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Introduction

Lignin is a polymer composed of a variety of cross-linked aromatic sub-units and accounts for up to 30 wt% of woody biomass. It represents the largest source of potentially renewable aromatics.¹ The major source of industrial lignin is derived from pulp and paper manufacturing where, once separated from the cellulose fibres and recovered from black liquour, it is typically burnt as a low grade fuel. Despite its availability and volume, lignin is currently an under-valorised resource, with only ~2% of the lignin produced annually being used for commercial applications other than process heat in the pulping operations.^{2,3} The established nature and scale of the petrochemical industry, combined with the technical challenges presented by the structural complexity of lignin, have provided limited incentive to valorise lignin to aromatic chemicals. However, the renewed push for renewable chemicals is changing the landscape, and new opportunities are emerging.⁴

Cobalt is one of the largest scale homogeneous oxidation catalysts in industrial chemistry, primarily in the conversion of al-

Investigating homogeneous Co/Br⁻/H₂O₂ catalysed oxidation of lignin model compounds in acetic acid[†]

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Oxidation of α -O-4, β -O-4 and monomeric lignin model compounds by Co/Br⁻/H₂O₂ in acetic acid at 70 °C was investigated. Co and Br⁻ were introduced as cobalt acetate tetrahydrate and KBr respectively. The degree of methoxylation of the substrate was found to affect its reactivity. For the α -O-4 model compounds, increased methoxylation of the benzyl moiety influenced product selectivity, while increased methoxylation of the phenolic moiety increased substrate conversion. The β -O-4 model compounds exhibited similar conversions to the α -O-4 models, but afforded a lesser amount of monomeric products. The formation of phenol and guaiacol from α -O-4 bond cleavage inhibited substrate conversion and sequestered oxidation products due to the formation of phenoxy radicals and polyguaiacols. Similar to the α -O-4 model compounds, increased methoxylation of the monomers changed the types of products formed, from polyphenols (phenol and guaiacol) to quinones (syringol). The behaviour of syringol was explored extensively, revealing that the corresponding 1,4-hydroquinone strongly inhibited syringol oxidation, and the syringol oxidation product, 4,4'-diphenoquinone, was susceptible to over-oxidation. The deleterious effects of phenols on oxidation of an α -O-4 model could be reduced by substitution of the Br⁻ cocatalyst with *N*-hydroxyphthalimide (NHPI), improving substrate conversion and product selectivity.

kyl aromatics to their respective aldehydes, alcohols and carboxylic acids. The AMOCO Mid Century Process (Schemes 1 and 2), utilises cobalt and manganese acetates with hydrobromic acid in acetic acid in the presence of pure oxygen.⁵ The success of this system revolves around several factors including its high activity over a broad range of temperatures (25-300 °C), substrate flexibility, simple product recovery, high yields (>90%), and simple catalyst components.^{6,7} The fundamental system operates with a cobalt salt, a source of bromide, and an oxidant (typically O_2 or H_2O_2). Cobalt (typically as the acetate) reacts rapidly with peroxides and peracids, and generates benzylic radicals via a Co(III) species. Bromide (HBr, NaBr or KBr) facilitates both rapid generation of benzylic radicals and reduction of Co(III) to Co(III). Adding different metal acetates (Mn, Zr) to the cobalt system can result in even higher activities and selectivities, e.g. replacing 20% Co with Mn resulted in a 5-fold increase in the rate of oxidation of the intermediate p-toluic acid.⁸⁻¹⁰ In addition,



Scheme 1 AMOCO Mid-Century method for the oxidation of *p*-xylene to terephthalic acid. Adapted from Partenheimer.⁶



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 $\mbox{Scheme 2}$ $\mbox{General}$ mechanism for the AMOCO MC catalyst. Adapted from Partenheimer. 6

cyclohexane can be oxidised by a similar catalytic system, ultimately to adipic acid in the DSM process.¹¹ Both current largescale industrial oxidations operate at ca. 170 °C and 10-30 atmospheres of air and use cobalt-based catalysts. They differ, however, in that the cyclohexane oxidation is performed selectively to the alcohol and ketone at low conversions, whereas the arene is oxidised to the carboxylic acid in high conversion and employs a bromide co-catalyst. The specific structure/speciation of the Co/Br⁻ catalyst is unknown, but investigations by a number of different researchers have attempted to reveal fundamental aspects. Solution studies of cobalt acetate and bromide in acetic acid and water (5-15 wt%), comparable to industrial conditions, report that the catalyst solution contains a mixture of different active catalyst species. As the fraction of water in the solvent increases less bromide is coordinated directly by cobalt centres, but instead has been suggested to remain in a second coordination sphere held there by ion pairing.¹² A number of published kinetic studies of bromide speciation have suggested that the main active species are metal(II) dibromides. These species are oxidised by metal(m) centres and subsequently undergo spontaneous reductive elimination to generate dibromide radical anions.^{13–15} At least three different cobalt(m) species, including dimers and a mixed valence Co(II/III) trimer, have been proposed while studies of oxidised acetic acid/water solutions of cobalt acetate in the presence of pyridine have revealed dimeric, trimeric, cubane and octo cobalt(m) structures.¹⁶

It is instructive to note that Neuenschwander and Hermans¹⁷ have described a simplified scheme of a thermal and catalytic free radical hydrocarbon autoxidation (reactions 1–4), which can be described analytically by eqn (E):

The radical initiation occurs *via* a thermal step

$$ROOH + RH \xrightarrow{k_2} RO' + H_2O + R'$$
(1)

And a catalytic step

$$ROOH + Co^{II} \xrightarrow{k_{cat}} Co^{III} - OH + RO$$
 (2)

The radical termination is given by

$$ROO' + ROO' \xrightarrow{k_t} ROH + Q = O + O_2$$
(3)

The propagation reaction is

$$ROO' + RH \xrightarrow{k_p} ROOH + R'$$
(4)

At steady-state, the rate of termination equals the rate of initiation, and so

$$k_2$$
[ROOH][RH] + k_{cat} [ROOH][Co^{II}] = k_t [ROO[·]]² (A)

So

$$\left[\text{ROO'}\right]^2 = \frac{\left[\text{ROOH}\right]\left(k_2\left[\text{RH}\right] + k_{\text{cat}}\left[\text{Co''}\right]\right)}{k_t} \tag{B}$$

If the rate of propagation, $r_{\rm p}$, is given by

$$\frac{d[RH]}{dt} = r_{p} = k_{p} [ROO^{\cdot}][RH]$$
(C)

Then, substituting for [ROO[•]]

$$r_{\rm p} = k_{\rm p} \left[\rm RH \right] \sqrt{\frac{k_2 \left[\rm ROOH \right] \left[\rm RH \right] + k_{\rm cat} \left[\rm ROOH \right] \left[\rm Co^{\rm u} \right]}{k_{\rm t}}} \qquad (\rm D)$$

$$\frac{d[RH]}{dt} = k_{p}[RH] \sqrt{\frac{k_{2}[ROOH][RH] + k_{cat}[ROOH][Co^{ii}]}{k_{t}}} \qquad (E)$$

