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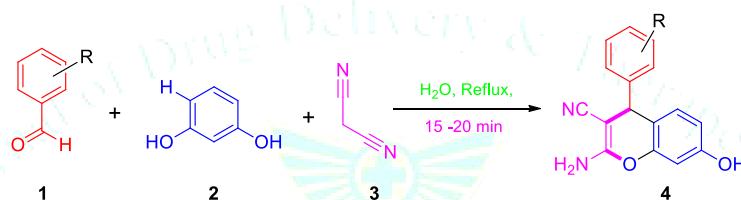
Research Article

## A Benign Synthesis of 2-Amino-3-Cyano-4H-Benzopyrans via Domino Reaction

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### ABSTRACT

A green and operationally simple approach domino reaction has been developed for the synthesis of 2-amino-3-cyano-4H-chromene derivatives from aromatic aldehydes, resorcinol and malononitrile in aqueous medium. This work represents the first example of catalyst free and organic solvents free multi-component reactions for the synthesis of pharmaceutically important chromene derivatives. The structures of the synthesized compounds were confirmed by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, Mass and single crystal XRD.



**Keywords:** Benzopyrans, malononitrile, Michael addition reaction, domino reaction, water mediated synthesis.

**Article Info:** Received 04 July 2019; Review Completed 23 Aug 2019; Accepted 26 Aug 2019; Available online 30 Aug 2019



### Cite this article as:

Silambarasan S, Abdul Nasser AJ, A Benign Synthesis of 2-Amino-3-Cyano-4H-Benzopyrans via Domino Reaction, Journal of Drug Delivery and Therapeutics. 2019; 9(4-A):271-279 <http://dx.doi.org/10.22270/jddt.v9i4-A.3417>

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### INTRODUCTION

Chromene (benzopyran) is a heterocyclic ring system in which a benzene ring and a pyran ring are fused together. The chromene nucleus containing natural alkaloids are anthocyanins, tocopherols and flavonoids. Moreover, a variety of natural and synthetic chromene derivatives has an important biological and pharmacological applications, such as antimicrobial, [1] anti-inflammatory, [2] antiproliferative, [3] antioxidant, [4] herbicidal, analgesic and anticonvulsant, [5] antitubercular, [6] anticoagulant, estrogenic antispasmodic, estrogenic, [7] TNF- $\alpha$  inhibitor effects and activities, [8] as well as inhibitor of diabetes-induced vascular dysfunction.[9] Moreover 7-Hydroxy-6-methoxy-

4H-chromene **A** (Fig. 1) is an example of naturally occurring 4H-chromene, which was obtained from the flowers of *Wisteria sinensis* and is one of their fragrance components.[10] Among different types of chromene systems, 2-amino-4H-chromenes have been reported to exhibit highly useful proapoptotic properties for the treatment of a wide range of cancer ailments.[11] In cancer chemotherapy, 2-amino-4H-chromene **B** was marked for drug development due to its high inhibition of tumor-associated Bcl-2 proteins.[12] A modified 4H-chromene structure **C** was able to induce apoptosis (programmed cell death) in several cancer cell lines.[13]

