

Communication

# Synthesis of 2-Aminochromene Derivatives Catalyzed by KF/Al<sub>2</sub>O<sub>3</sub>

WANG, Xiang-Shan\* (王香善) SHI, Da-Qing (史达清) TU, Shu-Jiang (屠树江)

Department of Chemistry, Xuzhou Normal University, Xuzhou, Jiangsu 221116, China

A series of 2-aminochromene derivatives including 2-amino-benzo[*h*]chromene, 2-amino-benzo[*f*]chromene and 2-amino-pyrano[3,2-*h*]quinolin derivatives was synthesized from aryl-aldehyde, malononitrile or ethyl cyanoacetate and 1-naphthol or 2-naphthol or 8-hydroxyquinoline in refluxing ethyl alcohol catalyzed by KF-Al<sub>2</sub>O<sub>3</sub>. The structures were confirmed by X-ray analysis.

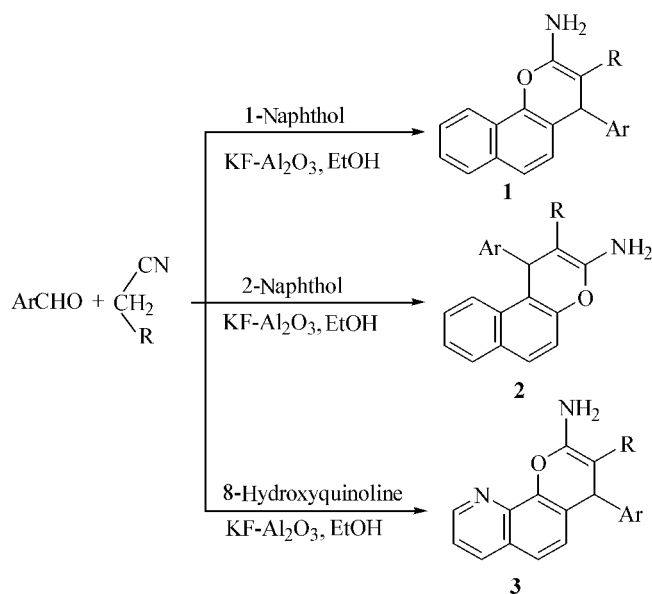
**Keywords** 2-aminochromene, 1-naphthol, 2-naphthol, 8-hydroxyquinoline, synthesis

2-Aminochromene is an important class of compounds found as the main compounds of many naturally occurring products employed as cosmetics and pigments<sup>1</sup> and utilized as potential biodegradable agrochemicals.<sup>2-4</sup> Fluoride salts have been used as potential base in a variety of synthetic reactions in recent years.<sup>5,6</sup> However, low solubility of fluoride salts in usual solvents hampers their wide applications in organic synthesis. On the other hand, there has been increasing use of inorganic solid supports as catalyst resulting in higher selectivity, milder reaction conditions and easier work-up for many reactions.<sup>7,8</sup> In our previous paper,<sup>9-12</sup> we reported that alumina coated with potassium fluoride (KF-alumina) is a versatile solid-supported reagent for Knoevenagel reaction, Michael addition condensation and many other reactions. Herein we report the synthesis of 2-aminochromene derivatives catalyzed by KF-Al<sub>2</sub>O<sub>3</sub>.

When arylaldehyde, malononitrile or ethyl cyanoacetate and 1-naphthol were treated with KF-Al<sub>2</sub>O<sub>3</sub> in refluxing ethyl alcohol, the 2-amino-4-aryl-4*H*-benzo[*h*]chromene derivatives (**1**) were obtained in moderate to good yields (72%—91%). If 2-naphthol was added instead of 1-naphthol, the 2-amino-4-aryl-4*H*-benzo[*f*]chromene derivatives (**2**) were obtained as the desired products. Similarly, 2-amino-pyrano[3,2-*h*]quinolin derivatives (**3**) were obtained successfully when 1-naphthol was substituted by 8-hydroxyquinoline in the same reaction condition (Scheme 1). The synthetic data of **1**, **2** and **3** are listed in Table 1.

