



**HAL**  
open science

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

Aida Chaker, Ennaji Najahi, Françoise Nepveu, Fakher Chanchoub

► **To cite this version:**

Aida Chaker, Ennaji Najahi, Françoise Nepveu, Fakher Chanchoub. Microwave-assisted synthesis of chromeno[2,3-d]pyrimidinone derivatives. *Arabian Journal of Chemistry*, 2017, 10 (Supp 2), pp.S3040-S3047. 10.1016/j.arabjc.2013.11.045 . hal-03149839

**HAL Id: hal-03149839**

**<https://ut3-toulouseinp.hal.science/hal-03149839>**

Submitted on 23 Feb 2021

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



## REVIEW

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



Aida Chaker <sup>a,b</sup>, Ennaji Najahi <sup>b</sup>, Françoise Nepveu <sup>b</sup>, Fakher Chabchoub <sup>a,\*</sup>

<sup>a</sup> Université de Sfax, Faculté des Sciences, Laboratoire de chimie appliquée, hétérocycles, corps gras et polymères, 3000 Sfax, Tunisia

<sup>b</sup> Université de Toulouse III, UPS, UMR 152 PHARMA-DEV, 118 Route de Narbonne, F-31062 Toulouse cedex 9, France

Received 14 March 2013; accepted 16 November 2013

Available online 28 November 2013

## KEYWORDS

Microwave irradiation;  
Chromeno[2,3-*d*]pyrimidinones;  
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.

© 2013 King Saud University. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

## Contents

|   |       |
|---|-------|
| 1. Introduction . . . . .   | S3041 |
| 2. Experimental. . . . .  | S3041 |
| 2.1. General procedure for synthesis of compounds <b>1(a–e)</b> and <b>2(a–d)</b> . . . . .                                 | S3042 |
| 2.1.1. Ethyl-3-amino-1-phenyl-1 <i>H</i> -benzo[ <i>f</i> ]chromene-2-carboxylate ( <b>1a</b> ) . . . . .                   | S3042 |
| 2.1.2. Ethyl-3-amino-1- <i>p</i> -methylphenyl-1 <i>H</i> -benzo[ <i>f</i> ]chromene-2-carboxylate ( <b>1b</b> ) . . . . .  | S3042 |
| 2.1.3. Ethyl-3-amino-1- <i>p</i> -methoxyphenyl-1 <i>H</i> -benzo[ <i>f</i> ]chromene-2-carboxylate ( <b>1c</b> ) . . . . . | S3042 |
| 2.1.4. Ethyl-3-amino-1- <i>o</i> -methoxyphenyl-1 <i>H</i> -benzo[ <i>f</i> ]chromene-2-carboxylate ( <b>1d</b> ) . . . . . | S3042 |
| 2.1.5. Ethyl-3-amino-1- <i>o</i> -chlorophenyl-1 <i>H</i> -benzo[ <i>f</i> ]chromene-2-carboxylate ( <b>1e</b> ) . . . . .  | S3042 |
| 2.1.6. Ethyl-2-amino-4-phenyl-4 <i>H</i> -benzo[ <i>h</i> ]chromene-3-carboxylate ( <b>2a</b> ) . . . . .                   | S3042 |
| 2.1.7. Ethyl-2-amino-4- <i>p</i> -methylphenyl-4 <i>H</i> -benzo[ <i>h</i> ]chromene-3-carboxylate ( <b>2b</b> ) . . . . .  | S3042 |
| 2.1.8. Ethyl-2-amino-4- <i>p</i> -methoxyphenyl-4 <i>H</i> -benzo[ <i>h</i> ]chromene-3-carboxylate ( <b>2c</b> ) . . . . . | S3042 |
| 2.1.9. Ethyl-2-amino-4- <i>m</i> -methoxyphenyl-4 <i>H</i> -benzo[ <i>h</i> ]chromene-3-carboxylate ( <b>2d</b> ) . . . . . | S3042 |

\* Corresponding author. Tel.: +216 23567881; fax: +216 74766606.

E-mail address: [fakher.chabchoub@yahoo.fr](mailto:fakher.chabchoub@yahoo.fr) (F. Chabchoub).