Furthermore, Hermans has recently reviewed free radical hydrocarbon oxidations18 and Adamian and Gong have discussed the specific case of *p*-xylene oxidation catalysed by a combination of Co/Mn/Br⁻ derivatives, illustrating the complexity of the process.¹⁵ Our own experience with cobaltcatalysed hydrocarbon oxidation included the investigation of the partial oxidation of 4-tert-butyltoluene to 4-tertbutylbenzaldehyde (37% yield, 79% selectivity) using Co/Br at 70 °C with H₂O₂ as the oxidant.¹⁹ In addition, we have also investigated the catalytic reaction of a model cobalt(III) acetate complex with H₂O₂, observing the relatively rapid decomposition of H₂O₂ and the formation of O₂.²⁰ This is consistent with reports describing the ability of cobalt(III) species to react with peroxides, however, the exact mechanism is unknown. Spier, Neuenschwander and Hermans have noted that depending on the type of ligand coordinated to Co (acac vs. 2-ethylhexanoate) and the Co-OOR bond strength, peroxides may react through different mechanistic pathways.²¹ This catalytic system has been applied to the oxidation of other functional groups,²² including the curing of paints,²³ and the subtle effects of ligand variation are noted.24 As outlined by Partenheimer,²⁵ and recognising the relative distributions of oxidisable linkages in lignin, investigating the potential of this catalyst system to valorise lignin is attractive for several reasons:²⁶⁻²⁸ firstly, as a successful and

established industrial catalyst many developmental and engineering problems such as corrosion and catalyst/solvent recycling have been solved. Secondly, lignin break-down products or fragments contain a broad mixture of hydroxylated, methoxylated and alkylated aromatics. As lignin undergoes extraction and chemical modification during pulping, cleavage of sub-units increases the frequency of phenolic hydroxyl groups from 7-13% to over 70%, based on aminolysis.^{29,30} Some of these fragments, either received from the process, or in pure form as model compounds, have been already investigated with Co/Mn/Br⁻ catalyst systems.³¹ However, these studies, performed at high temperature and pressure, were not sufficiently selective to warrant further commercially targeted development. It was found that the aromatic hydroxyl group inhibited the rate of oxidation of the benzylic group, but acetylation of the hydroxyl group improved the rate significantly.²⁵ In addition, application of the catalyst system to commercial grade organosolv lignin has also been performed under various conditions. Use of a Co/ Mn/Zr/Br catalyst at 180 °C and 138 bar afforded 10.9 wt% hydroxyaromatic benzaldehydes and acids.²⁵ Another example describes the use of a Co/Mn/Br⁻ catalyst to oxidise four different types of lignin under variable oxygen pressures (0.5-1.5 MPa) at 210 °C to yield vanillin and vanillic acid in 4-4.5 wt% based on the initial amount of lignin.³² Thus, these examples suggest that the catalyst system might not be selective enough to convert industrial grade lignin to economically attractive yields of valuable products due to the complexities associated with C-C and C-O bond cleavage and the repolymerisation of cleavage products. Alternatively, pretreatment procedures could be employed to afford less complex mixtures of relatively smaller oligomers or related compounds such as syringyl derivatives.33-35 We are currently unaware of any use of the Co/Br⁻ or a derivative catalyst system to oxidise exclusively phenolic substrates. However, the use of either cobalt or manganese acetate with excess H₂O₂ has been demonstrated for the oxidation of selected phenols to their respective benzoquinones in 30-75% yield.³⁶ This is important as phenol reactivity is distinct to that of alkyl or mixed alkyl/hydroxyl substituted aromatics. As reported previously, phenols are found to be strong anti-oxidants and inhibitors of alkylaromatic oxidations via the formation of long-lived phenoxy radicals that can terminate chain propagation by means of a number of processes, including the generation of unwanted side products, such as quinones, which may also act as inhibitors.³⁷⁻⁴³

The foregoing discussion raises several questions, which need to be answered to determine the in-principle viability of low temperature and pressure oxidations with a Co/H_2O_2 system: (i) what is the efficacy of catalysis for realistic model compounds and for lignin itself under milder conditions (70 °C with H_2O_2 , rather than O_2 under pressure, as the oxidant); (ii) is the simplified analysis of Neuenschwander and Hermans, notwithstanding the complexity of the chemistry described for *p*-xylene oxidation by Adamian and Gong, pertinent under these conditions and for these substrates;^{15,17} (iii)



Fig. 1 Lignin model compounds, from left to right: monomers, α -O-4 (red link) and β -O-4 (blue link) models.

might other agents such as NHPI, be a more selective radical promoter in lignin oxidation chemistry than the more commonly used bromide system.^{44,45} Accordingly, in the present study we report the use of Co/Br⁻/H₂O₂ in acetic acid at 70 °C and 1 atm for the oxidation of a series of lignin model compounds with varying degrees of methoxylation including phenolic monomers, and α -O-4 and β -O-4 models (Fig. 1), and of organosolv lignin. Cobalt and Br⁻ were introduced as cobalt acetate tetrahydrate and KBr respectively. A preliminary assessment of the applicability of the analytical solution to the Neuenschwander and Hermans rate equation was conducted using syringol as a simple substrate.

Experimental

Chemicals

All chemicals were used as received unless otherwise specified. Glacial acetic acid, potassium bromide, potassium carbonate, and sodium hydroxide (Ajax), 3,4-dimethoxybenzaldehyde (3,4DMB-CHO), 3,4-dimethoxybenzyl alcohol (3,4DMB-OH), 3,4-dimethoxybenzyl acetate (3,4DMB-OAc), 3,4-dimethoxy acetophenone, 2,6-dimethoxyphenol (syringol), 2,6-dimethoxy-1,4-benzoquinone (2,6DMBZQ), 2,6-dimethoxy-1,4-hydroquinone (2,6DMHQ), N-bromosuccinimide, benzoic acid, phthalic anhydride, sodium hydride (60% w/w in mineral oil), vanillin, (Sigma Aldrich), N-hydroxyphthalimide (Alfa Aesar), aqueous hydrogen peroxide (30% w/v), 2-phenylethyl bromide, copper(II) bromide, phosphorus tribromide, potassium hydroxide, toluene (Merck), cobalt(II) acetate tetrahydrate, benzaldehyde (Asia Pacific), phenyl benzoate (British Drug Houses) were of reagent grade. Organosolv lignin was purchased from GreenValue Enterprises and was produced by the Alcell process. The feedstock was a mixture of eastern Canadian hardwoods (~50% maple, 30% birch and 20% poplar). Chloroform-d, acetic acid-d₄ (Cambridge Isotope Laboratories) were diagnostic grade. All water used was de-ionised with a Milli-Q (Millipore) Ultra Pure Water System. Guaiacol (Sigma Aldrich) was vacuum distilled and stored under nitrogen before use. Phenol (Sigma Aldrich) was recrystallised from hexanes before use. Synthesis and

purification of α -O-4 and β -O-4 model compounds, and 4-bromo-2,6-dimethoxyphenol (4Br2,6DMP) was performed following published procedures (see ESI†).

Instrumentation

Gas chromatography-mass spectrometry (GC-MS) was performed using a Shimadzu GCMS-QP2010 and gas chromatography using an FID (GC-FID) was performed using a Shimadzu GC 2010 Plus. Both gas chromatographs were fitted with a Restek Rtx-5MS column (30 mm × 0.25 mm, I.D.; 0.25 µm thickness) and a Shimadzu AOC-20i auto injector. Data were collected and analysed using Shimadzu LabSolutions GCMSsolution version 2.72 and Shimadzu LabSolutions GCsolution version 2.41 respectively. Atmospheric pressure chemical ionisation mass spectroscopy (APCI-MS) and electrospray ionisation mass spectroscopy (ESI-MS) data were acquired using a Bruker amaZon SL mass spectrometer. ¹H NMR (300.13 MHz) and ¹H NMR (200.13 MHz) spectra were recorded on a Bruker Avance DPX300 and a Bruker Avance DPX200 spectrometer respectively, both at 300 K. Spectra were collected and processed using Bruker TopSpin 3.0 software and referenced internally to residual solvent signals or tetramethylsilane (TMS, δ 0.00 ppm). The melting points of compounds were determined in air using a Stanford Research Systems OptiMelt Automated Melting Point System, and a Gallenkamp melting point apparatus, and were reported uncorrected to a known standard.

