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Novel insights on biomass delignification with acidic deep eutectic solvents: a mechanistic study of β-O-4 ether bond cleavage and the role of the halide counterion on the catalytic performance.

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Abstract

The development of innovative technologies for an efficient, yet eco-friendly, biomass delignification is required to achieve higher sustainability than traditional processes. In this context, the use of deep eutectic solvents (DES) for the delignification process could fulfil these requirements and stands today as a promising alternative.

This work focuses on understanding the fundamental chemistry behind the cleavage of β-O-4 ether bond present in 2-phenxy-1-phenylethanol (PPE), a lignin model compound, with three acidic DES, including Propionic acid/Urea (PA:U), Lactic acid/Choline Chloride (LA:ChCl) and p-Toluenesulphonic acid/Choline chloride (pTSA:ChCl). The acidic nature of each DES influenced the efficiency of PPE cleavage and determined the extent of further side reactions of cleavage products. Although PA:U (2:1) demonstrated ability to dissolve lignin, it is unable to cleave β-O-4 ether linkage in PPE. On the other hand, LA:ChCl (10:1) allowed PPE cleavage, but an esterification between the PPE and lactic acid as well as oligomerization of lactic acid were detected. Among examined solvents, pTSA:ChCl (1:1) demonstrated the highest performance on the PPE cleavage, although the high acidity of this system lead to condensation of cleavage products at prolonged time. The presence of water decreases the ability of DES for the cleavage, but the extension of undesired side reactions was also reduced.

Finally, the analysis of intermediates and products of the reactions allowed the identification of a chlorinated species of PPE that precedes the cleavage reaction. A kinetic study using pTSA:ChCl (1:1) and pTSA:ChBr (1:1) was performed to unveil the role of the halide counterion present in DES on the cleavage of β-O-4 ether bond and a new reaction mechanism was herein proposed and supported by density functional theory (DFT) calculations.

Keywords

Deep eutectic solvents, lignin model compound, ether bond cleavage, reaction mechanism, sustainable delignification.
1. Introduction

Lignin is one of the major components of lignocellulosic biomass (15-40 wt%) and after cellulose is the second most abundant resource in nature.\(^1\) It consists of branched phenylpropanoid units, including \(p\)-coumaryl, coniferyl and sinapyl alcohols linked through different C-O and C-C bonds.\(^2\)

The carbon atoms in the aliphatic side chains of phenylpropane units are usually labelled as \(\alpha\), \(\beta\) and \(\gamma\), while those in the aromatic ring are numbered from 1 to 6. Based on this nomenclature, the major linkages between lignin building blocks are \(\beta-O-4\), \(\beta-\beta\) and \(\beta-5\). Minor linkages, like \(\alpha-O-4\) and \(\beta-1\), are also present.\(^3\) Due to its aromatic character, lignin has been drawing attention as raw material to produce fuels, chemicals and materials in the frame of the biorefinery concept to replace overused aromatic hydrocarbons stemming from fossil resources.\(^4,5\)

The cleavage of lignin chemical linkages, along with the disruption of lignin-polysaccharide bonds, allows the lignin extraction from biomass in a process called delignification. The type and extent of delignification dictates the size of the extracted lignin macromolecules as well as its chemical composition and modification. Therefore an efficient delignification is one of the key steps on the entire biomass valorisation chain and has a direct impact on the quality of lignin for further conversion and commercialization.\(^6,7\) Amongst lignin chemical linkages, aryl ether bonds (\(\beta-O-4\)) are the most abundant and can reach more than 50% content of all bonding motifs.\(^8\)

This type of linkage is stable (52–75 kcal·mol\(^{-1}\)) and often requires high energy towards cleavage.\(^9\) In this sense, an efficient and selective disruption of \(\beta-O-4\) ether bond is a challenge to overcome, where the use of catalysts is crucial as their unique properties enable to control the activation routes of cleavage. However, the use of hazardous and toxic catalysts is usually approached in traditional delignification technologies, such as Kraft (NaOH and Na\(_2\)S),\(^10\) soda (NaOH)\(^11\) and sulphite (e.g. Mg(HSO\(_3\))\(_2\))\(^12\) to produce high quality cellulose fibres. Other disadvantages including lack of selectivity in the chemical cleavage and high energy demand for delignification have been also pointed out in these technologies.\(^5\) Although delignification is efficiently achieved with those processes, the last drawbacks lead to low quality lignin samples
with highly dispersed molecular weights, high condensation degrees and contamination with sulphur, which compromises further application. A possible solution lies in addressing selective and sustainable technologies where the application of green solvents, catalysts and reagents is imperative to surpass those limitations.

The cleavage of \( \beta-O-4 \) ether bonds in lignin and lignin model compounds has been approached by heterogeneous and homogeneous catalysis.\(^5\)\(^,\)\(^13\) The engagement of supported or unsupported metal catalysts, including Pd,\(^8\) Ce,\(^14\) V,\(^15\) Ni,\(^9\) Cu\(^16\) and Ru\(^17\) are some successful examples of heterogeneous catalysis. However, once the surface of the catalyst is saturated with lignin fragments, the reaction cannot proceed for a new turn making it as a disadvantage.\(^18\) In this context, homogeneous catalysis is probably a suitable alternative since the reaction occurs solely in a liquid phase, thus reducing mass transfer limitations. Moreover, a metal-free and a less costly catalyst looks advantageous for application in these processes.\(^19\)

Ground-breaking homogeneous catalysis for lignin depolymerization within a green framework have been developed with Ionic Liquids (ILs) that can act as both solvent and catalyst. Although lignin oxidative cleavage has been shown elsewhere using non-acidic ILs,\(^19\) the cleavage of lignin ether bonds promoted by acidic ILs is the most common approach and it has been well scrutinised in literature.\(^19\)\(^–\)\(^25\) Ekerdt and co-workers were the first to try acidic cleavage of lignin model compounds, guaiacylglycerol-\(\beta\)-guaiacyl ether (GG) and veratrylglycerol-\(\beta\)-guaiacyl ether (VG), with 1-H-3-methylimidazolium chloride ([Hmim]Cl).\(^20\)\(^,\)\(^21\) The researchers described a \( \beta-O-4 \) ether bond cleavage of model compounds by an acid-catalysed dehydration and coupling in the first place, forming intermediates. Afterwards, a molecule of water attacks the \( \beta \)-carbon of the intermediates allowing for ether bond cleavage.\(^20\) Another work showed that 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]HSO\(_4\)) was able to disrupt the ether bond from benzyl phenyl ether (BPE).\(^22\) The Bronsted acid character of this IL demonstrated high efficiency in BPE cleavage, but degradation of hydrolysis products (e.g. phenol) was also detected.\(^22\) On the other hand, acidic SO\(_3\)H-functionalized imidazolium ILs demonstrated high ability to perform
cleavage of 2-(2-methoxyphenoxy)-1-phenylethanol (MPPE)\textsuperscript{23} and VG.\textsuperscript{25} Jing \textit{et al.} referred to an unconventional E1 elimination with five successive steps: i) protonation-dehydration; ii) $\beta$-H elimination; iii) protonation; iv) hydroxylation; and v) $\beta$-O-4 bond cleavage.\textsuperscript{25} The authors highlighted the first step as the limiting one and the IL plays a major role to overcome it. In case of 1-methyl-3-(3-sulphopropyl)-imidazolium hydrogensulphate ($[\text{C}_3\text{SO}_3\text{Hmim}]\text{HSO}_4$), the cation acts as a Brønsted acid, while the IL anion plays a dual role of Brønsted base and proton shuttle to increase the cleavage efficiency.\textsuperscript{25} Hallett and co-workers reached similar conclusions by testing several $\beta$-O-4 lignin model compounds and [HSO$_4$]-based ILs.\textsuperscript{24} They observed that HSO$_4^-$ anion is effective at cleaving the $\beta$-O-4 ether linkage, but anion–cation interaction also plays a significant role in the solvation of the solute to promote an increased rate of reaction.\textsuperscript{24} Although the use of ILs looks promising to reach high efficiency in lignin ether bond cleavage and to promote high selectivity in lignin extraction from biomass, their industrial application in biomass processing and valorisation has been hindered.

