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ORIGINAL ARTICLE

# A convenient one-pot synthesis and anxietic activity of 3-cyano-2(1*H*)-iminopyridines and halogen derivatives of benzo[*h*]chromenes

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**KEYWORDS**

Benzo[*h*]chromene derivatives;
Iminopyridines;
Multicomponent reactions;
Anxietic activity

**Abstract** A general and easy method for the synthesis of 4,6-disubstituted-3-cyano-2(1*H*)-iminopyridine or 3-amino-6-chloro-1-aryl-1*H*-benzo[*h*]chromen-2-yl cyanide derivatives in the presence of high surface area MgO as a highly effective heterogeneous base catalyst is described. These compounds were synthesized using one-pot multicomponent reactions of the properly substituted acetophenone, appropriate aldehyde, ammonium acetate and malononitrile or three component reactions of 4-chloro-2-naphthol, aldehydes and malononitrile, respectively, in DMF. The compound of **7c** was evaluated for its anxiolytic activities.



## 1. Introduction

The development of efficient and novel synthetic methods for the construction of polyfunctionalized heterocyclic compounds have allocated a broad area of organic and medicinal chemistry (Domling and Ugi, 2000; Domling, 2006). Pyridines and benzo[*h*]chromene derivatives have recently received considerable attention due to their synthetic and pharmaceutical importance. So different approaches for their synthesis have been developed (Khafagy et al., 2002; El-Saghier et al., 2007). Among these heterocycles, pyridine derivatives are an important class in pharmaceutical discovery. 2-Amino-3-cyanopyridines and 3-cyano-2-pyridones are known to have diverse biological and pharmacological activities, particularly antimicrobial (Temple et al., 1992), antidepressant (Murata et al., 2005), cardiotonic (Shi et al., 2005) and anticancer activity (Abadi et al., 1999).

## 2. Results and discussion

These findings encouraged us to explore the synthesis of 2-amino-4-aryl-6-alkyl(aryl)-3-cyanopyridines through a

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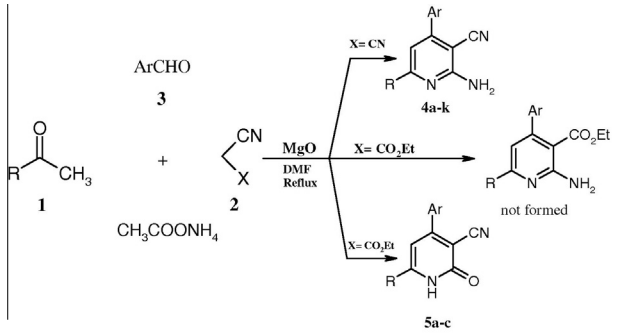



**4a**: R= $CH_3$, Ar= 4-$ClC_6H_4$, X= CN
**4b:** R= $CH_3$, Ar= 4-$(MeO)C_6H_4$, X= CN
**4c:** R= $CH_3$, Ar= 4-$MeC_6H_4$, X= CN
**4d:** R= $CH_3$, Ar= $C_6H_5$, X= CN
**4e:** R= $C_6H_5$, Ar= 4-$(MeO)C_6H_4$, X=CN
**4f:** R= 4-$(MeO)C_6H_4$, Ar= 4-$ClC_6H_4$, X=CN
**4g:** R= 4-$(MeO)C_6H_4$, Ar= 4-$(MeO)C_6H_4$, X=CN
**4h:** R= 2,4-$(MeO)_2C_6H_3$, Ar= $C_6H_5$, X= CN
**4i**: R= 2,4-$(MeO)_2C_6H_3$, Ar= 4-$ClC_6H_4$, X= CN
**4j:** R= 2,4-$(MeO)_2C_6H_3$, Ar= 4-$(MeO)C_6H_4$, X=CN
**5a:** R= 2,4-$(MeO)_2C_6H_3$, Ar= $C_6H_5$, X= $CO_2Et$
**5b:** R= 2,4-$(MeO)_2C_6H_3$, Ar= 4-$ClC_6H_4$, X= $CO_2Et$
**5c:** R= 2,4-$(MeO)_2C_6H_3$, Ar= 4-$(MO)C_6H_4$, X= $CO_2Et$

**Scheme 1** One-pot synthesis of 2-amino-4-aryl-6-alkyl(aryl)-3-cyanopyridines in the presence of MgO.

three-component reaction of a ketone such as acetone, cyclohexanone or acetophenone, aryl aldehydes, malononitrile and ammonium acetate in the presence of MgO as a highly effective heterogeneous base catalyst (Scheme 1).

