ratios, which are shown in Table **1**, were determined by integral height values of the 2',6'-H chemical shifts of the respective *Z* and *E* isomers. The total yields of the *Z* and *E* isomers are also listed in Table **1**. The multiplicity of the carbon atoms in the ^{13}C NMR spectra were obtained by DEPT analysis. Since many of the mixtures were unstable in DMSO (*vide infra*), the configuration of the major isomer was obtained by 1D NOE analysis, which determines the configuration in about 5 min.

The minor isomers were ignored. The *Z* configured compounds showed NOE between the proton at the C-4 position and the vinyl proton (see Fig. **1a**), whereas the *E*-configured compounds showed NOE between the C-4 and hydrogen at the C-2' (or C-6') (see Fig. **1b**). The *E* configuration of 5-chloro-3-(2',6'-dichlorobenzylidene)indolin-2-one (**11**),

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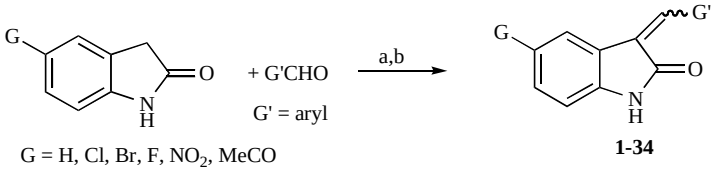


Scheme 1.

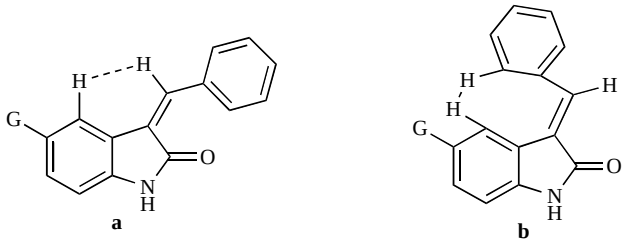
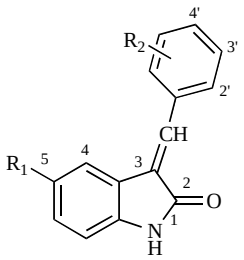


Fig. (1). a. NOE effect in *Z* configuration. **b**. NOE effect in *E* configuration.

Table 1. *Z*:*E* Isomer Ratios, 2,'6'-H Chemical Shifts of E and Z isomers, and Yield, % of E/Z Mixture



ID	Substitutent	Ratio, 2,'6'-H Chemical Shifts				Total	Major Isomer
	R_1	R_2	Z:E	*Z*	*E*	Yield, %	Configuration
1	H	3',5'-Br-4'-OH	10:90[a]	8.78	7.87	76	*E*
2	H	3',5'-Br	11:89	8.69	7.85	83	*E*
3	H	3',4',5'-OMe	90:10	7.98	7.03	88	*Z*
4	H	CH=CH-C_6H_4	50:50	7.75	7.40	b	-
5	H	2',6'-Cl	c	-	-	83	*E*[d]
6	H	2-NO_2	80:20	7.76	6.98	81	*Z*
7	Cl	3',5'-Br-4'-OH	5:95[e]	8.74	7.87	80	*E*
8	Cl	3',5'-Br	82:18	8.59	7.79	85	*Z*
9	Cl	3',5'-Br-4'-OAc	18:82	8.49	7.84	88	*E*
10	Cl	3',4',5'-OMe	77:23	7.97	7.02	90	*Z*
11	Cl	2',6'-Cl	c	-	-	92	*E*[f]
12	Cl	H	6:94	8.30	7.69	94	*E*
13	Cl	4'-CH_3	20:80	8.49	7.56	86	*E*
14	Cl	4'-OMe	4:96	8.55	7.69	87	*E*
15	Cl	4'-NMe_2	4:96	8.46	7.63	84	*E*
16	Br	3',5'-Br-4'-OH	5:95[g]	8.74	7.55	78	*E*
17	Br	3',5'-Br	91:9	8.59	7.57	81	*Z*

(Table 1). Contd…..

ID	Substitutent	Ratio, 2,'6'-H Chemical Shifts				Total	Major Isomer
	R_1	R_2	Z:E	*Z*	*E*	Yield, %	Configuration
18	Br	3',4',5'-OMe	90:10	8.01	7.06	80	*Z*
19	Br	4'-OMe	13:87	8.45	7.66	83	*E*
20	Br	4'-NMe_2	10:90	8.43	7.59	81	*E*
21	NO_2	3',5'-Br-4'-OH	70:30[h]	8.77	8.01	78	*Z*
22	NO_2	3',5'-Br	90:10	8.63	7.72	80	*Z*
23	NO_2	3',4',5'-OMe	88:12	8.07	7.16	83	*Z*
24	NO_2	2',6'-Cl	c	-	-	85[d]	*E*
25	NO_2	H	90:10	8.40	7.33	80	*Z*
26	NO_2	CH=CH-C_6H_5	9:91	7.79	7.59	81	*E*
27	NO_2	CH=CH-C_6-H_4-2'NO_2	11:89	8.16	7.86	83	*E*
28	NO_2	4'-Me	92:8	8.33	7.67	80	*Z*
29	NO_2	4'-NMe_2	90:10	8.48	7.68	81	*Z*
30	F	3',5'-Br-4'-OH	5:95[i]	8.74	7.87	70	*E*
31	F	3',5'-Br	26:74	8.59	7.88	88	*E*
32	F	3',4',5'-OMe	71:19	7.98	7.02	87	*Z*
33	F	H	12:88	8.35	7.65	86	*E*
34	COMe	3',5'-Br-4'-OH	90:10[h]	8.80	7.96	74	*Z*

[a]*Z:E* ratios were calculated on integral peak heights of the 2',6'-H signals. [b]Configuration, unless not stated, was determined by 1D NOE analysis. [c]*Z*/*E* ratio can not be determined by NOE analysis. [d]Configuration determined by analogy and comparison of spectral data to that of reference compound **11**. [f]Configuration determined by x-ray crystallographic analyses.

which does not exhibit NOE since the 2', 6'-H have been replaced by Cl was confirmed by x-ray crystallography [6]. The remaining 3-(2',6'-benzylidine) isomers were assigned to the *E* confirmation on the basis of analogy and the similarity of their ^{1}H NMR spectra with that of **11**.

With the NOE results in hand, we were able to confirm that the 2',6'-H chemical shifts assigned to the mixtures of *Z* and *E* in Table **1** were correct.

Of particular interest in Table **1** are the comparisons of the respective Z:E ratios of the 5-chloro- and 5-bromo de-

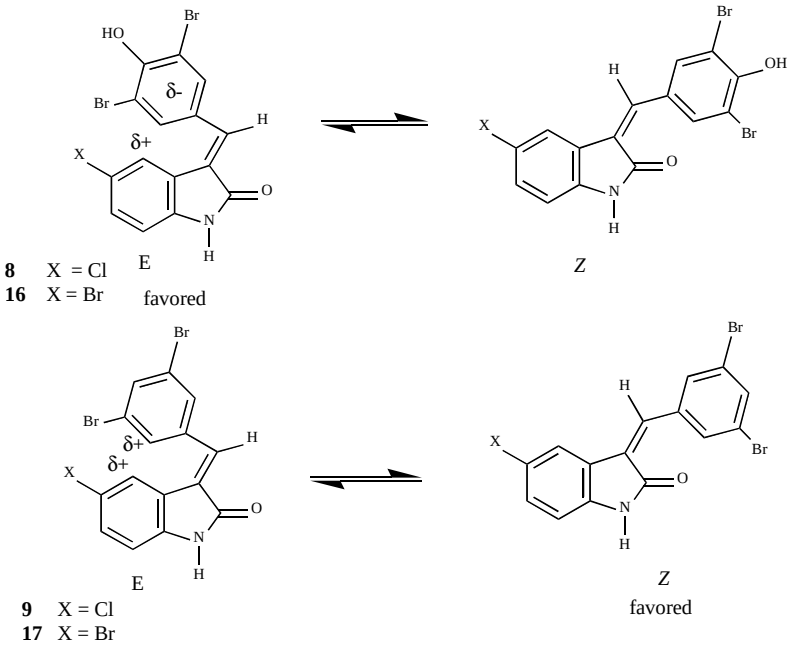


Fig. (2).

