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Differences in the Mechanisms of MnO₂ Oxidation between Lignin Model Compounds with the *p*-Hydroxyphenyl, Guaiacyl, and Syringyl Nuclei

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ABSTRACT: The purpose of this study was to examine how the rate and mechanism of MnO₂ oxidation differ between the phydroxyphenyl (H), guaiacyl (G), and syringyl (S) types of simple nonphenolic lignin model compounds as well as the *p*-ethylphenyl (E) type compounds. The oxidation was conducted using an excess amount of MnO_2 in a sulfate buffer solution at a pH value of 1.5 at room temperature. MnO₂ oxidized at least the G and S nuclei, although it commonly oxidizes alcohols present at the benzyl position. The oxidation rates of the benzyl alcohol derivatives were in the order of $G - S - \gg H - E$ -type, which suggests that the rates are determined by the electronic effects of their methoxy and ethyl functional groups on not only their benzyl positions but also their aromatic π -electron systems. The kinetic isotope effect was observed in the MnO₂ oxidations of the same derivatives deuterated at their benzyl hydroxymethyl groups. The observed magnitudes were in the order of $E - \gg H - S - S$ -type, suggesting that the contribution of oxidation of their aromatic nuclei, which is another reaction mode of the oxidation of their benzyl positions, increases in the reverse order.

KEYWORDS: aromatic nucleus, benzyl alcohol, guaiacyl, p-hydroxyphenyl, manganese dioxide, syringyl

INTRODUCTION

Lignin is commonly depolymerized and degraded to isolate a portion with inevitable structural alteration, to promote delignification and allow isolation of the other components (the carbohydrates), or to obtain lignin-based fine chemicals in a biomass conversion process of woody raw materials, including chemical pulping for paper making. Oxidation is one of the most common methods for these purposes, together with acidic and alkaline treatments. In an oxidation process, lignin should be selectively oxidized while minimizing degradation of the carbohydrates as far as possible. Establishment of a process to realize this requirement is desirable; the oxidation processes currently in practical use do not show satisfactory selectivity.

In our previous study, we applied an oxidation process employing manganese dioxide (MnO_2) as an oxidant at a pH value of 2 (in a sulfate buffer solution) and temperature of 70 $^{\circ}C$ to the prebleaching (oxygen delignification) stage of chemical pulping.¹ The latter half of the oxygen delignification stage was substituted with the MnO₂ oxidation process, which promoted delignification while suppressing the degradation of the carbohydrates relative to that observed in the common oxygen delignification stage without the substitution. The MnO₂ oxidation process therefore has potential to satisfy the above-described requirement. MnO2 is a recyclable oxidant because it is reduced to Mn2+ in the oxidation process and Mn^{2+} can be reconverted to MnO_2 by oxygen oxidation under alkaline conditions. This recyclability is another advantage of the MnO_2 oxidation process.

MnO₂ oxidation of lignin has been examined in only a few studies, at least from a pure chemistry viewpoint,^{2,3} although nonrecyclable permanganate (MnO₄⁻) oxidation of lignin has been reported fairly widely.⁴⁻¹⁴ It is generally known that MnO₂ oxidizes allyl and benzyl alcohols selectively among various types of alcohols to afford the corresponding conjugate and aromatic carbonyls, respectively, with the oxidation rates being higher in nonpolar organic solvents than in polar solvents.^{15–22} MnO_2 oxidation of other alcohols progresses only under severe conditions.^{17,23} However, if MnO_2 had oxidized only benzyl alcohols in the residual lignin, and consequently the corresponding α -carbonyl groups had just formed in our previous study,¹ in accordance with this general knowledge, sufficient delignification must not have been attained. Just introducing α -carbonyl groups does not contribute to delignification at the employed pH and temperature.

The aim of this study is to examine the mechanism of MnO₂ oxidation of lignin using model compounds. This paper is the first in a series and focuses mainly on the mechanism of MnO₂ oxidation of simple nonphenolic lignin model compounds consisting of the p-hydroxyphenyl (H), guaiacyl (G), and syringyl (S) nuclei. Scheme 1 shows the H-, G-, and S-type lignin model compounds as well as *p*-ethylphenyl type (E-type) compounds employed in this study. They are analogues of

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Scheme 1. Nonphenolic Lignin Model Compounds (the H-, G-, and S-Types) and *p*-Ethylphenyl Type Compounds (the E-Types) Employed in This Study



Scheme 2. Quantified Reaction Products as well as Another Possible One without Detection (Product B_H) in MnO₂ Oxidation

