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## REVIEW

# Microwave-assisted synthesis of chromeno[2,3-*d*]pyrimidinone derivatives



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## KEYWORDS

Microwave irradiation;  
Chromeno[2,3-*d*]pyrimidinone;  
Phenylhydrazine

**Abstract** New series of 10-anilino-9-alkyl-12-aryl-10,12-dihydro-11*H*-benzo[5,6] chromeno[2,3-*d*]pyrimidin-11-ones **5(a–e)** and 9-anilino-10-alkyl-7-aryl-7,9-dihydro-8*H*-benzo[7,8]chromeno[2,3-*d*]pyrimidin-8-ones **6(a–f)** were prepared in three steps with microwave irradiation. The procedure is easy, avoiding time-consuming syntheses is not costly.

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## 1. Introduction

The pyranopyrimidine moieties represent important building blocks in synthetic bioactive compounds, which show antibacterial (Ashraf and Abd El-Wahab, 2002), antimicrobial (Fathy et al., 2004), antifungal (Ahmed et al., 2000a, 2001; Mostafa et al., 2002), and antigenotoxic (Fakher et al., 2007) activities. Also, pyranopyrimidine derivatives can have antiplatelet, anti-thrombotic (Bruno et al., 2006), analgesic, anti-inflammatory, and antiphlogistic activities (Bruno et al., 2002, 2004). Therefore, the synthesis of this type of compounds has attracted considerable attention (Mehdi et al., 2005, 2006, 2008; Ahmed et al., 1997, 2000b,c, 2002; Abdel-Ghani et al., 1993; Zaki et al., 1991, 1999).

In our previous work, we synthesized a new class of naph-topyranopyrimidinones by reaction of imidates **3** with primary amines (Kamar et al., 2010).

The present work represents a new method for the synthesis of *N*-phenylamin-naph-topyranopyrimidinones using microwave irradiation as a convenient method and rapid which give better yields and higher purity of the products than the conventional method.

## 2. Experimental

Commercially reagent grade chemicals were used as received without additional purification. All reactions were followed by TLC (E. Merck Kieselgel 60 F-254), with detection by UV light at 254 nm. IR spectra were recorded on a Perkin-Elmer spectrometer. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded on an AC Bruker spectrometer at 300, 500 MHz (<sup>1</sup>H) and 75, 125 MHz (<sup>13</sup>C) using (CD<sub>3</sub>)<sub>2</sub>SO as solvent with (CD<sub>3</sub>)<sub>2</sub>SO (δ<sub>H</sub> 2.5) or (CD<sub>3</sub>)<sub>2</sub>SO (δ<sub>C</sub> 39.5). Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (0 ppm) as an internal reference and the following multiplicity abbreviations were used: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; *J* in hertz. Mass spectra (MS) were recorded on a gas chromatography (GC) MS spectrometer with an atmospheric pressure electrospray (API-ES) ionization source. Elemental analyses (C, H, and N) were performed at the Instituto de Química orgánica (Consejo Superior de Investigaciones Científicas, Spain). All solvents were dried by standard methods. The microwave assisted reactions were carried out in synthetic microwave: Monowave 300 with a maximum power of 300 W.

### 2.1. General procedure for synthesis of compounds **1(a–e)** and **2(a–d)**

A mixture of aromatic aldehyde (0.01 mmol), ethyl cyanoacetate (0.01 mmol), 2-naphthol (or 1-naphthol) (0.01 mmol) in ethanol (20 ml) in the presence of 0.2 equivalent of piperidine was irradiated for 10 min in a sealed tube. The irradiation was programmed to obtain a constant temperature (80 °C, 150 W). We obtained a robust product that was filtered, washed with cold ethanol, and dried, to give compounds **1(a–e)** and **2(a–d)** in good yields.

#### 2.1.1. Ethyl-3-amino-1-phenyl-1H-benzo[f]chromene-2-carboxylate (**1a**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.1.2. Ethyl-3-amino-1-p-methylphenyl-1H-benzo[f]chromene-2-carboxylate (**1b**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.1.3. Ethyl-3-amino-1-p-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate (**1c**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1686 (C=O), 3333–3421 (NH<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.06 (m, 3H), 3.82 (s, 3H), 4.03 (m, 2H), 5.85 (s, 1H), 6.74–8.27 (m, 10H, aromatic), 7.70 (s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>): 14.97, 34.62, 55.03, 59.34, 77.22, 117.32, 118.58, 123.51, 125.33, 127.58, 127.92, 128.29, 129.18, 129.78, 129.99, 131.10, 131.13, 131.71, 131.97, 144.59, 147.38, 161.23, 168.78.