rivative) of 3-(3',5'-dibromo-4'-hydroxybenzylidene)-2-ones, **7** and **16**, to those of the respective 4'dehydroxy 3-(3',5'-dibromobenzylidene) indolin-2-ones (**8** and **17**). As shown, the *Z*:*E* ratio of both **7** and **16** are approximately 10:90, whereas those of the 4'-dehydoxy compounds **8** and **17** approximately 5:95, indicating that the 4'-hydroxy derivatives exist mainly in the *E* configuration and the 4'dehydroxy derivatives adopt mainly the *Z* conformation. In our previous study [3] we found that the 4'-hydroxy containing compounds **7** and **16**, were superior neuroprotecting compounds compared to **8** and **17**. Our data here suggests then that not only is the presence of 4'-OH in the benzylidine portion of the indolin-2-one is required for neuroprotection, but also the compounds should exists as *E* isomers. A possible explanation for the reversal in *Z*: *E* ratios is presented in Fig. (**2**).

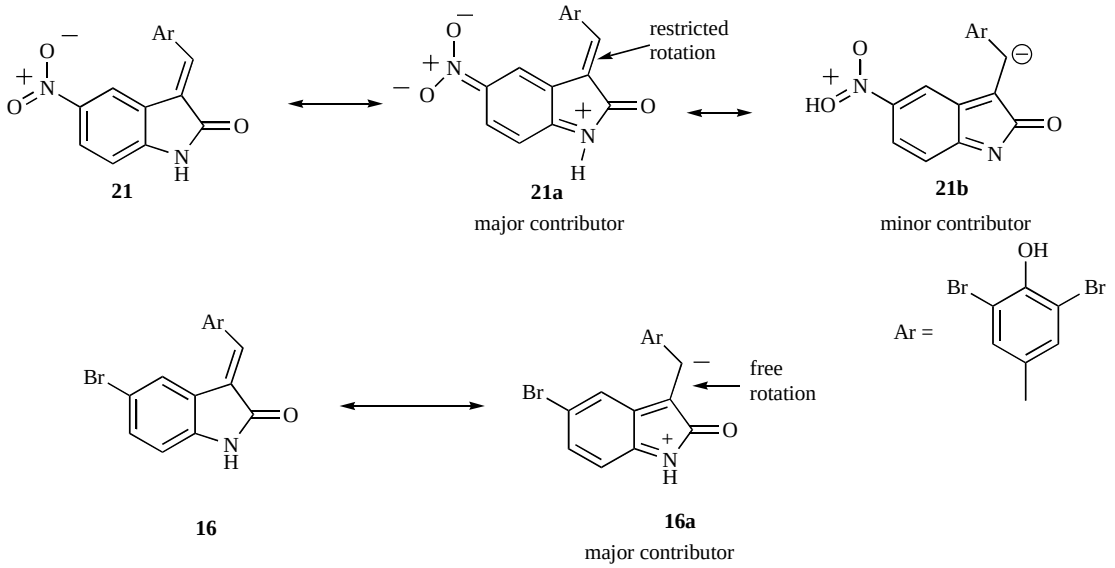
Two factors seem to be important in **7 a**nd 1**6** preference to exist in the *E* confirmation. First, the lone pair on 4'-OH can be delocalized onto the oxygen atom of the 2-keto group, which increases the strength of the hydrogen bond between the H-vinyl hydrogen and the oxygen of the 2-keto-group. This type of hydrogen bonding has been reported to be important in stabilizing *E* configurations [7]. Secondly, there is a favorable electrostatic interaction between the electron-rich phenyl group due to the 4'-OH group (making ring $\delta-$) and C-4 that now possesses a $\delta+$ charge due to a portion of its electronic density being drained towards the adjacent C-5 bearing the electronegative chlorine or bromine atom. These factors apparently overcome the unfavorable steric interaction between the two rings. In the case of the 4'-dehydroxy compounds **8** and **17**, the *Z* configuration is being favored due to the hydrogen bonding between the H-vinyl and 2'-H groups. However, the *E* configuration of these compounds are not favored because of electrostatic repulsion between C-4 and C'-2 both of which possess a $\delta+$ charge since each are adjacent to a carbon atom bearing an electronegative halogen atom. Note also that the 4-dehydroxy ring is now considerably less electron rich due to the lack of 4-'hydroxy group. Furthermore, there might be some hydrogen bonding between the keto oxygen atom and the 2'-H. on the 3',5'dibromo ring. Interestingly, in case of the parent indolin-2-ones 1 and 2 both exist in the *E* configuration presumable due to the lack of a electronegative 5-halogen atom, which doesn't allow significant electrostatic attraction between the two rings. In these cases, unfavorable steric effects between the two rings hinders the formation of the *Z* isomer. Further support for stabilization of the *E* by the *vinyl*-H and oxygen atom of the 2-keto was recently provided by an X-ray crystallographic study that showed 3-benzylidine-2-one exist as the *E* isomer [8].

As mentioned previously, the initial Z:E product ratios for many compounds listed in Table **1** obtained by using DMSO-d_6 as a solvent which increased in value .To obtain more information on the configurational isomerization, we studied 3',5'-dibromo-4-hydroxybenzylidine (**1**) and five 5-substituted analogs, namely, **7** (R_1 = Cl), **16** (R_1 = Br), **21** (R_1 = NO_2), **30** (R_1= F) and **34** (R_1= MeCO). The purified isomeric mixtures were dissolved into DMSO-d_6 and their ^{1}H NMR spectrum were obtained as quickly as possible (usually within 2 min after mixing). NMR spectrum were then obtained at 1 h intervals. With the exception of the 5-nitro derivatives **21** and **34**, the *Z*:*E* ratios of the four other compounds increase in value (that is to say the % of the *E* isomer increase at the expense of the *Z* isomer until they reached a constant value within 6 h of mixing). Thus, the *Z*:*E* ratio of **1** increased from 10:90 to 55:45, whereas both **7** and **16** increased from 5:95 to 70:30, and **30** increased from 5:95 to 80:20. In the exceptional cases, the initial ^{1}H NMR spectrum of the 5-nitro derivatives **21** and **34** revealed *Z:E* isomers ratio of 70:30, and 90:10, respectively both of which remained unchanged throughout the 7 h observational period. The results of these experiments are shown in Table **2**.

Attempts to carry out additional studies on these compounds using other solvents such as $CDCl_3$ failed due to solubility factors. A possible explanation of the influence of 5-substitutents on the *E* - *Z* isomerization of indolin-2-ones in DMSO-d_6 is given in Scheme **2**. Thus, by virtue of the nitro group in **21** being a–R group (electron-withdrawing by resonance) the lone pair electrons on the NH group can be delocalized into the 5-NO_2 moiety to give resonance structure **21a** and then further delocalized onto the benzylidine C=C to give the anionic resonance structure **21b**. Because the electronegativity of oxygen is much greater than carbon, structure **21a** is much more stable than **21b** and thus **21a** is a major contributor and **21b** is a minor contributor to the stability of **21**. Consequently, rotation about the benzylidene C=C in **21** is restricted. However, with a group such as 5-Br in compound **16 (**which is not a –R group) cannot participate in the delocalization process, thus the lone pair electrons on the NH group can only interact with the C=C to afford anionic C-C^- bond about which rotation can occur. In support of the above arguments, we found that compound **34**, which contains the –R 5-acetyl group, exists predominantly in the *Z* configuration (90%) in DMSO-d_6 and remains unchanged 6 h after mixing.

