Significant Lability of Guaiacylglycerol β-Phenacyl Ether under Alkaline Conditions

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It was observed that the β-O-4 bond cleavage of a dimeric phenolic lignin model compound with an α-carbonyl group at the B-ring, 2-(2-ethoxy-4-formylphenoxy)-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol (**I**), is extremely fast in a mild anaerobic alkaline treatment (0.45 mol/L NaOH, 95 °C, 0.8 MPa of N_2). This phenomenon significantly contrasts with the case of a common dimeric phenolic lignin model compound without any specific functional group, 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (**II**). The most plausible mechanism is the migration of the B-ring from the β- to the α-position following the S_NAr mechanism. Because this migration affords the alkaline labile phenolic α-O-4-type compound (**XI**), the formation of the quinone methide as well as the cleavage of the originally alkaline very stable alkyl-aryl ether bond is promoted. This promotion of the quinone methide formation explains why a relatively large amount of 4-hydroxy-3-methoxybenzaldehyde (**IV**) is produced from **I** in an oxygen–alkali treatment.

KEYWORDS: Alkyl-aryl ether; β-O-4; carbonyl; lignin; migration; quinone methide

INTRODUCTION

The most important utilization of wood has still been producing pulp for papermaking, although the use for bioethanol production and others has recently expanded. Therefore, the investigation of the pulping process is still the most interesting and necessary topic. Chemical pulp for papermaking is generally produced by the Kraft process in which NaOH and Na_2S are utilized as reagents. More than 90% of lignin is removed in this process, and the residual several percent is eliminated in subsequent bleaching processes.

There has been much research dealing with reactions of lignin (delignification) under alkaline conditions, because the pulping process is based on these reactions as described above. The delignification in the process is mainly attained by the cleavage of the β-O-4 bond (see **Figure 1** for the definition of β-O-4), which is the most abundant substructure in wood lignin. **Figure 1** illustrates the general mechanism for the cleavage of the nonphenolic β-O-4 bond under alkaline pulping conditions (generally ca. 2 mol/L NaOH, >150 °C). An alcoholate anion produced at an α-position attacks the neighboring β-carbon,

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resulting in a kind of intramolecular S_N2 reaction (back-side attack) (*1*). The contribution of the γ-position to this reaction is small (*2*). To advance this back-side attack sufficiently as a delignification reaction, conditions required are at least more severe than 1 mol/L NaOH and 130 °C (*3*).
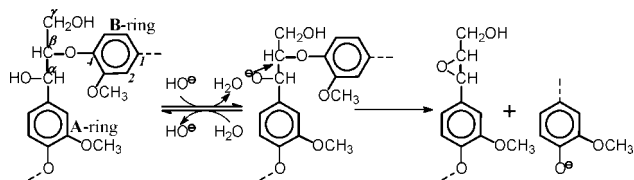
It is well known that functional groups affect the rate of the back-side attack (*4–6*). Among these, the effect of the carbonyl group is the most interesting. Gierer and Ljunggren reported that the alkyl-aryl ether bond of a β-O-4 substructure with an α-carbonyl group at the B-ring (see **Figure 1** for the definition of A- and B-rings) cleaves 40 times faster than that of another common β-O-4 substructure without any specific functional group, following the back-side attack mechanism (*7*).

In this paper, a dimeric phenolic lignin model compound with an α-carbonyl group at the B-ring, 2-(2-ethoxy-4-formylphenoxy)-1-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol (**I** in **Figure 2**), was subjected to mild anaerobic alkaline and oxygen–alkali treatments, and the effect of the carbonyl group is reevaluated by comparing the results with those obtained from the same treatments of a common dimeric phenolic lignin model compound without any specific functional group, 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (**II**). A reaction product obtained from the B-ring of **I** in a mild anaerobic alkaline treatment, 3-ethoxy-4-hydroxybenzaldehyde (**III**), and another reaction product derived from the A-ring of **I** and **II** in oxygen–alkali treatments, 4-hydroxy-3-methoxybenzaldehyde (**IV**), were quantified. Rational mechanisms are proposed for the β-O-4 bond cleavage in a mild anaerobic

Figure 1. General neighboring group participation mechanism for the cleavage of the nonphenolic β-O-4 bond under alkaline pulping conditions.
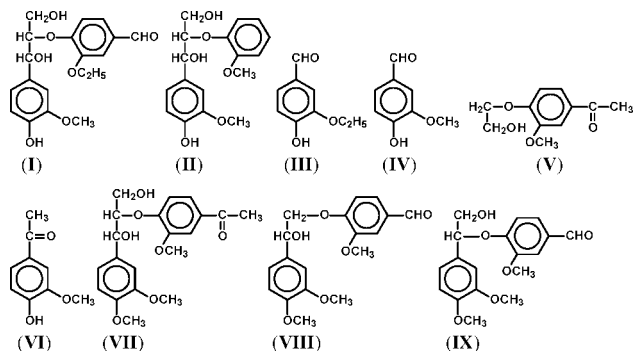
Figure 2. Chemical structure of the compounds used or referred to in this study.