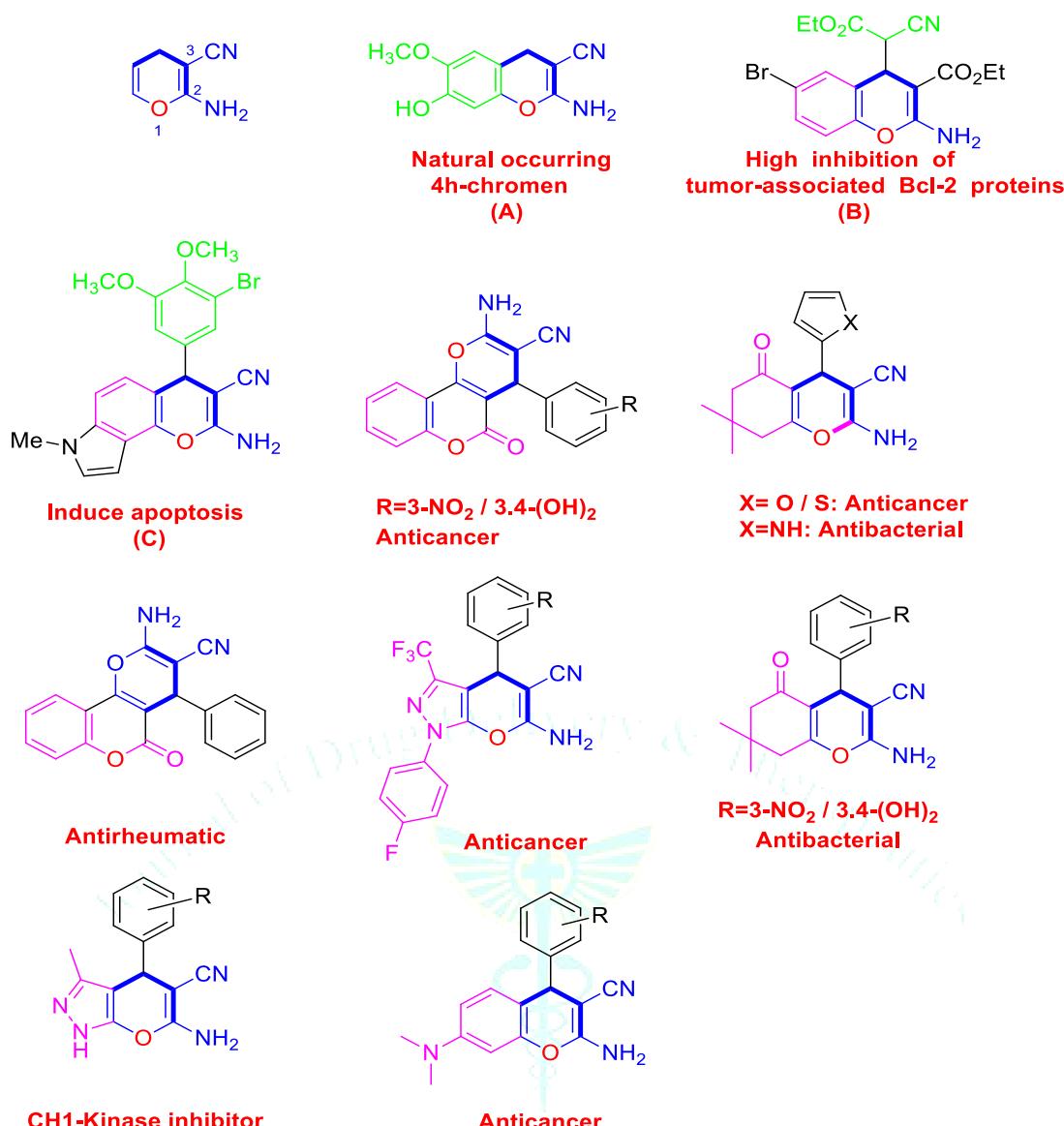


Figure 1: Structure of some biologically important 2-amino-3-cyano- 4H-chromenes

The biological records of these privileged motifs prompted us to develop an atom-economical, one pot, mild and greener method for the synthesis of chromene derivatives. Many synthetic procedures have appeared in the literature for the synthesis of 2-amino-7-hydroxy-4-phenyl-4H-chromene-3-carbonitrile; these generally utilize the homogeneous, heterogeneous catalysts and acid/base mediated harsh reaction conditions. Therefore, a new synthetic route associated with environmentally friendly reaction condition is highly desirable. One of the most important progresses to combine economic aspects with the environmental concerns is the use of green protocol techniques which has provided simple and efficient synthetic methods of great promise. The elimination of toxic organic solvent in the reaction medium, shorter reaction time, straightforward work-up, and providing good to excellent yields with stoichiometric amounts of reactants are apparent advantages that distinguish the green chemical methods from others techniques such as microwave or ultrasound irradiation.[14,15] In the present work, we describe the synthesis of 2-amino-7-hydroxy-4-phenyl-4H-chromene-3-carbonitrile derivatives *via* multi-component domino reaction in aqueous medium using aromatic aldehyde, resorcinol and malononitrile.

## RESULTS AND DISCUSSION

Initially, multicomponent domino reaction of malononitrile, aryl aldehyde and resorcinol was chosen as the model reaction. The effect of various reaction parameters such as the influence of solvent, formation of hydrogen bond and the effect of temperature were studied to optimize the reaction conditions (Table 1). It is important to note that K<sub>2</sub>CO<sub>3</sub> and Na<sub>2</sub>CO<sub>3</sub> with a molar ratio of 0.1 was found to be the catalyst for the three component reaction of malononitrile, aryl aldehyde and resorcinol affording a considerable yield of the desired product. Moreover in the absence of catalyst a significant product formation was observed under reflux condition (Table 1, entry 14).

The solvent temperature plays an important role in the reactivity (Table 1). We have investigated the effect of various protic, aprotic and non-polar solvents on the three component reaction of resorcinol, aryl aldehyde and malononitrile (Table 1, entry 1-14). In non-polar solvents such as 1,4-dioxane and Toluene, the yield of the reaction was found to be very low (10-20%) (Table 1, entry 5,6,11,12). Whereas in the case of polar aprotic solvents such as THF, acetonitrile, the yield of the reaction was found to be low (8-15%) (Table 1, entry 3,4,9,10). In the case of

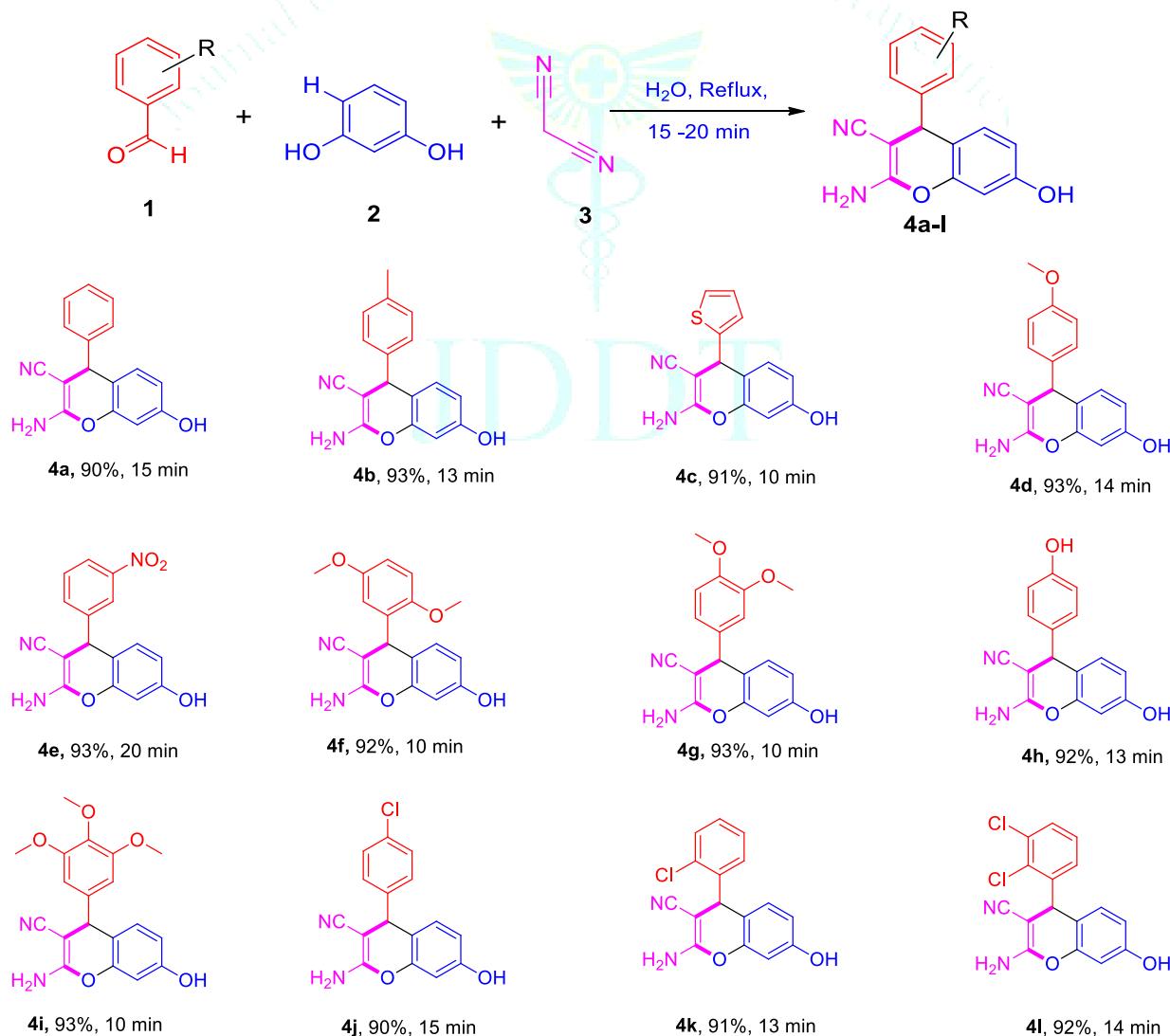
polar protic solvents such as ethanol and methanol (Table 1, entry 1,2,7,8), the yield of the desired product was considerable (50-65%). Further increase in the reaction temperature to reflux makes the reaction almost quantitative (Table 1, entry 14). From Table 1, it is clear that water was the best choice as solvent.

