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Oxidative cleavage of C–C bonds in lignin

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Lignin is an aromatic polymer that constitutes up to 30 wt% of woody biomass and is considered the largest source of renewable aromatics. Valorization of the lignin stream is pivotal for making biorefining sustainable. Monomeric units in lignin are bound via C–O and C–C bonds. The majority of existing methods for the production of valuable compounds from lignin are based on the depolymerization of lignin via cleavage of relatively labile C–O bonds within lignin structure, which leads to yields of only 36–40 wt%. The remaining fraction (60 wt%) is a complex mixture of high-molecular-weight lignin, generally left unvalorized. Here we present a method to produce additional valuable monomers from the high-molecular-weight lignin fraction through oxidative C–C bond cleavage. This oxidation reaction proceeds with a high selectivity to give 2,6-dimethoxybenzoquinone (DMBQ) from high-molecular-weight lignin in 18 wt% yield, thus increasing the yield of monomers by 32%. This is an important step to make biorefining competitive with petroleum-based refineries.

Lignocellulosic biomass is the most available renewable source of organic matter worldwide and it can potentially serve as an alternative to petroleum in the production of materials, chemicals and fuels. Lignocellulose consists of cellulose (30–50%), hemicellulose (20–35%) and lignin (15–30%)[1]; however, the main industrial pulping processes focus on the production of value-added products primarily from cellulose—leaving lignin and hemicellulose to serve as a heat and power source for the pulp mill[2]. Given the amount of lignin produced in nature (approximately 1.5 million tonnes per year)[3] and the amount of lignin generated at pulp mills (the most common type of biorefineries[4]; approximately 70 million tonnes per year), the development of new and more efficient methods to utilize all components of lignocellulose is gaining attention (Fig. 1).

A new approach to lignocellulose processing that has emerged over the past decade is the so-called lignin-first method, also known as early stage catalytic conversion of lignin or catalytic upgrading biorefinery[1,5]. The most reported method of this type is the reductive catalytic fractionation (RCF) of lignocellulose[6–8]. During this process, the lignin–carbohydrate complex is disassembled and lignin is released into solution along with hemicellulose. The lignin fragments are further reacted over a catalyst to give the theoretical maximum yield of monophenolic compounds from lignin. A majority of current lignin-first methods rely on the use of transition metal (Ni, Ru, Pd) catalysts, although some transition metal-free methodologies have also been developed (Fig. 1)[9–12].

These fractionation methods have a high retention of cellulose as a solid pulp, which can be further transformed by enzymatic hydrolysis into sugars or used in polymeric form for the production of fibres and other cellulose-based materials. Hemicellulose can be used as a hydrogen source for the fractionation process[13,14], retained in a solid pulp or isolated from the water phase as sugars or derivatives thereof.

In regard to lignin, most of the developed catalytic fractionation methodologies are limited to the production of monomeric value-added products via the cleavage of C–O bonds (mainly β-O-4′ bonds) with relatively low bond dissociation energies (~60 kcal mol^{-1})[15]. Monomeric products are easily separated by distillation and can be converted to versatile synthetic precursors. The theoretical maximum yield is a term widely used in the current literature to describe the yield of monomers predicted based on the β-O-4′ bond content in a feedstock. The theoretical maximum yield of lignin monomers is calculated as x^2, where x is the β-O-4′ bond content in lignin. Assuming that lignin is a polymer of infinite length and that the bonds are distributed randomly, the probability that a monomeric unit is attached to both neighbouring units via β-O-4’ bonds is x^2; therefore, given that the abundance of β-O-4′ bonds in lignin is approximately 60%, which is easily measured by thioacidolysis, the theoretical maximum yield of lignin monomers is approximately 36 wt%.

Aside from the monomeric compounds produced in a lignin-first process, more than half of the lignin oil remains unvalorized as an inseparable mixture of dimers and higher oligomers consisting of C–C bonds of high bond dissociation energy (80–120 kcal mol^{-1})[15]. Furthermore, the dimeric and oligomeric fraction is highly irregular which hampers its utilization. Lately, there has also been interest in valorizing the dimers and oligomers[16]. The difficulty in cleaving C–C bonds is illustrated by Wang's group that recently reported the Ru/NbOPO$_4$-catalysed cleavage of both C–C and C–O bonds in lignin[17]. To achieve the cleavage of both bonds, harsh reaction conditions—including high temperature (310 °C) and hydrogen gas—were required. Even such, the best cases still produced total yield of monomers of 31.9 wt%, in complex mixtures that are tedious to separate.

Here we present a protocol to overcome the theoretical maximum yield limitation by the production of further commercially valuable monomers from the high-molecular-weight fraction of lignin oil, yielding solely 2,6-dimethoxybenzoquinone (DMBQ) with high selectivity (Fig. 1). This protocol involves the oxidative cleavage of C–C bonds with (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO)-based oxidants (oxoammonium salts). We have performed a detailed mechanistic study to understand the fundamental steps in this transformation. Biological activity of benzoquinones makes them valuable compounds for medicinal chemistry and biochemistry. Benzoquinones are known to be involved in crucial biological processes such as respiration and photosynthesis on

