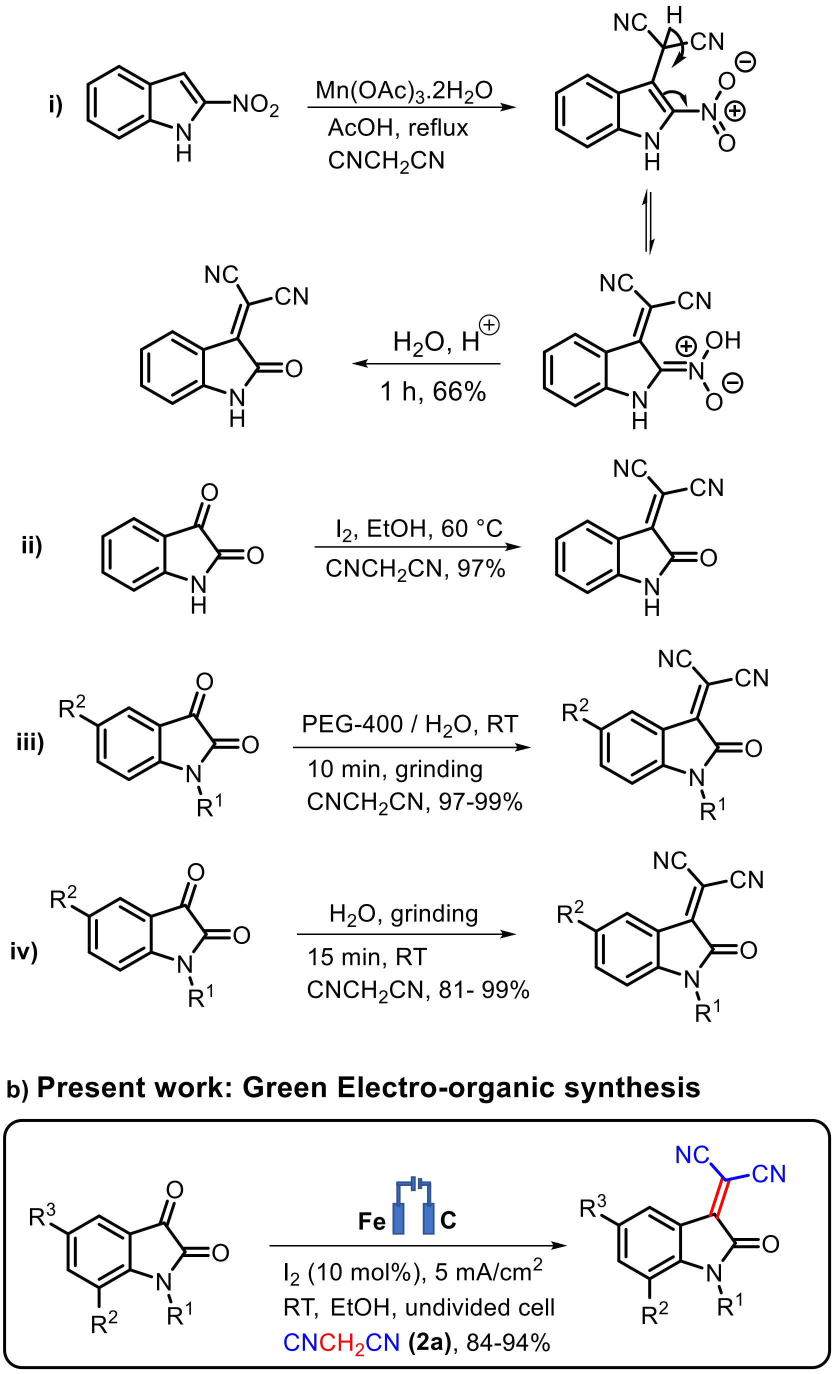
3.1. Introduction

The dicyano derivative of 2-(2-oxoindolin-3-ylidene) malononitrile, or isatylidene malononitrile, is an interesting Michael acceptor used to construct potential bioactive molecules. Because of the unique structural features and interesting biological properties of 2-(2-oxoindolin-3-ylidene) malononitrile, the design of new strategies for constructing this scaffold has attracted considerable interest. General interest in synthesizing isatylidene malononitriles -based structures comes not only from their structure properties and biological applications [1,4]. Many researchers have reported a two or three -or three-component reaction to synthesize isatylidene malononitriles as an intermediate. Isatylidene malononitriles have been prepared by many researchers [5,6] using different techniques. Among these, the most common methods for the synthesis of 2-(2-oxoindolin-3-ylidene) malononitriles are the condensation of isatins with malononitriles in the presence of a presence of a catalyst, such as a piperidine acetate,[7] DBU, Al_2O_3, $N(CH_2CH_2OH)_3$, chitosan [8,9].

Recently microwave irradiation [10,11] and iodine [12] at elevated temperatures have also been applied for the synthesis of isatylidene malononitriles. In the last few years molecular iodine has emerged as a powerful catalyst in various organic transformations as it is mild, soluble in common organic solvents, non-toxic, cost-effective, non-hazardous, and common organic solvents, nontoxic, cost-effective, non-hazardous, and environmentally benign catalyst for the synthesis of aa variety of heterocyclic compounds [13] It also constitutes an alternative to transition metal catalysis. It’s mild Lewis’s acidity and halogen bond activation favors the catalytic properties. Generally, organic synthesis reactions reported in the presence of molecular iodine occure at room temperature (25 °C) [14] However, most of these procedures have significant drawbacks such as long reaction times, low yields, harsh reaction conditions, tedious workup, and environmentally toxic or expensive reagents etc. Thus, there is still a need to develop a simple and general protocol for condensing isatin with malonitrile. Until now, molecular iodine-catalyzed transformations were carried out in conventional as well as under microwave and ultrasound irradiation only for such types of transformation. We are disclosing here the first report, to the best of my knowledge, on use of molecular iodine in the electro-organic synthesis of the dicyano derivative of 2-(2-oxindole-3-ylidene) malononitrile. Electro-organic synthesis is considered a clean and efficient synthetic methodology [15,16].

Molecular iodine is the exciting and essential catalyst of the present electro-organic synthesis. Using electron as a reagent, the following benefits were observed: the number of steps reduced, cleaner reaction mixtures, easier isolation of product, and pollution caused by the use of chemicals decreased significantly. Summary of previous strategies for the synthesis of dicyano 2(2-oxoindolin-3-ylidene) malononitrile derivatives using various methods with short comings of the methods *viz.* use of metallic catalyst,[17] temperature and access of only a few derivatives [18,19] their comparison with present green electro- organic synthesis catalysed with iodine are presented in **Scheme 1**.



Scheme 3.1 Strategies for the synthesis of dicyano 2-(2-oxoindolin-3-ylidene) malononitrile derivatives.

