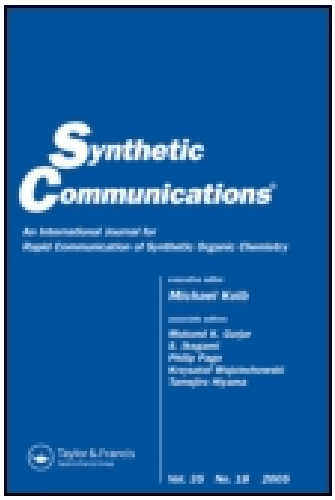

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# Synthesis of 2-Aminochromene Derivatives Catalyzed by $KF/Al_2O_3$

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# Synthesis of 2-Aminochromene Derivatives Catalyzed by $KF/Al_2O_3$

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## ABSTRACT

A series of 2-aminochromene derivatives include 2-aminobenzo-[*h*]chromene and naphtha[1,2-b;6,5-b′]dipyrans derivatives were synthesized from arylaldehyde, malononitrile or ethyl cyanoacetate with 1-naphthol or 1,5-naphthalenediol in refluxing ethyl alcohol catalyzed by $KF\text{-}Al_2O_3$. The structure of the products was confirmed by X-ray analysis.

*Key Words:* 2-Aminochromene; Naphtho[1,2-b;6,5-b′]dipyrans; Synthesis.

2-Aminochromene is an important class of compounds found as the main compounds of many naturally occurring products employed as cosmetics and

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pigments and utilized as potential biodegradable agrochemicals.[1–3] The utility of fluoride salts as potential base in variety of synthetic reactions has been recognized in recent years. Especially alumina coated with potassium fluoride (KF-alumina) as a catalyst resulting in higher selectivity, milder reaction conditions and easier work-up has been reported as a useful catalyst for many reactions.[4–6] In our previous paper, we have reported that alumina coated with potassium fluoride (KF-alumina) is a versatile solid-supported reagent for Knoevenagel reaction,[7] Michael addition condensation[8] and any other reactions.[9–11] Herein we report the synthesis of 2-aminochromene derivatives catalyzed by KF-$Al_2O_3$.

When arylaldehyde, malononitrile or ethyl cyanoacetate and 1-naphthol were treated with KF-$Al_2O_3$ in refluxing ethyl alcohol, the 2-amino-4-aryl-4*H*-benzo[h]chromene derivatives were obtained in slightly high yields (72–90%) (Table 1), if 1,5-naphthalenediol was added instead of 1-naphthol, the naphtho[1,2-b;6,5-b′] dipyrans derivatives were isolated in the same reaction condition in high yields (Sch. 1).

The structure of **1a** was confirmed by X-ray analysis,[12] and the crystal structure of **1a** was shown in Fig. 1. In the structure of **1a**, the pyran rings adopt boat conformation. In the structure of **1a**, the atoms C(1), C(2), C(4) and C(5) are on one plane, the atom O(1) and C(3) deviate from the plane by −0.0717 and −0.0710 Å, the dihedral angle between the plane and phenyl ring (C(14)–C(19)) is 88.55°.

***Table 1.*** The yields of the products.

| Entry | Ar | R | Yield (%) |
|---|---|---|---|
| **1a** | 2-$ClC_6H_4$ | $CO_2Et$ | 72 |
| **1b** | 4-$FC_6H_4$ | CN | 76 |
| **1c** | 4-$CH_3OC_6H_4$ | CN | 78 |
| **1d** | 3,4-$(CH_3O)_2C_6H_3$ | CN | 90 |
| **1e** | 3,4-$OCH_2OC_6H_3$ | CN | 74 |
| **2a** | $C_6H_5$ | CN | 83 |
| **2b** | 4-$ClC_6H_4$ | CN | 93 |
| **2c** | 4-$FC_6H_4$ | CN | 91 |
| **2d** | 4-$BrC_6H_4$ | CN | 86 |
| **2e** | 4-$CH_3OC_6H_4$ | CN | 96 |
| **2f** | 3-$NO_2C_6H_4$ | CN | 92 |
| **2g** | 3,4-$(CH_3O)_2C_6H_3$ | CN | 91 |
| **2h** | 2,4-$Cl_2C_6H_3$ | CN | 94 |





