EFFECT OF SOLVENT ON THE *β-O*-4 BOND CLEAVAGE OF A LIGNIN MODEL COMPOUND BY TERT-BUTOXIDE UNDER MILD CONDITIONS

Kineo Takeno, Tomoya Yokoyama,* and Yuji Matsumoto

The beta-*O*-4 bond cleavage of a non-phenolic *β-O*-4 type dimeric lignin model compound, 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)-ethanol (III), was examined in systems using potassium *tert*-butoxide as a base (0.5 mol/l) and *tert*-butanol (*t*BuOH), dimethylsulfoxide, 1,4-dioxane, or tetrahydrofuran as a solvent. The *β-O*-4 bond of compound III was cleaved in any system at 30°C, and 2-methoxyphenol (II) was liberated. The amount of compound II liberated was close to the quantitative yield on the basis of the amount of compound III that disappeared, except for the treatment in the *t*-BuOH system. The reaction rate was dependent on what solvent was used. Half-life periods for these systems were roughly about 6.0, 3.0, 0.7, and 0.2h, respectively. It seemed that the rates were very high when the polarity of the solvents was low. Two reaction products generated from the aromatic ring with two methoxyl groups of compound III, 4-acetyl-1,2-dimethoxybenzene and 3,4-dimethoxybenzoic acid, were detected in all the systems. A peculiar reaction product, 1,2-dimethoxybenzene, was detected in a fairly large quantity, only when the latter two solvents with low polarities were applied.

Keywords: Alkyl-aryl ether; Base; t-Butoxide; Half-life; Lignin

*Contact information: Laboratory of Wood Chemistry, Department of Biomaterial Sciences, Graduate School of Agricultural and Life Sciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-8657, Japan; * Corresponding author: yokoyama@woodchem.fp.a.u-tokyo.ac.jp*

INTRODUCTION

The cell wall of wood consists of three main components: cellulose, hemicellulose, and lignin. Lignin is second in abundance after the polysaccharides as a natural polymer on the earth. However, because few methods for unitization of lignin as a high value added product are currently established, lignin is often removed from lignocellulosic materials to isolate carbohydrates in biomass conversion processes. The most important steps in these lignin removal processes are cleavage of the *β-O*-4 bond (see Fig. 1 for definition of the nomenclature), the most abundant linkage type in lignin, and subsequent dissolution of the lignin fragments. Lignin is basically hydrophobic and dissolves more easily in an organic solvent system than in an aqueous system. It is expected, therefore, that lignin can be removed in an organic solvent system under conditions milder than those in an aqueous system since the hydrophobic nature can be expected to influence chemical reactions in the lignin removal.

Fullerton (1975) examined the *β-O*-4 bond cleavage of a phenolic *β-O*-4 type dimeric lignin model compound, 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)ethanol (I in Fig. 1), in various organic solvents. Table 1 lists the yield of 2-methoxyphenol (II in Fig. 1), which was liberated by the *β*-*O*-4 bond cleavage of compound I, when compound I was treated by Fullerton. The *β*-*O*-4 bond was cleaved even at 22°C when potassium *tert*-butoxide (KO*t*Bu) and dimethylsulfoxide (DMSO) were applied as a base and solvent, respectively.

Table 1. Summary of Various Base Treatments of Compound I Reported by Fullerton (1975)

Solvent	Base	Time (h)	Temperature (°C)	Yield of II (%)
H_2O	WL	2.0	170	70
H_2O	2N NaOH	2.0	170	30
DMSO	KO*t*Bu	2.0	170	49
DMSO	KO*t*Bu	0.3	75	81
DMSO	KO*t*Bu	17.0	22	51
DMSO	NaH	2.0	75	21
DMSO	$NaOCH_3$	5.0	75	45
CH_3OH	$NaOCH_3$	2.0	170	trace

WL: White liquor is a solution of NaOH (3.5 g) and $Na_2S{\cdot}9H_2O$ (3.1 g) in water (100 mL).

