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The BBr_3-Assisted Preparation of Aromatic Alkyl Bromides from Lignin and Lignin Model Compounds

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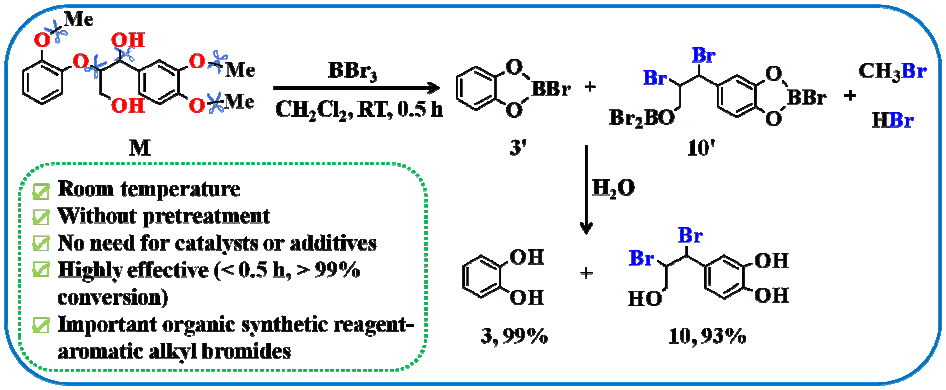
KEYWORDS: aromatic alkyl bromide, biomass, C-O bond, lignin model compound, nucleophilic substitution



ABSTRACT: For the first time, BBr_3-assisted nucleophilic substitution was applied to a variety of β-O-4 and α-O-4 model compounds for the highly effective cleavage of different C-O bonds, including C-$O_{α\text{-}OH}$, $C_β$-O/$C_α$-O and C_{Me}-O bonds (< 0.5 h and > 99% conversion for most cases). Without any pretreatment, the substitution proceeds at room temperature in the absence of any catalyst, or additive, selectively affording phenols and important organic synthesis reagents, aromatic alkyl bromides, in high to excellent yields (up to 98%). Preliminary studies also highlight the prospect of this method for the effective cleavage of different types of C-O bonds in real lignin, a total 14 wt% yield of aromatic alkyl bromide, 4-(1,2-dibromo-3-hydroxypropyl)benzene-1, 2-diol (**10**), has been obtained from a lignin extracted through this method.

INTRODUCTION

With the increasing demand for products derived from petroleum-dependent chemicals, finding alternative renewable energy and valuable chemical resources has become a target that needs to be tackled. As the most abundant source of renewable aromatics,[1] degradation of the highly-functionalised lignin exhibits great potential for the direct preparation of aromatic specialty and fine chemicals, circumventing the requirement for full defunctionalisation to BTX (benzene, toluene and xylenes) and subsequent refunctionalisation to desired platform chemicals.[2] However, so far lignin is highly underutilized and only less than 2% of lignin is used to deliver commercial products[3] due to its complicated structural characteristic of a variety of distinct and chemically different bonding motifs, each demanding different conditions for cleavage when selective depolymerization is targeted. This has greatly stimulated both the academic[4] and industrial[5] aspirations to develop effective methods for the degradation and valorization of lignin. Various value-added products, including aromatic alcohols, [3, 6] phenols,[7] aldehydes,[8] acid,[9] aliphatics,[10] etc. have been obtained under oxidizing, [7i, 9a, b, 11] reducing[7e, f, 12] or neutral[13] reaction conditions. Generally, a pretreatment strategy is required to achieve the effective cleavage of the C-O and/or C-C bonds in different lignin model compounds, either through the oxidation of the α-hydroxyl group of lignin models to a ketone structure with reduced dissociation energy[9b, 11] or through a protecting agent[14] to stabilize lignin during extraction. Therefore, more examples and new degradation technologies are still needed for the fundamental understanding towards the valorization of lignin to generate more renewable aromatic chemicals.

Organic reactions are closely linked with our life, the application of organic synthetic strategy always opens the door to solving problems due to its characteristic of easy controllability, forming and breaking chemical bonds under mild conditions.[15] Recently, we successfully applied the classic organic name reaction, Baeyer-Villiger (BV) oxidation, in the effective transformation of inert C-C bonds in lignin model compounds into active ester bonds, followed by alcoholysis reaction to yield esters and phenols in excellent yields.[16] As a fundamental class of reactions occurring at a saturated aliphatic carbon center, nucleophilic substitution has received the greatest

attention of organic chemists due to its great synthetic utility.[17] However, it is seldom reported for the degradation of lignin, despite that it is well-known that ether (C-O) bonds are abundant in lignin structure, as 50-65% of all linkages are β-O-4 bond and around 3-17% are α-O-4 bond,[1b,18] and ether bonds are prone to nucleophilic substitution. Herein we successfully applied the BBr_3-assisted nucleophilic substitution in the degradation of lignin model compounds and achieved highly effective cleavage of various types of C-O bonds for the first time, including C-$O_{\alpha\text{-OH}}$, C_β-O/C_α-O and C_{Me}-O bonds (< 0.5 h and > 99% conversion for most cases). Unlike the other degradation strategies, there is no requirement of pretreatment, catalyst or any additives for this method. More importantly, with strongly Lewis acidic and nucleophilic BBr_3, such a method enables us to obtain functionalized chemical platform, aromatic alkyl bromides, in high to excellent yields (up to 98%) at room temperature. To the best our knowledge, there has been no such report on the preparation of the useful aromatic alkyl bromides from lignin so far.