In the present work, after screening the various reaction conditions (**Tables 3.3–3.5**), we herein report a three-component reaction using isatin **1a** (1.0 mmol), malononitrile **2a** (1.0 mmol), and iodine (10 mol%) in ethanol (20 mL) to furnish the desired isatylidene malononitrile **3a** in 94% isolated yield. The electrochemical synthesis was carried out in an undivided cell equipped with carbon cloth (2 cm^2) as an anode and iron (2 cm^2) as a cathode at room temperature under a constant current density of 5 mA cm^{-2}. The progress of the reaction was monitored by TLC using a hexane/ethyl acetate (1:1, v/v) solvent mixture. Initially, we selected isatin **1a** and malononitrile **2a** as the model starting materials to optimize the reaction. The use of 1.0 equivalent of **1a**, **2a** and I_2 (0.1 mmol) was found to be optimal reaction conditions (**Table 3.5**). The yield decreased with no change in product observed when their equivalents were increased or decreased. Subsequently, the influence of solvents, time of reaction, and applied current density were studied (**Table 3.3 and 3.4**). We have performed electrolysis in various LR grade solvents such as EtOH, MeOH, MeCN, DCM and H_2O and found that reaction proceeded in all these solvents and was observed to be best in EtOH in terms of yield and reaction time (**Table 3.3**). The experiment manifested that no product was formed without any solvent, while a low conversion was observed in acetonitrile and dichloromethane (may be due to poor transfer of e^-) while ethanol enhanced the yield. The reaction with changes in equivalents ratio of substrates **1a** and **2a** along with iodine was also carried out, which showed no change in the product except very little variation in yields (**Table 3.5**). As shown in **Table 3.4** (**entries 4**), the applied current density of 5 mA cm^{-2} is optimal to synthesize isatylidene malononitrile derivatives owing to maximum yield. At the same time, lower or higher current densities resulted in decreased yield. With the optimized electrolysis parameters in hand, we applied the electro-organic synthesis method to a range of substrates to elucidate the reaction's scope (**Scheme 3.2**). We were contented to and that reaction works with a wide range of isatin derivatives. We carried out the reaction at room temperature under an air atmosphere and prepared isatylidene malononitrile with electron- donating or electron-neutral, or electron- withdrawing substituents, such as 5-methyl, 5-chloro, 5- bromo, 5-fluoro, 7-chloro, 7-bromo, *N*-methyl and *N*-phenyl by Knoevenagel condensation of isatin and malononitrile using I_2 successfully, leading to the corresponding products in good to very good yields (**Scheme 3.2**). To our delight, this transformation could be performed under an air atmosphere, affording the targeted products in excellent yields. These results demonstrated that this condensation reaction is relatively easy to handle and practically applicable under electro-organic synthesis conditions. Different substituents on the isatin core were well tolerated and furnished the respective products in very good to excellent yields. Expectedly, an electrical current is necessary for this reaction (**Table 3.4**).

Open circuit potential (OCP) was measured before applying fixed current density. An open circuit potential is equal to the electrochemical potential of the electrode with respect to the electrolyte of the reaction mixture. OCP was observed for different isatin derivatives, as shown in **Table 3.1**, in the electro-organic synthesis reaction mixture in a potential region of +1 V to -1 V for 6.67 min. In almost all cases, OCP was constant and varying with ±0.001 V in the reaction mixture containing **1b**, **1c**, and 1f. OCP was recorded for different electron-withdrawing and electron-donating substituents at 1, 5, and 7 positions of isatin substrates and shown in **Table 3.1**. Comparative OCP for the electro-organic synthesis of a reaction mixture containing (5- and 7-) substituted isatins (1.0 mmol) + iodine (10 mol%) + malononitrile (1.0 mmol) was studied prior to application of applied current density (**Figure 1**).

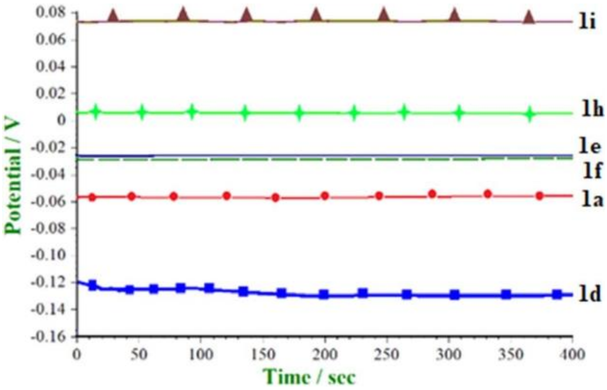


Figure 3.1 OCP electro-organic synthesis of reaction mixture.

The result showed that the 5-methyl derivative has lower OCP as the electron-donating group while 5-substituted –Br, –Cl, –F, and 7-Cl have higher OCP due to electron-withdrawing behaviour. Similar open circuit potential data were presented by Assary *et al* [20] for a broader set of aromatic nitrogen-containing molecules, especially quinoxaline derivatives in ethanol.

Table 3.1 OCP data for electro-organic synthesis of isatylidene malononitrile derivatives

Entry	Electrochemical reaction mixture (substrate +I_2 +**2a**)	Open circuit potential OCP (in volts)
1	**1a**	-0.056
2	**1b**	-0.008
3	**1c**	0.073
4	**1d**	-0.011
5	**1e**	-0.026
6	**1f**	-0.029
7	**1g**	0.0053
8	**1h**	-0.03
9	**1i**	0.074
10	**1j**	0.068
11	**1k**	0.06
12	**1a** + I_2 + **2a** + TEMPO	0.041

OCP of 5-halo substituted isatin was found to be in the following order: **1g** > **1e** > **1f** > **1h**, due to the −I effect, fluoro being highly electron withdrawing. Among alkyl/aryl substituents, the OCP values are in the following order: **1c** > **1b** > **1d**, where there is a +I effect from the conjugation of 5-methyl group.

Thus, electro-organic synthesis was carried out at a constant current density of 5 mA cm^{-2} for different times (∼1.5 h to ∼3 h), and the progress of the reaction was monitored by TLC plates (silica gel 60 F254). Loaded TLC plates were visualized in a UV chamber hexane and ethyl acetate (1:1) using pre-coated TLC plates (silica gel 60 F254). It is worth mentioning here that, the electron-withdrawing and electron-donating groups are compatible with the electro-organic synthesis, and the desired productwas obtained in 91% ± 3% yields.

3.2 Plausible Mechanism

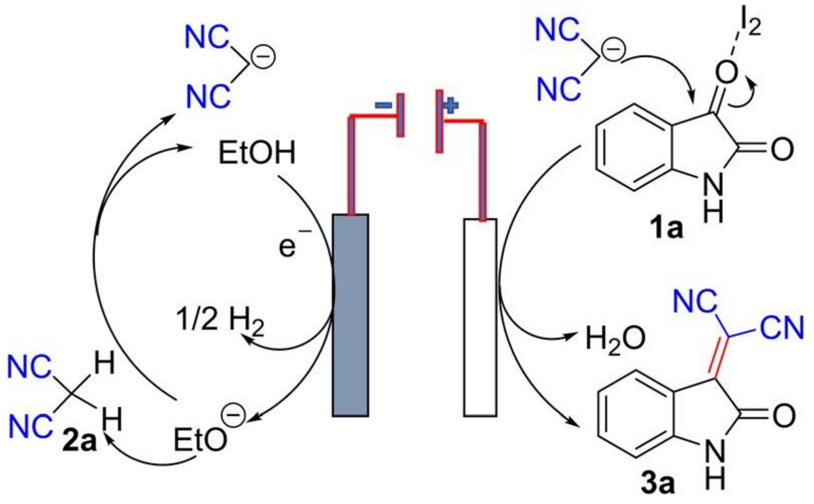


Figure 3.2 The Postulated reactions at each electrode in the reaction mixture.