OMe OMe MeO OMe OMe MeO OMe ÓМе ÓМе ÓМе ö ÓМе ÓМе ÓMe Ét B_G Ан A_{G} As AE B_H Bs Ан A_{G} As' AE Deuterated benzaldehyde analogues Benzaldehyde analogues 1,4-Benzoquinone analogues

benzene (methoxybenzene (H-type, $I_{\rm H}$), 1,2-dimethoxybenzene (G-type, $I_{\rm G}$), 1,2,3-trimethoxybenzene (S-type, $I_{\rm S}$), and ethylbenzene (E-type, $I_{\rm E}$)), benzyl alcohol (4-methoxybenzyl alcohol (H-type, $II_{\rm H}$), 3,4-dimethoxybenzyl alcohol (G-type, $II_{\rm G}$), 3,4,5-trimethoxybenzyl alcohol (S-type, $II_{\rm S}$), and 4-ethylbenzyl alcohol (E-type, $II_{\rm E}$)), and benzyl alcohol deuterated at the methylene of the benzylic hydroxymethyl group (1-hydroxy(²H₂)methyl-4-methoxybenzene (H-type, $III_{\rm H}$), 4-hydroxy(²H₂)methyl-1,2-dimethoxybenzene (G-type, $III_{\rm G}$), 5-hydroxy(²H₂)methyl-1,2,3-trimethoxybenzene (S-type, $III_{\rm S}$), and 1-ethyl-4-hydroxy(²H₂)methylbenzene (E-type, $III_{\rm E}$)).

EXPERIMENTAL SECTION

Materials. All chemicals used in this study except for the organic compounds described below were purchased from FUJIFILM Wako Pure Chemical Co. (Osaka, Japan), Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), or Sigma-Aldrich Japan K. K. (Tokyo, Japan) and used without further purification. Ultrapure H_2O prepared using a generator, Puric-Z (Organo Co., Tokyo, Japan), was used in all the experiments.

Preparation of Model Compounds and Authentic Compounds of Reaction Products. Compounds I (all the H-, G-, S-, and E-types) and II were commercially available and purified by flash chromatography (Isolera, Biotage Japan Ltd., Tokyo, Japan). Compounds III_H, III_G, and III_E were synthesized from commercially available 4-methoxybenzoic acid, 3,4-dimethoxybenzoic acid, and 4ethylbenzoic acid, respectively, by direct reduction with LiAlD₄ in dry THF and purified by flash chromatography. Compound III_S was synthesized from commercially available 3,4,5-trimethoxybenzoic acid by ethyl esterification in EtOH containing H_2SO_4 and successive reduction with NaBD₄ and LiCl in dry THF and then purified by flash chromatography.

Scheme 2 shows the quantified reaction products and another reaction product possibly generated in spite of no detection. The formers are analogues of benzaldehyde (H-type (A_H) , G-type (A_G) , S-type (A_S) , and E-type (A_E)), 1,4-benzoquinone (G-type (B_G) and S-type (B_S)), and benzaldehyde deuterated at the benzylic formyl group (H-type (A_H') , G-type (A_G') , S-type (A_S') , and E-type (A_E')). The latter is 1,4-benzoquinone (H- (or E-) type (B_H)). Products **A** were purchased and purified by flash chromatography for use in authentic compounds for identification, for preparing their calibration lines for quantification, and for reacting them as starting materials in the MnO₂ oxidations described below. Products **B**_G and **B**_S were isolated from reaction solutions of the MnO₂ oxidations of compounds **I**_G and **II**_S.

respectively, and purified by flash chromatography for the same purposes. Product B_H was purchased and purified by flash chromatography for the same purposes. Products A' were obtained from the corresponding compounds III by oxidizing them with MnO_2 in CH_2Cl_2 at room temperature and purified by flash chromatography for the same purposes.

All the reaction products shown in Scheme 2 except for product B_H were identified on the basis of their ¹H- and ¹³C-NMR (JNM-A500, 500 MHz, JEOL Ltd., Tokyo, Japan) and GC/MS (GC2010/PARVUM2, Shimadzu Co., Kyoto, Japan) spectra. These assignments and the MS spectra are shown in the Supporting Information.

