Green Chemistry

Cutting-edge research for a greener sustainable future

Accepted Manuscript

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rsc.li/greenchem

Volume 20
Number 9
7 May 2018
Pages 1919-2160

ISSN 1463-9262

ROYAL SOCIETY
OF CHEMISTRY

PAPER
Paul T. Anastas et al.
The Green ChemisTREE: 20 years after taking root with the 12 principles
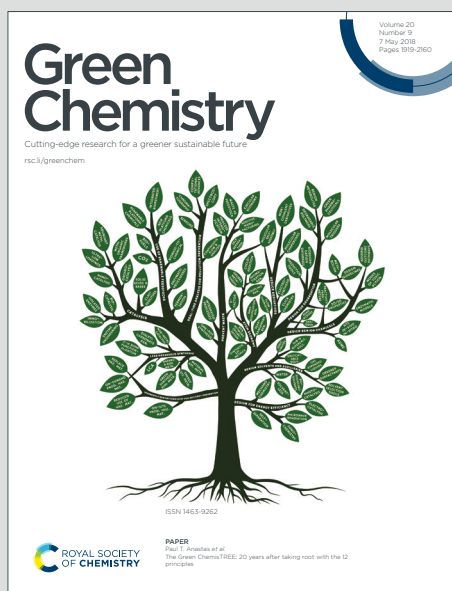
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1 **Novel insights on biomass delignification with acidic deep**

2 **eutectic solvents: a mechanistic study of β-O-4 ether bond**

3 **cleavage and the role of the halide counterion on the catalytic**

4 **performance.**

5

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14

15   **Abstract**

16   The development of innovative technologies for an efficient, yet eco-friendly, biomass

17   delignification is required to achieve higher sustainability than traditional processes. In this

18   context, the use of deep eutectic solvents (DES) for the delignification process could fulfil these

19   requirements and stands today as a promising alternative.

20   This work focus on understanding the fundamental chemistry behind the cleavage of β-O-4

21   ether bond present in 2-phenoxy-1-phenylethanol (PPE), a lignin model compound, with three

22   acidic DES, including Propionic acid/Urea (PA:U), Lactic acid/Choline Chloride (LA:ChCl) and *p*-

23   Toluenesulphonic acid/Choline chloride (pTSA:ChCl). The acidic nature of each DES influenced

24   the efficiency of PPE cleavage and determined the extent of further side reactions of cleavage

25   products. Although PA:U (2:1) demonstrated ability to dissolve lignin, it is unable to cleave β-

26   O-4 ether linkage in PPE. On the other hand, LA:ChCl (10:1) allowed PPE cleavage, but an

27   esterification between the PPE and lactic acid as well as oligomerization of lactic acid were

28   detected. Among examined solvents, pTSA:ChCl (1:1) demonstrated the highest performance on

29   the PPE cleavage, although the high acidity of this system lead to condensation of cleavage

30   products at prolonged time. The presence of water decreases the ability of DES for the cleavage,

31   but the extension of undesired side reactions was also reduced.

32   Finally, the analysis of intermediates and products of the reactions allowed the identification of

33   a chlorinated species of PPE that precedes the cleavage reaction. A kinetic study using pTSA:ChCl

34   (1:1) and pTSA:ChBr (1:1) was performed to unveil the role of the halide counterion present in

35   DES on the cleavage of β-O-4 ether bond and a new reaction mechanism was herein proposed

36   and supported by density functional theory (DFT) calculations.

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41   **1. Introduction**

42   Lignin is one of the major components of lignocellulosic biomass (15-40 wt%) and after cellulose

43   is the second most abundant resource in nature.[1] It consists of branched phenylpropanoid units,

44   including *p*-coumaryl, coniferyl and sinapyl alcohols linked through different C-O and C-C bonds.[2]

45   The carbon atoms in the aliphatic side chains of phenylpropane units are usually labelled as α, β

46   and γ, while those in the aromatic ring are numbered from 1 to 6. Based on this nomenclature,

47   the major linkages between lignin building blocks are β-O-4, β-β and β-5. Minor linkages, like α-

48   O-4 and β-1, are also present.[3] Due to its aromatic character, lignin has been drawing attention

49   as raw material to produce fuels, chemicals and materials in the frame of the biorefinery concept

50   to replace overused aromatic hydrocarbons stemming from fossil resources.[4,5]

51   The cleavage of lignin chemical linkages, along with the disruption of lignin-polysaccharide

52   bonds, allow the lignin extraction from biomass in a process called delignification. The type and

53   extent of delignification dictates the size of the extracted lignin macromolecules as well as its

54   chemical composition and modification. Therefore an efficient delignification is one of the key

55   steps on the entire biomass valorisation chain and has a direct impact on the quality of lignin for

56   further conversion and commercialization.[6,7] Amongst lignin chemical linkages, aryl ether bonds

57   (β-O-4) are the most abundant and can reach more than 50 % content of all bonding motifs.[8]

58   This type of linkage is stable (52–75 kcal·mol^{-1}) and often requires high energy towards

59   cleavage.[9] In this sense, an efficient and selective disruption of β-O-4 ether bond is a challenge

60   to overcome, where the use of catalysts is crucial as their unique properties enables to control

61   the activation routes of cleavage. However, the use of hazardous and toxic catalysts is usually

62   approached in traditional delignification technologies, such as Kraft (NaOH and Na_2S),[10] soda

63   (NaOH)[11] and sulphite (*e.g.* $Mg(HSO_3)_2$)[12] to produce high quality cellulose fibres. Other

64   disadvantages including lack of selectivity in the chemical cleavage and high energy demand for

65   delignification have been also pointed out in these technologies.[5] Although delignification is

66   efficiently achieved with those processes, the last drawbacks lead to low quality lignin samples

67   with highly dispersed molecular weights, high condensation degrees and contamination with

68   sulphur, which compromises further application.[5] A possible solution lies in addressing selective

69   and sustainable technologies where the application of green solvents, catalysts and reagents is

70   imperative to surpass those limitations.

71   The cleavage of β-O-4 ether bonds in lignin and lignin model compounds has been approached

72   by heterogeneous and homogeneous catalysis.[5,13] The engagement of supported or

73   unsupported metal catalysts, including Pd,[8] Ce,[14] V,[15] Ni,[9] Cu[16] and Ru[17] are some successful

74   examples of heterogeneous catalysis. However, once the surface of the catalyst is saturated with

75   lignin fragments, the reaction cannot proceed for a new turn making it as a disadvantage.[18] In

76   this context, homogeneous catalysis is probably a suitable alternative since the reaction occurs

77   solely in a liquid phase, thus reducing mass transfer limitations. Moreover, a metal-free and a

78   less costly catalyst looks advantageous for application in these processes.[19]

79   Ground-breaking homogeneous catalysis for lignin depolymerization within a green framework

80   have been developed with Ionic Liquids (ILs) that can act as both solvent and catalyst. Although

81   lignin oxidative cleavage has been shown elsewhere using non-acidic ILs,[19] the cleavage of lignin

82   ether bonds promoted by acidic ILs is the most common approach and it has been well

83   scrutinised in literature.[19–25] Ekerdt and co-workers were the first to try acidic cleavage of lignin

84   model compounds, guaiacylglycerol-β-guaiacyl ether (GG) and veratrylglycerol-β-guaiacyl ether

85   (VG), with 1-H-3-methylimidazolium chloride ([Hmim]Cl).[20,21] The researchers described a β-O-4

86   ether bond cleavage of model compounds by an acid-catalysed dehydration and coupling in the

87   first place, forming intermediates. Afterwards, a molecule of water attacks the β-carbon of the

88   intermediates allowing for ether bond cleavage.[20] Another work showed that 1-butyl-3-

89   methylimidazolium hydrogensulphate ([bmim]HSO$_4$) was able to disrupt the ether bond from

90   benzyl phenyl ether (BPE).[22] The Bronsted acid character of this IL demonstrated high efficiency

91   in BPE cleavage, but degradation of hydrolysis products (*e.g.* phenol) was also detected.[22] On

92   the other hand, acidic SO$_3$H-functionalized imidazolium ILs demonstrated high ability to perform

93   cleavage of 2-(2-methoxyphenoxy)-1-phenylethanol (MPPE)[23] and VG.[25] Jing *et al.* referred to an

94   unconventional E1 elimination with five successive steps: i) protonation-dehydration; ii) β-H

95   elimination; iii) protonation; iv) hydroxylation; and v) β−O−4 bond cleavage.[25] The authors

96   highlighted the first step as the limiting one and the IL plays a major role to overcome it. In case

97   of 1-methyl-3-(3-sulphopropyl)-imidazolium hydrogensulphate ([C_3SO_3Hmim]HSO_4), the cation

98   acts as a Brønsted acid, while the IL anion plays a dual role of Brønsted base and proton shuttle

99   to increase the cleavage efficiency.[25] Hallett and co-workers reached similar conclusions by

100   testing several β-O-4 lignin model compounds and [HSO_4]-based ILs.[24] They observed that HSO_4^-

101   anion is effective at cleaving the β-O-4 ether linkage, but anion–cation interaction also plays a

102   significant role in the solvation of the solute to promote an increased rate of reaction.[24] Although

103   the use of ILs looks promising to reach high efficiency in lignin ether bond cleavage and to

104   promote high selectivity in lignin extraction from biomass, their industrial application in biomass

105   processing and valorisation has been hindered.

