Synthesis of Biomass-Derived Ethers for Use as Fuels and Lubricants

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Ethers synthesized from biomass-derived compounds have exceptional properties as fuels, lubricants, and specialty chemicals and can serve as replacements for petroleum-derived products. Recent efforts have identified heterogeneous catalysts for the selective synthesis of ethers from alcohols, aldehydes, ketones, furans, esters, olefins, carboxylic acids, and other molecules derived from biomass. This Review highlights the scope of etherification reactions and provides insights into the choice of catalysts and reaction conditions best suited for producing targeted ethers from the available starting materials. First, the properties of ethers for specific applications and the methods by which synths for ether synthesis can be obtained from biomass are discussed. Then the progress that has been made on the synthesis of ethers via the following methods is summarized: direct etherification of alcohols; reductive etherification of alcohols with aldehydes or ketones; etherification of furanic compounds, esters, and carboxylic acids; and the addition of alcohols to olefins. Next, the mechanisms of these reactions and catalyst properties required to promote them are discussed, with the goal of understanding how reaction conditions can be tuned to optimize catalyst activity and selectivity towards desired ethers. The Review closes by examining the tradeoffs between catalyst selectivity, activity, stability, and reaction conditions required to achieve the most economically and environmentally favorable routes to biomass-derived ethers.

1. Introduction

The increasing global consumption of petroleum-derived fuels and chemicals has resulted in rapid generation of atmospheric CO$_2$, the accumulation of which has adverse effects on the global climate.

One strategy for lowering the overall emission of CO$_2$ from the combustion of petroleum-derived fuels and lubricants is to replace them with similar products derived from renewable sources. This approach has the potential to be both environmentally responsible and economical, particularly if policy changes incentivize the use of non-fossil energy resources in the future. An attractive feedstock for producing sustainable fuels and specialty chemicals is lignocellulosic biomass, because it does not compete with food feedstocks and would otherwise be considered waste.

There have been many recent developments in the production of fuels and specialty chemicals from biomass. Various catalytic pathways involving condensation, reduction, acetalization, and dehydration have been identified for producing liquid fuels from biomass-derived platform chemicals. Ethers have emerged as a class of molecules with excellent properties that can be used to meet the growing demands for gasoline additives, cetane enhancers for diesel fuel, automotive lubricants, and other valuable products.

What makes ethers attractive for meeting these applications is that they can be produced from biomass-derived carbohydrates and triglycerides with a minimum consumption of molecular hydrogen, unlike the synthesis of fuels from the hydrogenation of furan-containing condensation products or aldol condensation products derived from biomass. This latter characteristic is important since currently nearly all hydrogen is produced by steam reforming of methane, a process that produces a mole of fossil-based CO$_2$ per four moles of H$_2$.

Our objective is to review recent reports of ether synthesis from biomass-derived platform molecules and understand how heterogeneous catalysts promote these reactions. To this end, we examine the roles of Brønsted and Lewis acid sites on the reaction mechanism and the role of substrate composition and structure. Our ultimate aim is to identify the combination of catalyst properties required to achieve high ether selectivity for a specified class of synths. Meeting this objective is not easy since etherification can occur by direct etherification of alcohols and reductive etherification alcohols with aldehydes, furans, ketones, carboxylic acids, esters, and olefins. The etherification of glycerol is also discussed briefly because several recent reviews have discussed glycerol conversion to ethers, solketal, acrolein, propylene glycol, polymers, propanediol, glycerol oxidation products, fuel additives, and other value-added products. William-son ether synthesis and other homogeneous routes are not discussed as these processes require catalyst separation and produce salts. Instead, we focus exclusively on the use of heterogeneous catalysts due to their ease of separation from products.

We begin by discussing the fuel and lubricant properties of ethers obtained by the etherification of biomass-derived platform molecules and the methods for sourcing these molecules from biomass. This is followed by a discussion of ether formation through direct etherification of alcohols, reductive etherification of alcohols and carbonyl compounds, and etherification of olefins with alcohols. Through this discussion, we describe the reaction conditions and catalyst properties required for...
selective ether synthesis and specifically discuss the role of cooperative effects between Brønsted and Lewis acid sites in controlling ether selectivity. Finally, we offer a roadmap for producing targeted ethers from available starting materials in high selectivity by utilizing knowledge of the effects of reactant structure, catalyst properties, and reaction conditions.

2. Applications and Fuel and Lubricant Properties of Biomass-Derived Ethers

Figure 1 shows some example structures of ethers synthesized from biomass-derived molecules that have properties making them suitable as diesel fuels, cetane boosters, octane boosters, automotive lubricants, and other products. Ethers that could serve as diesel are shown in Table 1. Symmetrical, linear ethers such as di-n-hexyl ether and di-n-octyl ether have high energy densities and high cetane numbers, which result in decreased ignition delay in diesel vehicles. Addition of diethyl ether to ethanol biodiesel blends also reduces the ignition delay, exhaust-gas oxygen, smoke emissions, and particulate matter. Linear asymmetrical ethers such as ethyl octyl ether and butyl hexyl ether also have high cetane numbers and can be added to diesel blends.

For use as gasoline additives, short-chain branched ethers are suitable owing to their high octane numbers. The increased substitution of these ethers results in a higher ignition delay, allowing the fuel to be used in gasoline engines, which operate at high compression ratios. An example is ethyl-tert-butyl ether (ETBE), which has an octane number of 112. Not only can ETBE be produced from renewable sources, but it also has a higher boiling point, a lower flash point, lower blending Reid vapor pressure, and lower solubility in water than methyl-tert-butyl ether. Over the years, the global consumption of ETBE for use in gasoline has increased as ETBE has excellent gasoline-additive properties, has reduced environmental toxicity and improved biodegradability compared to methyl-tert-butyl ether (MTBE), is less soluble in water, and its synthesis utilizes renewable ethanol.

Monoethers and diethers derived from furans such as 5-(ethoxymethyl)furfural-2-carboxaldehyde (EMF) and 2,5-bis(ethoxymethyl)furan (BEMF) have excellent cetane numbers and can be added to diesel or used as a drop-in fuel. EMF has an energy density of 8.7 kWh L\(^{-1}\), comparable to gasoline (8.8 kWh L\(^{-1}\)) and diesel (9.7 kWh L\(^{-1}\)), and superior to that of ethanol (6.1 kWh L\(^{-1}\)).

Ethers derived from biomass also have the potential to replace petroleum-derived automotive lubricants. Transport vehicles consume almost 30% of energy produced today, and of that approximately one third is lost due to friction and wear. This gives rise to a global demand for lubricants of around 35 million tonnes per year, with automotive lubricants accounting for about 15% of the total lubricant consumption. The performance of automotive lubricants is judged by a number of criteria, including the kinematic viscosity (KV) at 40 and 100 °C (KV\(_{40}\) and KV\(_{100}\), respectively), the viscosity index (VI), the pour point (PP), the oxidation stability (DSC onset temperature), the volatility (TGA Noack), and the cold-cranking simulator viscosity (CCS). The currently used synthetic automotive lubricant consists of poly-alpha-olefins (PAO), which are derived from petroleum through the oligomerization of \(\alpha\)-olefins. However, as shown in Table 2, recent
reports showed that branched ethers such as 11-[(2-ethylhexyl)oxy]methyltricosane have comparable lubricant properties and can be synthesized from renewable sources. Branches in the alkyl portions of ethers reduce the PP and increase the viscosity of the ether, enhancing the lubricant properties. Other ethers such as alkylated diphenyl ether and glycerol ethers have excellent lubricant properties. Glycerol ethers and polyethers also have applications as surfactants and fuel additives. Monododecyl polyglyceryl ether (MAGE) and multidodecyl polyglyceryl ethers produced from the etherification of glycerol with dodecanol have excellent surfactant properties. Other monoether glycerol ethers were shown to be suitable for pharmaceutical applications because of their anti-inflammatory, antibacterial, anti-tumor, and antifungal properties. Di- and tri-tert-butyl ethers are soluble in diesel fuel and can be added as oxygenates to decrease the viscosity and cloud points.

One of the important considerations in utilizing ethers as fuels and lubricants is their propensity to form peroxides. There is a delicate balance with peroxide formation, because some peroxide formation is beneficial for ignition properties of the fuel but too much peroxide formation can lead to stability and safety concerns. The peroxide number is a measure of a tendency for a material to form peroxides. Compounds are classified based upon their peroxide numbers to ensure safe handling. For example, diethyl ether is classified as a group B compound for peroxide formation, meaning it must be discarded or used after one year of storage. On the other hand, MTBE forms peroxides more slowly than tetrahydrofuran (THF), 2-methyl-

<table>
<thead>
<tr>
<th>Ether</th>
<th>Blending cetane number</th>
<th>Blending cloud point [°C]</th>
<th>Blending cold filter plugging point [°C]</th>
</tr>
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<tbody>
<tr>
<td>dimethyl ether</td>
<td>55–66</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>diethyl ether</td>
<td>&gt; 125</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>di-n-butyl ether</td>
<td>85</td>
<td>–20</td>
<td>–13</td>
</tr>
<tr>
<td>di-n-pentyl ether</td>
<td>109</td>
<td>–22</td>
<td>–20</td>
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<tr>
<td>di-n-hexyl ether</td>
<td>117</td>
<td>–7</td>
<td>–5</td>
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<tr>
<td>di-n-heptyl ether</td>
<td>117</td>
<td>–7</td>
<td>–5</td>
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<tr>
<td>di-n-octyl ether</td>
<td>118,119</td>
<td>–17</td>
<td>–15</td>
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<td>89</td>
<td>–</td>
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<tr>
<td>ethyl octyl ether</td>
<td>100, 98</td>
<td>–</td>
<td>–</td>
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<tr>
<td>n-butyl hexyl ether</td>
<td>94</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>n-heptyl propyl ether</td>
<td>94</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>reference: diesel fuel</td>
<td>48–51</td>
<td>–2 to 5</td>
<td>–4 to 3</td>
</tr>
</tbody>
</table>

Figure 1. Applications of selected biomass-derived ethers.