Preparation of MnO₂ for the Reaction. To 700 mL of a H₂O solution containing 0.20 mol $MnSO_4$ ·H₂O was added dropwise 100 mL of 4.0 mol L⁻¹ NaOH. The resultant solution was bubbled with O₂ for 60 min with stirring at room temperature. The suspension was neutralized with 150 mL of 1.0 mol L⁻¹ H₂SO₄ with stirring for 30 min. The dropwise addition of 4.0 mol L⁻¹ NaOH and successive O₂ bubbling were then repeated to further advance the oxidation. The obtained precipitates (mostly MnO₂) were collected by filtration under reduced pressure, washed with H₂O until the filtrate became neutral, and air-dried for further use. To examine the oxidation powers, the precipitates were ground into powder in a mortar and iodometrically titrated. The content was 84.9% of the theoretical value.

 MnO_2 Oxidation Reaction. All reactions were conducted in a round-bottom glass flask (200 mL volume) equipped with a magnetic stirrer. A sulfate buffer solution (0.50 mol L⁻¹, pH 1.5) was prepared in advance by mixing Na_2SO_4 and H_2SO_4 solutions (0.50 mol L⁻¹ each).

The precipitates of MnO₂ obtained above were ground into powder in a mortar. The powder (1.2 mmol (oxidation power basis: $1.2 \times 84.9/100 = 1.02$ mmol), oven-dry basis) was aged in sulfate buffer solution (50 mL) for 120 min in a glass flask at room temperature. Another sulfate buffer solution (10 mL) consisting of the same sulfate components and containing one of the compounds shown in Scheme 1 or 2 (12 µmol) as a starting material was added to the sulfate buffer solution containing the MnO₂ powder to initiate the reaction at room temperature. The initial concentrations of the compound and MnO₂ (insoluble solid) were 0.20 and 20 mmol L⁻¹, respectively. Each reaction was conducted three times to confirm the reproducibility.

Quantification. A specific amount of the reaction solution was withdrawn at prescribed reaction times and poured into a glass tube to which a saturated NaHCO₃ solution had already been added for neutralization. The mixture was extracted with CH_2Cl_2 containing an internal standard compound, 1,2,3-trimethoxybenzene or 3,4-dimethoxybenzaldehyde (veratraldehyde), and twice further (without

the internal standard compound) in the glass tube. The organic layers were combined, dried over anhydrous Na_2SO_4 , filtered with a membrane filter, and injected into an HPLC instrument with an ultraviolet–visible (UV–vis) absorption detector (LC-2010C_{HT}, Shimadzu Co.) for quantification based on an absorbance at 280 nm.

In HPLC analyses, an HPLC column, Luna 5 u C18(2) 100 Å (length: 150 mm; inner diameter: 2.0 mm; particle size: 5.0 μ m; Phenomenex, Inc., Torrance, CA, USA), was used at an oven temperature of 40 °C with a solvent flow rate of 0.2 mL min⁻¹. The types of solvent and gradients were as follows: For the reactions of the H-, G-, and S-type compounds, the gradient of MeOH/H₂O (v/v) was from 30/70 to 40/60 for 30 min and then maintained for 10 min. For the reactions of the E-type compounds except for compound I_E, the gradient of MeOH/H₂O (v/v) was from 30/70 to 50/50 to 60/40 for 15 min, and maintained for 10 min. For the reactions of compound I_E, the gradient of MeOH/H₂O (v/v) was from 40/60 to 50/50 for 10 min, from 50/50 to 85/15 for 20 min, and maintained for 10 min.

RESULTS AND DISCUSSION

Preparation of MnO2. Commercially available active MnO₂ (FUJIFILM Wako Pure Chemical Co.) was ground into powder. The oxidation power was iodometrically titrated to be 90.2% of the theoretical value by the method described above. The MnO₂ powder was applied to the oxidation of compound II_G under conditions identical to those described above. When the logarithmic plot for the disappearance of compound II_G was approximated to a pseudo-first-order reaction, the approximation was rather bad. The disappearance was gradually accelerated when compared with that which was supposed to follow a pseudo-first-order reaction from the initial stage. The rate reached a ceiling level at a reaction time of about 120 min. In contrast, the disappearance followed a pseudo-first-order reaction well from the initial stage at a rate similar to the above ceiling level, when the MnO₂ powder had primarily been aged following the procedure described above. The observed acceleration of the oxidation using the MnO₂ powder without the pre-aging thus suggests that the MnO₂ powder was aged and became more active during the oxidation. This clarified that pre-aging is necessary for the commercial MnO₂.