106   In the last years, another class of green solvents called Deep Eutectic Solvents (DES) has been

107   explored as a promising and more economical alternative to ILs. DES are mixtures composed of

108   at least a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) species, which

109   establish stronger hydrogen-bonding interactions than those present in the neat precursors (at

110   hypothetical liquid state), leading to a significant depression of the melting temperature of the

111   mixture in comparison to that of the individual compounds.[26] This allows some DES to be liquid

112   at room temperature and to be applied as solvents. Most DES and particularly those based on

113   naturally occurring HBAs and HBDs have been shown to possess low toxicity and high

114   biodegradability.[26] Similar to ILs, DES properties can be tailored for a certain purpose by

115   considering the substitution of HBD and/or HBA in its preparation.

116   In 2013, the Confederation of European Paper Industries (CEPI) referred to DES as the most

117   promising platform for the future biomass valorisation aiming at increasing added value and

118   reduce the CO_2 emissions in the frame of the European low-carbon bio-economy strategy.[27] This

119   was a driving force for the research and development of new biomass fractionation processes

120   with DES. In particular, acidic DES, such as lactic acid/choline chloride (LA:ChCl), have been

121   demonstrated as capable solvents to delignify biomass.[28–32] However, few studies in literature

122   shortly addressed the mechanisms behind biomass delignification triggered by DES.[29,33–35] Ji and

123   co-worker Lv showed that among LA:ChCl components lactic acid is the main responsible for

124   lignin solubility.[36] By using density functional theory (DFT) and molecular dynamics calculations,

125   the researchers showed that lactic acid, rather than Cl⁻, provides strong non-covalent

126   interactions with hydroxyl groups of a lignin model compound (VG).[36] In another study, Alvarez-

127   Vasco *et al.* disclosed the functionalities of LA:ChCl in the extraction of lignin from biomass.[29] By

128   demonstrating the cleavage of GG model compound with LA:ChCl (non-defined ratio) the

129   authors found out that the reaction mechanism is similar to lignin acidolysis catalysed by HCl. In

130   addition, the 2D HQSC NMR analysis of extracted lignin showed a selective cleavage of lignin β-

131   O-4 ether bonds mediated by LA:ChCl.[29,34] On the other hand, Smink *et al.* observed that ChCl

132   has a positive impact on this delignification process, since at low molar ratios like 250:1 (LA:ChCl)

133   the obtained delignification efficiency was higher than that of lactic acid alone.[33] Although

134   testing other DES system (Glycerol:ChCl with $AlCl_3 \cdot 6H_2O$), Xia et al. demonstrated through DFT

135   that hydrogen bonding strength between OH and Cl⁻ is higher than that existing between OH

136   and O in lignin.[35] Therefore, multisite chloride anions from $AlCl_3$ were required for an efficient

137   disruption of hydrogen bonding network in lignocellulose (or lignin) allowing then for lignin

138   cleavage and its subsequent extraction.[35] However, no particular role was attributed to ChCl in

139   the cleavage reaction, but rather to the acidic protons of HBD[29,33,34] or to additional acidic active

140   sites, such as the Lewis acid $AlCl_3$.[35]

141   A full overview of the delignification mechanisms mediated by acidic DES especially on the

142   cleavage of β-O-4 ether bonds is still needed and should be complemented by computational

143   studies using electronic structure calculations (*e.g.* DFT) to support the experimental results. In

144   this context, a comprehensive study revealing new insights on the mechanisms of β-O-4 ether

145   bond cleavage mediated by acidic DES is herein provided. In this respect, the cleavage of a lignin

146   model compound, 2-phenoxy-1-phenylethanol (PPE), by three different DES, namely LA:ChCl (as

147   reference), Propionic acid/Urea (PA:U) and *p*-Toluenesulphonic acid/Choline chloride

148   (pTSA:ChCl) was examined. The influence of temperature, water and catalytic amounts of a

149   mineral acid on the cleavage performance of DES was also investigated. Finally, the obtained

150   results unveil a possible role of the HBA halide counterion in the cleavage of β-O-4 ether bond,

151   which is discussed for the first time in this study. A computational study based on DFT

152   calculations was also addressed to support the mechanistic insights proposed in this work.

153

154   **2.   Experimental**

155   **2.1.   Materials**

156   2-Phenoxy-1-phenylethanol (98 wt% purity) was purchased from Fluorochem Ltd. Different

157   HBAs and HBDs precursors for DES preparation were used: DL-lactic acid (85 wt% purity, [α]= -

158   0.05 at 25 °C), choline chloride (99 wt% purity), propionic acid (99 wt% purity) were purchased

159   from Fisher Scientific, while *p*-toluene sulphonic acid monohydrate (>98 wt% purity) was

160   supplied from TCI chemicals and urea ACS grade (>99.5 wt% purity) was purchased from

161   PanReac AppliChem, ITW reagents. Deionised water used in experiments was produced by

162   Simplicity® Water Purification System. Sulphuric acid (>95 wt% purity, analytical reagent grade)

163   purchased from Fisher Scientific was used as catalyst for reaction assays. Ethyl acetate (99.9 wt%

164   purity, analytical reagent grade) supplied by Fisher Scientific was used as extracting solvent of

165   reaction products for GC/MS analysis. Phenol (99.5 wt% purity, analytical reagent grade) was

166   used as GC standard and was purchased from Merck, while methyl benzoate (99 wt% purity)

167   supplied by Sigma was employed as internal standard. Supelco® 4 mL vials with solid caps

168   containing PTFE/Liner supplied by Sigma-Aldrich were employed in the reaction trials.

169   **2.2.   Methodology**

170   **2.2.1.   Preparation of DESs and DESs aqueous solutions**

171   Prior to DES preparation, the moisture of the different precursors (HBAs and HBDs) was

172   determined by a Metrohm 831 Karl Fisher coulometer. Afterwards, the precursors were weighed

173   to specific molar ratios (Table 1), placed in sealed glass vials with constant stirring and heated at

174   60 °C until a transparent liquid was formed. The liquid mixture was kept for 1h at this

175   temperature before returning to room temperature.

176   The effect of water and acidity on ether cleavage was also studied in this work. In this context,

177   aqueous solutions of each DES were prepared to 50 wt% water content considering the initial

178   moisture of DES precursors. These aqueous solutions were made in duplicate. One was used as

179   prepared, while 2.5 wt% sulphuric acid was added to the other.

180

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

DES	Molar ratio (HBD/HBA)
Lactic acid/Choline Chloride (LA:ChCl)	10:1
Propionic acid/Urea (PA:U)	2:1
p-Toluene Sulphonic acid/Choline Chloride (PTSA:ChCl)	1:1

182

183   **2.2.2.   Reactions of the lignin model compound with DES or DES aqueous solutions.**

184   Approximately 20 mg of 2-phenoxy-1-phenylethanol (PPE) was weighed into 4 mL vials with a

185   magnetic stirrer and was followed by the addition of 1.0 g of DES or DES aqueous solution. The

186   vials were sealed and placed into an aluminium disk with appropriate cavities to run the desired

187   reactions. The aluminium disk supporting the vials was transferred to a heating plate with

188   temperature control and reactions were performed at 80 °C or 120 °C during 8h. After this

189   period, vials were lifted out from the aluminium disk and were cooled down and stored at the

190   freezer (-20 °C). All experiments were performed at least in duplicate and results were expressed

191   as means (less than 5% variation).

2.2.3. Sample preparation for analysis

192

193 The resulting products and unreacted PPE were extracted from DES solution samples. Then, 1.0

194 mL deionised water and 1.0 mL ethyl acetate were added to the system and followed by vigorous

195 stirring. This procedure allowed to form a biphasic system in which unreacted PPE and resulting

196 products were easily extracted to the organic upper phase. This phase was collected to a new

197 vial and 1.0 mL of ethyl acetate was added again to the reaction system for a new extraction

198 step. This was repeated 3 times and organic phases were collected to the same container. The

199 volume of total organic phase was adjusted to 3.9 mL and finally 100 µL of methyl benzoate

200 dissolved in ethyl acetate at known concentration was added as internal standard. The samples

201 were filtrated and analysed by GC/MS.

2.2.4. GC/MS analysis

202

203 The analyses were performed using a gas chromatograph-mass spectrometer Shimadzu QP2010

204 Ultra, equipped with an AOC-20i autosampler and high-performance quadrupole mass filter. The

205 separation of reaction products was carried out in a DB-5 ms column (30 m length, 0.25 mm i.d.

206 and 0.25 µm film thickness) using helium as the carrier gas (40 cm s^{-1}). The chromatographic

207 conditions were as follows: isothermal at 80 °C for 5 min, ramped from 80 to 250 °C (8 °C min^{-1}),

208 ramped from 250 to 300 °C (4 °C min^{-1}) and then isothermal at 300 °C for 5 min; injector

209 temperature of 320 °C; and split ratio equal to 1:10. The MS was operated in the electron impact

210 mode with electron impact energy of 70 eV and data was collected at a rate of 1 scan s^{-1} over a

211 range of m/z 50–1000. The ion source was kept at 200 °C and the interface temperature at

212 300 °C.