Table 1. Representative linear alkyl ethers and selected diesel-fuel properties.
THF, and 2,5-dimethyl furan.\textsuperscript{[69]} Another important consideration is the fact that the addition of oxygenates to fuel blends also impacts the exhaust emissions, lowering CO and other unregulated emissions such as benzene and 1,3-butadiene.\textsuperscript{[70]} A review by Di Nicola and co-workers provides greater detail about emissions from ethers and organic carbonate fuel additives.\textsuperscript{[70]}

### 3. Platform Molecules from Biomass-Derived Feedstocks

A variety of synthons derived from the carbohydrate fraction of biomass can be used to produce ethers. These include aldehydes, ketones, alcohols, and furans. Scheme 1 illustrates pathways for producing these synthons starting from C\textsubscript{5} and C\textsubscript{6} sugars. Recent investigations of ABE (acetone–butanol–ethanol) fermentation of glucose using clostridium acetobutylicum have shown that a mixture of butanol, acetone, and ethanol can be produced with the molar ratio of 6:3:1.\textsuperscript{[71, 72]} These products can be further upgraded to afford higher carbon number alcohols and ketones, such as 2-pentanone, 2-heptanone, 4-heptanone, 6-undecanone, and methyl isobutyl ketone (MIBK).\textsuperscript{[7, 73, 74]} Some of these compounds can also be prepared from furfural and 5-hydroxymethyl furfural (HMF) by the dehydration of xylose and glucose, respectively.\textsuperscript{[75–77]}

Condensation of furfural with acetone in the presence of hydrogen produces 1-octanol.\textsuperscript{[78]} Other linear alcohols such as 1-hexanol and 1-dodecanol can be accessed from furfural using engineered Escherichia coli\textsuperscript{[79]} and through hydrolysis of triglycerides and fatty acids,\textsuperscript{[80]} respectively. Furfural can be converted to 1-pentanol through hydrogenation to furfuryl alcohol followed by hydrolysis to produce levulinic acid, which can then be hydrogenated to form 1-pentanol.\textsuperscript{[80, 81]} The carbon number of linear alcohols can be further increased via the Guerbet pathway, which affords branched alcohols such as 2-ethyl-1-hexanol, 2-hexyl-1-decanol, and 2-decyl-1-tetradecanol.\textsuperscript{[82]} Olefins derived from biomass are also useful synthons for producing ethers. For example, isobutene can be selectively formed from acetone or ethanol over zinc oxide dispersed on zirconia in the presence of water,\textsuperscript{[83, 84]} or through fermentation of biomass-derived sugars.\textsuperscript{[85]} Other olefins such as octene, decene, and 2-ethyl hexene can be prepared via unimolecular dehydration of biomass-derived alcohols.

| Table 2. Comparison of lubricant properties of PAO and C\textsubscript{32} ether.\textsuperscript{[16]} |
|-----------------|---------|------|-------|-----------------|-------|------|
| Lubricant       | KV\textsubscript{100} [cSt] | KV\textsubscript{40} [cSt] | VI    | PP [°C] | DSC oxidation onset [°C] | TGA Noack [wt %] | CCS [cP] |
| 11-[[2-ethylhexyl]oxy]methyl]tricosane | 3.5     | 12.0 | 145   | –36    | 206              | 5.1       | 769   |
| Reference: PAO  | 4.0     | 17.8 | 126   | –75    | 221              | 18.8      | 1276  |

Scheme 1. Overview of processes for deriving alcohols, aldehydes, ketones, and furans from biomass-derived feedstocks.
Glycerol is another abundant and inexpensive biomass-derived platform chemical obtained as a byproduct of biodiesel production. Sources of triglycerides for the generation of biodiesel include various vegetable oils, waste oil products, and algae.[4,5]

4. Synthesis of Ethers from Biomass-Derived Platform Chemicals

A number of different pathways are available for obtaining biomass-derived synths for the production of ethers, as shown in Scheme 1. The choice of synthetic pathway depends on the composition of the feedstock and the desired final product and selectivity. In this section, we discuss the scope of direct etherification of alcohols; the reductive etherification of alcohols with aldehydes, ketones, esters, and carboxylic acids in the presence of hydrogen; direct and reductive etherification of furanic compounds; and the etherification of olefins by reaction with alcohols. For each of these methods, we examine the reaction mechanism and the activity and selectivity of known catalysts and discuss adjustments that can be made to the reaction conditions to obtain the maximum product yield.

4.1. Direct etherification of alcohols

4.1.1. Direct etherification of linear and branched alcohols

Direct etherification of alcohols over a solid-acid catalyst involves the bimolecular dehydration of two alcohols in the absence of a reducing agent to produce ether and water (solid green arrow in Figure 2a). Solid-acid-catalyzed etherification of alcohols in the liquid phase enables the production of ethers in a single phase and can be performed in the presence of a solvent or using the alcohol as the solvent itself. One of the advantages of the latter approach is that it eliminates the need for solvent separation. Various polymeric resins, metal oxides, and other solid-acid catalysts are effective for the direct etherification of linear alcohols. The competing reaction in the presence of an acid catalyst is unimolecular dehydration of the alcohol to form an olefin, a product that is thermodynamically favored over ether formation at elevated temperatures. For example, Figure 2b shows that the unimolecular dehydration of 1-dodecanol is thermodynamically favored over formation of didodecyl ether at temperatures above ≈ 350 K.[86] Other linear and branched alcohols such as 1-hexanol, 2-hexanol, and 3-hexanol follow the same trend of increasing thermodynamic preference for unimolecular dehydration with increasing temperature.[87] Olefins are not desired in fuel and lubricant blends because they tend to form gums.[88] Moreover, as shown in Figure 2a, primary olefins can rehydrate to form secondary alcohols; this can result in the formation of branched ethers, which changes fuel properties such as the cetane number.[89] Olefins can also oligomerize to form larger olefins and coke, resulting in catalyst deactivation. Other challenges with direct etherification are associated with the inhibiting effects of water and ether on reaction rates and selectivities towards ethers.[86, 90]

To achieve high ether selectivities, the catalyst must either be operated at temperatures below the temperature at which unimolecular dehydration becomes thermodynamically preferred or have an intrinsic selectivity for etherification versus dehydration. The most desirable catalyst has high activity (turnover number), low activation energy for etherification, high selectivity for etherification, high thermal stability, and can be reused. Table 3 lists a number of heterogeneous catalysts and reaction conditions that are effective for the direct liquid-phase etherification of linear alcohols to symmetrical ethers. The reported solid-acid catalysts employed for direct etherification include Brønsted-acid catalysts, Lewis-acid catalysts, and catalysts with both Brønsted and Lewis acid sites. Among these are acidic resins, metal oxides, and other solid-acid catalysts. The desired acid strength for etherification is not clearly defined, with some studies suggesting that etherification requires high acid-site density and low acid strength[13] and others suggesting that acid strength only affects rates but not selectivity.[91] Published studies suggest that bimolecular etherification of alcohols requires that two alcohol molecules interact favorably with one another. This condition can be achieved either by using a catalyst with strong acid sites located within large pores that provide a high local concentration of alcohol or by using a catalyst with two proximate active sites for adsorption of both alcohols.

Brønsted-acid catalysts involve proton donor sites. Polymeric resins such as Amberlyst and Nafion contain Brønsted-acidic H atoms attached to sulfonic acid groups. Amberlyst 70 is a macroporous sulfonic styrene–divinyl benzene (DVB) resin catalyst with a surface area of 36 m²g⁻¹ and an acid site concentration of 1.5 mmoles/g.[87] Other linear

![Figure 2](https://www.chemsuschem.org/2019/12/2835-2858)

**Figure 2.** a) Reaction pathway for acid-catalyzed direct etherification of alcohols (solid green arrow) and side-product formation (dashed red arrows), b) Gibbs free energies of formation for 1-dodecanol etherification (green, solid) and unimolecular dehydration (red, dashed).
Nafion NR-50 is a sulfonated Brønsted–[94] acid catalyst that has a fluorinated backbone, as shown in Figure 3a. Amberlyst 70 and Amberlyst NR-50 stand out as active and selective Brønsted-acid catalysts for the direct etherification of the linear primary alcohols 1-octanol, 1-hexanol, and 1-pentanol.[92–94] Table 3, entries 1, 2, 5, 6, 8, 9, and 11, show that Amberlyst 70, Nafion NR-50, as well as the resins Purolite CT-224, Amberlyst DL-H/03, and Dowex 50WX4 are highly selective for ether formation of 3 equiv H+ kg⁻¹.[97] and other resins such as Amberlyst 15 are even less thermally stable and are not recommended for use above 393 K. Moreover, regeneration of resin catalysts requires solvents and separation processes that consume energy and generate additional waste.

In a study of octanol etherification over gel-type and macroporous polymeric resins, the best selectivity to di-ether was observed for catalysts with a low degree of cross-linking.[41] Resins with a low cross-linking degree (Amberlyst 39 and Amberlyst 70) were also found to be more selective for the etherification of 1-hexanol and 1-pentanol than catalysts with higher degrees of cross-linking with DVB.[99] As shown in Figure 3a, a high degree of DVB cross-linking (pink) results in more confined pore volumes and thus less accessibility to the catalyst.
active sites by long-chain alcohols. Solvent effects on polymer swelling are also important as they introduce mass-transfer limitations due to variation in the number of accessible acid sites with time. Cooley et al. examined the microscopic and bulk swelling behavior of Nafion perfluorinated ionomer membranes in mixtures of water and ethanol using small-angle X-ray diffraction and optical microscopy. While the microscopic swelling decreased with increasing ethanol content, the bulk swelling increased dramatically with increasing ethanol content. They concluded that the ethanol plasticiizes the fluorocarbon matrix in Nafion, which allows the ionic material to form numerous smaller clusters compared to membranes swollen solely with water. A lower degree of cross-linking generally results in greater swelling of the resins, and as a result improved accessibility of the active centers for etherification.