We examined the substrate scope of substituted benzaldehydes (**1a-1l**) under optimized reaction condition for the synthesis of chromene derivatives (**4a-4l**). All the electron donating and electron withdrawing aldehydes are compatible with optimized reaction condition afforded the excellent yield 80-93%.

**Table 1** Optimization of reaction conditions

| Entry | base                            | solvent<br>(1 equiv) | Temp (°C) | Time<br>(min) | Yield <b>4a</b><br>(%) |
|-------|---------------------------------|----------------------|-----------|---------------|------------------------|
| 1     | Na <sub>2</sub> CO <sub>3</sub> | EtOH                 | 60        | 30            | 50                     |
| 2     | "                               | MeOH                 | 50        | 30            | 55                     |
| 3     | "                               | THF                  | 50        | 30            | 10                     |
| 4     | "                               | Acetonitrile         | 60        | 30            | 8                      |
| 5     | "                               | Dioxane              | 60        | 30            | 15                     |
| 6     | "                               | Toluene              | 80        | 30            | 10                     |
| 7     | K <sub>2</sub> CO <sub>3</sub>  | EtOH                 | 60        | 30            | 60                     |
| 8     | "                               | MeOH                 | 50        | 30            | 65                     |
| 9     | "                               | THF                  | 50        | 30            | 15                     |
| 10    | "                               | Acetonitrile         | 60        | 30            | 10                     |
| 11    | "                               | Dioxane              | 60        | 30            | 20                     |
| 12    | "                               | Toluene              | 80        | 30            | 12                     |
| 13    | -                               | H <sub>2</sub> O     | 60        | 30            | 50                     |
| 14    | -                               | H <sub>2</sub> O     | reflux    | 15-20         | 80-93                  |

**Scheme 1** Synthesis of 2-amino-3-cyano- 4H-chromenes derivatives (**4a-l**)



## Single-crystal X-Ray study

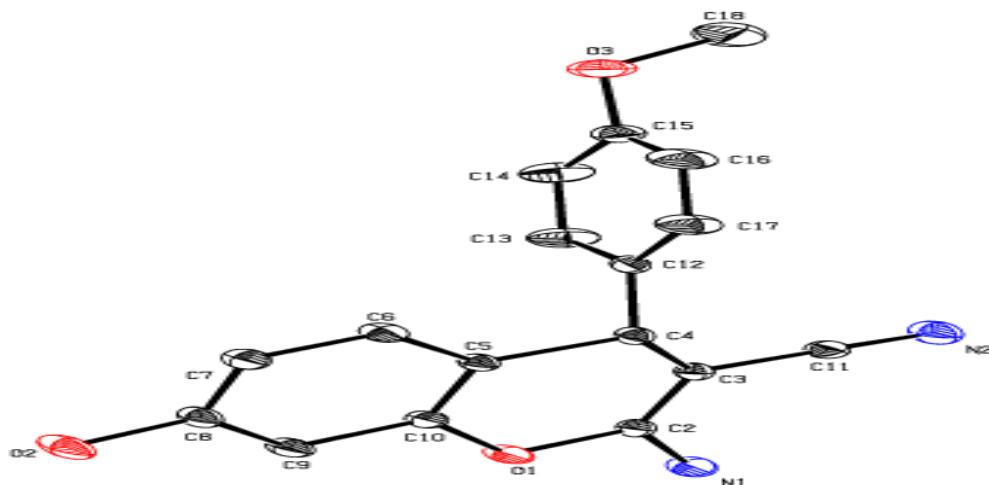
**Refinement:** Crystal data collection and structure refinement details are summarized in **Table 2**

Table 2. Crystallographic data for **4d** and **4k**

| Compound                          | 4d  | 4k  |
|-----------------------------------|---|---|
| Identification code               | mrb-4   | mrb-12  |
| Empirical formula                 | C <sub>17</sub> H <sub>11</sub> N <sub>2</sub> O <sub>3</sub>   | C <sub>16</sub> H <sub>11</sub> C <sub>1</sub> N <sub>2</sub> O <sub>2</sub>  |
| Formula weight                    | 287.30  | 270.31  |
| Temperature                       | 293(2) K  | 296(2) K  |
| Wavelength                        | 0.71073 Å   | 0.71073 Å   |
| Crystal system                    | Triclinic,  | Monoclinic,   |
| Space group                       | P1  | P21/n   |
| Unit cell dimensions              | a = 6.2316(3) Å $\alpha$ = 116.255(2) $^{\circ}$ .<br>b = 11.0207(6) Å $\beta$ = 90.099(2) $^{\circ}$ .<br>c = 11.8732(6) Å $\gamma$ = 96.165(2) $^{\circ}$ .<br>725.95(6) Å <sup>3</sup> | a = 6.6658(3) Å $\alpha$ = 90 $^{\circ}$<br>b = 30.1600(16) Å $\beta$ = 106.088(2) $^{\circ}$ .<br>c = 7.2193(4) Å $\gamma$ = 90 $^{\circ}$ .<br>1394.53(12) Å <sup>3</sup> |
| Volume                            |   |   |
| Z, Density (calculated)           | 2, 1.314 Mg/m <sup>3</sup>  | 4, 1.287 Mg/m <sup>3</sup>  |
| Absorption coefficient            | 0.086 mm <sup>-1</sup>  | 0.078 mm <sup>-1</sup>  |
| F(000)                            | 298   | 568   |
| Crystal size                      | 0.20 x 0.22 x 0.20 mm   | 0.15 x 0.10 x 0.10 mm   |
| Theta range for data collection   | 3.72 to 36.41 $^{\circ}$  | 1.35 to 26.70 $^{\circ}$  |
| Index ranges                      | -10<=h<=10, -18<=k<=18, -19<=l<=19  | -6<=h<=8, -38<=k<=38, -9<=l<=8  |
| Reflections collected             | 31554 / 6513 [R(int) = 0.0402]  | 21899 / 2942 [R(int) = 0.0335]  |
| Completeness to theta =           |   | 99.70%, 25.000 $^{\circ}$   |
| Refinement method                 | 91.8 %, 24.998 $^{\circ}$   | Full-matrix least-squares on F <sup>2</sup>   |
| Data / restraints / parameters    | Full-matrix least-squares on F <sup>2</sup>   | 2942 / 0 / 191  |
| Goodness-of-fit on F <sup>2</sup> |   | 1.111   |
| Final R indices [I>2sigma(I)]     | 6513 / 2 / 209  | R1 = 0.0407, wR2 = 0.1070   |
| R indices (all data)              | 1.072   | R1 = 0.0684, wR2 = 0.1384   |
| Largest diff. peak and hole       | R1 = 0.1496, wR2 = 0.3302<br>R1 = 0.1990, wR2 = 0.3606<br>1.069 and -0.760 e. Å <sup>-3</sup>   | 0.319 and -0.210 e. Å <sup>-3</sup>   |