Catalytic testing

The following procedures were derived from van de Water et al.19 Oxidation of lignin model compounds was conducted with a mole ratio of cobalt acetate tetrahydrate, to substrate, to potassium bromide and excess hydrogen peroxide (per aliquot) of 1:45:8:15-18, heated at 70 °C in a 100 mL multi-necked round bottom flask with a magnetic stirrer, and an un-capped reflux condenser open to the atmosphere. Products were identified by GC-MS and comparing the EI-MS spectra with those in the (NIST05) database. Substrates and products were quantified by GC-FID using individual co-efficient factors determined from calibration curves of authentic samples. Chlorobenzene was used as an internal standard. Conversions are expressed as a percentage defined as (moles of initial substrate - moles of final substrate) × 100. Selectivities are expressed as a percentage defined as (moles of product/moles of converted substrate) × 100. Yields are expressed as a percentage defined as (conversion percentage × selectivity percentage)/100. Mass balances are calculated from the calibrated substrates and products measured by GC-FID, or gravimetrically. Oxidation of α -O-4 model compounds, guaiacol, phenol, 3,4DMB-OH, and toluene involved reacting Co(OAc)2·4H2O (0.08 mmol), substrate (3.6 mmol) and KBr (0.67 mmol) in acetic acid (10 mL) with aliquots of H_2O_2 (11 × 150 µL) added every 12 min for 2 h, and samples (150 µL) taken every 20 min (samples taken every 10 min for the first hour of 3,4DMB-OH oxidation). Oxidation of β -O-4 model compounds involved reacting Co(OAc)₂·4H₂O (0.06 mmol), substrate (2.7 mmol) and KBr (0.5 mmol) in acetic acid (7.5 mL) with H_2O_2 (10 × 113 µL) added every 12 min for 2 h, and samples (150 µL) taken every 20 min. Oxidation of syringol involved reacting Co(OAc)₂·4H₂O (0.24 mmol), syringol (10.8 mmol) and KBr (2 mmol) in acetic acid (20 mL), H₂O₂ (375 µL aliquot) was added every 12 min for either 2.5 h, or 1 h followed by 1 h of heating. Samples (200 µL) were taken 5 min after H₂O₂ addition. Oxidation of 3,3',5,5'-tetramethoxy-4,4'diphenoquinone (coerulignone) and 2,6DMBZQ as substrates were conducted similarly to syringol. Samples were extracted into ethyl acetate for analysis by a Shimadzu GC-2010 Plus GC-FID installed with a Rtx-5MS capillary column, 30 mm × 0.25 mm \times 0.25 μ m. The GC oven ramp method employed for all substrates, except B2, was 3 min isothermally at 50 °C followed by a ramp of 15 °C min⁻¹ to 300 °C which temperature was held for 5 min, giving a total method time of 24.67 min. The GC oven ramp method employed for analysis of B2 was 3 min isothermally at 50 °C, followed by a ramp of 10 °C min⁻¹ to 300 °C which temperature was held for 5 min, giving a total method time of 33 min. For reactions with coerulignone, the product was washed with methanol (20-30 mL) and dried in air for 5-10 minutes followed by oven drying at 80 °C for up to 4 h. Repeat experiments of the catalytic oxidation of syringol were performed to determine the experimental error of the catalytic testing procedure. The standard deviation of the data points of the substrate and products was <3%. All other substrates were reacted in the catalyst system once unless otherwise specified. Coerulignone was identified by melting point, mass spectroscopy and elemental analysis (ESI). The residue from reactions involving syringol was collected by removing the acetic acid in vacuo to afford a dark red/brown amorphous material. This was then washed with dichloromethane $(5 \times 50 \text{ mL})$ to remove the remaining soluble organics and dried in an oven at 80 °C for up to 4 h leaving a dry brown powder/residue. Analysis of the organic filtrate by GC-MS identified syringol, 2,6DMBZQ, 2,6DMHQ and 4Br2,6DMP. Oxidation of organosolv lignin was conducted similarly to syringol for 2 h, however a time-course analysis was not performed. After 2 h the reaction was cooled to room temperature and diethyl ether and water (40 mL each) were added to the reaction mixture to precipitate the unreacted lignin. The mixture was filtered and the lignin residue washed with diethyl ether and water (3×20) mL each) followed by drying at 60 °C overnight. The combined aqueous fraction was extracted with diethyl ether until the organic fractions were colourless (5×100 mL). The ethereal fractions were combined and concentrated in vacuo followed by redissolving of the products in ethyl acetate in a volumetric flask (10 mL) and analysis by GC-MS, and quantification by GC-FID using chlorobenzene as an external standard.

Results and discussion

Catalytic oxidation of α -O-4 and β -O-4 model compounds

The efficacy of the Co/Br⁻/H₂O₂ catalyst system was evaluated for lignin model compounds first. Results for the catalytic oxidation of α -O-4 and β -O-4 model compounds by Co/Br⁻/H₂O₂

Catalysis Science & Technology





are summarised in Table 1. The unsubstituted α -O-4 model compound, A1, exhibited a relatively slow rate of conversion (17% overall) over 2 h with minimal change to the mass balance of the benzyl moiety (96%) (Fig. S1[†]). Benzaldehyde was identified as the major product with a small amount of phenyl benzoate (1.1%) also identified. Small amounts of phenol and bromophenol isomers (<1%) were observed by GC-MS (Fig. S2[†]). Due to the small amounts detected of the latter species and the rapid oxidation of phenols to quinones and CO_2 , the mass balance of the phenyl moiety could not be determined accurately. Methoxylation at the para- and ortho-positions of the benzyl moiety of the α -O-4 linkage gives substrate A2. Under the standard oxidation conditions, when comparing to A1, the product distribution is significantly altered, yielding 3,4-dimethoxybenzyl acetate (3,4DMB-OAc) and decreased selectivity for the corresponding benzaldehyde (from 12% to 8%, Fig. S3[†]). In contrast to the phenylbenzoate observed for A1, no corresponding phenyl-3,4dimethoxybenzoate was observed for A2. Phenol and bromo-

phenol products were barely detectable, attributed to their rapid oxidation. Similarly to A1 however, A2 exhibited a relatively slow rate of conversion (14% overall) over 2 h and comparable mass balance values. The formation of 3,4DMB-OAc is attributed to the stabilising effect of the methoxy groups on the intermediate benzylic radical.⁴⁶ Assuming the benzyl moiety has been cleaved, greater stability of the benzylic



Scheme 3 The equilibrium established between benzylic radicals and O_2 . The electron-donating methoxy substituents impart stability to the benzylic radical.