Figure 3. Yield of **III** and **IV** in the mild anaerobic alkaline and the oxygen–alkali treatments of **I** or **II**.

alkaline treatment of **I** and for the oxidation in an oxygen–alkali treatment of **I**.

MATERIALS AND METHODS

Materials. Figure 2 illustrates the chemical structure of the compounds used or referred to in this study. Dimeric lignin model compounds, **I** and **II**, were synthesized according to the methods of Katayama et al. (8) and Li et al. (9). These compounds were purified using a preparative medium-pressure liquid chromatograph (YFLC-540; Yamazen Co., Osaka, Japan) on a silica gel column (Ultrapack SI-40C; Yamazen Co.). The eluent was a mixture of chloroform/ethanol (10/1). The structures were confirmed by ^{1}H NMR. A semiconductor grade of NaOH and FeCl$_3$ (Sigma-Aldrich Japan K. K., Tokyo, Japan) and ultrapure water were used in all of the experiments.

Alkaline Treatment under Anaerobic and Aerobic Conditions. An aqueous solution containing NaOH and FeCl$_3$ (4 mL) was bubbled with nitrogen and added to a stainless steel reactor equipped with a Teflon inscribed tube and lid. To the reactor was added 0.4 mL of an ethanol solution containing **I** or **II**. After the air in the reactor was replaced with nitrogen and the reactor was pressured with 0.8 MPa of nitrogen, the reactor was soaked in a water bath (95 °C) at which the reaction time was defined as 0. Four reactions were run for 0, 15, 50, and 100 min. Oxygen–alkali treatments (0.8 MPa) were also carried out following the same procedure. The concentrations of the additives and **I** (or **II**) were as follows: NaOH, 0.45 mol/L; FeCl$_3$, 0.33 mmol/L; **I**, 2.6 mmol/L (or **II**, 3.1 mmol/L). Because **I** or **II** was primarily dissolved into ethanol, the reaction solution was 9.1% aqueous ethanol.

Quantification of Degradation Products. After the reactor was cooled in an ice–water for 1 min, the lid was opened, and an alkaline solution of an internal standard (4-hydroxy-3,5-dimethoxybenzaldehyde) was added. The lid was closed again, and the resultant solution was shaken well. The solution was transferred into a glass beaker. Then, the solution was acidified with hydrochloric acid and extracted with dichloromethane three times. The dichloromethane layers were collected and dried over anhydrous sodium sulfate. A portion of the dichloromethane solution was transferred into a micro tube and dried by a current of nitrogen. The content was trimethylsilylated with 75 μL of N,O-bis(trimethylsilyl)acetamide at 100 °C for 5 min and injected into a gas chromatograph.

Quantitative analyses for **III** and **IV** were performed on a GC-17A instrument (Shimadzu Co., Kyoto, Japan) equipped with a flame ionization detector using helium as a carrier gas. The temperatures of
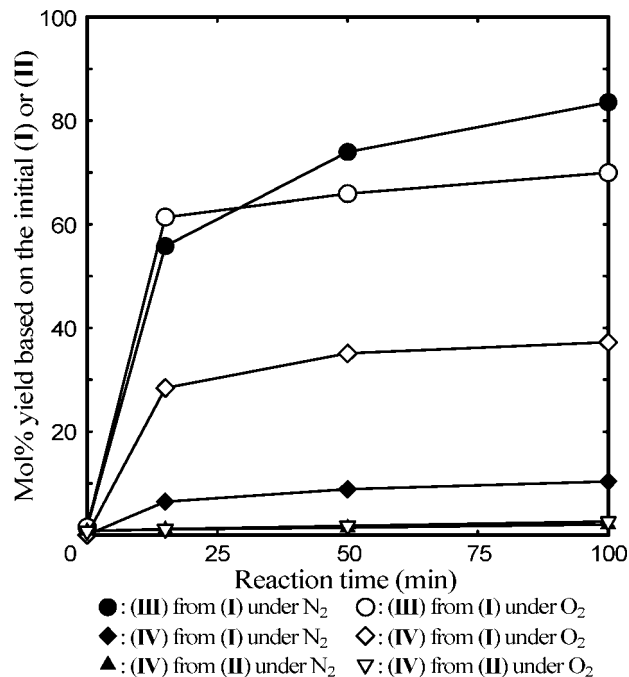
the injector and detector were 280 °C. Separations were achieved on a capillary column of NB-1 (30 m × 0.25 mm × 0.4 μm film thickness; GL Sciences Inc., Tokyo, Japan). The temperature program was from 150 to 280 °C at a rate of 5 °C/min while maintaining the initial and final temperatures for 10 and 20 min, respectively.

