Accepted Manuscript

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PII: S0040-4039(13)01229-X
DOI: http://dx.doi.org/10.1016/j.tetlet.2013.07.080
Reference: TETL 43278

To appear in: *Tetrahedron Letters*

Received Date: 19 May 2013
Revised Date: 29 June 2013
Accepted Date: 12 July 2013

Please cite this article as: Bahrami, K., Khodaei, M.M., Naali, F., Yousefi, B.H., Synthesis of polysubstituted pyridines *via* reactions of chalcones and malononitrile in alcohols using Amberlite IRA-400 (OH^-), *Tetrahedron Letters* (2013), doi: http://dx.doi.org/10.1016/j.tetlet.2013.07.080

Synthesis of polysubstituted pyridines *via* reactions of chalcones and malononitrile in alcohols using Amberlite IRA-400 (OH^-)

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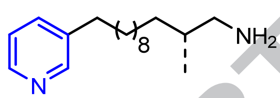
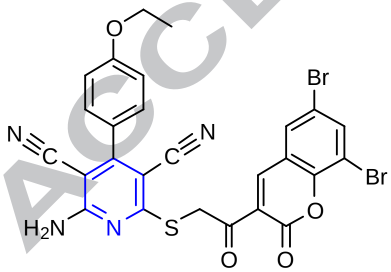
Abstract— Polysubstituted pyridine derivatives were synthesized through economical one-pot multicomponent reactions of different α,β-unsaturated ketones, malononitrile and ethanol or methanol in the presence of Amberlite IRA-400 (OH^-) at room temperature. The catalyst is recyclable several times without substantial loss of activity. Other valuable features include the wide range of functional group tolerance, easy and clean synthesis with a simple work-up procedure, and excellent yields under mild conditions.

An increasing number of studies have reported on the environmentally friendly production of fine chemicals using recyclable solid base catalysts *via* multi-component reactions (MCRs). MCRs are considered to be superior synthetic strategies,[1] and are highly efficient and atom economic. Compared to conventional organic reactions, MCRs represents environmentally friendly processes by reducing the number of steps, energy consumption, and waste production.[2]



Niphatesine C (antimicrobial)[4]



A potent inhibitor of HIV-1 integrase[8d]

Figure 1. Examples of pyridine frameworks as drug candidates.

The pyridine framework is found in natural products, pharmaceuticals, and functional materials[3-5] (Figure 1). It is also of widespread interest in coordination and supramolecular chemistry, as well as in materials science.[6] As a result, endeavors to develop new routes to pyridines have occupied the synthetic community for several decades, and constitute an active area of research.[7] Among them, the direct condensation of carbonyl compounds with a source of ammonia is well documented,[8] but suffers from limitations in the substrates,[9] or involves an oxidative agent.[10] Thus, the development of efficient synthetic pathways toward these compounds remains both an industrial and an academic challenge.[11]

Chemical synthesis is greatly facilitated by catalysis and further by catalyst recovery and recycling. Catalyst reuse increases the overall productivity and cost effectiveness of chemical transformations while minimizing their environmental impact, ultimately contributing considerably to the sustainability of chemical processes. In this regard, ion-exchange resins have certain inherent advantages over conventional acid and base catalysts. Their insolubility renders them environmentally compatible since the cycle of loading/regeneration/reloading allows them to be used for many years. At the end of the reaction, the resin can be separated quantitatively by filtration and recycled.

Ion-exchange resins are used in a variety of specialized applications such as chemical processing, pharmaceuticals, mining, food, and beverage processing.[12] Organic reactions in the presence of ion-exchange resins is a growing field of research as the demand for clean and eco-friendly chemical processes is increasing. Their applicability as catalysts has been recognized in numerous publications.[12b,c, 13-19]