213 Chromatographic peaks were identified by comparing their retention times and their mass

214 spectra with the equipment mass spectral library (NIST14s MS Library Database or WILEY229 MS

215 Library Database). Quantitative analysis was performed through calibration curves of PPE and

216 phenol for the quantification of non-cleaved and cleaved products, respectively. In this process,

217   the response factor of each compound was contrasted with the response factor of the internal

218   standard.

2.2.1. Density functional theory calculations

220   The Gaussian 09 code[37] was used to perform all the density functional theory (DFT) calculations.

221   The M06-2X/6-311G(d,p) approach[38,39] was employed in the geometry optimization of the

222   minima and first-order saddle points on the potential energy surfaces, and in the calculation of

223   the vibrational frequencies. The latter were used to validate the structures as minima (absence

224   of imaginary frequencies) or as transition states (single imaginary frequency), and to compute

225   the zero-point energies and the thermal contributions at T=298.15 K. Additionally, the transition

226   state structures were confirmed to connect the relevant initial and final states by following the

227   corresponding intrinsic reaction coordinate. Optimized Cartesian coordinates are provided as

228   Electronic Supplementary Information.

229

3. Results and Discussion

231   The application of DES in biomass delignification has been successfully demonstrated in several

232   works, mainly using LA:ChCl as delignification media.[29] The study of the molar ratio between LA

233   and ChCl has been also shown and a high molar ratio of LA (*e.g.* 5:1, 10:1 and 15:1)[28,40–42] was

234   observed to favour delignification. Furthermore, a small content of ChCl showed a positive

235   impact on delignification when contrasting to pure lactic acid,[43] although a reasonable

236   explanation about the role of ChCl has not been disclosed yet. Giving its relevance on biomass

237   delignification, LA:ChCl (10:1) was selected in this work as reference for the cleavage of PPE.

238   Two other acidic DES, namely PA:U and pTSA:ChCl, were also studied for PPE cleavage trials.

239   Among several examined DES and different molar ratios, PA:U (2:1) and pTSA:ChCl (1:1) revealed

240   the highest solubility values for lignin monomeric compounds (*e.g.* syringaldehyde) and

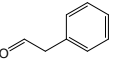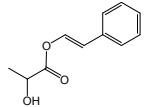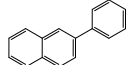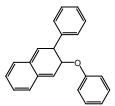241   technical lignins (Kraft and organosolv) as demonstrated elsewhere.[44,45] This was the reason they
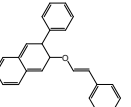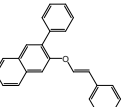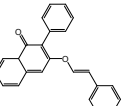
242   were selected, although the acidity character of both DES was also a key factor to unveil the

243   cleavage of PPE in this study.

244   **3.1.   Identification of reaction products**

245   After the reaction of PPE with the studied DES, a series of compounds were produced in each

246   system, identified by GC/MS and categorized in two distinct groups: i) compounds resulting from

247   β-O-4 cleavage of PPE (Table 2); and ii) PPE derived compounds in which no cleavage was

248   observed (Table 3).

249

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

Entry	Name	Chemical structure	M_w	Retention time (min)	DES system		
					PA:U (2:1)	LA:ChCl (10:1)	PTSA:ChCl (1:1)
1	phenol		94	4.7	-	●	●
2	2-phenylacetaldehyde		120	6.4	-	●	●
3	2-phenylacetaldehyde lactate		192	15.3	-	●	-
4	2-phenylnaphthalene		204	22.6	-	-	●
5	2-phenylnaphthalene derivative 1		298	31.9	-	-	●
6	2-phenylnaphthalene derivative 2		324	32.7	-	-	●
7	2-phenylnaphthalene derivative 3		322	36.2	-	-	●
8	2-phenylnaphthalene derivative 4		338	36.6	-	-	●

251

252   In the first group, phenol **(1)** and 2-phenylacetaldehyde **(2)** were produced directly from PPE

253   cleavage, while other compounds were formed from cleaved compounds, either from reaction

254   with DES **(3)** or through their own condensation **(4-8)**. On the other hand, non-cleaved products,

255   including PPE dehydrated intermediate **(9)**, PPE with the hydroxyl group substituted by chloride

256   **(10)**, or esterified with propionate **(11)**, lactate **(12)**, carbamate **(13)** and dilactate **(14)** were also

257   found. The formation of these structures depends on the applied DES and the details on the

258   reaction pathways will be presented below.

259

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

| Entry	Name	Chemical structure	M_w	Retention Time (min)	DES system		
					PA:U (2:1)	LA:ChCl (10:1)	PTSA:ChCl (1:1)
9	2-phenoxyvinylbenzene		196	18.9	●	●	●
10	1-chloro-2-phenoxyethylbenzene (PPE-Cl)		232	20.6	-	●	●
11	PPE propionate		270	22.8	●	-	-
12	PPE lactate		286	24.3	-	●	-
13	PPE carbamate		257	25.2	●	-	-
14	PPE dilactate		358	28.0	-	●	-

261

262   ## 3.2.   The influence of DES and temperature on β-O-4 ether bond cleavage

263   The ability for PPE conversion was first scrutinised between neat PA:U (2:1), LA:ChCl (10:1) and

264   pTSA:ChCl (1:1) in reactions at 80 and 120 °C for 8 h. The results of PPE conversion are

265   highlighted as molar yields of non-cleaved products (solid bar) and cleaved products (dashed

266   bar) in Figure 1. On the other hand, product distributions obtained for each reaction system are

267   reported in Table 4.

268   At first glance, PPE conversion was achieved in all DES at both temperatures. The PA:U (2:1) was

269   the less efficient system reaching up to 24.4 mol% conversion at 120 °C. However, only non-

270   cleaved products were detected in any condition, showing the inability of PA:U (2:1) for the

271   disruption of β-O-4 ether bond in PPE. On the other hand, LA:ChCl (10:1) allowed 51.8 mol% PPE

272   conversion at 120 °C, from which almost half of the products were derived from the ether bond

273   cleavage. Nevertheless, the energy supplied at 80 °C during 8 h was not enough for LA:ChCl

274   (10:1) to cleave PPE. At the same temperature, pTSA:ChCl (1:1) converted 84.1 mol% PPE and

275   was capable to disrupt β-O-4 ether bond, totalizing 23.4 mol% yield of cleavage compounds. By

276   increasing the temperature, total PPE conversion was achieved in this system, in which 89.9

277   mol% stemmed from cleavage products. These results demonstrated clearly the superior

278   performance of pTSA:ChCl for β-O-4 ether bond cleavage and a rough correlation between the

279   acidity of DES and its ability for β-O-4 cleavage can be established. The more acidic is the HBD,

280   the higher is the cleavage of PPE ether bond. The cleavage efficiency can be ordered as the

281   following: *p*-toluenesulphonic (pKa=-1.34) > lactic (pKa=3.86) > propionic (pKa=4.88), despite

282   the molar ratio of HBD and HBA is not equivalent among the studied DES.

283   PA:U (2:1), although being reported as good solvent for lignin,[44,45] does not seem to be able to

284   break the desired bonds in lignin to perform biomass delignification, at least under the examined

285   conditions. On the other hand, LA:ChCl (10:1) allowed only moderate cleavage of PPE ether bond

286   at 120 °C, which might explain previously reported results.[46] Up to now, pTSA:ChCl (1:1) was

287   never used as solvent or catalyst in biomass delignification, but the disclosed results show the

288   high potential of this system to be applied for such purpose at milder temperatures (*e.g.* 80 °C)

289   than those used for LA:ChCl (10:1).[29,40]

290   The product distribution from PPE reaction changed depending on the applied DES and

291   temperature (Table 4), which allows to understand the main reaction mechanisms taking place

292   in each system.

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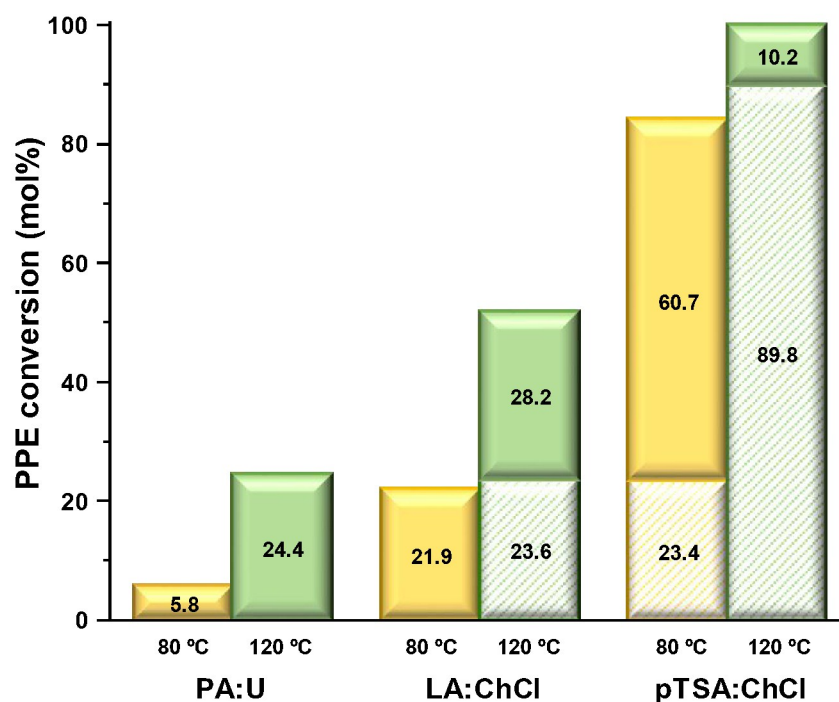
294

295   **Figure 1.** The effect of examined DES (PA:U – 2:1; LA:ChCl – 10:1; and pTSA:ChCl – 1:1) and

296   temperature on the conversion of PPE in a reaction period of 8 h. The PPE conversion yield is

297   established as the sum of the yields of non-cleaved products (solid) and cleaved products

298   (dashed).

