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Reddi Mohan Naidu Kalla, Mi Ri Kim, Il Kim

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Dibutylamine-catalyzed efficient one-pot synthesis of biologically potent pyrans

Reddi Mohan Naidu Kalla, Mi Ri Kim, Il Kim *

BK21 PLUS Center for Advanced Chemical Technology, Department of Polymer Science and Engineering, Pusan National University, Busan 609-735, Republic of Korea
Fax: +82-51-5137720; Tel.: +82-51-5102466; E-mail: ilkim@pusan.ac.kr

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ABSTRACT

An expedient, eco-friendly, and efficient procedure for the preparation of novel pyran derivatives have been developed through a solvent-free, one-pot reaction of various aldehydes, malononitrile, and either methylacetoacetate or ethyl benzoylacetate in the presence of dibutylamine (2.5 mol%) at room temperature. This procedure is advantageous because it is mild, environmentally friendly, gives high yields, and requires short reaction times. Furthermore, the product did not necessitate separation via extraction and column chromatography.

1. Introduction

Sustainable chemistry emphasizes the development of operationally simple and eco-friendly routes to the synthesis of biologically potent organic and medicinal compounds, which are the most significant objective compounds in synthetic chemistry. Conducting reactions in the absence of a solvent (i.e., neat conditions) is an important aspect of green chemistry;[1,2] furthermore, the completion of various transformations via a single process is highly compatible with the goals of green chemistry. A one-pot reaction in which three or more reactants combine to form a new compound without isolation of any intermediate is known as a multi-component reaction (MCR)[3] and is highly attractive because of their ability to generate two or more C–C, C–N, or C–O bonds in a single step.

Organocatalysis is presently one of the fastest growing fields of research in organic chemistry.[4] Even though chemical transformations that use organic catalysts, or organocatalysts, are currently standard and have been over the last century, the application of small natural molecules as organocatalysts in MCRs for diversity-oriented syntheses (DOSs) offers many advantages; e.g., they do not require moisture-sensitive Lewis acids, air-sensitive reagents, toxic metals, nor an inert atmosphere.

Synthetic heterocyclic compounds are most important in the fields of organic and medicinal chemistry because these compounds have a broad range of pharmacological applications. Pyrans are an important class of oxygen heterocycles that have various biological properties such as anti-leishmanial,[5] anti-HIV,[6] antioxidant,[7] anti-tumor,[8] and central nervous system (CNS) activities and effects;[9] they are also used for treatment of Alzheimer's disease[10] and schizophrenia.[11] Furthermore, some pyran derivatives have also been used for the preparation of laser dyes,[12]cosmetics and pigments,[13] agrochemicals,[14] nonlinear optical (NLO) properties,[15] photo chromic materials,[16] and photovoltaic application.[17,18] In addition, they also serve as intermediates for the synthesis of organic compounds, including lactones, imidoesters,[19] polyazanaphthalenes,[20] pyridin-2-ones,[21] pyrano[2]-pyrimidines,[22] and pyranopyridinederivatives.[23] The generation of pyrans are of significant interest given their wide range of applications. A variety of catalytic methods have been reported for the synthesis of pyrans; these include heterogeneous catalysis,[24–26] ionic liquids,[27] and base-promoted reactions under microwave irradiation[20] and thermal heating[28]. Chemical reactions under microwave irradiation at high temperatures in the presence of acids or metal catalysts are favourable for side reactions such as Knoevenagel condensation (KC) that form byproducts. Hence, the development of similar milder and environmentally sustainable procedures for the preparation of pyrans is needed.

Currently, reactions conducted under neat conditions were used for the synthesis of various chemicals. Furthermore, the cost effectiveness and reaction rates of various organic transformations are also being improved. The most significant goals of sustainable chemistry are to reduce the use of organic solvents, toxic reagents, and laborious work-up procedures associated with the synthesis of compounds. An extensive survey of the literature revealed that there are, to the best of our knowledge, no reports on the synthesis of pyrans promoted by a dibutylamineorganocatalyst. This is a continuation of our ongoing research interest in the growth of efficient, inexpensive, and new methodologies.[29–34] Herein, we report the eco-friendly one-pot synthesis of pyrans through a three-component condensation of aldehyde, malononitrile (MN), and methylacetoacetate (MAA) or ethyl benzoylacetate (EBA) in