In the last years, another class of green solvents called Deep Eutectic Solvents (DES) has been explored as a promising and more economical alternative to ILs. DES are mixtures composed of at least a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) species, which establish stronger hydrogen-bonding interactions than those present in the neat precursors (at hypothetical liquid state), leading to a significant depression of the melting temperature of the mixture in comparison to that of the individual compounds.\textsuperscript{26} This allows some DES to be liquid at room temperature and to be applied as solvents. Most DES and particularly those based on naturally occurring HBAs and HBDs have been shown to possess low toxicity and high biodegradability.\textsuperscript{26} Similar to ILs, DES properties can be tailored for a certain purpose by considering the substitution of HBD and/or HBA in its preparation.

In 2013, the Confederation of European Paper Industries (CEPI) referred to DES as the most promising platform for the future biomass valorisation aiming at increasing added value and reduce the CO$_2$ emissions in the frame of the European low-carbon bio-economy strategy.\textsuperscript{27} This
was a driving force for the research and development of new biomass fractionation processes with DES. In particular, acidic DES, such as lactic acid/choline chloride (LA:ChCl), have been demonstrated as capable solvents to delignify biomass. However, few studies in literature shortly addressed the mechanisms behind biomass delignification triggered by DES. Ji and co-worker Lv showed that among LA:ChCl components lactic acid is the main responsible for lignin solubility. By using density functional theory (DFT) and molecular dynamics calculations, the researchers showed that lactic acid, rather than Cl, provides strong non-covalent interactions with hydroxyl groups of a lignin model compound (VG). In another study, Alvarez-Vasco et al. disclosed the functionalities of LA:ChCl in the extraction of lignin from biomass. By demonstrating the cleavage of GG model compound with LA:ChCl (non-defined ratio) the authors found out that the reaction mechanism is similar to lignin acidolysis catalysed by HCl. In addition, the 2D HQSC NMR analysis of extracted lignin showed a selective cleavage of lignin β-O-4 ether bonds mediated by LA:ChCl. On the other hand, Smink et al. observed that ChCl has a positive impact on this delignification process, since at low molar ratios like 250:1 (LA:ChCl) the obtained delignification efficiency was higher than that of lactic acid alone. Although testing other DES system (Glycerol:ChCl with AlCl₃·6H₂O), Xia et al. demonstrated through DFT that hydrogen bonding strength between OH and Cl⁻ is higher than that existing between OH and O in lignin. Therefore, multisite chloride anions from AlCl₃ were required for an efficient disruption of hydrogen bonding network in lignocellulose (or lignin) allowing then for lignin cleavage and its subsequent extraction. However, no particular role was attributed to ChCl in the cleavage reaction, but rather to the acidic protons of HBD or to additional acidic active sites, such as the Lewis acid AlCl₃. A full overview of the delignification mechanisms mediated by acidic DES especially on the cleavage of β-O-4 ether bonds is still needed and should be complemented by computational studies using electronic structure calculations (e.g. DFT) to support the experimental results. In this context, a comprehensive study revealing new insights on the mechanisms of β-O-4 ether
bond cleavage mediated by acidic DES is herein provided. In this respect, the cleavage of a lignin model compound, 2-phenoxy-1-phenylethanol (PPE), by three different DES, namely LA:ChCl (as reference), Propionic acid/Urea (PA:U) and \(\text{p-Toluenesulphonic acid/Choline chloride}\) (pTSA:ChCl) was examined. The influence of temperature, water and catalytic amounts of a mineral acid on the cleavage performance of DES was also investigated. Finally, the obtained results unveil a possible role of the HBA halide counterion in the cleavage of \(\beta\)-O-4 ether bond, which is discussed for the first time in this study. A computational study based on DFT calculations was also addressed to support the mechanistic insights proposed in this work.

2. Experimental

2.1. Materials

2-Phenoxy-1-phenylethanol (98 wt% purity) was purchased from Fluorochem Ltd. Different HBAs and HBDs precursors for DES preparation were used: DL-lactic acid (85 wt% purity, \([\alpha] = -0.05\) at 25 °C), choline chloride (99 wt% purity), propionic acid (99 wt% purity) were purchased from Fisher Scientific, while \(\text{p-toluene sulphonlic acid monohydrate (>98 wt% purity)}\) was supplied from TCI chemicals and urea ACS grade (>99.5 wt% purity) was purchased from PanReac AppliChem, ITW reagents. Deionised water used in experiments was produced by Simplicity® Water Purification System. Sulphuric acid (>95 wt% purity, analytical reagent grade) purchased from Fisher Scientific was used as catalyst for reaction assays. Ethyl acetate (99.9 wt% purity, analytical reagent grade) supplied by Fisher Scientific was used as extracting solvent of reaction products for GC/MS analysis. Phenol (99.5 wt% purity, analytical reagent grade) was used as GC standard and was purchased from Merck, while methyl benzoate (99 wt% purity) supplied by Sigma was employed as internal standard. Supelco® 4 mL vials with solid caps containing PTFE/Liner supplied by Sigma-Aldrich were employed in the reaction trials.
2.2. Methodology

2.2.1. Preparation of DESs and DESs aqueous solutions

Prior to DES preparation, the moisture of the different precursors (HBAs and HBDs) was determined by a Metrohm 831 Karl Fisher coulometer. Afterwards, the precursors were weighed to specific molar ratios (Table 1), placed in sealed glass vials with constant stirring and heated at 60 °C until a transparent liquid was formed. The liquid mixture was kept for 1h at this temperature before returning to room temperature.

The effect of water and acidity on ether cleavage was also studied in this work. In this context, aqueous solutions of each DES were prepared to 50 wt% water content considering the initial moisture of DES precursors. These aqueous solutions were made in duplicate. One was used as prepared, while 2.5 wt% sulphuric acid was added to the other.

