High Yields of Aromatic Monomers from Acidolytic Oxidation of Kraft Lignin in a Biphasic System

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ABSTRACT: In this work, acidic oxidation in a biphasic water/octanol system was applied to mitigate condensation and increase the yields of high-value aromatic monomers from Kraft lignin, a waste product, and an industrially relevant feedstock. Biphasic depolymerization (BPD) is a one-pot multistep technique in which target molecules are protected from degradation in the reactive aqueous milieu (necessary for the cleavage of β-O-4 bonds as well as the recalcitrant high dissociation energy carbon–carbon moieties) by an in situ transfer of the products into the protective octanol phase. The results have shown overall monomeric yields up to 13 wt % and yields of vanillin up to 7 wt % (FeCl₃ as a catalyst and O₂ as an oxidant), significantly outperforming the previously reported monophasic and biphasic outcomes for Kraft lignin. In addition to increased yields, BPD also resulted in an expansion of the product pool from few molecules typically reported in the literature to 64 aromatic monomers detected at various concentration levels in the current work. The identified aromatic alcohols, carbonyl compounds, and carboxylic acids incorporating varying side chain lengths show potential as green and sustainable replacements to BTX (benzene, toluene, and xylene) petrochemicals. BPD as a process coupled mild conversion conditions, cheap oxidants, and common homogeneous catalysts with an in situ separation of the products from the reaction mixture to yield excellent results in converting industrial waste and recalcitrant feedstocks into value.

INTRODUCTION

Lignin is a significant natural resource, and its valorization to high-value aromatic monomers will be the key to unlocking the sustainability of the next generation holistic biorefineries. Major advancements in the field of lignin conversion have been achieved in recent years with the emergence of “lignin-first” approaches prioritizing valorization of the naturally occurring biopolymer alongside the carbohydrate fraction. Strategies applying “protective capping” preventing condensation of the β-O-4 bonds during the extraction were shown to result in excellent selectivities and nearly theoretical yields of high-value target molecules, particularly when combined with depolymerization schemes such as acidolysis, which maximizes the availability of aromatics by cleaving ether bonds in both phenolic and nonphenolic units. Secondary condensation of lignin and its conversion products is the main challenge and the focal point of the current research in the field. Deuss et al. identified the aldehyde products responsible for the undesired condensation pathways during acidolysis and were able to stabilize them by stoichiometrical trapping via acetal formation, hydrogenation, and decarbonylation, increasing the yields of low molecular weight products from organosolv lignin from 10.1 to 27.0, 37.4, and 13.1 wt %, respectively. A similar tandem approach was applied by Lohr et al., who succeeded in the stabilization of targets via ether/ester C–O bond hydrolysis, and Jastrzebski et al., who combined a Lewis acid-catalyzed cleavage of β-O-4 with Rh-catalyzed decarbonylation.

Not surprisingly, more sustainable and industrially relevant technical lignins have also attracted increasing scientific interest. However, while significant advances for technical lignins have been achieved in the field of macromolecular applications, the progress in the production of high-value monomers has been insignificant in comparison. This has been attributed to the recalcitrant structure of the feedstock and the aggressive nature of the applied depolymerization processes. In order to break the high dissociation energy carbon–carbon moieties that were formed from β-O-4 linkages during the extraction, acidolytic oxidation involving strong acids, powerful oxidants, and effective catalysts is required. However, the enhanced reaction severity has the
untended effect of causing thermal decomposition, retroaldol condensation, and over-oxidation of reactive intermediates and target molecules, leading to low empirical yields (typically below 3 wt %), as shown in studies by Voitl et al. and Werhan et al. In order to mitigate the undesired pathways, chemical quenching has been applied with some success. Von Rohr and co-workers have demonstrated that condensation can be mitigated by a competitive coupling of reactive benzylic carbenium sites in Kraft lignin with alcohols such as methanol, leading to modest yield improvements from 2.6 to 5.2 wt %.19,20