 MnO_2 was synthesized from Mn^{2+} by the method described above, and the obtained precipitates were ground into powder. This synthesized MnO_2 powder was applied to the oxidation of compound II_G with or without pre-aging. The disappearance approximated well to a specific pseudo-first-order reaction from the initial stage, regardless of conducting pre-aging. It was faster than that observed when the above-described commercial MnO_2 powder was used, which was surprising because the synthesized MnO_2 powder had less oxidation power (84.9%) than the commercial powder (90.2%). This clarified that preaging is not necessary for the synthesized MnO_2 powder.

The observed difference between the commercial and the synthesized MnO_2 powders must have arisen from their physical properties. Physical properties of commercially available MnO_2 are often dependent on the vender. Thus, the synthesized MnO_2 powder, whose physical properties are possibly prepared to be constant anytime, was employed in this study. Because any aging and the consequent activity change during the MnO_2 oxidation process interfere with ready analysis, pre-aging was applied to the synthesized MnO_2 powder in spite of its unnecessity.

Choice of the E-Type Compounds. Reactivity at the benzyl position of an aromatic compound with functional groups on the aromatic nucleus in a chemical reaction commonly correlates well with their Hammett's substituent constants (σ values), when they are located at the *para* and/or meta of the benzyl carbon and the reactivity is relatively compared with that of an analogous aromatic compound with other or no functional groups present at both positions. The Etype compounds were employed in this context. The total σ value of two methoxy groups of the G-type compounds is -0.153 (= -0.268 (para) + 0.115 (meta)), which is close to that of the ethyl group of the E-type compounds (-0.151). Each E-type compound can thus be expected to have similar reactivity to the corresponding G-type compound in a reaction occurring at their benzyl positions, provided that the reaction is affected only by the electronic factors that originate in the functional groups and appear locally at the benzyl positions. Thus, the reactivities of the G- as well as the other types are compared with those of the E-types in the following sections.

 MnO_2 Oxidation of Benzene Analogues (Compounds I). Although MnO_2 is an oxidant that selectively oxidizes an analogue of allyl or benzyl alcohol, as described in the Introduction section, it was examined by employing compounds I whether or not MnO_2 can oxidize the aromatic nucleus of an aromatic compound without benzylic hydroxy group and a substructure corresponding to the side-chain portion in lignin and whether the progress of this oxidation is dependent on the type of aromatic nucleus.

Compound I_H disappeared in MnO₂ oxidation and remained with a recovery yield $(\pm$ standard deviation calculated from three duplicated runs) of $81.0 \pm 2.0\%$ at a reaction time of 660 min, although no other peaks of any size appeared on the HPLC chromatogram. These results were considered to indicate that the aromatic nucleus of compound I_H was degraded to afford reaction products that do not exhibit an absorbance at around 280 nm and/or that it just volatilized. When compound I_H was reacted in the absence of MnO₂ under otherwise exactly the same conditions where it must stably have existed, it disappeared and remained with the same recovery yield as for MnO2 oxidation. Compound IH must therefore have volatilized and not have been oxidized by MnO₂. Because exactly the same phenomena were observed in the reactions of compound I_E with and without MnO₂, it must also have volatilized and not been oxidized by MnO₂. Incidentally, because product B_H was afforded when compound I_H was subjected to the MnO₂ oxidation applying 1.0 mol L^{-1} H₂SO₄ under otherwise the same conditions, the oxidation power of MnO₂ is dependent on the system acidity. It can be excluded from an explanation for these observed phenomena that polymers formed but they were not detected by the HPLC analysis, when the employed conditions are taken into consideration.

Compound I_G or I_S disappeared in MnO₂ oxidation and remained with a recovery yield of 60.8 ± 1.1% or 60.0 ± 1.2%, respectively, at a reaction time of 660 min, although neither compound disappeared in the reaction without MnO₂. Product B_G or B_S was afforded as the exclusive major reaction product with a yield of 20.9 ± 1.1% or 13.2 ± 0.1%, respectively, at the same reaction time. Many small peaks in addition to the large peak of product B_G or B_S appeared on the HPLC chromatogram of the reaction solution withdrawn at this reaction time, indicating the formation of many minor reaction products. The proportion of the amount of afforded product B_G or B_S to that of disappearing compound I_G or I_S , respectively, did not vary largely during the reaction. Product