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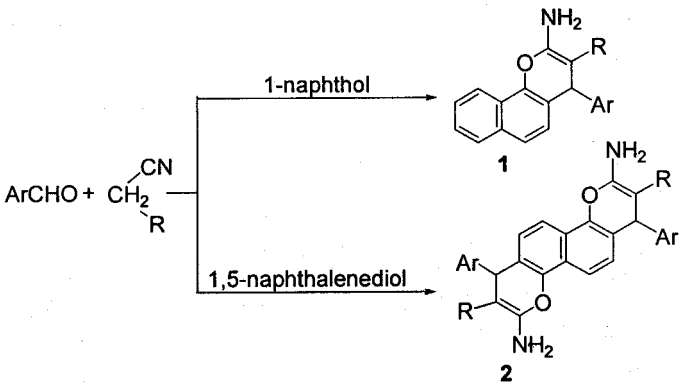


*Scheme 1.*

## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr. $^1$H NMR spectra were obtained for solution in DMSO-$d_6$ with $Me_4Si$ 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.

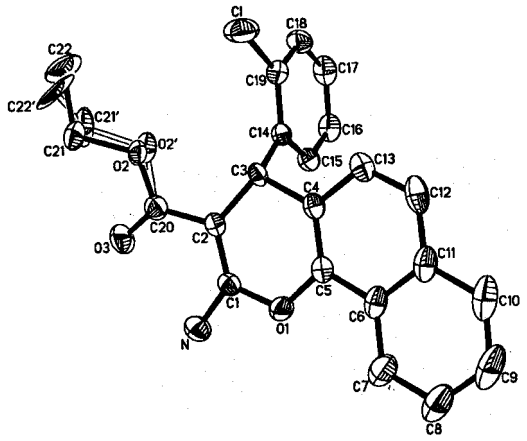


***Figure 1.*** Structure of the compound **1**a.





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## General Procedure

A dry 50 mL flask was charged with arylaldehyde (5 mmol), malononitrile (5 mmol) or ethyl cyanoacetate (5 mmol), 1-naphthol (5 mmol) or 1,5-naphthalenediol (3 mmol), KF-alumina (500 mg) and ethyl alcohol (15 mL), The mixture was stirred at 80°C for 5–6 h, then cooled to room temperature. The mixture was poured into 200 mL 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**.

**1a**. 72%, m.p. 161–163°C; $^1$H NMR (DMSO-$d_6$) $\delta$: 1.00 (t, $J = 7.2$ Hz, 3H, $CH_3$), 3.92 (q, $J = 7.2$ Hz, 2H, $OCH_2$), 5.60 (s, 1H, CH), 7.12–7.25 (m, 4H, ArH), 7.38 (d, $J = 8.4$ Hz, 1H, ArH), 7.54–7.65 (m, 3H, ArH), 7.83 (s, 2H, $NH_2$), 7.86 (d, $J = 7.2$ Hz, 1H, ArH), 8.30 (d, $J = 9.6$ Hz, 1H, ArH); IR (KBr, $\nu$, cm$^{-1}$): 3403, 3291, 3030, 2977, 1667, 1612, 1518, 1462, 1447, 1401, 1307, 1276, 1220, 1158, 1047, 1036, 827, 815, 776, 741, 699 cm$^{-1}$. Anal. calcd for $C_{22}H_{18}ClNO_3$: C 69.57, H 4.78, N 3.69; Found C 69.45, H 4.89, N 3.63.