Peer review under responsibility of King Saud University.



Production and hosting by Elsevier

|         |  |       |
|---------|--|-------|
| 2.2.    | General procedure for synthesis of imidate <b>3(a-j)</b> and <b>4(a-f)</b> . . . . .   | S3042 |
| 2.2.1.  | Ethyl-3-[(ethoxyethylidene)amino]-1-phenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3a</b> ) . . . . .                                 | S3042 |
| 2.2.2.  | Ethyl-3-[(ethoxyethylidene)amino]-1-p-methylphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3b</b> ) . . . . .                         | S3042 |
| 2.2.3.  | Ethyl-3-[(ethoxyethylidene)amino]-1-p-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3c</b> ) . . . . .                        | S3042 |
| 2.2.4.  | Ethyl-3-[(ethoxyethylidene)amino]-1-o-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3d</b> ) . . . . .                        | S3042 |
| 2.2.5.  | Ethyl-3-[(ethoxyethylidene)amino]-1-o-chlorophenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3e</b> ) . . . . .                         | S3043 |
| 2.2.6.  | Ethyl-3-[(ethoxypropylidene)amino]-1-phenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3f</b> ) . . . . .                                | S3043 |
| 2.2.7.  | Ethyl-3-[(ethoxypropylidene)amino]-1-p-methylphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3g</b> ) . . . . .                        | S3043 |
| 2.2.8.  | Ethyl-3-[(ethoxypropylidene)amino]-1-p-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3h</b> ) . . . . .                       | S3043 |
| 2.2.9.  | Ethyl-3-[(ethoxypropylidene)amino]-1-o-methoxyphenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3i</b> ) . . . . .                       | S3043 |
| 2.2.10. | Ethyl-3-[(ethoxypropylidene)amino]-1-o-chlorophenyl-1H-benzo[f]chromene-2-carboxylate ( <b>3j</b> ) . . . . .                        | S3043 |
| 2.2.11. | Ethyl-2-[(ethoxyethylidene)amino]-4-phenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4a</b> ) . . . . .                                 | S3043 |
| 2.2.12. | Ethyl-2-[(ethoxyethylidene)amino]-4-p-methylphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4b</b> ) . . . . .                         | S3043 |
| 2.2.13. | Ethyl-2-[(ethoxyethylidene)amino]-4-p-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4c</b> ) . . . . .                        | S3043 |
| 2.2.14. | Ethyl-2-[(ethoxyethylidene)amino]-4-m-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4d</b> ) . . . . .                        | S3043 |
| 2.2.15. | Ethyl-2-[(ethoxypropylidene)amino]-4-phenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4e</b> ) . . . . .                                | S3043 |
| 2.2.16. | Ethyl-2-[(ethoxypropylidene)amino]-4-p-methylphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4f</b> ) . . . . .                        | S3043 |
| 2.2.17. | Ethyl-2-[(ethoxypropylidene)amino]-4-p-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4g</b> ) . . . . .                       | S3043 |
| 2.2.18. | Ethyl-2-[(ethoxypropylidene)amino]-4-m-methoxyphenyl-4H-benzo[h]chromene-3-carboxylate ( <b>4h</b> ) . . . . .                       | S3044 |
| 2.3.    | General Procedure for synthesis compounds <b>5(a-e)</b> and <b>6(a-f)</b> . . . . .  | S3044 |
| 2.3.1.  | 10-Anilino-9-methyl-12-phenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3- <i>d</i> ] pyrimidin-11-one ( <b>5a</b> ) . . . . .          | S3044 |
| 2.3.2.  | 10-Anilino-9-methyl-12-p-methylphenyl-10,12-dihydro-11H-benzo[5,6]chromeno [2,3- <i>d</i> ]pyrimidin-11-one ( <b>5b</b> ) . . . . .  | S3044 |
| 2.3.3.  | 10-Anilino-9-ethyl-12-phenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3- <i>d</i> ] pyrimidin-11-one ( <b>5c</b> ) . . . . .           | S3044 |
| 2.3.4.  | 10-Anilino-9-ethyl-12-o-methoxyphenyl-10,12-dihydro-11H-benzo[5,6]chromeno [2,3- <i>d</i> ] pyrimidin-11-one ( <b>5d</b> ) . . . . . | S3044 |
| 2.3.5.  | 10-Anilino-9-ethyl-12-o-chlorophenyl-10,12-dihydro-11H-benzo[5,6]chromeno[2,3- <i>d</i> ] pyrimidin-11-one ( <b>5e</b> ) . . . . .   | S3044 |
| 2.3.6.  | 9-Anilino-10-methyl-7-phenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ]pyrimidin-8-one ( <b>6a</b> ) . . . . .                | S3044 |
| 2.3.7.  | 9-Anilino-10-methyl-7-p-methylphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ] pyrimidin-8-one ( <b>6b</b> ) . . . . .       | S3044 |
| 2.3.8.  | 9-Anilino-10-methyl-7-p-methoxyphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ] pyrimidin-8-one ( <b>6c</b> ) . . . . .      | S3044 |
| 2.3.9.  | 9-Anilino-10-methyl-7-m-methoxyphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ] pyrimidin-8-one ( <b>6d</b> ) . . . . .      | S3044 |
| 2.3.10. | 9-Anilino-10-ethyl-7-phenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ]pyrimidin-8-one ( <b>6e</b> ) . . . . .                 | S3045 |
| 2.3.11. | 9-Anilino-10-ethyl-7-p-methylphenyl-7,9-dihydro-8H-benzo[7,8]chromeno[2,3- <i>d</i> ] pyrimidin-8-one ( <b>6f</b> ) . . . . .        | S3045 |
| 3.      | Result and discussion . . . . .  | S3045 |
| 4.      | Conclusion . . . . .   | S3047 |
|         | Acknowledgements . . . . .   | S3047 |
|         | References . . . . .   | S3047 |

