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Vilsmeier-Haack reagent: A facile synthesis of 2-(4-chloro-3,3-dimethyl-7-phenoxyindolin-2-ylidene)malonaldehyde and transformation into different heterocyclic compounds

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2-(5-Chloro-2-phenoxyphenyl)hydrazine was converted to corresponding 3H-indole by Fischer method utilizing the isopropyl methyl ketone in acetic acid. The reaction of 3H-indole with Vilsmeier-Haack reagent furnished aminomethylene malonaldehyde in excellent yield while the reactions of malonaldehyde with hydrazine, arylhydrazines, amines, cyanoacetamide and hydroxylamine hydrochloride, led to the corresponding pyrazole derivatives, enamines, cyanopyridone, and cyanoacetamide derivatives respectively.

1. Introduction

Chloromethyleneiminium salts, commonly known as highly versatile Vilsmeier-Haack reagent,[1] usually generated *in situ* by the treatment of $POCl_3$ with an *N*,*N*-disubstituted formamides (*e.g.,* DMF), is very useful in the synthetic transformations. Selected applications of this reagent include: formylation,[2,3] cyclohaloaddition,[4] cyclization[5] and ring annulations.[6] A wide variety of alkene derivatives,[7] carbonyl compounds,[8] activated methyl and methylene groups bearing chemicals,[9] and oxygen[10] as well as nitrogen nucleophiles[11] undergo the reactions with Vilsmeier reagent to yield the corresponding iminium salts.

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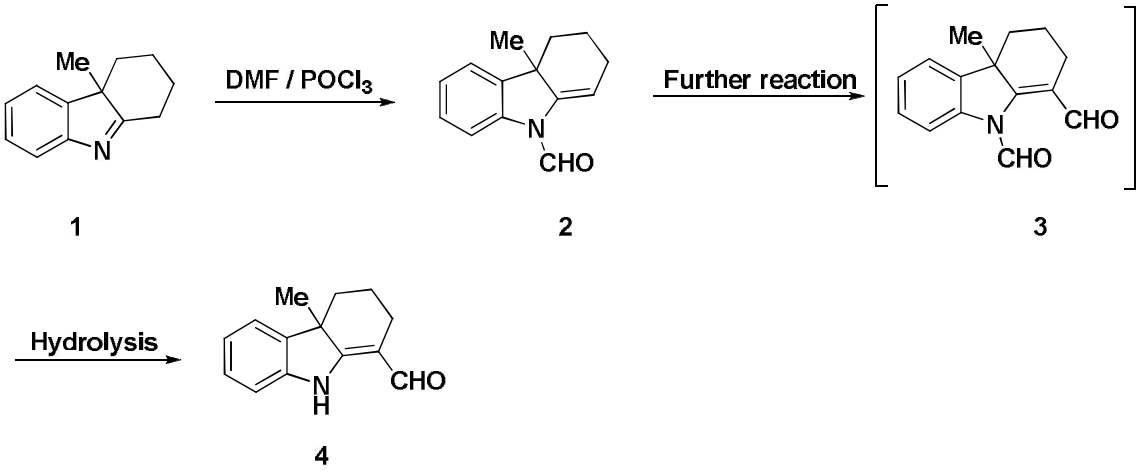
In 1959, Fritz[12] reported the *N*-formylation of a 3,3-disubstituted 3*H*-indole (indolenine) **1** leading to **2** by utilization of Vilsmeier reagent formed from DMF and $POCl_3$. Further reaction of **2** with the Vilsmeier reagent, followed by hydrolysis produced compound **4**. Formation of this product probably involves the intermediate **3**, from which the *N*-formyl group is hydrolytically removed during work-up (**Scheme 1**).

