

Overview

Recent Developments in Catalytic Reductive Etherifications

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Abstract

Ether derivatives are versatile organic compounds and have been applied in various fields of academia and the chemical industry. Therefore, it is highly desirable to create procedures for their manufacture that are more efficient and sustainable. Catalytic reductive etherification with carbonyl moieties such as ketones/ aldehydes and carboxylic acid derivatives has recently been recognized as a possible tool among the several techniques reported for ether production. These procedures offer promising methods to selectively produce ethers with higher molecular structures, both symmetrical and asymmetrical. This Review provides an update on current developments in the field of catalytic reductive etherification, which synthesizes ethers utilizing alcohol and an aldehyde substrate. Applications for organic synthesis and catalyst design are given special attention.

Keywords: Etherification; Catalysis; Carbonyl compounds; Polyether; Redox reactions

1.0 Introduction

Ether synthesis is a frequent transition in both industrial and academic reactions due to an important class of organic compounds [1-5]. It is present as a functional group in a variety of organic compounds, such as simple cyclic and acyclic alkyl ethers, and cyclic alkyl ethers based on the 1,2-ethanediol unit that is employed as organic solvents. For example, ether functionality can be found in many bioactive components, flavorings, solvents, natural or organic products, and polymers, demonstrating the functional group's enormous relevance in a wide range of contexts. Furthermore, the application of biomass-derived ethers as surfactants, lubricants, and fuel additives has recently attracted a lot of attention. Therefore, it is highly desirable to create procedures for their manufacture that are more efficient and sustainable. Ethers and their

derivatives are extensively employed in liquid fuels (oxygenated fuel additives), pharmaceutical industries such as medicines, surfactants (non-ionic surfactants), and polymers [3, 6-9].

Reductive etherification is a method for producing ethers from alcohol, and carbonyl compounds (e.g., aldehydes and ketone) in a single step. Due to the high accessibility, low cost, simple handling, under a hydrogen atmosphere, and wide structural diversity of aldehydes and ketones, this technique offers a priceless synthetic substitute for the straightforward production of a large range of complicated ethers, both symmetrical and asymmetrical and also it has been discovered that this process is particularly selective for etherification of some frequently encountered carbonyl components including octanal, cyclohexanone, benzaldehyde, and others [7].

Reductive etherification and direct etherification are the two types of etherification [3,10]. The direct etherification procedure includes intermolecular dehydration that is acid-catalyzed after the C=O bonding is saturated to C-OH, for intermolecular dehydration to effectively convert the alcohols, It is necessary to use Lewis acids or Bronsted acids. Aldehydes are acetalized during the reductive-etherification process as an intermediate step, and the final ethers are created by hydrogenation of the (partial) acetal through hydrogenolysis and dehydration, due to a lack of acid sites, the side-product production of alcohol reduced the ether yield [10,11]. The reductive etherification reaction is a simple way to generate either symmetric or asymmetric ether by the coupling reaction with aldehyde ketone with uses a lewis acid, Brönsted acid, and metal catalyst of various types and also can be conveniently performed using a catalyst [4,12] The parameters such as solvents and reactant amounts affected on reductive etherification reaction [13], and polymers of a modest molecular weight were formed in yields ranging from low to high. The development of the related reductive etherification reactions, however, has not yet developed to their full potential [1,14]. Because of these reasons, it becomes critically important to design a practical and effective method for producing ether derivatives.

2.0 Polyether Synthesis By Reductive Etherification Reaction

Polyethers are special class chemistry of polymers and are widely applied on both an industrial and scientific scale. The characteristic properties of polyethers are based on the C–O–C bonds of the primary and/or secondary chains, which provide the polymer with a significant amount of

flexibility and easy workability under the decomposition temperature. Applications have been used from the field of biomedicine to materials science.

However, the strategies currently adopted for their synthesis necessitate dire conditions, including ionic polymerization and fewer options for antecedent monomers. In this work, reductive etherification facilitated by chlorodimethylsilane was developed as a flexible method for polyether production. Therefore, employing nitromethane as the polymer solvent, 1,4-butanediol and terephthalaldehyde were initially combined in the absence of chlorodimethylsilane. at room temperature to show the best parameters for the suggested system. The various diols, Terephthalaldehyde (as well as its isomers) was then reacted with under optimum condition to develop polyether libraries, ranging from linear to sterically congested diols.

