

## **I<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub>: An efficient catalyst for the synthesis of 5-aryl-2,6-dicyano-3-methylanilines**

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**Abstract.** Molecular iodine in the presence of potassium carbonate has been found to be an efficient and eco-friendly catalyst for the synthesis of polysubstituted dicyanoanilines from aldehydes, acetone and malononitrile under solvent-free thermal condition. The experimental procedure is simple, includes shorter reaction times (less than 10 min) and results in excellent yield of the products.

**Keywords.** Acetone; aldehydes; molecular iodine; malononitrile; potassium carbonate; solvent-free condition.

### **1. Introduction**

One-pot multicomponent reactions (MCRs) have been found to be attractive synthetic strategies to generate multiple molecular scaffolds and to increase structural as well as skeletal diversity from simple and easily available molecules.<sup>1</sup> It is a vital field of chemistry involving the synthesis of complicated molecules which can be achieved in a very fast, efficient, and time saving manner without the isolation of any intermediates.<sup>2</sup>

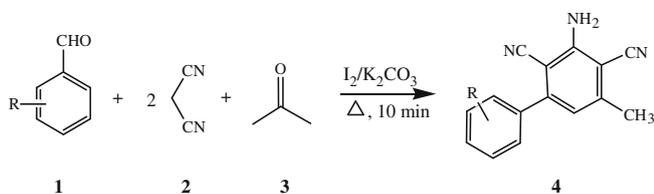
Photo-induced intramolecular electron transfer (PIET) leading to a charge separation in a supramolecular structure plays a fundamental role in the dynamics of concomitant processes involved in the photosynthesis, in biology, in photonics or in the solar energy conversion.<sup>3</sup> One of the factors that tune the efficiency of the PIET is the distance between the acceptor and the donor groups. To obtain a long-lived charge separation, much attention has been devoted to the investigation of the acceptor–donor–acceptor (A–D–A) systems comprising one electron donor and two electron acceptors.<sup>4</sup>

3,5-Diaryl-2,6-dicyanoanilines have been prepared from acetone and arylidenemalononitriles or 1-arylethylidenemalononitriles in the presence of piperidine.<sup>5</sup> The reaction between malononitrile and  $\alpha,\beta$ -unsaturated ketones can also give 3,5-diaryl-2,6-dicyanoanilines, but in poor yield (5–20%).<sup>6</sup> One-pot three-component reactions of aromatic aldehydes, mal-

ononitrile and acetone in the presence of basic catalysts have also been reported to give the desired products.<sup>7–11</sup> Recently, Mehdi *et al.* have reported the synthesis of dicyanoanilines by the reaction of nitrostyrenes and malononitrile in the presence of sodium carbonate.<sup>12</sup> These protocols suffer from several drawbacks, such as multistep reactions (linear synthesis), long reaction times, use of excess amounts of volatile organic solvents, harsh refluxing conditions, use of toxic chemicals and especially lower product yields. Hence, it becomes a necessity to develop a protocol in which environmentally benign catalyst is used and the desired product is obtained in high to excellent yields which can find application in pharmaceutical industry. Previously, we have reported the synthesis of 5-aryl-2,6-dicyano-3-methylanilines in the presence of sodium methoxide under grindstone method.<sup>13</sup> Since grindstone method is not a prudent method, we have developed a solvent-free thermal reaction using an environment friendly catalyst iodine/potassium carbonate.

An increase in public concern over environmental hazards, eco-friendly solvents like water and solvent-free reactions have found many applications. Use of the green chemical technologies have many advantages such as low cost, reduced pollution, enhanced rate of reaction and simple work-up procedure. On the other hand, 'Iodine' being a mild Lewis acid as well as an oxidant has been used in many organic transformations and in organic synthesis. The advantages include its environment-friendly nature, non-toxicity, ready availability, low cost and it affords products in excellent yield with high selectivity.<sup>14</sup>

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R = H; 4-OCH<sub>3</sub>; 3,4-(OCH<sub>3</sub>)<sub>2</sub>; 4-CH<sub>3</sub>; 4-Cl; 4-NO<sub>2</sub> and Furan-2-yl