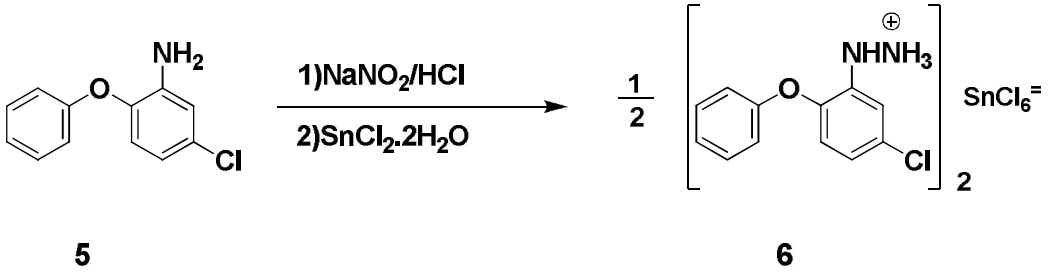


Scheme 1

Recently, we demonstrated[13-15] that the 2-CH_3 formylation reaction of some of 2,3,3-trimethylindolenines (3*H*-indoles) by Vilsmeier reagent furnished aminomethylene malonaldehydes. Thus formed 1,3-dialdehyde compounds undergo reaction with various nucleophiles to yield a wide range of new heterocyclic compounds. As an extension of our previous studies, herein we demonstrated the formylation of another indolenine to produce corresponding malonaldehyde as well as synthesis of various heterocyclic compounds by condensations of malonaldehyde with various arylhydrazines and cyanoacetamide leading to both 5- and 6-membered heterocycles, respectively.

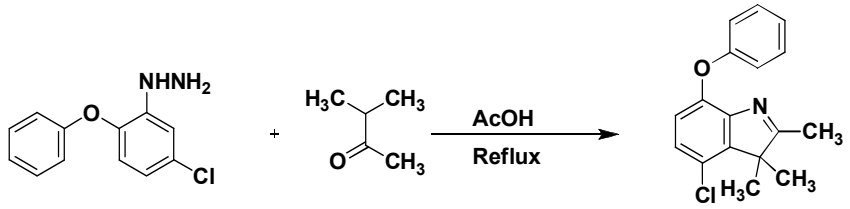
2. Results and Discussion

5-Chloro-2-phenoxyaniline **5** was diazotized with $NaNO_2$/HCl. The formed diazonium salt was then reduced by stannous chloride dihydrate in $HCl_{(aq)}$ to produce the corresponding bis- hydrazinium hexachloro stannate **6**, revealed by atomic absorption analysis,. A neutralization of obtained reaction mixture by NaOH(aq.) furnished free base of aryl hydrazine **7** (**Scheme 2**).



Scheme 2

Reaction of **7** with isopropyl methyl ketone in a Fischer reaction condition furnished the 3*H*-indole **8** in a good yield (**Scheme 3**).

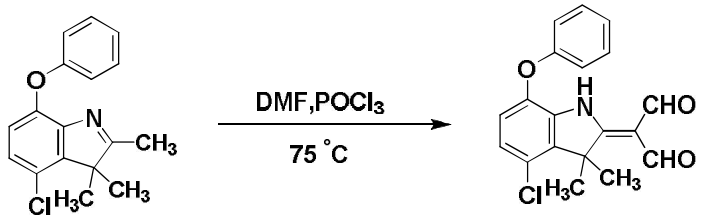


7 8

Scheme 3

The structure of 3*H*-indole **8** was confirmed on the basis of analysis of ^{1}H-NMR spectrum possessing six-hydrogen singlets for the geminal methyl groups, at δ 1.55 ppm and three-hydrogen singlet signals for the imine-methyl group, at δ 2.29 ppm.

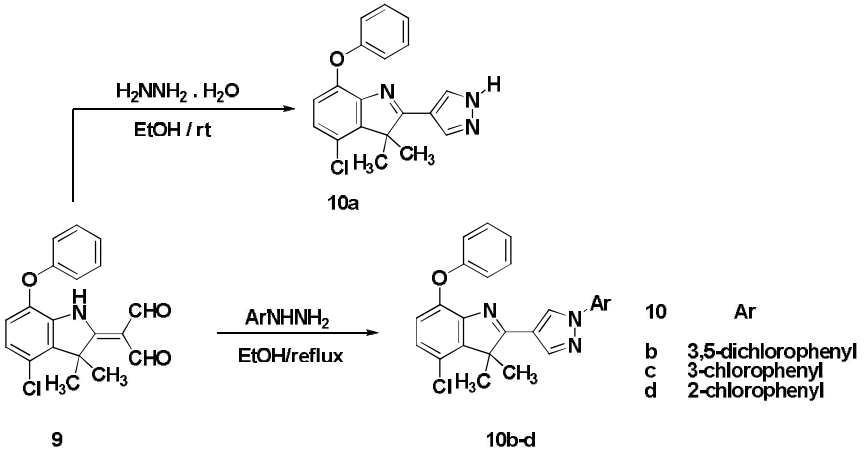
The reaction of **8** with Vilsmeier reagent at 75°C, led to diformylation of imine-methyl group in excellent yield (**Scheme 4**). The structure of malonaldehyde **9** was confirmed by its spectral data. The IR absorptions at 3159 and 1675 ,1639 cm^{-1} support a presence of N-H and two carbonyl groups, thus in ^{1}H-NMR spectrum signal for the *N*-hydrogen appearing at δ 13.55 ppm and two aldehyde hydrogens at δ 9.75 ppm. The ^{13}C-NMR spectrum of **9** showed the presence of two carbon signals at 187.66 and 192.64 ppm corresponding to CHO groups.



