A Facile Four-component Synthesis Of Pyrazolophthalazines Using Tetrabutylammonium Bromide As Efficient Ionic Liquid Catalyst

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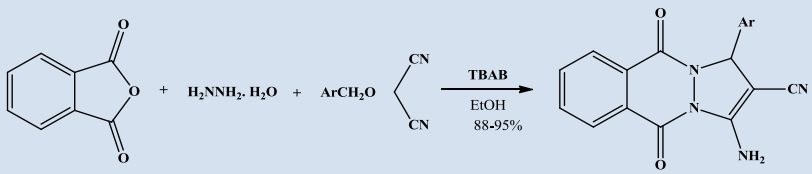
Abstract

An efficient method for the synthesis of pyrazolophthalazine derivatives was developed by using tetrabutylammonium bromide (TBAB) as ionic liquid catalyst in excellent yields (88-95%).

Introduction: Most of the significant advances against disease have been made by designing and testing new structures, which are often heteroaromatic derivatives. In addition, over 80% of the top small molecule drugs by U.S. retail sales in 2010 contain at least one heterocyclic fragment in their structure. Therefore, researchers are on a continuous pursuit to design and produce better pharmaceuticals, pesticides, insecticides, rodenticides, and weed killers by following natural models. A significant part of such biologically active compounds is composed of heterocycles [1]. Moreover, phthalazine derivatives possess a versatile pharmacological properties including anticonvulsant, vasorelaxant, and cardiotonic activities.

Methods and Results: We report here an efficient method for the synthesis of pyrazolophthalazine derivatives by a four-component reaction of equimolar amounts of phthalic anhydride, hydrazine hydrate, arylaldehydes and malononitrile in the presence of 20 mol tetrabutylammonium bromide (TBAB) ionic liquid as catalyst, in excellent yields.



Conclusions:

The protocol described here produced the desired pyrazolophthalazines in excellent yields (88-95%) and lower reaction times. The catalyst was reused at least 5 times without appreciable reduction in catalytic activities.

Keywords: Phthalazine, Pyrazolophthalazine, TBAB, Malononitrile.

[1] (a) Balaban, A. T.; Oniciu, D. C.; Katritzky, A. R. *Chem. Rev.* **2004**, *104*, 2777.(b) Global Pharmaceutical Research and Development, Neuroscience Research, Abbott Laboratories, 100 Abbott Park Road, Abbott Park,Illinois 60064.