Zeolites, such as H-BEA pictured in Figure 3b, are also strong acids, but have superior thermal stability to resins and can be regenerated easily by calcination. The Brønsted acid site in zeolites is generated when a Si atom (4+) in the framework structure is replaced by an Al atom (3+), requiring a proton to balance the charge; thus, the higher the Al/Si ratio, the higher the Brønsted acid site density. However, zeolites tend to catalyze undesired side reactions, such as unimolecular dehydration, and produce coke, which results in catalyst deactivation. Table 3 shows the selectivity to didodecyl ether for dodecanol etherification over H-BEA at 393 K is only 61%, compared to 97% and 98% for Amberlyst 70 and Nafion NR-50, respectively. Moreover, while Amberlyst 70, Nafion NR-50, and tungstated zirconia (WO\textsubscript{5}/ZrO\textsubscript{2}) exhibit similar activation energies for 1-hexanol etherification (108–127 kJ mol\textsuperscript{-1}), the activation energy for the H-BEA-25 is significantly higher (148±11 kJ mol\textsuperscript{-1}). A study of Zeolite HUSY suggests that its higher surface hydrophilicity leads to the retention of a portion of the byproduct water inside the pores, thereby reducing its etherification activity at low temperatures. If high reaction temperatures and ease of catalyst regeneration are desired at the expense of selectivity, then zeolites such as H-BEA could be employed as solid Brønsted acids.

Another class of solid acids are Lewis-acid catalysts such as zirconia, alumina, silica, and aluminosilicates. At 393 K, Lewis-acidic zirconia, γ-alumina, mesostructured silica, and mesostructured aluminosilicate have all been shown to be inactive for the liquid-phase etherification of 1-dodecanol. While \( \eta \) alumina has been shown to be active for etherification of C\(_6\)-C\(_{12}\) linear alcohols at 523 K (Table 3, entries 33–38), it is not highly selective. We have shown that WO\textsubscript{5}/ZrO\textsubscript{2}, a solid-acid catalyst containing both Brønsted and Lewis acid sites, promotes the direct etherification of primary linear alcohols ranging from \( n \)-hexanol to \( n \)-dodecanol, with ether selectivities of over 94% at 393 K. WO\textsubscript{5}/ZrO\textsubscript{2} is also highly active. The turnover frequency (TOF) normalized per Brønsted acid site at 393 K for 1-hexanol etherification is 1.3 s\textsuperscript{-1}, which is significantly higher than the TOFs for the etherification of 1-pentanol over Amberlyst 70, Nafion NR50, Zeolite HBEA-25, Amberlyst 36, Purolite CT-224, Amberlyst DL-H/03, Amberlyst DL-I/03, and Dowex 50WX4 (0-0.4 s\textsuperscript{-1}) at the same temperature and reactant concentration. We hypothesized that WO\textsubscript{5}/ZrO\textsubscript{2} is an effective catalyst for the etherification of alcohols because Brønsted and Lewis acid sites on the surface of the catalyst work cooperatively to promote bimolecular etherification over unimolecular dehydration, as illustrated in Figure 4. In contrast to acidic resins, WO\textsubscript{5}/ZrO\textsubscript{2} exhibits high thermal stability and facile catalyst regeneration, making it an excellent choice of catalyst for the synthesis of symmetrical linear ethers.

In addition to forming linear symmetrical ethers, direct etherification of alcohols can be used to synthesize asymmetrical ethers such as ethyl octyl ether. As shown in Table 4, Amberlyst 121, Dowex 50WX2, and Purolite CT-224 are most selective for producing ethyl octyl ether from equimolar feed ratios of ethanol and octanol, although symmetrical ethers are still formed. As shown in Table 3, the alkyl chain length of the alcohols does not have a significant effect on the ether selectivity or the activation energies for etherification and dehydration over WO\textsubscript{5}/ZrO\textsubscript{2} (entries 22–27) and Amberlyst 70 (entries 1, 9, and 28). Because of the negligible changes in kinetics with increasing linear alcohol chain length, mixtures of linear alcohols couple in a nearly statistical manner. Our recent study of alcohol etherification over WO\textsubscript{5}/ZrO\textsubscript{2} showed that equimolar mixtures of 1-hexanol, 1-heptanol, 1-octanol, 1-nonanol, 1-decanol, 1-undecanol, and 1-dodecanol produce a nearly statistical distribution of C\(_{12}\)-C\(_{24}\) ethers at 393 K. In another study, Walsh et al. demonstrated that short-chain (C\(_2\)-C\(_6\)) alcohols couple to form a nearly statistical distribution of ethers over Nafion SAC-13 and Purolite CT-175 in the presence of supercritical CO\textsubscript{2}. Thus, the cross-coupling of alcohols is desirable for producing mixtures of ethers for diesel blends but not when pure asymmetrical ether products are desired because homocoupling of alcohols will also occur.

The synthesis of ethyl hexyl ether and ethyl octyl ether was also investigated using diethyl carbonate as an ethylating agent, where two moles of alcohols are added to one mole of diethyl carbonate to produce two moles of asymmetrical ethers, one mole of H\(_2\)O, and one mole of CO\textsubscript{2}. Carbonates such as dimethyl and diethyl carbonate are now considered “green reagents” because they can be prepared from the catalytic oxidative carbonylation of methanol or ethanol with CO\textsubscript{2} rather than from phosgene. However, Tejero and co-workers compared the synthesis of ethyl octyl ether through...
etherification of octanol using diethyl carbonate and through direct etherification of ethanol and octanol and concluded that direct etherification was the most effective method for producing ethyl octyl ether over acidic ion-exchange resins.\cite{107} The authors found that at long reaction times the yields of ethyl octyl ether were similar for the two synthetic methods; but, at early reaction times direct etherification of ethanol and octanol resulted in higher rates of ethyl octyl ether formation. Furthermore, they suggested that direct etherification is preferable to etherification of alcohol with carbonate because it does not produce CO$_2$.\cite{107}

Direct etherification of branched alcohols in the absence of a solvent was also investigated over WO$_x$/ZrO$_2$. Our studies concluded that primary alcohols with carbon branches at least three carbon atoms away from the hydroxyl group are highly selective to ether formation. However, as the carbon branch approached the $\alpha$- and $\beta$-carbon atoms of the alcohol, the selectivity to ether drastically dropped, as shown in Table 3 (entries 16–21) and illustrated in Figure 5.\cite{98} Other studies also showed that substituted alcohols, such as 2-butanol, readily undergo unimolecular dehydration over tungsten oxide catalysts, while etherification is negligible.\cite{110}

In our previous study of the kinetics and mechanism of etherification and dehydration over WO$_x$/ZrO$_2$, measurements of kinetic isotope effects revealed that the rate-limiting step for unimolecular dehydration is the cleavage of the $\beta$-C–H bond of the alcohol.\cite{86} Kinetic isotope studies of ethanol dehydration over $\gamma$-Al$_2$O$_3$ also suggested that this is the rate-limiting step.\cite{111,112} The addition of alkyl branches to the $\alpha$- and $\beta$-carbon atoms of the alcohol increases the stability of the carbocation intermediate involved in the unimolecular dehydration, thereby promoting olefin formation. This evidence, coupled with the fact that activation barriers for dehydration decrease with increasing substitution of the alcohol,\cite{86,112} suggests that direct etherification is limited to primary alcohols with no branches or with branches located a sufficient distance from the hydroxyl group.

Measurements of the kinetics of ethanol dehydration and etherification in the gas phase also revealed important considerations concerning the inhibition by ethanol–water dimers as well as more complicated dimer and trimer species.\cite{90,111,113–115} Inhibition by water was observed for primary linear alcohol etherification over WO$_x$/ZrO$_2$ as shown in Figure 4,\cite{86} which was also observed for 1-octanol etherification over zeolite BEA\cite{95} and for 1-pentanol etherification over Amberlyst 70.\cite{97} The removal of water is thus an important consideration for improving selectivity towards ethers across a variety of catalysts, particularly if the reaction is operated in a batch process at high conversions. In this connection, we note that Tejero et al. found that water removal during the etherification of 1-pentanol over Purolite CT-224 by distillation improved ether selectivity.\cite{116}

Ether selectivity can also be improved by eliminating both external and internal mass-transfer limitations. In addition to considering the molecular size of adsorbing species and swel-

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**Table 4.** Synthesis of ethyl octyl ether via direct etherification of ethanol and octanol catalyzed by solid acids.\cite{107}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Selectivity to ethyl octyl ether</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amberlyst 15</td>
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<tr>
<td>2</td>
<td>Amberlyst 35</td>
<td>15.2\cite{104}</td>
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<td>3</td>
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<td>Amberlyst 70</td>
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<tr>
<td>7</td>
<td>Purolite CT-224</td>
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<td>8</td>
<td>Amberlyst 31</td>
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<td>9</td>
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<td>11</td>
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<td>[14]</td>
</tr>
<tr>
<td>12</td>
<td>Amberlyst 70</td>
<td>25.5 from EtOH, 69.4 from octanol</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Purolite CT-224</td>
<td>26.2 from EtOH, 72.4 from octanol</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Dowex 50Wx2</td>
<td>26.1 from EtOH, 73.7 from octanol</td>
<td></td>
</tr>
</tbody>
</table>

[a] Molar ratio octanol/ethanol 1:1 at 423 K. [b] Moles of ethanol reacted to form ethyl octyl ether + moles of octanol reacted to form ethyl octyl ether/moles of ethanol and octanol reacted x 100%.