Table 2. *Z*:*E* Ratios as a Function of Time in DMSO-d_6

Compound	Initial	1h	2h	3h	4h	5h	6h	7h
1	10:90	18;82	29:71	39:61	47:53	51:49	55:45	55:45
7	4:96	14:86	31:69	42:58	53:47	65:35	72:28	72:28
16	5:95	15:85	32.68	44:56	52:38	62:38	70:30	70:30
21	70:30	70:30	70:30	70:30	70:30	70:30	70:30	70:30
30	5:95	17:83	31;69	43:57	55:45	69:31	80:20	80;20
34	90:10	90:10	90:10	90:10	90:10	90:10	90:10	90:10

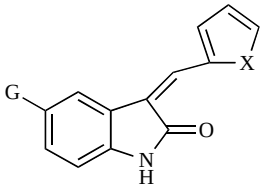


Scheme 2.

Chemical Synthesis of 3-(hetarylmethylene)indolin-2-ones

As shown in Table **3**, six 3-(pyrrol-2-yl) (**35**-**40**) and four 3-(thiophen-2-yl) (**41**-**44**) derivatives were prepared in yields ranging from 80-90% by method B [5], whereas the three (2-furan-2-yl) compounds, **45**-**47** were prepared by method C of Xiong *et al.* [9] in 83-86% yields. TLC analysis of reaction mixture indicated that only one isomer was formed. The configuration of these compounds, which are stable in DMSO-d_6, were obtained by 2D NOE analysis. These analyses established a NOE between the vinyl proton and C-4 proton in

Table 3. *Z*/E Product Ratios, Chemical Shifts of H-vinyl and H-4 and Yield, % of *Z* or *E* Isomer



Substitutent

Entry	G	X	% Z[a]	% E[b]	Yield
35	H	N	100	0	86
36	Cl	N	100	0	90
37	Br	N	100	0	83
38	COMe	N	100	0	82
39	NO_2	N	100	0	80
40	F	N	100	0	85
41	H	S	100	0	80
42	NO_2	S	100	0	81
43	Br	S	100	0	86
44	F	S	100	0	80
45	H	O	0	100	85
46	Br	O	0	100	86
47	NO_2	O	0	100	83

[a]2D NOE observed between the H-vinyl and C-4 hydrogen. [b]2D NOE not observed between the H-vinyl and C-4 hydrogen.

compounds **35-40** confirming the *Z* configuration of these compounds. On the other hand, the *E* configurations of compounds **45-47** were confirmed by the absence of NOE between the vinyl proton and C-4 proton. The fascination of compounds **35-40** to adopt the *Z* configuration most likely reflects favorable intramolecular H-bonding interactions between the NH of the pyrrole ring with the oxygen atom of the 2-keto oxygen atom [5] or favorable electrostatic interactions in **41-44** between the partial positive sulfur atom of the thiophene ring and the oxygen atom of the 2-keto oxygen atom [5]. In the exceptional cases, compounds **45-47** entirely exist in the *E*-configuration most likely due to electron repulsion between the electron lone pair on the oxygen atoms of the furan ring, and oxygen atom of the 2-keto group [5].

CONCLUSIONS

In conclusion, a wide variety of 3-benzylideneindolin-2-ones, 5-substituted 3-benzylideneindolin-2-ones, and 3-(hetarylmethylene)indolin-2-ones have been synthesized. Where possible, compounds have been assigned a *Z* or *E* configurations by 1D NOE analysis (if the compounds are unstable in DMSO-d_6) or by 2D NOE analysis (if the compounds are stable in DMSO-d_6). The 5-chloro-2',6'dichloro indolin-2-one **11** was assigned by the *E* configuration on the basis of x-ray crystallographic analysis. Additionally, a study on the effect of the NMR solvent, on 3-(3', 5'-dibromo-4'-hydroxybenzylidene)indolin-2-one (**1**) and its 5-halo, 5-nitro- and 5-acetyl analogs as a function of time were carried out. Of these, the *Z:E* ratios of **1** and its 5-halo derivatives were found to increase with time, whereas that of the 5-nitro and 5-acetyl analogs remained constant over time. An explanation in terms of extent of electronic delocalization of the lone pair on the NH of the indolin-2-one ring with the 5-substituent and 3-benzylidene C=C is presented.

ACKNOWLEDGEMENTS

We thank the Welch Foundation (Grant N-118) NIH (NS047201) and DARPA (HR0011-06-1-0032) for partial funding for this work.

EXPERIMENTAL SECTION

Melting points were taken on a Mel-Temp apparatus and are uncorrected. NMR spectra were recorded on a Brucker-400MHz and/or JEOL-500MHz Spectrometer. Chemical shifts are reported in parts per million (δ) downfield from TMS. Coupling constants are reported in hertz (Hz). Chemicals were purchased from Sigma Aldrich chemical company and were used as received. HRMS analyses were performed by the Washington University Center for Biomedical and Bioorganic Mass Spectrometry: A NIH-supported resource center.

Synthesis of 3-benzylidene Derivatives

Method A: Compounds 1, 7, 16, 21, 30, and 34 were prepared according to the method (A) of Andreani *et al*. [4]. In a typical experiment, 3',5'-dibromo-4'-hydroxybenzaldehyde (2 mmol) was treated with the appropriate indolinone (2 mmol), anhydrous sodium acetate (4 mmol) in 20 ml of acetic acid. After the reaction mixture was refluxed for 3 h, it was cooled and evaporated under reduced pressure. The residue was poured onto crushed ice, and the resulting precipitate was collected by filtration (70-80% yields) and recrystallized from ethanol.

Method B: Compounds 2-6, 8-15, 17-20, 22-29, 31-33, were prepared by the method (B) of Sun *et al*. [5]. In a typical experiment, the appropriate aldehyde (1 mmol) was dissolved in ethanol (10 mL) and treated with the equivalent of the corresponding indolin-2-one (1 mmol) and piperidine (0.1 mmol). The reaction mixture was refluxed for 3-5 h then cooled to rt. During that time a precipitate formed which was collected by filtration (80-95% yield) and recrystallized from ethanol.

Synthesis of 3- (hetaryl-2-methyl)indoline-2-ones

Method B: The 3-(2'-pyrroles) (35-40) and 3-(2'-thienyl) (41-44) derivatives were prepared by Method B as described above.

Method C: The-3-(2'-furanyl) derivatives (45-47) were prepared by Method C of Xiong *et al*. [8]. In a typical reaction a mixture containing oxindole (1equiv), furan-2-carboxaldehyde (1.2 equiv), and piperidine (0.1 equiv) in (8 mL of methanol) was stirred at room temperature for 30 min. After the mixture was cooled to 0 ˚C, the reaction was stirred overnight. The resulting precipitate was filtered, washed with cold methanol, and dried to give the target compounds (80-90% yield). The resulting compounds were recrystallized from ethanol.

The melting points, spectral properties and HRMS analyses and configuration or the major isomers, which were determined, where appropriate, by 1D NOE analysis for compounds 1-34 and by 2D NOE analysis for compounds 35-47.

(E)-3-(3', 5'-Dibromo-4'-hydroxybenzylidene)indolin-2-one (1) was obtained as a yellow solid; mp 238-241 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.56 (s, 1H, NH-1), 7.87 (s, 2H, H-2,6'), 7.45 (d, J = 4.60 Hz, 2H, H-vinyl, H-7), 7.20 (t, J = 7.45 Hz, 1H. H-6), 6.85 (t, J = 6.25 Hz, 2H, H4,5);. 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 152.3 (C), 143.5 (C), 133.7 (CH), 133.6 (CH) 130.8 (CH), 129.8 (C), 128.3 (C), 122.4 (CH), 121.7 (CH), 121.1 (C), 112.3 (2xC), 110.8 (CH); HRMS Calcd. for C15H9Br2NO2: 392.9000. Found: 392.2002.