8 9

Scheme 4

1,3-Dicarbonyl compounds can be used as important building blocks in the syntheses of various heterocycles[16] , which often show high biological activities[16,17]. The reaction of the substrate **9** with hydrazine hydrate and substituted arylhydrazines at room temperature and reflux conditions, respectively, afforded desired products **10a-d** in quantitative yields (**Scheme 5**).

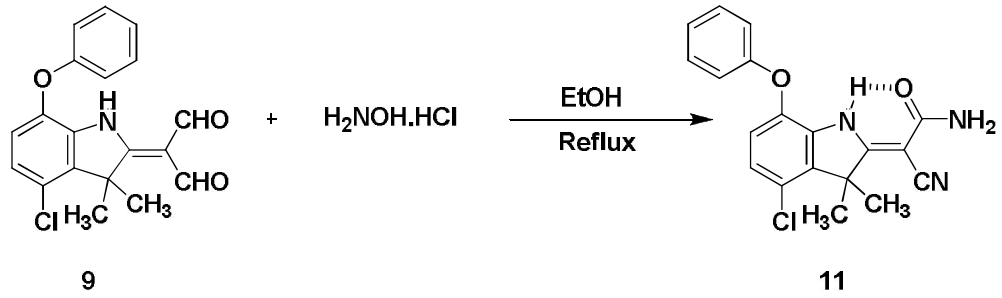


9 10b-d

Scheme 5

As extension of this work, we also examined the reactions of hydroxylamine hydrochloride, cyanoacetamide and arylamines with aminomethylene malonaldehyde **9**.

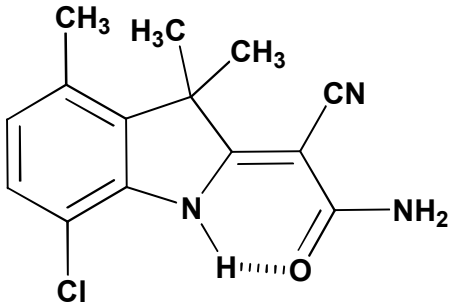
The corresponding cyanoacetamide derivative **11** was readily achieved by refluxing a mixture of malonaldehyde **9** and hydroxylamine hydrochloride in ethanol (**Scheme 6**).



9 **11**

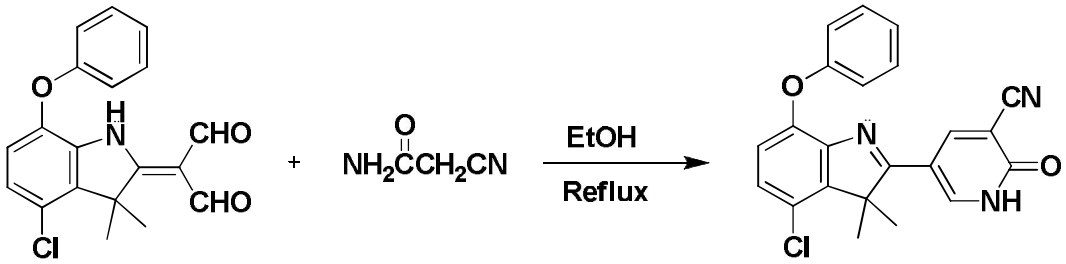
Scheme 6

The X-ray diffraction data for similar compound[18] showed that the orientation of the acetamide group arises from intramolecular hydrogen bonding between the indole N-H and the carbonyl group (**Scheme 7**).