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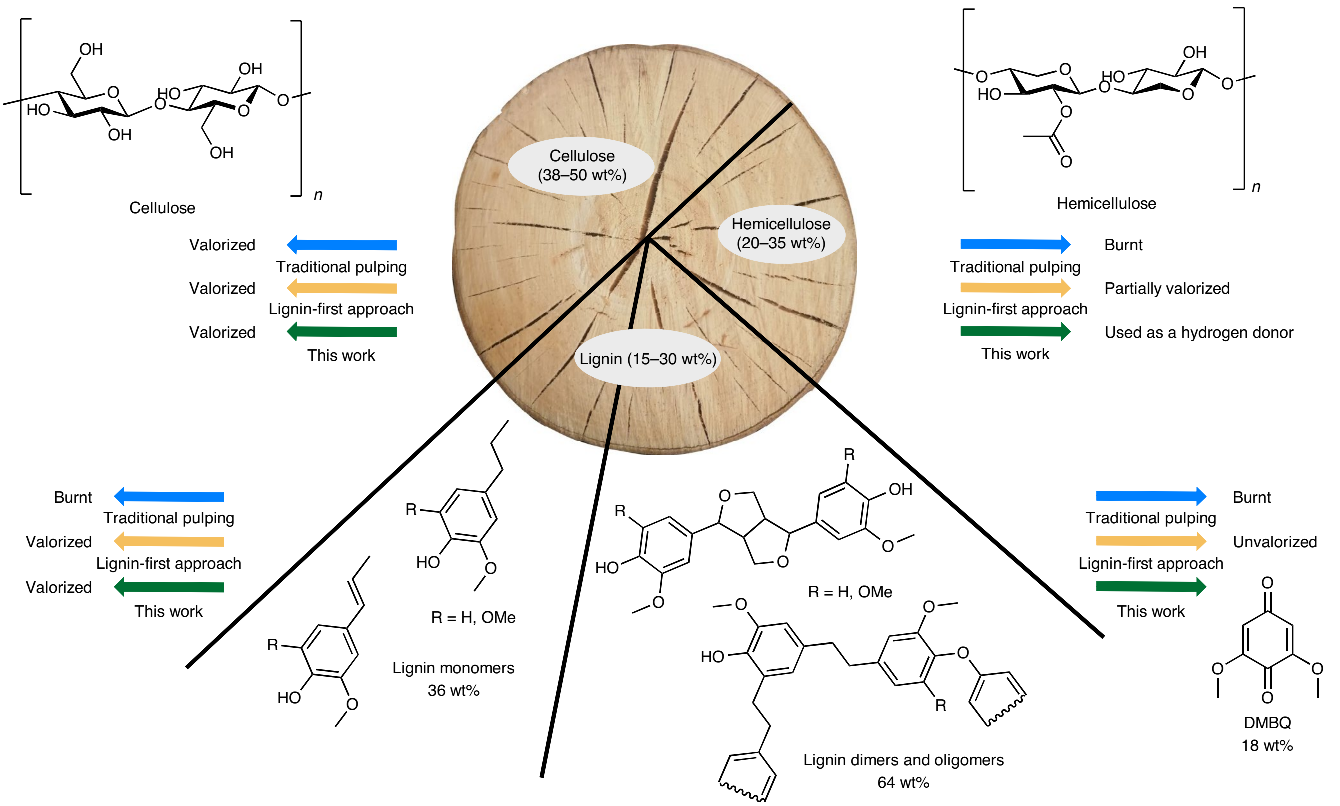


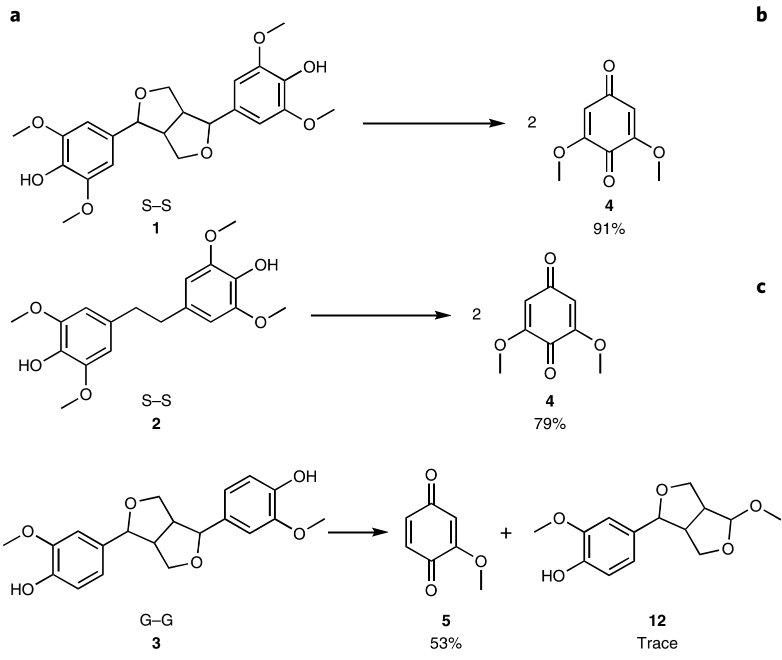
Fig. 1 | Valorization strategy of woody biomass. In traditional pulping only the cellulose part of the biomass is valorized, whereas lignin and hemicellulose are burnt to produce heat and energy for the pulp mill. In the lignin-first approach, cellulose is valorized and hemicellulose and lignin are partially valorized, where lignin is converted into valuable monomers (up to 36 wt%) via in-situ depolymerization, whereas lignin dimers and oligomers (64 wt%) are unvalorized. In this work we expand the lignin-first approach and develop a method for the production of additional monomers from the mixture of lignin dimers and oligomers via oxidation with Bobbitt's salt to give 2,6-dimethoxybenzoquinone (DMBQ).

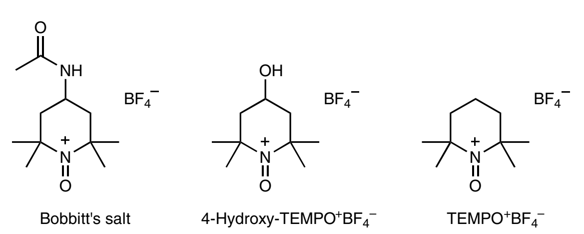
a cellular level[18]. They are used as building blocks for the synthesis of antitumour compounds chaloxone and *Streptomyces* metabolite LL-C10037α[19–21]. Studies on hydroxylated derivatives of DMBQ revealed their high stability under physiological conditions and strong radical scavenging properties[22]. Thus, examples of possible application of DMBQ include antifungal, antitumor or antioxidant agents. Furthermore, DMBQ was found to be an excellent biomimetic electron-transfer mediator for ruthenium-catalysed aerobic oxidation of alcohols due to the low oxidation potential of the corresponding dimethoxyhydroquinone[23,24]; however, benzoquinones are currently produced via the oxidation of petroleum-derived aromatic compounds with metal-based oxidants, presenting environmental concerns. Our greener pathway to the production of benzoquinones is thus expected to be of interest to the chemical industry.