We have focused on KO*t*Bu as a base and have already described that the *β*-*O*-4 bond of a non-phenolic *β*-*O*-4 type dimeric lignin model compound, 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethanol (III in Fig. 1), is clearly cleaved under mild conditions, and beech wood meal is sufficiently delignified in the KO*t*Bu/DMSO system under conditions much milder than those for a common alkaline pulping process (Takeno *et al*. 2010). On the other hand, beech wood meal is not delignified in the KO*t*Bu/*tert*-butanol (*t*BuOH) system, and sufficient delignification is not attained for beech wood chip even in the KO*t*Bu/DMSO system. It seemed that this insufficient delignification of the chip was due to the difficulty of penetration of KO*t*Bu into the chip (Takeno *et al*. 2010).

In this study, the effect of solvent on the *β*-*O*-4 bond cleavage of compound III is further examined using KO*t*Bu as a base and *t*BuOH, DMSO, 1,4-dioxane (Diox), or tetrahydrofuran (THF) as a solvent to understand the chemistry of the system using KO*t*Bu as a base. Compound III does not have a phenolic hydroxyl group, and it is more suitable for a model compound of native lignin than compound I. Another dimeric non-phenolic C_6-C_3 type lignin model compound, 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)propane-1,3-diol, is commonly used in this kind of experiment. Although this model compound has two hydroxyl groups in the side chain and the stereoisomers, the reaction occurring in the system is much more complex than that of compound III. On the basis of this fact and the purpose of this study, compound III was chosen as a main model compound applied in this study.

EXPERIMENTAL

Materials

Compounds III and IX were synthesized according to the method of Adler *et al.* (1952). Compound III was dissolved in methanol containing sulfuric acid, and the mixture was kept at 50°C for 3h with stirring, which afforded compound VIII. Compound IX was synthesized from 2-bromopropane by substituting bromide with 2-methoxyphenol in acetone containing potassium carbonate. The other chemicals were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan) or Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan). All the compounds applied as starting materials were recrystallized before use. High-purity anhydrous KO*t*Bu, *t*BuOH, DMSO, Diox, and THF were purchased from Sigma-Aldrich Japan K. K. (Tokyo, Japan) and used without further purification. The chemical structures of compounds used and referred to in this paper are shown in Fig. 1.

The structure and purity of compound III were confirmed by ^{1}H-NMR (JNM-A500, 500MHz, JEOL Ltd., Tokyo, Japan) and GC/MS (GC2010/PARVUM2, Shimadzu Co., Kyoto, Japan). ^{1}H-NMR (CD_3COCD_3): δ 3.78-3.83 (s, 9H, 3 -OC$\underline{H}_3$), 3.99 (dd, 1H, $J=9.9$, 7.7, Cβ-$\underline{H}_a$), 4.08 (dd, 1H, $J=9.9$, 4.2, Cβ-$\underline{H}_b$), 4.97 (m, 1H, $J=7.7$, 4.2, Cα-$\underline{H}$), 6.74-7.19 (m, 7H, aromatic). MS m/z (rel. int.): 304 (M^+, 6), 286 (44), 271 (9), 257 (11), 226 (22), 211 (6), 180 (17), 167 (57), 151 (55), 139 (41), 124 (43), 109 (41), 91 (37), 77 (100), 65 (40), 51 (57).

