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The One-step Synthesis of C,D-dihydropyrano[F] Chromene Derivatives in Under Grinding as An Environmentally Frinendly Alternative

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ABSTRACT

1,4-diazabicyclo[2.2.2]octane (DABCO) was used as a catalyst for one-pot, three-component condensation reactions consisting of aromatic aldehydes, malononitrile and β-Naphtol under grinding at room temperature, to afford the corresponding dihydropyrano[c]chromenes in high yields. This method has the advantages of a simple operation, mild reaction conditions, high yields, by using a less toxic and low cost chemical as a catalyst.

Key words: One-step synthesis, Chromene, Environment friendly.

INTRODUCTION

There has been considerable interest in chromenes and their benzoderivatives, not least because of their value for a variety of industrial, biological, and chemical synthetic uses.[1] As a result, a large number of methods have appeared describing novel synthesis of these heterocycles.[2] 2-Amino-4H-benzochromenes have been of interest because of their biological activity[3] and a few methods have been reported for their synthesis.[4]

In this paper we focus on the preparation of 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile derivatives 4 (Scheme 1) in grinding media.

Due to the diverse biological properties of this compound class, there is a widespread interest in their synthesis. Compounds with an uracil moiety antitumor, antibacterial, antihypertensive, vasodilator, bronchiodilator, hepatoprotective, cardiotonic, and antiallergic activities. Some of them exhibit antimalarial, antifungal analgesics, and herbicidal properties[5-9].

Previous methods for the synthesis of 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile have been reported in which a two-component reaction between arylidene malononitrile with β-Naphtole occurred under harsh thermal conditions. Also, a microwave-assisted one-pot three-component cyclocondensation of Phenols, benzaldehyde derivatives, and alkylnitrile in the absence or presence of triethylamine, Diammonium hydrogen phosphate (DAHP) has been reported. These methods exhibit some disadvantages such as: harsh conditions, long reaction times, low yields, and effluent pollution.[10]

RESULTS AND DISCUSSION

Herein we report a simple synthesis of 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile as a domino Knoevenagel–Michael condensation, catalyzed by 0.1 eq mol of DABCO in aqueous media at room temperature (Scheme 1). Although we have not yet established the mechanism of the one-pot reaction between benzaldehyde derivatives, malononitrile and â-Naphtole in the presence of DABCO, a possible explanation is presented in Scheme 2. The higher reactivity of the iminium group is utilized to facilitate Knoevenagel condensation between aryl aldehyde 1 and malononitrile 2, which proceeds via intermediate 5. After dehydration, olefin 6 is produced. DABCO also catalyzes the generation of a proposed β-Naphtoxide and this intermediate adds to olefin 5 to generate 4, after proton transfer, tautomerization andnhydrolysis of intermediate 7 (Scheme 2 and table 1).

The structures of compounds 4 were deduced from their ^{1}H NMR, ^{13}C NMR and IR spectral data and their molecular weight confirmed by mass spectrometry. ^{1}H NMR and ^{13}C NMR spectroscopy were especially useful to elucidate the structures of products. The mass spectra of these compounds detected the expected molecular ion signals. Selected spectroscopic data have been given in general procedure section. The results obtained in the reaction of a series of representative aldehydes with malononitrile and β-Naphtole. The effect of substituents on the aromatic ring did not show special effects in terms of yields under these reaction conditions. We have developed an easier, practically convenient, novel, ecologically safe method for the synthesis of 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile derivatives using a green chemistry protocol. We suggest DABCO as a green and effective catalyst that does not use harmful organic solvents for these reactions.

Table 1: 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile 4a–g in under grinding using DABCO Yields refer to pure isolated products characterized b y IR, ^{1}H and ^{13}C N MR spectroscopy and mass spectrometry

Product	Ar	Time (min)	Yield
4a	3-Chloro -C_6H_4	10	89
4b	4-Chloro -C_6H_4	8	83
4c	4-Cyano -C_6H_4	10	91
4d	2,3- diChloro -C_6H_3	6	96
4e	3-hydroxy -C_6H_4	14	92
4f	3-nitro -C_6H_4	12	95
4g	4-trifluoro -C_6H_4	12	85
4h	C_6H_5	9	88
4i	4-dimethyl- amino- C_6H_4	3	92
4k	4-Br- C_6H_4	9	83