#### 2.1.4. Ethyl-3-amino-1-o-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate (**1d**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.1.5. Ethyl-3-amino-1-o-chlorophenyl-1H-benzo[f]chromene-2-carboxylate (**1e**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.1.6. Ethyl-2-amino-4-phenyl-4H-benzo[h]chromene-3-carboxylate (**2a**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1662 (C=O), 3372–3260 (NH<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.10 (m, 3H), 4.01 (m, 2H), 5.04 (s, 1H), 7.04–8.33 (m, 11H, aromatic), 7.64 (s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  14.74, 40.57, 59.08, 76.86, 121.16, 121.46, 123.29, 124.18, 126.48, 126.92, 126.99, 127.07, 127.79, 128.11 (double intensity), 128.67 (double intensity), 132.97, 143.29, 148.29, 161.26, 168.70.

#### 2.1.7. Ethyl-2-amino-4-p-methylphenyl-4H-benzo[h]chromene-3-carboxylate (**2b**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1672 (C=O), 3315–3452 (NH<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.10 (m, 3H), 2.28 (s, 3H), 4.00 (m, 2H), 4.98 (s, 1H), 6.98–8.29 (m, 10H, aromatic), 7.62 (s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  14.77, 20.99, 40.83, 59.08, 76.98, 121.25, 121.86, 123.36, 124.11, 126.85, 126.90,

127.08, 127.67, 128.09 (double intensity), 129.22 (double intensity), 132.94, 135.42, 143.26, 145.36, 161.21, 168.76.

#### 2.1.8. Ethyl-2-amino-4-p-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate (**2c**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1665 (C=O), 3274–3360 (NH<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.09 (m, 3H), 3.66 (s, 3H), 4.01 (m, 2H), 4.97 (s, 1H), 6.76–8.34 (m, 10H, aromatic), 7.74 (s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  14.79, 39.98, 55.39, 59.08, 77.13, 114.03 (double intensity), 121.12, 121.78, 123.29, 124.12, 136.85, 126.91, 127.12, 128.10 (double intensity), 128.73, 132.91, 140.48, 143.22, 157.97, 161.16, 168.77.

#### 2.1.9. Ethyl-2-amino-4-m-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate (**2d**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1663 (C=O), 3393–3280 (NH<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.09 (m, 3H), 3.68 (s, 3H), 4.02 (m, 2H), 5.01 (s, 1H), 6.67–8.32 (m, 10H, aromatic), 7.63 (s, 2H, NH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  14.26, 40.04, 54.83, 58.60, 76.25, 110.78, 113.51, 119.50, 120.65, 120.86, 122.78, 123.65, 126.41, 126.43, 126.51, 127.60, 129.28, 132.49, 142.81, 149.35, 159.05, 160.81, 168.21.

### 2.2. General procedure for synthesis of imidate **3(a–j)** and **4(a–f)**

A stirred mixture of (0.01 mmol) of **1** or **2**, a catalytic amount of acetic acid in (0.06 mmol) orthoesters (ethyl orthoacetate or ethyl orthopropionate) was irradiated for 10–15 min. The irradiation was programmed to obtain a constant temperature (140 °C, 150 W). The solid product formed was collected by filtration and recrystallized with a suitable solvent (hexane/ether 5:5), to afford the expected compounds **3(a–j)** or **4(a–f)**.

#### 2.2.1. Ethyl-3-[(ethoxyethylidene)amino]-1-phenyl-1H-benzo[f]chromene-2-carboxylate (**3a**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.2.2. Ethyl-3-[(ethoxyethylidene)amino]-1-p-methylphenyl-1H-benzo[f]chromene-2-carboxylate (**3b**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

#### 2.2.3. Ethyl-3-[(ethoxyethylidene)amino]-1-p-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate (**3c**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1664 (C=O), 1596 (N=C); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.32 (t, 3H, *J* = 7.2 Hz), 1.45 (m, 3H), 2.09 (s, 3H), 3.91 (s, 3H), 4.19 (q, 2H, *J* = 7.2 Hz), 4.45 (m, 2H), 5.83 (s, 1H), 6.85–8.46 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  13.80, 14.13, 17.31, 33.55, 55.32, 59.58, 63.17, 92.80, 111.10, 117.16, 118.22, 120.63, 123.96, 124.59, 126.68, 127.75, (double intensity): 128.55, 131.14, 131.29, 131.59, 134.21, 148.38, 156.38, 159.67, 166.77, 167.45.