RESULTS AND DISCUSSION

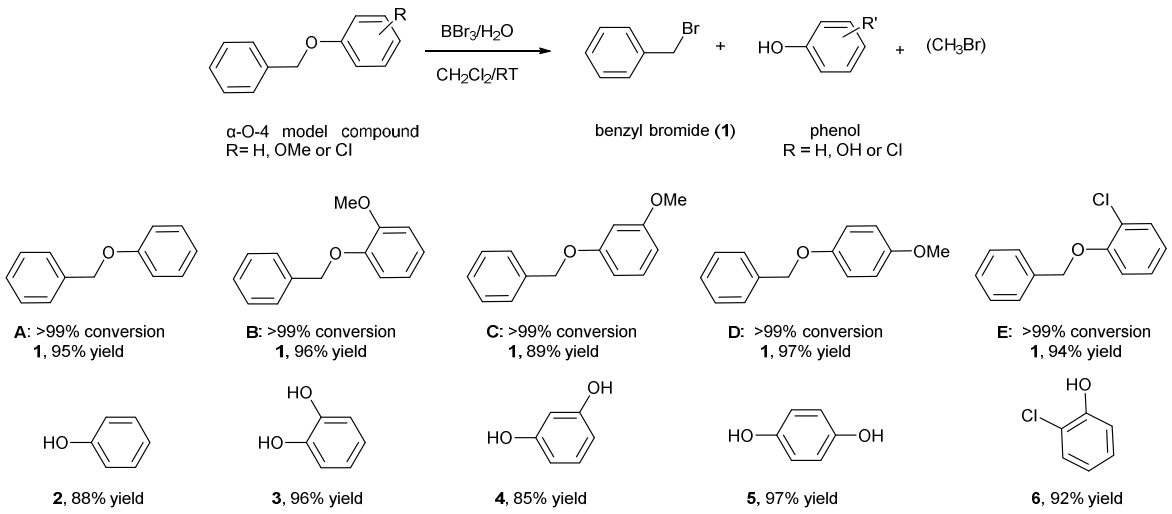


Figure 1. BBr_3-assisted the cleavage C-O bonds in α-O-4 lignin model compounds. The conversions and yields were measured by HPLC.

We initiated the study with the reaction of α-O-4 (benzylphenylether, **A**) or β-O-4 model (2-phenoxyethyl)benzene, **F**) with a series of boron halides, BX_3 (X = F, Cl, Br, I) (table S1). We discovered that

the reactivity is increased with the decrease of the electronegativity: $BF_3{\cdot}OEt_2 < BCl_3 < BBr_3 \approx BI_3$. $BF_3{\cdot}OEt_2$, is completely ineffective for both models; BCl_3 only works for α-O-4 linkage; while BI_3 and BBr_3 are highly effective for both models. However, the cost and difficulty in handling of BI_3 restrict its application. Therefore, the less expensive BBr_3 was chosen for the reaction. The bromine atom participates in the nucleophilic substitution and is retained in the final product, and thus we performed the following experiments to investigate the utilization efficiency of BBr_3 since each BBr_3 provides 3 equiv. of bromine atoms. It turned out that 0.33 equiv. of BBr_3 obtained 71% conversion of **A** and 0.5 equiv. of BBr_3 afforded 90% conversion (table S2), which indicated that at least two of three bromines of BBr_3 are effective for the cleavage of C-O bonds. In the presence of 1 equiv. of BBr_3, 95% yield of benzyl bromide (**1**) and 88% yield of phenol (**2**) was produced within 0.5 h at room temperature. Near quantitative conversions were obtained for all α-O-4 models under optimized conditions (Figure 1). It is noted that the position of methoxy group also has a significant impact on the reactivity and the BBr_3 amount. For **B** with ortho-methoxy group, only 1 equiv. of BBr_3 is needed to cleave both C_α-O and C_{Me}-O bonds to furnish excellent yields of **1** in 96% and o-benzenediol (**3**) in 96%, which also confirmed that at least two of three bromines of BBr_3 are in effect. Therefore, the amount of BBr_3 was optimized with 0.5 equiv. BBr_3 per C-O bond in the lignin model compound for the reaction. It turned out that we could achieve optimal results for most cases with such a feed ratio.

Methyl bromide (CH_3Br, Figure S10) is obtained as the bromination product of the methoxy group. However, the accurate yield of CH_3Br was not obtained due to its volatility. For **C** or **D** with meta- or para-methoxy group, 1 equiv. of BBr_3 produced **1** in high to excellent yield (80% for **C**; 97% for **D**) along with incomplete cleavage products of C_{Me}-O bonds (table S2, entries 5 and 7, **4a**, 36% for **C**; **5a**, 47% for **D**). Therefore, extra BBr_3 (2 equiv.) and extended reaction time (36 h) are needed to obtain high yield of m-benzenediol (**4**, 85% for **C**) or p-benzenediol (**5**, 97% for **D**), respectively. It is noted that BBr_3 is quite effective for model B with ortho-methoxy group that needs only 0.5 h to cleave all C-O bonds (entry 4, table S2), whereas it took much longer reaction time (36 h) and more BBr_3 (2 equiv. BBr_3) to achieve the complete breakdown of all C-O bonds for model C with meta-methoxy group (entry 6, table S2) and model D with para-methoxy group (entry 8, table S2). For **E** with

adjacent electron-withdrawing Cl substituent, only 0.5 equiv. of BBr_3 is needed to achieve excellent yield of **1** (94%) and 2-chlorophenol (**6**, 92%) within 0.5h. Previously, BBr_3 was merely reported as a deprotection reagent for the demethylation[19] or depropargylation[20] in aryl ethers to afford phenols with a more reactive hydroxyl group under specific reaction condition. It was noted that such BBr_3-assisted demethylation is only effective for the cleavage of C_{Me}-O bond, leaving the other type of C-O bonds intact; while BBr_3-assisted depropargylation only works for the cleavage of $C_{propargyl}$-O bond, the methoxy group is notably stable under the reaction conditions, although BBr_3 is known to be an effective reagent for cleaving aryl ethers.[21]