Scheme 7

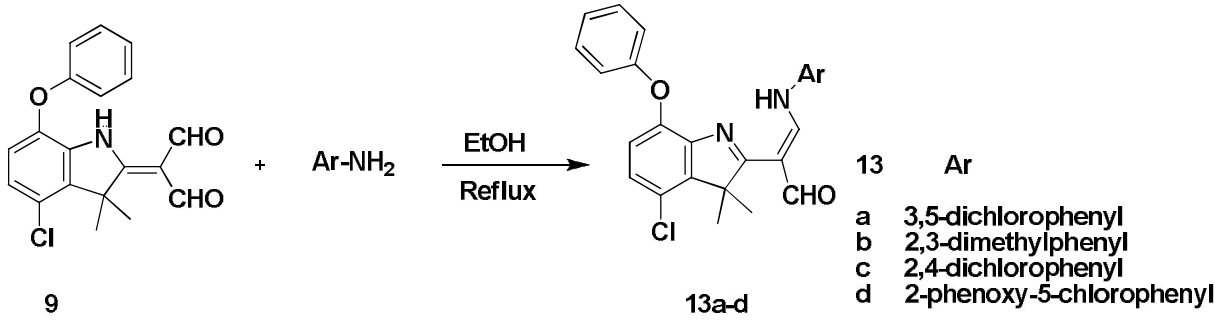
The compound **9** was allowed to react with cyanoacetamide under reflux condition in ethanol to obtain cyanopyridone derivative **12**. The structure of compound **12** was elucidated from its spectral data. The ^{1}H-NMR spectrum showed two singlet at δ 8.42 and 8.66 ppm respectively, belonged to two protons of pyridone. The broad singlet appearing around δ 13.07 ppm confirmed the presence of pyridone N-H bond (**Scheme 8**).



9 **12**

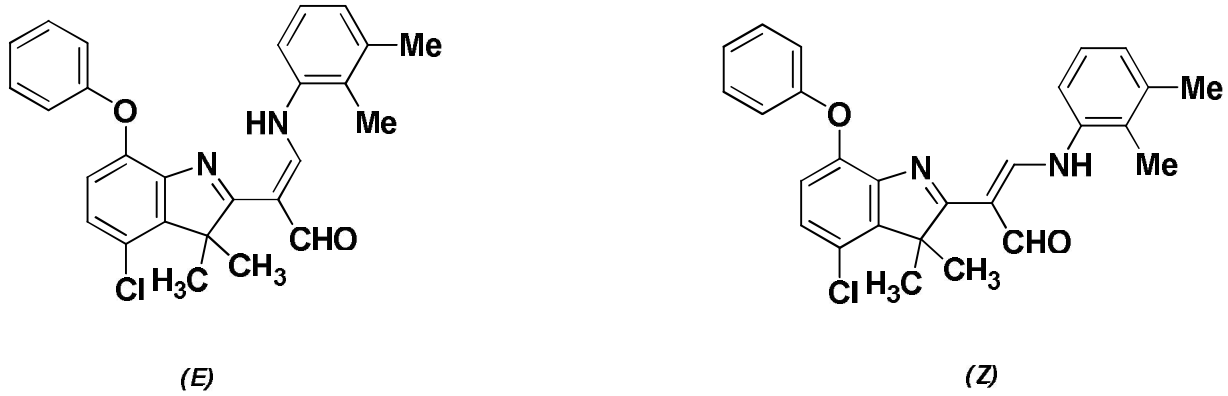
Scheme 8

Finally, attempt to synthesis quinoline derivatives starting from arylamines and malonaldehyde **9** was unsuccessful but this condensation gave enamines **13a-d** in high yields (**Scheme 9**).



Scheme 9

A study of the ^{1}H-NMR spectrum of enamine **13b** showed that both *E* and *Z* isomers of 13b have been formed in a ratio 1:1. Thus, there were two singlets at δ 8.39 and δ 8.43 ppm in a ratio 1:1, corresponding to CH=N and a pair of siglets at δ 14.08 and δ 14.12 ppm, again in a ratio of 1:1 assigned to NH protons (**Scheme 10**).



Scheme 10

3. Conclusion

In summary, we have examined the reaction of 3*H*-indole with Vilsmeier-Haack reagent. This study revealed that the formed malonaldehyde from formylation reaction could be cyclized using various arylhydrazines and cyanoacetamide to afford substituted pyrazoles and cyanopyridone. Also, reaction of malonaldehyde with hydroxylamine and primary aromatic amines furnished cyanoacetamide and enamine derivatives, respectively.

Acknowledgements

The authors are grateful to the University of Urmia for financial support of this work.

4. Experimental

Melting points were measured on an electrothermal IA9200 apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance AQS 300 MHz spectrometer, at 300 MHz and 75 MHz

respectively. Chemical shifts δ are in parts per million (ppm) measured in $CDCl_3$ and DMSO-d_6 as solvents and related to TMS as the internal standard. IR spectra were recorded on a Thermonicolet-Nexus 670 FT-IR instrument. Elemental analyses were performed on Heraeus CHN-O rapid analyzer.

4-Chloro-2,3,3-trimethyl-7-phenoxy-3*H*-indole (8).