#### 2.2.4. Ethyl-3-[(ethoxyethylidene)amino]-1-o-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate (**3d**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.5. Ethyl-3-[(ethoxyethylidene)amino]-1-*o*-chlorophenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3e**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.6. Ethyl-3-[(ethoxypropylidene)amino]-1-phenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3f**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.7. Ethyl-3-[(ethoxypropylidene)amino]-1-*p*-methylphenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3g**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.8. Ethyl-3-[(ethoxypropylidene)amino]-1-*p*-methoxyphenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3h**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1678 (C=O), 1613 (C=N); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.05 (t, 3H, *J* = 7.2 Hz), 1.13 (m, 3H), 1.28 (t, 3H, *J* = 7.2 Hz), 2.30 (q, 2H, *J* = 7.2 Hz), 3.78 (s, 3H), 4.01 (m, 2H), 4.25 (q, 2H, *J* = 7.2 Hz), 5.95 (s, 1H), 6.68–7.65 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.85, 14.48, 14.63, 25.40, 34.10, 55.81, 60.10, 63.35, 93.26, 111.45, 117.35, 118.77, 121.16, 124.31, 124.78, 126.93, 127.99 (double intensity), 128.63, 131.32, 131.55, 131.88, 134.61, 148.69, 156.69, 159.60, 167.10, 169.60.

2.2.9. Ethyl-3-[(ethoxypropylidene)amino]-1-*o*-methoxyphenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3i**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.10. Ethyl-3-[(ethoxypropylidene)amino]-1-*o*-chlorophenyl-1*H*-benzo[*f*]chromene-2-carboxylate (**3j**)

Data supporting its chemical structure are reported in Ref. (Kamar et al., 2010).

2.2.11. Ethyl-2-[(ethoxyethylidene)amino]-4-phenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4a**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1662 (C=O), 1596 (C=N); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.13 (m, 3H), 1.32 (t, 3H, *J* = 6.9 Hz), 1.95 (s, 3H), 3.98 (m, 2H), 4.30 (q, 2H, *J* = 6.9 Hz), 5.16 (s, 1H), 7.04–8.18 (m, 11H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 14.15 (double intensity), 17.62, 42.72, 59.81, 63.13, 92.97, 119.75, 121.33, 123.68, 124.08, 126.18, 126.22, 126.70, 127.57, 127.97 (double intensity), 128.32 (double intensity), 128.64, 129.42, 133.05, 144.30, 146.92, 159.14, 166.53, 166.85.

2.2.12. Ethyl-2-[(ethoxyethylidene)amino]-4-*p*-methylphenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4b**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1662 (C=O), 1613 (C=N); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.12 (m, 3H), 1.32 (t, 3H, *J* = 6.9 Hz), 1.94 (s, 3H), 2.16 (s, 3H), 4.01 (m, 2H), 4.29 (q, 2H, *J* = 6.9 Hz), 5.12 (s, 1H), 7.03–8.08 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 14.10, 14.18, 17.61, 21.01, 42.30, 59.80, 63.71, 93.11, 119.97, 121.33, 123.70, 124.09, 126.14, 126.15, 127.41, 128.28, 128.85, 129.04, 129.32, 130.90, 133.02, 135.88, 144.06, 144.28, 159.04, 166.58, 166.83.

2.2.13. Ethyl-2-[(ethoxyethylidene)amino]-4-*p*-methoxyphenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4c**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1661 (C=O), 1593 (N=C); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.19 (m, 3H), 1.30 (t, 3H, *J* = 7.2 Hz), 1.89 (s, 3H), 3.84 (s, 3H), 4.05 (m, 2H), 4.25 (q, 2H, *J* = 7.2 Hz), 5.66 (s, 1H), 7.00–8.03 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.37, 14.46, 17.63, 38.39, 55.10, 60.09, 63.14, 93.60, 117.41, 117.82, 123.62, 125.28, 127.55, 128.28 (double intensity), 129.01 (double intensity), 129.32, 129.42, 130.62, 131.40, 135.89, 143.31, 147.84, 158.64, 165.96, 167.19.

2.2.14. Ethyl-2-[(ethoxyethylidene)amino]-4-*m*-methoxyphenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4d**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1653 (C=O), 1584 (N=C); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.11 (m, 3H), 1.34 (t, 3H, *J* = 7.1 Hz), 2.02 (s, 3H), 3.69 (s, 3H), 3.98 (m, 2H), 4.32 (q, 2H, *J* = 7.0 Hz), 5.20 (s, 1H), 6.71–8.14 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.39 (double intensity), 17.82, 42.19, 55.39, 59.95, 63.26, 92.53, 111.79, 114.24, 120.02, 120.29, 121.07, 123.27, 124.54, 126.79, 127.01, 127.18, 128.17, 130.03, 133.07, 143.89, 148.72, 159.11, 159.68, 165.95, 167.18.