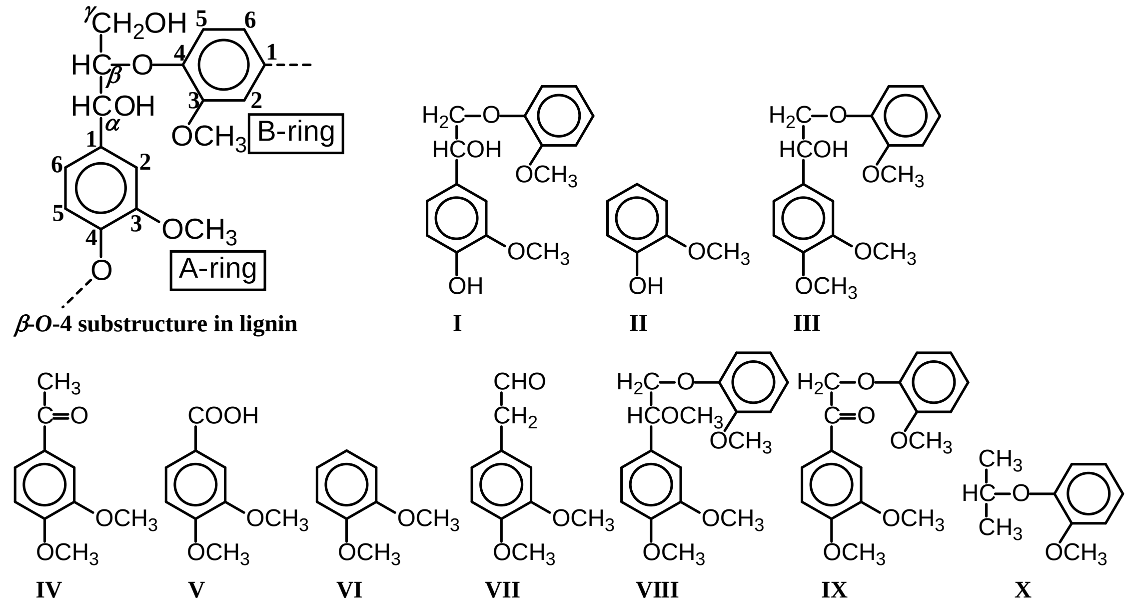

Fig. 1. Chemical structures of model compounds used and referred to in this paper

KO*t*Bu Treatment of Compound III

To a round-bottomed Teflon flask was added 30mL of 0.50mol/L KO*t*Bu solution dissolved in *t*BuOH, DMSO, Diox, or THF. Compound III (45.6mg) was added to the solution and the reaction was initiated. The concentration of compound III in the resulting solution was 5.0mmol/L. The prepared mixture was kept at 30°C with stirring. The reaction system was thoroughly flushed with nitrogen before the addition of the solution.

Quantification of Compound III and Reaction Products

At prescribed times, 1.0mL of the reaction solution was withdrawn, and added to a glass tube containing an internal standard solution (2,5-dichlorophenol in methanol) and acetic acid for neutralization. After filtration, the resulting mixture was injected into an HPLC (LC-10A, Shimadzu Co., Kyoto, Japan) equipped with an SPD-M10A detector (280nm, Shimadzu Co.) to determine the concentration of residual compound III and reaction products, compound II, 4-acetyl-1,2-dimethoxybenzene (IV in Fig. 1), 3,4-dimethoxybenzoic acid (V in Fig. 1), and 1,2-dimethoxybenzene (VI in Fig. 1). The reaction products were identified by comparing their retention times in the HPLC analyses, their UV absorbances (190~370nm) analyzed by the SPD-M10A detector, and their MS spectra analyzed by the GC/MS with those of the authentic compounds. MS (m/z, rel. int.) compound II: 124 (M^+, 87), 109 (100), 81 (61), 53 (14); compound IV: 180 (M^+, 54), 166 (11), 165 (100), 137 (10), 77 (12); compound V: 182 (M^+, 100), 167 (24), 121 (11), 111(15), 95 (11), 79 (11), 77 (14), 51 (11); compound VI: 138 (M^+, 100), 123 (43), 95 (43), 77 (29), 65 (15), 52 (17), 51 (12).

The conditions for HPLC analysis were as follows. Column: Luna 5u C18 (2) 100A (150mm x 4.6mm, Phenomenex, Inc., CA, USA), oven temperature: 40°C, flow rate: 1.2mL/min, solvent system: CH_3OH/0.1mol/L acetate buffer (20/80 (v/v)) for 8min; gradient to 50/50 for 22min and maintained for 10min; gradient to 20/80 for 0.1min and maintained for 5min, total time: 45.1min. The conditions for GC/MS analysis were as follows. Column: IC-1 (30m x 0.25mm x film thickness 0.4µm, GL Sciences Inc., Tokyo, Japan), carrier gas: He, injector temperature: 240°C, interface temperature: 250°C, temperature program: 90°C maintained for 3min; raised to 240°C at 10°C/min heating rate and maintained for 14.5min, total analytical time: 32.5min.

RESULTS AND DISCUSSION

Two aromatic rings of the dimeric lignin model compounds used are named as A-ring and B-ring, and these are schematically shown on the *β-O*-4 type substructure in lignin in Fig. 1. The name of each carbon in the model compounds is also shown. In this study, the non-phenolic *β-O*-4 type dimeric lignin model compound III was treated with 0.5mol/L KO*t*Bu in *t*BuOH, DMSO, Diox, or THF at 30°C, and the cleavage of the *β-O*-4 bond was examined.