We found that a mixture of ketones **1**, aryl aldehydes **2**, malononitrile and ammonium acetate in the presence of high surface area MgO as a highly effective heterogeneous base catalyst and as an inexpensive and readily available catalyst, afforded 4,6-disubstituted-3-cyano-2(1*H*)-iminopyridines in good to excellent yields and in a short experimental time (Table 1). Many of the standard procedures require either longer reaction times or in some cases lead to mixtures of products and proceed in low yields (Murata et al., 2005; Shi et al., 2005; Abadi et al., 1999).

The formation of products **4a–j** can be rationalized by the initial formation of imine **I** from aldehyde and ammoni-um acetate, imine **I** reacts with alkylidenemalononitrile **II** (from condensation of aromatic aldehyde with malo- nonitrile) to give **III**, followed by cycloaddition, isomerization, aromatization to afford the 2-amino-3-cyanopyridine derivatives **4** (Scheme 2).

Encouraged by these results, we also developed our investigation and replaced the activated phenolic compounds such as α-naphthol or 4-chloro-1-naphthol **6** instead of ketones in same conditions (Scheme 3).

The three-component reaction of malononitrile, aldehydes and phenolic β-naphthol **8**, is extended to the formation of 2-amino-fused chromenes **9a–c** in the presence of magnesium oxide (MgO) as a highly effective heterogeneous base catalyst (Scheme 4).

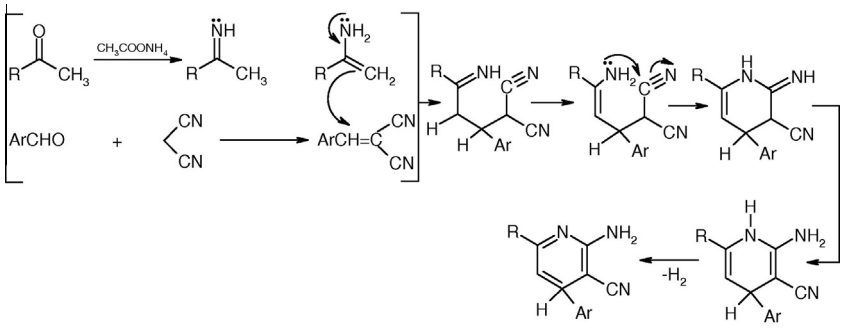
2-Amino-chromenes and fused chromenes are an important class of compounds found as the main components of many naturally occurring products employed as cosmetics and pigments (and utilized as potential biodegradable agrochemicals (Hafez et al., 1987; Abdel Galil et al., 1982). Numerous reports delineate the antitumor (Mohr et al., 1975), antimicrobial activities (Bedair et al., 2000), and the central nervous system (CNS) activity (Eiden and Denk, 1991) of these compounds. Similarly, in recent years, considerable attention has been focused on the development of new methodologist to synthesize many kinds of chromene ring system. These compounds are generally prepared by reacting malononitrile, an aldehyde and an activated phenol in organic solvents (i.e. acetonitrile, ethanol) and in the presence of organic bases like piperidine, which are frequently utilized in stoichiometric amounts (Ballini et al., 2001; Khafagy et al., 2002). In the present study we found that these compounds could be synthesized in a one step procedure in the presence of high surface area MgO as a highly effective heterogeneous base catalyst in excellent yields and in a short reaction time (Table 2).

