Chapter-5

I_2/TBHP Mediated Oxidative Coupling of Indole with Active methylene Compounds Via C-C and C-O bond formation

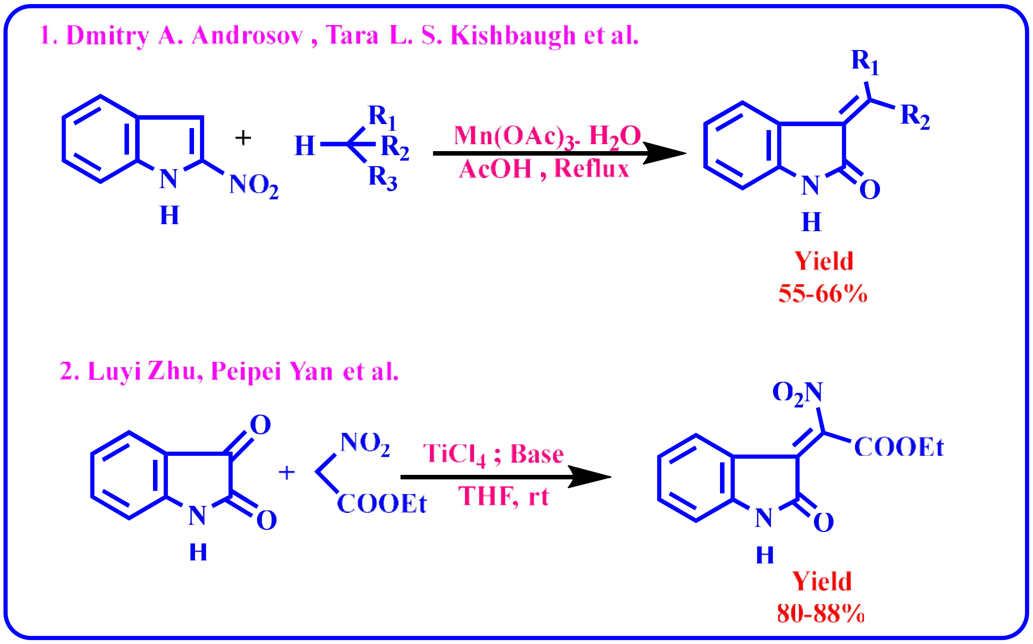
5.1 Introduction

Forming a carbon-carbon unsaturated bond by oxidative coupling reaction is important synthesis.[1] Over the past two decades, the oxidative coupling has been recognized as a green, environment-friendly, and economical synthesis. Unsaturated bond-containing compounds are broadly found in natural compounds, and such combinations are also used in pharmaceuticals, agrochemicals, functional materials, bulk materials, etc.[2]

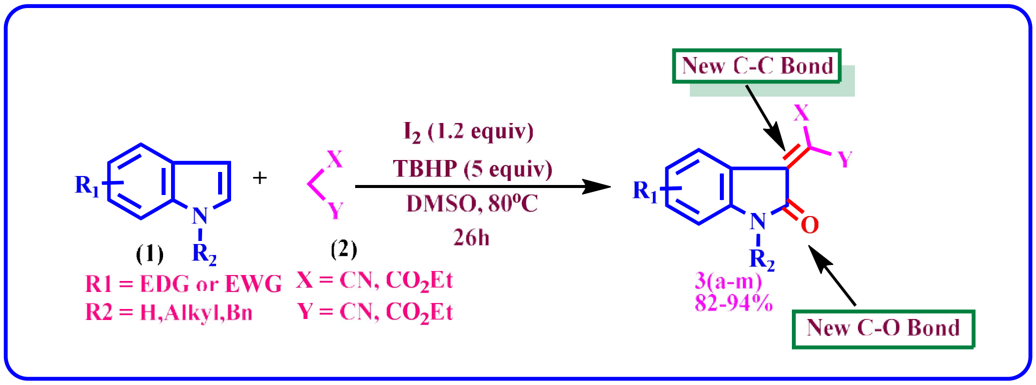
The most essential pharmacologically significant structural motifs of natural indole alkaloids and bioactive molecules are 3-ylidene oxindole components formed from indole derivatives and active methylene molecules, which show powerful anticancer [3], antifungal,[4], and antiviral activities.[5] For instance, a protein kinase inhibitor, indirubin[6], is Chinese herbal medicine; Nintedanib (Ofev) is used for the treatment of idiopathic pulmonary fibrosis (IPF) & cancer[7] etc., Oxindole and related compounds also present inhibitory effects on CDKs. A moment ago, 3-ylidene oxindole acetamides, an antitumor agent, showed a corresponding profile towards roscovitine. Moreover, 3-ylidene oxindoles are the central part of biologically active natural products alkaloids (including neolaugerine,[8] continu A, and costinine [9]. Attributable to the biological and medicinal importance of such compounds, many synthetic strategies have been forcefully developed. Some of the reported methods for reacting indole derivatives and active methylene are traditional Wittig, Knoevenagel reaction[10], palladium-catalyzed Heck–Suzuki– Miyaura domino reactions[11], using metal as a costly catalyst, and more toxic motivation [12], and some other techniques [13,14]. But these methods undergo some disadvantages like complex workup, large waste generation, low yield, and are environmentally unfriendly. Henceforth, there is a pronounced requirement to develop an economical and environment-friendly approach as a substitute for using metal catalysts that adversely impact the environment.

Although only one report is available to synthesize such compounds by oxidative coupling of indolin-2-ones with active methylenes, there is no report on the oxidative coupling of indole and active methylene compounds. Because of the above and our continuing interest[15] in developing green, environmentally benign, and sustainable methods, a new approach was established for the oxidative coupling of indole and active methylene compounds using I_2/TBHP at 80° C in the presence of DMSO (**Scheme 5.1**).