Results and discussion

Selection of model compounds. We commenced our studies with the isolation and characterization of the fraction of lignin dimers and oligomers (DO) obtained during the RCF of birch wood. Lignin oil (consisting of value-added monophenolic products and a high-molecular-weight fraction) was isolated by dichloromethane (DCM)/water extraction and distilled to remove the monophenolic products (the mass balance and the pulping conditions are presented in Supplementary Table 1). The size-exclusion chromatogram of the residue revealed the presence of only dimers, trimers and higher oligomers, indicating the successful removal of monophenolic compounds (see Supplementary Appendix 3). Gas chromatography–mass spectroscopy analysis of the DO fraction showed that the main observed dimer is a β-β′ structure formed between two syringol units. This dimer constituted 3.9 wt% of the DO fraction, indicative of a high percentage of higher oligomers in the mixture (Supplementary Table 3). Other dimers with β-1′ and β-5′ structures were also observed. Notably, the reductive conditions used during the fractionation process led to hydrogenolysis at the benzylic positions in the β-1' and β-5' dimers (Supplementary Appendix 1). Thus, the generated dimers are different from those present in native lignin, which governed our choice of the model compound representing β-1′ dimer (where the benzylic position is reduced). The structures of the obtained dimers are in agreement with those previously reported[25]. The S/G ratio of phenolic units (that is, the ratio between syringyl and guaiacyl units) in the DO fraction was measured by quantitative ^{31}P NMR (Supplementary Table 4 and Supplementary Fig. 1)[26], and a value of 5/1 was determined, indicating a high prevalence of S units in the DO fraction; thus, for initial optimization, we synthesized model compounds **1** and **2**, which represent β-β′ and β-1′ dimers, respectively (Fig. 2a). To use model compounds is a general practice in lignin chemistry to study the mechanism of specific bond cleavage in the complex lignin structure. Although the G unit is less representative of the substrate used in the current study (birch wood), it might be relevant for other types of biomass; thus, model compound **3**, which represents the β-β′ G–G dimer, was also prepared and studied (Fig. 2a).

Optimization of reaction conditions. Oxidative cleavage of lignin has a long history. For example, vanillin is industrially produced by oxidative cleavage of lignosulfonates[27], and the oxidative degradation of residual lignin is known to occur in bleaching and has





c

Entry	Model	Oxidant	Solvent	Water (wt%)	4/5 Yield (%)
1	1	Bobbitt's salt (6)	MeCN	0.6	22[a]
2	1	Bobbitt's salt (6)	MeOH	0	31[a]
3	1	Bobbitt's salt (6)	MeOH	0.16	66[a]
4	1	Bobbitt's salt (6)	MeOH	0.4	91[a]
5	1	Bobbitt's salt (6)	MeOH	1.25	76[a]
6	1	4-Acetamido-TEMPO (6)	MeOH	0.4	—
7	1	TEMPO^{+}BF$_4^{-}$ (6)	MeOH	0.4	94[a]
8[c]	1	4-HydroxyTEMPO^{+}BF$_4^{-}$ (6)	MeOH	0.4	92[a]
9[d]	2	Bobbitt's salt (10)	MeOH	0.4	79[a]
10	3	Bobbitt's salt (10)	MeOH	0.4	66[b]

Fig. 2 | Oxidation of lignin model compounds. a, The main products of the oxidation of β-β′ and β-1′ model compounds. Oxidation of model compounds bearing syringyl moieties (**1** and **2**) results in selective formation of dimethoxybenzoquinone **4**, whereas oxidation of model compound **3** bearing guaiacyl units leads to formation of a more complex mixture of products including methoxybenzoquinone **5**. **b**, The TEMPO-based oxidants and their analogues used in this study. **c**, Optimization of the reaction conditions for oxidation of model compounds **1**, **2** and **3**. Reaction conditions: 30 mg model compound, 1 h, r.t., 4 ml solvent. [a]Yields relative to 2 equiv. of product formed. [b]Yield relative to 1 equiv. of product formed. [c]The oxidant was used as a mixture of the reduced and oxidized forms of the corresponding TEMPO derivative. [d]*T* = 100 °C. S, syringyl; G, guaiacyl. The numbers in brackets in the oxidant column represent the number of equivalents used.

been applied to pulp to improve its brightness. These processes, although generating benzoquinones as products of lignin degradation, are generally focused on the degradation of lignin rather than valorization and thus lack selectivity[28–30]. More recently, metal-catalysed oxidation reactions of lignin model compounds have been reported[31–35]; however, these studies are related to β-O-4′ lignin models. In addition to model studies, cobalt-catalysed aerobic oxidation of poplar lignin was reported where DMBQ was obtained in 1.7 wt% yield[34]. Wang's group has expanded the oxidative approach to native β-1′ motifs via photocatalytic cleavage of lignin model compounds[36,37]. The reactivity of a β-β′ motif without free phenolic groups under oxidative conditions (2,3-dichloro-5,6-dicyano-1,4-benzoquinone oxidation) was investigated by Westwood's group and resulted in the formation of pyran-4-one without cleavage of the C–C bonds[38].

Stahl's group has contributed to the research field by performing extensive studies to develop metal-free oxidation reactions of alcohol functionalities in lignin, which facilitate the subsequent cleavage of β-O-4′ bonds to form monomeric products[39,40]; however, C–C bond cleavage of β-β′, β-1′ or other motifs from the oligomeric fractions obtained by RCF was not a focus in these studies. Furthermore, the oxidation of phenolic compounds by oxoammonium salts was studied in the early period of the development of oxoammonium salt oxidation reactions. The main products of the reaction of phenolic compounds were dimeric quinone structures[41,42].