---

**Figure 4.** Mechanism of direct etherification and dehydration of linear alcohols over cooperative Brønsted (BA) and Lewis (LA) acid sites of WO$_x$/ZrO$_2$ (adapted from Ref. [86]).
ling of pore sizes caused by alcohols and solvent (if the solvent is different than the alcohol), external mass transfer can be improved by operating at high stirring rates, whereas small particle sizes reduce the effects of internal mass transfer. Improper mixing hinders bimolecular interactions of alcohols, especially for alcohols with long chains, such as 4-hexyl-dodecanol (Figure 5), resulting in decreased selectivity with increased chain length due to external mass-transfer limitations.\[13, 96\]

The preceding discussion suggests that catalysts with both large pore volumes and small particle sizes enable selective ether synthesis via direct etherification from a wide variety of alcohols. Consistent with this conclusion, a recent study of ethanol dehydration over the metal–organic framework (MOF) UiO-66, which contains nodes in the form of a $\text{Zr}_6\text{O}_{18}$ cluster, demonstrated that the catalyst exhibits 100% selectivity to diethyl ether between 473 and 523 K.\[114\] The authors suggest that the key to achieving high ether selectivity is the breaking of node-linker bonds, which forms defect sites proximate to open sites that facilitate effective bond formation between the alcohols. The authors found that the rate of etherification was three times greater for MOF UiO-66 (200 nm particle diameter) than for MOF UiO-67 (800 nm particle diameter), suggesting that transport limitations in the pores are significant.\[114\] In practice, though, this catalyst may not be suitable for selective ether formation because although vacancy sites produce more catalytically active sites they also contribute to a loss of crystallinity and, thus, stability.\[114\]

In summary, to achieve high yields of ethers from alcohols via direct etherification a balance must be struck between catalyst selectivity, activity, and thermal stability. Moreover, the reactants in the reactor in which etherification is carried out must be well mixed and water produced by the reaction should be separated from the reactant mixture. Catalysts with confined spaces such as zeolites and resins with a high degree of cross-linking exhibit lower selectivity to ether, suggesting that pore confinement isolates alcohols and facilitates unimolecular dehydration. Achieving a high local concentration of alcohols at the catalyst surface is necessary to promote bimolecular etherification. This can be achieved either using Brønsted-acid catalysts with large pores that swell up in the presence of the solvent, such as Amberlyst 70, or through adsorption of alcohols onto catalysts containing proximate Brønsted and Lewis acid sites that facilitate the cross-coupling reaction, as occurs for WO$_x$/ZrO$_2$. Still, the method of direct etherification is only applicable for producing symmetrical ethers from linear alcohols or blends of asymmetrical and symmetrical ethers from a feed composed of a mixture of linear alcohols. If high selectivities of linear asymmetrical ethers or ethers with branches closer than three carbon atoms away from the hydroxyl group are desired, the method of reductive etherification of an alcohol and an aldehyde or ketone is preferred. This method is discussed in Section 4.2.

4.1.2. Synthesis of mono-, di-, and triethers via the direct etherification of glycerol and polyols with alcohols

Glycerol is an inexpensive byproduct of biodiesel production and has emerged as an attractive platform molecule for the production of fuels and specialty chemicals. As mentioned in the introduction, the valorization of glycerol through acetalization, dehydration to acrolein, conversion to 1,3-propanediol, and other methods has been studied and reviewed extensively.\[21–38\] Therefore, we will only highlight a few examples of glycerol valorization to fuels and lubricants via direct etherification using solid-acid catalysts.
Table 5. Scope of some ethers produced from the direct etherification of glycerol with alcohols.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Amberlyst 70 (10 wt %)</td>
<td>403</td>
<td>24</td>
<td>1-dodecanol</td>
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<td>57</td>
<td>0</td>
</tr>
<tr>
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<td>1-dodecanol</td>
<td>4</td>
<td>36</td>
<td>5</td>
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<tr>
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<td>1-butanol</td>
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<td>1-pentanol</td>
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<td>13</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
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<td>24</td>
<td>1-hexanol</td>
<td>4</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>Amberlyst 70 (10 wt %)</td>
<td>403</td>
<td>24</td>
<td>1-octanol</td>
<td>4</td>
<td>36</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
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<td>353</td>
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<td>1-phenylpropan-1-ol</td>
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<td>8</td>
<td>SiO₂-SO₃H (1.7 mol %)</td>
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<td>SiO₂-SO₃H (2.5 mol %)</td>
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<tr>
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<tr>
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<tr>
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<tr>
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<td>tert-butanol</td>
<td>4</td>
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<td>NA</td>
</tr>
<tr>
<td>16</td>
<td>Amberlyst 15</td>
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<td>6</td>
<td>isobutanol</td>
<td>0.25</td>
<td>100</td>
<td>NA</td>
</tr>
<tr>
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<td>isobutanol</td>
<td>0.25</td>
<td>78.9</td>
<td>NA</td>
</tr>
<tr>
<td>18</td>
<td>Amberlyst 15</td>
<td>343</td>
<td>6</td>
<td>isobutanol</td>
<td>0.25</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>19</td>
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<td>6</td>
<td>1-butanol</td>
<td>0.25</td>
<td>85.1</td>
<td>NA</td>
</tr>
<tr>
<td>20</td>
<td>Amberlyst 15</td>
<td>393</td>
<td>6</td>
<td>ethanol</td>
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<td>NA</td>
</tr>
<tr>
<td>21</td>
<td>Amberlyst 15</td>
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<td>6</td>
<td>ethanol</td>
<td>0.1</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>22</td>
<td>Amberlyst 15</td>
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<td>ethanol</td>
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<td>NA</td>
</tr>
<tr>
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<td>DBSA</td>
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<td>24</td>
<td>1-dodecanol</td>
<td>4</td>
<td>26</td>
<td>72</td>
</tr>
</tbody>
</table>

[a] Selectivity to isobutene. [b] Product distribution [wt %], with remainder 28.6 wt % tert-butanol and 6.4 wt % glycerol.

Bromsted-acid catalysts such as Amberlyst 70, Amberlyst 15, Amberlyst 35, sulfated zirconia, sulfonated silica, and zeolite H-BEA are effective for catalyzing the etherification of glycerol with a variety of alcohols in the liquid phase.[117-122] Table 5 illustrates a number of examples of solid-acid-catalyzed direct etherification of glycerol with alcohols. In general, the major product for the monoether is 1a, whereas 1b is the minor product formed by the more sterically difficult etherification of the middle hydroxyl group of the glycerol. Similarly, 2b is the minor product for the diethers. The triether (3) is a result of etherification of each of the hydroxyl groups of glycerol with alcohols. The bimolecular etherification of two alcohols (4) as well as the oligomerization of glycerol (5) also occurs. Notably, in the case of ethanol etherification with glycerol, the side reaction of diethyl ether formation did not have a significant effect on the rates of formation of the desired products.[123] To maximize yields of mono-, di-, and triglycerol ethers, it is important to consider the effects of the catalyst properties, alcohol structure, temperature, and water removal to optimize the kinetics.

To synthesize mono-, di-, and triethers of glycerol with linear alcohols, one must consider the tradeoff between etherification activity and selectivity. For the etherification of glycerol with ethanol over Amberlyst 15 shown in Table 5, entries 20–22, no reaction occurred below 433 K.[120] Although this reaction is highly selective to the monoether, the catalyst is not reusable as Amberlyst 15 is unstable above 393 K. Similarly, the etherification of glycerol with butanol over Amberlyst 15 is active at 433 K, reaching a monoether yield of up to 70% at a glycerol conversion of 85.1%, but is not active at 343 K, as shown in Table 5, entries 18–19.[122] Therefore, for these reactions, it is recommended that a more thermally stable catalyst such as Amberlyst 70 or a metal oxide is used because high temperatures are required.

For the synthesis of glycerol ethers using alcohols such as 1-dodecanol and 1-octanol, there are additional challenges due to mass-transfer limitations introduced by the poor solubility of long-chain alcohols in glycerol. As shown in Table 5, entry 8, a temperature of 353 K is insufficient for etherification of 1-dodecanol with glycerol over sulfonated silica, a catalyst that is active under the same conditions for the etherification of glycerol with benzyl alcohol to produce a monoether (entry 10).[61] Adding a surfactant promotes etherification of glycerol with long-chain alcohols such as 1-dodecanol in the liquid phase to improve solubility. For example, Jérôme and co-workers used dodecylbenzene sulfonic acid (DBSA) to enable emulsification.
of the reaction medium, which resulted in yields of mono-decyl glycerol ethers of 30% at 403 K (Table 5, entry 23). De Campo and co-workers also demonstrated that using a well-tuned amphiphilic polystyrene–polystyrene sulfonic acid (PST-PSSA) copolymer, a surfactant acid catalyst grafted on silica, significantly increased ether formation from 1-dodecanol and glycerol by facilitating better contact between the two reactants.\textsuperscript{[50]}

Amberlyst 70 and sulfonic acid supported on silica are effective for the synthesis of monoethers from linear and benzyl alcohols (Table 5, entries 2–7, 9, and 10).\textsuperscript{[18, 61]} Amberlyst 15 is effective for producing di- and triethers from the reaction of glycerol with isobutanol to produce diesel additives (Table 5, entry 16).\textsuperscript{[120]} If high yields of di- and triethers are desired, water must be removed during the synthesis to increase the conversion. Frusteri and co-workers used a membrane to selectively remove water and shift the equilibrium of the reaction towards the formation of polyethers for the etherification of glycerol with tert-butyl alcohol\textsuperscript{[119, 121]} as well as butanol.\textsuperscript{[122]} De Campo et al. also used a water removal process to increase selectivity of alkyl polyglyceryl ether (AGEM) during the etherification of 1-dodecanol and glycerol over sulfonated silica catalysts, leading to yields of AGEM > 80% at 423 K.\textsuperscript{[50]}

The effectiveness of strong solid Brønsted acids for glycerol etherification reactions depends on several catalyst properties including hydrophilicity, accessibility, and thermal and mechanical stability. In a study of glycerol etherification with ethanol over solid-acid catalysts, Pariente et al.\textsuperscript{[123]} suggested that the hydrophobicity of the catalyst is an important factor in determining etherification activity. The authors found that strongly hydrophobic catalysts were less effective for glycerol etherification because they did not allow adsorption of glycerol; however, hydrophilic catalysts that adsorb glycerol too strongly also resulted in lower etherification rates. For example, Nafion NR50, a hydrophobic strongly Brønsted-acidic fluorinated sulfonated polystyrene resin, did not catalyze the etherification of glycerol but it did catalyze bimolecular etherification of the alcohol. The authors also studied the etherification of glycerol with ethanol over a series of zeolites with varying silica-to-alumina ratios and found that there is a tradeoff between the silica-to-alumina ratio and the etherification activity. As the alumina content was increased, a higher density of acid sites was generated, which contributed to an increase in the etherification rate; however, the surface also became more polar, thus decreasing the glycerol etherification rate due to the increased hydrophobicity. The authors found that a compromise could be achieved with zeolites with intermediate alumina content (Si/Al ratios around 25), which were the most effective for glycerol etherification. Amberlyst 15 and Amberlyst 35 were also effective for glycerol etherification at 433 K, with selectivities towards monoethoxy glyceryl ethers of 100% and 90% (remainder diethers) at glycerol conversions of 32% and 52%, respectively. While the zeolites were found to be active at 473 K and more thermally stable, they also exhibited lower selectivity. The tradeoff between selectivity and thermal stability of the catalyst is thus a concern for direct etherification of glycerol as well as for primary alcohols, as discussed earlier, as higher temperatures not only increase rates of etherification but also catalyze the unimolecular dehydration of alcohols to olefins, especially for substituted alcohols such as isobutanol, 2-propanol, and for Guerbet alcohols.