2.2.15. Ethyl-2-[(ethoxypropylidene)amino]-4-phenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4e**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1681 (C=O), 1588 (N=C); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.10 (t, 3H, *J* = 7.2 Hz), 1.33 (m, 3H), 1.41 (t, 3H, *J* = 7.2 Hz), 2.38 (q, 2H, *J* = 7.2 Hz), 4.15 (m, 2H), 4.33 (q, 2H, *J* = 7.2 Hz), 5.64 (s, 1H), 7.12–8.25 (m, 11H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.25, 12.89, 13.17, 23.98, 37.85, 58.69, 61.78, 99.49, 116.92, 118.86, 121.38, 124.58, 125.20, 125.61, (double intensity): 127.35, (double intensity): 127.55, 127.36, 127.65, 129.86, 132.22, 145.66, 147.92, 158.73, 165.58, 168.30.

2.2.16. Ethyl-2-[(ethoxypropylidene)amino]-4-*p*-methylphenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4f**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1685 (C=O), 1592 (N=C); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.15 (t, 3H, *J* = 7.2 Hz), 1.33 (m, 3H), 1.48 (t, 3H, *J* = 7.2 Hz), 2.25 (s, 3H), 2.35 (q, 2H, *J* = 7.2 Hz), 4.22 (m, 2H), 4.40 (q, 2H, *J* = 7.2 Hz), 5.79 (s, 1H), 7.01–8.28 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.02, 12.88, 13.22, 21.23, 23.87, 37.59, 59.60, 61.56, 93.91, 115.52, 116.76, 122.78, 123.68, 125.69, 125.58, (double intensity): 127.34, (double intensity): 127.42, 127.45, 127.75, 129.92, 130.40, 145.26, 146.82, 157.43, 165.12, 168.35.

2.2.17. Ethyl-2-[(ethoxypropylidene)amino]-4-*p*-methoxyphenyl-4*H*-benzo[*h*]chromene-3-carboxylate (**4g**)

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1683 (C=O), 1595 (N=C); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.08 (t, 3H, *J* = 7.0 Hz), 1.12 (m, 3H), 1.32 (t, 3H, *J* = 7.0 Hz), 2.33 (q, 2H, *J* = 7.0 Hz), 3.41 (s, 3H), 3.64 (m, 2H), 4.29 (q, 2H, *J* = 7.0 Hz), 5.10 (s, 1H), 6.66–7.40 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 10.45, 14.03, 14.18, 22.62, 41.81, 56.90, 59.71, 62.97, 92.91, 113.50, 113.66, 115.58, 120.05, 121.25, 123.69, 124.02, 126.12, 126.46, 127.55, 128.30, 129.10, 132.98, 139.38, 144.23, 158.09, 158.70, 166.64, 169.78.

2.2.18. *Ethyl-2-[(ethoxypropylidene)amino]-4-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate (4h)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1680 (C=O), 1600 (N=C); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.08 (t, 3H, *J* = 7.0 Hz), 1.13 (m, 3H), 1.35 (t, 3H, *J* = 7.0 Hz), 2.35 (q, 2H, *J* = 7.0 Hz), 3.70 (s, 3H), 3.97 (m, 2H), 4.32 (q, 2H, *J* = 7.0 Hz), 5.19 (s, 1H), 6.71–8.12 (m, 10H, aromatic); <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 10.79, 14.37, 14.41, 25.10, 42.12, 55.38, 59.91, 63.21, 92.28, 111.28, 114.16, 120.13, 120.21, 120.93, 123.25, 124.57, 126.80, 127.01, 127.24, 128.20, 130.01, 133.07, 143.88, 148.69, 158.91, 159.69, 165.98, 169.93.

2.3. General Procedure for synthesis compounds 5(a–e) and 6(a–f)

A suspension of the compound 3 or 4 (0.01 mmol), phenylhydrazine (0.01 mmol), a catalytic amount of acetic acid in toluene 4 (mL) was irradiated for 15 min in a sealed tube. The irradiation was programmed to obtain a constant temperature (105 °C, 300 W). After cooling, the precipitated solid was filtered, washed with ether, and dried to obtain compounds 5(a–e) or 6(a–f).