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Table 1. Observed Pseudo-First-Order Reaction Rate Constants (k_{obs}) , Squares of the Correlation Coefficients (R^2) in the Approximations, and Ratios of k_{obs} Values between Compounds II and III $(k_{obs}(II)/k_{obs}(III))$ for Estimation of the Magnitudes of the Kinetic Isotope Effects

| C.I ^a | $k_{\rm obs}{}^{b}$ | R^{2c} | C.II ^d | $k_{obs}^{\ b}$ | R^{2c} | C.III ^e | $k_{ m obs}{}^{m b}$ | R^{2c} | $k_{\rm obs}({ m III})/k_{\rm obs}({ m IIII})$ |
|------------------|---------------------|----------|-------------------|-----------------|----------|--------------------|----------------------|----------|--|
| I _H | | | II_{H} | 14.7 ± 0.1 | 0.995 | III_{H} | 3.13 ± 0.09 | 0.995 | $k_{\rm obs}({\rm II}_{\rm H})/k_{\rm obs}({\rm III}_{\rm H}) = 4.7$ |
| | | | | | 0.997 | | | 0.986 | |
| | | | | | 0.995 | | | 0.987 | |
| I_G | 7.96 ± 0.05 | 0.986 | II_G | 911 ± 23 | 0.999 | III_G | 227 ± 8 | 1.00 | $k_{\rm obs}({\rm II}_{\rm G})/k_{\rm obs}({\rm III}_{\rm G}) = 4.0$ |
| | | 0.972 | | | 0.985 | | | 1.00 | |
| | | 0.998 | | | 0.988 | | | 1.00 | |
| Is | 8.08 ± 0.14 | 0.987 | IIs | 343 ± 18 | 0.962 | III _s | 127 ± 2 | 0.983 | $k_{\rm obs}({\rm III}_{\rm S})/k_{\rm obs}({\rm IIII}_{\rm S}) = 2.7$ |
| | | 0.983 | | | 0.968 | | | 0.985 | |
| | | 0.991 | | | 0.994 | | | 0.983 | |
| IE | | | IIE | 2.09 ± 0.06 | 0.995 | III _E | 0.244 ± 0.008 | 0.961 | $k_{\rm obs}({\rm III_E})/k_{\rm obs}({\rm III_E}) = 8.6$ |
| | | | | | 0.992 | | | 0.958 | |
| | | | | | 0.991 | | | 0.941 | |

^{*a*}Compounds I. ^{*b*}Unit: $\times 10^{-4}$ min⁻¹. The values after the "±" marks are the standard deviations of three duplicated runs. ^{*c*}The value obtained from each of three duplicated runs. ^{*d*}Compounds II. ^{*e*}Compounds III.

 B_G or B_S was stable under the employed conditions when subjected to MnO₂ oxidation as a starting compound. The disappearance of compound I_G or I_S and concomitant formation of product B_G or B_S , respectively, are shown in Figure S1 in the Supporting Information.

The above observations confirm that MnO_2 cannot oxidize the H- and E- but can oxidize the G- and S-type aromatic nuclei to afford products B_G and B_S , respectively, as the exclusive major reaction products under the employed conditions in spite of the slow progress. The labilities of the G- and S-type aromatic nuclei do not seem to be different.

The disappearance of compound I_G or I_s was approximated to a pseudo-first-order reaction to obtain the pseudo-first-order reaction rate constant k_{obs} , which is listed in Table 1. The approximations were fairly good in most of the six runs (two compounds × three duplications; see the R^2 values in Table 1).

MnO₂ **Oxidation of Benzyl Alcohol Analogues** (**Compounds II**). Compound II_H was oxidized in MnO₂ oxidation, and product A_H formed as the exclusive major reaction product. The recovery yield and yield of product A_H were 52.7 ± 0.1% and 39.3 ± 0.7%, respectively, at a reaction time of 660 min. The total of these was 92.0%, indicating that side reactions contributed only slightly. Few small peaks appeared on the HPLC chromatogram of the reaction solution withdrawn at this reaction time. Compound II_H was stable in the absence of MnO₂ under otherwise the same conditions. Product A_H was stable under the employed conditions when it was subjected to MnO₂ oxidation as a starting compound.

All the observed phenomena in the MnO_2 oxidation of compound II_G were the same as those of compound II_H except for the remarkably higher rate. The recovery yield and yield of product A_G were $4.3 \pm 0.4\%$ and $87.2 \pm 8.7\%$, respectively, at a reaction time of 30 min. The total of these was thus 91.5%. Product A_G was stable under the employed conditions when subjected to MnO_2 oxidation as a starting compound.