The structures of **1a**, **2a** and **3a** were confirmed by X-ray analysis. The selected crystallographic data are

Scheme 1



listed in Table 2, and the crystal structures of **1a**, **2a** and **3a** are shown in Figs. 1, 2 and 3, respectively. In the structures of **1a** and **2a**, the pyran rings adopt boat conformation. In the molecular structure of **1a**, the atoms  $\alpha(1)$ ,  $\alpha(2)$ ,  $\alpha(4)$  and  $\alpha(5)$  are on one plane, while the atoms  $\alpha(1)$  and  $\alpha(3)$  deviate from the plane by  $-0.00717$  and  $-0.00710$  nm respectively, and the dihedral angle between the plane and phenyl ring [C(14)—C(19)] is  $88.55^\circ$ . In the structure of **2a**, the atoms  $\alpha(1)$  and  $\alpha(3)$  deviate from the plane by  $-0.01936$  and  $-0.03014$  nm, respectively. The dihedral angle between the plane and phenyl ring [C(17)—C(22)] is  $91.94^\circ$ . While in the structure of **3a**, the pyran ring adopts half-chair conformation: the atoms  $\alpha(1)$ ,  $\alpha(2)$ ,  $\alpha(4)$ ,  $\alpha(5)$  and O are on one plane, while the atom  $\alpha(3)$  deviates from the plane by  $0.00806$  nm. The torsion angle values of  $\alpha(4)-C(5)-O-C(1)$  [ $-1.3(5)^\circ$ ] and  $\alpha(2)-C(1)-O-C(5)$  [ $0.2(5)^\circ$ ] close to  $180^\circ$  also show that these atoms of the pyran ring are extremely flattened. The dihedral angle between the plane and phenyl ring [ $\alpha(13)-\alpha(18)$ ] is  $89.35^\circ$ .

\* E-mail: xswang@xznz.edu.cn

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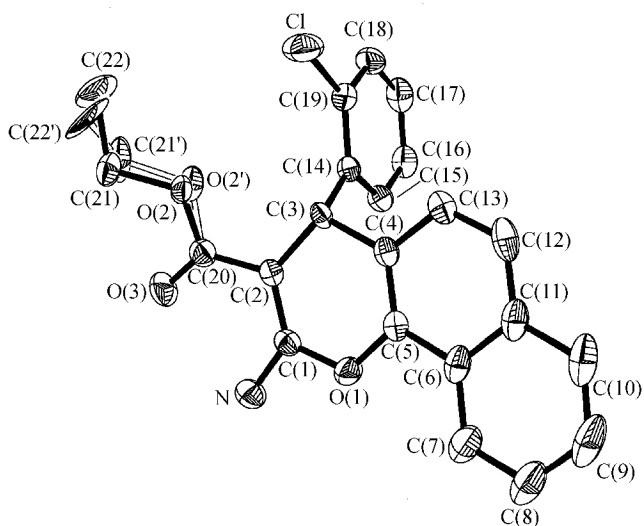


Fig. 1 Structure of the compound 1a.

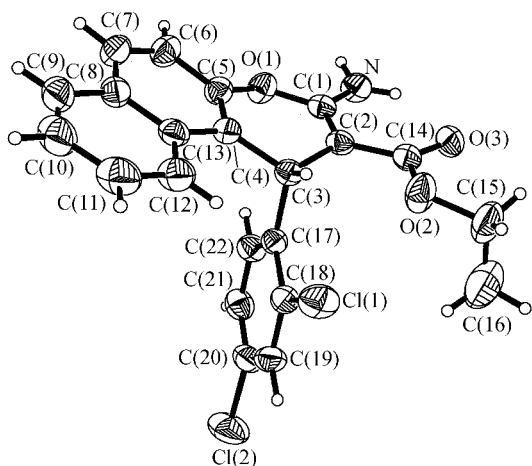


Fig. 2 Structure of the compound 2a.