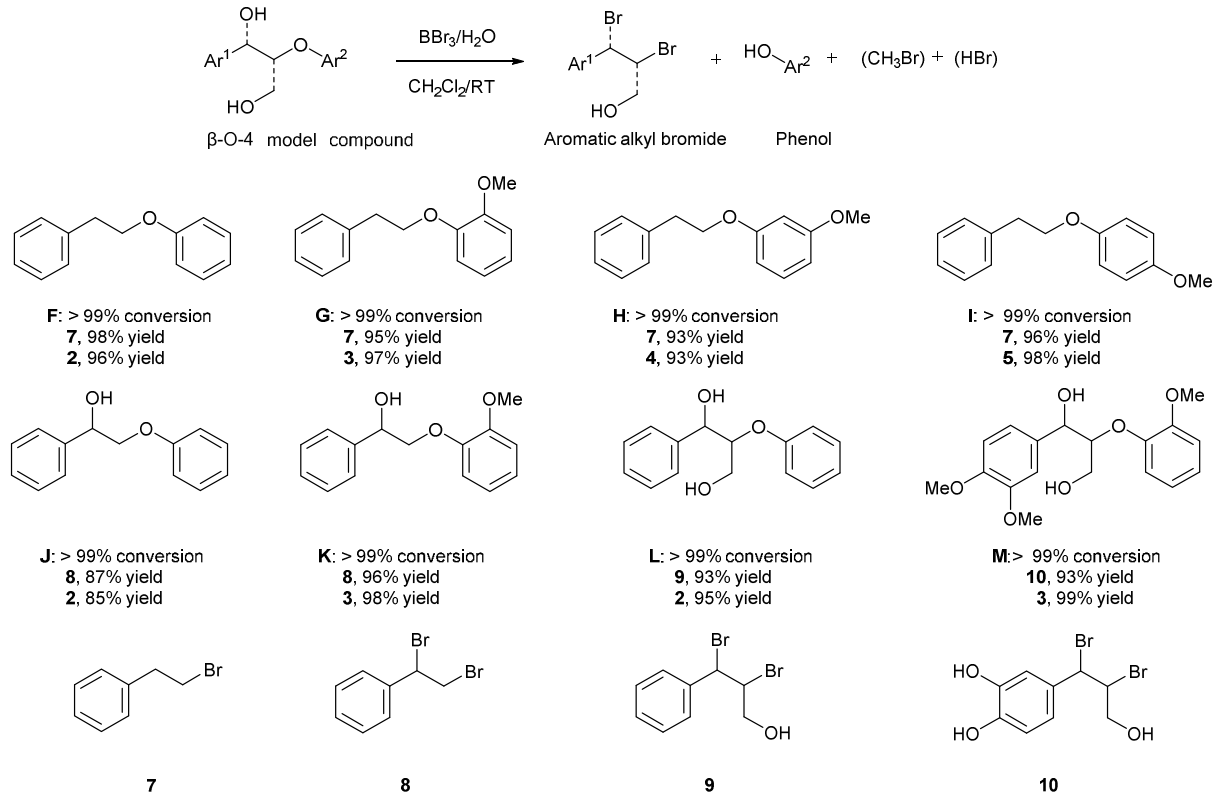
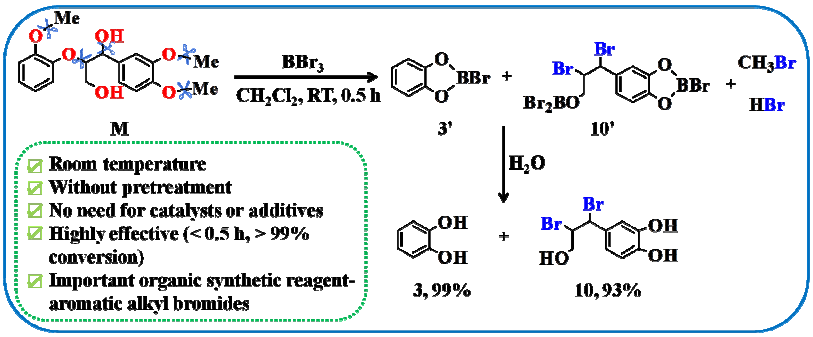


Figure 2. BBr_3-assisted the cleavage C-O bonds in β-O-4 lignin model compounds. The conversions and yields were measured by HPLC.

These results inspired us to apply the BBr_3-assisted nucleophilic substitution to β-O-4 models, the most abundant linkage in lignin. To our gratification, BBr_3 is highly effective for the cleavage of various C-O bonds and achieves near quantitative conversions for all models, including complex G-type model **M** (Figure 2). Excellent yields of 2-bromoethyl benzene (**7**, 98%) and phenol (**2**, 96%) were obtained for **F** within 0.5h at room temperature, while **G**, **H**, and **I** with ortho-, meta- and para-methoxy group all achieved high yields of **7** (**G**, 95%; **H**, 93%; **I**,

96%), phenols (**3** for **G**, 97%; **4** for **H**, 93%; **5** for **I**, 98%) along with CH_3Br. To avoid the formation of byproducts, the experiments were carried out at 5°C for **H** and **I**, as it took more than 36h to reach completion. Besides ether bond, this method is also quite effective for the cleavage of C-$O_{\alpha\text{-OH}}$ bond in **J** and **K** with α-hydroxyl (OH) group, affording high yield of 1, 2-dibromoethyl benzene (**8**) (87% for **J**; 96% for **K**) and phenols (**2** for **J**, 85%; **3** for **K**, 98%). It is noted that the presence of -OH group led to the formation of hydrogen bromide (HBr) (Figure S18). However, the accurate yield of HBr was not obtained due to its volatility. Interestingly, for **L** containing both α- and γ-OH group, it is effective for the cleavage of C_β-O and C-$O_{\alpha\text{-OH}}$ bonds but not for C-$O_{\gamma\text{-OH}}$ bond, furnishing high yield of 2, 3-dibromo-3-phenylpropan-1-ol (**9**) and **2** in 93% and 95%, respectively. Of greater significance is the effectiveness of this facile method with G-type β-O-4 model (**M**); excellent yield of 4-(1,2-dibromo-3-hydroxypropyl)benzene-1, 2-diol (**10**) and o-benzenediol **3** is achieved in 93% and 99% yield, respectively (Scheme 1), with the requirement of 4 equiv. BBr_3.

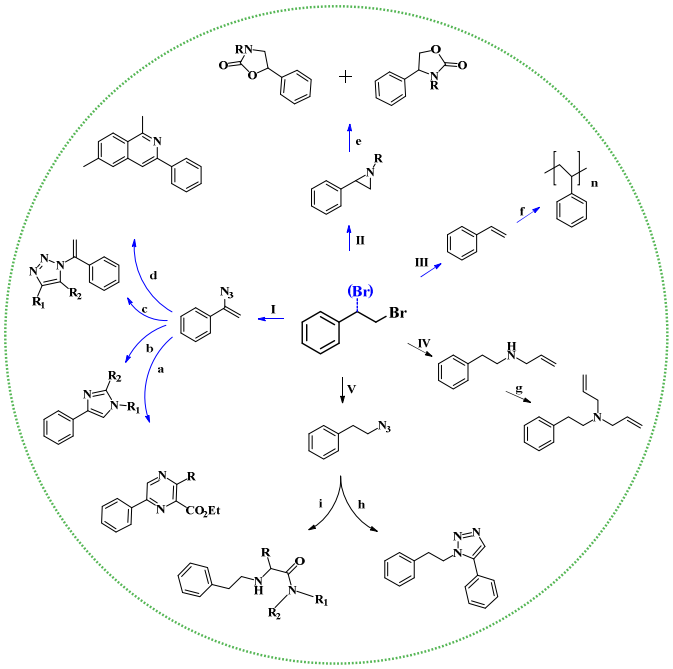
Scheme 1. BBr_3-assisted the cleavage of C-O bonds in G-type β-O-4 model M.