In contrast, compound II_s afforded products A_s and B_s as the exclusive major and prominent secondary reaction product, respectively, although all of the other phenomena were the same as those of compound II_g except for the slower oxidation. The S nucleus of compound II_s was oxidized in MnO_2 oxidation. The recovery yield and yields of products A_s and B_s were 3.5 \pm 0.7%, 66.0 \pm 1.2%, and 7.8 \pm 0.2%, respectively, at a reaction time of 120 min. The total of these was thus 77.3%, which was lower than those of compounds II_H and II_G . The oxidation of the aromatic nucleus (S nucleus) may thus increase reactions affording unidentified reaction products. Because few small peaks appeared on the HPLC chromatogram, the oxidation of the aromatic nucleus must have afforded aliphatic reaction products accompanying the degradation of the S nucleus. Product A_S or B_S was stable under the employed conditions when subjected to MnO_2 oxidation as a starting compound.

All the observed phenomena in the MnO₂ oxidation of compound II_E were the same as those of compound II_H except for the slower oxidation. The recovery yield and yield of product A_E were 87.0 ± 0.1% and 13.2 ± 0.1%, respectively, at a reaction time of 660 min. The total of these was 100.2%, indicating that this oxidation reaction was quantitative. Product A_E was stable under the employed conditions when subjected to MnO₂ oxidation as a starting compound. Each disappearance of compounds II and concomitant formation of the reaction products are shown in Figure S2 in the Supporting Information.

Each disappearance of compounds II was approximated to a pseudo-first-order reaction, and the value of k_{obs} is listed in Table 1. The approximations were good in most of the 12 runs (four compounds × three duplications; see the R^2 values in Table 1). The rates were in the order of compounds II_G > II_S \gg II_H > II_E. If the MnO₂ oxidations had been affected only by the electronic effects originating in the functional groups on their aromatic nuclei and appearing locally only at their benzyl positions, the rates should have been in the order of compounds II_H > II_G \geq II_E > II_S on the basis of their Hammett's σ values, which are -0.268, -0.153, -0.151, and -0.038, respectively. This inconsistency suggests that the MnO₂ oxidations are affected by not only the electronic effects on the benzyl positions but also some other factors.

These other factors are discussed here. Previous studies proposed that allyl or benzyl alcohols can form the π -complex type of interaction with Lewis acid sites on the surface of MnO₂ aggregates, and hence these alcohols are oxidized by MnO₂ much more readily than other types of alcohols.^{18,24,25} On the basis of this proposal, MnO₂ is presumed to readily oxidize an analogue of benzyl alcohol with high electron density in its aromatic nucleus owing to the ready formation of the π -complex type of interaction with it. In this context, the

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Scheme 3. Three Possible Reaction Modes in the MnO₂ Oxidations of the Benzyl Alcohol Analogues (Compounds II and III)^a



^aThe former is representatively described, although the latter also undergoes these modes.

slowest MnO₂ oxidation of compound II_E can be explained as follows: Compounds II_H, II_G, and II_S with the methoxy group substituent(s) have the aromatic nuclei with electron densities higher than that of compound II_E with the ethyl group substituent, resulting in rapid or ready formation of the π complex type of interaction with MnO₂. The methoxy groups resonantly donate their lone pairs to the π -electron systems of their aromatic nuclei, which consequently increase their electron densities higher than that of compound II_{E} elevated only inductively by the ethyl group. The faster MnO₂ oxidations of compounds II_G and II_S than that of compound II_H can result from the high electron densities of their aromatic nuclei, owing to the presence of plural methoxy groups. Because the MnO₂ oxidation of the benzyl position of compound IIs is relatively suppressed by the electronwithdrawal inductive effect originating in two meta-substituted methoxy groups, the MnO2 oxidation of compound IIs must have been suppressed and slower than that of compound IIG. Instead, the oxidation of the aromatic S nucleus of compound II_S progressed to afford product B_S as the secondary prominent reaction product, owing to the quite high electron density of the S nucleus.

Although MnO_2 can oxidize the aromatic nucleus of not only the S-type (compound I_S) but also G-type (compound I_G), as shown in the previous section, product B_G was not detected in the MnO_2 oxidation of compound II_G . This is probably because the oxidation of the benzyl position of compound II_G is fast enough to be exclusive in competing with the oxidation of the G nucleus.

