

# 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 <sup>1</sup>HNMR, <sup>13</sup>C NMR, 1D and 2D NOE analysis, and HRMS. An investigation of the effect of certain 5-substituents on the *E* to *Z* ratios in DMSO-*d*<sub>6</sub> 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 neuronal 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 com-

mercially 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.

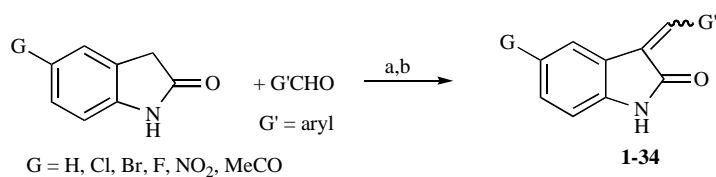
## Chemical Synthesis of 3-(benzylidene)indolin-2-ones

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 <sup>13</sup>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.

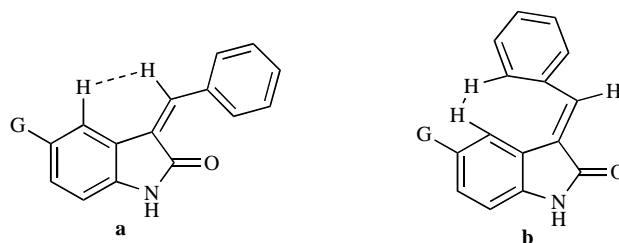
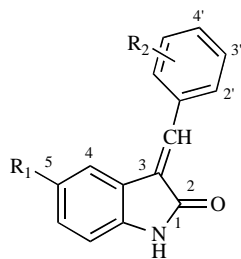
The minor isomers were ignored. The *Z* configured compounds showed NOE between the proton at the C-4 position and the vinyl proton (see Fig. 1a), whereas the *E*-configured compounds showed NOE between the C-4 and hydrogen at the C-2' (or C-6') (see Fig. 1b). The *E* configuration of 5-chloro-3-(2',6'-dichlorobenzylidene)indolin-2-one (**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	Substituent	Ratio, 2,6'-H Chemical Shifts				Total Yield, %	Major Isomer Configuration
		R <sub>2</sub>	Z:E	Z	E		
1	H	3',5'-Br-4'-OH	10:90 <sup>a</sup>	8.78	7.87	76	<i>E</i>
2	H	3',5'-Br	11:89	8.69	7.85	83	<i>E</i>
3	H	3',4',5'-OMe	90:10	7.98	7.03	88	<i>Z</i>
4	H	CH=CH-C <sub>6</sub> H <sub>4</sub>	50:50	7.75	7.40	b	-
5	H	2',6'-Cl	c	-	-	83	<i>E</i> <sup>d</sup>
6	H	2-NO <sub>2</sub>	80:20	7.76	6.98	81	<i>Z</i>
7	Cl	3',5'-Br-4'-OH	5:95 <sup>e</sup>	8.74	7.87	80	<i>E</i>
8	Cl	3',5'-Br	82:18	8.59	7.79	85	<i>Z</i>
9	Cl	3',5'-Br-4'-OAc	18:82	8.49	7.84	88	<i>E</i>
10	Cl	3',4',5'-OMe	77:23	7.97	7.02	90	<i>Z</i>
11	Cl	2',6'-Cl	c	-	-	92	<i>E</i> <sup>d</sup>
12	Cl	H	6:94	8.30	7.69	94	<i>E</i>
13	Cl	4'-CH <sub>3</sub>	20:80	8.49	7.56	86	<i>E</i>
14	Cl	4'-OMe	4:96	8.55	7.69	87	<i>E</i>
15	Cl	4'-NMe <sub>2</sub>	4:96	8.46	7.63	84	<i>E</i>
16	Br	3',5'-Br-4'-OH	5:95 <sup>e</sup>	8.74	7.55	78	<i>E</i>
17	Br	3',5'-Br	91:9	8.59	7.57	81	<i>Z</i>

(Table 1). Contd.....