Table 1. List of deep eutectic solvents examined in this work.

<table>
<thead>
<tr>
<th>DES</th>
<th>Molar ratio (HBD/HBA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactic acid/Choline Chloride (LA:ChCl)</td>
<td>10:1</td>
</tr>
<tr>
<td>Propionic acid/Urea (PA:U)</td>
<td>2:1</td>
</tr>
<tr>
<td>p-Toluene Sulphonic acid/Choline Chloride (PTSA:ChCl)</td>
<td>1:1</td>
</tr>
</tbody>
</table>

2.2.2. Reactions of the lignin model compound with DES or DES aqueous solutions.

Approximately 20 mg of 2-phenoxy-1-phenylethanol (PPE) was weighed into 4 mL vials with a magnetic stirrer and was followed by the addition of 1.0 g of DES or DES aqueous solution. The vials were sealed and placed into an aluminium disk with appropriate cavities to run the desired reactions. The aluminium disk supporting the vials was transferred to a heating plate with temperature control and reactions were performed at 80 °C or 120 °C during 8h. After this period, vials were lifted out from the aluminium disk and were cooled down and stored at the freezer (-20 °C). All experiments were performed at least in duplicate and results were expressed as means (less than 5% variation).
2.2.3. Sample preparation for analysis

The resulting products and unreacted PPE were extracted from DES solution samples. Then, 1.0 mL deionised water and 1.0 mL ethyl acetate were added to the system and followed by vigorous stirring. This procedure allowed to form a biphasic system in which unreacted PPE and resulting products were easily extracted to the organic upper phase. This phase was collected to a new vial and 1.0 mL of ethyl acetate was added again to the reaction system for a new extraction step. This was repeated 3 times and organic phases were collected to the same container. The volume of total organic phase was adjusted to 3.9 mL and finally 100 μL of methyl benzoate dissolved in ethyl acetate at known concentration was added as internal standard. The samples were filtrated and analysed by GC/MS.

2.2.4. GC/MS analysis

The analyses were performed using a gas chromatograph-mass spectrometer Shimadzu QP2010 Ultra, equipped with an AOC-20i autosampler and high-performance quadrupole mass filter. The separation of reaction products was carried out in a DB-5 ms column (30 m length, 0.25 mm i.d. and 0.25 μm film thickness) using helium as the carrier gas (40 cm s⁻¹). The chromatographic conditions were as follows: isothermal at 80 °C for 5 min, ramped from 80 to 250 °C (8 °C min⁻¹), ramped from 250 to 300 °C (4 °C min⁻¹) and then isothermal at 300 °C for 5 min; injector temperature of 320 °C; and split ratio equal to 1:10. The MS was operated in the electron impact mode with electron impact energy of 70 eV and data was collected at a rate of 1 scan s⁻¹ over a range of m/z 50–1000. The ion source was kept at 200 °C and the interface temperature at 300 °C.

Chromatographic peaks were identified by comparing their retention times and their mass spectra with the equipment mass spectral library (NIST14s MS Library Database or WILEY229 MS Library Database). Quantitative analysis was performed through calibration curves of PPE and phenol for the quantification of non-cleaved and cleaved products, respectively. In this process,
the response factor of each compound was contrasted with the response factor of the internal
standard.

2.2.1. Density functional theory calculations

The Gaussian 09 code\textsuperscript{37} was used to perform all the density functional theory (DFT) calculations. The M06-2X/6-311G(d,p) approach\textsuperscript{38,39} was employed in the geometry optimization of the minima and first-order saddle points on the potential energy surfaces, and in the calculation of the vibrational frequencies. The latter were used to validate the structures as minima (absence of imaginary frequencies) or as transition states (single imaginary frequency), and to compute the zero-point energies and the thermal contributions at $T=298.15$ K. Additionally, the transition state structures were confirmed to connect the relevant initial and final states by following the corresponding intrinsic reaction coordinate. Optimized Cartesian coordinates are provided as Electronic Supplementary Information.

3. Results and Discussion

The application of DES in biomass delignification has been successfully demonstrated in several works, mainly using LA:ChCl as delignification media.\textsuperscript{29} The study of the molar ratio between LA and ChCl has been also shown and a high molar ratio of LA (e.g. 5:1, 10:1 and 15:1)\textsuperscript{28,40–42} was observed to favour delignification. Furthermore, a small content of ChCl showed a positive impact on delignification when contrasting to pure lactic acid,\textsuperscript{43} although a reasonable explanation about the role of ChCl has not been disclosed yet. Giving its relevance on biomass delignification, LA:ChCl (10:1) was selected in this work as reference for the cleavage of PPE. Two other acidic DES, namely PA:U and pTSA:ChCl, were also studied for PPE cleavage trials. Among several examined DES and different molar ratios, PA:U (2:1) and pTSA:ChCl (1:1) revealed the highest solubility values for lignin monomeric compounds (e.g. syringaldehyde) and technical lignins (Kraft and organosolv) as demonstrated elsewhere.\textsuperscript{44,45} This was the reason they
were selected, although the acidity character of both DES was also a key factor to unveil the cleavage of PPE in this study.

3.1. Identification of reaction products

After the reaction of PPE with the studied DES, a series of compounds were produced in each system, identified by GC/MS and categorized in two distinct groups: i) compounds resulting from β-O-4 cleavage of PPE (Table 2); and ii) PPE derived compounds in which no cleavage was observed (Table 3).

Table 2. Identification of PPE cleavage products formed with examined DES.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Name</th>
<th>Chemical structure</th>
<th>(M_w)</th>
<th>Retention time (min)</th>
<th>DES system</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>phenol</td>
<td><img src="phenol" alt="Chemical Structure" /></td>
<td>94</td>
<td>4.7</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>2-phenylacetaldehyde</td>
<td><img src="2-phenylacetaldehyde" alt="Chemical Structure" /></td>
<td>120</td>
<td>6.4</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>2-phenylacetaldehyde lactate</td>
<td>![Chemical Structure](2-phenylacetaldehyde lactate)</td>
<td>192</td>
<td>15.3</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>2-phenylnaphthalene</td>
<td><img src="2-phenylnaphthalene" alt="Chemical Structure" /></td>
<td>204</td>
<td>22.6</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>2-phenylnaphthalene derivative 1</td>
<td>![Chemical Structure](2-phenylnaphthalene derivative 1)</td>
<td>298</td>
<td>31.9</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>2-phenylnaphthalene derivative 2</td>
<td>![Chemical Structure](2-phenylnaphthalene derivative 2)</td>
<td>324</td>
<td>32.7</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>2-phenylnaphthalene derivative 3</td>
<td>![Chemical Structure](2-phenylnaphthalene derivative 3)</td>
<td>322</td>
<td>36.2</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>2-phenylnaphthalene derivative 4</td>
<td>![Chemical Structure](2-phenylnaphthalene derivative 4)</td>
<td>338</td>
<td>36.6</td>
<td>-</td>
</tr>
</tbody>
</table>
In the first group, phenol (1) and 2-phenylacetaldehyde (2) were produced directly from PPE cleavage, while other compounds were formed from cleaved compounds, either from reaction with DES (3) or through their own condensation (4-8). On the other hand, non-cleaved products, including PPE dehydrated intermediate (9), PPE with the hydroxyl group substituted by chloride (10), or esterified with propionate (11), lactate (12), carbamate (13) and dilactate (14) were also found. The formation of these structures depends on the applied DES and the details on the reaction pathways will be presented below.