Previous work



Present Work

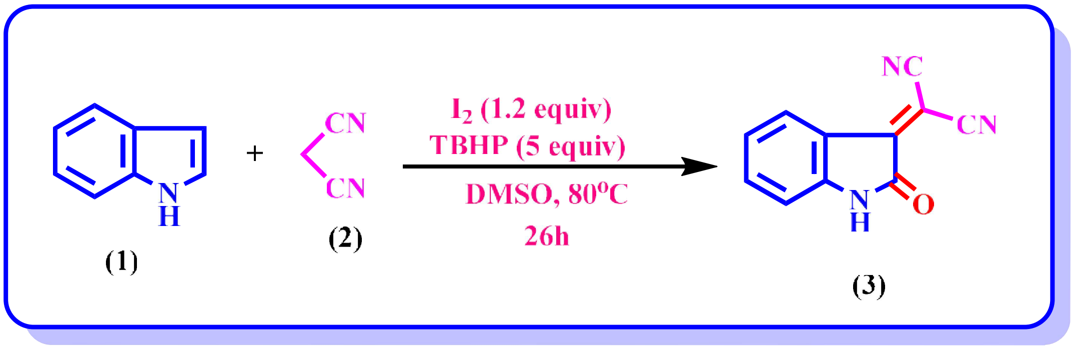


Scheme 5.1 Oxidative coupling of indole and active methylene compound

5.2 Results and Discussion

To determine the optimum reaction condition for this conversion, the reaction of indole (1mmol) (**1**) and malononitrile (1mmol) (**2**) was selected as a model reaction (**Table 5.1**) and various parameters were examined. First of all, the effect of oxidant TBHP was examined. While the reaction was carried out at 100^0 C with 1.2 equivalent of catalyst I_2 and 2 equivalent of TBHP(aq), only a trace amount of the product was isolated (**Table 5.1, entry 1**). As the amount of oxidant was increased, the % yield of the product was also increased. But after 5 equivalent of TBHP(aq), there was no increase in the % yield of the product (**Table 5.1, entry 6**). Thus the optimum condition of TBHP(aq) was taken as 5 equivalent (**Table 5.1, entry 4**). The effect of TBHP decane was also seen, and the result shows that TBHP (aq) was better (**Table1, entry 6**). Further, the amount of catalyst was screened. The % yield was increased with the increasing amount of catalyst (**Table 5.1, entries 7-9**). Even on increasing the amount of catalyst from 1.2 to 1.3 equivalent, there was no increase in the yield of the product (**Table 5.1, entry 9**). Thus the amount of catalyst was fixed as 1.2, equivalent for further studies. Subsequently, the effect of some other solvents like DMF and DCM were also examined, but no one could provide the expected yield of the product (**Table 5.1, entries 10-11**). Different catalysts, KI, TBAI, NH_4I, and NaI, were also screened, but none of them would match the catalytic efficacy of I_2 (**Table 5.1, entries 12–15**). Other oxidants like DTBP, DDQ, $K_2S_2O_8$, and H_2O_2 were also screened, but no one could afford the estimated yield of the product (**Table 5.1, entries 16-19)**. Consequently, the effect of various temperatures was also screened, and it was found that the temperature 80^{0}C provides the best yield (**Table 5.1, entries 20-23**).

Table 5.1 Optimization of reaction conditions for the synthesis of (3a)

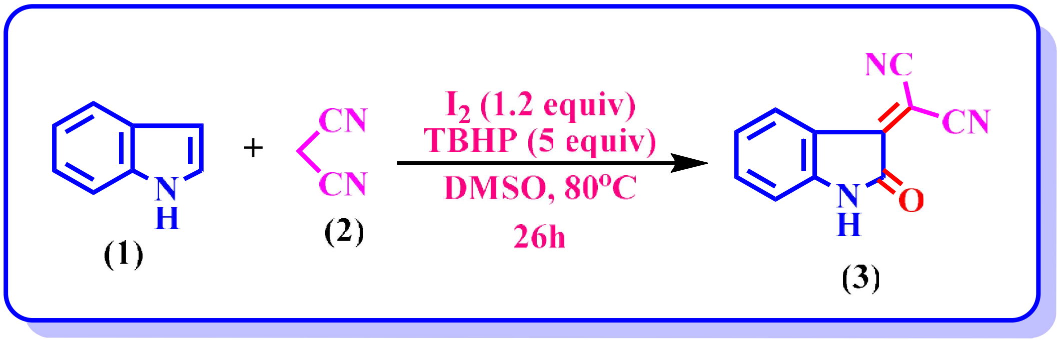


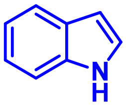
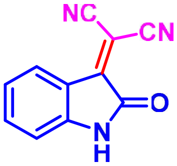
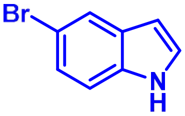
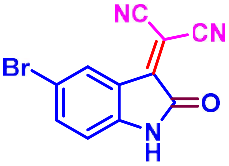
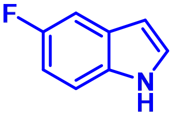
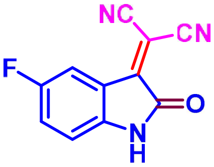
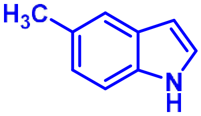
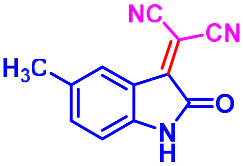
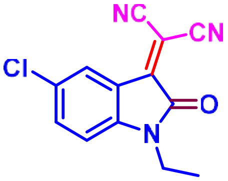
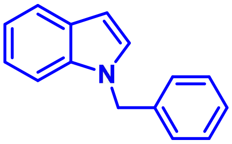
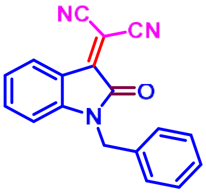
Entry	Oxidant (Equivalent)	Catalyst (equiv.)	Solvent	Temperature (° C)	Yield^b (%)
1	TBHP (2)	I_2 (1.2)	DMSO	80	trace
2	TBHP (3)	I_2 (1.2)	DMSO	80	48
3	TBHP (4)	I_2 (1.2)	DMSO	80	66
4	**TBHP (5)**	I_2 (1.2)	**DMSO**	80	**80**
5	TBHP (6)	I_2 (1.2)	DMSO	80	78
6	TBHP(5)(dec)	I_2 (1.2)	DMSO	80	55
7	TBHP (5)	I_2 (1.0)	DMSO	80	trace
8	TBHP (5)	I_2 (1.1)	DMSO	80	25
9	TBHP (5)	I_2 (1.3)	DMSO	80	46
10	TBHP (5)	I_2 (1.2)	DMF	80	50
11	TBHP (5)	I_2 (1.2)	DCM	80	52

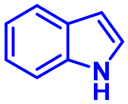
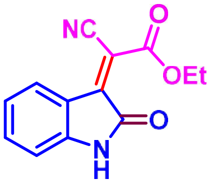
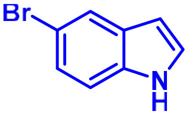
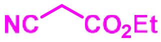
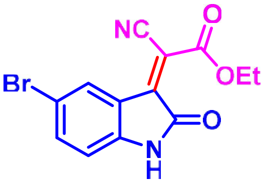
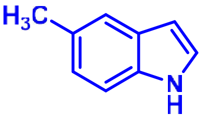
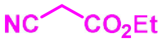
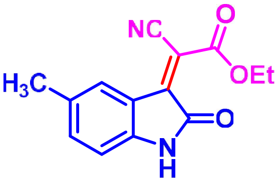
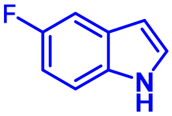
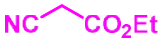
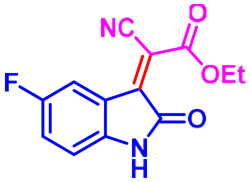
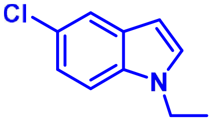
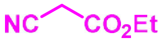
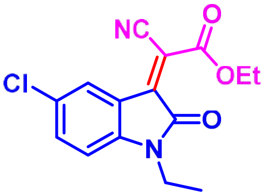
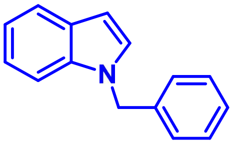
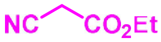
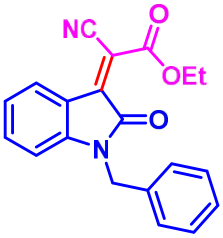
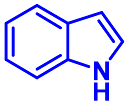
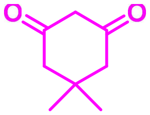
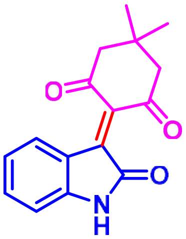
12	TBHP (5)	KI	DMSO	80	42
13	TBHP(5)	TBAI	DMSO	80	37
14	TBHP(5)	NH_4I	DMSO	80	28
15	TBHP(5)	NaI	DMSO	80	35
16	DTBP	I_2 (1.2)	DMSO	80	NIL
17	DDQ	I_2 (1.2)	DMSO	80	38
18	$K_2S_2O_8$	I_2 (1.2)	DMSO	80	24
19	H_2O_2	I_2 (1.2)	DMSO	80	48
20	TBHP(5)	I_2 (1.2)	DMSO	40	n.d.
21	TBHP(5)	I_2 (1.2)	DMSO	60	47
22	TBHP(5)	I_2 (1.2)	DMSO	100	62
23	TBHP(5)	I_2 (1.2)	DMSO	110	52