On the other hand, in addition to the polyethers with the anticipated alternating units, the synthesis of polyethers was found to be due to the self-condensation of terephthalaldehyde in every instance. The suggested methodology resulted in a polyether with a strong alternating unit concentration of up to 93 percent and a molecular weight of approximately 110.4 kDa. Process and eventually studies of the model showed how adaptable and durable the proposed method and the polymerization process were mechanically investigated. Given the unlimited source of diols, it is expected that the methods presented may be potential candidates for the synthesis of polyethers with different skeletons.

3.0 Furfural derivative-derived fuels and fuel additives Via Reductive Etherification Reaction

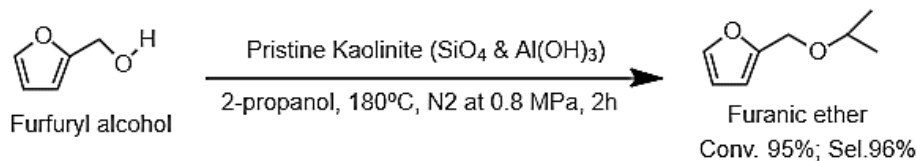
Since the turn of the century, all nations have relied on fossil fuels as energy and chemical sources, and its dependence has made fossil fuels an essential part of the global economy [3,15]. Due to the depletion of fossil fuel resources, the potential of replacing fuel with renewable energy has attracted considerable interest [7]. Since fossil fuels are non-renewable, several factors can affect their availability, including population increase and the exhaustion of oil reserves, which has led to inflated prices, and political unrest, notably in the wake of the 1970s oil crisis. Biomass, wind, solar, geothermal, hydroelectricity, and other renewable energy sources are some of the alternatives.

The etherification of furfural and its derivatives is a promising and known strategy for producing fuel additives [16]. Furfural is one of the base compounds that can be converted into a combination of chemicals and fuels with added value, including furan, tetrahydrofuran, furfuryl alcohol, 2-methyl furan, and 2-methyl tetrahydrofuran. They can be made from starch and lignocellulose, respectively. They produce several monomers with six carbons or lower as the product, and they do not constitute highly traded compounds [17].

One of the methodologies used to make furanic ethers is the reductive etherification technique, also known as direct furfural conversion, using acetal or furfuryl alcohol as an intermediary [3,15]. This method effectively converted furfuryl alcohol into the corresponding ether while reducing the undesirable side effects [10]. Besides that, the etherification of furanic chemicals generated from biomass to produce biofuel has a variety of uses as fuel additives [3,18,19]. Biomass with wide precursors and the richest and most diverse natural carbon source can be used to produce green products like biofuels or alternative additives without having an impact on human food consumption [12]. An acid catalyst is also necessary for the etherification of furanyl alcohol to proceed.

Modified zeolites, metal oxides, reformulated montmorillonites, metal chlorides, and resins are a few examples of acidic catalysts that have been developed to generate furanic ethers. Zeolite-based catalysts are the most frequently employed for the etherification of furanyl alcohol. Brønsted or Lewis acid had an impact on furfuryl alcohol conversion into furfuryl ethers. The potential of furfuryl ethers as a fuel additive has been recognized [10]. There are also numerous ways to transform furan into liquid fuel, including arenes-based Friedel-Crafts alkylation [20], condensation of aldol with ketone [2], and Baylis-Hillman processes involving methyl acrylate with 5-hydroxymethylfurfural [21].

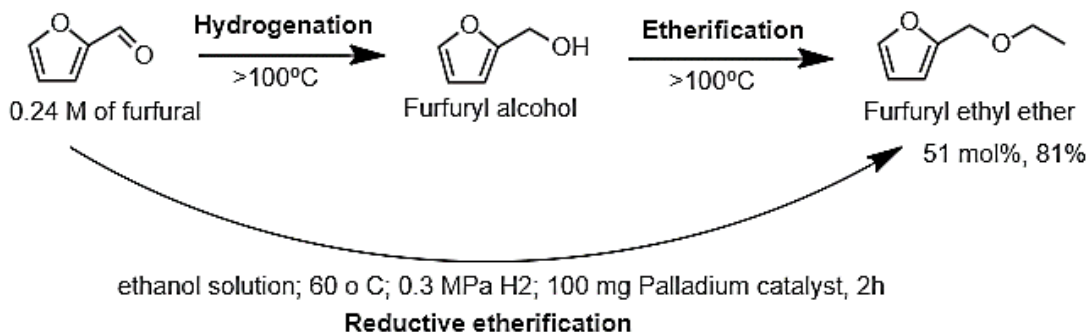
The application of kaolinite as an acid catalyst for the production of furanic ethers using furfuryl alcohol was demonstrated [3,15]. Kaolinite also known as $\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4$ is a kaolin group dioctahedral 1:1 clay natural component of tetrahedral SiO_4 and octahedral gibbsite $\text{Al}(\text{OH})_3$ sheets. It offers substantial environmental benefits in the green and natural chemistry production of biodiesel-derived products as illustrated in Scheme 1 [21].