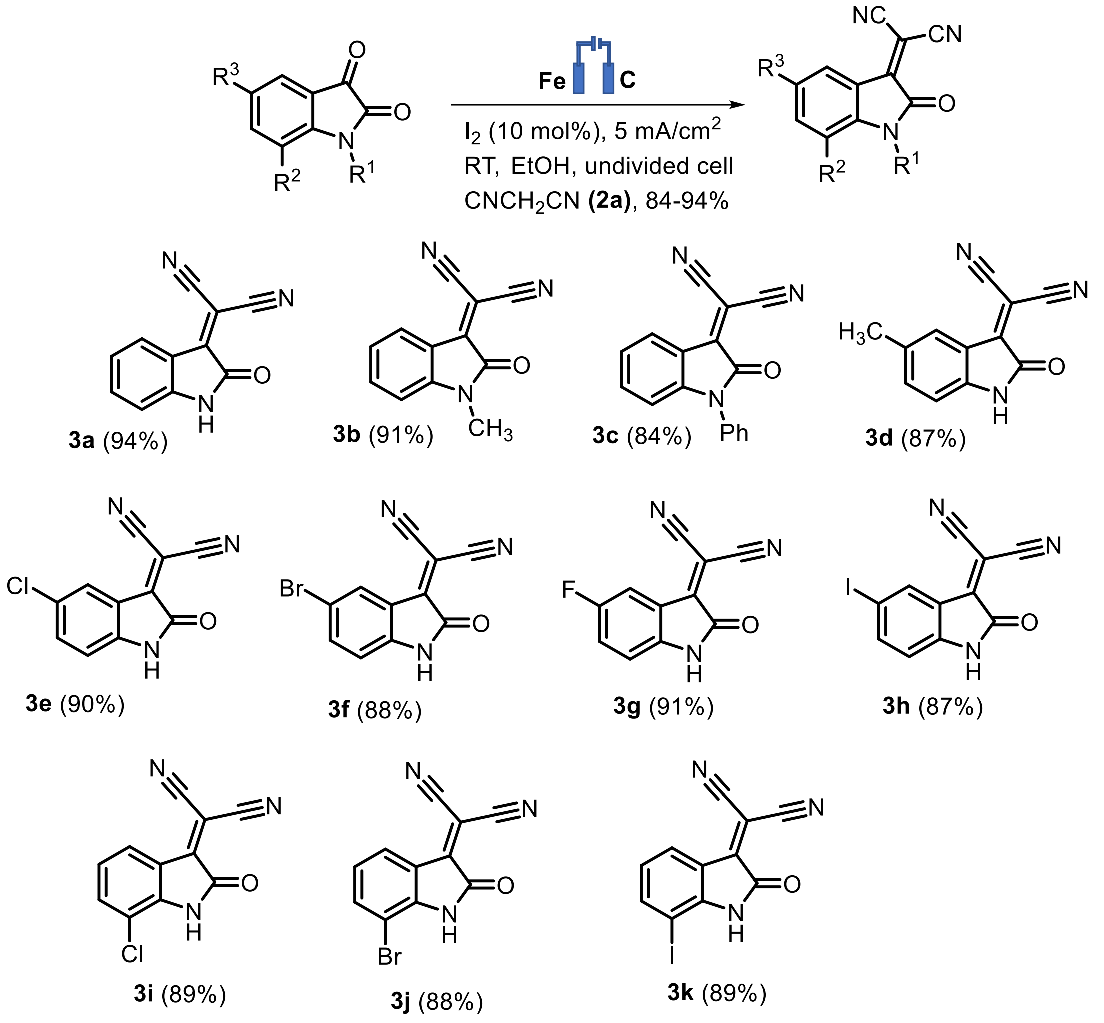
From the experimental data, it can be inferred that the strong -I effect raised the redox potential for the electro-organic synthesis. For example, 5-halo substituted isatin derivative (-Cl, -Br, -I) show electron-releasing behavior and thus have low redox potential. However -F behave differently because of the strong -I effect and high redox potential for products electro-organic synthesis [21].

Therefore, the redox potential for the synthesis of **3g** is comparatively higher than the electro-organic synthesis of **3e**, **3f**, and **3h** (**Table 3.2**). We were interested to see whether reaction proceeded through free radical intermediate formation or not, therefore a reaction was performed using **1a** and **2a** by adding TEMPO (free radical scavenger), adopting As 0.041 V. However, synthesis has initiated at -0.03 V relatively higher reduction potential than that of the standard reaction mixture and furnished the final product in ~2 h 45 min. optimized standard reaction conditions.

Table 3.2 Data for electro-organic synthesis of isatylidene malononitrile derivative (**3a-k**).

Entry	(Substrate +I_2 + 2a)	Potential (in volts)	Time (seconds)	Products	Yields (%)
1	**1a**	(-0.058 to -0.0560)	8.78×10^3	**3a**	94
2	**1b**	(-0.11 to -0.09)	6.31×10^3	**3b**	91
3	**1c**	(0.058 to -0.050))	1.06×10^4	**3c**	84
4	**1d**	(-0.14 to -0.13)	1.06×10^4	**3d**	87
5	**1e**	(-0.028 to -0.026)	6.0×10^3	**3e**	90
6	**1f**	(-0.030 to -0.026)	1.06×10^4	**3f**	88
7	**1g**	(0.004 to 0.087)	7.5×10^3	**3g**	91
8	**1h**	(-0.031 to – 0.030)	1.05×10^4	**3h**	87
9	**1i**	(0.065 to 0.050)	1.00×10^4	**3i**	89
10	**1j**	(0.071 to 0.045)	1.04×10^4	**3j**	88
11	**1k**	(0.058 to 0.035)	1.05×10^4	**3k**	89
12	**1a** + I_2 +**2a** +TEMPO	(-0.0315 to 0.0310)	1.01×10^4	**3a**	88

It was observed that, formation of desired product **3a** (88%) took place (**Table 3.2, entry 12**), which confirms there is no radical value of OCP was noted under a wavelength of 254 ƛ.



Scheme 3.2 Electro-organic synthesis of dicyano 2-(2-oxoindolin-3ylidene) malononitriles.