The accessibility of acid sites also plays a fundamental role in promoting catalyst activity, as it was found that catalysts with larger pore volumes are more active.\textsuperscript{[119]} The kinetics of glycerol etherification with alcohols depends greatly on the reactant concentration and temperature. For example, Frusteri et al. found that the molar ratio of alcohol to glycerol for tert-butanol etherification with glycerol over Amberlyst 15 did not affect the product distribution.\textsuperscript{[119]} However, Jaworski et al. reported that for the etherification of benzyl alcohol with glycerol over sulfonated zirconia, mono- and diether formation rates were first order in benzyl alcohol concentration, but benzyl alcohol self-condensation was second order with respect to benzyl alcohol.\textsuperscript{[119]} They also found that benzyl alcohol self-condensation had a higher activation energy than mono- and diether formation, suggesting an explanation for the higher selectivity towards cross-etherification at lower temperatures.\textsuperscript{[118]}

Several approaches can be considered to address the tradeoff between activity and selectivity that occurs with increasing temperature of etherification. Batch reactors coupled with water-permselective membranes can enhance ether selectivity by removing water. As temperature is increased, membrane effectiveness increases, but unimolecular dehydration of alcohols also increases.\textsuperscript{[122]} Therefore, developing stable membrane separators that are effective at lower temperatures could improve ether selectivity. Further modification of the acid–base properties of the catalysts could also enable tuning of product distributions for glycerol etherification. For example, Ruppert et al. found that the rates of etherification of glycerol to produce di- and triglycerides over CaO, SrO, and BaO at 533 K increase with increasing basicity of the catalyst.\textsuperscript{[124]} Understanding the role of Lewis acidity and basicity could enable the development of catalysts that optimize glycerol adsorption and reaction to form ethers.\textsuperscript{[125]}

### 4.2. Reductive etherification of alcohols with aldehydes, ketones, esters, and carboxylic acids

Asymmetrical ethers with and without branching are desirable as cetane boosters and as automotive lubricant base oils. As noted above, direct etherification of a branched alcohol and a linear alcohol is ineffective for the synthesis of asymmetrical branched ethers because substituted alcohols and alcohols with carbon chain branches on the α- and β-carbon atoms readily undergo dehydration. This method is also relatively ineffective for the synthesis of asymmetrical linear ethers because the alcohols will self-couple to generate symmetrical ethers. Reductive etherification of alcohols with aldehydes and ketones provides an alternative approach for producing high yields of symmetrical and asymmetrical ethers with a variety of structures and degrees of carbon chain branches.\textsuperscript{[16, 19, 126]}

Scheme 2a shows a general scheme for the reductive etherification of a carbonyl compound with an alcohol to produce an asymmetrical ether. The overall reductive etherification reac-
tion of an alcohol with an aldehyde or ketone to produce an ether and water occurs in the presence of $\text{H}_2$, a catalyst for $\text{H}_2$ activation, such as carbon-supported Pd, and an acid catalyst.

The heterogeneously catalyzed reductive etherification of aldehydes and ketones with an alcohol allows flexibility in the choice of both reactants, enabling the utilization of biomass-derived alcohols with carbon chain branches produced via the Guerbet reaction as well as carbonyl compounds obtained from a variety of biomass sources (Scheme 1). This method is therefore suitable for the selective synthesis of symmetrical or asymmetrical primary or secondary ethers. Reductive etherification of carbonyl compounds can also be performed using polyols such as glycerol to produce surfactants, fuel additives, and other value-added products.\(^{\text{127-129}}\) Drawbacks of the reductive etherification synthesis are the requirement of hydrogen and the use of precious-metal catalysts. In addition, there are some limitations to the scope of aldehydes for the synthesis; for example, the carbonyl group of an aromatic aldehyde can be reduced rapidly, thereby reducing the extent of etherification.\(^{\text{19}}\)

We recently demonstrated that a wide variety of ethers suitable for use as fuels and lubricants can be synthesized from biomass-derived platform molecules.\(^{\text{16}}\) Representative ethers prepared with high yields are shown in Table 6. These reactions were carried out at 393 K using a combination of Pd/C and $\text{H}_2$ as well as silica-supported 4-ethylbenzenesulfonic acid (EBSA/$\text{SiO}_2$). To utilize Guerbet alcohols, four equivalents of aldehyde or ketone were required per equivalent of alcohol.\(^{\text{16}}\) Amberlyst 15 was also an effective acid catalyst for this reaction. Unlike direct etherification, this method enabled the use of substituted alcohols and Guerbet alcohols, since dehydration of the alcohols to olefins is not observed. Thus, carbonyl compounds and alcohols can be selected independently to produce either symmetrical or asymmetrical ethers.

The mechanism of reductive etherification is not known, but it was proposed to proceed via hemiacetal or acetal intermediates (Scheme 3).\(^{\text{16, 19, 126}}\) The first step is the acid-catalyzed activation of the carbonyl group, which is followed by addition of an alcohol to form the hemiacetal or acetal intermediate. These intermediates can undergo hydrogenolysis to form ether directly or undergo a two-step process of acid-catalyzed dehydration or loss of alcohol followed by hydrogenation over Pd/C.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
Entry & Carbonyl (C) & Alcohol (A) & C/A & Ether & Yield [%]/(conversion of limiting substrate [%]) \\
\hline
1 & 2-heptanone & butanol & 1:4 & & 88/(100) \\
2 & 2-ethylhexanal & butanol & 1:4 & & 85/(100) \\
3 & 2-heptanone & 2-decyl-1-tetradecanol & 4:1 & & 91/(100) \\
4 & butanal & 2-decyl-1-tetradecanol & 4:1 & & 88/(97) \\
5 & isobutanal & 2-decyl-1-tetradecanol & 4:1 & & 86/(100) \\
6 & cyclopentanone & 2-decyl-1-tetradecanol & 4:1 & & 87/(100) \\
7 & 8-pentadecanone & 2-hexyl-decanol & 4:1 & & 88/(93) \\
8 & octanal & 2-decyl-1-tetradecanol & 4:1 & & 59/(94) \\
9 & 2-ethylhexanal & 2-decyl-1-tetradecanol & 4:1 & & 51/(79) \\
\hline
\end{tabular}
\caption{Conversion of biomass-derived carbonyl compounds and alcohols to ethers from Ref. [16].\(^{\text{a}}\)}
\end{table}

\(^{\text{a}}\) Reagents and conditions: carbonyl compound (2 or 8 mmol), alcohol (2 or 8 mmol), 5% Pd/C (2.5 mol%), EBSA/$\text{SiO}_2$ (entries 1, 2: 2.5 mol%; entries 3, 6, 7: 10 mol%; entries 4, 5, 8, 9: 5 mol%), 393 K, 1034 kPa $\text{H}_2$, 5 h.
In addition to the synthesis of lubricant-range ethers from biomass-derived alcohols, reductive etherification was employed for the synthesis of glycerol ethers (Scheme 2b). Lemaire and co-workers prepared glycerol ethers selectively via the reductive etherification of glycerol with aldehydes, ketones, carboxylic acids, methyl esters, and triglycerides. These reactions were performed with a combination of carbon-supported Pd, H₂, and an acid catalyst.

The mechanism for glycerol etherification with a carboxylic acid in the presence of molecular hydrogen proposed by Lemaire and co-workers is shown in Scheme 4. The major product is shown in green. Minor products involve the ether formed from the middle hydroxyl group as well as the unreduced ester. The proposed mechanism for etherification of glycerol with the methyl ester proceeds similarly, except that the hydroxy group is replaced with a methoxy group. Lemaire and co-workers also demonstrated that glycerol ethers can be produced from the reductive etherification of triglycerides directly with glycerol in a two-step process. First, glycerol and triolein are esterified using 10 wt% BaO/Al₂O₃ at 473 K, followed by reduction in 50 bar H₂ with 10 wt% Amberlyst 15 and 1 mol% Pd/C at 393 K, resulting in an isolated yield of 34% of the monoether.
4.3. Synthesis of ethers from furanics via direct and reductive etherification

Furfural and other furanic compounds have emerged as a class of useful platform molecules that can be readily produced from biomass via the dehydration of sugars derived from cellulose and hemicellulose or synthesized directly from biomass feedstocks.\textsuperscript{[75, 76, 130, 131]} Ethers obtained from these platform molecules, such as alkoxymethyl furfural, can be used as biofuels and specialty chemicals.\textsuperscript{[75, 132, 133]} Both direct and reductive etherification were employed to upgrade these synthons to furanylethers. Ethersification of furans with alcohols presents challenges similar to those for the direct ethersification of alcohols in terms of activity and selectivity. Undesired side reactions such as the unimolecular and bimolecular dehydration of alcohols make the task of synthesizing asymmetrical ethers challenging. In addition, there is a tradeoff between reaction rate and selectivity for producing ethers as increasing temperature improves total product yield but decreases selectivity for direct etherification.\textsuperscript{[134]} Several recent efforts by our group and others to produce ethers from both direct and reductive ethersification of furfural, furfuryl alcohol, and HMF are shown in Scheme 5. Below, we discuss recent efforts to synthesize furanylethers via direct ethersification of furanyl alcohols with linear alcohols, reductive etherification of furans with alcohols, and transfer hydrogenation/etherification reactions.