299

300   Without any cleavage, the PPE conversion using PA:U (2:1) allowed three different reactions,

301   namely dehydration, esterification and carbamation of PPE, giving rise to products **9**, **11** and **13**,

302   respectively (Table 4). Probably, due to the higher propionic acid content in PA:U (2:1) the

303   esterification is favoured to the detriment of other reactions, and is more noticeable at 120 °C.

304   The use of LA:ChCl (10:1) allowed the cleavage of PPE, but other side reactions, including

305   esterification, were also observed. At 80 °C, the esterification of PPE with lactic acid is the major

306   phenomenon leading to the formation of PPE lactate (**12**). Moreover, oligomerization of this

307   compound also occurred forming PPE dilactate (**14**) and trilactate derivatives (negligible

308   amounts). Further lactic acid polymerization products with PPE may be generated, but due to

309   their higher molecular weight they were not detected by GC/MS analysis.

310

311   **Table 4.** Product yield distribution of PPE conversion with PA:U (2:1), LA:ChCl (10:1) and

312   pTSA:ChCl (1:1) systems at both 80 and 120 °C.

| | Product distribution (%) | | | | | |
| Entry | Reaction at 80 °C | | | Reaction at 120 °C | | |
	PA:U	LA:ChCl	pTSA:ChCl	PA:U	LA:ChCl	pTSA:ChCl
1	0.0 ± 0.0	0.0 ± 0.0	16.3 ± 0.8	0.0 ± 0.0	23.5 ±0.4	57.7 ± 0.5
2	0.0 ± 0.0	0.0 ± 0.0	7.8 ± 0.6	0.0 ± 0.0	10.8 ± 0.4	0.0 ± 0.0
3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	11.3 ± 0.1	0.0 ± 0.0
4	0.0 ± 0.0	0.0 ± 0.0	1.4 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	13.7 ± 0.5
5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	6.9 ± 0.1
6	0.0 ± 0.0	0.0 ± 0.0	1.5 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	9.4 ± 0.2
7	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.9 ± 0.1
8	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1.2 ± 0.1
9	21.8 ± 1.5	6.5 ± 0.5	4.8 ± 0.1	6.4 ±0.6	2.6 ± 0.1	1.7 ± 0.2
10	0.0 ± 0.0	4.4 ± 0.1	67.3 ± 1.7	0.0 ± 0.0	2.1 ± 0.2	3.7 ± 0.2
11	45.4 ± 1.9	0.0 ± 0.0	0.0 ± 0.0	55.5 ± 0.9	0.0 ± 0.0	0.0 ± 0.0
12	0.0 ± 0.0	77.8 ± 0.7	0.0 ± 0.0	0.0 ± 0.0	40.9 ± 0.7	0.0 ± 0.0
13	32.8 ± 0.3	0.0 ± 0.0	0.0 ± 0.0	38.1 ± 1.5	0.0 ± 0.0	0.0 ± 0.0
14	0.0 ± 0.0	11.3 ± 0.2	0.0 ± 0.0	0.0 ± 0.0	8.8 ± 0.1	0.0 ± 0.0
15	0.0 ± 0.0	0.0 ± 0.0	0.9 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	4.8 ± 0.2

313   **(1)** phenol; **(2)** 2-phenylacetaldehyde; **(3)** 2-phenylacetaldehyde lactate; **(4)** 2-phenylnaphthalene; **(5)** 2-phenylnaphthalene

314   derivative 1; **(6)** 2-phenylnaphthalene derivative 2; **(7)** 2-phenylnaphthalene derivative 3; **(8)** 2-phenylnaphthalene derivative 4; **(9)**

315   2-phenoxyvinylbenzene; **(10)** 1-chloro-2-phenoxyethylbenzene; **(11)** PPE propionate; **(12)** PPE lactate; **(13)** PPE carbamate; **(14)** PPE

316   dilactate; **(15)** non-identified. Errors are expressed as standard deviation.

317

318   At higher temperature (120 °C) the capacity of LA:ChCl (10:1) to form PPE ester derivatives is

319   similar to its cleavage ability. The cleavage products, including phenol (**1**), 2-phenylacetaldehyde

320   (**2**) and 2-phenylacetaldehyde lactate derivative (**3**) accounting for 23.5 %, 10.8 % and 11.3 %,

321   respectively, revealed to be half of the product's content (Table 4). While products **1** and **2**

322   directly result from the acid-catalysed PPE cleavage, the latter species, **3**, was formed through

323   the esterification of the alcohol-based isomer of **2** with lactic acid, as demonstrated in Figure 2.

324   Therefore, besides the esterification of PPE and lactic acid oligomerization, cleavage products

325   also suffer esterification as secondary reaction. Moreover, the chlorinated compound **10**,

326   abbreviated as PPE-Cl, which basically was formed through substitution of PPE hydroxyl group

327   by a chloride anion from ChCl, was also detected. However, low PPE-Cl contents were observed

328   at both temperatures (4.4 % and 2.1 % at 80 and 120 °C, correspondingly).

329   These results clearly show the limitations of using LA:ChCl (10:1) in biomass delignification

330   processes. The acidity of lactic acid allow the cleavage of lignin ether bonds and further lignin

331   extraction,[28,29,40,46,47] but additional esterification may also occur either with original lignin

332   hydroxyl groups or those formed after acidic cleavage. Besides, the lactic acid oligomerization

333   could be a disadvantage for solvent recovery and reuse.

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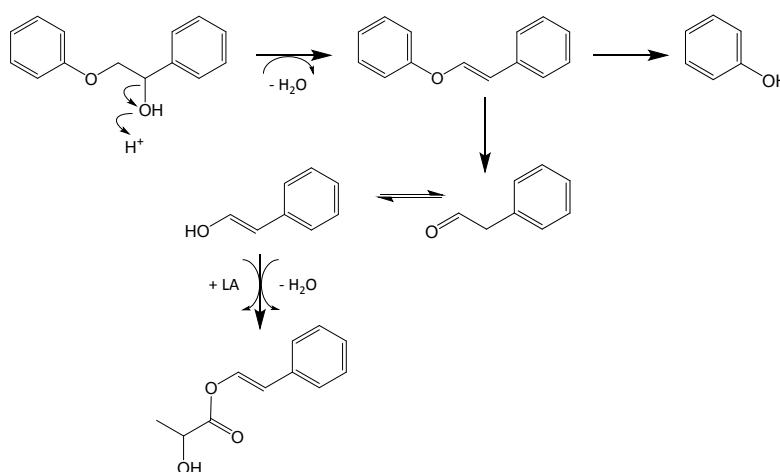
335

336   **Figure 2.** PPE cleavage in presence of LA:ChCl (10:1) and subsequent esterification of the

337   cleavage product.

338

339   Finally, PPE conversion with pTSA:ChCl (1:1) revealed a different behaviour in product

340   distribution (Table 4). In this case, no esterification products were identified at any temperature,

341   but instead a rather high phenol content (57.7 % at 120 °C) and low content of 2-

342   phenylacetaldehyde (1.7 % at 120 °C) was observed. According to the stoichiometry of PPE

343   cleavage, the molar amount of 2-phenylacetaldehyde should be equal to the phenol molar

344   content, in case none of these products participate in further reactions. However, 2-

345   phenylacetaldehyde was doubly consumed by self-cyclization, followed by two dehydration

346   steps producing 2-phenylnaphthalene **(4)**, as described in Figure 3. This reaction is highlighted

347   elsewhere[48] and it was also identified in the cleavage of β-O-4 lignin model compounds with

348   SO_3H-based ILs.[23] Furthermore, other side reactions contemplating the condensation of 2-

349   phenylnaphthalene intermediates with 2-phenylacetaldehyde and phenol allowed the

350   formation of compounds **(5-8)**. Therefore, pTSA:ChCl (1:1) demonstrated to be an excellent

351   system to provide β-O-4 ether bond cleavage, but it also triggers a series of condensation

352   reactions involving the cleavage products as substrates, especially at high temperature (120 °C).