Scheme 1: Etherification of Furfuryl alcohol to furanic ether in the presence of pristine kaolinite

The efficiency of pure kaolinite was exhibited by an etherification procedure with excellent catalytic efficiency and reusability to generate biodiesel-based products from furfuryl alcohol produced from biomass. The kaolinite catalyst's capacity to be recycled was investigated to figure out the advantages of using this catalyst in the etherification reaction economically and even after the fifth run, the catalyst demonstrated high stability and catalytic performance [3,22].

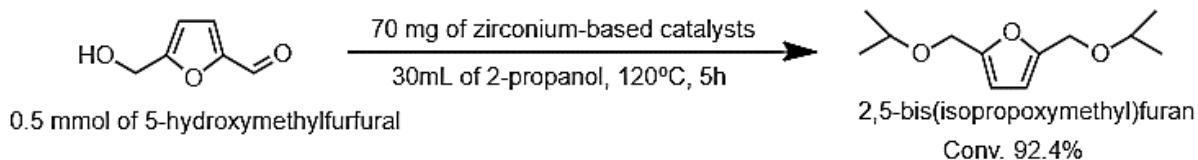
Yun *et al.* reported the reductive etherification furfural into ethyl furfuryl ether with high yield in ethanol under mild conditions, as shown in Scheme 2 [17].



Scheme 2: The path of the reaction that transforms furfural into ethyl furfuryl ether during reductive etherification

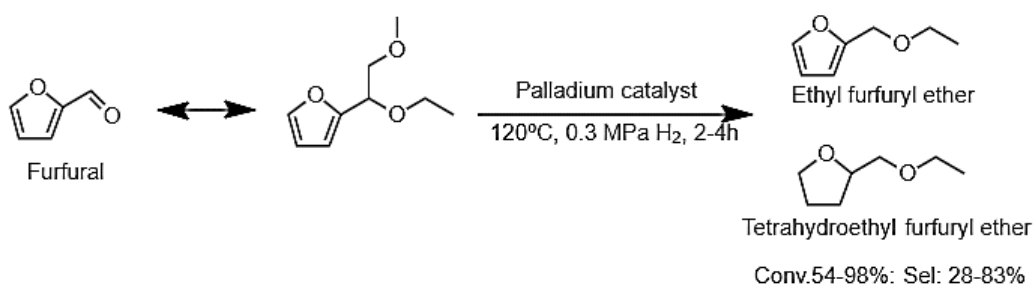
Wang *et al.* created a simple hydrothermal methodology to generate zirconium-based catalysts from biomass, sulfosalicylic acid, and zirconium salt [7]. As-prepared solid acid or bifunctional catalyst with multifunctional Brønsted acid sites was applied for the single pot reductive etherification of 5-hydroxymethylfurfural (HMF) through the Meerwein-Ponndorf-Verley reaction. The final product, furanic diether of 2,5-bis(isopropoxymethyl)furan (BPMF), was prepared in 2-propanol with a 92.4% yield, which is applicable as a fuel additive or biofuel, as

shown in Scheme 3 [7]. In addition, the catalyst exhibits strong catalytic activity for converting the aldehyde to the respective ester.



Scheme 3: Conversion 5-hydroxymethylfurfural (HMF) to 2,5-bis(isopropoxymethyl)furan (BPMF) via reductive etherification

Guo *et al.* reported a simple method for producing furfuryl ether *via* the etherification of furfural in one step over supported Palladium catalysts, as illustrated in Scheme 4 [10]. It is still difficult to prepare a reusable Palladium catalyst for reductive etherification. In their study, various SiO₂-supported Palladium catalysts were developed, ranging from 2.2 to 28 nm in terms of particle size. Their results provide an understanding of the particle size role in the rivalry among hydrogenation and hydrolysis of C=O in furfural onto Palladium surfaces. In one-step reductive etherification, Palladium nanoparticles larger than 3 nm were preferable. Pd/ZSM-5 bifunctional catalyst with Palladium nanoparticles bigger than 3 nm were prepared. In addition, the acidity was decreased in the presence of amino organosilane. The bifunctional catalyst successfully produced the desired ether *via* both direct and reductive etherification in a single pot.



