Review Article

Chemical Review and Letters
journal homepage: www.chemrevlett.com
ISSN (online): 2645-4947 (print) 2676-7279

Synthesis and crystallization procedure of piperidin-4-one and its derivatives: An update

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ARTICLE INFO

Article history:
Received 23 March 2021
Received in revised form 6 June 2021
Accepted 17 June 2021
Available online 30 October 2021

Keywords:
Piperidin-4-ones
2,6-disubstituted piperidin-4-ones
Recrystallization
Chair conformation
Boat conformation

ABSTRACT

Piperidine is a heterocyclic chemical molecule that is forming by hydrogenating pyridine. In natural and pharmaceutically active drugs, the piperidine ring is an essential molecular component. Several crystal structures of piperidine-4-ones and their derivatives are reported for their medicinal value. While several methods of piperidin-4-one crystallization have been developed to obtain a crystal structure, novel approaches are still needed. A review of the synthesis and crystallization procedure of piperidin-4-ones and its derivatives is outlined in this review paper.

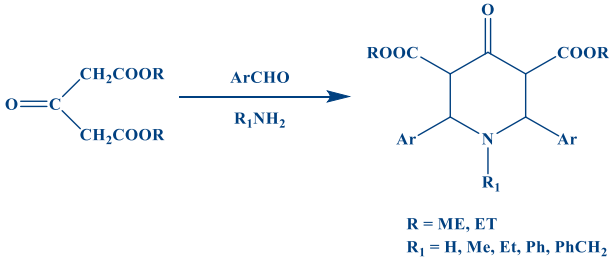
1. Introduction

Over the last decade, clinical and preclinical studies have mentioned thousands of piperidine compounds. Considerable attention has also been drawn to the importance of analgesic and anti-inflammatory activities containing compounds and the synthesis of piperidine-4-one derivatives [1]. There are many biological activities of piperidine derivatives, such as analgesic, antihypertensive, antiviral central nervous system depressant, antibacterial, antifungal, etc. [2-6]. Watson et al. reported that there were thousands of piperidine compounds mentioned in clinical and preclinical studies over the last 10 years [7].

There are vital biological profiles of nitrogen-containing heterocycles. For example, the sub-structure of piperidine is ubiquitous. Structural features of many alkaloids, natural products, and candidates for drugs [8]. Crystallization is a method used for the purification of solid compounds by chemists. It is one of the fundamental processes that must be mastered by and chemist to become competent in the laboratory. Impurities are removed from the growing crystals and filtration will isolate the pure solid crystals from the dissolved impurities. While several piperidine-4-ones and its derivatives crystallization techniques have been developed to obtain a crystal structure.

2. Synthesis of piperidine-4-ones by Mannich condensation

The Mannich condensation reaction between substituted aromatic aldehydes, ethyl methyl ketone, and ammonium acetate in ethanol medium ware synthesized as substituted 4-piperidones. Mannich first recognized the formation of β-amino carbonyl compounds (Mannich bases) from the reaction of an active methylene compound with formaldehyde and amine [9]. Baliah et al [10-15] developed an elegant 2, 6-diphenylpiperidine-4-ones synthesis method based on the earlier work of Petrenko-Kritschenko et al. [16-19]. The previous reaction involved the condensation of an acetone dicarboxylic acid ester with an aromatic aldehyde and ammonia or a primary amine, resulting in the formation of 2,6-diaryl-4oxopiperidine-3,5-dicarboxylate or its N-substituted derivatives as shows in scheme 1.



Scheme 1: Synthesis of piperidine-4-ones by Mannich condensation

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