353   Furthermore, similar to LA:ChCl (10:1) system, PPE chlorinated derivatives were also detected

354   in the pTSA:ChCl (1:1) reaction medium. Surprisingly, PPE-Cl was the major component among

355   detected products achieving 67.3 % at 80 °C, while much lower content was observed at 120 °C

356   (3.7 %). This suggests that PPE-Cl could be an intermediate of the cleavage. This aspect will be

357   further explored below.

358

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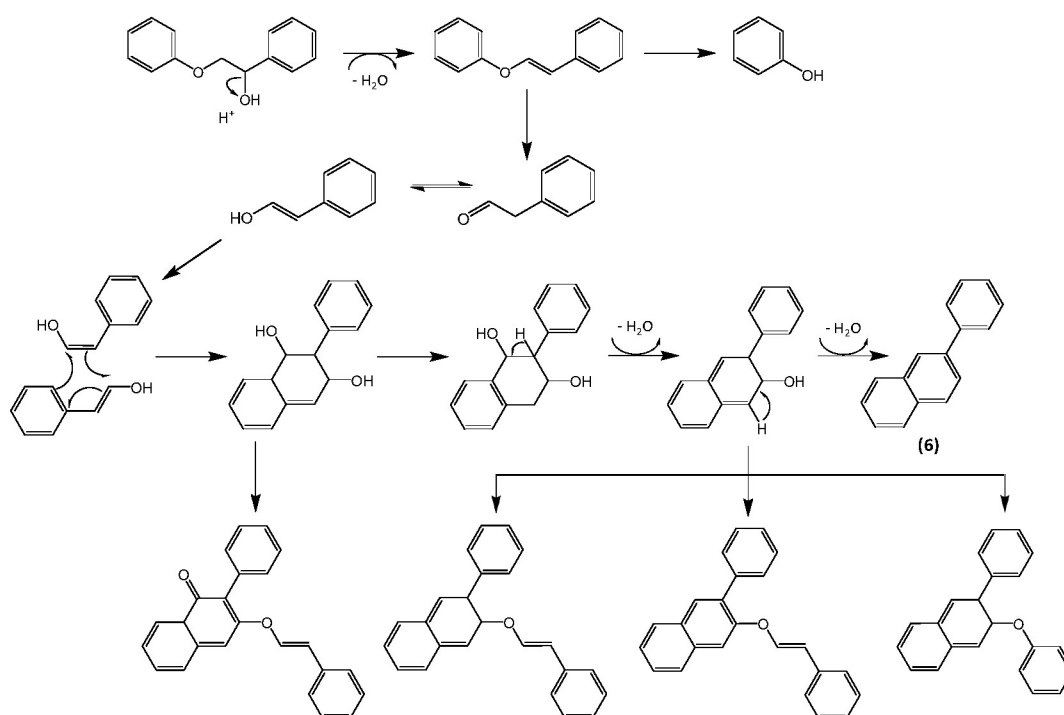
Figure 3. PPE cleavage in presence of LA:ChCl (10:1) and subsequent cyclization of two molecules of 2-phenylacetaldehyde with double dehydration to form 2-phenylnaphthalene. Different derivatives of 2-phenylnaphthalene stemming from the reaction of intermediates with 2-phenylacetaldehyde and phenol were also detected by GC/MS.

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

The addition of water and catalytic amounts of H_2SO_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_2SO_4 were examined at both 80 °C and 120 °C and contrasted with trials using neat DES, water and 2.5 wt% H_2SO_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

375 solutions was reduced, although less pronounced with the last system. For instance, PPE

376 conversion and cleavage yields obtained with LA:ChCl (10:1) decreased from 51.8 mol% and 23.6

377 mol%, respectively, to 18.8 mol% and 9.6 mol% with its aqueous solution counterpart. However,

378 the addition of water seems to be meaningful in avoiding undesired side reactions, such as PPE

379 esterification and condensation of cleavage products. For PA:U (2:1) and LA:ChCl (10:1) aqueous

380 solutions, the production of PPE derived esters was highly reduced at both temperatures.

381 Furthermore, the formation of condensed products decreased to almost a half (from 32.2 mol%

382 to 19.7 mol% at 120 °C) when adding water to pTSA:ChCl (1:1). Although water reduces the

383 efficacy of DES on the ether bond cleavage by diluting DES and decreasing its acidity, the

384 extension of the reaction may be enough to achieve lignin extraction from biomass, while

385 simultaneously preventing undesired side reactions.

386

387 **Table 5.** Molar yields of PPE conversion, cleaved and non-cleaved products using neat DES and

388 DES aqueous solutions, with or without H_2SO_4 (2.5 wt%), at 80 °C and 120 °C.

Entry	PPE conversion (mol%)	Cleavage products (condensed) (mol%)	Non-cleaved products(mol%)		
			Esters[a] (mol%)	PPE-Cl (mol%)	Others[b] (mol%)
Reactions at 80 °C					
PA:U	5.8 ± 0.9	0.0 ± 0.0 (0.0 ± 0.0)	2.6 ± 0.3	0.0 ± 0.0	3.2 ± 0.6
PA:U/H₂O	1.9 ± 0.6	0.0 ± 0.0 (0.0 ± 0.0)	0.7 ± 0.2	0.0 ± 0.0	1.2 ± 0.4
PA:U/H₂O/H₂SO₄	4.8 ± 1.1	0.0 ± 0.0 (0.0 ± 0.0)	3.4 ± 0.8	0.0 ± 0.0	1.4 ± 0.3
LA:ChCl	21.9 ± 1.8	0.0 ± 0.0 (0.0 ± 0.0)	19.5 ± 1.7	1.0 ± 0.0	1.4 ± 0.1
LA:ChCl/H₂O	3.8 ± 0.5	0.0 ± 0.0 (0.0 ± 0.0)	2.5 ± 0.3	0.0 ± 0.0	1.3 ± 0.2
LA:ChCl/H₂O/H₂SO₄	8.1 ± 0.7	0.0 ± 0.0 (0.0 ± 0.0)	5.8 ± 0.4	0.8 ± 0.1	1.5 ± 0.2
pTSA:ChCl	84.1 ± 2.4	23.4 ± 0.6 (3.2 ± 0.2)	0.0 ± 0.0	56.6 ± 1.7	4.1 ± 0.1
pTSA:ChCl/H₂O	16.8 ± 1.7	12.7 ± 1.4 (1.7 ± 0.2)	0.0 ± 0.0	1.4 ± 0.1	2.7 ± 0.2
pTSA:ChCl/H₂O/H₂SO₄	18.1 ± 1.8	12.6 ± 1.2 (2.1 ± 0.3)	0.0 ± 0.0	2.5 ± 0.3	3.0 ± 0.3
Reactions at 120 °C					
H₂O	0.7 ± 0.2	0.0 ± 0.0 (0.0 ± 0.0)	0.0 ± 0.0	0.0 ± 0.0	0.7 ± 0.2
H₂O/H₂SO₄	0.7 ± 0.3	0.0 ± 0.0 (0.0 ± 0.0)	0.0 ± 0.0	0.0 ± 0.0	0.7 ± 0.3

PA:U	24.4 ± 0.8	0.0 ± 0.0 (0.0 ± 0.0)	13.5 ± 0.4	0.0 ± 0.0	10.9 ± 0.4
PA:U/H$_2$O	5.1 ± 0.9	0.0 ± 0.0 (0.0 ± 0.0)	2.8 ± 0.5	0.0 ± 0.0	2.3 ± 0.4
PA:U/H$_2$O/H$_2$SO$_4$	5.3 ± 0.5	0.0 ± 0.0 (0.0 ± 0.0)	3.1 ± 0.3	0.0 ± 0.0	2.2 ± 0.2
LA:ChCl	51.8 ± 2.2	23.6 ± 0.9 (5.9 ± 0.1)	25.7 ± 1.0	1.1 ± 0.2	1.4 ± 0.1
LA:ChCl/H$_2$O	18.8 ± 0.7	9.6 ± 0.3 (0.0 ± 0.0)	7.6 ± 0.3	0.0 ± 0.0	1.6 ± 0.1
LA:ChCl/H$_2$O/H$_2$SO$_4$	36.6 ± 1.1	29.2 ± 0.5 (4.2 ± 0.5)	5.0 ± 0.3	0.9 ± 0.1	1.5 ± 0.2
pTSA:ChCl	100.0 ± 0.0	89.8 ± 1.6 (32.2 ± 0.8)	0.0 ± 0.0	3.7 ±0.2	6.5 ±0.4
pTSA:ChCl/H$_2$O	89.7 ± 2.5	79.4 ± 1.3 (19.7 ± 0.3)	0.0 ± 0.0	1.4 ± 0.1	8.9 ± 1.1
pTSA:ChCl/H$_2$O/H$_2$SO$_4$	97.8 ± 1.2	88.9 ± 1.5 (26.7 ± 0.5)	0.0 ± 0.0	1.6 ± 0.1	7.3 ± 0.6

389   a) Comprises compounds **11**, **12** and **14** from Table 2; b) comprises other non-cleavage compounds, including **9** and **13** from Table

390   2, and others (*e.g.* PPE dimer). Errors are expressed as standard deviation.