Effect of Solvent on the *β-O*-4 Bond Cleavage of Compound III

Figure 2 shows the result of the treatments of compound III in the KO*t*Bu/*t*BuOH system. Compound II was liberated from the B-ring of compound III accompanying the *β-O*-4 bond cleavage. The yield of compound II was not quantitative, but about 80 to 85% on the basis of the amount of compound III that disappeared at any reaction time. Because compound II was found to be fairly stable under the conditions identical to those for the treatment of compound III except under ordinary pressure, it is suggested that about 15 to 20% of compound III disappears *via* reactions without being accompanied by the *β-O*-4 bond cleavage. Two reaction products, compounds IV and V, originated from the A-ring of compound III were identified and quantified. Total yield of compounds III, IV, and V, which are structurally constituted from the A-ring portion of compound III, was about 75% at the end of the reaction. There was only one unidentified major peak in the HPLC chromatogram other than the identified compounds, although compound II was not quantitatively afforded, while the total yield of compounds III, IV, and V was approximately 75%. Further detailed identification is required to quantitatively analyze the whole degradation products. Because the amount of compound IV decreased in the final stage of the reaction and the formation mechanism of compound V from compound III is currently unclear, further research was done to determine if compound V was produced from compound IV. When compound IV was similarly treated in the *t*BuOH system as a starting compound, compound V was afforded at a rate slow enough to judge that the conversion of compound IV into compound V is not the main route for the formation of compound V in the treatment of compound III. Total yield of compounds IV and V gradually decreased and reached about 80%, when the yield of the starting compound IV was 35%. Other reaction products could not be identified.

The disappearance of compound III in the *t*BuOH system was slow at the initial phase, but immediately accelerated. It was well approximated to a pseudo-first-order reaction after a reaction time of about 2h when the yield of compound III was still approximately 90%. The disappearance of compound III was faster in this study where the Teflon flask was used than in our previous study where a glass flask was applied (Takeno *et al.* 2010). Material of the glassware probably dissolved in the reaction solution. This dissolution consumed *tert*-butoxide and neutralized the reaction solution.

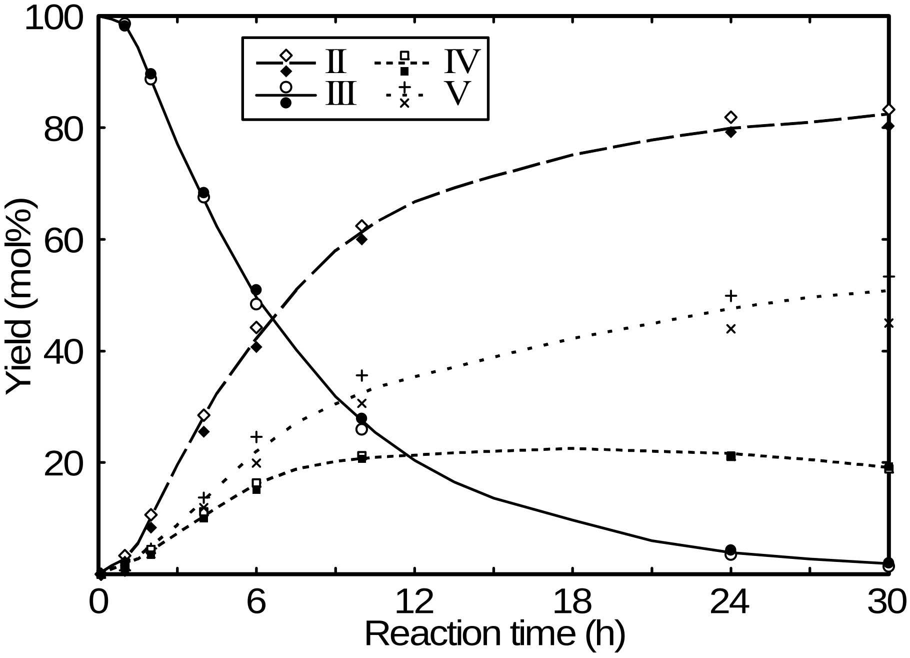

Fig. 2. Change in the yields of compounds II, III, IV, and V when compound III was treated in the KO*t*Bu/*t*BuOH system