Inspired by the previous efforts, we sought to develop a benign and selective oxidation procedure to cleave lignin C–C bonds in the low-value DO fraction and convert a portion of the compounds in this fraction to DMBQ with high selectivity. The above-mentioned reactions using oxoammonium salts (Fig. 2b) were conducted in a MeCN or DCM solvent[41,42]. We expected that the addition of a suitable nucleophile would help prevent the formation of undesirable dimeric products due to attack by a nucleophilic arene on the electrophilic intermediate after initial oxidation. Indeed, when the reaction was performed in a MeCN/H_2O mixture, DMBQ **4** was isolated in 22% yield along with unidentified by-products (Fig. 2c, entry 1). Replacing MeCN with MeOH and optimizing the amount of added water led to facile formation of DMBQ. Under the optimized reaction conditions, DMBQ was isolated in 91% yield (Fig. 2c, entry 4). No other products were detected in the crude mixture. The reaction with an oxidant in its radical form (4-acetamido-TEMPO) resulted in no conversion of the starting material, indicating that an oxidized form (Bobbitt's salt) is required (Fig. 2c, entry 6). Tetrafluoroborate salts of 4-hydroxy-TEMPO and TEMPO were also tested (Fig. 2c, entries 7 and 8). It is worth mentioning that 4-substituted derivatives of TEMPO (for example, Bobbitt's salt, TEMPOL) are less expensive alternatives to TEMPO-derived oxidants as they can be prepared from triacetonamine, which is available at a low price (US$3 per kilogram)[43]. Because Bobbitt's salt is commercially available and gave good results, this oxidant was chosen for further optimization.

Another common motif found in the DO mixture is a reduced β-1′ dimer with two bridging carbon atoms, represented by model compound **2**. To convert model **2** to DMBQ **4**, an increased amount of oxidant and a higher temperature (100 °C) were required (see the 'Mechanistic studies' section for further explanation). The final product **4** was generated in 79% isolated yield (Fig. 2c, entry 9).

The reaction with model compound **3**—under the same conditions used for model **2**—resulted in a more complex mixture of cleaved products, due to the free 5-position of the aryl of the G unit. Methoxybenzoquinone **5** was isolated in 53% yield (relative to 1 equiv. of product formed) along with trace amounts of compound **12** (Fig. 2a and entry 10 of Fig. 2c; see Supplementary Section 8.5 for more details).