The X-ray diffraction analysis reveals that the benzopyran ring of the compound **4d**, C<sub>17</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>, is planar [maximum deviation = 0.080 (2) Å] and the methoxyphenyl ring is also in planar conformation. The benzopyran derivative is almost perpendicular to the methoxyphenyl ring [dihedral angle = 88.75 (5) $^{\circ}$ ]. The ORTEP plot of the molecule is shown in Fig.2. The methoxyphenyl substituted benzopyran compound crystallise in triclinic P1 space group. In the structure, the benzopyran and methoxyphenyl rings are planar. The benzopyran ring makes a dihedral angle of

90.857 (5) $^{\circ}$  with the methoxyphenyl ring and confirms the fact that the two moieties are in axial orientation. The orientation of the benzopyran and methoxyphenyl rings also confirmed from the torsion angle values of [C3—C4—C12—C13=] 75.6 (2) $^{\circ}$  & [C3—C4—C12—C17=] -105.3 (2) $^{\circ}$ , respectively. In the benzopyran moiety, the attached carbonitrile, amino and hydroxy groups lie in a same plane, with the maximum deviation of atom N2[-0.055 (2) Å]. The sum of the bond angles around atom N1 of the pyran ring is in accordance with sp<sup>2</sup> hybridization state[360 $^{\circ}$ ]

Figure 2: ORTEP diagram of **4d**

The benzopyran ring of the compound **4k**,  $C_{16}H_{11}N_2O_2Cl$  is planar [maximum deviation = 0.079 (2) Å] and the chlorophenyl ring is also in planar conformation. The benzopyran derivative is almost perpendicular to the chlorophenyl ring [dihedral angle = 86.85 (6)°]. The ORTEP plot of the molecule is shown in Fig.3. The chlorophenyl substituted benzopyran compound crystallise in monoclinic  $P2\bar{1}/c$  space group. In the structure, the benzopyran and chlorophenyl rings are planar. The benzopyran ring makes a dihedral angle of 86.85 (6)° with the chlorophenyl ring and confirms the fact that the two moieties are in axial

orientation. The chlorophenyl moiety is also planar with the maximum deviation noted for atom CL12 as -0.040 (1) Å. The orientation of the benzopyran and chlorophenyl rings also confirmed from the torsion angle values of [C3—C4—C11—C12=] 76.5 (2)° & [C3—C4—C11—C16=] -100.4 (2)°, respectively. In the benzopyran moiety, the attached carbonitrile, amino and hydroxy groups lie in a same plane, with the maximum deviation of atom N2[-0.053 (2) Å]. The sum of the bond angles around atom N1 of the pyran ring is in accordance with  $sp^2$  hybridization state [360°].