As an alternative approach, we proposed to mitigate condensation by application of biphasic depolymerization (BPD) involving an in situ removal of the conversion products from the reactive aqueous environment containing acids, catalysts, and oxidants into an inert protective organic phase, octanol. While previous research in the BPD field focused largely on solubilization of lignin promoting conversion of the carbohydrate fraction, the current study targets the production of high-value aromatic monomers (a broad spectrum of theoretically predicted aromatic oxygenates) from highly modified technical lignin (Kraft lignin) via acidolytic oxidation in the presence of cheap oxidants and common catalysts coupled to an in situ target extraction. Based on its excellent solvent properties combining low volatility, low toxicity, high solubility of aromatic oxygenates with low solubility for catalysts and lignin, and green status (can be produced from biomass), 1-octanol was handpicked as the organic extractive phase for the current system. An in-depth qualitative and quantitative characterization of reaction products was performed via high-resolution mass spectrometry (HRMS) and data mining. The applied workflow combined molecular identification and quantification of known targets such as vanillin, a screening for suspected conversion products, as well as nontargeted mining of novel compounds. The goal was to identify and quantify as many aromatic monomers as feasible with the highest degree of confidence possible, as well as to elucidate the complex pathways of acidolysis and oxidation based on the expanded lignomic chemical space.

## EXPERIMENTAL SECTION

### Materials

In a set of BPD experiments, Kraft lignin was converted at pH = 1 in an octanol/water 50/50 vol % mixture in the presence of catalysts and oxidants. Lignin used in this study was Kraft pine lignin Indulin AT (Ingevity, 5255 Virginia Ave, North Charleston, SC, US) in the form of free-flowing brown powder with no insolubles in warm aqueous solution of 5% NaOH and the following characteristics: moisture 3.5 wt %, ash 1.9 wt %, and average molar mass 8000 g/mol as declared by the supplier. Two common lignin conversion catalysts, FeCl₃ [iron(III) chloride from Sigma-Aldrich, MW = 162.20, CAS: 7705-08-0, ≥99.99%] and H₂[P(MoO₁₀)₄]:H₂O [phosphomolybdic acid hydrate from Tokyo Chemical Industry, MW = 1825.25 (anhydrous basis) g/mol, CAS: 51429-74-4, ≥99.99%, designated as HPMoO], were tested to enable an easy comparison to the large body of literature about monophase conversion and supplemented with anthraquinone (C₁₄H₁₂O₂, MW = 208.21 g/mol, CAS 84-65-1, designated as AQ), a novel catalyst applied so far exclusively for alkaline oxidation of lignin. The catalysts were combined in a full factor design (Table 1) with Ar (argon inert gas, ≥99.98%), O₂ (≥99.998%), and H₂O₂ (30 wt % in H₂O, ACS reagent from Sigma-Aldrich, MW = 34.04 g/mol, CAS: 7722-84-1) as green oxidants. In a set of preliminary experiments, a number of organic solvents (octanol, decalin, heptane, and toluene) covering a range of polarities were evaluated based on their properties: solubility in the carrier (water), the partition coefficient (for the feedstocks, catalysts, and oxidants—low, for the solutes—high), behavior under biphasic conditions, and the possibility for sustainable production from biomass. Volatility was not considered because the envisioned separation was not based on evaporation but on the much less energy-extensive extraction scheme. Typical biphasic solvents, according to the literature, include alkylphenols (often toxic), γ-valerolactone (green and can be produced from biomass but requires salts for biphasic system formation, thus making the analytics more complex, as well as introducing precipitation and corrosion in reactors), poly(ethylene glycol) (the same as γ-valerolactone), and dodecane (lack of polarity and affinity for aromatic oxygenates). One-octanol (99.5% purchased from TCI and purified by three consecutive extractions in equal volumes of 0.05 HCl, followed by drying with an inert drying agent, sodium sulfate, Na₂SO₄ for 3 h) was selected as the organic extractive phase based on its excellent solvent properties combining high solubility of aromatic oxygenates with low solubility for catalysts and lignin. Solvents for analysis purchased from Sigma-Aldrich included acetonitrile (ACN), methanol (MeOH), formic acid (HCOOH), and high-purity water. All were of HPLC grade (purity ≥ 99.99%). Concentrated HCl from Sigma-Aldrich was used for the adjustment of pH (37 wt %, hydrochloric acid, ACS reagent from Sigma-Aldrich, MW 36.46, CAS: 7647-01-0). Unless stated otherwise, all commercially available chemicals were used without further purification.