Three component reactions of salicylaldehyde, malononitrile and a ketone **11a–c** in the presence of high surface area MgO afforded the 4-(2-hydroxyphenyl)-6-alkyl-3-cyano-2(1*H*)-iminopyridine derivatives **12a–c** (Scheme 5). Structures of these compounds were established on the basis of IR spectra which showed the presence of CN at 2200–2210 $cm^{-1}$ and OH (phenolic proup) at 3200–2900 $cm^{-1}$ (broad peak), respectively.

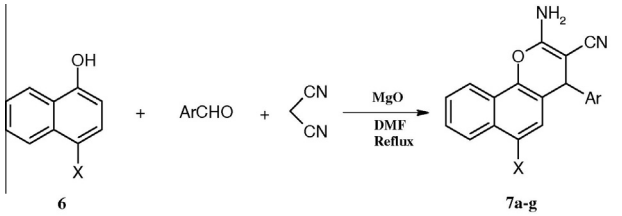
Hutchings and co-workers investigated the reaction of a high surface area form of MgO as a catalyst for a number of different Michael additions and Knoevenagel condensations

**Table 1** Synthesis of **4a–i** in the presence of base catalysts.

| Com. No. | [Without Catalyst] | | Commercial (MgO) | | High surface area (MgO) | | M. P. °C | M. P. reported °C [Ref.] |
|---|---|---|---|---|---|---|---|---|
| | Time (h) | Yield (%) | Time (h) | Yield (%) | Time (min) | Yield (%) | Observed | |
| **4a** | 6 | 53 | 4 | 68 | 9 | 86 | 170–172 | 172–173 (Shi et al., 2005) |
| **4b** | 6 | 44 | 5 | 50 | 10 | 81 | 238–240 | 241–242 (Kambe et al., 1980) |
| **4c** | 6 | 65 | 4 | 69 | 9 | 79 | 255–257 | 258–260 (Kambe et al., 1980) |
| **4d** | 6 | 45 | 4.5 | 68 | 9 | 80 | 234–235 | 236–237 (Kambe et al., 1980) |
| **4e** | 5 | 42 | 4 | 47 | 9 | 83 | 182–184 | 180–182 (Shi et al., 2005) |
| **4f** | 8 | 59 | 4 | 62 | 7 | 85 | 194–196 | 195–196 (Shi et al., 2005) |
| **4g** | 6 | 57 | 4 | 66 | 8 | 84 | 159–160 | 159–60 (Shi et al., 2005) |
| **4h** | 8 | 38 | 5 | 55 | 10 | 85 | 187–188 | 188–190 (Abadi et al., 1999) |
| **4i** | 6 | 60 | 4 | 70 | 9 | 87 | 186–188 | 186–188 (Abadi et al., 1999) |
| **4j** | 6 | 41 | 4 | 65 | 8 | 84 | 216–218 | 217–219 (Abadi et al., 1999) |
| **5a** | 10 | 36 | 5 | 55 | 15 | 72 | 165–168 | 168–70 (Abadi et al., 1999) |
| **5b** | 10 | 35 | 4.5 | 60 | 12 | 78 | 235–237 | 240–42 (Abadi et al., 1999) |
| **5c** | 10 | 30 | 6 | 55 | 12 | 70 | 227–230 | 231–233 (Abadi et al., 1999) |



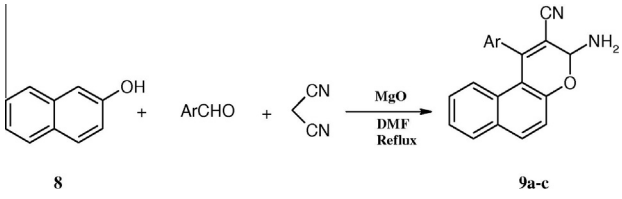
**Scheme 2** A reasonable mechanism for the formation of the products **4a**–**k**.