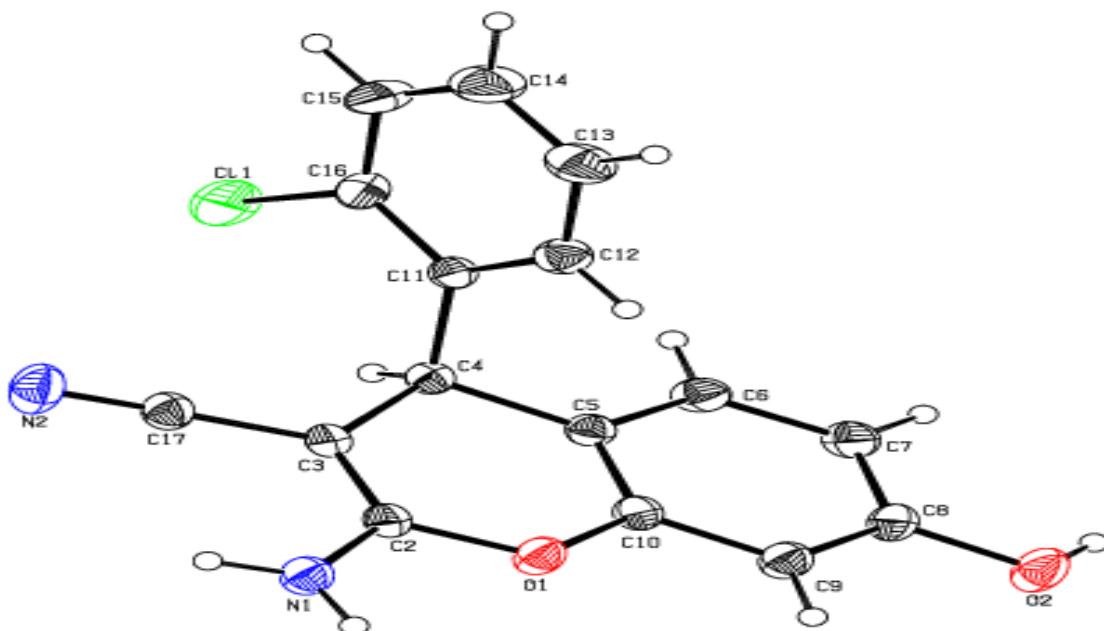


Figure 3: ORTEP diagram of **4k**

## Experimental

All the chemicals used were purchased from Merck AnalaR grade and purified wherever necessary using the standard purification method. The purity of compounds were checked by TLC using silica gel-G plate and visualized by iodine vapours. The melting points were recorded in open capillary tube and uncorrected. The FT-IR spectra were recorded in SHIMADZU FT-IR Affinity-I spectrometer using KBr pellets and PerkinElmer. The  $^1H$ -NMR and  $^{13}C$ -NMR spectra were obtained in DMSO-d<sub>6</sub> on BRUKER 300 MHZ and 500MHZ instrument with TMS as an internal standard and the chemical shift values are presented in ppm. The mass spectra were taken on SHIMADZU GC-MS QP 2010 spectrometer operating at an ionization potential of 70ev.

### General experimental procedure for the Synthesis of 2-amino-7-hydroxy-4-phenyl-4H-chromene-3-carbonitrile

To a stirred solution of substituted benzaldehyde (0.05 mol) in water was added resorcinol (0.05 mol) and malononitrile (0.05 mol) at room temperature and refluxed for 15 - 20 minutes. The progress of the reaction was monitored by thin layer chromatography using silica gel-G plates. The reaction mixture was cooled and allowed to 30 minutes. The precipitated solid was filtered at suction pump. The crude solid obtained was recrystallized by methanol.

### 2-Amino-7-hydroxy-4-phenyl-4H-chromene-3-carbonitrile **4a**

IR: (KBr cm<sup>-1</sup>) 3425 (OH), 3332, 3219 (NH<sub>2</sub>), 2193(CN), 1651 (C=C Vinyl nitrile) 1587 (C=C Aromatic),  $H^1$  NMR (300 MHz DMSO -d<sub>6</sub>):  $\delta_H$  4.63 (S, 1H), 6.43 (d,  $J$ =2.4, 1H), 6.48-6.52 (m, 1H) 6.81 (d,  $J$ =8.7, 1H), 6.89 (s, 2H) 7.16-7.22(m, 3H), 7.29 (t,  $J$ =6.9, 2H), 9.74 (s, 1H),  $^{13}C$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_C$  56.22, 102.15, 112.36, 113.71, 120.68, 126.61, 127.35, 128.56, 129.90, 146.35, 148.82, 157.06, 161.23.

### 2-Amino-7-hydroxy-4-(*p*-tolyl)-4H-chromene-3-carbonitrile **4b**

IR: (KBr cm<sup>-1</sup>) 3410(OH), 3340, 3230 (NH<sub>2</sub>), 2181(CN), 1641 (C=C Vinyl nitrile) 1587 (C=C Aromatic),  $H^1$  NMR (300 MHz):  $\delta_H$  2.24 (s, 3H), 4.58 (s, 1H), 6.44 (d,  $J$ =2.1,1H), 6.48-6.52 (m, 1H), 6.78(d,  $J$ =8.4, 1H), 6.86 (s, 2H), 7.04-7.12 (m, 4H), 9.72 (s, 1H),  $^{13}C$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_C$  20.55, 56.39, 102.12, 112.31, 113.87, 120.70, 127.28, 129.10, 135.68, 143.40, 148.78, 156.99, 160.14.

### 2-Amino-7-hydroxy-4-(thiophen-2-yl)-4H-chromene-3-carbonitrile **4c**

IR: (KBr cm<sup>-1</sup>) 3421(OH), 3332, 3219 (NH<sub>2</sub>), 2193(CN), 1654 (C=C Vinyl nitrile) 1589 (C=C Aromatic),  $H^1$  NMR (300 MHz DMSO -d<sub>6</sub>):  $\delta_H$  4.9 (s, 1H), 6.40 (d,  $J$ =2.4, 1H), 6.52-6.56 (m, 1H), 6.91-6.94 (m, 1H), 6.97 (t,  $J$ =3.6, 2H), 6.99 (s, 2H), 7.34-

7.36 (m, 1H), 9.77 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  56.39, 102.15, 112.37, 113.49, 120.50, 124.00, 125.02, 126.72, 129.85, 148.51, 151.48, 157.30, 160.28.

**2-Amino-7-hydroxy-4-(4-methoxyphenyl)-4H-chromene-3-carbonitrile 4d**

IR: (KBr cm<sup>-1</sup>) 3415(OH), 3334, 3221 (NH<sub>2</sub>), 2187(CN), 1655 (C=C Vinyl nitrile) 1587 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  3.71 (s, 3H), 4.58 (s, 1H), 6.42 (d,  $J$ =2.1, 1H), 6.48-6.52 (m, 1H), 6.85-7.13 (m, 6H), 9.71 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  54.96, 56.56, 102.09, 112.30, 113.88, 114.03, 120.72, 128.41, 129.91, 130.13, 138.46, 148.73, 156.94, 157.93, 160.05.

**2-Amino-7-hydroxy-4-(3-nitrophenyl)-4H-chromene-3-carbonitrile 4e**

IR: (KBr cm<sup>-1</sup>) 3450(OH), 3334, 3221 (NH<sub>2</sub>), 2190(CN), 1658 (C=C Vinyl nitrile) 1587 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  4.96 (s, 1H), 6.52 (d,  $J$ =2.4 Hz, 1H), 5.5-5.58 (m, 1H), 6.87 (d,  $J$ =8.4 Hz, 1H), 7.11 (s, 2H), 7.63-7.72 (m, 2H), 8.08-8.14 (m, 2H), 9.87 (s, 1H);  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  55.31, 112.49, 112.66, 120.40, 121.74, 121.82, 129.96, 130.27, 134.27, 147.89, 148.53, 148.88.

**2-Amino-4-(2,5-dimethoxyphenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4f**

IR: (KBr cm<sup>-1</sup>) 3406(OH), 3338, 3223 (NH<sub>2</sub>), 2187(CN), 1657 (C=C Vinyl nitrile) 1503 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  3.63 (s, 3H), 3.71 (s, 3H), 4.93 (s, 3H), 6.39 (d,  $J$ =2.0 Hz, 1H), 6.46-6.48 (m, 1H), 6.53 (d,  $J$ =3.0 Hz, 1H), 6.73-6.76 (m, 1H), 6.82 (s, 2H), 6.84 (d,  $J$ =8.5 Hz, 1H), 6.90 (d,  $J$ =9.0 Hz, 1H), 9.67 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  55.56, 55.66, 56.71, 102.56, 111.98, 112.65, 113.26, 114.25, 115.54, 121.24, 129.69, 135.78, 149.57, 151.06, 153.75, 157.39, 161.41.