### Experiments

The experiments were designed to cover a wide pool of possible depolymerization products. The conversion was carried out in a Biotage Initiator microwave reactor in organic synthesis mode at pH = 1, T = 170 °C, t = 40 min, 1 mg/mL lignin loading (concentration of lignin in the reactive phase), and 10 mM catalyst loading. Typically, 2 mg of Kraft lignin Indulin AT was loaded together with 2 mL of 0.05 M HCl aqueous catalyst/oxidant (H₂O₂ = 2 mM) solution and 2 mL of purified and dried octanol (triple

| run | Cat | Oxi | run | Cat | Oxi | run | Cat | Oxi | run | Cat | Oxi |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| R₁ | noCat | Ar | R₂ | noCat | O₂ | R₃ | noCat | H₂O₂ |
| R₄ | AQ | Ar | R₅ | AQ | O₂ | R₆ | AQ | H₂O₂ |
| R₇ | HPMoO | Ar | R₈ | HPMoO | O₂ | R₉ | HPMoO | H₂O₂ |
| R₁₀ | FeCl₃ | Ar | R₁₁ | FeCl₃ | O₂ | R₁₂ | FeCl₃ | H₂O₂ |

“All runs were performed at T = 170 °C, t = 40 min, and 2 mg of lignin loading (1 mg/mL in the reactive phase). Cat-catalyst (10 mM loading), Oxi-oxidant (2 mM H₂O₂ loading).
extraction with 0.05 M HCl, followed by 3 h with Na₂SO₄ into a 10 mL reaction vial containing a magnetic stirrer and then sealed. In the runs with O₂ as the oxidant, the sealed mixtures were saturated with oxygen for 15 min at 30 mL/min. In the runs with Ar, the samples were purged with argon for 15 min. Stirring at 1200 rpm ensured a stable emulsion of octanol in water. The use of microwave as the source of energy ensured very fast heating and cooling (Figure S1), effectively emulating conditions in a continuous system, which will ultimately be the reactor type applied for a large-scale conversion. Furthermore, the Biotage Initiator microwave reactor system made it possible to run the experiments in a semiautomated way with an autosampler. Last but not least, microwave radiation has been shown to significantly reduce the reaction time and improve the yields and selectivity of target products from biomass. The reproducibility of the experimental procedure, assessed based on triplicates of the runs with oxygen as the catalyst, was below 10% (relative standard deviation).

**Analytics.** The samples were filtered through a 0.22 μm filter and prepared by transferring 180 μL of the sample and 20 μL of internal standard-vanillin-(phenyl-13C₆) into a 0.3 mL chromatography vial and sealed. The chromatographic separation was performed with Ultra-High-Performance Liquid Chromatography (UHPLC, Thermo Scientific, Dionex Ultimate 3000 series RS), mobile phase A (1% ACN, 1% MeOH, and 0.2% HCOOH), mobile phase B (100 vol % MeOH), flow 0.700 mL/min, injection 1 μL, followed by HRMS with a Q Exactive hybrid quadrupole-orbitrap mass spectrometer (Thermo Scientific, positive mode electrospray ionization, full scan MS1 and dd-MS2, isolation window of 1 m/z, range 50–750 m/z, resolution 70,000 for MS1 and 17,500 for dd-MS2). The raw data were processed in Compound Discoverer 3.1. Figure S2 shown in Supporting Information summarizes the raw data processing method.