**Table 3.** Identification of non-cleaved products after PPE conversion with examined DES.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Name</th>
<th>Chemical structure</th>
<th>M&lt;sub&gt;w&lt;/sub&gt;</th>
<th>Retention Time (min)</th>
<th>DES system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PA:U (2:1)</td>
<td>LA:ChCl (10:1)</td>
</tr>
<tr>
<td>9</td>
<td>2-phenoxyvinylbenzene</td>
<td><img src="image" alt="Structure" /></td>
<td>196</td>
<td>18.9</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>1-chloro-2-phenoxyethylbenzene (PPE-Cl)</td>
<td><img src="image" alt="Structure" /></td>
<td>232</td>
<td>20.6</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>PPE propionate</td>
<td><img src="image" alt="Structure" /></td>
<td>270</td>
<td>22.8</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>PPE lactate</td>
<td><img src="image" alt="Structure" /></td>
<td>286</td>
<td>24.3</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>PPE carbamate</td>
<td><img src="image" alt="Structure" /></td>
<td>257</td>
<td>25.2</td>
<td>-</td>
</tr>
<tr>
<td>14</td>
<td>PPE dilactate</td>
<td><img src="image" alt="Structure" /></td>
<td>358</td>
<td>28.0</td>
<td>-</td>
</tr>
</tbody>
</table>
3.2. The influence of DES and temperature on β-O-4 ether bond cleavage

The ability for PPE conversion was first scrutinised between neat PA:U (2:1), LA:ChCl (10:1) and pTSA:ChCl (1:1) in reactions at 80 and 120 °C for 8 h. The results of PPE conversion are highlighted as molar yields of non-cleaved products (solid bar) and cleaved products (dashed bar) in Figure 1. On the other hand, product distributions obtained for each reaction system are reported in Table 4.

At first glance, PPE conversion was achieved in all DES at both temperatures. The PA:U (2:1) was the less efficient system reaching up to 24.4 mol% conversion at 120 °C. However, only non-cleaved products were detected in any condition, showing the inability of PA:U (2:1) for the disruption of β-O-4 ether bond in PPE. On the other hand, LA:ChCl (10:1) allowed 51.8 mol% PPE conversion at 120 °C, from which almost half of the products were derived from the ether bond cleavage. Nevertheless, the energy supplied at 80 °C during 8 h was not enough for LA:ChCl (10:1) to cleave PPE. At the same temperature, pTSA:ChCl (1:1) converted 84.1 mol% PPE and was capable to disrupt β-O-4 ether bond, totalizing 23.4 mol% yield of cleavage compounds. By increasing the temperature, total PPE conversion was achieved in this system, in which 89.9 mol% stemmed from cleavage products. These results demonstrated clearly the superior performance of pTSA:ChCl for β-O-4 ether bond cleavage and a rough correlation between the acidity of DES and its ability for β-O-4 cleavage can be established. The more acidic is the HBD, the higher is the cleavage of PPE ether bond. The cleavage efficiency can be ordered as the following: p-toluenesulphonic (pKa=-1.34) > lactic (pKa=3.86) > propionic (pKa=4.88), despite the molar ratio of HBD and HBA is not equivalent among the studied DES.

PA:U (2:1), although being reported as good solvent for lignin,⁴⁴,⁴⁵ does not seem to be able to break the desired bonds in lignin to perform biomass delignification, at least under the examined conditions. On the other hand, LA:ChCl (10:1) allowed only moderate cleavage of PPE ether bond at 120 °C, which might explain previously reported results.⁴⁶ Up to now, pTSA:ChCl (1:1) was never used as solvent or catalyst in biomass delignification, but the disclosed results show the
high potential of this system to be applied for such purpose at milder temperatures (e.g. 80 °C) than those used for LA:ChCl (10:1).\textsuperscript{29,40} The product distribution from PPE reaction changed depending on the applied DES and temperature (Table 4), which allows to understand the main reaction mechanisms taking place in each system.

![PPE conversion chart](chart.png)

**Figure 1.** The effect of examined DES (PA:U – 2:1; LA:ChCl – 10:1; and pTSA:ChCl – 1:1) and temperature on the conversion of PPE in a reaction period of 8 h. The PPE conversion yield is established as the sum of the yields of non-cleaved products (solid) and cleaved products (dashed).

Without any cleavage, the PPE conversion using PA:U (2:1) allowed three different reactions, namely dehydration, esterification and carbamation of PPE, giving rise to products 9, 11 and 13, respectively (Table 4). Probably, due to the higher propionic acid content in PA:U (2:1) the esterification is favoured to the detriment of other reactions, and is more noticeable at 120 °C.
The use of LA:ChCl (10:1) allowed the cleavage of PPE, but other side reactions, including esterification, were also observed. At 80 °C, the esterification of PPE with lactic acid is the major phenomenon leading to the formation of PPE lactate (12). Moreover, oligomerization of this compound also occurred forming PPE dilactate (14) and trilactate derivatives (negligible amounts). Further lactic acid polymerization products with PPE may be generated, but due to their higher molecular weight they were not detected by GC/MS analysis.

Table 4. Product yield distribution of PPE conversion with PA:U (2:1), LA:ChCl (10:1) and pTSA:ChCl (1:1) systems at both 80 and 120 °C.

<table>
<thead>
<tr>
<th>Entry</th>
<th>PA:U</th>
<th>LA:ChCl</th>
<th>pTSA:ChCl</th>
<th>PA:U</th>
<th>LA:ChCl</th>
<th>pTSA:ChCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>16.3 ± 0.8</td>
<td>0.0 ± 0.0</td>
<td>23.5 ± 0.4</td>
<td>57.7 ± 0.5</td>
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<tr>
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<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>7.8 ± 0.6</td>
<td>0.0 ± 0.0</td>
<td>10.8 ± 0.4</td>
<td>0.0 ± 0.0</td>
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<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>11.3 ± 0.1</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>4</td>
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<td>0.0 ± 0.0</td>
<td>1.4 ± 0.1</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>13.7 ± 0.5</td>
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<td>0.0 ± 0.0</td>
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<td>0.0 ± 0.0</td>
<td>1.5 ± 0.1</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
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<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>8</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>1.2 ± 0.1</td>
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<tr>
<td>9</td>
<td>21.8 ± 1.5</td>
<td>6.5 ± 0.5</td>
<td>4.8 ± 0.1</td>
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<td>2.6 ± 0.1</td>
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<td>4.4 ± 0.1</td>
<td>67.3 ± 1.7</td>
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<td>2.1 ± 0.2</td>
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<td>0.0 ± 0.0</td>
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<tr>
<td>13</td>
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<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>38.1 ± 1.5</td>
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</tr>
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<td>14</td>
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<td>11.3 ± 0.2</td>
<td>0.0 ± 0.0</td>
<td>8.8 ± 0.1</td>
<td>0.0 ± 0.0</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td>0.9 ± 0.1</td>
<td>0.0 ± 0.0</td>
<td>4.8 ± 0.2</td>
<td></td>
</tr>
</tbody>
</table>