2.3.1. *10-Anilino-9-methyl-12-phenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3-d]pyrimidin-11-one (5a)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1676 (C=O), 3435 (NH); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 2.18 (s, 3H), 5.91 (s, 1H), 7.07–7.90 (m, 17H, aromatic); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 15.37, 36.77, 101.88, 116.66, 117.52, 123.80, 125.05, 126.70, 127.21, 127.60, 127.70, 128.49, 128.54 (double intensity), 128.67 (double intensity), 129.49, 129.58, 130.09, 130.20, 131.13, 131.61, 137.14, 143.73, 148.33, 158.34, 159.84, 162.79. MS (APCI<sup>+</sup>): *m/z* 432 (M + H)<sup>+</sup>.

2.3.2. *10-Anilino-9-methyl-12-p-methylphenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3-d]pyrimidin-11-one (5b)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1678 (C=O), 3421 (NH); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 2.18 (s, 3H), 2.22 (s, 3H), 5.88 (s, 1H), 6.99–7.93 (m, 16H, aromatic). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 15.38, 21.11, 36.32, 102.05, 116.82, 117.52, 123.81, 125.03, 127.20, 127.64, 127.73, 128.50, 129.20 (double intensity), 129.38 (double intensity), 129.56 (double intensity), 130.08, 130.16, 131.15, 131.61, 136.23, 137.18, 140.89, 148.30, 158.22, 159.80, 162.81. MS (APCI<sup>+</sup>): *m/z* 446 (M + H)<sup>+</sup>.

2.3.3. *10-Anilino-9-ethyl-12-phenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3-d]pyrimidin-11-one (5c)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1685 (C=O), 3390 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.33 (t, 3H, *J* = 7.2 Hz), 2.39 (q, 2H, *J* = 7.2 Hz), 5.97 (s, 1H), 6.83–8.21 (m, 17H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.39, 17.57, 35.52, 92.49, 111.93, 112.47, 117.73, 120.94, 123.37, 125.07, 125.59, 127.35, 127.60, 127.92, 128.33, 128.92 (double intensity), 129.05 (double intensity), 129.12, 129.24, 130.15, 130.76, 131.01, 131.18, 133.95, 148.23, 159.12, 167.26. MS (APCI<sup>+</sup>): *m/z* 446 (M + H)<sup>+</sup>.

2.3.4. *10-Anilino-9-ethyl-12-o-methoxyphenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3-d]pyrimidin-11-one (5d)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1681 (C=O), 3435 (NH); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.29 (t, 3H, *J* = 7.2 Hz), 2.40 (q, 2H, *J* = 7.2), 3.82

(s, 3H), 5.90 (s, 1H), 6.77–8.21 (m, 16H, aromatic). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.92, 28.30, 31.95, 55.83, 101.19, 111.66, 117.40, 120.75, 123.88, 124.60, 126.72, 127.87, 127.93, 128.21, 128.71 (double intensity), 129.24 (double intensity), 129.79, 129.83, 131.14, 131.28, 131.51, 132.25, 136.78, 148.27, 156.79, 160.73, 161.79, 162.61. Anal. calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>3</sub>: C, 75.77; H, 5.30; N, 8.84. Found: C, 75.63; H, 5.41; N, 8.94. MS (APCI<sup>+</sup>): *m/z* 476 (M + H)<sup>+</sup>.

2.3.5. *10-Anilino-9-ethyl-12-o-chlorophenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3-d]pyrimidin-11-one (5e)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1682 (C=O), 3410 (NH); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.22 (t, 3H, *J* = 7.2 Hz), 2.39 (q, 2H, *J* = 7.2 Hz), 5.92 (s, 1H), 7.00–8.19 (m, 16H, aromatic). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.84, 29.01, 34.57, 101.10, 116.76, 117.56, 123.88, 124.98, 127.06, 127.21, 127.84, 127.89, 127.95, 128.46, 129.36, 129.53, 129.92, 129.96 (double intensity), 131.36, 131.37, 131.79, 133.10, 136.56, 141.41, 148.19, 160.40, 162.43, 162.52. Anal. calcd. for C<sub>30</sub>H<sub>25</sub>N<sub>3</sub>O<sub>3</sub>Cl: C, 72.57; H, 4.62; N, 8.75; Cl, 7.39. Found: C, 72.35; H, 4.77; N, 8.63; Cl, 7.20. MS (APCI<sup>+</sup>): *m/z* 480 (M + H)<sup>+</sup>.