**6** **7a-g**

**7a:** Ar= 4-$NO_2C_6H_4$, X= H
**7b:** Ar= 3-$NO_2C_6H_4$, X= H
**7c:** Ar= 4-$ClC_6H_4$, X= H
**7d:** Ar= 4-(MeO)$C_6H_4$, X= H
**7e:** Ar= 4-$FC_6H_4$, X= Cl
**7f:** Ar= 4-$ClC_6H_4$, X= Cl
**7g:** Ar= 4-$BrC_6H_4$, X=Cl

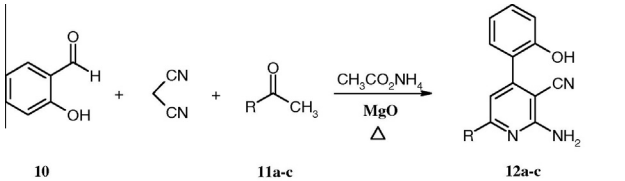
**Scheme 3** One-pot synthesis of 2-amino-3-cyano-4-aryl-4*H*-benzo[*h*]-chromene in the presence of MgO.



**8** **9a-c**

**Scheme 4** Three-component reaction of malononitrile, aldehydes and phenolic β-naphthol in the presence of MgO.

and it was found to be very active and reusable (Chunli et al., 2005). We sought to develop a route that is simple to perform and that allows to reuse the catalyst for a number of times, and



**10** **11a-c** **12a-c**

**12a:** R=$CH_3$, R"= H
**12b:** R= 4-$MeOC_6H_4$, R"= H
**12c:** R= 2-$ClC_6H_4$, R"= H

**Scheme 5** Three component reaction of salicylaldehyde, malononitrile and a ketone **11a**–**c** in the presence of MgO.

was tried to focus on solvents, where the product will be precipitated out from the reaction mixture when the reaction is completed. As shown in Tables 1 and 2 the yields of reactions are markedly affected by the catalyst, and optimum results were obtained when reactions were run in dimethylformamide (DMF) and in the presence of high surface area MgO. In order to optimize the reaction conditions for preparing compounds **4, 5, 7, 9** and **12** the effect of base catalyst and solvents such as water, ethanol, acetonitrile and dimethylformamide under different reaction conditions were investigated. Yields are relatively higher when DMF was used as a solvent in comparison with other solvents. We also attempted to reuse the catalyst in three-component reaction of acetone, benzaldehyde, malononitrile and ammonium acetate in dimethylformamide (DMF) as a solvent to prepare compound **4d** for three times. It should be noted that the catalytic activity also decreased after each use (Table 3).

The compounds **4a–f** are known in the literature (Abadi et al., 1999; Kambe et al., 1980; Hafez et al., 1987; Abdel Galil

**Table 2** Synthesis of **7a**–**g** and **9a**–**c** in the presence of base catalysts.

| Com. No. | [Without Catalyst] | | Commercial (MgO) | | High surface area (MgO) | | M. P. °C observed | M. P. reported °C [Ref.] |
|---|---|---|---|---|---|---|---|---|
| | Time (h) | Yield (%) | Time (h) | Yield | Time (min) | Yield | | |
| **7a** | 6 | 50 | 3.5 | 70 | 5 | 97 | 237–240 | 239.5–241 (Ballini et al., 2001) |
| **7b** | 6 | 45 | 3.5 | 70 | 8 | 95 | 212–213 | 214.5–216 (Ballini et al., 2001) |
| **7c** | 6 | 45 | 4 | 68 | 8 | 95 | 231–233 | 231–232.5 (Ballini et al., 2001) |
| **7d** | 6 | 40 | 4 | 65 | 12 | 91 | 183-185 | 183–184.5 (Ballini et al., 2001) |
| **7e** | 4 | 60 | 3 | 75 | 7 | 95 | 242–244 | 246 (Khafagy et al., 2002) |
| **7f** | 5 | 45 | 3.5 | 65 | 9 | 92 | 221–223 | 224 (Khafagy et al., 2002) |
| **7g** | 5 | 50 | 3.5 | 65 | 8 | 95 | 224–226 | 226 (Khafagy et al., 2002) |
| **9a** | 6 | 65 | 4 | 70 | 9 | 88 | 206-208 | 207–208.5 (Ballini et al., 2001) |
| **9b** | 6 | 62 | 4 | 69 | 5 | 91 | 189–190 | 188–189 (Ballini et al., 2001) |
| **9c** | 6 | 60 | 4 | 66 | 12 | 83 | 191–193 | 190–191.5 (Ballini et al., 2001) |