Real lignin structure is quite complex and contains various C-O bonds, including C-$O_{\alpha\text{-OH}}$, C-$O_{\gamma\text{-OH}}$, C_β-O/C_α-O and C_{Me}-O bonds. The investigation of their reactivities would be beneficial to the design and development of efficient lignin degradation system in the future. Taking β-O-4 model as example, we discovered that their reactivities followed the order in this study: C-$O_{\alpha\text{-OH}}$ > C_β-O > C_{Me}-O >> C-$O_{\gamma\text{-OH}}$, which was confirmed by the following experiments. First, model **J** with both $O_{\alpha\text{-OH}}$ and C_β-O bond was chosen for the substrate to react with BBr_3 in different ratios and found that 1 equiv. of BBr_3 was needed to achieve near quantitative conversion to the α-OH brominated product, (1-bromo-2-phenoxyethyl)benzene (**8'**), as the major product along with trace amount

of cleavage product ((1,2-dibromoethyl)benzene, **8**) of C_β-O bond within one min. Increasing the amount of BBr_3 also increased the the yield of **8**. With 2 equiv. of BBr_3 and 0.5 h reaction time, only negligible amount of **8'** was observed (Figure S25). These results indicated that the cleavage of C-$O_{\alpha\text{-OH}}$ bond is easier than that for C_β-O bond. Moreover, increasing the BBr_3 amount will speed up the formation of **8**. The more BBr_3 amounts employed, the faster reaction activities will be obtained, which was also well demonstrated by the degradation of model **F** with different amounts of BBr_3 (Figure S29 and S30), which is the characteristic of bimolecular nucleophilic substitution (SN2) reaction mechanism.[22] Second, experimental data revealed that the cleavage of C_β-O bond is easier than that for C_{Me}-O since only 0.5 h is needed to cleave C_β-O bond but it took 36 h to complete the cleavage of C_{Me}-O bond for both model **H** and **I** (Figure S26 and S27). Third, the BBr_3-assisted method is ineffective for the cleavage of C-$O_{\gamma\text{-OH}}$ bond, which was confirmed by the following experiment: first, BBr_3 reacted with 2,3-dibromo-3-phenylpropan-1ol (**9**) with a γ-OH to yield dibromo(2,3-dibromo-3-phenylpropoxy)borane (**9'**) after the elimination of one molecule of HBr. Compound **9'** was hydrolyzed back to **9** during the aqueous quenching process (Figure S28). It is also noted that the dr value of epimerization observed was slightly changed from 67:33 (before reaction for Model **L**) to 64:36 (after reaction for compound **9'**) during the in-situ NMR reaction (Figure S31), which also indicated the BBr_3-assisted nucleophilic substitution mainly adopts the SN2 mechanism. Detailed mechanistic study of this BBr_3-assisted nucleophilic substitution remains to be elucidated; however, the above-mentioned investigations towards the reactivity of these C-O bonds will provide an important foundation for the future development of lignin depolymerization.

Scheme 2. Chemical transformation of aromatic alkyl bromide 7 or 8 to useful chemical platform: I) NaN_3, DMSO; NaOH, DMSO; [23] **a. toluene, reflux; [Cu], DCE, 90°C to 150 °C;** [24] **b. I_2, TBHP, DMA, 100 °C;** [25] **c. DBU, DMSO;** [26] **d. $Pd(OAc)_2$, toluene, 90 °C;** [27] **II) RNH_2, H_2O; e. CO_2, Cat.;** [28] **III) cat. base, light;** [23] **f. $AliBu_3/[Ph_3C][B(C_6F_5)_4]$;** [29] **IV) K_2CO_3, allyl amine; g. Acryloyl chloride, Et_2N, CH_2Cl_2, 0 °C to rt;** [30] **V) NaN_3, DMF, 80°C; h.** [23] **[Ru] dioxane 60°C;** [26] **i. amide, Tf_2O, DCE.** [23]



Unlike the other degradation strategies, a key advantage of our method is that there is no need for any pretreatment, catalyst or additives. Although stoichiometric amount of BBr_3 was employed for the nucleophilic reagent, we achieved not only highly effective cleavage of various C-O bonds in lignin model compounds, but also obtained a variety of aromatic alkyl bromide products at room temperature from the bromination of aryl ether, which are very important organic synthetic reagents since these reactive Br motifs leave the further derivation potential to form diverse value-added aromatic products. The potential relevance of such aromatic alkyl bromides to the valorization of lignin was confirmed by several chemical transformations starting from mono-bromo product **7** or di-bromo product **8** (scheme 2). Products includes important heterocyclic compounds,[28] polymerizable monomers, such as styrene,[29] ally-N-alkyl/aryl-amines,[30] etc. Especially, such aromatic alkyl bromides could be converted to azide compounds,[23] which are known to be very important synthetic reagents for a wide range of chemical transformations, affording N-heterocyclic products of pyrazines,[24] imidazoles,[25] 1,2,3-triazoles,[26] and isoquinolines.[27] These compounds are known to have found vast applications in organic and bio-organic, medicinal and pharmaceutical, polymer and materials chemistry.

The BBr_3-assisted method is highly effective for the cleavage of various types of C-O bonds in both α-O-4 and β-O-4 models, especially models with ortho-methoxy group, which is commonly observed in the lignin. Therefore,

we anticipated this method would also exhibit good activity in the lignin depolymerization. Formacell Lignin was extracted from a native pine tree through a Formacell process, yielding around 5.4 wt% of soluble pine-lignin (for details see SI). The 2D HSQC NMR spectra clearly indicates that the soluble lignin was rich in Guaiacyl (G) units mainly composed of β-O-4 linkage and the absence of Syringyl (S) residues (Figure S32). Therefore, we compared the in-situ NMR spectrum obtained from the BBr_3-assisted degradation of Formacell lignin with that obtained for G-type β-O-4 model **M** and observed that major peaks found in the aromatic and aliphatic region of the depolymerized lignin products are similar to those for G-type β-O-4 model **M** as shown in the ^1H NMR spectra (Figure 3), indicating that this method is also effective for the Formacell lignin and yields similar degradation products to those obtained for model **M**. 2D HSQC spectrum of the depolymerized Formacell lignin (Figure 33B) further revealed that most of the G units were successfully cleaved to produce the same monomeric aromatic alkyl bromide **10'** as that obtained for Model **M** (Figure 33B). GPC traces also provide further evidence for the successful application of BBr_3-assisted substitution in the degradation of Formacell lignin at room temperature. As can be seen from Figure S35, the GPC trace for products obtained after depolymerization shifted to a smaller molecular weight region with a narrower molecular weight distribution ($Đ = 2.12$), while the molecular weight (M_w) value decreased from 1724 $g \cdot mol^{-1}$ for Formacell lignin to 713 $g \cdot mol^{-1}$ for products obtained after depolymerization. Using Formacell lignin, HPLC analyses indicated that aromatic alkyl bromide **10** is formed in 14 wt% yield after 5 h at room temperature in the presence of 144 wt% BBr_3 followed by hydrolysis process (Scheme S6). In short, preliminary investigation indicates that this BBr_3-assisted nucleophilic substitution is also quite effective for real lignin. Extending investigations on different lignins are under progress.