radical reduces its rate of interaction with molecular oxygen.⁷ This would be consistent with a relatively higher concentration of the more stable benzylic radical due to a greater resonance stabilisation than that present in its corresponding benzylperoxy radical (Scheme 3). In addition to methoxylation at the 3- and 4-positions of the benzyl moiety of A2, the methoxylation of the phenolic moiety in the ortho-position of A3 resulted in significant improvements in the rate and overall conversion (47% over 2 h) of the substrate A3 compared with A1 and A2 (Fig. S4[†]). In contrast to A2, 3,4DMB-OAc was the major product of A3 oxidation, while the yield of the corresponding benzaldehyde dropped significantly. In addition a greater amount of the phenolic moiety (guaiacol, 6%) was detected. Similarly to the observations with both A1 and A2, a small amount of the brominated phenolic moiety (bromoguaiacol) was detected by GC-MS. The improved substrate conversion of A3 (as compared to A1 and A2) is attributed to the increased stability of the phenoxy radical generated from guaiacol, compared to that generated from phenol, due to the electron donating effect of the methoxy group in the *ortho* position.⁴⁷ The improved conversion can be further rationalised from the calculated C-O bond dissociation energies (BDE) of A1, A2 and A3 (56.43, 56.24 and 51.32 kcal/mol respectively).⁴⁸ Addition of methoxy groups at the ortho-position on the phenolic moiety of the $\alpha\text{-}O\text{-}4$ model compounds led to the largest changes in the C-O BDE and this change was attributed to greater steric hindrance of the methoxy group added.⁴⁸ However, despite the increased conversion of A3 compared to A1 and A2, the overall mass balance for the reaction was lower, indicating an alternative reaction pathway, such as polymerisation.

The unsubstituted β -O-4 model compound (B1) vielded a conversion (19% over 2 h) similar to the unsubstituted α -O-4 model (A1), plateauing after 80 min (Fig. S5⁺). Benzaldehyde was the only major product quantified (4.6% yield), however, no colour change, the observation of which can indicate the formation of phenoxy-radicals or polyphenols was observed. Based on the intensity of the peaks in both the GC-MS and GC-FID chromatograms, it is clear that a significant amount of the substrate underwent bromination (Table 1, Fig. S6[†]). The exact isomer formed could not be identified conclusively, the fragmentation pattern suggesting bromination of the phenolic moiety (Fig. S7[†]). By assuming the brominated ether to have a similar FID molar signal response as to that of the substrate, the yield of the brominated product was approximated at 10% (Fig. S8†). This estimate is in line with expectations based on the previous observations of low conversion and high mass balances of the benzyl moieties of A1 and A2 over 2 h of reaction. In addition, hydroxyphenylethyl phenyl ether and phenacyl phenyl ether were also observed as minor products, presumably arising from an analogous oxidation process for the α -carbon that results in the phenyl benzoate observed in the oxidation of A1 (<1%, Table 1, Fig. S6[†]). Despite the similar rates of conversion of B1 and A1, the yield of benzaldehyde from the conversion of B1 was 3 times less than

that from A1. This is likely a consequence of the higher BDE values for C-C bonds compared with C-O bonds.48 Furthermore, reaction pathways such as bromination, and hydroxylation of the α -carbon proceeded to the extent that these species were just observable spectrometrically. From the pattern of substrate reactivity observed with the α -O-4 model compounds it was expected that the more elaborately functionalised (and thus more realistic) B-O-4 model compound, B2, would exhibit greater conversion and cleavage in the Co/Br-H2O2 system than B1. After 2 h 38% of the substrate was converted, then the rate of conversion appeared to plateau after a further 40 min (Fig. S9(a)[†]). The dimeric molecule 1-(3,4-dimethoxyphenyl)-2-(2methoxyphenoxy)ethanone was identified as the major product, indicating oxidation at the α -carbon and elimination of the primary alcohol of B2. Smaller amounts of 3,4DMB-CHO and guaiacol were also observed. Analysis of the reaction mixture by GC-MS revealed a mixture of aromatic monomer species (Fig. S10(a and b)⁺). Apart from the bromoguaiacol species, many of the low intensity ion peaks could not be reliably identified by the NIST library, however, structures consistent with the m/z ratio of the ion peak are proposed. The relatively low intensity ion peaks of these products suggests that they are present in the reaction at very low concentrations. In addition to aromatic monomeric species, two ion peaks with an m/z ratio consistent with the dimeric species 1-(3,4-dimethoxyphenyl)-2-(2methoxyphenoxy)-2-propen-1-one and acetylation of one of the alcohol groups of B2 were also observed (Fig. S10(c)[†]). In comparison to B1, bromination of the substrate was not observed, but a similar yield of the benzaldehyde product was obtained. The higher BDE values for C-C bonds compared with C-O bonds, cited earlier in the discussion of B1, may direct selectivity to dimeric oxidation products over monomeric products. In contrast to the α -O-4 model compounds A2 and A3, the presence of 3,4DMB-OAc was not detected. The mass balance for the reaction of B2 was slightly lower compared to B1 (when including the estimated yield of brominated B1), consistent with the behaviour of the α -O-4 model compounds with increased methoxylation of the phenolic moiety. The colour of the reaction turned dark orange during H₂O₂ addition, suggesting the formation of species with an extended π -system, such as polyphenolics. In comparison to earlier results obtained by DiCosimo et al., oxidation of B2 using a similar catalyst system (Co(II) acetate in 80% acetic acid at 170 °C and 3.45 MPa, 4% O₂ in N₂) reported 49% substrate conversion to afford 3,4DMB-CHO, 3,4-dimethoxybenzoic acid, guaiacol as the major products. Acetylation of the substrate at either the primary alcohol or both the primary and secondary alcohol was also observed, but no products consistent with the elimination of the primary alcohol of the substrate were reported.49 The authors also investigated the stability of B2 in the absence of the Co(II) catalyst (80% acetic acid at 170 °C and 3.45 MPa, 4% O2 in N2) observing 77% conversion of the substrate and affording a higher

selectivity for acetylation of the substrate relative to the monomeric products. In this work, heating B2 in acetic acid at 70 °C for 2 h demonstrated a negligible change in the amount of substrate, confirming that the Co/Br⁻/H₂O₂ catalyst is primarily responsible for the conversion of B2. Analysis of the reaction mixture by GC-MS revealed the presence of an ion peak consistent with the acetylation of B2 at either the primary or secondary alcohol (Fig. S11†).

Behaviour of phenol and guaiacol

The low conversion of A1 and A2, and the decrease in the mass balance for catalytic oxidation of A3 and B2 are attributed to the formation of phenoxy radicals and polymeric species. A colour change to red-brown after addition of H2O2 was observed for all α -O-4 model compounds, indicative of the formation of phenoxy radicals.⁵⁰ These species are known radical scavengers, reducing the availability of catalytically useful radicals (benzylic) and terminating the propagating radical species.^{51,52} As phenols undergo an increasing degree of polymerisation the antioxidant activity increases due to the greater number of hydroxyl groups and extended π -system, affording greater stability of the polymer.⁵³ Catalytic oxidation of either phenol or guaiacol revealed the monomers reacted more rapidly than the α - and β -O-4 compounds. Similar to the α -O-4 model compounds, increased methoxylation of the phenolic substrate resulted in a greater rate of conversion (Fig. S12 and S14[†]). GC-MS analysis detected only small amounts of the brominated substrate as well as 2-methoxyhydroquinone (species identified by the NIST library), but may also be methoxy resorcinol or methoxy catechol (Fig. S13 and S15[†]). Large molecular weight products (larger than dimers), not detectable by GC, were detected by APCI-MS analysis. Consistent with this, interrogation of the guaiacol reaction mixture revealed the presence of multiple ions with a m/z ratio comparable to structures of guaiacol and hydroxylated guaiacol derived oligomers including guaiacol dimer (m/z = 247.04), trimer (m/z = 369.16), tetramer (m/z = 491.13) and pentamer (m/z = 613.15) species (Fig. S16[†]), confirming that phenolic substrates undergo oxidative radical polymerisation in the Co/Br-/H2O2 system. Quinones and organic acids were not detected by GC-MS for the catalytic oxidation of guaiacol and phenol, suggesting overoxidation is not a major pathway for these substrates under the conditions employed.