(E)-3-(3', 5'-Dibromobenzylidene)indolin-2-one (2) was obtained as a yellow solid; mp 245-247 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.63 (s, 1H, NH-1), 7.90 (s, 1H, H-4'), 7.85 (s, 2H, H-2', 6'), 7.49 (s, 1H, H-vinyl), 7.26 (d, J = 7.45 Hz, 1H, H-4), 7.21 (t, J = 7.45 Hz, 1H, H-6), 6.85 (m, 1H, H-5, 7); 13C NMR (500 MHz, DMSO-d6) δ 168.6 (CO), 143.9 (C), 139.2 (C), 134.2 (CH), 132.7 (CH), 131.4 (CH), 131.1 (CH), 130.3 (C), 123.2 (C), 122.8 (CH), 121.8 (CH), 120.9 (C), 110.9 (CH); HRMS Calcd. for C15H10Br2NO: 377.0540. Found: 377.0534.

(Z)-3-(3', 4', 5'-Trimethoxybenzylidene)indolin-2-one (3) was obtained as a light yellow solid; mp 200-202 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.55 (s, 1H, NH-1), 7.98 (s, 2H, H-2',6'), 7.73 (s, 1H, H-vinyl), 7.64 (d, J = 7.45 Hz, 1H, H-4), 7.17 (t, J = 7.45 Hz, 1H, H-6), 6.97 (t, J = 7.45 Hz, 1H, H-5), 6.81 (d , J = 8.05 Hz, 1H, H-7), 3.81 (s, 6H, 2xOCH3), 3.71 (s, 3H, OCH3). 13C NMR (500 MHz, DMSO-d6) δ 167.8 (CO), 152.7 (C), 140.9 (C), 140.2 (C), 137.8 (CH), 130.0 (C), 129.1 (CH), 126.1 (C), 125.7 (C), 121.5 (CH), 119.9 (CH), 110.6 (CH), 109.8 (CH), 60.7 (OCH3), 56.4

(OCH3); HRMS Calcd. for C18H17NO4: 311.3319. Found: 311.3323.

3-(3'-Phenylallylidene)indolin-2-one (4) was obtained as an orange solid; mp 203-205 oC (lit. [10] 205-206 oC).

(E)-3-(2',6'-Dichlorobezylidene)indolin-2-one (5) was obtained as a red solid; mp 179-181oC (lit. [10] 164 oC).1H NMR (500 MHz, DMSO-d6) δ 10.78 (s, 1H, NH-1), 7.60 (d, J = 8.60 Hz, 2H, H-3',5'), 7.49 (t, J = 8.60 Hz, 1H, H-4'), 7.38 (s, 1H, H-vinyl), 7.19 (t, J = 8.60 Hz, 1H, H-5), 6.82 (d, J = 8.60 Hz, 1H, H-4), 6.74 (t, J = 8.0 Hz, 1H, H-6), 6.45 (d, J = 8.0 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 168.0 (CO), 143.5 (C), 133.7 (C), 132.3 (C), 131.8 (CH), 131.4 (CH), 129.1 (CH), 128.7 (CH), 123.3 (CH), 122.1 (CH), 121.2 (C), 110.7 (CH).

(Z-3-(2'-Nitrobenzylidene)indolin-2-one (6) was obtained as a light red solid; mp 239-241 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.70 (s, 1H, NH-1), 8.30 (d, 1H, J = 8.0 Hz, H-4), 7.76-7.92 (m, 4H, H-3', 5', H-vinyl), 7.29 (t, J = 7.2 Hz, 1H, H-4'), 6.73-6.89 (m, 3H, H-5,6,7). 13C NMR (500 MHz, DMSO-d6) δ 168.5 (CO), 147.6 (C), 143.5 (C), 135.0 (CH), 133.0 (CH), 131.5 (CH), 131.1 (CH), 130.9 (CH), 129.0 (C), 125.7 (CH), 122.9 (CH), 121.7 (CH), 110.8 (CH); HRMS Calcd. for C15H10N2O3: 266.069. Found: 266.0679.

(E)- 3-(3',5'-Dibromo-4-hydroxybenzylidene)-5-chloroindolin-2-one (7) was obtained as a yellow solid; mp 190-193 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.70 (s, 1H, NH-1), 7.87 (s, 2H, H-2',-6'), 7.49 (s, 1H, H-vinyl), 7.37 (s, 1H, H-4), 7.20 (d, J = 8.0 Hz, 1H, H-7), 6.82 (d, J = 8.0 Hz, 1H, H-6). 13C NMR (500 MHz, DMSO-d6) δ 168.6 (CO), 152.7 (C), 142.3 (C), 135.4 (CH), 133.8 (CH), 130.1 (CH), 128.7 (C), 127.2 (C), 125.4 (C), 122.9 (C), 122.2 (CH), 112.3 (C), 112.1 (CH); HRMS Calcd. for C15H8Br2ClNO2: 426.8610. Found: 426.8617.

(Z)-3-(3',5'-Dibromobenzylidene)-5-chloroindolin-2-one (8) was obtained as a light orange solid; mp 294-297 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.82 (s, 1H, NH-1), 8.59 (s, 2H, H-2', 6'), 7.90 (s, 1H, H-4'), 7.85 (s, 1H, H-vinyl), 7.75 (d, J = 6.85 Hz, 1H, H-4), 7.23 (d, J = 8.60 Hz, 1H, H-6), 6.81 (d, J = 8.60 Hz, 1H, H-7); NOE between H-vinyl and H-4; 13C NMR (500 MHz, DMSO-d6) δ 168.2 (CO), 141.9 (C), 138.2 (C), 135.4 (CH), 135.3 (CH), 133.7 (CH), 129.7 (CH), 126.5 (C), 125.5 (C), 122.7 (C), 120.9 (CH), 111.6 (CH); HRMS Calcd. for C15H9Br2ClNO: 411.3719. Found: 411.3713.

(E)-2,6-Dibromo-4-(5'-chloro-2'-oxoindolin-3-ylidene) methyl)phenyl acetate (9) was obtained as a light brown solid; mp 148-150 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.80 (s, 1H, NH-1), 7.84 (s, 2H, H-2', 6'), 7.52 (s, 1H, H-vinyl), 6.68 (s, 1H, H-4), 6.64 (d, J = 8.45 Hz, 1H, H-6), 6.02 (d, J = 8.45 Hz, 1H, H-7); HRMS Calcd. for C17H10Br2ClNO3: 411.8719. Found: 411.8706.

(Z)-5-Chloro-3-(3', 4', 5'-trimethoxybenzylidene)indolin-2-one (10) was obtained as a yellow solid; mp 269-271 oC. 1H NMR (400 MHz, DMSO-d6) δ 10.64 (s, 1H, NH-1), 7.97 (s, 2H, H-2',6'), 7.83 (s, 1H, H-vinyl), 7.72 (d, J = 2.0 Hz, 1H, H-4), 7.15 (dd, J = 8.0, 2. 0 Hz, 1H, H-7), 6.76 (d, J = 8.0 Hz, 1H, H-6), 3.76 (s, 6H, 2xOCH3), 3.68 (s, 3H, OCH3). 13C NMR (400 MHz, DMSO-d6) δ 167.9 (CO), 153.1 (C), 141.0 (C), 140.1(CH), 139.9 (C), 130.2 (C), 128.7 (CH), 128.0 (C), 126.2 (C), 125.2 (C), 120.3 (CH), 111.5 (CH), 111.3 (CH), 61.0 (OCH3), 56.7 (OCH3); HRMS Calcd. for C18H16ClNO4: 396.0768. Found: 396.0770

(E)- 5-Chloro-3-(2',6'-dichlorobenzylidene)indolin-2-one (11) was obtained as a yellow solid; mp 197-199 oC. 1H NMR (400 MHz DMSO-d6) δ 10.88 (s, 1H, NH-1), 7.69 (d, J = 7.88 Hz, 2H, H-3', 5'), 7.54-7.68 (m, 2H, H-vinyl, H-4'), 7.30 (d, J = 8.0 Hz, 1H, H-4), 6.90 (d, J = 8.2 Hz, 1H, H-6), 6.36 (d, J = 8.2 Hz, 1H, H-7); 13C NMR (400 MHz, DMSO-d6) δ 167.9 (CO), 142.6 (C), 133.9 (C), 132.7 (C), 132.5 (CH), 131.8 (C), 131.3 (CH), 131.0 (CH), 129.6 (CH), 126.2 (C), 123.1 (CH), 112.6 (CH).