A possible mechanism for the formation of compounds II and IV in the *t*BuOH system is proposed in Fig. 3. Another possible reaction product, 3,4-dimethoxyphenylacetaldehyde (VII in Fig. 1), was not detected at all. Compound VII may easily undergo base-induced reactions and be converted into further degradation products even if it is potentially formed. An elimination reaction on the basis of the E2 mechanism, which is shown as the dotted line in Fig. 3, may be excluded from a plausible mechanism for the formation of compound IV owing to the significantly high stability of 1-methoxy-2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethane (VIII in Fig. 1) under the conditions identical to those in the KO*t*Bu/*t*BuOH treatment of compound III. It should be rational to consider that the tendency for compound III to undergo this E2 type elimination reaction is similar to that for compound VIII. The formation mechanism of compound V from compound III has not yet been clarified.

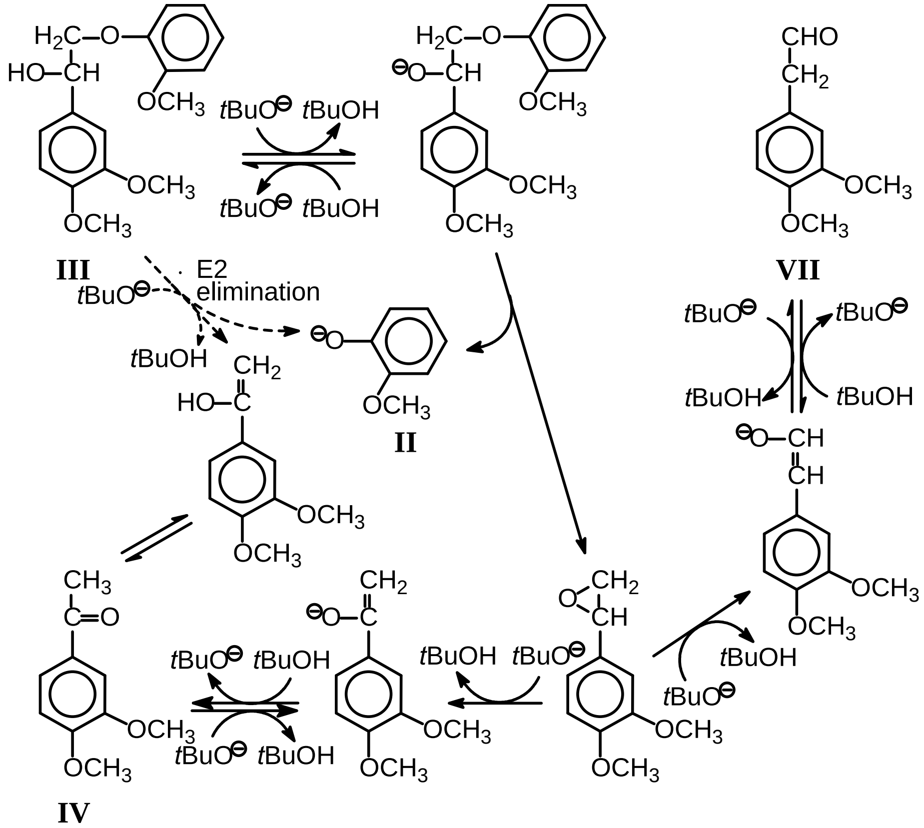

Fig. 3. Possible mechanism for the formation of compounds II and IV from compound III

Figure 4 shows the change in the yields of compounds II, III, IV, and V when compound III was treated in the DMSO system. The reaction was faster in this study than in the previous study, which was similar to the results obtained in the *t*BuOH system (Takeno *et al.* 2010). The liberation of compound II from the B-ring of compound III was nearly quantitative after accompanying the *β-O*-4 bond cleavage, which is different from the *t*BuOH system. Compounds IV and V were identified and quantified as reaction products originated from the A-ring portion of compound III. Total yield of compounds

III, IV, and V was only less than 50%. There were several unidentified minor peaks in the HPLC chromatogram other than the identified compounds, which is also different from the *t*BuOH system. It is suggested that reactions in the DMSO system are not exactly the same with those in the *t*BuOH system, although a possible mechanism in the DMSO system is also shown by Fig. 3.