4.3.1. Direct etherification of ethanol and HMF

The direct etherification of furfuryl alcohol, HMF, and 2,5-bis(hydroxymethyl)furan (BHMF) with linear alcohols is represented in Scheme 5 by the dashed green lines. One reaction of particular interest is the direct ethersification of HMF with ethanol to produce EMF and ethyl levulinate (EL).\textsuperscript{[134–139]} Both products can serve as platform molecules for the synthesis of fuels and, hence, understanding which reaction conditions favor either EMF or EL production would enable the suitable choice of reaction conditions to make one of these two products. Table 7 summarizes the effectiveness of solid-acid catalysts for selective production of EMF or EL and compares the yields with those obtained using sulfuric acid.

In a study on the ethersification of HMF with ethanol, Lanzafame et al.\textsuperscript{[135]} suggested that the selectivity to EMF or EL is determined by the presence of either Lewis or Brønsted acidity, respectively. They achieved EMF yields of 76% and EL yields of 23% at 100% conversion of HMF for the direct ethersification of HMF with ethanol over Zr-modified SBA-15 (Z-SBA-15) for 5 h at 413 K. Under the same reaction conditions but using Amberlyst 15 as the catalyst, they observed a >99% yield of EL at 100% conversion of HMF.\textsuperscript{[135]} In fact, they found that purely Brønsted-acidic catalysts, such as H\textsubscript{2}SO\textsubscript{4}, Amberlyst 15, and Al-MCM-41 (Si/Al 25), favored formation of EL. However, introduction of Lewis acid sites, such as Zr\textsuperscript{4+} into SBA-15 or extra-framework-isolated Al\textsuperscript{3+} sites in Al-MCM-41 (Si/Al 50), resulted in higher selectivity to EMF.\textsuperscript{[132]}

Our group and others showed that high selectivities towards EMF can be achieved using the Brønsted-acid catalyst Amberlyst 15. We observed EMF yields of over 55% from the ethersification of HMF and ethanol at 348 K for 24 h.\textsuperscript{[134]} Similarly, Che et al. observed EMF yields of over 62% for the ethersification of HMF and ethanol at 363 K for 2 h.\textsuperscript{[138]} Ether formation is favored at lower temperatures, which suggests that to produce EMF in high yields longer reaction times and lower temperatures are preferred; under such conditions, Lewis acid sites are not needed to produce EMF selectively. Amberlyst 15 is an excellent candidate for carrying out reactions at lower tempera-

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Scheme5.png}
\caption{Synthesis of furanylethers via direct and reductive ethersification of biomass-derived platform molecules. References are noted in brackets.}
\end{figure}
In addition to ethanol, direct etherification of HMF over solid-acid catalysts was achieved with other alcohols, such as 1-butanol, 2-butanol, tert-butanol,[143,144] and linear C₄-C₁₈ alcohols.[145,146] For example, Arias et al. investigated the cross-etherification of C₄-C₁₈ n-alcohols with HMF to produce asymmetrical ethers for applications as biodegradable surfactants over zeolites H-BEA, HY, H-MOR, H-MFI, ITQ-2, and MCM-41 at 373 K.[47] This work identified H-BEA as an effective catalyst, enabling the attainment of ether yields over 92%.

HMF can also undergo self-etherification to produce 5,5'-oxy(bis-methylene)-2-furaldehyde (OBMF), a useful precursor for the synthesis of crown ethers, polyurethanes, polyamides, and other polymers.[144] Sn-montmorillonite gave almost complete conversion of HMF with 98% selectivity to OBMF using nonpolar aprotic dichloroethane as a solvent at 373 K.[141]

### 4.3.2. Direct etherification of furfural and methyl furfural with ethanol

The direct etherification of furfural with ethanol or methanol to produce alkyl tetrahydrofurfuryl ether can also be achieved over solid-acid catalysts. Cao et al. demonstrated that H-MFI (Si/Al 25) was effective in the etherification of furfuryl alcohol with methanol and ethanol, obtaining selectivities to methyl furfural ether and ethyl furfuryl ether of 58.9% and 44.8%, respectively, at 298 K for 24 h using methanol or ethanol as the solvent.[142]

Methyl furfuryl alcohol (MFA) can be produced from HMF via selective hydrogenation over a Ru–MoOₓ/C catalyst.[143] The etherification of MFA with ethanol to produce 2-(ethoxymethyl)-5-methylfuran (EMMF) was achieved over Amberlyst 15. Recent work in our group demonstrated EMMF selectivities and yields of over 98% over Amberlyst 15 at 298 K.[144] Amberlyst 15 was also effective for the direct etherification of other alcohols such as butanol and other furans (e.g., BHMF). It was proposed that the high selectivity towards asymmetrical ethers is achieved through the formation of a solvation shell of polar C₄–C₈ alcohols that form around the active site of the catalyst, enhancing the cross-coupling reaction (Figure 6).[144]

### 4.3.3. Direct etherification of BHMF

Amberlyst 15 and zeolites are effective for the direct etherification of furan compounds with alcohols. For the direct etherification of BHMF with ethanol, yields of up to 80% 2,5-bis(ethoxymethyl)furan and 6% [5-(ethoxymethyl)furan-2-yl)methanol can be achieved.
thanol were achieved using 5 mol% catalyst loading of Amberlyst 15 at 313 K for 16 h.\[134\] Etherification of 2,5-bis(methoxymethyl)furan (BMFF) and BHMF with methanol is also highly selective over zeolites. Fang et al. achieved ether selectivities of over 95% over 1.5% Sn-ZSM-5 at 338 K.\[145\] The authors suggest that the main and side reactions, such as furan ring opening and polymerization, are dictated by pore structure as well as synergistic effects between Brønsted and Lewis acidity.\[146\]

4.3.4. Reductive etherification of HMF, furfural, alkoxymethyl furfural, and levulinic acid with alcohols

The cross-etherification of alcohols is limited by the tendency of branched alcohols, such as isopropanol, to undergo unimolecular dehydration, as discussed in Section 4.1. One way to suppress this side reaction and improve the selectivity to cross-etherification products is to employ reductive etherification. Some examples of reductive etherification routes to producing ethers from furans are illustrated in Scheme 5 by the dotted red lines. We used reductive etherification for the production of 2,5-bis(alkoxymethyl)furan via the reaction of HMF with ethanol and butanol.\[134\] Yields of the diether [2,5-bis(ethoxymethyl)furan] of up to 59%, with 7% of the monoether [5-(ethoxymethyl)furan-2-yl)methanol] and 1% 2-(diethoxymethyl)-5-(ethoxymethyl)furan, were produced using 5 mol% Amberlyst 15 and 1 mol% Pt/alumina at 348 K for 24 h in the presence of 200 psi H₂. Wu et al. demonstrated that Pd supported on TiO₂, Al₂O₃, SiO₂, and active carbon are also effective for the reductive etherification of furfural with ethanol at 333 K with 0.3 MPa of H₂.\[146\] Yields of up to 81% of furfuryl ethyl ether (FEE) were obtained over 0.7 wt% Pd/C with minor formation of 2-(diethoxymethyl)furan (4%), furfuryl alcohol (10%), and tetrahydrofurfuryl alcohol (3%).\[146\] The authors suggested that palladium hydride, formed in situ, catalyzes the formation of the key intermediate, 2-(diethoxymethyl)furan.\[146\] They also suggested that the key to achieving a high yield of ether is the balance between the proton-donating ability and hydrogenolysis activity of palladium hydride, which requires tuning of Pd loading, hydrogen pressure, and reaction temperature.\[146\]

Reductive etherification of alcohols with levulinic acid or ethyl levulinate can also be employed for the synthesis of sustainable nonvolatile organic compounds as solvents or biofuels.\[142,148\] Recent efforts revealed that methanol, ethanol, n-butanol, and n-heptanol can undergo reductive etherification with levulinic acid to produce alkyl 4-alkoxypentanoates (4-alkoxyvalerates) in 54–77% yield under hydrogen at 473–493 K and 1000 psig in the presence of a Pd/C catalyst.\[147\] Introducing acidity improved the yield and selectivity of ethyl-4-ethoxy-pentanoate (EEP) by reductive etherification of ethanol with ethyl levulinate at 413 K; addition of zeolite beta as a co-catalyst with Pd/SiO₂-carbon enabled the attainment of EEP yields of 93% at 100% conversion of ethyl levulinate.\[146\]

4.3.5. Etherification via transfer hydrogenation for the synthesis of furanyl ethers

Transfer-hydrogenation etherification has also emerged as a method of synthesizing furanyl ethers. A few illustrations of HMF etherification by transfer hydrogenation are presented in Scheme 5 by the dotted blue lines. In this case, the alcohol serves as the solvent, reactant, and hydrogen-transfer agent. Jae et al.\[149\] demonstrated that Lewis-acidic Sn-BEA and Zr-BEA are effective catalysts for the transfer hydrogenation and etherification of HMF with 2-propanol and 2-butanol at 453 K. Yields of over 80% of 2,5-bis(isopropoxymethyl)furan were reported. They proposed a mechanism and reaction pathway for the formation of 2,5-bis(alkoxymethyl)furan from HMF via direct etherification and etherification via transfer hydrogenation using isopropanol.\[149\] This reaction pathway is shown more generally for alcohols in Scheme 6. HMF is first converted to BHMF via transfer hydrogenation by an alcohol. BHMF then undergoes direct etherification with another alcohol molecule to produce the monoether and a second etherification with another alcohol molecule to produce the diether.\[149\] The proposed rate-limiting step is the Meerwein–Ponnendorf–Verley (MPV) conversion of HMF to BHMF via hydrogen transfer from the alcohol. Román-Leshkov and co-workers also identified Lewis-acidic zeolites as effective catalysts for the coupled transfer hydrogenation and etherification of HMF with ethanol and butanol at 393 K for 24 h and 791 kPa in a 100 mL stainless-steel Parr reactor.\[49\] The authors found that Sn-BEA showed the highest stability and selectivity for etherification whereas Hf-BEA and Zr-BEA appeared to be more active for the MPV reduction. Hard Lewis-acid centers, such as Zn and Sn, were found to be particularly effective in stabilizing the transition state of the rate-limiting hydride-transfer step whereas the weaker Lewis-acid centers, such as Ti and Ta, were less effective in catalyzing hydrogen transfer.\[49\] Primary alcohols are less likely to donate a hydrogen atom as 2-butanol is more effective than 1-butanol.\[49\] Thus, for the etherification of sub-
stituted alcohols with furans, hydrogen-transfer reductive etherification is an attractive option. Still, it is important to note that etherification via transfer reductive hydrogenation is typically done in a batch reactor to support the hydrogen-transfer step, which can limit the process scalability and increase the concentration of water in the vessel, thus inhibiting both the transfer hydrogenation and etherification reactions.