(E)-3-Benzylidene-5-chloroindolin-2-one (12) was obtained as a yellow solid; mp 208-211 oC. 1H NMR (400 MHz DMSO-d6) δ 10.76 (s, 1H, NH-1), 7.68-7.73 (m, 3H, H-2',6', vinyl), 7.53-7.56 (m, 3H, H-3', 5',4), 7.49 (d, J = 8.05 Hz, 1H, H-6), 7.28 (t, J = 8.60 Hz, 1H, H-4'), 6.87 (d, J = 8.05 Hz, 1H, H-7); 13C NMR (400 MHz, DMSO-d6) δ 169.1 (CO), 142.5 (C), 138.6 (C), 134.9 (CH), 130.5 (CH), 129.7 (CH), 125.7 (CH), 123.3 (CH), 122.6 (CH), 112.4 (CH); HRMS Calcd. for C15H10ClNO: 255.0451. Found: 255.0459.

(E)- 5-Chloro-3-(4'-methybenzylidene)indolin-2-one (13) was obtained as a light yellow solid; mp 220-223 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.69 (s, 1H, NH-1), 7.64 (s, 1H, H-vinyl), 7.56 (d, J = 8.20 Hz, 2H, H-2',6'), 7.45 (s, 1H, H-4), 7.30 (d, J = 7.45 Hz, 2H, H-3',5'), 7.23 (d, J = 8.05 Hz, 1H, H-6), 6.85 (d, J = 8.05 Hz, 1H, H-7), 2.35 (s, 3H, CH3); 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 142.1 (C), 140.7 (C), 138.4 (CH), 131.6 (C), 129.9 (CH), 126.6 (C), 125.4 (C), 122.1 (C), 111.9 (CH), 21.6 (CH3); HRMS Calcd. for C16H12ClNO: 269.0607. Found: 269.0611.

(E)-5-Chloro-3-(4'-methoxybenzylidene)indolin-2-one (14) was obtained as a yellow solid; mp 257-260 oC. 1H NMR (400 MHz, DMSO-d6) δ 10.69 (s, 1H, NH-1), 7.69 (d, J = 8.48 Hz, 2H, H-2',6'), 7.54 (d, J = 8.0 Hz, 1H, H-4), 7.25 (s, 1H, H-vinyl), 7.15 (t, J = 8.0 Hz, 1H, H-6), 7.10 (d, J = 8.50 Hz, 2H, H-3', 5'), 6.80-6.88 (m, 2H, H-3', 5'), 3.83 (s, 3H, OCH3); 13C NMR (400 MHz, DMSO-d6) δ 169.4 (CO), 161.7 (C), 142.2 (C), 139.7 (C), 138.7 (CH), 135.6 (CH), 132.4 (CH), 129.9 (CH), 127.0 (C), 125.7 (C), 125.6 (C), 123.6 (C), 122.2 (CH), 115.2 (CH), 112.2 (CH), 56.2 (OCH3); HRMS Calcd. for C16H12ClNO2: 265.0557. Found: 265.0576.

(E)-5-Chloro-3-(4'-(dimethylamino)benzylidene)indolin-2-one (15) was obtained as a orange solid; mp 257-260 oC. 1H NMR (400 MHz, DMSO-d6) δ 10.59 (s, 1H, NH-1), 7.70 (s, 1H, H-4), 7.63 (d, J = 7.88 Hz, 1H, H-2',6'), 7.59 (s, 1H, H-vinyl), 7.21 (d, J = 7.88 Hz, 1H, H-3'), 6.82-6.87 (m, 3H, 5,7,5'), 3.04 (s, 6H, N(CH3)2); 13C NMR (400 MHz, DMSO-d6) δ 169.9 (CO), 152.5 (C), 141.5 (C), 140.1 (CH), 133.0 (CH), 128.8 (CH), 125.5 (C), 124.4 (CH), 121.8 (C), 121.7 (C), 121.4 (C), 112.3 (CH), 111.8 (CH), 40.8 (N(CH3)2); HRMS Calcd. for C17H15ClN2O: 298.0873. Found: 298.0881.

(E)-5-Bromo-3-(3', 5'-dibromo-4'-hydroxybenzylidene-indolin-2-one (16) was obtained as a yellow solid; mp 148-150 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.70 (s, 1H,

NH-1), 7.87 (s, 2H, H-2',6'), 7.54 (s, 1H, H-vinyl), 7.50 (s, 1H, H-4), 7.36 (d, J = 8.60 Hz, 1H, H-7), 6.80 (d, J = 8.60 Hz, 1H, H-6); 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 152.7 (C), 142.3 (C), 135.3 (CH), 133.8 (CH), 129.5 (CH), 128.9 (C), 127.5 (C), 124.4 (C), 120.9 (C), 111.2 (CH), 110.8 (C), 110.1 (CH); HRMS Calcd. for C15H8Br3NO2: 470.9408. Found: 470.9419.

(Z)-5-Bromo-3-(3', 5'-dibromobenzylidene)indolin-2-one (17) was obtained as a yellow solid; mp 282-284 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.80 (brs, 1H, NH), 8.59 (s, 2H, H-2',6'), 7.87-7.94 (m, 3H, H-4', H-vinyl, H-4), 7.35-7.38 (m, 1H, H-6), 6.76 (d, J = 8.02 Hz). HRMS Calcd. for C15H8Br3NO: 470.9408. Found: 470.9416.

(Z)-5-Bromo-3-(3', 4', 5'-trimethoxybenzylidene)indolin-2-one (18) was obtained as a yellow solid; mp 250-252 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.68 (brs, 1H, NH), 8.01 (s, 2H, H-2,6'), 7.89 (s, 1H, H-vinyl), 7.87 (s, 1H, H-4), 7.31 (dd, J = 1.1, 9.1 Hz, 1H, H-6), 6.76 (d, J = 8.6 Hz, 1H, H-7), 3.81 (s, 6H, 2XOCH3), 3.72 (s, 3H, OCH3); 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 152.8 (C), 140.5 (C), 139.9 (CH), 131.2 (CH), 130.0 (C), 128.2 (C), 124.5 (C), 122.7 (CH), 113.5 (C), 111.7 (CH), 110.9 (CH), 60.7 (CH3), 56.4 (CH3); HRMS Calcd. for C18H16BrNO4: 375.0232. Found: 375.0237.

(E)-5-Bromo-3-(4'-methoxybenzylidene)indolin-2-one (19) was obtained as a light yellow solid; mp 220-222 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.68 (brs, 1H, NH), 7.66-7.68 (m, 3H, H-4, H-2',6'), 7.62 (s, 1H, H-vinyl), 7.36 (dd, J = 1.72, 8.02 Hz, 1H, H-6), 7.08 (d, J = 8.59 Hz, 2H, H-3',5'), 6.81 (d, J = 8.59 Hz, 1H, H-7), 3.82 (s, 3H, OCH3). HRMS Calcd. for C16H12BrNO2: 329.0051. Found: 329.0059.

(E)-5-Bromo-3-(4'-(dimethylamino)benzylidene) indolin-2-one (20) was obtained as a brick red solid; mp 238-240 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.55 (brs, 1H, NH), 7.80 (d, J = 6.8 Hz, 1H, H-4), 7.59 (d, J = 9.1 Hz, 2H, H-2',6'), 7.54 (s, 1H, H-vinyl), 7.20-7.32 (dd, J = 1.72, 8.05 Hz, 1H, H-6), 6.76-6.83 (m, 3H, H-3',5', H-7), 3.00 (s, 6H, N(CH3)2). HRMS Calcd. for C17H15BrN2O: 342.0368. Found: 342.0376.