**Table 3** Reusability of high surface area MgO.

| Entry | Catalyst | Time (min) | Yield (%) |
|---|---|---|---|
| 1 | MgO (1st use) | 9 | 80 |
| 2 | MgO (2nd use) | 15 | 70 |
| 3 | MgO (3rd use) | 25 | 50 |

et al., 1982). The IR spectra and melting point of all known compounds were consistent with those reported in the literature. Structures **4g–i** were established on the basis of IR measurements which showed the presence of CN at the region 2235–2238 $cm^{-1}$ and two sharp bands at 3500–3450 and 3390–3380 $cm^{-1}$ due to asymmetric and symmetric vibrations of the $NH_2$ group. The $^1H$ and $^{13}C$ NMR and mass spectra were also in accordance with the proposed structures.

### 2.1. Pharmacology

Previous study has been shown that the chromenes and fused chromenes have biological effects, one of the site for the action of this compound is the central nervous system (CNS) (Eiden and Denk, 1991; El-Agrody et al., 2000; Bianchi and Tava, 1987; Hogg, 1996; Taylor et al., 1998; Smith et al., 1998). Anxiety disorders are the most common mental illnesses in the world and become a very important area of research interest in psychopharmacology. With regard to the documented history of these compounds in relation to their effect on anxiety the aim of the present study was to evaluate the probably anxiolytic effects of the new heterocyclic 2-amino-3-cyano-4-(4-chlorophenyl)-4*H*-benzo[*h*]-chromene ($C_{19}H_{13}ClNO$) **7c** on the Elevated Plus-Maze (EPM).

## 3. Material and methods

### 3.1. Model of anxiety

Male NMRI rats (Pasteur, Tehran) 250–300 g were housed in cage (seven in each cage) and kept in a room with controlled temperature (22–25 °C).The Rats were maintained on a 12:12 light-dark cycle and had access to food and water ad libitum. Test was performed only after the rat had acclimated to the above environment for at least 7 days. All experiments were carried out between 08:00 and 13:00. Each rat received a single intraperitoneal (ip) injection of compound **7c** (different doses) or vehicle CMC + Toeen 80% and was tested once in the EPM. All procedures were approved by the Ethical committee of the Shahid Bahonar University of Kerman and conducted in accordance with the internationally accepted principles for laboratory animal use and care.

### 3.2. Elevated Plus-Maze

The EPM test is described in detail elsewhere (Abadi et al., 1999; Abdel Galil et al., 1982). Briefly, the apparatus comprised two open arms (35 × 5 cm) and two closed arms (30 × 5 × 15 cm) that extended from a common central platform (5 × 5 cm). The floor and walls of each arm were made of wood and painted black. The entire maze was elevated to a height of 60 cm above floor level. Testing was conducted in a quiet room illuminated only by a dim light. Rats were given

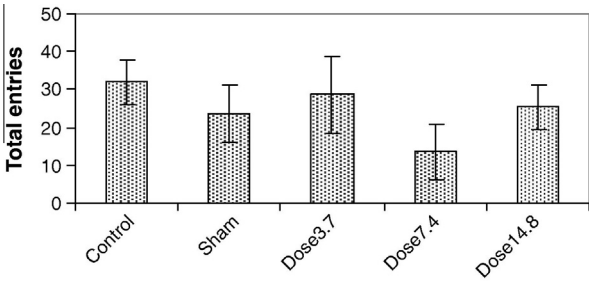



**Figure 1** Effects of vehicle (Toeen 80% + CMC) and compound **7c** (3.7, 7.4 and 14.8 mg/kg) on total entries. Data are presented as mean ± SEM, (one-way ANOVA following by Tukey test. $n = 7$).