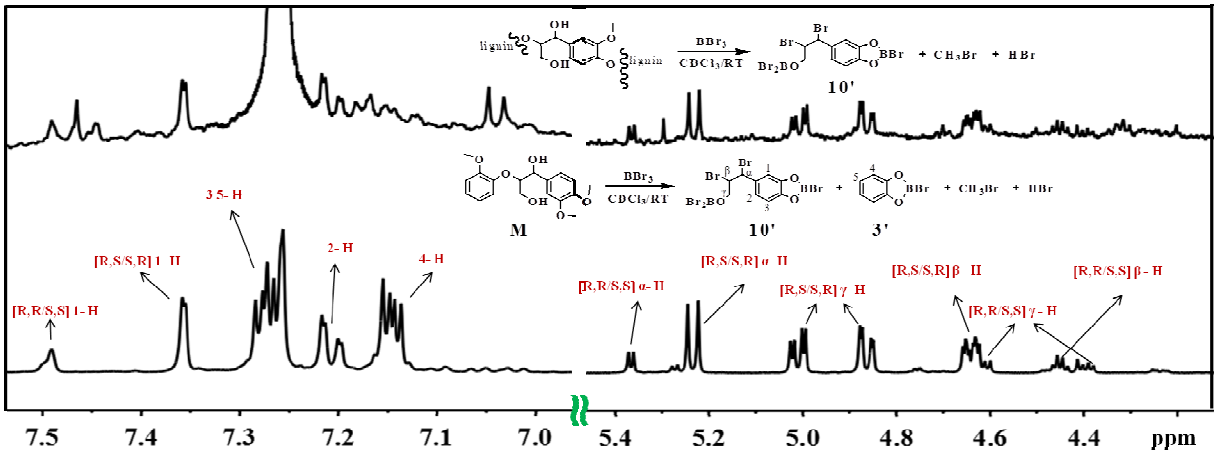


Figure 3. Overlay of ^{1}H NMR spectrum of BBr_3-assisted depolymerization of Formacell lignin (derived from pine wood) (above) and G-type β-O-4 model M (below).

CONCLUSIONS

In summary, we have successfully applied the BBr_3-assisted nucleophilic substitution to the highly effective cleavage of various C-O bonds in β-O-4 and α-O-4 lignin model compounds at room temperature for the first time, affording important organic synthetic reagent, aromatic alkyl bromides along with phenol derivatives in excellent yields (up to 98% yield). This method is featured with commercial available reagent, simple but highly effective at room temperature, and no need for pretreatment, catalysts or additives. More importantly, this strategy also exhibits good activity and chemoselectivity to the real lignin and produced similar monomeric aromatic alkyl bromides and phenols as that obtained for G-type lignin model compounds, producing di-bromo product **10** as the major product in a 14 wt% yield from G-type lignin extracted from native pine tree. Experimental data revealed the BBr_3-assisted method mainly adopted SN2 reaction mechanism and the reactivity for the cleavage of C-O bonds followed the order: $C\text{-}O_{\alpha\text{-}OH} > C_{\beta}\text{-}O > C_{Me}\text{-}O >> C\text{-}O_{\gamma\text{-}OH}$. The successful cleavage of different C-O bonds in both lignin model compounds and real lignin extracted from native pine tree achieved by BBr_3-assisted substitution reaction provides the significant important foundation to the depolymerization and valorization of lignin. Relevant work is currently under way.

EXPERIMENTAL SECTION

General Methods. All syntheses and manipulations of air- and moisture-sensitive materials were carried out in

flamed Schlenk-type glassware on a dual-manifold Schlenk line, a high-vacuum line, or a nitrogen-filled glovebox. Air sensitive NMR samples were conducted in Teflon-valve sealed J. Young-type NMR tubes. NMR spectra were recorded on a Varian Inova 300 (300 MHz, ^{1}H; 75 MHz, ^{13}C) or Bruker Avance II 500 (500 MHz, ^{1}H; 126 MHz, ^{13}C) instrument at room temperature. Chemical shifts for ^{1}H and ^{13}C spectra were referenced to internal solvent resonances and are reported as parts per million relative to $SiMe_4$. Fourier transformation infrared (FTIR) spectra were recorded on a Brucker VERTEX. Mass spectra were recorded on the Bruker MicroTOF Q II.

Boron trifluoride (1.0 M solution in ether), Boron trichloride (1.0 M solution in hexanes), Boron tribromide, Boron triiodide were purchased from Adamas-beta. Phenethyl alcohol, 2-Bromoacetophenone, guaiacol, diisopropylamine, n-BuLi (1.6 M solution in hexanes), 3, 4-dimethoxybenzaldehyde, 2-bromo-4'-methoxyacetophenone, and the standard substances benzyl bromide (**1**), phenols (**2** to **5**), 3-methoxyphenol (**4a**), 4-methoxyphenol (**5a**), (1,2-dibromoethyl) benzene (**8**) were purchased from J&K. Solvents were purchased from Titan. All chemicals were used as received unless otherwise specified as follows. THF was refluxed over sodium/potassium alloy distilled under nitrogen atmosphere and dichloromethane (CH_2Cl_2) was dried over CaH_2 and distilled before use, then stored over activated 4 Å molecular sieves. $CDCl_3$ was dried over molecular sieves 4 Å. Standard substances (2-Bromoethyl)benzene (**7**), 2,3-Dibromo-3-phenyl-propan-1-ol (**9**), 4-(1,2-Dibromo-3-hydroxy-propyl)-benzene-1,2-diol (**10**) were synthesized in our laboratory as described in the cleavage of C-O bond in β-O-4 lignin model compounds. The spectrum of compounds **7**[31] and **9**[32] were in agreement with those described in the literature. α-O-4 and β-O-4 lignin model compounds **A** to **I**,[33] **J** and **K**,[13b] **L** and **M** [34] were prepared according to a literature procedure.

The reaction mixture was analyzed by using Waters High Performance Liquid Chromatograph (HPLC) system equipped with autosampler, C18 column (Length: 150mm, Internal diameter: 4.6mm, 35 °C) and UV/Vis detector (λ = 256 nm). A) CH_3OH:H_2O (3:1) as a mobile phase with a flow rate of 1mL/min, B) CH_3OH:H_2O (1:4) as a mobile phase with a flow rate of 0.8 mL/min, C) CH_3CN:H_2O (1:1) as a mobile phase with a flow rate of 0.6 mL/min were used for HPLC analysis.