2.3.6. *9-Anilino-10-methyl-7-phenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (6a)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1683 (C=O), 3331 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.95 (s, 3H), 5.97 (s, 1H), 6.82–8.21 (m, 17H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.39, 33.61, 92.49, 111.93, 112.47, 117.34, 117.80, 120.94, 121.06, 123.37, 123.62, 125.07, 127.35, 127.60, 127.92, 128.33, 128.92, 130.15, 130.76, 131.10, 133.95, 148.23, 156.37, 159.12, 165.98, 167.26. MS (APCI<sup>+</sup>): *m/z* 432 (M + H)<sup>+</sup>.

2.3.7. *9-Anilino-10-methyl-7-p-methylphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (6b)*

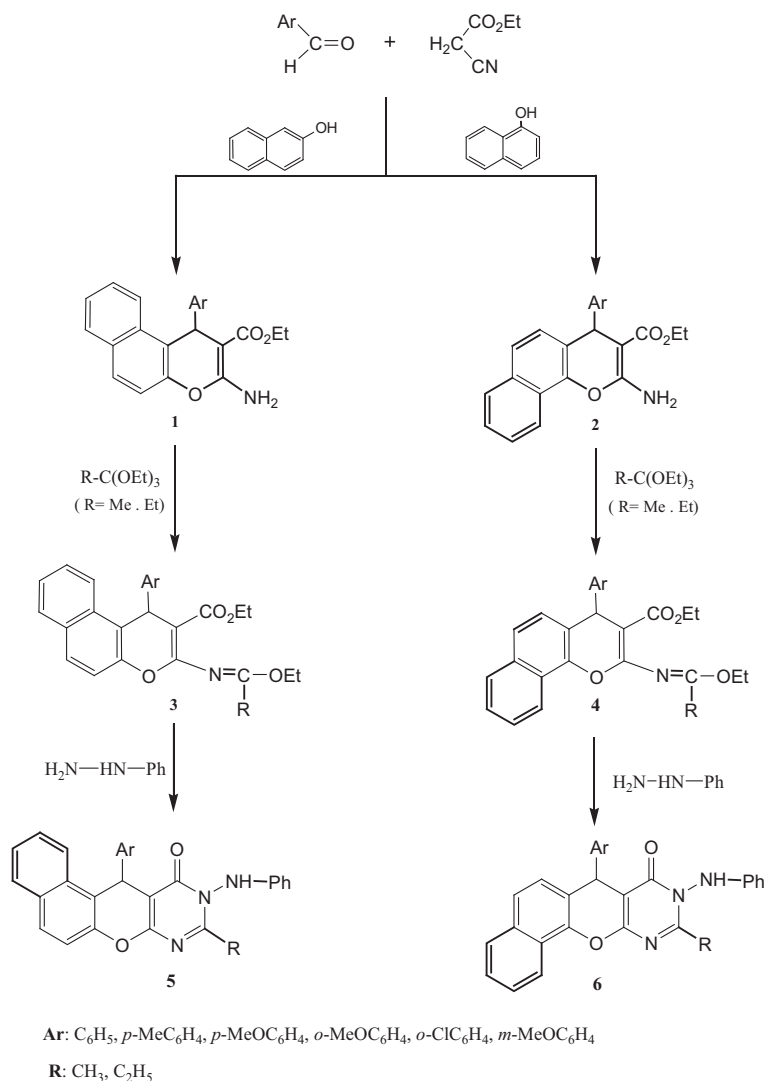
IR (cm<sup>-1</sup>):  $\nu_{\max}$  1679 (C=O), 3300 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.22 (s, 3H), 2.34 (s, 3H), 5.89 (s, 1H), 6.71–8.12 (m, 16H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.37, 23.12, 35.10, 92.28, 111.93, 117.34, 117.80, 120.94, 121.06, 123.37, 123.62, 125.07, 127.35, 127.60, 127.92, 128.33, 128.92, 129.05, 130.15, 130.76, 131.01, 131.18, 133.95, 148.23, 156.37, 159.12, 165.98, 167.26, 167.61. MS (APCI<sup>+</sup>): *m/z* 446 (M + H)<sup>+</sup>.

2.3.8. *9-Anilino-10-methyl-7-p-methoxyphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (6c)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1685 (C=O), 3360 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.21 (s, 3H), 3.72 (s, 3H), 5.88 (s, 1H), 7.34–7.69 (m, 16H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.19, 35.80, 55.41, 100.32, 111.83, 114.83, 119.45, 120.59, 121.19, 123.61, 124.92, 127.13, 127.27, 127.40, 128.26, 128.43, 128.58 (double intensity), 129.61, 130.02, 133.26, 137.67, 144.08, 147.21, 159.54, 159.65, 160.49, 162.33, 162.68. MS (APCI<sup>+</sup>): *m/z* 462 (M + H)<sup>+</sup>.