(1) phenol; (2) 2-phenylacetaldehyde; (3) 2-phenylacetaldehyde lactate; (4) 2-phenynaphthalene; (5) 2-phenynaphthalene derivative 1; (6) 2-phenynaphthalene derivative 2; (7) 2-phenynaphthalene derivative 3; (8) 2-phenynaphthalene derivative 4; (9) 2-phenoxyvinylbenzene; (10) 1-chloro-2-phenoxyethylbenzene; (11) PPE propionate; (12) PPE lactate; (13) PPE carbamate; (14) PPE dilactate; (15) non-identified. Errors are expressed as standard deviation.
At higher temperature (120 °C) the capacity of LA:ChCl (10:1) to form PPE ester derivatives is similar to its cleavage ability. The cleavage products, including phenol (1), 2-phenylacetaldehyde (2) and 2-phenylacetaldehyde lactate derivative (3) accounting for 23.5 %, 10.8 % and 11.3 %, respectively, revealed to be half of the product’s content (Table 4). While products 1 and 2 directly result from the acid-catalysed PPE cleavage, the latter species, 3, was formed through the esterification of the alcohol-based isomer of 2 with lactic acid, as demonstrated in Figure 2. Therefore, besides the esterification of PPE and lactic acid oligomerization, cleavage products also suffer esterification as secondary reaction. Moreover, the chlorinated compound 10, abbreviated as PPE-Cl, which basically was formed through substitution of PPE hydroxyl group by a chloride anion from ChCl, was also detected. However, low PPE-Cl contents were observed at both temperatures (4.4 % and 2.1 % at 80 and 120 °C, correspondingly).

These results clearly show the limitations of using LA:ChCl (10:1) in biomass delignification processes. The acidity of lactic acid allow the cleavage of lignin ether bonds and further lignin extraction, but additional esterification may also occur either with original lignin hydroxyl groups or those formed after acidic cleavage. Besides, the lactic acid oligomerization could be a disadvantage for solvent recovery and reuse.

**Figure 2.** PPE cleavage in presence of LA:ChCl (10:1) and subsequent esterification of the cleavage product.
Finally, PPE conversion with pTSA:ChCl (1:1) revealed a different behaviour in product
distribution (Table 4). In this case, no esterification products were identified at any temperature,
but instead a rather high phenol content (57.7 % at 120 °C) and low content of 2-
phenylacetaldehyde (1.7 % at 120 °C) was observed. According to the stoichiometry of PPE
cleavage, the molar amount of 2-phenylacetaldehyde should be equal to the phenol molar
content, in case none of these products participate in further reactions. However, 2-
phenylacetaldehyde was doubly consumed by self-cyclization, followed by two dehydration
steps producing 2-phenylnaphthalene (4), as described in Figure 3. This reaction is highlighted
elsewhere\textsuperscript{48} and it was also identified in the cleavage of β-O-4 lignin model compounds with
SO\textsubscript{3}H-based ILs.\textsuperscript{23} Furthermore, other side reactions contemplating the condensation of 2-
phenylnaphthalene intermediates with 2-phenylacetaldehyde and phenol allowed the
formation of compounds (5-8). Therefore, pTSA:ChCl (1:1) demonstrated to be an excellent
system to provide β-O-4 ether bond cleavage, but it also triggers a series of condensation
reactions involving the cleavage products as substrates, especially at high temperature (120 °C).
Furthermore, similar to LA:ChCl (10:1) system, PPE chlorinated derivatives were also detected
in the pTSA:ChCl (1:1) reaction medium. Surprisingly, PPE-Cl was the major component among
detected products achieving 67.3 % at 80 °C, while much lower content was observed at 120 °C
(3.7 %). This suggests that PPE-Cl could be an intermediate of the cleavage. This aspect will be
further explored below.
359 \textbf{Figure 3.} PPE cleavage in presence of LA:ChCl (10:1) and subsequent cyclization of two molecules of 2-phenylacetaldehyde with double dehydration to form 2-phenynaphthalene. Different derivatives of 2-phenynaphthalene stemming from the reaction of intermediates with 2-phenylacetaldehyde and phenol were also detected by GC/MS.

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3.3. Controlling the reactions by adding water and sulphuric acid to DES reaction media

The addition of water and catalytic amounts of H$_2$SO$_4$ to DES in the reaction with PPE were studied thereafter to scrutinise the influence of these parameters on DES catalytic cleavage of PPE and on the extent of side reactions taking place in each system. Experiments with DES aqueous solutions at 50 wt% water content with or without 2.5 wt% H$_2$SO$_4$ were examined at both 80 °C and 120 °C and contrasted with trials using neat DES, water and 2.5 wt% H$_2$SO$_4$ aqueous solution. The obtained molar yields of PPE conversion, including PPE cleaved and non-cleaved products, are presented in Table 5.

The collected data shows clearly that at both temperatures DES reactivity decreases when water is added. The cleavage performance of both LA:ChCl (10:1) and pTSA:ChCl (1:1) aqueous
solutions was reduced, although less pronounced with the last system. For instance, PPE conversion and cleavage yields obtained with LA:ChCl (10:1) decreased from 51.8 mol% and 23.6 mol%, respectively, to 18.8 mol% and 9.6 mol% with its aqueous solution counterpart. However, the addition of water seems to be meaningful in avoiding undesired side reactions, such as PPE esterification and condensation of cleavage products. For PA:U (2:1) and LA:ChCl (10:1) aqueous solutions, the production of PPE derived esters was highly reduced at both temperatures. Furthermore, the formation of condensed products decreased to almost a half (from 32.2 mol% to 19.7 mol% at 120 °C) when adding water to pTSA:ChCl (1:1). Although water reduces the efficacy of DES on the ether bond cleavage by diluting DES and decreasing its acidity, the extension of the reaction may be enough to achieve lignin extraction from biomass, while simultaneously preventing undesired side reactions.

Table 5. Molar yields of PPE conversion, cleaved and non-cleaved products using neat DES and DES aqueous solutions, with or without H$_2$SO$_4$ (2.5 wt%), at 80 °C and 120 °C.