(Z)- 3-(3', 5'-Dibromo-4-hydroxybenzylidene)-5-nitroindolin-2-one (21) was obtained as a light orange solid; mp 325-327 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.30 (s, 1H, NH-1), 8.77 (s, 2H, H-2', 6'), 8.55 (s, 1H, H-vinyl), 8.10 (d, J = 8.60 Hz, 1H, H-4), 7.36 (d, J = 8.90 Hz, 1H, H-7), 6.94 (d, J = 8.90 Hz, 1H. H-6). HRMS Calcd. for C15H8Br2N2O3: 421.8902. Found: 421.8918.

(Z)-3-(3', 5'-Dibromobenzylidene)-5-nitroindolin-2-one (22): was obtained as a yellow solid; mp 304-306 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.38 (brs, 1H, NH), 8.61-8.63 (m, 3H, H-2',6', H-4'), 8.12-8.18 (m, 2H, vinyl-H, H-4), 7.92-7.96 (m, 1H, H-6), 6.98 (d, J = 9.16 Hz, H-7). HRMS Calcd. for C15H8Br2N2O4: 437.8851. Found: 437.8861.

(Z)- 3-(3', 4', 5'-Trimethoxybenzylidene)-5-nitroindolin-2-one (23) was obtained as a yellow solid; mp 300-302 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.27 (brs, 1H, NH), 8.63 (s, 1H, H-4), 8.14- 8.12 (m, 2H, 1H-vinyl, H-6), 8.07 (s, 2H, H-2',6'), 7.00 (d, J = 8.6 Hz, 1H, H-7), 3.83 (s, 6H, 2XOCH3), 3.74 (s, 3H, OCH3); 13C NMR (500 MHz, DMSO-d6) δ 169.5 (CO), 168.0 (C), 153.5 (C), 152.8 (C), 148.0 (C), 141.7 (CH), 140.1 (CH), 126.8 (CH), 125.4 (CH), 118.3 (CH), 115.6 (CH), 111.2 (CH), 110.5 (CH), 109.8 (CH), 108.1 (CH), 60.7 (CH3), 56.5 (CH3), 56.3 (CH3); HRMS Calcd. for C18H16N2O6: 356.1008. Found: 356.1014.

(E)-3-(2', 6'-Dichlorobenzylidene)-5-nitroindolin-2-one (24) was obtained as a light yellow solid; mp 282-284 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.46 (brs, 1H, NH), 8.15 (dd, J = 2.2, 9.1Hz, 1H, H-4), 7.66-7.70 (m, 3H, H-3',5', H-vinyl), 7.57-7.60 (m, 1H, H-4'), 7.26 (d, J = 2.29 Hz, 1H, H-6), 7.04 (d, J = 8.59 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 168.1 (CO), 149.1 (C), 142.4 (C), 133.6 (C), 132.4 (CH), 132.4 (C), 132.0 (C), 130.5 (C), 129.4 (CH), 127.9 (CH), 121.4 (C), 118.4 (C), 111.0 (CH); HRMS Calcd. for C15H8Cl2N2O3: 333.9912. Found: 333.9923.

(Z)-3-Benzylidene-5-nitroindolin-2-one (25) was obtained as a yellow solid; yield 80%; mp 220-222 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.32 (brs, 1H, NH), 8.67 (d, J = 2.29 Hz, 1H, H-4), 8.39-8.40 (m, 2H, H-2',6'), 8.20 (s, 1H, H-vinyl), 8.14 (dd, J = 2.3, 8.6 Hz, 1H, H-6), 7.47-7.48 (m, 3H, H-3',4',5'), 6.97 (d, J = 8.6 Hz, 1H, H-7). HRMS Calcd. for C15H10N2O3: 266.0691. Found: 266.0699.

(E)-5-Nitro-3-(E)-3-phenylallylidene)indolin-2-one (26) was obtained as a yellow solid; mp 302-304 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.22 (brs, 1H, NH), 8.51 (s, 1H, H-4), 8.37-8.42 (m, 1H, H-9), 8.09-8.11 (m, 1H, Hb), 7.98 (dd, J = 2.29, 11.4 Hz, 1H, H-7), 7.59-7.60 (m, 2H, 2',6'-H), 7.36-7.47 (m, 3H, 3,4',5'-H), 7.26 (d, J = 16.04 Hz, 1H, Hc), 6.97 (dd, J = 1.72, 8.6 Hz, 1H, Hb); 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 146.8 (C), 145.4 (CH), 142.5 (CH), 140.0 (CH), 136.3 (C), 130.5 (CH), 129.7 (CH), 129.5 (C), 128.8 (C), 128.2 (CH), 125.7 (CH), 124.8 (C), 124.1 (CH), 123.6 (C), 116.2 (CH), 110.0 (CH); HRMS Calcd. for C17H12N2O3: 292.0848. Found: 292.0857.

(E)-5-Nitro-3-(2'-nitrophenyl)allylidene) indolin-2-one (27) was obtained as a yellow solid; mp 325-327 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.26 (brs, 1H, NH), 8.57 (s, 1H, H-4), 8.35-8.40 (m, 1H, Ha), 8.08-8.13 (m, 2H, H-3', H-6), 8.02 (d, J = 7.45 Hz, 1H, H-7), 7.86 (d, J = 7.45 Hz, 1H, H-6'), 7.78 (t, J = 8.02 Hz, 1H, H-5'), 7.62 (t, J = 7.45 Hz, 1H, H-4'), 7.45(d, J = 14.89 Hz, 1H, Hc), 6.96 (d, J = 8.02Hz, 1H, Hb); 13C NMR (500 MHz, DMSO-d6) δ 168.7 (CO), 148.9 (C), 147.2 (C), 143.0 (C), 138.5 (CH), 138.1 (CH), 134.0 (CH), 130.6 (CH), 128.8 (CH), 128.5 (CH), 126.0 (CH), 125.0 (CH), 116.6 (CH), 110.1 (CH); HRMS Calcd. for C17H11N3O5: 337.0699. Found: 337.0689.

(Z)-3-(4'-Methylbenzylidene)-5-nitroindolin-2-one (28) was obtained as a yellow solid; mp 263-265 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.29 (brs, 1H, NH), 8.66 (d, J = 1.72 Hz, 1H, H-4), 8.35 (d, J = 8.02 Hz, 2H, H-2',6'), 8.16 (s, 1H, H-vinyl), 8.12 (dd, J = 2.2, 9.7 Hz, 1H, H-6), 7.29 (d, J = 8.59 Hz, 2H, H-3',5'), 6.97 (d, J = 8.5 Hz, 1H, H-7), 2.35 (s, 1H, CH3). HRMS Calcd. for C16H12N2O3: 294.0879. Found: 294.0885.

(Z)-3-(4'-(Dimethylamino)benzylidene)-5-nitroindolin-2-one (29) was obtained as a orange solid; mp 295-297 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.13 (brs, 1H, NH), 8.54 (d, J = 2.29 Hz, 1H, H-4), 8.48 (d, J = 9.16 Hz, 2H, H-2',6'),

8.02 (dd, J = 2.3, 8.59 Hz, 1H, H-6), 7.98 (s, 1H, H-vinyl), 6.93 (d, J = 8.52 Hz, 1H, H-7), 6.76 (d, J = 8.89 Hz, 2H, H-3',5'), 3.03 (s, 6H, N(CH3)2); 13C NMR (500 MHz, DMSO-d6) δ 168.3 (CO), 153.0 (C), 145.1 (C), 142.4 (CH), 142.2 (C), 136.2 (CH), 127.6 (C), 123.6 (CH), 122.2 (C), 117.6 (C), 114.4 (CH), 111.6 (CH), 109.2 (CH), 40.2 (CH3), 40.1 (CH3); HRMS Calcd. for C17H15N3O3: 309.1113. Found: 309.1120.