## 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 naphthopyranopyrimidinones 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-naphthopyranopyrimidinones 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>): 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>): 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>): 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>): 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>): 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)*

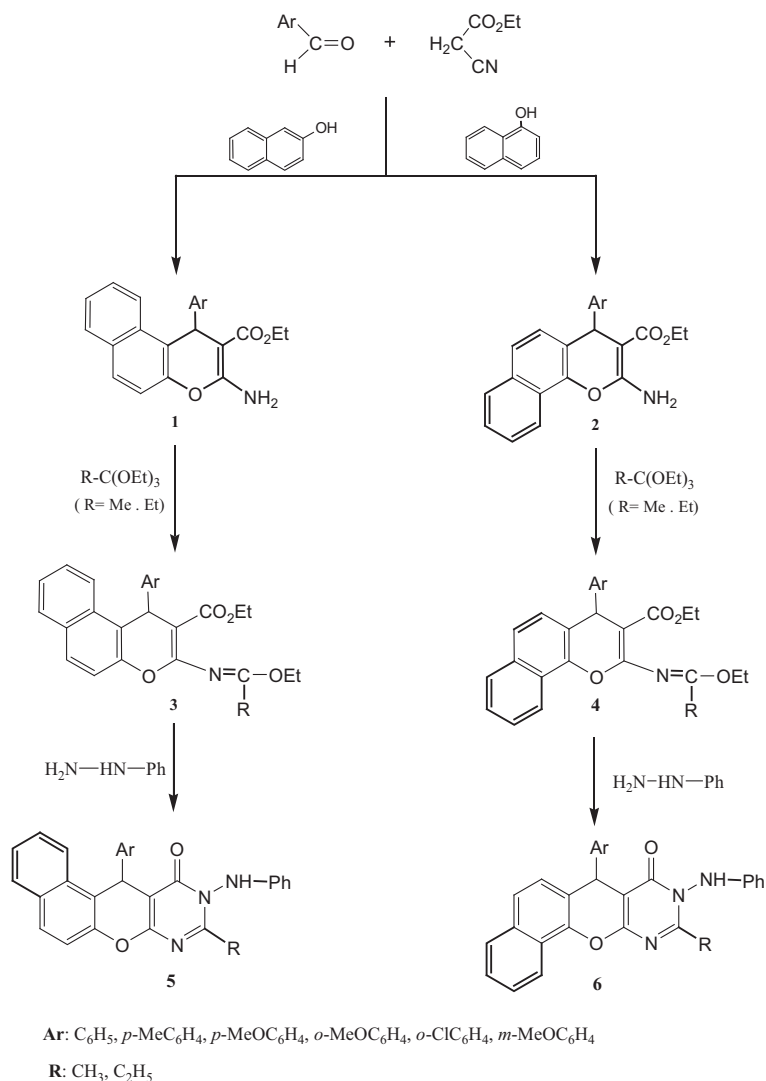
IR (cm<sup>-1</sup>):  $\nu_{\max}$  1679 (C=O), 3300 (NH); <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.22 (s, 3H), 2.34 (s, 3H), 5.89 (s, 1H), 6.71–8.12 (m, 16H, aromatic). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 14.37, 23.12, 35.10, 92.28, 111.93, 117.34, 117.80, 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).