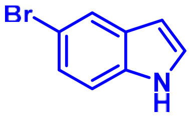
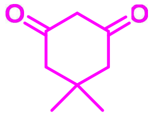
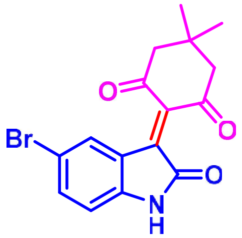
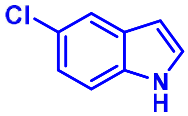
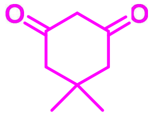
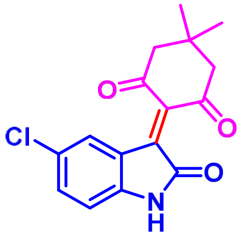
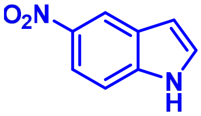
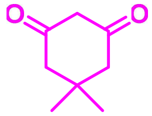
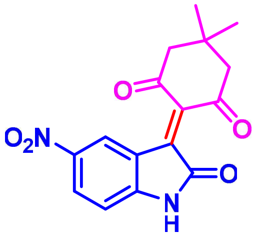
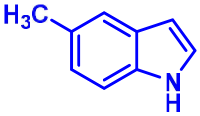
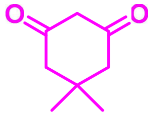
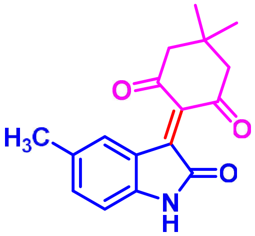
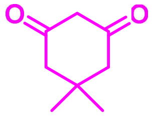
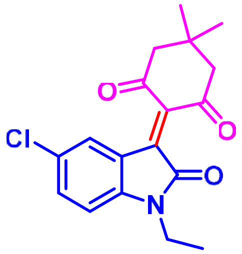
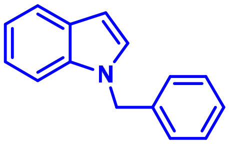
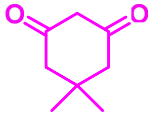
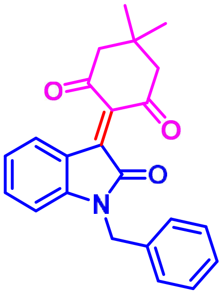
Using the optimized reaction conditions in hand, the scope of the substrate was explored to develop a reaction of a wide range of different indole **(1a),** 5-bromo-1H-indole **(1b),** 5-floro-1H-indole **(1c),** 5-methyl-1H-indole **(1d**), 1-ethyl-5-methyl-1H-indole **(1e),** 1-benzyl-1H-indole **(1f),** 5-nitro-1H-indole **(1p)** with active methylene compounds malanonitrile **(2a),** ethylcynoacetate **(2k),** 5,5-dimethylcyclohexane-1,3-dione **(2m).** All the substrates effectively converted to the corresponding compounds in good to excellent yields.

Table 5.2 Screening of substrates for the synthesis of 2-(2-Oxoindolin-3-ylidene) malononitrile



Entry	1	2	3ᵃ	Yieldᵇ(%)
3a				88
3b				86
3c				85
3d				86
3e				86
3f				85

3g				**85**
3h				**84**
3i				**84**
3j				**81**
3k				**82**
3l				**96**
3m				**84**

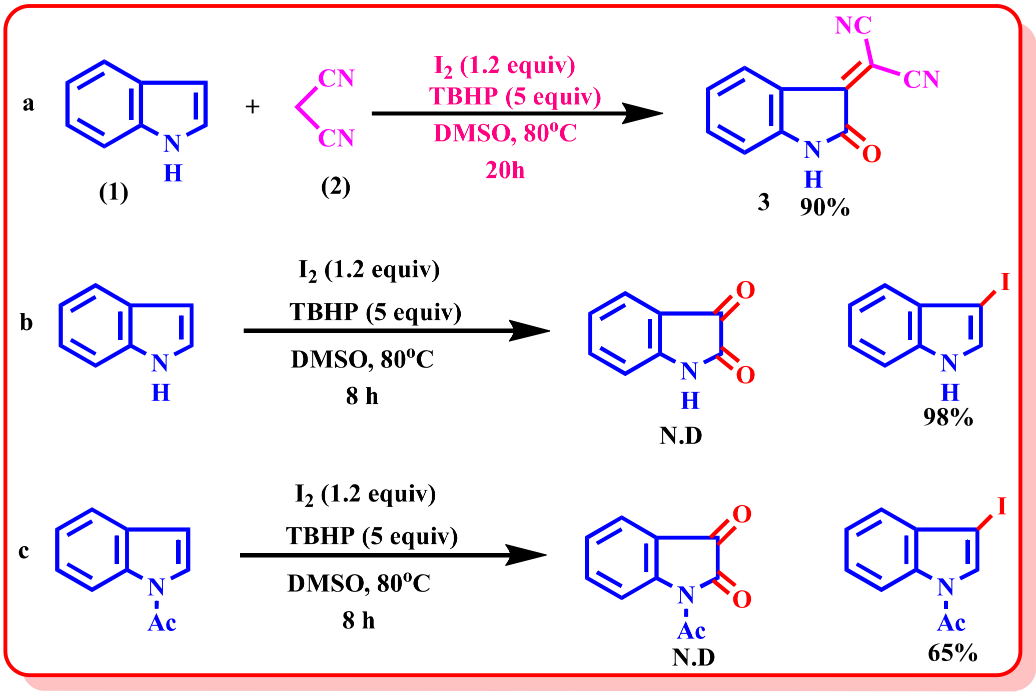
3n				**84**
3o				**83**
3p				**82**
3q				**83**
3r				**84**
3s				**82**