**Data Reduction and Mining.** The data reduction process involved following steps: a) blind (octanol/water with corresponding catalysts and oxidants, no lignin) and background subtraction (instrument blanks), b) filtration according to formula (C₆H₅NnOoS) and abundance (10° as the min peak area in at least one sample group, peak present in all replicates of each sample group, peak present in at least three sample groups), as well as c) evaluation of peak quality (shape and RT-retention time, min), d) instrumental reproducibility (CV < 25%), and e) annotation quality (at least three independent confirmations from a list of four: predicted composition, mass list with suspects, mzCloud spectral library, and ChemSpider compound library).

The resulting lignomic space was evaluated based on the obtained exact masses, RT, and MS2 (mass spectrometric fragmentation information) as follows: (1) targeted matching against a vanillin standard; (2) suspect screening (comparison to a mass list of 250 suspected lignin conversion products compiled from literature and theoretical conversion pathways); and (3) nontargeted screening (true unknowns). This approach resulted in a well-curated list of 204 lignin conversion products assigned based on their unambiguous molecular formula (and wherever available, the likely molecular ID) into five classes: (a) monomeric aromatics (64 species), (b) aliphatics (23 species), (c) cyclics (42 species), (d) lignin fragments (21 species), and (e) condensates (54 species). The aromatic monomers (suspects as well as unknowns) were prioritized toward identification via a combined search for candidates in mzCloud spectral database and compound databases within ChemSpider (based on formula and mass including mzLogic option) and supplemented by fragment ion search algorithm (FISh) evaluation. The results were compiled, and the best-performing candidates were selected based on a combined score. The list of 64 monomers (file Monomers_64species.xlsx in Supporting Information) was narrowed down to 39 features representing 30 structurally distinct aromatic oxygenates and 9 isomers (file MolecularID_30species.xlsx in Supporting Information). These species were further classified as (1) alcohols, (2) carboxyls, and (3) carboxylic acids, based on their functional group content, as well as (a) species with either one or two carbons in the side chain (1C2C), (b) intact propyl chains with single bonds (IPCs), and (c) styryl ethers with IPCs with double conjugated bonds (SEIPCs), based on the length of their side chain (file M-ID_functionality_side-chain-length.xlsx in Supporting Information).

**Quantification.** The yields (Ym) were obtained according to eqs 1–3 based on the masses (m) calculated from concentrations (Cm) measured as areas (AIS). The concentrations were determined against an external calibration curve for vanillin (0.1–100 μM, R² = 0.99, SD < 5%, slope = 0.98) normalized to an internal standard (AIS) and vanillin (phenyl-13C₆) and corrected for dilution (df, dilution factor). The areas measured across all runs were recalculated into yields on a dry lignin mass basis (lignin water content 0.035 wt %) for all 204 conversion products in both aqueous as well as octanol phase (file Yields_per_Run.xlsx in Supporting Information) for the sake of data analysis but were only meaningful for the aromatic monomers, for which similar ionization efficiencies, as well as matrix suppression behavior, can be expected as for the applied standard compound. The trends in the obtained yields were assessed by appropriate univariate analyses (one-way and two-way ANOVA) and various machine learning and data mining methods, including unsupervised clustering (hierarchical and k-means), data reduction via principal component analysis (PCA), and supervised tree ensemble methodology. The yield values were reported with standard analytical errors. More detailed information about the experimental and analytical methodologies is available in Supporting Information.

**RESULTS AND DISCUSSION**

**Lignomic Space.** Thanks to its amphiphilic nature, Kraft lignin was located on the interface between the octanol droplets and the continuous water phase during the conversion, creating an emulsion with a large surface area available for conversion and product transfer. While the
aqueous phase contained the active elements necessary for catalytic acidolysis and oxidation, octanol was the inert environment in which the lignin depolymerization products were extracted. A visual inspection of the reactive system post-conversion revealed an intensely colored octanol phase and a colorless aqueous fraction indicating a successful in situ transfer confirmed by the subsequent quantitative HRMS analysis, which also demonstrated the formation of a complex lignomic chemical space (Figure 1) composed of aromatic monomers, aliphatics, cyclics, condensates, and lignin fragments. Incorporating oxygen into the products, particularly the aromatic monomer fraction, was observed (O/C ≥ 0.3), thus identifying oxidation as a significant conversion pathway. While aliphatics were small molecular weight lignin conversion byproducts, cyclics, which were most abundant in the presence of O2 and H2O2, seemed to originate from the condensation of octanol. The comparisons of abundances for classes are depicted in Figures S3–S8 in Supporting Information.