EXPERIMENTAL

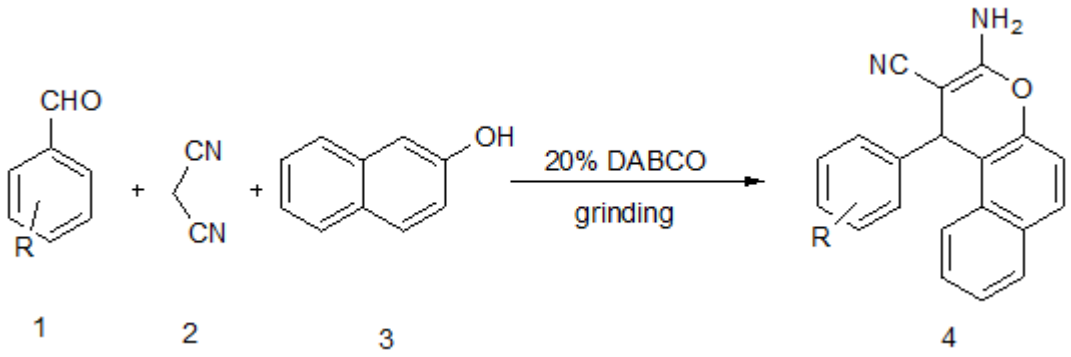
All of the chemical materials used in this work were purchased from Merck and Fluka and used without further purification. Melting points were

determined with an Electro thermal 9100 apparatus and were uncorrected. IR spectra were obtained on an ABB FT-IR (FTLA 2000) spectrometer. ^{1}HNMR and ^{13}C NMR spectra were recorded on a Bruker DRX-300 AVANCE at 300 and 75MHz (respectively) using TMS as internal standard and $CDCl_3$ as solvent. Mass spectra data were obtained using a GC-MS Hewlett Packard (EI, 20 e V) instrument.

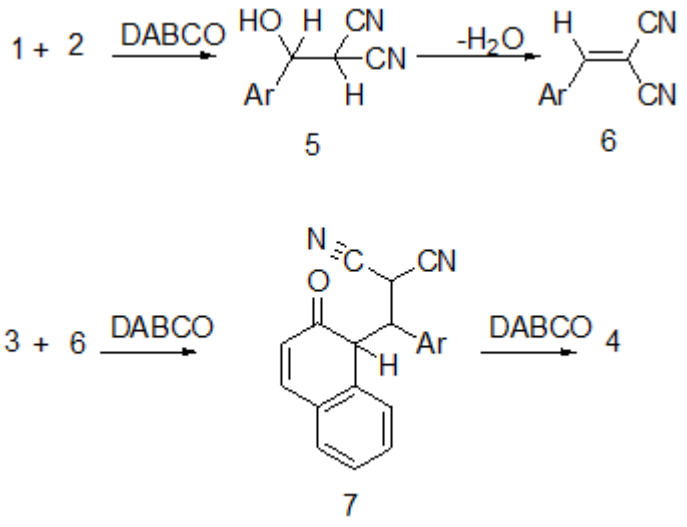
Synthesis 3-amino-1-phenyl-1H-benzo[f] chromene- 2-carbonitrile derivatives

A solution of aromatic aldehyde 1 (1 mmol), malononitrile 2 (1.2 mmol), β-Naphtole 3 (1 mmol), and 1,4-diazabicyclo[2.2.2]octane (DABCO) (22.4 mg, 20 mol %) in under grinding was stirred at room temperature for 3-15 min. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the mixture was then concentrated under reduced pressure, and 5 ml of water/ethanol(1:1) was added. The remaining solid was collected by filtration. Further purification was done by recrystallization in EtOH.

3-amino-1-(3-chlorophenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 202–204 ^{0}C. IR (KBr, cm^{-1}) 3431, 3328, 2182, 1646, 1588. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.40 (s, 1H, H-4), 6.34 (brs, 2H, NH2), 7.23–7.38 (m, 5H, H-Ar), 7.44–7.48 (m, 2H, H-Ar), 7.87–7.98 (m, 2H, H-Ar). ^{13}C



Scheme 1: Synthesis 3-amino-1-phenyl-1H-benzo[f] chromene-2-carbonitrile by 20% DABCO in under grinding



Scheme 2: The proposed mechanism for the synthesis of 3-amino-1-phenyl-1H-benzo[f]chromene-2-carbonitrile in under grinding catalyzed by 1,4-diazabicyclo[2.2.2]octane (DABCO)

NMR (75 MHz, CDCl3, ppm) δ 59.08, 111.50, 115.09, 118.33, 119.49, 120.66, 120.86, 123.38, 123.93, 126.44, 126.48, 126.59, 127.67, 133.27, 137.20, 143.06, 145.77, 147.60, 159.89. HR-MS (70 eV, EI): $C_{20}H_{13}N_2O^{35}Cl$ $[M]^{+\cdot}$ found: 332.0705; calc. 332.0716; $C_{20}H_{13}N_2O^{37}Cl$ $[M+2]^{+\cdot}$ found: 334.0695; calc. 334.0703.