The disappearance of compound III in the DMSO system was fairly faster than that in the *t*BuOH system in the early stage of the reaction. However, it became slow with the progress of the reaction in the DMSO system, and finally, compound III disappeared from the DMSO system at a reaction time similar to that in the *t*BuOH system. The disappearance of compound III in the DMSO system was not well approximated to a pseudo-first-order reaction through the whole reaction period owing to the decrease in the disappearance rate with the progress of the reaction. The reason for the rate decrease in the DMSO system has not been identified. The consumption of KO*t*Bu during the reaction cannot be a reason for the rate decrease owing to its relatively high concentration.

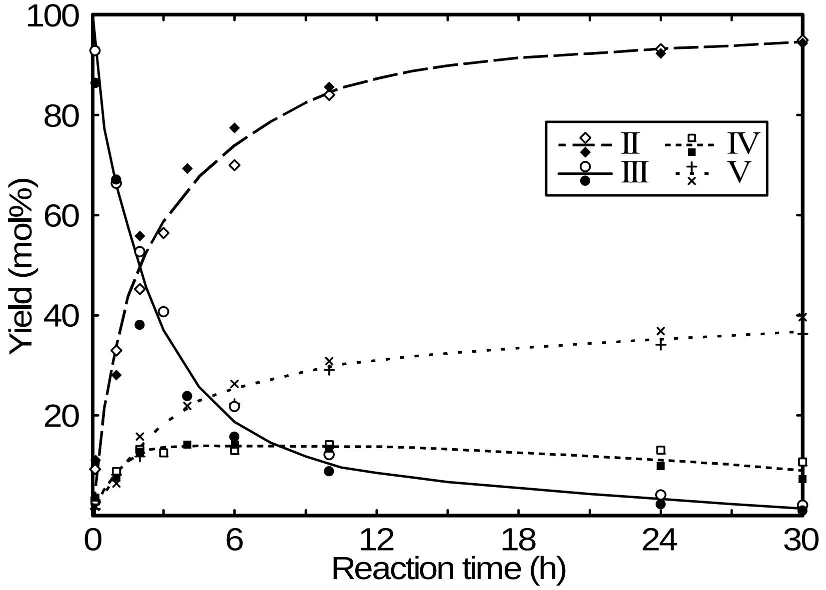

Fig. 4. Change in the yields of compounds II, III, IV, and V when compound III was treated in the KO*t*Bu/DMSO system

Figure 5 shows the change in the yields of compounds II, III, IV, V, and VI when compound III was treated in the Diox system. Compound II was quantitatively liberated from the B-ring of compound III. Compounds IV, V, and VI were detected as reaction products from the A-ring of compound III, and total yield of these compounds was close to 100% at any reaction time on the basis of the amount of compound III that disappeared, which is different from the previous two systems. The disappearance of compound III was significantly more rapid than those in the previous two systems. The reaction became slow with the progress of the reaction except in the initial phase when compared with a pseudo-first-order reaction, and hence, the disappearance of compound III was not well approximated to the reaction.

Figure 6 shows the change in the yields of compounds II, III, IV, V, and VI when compound III was treated in the THF system. Compound II was quantitatively liberated from the B-ring of compound III. Compounds IV, V, and VI were detected as reaction products from the A-ring of compound III, and total yield of these compounds was close to 100% at any reaction time on the basis of the amount of compound III that disappeared. The disappearance of compound III was most rapid among the systems studied. The disappearance could be approximated to a pseudo-first-order reaction for the whole reaction period.

Compound VI was obtained only in the Diox and THF systems. This compound is apparently a reduction product. The formation mechanism is not yet clear. Because the yield of compound VI was about 80% on the basis of the amount of compound IV that disappeared when compound IV was similarly treated in the THF system as a starting compound, it was suggested that compound VI is mainly produced *via* compound IV in the treatment of compound III. The formation of compound VI will be examined in detail as part of future work.