**Scheme 1.** Synthesis of polysubstituted dicyanoanilines.

Previously, we have reported the use of iodine in the synthesis of many biologically important molecules like  $\beta$ -acetamido- $\beta$ -aryl-propiophenones,<sup>15</sup> aryl-14*H*-dibenzo [*a*, *j*]xanthenes,<sup>16</sup> *N*, *N'*-disubstituted ureas/thioureas,<sup>17</sup>  $\beta$ -enaminones,<sup>18</sup> azines,<sup>19</sup> and 4,6-diarylpyrimidin-2(1*H*)-ones.<sup>20</sup> Since our laboratory is specialized in the synthesis of biologically important molecules or their precursors, we extended our work to the synthesis of polysubstituted dicyanoanilines (2,6-dicyano-aryl-anilines) by a one-pot three component reaction of aryl aldehydes, malononitrile and acetone using a mixture of I<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub> as a catalyst by a solvent-free thermal reaction as shown in scheme 1.

## 2. Experimental

### 2.1 Materials and apparatus

The chemicals used were commercial reagents. Melting points were determined using a Raaga, Chennai, Indian make melting point apparatus. Reactions were monitored on TLC by comparison with the authentic samples. Nuclear magnetic resonance spectra were obtained on a 400 MHz Bruker AMX spectrometer in DMSO-*d*<sub>6</sub> using TMS as a standard. LC-Mass spectra were performed on an Agilent Technologies 1200 series instrument. Infrared spectra were recorded using Shimadzu FT-IR-8400s Spectrophotometer as KBr pellets.

### 2.2 Typical experimental procedure for the synthesis of 4a

A mixture of benzaldehyde (5.0 mmol), malononitrile (10.0 mmol), acetone (5.0 mmol), Iodine (0.25 mmol) and K<sub>2</sub>CO<sub>3</sub> (0.25 mmol) was mixed well. The resulting mixture was heated on a pre-heated oil bath for 10 min at 80°C. At the end of the reaction, the liquefied reaction mixture suddenly turned into a solid; water (10 mL) was then added to the flask and stirred for several minutes and filtrated through a sintered funnel to

afford the crude product, which was further purified by recrystallization using absolute ethanol.

### 2.3 Spectral data of some of the products

**4a:** IR (KBr)  $\nu_{\max}$  = 3467, 3348, 3238, 2225, 1643, 1560, 1419, 1286, 752, 696 cm<sup>-1</sup>; <sup>1</sup>HNMR (DMSO, 400 MHz):  $\delta$  2.45 (s, 3H, CH<sub>3</sub>), 6.71 (s, 2H, NH<sub>2</sub>), 6.76 (s, 1H, C-H), 7.50–7.55 (m, 5H, H-Ar) ppm; <sup>13</sup>C NMR (DMSO, 100 MHz):  $\delta$  21.6, 98.0, 116.0, 125.3, 128.5, 130.0, 135.0, 139.0, 150.0, 150.9 ppm; HRMS (M+Na): 256.0849

**4b:** IR (KBr)  $\nu_{\max}$  = 3465, 3342, 3236, 2223, 1643, 1560, 1519, 1411, 1261, 1033, 823 cm<sup>-1</sup>; <sup>1</sup>HNMR (DMSO, 400 MHz):  $\delta$  2.44 (s, 3H, CH<sub>3</sub>), 3.83 (s, 3H, OCH<sub>3</sub>), 6.65 (s, 2H, NH<sub>2</sub>), 6.73 (s, 1H, C-H), 7.07–7.09 (d, 2H, *J* = 8 Hz, H-Ar), 7.50–7.52 (d, 2H, *J* = 8 Hz, H-Ar) ppm; <sup>13</sup>C NMR (DMSO, 100 MHz):  $\delta$  20.1, 54.18, 91.8, 94.4, 112.9, 114.5, 115.3, 118.0, 128.6, 128.8, 146.3, 148.2, 152.4, 159.2 ppm; HRMS (M+Na): 263.1055