For the catalytic oxidation of A3, similar to the oxidation of guaiacol, large molecular weight products were detected by APCI-MS: a complex spectrum was obtained displaying ions with a m/z ratio consistent with a guaiacol trimer (m/z = 369.16) and protonated guaiacol pentamer (m/z = 613.27) species. Species containing fragments consistent with both benzyl (m/z = 150) and guaiacyl (m/z = 122) moieties less two hydrogens each were also detected (Fig. S17†). These observations demonstrate that the progressive decrease in mass balance for the oxidation of A3 is due to the increasing formation of oligomeric and polymeric species derived from the radical coupling of phenolic

monomer moieties. Due to the radical scavenging ability of phenol and guaiacol, the effect of these molecules on the oxidation of a benzylic substrate was investigated. 3,4DMB-OH was chosen as the test substrate due to its resemblance to the benzyl moiety of the α -O-4 model compounds A2 and A3. Catalytic oxidation of 3,4DMB-OH in the Co/Br⁻/H₂O₂ system resulted in complete conversion of the substrate after 50 min to afford 3,4DMB-CHO (93% selectivity) and 3,4DMB-OAc (7% selectivity) (Fig. S18[†]). Addition of either phenol or guaiacol at 5 mol% (with respect to substrate) reduced the conversion of 3,4DMB-OH (68% and 61% respectively), and reduced the mass balance to \sim 80%, indicative of the formation of oligometic/polymetic phenols (Fig. S19 and S20[†]). In a similar trend to that observed for the α -O-4 model compounds A2 and A3, which feature the dimethoxybenzyl moiety, the yield and selectivity of 3,4DMB-OAc increased at the expense of the yield and selectivity of 3,4DMB-CHO in the presence of phenols and to a greater extent in the presence of guaiacol. At even higher concentrations of phenol or guaiacol (20 mol%) the conversion decreased even more (\sim 38%), while the mass balance remained relatively unchanged (Fig. S21 and S22[†]). The selectivity for 3,4DMB-OAc increased further with it becoming the major product, while the yield of 3,4DMB-CHO dropped to less than 10%. It is noteworthy that regardless of the type or amount of phenolic additive, the yields of 3,4DMB-OAc were all nearly identical (14, 13, 18, 14 mol%). Due to the reduced formation of benzylic radicals in the presence of phenols, 3,4DMB-OH is more likely to undergo acetylation in the presence of excess acetic acid. These results demonstrate clearly that phenols both inhibit the conversion of benzylic substrates, including a-O-4 model compounds, and demonstrate that product selectivity can be directed by the type of phenol employed.

Catalytic oxidation of syringol

Results for the catalytic oxidation of syringol by Co/Br-/H2O2 are summarised in Table 2. The substrate behaved similarly to phenol and guaiacol in that after addition of H₂O₂ the reaction turned dark red indicating the formation of phenoxy radicals. However, unlike the cases of the other phenolic monomers several products arising from distinct processes were detected. Over a 2.5 h period, with peroxide addition in aliquots, 96% of the syringol was consumed (Fig. S23[†]). Immediately after initiating the reaction with H₂O₂, a dark purple precipitate formed which was later identified as coerulignone by ESI-MS. Analysis by GC-FID and GC-MS revealed the formation of 2,6DMBZQ and 4Br2,6DMP as minor products, and a very small amount of 2,6DMHQ (<1%) (Fig. S24[†]). However the products and unreacted substrate accounted for only 63% of the mass balance. Removal of the solvent and extraction of the volatile organic molecules yielded a brown residue that is suspected to be the result of polymerisation of phenoxy radicals, and accounted for 31% of the mass balance (based on the initial mass of the substrate). Analysis of the residue by APCI-MS revealed multiple high molecular weight species (similar to those generated

Substrate	Conversion (mol%)	Products (yield mol%, selecti	ivity%)		Mass balance (mol%)
OH OH O	96	(Coerulignone) $0 \rightarrow 0 \rightarrow 0$ $0 \rightarrow 0 \rightarrow 0$	(2,6DMBZQ)	(4Br2,6DMP) OH O Br	(63) ^{<i>a</i>}

Table 2 Results for the Co/Br $^{-}$ /H₂O₂ catalysed oxidation of syringol, 2.5 h H₂O₂ addition

 a A significant amount of the substrate was converted to a non-tractable residue (31%, based on the mass of starting material) which was recovered by removing the solvent.

from guaiacol) consistent with structures composed of syringyl moieties (less two hydrogens, m/z = 152) (Fig. S25†). Methoxy groups in both *ortho* positions of syringol promote the dimerisation of the phenoxy radical, the product of which is then oxidised to form the highly insoluble coerulignone (Scheme S1†). Formation of the benzoquinone is possible by reaction of the phenoxy radical with a hydroxyl radical to form the hydroquinone, followed by oxidation by a either a bromine radical or hydroxyl radical. The benzoquinone could also be formed by the reaction of the phenoxy radical with O₂ in the *para* position, forming a *p*-Ph-O₂[•] adduct. Dimerisation of the benzoquinone, hydroquinone and O₂.⁵⁴ Formation of the bromophenol is likely a consequence of the phenoxy radical reacting with a bromine radical (Scheme S2†).

Variation of initial co and phenolic substrate concentration

To better understand the reactivity of phenolic substrates with the Co/Br⁻ catalyst, variation of the initial concentrations of Co catalyst and substrate were performed. Syringol was used as the test substrate due to its broader product distribution compared to phenol and guaiacol, and its prevalence in organosolv and hardwood lignin extracts.^{33,55,56} The conversion of syringol began to decrease significantly from 82 to 71 mol% when the initial concentration of Co was less than 6 mM (Table 3). Additionally, increased yields of 4Br2,6DMP, from 4 to 22%, were observed. This result indicates that when the Co:Br⁻ ratio decreases, more of the bromide anion is sequestered as the catalytically inactive form 4Br2,6DMP. Similar behaviour of deactivation has been observed by others for the oxidation of alkyl aromatics by the formation of catalytically inactive benzyl bromides and rapid bromination of phenol by-products.^{57,58} It has also been reported that in Co/Br⁻ catalysed systems the bromide anion may exist within the second coordination sphere of the metal through ion pairing.¹² With less Co present in the reaction to coordinate bromide, the co-catalyst is more likely to be sequestered by phenoxy radicals. Decreasing initial Co concentrations also resulted in decreasing yields of coerulignone (from 42 to 16%), a small overall decrease of the yield of 2,6DMBZQ (from 9 to 4%), and significant decreases in the residue recovered from solvent removal. Based on these results the yield of coerulignone appears dependent on the concentration of Co across the range of 0.6 to 12 mM. This interpretation is supported by a control reaction in which Co was absent, affording <1% of coerulignone (Fig. S26⁺). Previous studies concerning oxidation of 2,6-disubstituted phenols by Co-O₂ complexes demonstrated higher ratios of benzoquinone (BZQ) to diphenoquinone (DPQ) with increasing Co concentration in non-polar solvents.⁵⁹ However, the ratio of BZQ to DPQ significantly decreases with increased temperature in polar solvents, with DPQ (4,4 C-C bonding) being favoured in acidic solvents.43,60

In contrast to decreasing the initial Co concentration, decreasing the initial substrate concentration increased conversion of the substrate (Table 4). The yields of coerulignone were reduced and the yields of 4Br2,6DMPs remained relatively unchanged, however the yields of 2,6DMBZQ increased significantly (22%, 42% selectivity). With less substrate

Table 3	Results for the catalytic oxidation of syringol using different initial concentrations of Co (as Co(OAc) ₂ ·4H ₂ O), 1 h of H ₂ O ₂ addition						
Entry	[Co] ₀ (mM)	Conversion (mol%)	Coerulignone (yield, mol%)	2,6DMBZQ (yield, mol%)	4Br2,6DMP (yield, mol%)	Residue (%)	Mass balance ^c (%)
1	24	85	46	6	2	22	69
2	12^a	82	42	8	4	20	72
3	6	82	32	9	8	N/A^b	67
4	3	71	21	7	11	6	68
5	0.6	65	16	4	11	7	66

^a Same initial concentration as results in Table 2. ^b N/A: residue was not recovered. ^c Based on substrate and identified products.