A mixture of arylhydrazine **7** (5 g, 21 mmol) and isopropyl methyl ketone (2.01 g, 23 mmol) was heated at reflux in acetic acid (20 mL) overnight and then cooled, diluted with H_2O (50 mL), and neutralized with NaOH solution (2N), the aqueous solution was extracted with EtOAc (3×30 mL). The combined organic layers dried over Na_2SO_4 and solvent was evaporated to give 14 (4g, 65%) as a viscous oil which was solidified on standing; FT-IR (KBr) ν_{max}/cm^{-1}: 3065, 2969, 2930, 2869,1592, 1261, 752; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.55 (s, 6H, 2×CH_3), 2.29 (s, 3H, ×CH_3), 6.74 (d, *J*=8.7 Hz, 1H), 7.01 (d, *J*=8.7 Hz, 1H), 7.07-7.13 (m, 3H), 7.36 (t, *J*=8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.36, 20.44, 55.47, 116.75, 117.37, 118.66, 122.97, 125.67, 129.05, 142.25, 146.28, 155.70, 187.72; Anal. Calcd. for $C_{17}H_{16}ClNO$: C, 71.45%; H, 5.64%;N, 4.90%. Found: C, 71.38; H, 5.40%; N, 4.82%.

2-(4-Chloro-3,3-dimethyl-7-phenoxyindolin-2-ylidene)malonaldehyde (9).

To *N,N*-dimethyl- formamide (3.5 mL, 45.6 mmol) cooled in an ice bath was added dropwise phosphorus oxychloride (2.08 mL, 22.8 mmol) with stirring at below 5 °C. After that addition, 3H-indole **8** (2.18 g, 7.6 mmol) was added slowly. The cooling bath was removed and the reaction mixture was stirred at 75 ^{o}C for 6 h. The resulting solution was added to ice-cooled water and made alkaline with NaOH (aq.) solution (pH = 8-9). The resulting precipitate was collected by filtration, dried in air and recrystallized from ethanol to give yellow crystals. Yield 84%; mp 178-180 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3159, 3067, 2978, 2937, 2733, 1675, 1639, 1259, 767; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.95 (s, 6H, 2×CH_3), 6.79 (d, *J*=8.7 Hz, 1H), 7.05 (d, *J*=8.7 Hz, 1H), 7.09 (d, *J*=7.8, 2H), 7.21 (t, *J*=7.2 Hz, 1H), 7.41 (t, *J*=7.5 Hz, 2H), 9.79 (s, 2H, 2×CHO), 13.55(bs, 1H, -NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 19.69, 53.86, 109.23, 118.37, 119.11, 123.53, 124.76, 127.32, 130.20, 131.69, 137.43, 142.36, 155.31, 178.50, 187.66, 192.64; Anal. Calcd. for $C_{19}H_{16}ClNO_3$: C, 66.77%; H, 4.72%;N, 4.10%. Found: C, 66.70; H, 7.85%; N, 4.22%.

4-Chloro-3,3-dimethyl-7-phenoxy-2-(1H-pyrazol-4-yl)-3*H*-indole (10a).

A mixture of the malonaldehyde **9** (0.1 g, 0.29 mmol) and hydrazine monohydrate (0.09 g, 1.46 mmol), in absolute ethanol (15 mL) was stirred at room temperature overnight. After this time, the solvent evaporated and ethyl acetate (20 mL) was added to the residue. The organic layer was washed with water, dried over Na_2SO_4 and solvent evaporated. Resulting yellow precipitate crystallized from ethanol. Yield 92%; mp 211-213°C; FT-IR (KBr) ν_{max}/cm^{-1}: 3160, 2973, 2934, 1593, 1569, 1472, 1259, 954, 778; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.63 (s, 6H, 2×CH_3), 6.74 (d, *J*=8.4 Hz, 1H), 7.01-7.11 (m, 4H), 7.26-7.32 (m, 2H), 8.37 (s, 2H, Pyrazole), 10.22 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 21.38, 55.95, 117.00, 118.32, 119.45, 122.95, 123.97, 126.92, 129.87, 135.25, 143.19, 144.38, 147.42, 156.39, 179.97; Anal. Calcd. for $C_{19}H_{16}ClN_3O$: C, 67.56%; H, 4.77%;N, 12.44%. Found: C, 67.70; H, 4.88%; N, 12.32%.

General procedure for synthesis of (10b-d).