3-amino-1-(4-chlorophenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 206–208 ^{0}C. IR (KBr, cm^{-1}) 3409, 3322, 3029, 2223, 1630, 1586. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.36 (s, 1H, H-4), 7.11 (brs, 2H, NH2), 7.25 (d, 1H, J=8.4 Hz, H-Ar), 7.29 (d, 1H, J=8.4 Hz, H-Ar), 7.35 (d, 1H, J= 8.9 Hz, H-Ar), 7.38–7.45 (m, 3H, H-Ar), 7.80 (d, 1H, J= 8.2 Hz, H-Ar), 7.88 (d, 1H, J= 7.8 Hz, H-Ar), 7.92 (d, 1H, J= 9.0 Hz, H-Ar). 13C NMR (75 MHz, CDCl3, ppm) δ: 61.18, 112.37, 113.48, 114.40, 116.68, 123.58, 125.28, 127.40, 128.56, 128.63, 129.13, 129.27, 129.92, 30.08, 131.43, 131.86, 147.10, 158.34, 158.68. HR-MS (70 eV, EI): $C_{20}H_{13}N_2O^{35}Cl$ $[M]^{+\cdot}$ found: 332.0705; calc. 332.0716; $C_{20}H_{13}N_2O^{37}Cl$ $[M+2]^{+\cdot}$, found: 334.0695; calc. 334.0703.

3-amino-1-(4-cyanophenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 285–287 ^{0}C. IR (KBr, cm^{-1}) 3440, 3301, 2223, 2182, 1653, 1591. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.49 (s, 1H, H-4), 6.41 (brs, 2H, NH2), 7.37 (d, 1H, J= 8.9 Hz, H-Ar), 7.44–7.49 (m, 2H, H-Ar), 7.48 (d, 2H, J= 8.9 Hz, H-Ar), 7.70 (d, 2H, J =7.5 Hz, H-Ar), 7.82–7.85 (m, 1H, H-Ar), 7.92–7.95 (m, 1H, H-Ar), 7.98 (d, 1H, J=8.9 Hz, H-Ar). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 58.93, 110.55, 114.49, 116.83, 118.28, 119.00, 123.51, 125.18, 127.30, 128.26, 128.66, 130.08, 130.55, 131.49, 132.66, 147.44, 150.73, 159.84. HR-MS (70 eV, EI): $C_{21}H_{13}N_3O$: $[M]^{+\cdot}$ found 323.1058; calc. 323.1058.

3-amino-1-(2,3- dichlorophenyl)-1H-benzo[f]chromene -2-carbonitrile, mp: 319–322 ^{0}C. IR (KBr, cm^{-1}) 3439, 3322, 2135, 1630, 1589. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) ä: 5.94 (s, 1H, H-4), 6.38 (brs, 2H, NH2), 7.03 (d, 1H, J= 7.8 Hz, H-Ar), 7.21 (t, 1H, J=7.8 Hz, H-Ar), 7.35 (d, 1H, J=8.9 Hz, H-Ar), 7.41–7.54 (m, 3H, H-Ar), 7.70 (d, 1H, J= 8.3 Hz, H-Ar), 7.94 (d, 1H, J= 7.9 Hz, H-Ar), 7.98 (d, 1H, J= 9.0 Hz, H-Ar). HR-MS (70 eV, EI): $C_{20}H_{12}N_2O_{35}Cl_2$ $[M]^{+\cdot}$ found 366.0319; calc. 366.0327; $C_{20}H_{12}N_2O_{35}Cl_2$ $[M]^{+\cdot}$ found 366.0319; calc. 366.0327; $C_{20}H_{12}N_2O^{35}Cl^{37}Cl$ $[M+2]^{+\cdot}$ found 368.0282; calc. 368.0297; $C_{20}H_{12}N_2O^{37}Cl2$ $[M + 4]^{+\cdot}$ found 370.0261; calc. 370.0267.