BX_3 (X=F, Cl, Br, I) assisted the cleavage of C-O bonds in lignin model compounds. The procedure is detailed for the conversion of lignin model compounds to aryl alkyl halides, using BX_3 (X=F, Cl, Br, I) as the nucleophile. When BBr_3 and BI_3 were used to cleave the lignin model compounds, near quantitative conversion of lignin model compound could be obtained (Table S1).

General procedure: A 10 mL round bottom flask equipped with a magnetic stir bar was charged with lignin model compounds (0.1 mmol, 1 equiv.) and anhydrous dichloromethane (2 mL), the mixture was stirred until complete dissolution of the starting materials, then BX_3 (n equiv., n is determined by the different models) was added to the mixture under nitrogen atmosphere at room temperature (RT). The reaction mixture was stirred at RT for 0.5 h. The following experiments were carried out under the same conditions, unless otherwise specified. After that the reaction mixture was monitored by High Performance Liquid Chromatograph (HPLC) system. The solvent was then evaporated under reduced pressure and the crude residue was purified by flash chromatography (using pentane/ethyl acetate mixture as the eluent). (The in-situ NMR studies were run with a 0.1 mmol scale of substrate and 0.6 mL $CDCl_3$ in a teflon-valve sealed J. Young type NMR tube).

Typical procedure for the cleavage of C-O bonds in lignin model compounds. The procedure is detailed for the conversion of lignin model compounds to aryl alkyl halides, using BBr_3 as the nucleophile. All lignin models, **A** to **M**, could be completely converted to phenols and important organic synthetic reagents, aromatic alkyl bromides, in high to excellent yields (85% to 99%).

General procedure: A 10 mL round bottom flask equipped with a magnetic stir bar was charged with lignin model compounds (0.1 mmol, 1 equiv.) and anhydrous dichloromethane (2 mL), the mixture was stirred until complete dissolution of the starting materials, then BBr_3 (n equiv, n is determined by the different models) was added to the mixture under nitrogen atmosphere at room temperature (RT). The reaction mixture was stirred at RT for 0.5 h (The reactions of model **H-I** were stirred for 36 h at 5 °C) and then analyzed by High Performance Liquid Chromatograph (HPLC). The solvent was then evaporated under reduced pressure and the crude residue was purified by flash chromatography (using pentane/ethyl acetate mixture as the eluent). In-situ NMR studies

were carried out with 0.1 mmol scale of substrate and 0.6 mL $CDCl_3$ in a teflon-valve sealed J. Young type NMR tube and showed the near quantitative conversion of lignin model compounds with BBr_3, which is consistent with the HPLC results (Figure S9-18 and S20).

Spectral Data for products. Benzyl bromide (**1**):^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.42 (d, J =7.1Hz, 2H, *Ph*), 7.37 (t, J =7.5Hz, 2H, *Ph*), 7.32 (t, J =7.5Hz, 1H, *Ph*), 4.52 (s, 2H, PhCH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 137.9, 129.1 (2C), 128.9 (2C), 128.5, 33.7.

Phenol (**2**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.28 (t, J =7.5Hz, 2H, *Ph*), 6.97 (t, J =7.5Hz, 2H, *Ph*), 6.87 (d, J =5Hz, 2H, *Ph*) 4.72 (s, 1H, O*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 155.2, 129.8 (2C), 121.1, 115.5 (2C).

Dibromo(phenoxy)borane (**2'**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.38 (t, J = 5Hz, 2H, *Ph*), 7.22-7.27 (t, J =7.5Hz, 1H, *Ph*), 7.18 - 7.01 (d, J =10Hz, 2H, *Ph*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 154.1, 123.0 (2C), 125.8, 120.1 (2C).

Pyrocatechol (**3**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.90 - 6.86 (m, 2H, Ph), 6.84 - 6.80 (m, 2H, *Ph*), 5.33 (s, 1H, O*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 143.7 (2C), 121.4 (2C), 115.7 (2C).

2-bromobenzo[d][1, 3, 2]dioxaborole (**3'**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.40 - 7.22 (m, 2H, *Ph*), 7.22 - 7.05 (m, 2H, *Ph*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 148.7 (2C), 123.7 (2C), 112.9 (2C).

Resorcinol (**4**): ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 9.15 (s, 2H, O*H*), 6.93 (t, J = 7.9 Hz, 1H, *Ph*), 6.27 - 6.18 (m, 3H, *Ph*). ^{13}C NMR (126 MHz, DMSO-d_6) δ (ppm) = 158.9 (2C), 130.2, 106.7 (2C), 103.0.

3-methoxyphenol (**4a**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.14 (t, J = 8.0 Hz, 1H, *Ph*), 6.53 - 6.48 (m, 1H, *Ph*), 6.47 - 6.41 (m, 2H, *Ph*), 5.33 (s, 1H, O*H*), 3.78 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 161.0, 156.8, 130.3, 108.0, 106.6, 101.7, 55.4.

1, 3-bis((dibromoboryl)oxy)benzene (**4'**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.40 (t, J = 8.3 Hz, 1H, *Ph*), 6.95 (dd, J = 8.3, 2.3 Hz, 2H, *Ph*), 6.80 (t, J = 2.2 Hz, 1H, *Ph*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 154.4, 130.7, 117.4, 112.9.

Hydroquinone (**5**): ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) = 8.62 (s, 2H, O*H*), 6.56 (s, 4H, *Ph*). ^{13}C NMR (126 MHz, DMSO-d_6) δ (ppm) = 150.19 (2C), 116.12 (4C).

4-methoxyphenol (**5a**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.86 - 6.70 (m, 4H, *Ph*), 4.86 (s, 1H, O*H*), 3.77 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 153.8, 149.6, 116.2 (2C), 115.0 (2C), 56.0.

1, 4-bis((dibromoboryl)oxy)benzene (**5'**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.06 (s, 4H, *Ph*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 151.3 (2C), 121.4 (4C).

2-Chlorophenol (**6**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.33 (dd, J = 8.0, 1.5 Hz, 1H, *Ph*), 7.19 (td, J = 8.2, 1.6 Hz, 1H, *Ph*), 7.05 (dd, J = 8.2, 1.6 Hz, 1H, *Ph*), 6.88 (td, J = 7.7, 1.5 Hz, 1H, *Ph*), 5.65 (s, 1H, O*H*). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 151.4, 129.1, 128.5, 121.5, 120.0, 116.4.