<table>
<thead>
<tr>
<th>Entry</th>
<th>PPE conversion (mol%)</th>
<th>Cleavage products (condensed) (mol%)</th>
<th>Non-cleaved products (mol%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Esters$^a$ (mol%)</td>
<td>PPE-Cl (mol%)</td>
</tr>
<tr>
<td><strong>Reactions at 80 °C</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA:U</td>
<td>5.8 ± 0.9</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>2.6 ± 0.3</td>
</tr>
<tr>
<td>PA:U/H$_2$O</td>
<td>1.9 ± 0.6</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>0.7 ± 0.2</td>
</tr>
<tr>
<td>PA:U/H$_2$O/H$_2$SO$_4$</td>
<td>4.8 ± 1.1</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>3.4 ± 0.8</td>
</tr>
<tr>
<td>LA:ChCl</td>
<td>21.9 ± 1.8</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>19.5 ± 1.7</td>
</tr>
<tr>
<td>LA:ChCl/H$_2$O</td>
<td>3.8 ± 0.5</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>2.5 ± 0.3</td>
</tr>
<tr>
<td>LA:ChCl/H$_2$O/H$_2$SO$_4$</td>
<td>8.1 ± 0.7</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>5.8 ± 0.4</td>
</tr>
<tr>
<td>pTSA:ChCl</td>
<td>84.1 ± 2.4</td>
<td>23.4 ± 0.6 (3.2 ± 0.2)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>pTSA:ChCl/H$_2$O</td>
<td>16.8 ± 1.7</td>
<td>12.7 ± 1.4 (1.7 ± 0.2)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>pTSA:ChCl/H$_2$O/H$_2$SO$_4$</td>
<td>18.1 ± 1.8</td>
<td>12.6 ± 1.2 (2.1 ± 0.3)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td><strong>Reactions at 120 °C</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_2$O</td>
<td>0.7 ± 0.2</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>H$_2$O/H$_2$SO$_4$</td>
<td>0.7 ± 0.3</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Compound</td>
<td>Yield 1</td>
<td>Yield 2</td>
<td>Yield 3</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>PA:U</td>
<td>24.4 ± 0.8</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>13.5 ± 0.4</td>
</tr>
<tr>
<td>PA:U/H2O</td>
<td>5.1 ± 0.9</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>2.8 ± 0.5</td>
</tr>
<tr>
<td>PA:U/H2O/H2SO4</td>
<td>5.3 ± 0.5</td>
<td>0.0 ± 0.0 (0.0 ± 0.0)</td>
<td>3.1 ± 0.3</td>
</tr>
<tr>
<td>LA:ChCl</td>
<td>51.8 ± 2.2</td>
<td>23.6 ± 0.9 (5.9 ± 0.1)</td>
<td>25.7 ± 1.0</td>
</tr>
<tr>
<td>LA:ChCl/H2O</td>
<td>18.8 ± 0.7</td>
<td>9.6 ± 0.3 (0.0 ± 0.0)</td>
<td>7.6 ± 0.3</td>
</tr>
<tr>
<td>LA:ChCl/H2O/H2SO4</td>
<td>36.6 ± 1.1</td>
<td>29.2 ± 0.5 (4.2 ± 0.5)</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td>pTSA:ChCl</td>
<td>100.0 ± 0.0</td>
<td>89.8 ± 1.6 (32.2 ± 0.8)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>pTSA:ChCl/H2O</td>
<td>89.7 ± 2.5</td>
<td>79.4 ± 1.3 (19.7 ± 0.3)</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>pTSA:ChCl/H2O/H2SO4</td>
<td>97.8 ± 1.2</td>
<td>88.9 ± 1.5 (26.7 ± 0.5)</td>
<td>0.0 ± 0.0</td>
</tr>
</tbody>
</table>

a) Comprises compounds 11, 12 and 14 from Table 2; b) comprises other non-cleavage compounds, including 9 and 13 from Table 2, and others (e.g., PPE dimer). Errors are expressed as standard deviation.

On the other hand, the addition of 2.5 wt% H2SO4 was envisaged to increase the reactivity of aqueous DES systems for PPE cleavage. It was particularly successful with LA:ChCl (10:1) and pTSA:ChCl (1:1) at 120 °C by increasing the cleavage performance in comparison to DES solely with water. In case of aqueous LA:ChCl system with H2SO4, the cleavage yield (29.2 mol%) was even higher than that of neat DES (23.6 mol%), and the esterification of PPE was reduced by approximately 5-fold (from 25.7 mol% to 5.0 mol%). Finally, no positive effect of H2SO4 addition was observed for PA:U (2:1) since no PPE cleavage was promoted, showing once more the ineffective performance of PA:U (2:1) medium to promote such cleavage. Moreover, PPE cleavage using an aqueous solution of 2.5 wt% H2SO4 was also tested as a control, and no cleavage was observed, which means the chemical environment shaped by DES is an important factor to promote disruption of lignin ether bonds.

Table 5 also shows intriguing molar yields of PPE-Cl when using choline chloride-based DES. The molar yield of PPE-Cl is always very low in both LA:ChCl (10:1) and pTSA:ChCl (1:1) systems, excepting for the experiment at 80 °C with neat pTSA:ChCl (1:1) that revealed a PPE-Cl molar yield of 56.6 mol% from a total of 84.1 mol% PPE conversion. This was highlighted above in the product distribution of this reaction (67.7 % PPE-Cl). PPE-Cl can in fact be an intermediate species formed before PPE cleavage that is stable only in neat pTSA:ChCl (1:1). However, for the
same DES at 120 °C the yield of PPE-Cl was only 3.7 mol%. This could be associated to the high
cleavage extent promoted by neat pTSA:ChCl (1:1) at that temperature that simply consumed
PPE-Cl. This raises the question regarding the role of the halide counterion in DES on ether bond
cleavage. Up to now, the influence of the chloride anion on the ability of DES to disrupt lignin
chemical bonds and to extract lignin from biomass has not been studied. Therefore, to sort out
some evidences about a possible role of the halide on PPE cleavage, a kinetic study using
pTSA:ChCl (1:1) and pTSA:ChBr (1:1) was performed.

3.4. The role of the halide counterion on the PPE ether bond cleavage

The reactions of PPE cleavage were performed at 120 °C and the released products from each
DES were quantified along the reaction time. Figure 4 shows the PPE conversion yields, cleavage
yields and the corresponding formation of PPE-Cl and PPE-Br over time. In both cases, a yield
inversion between the halide intermediate and PPE cleavage was observed, confirming that PPE-
Cl and PPE-Br are formed before cleavage and are consumed along the time. However, the
formation vs consumption of each intermediate, as well as the rate of PPE cleavage, differ
between examined DES. In case of pTSA:ChCl (1:1), almost half of the initial amount of PPE was
in the form of PPE-Cl after 30 min, while the cleavage yield was already 42.8 mol%. The
consumption of PPE-Cl to give cleavage products was pronounced, but at the end of reaction
(8h) PPE-Cl was not totally converted and the cleavage yield reached 89.8 mol%. On the other
hand, the consumption of PPE-Br is much faster than PPE-Cl. At only 5 min, 62.3 mol% of
cleavage products was accomplished and 32.7 mol% PPE-Br was detected. Effectively, total PPE
cleavage was achieved in only 1h reaction with total consumption of PPE-Br. The better
performance of bromide than chloride for ether bond cleavage was also reported in acidic ILs,
whereas [Hmim]Br demonstrated faster cleavage of GG and VG model compounds than
[Hmim]Cl. 21

The main reason for the higher efficiency of pTSA:ChBr (1:1) in the cleavage of PPE is associated
to the stronger nucleophilicity of the bromide anion in comparison to chloride. Bromide allows
a faster substitution of the hydroxyl group in PPE to form the corresponding halide intermediate that precedes the ether bond cleavage. Surprisingly, these halide intermediates were never reported in mechanisms of β-O-4 ether bond cleavage using for instance HCl and HBr as catalysts\(^{49,50}\) or in acidic systems containing halide-based ILs.\(^{20,21,51}\) Therefore, using choline halide-based DES with a strong organic acid, like pTSA:ChCl and pTSA:ChBr, seems to mediate a different mechanism of β-O-4 ether bond cleavage.