**4.4. Etherification by alcohol addition to an olefin**

Branched ethers produced by the addition of an alcohol to an olefin, such as MTBE, ETBE, tert-amyl methyl ether, and tert-amyl ethyl ether (TAAEE), are useful fuel additives that can be generated from biomass-derived molecules. During the direct etherification of tert-butanol with linear alcohols, tert-butanol tends to favor dehydration to isobutene, producing water, thereby reducing ether selectivity. The reaction of an alcohol and an olefin to yield an ether is stoichiometric; however, there are many challenges to the synthesis of ethers by the addition of an alcohol to an olefin. These include reactor design, side-product formation, and product inhibition. This section discusses these challenges and identifies how the yield of the desired ether products can be improved.

One key challenge in the reaction of olefins with alcohols is the fact that for gaseous olefins, such as isobutene, the reaction cannot be performed in a single phase. For example, the formation of methyl tert-butyl ether is often completed in a two-step process: isobutanol is first dehydrated over a SiO₂–Al₂O₃ catalyst at 498 K, then reacted with isobutene over Amberlyst 15 at 323 K, achieving a yield of MTBE and methyl isobutyl ether (MIBE) of approximately 28% with a MTBE/MIBE ratio of 11.7:1.\(^{[150]}\) Not only is the ether selectivity fairly low but the second step involves either bubbling a gas through a liquid, which introduces mass-transfer limitations, or operating at higher pressure to keep all reactants in the liquid phase.\(^{[151]}\)

The formation of side products is also a key concern as isomerization and dimerization of olefins, as well as alcohol dehydration, adversely affect selectivity to the desired ethers. Scheme 7 provides an overview of the reaction pathway and side products formed from the addition of primary alcohols to linear olefins. In the presence of an acid catalyst, olefins can undergo oligomerization, producing higher carbon-number products that can further oligomerize and contribute to coke formation and, hence, catalyst deactivation. In addition, alcohols can undergo unimolecular dehydration to form olefins or direct etherification to form symmetrical ethers. When olefins are reacted with glycerol or polyols, the polymerization of the alcohols to polyethers is also a concern. As shown in Scheme 7, primary olefins can readily isomerize to form secondary olefins,\(^{[151]}\) which can also react with alcohol to produce a variety of ether products depending on which side of the double bond the alcohol adds to. Karinen et al. found that as the temperature was increased from 333 to 353 K, the ratio of olefin isomerization to etherification increases for reactions of methanol, ethanol, 1-propanol, 1-butanol, 2-butanol, and isobutanol with 2-methyl-1-butene and 2,4,4-trimethyl-1-pentene over Amberlyst 15.\(^{[151]}\) Other authors suggested that isobutene dimerization over Amberlyst 35 and Purolite CT-275 increases with increasing temperature and increasing olefin-to-alcohol ratio.\(^{[152]}\) For side reactions involving alcohol dehydration, the production of water presents additional challenges. Water can readily react with 1,1-disubstituted olefins to form tertiary alco-
and thereby inhibit active sites on the catalyst, decreasing rates of both isomerization and etherification.

The challenges noted above can be overcome in several ways to control product selectivity. These include the choice of catalyst, the ratio of olefins to alcohols, the choice of alcohol and olefin structures, the temperature, and water removal. Scheme 8 shows some sample reactions of olefins with alcohols to produce useful ether products. Amberlyst 35 is an effective catalyst for producing asymmetrical ethers from a variety of alcohols and olefins. As shown in Scheme 8a, glycerol can be reacted with isobutene to form mono-, di-, and tri-tert-butyl ethers. Klpačková et al. reported yields of di- and triethers from glycerol of up to 89% at 100% conversion of glycerol at 333 K and demonstrated that Amberlyst 35 is highly selective for the etherification of isobutene with ethylene glycol compared with para-toluene sulfonic acid (p-TSA) and large-pore zeolites H-Y and H-BEA. Karinen and Krause found that for the etherification of glycerol with isobutene over Amberlyst 35, optimal selectivity towards ethers was achieved with an isobutene-to-glycerol molar ratio of 3:1 at 353 K. By controlling the reaction conditions, it is possible to tune the distribution of ethers to match desired fuel blends, thus avoiding costly separations. As mentioned in Section 2, di- and tri-tert-butyl glyceryl ethers are preferred for diesel blends because of their solubility in diesel fuel and their properties such as viscosity and cloud points. Klpačková et al. found that the highest yields of di- and tri-tert-butyl glyceryl ethers were achieved over Amberlyst 35. Although glycerol conversion was highest over zeolite HBEA, the reaction to form tri-tert-butyl glycerol ether was sterically hindered; thus, the selectivity was low. The reaction of isobutene with ethanol or butanol produces ETBE and butyl-tert-butyl ether (BTBE), respectively, as shown in Scheme 8a. Tejero et al. found Amberlyst 35 to be the most effective catalyst for this reaction compared to Amberlyst 16, Amberlyst 39, Amberlyst 46, Amberlyst 70, and Purolite CT-275, at temperatures between 315 and 353 K. Amberlyst 35 was also effective for the etherification of 2-methyl-1-butene and 1-octene. Check the reviews.
2,4,4-trimethyl-1-pentene with various C_{3}-C_{6} alcohols between 333 and 353 K in the liquid phase (Scheme 8c)\cite{155} and for the etherification of C_{5}-olefins with methanol in the liquid phase between 323 and 363 K.\cite{113}

Badia et al. suggested that Amberlyst 35 is the most promising catalyst because of its strong acidity and rigid polymer backbone, which enhance the reaction rate.\cite{117} However, according to Ruppert et al., catalyst hydrophilicity and pore structure are the most critical catalyst properties for achieving high ether selectivity.\cite{158} While Bajus et al. suggest that H-BEA is not effective for etherification reactions of olefins and alcohols,\cite{154} Ruppert et al.\cite{158} reported that H-BEA is to be more selective for the etherification of glycerol and other glycols with 1-octene, 1-dodecene and 1-hexadecene compared to Amberlyst 70, p-TSA, H-Y, USY, and H-MFI (Scheme 8d). Using H-BEA, selectivities towards mono- and diocetyl ethers from glycols such as ethylene glycol and 1,2-propylene glycol of up to 85–95% were achieved at glycol conversions between 15–20% at temperatures between 393 and 413 K.\cite{158} Silica-supported sulfated zirconia, Amberlyst 16W, and Amberlyst 15 were also employed as catalysts for the reactions of C_{6} olefins with methanol (Scheme 8b),\cite{159} etherification of isomylanes (2-methyl-1-butene and 2-methyl-2-butene) with methanol, ethanol, and n-propanol (Scheme 8c)\cite{40} and isobutene with butanol (Scheme 8a),\cite{160} respectively, for temperatures between 333 and 353 K. Although zeolites introduce pore-volume constraints, they are thermally stable above 423 K, unlike Amberlyst 35 and Amberlyst 16. Still, the majority of alcohol additions to olefins are performed between 323 and 363 K, which is well within the range of thermal stability of resin catalysts. The catalysts that are effective for the etherification of olefins with alcohols contain large pore volumes or no pores and have high acid capacities, suggesting that Amberlyst 35 is a promising candidate for these reactions.

The ratio of alcohol to olefin strongly affects the kinetics of the reaction. Hatchings et al. observed that the kinetics of etherification varies with the ratio of reactants.\cite{161} For the reaction of isobutene with methanol or n-butanol over Amberlyst 15, at lower isobutene-to-alcohol ratios, the rate of etherification is zero order in alcohol and first order in olefin whereas at higher alcohol to isobutene ratios the reaction is first order in alcohol and zero order in olefin. These observations suggest that when the surface is saturated with alcohol, the rate-limiting step is the protonation of the olefin by the solvated proton, and when the surface is saturated with olefin acids coordinated to the sulfonic acid groups the rate-limiting step is the interaction of the olefin with the alcohol.\cite{161}

Scheme 9 shows a proposed mechanism for the reaction of isobutene with an alcohol and demonstrates how solvated alcohols can assist in the protonation of the olefin. In the general mechanism suggested by Tretbar et al. the olefin is first protonated by the acid site, leaving a stabilized carbocation intermediate, which then accepts electrons from the oxygen atom of the alcohol, forming a protonated ether, which, in turn, desorbs in the final step to form the asymmetrical ether.\cite{160} The upper pathway in Scheme 9 shows how the alcohol can be protonated by the acid site and then proceed to readily donate an acidic hydrogen to the olefin. For this mechanism, the rate-limiting step would be protonation of the olefin, resulting in a first order dependence of the rate of etherification on the olefin concentration. This conclusion is consistent with the observation that the reaction is first order in olefin and zero order in alcohol at low isobutene-to-alcohol ratios.\cite{45,150,161}

The alcohol structure also affects the mechanism for the addition of an alcohol to an olefin. Ancillotti and Fattore suggested that when isobutene is reacted with higher alcohols, the reactivity order is related to the alcohol basicity, which dictates the proton-transfer ability of ROH.\cite{162} Therefore, in the case where the alcohol-to-olefin ratio is greater than or equal to one, the alcohol acts as a solvent. Karinen et al. showed that etherification and dehydration rates increase with decreasing alcohol polarity and with increasing carbon number of the alcohol, owing to the acidity and Mulliken charges of the oxygen atom of the alcohol.\cite{153} The groups of Scurrrell and Rognoni also point out that the higher reactivity of n-butanol over methanol for etherification of tertiary olefins over Amberlyst 15 reflects the higher acidity of the proton on n-butanol than on methanol.\cite{161,163} The authors suggest that the excess of alcohol breaks up the network of hydrogen-bonded sulfonic acid groups, which aids in solvating and, hence, dissociating the proton.\cite{161} By contrast, Linnekoski et al. found that methanol, ethanol, and 1-propanol affect the rate of olefin isomerization but not the etherification rate for alcohol addition to isomylanes.\cite{40} This trend was explained by the fact that 2-methyl-1-butene isomerizes to 2-methyl-2-butene more rapidly in the presence of more acidic protons caused by more basic alcohols. The more substituted olefin, 2-methyl-2-butene, is more stable and thus less reactive for etherification, so the effects of increased acid strength cancel each other out, resulting in no net change in the etherification rate. The solvation effects of alcohols are consistent with the mechanism proposed in Scheme 9, in which the rate-limiting step for etherification is the protonation of the olefin.