391

392   On the other hand, the addition of 2.5 wt% H$_2$SO$_4$ was envisaged to increase the reactivity of

393   aqueous DES systems for PPE cleavage. It was particularly successful with LA:ChCl (10:1) and

394   pTSA:ChCl (1:1) at 120 °C by increasing the cleavage performance in comparison to DES solely

395   with water. In case of aqueous LA:ChCl system with H$_2$SO$_4$, the cleavage yield (29.2 mol%) was

396   even higher than that of neat DES (23.6 mol%), and the esterification of PPE was reduced by

397   approximately 5-fold (from 25.7 mol% to 5.0 mol%). Finally, no positive effect of H$_2$SO$_4$ addition

398   was observed for PA:U (2:1) since no PPE cleavage was promoted, showing once more the

399   ineffective performance of PA:U (2:1) medium to promote such cleavage. Moreover, PPE

400   cleavage using an aqueous solution of 2.5 wt% H$_2$SO$_4$ was also tested as a control, and no

401   cleavage was observed, which means the chemical environment shaped by DES is an important

402   factor to promote disruption of lignin ether bonds.

403   Table 5 also shows intriguing molar yields of PPE-Cl when using choline chloride-based DES. The

404   molar yield of PPE-Cl is always very low in both LA:ChCl (10:1) and pTSA:ChCl (1:1) systems,

405   excepting for the experiment at 80 °C with neat pTSA:ChCl (1:1) that revealed a PPE-Cl molar

406   yield of 56.6 mol% from a total of 84.1 mol% PPE conversion. This was highlighted above in the

407   product distribution of this reaction (67.7 % PPE-Cl). PPE-Cl can in fact be an intermediate

408   species formed before PPE cleavage that is stable only in neat pTSA:ChCl (1:1). However, for the

409   same DES at 120 °C the yield of PPE-Cl was only 3.7 mol%. This could be associated to the high

410   cleavage extent promoted by neat pTSA:ChCl (1:1) at that temperature that simply consumed

411   PPE-Cl. This raises the question regarding the role of the halide counterion in DES on ether bond

412   cleavage. Up to now, the influence of the chloride anion on the ability of DES to disrupt lignin

413   chemical bonds and to extract lignin from biomass has not been studied. Therefore, to sort out

414   some evidences about a possible role of the halide on PPE cleavage, a kinetic study using

415   pTSA:ChCl (1:1) and pTSA:ChBr (1:1) was performed.

416   **3.4.   The role of the halide counterion on the PPE ether bond cleavage**

417   The reactions of PPE cleavage were performed at 120 °C and the released products from each

418   DES were quantified along the reaction time. Figure 4 shows the PPE conversion yields, cleavage

419   yields and the corresponding formation of PPE-Cl and PPE-Br over time. In both cases, a yield

420   inversion between the halide intermediate and PPE cleavage was observed, confirming that PPE-

421   Cl and PPE-Br are formed before cleavage and are consumed along the time. However, the

422   formation *vs* consumption of each intermediate, as well as the rate of PPE cleavage, differ

423   between examined DES. In case of pTSA:ChCl (1:1), almost half of the initial amount of PPE was

424   in the form of PPE-Cl after 30 min, while the cleavage yield was already 42.8 mol%. The

425   consumption of PPE-Cl to give cleavage products was pronounced, but at the end of reaction

426   (8h) PPE-Cl was not totally converted and the cleavage yield reached 89.8 mol%. On the other

427   hand, the consumption of PPE-Br is much faster than PPE-Cl. At only 5 min, 62.3 mol% of

428   cleavage products was accomplished and 32.7 mol% PPE-Br was detected. Effectively, total PPE

429   cleavage was achieved in only 1h reaction with total consumption of PPE-Br. The better

430   performance of bromide than chloride for ether bond cleavage was also reported in acidic ILs,

431   whereas [Hmim]Br demonstrated faster cleavage of GG and VG model compounds than

432   [Hmim]Cl.[21]

433   The main reason for the higher efficiency of pTSA:ChBr (1:1) in the cleavage of PPE is associated

434   to the stronger nucleophilicity of the bromide anion in comparison to chloride. Bromide allows

435 a faster substitution of the hydroxyl group in PPE to form the corresponding halide intermediate

436 that precedes the ether bond cleavage. Surprisingly, these halide intermediates were never

437 reported in mechanisms of β-O-4 ether bond cleavage using for instance HCl and HBr as

438 catalysts[49,50] or in acidic systems containing halide-based ILs.[20,21,51] Therefore, using choline

439 halide-based DES with a strong organic acid, like pTSA:ChCl and pTSA:ChBr, seems to mediate a

440 different mechanism of β-O-4 ether bond cleavage.
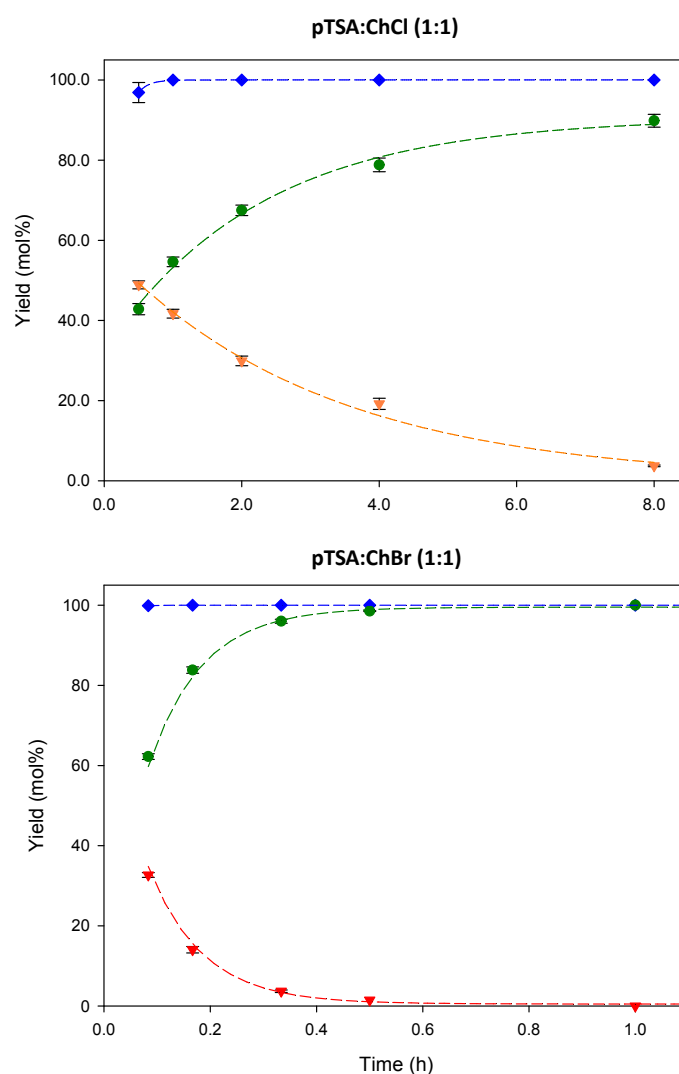
441

442 **Figure 4.** The yields of PPE conversion (◆), cleavage (●) and the content of chlorinated (▼) and

443 brominated (▼) PPE compounds in reactions at 120 °C using pTSA:ChCl (1:1) (at the top) and

444 pTSA:ChBr (1:1) (at the bottom), correspondingly. Note that different time scales were

445 employed for clarity of results. The lines are merely a guide for the eye.

446

447   The acidic cleavage of aryl ether bonds in lignin model compounds has been studied by several

448   researchers along the years and the following mechanistic steps have been commonly

449   suggested: i) protonation of hydroxyl group at α-carbon; ii) dehydration at α-carbon and

450   deprotonation at β-carbon; iii) formation of carbocation and/or enol-ether intermediate; iv)

451   hydroxylation at β-carbon and v) β−O−4 ether bond cleavage.[25] Although slight different

452   nuances and more detailed steps have been reported, in general this mechanism has been

453   associated to aqueous acidic mediums containing H_2SO_4, HCl and HBr,[49,50] and also to acidic ILs,

454   including [Hmim]Cl and [Hmim]Br,[20,21] SO_3H-based and HSO_4-based ILs.[23–25] In other words, it

455   corresponds to an acid-catalysed cleavage mechanism, where the acidic proton plays the major

456   role on the cleavage reaction. From these studies, some researchers found that the initial

457   dehydration of the lignin model compound is the limiting step determining the cleavage reaction

458   rate.[24,25,52] Sturgeon *et al.* performed DFT calculations and showed that in PPE cleavage reaction

459   pathway the highest ΔG was related to the dehydrated form of PPE, thus the most energy

460   dependent intermediate.[52] In this context, De Gregorio *et al.* mentioned that acidic ILs by playing

461   both catalytic and solvent roles allow stabilization of intermediates, decreasing ΔG, and by this

462   the cleavage reaction rate increases.[24] This poses the following question: can acidic deep

463   eutectic solvents containing halide counterions act on the ether bond cleavage similarly?