Table 4 Results for the catalytic oxidation of syringol using different initial concentrations of substrate, 1 h of H₂O₂ addition

Entry	[Syringol] ₀ (M)	Conversion (mol%)	Coerulignone (yield, mol%)	2,6DMBZQ (yield, mol%)	4Br2,6DMP (yield, mol%)	Residue (%)	Mass balance ^c (%)	Rate constant ^d (\min^{-1})
1	1.08	59	33	4	3	N/A ^b	81	0.0120
2	0.54^{a}	82	42	8	4	20	72	0.0213
3	0.27	98	31	16	5	N/A	54	0.0440
4	0.14	100	27	22	3	57	52	0.0970

 a Same initial concentration as results in Table 2. b N/A: residue was not recovered. c Based on substrate and identified products. d As an approximation to facilitate general comparisons of the relative rates, pseudo-first order rate constants were obtained by fitting the initial rates as first-order.

present fewer phenoxy radicals are produced in situ, reducing the probability of dimerisation. With relatively higher concentrations of Co, O2 and H2O2, phenoxy radicals are more likely to follow reaction pathways to form benzoquinone. To approximately compare the relative rates of the catalytic oxidation of syringol for different initial syringol concentrations, pseudo-first order rate constants were obtained from plotting the natural logarithm of syringol concentration vs. time for the initial part of the reaction. Plotting the pseudo-first order rate constants against the initial syringol concentration revealed that the initial pseudo-first order rate constant of syringol conversion is inversely proportional to the initial syringol concentration (Fig. S27 and S28†). Again, similar behaviour (increased substrate conversion, BZQ yield) has been observed for oxidation of 2,6-disubstituted phenols by Co-O₂ complexes when lowering the substrate concentration but maintaining the Co concentration (0.017 M Co and 0.66, 0.33 M substrate⁵⁹ vs. 0.012 M Co and 1.08, 0.54, 0.27, 0.17 M substrate, this work).

The effects of quinones and hydroquinones on the reaction of syringol

It is well known that phenols and quinones are inhibitors of the oxidation of benzylic carbons on aromatic molecules, however it is unclear if phenol oxidation in the $Co/Br^-/H_2O_2$

system is affected by oxidation products such as hydroquinones and quinones. Time-course experiments involving the addition of an equimolar amount of 2,6DMBZQ or 2,6DMHQ with syringol were performed with peroxide addition for 1 h (Fig. 2 and 3, Table 5, Fig. S29[†]). For the addition of equimolar 2,6DMBZQ the conversion of syringol was not dramatically inhibited (Fig. 2). However, at higher concentrations (~0.25 M) 2,6DMBZQ is partially insoluble, and due to the similar retention time/peak overlap of 4Br2,6DMP both molecules could not be accurately monitored. In comparison to the absence of added 2,6DMBZQ (Table 5, entry 1), the conversion of syringol and the observed pseudo-first order rate constant are slightly lower (82%, 0.0213 min⁻¹ vs. 79%, 0.0193 min^{-1} , Table 5, entry 2). The yield of coerulignone is slightly less (32% vs. 42%), suggesting that the dimerisation of syringyl radicals may have been inhibited.

In the presence of equimolar 2,6DMHQ, the catalytic oxidation of syringol was strongly inhibited (Fig. 3), while 2,6DMHQ was rapidly oxidised to 2,6DMBZQ. Unlike 2,6DMBZQ, 2,6DMHQ remained soluble at higher concentration. However, the rapid formation of 2,6DMBZQ meant that the product and 4Br2,6DMP could not be monitored accurately. The data suggests that until the concentration of 2,6DMHQ drops below 10% of its initial value the conversion of syringol is strongly inhibited. The pseudo-first order rate constant for the conversion of 2,6DMHQ was 0.104



Fig. 2 Time-course profile of the catalytic oxidation of syringol with $Co/Br^{-}/H_2O_2$ showing only syringol consumption with and without the presence of equimolar 2,6DMBZQ.



Fig. 3 Time-course profile of the catalytic oxidation of equimolar syringol and 2,6DMHQ with Co/Br $^-/H_2O_2.$

Paper

Entry	Substrate(s)	Syringol conversion (mol%)	Coerulignone (yield, mol%)	Rate constant ^{<i>a</i>} (syringol, min ⁻¹)	Rate constant ^a (2,6DMHQ, min ⁻¹)
1	Syringol (1 h H ₂ O ₂)	82	42	0.0213	N/A
2	Syringol, 2,6DMBZQ (1 h H ₂ O ₂)	79	32	0.0193	N/A
3	Syringol, 2,6DMHQ (1 h H ₂ O ₂)	36	6	0.0110	0.104
4	Syringol (2.5 h H_2O_2)	96	41	0.0254	N/A
5	Syringol, 2,6DMHQ (2.5 h H_2O_2)	80	35	0.0183	0.0944

^{*a*} As an approximation to facilitate general comparisons of the relative rates, pseudo-first order rate constants were obtained by fitting the initial rates as first-order.

min⁻¹ (Table 5, entry 3), approximately five times greater than that for syringol (0.0213 min⁻¹). Extending the H_2O_2 addition for 2.5 h syringol conversion continued until plateauing at 80% after 2 h (Fig. S30[†]). Similar to the equimolar addition of 2,6DMBZQ (Table 5, entry 2), the pseudofirst order rate constant and coerulignone yield were slightly lower compared to the reaction of only syringol for 2.5 h (0.0183 min⁻¹, 35% vs. 0.0254 min⁻¹, 41%, Table 5, entries 4 and 5). The relatively rapid reaction of 2,6DMHO may explain its presence in only very low concentrations (<1%) observed in samples from the catalytic oxidation of syringol. Furthermore, the inhibition of syringol conversion by 2,6DMHQ may explain why relatively higher initial concentrations of syringol result in lower amounts of syringol conversion. With a higher syringol to cobalt ratio, more 2,6DMHQ is generated, which inhibits syringol conversion. The mechanism of inhibition of syringol conversion by 2,6DMHQ would be consistent with a disproportionation pathway: in the absence of radical scavengers, neutral semiquinone radicals decay through bimolecular selfreactions that afford the respective quinone and hydroquinone.43 The generation of both syringyl and 2,6dimethoxysemiquinone radicals could result in the transfer of a hydrogen radical from a 2,6-dimethoxysemiquinone radical to a syringyl radical (Scheme 4). However, this assumes the rate of H-atom transfer between the phenoxy radical species is significantly greater than the rate of other reaction pathways such as syringyl radical dimerisation to form coerulignone.



Scheme 4 Proposed scheme of H⁻ transfer from a 2,6dimethoxysemiquinone radical to a syringyl radical.