**2-Amino-4-(3,4-dimethoxyphenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4g**

IR: (KBr cm<sup>-1</sup>) 3435(OH), 3332, 3233 (NH<sub>2</sub>), 3070(CH-Ar), 2135(CH-Aliphatic), 2194 (CN), 1643 (C=C Vinyl nitrile) 1571 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  3.84 (s, 3H), 3.98 (s, 3H), 4.59 (s, 1H), 6.42 (d,  $J$ =2.4 Hz, 1H), 6.50-6.52 (m, 1H), 6.67-6.70 (m, 1H), 6.80 (d,  $J$ =1.8 Hz, 1H), 6.83 (s, 2H), 6.86-6.90 (m, 2H), 9.71 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  54.66, 55.40, 56.38, 102.08, 111.18, 112.27, 113.91, 115.80, 121.46, 125.97, 129.88, 138.84, 147.53, 148.23, 150.30, 156.93, 160.14, 161.24, 165.85.

**2-Amino-7-hydroxy-4-(4-hydroxyphenyl)-4H-chromene-3-carbonitrile 4h**

IR: (KBr cm<sup>-1</sup>) 3481(OH), 3354, 3254 (NH<sub>2</sub>), 2193 (CN), 1652 (C=C Vinyl nitrile) 1588 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  4.49 (s, 1H), 3.98 (s, 3H), 4.49 (s, 1H), 6.39 (s, 1H), 6.47 (d,  $J$ =8.5 Hz, 1H), 6.67 (d,  $J$ =8 Hz, 2H), 6.67 (s, 1H),

6.78 (s, 2H), 6.95 (d,  $J$ =8.5 Hz, 2H), 9.28 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  57.23, 102.53, 112.73, 114.78, 115.68, 121.24, 128.83, 130.36, 137.27, 149.22, 156.50, 157.33, 160.51.

**2-Amino-7-hydroxy-4-(3,4,5-trimethoxyphenyl)-4H-chromene-3-carbonitrile 4i**

IR: (KBr cm<sup>-1</sup>) 3410(OH), 3333, 3222 (NH<sub>2</sub>), 3073(CH-Ar), 2945(CH-Aliphatic), 2194 (CN), 1658 (C=C Vinyl nitrile) 1592 (C=C Aromatic), H<sup>1</sup> NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_H$  3.62 (s, 3H), 3.71 (s, 6H), 4.58 (s, 1H), 6.39 (s, 1H), 6.47-6.50 (m, 3H), 6.85 (s, 2H), 6.85 (d,  $J$ =8.5 Hz, 1H), 9.69 (s, 1H),  $^{13}\text{C}$  NMR (300 MHz DMSO-d<sub>6</sub>):  $\delta_c$  56.25, 56.37, 60.37, 102.60, 105.01, 112.79, 113.97, 121.18, 130.33, 136.61, 142.44, 149.12, 157.51, 160.80.

**2-Amino-4-(2,3-dichlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4j**

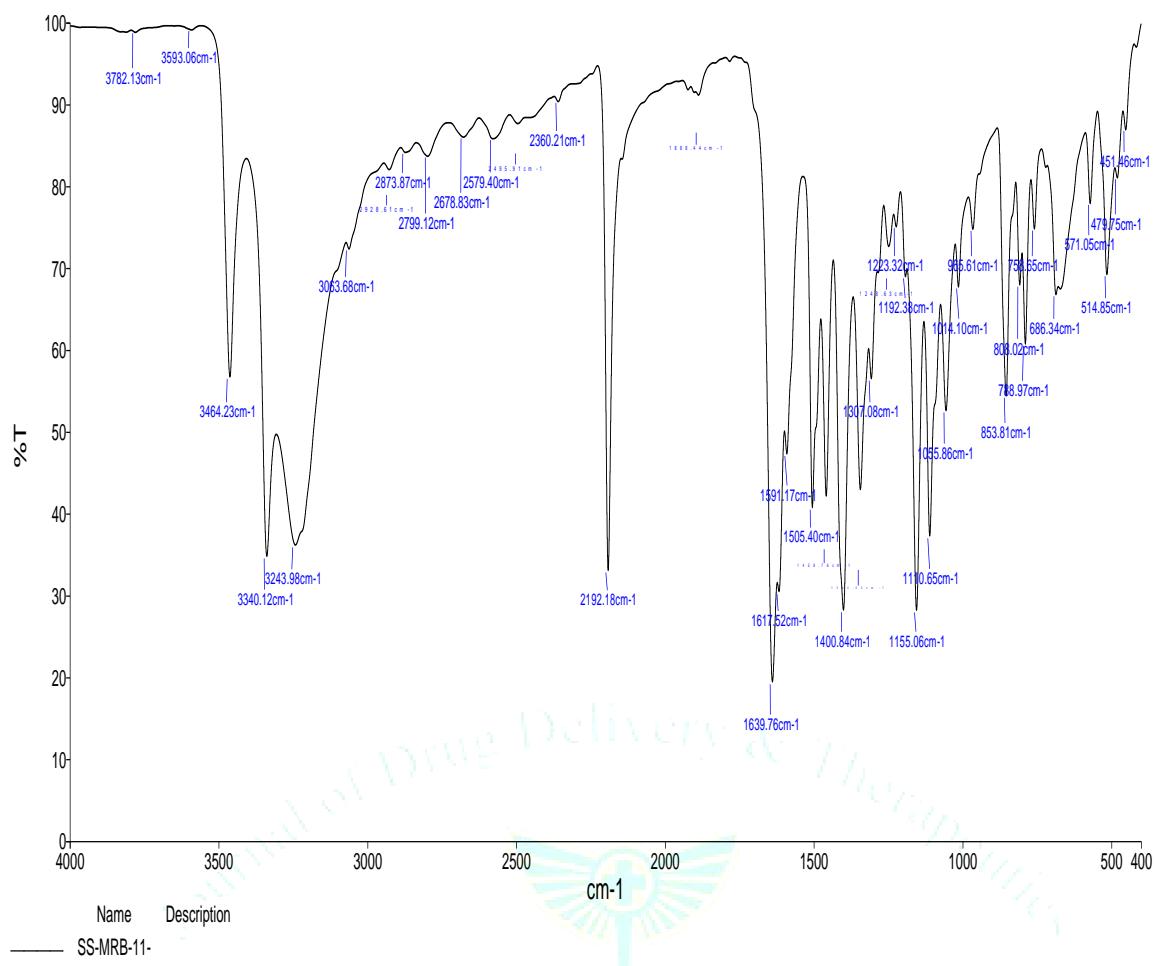
IR: (KBr cm<sup>-1</sup>) 3406 (OH), 3342, 3266 (NH<sub>2</sub>), 3035 (CH-Ar), 2928 (CH-Aliphatic), 2195 (CN), 1643 (C=C) 1461 (C=C), 1154 (C-C), 1109 (C-O-C), 1342 (C-N), H<sup>1</sup> NMR (500 MHz DMSO-d<sub>6</sub>):  $\delta_H$  5.21 (s, 1H), 6.41 (d,  $J$ =20.5 Hz, 1H), 6.42-6.49 (m, 1H), 6.72 (d,  $J$ =8.5 Hz, 1H), 6.99 (s, 2H), 7.17 (d,  $J$ =7.5 Hz, 1H), 7.31-7.34 (m, 1H), 7.51 (d,  $J$ =8 Hz, 1H), 9.80 (s, 1H),  $^{13}\text{C}$  NMR (500 MHz DMSO d<sub>6</sub>):  $\delta_c$  54, 102.75, 112.36, 113.05, 120.67, 129.09, 129.62, 129.67, 130.03, 130.45, 149.50, 157.96, 161.00.