464   Alvarez-Vasco *et al.* reported that β-O-4 ether bond cleavage with the acidic LA:ChCl follows the

465   mechanism from the lignin acidolysis with HCl, but no role to chloride anion was identified on

466   this process.[29]

467   The results obtained in this study allow to propose another mechanism showing a possible role

468   of the halide counterion in DES. An example with Cl⁻ anion from PTSA:ChCl is depicted in Figure

469   5 and the mechanistic steps can be described as the following: i) protonation of hydroxyl group;

470   ii) nucleophile attack of the halide anion at α-carbon and release of oxonium ion (dehydration);

471   iii) formation of halide PPE intermediate; iv) dehydrochlorination and formation of enol-ether

472 intermediate; v) ether bond cleavage. Basically, a fast dehydration of PPE is achieved and a

473 stable intermediate is formed, which in turn decreases the energy needed to perform the ether

474 bond cleavage (lower ΔG).

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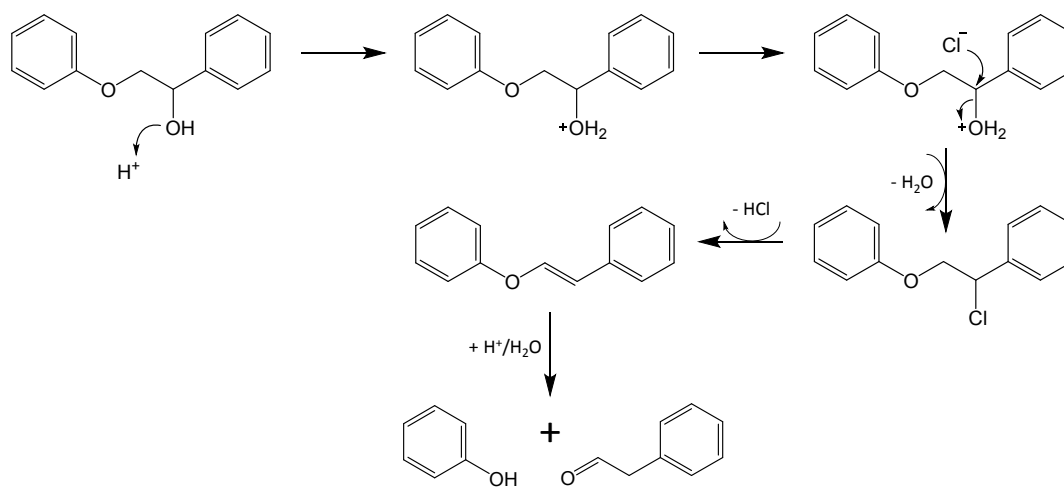
476

477 **Figure 5.** A proposed mechanism of PPE cleavage in presence of pTSA:ChCl (1:1) showing the

478 formation of a chlorinated intermediate with further dehydrochlorination enhancing the rate of

479 β-O-4 ether bond cleavage. The same mechanism can be considered for bromide using

480 pTSA:ChBr (1:1).

481

482 The proposed mechanism for PPE cleavage was analysed in this work by means of DFT

483 calculations. Based on the experimental results described above, a deep focus was put on the

484 first steps corresponding to the protonation of hydroxyl group, the dehydration at α-carbon (i.e.,

485 water release) and the deprotonation at β-carbon (i.e., formation of the enol-ether

486 intermediate: double bond between α and β carbons). Particularly, the role of the halide anions

487 in the process was inspected upon comparison of the free energy profiles for the reaction of PPE

488 with pTSA in the presence and in the absence of the halide species (Figure 6). The results in

489 Figure 6 clearly support that water release from PPE is more favourable in the presence of the

490 chloride or bromide anions. As it can be seen in the structural models inserted in Figure 6, the

491   halide anion binds the α-carbon during the dehydration step, stabilizing not only the transition

492   state structure but also the dehydrated intermediate species. With respect to the initial

493   configuration, the transition state structure for the reaction without the halide anions is > 12

494   kcal/mol above those calculated in the presence of Cl⁻ or Br⁻ species. Also, in the case of the

495   reaction solely with pTSA, the final state of the dehydration step is significantly more unstable

496   than the initial state (50 kcal/mol), while in the presence of the halide species, the 1-

497   chloro/bromo-2-phenoxyethyl)benzene intermediate is only 3/6 kcal/mol less stable than the

498   initial state, respectively.

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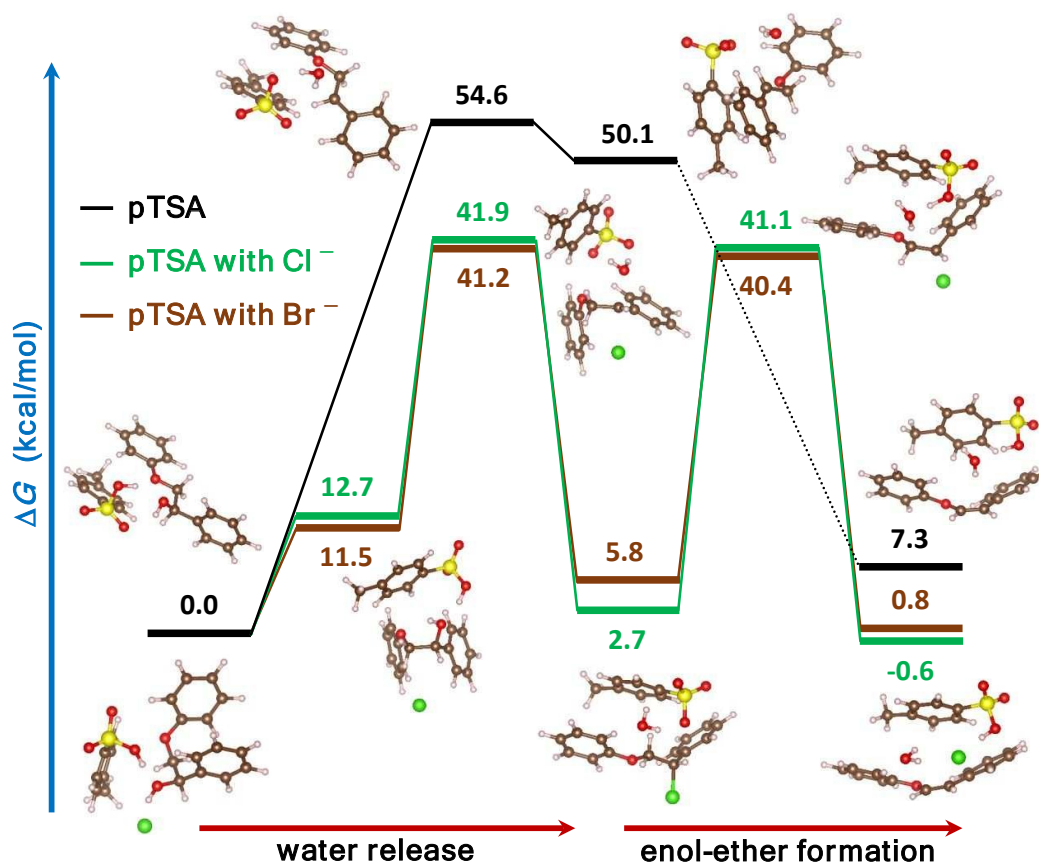
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501   **Figure 6.** Calculated free energy profiles for the first steps of the PPE cleavage in the presence

502   of pTSA (black lines), of pTSA with Cl⁻ (green lines) and of pTSA with Br⁻ (brown lines). Colour

503   code for spheres: white is H; brown is C; red is O; yellow is S and green is Cl⁻. Ball and stick models

504 show the optimized structures for the reaction in the absence and in the presence of halide (only

505 chloride models are shown because of their similarities with the bromide counterpart species).

506

507 Very recently, Jing et al.[25] reported the results of a computational study for the catalytic

508 breakage of the β-O-4 linkage in veratrylglycerol-β-guaiacyl ether, used as a lignin model. Their

509 DFT calculations have also shown that the product of the dehydration step (i.e., the cation at

510 the α-carbon) is much more unstable than the reactants since the transition state structure is

511 closely related to the carbocation species than to the reactants.

512 In the presence of the halide anions, the carbocation species is not formed since the halide anion

513 binds the α-carbon as water molecule is released, with a concomitant stabilization of the

514 dehydration step. Interestingly, the energy variation of this elementary step is very similar for

515 both halide anions. However, the formation of the 2-phenoxyvinylbenzene from the 1-

516 chloro/bromo-2-phenoxyethyl)benzene intermediate occurs more favourably when the halide

517 is bromide, which agrees with the fact that bromide is better leaving group than chloride.

518 Encouragingly, these results support the faster PPE conversion observed experimentally (Figure

519 4) when using pTSA:ChBr (1:1) rather than pTSA:ChCl (1:1), besides the higher nucleophilicity of

520 bromide mentioned above.