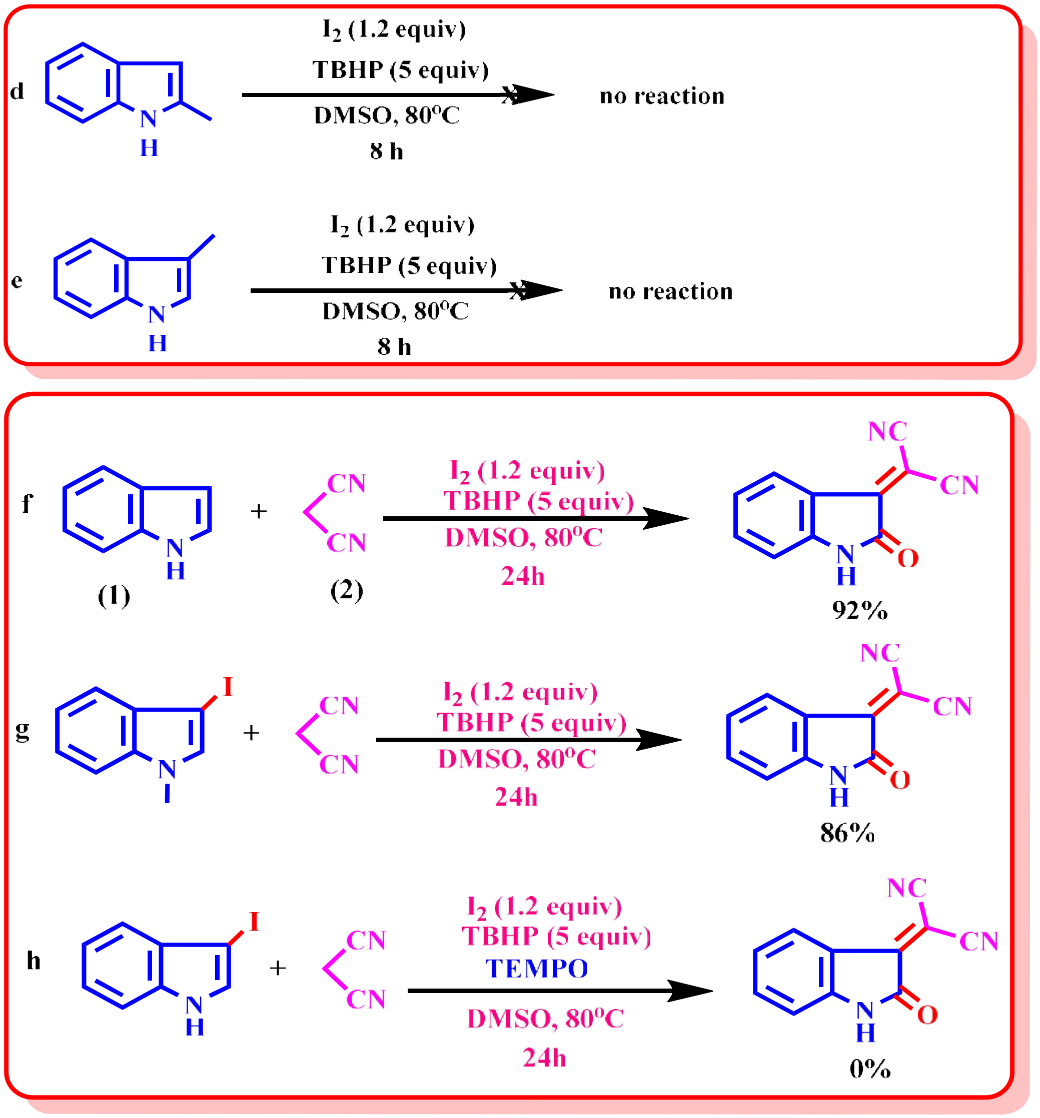
[a]Products were characterized by ^{1}H, ^{13}C NMR and IR analysis.

[b] Isolated yield.

5.3 Control Experiments

To know the mechanism of this reaction, some control experiments were attempted. Under optimized conditions, indole **1** was subjected to the reaction, which provided 3-iodoindole rather than isatin (**Scheme 5.2,** reaction b). To confirm the intermediacy of 3-iodoisatin, the reaction of 1- acetylindole was carried out under optimized conditions, which delivered 1-acetyl -3-iodoindole in 65% yield rather than 1-acetylisatin (**Scheme 5.2,** reaction c). Further to confirm the intermediacy of 3-iodoisatin, the reaction of 2- methyl-indole and 3-methyl-indole was carried out under optimized conditions, which did not provide intermediate isatin (**Scheme 5.2,** reaction d & e). Under standard conditions, when 3-iodoindole was exposed to the reaction, the desired product was formed in 94% yield (**Scheme 5.2,** reaction g). Such an outcome confirms that 3-iodoindole was the possible intermediate. As the reaction was carried out with TEMPO (3 equiv.), the formation of the product was suppressed entirely (**Scheme 5.2,** reaction h).

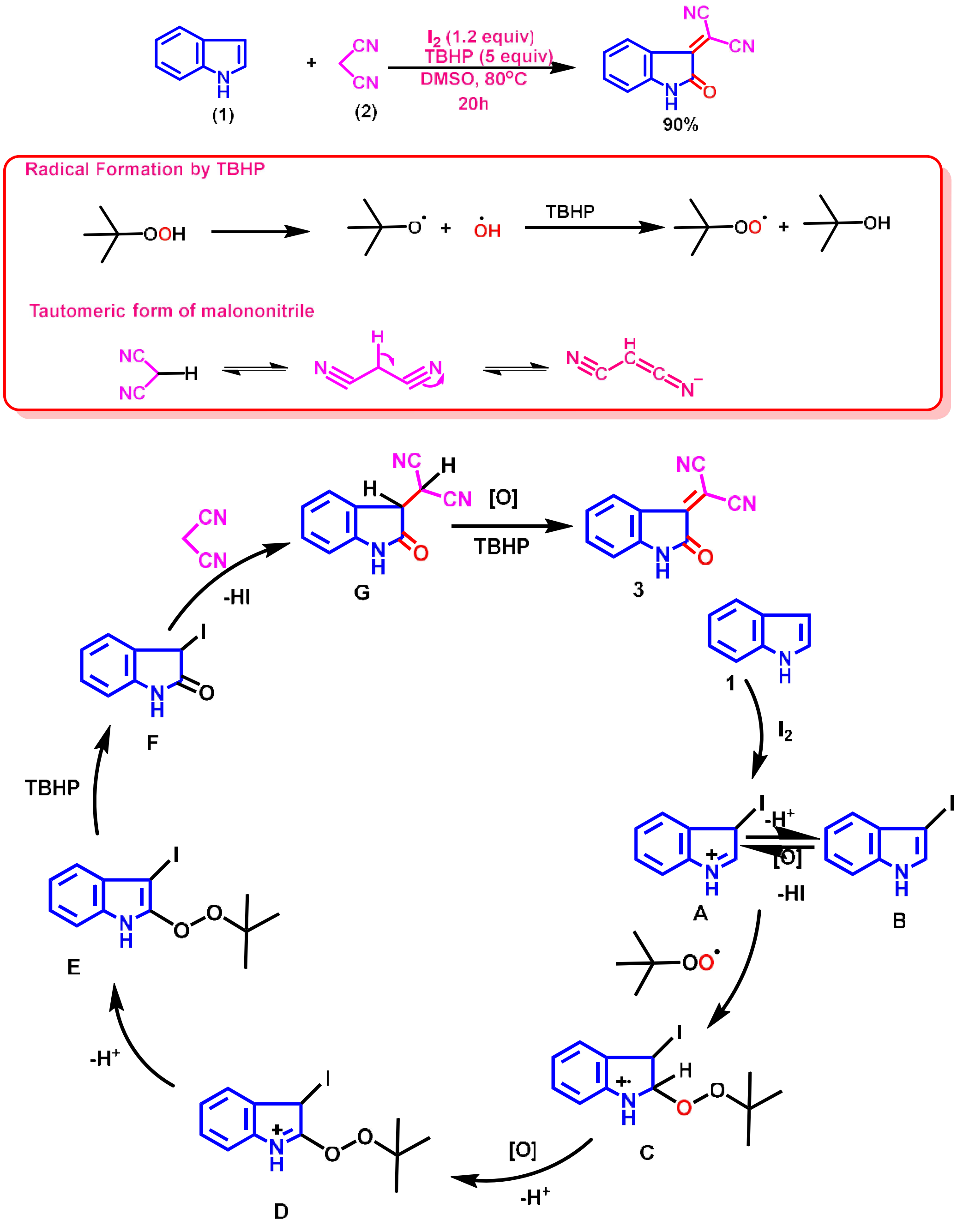




Scheme 5.2 Control experiments to establish the mechanism of the reaction

5.4 Mechanism for coupling of indole with active methylene groups

Following the above facts and reported literature [16−18], a probable mechanism of this reaction was suggested (**Scheme 5.3**). In starting, I_2 provides iminium intermediate **A** via reaction with indole. This intermediate interacts with a *tert*-butylperoxy free radical[17] to provide intermediate **C** [17,18]. Then this intermediate **C** is oxidized with TBHP to provide intermediate **D**, which upon isomerization and oxidation with TBHP provide 3-iodoindolin-2- one(**F**). Now 3-iodoindolin-2- one (**F**) reacts with malononitrile to provide **G**, which provides the final product **3** upon oxidation with TBHP.