RESULTS AND DISCUSSION

Anaerobic Alkaline Treatment. Gierer and Ljunggren reported lots of kinetic data concerning the β-O-4 bond cleavage of several dimeric lignin model compounds (7). We can estimate the extent of the β-O-4 bond cleavage of these dimeric model compounds in a reaction for 100 min under the conditions employed in this study (0.45 mol/L NaOH, 95 °C) assuming the back-side attack mechanism, when an Arrhenis plot is created for each compound using the kinetic data presented in the literature. When 2-(4-acetyl-2-methoxyphenoxy)ethanol (**V**) is assumed to be subjected to the mild anaerobic alkaline treatment for 100 min under the conditions employed in this study, the mole percent yield of 4-acetyl-2-methoxyphenol (**VI**) produced from the β-O-4 bond cleavage of **V** (based on the initial amount of **V**) can be estimated at 0.3%. Gierer and Ljunggren also suggested that a dimeric model compound, 2-(4-acetyl-2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)propane-1,3-diol (**VII**) with an A-ring, affords **VI** about 8 times faster than **V** due to the presence of the A-ring (7). On the basis of this suggestion, the mole percent yield of **VI** produced from the β-O-4 bond cleavage of **VII** (based on the initial amount of **VII**) can be estimated at 4.1%, when **VII** is assumed to be subjected to the mild anaerobic alkaline treatment for 100 min under the conditions employed in this study. The mole percent yield of **III** from **I** (based on the initial **I**) in the mild anaerobic alkaline treatment in this study is shown by the ● in **Figure 3**. As can be seen, the mole percent yield at 100 min was about 83%. This is extremely larger than the estimated value, 4.1%, for **VII**. Furthermore, it is presumed that the β-O-4 bond cleavage of **I** by the back-side attack mechanism is slower than **VII** due to the presence of the already ionized phenolic hydroxyl group in **I**. These yield estimations suggest that the β-O-4 bond
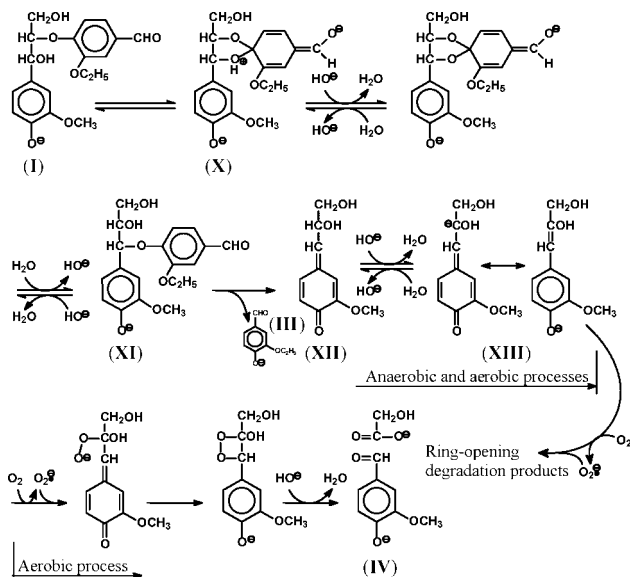
Figure 4. Mechanism proposed for the reaction route from **I** to **III** and **IV** in the mild anaerobic alkaline and the oxygen–alkali treatments.

cleavage of **I** under the conditions employed in this study does not follow the back-side attack mechanism shown in **Figure 1**.

It was reported by Criss et al. that in a quite mild alkaline treatment (0.34 mol/L NaOH, room temperature) of a dimeric nonphenolic lignin model compound with an α-carbonyl group at the B-ring, 2-(4-formyl-2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethanol (**VIII**), the B-ring migrates to the α-position and an equilibrium is established between **VIII** and 2-(4-formyl-2-methoxyphenoxy)-2-(3,4-dimethoxyphenyl)ethanol (**IX**) (*10*). The equilibrium is also established in the case of using **IX** as a starting compound. The mechanism presented and proved in the literature is an aromatic nucleophilic substitution reaction (S_NAr; cf. **Figure 4**), in which the alcoholate oxygen at the α-position attacks the C4 carbon of the B-ring and an intermediate with a five-membered ring (a kind of **X**) forms. This knowledge makes it rational to apply this mechanism to the phenomenon observed in this study, although there are the structural differences between **I** and **VIII**, the phenolic and nonphenolic A-rings, the presence and absence of the γ-position, and the formyl and acetyl functional groups at the B-rings, respectively.