**1b**. 76%, m.p. 235–237°C; $^1$H NMR (DMSO-$d_6$) $\delta$: 4.95 (s, 1H, CH), 7.09–7.12 (m, 2H, ArH), 7.15 (s, 2H, $NH_2$), 7.21–8.23 (m, 8H, ArH); IR (KBr, $\nu$, cm$^{-1}$): 3465, 3356, 2191, 1659, 1590, 1529, 1410, 1349, 1260, 1217, 1178, 1081, 1028, 903, 859, 812, 762, 738, 725 cm$^{-1}$. Anal. calcd for $C_{20}H_{13}FN_2O$: C 75.94, H 4.14, N 8.86; Found C 76.12, H 4.11, N 8.77.

**1c**. 78%, m.p. 192–194°C, (Lit.:[13] 182°C); $^1$H NMR (DMSO-$d_6$) $\delta$: 3.71 (s, 3H, $CH_3O$), 4.84 (s, 1H, CH), 6.87 (d, $J = 8$ Hz, 2H, ArH), 7.08–7.10 (m, 3H, $NH_2$ + ArH), 7.16–8.23 (m, 7H, ArH); IR (KBr, $\nu$, cm$^{-1}$): 3426, 3336, 2187, 1642, 1591, 1509, 1407, 1233, 1214, 1181, 1141, 1081, 1035, 817, 797, 763, 748, 731cm$^{-1}$.

**1d**. 90%, m.p. 209–211°C; $^1$H NMR (DMSO-$d_6$) $\delta$: 3.71 (s, 6H, $2CH_3O$), 4.84 (s, 1H, CH), 6.73 (d, $J = 8$ Hz, 1H, ArH), 6.90 (s, 2H, $NH_2$), 7.09–8.23 (m, 8H, ArH); IR (KBr, $\nu$, cm$^{-1}$): 3470, 3324, 2194, 1649, 1583, 1517, 1465, 1410, 1286, 1263, 1235, 1184, 1142, 1099, 1083, 1045, 968, 861, 844, 812, 743, 728 cm$^{-1}$. Anal. calcd for $C_{22}H_{18}N_2O_3$: C 73.73, H 5.06, N 7.82; Found C 73.59, H 5.14, N 7.73.

**1e**. 74%, m.p. 244–245°C; $^1$H NMR (DMSO-$d_6$) $\delta$: 4.84 (s, 1H, CH), 5.97 (s, 2H, $OCH_2O$), 6.74 (d, $J = 8$ Hz, 2H, ArH), 6.84 (d, $J = 8$ Hz, 1H, ArH), 7.11–7.13 (m, 3H, $NH_2$ + ArH), 7.55 + 8.22 (m, 5H, ArH); IR (KBr, $\nu$, cm$^{-1}$): 3433, 3339, 2183, 1639, 1590, 1492, 1453, 1411, 1283, 1261, 1184, 1070, 1027, 834, 814, 751, 717 cm$^{-1}$. Anal. calcd for $C_{21}H_{14}N_2O_3$: C 73.68, H 4.12, N 8.18; Found C 73.55, H 4.32, N 8.07.





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**2a**. 83%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 4.91 (s, 2H, 2CH), 7.11 (s, 4H, $2NH_2$), 7.24–7.91 (m, 14H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3452, 3332, 3230, 3017, 2848, 2196, 1649, 1589, 1493, 1450, 1382, 1118, 1040, 759, 707 $cm^{-1}$, Anal. calcd for $C_{30}H_{20}N_4O_2$: C 76.91, H 4.30, N 11.96; Found C 76.85, H 4.32, N 11.87.

**2b**. 93%, m.p. >300°C (Lit.:[14] >300°C), $^1$H NMR (DMSO-$d_6$) $\delta$: 4.96 (s, 2H, 2CH), 7.17 (s, 4H, $2NH_2$), 7.22–7.91 (m, 12H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3450, 3330, 3057, 2220, 1634, 1561, 1472, 1440, 1380, 1250, 1140, 1016, 840 $cm^{-1}$.