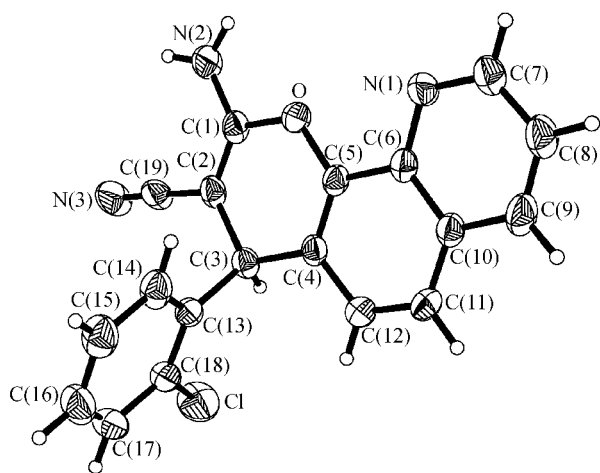
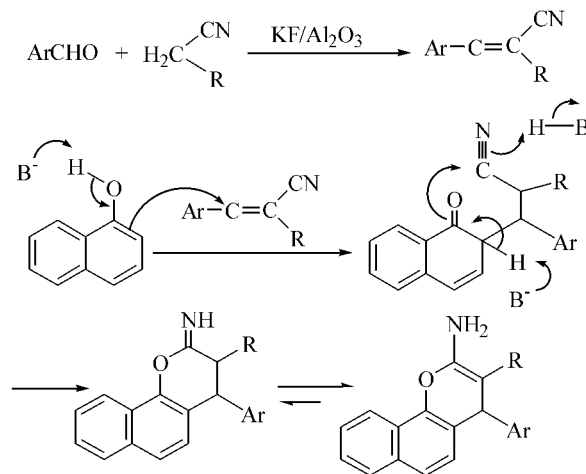


Fig. 3 Structure of the compound 3a.

According to the structures of products, a sequential reaction of the Knoevenagel reaction, Michael addition condensation and intramolecular cyclization may take place

in the formation of the product. The possible mechanism is shown in Scheme 2 (using the formation of compound 1 as example).

Scheme 2



#### Typical experimental procedure

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TEN-SOR 27 spectrometer in KBr.  $^1\text{H}$  NMR spectra were obtained from solution in  $\text{DMSO}-d_6$  with  $\text{Me}_4\text{Si}$  as internal standard using an Inova-400 spectrometer. Elemental analyses were carried out using Carlo Erba 1110 analyzer. X-Ray diffraction was measured on a Siemens P4 diffractometer.

A dry 50 mL flask was charged with arylaldehyde (5 mmol), malononitrile (5 mmol) or ethyl cyanoacetate (5 mmol), 1-naphthol (5 mmol) or 2-naphthol (5 mmol) or 8-hydroxyquinoline (5 mmol), KF-alumina (500 mg) and ethyl alcohol (15 mL). The mixture was stirred at  $80\text{ }^\circ\text{C}$  for 5–6 h, then cooled to room temperature. The mixture was poured into 200 mL of water; the yellow solid was filtered off and washed with water. The crude product was purified by recrystallization from DMF and water to give 1 or 2 or 3.

#### Selected spectral data

**1a** Yield 72%, m. p.  $161\text{--}163\text{ }^\circ\text{C}$ ;  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$ : 1.00 (t,  $J = 7.2\text{ Hz}$ , 3H,  $\text{CH}_3$ ), 3.92 (q,  $J = 7.2\text{ Hz}$ , 2H,  $\text{OCH}_2$ ), 5.60 (s, 1H, CH), 7.12–7.25 (m, 4H, ArH), 7.38 (d,  $J = 8.4\text{ Hz}$ , 1H, ArH), 7.54–7.65 (m, 3H, ArH), 7.83 (s, 2H,  $\text{NH}_2$ ), 7.86 (d,  $J = 7.2\text{ Hz}$ , 1H, ArH), 8.30 (d,  $J = 9.6\text{ Hz}$ , 1H, ArH); IR (KBr)  $\nu$ : 3403, 3291, 3030, 2977, 1667, 1612, 1518, 1462, 1447, 1401, 1307, 1276, 1220, 1158, 1047, 1036, 827, 815, 776, 741, 699  $\text{cm}^{-1}$ . Anal. calcd for  $\text{C}_{22}\text{H}_{18}\text{ClNO}_3$ : C 69.57, H 4.78, N 3.69; found C 69.45, H 4.89, N 3.63.