**4g:** IR (KBr)  $\nu_{\max}$  = 3413, 3355, 2221, 1668, 1525, 1419, 1350, 740, 698 cm<sup>-1</sup>; <sup>1</sup>HNMR (DMSO, 400 MHz):  $\delta$  2.38 (s, 3H, CH<sub>3</sub>), 6.25 (s, 1H, C-H), 6.99 (s, 2H, NH<sub>2</sub>), 7.42–7.44 (d, 2H, *J* = 8.4 Hz, H-Ar), 7.76–7.79 (d, 1H, *J* = 8.4 Hz, H-Ar) ppm; <sup>13</sup>C NMR (DMSO, 100 MHz):  $\delta$  20.4, 87.0, 91.6, 115.8, 117.0, 120.2, 124.6, 128.0, 128.0, 143.6, 146.8, 147.2, 152.6 ppm; HRMS (M+Na): 278.0800

## 3. Results and discussion

A test reaction using benzaldehyde (5 mmol), malononitrile (10 mmol) and acetone (5 mmol) under solvent-free thermal condition in the absence of catalyst was carried out. The contents were taken in a round bottom flask fitted with a reflux condenser and heated in an oil bath at 80°C, it was observed that, even Knoevenagel condensation between benzaldehyde and malononitrile did not occur after 2 h.

Ren and Cai have reported the Knoevenagel condensation between aldehydes and active methylene compounds in the presence of I<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub> in EtOH or DMF.<sup>21</sup> Knoevenagel condensation of aldehydes with active methylene compounds is also possible in the presence of I<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub>/KI in water (Ren and Cai).<sup>22</sup> It has been found that, use of only I<sub>2</sub> or K<sub>2</sub>CO<sub>3</sub> alone for the synthesis of this adduct results in low yield and requires longer reaction duration.

**Table 1.** Optimization of the reaction conditions.

Entry	Solvent	I <sub>2</sub> (mmol)	K <sub>2</sub> CO <sub>3</sub> (mmol)	Temperature (°C)	Time (h/min)	Yield (%)
1	EtOH	1.0	1.0	28-30 <sup>a</sup>	5 h	30
2	EtOH	1.0	1.0	Reflux <sup>a</sup>	2 h	40
3	H <sub>2</sub> O	1.0	1.0	Reflux <sup>a</sup>	2 h	36
4	Solvent-free	1.0	1.0	80 <sup>b</sup>	10 min	70
5	Solvent-free	0.75	0.75	80 <sup>b</sup>	10 min	80
6	Solvent-free	0.50	0.50	80 <sup>b</sup>	10 min	86
7	Solvent-free	0.25	0.25	80 <sup>b</sup>	10 min	92
8	Solvent-free	0.12	0.12	80 <sup>b</sup>	10 min	85

<sup>a</sup> Benzaldehyde (5 mmol), malononitrile (10 mmol) and acetone (30 mmol)

<sup>b</sup> Benzaldehyde (5 mmol), malononitrile (10 mmol) and acetone (5 mmol)

<sup>c</sup> Isolated yields

Since the mechanism of synthesis of 2,6-dicyano-aryl-anilines involves the formation of Knoevenagel adduct in the first step,<sup>7</sup> we decided to add equal amounts of I<sub>2</sub> and K<sub>2</sub>CO<sub>3</sub> (1 mmol each) in EtOH to the mixture of benzaldehyde, malononitrile and acetone at 25°C. After vigorous stirring for 5 h, only 30% of the desired product was obtained. To increase the yield and to optimize the reaction conditions, we refluxed the reactants in EtOH and in water. Under reflux in EtOH, the yield did improve; when water was used as a solvent under reflux condition, there was not much improvement in the yield. When we heated the reactants on a pre-heated oil bath at 80°C under solvent-free condition, satisfactory yield was obtained in a short duration (92%, 10 min), hence, all the other reactions were carried out under solvent-free thermal condition at 80°C for 10 min (scheme 1).

To study the catalytic activity of the iodine/potassium carbonate mixture; the reaction was carried out with various amounts of I<sub>2</sub> and K<sub>2</sub>CO<sub>3</sub>. The summary of the

optimization of the reaction conditions has been tabulated in table 1.