ID	Substituent R <sub>1</sub>	Ratio, 2',6'-H Chemical Shifts				Total Yield, %	Major Isomer Configuration
		R <sub>2</sub>	Z:E	Z	E		
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 <sub>2</sub>	10:90	8.43	7.59	81	E
21	NO <sub>2</sub>	3',5'-Br-4'-OH	70:30 <sup>b</sup>	8.77	8.01	78	Z
22	NO <sub>2</sub>	3',5'-Br	90:10	8.63	7.72	80	Z
23	NO <sub>2</sub>	3',4',5'-OMe	88:12	8.07	7.16	83	Z
24	NO <sub>2</sub>	2',6'-Cl	c	-	-	85 <sup>d</sup>	E
25	NO <sub>2</sub>	H	90:10	8.40	7.33	80	Z
26	NO <sub>2</sub>	CH=CH-C <sub>6</sub> H <sub>5</sub>	9:91	7.79	7.59	81	E
27	NO <sub>2</sub>	CH=CH-C <sub>6</sub> H <sub>4</sub> -2'NO <sub>2</sub>	11:89	8.16	7.86	83	E
28	NO <sub>2</sub>	4'-Me	92:8	8.33	7.67	80	Z
29	NO <sub>2</sub>	4'-NMe <sub>2</sub>	90:10	8.48	7.68	81	Z
30	F	3',5'-Br-4'-OH	5:95 <sup>e</sup>	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 <sup>b</sup>	8.80	7.96	74	Z

<sup>a</sup>Z:E ratios were calculated on integral peak heights of the 2',6'-H signals. <sup>b</sup>Configuration, unless not stated, was determined by 1D NOE analysis. <sup>c</sup>Z/E ratio can not be determined by NOE analysis. <sup>d</sup>Configuration determined by analogy and comparison of spectral data to that of reference compound **11**. <sup>e</sup>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'-benzylidene) isomers were assigned to the *E* confirmation on the basis of analogy and the similarity of their <sup>1</sup>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-

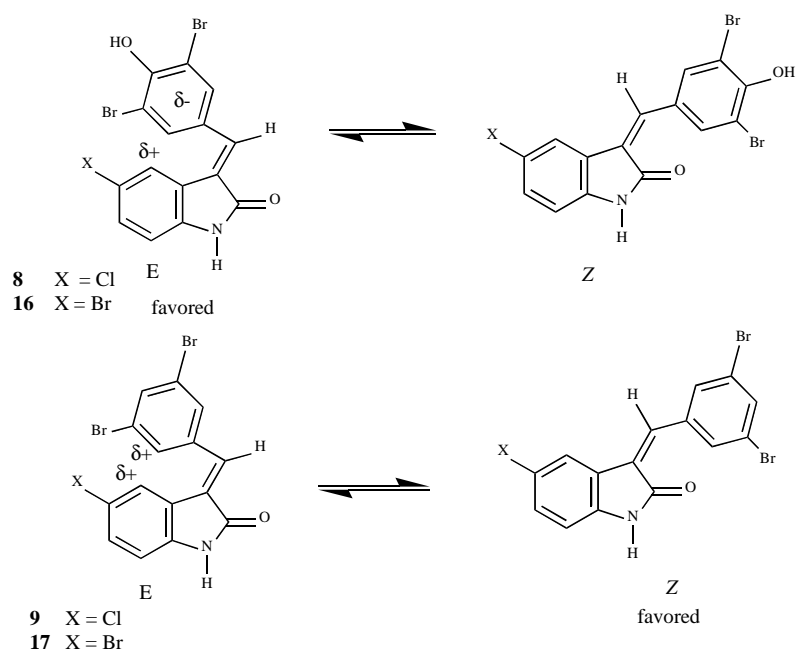
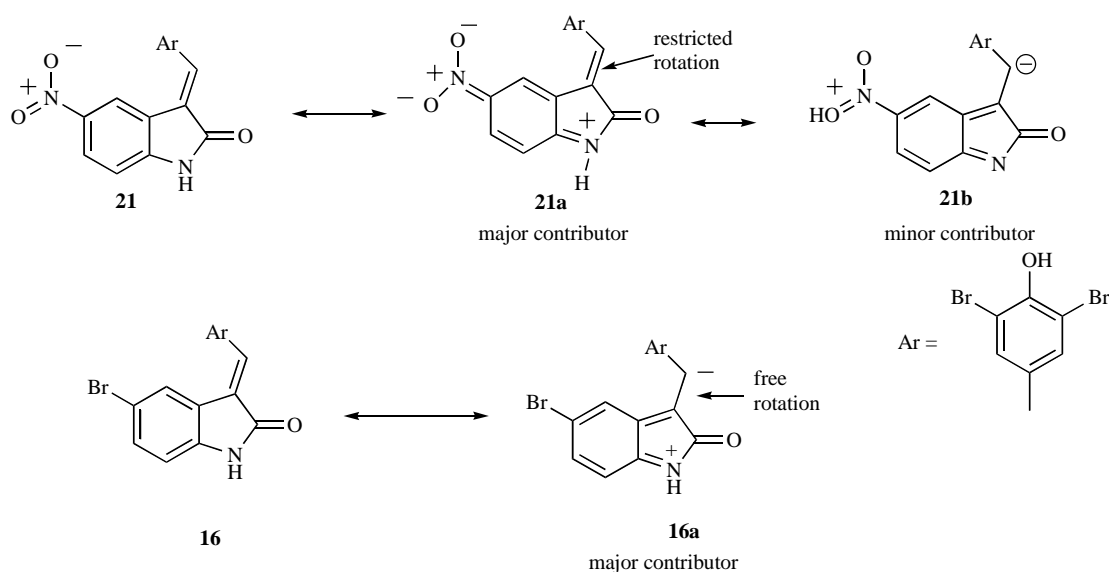