(E)-3-(3', 5'-Dibromo-4'-hydroxybenzylidene)-5-fluoro-indolin-2-one (30) was obtained as a yellow solid; mp 173-175 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.58 (s, 1H, NH-1), 7.87 (s, 2H, H-2', 6'), 7.51 (s, 1H, H-vinyl), 7.17 (d, J = 9.20 Hz, 1H, H-4), 7.07 (dt, J = 2.90, 9.20 Hz, 1H, H-7), 6.81 (dd, J = 4.8 0, 8.60 Hz, 1H, H-6); 13C NMR (500 MHz, DMSO-d6) δ 168.9 (CO), 158.5 (C), 152.7 (C), 139.9 (C), 135.2 (CH), 133.8 (CH), 128.7 (C), 127.8 (C), 122.1 (C), 117.1 (CH), 112.3 (C), 111.4 (CH), 109.5 (CH), HRMS Calcd. for C15H8Br3NO2: 410.8906. Found: 410.8913.

(E)-3-(3', 5'-Dibromobenzylidene)-5-fluoroindolin-2-one (31) was obtained as a yellow solid; mp 290-293 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.66 (s, 1H, NH-1), 7.94 (s, 1H, H-4'), 7.88 (s, 2H, H-2', 6'), 7.58 (s, 1H, H-vinyl), 7.07-7.11 (m, 2H, H-6, 4), 7.21 (d, J = 8.85 Hz, 1H, H-6), 6.83-6.85 (m, 1H, H-7). HRMS Calcd. for C15H8Br2FNO: 394.8957. Found: 394.8969.

(Z)-5-Fluoro-3-(3', 4', 5'-trimethoxybenzylidene)indolin-2-one (32) was obtained as a yellow solid; mp 194-196 oC. 1H NMR (400 MHz, DMSO-d6) δ 10.49 (s, 1H, NH-1), 7.91 (s, 2H, H-2',6'), 7.73 (s, 1H, H-vinyl), 7.47 (dd, J = 2.4, 8.7 Hz, 1H, H-4), 6.75-6.89 (m, 1H, H-7), 6.69-6.73 (m, 1H, H-6), 3.74 (s, 6H, 2xOCH3), 3.64 (s, 3H, OCH3); 13C NMR (400 MHz, DMSO-d6) δ 168.1 (CO), 159.9 (C), 153.1 (C), 140.9 (C), 139.9 (CH), 137.4 (C), 130.1 (C), 127.6 (C), 126.0 (C), 115.7 (CH), 111.2 (CH), 110.9 (CH), 108.0 (CH), 61.0 (OCH3), 56.9 (OCH3); HRMS Calcd.. for C18H16FNO4: 329.1063. Found: 329.1073.

(E)-3-Benzylidene-5-fluoroindolin-2-one (33) was obtained as a yellow solid; mp 195-198 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.61 (s, 1H, NH-1), 7.65-7.68 (m, 3H, H-2',6', vinyl), 7.48-7.53 (m, 3H, H-3', 5',4), 7.47 (d, J = 8.60 Hz, 1H, H-6), 7.06 (t, J = 8.75 Hz, 1H, H-4'), 6.84 (d, J = 8.60 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 169.0 (CO), 139.8 (C), 138.0 (CH), 134.5 (C), 130.5 (CH), 129.7 (CH), 129.4 (CH), 117.1 (CH), 111.3 (CH), 109.7 (CH); HRMS Calcd. for C15H10FNO: 239.0746. Found: 239.0754.

(Z)-5-Acetyl-3-(3', 5'-dibromo-4'-hydroxybenzylidene) indolin-2-one (34) was obtained as a yellow solid; mp 286-289 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.03 (s, 1H, NH-1), 10.72 (s, 1H, OH), 8.80 (s, 2H, H-2', 6'), 8.28 (s, 1H, H-vinyl), 7.91 (d, J = 6.85 Hz, 1H, H-4), 7.83 (d, J = 8.05 Hz, 1H, H-7), 6.88 (dd, J = 8.05, 4.05 Hz, 1H, H-6), 2.47 (s, 3H, CH3); 13C NMR (500 MHz, DMSO-d6) δ 197 (CO), 168.1 (CO), 153.4 (C), 145.0 (C), 136.9 (CH), 136.1 (CH), 131.1 (C), 130.4 (CH), 129.0 (C), 125.4 (C), 120.4 (CH), 111.6 (C), 109.5 (CH), 27.0 (CH3); HRMS Calcd. for C17H11Br2NO: 434.9106. Found: 434.9120.

(Z)-3-(1H-Pyrrol-2'-yl)methylene)indolin-2-one (35) was obtained as a light yellow solid; mp194-196 OC. The 1H NMR was identical to that reported previously [5];13C NMR (500 MHz, DMSO-d6) δ 169.7 (CO), 139.5 (C), 130.1 (C), 127.4 (CH), 126.8 (CH), 126.1 (CH), 125.7 (C), 121.7 (CH), 120.8 (CH), 119.0 (CH), 117.3 (C), 111.9 (CH), 110.0 (CH).

(Z)-5-Chloro-(1H-pyrrol-2'-yl)methylene)indoline-2-one (36) was obtained as a orange red solid; mp 260-262 oC. 1H NMR spectra was identical to that reported previously [5]; 13C NMR (400 MHz, DMSO-d6) δ 169.9 (CO), 138.3 (C), 130.3 (C), 128.8 (CH), 128.0 (C), 127.4 (CH), 126.9 (CH), 126.4 (C), 122.1 (CH), 119.3 (CH), 116.4 (C), 112.6 (CH), 111.6 (CH);

(Z)- 5-Bromo (3-(1H-pyrrol-2'-yl)methylene)indolin-2-one (37) was obtained as a yellow solid; mp 262-265 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.98 (brs, 1H, NH), 7.86 (s, 1H, H-vinyl), 7.84 (d, J = 1.72 Hz, H-4), 7.36-7.38 (m, 1H, H-5'), 7.24 (dd, J = 2.29, 8.0 Hz, 1H, H-6), 6.78-6.81 (m, 2H, H-7, H-3'), 6.34-6.35(m, 1H, H-4'); 13C NMR (500 MHz, DMSO-d6) δ 169.4 (CO), 138.3 (C), 130.0 (C), 129.4 (CH), 128.5 (CH), 128.1 (C), 127.1 (CH), 121.9 (CH), 121.7 (CH), 115.8 (C), 113.8 (C), 112.3 (CH), 111.8 (CH); HRMS Calcd. for C13H9BrN2O: 287.9898. Found: 287.9890.

(Z)- 5-Acetyl-3-(1H-pyrrol-2'-yl)methylene)indolin-2-one (38) was obtained as a light brown solid; mp 132-134 oC . 1H NMR (500 MHz, DMSO-d6) δ 11.23 (brs, 1H, NH), 8.26 (d, J = 1.72 Hz, 1H, H-4), 7.95 (s, 1H, H-vinyl), 7.79 (dd, J = 1.72, 8.6 Hz, 1H, H-6), 7.35-7.37 (m, 1H, H-5'), 6.95 (d, J = 8.02 Hz, 1H, H-7), 6.85-6.88 (m, 1H, H-3'), 6.35-6.36 (m, 1H, H-4'), 2.54 (s, 3H, CH3); 13C NMR (500 MHz, DMSO-d6) δ 197.3 (CO), 170.1 (CO), 143.2 (C), 131.2 (C), 130.1 (CH), 128.4 (CH), 128.3 (CH), 127.0 (CH), 125.8 (C), 121.9 (CH), 119.4 (CH), 116.0 (CH), 112.3 (CH), 109.7 (CH), 27.0 (CH3); HRMS Calcd for C15H12N2O2: 252.0899. Found: 252.0905.

(Z)-5-Nitro-3-(1H-pyrrol-2-yl)methylene)indolin-2-one (39) was obtained as a yellow solid; mp 308-310 oC. The1H NMR spectrum was identical to that previously reported [5]; 13C NMR (500 MHz, DMSO-d6) δ 170.1 (CO), 144.5 (C), 142.7 (C), 130.15(CH), 130.1 (C), 128.2 (CH), 126.6 (C), 123.4 (CH), 123.2 (CH), 114.6 (CH), 112.7 (CH), 109.9 (CH).