**2-Amino-4-(4-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4k**

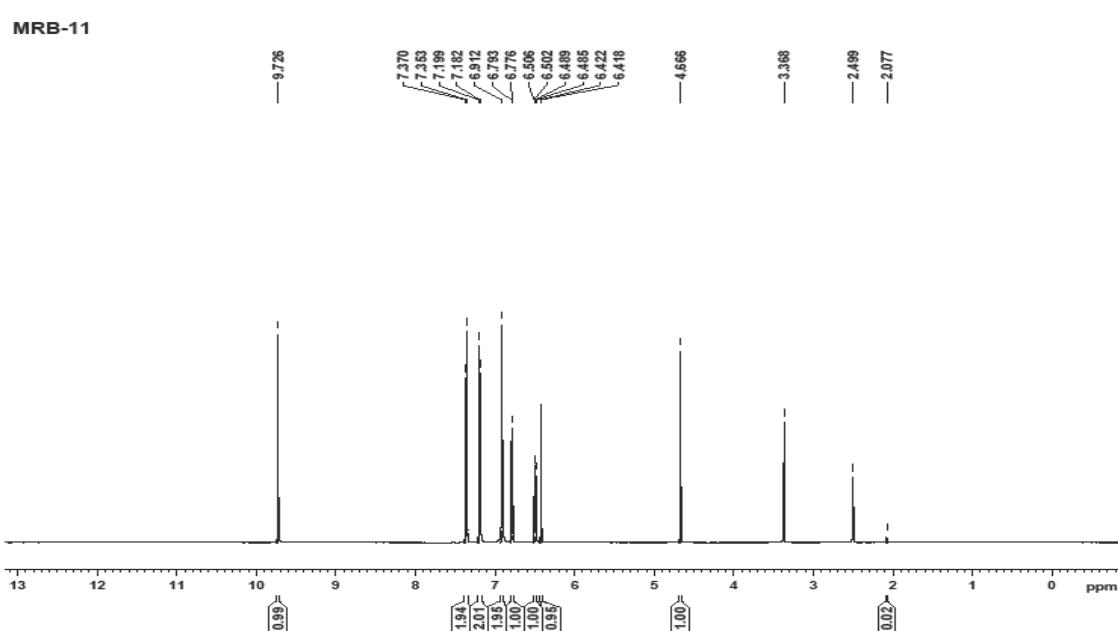
IR: (KBr cm<sup>-1</sup>) 3464 (OH), 3340, 3243 (NH<sub>2</sub>), 3063 (CH-Ar), 2928 (CH-Aliphatic), 2192 (CN), 1639 (C=C) 1458 (C=C), 1155 (C-C), 1110 (C-O-C), 1344 (C-N), H<sup>1</sup> NMR (500 MHz DMSO-d<sub>6</sub>):  $\delta_H$  6.41 (d, 1H,  $J$ =2 Hz, H-Ar), 6.48-6.50 (dd, 1H,  $J$ =2, 6.5 Hz, H-Ar), 6.77 (d, 1H,  $J$ =8.5 Hz, H-Ar), 6.91 (s, 2H, NH<sub>2</sub>), 7.18 (d, 2H,  $J$ =8.5 Hz, H-Ar), 7.35 (d, 2H,  $J$ =8.5 Hz, H-Ar), 9.72 (s, 1H, OH),  $^{13}\text{C}$  NMR (500 MHz DMSO d<sub>6</sub>):  $\delta_c$  56.35, 102.71, 112.95, 113.67, 120.97, 129.03, 129.75, 130.36, 131.71, 145.76, 149.30, 157.69, 160.72.