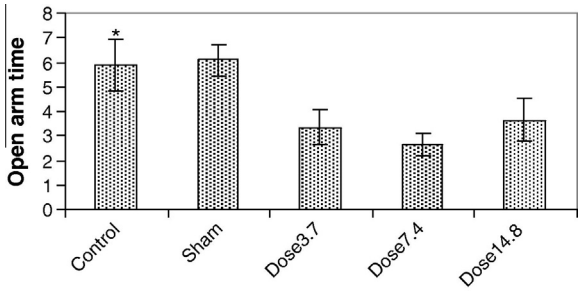



**Figure 2** Effects of vehicle (Toeen 80% + CMC) and compound **7c** (3.7, 7.4 and 14.8 ml/kg) on open arm time. Control. Data are presented as mean ± SEM. (one-way ANOVA following by Tukey test. $n = 7$). $^*P < 0.05$ vs dose 7.4.

a single ip dose of compound **7c** 30 min before their placement on the EPM. To begin a test session, the animals were placed on the open arm facing the center of the maze. An entry into an arm was defined as the animal placing all four paws over the line marking that area. The number of entries and the time spent in the open arm closed arms were recorded during a 5 min test period. The percentage of open arm entries (open/total × 100 entries was calculated for each animal × 24). Between each trial, the maze was wiped clean with a damp sponge and dried with paper towels.

### 3.3. Statistics

Statistical analysis performed using one-way analysis of variance (ANOVA) with post hoc TUKEY test. $P < 0.05$ was considered significant. All data are expressed as mean ± SEM.

### 3.4. Results

Related to total entries there was no significant difference between groups (Fig. 1).

The compound **7c** at a dose of 7.4 mg/kg significantly decreased the percentage of time spent ($P < 0.05$) in the open arms (Fig. 2).

## 4. Conclusions

In conclusion, we have developed a general and easy method for the synthesis of 4,6-disubstituted-3-cyano-2(1*H*)-imino-

pyridine or 3-amino-6-chloro-1-aryl-1*H*-benzo[*h*]chromen-2-yl cyanide derivatives in the presence of high surface area MgO as a highly effective heterogeneous base catalyst. The catalysts show environmental friendly character, which is inexpensive and easily obtained. EPM is a model which uses the natural fear of rodents to avoid open and elevated places. The results show that vehicle did not statistically change the measured EPM parameter. The compound **7c** decreased open arm time, this behavioral alteration induced by **7c** in the EPM provided anxiogenes effect at 7.4 mg/kg, so we can conclude that this compound has stimulation effect rather than sedation. The results also show that compound **7c** at all doses did not statistically change total entries. This effect further confirms the absence of sedation properties of **7c**. Based on the core composition of this heterocycle, the anxiolytic activity was expected, but the reverse was observed.

## 5. Experimental section

Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. IR spectra were measured on a Mattson 1000 FT-IR spectrometer. The proton and carbon NMR spectra were recorded with a BRUKER DRX-500 AVANCE spectrometer at 500 and 125.77 MHz, respectively. Mass spectra were recorded on a MS-QP2000A Shimadzu mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were performed using a Heracus CHN-O-Rapid analyzer.

### 5.1. Preparation of high surface area MgO

The catalyst used in this study was obtained by rehydrated $Mg(OH)_2$ at 450 °C for 2 h. A calcination temperature of 400–500 °C gave maximum conversion. When the catalyst was calcined above 500 °C, the activity of MgO decreased and continued to decrease as the calcination temperature increased. The maximum surface area was obtained after calcining the samples at 400–500 °C (Chunli et al., 2005).

### 5.2. General procedure for compounds **4** and **5**

A mixture of aldehyde (2 mmol), appropriate ketone (2 mmol), ammonium acetate (2 mmol) and malononitrile or ethyl cyanoacetate (2 mmol), and MgO (50 mg) in DMF (20 mL) was refluxed with stirring for the time reported in Table 1 (the progress of the reaction being monitored by TLC and hexane/ethyl acetate was used as an eluent). After completion of the reaction the catalyst was separated from the reaction mixture by centrifugation and then was poured into ice cold water; the crude product was filtered, dried and recrystallized from 96% ethanol.

