An Essay on:

Evaluation of the Synthesis, Reactions and Biological Activities of Quinolines

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Introduction

For many years, the synthesis of quinoline and its derivatives has been of considerable interest in organic and medicinal chemistry since a large number of natural products and drugs contain this heterocyclic nucleus. While versatile methods for the synthesis of the quinoline ring system have been developed, many of them suffer from harsh reaction conditions, poor yields, and (or) the use of expensive catalysts. Thus, simple, general, and efficient procedures for the synthesis of this important heterocycle are still in demand.

As one of the most frequently used pathways to prepare quinoline derivatives, Friedlander synthesis involves a condensation of 2-aminobenzaldehyde with an aldehyde, ketone, or polyfunctional carbonyl compound having a reactive α-methylene group. This classical process is usually carried out either by refluxing an aqueous or alcoholic solution of the reactants in the presence of a base or by heating a mixture of substrates at temperatures ranging from 150 to 220 °C in the absence of solvent and catalyst to produce the corresponding 2- and 3-substituted quinolines in moderate yields. Unfortunately, attempts to extend this method to the preparation of 4-substituted quinolines from 2-aminoaryl ketones appear to have met with very limited success. Subsequent studies showed that problems resulting from the classical Friedlander procedure can be overcome by using acid catalysis. For example, it has been reported that drops of concentrated sulfuric acid or 6 mol/L hydrochloric acid can be used as efficient catalysts in the Friedlander condensation procedure.
With this method, various structurally varied substrates, including 2 aminobenzophenone, can give the corresponding quinolines in moderate to high yields. However, this method still has some drawbacks, notably use of very strong acids as the catalyst, use of excessive glacial acetic acid as the solvent, or even requiring the use of a metal bath that can maintain a reaction temperature as high as 200 °C, thus making this method unsuitable for scale up in an environmentally benign and economical way.

Room temperature ionic liquids based on the 1,3-dialkylimidazolium cation are attracting increasing interest as alternative reaction media. The desirable advantages of ionic liquids, include their lack of vapor pressure, wide liquid range, and thermal stability, have made them exceptional reaction media as well as environmentally benign solvents in organic synthesis. In line with our research program of using ionic liquids as novel reaction media in organic reactions.