Fig. (2).





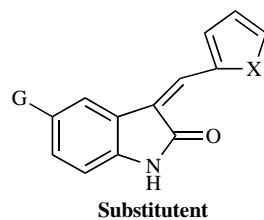
Scheme 2.

### 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



Entry	G	X	% Z <sup>a</sup>	% E <sup>b</sup>	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 <sub>2</sub>	N	100	0	80
40	F	N	100	0	85
41	H	S	100	0	80
42	NO <sub>2</sub>	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 <sub>2</sub>	O	0	100	83

<sup>a</sup>2D NOE observed between the H-vinyl and C-4 hydrogen. <sup>b</sup>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*<sub>6</sub>) or by 2D NOE analysis (if the compounds are stable in DMSO-*d*<sub>6</sub>). 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

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## EXPERIMENTAL SECTION

Melting points were taken on a Mel-Temp apparatus and are uncorrected. NMR spectra were recorded on a Bruker-400MHz and/or JEOL-500MHz Spectrometer. Chemical shifts are reported in parts per million ( $\delta$ ) 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 precipi-

tate 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'-furyl) 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. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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); <sup>13</sup>C NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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 C<sub>15</sub>H<sub>9</sub>Br<sub>2</sub>NO<sub>2</sub>: 392.9000. Found: 392.2002.

(*E*)-3-(3', 5'-Dibromobenzylidene)indolin-2-one (**2**) was obtained as a yellow solid; mp 245-247 oC. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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); <sup>13</sup>C NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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 C<sub>15</sub>H<sub>10</sub>Br<sub>2</sub>NO: 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. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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, 2xOCH<sub>3</sub>), 3.71 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  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 (OCH<sub>3</sub>), 56.4

(OCH<sub>3</sub>); HRMS Calcd. for C<sub>18</sub>H<sub>17</sub>NO<sub>4</sub>: 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'-Dichlorobenzylidene)indolin-2-one (5) was obtained as a red solid; mp 179-181 oC (lit. [10] 164 oC). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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). <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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). <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Br<sub>2</sub>ClNO<sub>2</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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; <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>9</sub>Br<sub>2</sub>ClNO: 411.3719. Found: 411.3713.

(E)-2,6-Dibromo-4-(5'-chloro-2'-oxoindolin-3-ylidene)methylphenyl acetate (9) was obtained as a light brown solid; mp 148-150 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>17</sub>H<sub>10</sub>Br<sub>2</sub>ClNO<sub>3</sub>: 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. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) 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, 2xOCH<sub>3</sub>), 3.68 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) 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 (OCH<sub>3</sub>), 56.7 (OCH<sub>3</sub>); HRMS Calcd. for C<sub>18</sub>H<sub>16</sub>ClNO<sub>4</sub>: 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. <sup>1</sup>H NMR (400 MHz DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) 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. <sup>1</sup>H NMR (400 MHz DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>10</sub>ClNO: 255.0451. Found: 255.0459.

(E)- 5-Chloro-3-(4'-methoxybenzylidene)indolin-2-one (13) was obtained as a light yellow solid; mp 220-223 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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, CH<sub>3</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 (CH<sub>3</sub>); HRMS Calcd. for C<sub>16</sub>H<sub>12</sub>ClNO: 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. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) 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, OCH<sub>3</sub>); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) 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 (OCH<sub>3</sub>); HRMS Calcd. for C<sub>16</sub>H<sub>12</sub>ClNO<sub>2</sub>: 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. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) 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(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) 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(CH<sub>3</sub>)<sub>2</sub>); HRMS Calcd. for C<sub>17</sub>H<sub>15</sub>ClN<sub>2</sub>O: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Br<sub>3</sub>NO<sub>2</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Br<sub>3</sub>NO: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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, 2XOCH<sub>3</sub>), 3.72 (s, 3H, OCH<sub>3</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 (CH<sub>3</sub>), 56.4 (CH<sub>3</sub>); HRMS Calcd. for C<sub>18</sub>H<sub>16</sub>BrNO<sub>4</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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, OCH<sub>3</sub>). HRMS Calcd. for C<sub>16</sub>H<sub>12</sub>BrNO<sub>2</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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(CH<sub>3</sub>)<sub>2</sub>). HRMS Calcd. for C<sub>17</sub>H<sub>15</sub>BrN<sub>2</sub>O: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>4</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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,