3-amino-1-(3-hydroxyphenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 280–282 ^{0}C. IR (KBr, cm^{-1}) 3419, 3327, 2187, 1642, 1586. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.40 (s, 1H, H-4), 6.23 (brs, 2H, NH2), 6.63–6.67 (m, 2H, H-Ar), 6.77 (d, 1H, J= 7.6 Hz, H-Ar), 7.10 (t, 1H, J= 7.6 Hz, H-Ar), 7.34 (d, 1H, J= 8.9 Hz, H-Ar), 7.40–7.49 (m, 2H, H-Ar), 7.92 (t, 3H, J= 8.9 Hz, H-Ar), 8.35 (brs, 1H, OH). ^{13}C NMR (75 MHz, CDCl3, ppm) δ: 60.18, 113.82, 114.10, 115.81, 116.73, 118.36, 119.44, 123.84, 124.96, 126.99, 128.46, 129.47, 129.65, 130.89, 131.43, 147.12, 147.30, 157.78, 159.60. ESI: $C_{20}H_{15}N_2O_2$ [M + 1]+ found 315.11280; calc. 314.1129; C20H14N2O2Na $[M+Na]^+$ found 337.09475; calc. 337.09493; $C_{40}H_{28}N_4O_4Na$ [2M +Na]$^+$ found 651.20028; calc. 651.20047.

3-amino-1-(3-nitrophenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 239–241 ^{0}C. IR (KBr, cm^{-1}) 3464, 3357, 2192, 1657, 1590. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.61 (s, 1H, H-4), 7.15 (brs, 2H, NH2), 7.38 (d, 1H, J= 8.9 Hz, H-Ar), 7.42–7.48 (m, 2H, H-Ar), 7.57 (t, 1H, J= 7.8 Hz, H-Ar), 7.65 (m, 1H, H-Ar), 7.85 (d, 1H, J= 7.5 Hz, H-Ar), 7.91–7.96 (m, 2H, H-Ar), 8.00 (d, 1H, J=6.3 Hz, H-Ar), 8.05 (m, 1H, H-Ar). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 57.42, 115.04, 117.32, 120.66, 121.78, 122.29, 123.93, 125.60, 127.85, 129.05, 130.37, 130.52, 130.89, 131.31, 134.17, 147.43, 148.33, 148.44, 160.44. HR-MS (70 eV, EI): $C_{20}H_{13}N_3O_3$ $[M]^{+\cdot}$ found 343.0977; calc. 343.0957.

3-amino-1-(4-trifluoromethylphenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 215–217 ^{0}C. IR (KBr, cm^{-1}): 3470, 3358, 2193, 1739, 1576. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.48 (s, 1H, H-4), 6.37 (brs, 2H, NH2), 7.37 (d, 1H, J=8.9 Hz, H-Ar), 7.41–7.50 (m, 4H, H-Ar), 7.64 (d, 2H, J= 8.2 Hz, H-Ar), 7.84–7.94 (m, 4H, H-Ar), 7.98 (d, 1H, J= 8.9 Hz, H-Ar). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) ä: 58.93, 114.75, 116.82, 119.16, 122.59, 123.55, 125.12, 125.73, 127.25, 127.96, 128.15, 128.60, 130.00, 130.59, 131.48, 147.40, 149.96, 159.79. HR-MS (70 eV, EI) $C_{21}H_{13}N_2OF_3$ $[M]^{+\cdot}$ found 366.0980; calc. 366.0967.

3-amino-1-(phenyl)-1H-benzo[f]chromene-2-carbonitrile, mp: 288-290 ^{0}C. IR (KBr, cm^{-1}) 3450, 3345, 2180, 1640, 1580. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.30 (s, 1H, H-4), 6.8 (brs, 2H, NH2), 7.23–7.38 (m, 5H, H-Ar), 7.44–7.48 (m, 5H, H-Ar). ^{13}C NMR (75 MHz, CDCl3, ppm) δ 59.08, 111.50, 115.09, 118.33, 119.49, 120.66, 120.86, 123.38, 123.93, 126.44, 126.48, 126.59, 127.67, 128.27, 130.20, 143.06, 145.77, 147.60, 159.89. HR-MS (70 eV, EI): $C_{20}H_{14}N_2O$ $[M]^{+\cdot}$ found: 298.11; calc. 298.09

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