A Brief Review: Microwave Assisted Ethers Synthesis

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Abstract

Ethers play a key role in the synthesis of pharmaceutical, biological, industrial, and natural products. This review paper describes the survey of literature regarding the number of microwave techniques for the synthesis of ethers in the recent times.

Keywords: Ethers; Pharmaceutical; Microwave synthesis

Introduction

Carbon-oxygen bond formation is a valuable reaction in organic synthesis and has generated considerable interest in recent years. Ethers are significant solvents and synthetic important supplements for the production of fragrances, cosmetics, pharmaceuticals, and dyestuffs [1,2]. The Williamson reaction is the best technique for the synthesis of symmetrical and unsymmetrical ethers. The Williamson reaction generally involves the employment of an alkali-metal salt of the hydroxyl compound and an alkyl halide. These reactions are generally carried out using organic solvents or with phase-transfer catalysts in the presence of a base followed by refluxing for times long [3-6]. Ether formation can also be accomplished using green solvents, ionic liquids, Mitsunobu reaction, coupling processes, ultrasonic reactions and solvent-free conditions [7-11].

Over the last decades, green Chemistry has become a research field of great interest. The enhancing requirement to minimize pollution and its influences, and the consequent risk for the human health and the environment, has brought towards a novel and safer procedure to chemical processes and compounds, defined in the principles of Green Chemistry. For this purpose, microwave technology, one of synthetic green techniques, has been successfully applied in organic chemistry.

The start of the fast growth of microwave assisted protocols in organic synthesis was ignited in 1986 by pioneering papers by Gedye et al. [12]. The uptake of microwave chemistry as a general means in synthesis laboratories has been gradual and steady since the introduction of chemical microwave systems [13]. The microwave offer easy, clean, speed, convenient, and economic techniques for the synthesis of a large number of organic compounds [14]. Microwave synthesis is obtaining importance as an instrument for the synthesis of a wide range of valuable and important compounds [15]. Now, in this paper, we wish to investigate microwave techniques for the synthesis of ethers derivatives and we will study results and benefits of these techniques.
The synthesis of ethers using microwave techniques

Alkylation alcohols are the most common strategy for synthesis of alkyl aryl ethers. For example, Wang et al. [16] used microwave irradiation in the presence of sodium hydroxide for the conversion of alcohols to alkyl aryl ethers. The reactions were carried out in less than 5 min at room temperature (SCHEME 1). Products were isolated in excellent yields (78% to 100%).

![Scheme 1](image)

**SCHEME 1. Conversion of alcohols to alkyl aryl ethers.**

In the year of 1998, a mild and rapid strategy was reported for the synthesis of various ether derivatives [17]. The mixture of potassium carbonate and potassium hydroxide in the presence of tetra-n-butyl ammonium bromide was introduced as an efficient and valuable system to synthesize symmetrical and unsymmetrical ethers in high yields. The reactions were accomplished under microwave irradiation (SCHEME 2). The variety of products, short reaction times (45-100 second) and use of mild conditions were the most important indices of this methodology.

![Scheme 2](image)

**SCHEME 2. The mixture of potassium carbonate and potassium hydroxide in the presence of tetra-n-butyl ammonium bromide.**

In 2000, Mitra et al. [18] reported a rapid and high-yielding methodology for O-methylation of a library of phenols under microwave irradiation. Dimethyl sulfate was used as methylating reagent. The reactions were carried out in the presence of potassium carbonate in acetone as solvent (SCHEME 3). The products were achieved in good to excellent yields.
The reactions were carried out in the presence of potassium carbonate in acetone as solvent. The coupling of alcohols with aryl halides is a general and useful route for the synthesis of diaryl ethers. In this regard, Li et al. [19] exploited microwave irradiation in the presence of potassium carbonate and dimethyl sulfoxide for the transformation of alcohols to various diaryl ethers.

**SCHEME 4.** Microwave irradiation in the presence of potassium carbonate and dimethyl sulfoxide for the transformation of alcohols to various diaryl ethers.

O-Alkylation was explored and accomplished by carrying out the reaction between aliphatic or aromatic alcohols and alkyl halides using CsF-Celite under microwave irradiation [20]. CsF-Celite was acted both efficient catalyst and reaction medium. It is noteworthy that alkyl aryl sulfides were obtained in very excellent yields and appropriate times (2 min to 7 min).

**SCHEME 5.** Reaction between aliphatic or aromatic alcohols and alkyl halides using CsF-Celite under microwave irradiation.

1,10-phenanthroline in the presence of cesium carbonate was designed as good and convenient system for the coupling aliphatic alcohols with aryl iodide [21]. Alkyl aryl ether derivatives were prepared using in high yields under microwave reaction conditions. To increase the efficiency of system, copper (I) iodide was added as catalyst into the reaction medium.

**SCHEME 6.**
SCHEME 6. 1,10-phenanthroline in the presence of cesium carbonate for the coupling aliphatic alcohols with aryl iodide.

To synthesis of diaryl ethers, in the year of 2010, Benaskar et al. [22] surprisingly discovered that the coupling phenols with hetero-aryl halides could also be accomplished using copper source and cesium carbonate under microwave condition. Dimethylacetamide was used as solvent to carry out reactions SCHEME 7. The high yield of products, simple isolation and mild reaction conditions demonstrated high efficiency of this methodology for the synthesis of diaryl ethers.

SCHEME 7. Coupling phenols with hetero-aryl halides using copper source and cesium carbonate under microwave condition.

Conclusion

This short review focuses on the application of microwave technology in synthesis of ethers. Microwave is an efficient strategy toward the aim of green chemistry, and is recommended to use in organic transformations. Rapid reactions, high purity of products, less side-products, excellent yields, high reactivity, wider usable range of temperature, higher energy efficiency, sophisticated measurement, safety technology and modular systems enable changing from mg to kg scale are the best important advantages of this technology (use of microwave techniques in organic synthesis). In result, we foresee the development of major applications of microwave techniques for synthesis of organic compounds.

REFERENCES