2XOCH<sub>3</sub>), 3.74 (s, 3H, OCH<sub>3</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 (CH<sub>3</sub>), 56.5 (CH<sub>3</sub>), 56.3 (CH<sub>3</sub>); HRMS Calcd. for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>8</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>17</sub>H<sub>11</sub>N<sub>3</sub>O<sub>5</sub>: 337.0699. Found: 337.0689.

(Z)-3-(4'-Methylbenzylidene)-5-nitroindolin-2-one (28) was obtained as a yellow solid; mp 263-265 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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, CH<sub>3</sub>). HRMS Calcd. for C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 (CH<sub>3</sub>), 40.1 (CH<sub>3</sub>); HRMS Calcd. for C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: 309.1113. Found: 309.1120.

(E)-3-(3', 5'-Dibromo-4'-hydroxybenzylidene)-5-fluoroindolin-2-one (30) was obtained as a yellow solid; mp 173-175 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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,  $J = 4.8, 8.60$  Hz, 1H, H-6); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>15</sub>H<sub>8</sub>Br<sub>3</sub>N<sub>2</sub>O: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>15</sub>H<sub>8</sub>Br<sub>2</sub>FNO: 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. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  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, 2xOCH<sub>3</sub>), 3.64 (s, 3H, OCH<sub>3</sub>); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 (OCH<sub>3</sub>), 56.9 (OCH<sub>3</sub>); HRMS Calcd. for C<sub>18</sub>H<sub>16</sub>FNO<sub>4</sub>: 329.1063. Found: 329.1073.

(E)-3-Benzylidene-5-fluoroindolin-2-one (33) was obtained as a yellow solid; mp 195-198 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>15</sub>H<sub>10</sub>FNO: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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, CH<sub>3</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 (CH<sub>3</sub>); HRMS Calcd. for C<sub>17</sub>H<sub>11</sub>Br<sub>2</sub>NO: 434.9106. Found: 434.9120.

(Z)-3-(1H-Pyrrol-2'-yl)methyleneindolin-2-one (35) was obtained as a light yellow solid; mp 194-196 OC. The <sup>1</sup>H NMR was identical to that reported previously [5]; <sup>13</sup>C NMR

(500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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)methyleneindoline-2-one (36) was obtained as a orange red solid; mp 260-262 oC. <sup>1</sup>H NMR spectra was identical to that reported previously [5]; <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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'); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>13</sub>H<sub>9</sub>BrN<sub>2</sub>O: 287.9898. Found: 287.9890.

(Z)- 5-Acetyl-3-(1H-pyrrol-2'-yl)methyleneindolin-2-one (38) was obtained as a light brown solid; mp 132-134 oC. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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, CH<sub>3</sub>); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 (CH<sub>3</sub>); HRMS Calcd for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: 252.0899. Found: 252.0905.

(Z)-5-Nitro-3-(1H-pyrrol-2'-yl)methyleneindolin-2-one (39) was obtained as a yellow solid; mp 308-310 oC. The <sup>1</sup>H NMR spectrum was identical to that previously reported [5]; <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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)methyleneindoline-2-one (40) was obtained as a yellow solid; mp 240-243 oC. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  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'); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>13</sub>H<sub>9</sub>FN<sub>2</sub>O: 228.0699. Found: 228.0705.

(Z)-3-(Thien-2'-yl)methyleneindolin-2-one (41) was obtained as a light yellow solid; mp 210 oC (Lit. [10] 210 oC). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>)  $\delta$  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 C<sub>13</sub>H<sub>8</sub>NOS: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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, 8.55 Hz, 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>S: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>13</sub>H<sub>8</sub>BrNOS: 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>13</sub>H<sub>8</sub>FNO<sub>2</sub>: 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). <sup>1</sup>H NMR identical to that previously reported [10]; <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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. <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 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'); <sup>13</sup>C NMR (500 MHz, DMSO-d<sub>6</sub>) 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 C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>4</sub>: 256.0484. Found: 256.0491.

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