A mixture of the malonaldehyde **9** (0.1 g, 0.29 mmol) and aryl hydrazinium chloride (0.29 mmol), in absolute ethanol (15 mL) was heated at reflux and stirred for 2-5 h. After cooling and concentrating the resulting crystals were collected by filtration and recrystallized from ethanol to give the corresponding pyrazoles.

4-Chloro-2-(1-(3,5-dichlorophenyl)-1H-pyrazol-4-yl)-3,3-dimethyl-7-phenoxy-3*H*-indole (10b).

Yield 71%; mp 165-168 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3119, 3087, 2974, 2933, 1591, 1467, 1258, 779; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.79 (s, 6H, 2×CH_3), 6.78 (d, *J*=7.8 Hz, 1H), 7.06 (d, *J*=7.8 Hz, 1H), 7.13-7.15 (m, 3H), 7.33-7.38 (m, 3H), 7.71 (s, 2H), 8.33 (s, 1H, Pyrazole), 8.68 (s, 1H, Pyrazole); ^{13}C NMR ($CDCl_3$): δ (ppm) 21.16, 55.59, 117.80, 118.22, 118.54, 119.56, 122.90, 123.89, 127.16, 127.87,129.79, 136.11, 140.74, 141.54, 143.42, 148.00, 156.62, 177.95; Anal. Calcd. for $C_{25}H_{18}C_{l3}N_3O$: C, 62.19%; H, 3.76%;N, 8.70%. Found: C, 62.26; H, 3.88%; N, 8.55%.

4-Chloro-2-(1-(3-chlorophenyl)-1H-pyrazol-4-yl)-3,3-dimethyl-7-phenoxy-3*H*-indole (10c).

Yield 77%; mp 143-145 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3114, 2969, 2929, 2870, 1594, 1483, 1203, 956, 771; ^{1}H NMR ($CDCl_3$): δ (ppm) δ (ppm) 1.76 (s, 6H, 2×CH_3), 6.78 (d, *J*=8.7 Hz, 1H), 7.06 (d, *J*=8.7 Hz, 1H), 7.15 (d, *J*=7.5, 2H), 7.16 (t, *J*=7.5 Hz, 1H), 7.32 (d, *J*=8.1 Hz, 1H), 7.38 (t, *J*=8.7, 1H), 7.42 (t, *J*=7.2, 2H), 7.65 (d, *J*=8.1, 1H), 7.84 (s, 1H), 8.33 (s, 1H, Pyrazole), 8.73 (s, 1H, Pyrazole); ^{13}C NMR ($CDCl_3$): δ (ppm) 21.26, 55.92, 117.27, 117.53, 118.53, 119.56, 119.82, 122.89, 123.90, 127.18, 127.43, 128.33, 129.79, 130.68, 135.48, 140.24, 141.21, 143.25, 147.84, 156.58, 178.32; Anal. Calcd. for $C_{25}H_{19}Cl_2N_3O$: C, 66.97%; H, 4.27%;N, 9.37%. Found: C, 66.82; H, 4.38%; N, 9.55%.

4-Chloro-2-(1-(2-chlorophenyl)-1H-pyrazol-4-yl)-3,3-dimethyl-7-phenoxy-3H-indole (10d).

Yield 62%; mp 123–125 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3125, 3068, 2974, 2932, 2875, 1567, 1487, 1248, 954, 753; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.74 (s, 6H, 2×CH_3), 6.78 (d, *J*=8.7 Hz, 1H), 7.04 (d, *J*=8.7 Hz, 1H), 7.12-7.15 (m, 3H), 7.34-7.43 (m, 4H), 7.55 (dd, J_o=7.5 Hz, J_m=2 Hz, 1H), 7.63 (dd, J_o=7.5 Hz, J_m=2 Hz, 1H), 8.39 (s, 1H, Pyrazole), 8.54 (s, 1H, Pyrazole); ^{13}C NMR ($CDCl_3$): δ (ppm) 20.26, 54.96, 115.77, 117.64, 118.41, 121.93, 122.67, 125.78, 126.63, 126.82, 127.28, 128.66, 128.70, 129,78, 131.10, 136.48, 140.00, 142.65, 144.65, 146.84, 155.82, 177.44; Anal. Calcd. for $C_{25}H_{19}Cl_2N_3O$: C, 66.97%; H, 4.27%;N, 9.37%. Found: C, 66.82; H, 4.38%; N, 9.55%.

(*Z*)-2-(4-Chloro-3,3-dimethyl-7-phenoxyindolin-2-ylidene)-2-cyanoacetamide (11).

