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

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## 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,  $\alpha$ -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.

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The increasing number of pyrrolo[1,2-*a*]benzimidazole derivatives having applications in biology and pharmacology,<sup>1–5</sup> 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.<sup>6–9</sup> One of the most important methods involves the 1,3-dipolar cycloaddition reaction of benzimidazolium ylides with electron-deficient alkynes or alkenes.<sup>10–16</sup> The classical multistep approach for the synthesis of pyrrolo[1,2-*a*]benzimidazoles, affording yields of up to 15%,<sup>10,11</sup> 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<sub>3</sub> were used together with an organic base such as triethylamine.<sup>13</sup>

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.<sup>17–21</sup> This is a three-component procedure starting with almost equimolar amounts of an *N*-heterocyclic compound, an  $\alpha$ -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

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