The mechanism proposed for the β-O-4 bond cleavage of **I** under the conditions employed in this study is illustrated in **Figure 4**. Once the α-O-4-type compound, 3-(2-ethoxy-4-formylphenoxy)-3-(4-hydroxy-3-methoxyphenyl)propane-1,2-diol (**XI**), forms by the migration of the B-ring, this compound easily converts into the corresponding quinone methide (**XII**) and the alkyl-aryl ether cleaves. To advance the quinone methide formation frequently, conditions required are only 1 mol/L NaOH and 10 °C for an α-O-4-type structure and, on the other hand, 1 mol/L NaOH and 140 °C for a β-O-4-type structure (*3*). The difficulty of the quinone methide formation from a β-O-4-type structure like **II** is due to the low leaving ability of the hydroxide anion from the α-position and the effect of an aqueous alkaline solvent.

The migration mechanism presented by Criss et al. is for nonphenolic β-O-4 substructures with α-carbonyl groups at the B-rings (*10*). When this mechanism operates on a phenolic β-O-4 substructure with an α-carbonyl group at the B-ring as in the reaction system of this study, the significant phenomenon

that the alkyl-aryl ether in the substructure cleaves is brought about. This phenomenon can develop a practical application described in the following section.

Oxygen–Alkali Treatment. The mole percent yield of **III** from **I** (based on the initial **I**) in the oxygen–alkali treatment is shown by the ○ in **Figure 3**. The yield at 15 min was almost the same as in the mild anaerobic alkaline treatment, and the formation rate gradually decreased, resulting in the approximately 70% yield at 100 min, which was lower than the yield at 100 min in the mild anaerobic alkaline treatment. The reaction product **III**, which carries an α-carbonyl group, is quite stable toward molecular oxygen under conditions of oxygen–alkali (*11*). However, because **III** can react with peroxides produced in the aerobic reaction system, it is anticipated that even if the amount of **III** produced in the oxygen–alkali treatment is the same as in the mild anaerobic alkaline treatment, some of them are probably transformed into other compounds.

As a noticeable result, the mole percent yield of **IV** (based on the initial **I**) in the oxygen–alkali treatment is shown by the ◇ in **Figure 3**. Almost no **IV** was produced in the oxygen–alkali treatment of **II** (▽ in **Figure 3**). In general, ring-opening degradation products are obtained when common phenolic lignin model compounds without a specific functional group, such as **II**, are treated under conditions of oxygen–alkali (*12, 13*). By considering the reaction mechanism, it is presumed that **IV** is produced by the oxidation of the quinone methide-type (**XII**) or the styrene-type structure (**XIII**), which is derived from **XII** by the abstraction of the β-proton. Therefore, the reaction route of **I** in the oxygen–alkali process can be the same as in the anaerobic alkaline process until the formation of **XII**, and **IV** is produced by the oxidation of **XII** or **XIII**. The difficulty of the quinine methide formation from **II** under the conditions employed reflects to the result that almost no **IV** is obtained from **II** in the oxygen–alkali process. Although the negligible amount of **IV** was the only product detected in the oxidation of **II**, much research ensures that a fairly large amount of **II** was oxidized and the A-ring of **II** must have been converted into ring-opening degradation products by the oxidation (*12–17*). Even in the oxygen–alkali treatment of **I**, the formation of **IV** and ring-opening degradation products should compete with each other. The yield of **IV** from **I** (◇ in **Figure 3**) in the oxygen–alkali treatment is about half of **III** (○ in **Figure 3**). This result must indicate that the oxidation of **XIII** results not only in the formation of **IV** but also in ring-opening degradation products.

Possible Practical Application. The results of Criss et al. (*10*) and those obtained in this study suggest the following phenomenon. Nonphenolic β-O-4 substructures with α-carbonyl groups at the B-rings are converted into corresponding nonphenolic α-O-4 substructures by the migration of the B-rings. When the phenolic hydroxyl group of an A-ring of one of these α-O-4 substructures is liberated during pulping reactions, the alkyl-aryl ether cleaves promptly. Therefore, if α-carbonyl groups can be introduced sufficiently into lignin by some oxidation methods, it is expected that portions of the β-O-4 polymer, such as endwise types, peel off a unit at a time from phenolic end residues under relatively mild alkaline conditions. This mechanism seems to give some idea for the development of oxidation-based cookings as sulfur-free methods.

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