**2c**. 91%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 4.95 (s, 2H, 2CH), 7.13–7.17 (m, 8H, $2NH_2$ + ArH), 7.22–7.91(m, 8H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3460, 3355, 3210, 3080, 2212, 1663, 1618, 1518, 1398, 1233, 1189, 1085, 837 $cm^{-1}$, Anal. calcd for $C_{30}H_{18}F_2N_4O_2$: C 71.42, H 3.60, N 11.11; Found C 71.38, H 3.82, N 11.03.

**2d**. 86%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 4.95 (s, 2H, 2CH), 7.17–7.24 (m, 10H, $2NH_2$ + ArH), 7.52 (d, $J = 8.4$ Hz, 4H, ArH), 7.89 (d, $J = 8.4$ Hz, 2H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3460, 3324, 3205, 2195, 1648, 1605, 1501, 1253, 1050, 863 $cm^{-1}$, Anal. calcd for $C_{30}H_{18}Br_2N_4O_2$: C 57.53, H 2.90, N 8.95; Found C 57.48, H 3.01, N 8.86.

**2e**. 96%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 3.73 (s, 6H, $2CH_3O$), 4.85 (s, 2H, 2CH), 6.88 (d, $J = 8.4$ Hz, 4H, ArH), 7.06 (s, 4H, $2NH_2$), 7.15 (d, $J = 8.8$ Hz, 4H, ArH), 7.21 (d, $J = 8.8$ Hz, 2H, ArH),; 7.87 (d, $J = 8.4$ Hz, 2H, ArH), IR (KBr, $\nu$, $cm^{-1}$): 3452, 3332, 3189, 2203, 1648, 1597, 1477, 1394, 1282, 1186, 1094, 827 $cm^{-1}$, Anal. calcd for $C_{32}H_{24}N_4O_4$: C 72.72, H 4.58, N 10.60; Found C 72.59, H 4.62, N 10.37.

**2f**. 92%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 5.22 (s, 2H, 2CH), 7.29–7.33 (m, 6H, ArH), 7.61–7.75 (m, 4H, ArH), 7.93 (d, $J = 8.4$ Hz, 2H, ArH), 8.13 (s, 4H, $2NH_2$); IR (KBr, $\nu$, $cm^{-1}$): 3400, 3316, 3196, 3050, 2187, 1665, 1605, 1513, 1401, 1253, 1094, 843, 775 $cm^{-1}$, Anal. calcd for $C_{30}H_{18}N_6O_6$: C 64.52, H 3.25, N 15.05; Found C 64.59, H 3.21, N 15.23.

**2g**. 91%, m.p. >260°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 3.71 (s, 6H, $2CH_3O$), 4.85 (s, 2H, 2CH), 6.72–6.90 (m, 6H, ArH), 7.08 (s, 4H, $2NH_2$), 7.28 (d, $J = 8.8$ Hz, 2H, ArH), 7.88 (d, $J = 8.4$ Hz, 2H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3444, 3340, 3197, 2187, 1649, 1588, 1521, 1382, 1341, 1293, 1074, 914, 811, 723 $cm^{-1}$, Anal. calcd for $C_{34}H_{28}N_4O_6$: C 69.38, H 4.79, N 9.52; Found C 69.27, H 4.85, N 9.39.

**2h**. 94%, m.p. >300°C, $^1$H NMR (DMSO-$d_6$) $\delta$: 5.43 (s, 2H, 2CH), 7.13 (d, $J = 8.4$ Hz, 2H, ArH), 7.24 (s, 4H, $2NH_2$), 7.28 (d, $J = 8.4$ Hz, 2H, ArH), 7.40 (d, $J = 8.4$ Hz, 2H, ArH), 7.63 (s, 2H, ArH), 7.90 (d, $J = 8.4$ Hz, 2H, ArH); IR (KBr, $\nu$, $cm^{-1}$): 3460, 3325, 3189, 2204, 1672, 1597, 1485, 1394, 1283, 1082, 1083, 826, 759 $cm^{-1}$, Anal. calcd for $C_{30}H_{16}Cl_4N_4O_2$: C 59.43, H 2.66, N 9.24; Found C 59.37, H 2.78, N 9.11.





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