### 5.3. General procedure for compounds **7** and **9**

A mixture of aldehyde **1** (2 mmol), malononitrile **2** (2 mmol), phenolic compound **4** (2 mmol) and MgO (50 mg) in DMF (20 mL) was refluxed with stirring for the time reported in Table 2. After completion of the reaction, as indicated by TLC, MgO was removed by filtration and excess dimethylformamide was distilled off. The crude product so obtained was recrystallized from ethanol to afford the pure product.

### 5.4. General procedure for compounds **12**

The foregoing method was carried out except that aldehyde and phenolic compounds were replaced by salicylaldehyde (Scheme 4).

#### 5.4.1. Spectral data for selected compounds

*5.4.1.1. 4-(4-Chlorophenyl)-6-methyl-2-amino-3-cyano-pyridine (**4a**).* Colorless crystals; mp 170–172 °C. $\nu_{max}$(KBr): 3390 and 3313 ($NH_2$), 3070 (ArH), 2211 (CN)cm$^{-1}$; $\delta_H$ (500 MHz, DMSO-$d_6$): 7.58 (2H, d, $^3J_{HH}$ = 7.9 Hz, ArH), 7.58 (2H, d, $^3J_{HH}$ = 7.9 Hz, ArH), 6.85 (2H, s, $NH_2$), 6.62 (1H, s, PryH), 2.36 (3H, s, CH3) ppm.

*5.4.1.2. 4-(4-Methoxyphenyl)-6-phenyl-2-amino-3-cyano-pyridine (**4e**).* Colorless crystals; mp 182–184 °C. $\nu_{max}$(KBr): 3452 and 3307 ($NH_2$), 3120 (ArH), 2210 (CN) cm$^{-1}$; $\delta_H$ (500 MHz, DMSO-$d_6$): 8.10–8.12 (2H, m, ArH), 7.55 (2H, d, $J$ = 8.0 Hz, ArH), 7.50–7.49 (3H, m, ArH), 7.32 (1H, s, CH), 7.10 (2H, d, $J$ = 8.0 Hz, ArH), 6.87 (2H, s, $NH_2$), 3.85 (3H, s, $OCH_3$) ppm.

*5.4.1.3. 6-(2,4-Dimethoxyphenyl)-4-phenyl-2-amino-3-cyano-pyridine (**4h**).* Pale yellow crystals; mp 187–188 °C. $\nu_{max}$(KBr): 3480, 3450 and 3300 ($NH_2$), 3075 (ArH), 2200 (CN) cm$^{-1}$. $\delta_H$ (500 MHz, DMSO-$d_6$): 7.85–6.70 (m, 11H, ArH and $NH_2$), 3.82 (6H, s, 2 and 4-$OCH_3$) ppm.

*5.4.1.4. 6-(2,4-Dimethoxyphenyl)-4-phenyl-3-cyano-(1H)-pyridinone (**5a**).* Pale yellow crystals; mp 165–168 °C. $\nu_{max}$(KBr): 3550–3200 ($NH_2$), 2212 (CN) cm$^{-1}$. $\delta_H$ (500 MHz, DMSO-$d_6$): 12.4 (1H, broad NH), 7.65–6.50 (m, 9H, ArH), 3.84 (6H, s, 2 and 4-$OCH_3$) ppm.

*5.4.1.5. 2-Amino-3-cyano-4-(4-nitrophenyl)-4H-benzo[h]-chromene (**7a**).* Yellow crystals; mp 237–240 °C. $\nu_{max}$(KBr): 3480-3300 ($NH_2$), 2211 (CN) cm$^{-1}$. $\delta_H$ (500 MHz, DMSO-$d_6$): 8.30 (d, 1H, $J$ = 7.7 Hz, H-10 or H-7), 8.15 (d, 2H, $J$ = 8.5 Hz, H-30 and H-50 or H-20 and H-60), 7.80 (d, 1H, $J$ = 7.6 Hz, H-7 or H10), 7.60 (d, 1H, $J$ = 8.5 Hz, H-6 or H-5), 7.30 (d, 2H, $J$ = 8.5 Hz, H-20 and H-60 or H-30 and H-50), 7.45–7.70 (m, 2H, H-8 and H-9), 7.30 (s, 2H, $NH_2$), 7.00 (d, 1H, $J$ = 8.5 Hz, H-5 or H-6), 5.20 (s, 1H, H-4) ppm.