Modelling the catalytic oxidation of syringol

As discussed above, to approximately compare the differences observed for the conversion of syringol under different conditions, pseudo-first order rate constants were obtained from the linear plots of the natural logarithm of the substrate concentration vs. time at the start of the reaction. While this treatment provides a convenient way to compare the behaviour of the substrate during the initial stage of the reaction (t < 65 min), it does not satisfactorily describe the behaviour of the substrate over the entirety of the reaction. The model based on pseudo-first order rate constants breaks down at lower concentrations of syringol, e.g. ~20% of the initial concentration (Fig. S31[†]), as its assumptions for its applicability (high concentration of substrate) become invalid. Recently, Neuenschwander and Hermans¹⁷ were able to successfully describe the thermal and catalytic initiation of the free radical hydrocarbon autoxidation of a-pinene. To test whether the rate equation of Neuenschwander and Hermans¹⁷ (eqn (E)) could be employed as a useful first approximation to model the entire catalytic reaction of syringol, an analytical solution for the concentration of substrate vs. time was developed consistent with the scheme of Neuenschwander and Hermans, *i.e.* there is a thermal and catalytic pathway, a steady-state in radical concentration, and that the concentrations of the peroxide (H₂O₂ in this case) and Co are constant. The timecourse of syringol oxidation was fitted using the analytical solution of the rate equation and the results are illustrated in Fig. 4. The derivation of the analytical solution of the rate equation is described in the ESI,† pp. 7-10. Although individual rate constants cannot be extracted, the good fit of the theoretical expression to the data indicate that the simplified mechanistic description of Neuenschwander and Hermans is a useful first approximation to describe the chemistry over the whole of the reaction and can be used as a basis for further in-depth microkinetic analysis of this complex system. In addition to Co, we also know that Br⁻ is involved in the catalytic step, however, it is added to speed up the reaction and may not be involved in the rate-determining step as described by Neuenschwander and Hermans, and discussed in detail by Adamian and Gong.^{15,17} Despite some Br⁻ being consumed in the bromination of the substrate, the concentration of Br remains in excess throughout the reaction (>60% of the initial Br⁻ concentration based on the 4Br2,6DMP concentration).



Fig. 4 Plot of the experimental data points for the catalytic oxidation of syringol over 2.5 h of peroxide addition, compared with the plot arising from the Neuenschwander and Hermans model, eqn (E), (including the standard error).

Over-oxidation of syringol-derived products

As reported above, a significant portion of syringol is recovered as a residue that is suspected to be the result of syringyl radical polymerisation. However, the literature provides scant examples of cobalt-catalysed formation of polyphenols.^{61,62} It is unknown whether the Co/Br⁻/H₂O₂ catalyst system could yield polymeric products, and whether any polymeric products would be resistant to over-oxidation. It is known that under Co/Br catalyst conditions both the acetic acid solvent and the aromatic substrate are subject to over-oxidation.^{58,63-66} The main by-products of solvent oxidation include CO₂ and CO, followed by smaller amounts of methyl acetate, acetoxyacetic acid, formic acid and methane. It has been demonstrated that solvent decomposition can be initiated by thermal decomposition of a Co(III) acetate species and formation of an acetoxy radical via homolysis of a Co(m)-O bond of an acetate ligand.⁶⁵ Products of substrate decomposition are similar to those from solvent decomposition, predominantly CO_x species and smaller amounts of organic acids, esters and brominated molecules.⁶⁶ Suspected mechanisms of substrate decomposition include decarboxylation of aromatic acids to produce CO_x species, or generation of phenols which are oxidised to quinones and CO2.6,42,43 Coerulignone and 2,6DMBZQ were both tested for over-oxidation and the results are summarised in Table 6. Monitoring of 2,6DMBZQ by GC-FID showed no

loss of the substrate, and the initial mass of 2,6DMBZQ was recovered. This suggests that the molecule is stable under the catalytic conditions and is not converted to organic acids or CO_x. Samples were also analysed by GC-MS, revealing a species corresponding to bromination of 2,6DMBZQ with a vield of <5% based on the co-efficient factor of 2,6DMBZQ (Fig. S32[†]). The reaction of coerulignone could not be monitored by GC-FID due to its extremely poor solubility, however, samples were still taken to observe any potential decomposition products. Samples analysed by GC-MS revealed tribromomethane and 2,2-dibromoacetic acid methyl ester (Fig. S33a[†]). Comparison of the chromatograms for the oxidation of coerulignone and a blank reaction indicate the brominated molecules are formed from the decomposition of coerulignone (Fig. S33b[†]). Conversion of coerulignone was determined gravimetrically by recovering the remaining material. A brown residue similar in appearance to the residue observed for the catalytic oxidation of syringol was also recovered. Like the syringol oxidation residue, the coerulignone residue was only soluble in acetic acid and was sparingly soluble in water. ¹HNMR spectroscopy of the coerulignone residue in acetic acid- d_4 revealed a complex spectrum with methoxy and phenolic signals similar to that for the syringol oxidation residue (Fig. S34-S36[†]). By extrapolation, the mass of coerulignone unaccounted for (23 and 57% of the mass balance, Table 6) corresponds to 5.7 and 5.6%, respectively, of the mass balance of syringol (for 1 h of H₂O₂ addition) in the earlier experiments. This suggests that excess H2O2 may directly affect conversion of coerulignone. Overall these results suggest the loss of coerulignone in the catalytic system could contribute to the poor mass balances recorded for the catalytic oxidation of syringol, including any contribution from CO/CO₂, which was not explicitly quantified.

Substitution of bromide with *N*-hydroxyphthalimide for catalytic oxidation of α -O-4 model compound (A3) and organosolv lignin

The highly corrosive conditions of the catalyst system, due to the presence of HBr, have encouraged the investigation of alternative radical promoter co-catalysts such as NHPI, which is converted to the phthalimide-*N*-oxyl (PINO) radical.⁴⁵ Co/NHPI systems have been demonstrated to oxidise toluene and other hydrocarbons effectively, but to the best of our knowledge have not been investigated for oxidation of lignin model compounds. Reaction of A3 with the Co/

Table 6 Results for the catalytic oxidation of 2,6DMBZQ and coerulignone in the Co/Br⁻/H₂O₂ system, 1 h of H₂O₂ addition

Run	Initial substrate, g ^{<i>a</i>}	Recovered substrate, g, (%)	Consumed substrate, g, (%)	Recovered residue, g, (%)	Mass balance (%)
2,6DMBZQ	0.455	0.455 (100)	0 (0)	0 (0)	100
Coerulignone1	0.412	0.27, (66)	0.142, (34)	0.047, (11)	77
Coerulignone2	0.165	0, (0)	0.165, (100)	0.071, (43)	43

^{*a*} The loadings of 2,6DMBZQ and coerulignone correspond to 25, and 25 and 10% of the loading for the catalytic oxidation of syringol (1.67 g, 10.8 mmol), 1 mole of coerulignone is equivalent to 2 moles of syringol.

Table 7	Results for the catalytic oxidation of organosolv lignin (1.67 g) with Co and either Br [−] or NHPI as co-catalysts, 2 h of H ₂ O ₂ ac	dition. Monomeric
aromatic	and quinone products contained in the organic extract of the reaction mixture were analysed only	

Run	Vanillin, mg (wt%)	Syringaldehyde, mg (wt%)	2,6DMBZQ, mg (wt%)	Total, mg (wt%)
Br ⁻ 1	2.8 (0.17)	7.2 (0.43)	18 (1.1)	28 (1.7)
Br ⁻ 2	3.6 (0.21)	9.1 (0.54)	22 (1.3)	35 (2.1)
NHPI 1	2.8 (0.17)	3.3 (0.2)	30 (1.8)	36 (2.2)
NHPI 2	2.5 (0.15)	2.0 (0.12)	28 (1.7)	33 (2.0)

The wt% product yields are calculated relative to the amount of initial lignin.