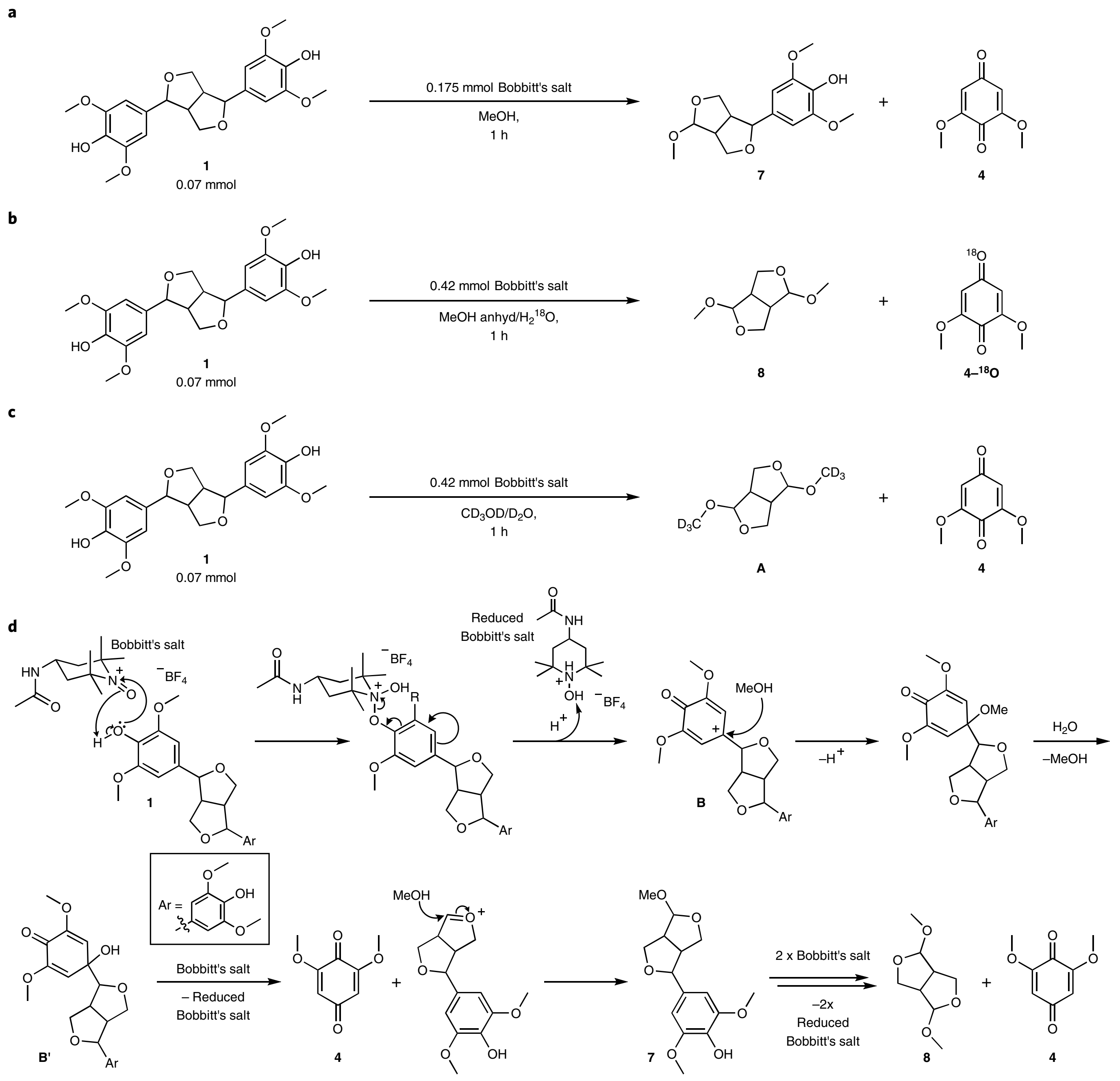


Fig. 3 | Mechanistic studies of the oxidation of model compound 1. a, Performing the reaction with a lower amount of oxidant allowed to detect intermediate product **7**, where cleavage of only one C–Aryl bond occurred. **b**, Oxidation of **1** in the presence of isotopically labelled water[18] showed that one of oxygen atoms in final product **4** stems from water. **c**, We performed the reaction in CD_3OD/D_2O solvent mixture to discern whether the oxidation of **1** proceeds via a quinone methide intermediate. No incorporation of deuterium in positions five and six occurred, indicating that quinone methide is not an intermediate in this transformation. **d**, The proposed mechanistic scheme for the oxidation of model **1**. We propose that reaction begins with the oxidation of the phenolic moiety of **1** to give **B**. Carbo-cation **B** is probably trapped by MeOH, followed by exchange to water (based on the isotopic labelling experiments) to form intermediate **B**′, oxidation of which results in the formation of final product **4**.

Mechanistic studies. We performed mechanistic studies to explain the differences in the reactivity of model compounds **1** and **2**, and to obtain a better understanding of the amount of oxidant required for the transformation. We initiated our studies using model compound **1**. Performing the reaction with a lower oxidant/substrate molar ratio (2.5) allowed us to isolate intermediate **7** (Supplementary Section 8.3 and Fig. 3a). When the reaction was performed with an oxidant/substrate molar ratio of 6, bicyclic product **8** (Fig. 3b) was isolated. The reaction in dry methanol with the addition of isotopically labelled water (H_2O; ref. [18]) resulted in the formation of mainly DMBQ with an incorporated ^{18}O atom (high-resolution mass spectroscopy: ^{18}O:^{16}O = 87:13; Fig. 3b), showing that water is the source of one of the oxygen atoms in compound **4**. To further elucidate the reaction mechanism, the reaction was performed in a CD_3OD/D_2O mixture. Gas chromatography–mass spectroscopy analysis of the reaction mixture revealed the formation of product **A** (Fig. 3c).