**2-Amino-4-(2-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4l**

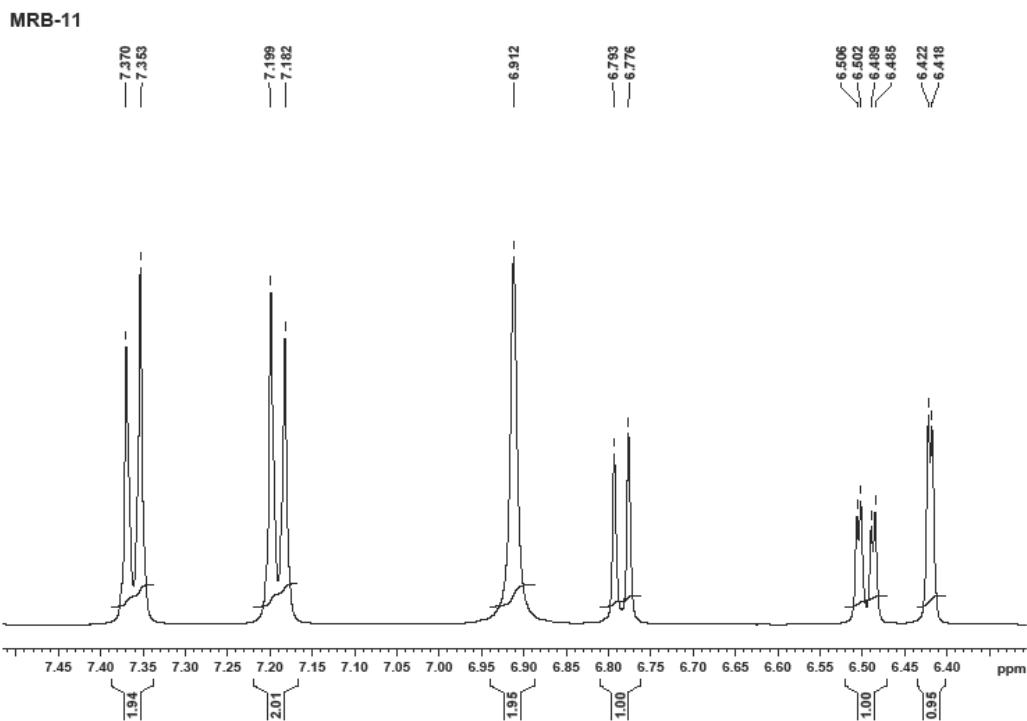
IR: (KBr cm<sup>-1</sup>) 3421 (OH), 3337, 3220 (NH<sub>2</sub>), 3070 (CH-Ar), 2922 (CH-Aliphatic), 2193 (CN), 1653 (C=C) 1461 (C=C), 1110 (C-O-C), 1301 (C-N), H<sup>1</sup> NMR (500 MHz DMSO-d<sub>6</sub>):  $\delta_H$  6.42 (d, 1H,  $J$ =1.5 Hz, H-Ar), 6.47-6.49 (dd, 1H,  $J$ =2.5, 6 Hz, H-Ar), 6.73 (d, 1H,  $J$ =8.5 Hz, H-Ar), 6.92 (s, 2H, NH<sub>2</sub>), 7.179-7.19 (t, 1H,  $J$ =7 Hz, H-Ar), 7.21-7.24 (q, 1H,  $J$ =1.5, 6 Hz, H-Ar), 7.28-7.31 (t, 1H,  $J$ =7.5 Hz, Ar-CH), 7.40 (d, 1H, 7.45 Hz, Ar-H), 9.74 (s, 1H, OH),  $^{13}\text{C}$  NMR (500 MHz DMSO d<sub>6</sub>):  $\delta_c$  55.37, 102.72, 112.96, 112.97, 120.76, 128.28, 129.00, 129.71, 130.18, 131.24, 132.30, 143.31, 149.48, 157.80, 160.98.



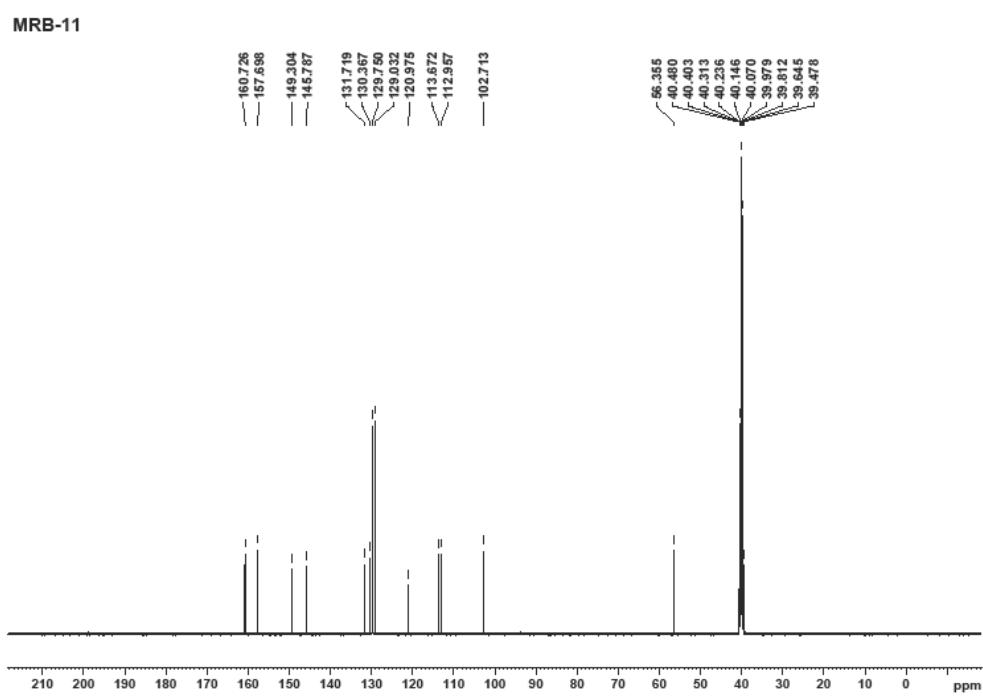
**Figure 4:** IR-Spectrum of 2-amino-4-(4-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4k



**Figure 5:** <sup>1</sup>H NMR-Spectrum of 2-amino-4-(4-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4k



**Figure 5a:**  $^1\text{H}$  NMR-Spectrum of 2-amino-4-(4-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4k



**Figure 6:**  $^{13}\text{C}$  NMR-Spectrum of 2-amino-4-(4-chlorophenyl)-7-hydroxy-4H-chromene-3-carbonitrile 4k

## CONCLUSION

In this work, cascade reaction has been carried out for the synthesis of 2-amino-3-cyanobenzopyrans 4k from malononitrile, aryl aldehyde and resorcinol in methanol, ethanol, acetone and water solvents using  $\text{K}_2\text{CO}_3$  or  $\text{Na}_2\text{CO}_3$

as base. Nevertheless, the use of water was successful for this reaction. Under the found conditions, the high yield for the products were achieved at short reaction time in aqueous medium. The structure of the products were confirmed by IR,  $^1\text{H}$ ,  $^{13}\text{C}$  NMR spectra and X-ray diffraction study.

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