(2-bromoethyl)benzene (**7**): 128 mg, 68% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.37 (t, J = 7. 5 Hz, 2H, *Ph*), 7.31 (t, J = 7. 5 Hz, 1H, *Ph*), 7.26 (d, J = 5.0 Hz, 2H, *Ph*), 3.61 (t, J = 7.7 Hz, 2H, CH_2Br), 3.21 (t, J = 7.7 Hz, 2H, PhCH_2). ^{13}C NMR (126MHz, $CDCl_3$) δ (ppm) = 139.0, 128.7 (2C), 128.7 (2C), 127.0, 39.5, 33.0.

(1,2-dibromoethyl)benzene (**8**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.56 - 7.31 (m, 5H, *Ph*), 5.16 (dd, J = 10.5, 5.0 Hz, 1H, PhC*H*), 4.09 (dd, J = 10.5, 5.5 Hz, 1H, CH_2Br), 4.04 (dd, J = 10.4, 10.4 Hz, 1H, CH_2Br). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 138.7, 129.3, 129.0 (2C), 127.8 (2C), 51.0, 35.2.

(1-bromo-2-phenoxyethyl)benzene (**8'**): ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.47 (d, J =10 Hz, 2H, *Ph*), 7.38 (t, J =7.5 Hz, 2H, *Ph*), 7.33 (t, J =7.5 Hz, 1H, *Ph*), 7.29 (t, J =7.5 Hz, 2H, *Ph*), 6.98 (d, J =10 Hz, 1H, *Ph*), 6.91 (d, J =10 Hz, 2H, *Ph*),5.24 (t, J = 7.0 Hz, 1H, PhC*H*Br), 4.52 (dd, J = 10.5, 7.0 Hz, 1H, CH_2O), 4.45 (dd, J = 10.0, 7.0 Hz, 1H, CH_2O). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) = 158.1, 138.7, 129.7 (2C), 129.0, 128.9 (2C), 128.0 (2C), 121.7, 115.1 (2C), 72.2, 50.7. GC/MS (EI, m/z [rel. intensity]) 278 [24], 196 [20], 186 [38], 184 [54], 104 [100], 94[16], 78 [38].

dibromo(2,3-dibromo-3-phenylpropoxy)borane **(9')**: ^{1}H NMR (500 MHz, $CDCl_3$) *erythro* isomer δ (ppm) = 7.55 - 7.30 (m, 5H, *Ph*), 5.22 (d, J = 10.5 Hz, 1H, PhC*H*), 5.01 (dd, J = 12.0, 4.4 Hz, 1H, CH_2), 4.88 (dd, J = 12.0, 3.0 Hz, 1H, CH_2), 4.71 - 4.67 (m, 1H, C*H*BrCH$_2$). ^{13}C NMR (126 MHz, $CDCl_3$) *erythro* isomer δ (ppm) = 139.2, 129.4,

129.0, 128.0, 74.7, 54.9, 52.1. ^{1}H NMR (500 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 7.55 - 7.30 (m, 5H, *Ph*), 5.33 (d, J = 5.7 Hz, 1H, PhC*H*), 4.62 (dd, J = 11.4, 5.5 Hz, 1H, CH_2), 4.53-4.49 (m, 1H, C*H*BrCH_2), 4.36 (dd, J = 11.5, 5.5 Hz, 1H, CH_2). ^{13}C NMR (126 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 137.4, 129.3, 128.9, 128.4, 73.3, 55.6, 53.2**.**

2-bromo-5-(1,2-dibromo-3-((dibromoboryl)oxy)propylbenzol[*d*][1,3,2]dioxaborole **(10')**: ^{1}H NMR (500 MHz, $CDCl_3$) *erythro* isomer δ (ppm) = 7.36 (d, J = 1.9 Hz, 1H, *Ph*), 7.28 - 7.26 (m, 1H, *Ph*), 7.21 (dd, J = 8.3, 1.9 Hz, 1H, *Ph*), 5.24 (d, J = 10.8 Hz, 1H, PhC*H*), 5.01 (dd, J = 12.0, 4.1 Hz, 1H, CH_2), 4.87 (dd, J = 12.0, 2.7 Hz, 1H, CH_2), 4.67 - 4.59 (m, 1H, C*H*BrCH_2). ^{13}C NMR (126 MHz, $CDCl_3$) *erythro* isomer δ (ppm) = 148.9, 148.5, 135.3, 123.8, 112.7, 112.2, 74.3, 53.2, 51.4. ^{1}H NMR (500 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 7.49 (t, J = 1.3 Hz, 1H, *Ph*), 7.28 - 7.26 (m, 1H, *Ph*), 7.21 (dd, J = 8.3, 1.9 Hz, 1H, *ph*), 5.37 (d, J = 5.2 Hz, 1H, PhC*H*), 4.67 - 4.59 (m, 1H, CH_2), 4.45 (q, J = 5.5 Hz, 1H, C*H*BrCH_2), 4.40 (dd, J = 11.1, 5.4 Hz, 1H, CH_2). ^{13}C NMR (126 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 148.63, 148.52, 133.4, 123.8, 113.2, 112.5, 73.1, 55.3, 53.8.

Typical procedure for the cleavage of L. The procedure is detailed for the conversion of lignin model compound **L** to phenol **2** and aromatic alkyl bromide, 2, 3-dibromo-3-phenylpropan-1-ol (**9**) in excellent yields, using BBr_3 as the nucleophile. The in-situ NMR studies showed the near quantitative conversion of lignin model compound **L** with BBr_3, which is consistent with the HPLC results (Figure S22).

General procedure: A 50 mL round bottom flask equipped with a magnetic stir bar was charged with β-O-4 lignin model compound **L** (200 mg, 1 equiv.) and anhydrous dichloromethane (6 mL), the mixture was stirred until complete dissolution of the starting materials, then BBr_3 (3 equiv.) was added to the mixture under nitrogen atmosphere. The reaction mixture was stirred at RT for 0.5 h. After that, the reaction was quenched by water, then the reaction mixture was extracted with dichloromethane (3 × 6 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. Then the mixtures were separated and purified by the fast chromatographic column (dichloromethane as the eluent) to obtain product **9** as a crystalline white solid (217 mg, 90% isolated yield) and **2** (isolated yield is not obtained due to its volatility). 2,3-dibromo-3-phenylpropan-1-ol (**9**):