521 The ability of chloride and bromide anions to speed up PPE cleavage was also investigated by

522 contrasting the cleavage kinetics of pTSA:ChCl (1:1) and pTSA:ChBr (1:1) with corresponding

523 aqueous solutions and pTSA aqueous solution as well. The obtained PPE cleavage yields are

524 depicted in Figure 7. Again, a negative influence of water on the ability of acidic DES to break β-

525 O-4 ether bond in PPE was observed. In case of aqueous solutions of pTSA:ChCl (1:1) and

526 pTSA:ChCl (1:1), the presence of 50 wt% water may cause significant dilution that compromises

527 the efficiency of the cleavage. However, rather than dilution, water also has a direct impact on

528 the reaction. As aforementioned, the PPE cleavage requires initial protonation of the substrate

529 followed by a dehydration step, thus the presence of high quantities of water, which also act as

530   reagent, will retard the reaction progress.[24,53] Since it directly affects the rate limiting step, the

531   negative influence of water is pronounced as demonstrated in Figure 7.

532   However, negligible contents of chlorinated or brominated PPE were always observed in the

533   reactions with pTSA:ChCl and pTSA:ChBr aqueous systems, indicating that such intermediates

534   are unstable or unfavourable in the presence of water reducing the cleavage rate. Nevertheless,

535   for pTSA aqueous solution, *i.e.* in absence of ChCl or ChBr, an even higher decrease of the PPE

536   cleavage efficiency was obtained (Figure 7). This means that in aqueous solutions the role of the

537   halide counterion in DES is preserved, although with a lower efficiency. Particularly in pTSA:ChCl

538   and pTSA:ChBr aqueous solutions, it is expected that polar protic solvents like water form

539   hydrogen bonds with halide, hindering it from attacking the α-carbon containing the leaving

540   group (oxonium ion – Figure 5) and to promote PPE dehydration.
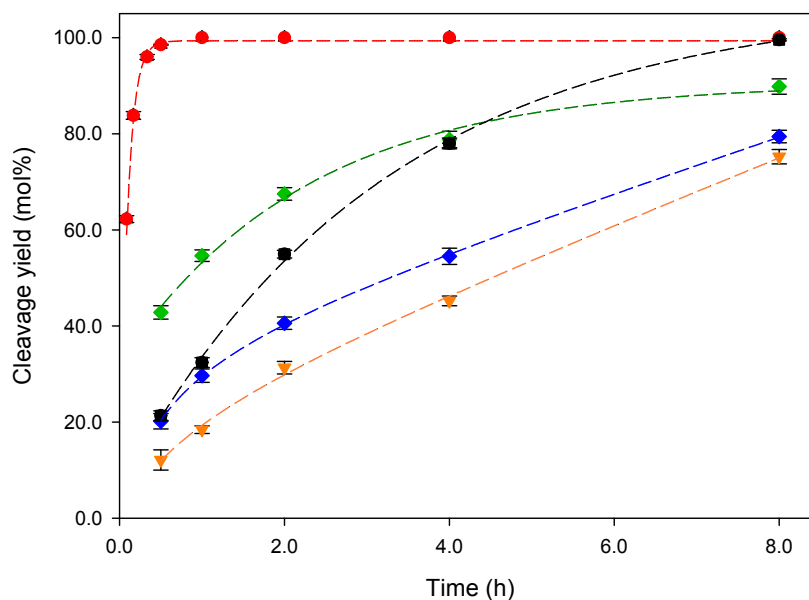
541

542   **Figure 7.** The PPE cleavage yields of pTSA:ChBr (1:1) (●), pTSA:ChCl (1:1) (●), pTSA:ChBr (1:1)

543   aqueous solution (50 wt% H_2O)(◆), pTSA:ChBr (1:1) aqueous solution (50 wt% H_2O) (◆), and

544   pTSA aqueous solution (≈70 wt% H_2O) (▼), at 120 °C during 8h. The lines are merely a guide for

545   the eye.

546

547   Finally, another evidence suggesting a beneficial role of the halide counterion is the prevention

548   of PPE dimerization. The formation of PPE dimer as consequence of the reaction between PPE

549   and its dehydrated form was favoured in aqueous solutions, especially with pTSA aqueous

550   system in the absence of ChCl or ChBr (data not shown). This phenomenon could be also

551   important when transposing to biomass delignification with DES, in which the presence of a

552   halide counterion may be beneficial to protect lignin from self-condensation.

553   **3.5.**   **pTSA:ChCl and pTSA:ChBr as promising media for β-O-4 ether bond cleavage**

554   Currently, there is no quantitative data about β-O-4 ether bond cleavage with DES, but a

555   benchmark between the most efficient DES herein proposed, namely pTSA:ChCl and pTSA:ChBr,

556   with the state-of-the-art can be performed. In 30 min, pTSA:ChCl (1:1) was capable to cleave

557   42.8 mol% of PPE at 120 °C, while pTSA:ChBr (1:1) allowed 62.3 mol% PPE cleavage in only 5 min

558   at the same temperature (Figure 7). These are cutting-edge results that are comparable to those

559   described in literature using other non-aqueous systems, including acidic ILs.[20–23] For instance,

560   the cleavage of GG model compound with [Hmim]Cl and [Hmim]Br was attempted in different

561   studies and approximately 35 % (130 °C/15 min) and 60 % (130 °C/20 min) guaiacol yield

562   (cleavage product) was achieved, respectively.[20,21] On the other hand, the cleavage of BPE model

563   compound with [bmim]HSO_4 demonstrated around 60 % guaiacol yield in only 5 min, although

564   the reaction was performed with microwave irradiation at very high temperature (180 °C).[22]

565   Moreover, Scott *et al.* demonstrated that SO_3H-functionalised imidazolium ILs were capable to

566   cleave MPPE and reached almost 60 % guaiacol at 140 °C for 5 min. These results achieved with

567   acidic ILs confirm that the acidic DES shown in this work present similar performance on the

568   cleavage of lignin model compounds at mild temperatures and short residence times. However,

569   a relevant issue must be highlighted when contrasting these results, namely the fact that GG is

570   a phenolic dimer, while BPE and PPE (studied in this work) are non-phenolic dimeric model

571   compounds. Sturgeon *et al.* tested the cleavage of phenolic (GG and VG) and non-phenolic

572   dimers (PPE) by acid catalysis in 0.2 M H_2SO_4 at 150 °C and observed that cleavage of phenolic

573   dimers can be 2 orders of magnitude faster than non-phenolic dimers. This suggests that GG

574   cleavage in pTSA:ChCl and pTSA:ChBr could be even faster or proceed at milder conditions than

575   ILs. Therefore, the results shared in this study place pTSA:ChCl and pTSA:ChBr as promising

576   solvents to apply in biomass delignification with higher sustainability than traditional processes.

577   The use of DES could be also an economical advantage over their IL counterparts and,

578   simultaneously, it could maintain or improve the selectivity and efficiency of lignin extraction.

579

580   **4.   Conclusions**

581   The present study gathered relevant insights regarding the influence of the acidic nature of DES

582   on the cleavage performance of PPE model compound that can be transposed to biomass

583   delignification processes. For instance, PA:U (2:1), that demonstrate ability to dissolve technical

584   lignins may not be able to delignify biomass, as consequence of its incapacity to disrupt β-O-4

585   ether bond as shown in this work. Moreover, LA:ChCl, which is reported in literature as one of

586   the most efficient DES performing biomass delignification, revealed some technical concerns.

587   Although LA:ChCl (10:1) demonstrated moderate ether bond cleavage of PPE that confirms its

588   ability for delignification, other side reactions including substrate esterification with

589   oligomerization of lactic acid were unleashed by this DES. Therefore, some offsets may result

590   from the use of LA:ChCl in biomass processing by producing modified lignin with lactic acid and

591   subsequent consumption of the solvent in the reaction. On the other hand, the cleavage

592   efficiency of PPE using pTSA:ChCl (1:1) was much higher, although the high acidity of this

593   medium allowed undesired condensation of cleavage products. The presence of water in DES

594   decreased the formation of condensed products, but the cleavage activity of DES was also

595   reduced. In this context, the addition of sulphuric acid at catalytic amounts allowed an increase

596   of the cleavage performance of DES aqueous solutions.

597   In the analysis of reaction products, halide intermediates that precede the PPE cleavage reaction

598   were herein reported for the first time. The kinetic study performed with pTSA: ChCl (1:1) and

599   pTSA: ChBr (1:1) demonstrated that PPE-Cl and PPE-Br intermediates are important to speed up

600   the cleavage reaction, which was confirmed by the results from DFT calculations. In literature,

601   the formation of a dehydrated form of PPE is considered the rate limiting step of the cleavage

602   reaction, which is overcome by the presence of a strong organic acid, (e.g. pTSA), a nucleophile

603   (Cl^- or Br^-) and the absence of water. The faster the hydroxyl group substitution of PPE by the

604   halide anion and its subsequent leaving to form the enol-ether intermediate, the faster is the

605   ether bond cleavage. For instance, 62.3 mol% of cleavage products was achieved with pTSA:ChBr

606   (1:1) at 120 °C in only 5 min, which represents one of the fastest β-O-4 ether bond cleavages

607   when benchmarked with the ultimate technologies, such as ILs. Therefore, the application of

608   acidic DES for β-O-4 ether bond cleavage was successfully demonstrated in this work, where

609   pTSA:ChBr and pTSA:ChCl stands as promising solvent systems with interesting catalytic

610   properties. In this context, biomass delignification trials with these DES should be addressed as

611   a forward step.

612

613   **Acknowledgments**

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