**Quantitative Assessment.** The calculations of monomeric yields have shown that the corresponding concentrations in octanol and aqueous fractions were 1 to 2 orders of magnitude apart (Figure S3 in Supporting Information), thus confirming the proof-of-concept for biphasic conversion.

Analysis of yield trends in the octanol fraction (Figure S4 in Supporting Information) revealed that, although no simple linear relationships could be confirmed by ANOVA, the efficiencies of oxidants and catalysts increased as follows: O2 > Ar > H2O2 and FeCl3 > noCat = HPMoO > AQ. A more detailed evaluation of the overall monomeric yields (Ym), as well as the yields of vanillin (Yv), is presented in Figure 2, showing that the combination of FeCl3 as a catalyst and O2 as an oxidant was particularly effective, resulting in 7 and 13 wt % for Yv and Ym respectively. The lowest yields were recorded for the AQ/H2O2 pair (1 and 2 wt % for Yv and Ym, respectively). According to the literature, the application of peroxydrate often results in ring-opening reactions giving effective conversion but overall low yields of aromatic monomers.42 In terms of vanillin yields alone, the current system outperformed both the monophasic (aqueous) acidolysis of Kraft lignin at similar conditions (Yv = 0.19 wt %), previously reported biphasic conversion in the presence of the CuSO4 catalyst (Yv ≈ 1 wt %),21 as well as the catalytic acidic oxidation of Kraft lignin in the presence of methanol, as demonstrated by Von Rohr and co-workers (Yv...
While monomeric yields above 10 wt % are typically reported for native lignin feedstocks, they are not expected for heavily modified technical lignins. Furthermore, while only a few aromatic monomers are typically reported as products from acidolysis of Kraft lignin, vanillin being the primary target of many studies, in the current setup, 64 aromatic oxygenates were detected by HRMS. Figure S9 shown in Supporting Information exhibits their respective yields.

**Molecular Identification.** 30 aromatic monomers from the pool of 64 detected species (file Monomers_64species.xlsx in Supporting Information) were associated with a high confidence molecular ID (level 2 and 3) according to Schymanski et al., meaning that either a probable structure (by library spectrum match or other diagnostic evidence) or at least tentative candidates (structure, substituent, and class) could be associated with each compound. An excerpt of the full list (file MolecularID_30species.xlsx in Supporting Information) is shown in Table 2. While most of the

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<th>Monomer</th>
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<th>Structure</th>
<th>RT (min)</th>
<th>MW (Da)</th>
<th>Yexp (%)</th>
<th>F</th>
<th>SCH</th>
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<tr>
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<td>132.0473</td>
<td>34</td>
<td>=O</td>
<td>1C2C</td>
<td></td>
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<tr>
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<td>C_{4}H_{4}O_{2}</td>
<td>2.42</td>
<td>136.0524</td>
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<td>1C2C</td>
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<tr>
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<td>0.3</td>
<td>-COOH</td>
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Table 2. Selected Aromatic Monomers

| Y_{exp} shows the percentage of the total yields explained by each monomer. F-functional groups and SCH-side chains. |

products originated from p-hydroxphenyl (H) and guaiacyl (G) phenyl propane structural units typical for softwood lignin from which the used Kraft lignin was derived, the detected trace amounts of ordinarily depleted softwood syringols were attributed to secondary reactions of H and G units. The functionalities present included alcohol, carbonyl, and carboxylic groups coupled to side chains with (1) 1−2 carbons (1C2C), (2) IPCs, and (3) SEIPCs. While 1C2C containing compounds originated most likely from the cleavage of propyl chains via oxidation, the presence of IPCs and SEIPCs indicated acidolysis. Analysis of the yield distribution across functional groups and side chains (Figure 3) demonstrated that carbonyl compounds with cleaved propyl chains (1C2C) were by far the most common products [e.g., vanillin (M2) and apocynin (M10) were responsible for 45% of the obtained aromatic yields]. Besides alcohols and carboxylic acids with IPCs, less common products included species with condensed side chains (M13 and M32) and molecules that underwent secondary reactions (M54 and M64), for example, acetoxylation.