2.3.9. *9-Anilino-10-methyl-7-m-methoxyphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-d]pyrimidin-8-one (6d)*

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1682 (C=O), 3334 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.15 (s, 3H), 3.69 (s, 3H), 5.87 (s, 1H), 6.90–7.69 (m, 16H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.16, 35.91, 55.39, 99.82, 110.85, 112.83, 119.49, 120.80, 121.23,



**Scheme 1** General reaction for the synthesis of compounds **5(a-e)** and **6(a-f)**.

123.81, 124.56, 127.33, 127.48, 127.55, 128.76, 128.48, 128.66, 129.62 (double intensity), 131.02, 133.46, 137.57, 144.15, 148.25, 159.59, 159.75, 160.46, 162.52, 162.77. MS (APCI<sup>+</sup>): *m/z* 462 (M + H)<sup>+</sup>.

**2.3.10. 9-Anilino-10-ethyl-7-phenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-*d*]pyrimidin-8-one (6e)**

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1678 (C=O), 3333 (NH); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.14 (t, 3H, *J* = 7.0 Hz), 2.35 (q, 2H, *J* = 7.0 Hz), 5.92 (s, 1H), 7.28–8.35 (m, 17H, aromatic). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.82, 28.93, 35.97, 100.42, 119.54, 121.27, 123.62, 124.95, 127.06, 127.18, 127.27, 127.41, 128.26, 128.49 (double intensity), 128.59 (double intensity), 128.79, 128.90, 129.60, 129.98, 130.03, 133.25, 137.18, 144.22, 145.68, 160.64, 162.39, 168.47. MS (APCI<sup>+</sup>): *m/z* 446 (M + H)<sup>+</sup>.

**2.3.11. 9-Anilino-10-ethyl-7-*p*-methylphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3-*d*]pyrimidin-8-one (6f)**

IR (cm<sup>-1</sup>):  $\nu_{\max}$  1674 (C=O), 3341 (NH); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 1.10 (t, 3H, *J* = 7.0 Hz), 1.95 (s, 3H), 2.31 (q, 2H, *J* = 7.0 Hz), 5.96 (s, 1H), 6.40–8.20 (m, 16H, aromatic). <sup>13</sup>C

NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 10.69, 20.54, 28.57, 37.21, 100.87, 118.49, 121.32, 123.47, 124.21, 125.89, 126.04, 126.20, 127.07, 127.44, 127.48 (double intensity), 128.07 (double intensity), 128.63, 128.84, 129.32, 129.40, 132.80, 135.75, 136.25, 141.56, 144.29, 159.97, 161.59, 162.41. MS (APCI<sup>+</sup>): *m/z* 460 (M + H)<sup>+</sup>.

### 3. Result and discussion

The expected benzo[5,6]chromeno[2,3-*d*]pyrimidin-11-one **5(a-e)** and benzo[7,8]chromeno[2,3-*d*]pyrimidin-8-one **6(a-f)** were obtained after three steps as shown in (Scheme 1), using both classical and microwave heating.

In the first step, the multi-component reaction of ethyl cyanoacetate, aromatic aldehyde and 2-naphthol or 1-naphthol under microwave irradiation led to synthesis of ethyl-3-amino-1-aryl-1*H*-benzo[*f*]chromene-2-carboxylate **1(a-e)** and ethyl-2-amino-4-aryl-4*H*-benzo[*h*]chromene-3-carboxylate **2(a-d)** with high yield (10 min, 150 W, 80 °C). In classical conditions need 24 h (Table 1).

**Table 1** Microwave-assisted synthesis of compounds **1(a–e)** and **2(a–d)**.

C.C			MW		
Compounds	Yield (%)	Time (h)	Yield (%)	Time (min)	M.p (°C)
<b>1a</b>	82	24	90	10	168–170
<b>1b</b>	72	24	75	10	194–196
<b>1c</b>	60	24	68	10	190–192
<b>1d</b>	60	24	73	10	188–190
<b>1e</b>	65	24	72	10	170–172
<b>2a</b>	66	24	88	10	160–162
<b>2b</b>	65	24	68	10	158–160
<b>2c</b>	62	24	79	10	162–164
<b>2d</b>	63	24	75	10	156–158

C.C: Classical condition. M.W: Microwave. M.p: Melting point.