This rise in reaction time may be due to the presence of TEMPO, which hindered the mass transfer of the reaction mixture at the electrode surface. Effect of substituents in the synthesis of isatylidene derivative: the effects of a methyl group can be seen on **3b** and **3d** synthesis in comparison to **3a** synthesis, the methyl group being electron donating, lower the reduction potential as well as the time of product formation by ~50 mV and ~25 min during **3b** synthesis. On the other hand, for the synthesis of **3d**, the reduction potential was lowered by 80 mV, and it took ∼15 min longer to attain the maximum yield. However, synthesis of **3c**, having a −I effect group, was found to raise the potential and reaction time by 100 mV and 32 min longer than **3a**. This may be due to a decrease in electron density owing to the electron-withdrawing tendency of the phenyl group to a greater extent. At the same time, the *N*-methyl group showed decreased redox potential than **3a** since it is present on a non-conjugated, non- aromatic ring and pushes its electron density towards C2, which affects the electrophilicity of C3 and thus lowers the reduction potential and is observed to have enhanced rate of reaction for the synthesis of **3b**. The introduction of electron donating groups (EDG) at the ring nitrogen increases the electron density and, hence, decreases the electron affinity and reduction potential. It is important to note that, in this electro-organic synthesis, explicit effects of electrolyte, solvent, reagents, concentration, and electrode materials play a significant role in deciding the fate of the reaction. Electron withdrawing groups (EWG) like Fluoride, chloride, and phenyl groups have increased the electron affinity and hence increased redox potential for synthesis. For instance, under the present experimental conditions, the OCP of 5-fluoro isatin for the synthesis of **3g** was 0.005 V, which was higher than which was higher than that of unsubstituted isatin. The formation of the **3b** product was faster than the **3c**, keeping **3a** reactivity in between, which may be owed to the +I effect of the methyl group and the steric effect of the phenyl group [22]. It was found that when the electrochemical reaction is controlled by the mass transfer step, the electrolysis current density relates to the magnitude of the concentration gradient of the substrate molecule or the intermediate species at the electrode surface and interface [23].

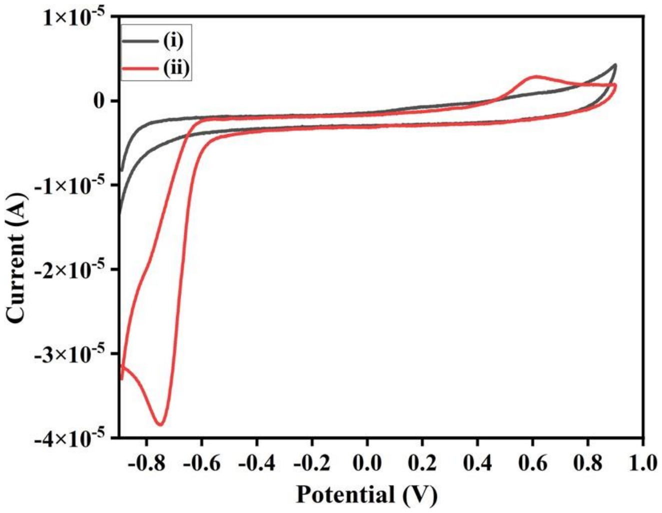


Figure 3.3 Cyclic voltammograms: (i) **1a** (ii) **3a.**

Overall, it was observed that chronopotentio graphs of (**3a-h**) have followed similar pattern (Fig.S1, ESI) and their potential region lies in 0.058 V, 0.004 V, -0.028 V, -0.030 V, -0.031 V, -0.058 V, -0.09 V, and -0.14 V in the order as follows: *N*-phenyl > -F > -Cl > -Br > -I > IS > N-methyl > $-CH_3$ with the high yield of **3a** (94%) and **3g** (91%) and other in good yield in the range of 84-90%. The better yield of **3g** can be conferred to the -I effect, which eventually affects the electrophilicity of the C3=O. It was observed that the synthesis of **3a**, **3b**, **3e**, and **3g** took relatively lesser time to furnish the final products. Importantly, it was observed that their synthesis got initiated at redox potentials or nearly OCP value. Electro organic synthesis of **3a** initiated with -0.055 V and raised to -0.059 V within 13 s. This shows that a reductive step follows initial oxidation. Due to the halogen bond activation mode of catalysis by molecular I_2, [24] wherein I_2 was reduced and further showed a plateau at the constant potential for 30 seconds, representing the transition time for the reaction.

It is followed by a continuous reduction process up to -0.061 V for about an initial 1000 s and followed by oxidation at -0.056 V and remains constant throughout the synthesis process. It indicates a more significant reaction and diffusion at the electrode surface [25].

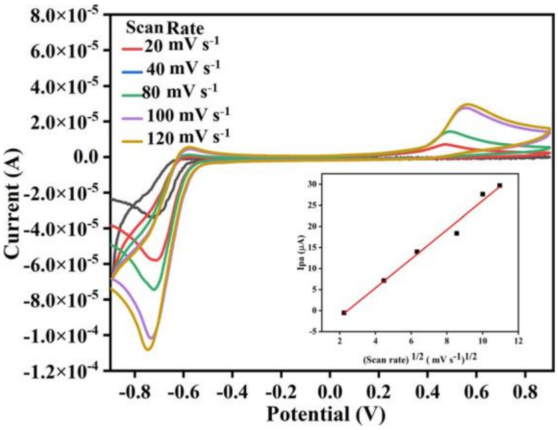


Figure 3.4 Cyclic voltammograms of **3c** at different scan rates. Inset shows the plot for I_{pa} vs. square root of scan rate.

Precipitate started to form after 16.67 min and continued to form until the reaction was completed. The progress of the reaction was observed by TLC. After completion of the reaction, the precipitate was washed with ethanol, filtered, and vacuum dried, followed by column chromatography to get pure vacuum dried, followed by column chromatography to get pure product. The details of the electro-organic synthesis of other compounds **3b-k**.

Cyclic voltammetry (CV) is a powerful and important electrochemical tool commonly used to investigate the reduction and oxidation process of molecular species. Therefore, CV measurements were carried out (**Figure 3.3**) using a glassy carbon (GCE) (d = 3mm) working electrode, Pt counter electrode (1 cm^2), and a non-aqueous $Ag/AgNO_3$ (0.1 M $AgNO_3$ in acetonitrile) as reference electrode, respectively and $NaClO_4$ (0.1 M) as supporting electrolytes was used.

Mechanical treatment of GCE was carried out as follows: polished using Alumina powder (particle size 0.01 µm) before each experiment, rinsed thoroughly, and cleaned with isopropyl alcohol (IPA). Then GCE was placed in an electrolyte, and various cyclic voltammograms were recorded until a steady state baseline voltammogram was obtained. This procedure ensured very reproducible experimental results. The cyclic voltammogram consists of two segments, i.e., anodic and cathodic (**Table 3.3**, ESI).