Scheme 4: Conversion furfural to Ethyl furfuryl ether or tetrahydroethyl ether via reductive etherification

Ortiz *et al.* investigated the transforming methyl levulinate into methyl 4-alkoxypentanoates through the reductive etherification of the fatty alcohols. The superior biomass-derived surfactants were produced. The Pd/C-based bifunctional catalyst provided complete conversion and selectivity after optimising the metal crystal size. Enol ether was generated as an intermediate, and then it underwent hydrogenation. Additional cyclic and aliphatic ketones and aldehydes generated with biomass could be proceeded using the palladium catalyst and reductive etherification with promising results. The essential micellar concentration and surface tension of the sodium salt of 4-alkoxypentanoic acid were evaluated to determine the surfactant characteristics, and they outperform traditional soaps extremely favourably [23].

4.0 Polyketone Modification Via Reductive Etherification Reaction

A simple post-polymerization modification technique from polyketone was described using a reductive etherification reaction mediated by chlorodimethylsilane. The polyketone system was developed through polymerization of acyclic diene metathesis under mild conditions. It interacted with various alcohols in the presence of chlorodimethylsilane to produce various polymers containing functional-alkoxy pendants [13].

This study also investigated the effect of various silane compounds on the reductive etherification reaction; however, none of them offered as high efficiency as the one generated by chlorodimethylsilane. Due to their intrinsic Si–H bond, organosilanes are important substances that are widely used as reductants to produce ethers from compounds containing carbonyls such as ketones and aldehydes [24]. Organosilanes can be used to synthesise two very different symmetrical and asymmetrical ethers, depending on the conditions of the reaction, for example, symmetrical ether can be produced by employing a carbonyl compound such as aldehydes and ketones in the existence of an organosilane without the use of alcohol, whereas alcohol can be used as the nucleophile to produce unsymmetrical ether. Aldehydes quickly produced two very different symmetrical and unsymmetrical ethers in greater yields while ketones were discovered to have low yields, especially when synthesising unsymmetrical ethers [24]. The same study also showed that under identical conditions, sulfur- and nitrogen-based nucleophiles might react favorably with aldehydes and ketones to produce thioethers and amines [21]. Chlorodimethylsilane which has both reductive and Lewis acid characteristics, has recently been shown by Lee and Morandi to be able to mediate reductive etherification reaction among ketones and alcohols to produce

unsymmetrical ethers [25]. The primary alcohols were reported to produce the related alkoxy structures with excellent efficiency, strong isolated yields, and broad tolerance levels for functional groups.

5.0 Anion-Binding Catalysis Via Reductive Etherification Reaction

One method for the reductive etherification of alcohols with aldehydes and ketones and produce ethers is based on the beneficial effects of a low-cost HCl, organocatalyst, a straightforward silane reductant, usage of a basic thiourea catalyst, and Brønsted acid with the proper reducing agent available such as 1,1,3,3-tetramethyldisiloxane. Multiple alcohols has been also involved in the reductive etherification reaction [24]. A technique for reductive etherification must enable the condensation of an aldehyde and ketone with an alcohol to produce an oxocarbenium ion or approximate analogous, mirroring the conditions for reductive amination.

Future Outlooks

In the past century, both small and major chemical enterprises as well as industries and academic reactions have employed several types of ether compounds for a wide variety of purposes. Therefore, novel synthesis techniques for these compounds have been developed by the synthetic and catalytic sectors. With this Review, we have attempted to provide an overview of the current methods in use for the reductive etherification of alcohols and carbonyl-based chemicals under catalytic conditions such as aldehydes, ketones, and carboxylic acid derivatives to produce ether. There has been a noticeable increase in the number of studies using these methodologies over the past ten years.

This overview shows that reductive etherification reaction is a very promising mild strategy for (a) generating alkoxy-functional polymers with variable functionality from polyketone, (b) synthesis of polyethers with different skeletons, (c) preparation fuels and fuel additives from furfural derivatives, (d) synthesis ethers through anion-binding catalyst of alcohols with aldehydes and ketones to produce ethers. In addition, it illustrates the more challenging reductive ester-to-ether transformation. Therefore, the development of novel reductive ether synthesis techniques that allow the production of ethers with the designed and favorite structural complexity is an interesting topic in the catalysis and organic synthesis. We anticipate that this review will serve as motivation for research scientists in the above high demand topic who intend to generate the innovative reductive etherification methods and techniques.

Authorship contribution statement

Lia Zaharani: Research, data analysis and collection, original draught writing, and editing; *Nader Ghaffari Khaligh*: Conceptual model, Resources, Supervision, Funding Acquirement, Project Planning, Visual analytics, Verification, Writing-review & editing.

Conflicts of interest

There are no apparent conflicts.

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