In addition to the choice of alcohol, the choice of olefin also contributes to the reaction kinetics. The more volatile the
olefin, the more pressure must be applied to maintain a liquid phase reaction. Generally, the longer the chain length the lower the volatility. The selection of isomer also affects the reaction rate because olefin isomers that are thermodynamically favored at equilibrium have a lower reactivity for etherification. Selecting less-substituted olefins can increase etherification rates, although isomerization is likely to occur. Karinen and Krause found that etherification rates of olefins with methanol were lower for olefins with longer carbon chains (C₅) compared to shorter chains (C₁). In addition, they found that the equilibrium between 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene was affected by steric hindrance, which is another concern when selecting an olefin for this reaction.

Temperature has a clear effect on ether selectivity. As discussed earlier, the optimal temperatures for etherification of olefins with alcohols is between 323 and 363 K. The tradeoffs between catalyst activity and selectivity are critical in optimizing for ether formation. In a prospective study by Soto et al. the equilibrium conversion, selectivity, and yield were optimized using a combination of experimental and numerical multiojective optimization to determine conditions most favorable for the liquid-phase etherification of isobutene and isomylene by addition of ethanol over Amberlyst 35. That study concluded that the optimal experimental conditions for maximizing the simultaneous production of ETBE and TAAE occurred for molar alcohol-to-olefin ratios of 0.9, C₅-to-C₁ olefin ratios of 0.5, and at a temperature of 323 K.

In summary, the reaction of alcohols with olefins produces asymmetrical ethers with a high degree of branching for use as fuel additives. Under the right conditions, high yields of mono- di- and triethers of glycerol with olefins as well as cross-coupling of monoolcohols with olefins can be achieved. Although this method of producing ethers could be employed to produce symmetrical linear ethers, the tendency for olefins to undergo isomerization and oligomerization suggests that direct etherification of alcohols is more appropriate for obtaining high selectivities towards linear symmetrical ethers. Thus, this reaction is best employed when the olefin is highly substituted and the desired product is an asymmetrical ether.

5. Role of Cooperative Brønsted and Lewis Acidity in Selective Ether Synthesis

Recent studies of alcohol etherification and dehydration over solid acids indicated that by tuning the strength and ratio of Brønsted and Lewis acid sites on the surface of the catalyst, the selectivity of the reaction can be adjusted. As mentioned in Section 4.1, our group has proposed that cooperative effects between Brønsted and Lewis acid sites on WO₃/Al₂O₃ promote the bimolecular etherification of 1-dodecanol to form didodecyl ether. Padovan et al. suggested that bifunctional Brønsted and Lewis acidic zeolites facilitate the production of butoxy methyl furan via the etherification of furfural and 2-butanol. They found that a bifunctional H-BEA containing 2 wt% Sn and 0.5 wt% Al gave high ether selectivity (>75%) and exhibited excellent stability. By contrast, monofunctional analogues or physical mixtures of the analogues were less selective and stable. Fang et al. also found that Sn-MFI was effective for the etherification of BHMF with methanol to produce BMMF, achieving a selectivity of 95%. The authors found that BMMF formation increased with increasing Lewis acidity of the catalyst.

Several studies revealed that the ratio of Brønsted-to-Lewis acid sites on the surface of a catalyst can be tuned to adjust the product distribution for glycerol dehydration reactions. Wang et al. studied the dehydration of glycerol to acrolein over Al/H-ZSM5 zeolite catalysts and suggested that a cooperative effect between Brønsted and Lewis acid sites on the surface of the catalyst is responsible for the high acrolein selectivity. Foo et al. studied the role of Lewis and Brønsted acid sites in the dehydration of glycerol over niobia and concluded that a higher ratio of Brønsted acid sites to Lewis acid sites results in higher acrolein selectivity, whereas a larger ratio of Lewis-to-Brønsted acid sites results in higher selectivity towards hydroxyacetone. Cooperative effects between Brønsted and Lewis acid sites on Sn-Beta were also proposed for ethanol dehydration. For example, Bukowski et al. proposed a concerted transition state involving both the Lewis-acidic Sn center and an adjacent weakly Brønsted-acidic framework silan group.

Because there is precedent for the role of Brønsted and Lewis acidity in controlling etherification and dehydration selectivity over metal oxides, the investigation of tuning Brønsted and Lewis acid sites by varying the ratio of Brønsted-to-Lewis acid sites, changing the strength of Lewis acid centers by varying the metal cations, and changing the density of Brønsted acid sites is a promising avenue for future improvement of ether selectivity that is not afforded by Brønsted-acidic polymeric resins.

6. Conclusions and Outlook

We have shown that ethers suitable for use as fuels, lubricants, and specialty chemicals can be synthesized from a variety of biomass-derived platform molecules through direct and reduc-tive etherification of alcohols, aldehydes, ketones, esters, carboxylic acids, and olefins. The best strategy for synthesizing ethers from biomass-derived compounds using heterogeneous catalysts depends on the structure of the reactants and the properties of the catalyst. In this Review, we have outlined the advantages and disadvantages of various methods for producing ethers from renewable sources. Here, we summarize the recommended synthesis routes for producing a particular type of ethers from a defined set of reactants.

Symmetrical ethers can be formed from linear alcohols via direct etherification over a solid acid, using the reactant alcohol as the solvent, at low temperatures and with minimal side-product formation. If there are carbon-chain branches on the alcohol, direct etherification is still viable as long as the branches are at least three carbon atoms away from the hydroxyl group of the alcohol. If mixtures of symmetrical and asymmetrical linear ethers are desired, direct etherification of a mixture of linear alcohols is a viable synthetic route. However,
if purely asymmetrical ethers are desired, we recommend reductive etherification of an alcohol and an aldehyde or ketone in the presence of a solid-acid catalyst and a hydrogenation catalyst, such as Pd/C. This method enables selective synthesis of asymmetrical or symmetrical ethers from alcohols with a significantly larger range of structures including branched alcohols, such as those produced from the Guerbet reaction, to create lubricant-range molecules, as well as secondary and tertiary alcohols for use as diesel and gasoline additives. Reductive etherification can also be used to prepare ethers via the reaction of alcohols with esters and carboxylic acids, and both direct and reductive etherification can also be employed for the valorization of glycerol and polyols for the synthesis of fuel additives and specialty chemicals.

Fuel additives can also be produced via direct, reductive, and transfer hydrogenation etherification of furfural and furans derived from biomass. For these methods, we discussed the reaction pathways and conditions for selective synthesis of the desired ethers based upon recent developments in the literature. Amberlyst 15 and zeolites stand out as selective catalysts for the direct etherification of ethanol with hydroxymethyl furfural. Amberlyst 15 is also an effective catalyst for the etherification of furfural or methyl furfural with ethanol and for the direct etherification of 2,5-bis(hydroxymethyl)furan (BHMF) with alcohols. Low temperatures and longer reaction times are preferred for these reactions. Reductive etherification of furans enables enhanced selectivity towards cross-etherification by limiting homocoupling of alcohols and can be achieved using a combination of an acid catalyst, Pd/C, and H₂ for reduction. For the etherification of substituted alcohols with furans, transfer-hydrogenation etherification is also a viable option as the alcohol can be used as both the reducing agent and the reactant, eliminating the need to supply molecular hydrogen.

The addition of an alcohol to an olefin is another method of producing ethers. The selectivity to ether in this reaction depends on avoidance of alcohol dehydration. This can be achieved by operating at temperatures between 323 and 363 K and using Amberlyst 35 as a catalyst. This synthesis method is most effective for the etherification of alcohols with highly substituted olefins, such as the synthesis of ethyl-tert-butyl ether.

Brensted-acidic resins with large pores that swell in the presence of solvent such as Amberlyst 70 are effective in promoting etherification of alcohols by increasing the concentration of alcohol around the active site. A high local concentration of alcohol can also be achieved using bifunctional catalysts that contain proximate adsorption sites for alcohols, such as the Brensted and Lewis acid sites on WO₃/ZrO₂. Future directions in employing tandem catalysts, tuning pore sizes, and identifying the site requirements for side reactions could enable finer enhancements of selectivity for both direct and reductive etherification reactions. Another promising approach, particularly for the synthesis of asymmetrical ethers via direct etherification, is the use of so-called “heterogenized” homogeneous acid catalysts. For example, the homogeneous cationic ruthenium-hydride complex [(C₆H₅)(PCy₃)(CO)RuH]⁺BF₄⁻ (PCy₃ = tricyclohexylphosphine) is known to catalyze the selective etherification of two different alcohols to form asymmetrical substituted ethers with a large scope of substrates and without the need for reactive reagents or protecting groups. Developing heterogeneous catalysts that enable selective asymmetrical ether synthesis without the need for reductive etherification could lower costs associated with operating under hydrogen pressure and would allow more flexibility in the choice of alcohol substrates.

The removal of water is also a major consideration in the synthesis of ethers, as water inhibits active sites for etherification, thus lowering the etherification rate and selectivity. Investigation into water removal with membranes and reactive distillation with recirculation is a physical method of improving ether yields. Further investigation into tuning feed ratios for direct and reductive etherification may also elucidate pathways towards producing blends of ethers for fuel and lubricant applications. Moving forward, investigation of multi-step processes for synthesizing ethers directly from biomass will be necessary to provide further insights into developing industrially relevant processes for synthesizing renewable ethers. Overall, these recent efforts to synthesize ethers from renewable sources using sustainable heterogeneous catalysis provide a vast scope of pathways towards utilizing biomass-derived platform molecules and have the potential to enable the production of fuels, lubricants, and specialty chemicals that could replace petroleum-derived products at low cost and with reduced adverse environmental effects.

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Conflict of interest

The authors declare no conflict of interest.

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