All the chosen substituted isatin (**3a-k**) exhibited well-defined diffusion-controlled quasi-reversible redox peak except 5-substituted derivatives. 5-Substituted derivatives showed a typical irreversible peak with an insignificant reduction in all cases while an oxidation peak for **3g** [26]. A study of the effect of scan rate is made to evaluate the mechanism and the feasibility of all product's electrochemical reactions involved at GCE in the electrolytic condition. (**Figure 3.4)** shows an exemplary cyclic voltammogram of **3c** where the oxidation and reduction current peaks increase with the increasing scan rate; however, in the case of oxidation, the increase of current is not as significant as for the reduction. For instance, in the case of **3c**, the linear dependence of peak current on the inverse of the square root of the sweep rate. (**Figure 3.4)** indicate that the migration of **3c** is proportional to the concentration of the species at the interface and hence it was a diffusion-controlled electrode process [27]. The inset shows the Randles-Sevcik plots for product **3c**, where the linear slope signifies the diffusion-controlled reaction. The linearity of the data points with a regression coefficient 0.98 indicates that the relationship is promising.

Cyclic voltammetry of isatin and malononitrile were not showing any peak, and hence redox inactive under the given reaction condition. However, iodine is quite reactive and exhibits quasi-reversible redox peaks. The interaction of I_2 with isatin showed a high current density compared to its interaction with malononitrile. This indicates that I_2 preferably interacts with the C3 position of isatin, being highly electrophilic rather than malononitrile. Moreover, the onset potential of the catalysis by I_2 via halogen bond activation and with **1a** is lower than that of **2a**. We monitored the anodic and cathodic peak currents, and peak potentials achieved during the interaction of I_2 reacted with **1a** and **2a**. CV was recorded in the potential range of +0.90V and -0.90 V in electrolytic solution (**Figure 3.5**), both **1a** and **2a** do not exhibit any redox activity. Whereas, when the CV was recorded in the standard electrolytic solution with dissolved I_2 + **1a** and I_2 + **2a** because with **1a,** the exchange of electrons is swift and interaction is more effective due to the involvement of partial negative charge of *O*-atom and lone pair of I_2. Hence, I_2 is bound with the carbonyl group at the C3-position of isatin and exhibits a higher peak current. Whereas in the latter case, the exchange of electrons is slower due to subsided electronegativity of the CN group due to the presence of methylene groups; hence interaction is weaker. This concept directs us to the inference that I_2 comes in contact with isatin at the anode and simultaneously malononitrile generates anion in the electrolytic solution, as shown in the given plausible mechanism (**Scheme 3.3** and **Figure 3.2**). Based on the above observations and a recent study [24], which supported that I_2 exhibits halogen bonding activation, which is a strong catalytic event, we can propose that, during synthesis, at the cathode, ethoxide ion generated and releases one electron to the cathode and former helps to generates malononitrile anion in solution. At the anode, isatin preferably undergoes a charge transfer reaction with I_2, which helps lower the activation energy for nucleophilic attack and thus facilitates the nucleophilic substitution at C3 position to furnish the product **3a** in excellent isolated yield.

3.3 Conclusions

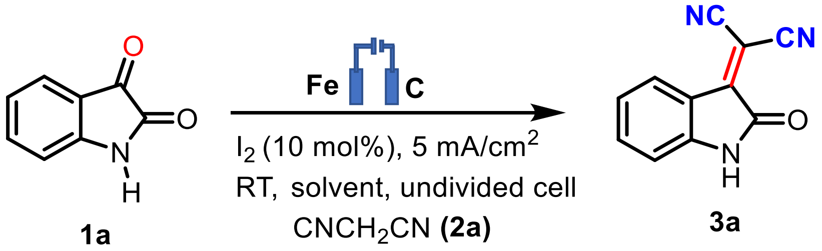
In conclusion, we have demonstrated that molecular iodine-catalyzed electro-organic synthesis of dicyano-isatylidene malononitrile derivatives can be achieved in a greener way at ambient temperature and cost-effective manner. This methodology can be used for the gram-scale synthesis of dicyano-isatylidene malononitrile derivatives. This finding will be helpful in the electro-organic synthesis of other isatin and indole derivatives which are biologically active compounds, and their synthesis and isolation are tedious. we are also in the process of elucidate further mechanistic details of these types of reactions in order to understand their scope and limitations, which will be disclosed in due course of time.

3.4 General experimental material and methods

All reactions were performed in an Electrochemical cell at room temperature (~25-26 °C). Solvents and chemicals were purchased from Merck. Prior to usage, all glassware underwent an extended 110 °C oven drying period. All commercial materials and solvents were used without purification unless otherwise indicated. Anhydrous acetonitrile, Methanol, and Ethanol were purchased from Sigma-Aldrich. A CHI-608C Potentiostat/ Galvanostat has been used for all electrochemical studies. All electrochemical experiments were performed in an undivided electrochemical cell using retried glassware. Each electro organic synthesis was performed using two electrodes system viz., carbon cloth (2 cm^2) as anode and iron cathode (2 cm^2) as cathode. All electrodes were purchased from Sinsil International India (CH Instruments). Thin-layer chromatography was performed using pre-coated plates contained from E. Merck (TLC silica gel 60 F254). TLC Plates were visualized by exposure to ultraviolet light (UV). The Column chromatography was performed on silica gel (100-200 mesh) using a mixture of ethyl acetate and hexane as eluent. Melting points were recorded on a digital melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded in Bruker Avance 500 MHz NMR spectrophotometer with operating frequencies of 500 MHz (^{1}H) and 125 MHz (^{13}C), respectively. Chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz.

The electro-organic synthesis was optimized by using different solvent (**Table 3.3**) and applied current density (**Table 3.4**).

Table 3.3. Reaction optimization in different solvents



Entry	Variation in Solvents[a]	Yields (%)
1	MeOH	75
2	CH_3CN	60
3	EtOH	94
4	DCM	47
5	DMF	50
6	H_2O	62

Laboratory Reagents (LR) grade solvents were used, which contained little moister. Reaction in CH_3CN, the DCM and DMF may be proceeding due to presence of this little moister and resulting poor yields.

Table 3.4. Variation of Applied current density under the standard condition

Entry	Applied Current density (mA/cm^2)	Yields (%)
1	No electricity	Not detected
2	2	Negligible
3	4	20
4	5	94
5	10	90
6	15	85

Screening the equivalent ratio of I_2/1a/2a: As shown in Table 3.5, the standard reaction entry 1, the proportion of I_2, **1a,** and **2a** was 0.1:1:1. As the concentration of I_2 is increased to its double, the yields slightly increases but on increasing the concentration of Isatin (**1a**) and malononitrile (**2a**) the yields was slightly decreases. This reaction was carried out in gram- scale adopting optimized reaction protocols which furnished product in very good isolated yields.