NHPI/H₂O₂ system, replacing Br⁻ with an equimolar amount of NHPI, resulted in improvements in substrate conversion and product yields (Fig. S37, Table S1[†]). The conversion of the substrate increased from 47 to 68%, while the yield of 3,4DMB-CHO increased from 1.2 to 8.2%, corresponding to a 5-fold improvement in selectivity. The yield and selectivity of guaiacol significantly improved (from 6 and 13%, to 29 and 43%), while the yield of 3,4DMB-OAc also improved slightly. The mass balance of the benzyl moiety of A3 exhibited a similar profile to A3 reacted in the presence of Co/Br, while the mass balance of the phenolic moiety improved relative to the improved yield of guaiacol. This improved guaiacol selectivity suggests that substitution of Brwith NHPI reduces the rate of polyguaiacol formation, which reduces inhibition of substrate conversion and the loss of oxidation products. Benzylic substrates undergo less conversion when using NHPI as a co-catalyst than when using Br⁻ (e.g. toluene, Fig. S38 and S39⁺). This is reflected by the less thermodynamically favoured hydrogen atom abstraction by PINO radicals compared to bromine radicals.⁶⁷ In addition, benzylic radicals have a shorter lifetime relative to phenoxy radicals.⁶ However, the greater stability of the PINO radical appears advantageous in the presence of more reactive molecules such as phenolics (relative to benzyls), compared to highly active bromine radicals. Rate constants reported for the reaction between dibromide radicals and methoxylated phenols are $\sim 10^8$ M⁻¹ s⁻¹, which may be considered close to diffusion control limited.⁶⁸ This would suggest that the higher reactivity of bromine radicals results in lower selectivity, causing an increase in guaiacol radical concentration and subsequent polyguaiacol formation.

Following these encouraging results, preliminary experiments using NHPI as a co-catalyst for oxidation of organosolv lignin were conducted. NHPI was compared against Br⁻ based on the yield of aromatic and quinone products extracted in the organic phase. For the lignin oxidation experiments, the molar ratio of the cobalt catalyst was doubled to reduce the probability of forming brominated phenols and aromatics, evidenced from variation of the cobalt concentration for syringol oxidation. Oxidation of organosolv lignin with Co/ Br⁻/H₂O₂ and analysis of the diethyl ether extract revealed three major products identified by GC-MS as vanillin, 2,6DMBZQ and syringaldehyde, and quantified by GC-FID (Table 7, Fig. S40†). Substitution of Br⁻ for an equivalent molar amount of NHPI resulted in the decrease of the wt% yield of syringaldehyde by a factor of 2–4 while the wt% yield of

vanillin was relatively unchanged. This is inconsistent with the improved aldehyde yield from the reaction of A3 with NHPI as a co-catalyst. The wt% yield of 2,6DMBZQ increased by a factor of 1.3-1.5, indicating less syringol was lost to polymerisation and over-oxidation. This is consistent with the increased guaiacol yield from the reaction of A3. No coerulignone was observed suggesting a relatively low concentration of free syringol generated from the lignin polymer, inferred from the syringol concentration variation experiments. In addition, a significant amount of the NHPI co-catalyst was converted to other species, including phthalic anhydride ($\sim 20 \text{ wt\%}$), suggesting deactivation of the catalyst system (Fig. S41⁺). These preliminary results demonstrate that NHPI could potentially be useful for improving the overall product yield from catalytic lignin oxidation, but further studies are necessary to understand and optimise the system. In comparison to the two literature examples (see ESI[†] for details, pp. 36–37), the yields of aromatic aldehydes, calculated as the wt% of the initial lignin, are \sim 5 times less.^{25,32} The other examples use more active catalyst compositions, such as Co/Mn/Br and Co/ Mn/Zr/Br, which are ~4 and 9 times more active towards alkyl aromatic substrates than Co/Br⁻ respectively.⁶ In addition, the other literature examples employ either a higher reaction temperature or pressure which has been shown to improve the yield of aromatic aldehydes. However, the complexity of the catalyst system and the variation of conditions between the different literature reports makes comparison of the performance of the different systems difficult.

Conclusions

The catalytic oxidation of lignin model compounds by Co/ Br⁻/H₂O₂ in acetic acid at 70 °C has been investigated, demonstrating the efficacy of the system to react with a variety of substrates, the successful application of a simplified mechanistic scheme, and the ability of NHPI to act as a more selective radical promoter for the oxidation of lignin model compounds. For the oxidation of model compounds, the degree of methoxylation of the substrate was observed to have a significant effect on its reactivity and the product distribution across all types of model compounds tested. For the α -O-4 model compounds the selectivity could be varied by methoxylation of the benzyl moiety while substrate conversion could be improved by methoxylation of the phenolic moiety. The improved substrate conversion is attributed to the greater stability of the guaiacyl radical (*vs.* phenoxy radical) and lower

C-O BDE. Similar behaviour was observed for the β-O-4 model compounds, with the addition of methoxy and alcohol functional groups increasing the complexity of the product distribution. The catalytic oxidation of phenolic monomers such as phenol and guaiacol resulted in the formation of polyphenols/guaiacols. These species were found to inhibit substrate conversion and reduce the mass balance of α -O-4 model compounds by incorporation of oxidation products into polymeric species. In comparison to phenol and guaiacol, catalytic oxidation of syringol yielded dipheno- and benzoquinones, the selectivity for the formation of which was dependent on the ratio of Co to substrate. However, the diphenoquinone was susceptible to over-oxidation. Analysis of the time-course data of syringol oxidation using the analytical solution to the rate equation of Neuenschwander and Hermans¹⁷ demonstrated that the oxidation could usefully be modelled to a first approximation by this simplified mechanistic scheme. The successful application of this mechanistic scheme will be explored for other aromatic substrates, such as 4-tert-butyltoluene, and other lignin model compounds in future investigations. The substitution of Br for NHPI as the radical promoting co-catalyst reduced the deleterious effects of phenols for the conversion of a model α -O-4 compound, improving the yield and selectivity of 3,4DMB-CHO and guaiacol products. Preliminary application of NHPI to an actual lignin source afforded a modest improvement in the vield of benzoquinone product, but, not unexpectedly, the total yield of aromatic aldehydes was lower. These results demonstrate that NHPI can be a more selective radical promoter for pure lignin model compounds than Br, while further investigation is necessary to improve the oxidation of lignin with Co/NHPI/H₂O₂.

Overall this study demonstrates the complexity of Co/Br⁻ catalysed oxidation of lignin substrates by revealing the effects of discrete structural changes to the substrate on the conversion and resulting product distribution. While the catalyst system is versatile enough to react with a variety of substrates, poor product selectivity from real lignin sources, and inhibition by substrate-derived phenols remain as critical issues. Despite the improved product yield when using NHPI with a model compound, the inconsistency when using an actual lignin source encourages further investigation of NHPI as the co-catalyst.

Nonetheless, the low temperature and pressure system shows much promise and further optimisation, including additives like Mn or Zr mirroring the commercial system, might lead to acceptable conversion at much higher selectivities.

Conflicts of interest

The authors declare no conflict of interest.

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