(Z)-5-Fluoro-(pyrrol-2'-yl)methylene)indoline-2-one (40) was obtained as a yellow solid; mp 240-243 oC. 1H NMR (400 MHz, DMSO-d6) δ 13.35 (s, 1H, NH-1'), 10.90 (s, 1H, NH-1), 7.85 (s, 1H, H-vinyl), 7.70 (d, J = 2.5 Hz, 1H, H-4), 7.38-7.40 (m, 1H, H-5'), 7.10 (dd, J = 2.5, 8.05 Hz, 1H, H-6), 6.95 (d, J = 8.05 Hz, 1H, H-7), 6.85 (dd, J = 1.60, 3.45 Hz, 1H, H-3'), 6.37-6.39 (m, 1H, H-4'); 13C NMR (400 MHz, DMSO-d6) δ 170.1 (CO), 160.1 (C), 135.9 (C), 130.3 (C), 128.6 (CH), 127.8 (CH), 121.9 (CH), 117.2 (C), 113.9 (C), 113.6 (CH), 112.6 (CH), 111.0 (C), 106.5 (CH); HRMS Calcd. for C13H9FN2O: 228.0699. Found: 228.0705.

(Z)-3-(Thien-2'-ylmethylene)indolin-2-one (41) was obtained as a light yellow solid; mp 210 oC (Lit. [10] 210 oC). 1H NMR (500 MHz, DMSO-d6) δ 10.58 (s, 1H, NH-1), 8.13 (d, J = 8.05 Hz, 1H, H-4), 7.96 (s, H, H-vinyl), 7.75-7.79 (m, 2H, H-2',4'), 7.25-7.28 (m, 2H, H-5,6), 7.00 (t, J = 7.45 Hz, 1H, H-3'), 6.89 (d, J =6.25 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 169.7 (CO), 143.1 (C), 137.6 (CH), 136.6 (C), 132.5 (CH), 130.4 (CH), 129.1 (CH), 127.6 (CH), 123.9 (C), 123.7 (CH), 121.7 (CH), 121.4 (C), 110.5 (CH); HRMS Calcd. for C13H8NOS: 226.0327. Found: 226.0337.

(Z)-5-Nitro-3-(thien-2'-ylmethylene) indolin-2-one (42) was obtained as a yellow solid; mp 291-293 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.28 (brs, 1H, NH), 8.63 (d J = 2.29 Hz, H-4), 8.52 (s, 1H, H-vinyl), 8.10 (dt, J = 2.29, 8.55Hz, 1H, H-6), 7.97-7.98 (m, 2H, H-3',5'), 7.24-7.26 (m, 1H, H-4'), 6.99 (dd, J = 8.55 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 168.0 (CO), 146.2 (C), 142.4 (C), 139.8 (CH), 137.6 (C), 136.7 (CH), 132.5 (CH), 128.4 (CH), 125.7 (C),125.2 (CH), 119.7 (C), 115.7 (CH), 109.9 (CH); HRMS Calcd for C13H8N2O3S: 272.0256. Found: 272 0268.

(Z)-5-Bromo-3-(thien-2'-ylmethylene)indolin-2-one (43) was obtained as a yellow solid; mp 265-266 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.69 (brs, 1H, NH), 8.22 (s, 1H, H-vinyl), 7.89-7.90 (m, 3H, H-4, H-3',5'), 7.31 (dd, J = 2.29, 8.05 Hz, 1H, H-6), 7.21-7.22 (m, 1H, H-4'), 6.77 (d, J = 8.02 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 167.4 (C), 139.9 (C), 138.8 (CH), 137.7 (C), 135.7 (CH), 131.0 (CH), 130.6 (CH), 128.2 (CH), 122.7 (CH), 120.9 (C), 113.5 (C), 111.8 (CH); HRMS Calcd. for C13H8BrNOS: 304.9510. Found: 304.9518.

(Z)-5-Fluoro-3-(thien-2'-ylmethylene)indolin-2-one (44) was obtained as a light yellow solid; 188-190 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.58 (s, 1H, NH-1), 8.15 (s, 1H, H-vinyl), 7.90-7.92 (m, 2H, H-2',4'), 7.56 (d, J = 9.15 Hz, 1H, H-4), 6.99 (t, J = 4.0 Hz, 1H, H-3'), 6.98 (dt, J = 1.20, 7.45 Hz, 1H, H-6), 6.79 (d, J = 7.45 Hz, 1H, H-7); 13C NMR (500 MHz, DMSO-d6) δ 167.8 (CO), 159.3 (C), 138.6 (CH), 137.7 (C), 137.1 (C), 135.5 (CH), 130.2 (CH), 128.2 (CH), 121.8 (C), 115.2 (CH), 110.7 (CH), 107.4 (CH); HRMS Calcd. for C13H8FNO2: 229.0539. Found: 229.0548.

(E)-3-(Furan-2'-ylmethylene)indoline-2-one (45) was obtained as a red solid; mp 178-181 oC (lit [10], mp 183). 1H NMR identical to that previously reported [10]; 13C NMR (500 MHz, DMSO-d6) δ 169.6 (CO), 151.0 (C), 147.9 (CH), 142.9 (C), 130.3 (CH), 125.1 (CH), 122.0 (CH), 121.4 (CH), 121.6 (C), 121.2 (C), 119.9 (CH), 114.1 (CH), 110.3 (CH); 169.6 (CO), 151.0 (C), 147.9 (CH), 142.9 (C), 130.3 (CH), 125.1 (CH), 122.0 (CH), 121.4 (CH), 121.6 (C), 121.2 (C), 119.9 (CH), 114.1 (CH), 110.3 (CH).

(E)- 5-Bromo-3-(furan-2'-ylmethylene)indolin-2-one (46) was obtained as a solid; mp 247-249 oC. 1H NMR (500 MHz, DMSO-d6) δ 10.68 (brs, 1H, NH), 8.39 (d, J = 1.72 Hz yellow, 1H, H-4), 8.22 (d, J = 1.15 Hz, 1H, H-5'), 7.40 (dd, J = 2.29, 8.0 Hz, 1H, H-6), 7.36 (s, 1H, H-vinyl), 7.30 (d, J = 3.44 Hz, 1H, H-3'), 6.80-6.81 (m, 2H, H-4', H-7); 13C NMR (500 MHz, DMSO-d6) δ 169.4 (CO), 151.0 (C), 148.4 (CH), 142.1(C), 132.4 (CH), 127.0 (CH), 123.9 (C), 122.6 (CH), 121.3 (C), 121.2 (CH), 114.3 (CH), 113.6 (C), 112.0 (CH).

(E)-3-(Furan-2'-ylmethylene)-5-nitroindolin-2-one (47) was obtained as a light green solid; mp 312-314 oC. 1H NMR (500 MHz, DMSO-d6) δ 11.27 (brs, 1H, NH), 9.14 (d, J = 2.29 Hz, 1H, H-4), 8.27 (d, J = 1.72 Hz, 1H, H-5'), 8.18 (dd, J = 2.29, 9.1 Hz, 1H, H-6), 7.49 (s, 1H, H-vinyl), 7.40 (d, J = 3.57 Hz, 1H, H-3'), 7.03 (d, J = 8.59 Hz, 1H, H-7), 6.84-6.85 (m, 1H, H-4'); 13C NMR (500 MHz, DMSO-d6) δ 170.0 (CO), 150.9 (C), 148.9 (CH), 148.5(C), 142.4 (C), 126.4 (CH), 123.7 (CH), 122.4 (CH), 122.0 (C), 120.3 (C), 119.8 (CH), 114.6 (CH), 110.1 (CH); HRMS Calcd. for C13H8N2O4: 256.0484. Found: 256.0491.

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Received: October 24, 2008 Revised: November 20, 2008 Accepted: November 24, 2008