Table 3.5 Gram-scale synthesis of **3a** under various ratio of substrate and Iodine

Entry	Variation	Yields (%)
1	I_2(0.1eq.)/**1a**/(1eq.)/**2a**(1eq.)	94
2	I_2(0.2eq.)/**1a**/(1eq.)/**2a**(1eq.)	96
3	I_2(0.1eq.)/**1a**/(2eq.)/**2a**(1eq.)	93
4	I_2(0.1 eq.)/**1a**/(2eq.)/**2a**(2eq.)	89

3.4.1 General procedure for the cyclic voltammetry experiments in three electrode setup:

Cyclic voltammetry experiments were carried out in a three-electrode cell setup under an Argon atmosphere at room temperature. working, counter, and reference electrodes were glassy carbon disc (0.07 cm^2), platinum plate (1 cm^2), and non-aqueous Ag/$AgNO_3$ submerged in acetonitrile solution and connected with a salt bridge, respectively. The standard electrolyte for cyclic voltammetric studies was 0.1 $NaClO_4$ (supporting electrolyte) in acetonitrile solution (20 mL). The potential range for experiment was + 0.9 V to -0.9 V at different scan rate from 10 mVs^{-1} to 120 mVs^{-1}.

Table 3.6 Cyclic Voltametric parameters for the reactants

Reactants	Epa/V	Ipa/µA	Epc	Ipc
I_2(0.182-0.7005)	0.368	35.5 µA	0.005	-104 µA
I_2/Isatin **1a** (0.1890. 7005)	0.377	76 µA	0.018	-82µA
Malononitrile **2a** (0.217-0.715)	0.377	41.2µA	0.018	-52µA

Table 3.6 indicated that during the entire reaction, the anode potential was similar for all and iodine oxidizes readily with **1a** and **2a** both but we observed I_2 charge transfer reaction is more facile with isatin and thus higher current was observed. Therefore, in this reaction process, most probable interaction of I_2 and isatin occurs.

Figure 3.5 shows chronopotentiometry curves for electro-organic synthesis of 1- and 5- substituted isatylidene malononitrile derivatives.

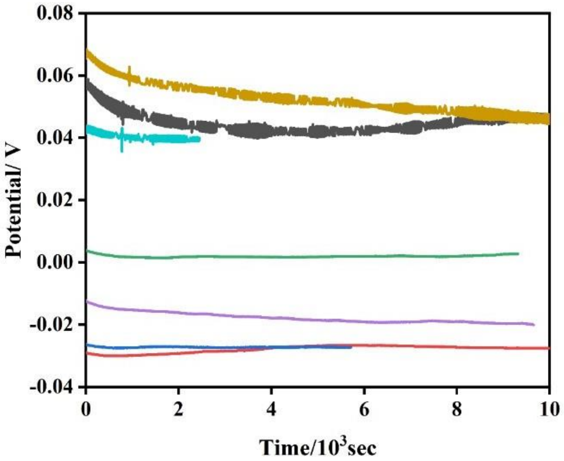


Figure 3. 5 Chronopotentiometric curves.

3.4.2 General procedure for the electrochemical synthesis of 2-(2-oxoindolin -3-ylidene) malononitrile 3a and its derivatives:

In an oven-dried undivided electrochemical cell equipped with a stir bar, isatin **1a** (1.0 mmol, 1.0 equiv.), I_2 (0.1 mmol, 1.0 equiv.) and malononitrile **2a** (1.0 mmol, 1.0 equiv.) in ethanol (10 mL) were combined and added. The anode and cathode were carbon cloth (20.0 mm ×10.0 mm×0.2 mm) and platinum plate (10.0 mm×10.0 mm×0.2 mm), respectively. For TLC purpose, solution was taken intermittently into the vial via syringes. The reaction mixture was continuously stirred and electrolyzed with a constant current density of 5 mA cm^{-2} at room temperature. When the reaction was finished, the pure product was washed and dried and further worked up by column chromatography on silica gel (100-200 mesh size) using hexane and ethyl acetate (2:1) as the eluent to furnished **3a** in 94% isolated yield. The product **3a** was confirmed by melting point and sample for NMR was prepared in DMSO-d_6 solvent. Similar reaction procedure was adopted for other substrates. All reactions proceed with high yields and no side products could be detected under the reaction conditions.

3.5 Electro-organic synthesis of 3b-3k derivative:

3b: After setting up the electrodes, an OCP measurement was taken which is found to be ranging from -0.008 to -0.01 V. After OCP, CP started at -0.1 V and fall down steeply to 0.008 V after the 950 s, followed by a plateau till the 2400 s and then rising up to 0.0091 V till the 3600 s and staying at 0.009 V for the next 4000 s. It again rises continuously to 0.01V up to product formation in 6310 s (~2 h and 15 min) which yields 91%.

3c: After setting up the electrode, an OCP measurement was taken which is found to be 0.07V. After OCP, CP started at 0.056 V which steeply fall to 0.047 V in 2000 s then fall to 0.042 V in 3200 s and remain there for up to 7250 s (2 hours) and raise slightly to 0.047 V to form the product after 10600 s which yields 84%. The conversion was very slow at 0.042 V.

3d: After setting up the electrodes, an OCP was found to be -0.01 V. Unlike synthesis of **3a**, here no raise in potential was observed which indicates that the electrochemical synthesis is very facile and reduction of electrophilic species has started at once and during the synthesis, it shows the variation of potential from -0.012 to -0.021 V for 10600 s. Such a reaction corresponds to high electron density at the reactant which facilitates a reduction reaction swiftly and it yields 87% of the product.

3e: After setting up the electrodes, an OCP was observed at -0.026 V. CP was initiated from OCP value and fall down to -0.0274 V in 500 s and then a plateau was observed for the next 500 s there after rise in potential was observed to -0.0271 V for 6000 s synthesis was followed by an almost constant potential of -0.0273 V. These steps in synthesis correspond to initial reduction and then diffusion of a reactive moiety at the electrode surface. Further, oxidation of reactive species followed by diffusion and then continuous synthesis of the product reaching towards the product formation in the electrochemical solution which yields 90%.

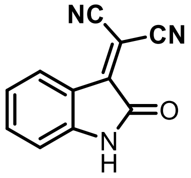
3f: Here, OCP was observed at -0.0288 V and CP was instigated from OCP value and came down to -0.030 V in 400 s and observed a plateau for 500 s and then raised slowly to -0.0267 V till 5110 s and formed a plateau for about 6675 s and then synthesized slowly at a constant potential of -0.027 V until single spot corresponding to 5-BIM was obtained in 10600 s. The chronopotentiometry graph indicates an initial reduction followed by oxidation of the reactive species and its diffusion towards the electrode surface and then the formation of the product in the electrochemical solution. It yields 88% of the product.

3g: Here, OCP was observed at 0.050 V and found to be very stable among all 5 substituted isatin derivatives. CP was started at 0.04 V and fall down to 0.002 V in the 700 s and react (oxidize) slowly up to the 1800 s to 0.001 s to 0.001 V then starts to reduce till 2600 s and then a limited mass transfer plateau (at 0.002 V) was observed (~7500 s) which shows product formation. Electro-organic synthesis curve shows that initial oxidation for 2 s is followed by a reductive step. This oxidation process may be due to the bonding interaction of isatin and I_2, where I_2 gets reduced. The plateau represents the transition time of the 30 s which corresponds to the greater extent of reaction and diffusion at the electrode surface and completes in 2 hours which yields 91%.