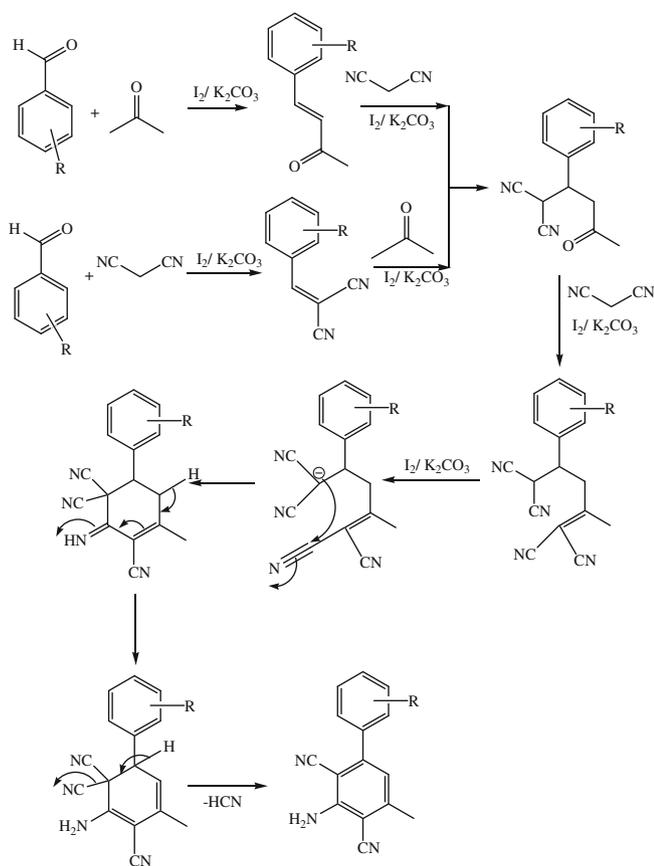
Using the optimized reaction condition (table 1, entry 7), the scope of the reaction was tested by extending the reaction to different aldehydes and it was found that, all the aldehydes displayed high reactivity and generated the products in good to excellent yields. The results in table 2 indicate that the aromatic aldehydes bearing both electron-donating and electron-withdrawing groups gave excellent yield of the desired products. In addition to aromatic aldehydes, heteroaromatic aldehyde such as furan-2-aldehyde also participated well in this protocol. All the 2,6-dicyano-aryl-anilines were characterized by comparison of their spectroscopic and physical data with authentic samples.

A tentative mechanism would include probable sequence of events involving the formation of Knoevenagel adduct and aldol condensation followed by Michael addition and Thorpe–Ziegler cyclization to give 2,6-dicyano anilines after tautomerization (scheme 2).

**Table 2.** I<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub> catalysed synthesis of 5-aryl-2,6-dicyano-3-methylanilines from aldehydes, malononitrile and acetone under solvent-free thermal condition.

Entry	Aldehyde R =	Product	Yield <sup>a</sup> %	Melting point (°C)	Lit. M. P. (°C)
a	H	<b>4a</b>	92	187	188–190 <sup>11</sup>
b	4-OCH <sub>3</sub>	<b>4b</b>	97	189	190 <sup>11</sup>
c	3,4-(OCH <sub>3</sub> ) <sub>2</sub>	<b>4c</b>	95	222	224–225 <sup>11</sup>
d	4-CH <sub>3</sub>	<b>4d</b>	91	219	200 <sup>11</sup>
e	Furan-2-yl	<b>4e</b>	90	196	198–199 <sup>12</sup>
f	4-Cl	<b>4f</b>	95	237	236–240 <sup>11</sup>
g	4-NO <sub>2</sub>	<b>4g</b>	89	228–230	—

<sup>a</sup>Isolated yield



**Scheme 2.** A plausible mechanism for the formation of dicyanoanilines.

#### 4. Conclusion

In conclusion,  $I_2/K_2CO_3$  catalysed one-pot three-component coupling of aldehydes, malononitrile and acetone has been achieved. The process is simple and efficient, generates a diverse range of fluorescent 5-aryl-1,2,6-dicyano-3-methylanilines in good to excellent yields. A high atom efficient reaction following green protocol with easy work-up, clean reaction profile and cost effectiveness of the catalyst are the advantages for the use of this protocol in industry. The synthetic applications of these products are under investigation.

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