Scheme 5.3 Plausible mechanism for the synthesis of 2-(2-Oxoindolin-3-ylidene) malononitrile

5.5 Conclusion

In summary, a metal-free oxidative coupling of indole and active methylene compound into the corresponding 3-ylidene oxindole has been developed via C-C and C-O bonds under mild reaction conditions. As far as we know, this is the first report on oxidative coupling of indole and active methylene compound to corresponding 3-ylidene oxindoles under metal-free conditions. The current I_2 / TBHP mediated oxidative coupling is easy to get to a variety of 3-ylidene oxindoles derivatives in good to excellent yields

5.6 Experimental Section

5.6.1 General experimental procedure for the synthesis of the compound of 3a

Indole (1 mmol) and DMSO (2 mL) were taken into a flask and energetically agitated at 80°C under an open atmosphere. To this, the mixture of I_2 (1.2 mmol), TBHP (5 equiv), and DMSO (15mL) were added dropwise. After one hour, malononitrile (1 mmol) was added to it. After completion of the reaction (as monitored by TLC) 5% $Na_2S_2O_3$ soln (10 mL) was added to the reaction mixture. Then the reaction mixture was extracted with EtOAc (3×15 mL), the organic layer was dried over Na2SO4, and the solvent evaporated under a vacuum. The obtained crude product after column chromatography on silica gel provides the pure product.

5.6.2 Characterization data of the compounds

2-(2-Oxoindolin-3-ylidene) malononitrile (4a)

Brick red crystal, m.p. 196 °C; 88% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.22 (s, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.57 (m, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.93

(d, *J* = 7.9 Hz, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 164.21, 151.08, 146.93, 138.28, 126.28, 123.38, 119.09, 113.52, 112.10, 81.06. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{11}H_6N_3O$, 196.0510; found- 196.0509.

2-(5-bromo-2-oxoindolin-3-ylidene) malononitrile (4b)

Purple crystal, m.p. 225 °C; 86% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.37 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.76 (m, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 7.4 Hz, 1H**). ^{13}C NMR (126 MHz, DMSO)** δ 177.85, 163.94, 163.78, 149.98, 145.99, 140.10, 128.10, 120.99, 114.37, 114.13. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{11}H_5BrN_3O$, 273.9615; found- 273.9613.

2-(5-fluoro-2-oxoindolin-3-ylidene) malononitrile (4c)

Purple crystal, m.p. 245 °C; 85% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.95 (s, 1H), 8.63 (d, *J* = 7.6 Hz, 1H), 8.44 (m, *J* = 8.1 Hz, 1H), 7.13 (s, 1H). **^{13}C NMR (126 MHz, DMSO)** δ 164.44, 151.62, 149.70, 142.82, 133.12, 121.11, 119.20, 112.36, 83.88. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{11}H_5FN_3O$, 214.0416; found- 214.0412 .

2-(5-Methyl-2-oxoindolin-3-ylidene) malononitrile (4d)

Reddish crystal, m.p. 183 °C; 86% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.11 (s, 1H), 7.65 (s, 1H), 7.40 (m, *J* = 8.1 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 2.28 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 164.27, 151.05, 144.89, 139.01, 132.39, 126.17, 119.12, 113.54, 111.98, 80.74, 20.92. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{12}H_8N_3O$, 210.0667; found- 210.0665.

2-(5-Chloro-1-ethyl-2-oxoindolin-3-ylidene) malononitrile (4e)

Black crystal, m.p. 190 °C; 86% yield; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.11 (d, *J* = 7.7 Hz, 1H), 7.56 (m, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 3.79 (t, 2H), 1.31 (t, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 161.72, 148.41, 144.65, 137.18, 129.35, 126.60, 119.33, 111.86, 110.72, 110.21, 84.08, 35.43, 12.42. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{13}H_9ClN_3O$, 258.0434; found- 258.0428.

2-(1-Benzyl-2-oxoindolin-3-ylidene) malononitrile (4f)

Purple solid, m.p. 201 °C; 85% yield; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.16 (m, *J* = 7.6 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.37 – 7.28 (m, 5H), 7.18 – 7.09 (m, 1H), 6.80 (m, *J* = 7.8 Hz, 1H), 4.94 (d, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 137.70, 129.12, 128.51, 128.35, 127.53, 127.01, 123.97, 88.65, 88.49, 44.22. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{18}H_{12}N_3O$, 286.0980; found- 286.0979.

Ethyl-2-cyano-2-(2-oxoindolin-3-ylidene) acetate (4g)

Dark red crystal, m.p. 220 °C; 85% yield ;**^{1}H NMR (500 MHz, DMSO)** δ 11.10 (s, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.01 (d, *J* = 0.7 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 4.39 (m, 2H), 1.27 (m, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 165.66, 161.81, 146.28, 145.79, 138.85, 136.53, 129.70, 122.65, 119.16, 111.33, 104.94, 63.61, 14.23. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{13}H_{11}N_2O_3$, 243.0769; found- 243.0769.

Ethyl-2-(5-bromo-2-oxoindolin-3-ylidene)-2-cyanoacetate (4h)

White crystal, m.p. 226 °C; 84% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.20 (s, 1H), 8.19 (s, 1H), 7.52 (s, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 4.46 – 4.32 (m, 2H), 1.39 – 1.23 (m, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 165.45, 161.62, 145.21, 135.67, 129.41, 114.27, 112.55, 13.98. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{13}H_{10}BrN_2O_3$, 320.9874; found- 320.9871.

Ethyl-2-cyano-2-(5-methyl-2-oxoindolin-3-ylidene) acetate (4i)

Red crystal, m.p. 220 °C; 84% yield; **^{1}H NMR (500 MHz, DMSO)** δ 10.98 (s, 1H), 7.92 (s, 1H), 7.30 (m, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 4.42 (s, 2H), 2.24 (s, 3H), 1.34 (t, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 165.76, 161.87, 145.90, 144.08, 137.14, 131.53, 129.82, 119.19, 114.71, 111.15, 63.65, 21.06, 14.22. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{14}H_{13}N_2O_3$, 257.0926; found- 257.0922.

Ethyl-2-cyano-2-(5-fluoro-2-oxoindolin-3-ylidene) acetate (4j)

Brown crystal, m.p. 228 °C; 81% yield;**^{1}H NMR (500 MHz, DMSO)** δ 11.74 (s, 1H), 10.12 (s, 1H), 8.37 (m, *J* = 7.8 Hz, 1H), 7.12 – 7.06 (m, 1H), 4.44 (m, 2H), 1.37 (m, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 173.38, 165.55, 156.59, 139.10, 137.47, 124.36, 116.34, 115.46, 111.05, 109.77, 103.06, 59.65, 16.55. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{13}H_{10}FN_2O_3$, 261.0675; found- 261.0671.