^{1}H NMR (500 MHz, $CDCl_3$) *erythro* isomer δ (ppm) =7.48 - 7.31 (m, 5H, *Ph*), 5.27 (d, J = 11.5 Hz, 1H, PhC*H*), 4.72 - 4.68 (m, 1H, C*H*BrCH_2), 4.33 (dd, J = 12.5, 4.5 Hz, 1H, CH_2), 4.25 (dd, J = 12.5, 2.6 Hz, 1H, CH_2), 2.11 (s, 1H, O*H*). ^{13}C NMR (126 MHz, $CDCl_3$) *erythro* isomer δ (ppm) = 140.0, 129.1, 128.9 (2C), 128.0 (2C), 66.0, 59.4, 52.4. ^{1}H NMR (500 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 7.48 - 7.31 (m, 5H, *Ph*), 5.35 (d, J = 6.5 Hz, 1H, PhC*H*), 4.53 - 4.49 (m, 1H, C*H*BrCH_2), 3.93 (dd, J = 12.5, 4.5 Hz, 1H, CH_2), 3.67 (dd, J = 12.5, 6.5 Hz, 1H, CH_2), 2.11 (br s, 1H, O*H*). ^{13}C NMR (126 MHz, $CDCl_3$) *threo* isomer δ (ppm) = 138.1, 129.1, 128.8 (2C), 128.4 (2C), 64.9, 61.9, 59.4, 55.5. GC/MS (EI, m/z [rel. intensity]) 213 [22], 197 [24], 185 [68], 105 [82], 104 [100], 77 [42]. Spectral data are consistent with that reported in the literature.[32] HRMS (ESI) calculated for $C_9H_9{}^{79}Br^{81}BrO^-$ [M - H]$^-$ 290.9020, found 290.8794.

Typical procedure for the cleavage of M. The procedure is detailed for the conversion of lignin model compound **M** to 4-(1,2-dibromo)3-hydroxypropyl)benzene-1,2-ol (**10**), using BBr_3 as the nucleophile. Yet, all of the substrate, **M**, could completely convert into phenol **3** and aromatic alkyl bromide **10** in excellent yields. The in-situ NMR studies showed the near quantitative conversion of lignin model compound **M** with BBr_3, which is consistent with the HPLC results (Figure S24).

General procedure: A 50 mL round bottom flask equipped with a magnetic stir bar was charged with β-O-4 lignin model compound **M** (200 mg, 1 equiv.) and anhydrous dichloromethane (6 mL), the mixture was stirred until complete dissolution of the starting materials, then BBr_3 (4 equiv.) was added to the mixture under nitrogen atmosphere, at RT. The reaction mixture was stirred at RT for 0.5 h and such reaction was monitored by HPLC. The solvent was then evaporated under reduced pressure and the crude residue was purified by flash chromatography (using pentane/ ethyl acetate (3:1) mixture as the eluent). After solvent removal under reduced pressure, **10** was obtained as a pale yellow solid (162 mg, 83%). To obtain pure lignin monomer standards, the resultant product was separated and purified by another silica gel column chromatography. The collected liquid was dried under reduced pressure in a rotary evaporator under nitrogen atmosphere at RT, and the yielded products were used for HPLC, IR, high resolution mass spectrometer (ESI-HRMS) and NMR analyses.

4-(1,2-dibromo)3-hydroxypropyl)benzene-1,2-ol (**10**): ^{1}H NMR (500 MHz, CD_3CN) δ (ppm) = 6.86 (d, J = 2.0 Hz, 1H, *Ph*), 6.79 (d, J = 8.1 Hz, 1H, *Ph*), 6.75 (dd, J = 8.1, 2.0 Hz, 1H, *Ph*), 6.69 (s, 1H, Ph-O*H*), 6.67 (s, 1H, Ph-O*H*), 4.79 (dd, J = 5.8 Hz, 4.3 HZ, 1H, PhC*H*Br), 4.26-4.23 (m, 1H, C*H*BrCH$_2$), 3.87 - 3.77 (m, 2H, CH_2), 3.22 (t, J = 5.2 Hz, 1H, CH_2O*H*). ^{13}C NMR (126 MHz, CD_3CN) δ (ppm) = 145.1 (2C), 134.8, 120.0, 118.3, 115.0, 75.6, 64.5, 61.8.; IR (film) ν_{max} 3383 (br), 2962, 1703, 1609, 1520, 1445, 1375, 1261, 1043, 972, 868, 803 cm^{-1}; HRMS (ESI) calculated for $C_9H_9{}^{79}Br^{81}BrO_3^-$ [M - H]$^-$ 322.8924, found 322.8782.

Extraction and characterization of Formacell lignin. Formacell Lignin was extracted using the Formacell process as described by Delmas etal.[35] In a 500 mL round-bottom flask equipped with a magnetic stir bar and a reflux condenser, 20 g of sawdust was used with a liquor to solid (L/S) ratio of 10.0/0.83. The cooking liquor is a mixture solution of formic acid/acetic acid/water in a 30/50/20 % volume ratio. The suspension was heated at 107 °C for 10 h (boiling point of water/formic acid azeotrope). After cooling to room temperature, the suspension was filtered under reduced pressure through G4 funnel and the solids were washed twice with 50 mL of the formic acid/acetic acid/water mixture solution. The solvents were then evaporated under reduced pressure from the dark colored solution containing lignin and the hemicellulose derivatives. The solid was washed with 25 mL of distilled water until the washings were colorless. After that n-hexane was used to remove the pine oil and some other soluble impurities, then the solid was separated into two parts by dichloromethane, the soluble pine-lignin (1.07 g, 5.4 wt%) and the insoluble pine-lignin (0.29 g, 1.5 wt%). Finally, the soluble lignin was dried overnight under primary vacuum and then used for 2D HSQC NMR and Gel-permeation chromatography (GPC) analyses. (The HSQC correlations were in agreement with those described in the literature for organosolv lignin (Figure S32).[11b])

Depolymerization of Formacell lignin. A 50 mL round bottom flask equipped with a magnetic stir bar was charged with the soluble Formacell lignin extracted from native pine tree (40 mg, approximatively 0.2 mmol) and anhydrous dichloromethane (2 mL). The mixture was stirred until complete dissolution of the starting materials, then BBr_3 (144 wt%) was added under nitrogen atmosphere at RT. The reaction mixture was stirred at RT for 5 h

and then quenched by water, extracted with ethyl acetate (5×3), washed with salt-saturated water and dried over Na_2SO_4, The solvent was removed from the combined organic layers under reduced pressure using a rotary evaporator under nitrogen atmosphere at 20 °C. A total mass yield of 46 mg mixtures was obtained, which is more than Formacell lignin since Br was introduced into the depolymerization product. HPLC was performed to determine the yield of aromatic alkyl bromide (**10**) and GPC was performed to analyze the molecular weight of the product obtained after depolymerization of extracted Formacell lignin.

ASSOCIATED CONTENT

Supporting Information Spectroscopic and analytical data as well as the original copy of ^{1}H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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