MnO₂ Oxidation of Deuterated Benzyl Alcohol Analogues (Compounds III). The observed phenomena in the MnO₂ oxidation of each of compounds III were mostly the same as those of the corresponding compounds II except that the rate was lower due to the appearance of the primary kinetic isotope effect (Table 1). The recovery yield of compound III_{H} and yield of product $A_{H}{'}$ were 81.7 \pm 0.5% and 16.9 \pm 0.3%, respectively, at a reaction time of 660 min. The total of these was 98.6%. Those of compound III_G and product A_G' were 1.9 \pm 0.2% and 86.6 \pm 0.2%, respectively, at a reaction time of 180 min. The total of these was 88.5%. In the MnO₂ oxidation of compound $III_{s'}$ products $A_{s'}$ and B_{s} formed as the exclusive major and secondary prominent reaction products, respectively. The recovery yield of compound IIIs and yields of products A_{s}' and B_{s} were 11.5 \pm 0.4%, 31.0 \pm 0.2%, and 18.1 \pm 0.0%, respectively, at a reaction time of 180 min. The total of these was 60.6%. The recovery yield of compound III_{E} and yield of product A_{E}' were 98.4 \pm 0.0% and 1.3 \pm 0.0%, respectively, at a reaction time of 660 min. The total of these was 99.7%. Each disappearance of compounds III and concomitant formation of the reaction products are shown in Figure S3 in the Supporting Information.

Regarding the observed aspects other than the rates, it should be noted that only the S-type compounds showed a significant difference between compounds III and II. The amount of afforded product A_{S}' was smaller than twice that of product B_{S} in the MnO₂ oxidation of compound III_S, while product A_{S} was afforded in an amount about 7–9 times as large as that of product B_{S} in the reaction of compound II_S. This significant difference in the S-type compounds suggests that in the oxidation of compound III_S, the S-nucleus oxidation is competitively and alternatively enhanced by suppressing the oxidation of the benzyl position due to the presence of the deuteriums and appearance of the kinetic isotope effect.

Possible Reaction Modes in MnO₂ Oxidation. Although MnO_2 commonly oxidizes alcohol groups present at the benzyl position,¹⁸ it certainly oxidized the G and S nuclei of compounds I_G and I_S , respectively, which do not have the benzyl position and substructures corresponding to the sidechain portion of lignin, under the employed conditions. On the basis of this observation, three possible reaction modes can be proposed for the MnO_2 oxidation of compounds II and III, as shown in Scheme 3.

Mode 1 is direct oxidation of the benzyl position to afford the corresponding benzaldehyde-type products A or A', which is the general mode of MnO₂ oxidation. Mode 2 begins with the oxidation of the aromatic nucleus but finally results in the oxidation of the benzyl position to afford products A or A'. In this mode, the aromatic cation radical must be the primary intermediate, which is generated by the one-electron oxidation of the aromatic nucleus by MnO₂. Mode 3 also begins with the oxidation of the aromatic nucleus and finally results in the oxidative degradation of the aromatic nucleus to afford product B or B^\prime as well as other unidentified aliphatic reaction products. It is discussed in the following paragraphs which is the major reaction mode in the MnO₂ oxidation of the H-, G-, S-, and E-type compounds on the basis of the magnitudes of the kinetic isotope effects, which are expressed by the ratios of the k_{obs} values of compounds II to those of the corresponding compounds III $(k_{obs}(II)/k_{obs}(III))$ listed in Table 1, focusing on how dependent the ratio is on the types of the H, G, S, and

E nuclei of compounds II and III. On the other hand, it is not discussed in this study which mechanism the MnO_2 oxidation follows, the consecutive two steps of one-electron oxidation or one step of two-electron oxidation, and how primarily generated intermediates are further oxidized by MnO_2 and rearrange to products **A** and **B**, although the aromatic cation radical is drawn as the intermediate on the way in Scheme 3. Other possible intermediates are not discussed in this study because any data obtained in this study cannot sufficiently contribute to distinguishing between the above-described two mechanisms of MnO_2 oxidation (two steps of one-electron oxidation and one step of two electrons) and tracing further rearrangements. However, it is valuable enough to clarify which mode (1, 2, or 3) is the major in the MnO_2 oxidation of the H-, G-, S-, and E-type compounds.

The ratio between the E-type compounds $(k_{obs}(II_E)/k_{obs}(III_E))$ is 8.6 and the largest among all types. This ratio seems to be a common magnitude as an expression of the primary kinetic isotope effect. As described in the previous section, MnO₂ cannot oxidize compound I_E , and the MnO₂ oxidation of compound II_E or III_E quantitatively affords product A_E or A_E' , respectively. On the basis of these facts, the MnO₂ oxidations of the E-type compounds II_E and III_E are presumed to progress exclusively *via* mode 1.