*5.4.1.6. 2-Amino-4-(2-hydroxyphenyl)-6-methyl-3-pyridylcyanide (**12a**).* A 0.40 g. red crystals, yield 90%; mp 234–236 °C; $\nu_{max}$(KBr): 3354, 3205 (broad, $NH_2$ and OH), 2212 (CN), 1617 (C=N), 1517 (Ar) cm$^{-1}$; $\delta_H$ (500 MHz, DMSO-$d_6$): 10.01 (1H, s, OH), 8.83–.25 (7H, m, arom and $NH_2$), 1.77 (3H, s, CH3); $\delta_C$ (125 MHz, DMSO-$d_6$)160.31, 159.37, 157.94, 151.30, 129.88, 128.64, 124.54, 120.35, 117.50, 117.12, 86.57, 71.05, 23.49 ($CH_3$).; MS, $m/z$ (%): 225 ($M^+$, 20), 101 (18), 83 (16), 77 (18), 59 (30), 43 (100). Anal. Calcd. For $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.65%. Found: C, 69.05; H, 4.81; N; 18.35.

*5.4.1.7. 2-Amino-4-(2-hydroxyphenyl)-6-(4-methoxyphenyl)-3-pyridylcyanide (**12b**).* A 0.53 g. red crystals, yield 85%; mp 238–240 °C; $\nu_{max}$(KBr): 3329, 3205 (broad, $NH_2$ and OH), 2212 (CN), 1620 (C=N), 1517 (Ar) cm$^{-1}$; $\delta_H$ (500 MHz, DMSO-$d_6$): 9.90 (1H, s, OH), 8.41–6.89 (11H, m, arom and

$NH_2$), 3.39 (3H, s, CH3); $\delta_C$ (125 MHz, DMSO-$d_6$) 167.77, 163.12, 160.18, 155.08, 151.85, 143.04, 132.72, 129.40, 124.66, 123.30, 119.30, 116.43, 116.35, 92.19, 81.01, 59.35 ($CH_3$).;MS, $m/z$ (%): 317 ($M^+$, 10), 312 (8), 209 (34), 121 (100), 83 (15), 77 (29), 59 (30). Anal. Calcd. For $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24%. Found: C, 71.65; H, 4.56; N; 12.95.

*5.4.1.8. 2-Amino-6-(2-chlorophenyl)-4-(2-hydroxyphenyl)-3-pyridylcyanide (**12c**)*. A 0.51 g red crystals, yield 80%; mp 235–237 °C; $\nu_{max}$(KBr): 3429, 3180 (broad, $NH_2$ and OH), 2212 (CN), 1666 (C═N), 1517 (Ar) $cm^{-1}$; $\delta_H$ (500 MHz, DMSO-$d_6$): 10.09 (1H, s, OH), 8.82(d, 1H, $J$ = 6.8 Hz, ArH), 8.40 (s, 1H, $H_5$), 7.70–6.98 (9H, m, arom and $NH_2$); $\delta_C$ (125 MHz, DMSO-$d_6$) 163.23, 160.97, 156.01, 152.80, 144.01, 140.97, 133.77, 129.30, 125.96, 124.28, 120.30, 117.40, 116.43, 116.35, 94.34, 79.89. MS, $m/z$ (%): 321 ($M^+$, 25), 285 (10), 77 (100), 59 (35). Anal. Calcd. For $C_{18}H_{12}ClN_3O$: C, 67.19; H, 3.76; N, 13.06%. Found: C, 66.87; H, 3.51; N; 12.85.

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