**Figure 4.** The yields of PPE conversion (●), cleavage (●) and the content of chlorinated (▼) and brominated (▼) PPE compounds in reactions at 120 °C using pTSA:ChCl (1:1) (at the top) and pTSA:ChBr (1:1) (at the bottom), correspondingly. Note that different time scales were employed for clarity of results. The lines are merely a guide for the eye.
The acidic cleavage of aryl ether bonds in lignin model compounds has been studied by several researchers along the years and the following mechanistic steps have been commonly suggested: i) protonation of hydroxyl group at α-carbon; ii) dehydration at α-carbon and deprotonation at β-carbon; iii) formation of carbocation and/or enol-ether intermediate; iv) hydroxylation at β-carbon and v) β–O–4 ether bond cleavage. Although slight different nuances and more detailed steps have been reported, in general this mechanism has been associated to aqueous acidic mediums containing H$_2$SO$_4$, HCl and HBr, and also to acidic ILs, including [Hmim]Cl and [Hmim]Br, SO$_3$H-based and HSO$_4$-based ILs. In other words, it corresponds to an acid-catalysed cleavage mechanism, where the acidic proton plays the major role on the cleavage reaction. From these studies, some researchers found that the initial dehydration of the lignin model compound is the limiting step determining the cleavage reaction rate. Sturgeon et al. performed DFT calculations and showed that in PPE cleavage reaction pathway the highest ΔG was related to the dehydrated form of PPE, thus the most energy dependent intermediate. In this context, De Gregorio et al. mentioned that acidic ILs by playing both catalytic and solvent roles allow stabilization of intermediates, decreasing ΔG, and by this the cleavage reaction rate increases. This poses the following question: can acidic deep eutectic solvents containing halide counterions act on the ether bond cleavage similarly? Alvarez-Vasco et al. reported that β-O-4 ether bond cleavage with the acidic LA:ChCl follows the mechanism from the lignin acidolysis with HCl, but no role to chloride anion was identified on this process.

The results obtained in this study allow to propose another mechanism showing a possible role of the halide counterion in DES. An example with Cl$^-$ anion from PTSA:ChCl is depicted in Figure 5 and the mechanistic steps can be described as the following: i) protonation of hydroxyl group; ii) nucleophile attack of the halide anion at α-carbon and release of oxonium ion (dehydration); iii) formation of halide PPE intermediate; iv) dehydrochlorination and formation of enol-ether.
intermediate; v) ether bond cleavage. Basically, a fast dehydration of PPE is achieved and a stable intermediate is formed, which in turn decreases the energy needed to perform the ether bond cleavage (lower $\Delta G$).

Figure 5. A proposed mechanism of PPE cleavage in presence of pTSA:ChCl (1:1) showing the formation of a chlorinated intermediate with further dehydrochlorination enhancing the rate of $\beta$-O-4 ether bond cleavage. The same mechanism can be considered for bromide using pTSA:ChBr (1:1).

The proposed mechanism for PPE cleavage was analysed in this work by means of DFT calculations. Based on the experimental results described above, a deep focus was put on the first steps corresponding to the protonation of hydroxyl group, the dehydration at $\alpha$-carbon (i.e., water release) and the deprotonation at $\beta$-carbon (i.e., formation of the enol-ether intermediate: double bond between $\alpha$ and $\beta$ carbons). Particularly, the role of the halide anions in the process was inspected upon comparison of the free energy profiles for the reaction of PPE with pTSA in the presence and in the absence of the halide species (Figure 6). The results in Figure 6 clearly support that water release from PPE is more favourable in the presence of the chloride or bromide anions. As it can be seen in the structural models inserted in Figure 6, the
halide anion binds the α-carbon during the dehydration step, stabilizing not only the transition state structure but also the dehydrated intermediate species. With respect to the initial configuration, the transition state structure for the reaction without the halide anions is > 12 kcal/mol above those calculated in the presence of Cl or Br species. Also, in the case of the reaction solely with pTSA, the final state of the dehydration step is significantly more unstable than the initial state (50 kcal/mol), while in the presence of the halide species, the 1-chloro/bromo-2-phenoxyethyl)benzene intermediate is only 3/6 kcal/mol less stable than the initial state, respectively.

Figure 6. Calculated free energy profiles for the first steps of the PPE cleavage in the presence of pTSA (black lines), of pTSA with Cl (green lines) and of pTSA with Br (brown lines). Colour code for spheres: white is H; brown is C; red is O; yellow is S and green is Cl. Ball and stick models
show the optimized structures for the reaction in the absence and in the presence of halide (only
chloride models are shown because of their similarities with the bromide counterpart species).

Very recently, Jing et al. reported the results of a computational study for the catalytic
breakage of the β-O-4 linkage in veratrylglycerol-β-guaiacyl ether, used as a lignin model. Their
DFT calculations have also shown that the product of the dehydration step (i.e., the cation at
the α-carbon) is much more unstable than the reactants since the transition state structure is
closely related to the carbocation species than to the reactants.

In the presence of the halide anions, the carbocation species is not formed since the halide anion
binds the α-carbon as water molecule is released, with a concomitant stabilization of the
dehydration step. Interestingly, the energy variation of this elementary step is very similar for
both halide anions. However, the formation of the 2-phenoxyvinylbenzene from the 1-
chloro/bromo-2-phenoxyethyl)benzene intermediate occurs more favourably when the halide
is bromide, which agrees with the fact that bromide is better leaving group than chloride.

Encouragingly, these results support the faster PPE conversion observed experimentally (Figure
4) when using pTSA:ChBr (1:1) rather than pTSA:ChCl (1:1), besides the higher nucleophilicity of
bromide mentioned above.

The ability of chloride and bromide anions to speed up PPE cleavage was also investigated by
contrasting the cleavage kinetics of pTSA:ChCl (1:1) and pTSA:ChBr (1:1) with corresponding
aqueous solutions and pTSA aqueous solution as well. The obtained PPE cleavage yields are
depicted in Figure 7. Again, a negative influence of water on the ability of acidic DES to break β-
O-4 ether bond in PPE was observed. In case of aqueous solutions of pTSA:ChCl (1:1) and
pTSA:ChCl (1:1), the presence of 50 wt% water may cause significant dilution that compromises
the efficiency of the cleavage. However, rather than dilution, water also has a direct impact on
the reaction. As aforementioned, the PPE cleavage requires initial protonation of the substrate
followed by a dehydration step, thus the presence of high quantities of water, which also act as
reagent, will retard the reaction progress.\textsuperscript{24,53} Since it directly affects the rate limiting step, the negative influence of water is pronounced as demonstrated in Figure 7.