3h: Here, OCP was found at -0.03 V and electro-organic synthesis took place at constant -0.3 V. Reaction completed in 10500 s which yields 87%.

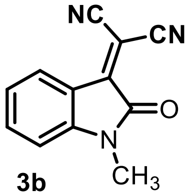
3i-3k: a constant OCP of 0.073 V ± 0.01 V was observed here. A similar pattern was observed for 7-substituted derivatives, for example in 3i, CP started at 0.06 ± 0.01 V and slowly fall down to 0.059 V in 900 s and then slowly downfall in the potential to 0.054 V took the next 3000 s while falling in the potential to 0.051 V took next 5800 s and finally reached to product formation at 0.046 V in (10000-10100 s) and yields final products in range of 88-89%. The conversion was very slow at 0.052 V.

3.6 Spectroscopic data of all compounds (3a-3k)



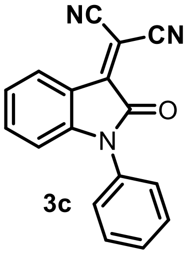
3a

2-(2-oxoindolin-3-ylidene) malononitrile (3a). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane, 1:4), Red Solid, Yield (94%); m.p.197-199 °C; **^{1}H NMR** (500 MHz, DMSO-d$_6$) δ = 11.21 (s, 1H, NH), 7.87 (d, J = 7.9 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 7.9 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, DMSO-d$_6$): δ = 163.8, 150.7, 146.5, 137.9, 125.9, 123.0, 118.7, 113.1, 111.7, 111.6, 80.7 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_5N_3O$ $[M+H]^+$ 196.0511, found 196.0521;



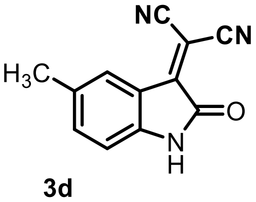
3b

2-(1-methyl-2-oxoindolin-3-ylidene) malononitrile (3b). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, yield (91%); m.p. 235-236 °C; **^{1}H NMR** (500 MHz, DMSO-d$_6$) δ = 7.92 (d, J = 7.9 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 3.16 (s, 3H). **^{13}C NMR** (125 MHz, DMSO-d$_6$): δ = 162.4, 149.8, 147.2, 137.7, 125.4, 123.4, 118.0, 112.9, 111.4, 110.5, 81.2, 26.2 ppm; HRMS (ESI) m/z: calcd for $C_{12}H_7N_3O$ $[M+H]^+$ 210.0667, found 210.0621;



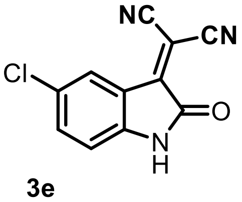
3c

2-(2-oxo-1-phenylindolin-3-ylidene) malononitrile (3c). The product was purified by silica gel column chromatography (Ethyl acetate :Hexane, 1:4) Red Solid, Yield (84%); m.p.197-199 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ = 8.05 (d, J = 7.9 Hz, 1H), 7.64 – 7.59 (m, 3H), 7.55 – 7.51 (m,1H), 7.50 – 7.49 (m, 1H), 7.49 – 7.47 (m, 1H), 7.30 – 7.25 (m, 1H), 6.82 (d, J = 8.0 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, DMSO- d_6) δ = 161.9, 149.9, 147.0, 137.7, 132.6, 129.8, 128.9, 126.7, 125.7,123.9, 118.2, 113.0, 111.4, 110.7, 81.2 ppm; HRMS (ESI) m/z: calcd for $C_{17}H_9N_3O$ $[M+H]^+$ 272.0824, found 272.0812;



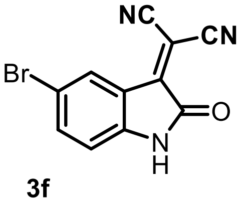
3d

2-(5-methyl-2-oxoindolin-3- ylidene) malononitrile (3d). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, Yield (87%); m.p. 263-266 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ = 11.10 (s, 1H, NH), 7.65 (s, 1H), 7.39 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 2.28 (s, 3H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ = 163.9, 150.7, 144.6, 138.7, 132.1, 125.8, 118.8, 113.2, 111.7, 111.6, 79.5, 19.9 ppm; HRMS (ESI) m/z: calcd for $C_{12}H_7N_3O$ $[M+H]^+$ 210.0667, found 210.0632;



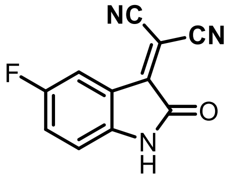
3e

2-(5-chloro-2-oxoindolin-3-ylidene) malononitrile (3e). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, Yield (90%); m.p. 221-223 °C; 1H NMR (500 MHz, DMSO-d_6: δ = 10.15 (s, 1H, NH), 6.56 (s, 1H), 6.41 (d, J = 7.9 Hz, 1H), 5.77 (d, J = 8.0 Hz, 1H), ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 163.8, 149.9, 145.4, 137.3, 126.9, 125.2, 120.2, 113.6, 112.3, 111.5, 82.2 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4ClN_3O$ $[M+H]^+$ 230.0121, found 230.0152;



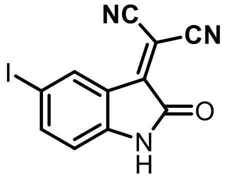
3f

2-(5-bromo-2-oxoindolin-3-ylidene) malononitrile (3f). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane,1:4) Brown Red Solid, Yield (88%); m.p.222- 224 °C; **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 11.16 (s, 1H, NH), 7.51 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.92 (s, 1H) ppm. **^{13}C NMR** (125 MHz, DMSO-d_6): δ = 163.7, 149.7, 145.78, 140.0, 128.0, 120.6, 114.4, 114.0, 112.9, 111.4, 82.6 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4BrN_3O$ $[M+H]^+$ 273.9616, found 273.9651;



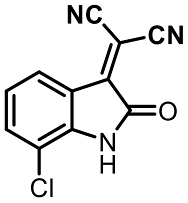
3g

2-(5-fluoro-2-oxoindolin-3-ylidene) malononitrile (3g). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, Yield (91%)**;** m.p**.** 232-233 °C**;** ^{1}**HNMR** (500 MHz, DMSO-d_6) δ = 10.80 (s, 1H, NH), 7.60 (s, 1H), 7.44 (dd, J = 8.0 Hz, J = 2.1 Hz,1H), 6.71 (d, J = 8.5 Hz, 1H) ppm. ^{13}**C NMR** (125 MHz, DMSO-d_6) δ = 164.2, 151.1, 146.9, 138.2, 126.3, 123.3, 119.1, 112.6 112.1, 81.0 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4FN_3O$ $[M+H]^+$ 214.0417, found 214.0432;