The ratio between the H- or G-type compounds is 4.7 $(k_{obs}(II_H)/k_{obs}(III_H))$ or 4.0 $(k_{obs}(III_G)/k_{obs}(III_G))$, respectively, which is smaller than that between the E-type compounds $(k_{obs}(II_E)/k_{obs}(III_E))$. Because the rate-determining step is the oxidation of the aromatic nucleus and hence the kinetic isotope effect does not appear when the MnO₂ oxidation progresses only via mode 2, any contribution of mode 2 to MnO₂ oxidation must decrease the ratio. On the basis of this fact, the MnO₂ oxidations of the H-type compounds II_H and III_H must progress via not only mode 1 but also mode 2, although MnO2 cannot oxidize the H nucleus in the oxidation of compound I_H. Mode 2 can become progressive in the MnO₂ oxidations of compounds II_H and III_H owing to the presence of their benzyl hydroxymethyl groups as an inductively electron-donating group. Similar discussion is possible for the MnO₂ oxidations of the G-type compounds (II_G and III_G). Because MnO₂ can oxidize compound I_G, the contribution of mode 2 is greater than that in the oxidations of compounds II_H and III_H, resulting in $k_{obs}(II_G)/k_{obs}(III_G)$ being smaller than $k_{obs}(II_H)/k_{obs}(III_H)$.

The ratio between the S-type compounds $(k_{obs}(II_S)/$ $k_{obs}(III_s)$) is 2.7, which is much smaller than the others. As described in the previous section, the MnO₂ oxidations of compounds IIs and IIIs afford products Bs, which clearly shows that MnO₂ oxidizes their S nuclei to afford the products. Thus, mode 3 contributes substantially to the MnO₂ oxidations of compounds II_s and III_s. The kinetic isotope effect does not naturally appear in mode 3, and hence the contribution of mode 3 to MnO₂ oxidation decreases the ratio. The electronwithdrawal inductive effects of the two meta-methoxy groups (σ value: +0.115 × 2) of compounds II_s and III_s decrease the contribution of mode 1, which further decreases the ratio. These facts indicate that modes 1, 2, and 3 all contribute to the MnO₂ oxidations of compounds II_s and III_s. Compounds II_s and III_s thus progress to mode 3 contrary to the lack of mode 3 in the MnO_2 oxidations of compounds II_G and III_G , although both the S- and G-type compounds are oxidized to be the cation radicals as the primary intermediates. This relative preference of mode 3 in the oxidations of the S-type

compounds is based on its higher electron density as well as relative resistance in the rearrangement of the aromatic cation radical to the benzyl radical accompanying the deprotonation from the benzyl position. The MnO_2 oxidation of the benzyl radical must readily progress to afford products **A**.

Final Statements. MnO2 oxidized the G and S nuclei of compounds I_G and I_S, respectively, which do not have substructures corresponding to the side-chain of lignin, although MnO₂ commonly oxidizes alcohol groups present at the benzyl positions. MnO₂ oxidized compounds II, the analogues of benzyl alcohol, with the rate in the order G - S- \gg H- > E-type. This order suggests that their reactivity is determined by the electronic effects of their methoxy and ethyl groups on not only their benzyl positions but also their aromatic π -electron systems. The magnitudes of the kinetic isotope effects in MnO₂ oxidations were estimated from the ratios of the k_{obs} values between compounds II and III, the nondeuterated and deuterated analogues of benzyl alcohol, respectively. Because the kinetic isotope effect did not appear when the MnO₂ oxidation began with their aromatic nuclei, the ratio decreased with increasing contribution of the oxidation of the aromatic nuclei. The observed ratios were in the order of E- \gg H- > G- \gg S-type, which suggests that the contribution of the oxidations of the aromatic nuclei increases in the reverse order.

Because any carbon–carbon bond does not cleave in modes 1 and 2, these modes may not contribute to delignification in a bleaching process of actual chemical pulp. Because mode 3 does not contribute to the oxidation of the G-type compounds, the MnO_2 oxidation may not be effective in a bleaching process of softwood pulp in contrast to that of hardwood pulp examined in our previous paper.¹ We will examine these in the next coming papers.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jafc.0c01956.

Assignments of ¹H- and ¹³C-NMR spectra of compounds III, products **A**, and products **B**; disappearances of compounds I and concomitant formations of products **B** in the MnO₂ oxidations of compounds I (Figure S1); disappearances of compounds II and concomitant formations of products **A** and **B** in the MnO₂ oxidations of compounds II (Figure S2); and disappearances of compounds III and concomitant formations of products **A'** and **B'** in the MnO₂ oxidations of products **A'** and **B'** in the MnO₂ oxidations of compounds III (Figure S3) (PDF)

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Notes

The authors declare no competing financial interest.

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