A solution of malonaldehyde **9** (0.1 g, 0.29 mmol) and hydroxylamine hydrochloride (0.02 g, 0.29 mmol) in absolute ethanol (15 mL) was refluxed for 2 hr. After this time, a solution standing overnight and then yellow precipitate was filtered off, washed with water and air- dried product was purified by recrystallization from ethanol. Yield 78%; mp 123–125 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3477, 3318, 3169, 2983, 2941, 2189, 1658, 1554, 1225, 780; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.88 (s, 6H, 2×CH_3), 5.40 (bs, H, NH_2), 5.95 (s, 1H, NH_2), 6.77 (d, *J* =8.4 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 2H), 7.17 (t, *J* = 6.3 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 11.71 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 21.03, 52.00, 69.85, 118.64, 118.80, 119.06, 123.91, 124.36, 125.34, 130.12, 133.10, 134.72, 140.68, 155.72, 168.89, 176.59; Anal. Calcd. for $C_{19}H_{16}ClN_3O_2$: C, 64.50%; H, 4.56%;N, 11.88%. Found: C, 64.76; H, 4.38%; N, 11.55%.

5-(4-Chloro-3,3-dimethyl-7-phenoxy-3*H*-indol-2-yl)-2-oxo-1,2-dihydropyridine-3-carbo- nitrile (12).

Cyanoacetamide (0.04 g, 0.48 mmol) was dissolved in hot EtOH (10 mL, 95%), then piperidine (0.11 g, 0.12 mL, 1.25 mmol) was added and the mixture was heated for 10 min. The malonaldehyde **9** (0.15 g, 0.44 mmol) was slowly added and the reaction mixture was refluxed overnight. After cooling the solution, formed precipitate was filtered off, washed with aqueous ethanol and finally dried in air. Yield 82%; mp 269-270 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3158, 3070, 2980, 2923, 2230, 1656, 1248, 753; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.63 (s, 6H, 2×CH_3), 6.91 (d, *J*=8.4 Hz, 1H), 7.03 (d, *J*=7.2 Hz, 2H), 7.13 (t, *J*=6.9, 1H), 7.22 (d, *J*=8.4, 1H), 7.31 (t, *J*=6.9, 2H), 8.42 (s, 1H, pyridine), 8.66 (s, 1H, pyridine), 13.07 (bs, 1H, -NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 20.46, 55.66, 104.84, 111.04, 116.03, 118.63,

120.51, 122.80, 123.89, 128.10, 130.44, 143.07, 144.68, 144.99, 147.25, 147.75, 157.30, 159.84, 178.85; Anal. Calcd. for $C_{22}H_{16}ClN_3O_2$: C, 67.78%; H, 4.14%;N, 10.78%. Found: C, 67.76; H, 4.28%; N, 10.55%.

General procedure for synthesis of (13a-d).

Primary aromatic amines (0.29 mmol) was added to the solution of polyphosphoric acid (0.06 g) in absolute ethanol (15 mL) at 70 °C. After 10 minutes, malonaldehyde **9** (0.29 mmol) was added to the hot solution and reaction mixture was refluxed overnight. After cooling the reaction mixture, resulting precipitate was collected, washed with ethanol and dried in air. The crude products recrystallized from ethanol.

(*E*)-2-(4-Chloro-3,3-dimethyl-7-phenoxy-3*H*-indol-2-yl)-3-(3,5-dichlorophenylamino)acryl-aldehyde (13a).

Yield 78%; mp 158-159 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3065, 2928, 1665,1629, 1487, 1250, 776; ^1H NMR ($CDCl_3$): δ (ppm) 1.86 (s, 6H, 2×CH_3), 6.69 (s, 2H), 7.00-7.17 (m, 6H), 7.35 (t, *J* =6.9 Hz, 1H), 8.24 (s, 1H, -CHO), 12-15 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 19.78, 56.40, 108.22, 115.54, 116.65, 118.37, 119.07, 122.09, 122.55, 124.88, 125.38, 127.43, 130.10, 135.99, 142.12, 143.10, 153.25, 157.44, 182.72, 186.79. Anal. Calcd. for $C_{25}H_{19}Cl_3N_2O_2$: C, 61.81%; H, 3.94%;N, 5.77%. Found: C, 61.68; H, 3.85%; N, 5.65%.

2-(4-Chloro-3,3-dimethyl-7-phenoxy-3H-indol-2-yl)-3-(2,3-dimethylphenylamino)acryl aldehyde (13b).