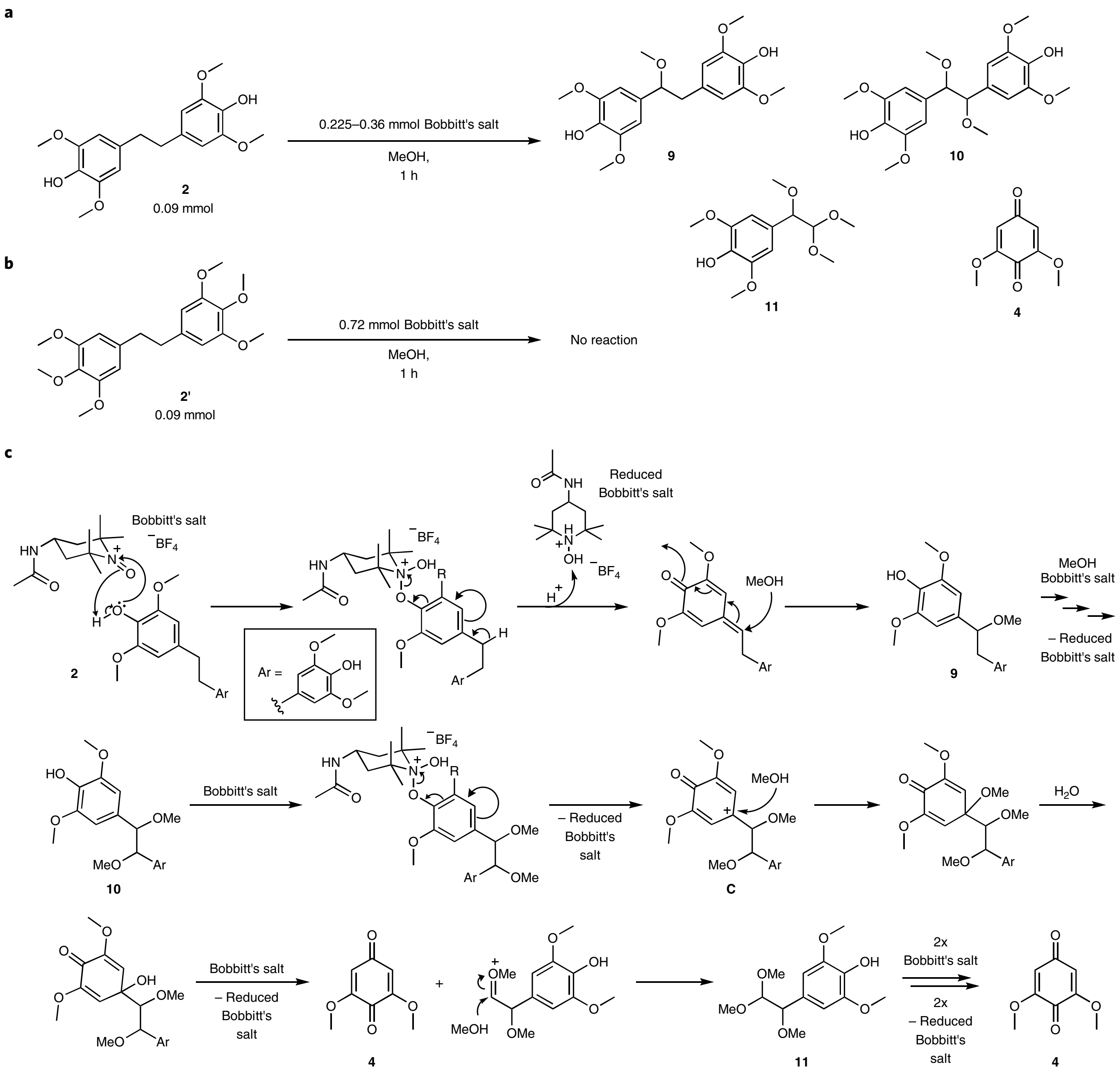


Fig. 4 | Mechanistic studies of the oxidation of model compound 2. a, Performing the reaction with a lower amount of oxidant allowed detection of intermediates **9** and **10**, showing that methoxylation of benzylic position occurs before the cleavage of C–Ar bonds. This is further supported by the detection of intermediate **11**, where one of the C–Ar bonds is cleaved. **b**, No reaction occurred when the oxidation of model compound **2**′ (lacking free phenolic moieties) was attempted, demonstrating the necessity of the phenolic group for the transformation. **c**, We propose that oxidation of model **2** begins with the formation of quinone methide followed by its reaction with MeOH, which results in the formation of product **9**. We propose that after the methoxylation of both benzylic positions of model **2**, the reaction proceeds in a similar fashion to the reaction with model **1**.

As the deuterium atom was not incorporated at positions 5 and 6 in the resulting product **A**, we conclude that no deprotonation of the benzylic position of **1** occurred (Fig. 3c); the mechanism thus does not involve the formation of a quinone methide intermediate.

Based on the aforementioned experiments and literature reports, we propose the following reaction mechanism (Fig. 3d): the reaction begins with the oxidation of the phenolic moiety of **1** to form dearomatized carbo-cation **B**, which is probably stabilized by a neighbouring oxygen atom from an ether group. Based on isotopic labelling experiments (Fig. 3b), we propose that nucleophilic attack by methanol followed by an ipso-substitution by water leads to **B**′. Oxidation of **B**′ furnishes the final product DMBQ **4**, along with bicyclic acetal **8**. The overall transformation of 1 mol of compound **1** thus requires 4 mol of oxidant.

When the reaction of model **2** was studied in a similar manner (with lower amounts of oxidant), intermediates **9**, **10** (with an oxidant/substrate molar ratio of 2.5) and **11** (with an oxidant/substrate molar ratio of 4) were isolated (Supplementary Section 8.4 and Fig. 4a). Products **9** and **10** indicate the initial formation of a quinone methide from **2**, followed by nucleophilic attack by methanol.