**Table 1** Preparation of **1**, **2** and **3**

Entry	Ar	R	m.p. ( lit. , °C )	Yield ( % )
<b>1a</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	224—225	72
<b>1b</b>	4-FC <sub>6</sub> H <sub>4</sub>	CN	235—237	76
<b>1c</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CN	254—256	73
<b>1d</b>	4-ClC <sub>6</sub> H <sub>4</sub>	CN	243—245 ( 232 ) <sup>3</sup>	80
<b>1e</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	207—209	91
<b>1f</b>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	CN	192—194 ( 182 ) <sup>4</sup>	78
<b>1g</b>	3 <i>A</i> -( CH <sub>3</sub> O ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CN	209—211	90
<b>1h</b>	3 <i>A</i> -OCH <sub>2</sub> OC <sub>6</sub> H <sub>3</sub>	CN	244—245	74
<b>2a</b>	2 <i>A</i> -Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CO <sub>2</sub> Et	199—200	79
<b>2b</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	175—177	72
<b>2c</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	203.6—204	70
<b>2d</b>	4-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	188—189 ( 168 ) <sup>3</sup>	76
<b>2e</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CN	274—276	80
<b>2f</b>	4-ClC <sub>6</sub> H <sub>4</sub>	CN	226—228 ( 208 ) <sup>3</sup>	83
<b>2g</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	279—281	70
<b>2h</b>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	CN	200—201 ( 192 ) <sup>4</sup>	82
<b>2i</b>	3 <i>A</i> -( OCH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CN	214—216	66
<b>3a</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CN	287—289	85
<b>3b</b>	C <sub>6</sub> H <sub>5</sub>	CN	268—270 ( 270 ) <sup>4</sup>	78
<b>3c</b>	4-ClC <sub>6</sub> H <sub>4</sub>	CN	222—224	80
<b>3d</b>	2 <i>A</i> -Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CN	241—243	70
<b>3e</b>	2-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	222—223	66
<b>3f</b>	2 <i>A</i> -Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CO <sub>2</sub> Et	203—204	64
<b>3g</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	200—202	61