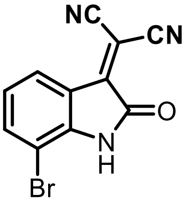
3h

2-(5-iodo-2-oxoindolin-3-ylidene) malononitrile (3h). The product was purified by silica gel column chromatography (Ethyl acetate: Hexane, 1:4) Red Solid, Yield (87%); m.p. 230-233 °C; ^{1}**H NMR** (500 MHz, DMSO-d_6) δ = 11.03 (s, 1H, NH), 7.44 (d, J = 8.9 Hz, 1H), 7.40 (d, J = 8.9 Hz, 1H), 6.92 (s, 1H) ppm. ^{13}**C NMR** (125 MHz, DMSO-d_6) δ = 164.1, 157.0; 150.6, 143.4, 125.0, 124.8, 113.4, 113.3,112.5,112.3, 82.7 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4IN_3O$ $[M+H]^+$ 321.9477, found 321.9432;



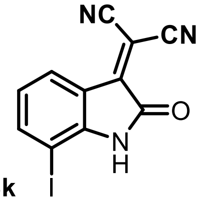
3i

2-(7-chloro-2-oxoindolin-3-ylidene) malononitrile (3i). The product was purified by column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, Yield (89%); m. p. 189-194 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ =11.31 (s, 1H, NH), 7.78 (d, J = 8.5 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.02 (t, J = 8.2 Hz, 1H) ppm; **^{13}NMR** (125 MHz, DMSO-d_6) δ = 163.8, 150.2, 143.7, 136.7, 124.3, 124.0, 120.4, 115.7, 112.8, 111.3, 82.1 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4ClN_3O$ $[M+H]^+$ 230.0121, found 230.0128;



3j

2-(7-bromo-2-oxoindolin-3-ylidene) malononitrile (3j). The product was purified by column chromatography (Ethyl acetate: Hexane,1:4) Brown Red Solid, Yield (88%); m.p. 190-195 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ = 10.63 (s, 1H, NH), 7.34 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 8.1 Hz, 1H), 6.87 (t, J = 8.0 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, DMSO-d_6) δ = 164.2, 150.7, 144.2, 137.1, 124.8, 128.5, 120.9, 116.2, 113.2, 111.8, 82.6 ppm; HRMS (ESI) m/z: calcd for $C_{11}H_4BrN_3O$ $[M+H]^+$ 273.9616, found 273.9625;



3k

2-(7-iodo-2-oxoindolin-3-ylidene) malononitrile (3k). The product was purified by column chromatography (Ethyl acetate: Hexane,1:4) Red Solid, Yield (89%); m.p.192-197 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ = 11.45 (s, 1H, NH), 7.66 (d, J = 8.1 Hz, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, DMSO-d_6) δ = 163.7, 150.2, 143.7, 136.6, 124.3, 124.0, 120.4, 115.7, 112.7, 111.3, 82.1 ppm; HRMS

(ESI) m/z: calcd for $C_{11}H_4IN_3O$ $[M+H]^+$ 321.9477, found 321.948;

^{1}H NMR (500MHz, DMSO-d_6) and ^{13}C NMR (125 MHz, DMSO-d_6) 3a-

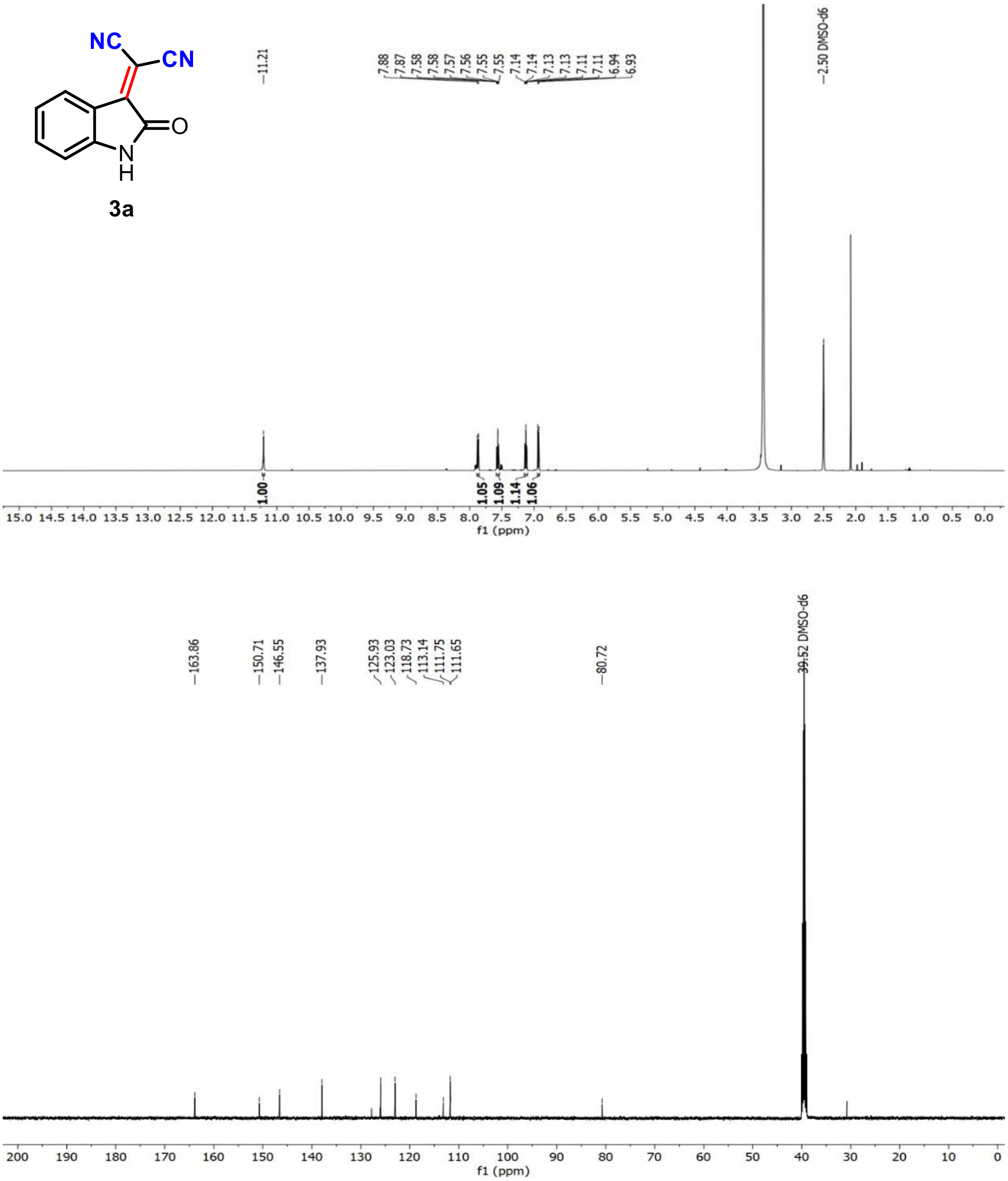


Figure 3.6 ^{1}H NMR ^{13}C NMR spectra of compound 3a in DMSO.

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