**Data Mining.** The univariate approach did not yield statistically significant trends, indicating either a lack of well-defined relationships or the inability of linear methods to describe the trends in the data. The follow-up data mining, both unsupervised and supervised, was applied to explore the second possibility. First, the samples were clustered with k-means and hierarchical clustering algorithms (based on the yields of monomers in octanol, chosen as the most interesting outcome of the study) in an attempt to find similarities independently of a priori knowledge of the samples. The k-means clustering method (k = 3 calculated based on elbow analysis, Figure S12 in Supporting Information) distinguished three clusters in the data based on the yields of aromatic monomers: cluster-1: FeCl3/Ar/O2, cluster-2: no catalyst/Ar/O2, FeCl3/H2O2, and HPMoO4/O2, and cluster-3: the remaining runs (see file k-means_M_importance.xlsx in Supporting Information). In all the three clusters, the yields of vanillin were the most important feature, with average yields of 6.5 (cluster-1), 3.1 (cluster-2), and 1.2 wt % (cluster-3). Besides vanillin, M10 (apocynin) and M42 (C_{6}H_{6}O_{5}) were also of importance, in each case showing the same trend of decreasing yields. The independently performed hierarchical clustering resulted in a similar outcome (see dendrogram shown in Figure S11, Supporting Information).

To explore further hidden trends in the data, a set of PCA was run for the corrected areas of all detected compounds. The PCA for all species with scores (projections of samples) colored according to the phase and oxidant and catalyst and loadings (projections of variables) colored according to the class of species resulted in multiple interesting observations. First of all, the composition differences between the aqueous and the octanol fractions were confirmed (separation along PC1 in the score plot shown in Figure S13 and the loading plot shown in Figure S14 in Supporting Information, additional plots in Figures S15 and S16). PCA on the octanol fraction alone revealed that the next biggest variation in the data was due to the differences between the experiments with FeCl3 and O2 (R2) and the remaining runs (separation along PC1 in the score plot shown in Figure S17, 40%). PC2, responsible for 22% of the variation in the data, was due to the application of different oxidants (a summarized version of the scores and loadings is shown in Figure 4, and the full version is shown in Figures S17−S19 in Supporting Information). From the loading plot for these

![Figure 3. Proportion of functional groups (alcohol, carbonyl, and carboxylic) and side chain types (1C2C, IPC, and SEIPC) among the identified monomers.](https://example.com/figure3.png)
samples, it could be seen that while a certain monomeric composition was associated with $R_k$, the presence of $\text{H}_2\text{O}_2$ was responsible for the majority of cyclic and aliphatic species. Once $R_k$ was removed from the analysis (Figures S20–S22 in Supporting Information), the latter trends dominated.

Finally, the monomeric yields for 64 species were fed into a supervised regression algorithm (using the conversion conditions transformed to dummy variables as input) to train a regression tree ensemble model to predict the yields. Because the data were extremely scarce compared to a typical machine learning application, the usual procedure (separating the data into train, test, cross-validation, and hyperparameter tuning sets) was simplified to an evaluation based on the out-of-bag performance. While this approach did not yield valid results for the majority of the monomers, reasonable predictions were obtained for $M_2$ (vanillin) and two unidentified species: $M_{16}$ and $M_{45}$. The results are summarized with measured versus predicted plots as shown in Figure 5, showing that the predictions’ performance decreased with increasing yields, that is, the models were not able to handle the runs with $\text{FeCl}_3$ producing outstandingly high yields. Increasing the number of runs, that is, filling the space with more data points for the supervised algorithms to learn from, would undoubtedly improve the results.