However, negligible contents of chlorinated or brominated PPE were always observed in the reactions with pTSA:ChCl and pTSA:ChBr aqueous systems, indicating that such intermediates are unstable or unfavourable in the presence of water reducing the cleavage rate. Nevertheless, for pTSA aqueous solution, \textit{i.e.} in absence of ChCl or ChBr, an even higher decrease of the PPE cleavage efficiency was obtained (Figure 7). This means that in aqueous solutions the role of the halide counterion in DES is preserved, although with a lower efficiency. Particularly in pTSA:ChCl and pTSA:ChBr aqueous solutions, it is expected that polar protic solvents like water form hydrogen bonds with halide, hindering it from attacking the α-carbon containing the leaving group (oxonium ion – Figure 5) and to promote PPE dehydration.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure7.png}
\caption{The PPE cleavage yields of pTSA:ChBr (1:1) (●), pTSA:ChCl (1:1) (●), pTSA:ChBr (1:1) aqueous solution (50 wt\% H\textsubscript{2}O) (●), pTSA:ChBr (1:1) aqueous solution (50 wt\% H\textsubscript{2}O) (●), and pTSA aqueous solution (=70 wt\% H\textsubscript{2}O) (◇), at 120 °C during 8h. The lines are merely a guide for the eye.}
\end{figure}
Finally, another evidence suggesting a beneficial role of the halide counterion is the prevention of PPE dimerization. The formation of PPE dimer as consequence of the reaction between PPE and its dehydrated form was favoured in aqueous solutions, especially with pTSA aqueous system in the absence of ChCl or ChBr (data not shown). This phenomenon could be also important when transposing to biomass delignification with DES, in which the presence of a halide counterion may be beneficial to protect lignin from self-condensation.

3.5. pTSA:ChCl and pTSA:ChBr as promising media for β-O-4 ether bond cleavage

Currently, there is no quantitative data about β-O-4 ether bond cleavage with DES, but a benchmark between the most efficient DES herein proposed, namely pTSA:ChCl and pTSA:ChBr, with the state-of-the-art can be performed. In 30 min, pTSA:ChCl (1:1) was capable to cleave 42.8 mol% of PPE at 120 °C, while pTSA:ChBr (1:1) allowed 62.3 mol% PPE cleavage in only 5 min at the same temperature (Figure 7). These are cutting-edge results that are comparable to those described in literature using other non-aqueous systems, including acidic ILs.20–23 For instance, the cleavage of GG model compound with [Hmim]Cl and [Hmim]Br was attempted in different studies and approximately 35% (130 °C/15 min) and 60% (130 °C/20 min) guaiacol yield (cleavage product) was achieved, respectively.20,21 On the other hand, the cleavage of BPE model compound with [bmim]HSO₄ demonstrated around 60% guaiacol yield in only 5 min, although the reaction was performed with microwave irradiation at very high temperature (180 °C).22 Moreover, Scott et al. demonstrated that SO₃H-functionalised imidazolium ILs were capable to cleave MPPE and reached almost 60% guaiacol at 140 °C for 5 min. These results achieved with acidic ILs confirm that the acidic DES shown in this work present similar performance on the cleavage of lignin model compounds at mild temperatures and short residence times. However, a relevant issue must be highlighted when contrasting these results, namely the fact that GG is a phenolic dimer, while BPE and PPE (studied in this work) are non-phenolic dimeric model compounds. Sturgeon et al. tested the cleavage of phenolic (GG and VG) and non-phenolic dimers (PPE) by acid catalysis in 0.2 M H₂SO₄ at 150 °C and observed that cleavage of phenolic
dimers can be 2 orders of magnitude faster than non-phenolic dimers. This suggests that GG cleavage in pTSA:ChCl and pTSA:ChBr could be even faster or proceed at milder conditions than ILs. Therefore, the results shared in this study place pTSA:ChCl and pTSA:ChBr as promising solvents to apply in biomass delignification with higher sustainability than traditional processes. The use of DES could be also an economical advantage over their IL counterparts and, simultaneously, it could maintain or improve the selectivity and efficiency of lignin extraction.

4. Conclusions

The present study gathered relevant insights regarding the influence of the acidic nature of DES on the cleavage performance of PPE model compound that can be transposed to biomass delignification processes. For instance, PA:U (2:1), that demonstrate ability to dissolve technical lignins may not be able to delignify biomass, as consequence of its incapacity to disrupt β-O-4 ether bond as shown in this work. Moreover, LA:ChCl, which is reported in literature as one of the most efficient DES performing biomass delignification, revealed some technical concerns. Although LA:ChCl (10:1) demonstrated moderate ether bond cleavage of PPE that confirms its ability for delignification, other side reactions including substrate esterification with oligomerization of lactic acid were unleashed by this DES. Therefore, some offsets may result from the use of LA:ChCl in biomass processing by producing modified lignin with lactic acid and subsequent consumption of the solvent in the reaction. On the other hand, the cleavage efficiency of PPE using pTSA:ChCl (1:1) was much higher, although the high acidity of this medium allowed undesired condensation of cleavage products. The presence of water in DES decreased the formation of condensed products, but the cleavage activity of DES was also reduced. In this context, the addition of sulphuric acid at catalytic amounts allowed an increase of the cleavage performance of DES aqueous solutions. In the analysis of reaction products, halide intermediates that precede the PPE cleavage reaction were herein reported for the first time. The kinetic study performed with pTSA: ChCl (1:1) and
pTSA: ChBr (1:1) demonstrated that PPE-Cl and PPE-Br intermediates are important to speed up the cleavage reaction, which was confirmed by the results from DFT calculations. In literature, the formation of a dehydrated form of PPE is considered the rate limiting step of the cleavage reaction, which is overcome by the presence of a strong organic acid, (e.g. pTSA), a nucleophile (Cl\textsuperscript{-} or Br\textsuperscript{-}) and the absence of water. The faster the hydroxyl group substitution of PPE by the halide anion and its subsequent leaving to form the enol-ether intermediate, the faster is the ether bond cleavage. For instance, 62.3 mol% of cleavage products was achieved with pTSA:ChBr (1:1) at 120 °C in only 5 min, which represents one of the fastest β-O-4 ether bond cleavages when benchmarked with the ultimate technologies, such as ILs. Therefore, the application of acidic DES for β-O-4 ether bond cleavage was successfully demonstrated in this work, where pTSA:ChBr and pTSA:ChCl stands as promising solvent systems with interesting catalytic properties. In this context, biomass delignification trials with these DES should be addressed as a forward step.

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