Ethyl-2-(5-chloro-1-ethyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (4k)

Black crystal, m.p. 213 °C; 82% yield; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.40 (s, 1H), 7.47 – 7.44 (m, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 4.51 – 4.48 (m, 2H), 3.81 (d, 2H), 1.47 (t, 3H), 1.29 (d, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 163.56, 161.26, 144.19, 135.13, 134.14, 130.12, 128.40, 125.34, 120.00, 110.08, 109.72, 63.71, 35.21, 13.97, 12.38. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{15}H_{14}ClN_2O_3$, 305.0692; found- 305.0690.

Ethyl-2-(1-benzyl-2-oxoindolin-3-ylidene)-2-cyanoacetate (4l)

Brown crystal, m.p. 220 °C; 96% yield; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.33 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.32 (m, 6H), 7.04 (t, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 4.96 (s, 2H), 4.49 (m, 2H), 1.47 (t, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.48, 164.45, 144.60, 140.90, 136.33, 129.93, 128.97, 128.42, 128.07, 127.49, 121.42, 115.82, 104.28, 60.23, 47.07, 13.64. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{20}H_{17}N_2O_3$, 333.1239; found- 333.1238.

5, 5-Dimethyl-2-(2-oxoindolin-3-ylidene) cyclohexane-1, 3-dione (4m)

Light orange crystal, m.p. 265 °C; 84% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.02 (d, *J* = 7.6 Hz, 1H), 7.55 (m, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 7.9 Hz, 1H), 6.87 6.67 (m, 1H), 2.50 – 1.77 (m, 4H), 1.10 – 0.89 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 194.61, 168.70, 151.24, 144.76, 138.85, 128.12, 125.16, 123.24, 118.32, 112.67, 50.63, 31.57, 26.44. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{16}H_{16}NO_3$, 270.1130; found .270.1127.

2-(5-Bromo-2-oxoindolin-3-ylidene)-5, 5-dimethylcyclohexane-1, 3-dione (4n)

Greyish yellow crystal, m.p. 271 °C; 84% yield; **^{1}H NMR (500 MHz, DMSO)** δ 10.33 (s, 1H), 7.75 – 6.76 (m, 3H), 2.40 – 1.94 (m, 4H), 1.05 – 0.95 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 183.66, 176.47, 150.03, 142.52, 140.50, 132.21, 127.38, 126.29, 120.07, 114.75, 113.16, 111.92, 110.48, 78.19, 32.25, 28.42, 27.96. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{16}H_{15}BrNO_3$, 348.0235 ; found- 348.0234.

2-(5-Chloro-2-oxoindolin-3-ylidene)-5,5-dimethylcyclohexane-1,3-dione (4o)

Orange crystal, m.p. 268 °C; 83% yield; **^{1}H NMR (500 MHz, DMSO)** δ 11.17 (s, 1H), 7.65 – 6.57 (m, 3H), 2.26 – 1.56 (m, 4H), 1.09 – 0.80 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 179.94, 170.27, 150.59, 141.76, 140.69, 126.78, 124.60, 122.99, 109.92, 106.59, 50.83, 32.09, 28.79. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{16}H_{15}ClNO_3$, 304.0740 ; found-304.0738 .

5,5-Dimethyl-2-(5-nitro-2-oxoindolin-3-ylidene)cyclohexane-1,3-dione (4p)

Yellow crystal, m.p. 265 ^oC; 82% yield; **^1H NMR (500 MHz, DMSO)** δ 11.32 (s, 1H), 8.50 – 8.43 (m, 1H), 8.11 – 8.01 (m, 1H), 6.82 (t, *J* = 8.4 Hz, 1H), 2.69 – 2.57 (m, 2H), 2.15 (m, 2H), 0.99 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 200.15, 168.68, 156.77, 135.25, 131.87, 128.72, 117.08, 112.96, 32.19, 27.90, 27.58. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{16}H_{15}N_2O_5$, 315.0980 ; found-315.0978 .

5,5-Dimethyl-2-(5-methyl-2-oxoindolin-3-ylidene)cyclohexane-1,3-dione (4q)

Red crystal, m.p. 258 ^oC 83% yield; **^1H NMR (500 MHz, DMSO)** δ 10.91 (d, *J* = 7.8 Hz, 1H), 7.40 (m, *J* = 7.9 Hz, 1H), 7.00 – 6.53 (m, 2H), 2.45 – 2.26 (m, 2H), 2.26 – 2.11 (m, 3H), 2.10 – 1.86 (m, 2H), 0.99 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 194.70, 182.19, 148.97, 139.35, 132.59, 128.26, 125.28, 122.45, 112.53, 101.36, 46.99, 33.66, 28.97, 27.28, 21.28. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{17}H_{18}NO_3$, 284.1286 ; found-284.1284 .

2-(5-Chloro-1-ethyl-2-oxoindolin-3-ylidene)-5,5-dimethylcyclohexane-1,3-dione (4r)

White crystal, m.p. 279 ^oC; 84% yield; **^1H NMR (500 MHz, $CDCl_3$)** δ 8.98 (d, *J* = 7.1 Hz, 1H), 6.85 (m, *J* = 7.8 Hz, 2H), 3.90 (m, 2H), 2.31 – 2.06 (m, 4H), 1.44 (t, 3H), 1.15 (d, 3H), 1.06 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 195.30, 169.18, 153.70, 143.75, 133.96, 128.26, 121.13, 109.47, 101.77, 54.79, 43.26, 31.55, 27.00, 11.57. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{18}H_{19}ClNO_3$, 332.1053 ; found-332.1051.

2-(1-Benzyl-2-oxoindolin-3-ylidene)-5,5-dimethylcyclohexane-1,3-dione (4s)

White crystal, m.p. 276 ^{o}C; 82% yield; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 9.00 (d, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.11 (m, *J* = 7.8 Hz, 1H), 6.90 (m, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 5.12 (m, 2H), 2.36 (m, 2H), 2.25 – 2.07 (m, 2H), 1.16 (s, 3H), 1.08 (d, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 208.50, 194.91, 168.78, 153.26, 145.51, 144.33, 135.65, 128.71, 128.33, 127.33, 124.20, 122.67, 120.29, 110.00, 50.69, 48.12, 31.44, 26.68. HRMS (ESI-TOF) m/z: $[M + H]^+$ calc. for $C_{23}H_{22}NO_3$, 360.1599 ; found-360.1595.