Yield 92%; mp 115-117 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3065, 2971, 2930, 2870, 2724, 1664, 1619, 1486, 1253, 770; ^1H NMR ($CDCl_3$): δ (ppm) 1.88 (s, 6H, 2×CH3), 2.24 (s, 3H, CH_3), 2,32 (s, 3H, -CH_3), 6.79 (d, J =7.8 Hz, 1H), 7.019-7.069 (m, 4H), 7.10 (d, *J* =7.8 Hz, 2H), 7.16 (d, *J* = 6 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 8.39 (s, 1H, H-C=N, One isomer), 8.43 (s, 1H, H-C=N, Another isomer) (9.73 (s, 1H, -CHO), 14.08 (bs, 1H, -NH, One isomer), 14.12 (bs, 1H, -NH, Another isomer); ^{13}C NMR ($CDCl_3$): δ (ppm) 12.39, 18.62, 19.47, 55.65, 106.65, 113.31, 117.34, 117.96, 122.28, 125.43, 125.56, 126.52, 128.74, 137.24, 137.30, 141.73, 143.03, 144.83, 153.00, 155.99, 182.76, 185.96. Anal. Calcd. for $C_{27}H_{25}ClN_2O_2$: C, 72.88%; H, 5.66%;N, 6.30%. Found: C, 72.68; H, 5.81%; N, 6.35%.

3-(5-Chloro-2-phenoxyphenylamino)-2-(4-chloro-3,3-dimethyl-7-phenoxy-3*H*-indol-2-yl) acrylaldehyde (13c).

Yield 86%; mp 138-139 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3066, 2976, 2936, 2871, 2734, 1678, 1617, 1494, 1255, 749; ^1H NMR ($CDCl_3$): δ (ppm) 1.82 (s, 6H, 2×CH_3), 6.56 (d, *J* = 8.7, 1H), 6.65 (d, *J* = 8.7, 1H), 6.81(d, *J* = 7.9, 2H), 6.86 (d, *J* = 7.9, 2H), 6.93 (d, *J* = 7.9, 1H), 6.97-7.00 (m, 2H), 7.04-7.11 (m, 3H), 7.21 (t, *J* = 6.5 Hz, 2H), 7.29 (d, *J* = 2.2, 1H), 8.40 (s, 1H, CH=N), 9.74 (s, 1H, -CHO), 13.94 (bs, 1H, -NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 18.52, 55.38, 107.62, 116.56, 116.65, 117.61, 118.69, 118.96, 121.43, 122.63, 123.41, 124.48, 125.66, 127.42, 128.66, 128.73, 130.81, 141.38, 141.45, 146.11, 146.46, 152.20, 154.24, 155.24, 181.65, 186.18. Anal. Calcd. for $C_{31}H_{24}Cl_2N_2O_3$: C, 68.51%; H, 4.45%;N, 5.15%. Found: C, 68.86; H, 4.70%; N, 5.42%.

3-(5-Chloro-2-phenoxyphenylamino)-2-(4-chloro-3,3-dimethyl-7-phenoxy-3H-indol-2-yl) acrylaldehyde (13d).

Yield 86%; mp 138-139 °C; FT-IR (KBr) ν_{max}/cm^{-1}: 3066, 2976, 2936, 2871, 2734, 1678, 1617, 1494, 1255, 749; ^1H NMR ($CDCl_3$): δ (ppm) 1.82 (s, 6H, 2×CH_3), 6.56 (d, *J* = 8.7, 1H), 6.65 (d, *J* = 8.7, 1H), 6.81(d, *J* = 7.9, 2H), 6.86 (d, *J* = 7.9, 2H), 6.93 (d, *J* = 7.9, 1H), 6.97-7.00 (m, 2H), 7.04-

7.11 (m, 3H), 7.21 (t, J = 6.5 Hz, 2H), 7.29 (d, J = 2.2, 1H), 8.40 (s, 1H, CH=N), 9.74 (s, 1H, -CHO), 13.94 (bs, 1H, -NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 18.52, 55.38, 107.62, 116.56, 116.65, 117.61, 118.69, 118.96, 121.43, 122.63, 123.41, 124.48, 125.66, 127.42, 128.66, 128.73, 130.81, 141.38, 141.45, 146.11, 146.46, 152.20, 154.24, 155.24, 181.65, 186.18. Anal. Calcd. for $C_{31}H_{24}Cl_2N_2O_3$: C, 68.51%; H, 4.45%;N, 5.15%. Found: C, 68.86; H, 4.70%; N, 5.42%.

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