#### Acknowledgements

The authors acknowledge the Ministry of Higher Education, Scientific Research and Technology in Tunisia for their financial support.

#### References

- Abdel-Ghani, A.E., Abdel-Aziz, F.M., Khadeir, M.N.M., El-Nagdi, M.H., 1993. Nitriles in heterocyclic synthesis: the reaction of polyhydric naphthalenes, 4-methylcoumarin-3-carbonitrile, and alkylidenemalononitrile with methylenemalononitrile. *Bull. Chem. Soc. Jpn.* 66, 464–468.
- Ahmed, H.B., Hussien, A.E., Nagwa, A.E.H., Kamal, A.R.A., Ahmed, M.E.A., 2001. Synthesis and antimicrobial activities of naphtho[2,1-*b*]pyrene, pyrano[2,3-*d*]pyrimidine, and pyrano[3,2-*e*][1,2,4]triazolo[2,3-*c*]pyrimidine derivatives. *Farmaco* 56, 965–973.
- Ahmed, H.B., Nagwa, A.E.H., Abd El-Latif, M.S., Fakery, A.H., Ahmed, M.E.A., 2000a. 4-Hydroxycoumarin in heterocyclic synthesis, part III: synthesis of some new pyrano[2,3-*d*]pyrimidine, 2-substitued[1,2,4]triazolo[1,5-*c*]pyrimidine, and pyrimido[1,6-*b*][1,2,4] triazine derivatives. *Farmaco* 55, 708–714.
- Ahmed, M.E.A., Fathy, A.E., Hussein, A.E., Hany, M.M., Ahmed, H.B., 2002. Synthesis of 9-methoxy and 9-acetoxy-3-amino-1-(4-methoxyphenyl)-1*H*-benzo[*f*]chromene-2-carbonitriles via 2-(imino-piperidin-1-yl-methyl)-3-(4-methoxyphenyl)acrylonitrile as intermediate. *Z. Naturforsch.* 57b, 579–585.
- Ahmed, M.E.A., Abd El-Latif, M.S., Fakery, A.H., Bedair, A.H., 2000b. Heteroaromatization with 4-hydroxycoumarin, part I:

- synthesis of some new pyranocoumarins and coumarinopyranopyrimidines. *J. Chem. Res. Synop.*, 26–27.
- Ahmed, M.E.A., El-Hakim, M.H., Abd El-Latif, M.S., Fakery, A.H., El-Sayed, E.M., El-Gharead, K.A., 2000c. Synthesis of pyrano[2,3-*d*]pyrimidine and pyrano[3,2-*e*][1,2,4] triazolo[2,3-*c*]pyrimidine derivatives with promising antibacterial activities. *Acta Pharm.* 50, 111–120.
- Ahmed, M.E.A., Emam, H.A., El-Hakim, M.H., Abd El-Latif, M.S., Fakery, A.H., 1997. Activated nitriles in heterocyclic synthesis: synthesis of pyrano[2,3-*d*]pyrimidine and pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives. *J. Chem. Res. Synop.*, 320–321.
- Ashraf, H.F., El-Wahab, Abd., 2002. Activated nitriles in heterocyclic synthesis: synthesis of new[1]benzopyrano[3',4':5,6]pyrano[2,3*d*]pyrimidine and [1] benzopyrano[3:5,6]pyrano [3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives with promising antibacterial activity. *Acta Pharm.* 52, 269–280.
- Bruno, O., Brullo, C., Schenone, S., Bondavalli, F., Ranise, A., Tognolini, M., Impicciatore, M., Ballabeni, V., Barocelli, E., 2006. Synthesis, antiplatelet, and antithrombotic activities of new 2-substitued benzopyrano[4,3-*d*]pyrimidin-4-cycloamines and 4-amino/cycloamino-benzopyrano[4,3-*d*]pyrimidin-5-ones. *Bioorg. Med. Chem.* 14, 121–130.
- Bruno, O., Brullo, C., Schenone, S., Bondavalli, F., Ranise, A., Tognolini, M., Ballabeni, V., Barocelli, E., 2004. Synthesis and pharmacological evaluation of 5*H*-[1]benzopyrano [4,3*d*]pyrimidines effective as antiplatelet = analgesic agents. *Bioorg. Med. Chem.* 12, 553–561.
- Bruno, O., Brullo, C., Schenone, S., Ranise, A., Bondavalli, F., Barocelli, E., Tognolini, M., Magnanini, F., Ballabeni, V., 2002. Progress in 5*H* [1]benzopyrano[4,3-*d*]pyrimidin-5-amine series: 2-methoxy derivatives effective as antiplatelet agents with analgesic activity. *Farmaco* 57, 753–758.
- Fakher, C., Mehdi, M., Hédi, B.M., Leila, C.G., Mansour, S., 2007. Synthesis and antigenotoxic activity of some naphtho[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives. *Eur. J. Med. Chem.* 42, 715–718.
- Fathy, A.E., Ashraf, H.F.A.E.W., Gameel, A.M.E.-H.A., Moustafa, M.K., 2004. Synthesis and antimicrobial evolution of naphtho [2,1-*b*]triazolo[1,5-*c*]pyrimidine derivatives. *Acta Pharm.* 54, 13–26.
- Mehdi, M., Fakher, C., Mansour, S., 2005. Action of primary amines and hydroxylamine on ethoxymethyleneaminonaphthopyranes: synthesis of new naphthopyrano[2,3-*d*]pyrimidines derivatives. *Heterocycl. Commun.* 9, 401–404.
- Mehdi, M., Fakher, C., Mansour, S., 2006. Synthèse et réactivité des pyranopyrimidines tosylés vis-à-vis du chlorure de thionyle: obtention des 1,2,3,5-thiatriazolopyrimidines. *Phosphorus Sulfur Silicon* 181, 1–6.
- Mehdi, M., Fakher, C., Rached, E., Mansour, S., 2008. Action du Disulfure de carbone et du phenylthioisocyanate sur des dérivés naphthopyraniques: obtention des naphthopyranopyrimidodithiones et des naphthopyranopyrimidodithiones. *Phosphorus Sulfur Silicon* 183, 1145–1151.
- Mostafa, M.K., Ashraf, H.F.A.E.-W., Fathy, A.E., Ahmed, M.E.-A., 2002. Synthesis of halogen derivatives of benzo[*h*]chromene and benzo[*a*]anthracene with promising antimicrobial activities. *II Farmaco.* 57, 715–722.
- Kamar, M., Fakher, C., Marco Contelles, J.C., Abdelouahid, S., Mansour, S., 2010. Convenient synthesis of 11-aryl-1,12-dihydro-1*h*-naphthopyrano[2,3-*d*] pyrimidin-12-ones. *Synthetic Commun.* 40, 3405–3414.
- Zaki, M.E.A., Fawzy, N.M., Swelam, S.A., 1999. Synthesis of fused azoles and *N*-heteroaryl derivatives based on pyrano[2,3-*c*]pyrazole. *Mol. Online* 3, 1–8.
- Zaki, K.H., Abd El-Hafez, A.A., Geiez, A.A., El-Dean, A.M.K., 1991. Nitriles in heterocyclic synthesis: reactions of pyrano[3,2-*h*]quinoline derivatives. *Bull. Chem. Soc. Jpn.* 64, 668–670.