**Table 2** Crystallographic data for **1a**, **2a** and **3a**

Crystallographic parameter	<b>1a</b>	<b>2a</b>	<b>3a</b>
Empirical formula	C <sub>22</sub> H <sub>18</sub> ClNO <sub>3</sub>	C <sub>22</sub> H <sub>17</sub> Cl <sub>2</sub> NO <sub>3</sub>	C <sub>19</sub> H <sub>12</sub> ClN <sub>3</sub> O
Color/shape	Pale yellow/block	Colorless/block	Pale yellow /block
Formula weight	379.82	414.27	333.77
Temperature	294(2) K	292(2) K	294(2) K
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	<i>C</i> 2/ <i>c</i>	<i>P</i> 2(1) <i>/n</i>	<i>P</i> -1
Unit cell dimensions	<i>a</i> = 2.5168(4) nm, $\alpha$ = 90°. <i>b</i> = 0.9584(1) nm, $\beta$ = 111.14(2)° <i>c</i> = 1.6503(3) nm, $\gamma$ = 90°	<i>a</i> = 1.4505(2) nm, $\alpha$ = 90°. <i>b</i> = 0.9037(1) nm, $\beta$ = 101.2(1)° <i>c</i> = 1.4913(2) nm, $\gamma$ = 90°	<i>a</i> = 0.7488(2) nm, $\alpha$ = 73.58(2)° <i>b</i> = 0.9127(3) nm, $\beta$ = 78.38(2)° <i>c</i> = 1.2253(3) nm, $\gamma$ = 75.39(2)°
Volume	3.7128(10) nm <sup>3</sup>	1.9175(4) nm <sup>3</sup>	0.7695(4) nm <sup>3</sup>
<i>Z</i>	8	4	2
Density ( calculated )	1.359 Mg/m <sup>3</sup>	1.435 Mg/m <sup>3</sup>	1.440 Mg/m <sup>3</sup>
<i>F</i> (000)	1584	856	344
Crystal size	0.52 × 0.40 × 0.26 mm <sup>3</sup>	0.56 × 0.52 × 0.24 mm <sup>3</sup>	0.54 × 0.32 × 0.28 mm <sup>3</sup>
$\theta$ Range	1.74° to 25.01°	1.79° to 24.99°	1.75° to 24.99°
Reflections collected	3711	4195	2913
Independent reflections	3270 [ <i>R</i> (int) = 0.0263 ]	3379 [ <i>R</i> (int) = 0.0126 ]	2684 [ <i>R</i> (int) = 0.0107 ]
Goodness-of-fit on <i>F</i> <sup>2</sup>	0.885	1.085	1.090
Final <i>R</i> indices [ <i>I</i> > 2 $\sigma$ ( <i>I</i> ) ]	<i>R</i> <sub>1</sub> = 0.0565, <i>wR</i> <sub>2</sub> = 0.1320	<i>R</i> <sub>1</sub> = 0.0444, <i>wR</i> <sub>2</sub> = 0.1177	<i>R</i> <sub>1</sub> = 0.0717, <i>wR</i> <sub>2</sub> = 0.2159
<i>R</i> indices ( all data )	<i>R</i> <sub>1</sub> = 0.1076, <i>wR</i> <sub>2</sub> = 0.1525	<i>R</i> <sub>1</sub> = 0.0699, <i>wR</i> <sub>2</sub> = 0.1272	<i>R</i> <sub>1</sub> = 0.0915, <i>wR</i> <sub>2</sub> = 0.2282
Largest diff. peak and hole	491 and -204 e·nm <sup>-3</sup>	428 and -255 e·nm <sup>-3</sup>	1613 and -547 e·nm <sup>-3</sup>

**2a** Yield 79% , m. p. 199—200 °C ; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ : 1.19 (t , *J* = 7.2 Hz , 3H , CH<sub>3</sub>) , 4.07 (q , *J* = 7.2 Hz , 2H , OCH<sub>2</sub>) , 5.81 (s , 1H , CH) , 7.25—7.55 (m , 6H , ArH) , 7.79 (s , 2H , NH<sub>2</sub>) , 7.92 (d , *J* = 8.8 Hz , 2H , ArH) , 8.14 (d , *J* = 8.8 Hz , 1H , ArH) ; IR (KBr) ν : 3400 , 3297 , 3045 , 2951 , 1673 , 1615 , 1526 , 1465 , 1401 , 1362 , 1306 , 1273 , 1222 , 1169 , 1101 , 1075 , 1032 , 867 , 849 , 831 , 810 , 787 , 741 cm<sup>-1</sup>. Anal. calcd for C<sub>22</sub>H<sub>17</sub>Cl<sub>2</sub>NO<sub>3</sub> : C 63.78 , H 4.14 , N 3.38 ; found C 63.75 , H 4.17 , N 3.61.

**3a** Yield 85% , m. p. 287—289 °C ; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ : 5.46 (s , 1H , CH) , 7.10 (d , *J* = 8.4 Hz , 1H , ArH) , 7.26—7.33 (m , 5H , NH<sub>2</sub> , ArH) , 7.45 (d , *J* = 7 Hz , 1H , ArH) , 7.60—7.65 (m , 2H , ArH) , 8.34 (d , *J* = 7 Hz , 1H , ArH) , 8.95 (d , *J* = 4.4 Hz , 1H , ArH) ; IR (KBr) ν : 3478 , 3324 , 2195 , 1656 , 1601 , 1498 , 1469 , 1388 , 1315 , 1106 , 1053 , 827 , 784 , 755 , 699 , 658 cm<sup>-1</sup>. Anal. calcd for C<sub>19</sub>H<sub>12</sub>ClN<sub>3</sub>O : C 68.37 , H 3.62 , N 12.59 ; found C 68.49 , H 3.55 , N 12.44.

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