**Reaction Mechanisms.** The protective extraction of depolymerization products during biphasic acidolysis and oxidation, followed by reliable identification and quantification allowed us to track conversion pathways in the biphasic system. The routes of acidolysis and oxidation in monophasic systems were described by Gierer and Nilvebrant and are summarized in Figure 6. In the first steps, lignin units are activated into carbenium ions (step 1), and with styrly ethers as intermediates (step 2), they can either undergo radical oxidation in the presence of an oxidant (step 3A) or acidolysis (step 3B) in its absence. Both pathways lead to carbonyl products, but while oxidation takes place typically via the cleavage of side chains at $C_\alpha$–$C_\beta$ resulting in vanillin and apocynin ($1C2C$ side chains), acidolysis proceeds through the reactive styrly ether (SEIPC) intermediates containing double bonds conjugated to the rings yielding Hibbert’s ketones and $C_2$-aldehyde-substituted phenolics. Because both the intermediates as well as the final products of acidolysis are highly unstable at acidic (aldol condensation) and oxidative conditions (direct electrophilic attack by molecular oxygen on the conjugated bond), they are not often reported as lignin conversion products. The presence of SEIPC species in the current samples, along with the more common $1C2C$ typical lignin conversion targets such as vanillin, showed that, in addition to protecting targets from degradation, the nonproductive pathways of condensation typical for acidolysis in the biphasic system turned toward monomer production, enhancing both the quantitative yields as well as expanding the aromatic space available from lignin. Furthermore, a positive correlation between the yields of monomers (Figure S10 in Supporting Information), corresponding to different conversion pathways, indicated a possibility for process tailoring toward specific pathways turning BPD into a chemical vending machine.

**Effect of the Iron Catalyst.** $\text{FeCl}_3$ was shown to be an extraordinarily effective catalyst doubling the yields of both vanillin and other aromatic monomers and outperforming common lignin conversion catalysts such as $\text{CuSO}_4$. Although the mechanisms of how transition metals help to convert
The current results, showing conversion in the presence and absence of the oxidant, indicated that iron supported the heterolytic cleavage of Cα–Cβ in addition to the acidolytic cleavage of β-O-4.51

**Sustainability of BPD.** Consideration of the sustainability of the process should be an essential part of any biomass valorization evaluation. BPD is a relatively simple and elegant one-pot multistep method combining green solvents (octanol can be produced from biomass, other solvents can be used) with mild conversion conditions. While the applied temperature and pH are not insignificant, they can be considered mild compared to typical thermochemical processes (300–500 °C and 200–300 bar) and the industrially applied lignocellulose pretreatment strategies used for, for example, the production of bioethanol. Low pH (pH = 1) must be used to promote the effective activation of lignin into carboxations. Both octanol (not consumed during the process) and the acidic aqueous phase (no changes in pH) have been studied in detail; the overall conversion pathways proposed by Gierer and Nilvebrant indicate a possibility of copper carrying out a similar function at low pH as at high pH, that is, subtraction of an electron from the styryl ether intermediate initiating a radical pathway leading to Cα-aldehyde-substituted phenolics. In both scenarios, Cu⁺ is reoxidized to Cu²⁺ by oxygen recuperating the catalyst, decreasing the potential of the oxidant to carry out a direct attack on lignin and its conversion products. On the other hand, studies have shown that iron is unable to act as an electron acceptor at alkaline conditions and its catalytic effect has instead been attributed to the formation of lignin–OH–Fe³⁺–O₂ complexes ensuring an efficient but controlled oxidant delivery.

The current results, showing conversion in the presence and absence of the oxidant, indicated that iron supported the heterolytic cleavage of Cα–Cβ in addition to the acidolytic cleavage of β-O-4.

