Tetrahedron Letters 51 (2010) 5443–5447

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Generation of pyrrolo[2,3-*d*]pyrimidines. Unexpected products in the multicomponent reaction of 6-aminopyrimidines, dimedone, and arylglyoxal

Jairo Quiroga [a,*], Paola A. Acosta [a], Silvia Cruz [b], Rodrigo Abonía [a], Braulio Insuasty [a], Manuel Nogueras [c,*], Justo Cobo [c]

[a] Grupo de Investigación de Compuestos Heterocíclicos, Department of Chemistry, Universidad del Valle, A.A. 25360, Cali, Colombia
[b] Department of Chemistry, Universidad de Nariño, A.A. 1175, Pasto, Colombia
[c] Department of Inorganic and Organic Chemistry, Universidad de Jaén, 23071 Jaén, Spain

ARTICLE INFO

Article history:
Received 25 May 2010
Revised 2 August 2010
Accepted 6 August 2010
Available online 12 August 2010

Keywords:
Pyrrolopyrimidines
Multicomponent reaction
Aminopyrimidines
Arylglyoxal
Dimedone

ABSTRACT

A series of 6-aryl-5-(1-cyclohexen-1-yl)pyrrolo[2,3-*d*]pyrimidines **9a**–**q** were obtained by the three-component reaction between 6-aminopyrimidines **6**, **7**, **8**, dimedone **2**, and arylglyoxal **5a**,**b**. The unexpected cyclization process was established by NMR and X-ray diffraction measurements.

The pyrrolo[2,3-*d*]pyrimidine ring system is a common motif in several natural products and biologically active molecules.[1a] Recently there has been a great interest in the synthesis of pyrrolo[2,3-*d*]pyrimidines due to their proven biological activity and medicinal utility. A number of pyrrolopyrimidine derivatives structurally related to toyocamycin, sangivamycin, and the seco nucleosides of tubercidin have antiviral activity.[1]

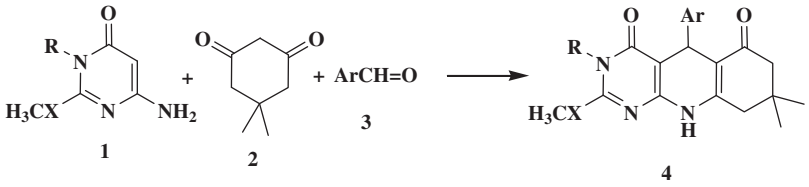
As the pyrrolo[2,3-*d*]pyrimidine heterosystem represents a 7-deazaanalogue of biogenic purine, it is an important class of compounds possessing notable biological activity.[2,3]

We recently reported a three component one-step reaction of 6-aminopyrimidin-4-ones **1** with dimedone **2** and benzaldehydes **3**, which yields pyrimido[4,5-*b*]quinolines[4] **4** via a simple, practical, and a very regioselective procedure (Scheme 1).

In the course of our research aimed at the preparation of bioactive nitrogen-containing heterocycles, we addressed the multicomponent synthesis of fused pyrido[2,3-*d*]pyrimidines.[5]

We report herein an extension of this three-component reaction with aminopyrimidines **1**, dimedone **2**, and arylglyoxales **5**, which yielded the formation of unexpected several pyrrolo[2,3-*d*]pyrimidine derivatives **9a**–**q** (Scheme 2, Table 1).

