Tetrahedron Letters 54 (2013) 1486–1488

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

Unexpected formation of pyrrolo[1,2-*a*]quinoxaline derivatives during the multicomponent synthesis of pyrrolo[1,2-*a*]benzimidazoles

Alina Nicolescu [a,b], Calin Deleanu [a,b,*], Emilian Georgescu [c], Florentina Georgescu [c], Ana-Maria Iurascu [b], Sergiu Shova [b,d], Petru Filip [a]

[a] *'C. D. Nenițescu' Centre of Organic Chemistry of the Roumanian Academy, Spl. Independenței 202-B, RO-060023 Bucharest, Romania*
[b] *'Petru Poni' Institute of Macromolecular Chemistry of the Roumanian Academy, Aleea Grigore Ghica Vodă 41-A, RO-700487 Iasi, Romania*
[c] *Research Center Oltchim, 1 Uzinei St., RO-240050 Râmnicu Vâlcea, Romania*
[d] *Institute of Chemistry, Academy of Sciences of the Republic of Moldova, Str. Academiei 3, MD-2028 Chişinău, Moldavia*

ARTICLE INFO

Article history:
Received 23 September 2012
Revised 26 December 2012
Accepted 10 January 2013
Available online 16 January 2013

Keywords:
Pyrrolo[1,2-*a*]quinoxalines
Pyrrolo[1,2-*a*]benzimidazoles
Synthesis
^{1}H, ^{13}C and ^{15}N NMR
Single crystal X-ray

ABSTRACT

New pyrrolo[1,2-*a*]benzimidazole and pyrrolo[1,2-*a*]quinoxaline derivatives are obtained via one-pot, three-component reactions from 1-benzylbenzimidazoles, α-bromocarbonyl compounds, and non-symmetrical activated acetylenic dipolarophiles in propylene oxide as both the reaction medium and acid scavenger, at room temperature. When the same reaction is performed in 1,2-epoxybutane at reflux temperature only the pyrrolo[1,2-*a*]benzimidazole derivative is obtained.

The increasing number of pyrrolo[1,2-*a*]benzimidazole derivatives having applications in biology and pharmacology,[1–5] justifies interest in the development of efficient synthetic methods for these compounds.

Several synthetic routes have been reported for the synthesis of pyrrolo[1,2-*a*]benzimidazole derivatives.[6–9] One of the most important methods involves the 1,3-dipolar cycloaddition reaction of benzimidazolium ylides with electron-deficient alkynes or alkenes.[10–16] The classical multistep approach for the synthesis of pyrrolo[1,2-*a*]benzimidazoles, affording yields of up to 15%,[10,11] starts with the preparation of benzimidazolium salts followed by their in situ conversion into benzimidazolium-*N*-ylides in the presence of a base and the dipolarophile. Improved yields have been reported when oxidant promoters such as CrO_3 were used together with an organic base such as triethylamine.[13]

Our group has developed a one-pot synthetic strategy based on a consecutive quaternization, in situ generation of a heterocyclic *N*-ylide, 1,3-dipolar cycloaddition, and aromatization sequence.[17–21] This is a three-component procedure starting with almost equimolar amounts of an N-heterocyclic compound, an α-bromocarbonyl derivative, and an electron deficient alkyne in the presence of an epoxide, which plays the role of both the reaction medium and acid scavenger. This proved to be a regiospecific, wide-in-scope synthesis, requiring simple reaction conditions and allowing final product separation through crystallization.

In the case of 1-benzylbenzimidazole, using 1,2-epoxybutane at reflux temperature, we obtained better yields of pyrrolo[1,2-*a*]benzimidazole derivatives. Thus, starting from 1-benzylbenzimidazole (**1**), phenacyl bromides **2a,b,** and electron deficient alkynes **3a,b** in 1,2-epoxybutane, we obtained pyrrolo[1,2-*a*]benzimidazole derivatives **5a,b** in 68%, and 73% yields, respectively (Scheme 1). The reaction was performed by mixing the components at reflux temperature for 24 h, followed by solvent evaporation and subsequent crystallization.

The reaction mechanism implies the formation of an intermediate benzimidazolium salt from 1-benzylbenzimidazole (**1**) and the phenacyl bromide **2**, followed by the generation of a benzimidazolium-*N*-ylide by the action of 1,2-epoxybutane, and finally a 1,3-dipolar cycloaddition reaction of the intermediate benzimidazolium-*N*-ylide with the activated alkyne **3** to give the corresponding dihydropyrrolo[1,2-*a*]benzimidazole **4** as the primary cycloadduct. Finally, the pyrrolo[1,2-*a*]benzimidazole derivative **5** is obtained by spontaneous aromatization of the primary cycloadduct **4**.

Surprisingly, if the same reactions were carried out in propylene oxide or 1,2-epoxybutane at room temperature for 60 h, almost

* Corresponding author. Tel.: +40 74 434 0456; fax: +40 21 312 1601.
E-mail address: calin.deleanu@yahoo.com (C. Deleanu).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.01.036