**Figure 6.** Pathways for lignin depolymerization at acidic conditions: (1) protonation of O at Cα, elimination of a neutral ROH, and formation of the benzylium ion, (2) elimination of H from Cβ leading to ring conjugated structures (RCSs), (3A) oxidative pathway, and (3B) hydrolysis at Cβ. While acidity activates the lignin structure into RCSs, the catalyst promotes the kinetics of the subsequent steps. The figure shows a compilation of mechanisms inspired by the work of Gierer and Nilvebrant.

**STEP 1:**
**Cleavage of Cα-OR". Phenolic and non-phenolic units**

**STEP 2:**
**Styrl ether formation. Elimination of H from Cβ**

**STEP 3A:**
**Radical oxidation with Cat/O₂: i) electron transfer from Cβ to Cat, ii) phenoxy radical + H₂O, iii) O₂ addition to hydroperoxy radical, iv) heterolytic cleavage of Cα and Cβ to carbonyl compounds.**

**STEP 3B:**
**Acidolysis in the absence of oxygen is based on acidic hydrolysis of the β-aryl ether bond.**
can be recycled. BPD performed well with a recalcitrant feedstock while utilizing common green and cheap catalysts and oxidants. Both the oxidant as well as the catalyst have to be recharged between the runs. Further studies are required to understand the exact role of iron during conversion in a large-scale process with higher lignin loading. Separation of the products from octanol can be obtained with an alkaline aqueous extraction, followed by acidification, precipitation, and filtration. Excluding process tailoring and pathway optimization, the complexity of the resulting product mixture will pose a significant purification challenge, and the products should be funneled toward nontargeted valorization.\textsuperscript{2,5,7} Last but not least, BPD is robust and tailorable and can be easily upscaled to become industrially relevant.

**CONCLUSIONS**

In this work, catalytic acidolysis and oxidation in the aqueous phase were applied to successfully depolymerize lignin into various aromatic monomers that were subsequently protected from condensation via extraction into protective inert octanol. Followed by the conversion, a coupling of identification, quantification, and data mining showed that biphasic processing significantly enhanced overall monomeric yields as well as expanded the product pool mixture. The highest yields (both $Y_v$ and $Y_m$) were obtained in the presence of $\text{FeCl}_3$ and $\text{O}_2$, outperforming the previously reported results for monophasic acidolysis, biphasic conversion in the presence of the $\text{CuSO}_4$ catalyst, as well as other condensation mitigating strategies. 30 of the 64 detected aromatic monomers could be associated with a high confidence molecular ID. The carbonyl compounds with cleaved propyl chains (1C2C) were by far the most common products (e.g., vanillin and apocynin). Because cleavage of propyl chains took place in the presence as well as the absence of oxidants, the mechanisms shifted between oxidation (in the presence of oxidants) as well as heterolytic acidolytic cleavage of $C_\alpha-C_\beta$ (in their absence). The detection of SEIPC species revealed that protective extraction prevented the degradation of specific target molecules as well as mitigated the destructive acidolytic pathways of the intermediates. Overall, biphasic processing is a promising condensation mitigation strategy and a sustainable lignin conversion scheme.

**ASSOCIATED CONTENT**

- **Supporting Information**
  The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.iecr.1c01776.
  
  A) Details about the experimental, analytical, and data mining procedures, including temperature/pressure profiles, sample preparation and analysis, raw data processing, compound discoverer workflow, and applied machine learning approaches; and B) Suppporting results, including box plots, marix plots, and correlation plots with class yields, as well as the outcomes from data mining via clustering and PCA (PDF)
  
  Data files: Monomers_64-species.xlsx, MolecularID_30-species.xlsx, M-ID_functionality_side-chain-length.xlsx, Yields_per_Run.xlsx, and k-means_M_importance.xlsx (ZIP)

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**Notes**

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

This research project was funded by Marie Curie Individual Fellowship (MSCA-IF-2017, grant agreement ID 794039), supported by the Swiss Innovation Agency Innosuisse (SCCER BIOSWEET) at the Paul Scherrer Institute. The authors thank ChemAxon (www.chemaxon.com) for the academic license of software tools (Standardizer, Marvin-Sketch, InstantJChem).

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