5.6.3.1 Spectrul data of Product 2-(2-oxoindolin-3-ylidene) malononitrile (4a)

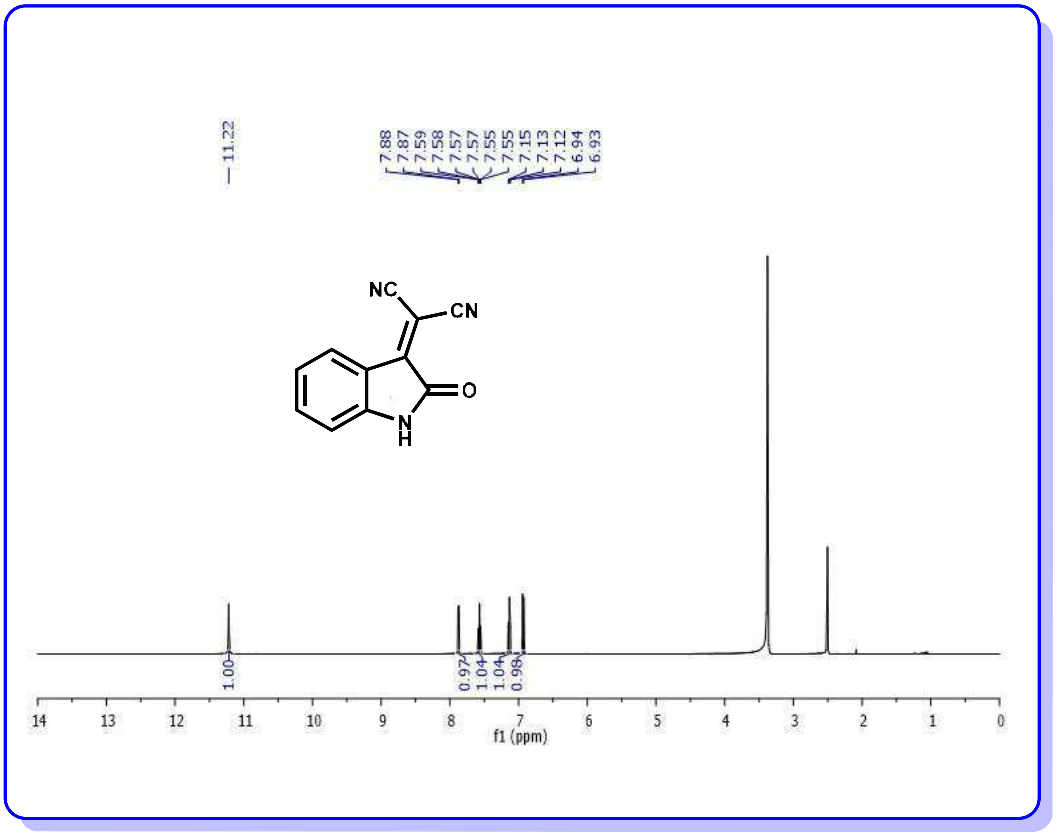


Figure 5.1 ^{1}H NMR of 2-(2-oxoindolin-3-ylidene) Malononitrile(4a)

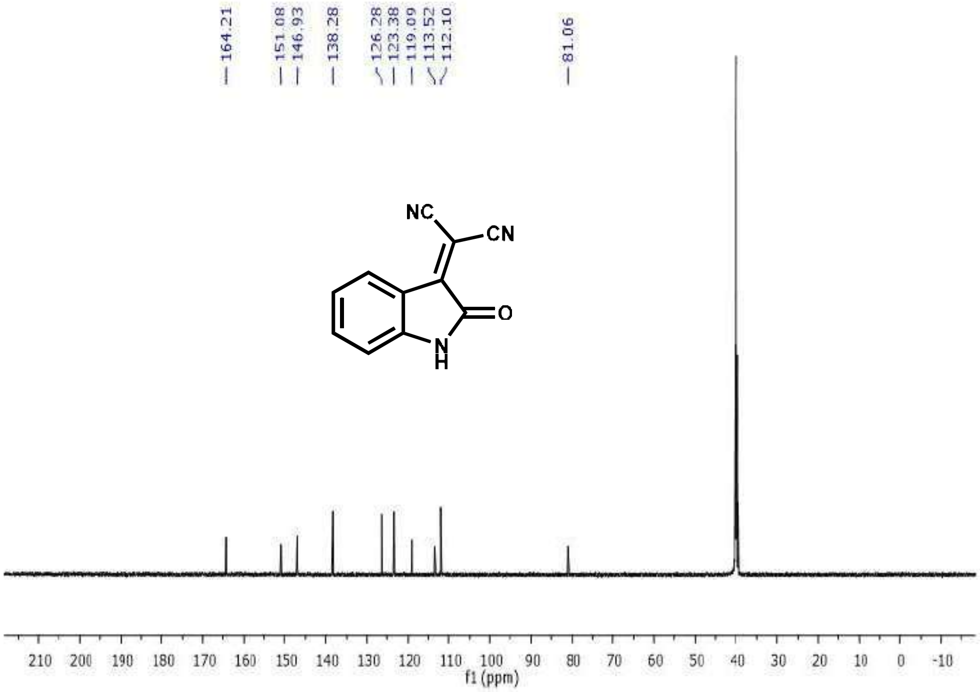


Figure 5.2 ^{13}C NMR of 2-(2-oxoindolin-3-ylidene) Malononitrile(4a)

5.6.3.2 Spectrul data of Product Ethyl-2-cyano-2-(2-oxoindolin-3-ylidene) acetate(4g)

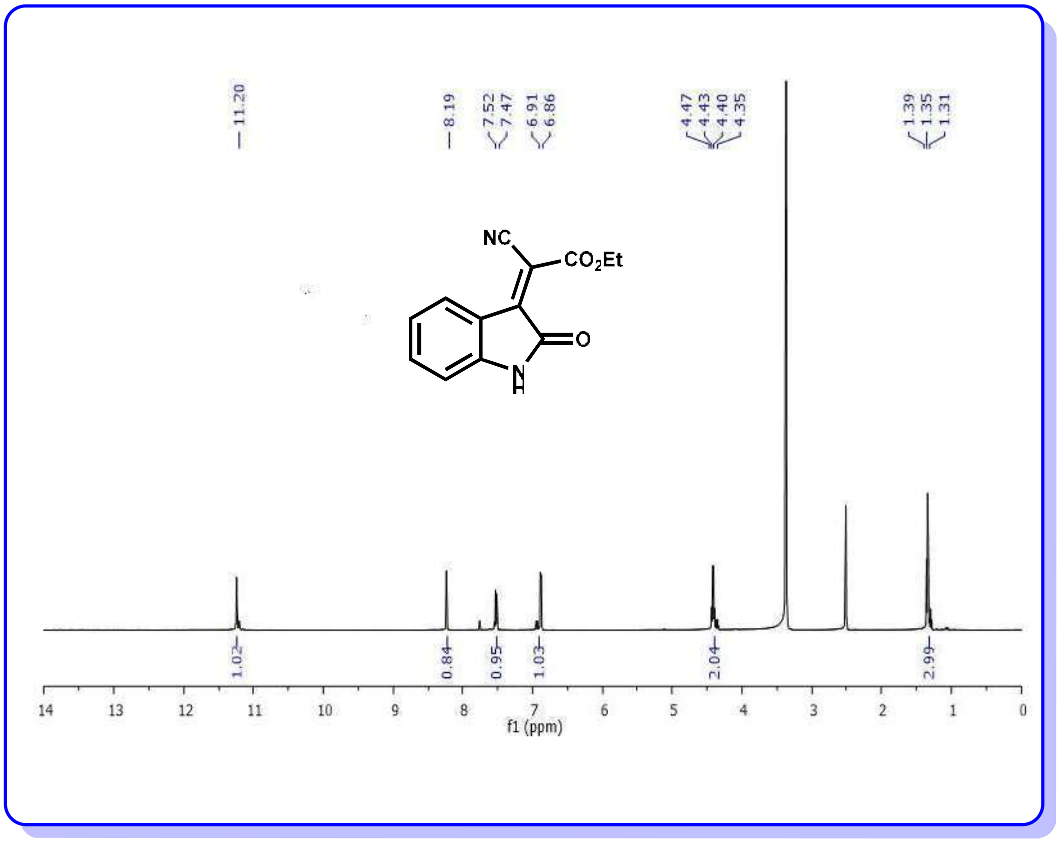


Figure 5.3 ^{1}H NMR of Ethyl-2-cyano-2-(2-oxoindolin-3-ylidene) acetate(4g)