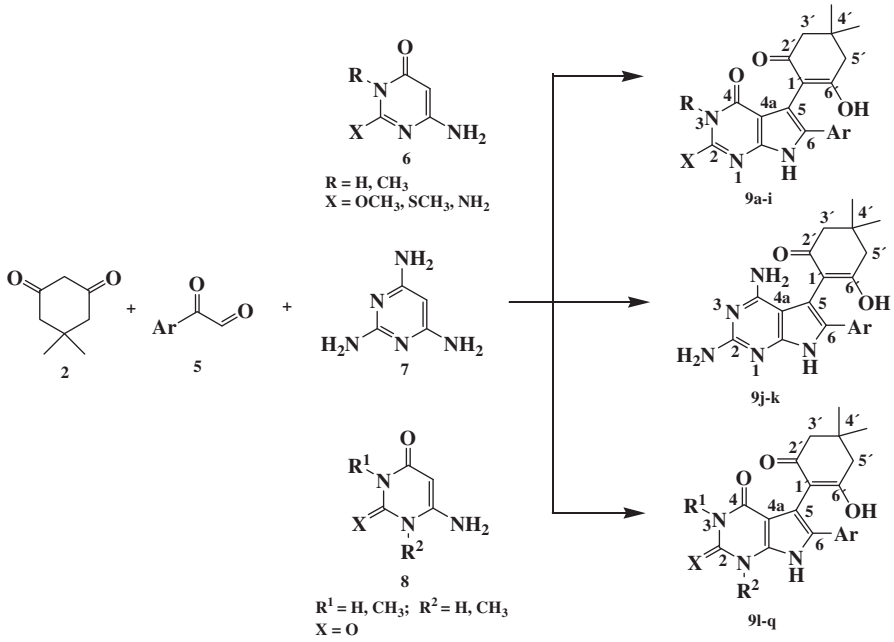
The structure of all new compounds was determined on the basis of their analytical techniques, 1D and 2D-NMR spectra, and MS, which agree with the proposed structures. Single crystal X-ray dif-



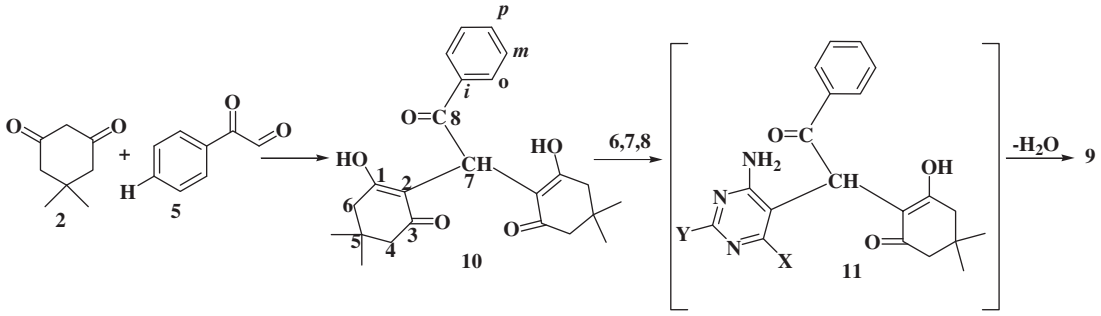
Scheme 1.

* Corresponding authors. Fax: +57 2 33392440 (J.Q.); fax: +34 618907111 (M.N.).
E-mail addresses: jaiquir@univalle.edu.co (J. Quiroga), mmontiel@ujaen.es (M. Nogueras).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.08.021



Scheme 2.

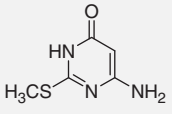
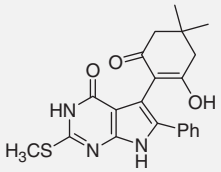
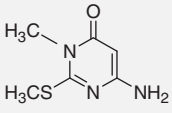
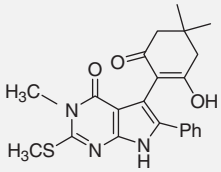


Scheme 3.

fraction analysis of compounds **9b**[6] was used to corroborate the postulated structures.[7]

A possible mechanism route for the described three-component reaction is outlined in Scheme 3. We consider that initially the dimedone reacts with the arylglyoxal to give the intermediate **10**. The last one reacts with the 6-aminopyrimidine leading to the formation of intermediate **11**, which suffers the cyclation with loss of a water molecule, to form final pyrrolopyrimidine **9**. As an evidence of this is the fact that the reaction of dimedone with phenylglyoxal led to the formation of product **10**, which was isolated and character-

Table 1
Pyrrolo[2,3-*d*]pyrimidine derivatives

Entry	Pyrimidine	Product	Mp (°C)	%	*m/z*
9a			280–282	50	395
9b			294–295	60	410