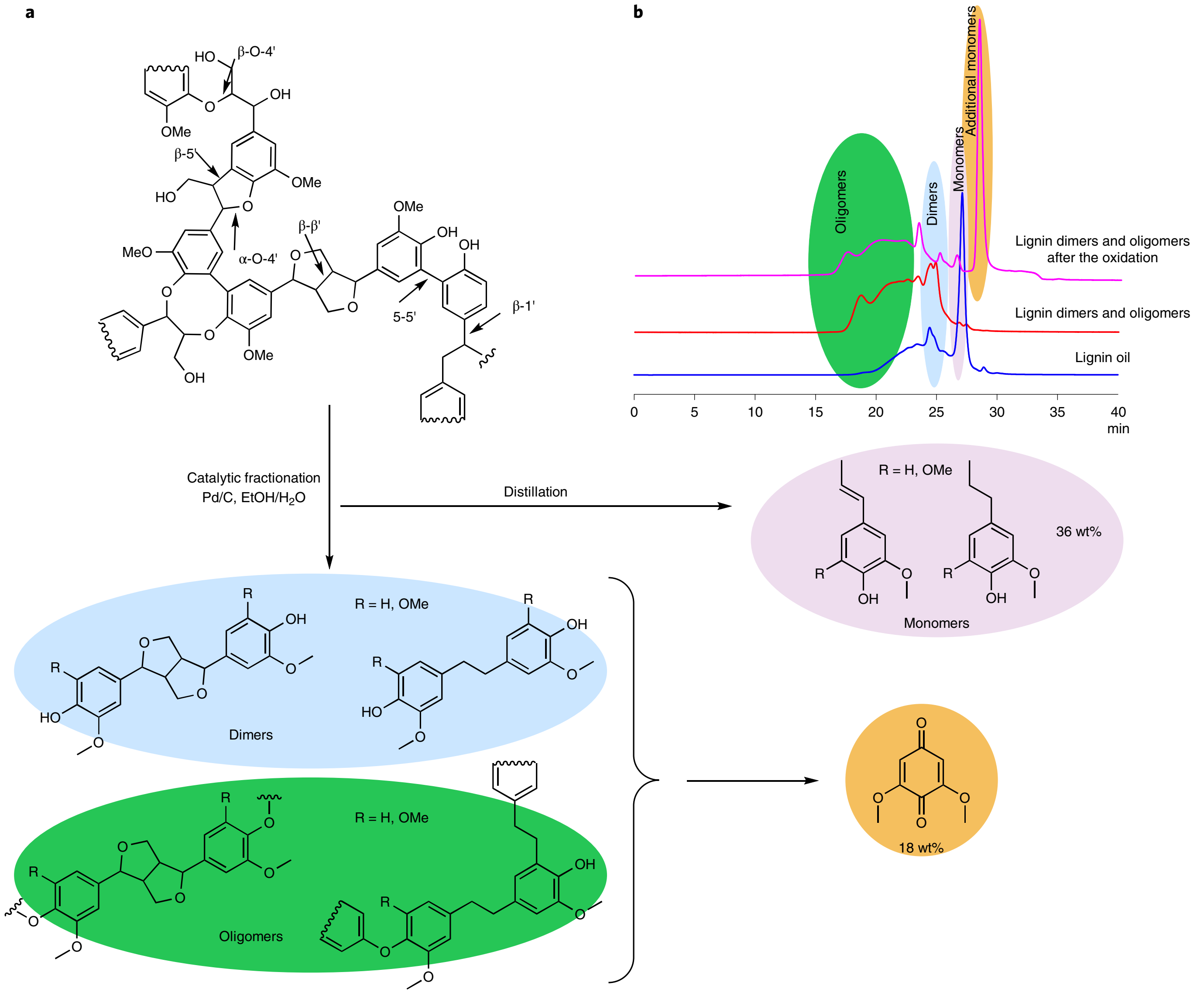


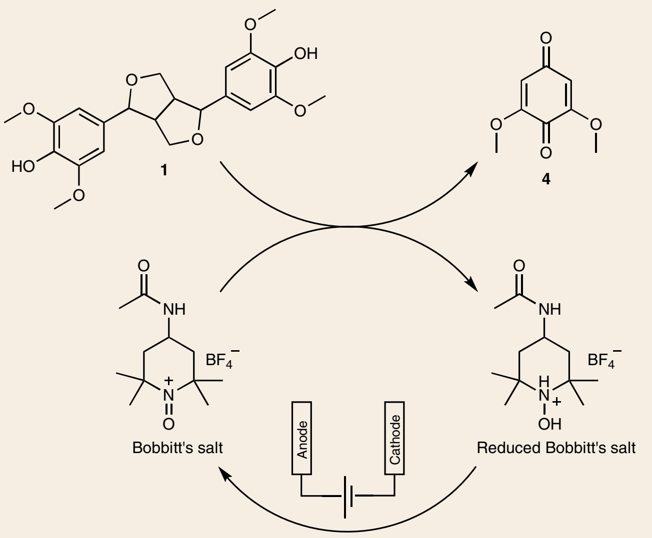
Fig. 5 | Oxidation of a mixture of dimers and oligomers obtained after pulping of birch wood. a, Reductive catalytic fractionation of wood generally leads to formation of maximum 36 wt% of monomers from lignin. An additional amount of monomeric product **4** is formed from the high-molecular-mass fraction of lignin via an oxidation developed in this work. **b**, Comparison of size-exclusion chromatograms of lignin oil obtained following catalytic fractionation (blue line), the fraction of dimers and oligomers obtained after the distillation of the monomers (red line), and the mixture obtained after the reaction (purple/pink line) illustrate the formation of additional number of monomeric products from the high-molecular-mass fraction of lignin via oxidation with Bobbitt's salt.

We propose that methoxylation of the benzylic position in model **2** plays an important role in the stabilization of carbo-cation **C** and thus facilitates the ipso attack of methanol and then water and subsequent cleavage of the model compound. The oxidation of **10** is similar to that of model compound **1**. When both phenolic groups of dimer **2** were methylated, no reaction occurred (Fig. 4b), indicating the necessity of a phenolic group for the transformation. According to the proposed mechanism, the oxidation of 1 mol of model **2** requires 6 mol of the oxidant, which explains why a higher oxidant loading was needed for model compound **2** (Fig. 4c).

Although methanol can be oxidized by Bobbitt's salt, only a slight excess of the oxidant (1.5 equiv. and 1.7 equiv. for models **1** and **2**, respectively) was required to obtain quantitative yields of products in both cases.

Regeneration of an oxidant. Oxoammonium salts are known to be easily recovered following completion of a reaction and can be regenerated via reoxidation with a terminal oxidant (for example, bleach) or electrochemically[44–46]. Electrochemical regeneration of a reduced form of an oxidant is a benign and sustainable method. The reduced form of Bobbitt's salt was collected as a white solid (Supplementary Section 11), which consisted of a hydroxylamine tetrafluoroborate salt and was redissolved in an aqueous solution of $NaBF_4$ as an electrolyte and subjected to an electrochemical oxidation process (Table 1). See Supplementary Section 11 for details on the electrochemical regeneration. We performed five consecutive reaction cycles with model compound **1** to demonstrate that the regenerated oxidant was active and can be reused (Table 1). The oxidant was active for five consecutive reactions and the DMBQ **4** could be isolated in 79–94% yield. It is worth mentioning that separating the oxidant from $NaBF_4$ was not required, and $NaBF_4$ can be collected together with reduced form of Bobbitt's salt from the solution of crude reaction mixture in DCM via extraction with water. The collected mixture can be subjected directly to the electrochemical

Table 1 | Oxidation of model compound 1 with the regenerated oxidant



Reaction cycle	4 Yield (%)
1st (Commercial Bobbitt's salt)	91
2nd	94
3rd	85
4th	77
5th	79

Following completion of the reaction, the oxidant was isolated from the reaction mixture and subjected to electrochemical regeneration. The regenerated Bobbitt's salt was used to perform the reaction again with a new portion of substrate. Five consecutive cycles were performed with a minimal drop in the yield of the product.

Table 2 | Optimization of reaction conditions for the mixture of lignin DOs

Entry	Temperature (°C)	Time (h)	Oxidant/ substrate (wt/wt)	4 Yield (mol%)[a]	4 Yield (wt%)[b]
1	100	0.5	4	73	18
2	100	0.5	2.2	60	15
3	100	0.5	6.7	71	17
4	r.t.	1	6.7	54	13

Reaction conditions: 50 mg substrate (mixture of dimers and oligomers obtained following distillation of lignin oil to remove monomers), 7 ml MeOH (0.4 wt% H_2O), Bobbitt's salt as the oxidant. [a]The mol% yield calculated based on the amount of phenolic syringyl (S) units in the mixture of DO. The mol% yield represents amount of product formed per aromatic unit bearing phenolic group. As according to mechanistic studies (Fig. 4b), the oxidative cleavage of dimeric and oligomeric lignin fragments requires a presence of free phenolic moiety the maximum possible mol% yield of **4** equals to amount of phenolic syringyl (S) units in the DO mixture. [b]Isolation yield.

regeneration (Supplementary Appendix 6). Likewise, following completion of the electrochemical reaction and removal of water, the mixture of the oxidant and electrolyte can be directly used in the next reaction cycle.