**Table 2** Microwave-assisted synthesis of imidates **3(a–j)** and **4(a–f)**.

C.C				MW			
Products	Ar	Orthoester	Yield (%)	Time (h)	Yield (%)	Time (min)	M.p (°C)
<b>3a</b>	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	81	24	88	10	120–122
<b>3b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	90	24	90	10	118–120
<b>3c</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	75	24	83	10	142–144
<b>3d</b>	<i>o</i> -MeOC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	84	24	85	15	144–146
<b>3e</b>	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	40	24	65	15	120–122
<b>3f</b>	C <sub>6</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	89	24	92	10	176–178
<b>3g</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	30	24	80	10	110–112
<b>3h</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	75	24	84	10	164–166
<b>3i</b>	<i>o</i> -MeOC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	83	24	85	15	162–164
<b>3j</b>	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	80	24	85	15	178–180
<b>4a</b>	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	42	24	65	25	130–132
<b>4b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	47	24	68	30	132–134
<b>4c</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	50	24	65	30	128–130
<b>4d</b>	<i>m</i> -MeOC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub> -C(OEt) <sub>3</sub>	44	24	59	25	126–128
<b>4e</b>	C <sub>6</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	35	24	53	25	134–136
<b>4f</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	38	24	57	30	130–132
<b>4g</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	40	24	68	30	128–130
<b>4h</b>	<i>m</i> -MeOC <sub>6</sub> H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> -C(OEt) <sub>3</sub>	35	24	54	30	126–128

C.C: Classical condition. M.W: Microwave. M.p: Melting point.

**Table 3** Microwave-assisted synthesis of compounds **5(a–e)** and **6(a–f)**.

C.C				MW		
Products	Ar	Yield (%)	Time (h)	Yield (%)	Time (min)	M.p (°C)
<b>5a</b>	C <sub>6</sub> H <sub>5</sub>	20	24	43	15	266–238
<b>5b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	20	24	48	15	268–270
<b>5c</b>	C <sub>6</sub> H <sub>5</sub>	37	24	50	15	270–272
<b>5d</b>	<i>o</i> -MeOC <sub>6</sub> H <sub>4</sub>	20	24	38	15	266–268
<b>5e</b>	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	35	24	45	15	264–266
<b>6a</b>	C <sub>6</sub> H <sub>5</sub>	18	24	42	15	264–266
<b>6b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	23	24	51	15	262–264
<b>6c</b>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	27	24	54	15	264–266
<b>6d</b>	<i>m</i> -MeOC <sub>6</sub> H <sub>4</sub>	20	24	35	15	258–260
<b>6e</b>	C <sub>6</sub> H <sub>5</sub>	48	24	67	15	268–270
<b>6f</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	30	24	48	15	270–272

C.C: Classical condition. M.W: Microwave. M.p: Melting point.



In the next step, we wanted to study and apply the microwave irradiation in order to make the conversion of compounds **1(a-e)** and **2(a-d)** to imidates **3(a-j)** and **4(a-f)**. At first, we used classical conditions to synthesize compounds **3** and **4** in order to have some reference by TLC [solvent system: (ethyl acetate):(hexane) = 1:4]. The compounds **1(a-e)** or **2(a-d)** were refluxed with orthoesters (ethyl orthoacetate or ethyl orthopropionate) for 24 h to afford products **3(a-j)** and **4(a-f)**. After that, we transposed this reaction under microwave heating. As a result, we obtained imidates **3** and **4** with a decrease of a time reaction (from 24 h to just 10–30 min) and the yields were considerably increased (Table 2).

Finally, we transformed the imidate into pyrimidinone **5(a-e)** and **6(a-f)** via treatment of compounds **3** or **4** with phenylhydrazine at 105 °C for 24 h or via irradiation with microwave (10–15 min, 105 °C, 300 W) (Table 3). In this case, we obtained essentially a diminution of time reaction and a slight increase in yields.

#### 4. Conclusion

To conclude, thanks to microwave irradiation we have synthesized ethyl-3-amino-1-aryl-1*H*-benzo[*f*]chromene-2-carboxylate (**a-e**) and ethyl-2-amino-4-aryl-4*H*-benzo[*h*]chromene-3-carboxylate (**a-d**) in 10 min. And, we have successfully prepared imidates. Finally, conversion of compounds **3(a-j)** and **4(a-f)** into the corresponding chromeno[2,3-*d*] pyrimidinone derivatives **5(a-e)** and **6(a-f)** was also performed under microwave heating in a short time (15 min).

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