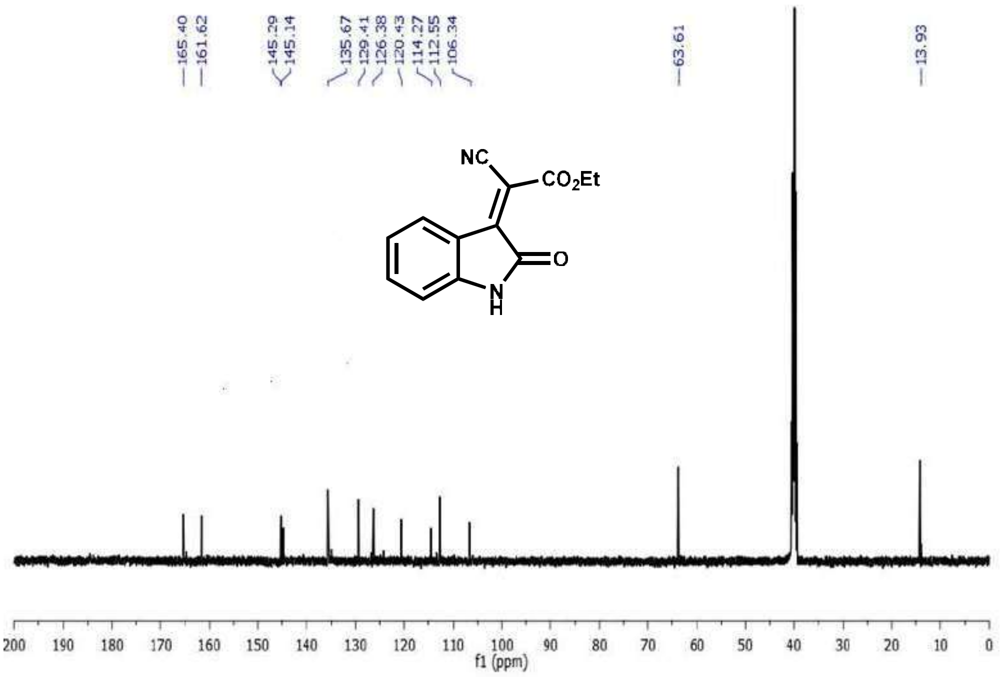


Figure 5.4 ^{13}C NMR of Ethyl-2-cyano-2-(2-oxoindolin-3-ylidene) acetate(4g)

5.6.3.3 Spectrul data of Product 5, 5-Dimethyl-2-(2-oxoindolin-3-ylidene) cyclohexane-1, 3-dione(4m)

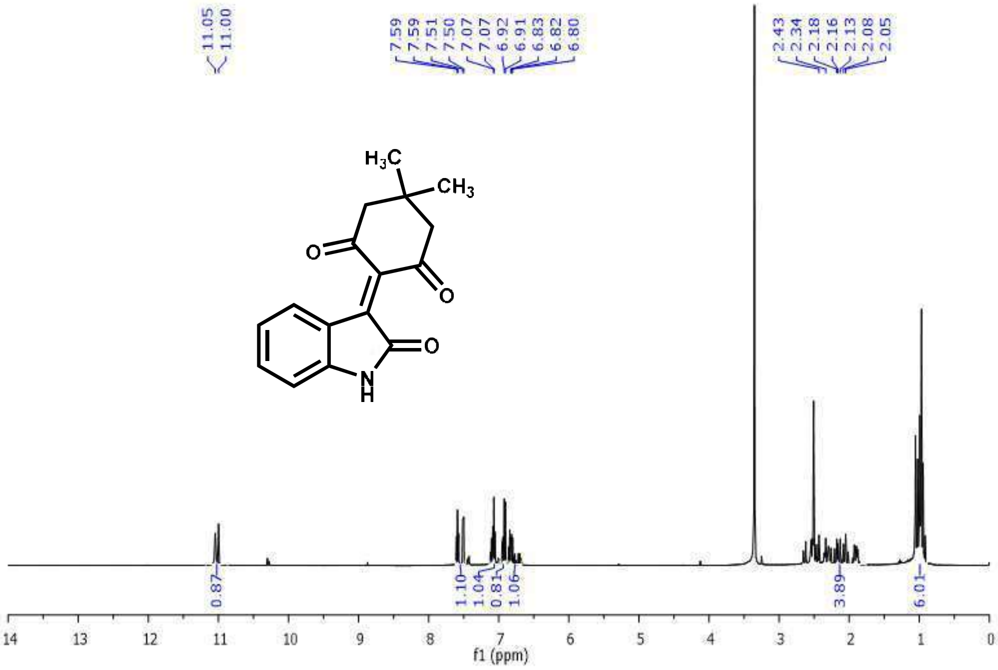


Figure 5.5 ^{1}H NMR of 5, 5-dimethyl-2-(2-oxoindolin-3-ylidene) cyclohexane-1, 3-dione(4m)

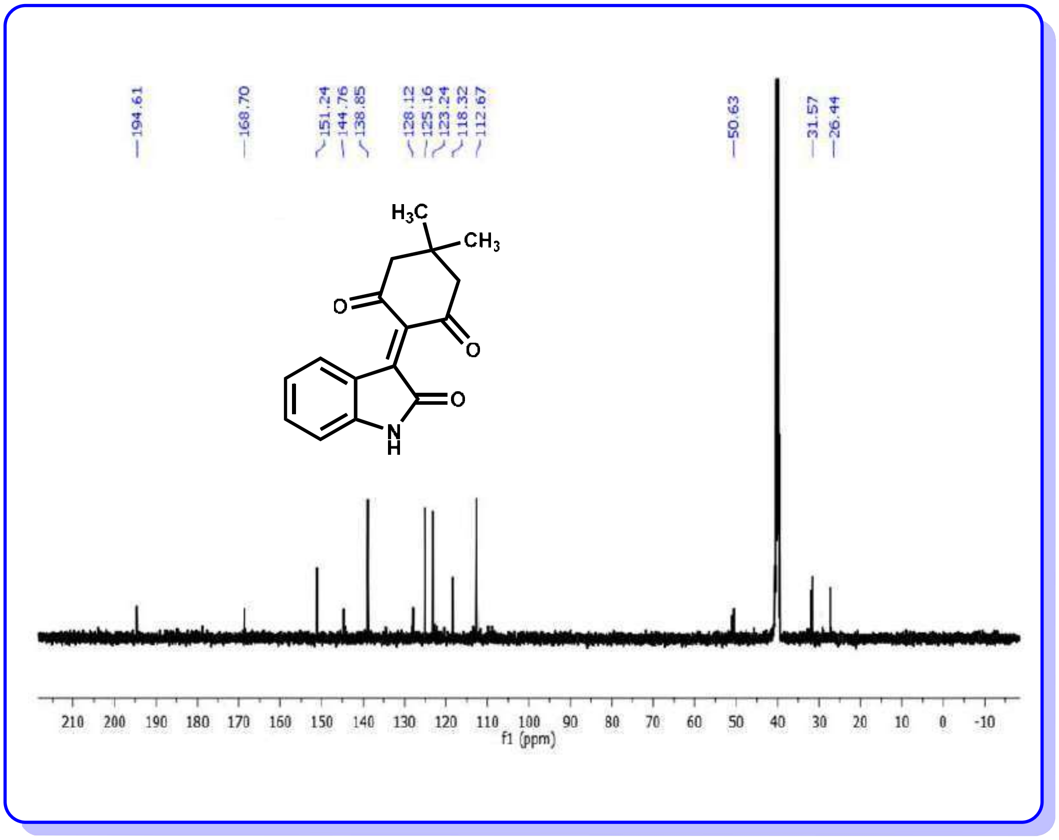


Figure 5.6 ^{13}C NMR of 5, 5-dimethyl-2-(2-oxoindolin-3-ylidene) cyclohexane-1, 3-dione(4m)

5.7 References

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