Reaction of the DO fraction obtained during catalytic fractionation of birch wood. Finally, the reactivity of the DO fraction obtained from catalytic fractionation of birch wood was probed using the optimized procedure (Fig. 5a; see Supplementary Section 5 for the catalytic fractionation conditions). Figure 5b shows the gel permeation chromatograms of the lignin oil obtained from the catalytic fractionation of birch wood, the DO fraction obtained after removal of the monomeric products by distillation, and the mixture obtained after oxidative treatment of the DO fraction. The figure clearly illustrates the formation of a further yield of monomeric products from the high-molecular-weight lignin fraction beyond the theoretical maximum yield.

The monomeric products formed during the catalytic fractionation of wood are derived from the quantitative cleavage of β-O-4′ bonds; thereby, DOs are almost fully composed of C–C bonds and DMBQ is generated via oxidative cleavage of these bonds. The optimization of the reaction conditions is presented in Table 2. We found that a higher reaction temperature is beneficial for the oxidation of the DO mixture, presumably due to better solubility (100 °C; compare entries 1 and 4 in Table 2). By varying the amount of the oxidant, we have determined the optimal oxidant to substrate (w/w) ratio of 4. As we discovered during our mechanistic investigation (Fig. 4b), the presence of phenolic groups is essential for the transformation. Taking into account the total amount of S phenolic units in DO estimated by ^{31}P NMR (Supplementary Fig. 1), the yield of 18 wt% DMBQ **4** corresponds to a 73 mol% yield (based on S units's phenolic group content in DO mixture used in the reaction). When the reaction mixture was subjected to ^{31}P NMR analysis, almost no phenolic groups were detected in the remaining crude mixture (Supplementary Fig. 2), which indicates substantial conversion of phenolic units into DMBQ **4**. Furthermore, we have performed the oxidation of birch lignin oil (containing lignin-derived monomers in addition to dimers and oligomers) and isolated DMBQ in 32 wt% yield (Supplementary Table 5; DMBQ was formed along with other monomeric products). The oxidant was isolated and regenerated via electrochemical oxidation. No considerable drop in yield of DMBQ **4** was observed, and the product was isolated in 31 wt% yield (Supplementary Table 5).

In conclusion, the presented protocol can be considered an extension of the lignin-first approach and addresses the main limitation of the majority of lignin-first methods, namely, the limitation of the theoretical maximum yield of monomers. We were able to produce an additional low-molecular-weight product (DMBQ **4**, 18 wt% yield) via the oxidative cleavage of C–C bonds within the DO fraction generated during the catalytic fractionation of wood. Thus, the total yield of monomers from the RCF and oxidation of DO constitutes 132% relative to the theoretical maximum yield.

$$\begin{aligned}&132\%\ \text{Monomer yield (relative to theoretical maximum yield)}\\&=\frac{18\ \text{wt}\%\times 0.64\ (\text{DO})+36\ \text{wt}\%\ (\text{monomers})}{36\ \text{wt}\%(\text{theoretical maximim})}\end{aligned}\qquad(1)$$

Performing the reaction in a green solvent (MeOH) under mild reaction conditions and using an inexpensive and benign oxidant (Bobbitt's salt, which was readily regenerated via electrochemical oxidation) contribute to the sustainability of the overall process. Previous lignin-first methodologies—developed over a century with a resurrected interest the past decade—enabled us to produce monophenolic compounds from quantitative C–O bond cleavage in lignin. This study makes progress in the research field by demonstrating the near-quantitive cleavage of C–C bonds in lignin fragments containing free phenolic groups. We hope that this inspires researchers to further development of the cleavage of C–C bonds within the residual lignin.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41557-021-00783-2.

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Methods

Oxidative cleavage of lignin model compounds. Lignin model (30 mg) and an oxidant were placed into a reaction flask, followed by addition of solvent (4 ml). The reaction mixture was stirred at room temperature. Following the completion of the reaction, the solvent was removed by rotary evaporator to give a crude product. The oxidant was separated via a DCM/water extraction. The organic phases were combined and evaporated by rotary evaporator. Crude product was purified by column chromatography (0.1–0.3% MeOH/DCM). The water phase was dried by air to recover a reduced form of an oxidant.

Oxidative cleavage of lignin DO. The reaction with DO mixture was performed in a similar fashion as with model compounds; 50 mg of mixture of DO obtained after the removal of monomeric products from the lignin oil was placed in a vial, corresponding amount of oxidant and solvent were added into a vial and the vial was capped. Following the completion of the reaction, the vial was cooled down to room temperature, opened, and solvent was removed by rotary evaporator. The reaction mixture was extracted with DCM/water, organic fractions were combined, dried over Na_2SO_4 and the solvents were evaporated under reduced pressure. The product was purified by column chromatography (DCM and MeOH) to yield 16 mg (0.095 mmol) of DMBQ.

Data availability

The data that support the plots within this paper and other findings of this study, such as ^1H NMR, ^{13}C NMR and HPLC spectra, as well as experimental procedures and quantum chemical calculations are available in the Supplementary Information.

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Author contributions

E.S. conceived the idea, designed the study along with J.S.M.S., and wrote the manuscript and the supporting information along with T.R. and J.S.M.S. E.S. performed all of the wood experiments (including the analysis) and wood-derived fractions. E.S. and T.R. performed the synthesis of model compounds and the mechanistic studies. M.D.M.-M. participated in the initial optimizations of the process and participated in the literature search. X.Y. and T.R. performed the electrocatalytic experiments under the supervision of M.J.

Competing interests

J.S.M. Samec is the founder of RenFuel, a company working on lignin valorization. The other authors do not declare any competing interests.

Additional information

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