Half-life periods of compound III in the *t*BuOH, DMSO, Diox, and THF systems are roughly about 6.0, 3.0, 0.7, and 0.2h, respectively, although the periods cannot strictly be applied to the comparison of reaction rates between these systems owing to the low approximations of the disappearances of compound III to pseudo-first-order reactions in the DMSO and Diox systems. It seems that compound III disappears more rapidly when the polarity of the solvent is low. It is not clear why the disappearance of compound III is rapid in the solvent with low polarity. A possible explanation is that solvation of the alcoholate anion at the α-position of compound III by solvent may be great when polarity of the solvent is high, and consequently, attack of the alcoholate anion on the neighboring β-carbon may be slow (Fig. 3). High polarity of solvent may also result in enhanced solvation of the base, KO*t*Bu, and consequently, alkalinity of the system may be low.

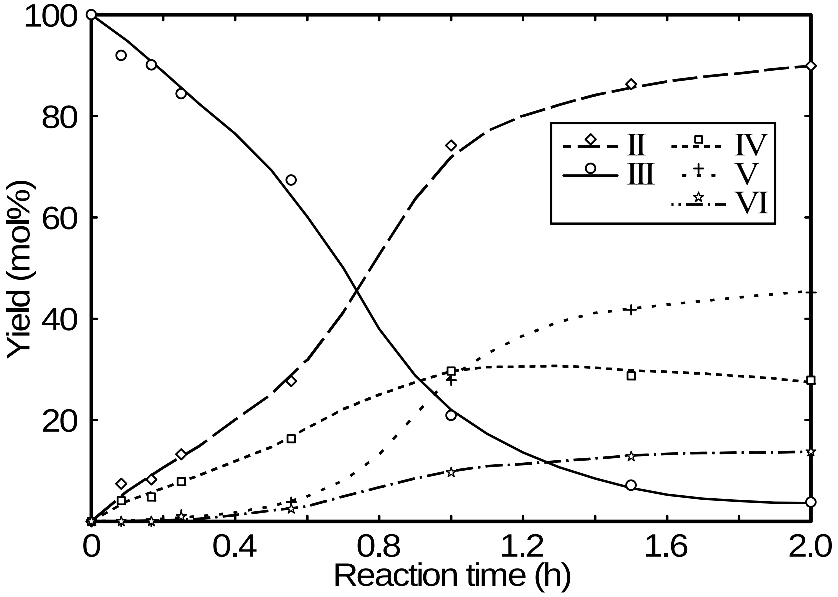

Fig. 5. Change in the yields of compounds II, III, IV, V, and VI when compound III was treated in the KO*t*Bu/Diox system

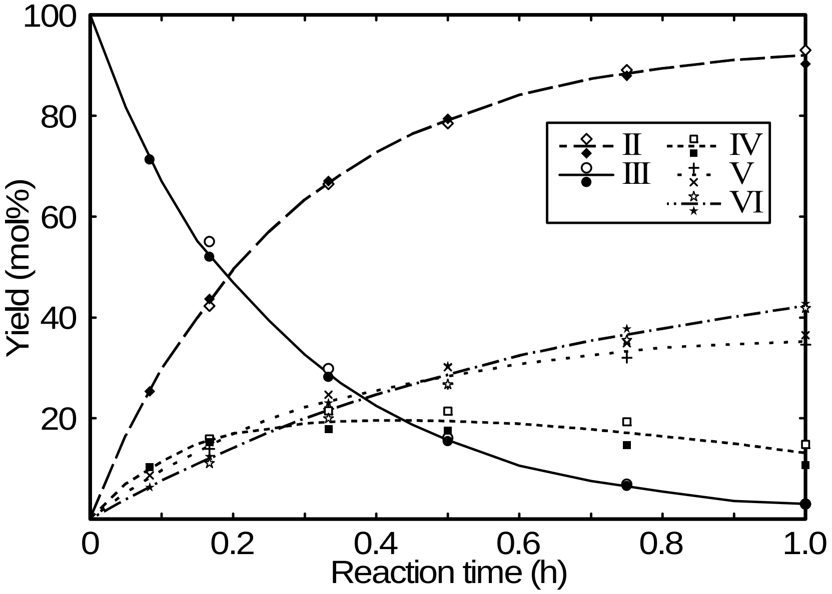

Fig. 6. Change in the yields of compounds II, III, IV, V, and VI when compound III was treated in the KO*t*Bu/THF system

Because not only the rates of the disappearance of compound III, but also reaction products obtained are different from each system, the reaction mechanism is not the same in all the systems. A possible mechanism is shown in Fig. 3 in any system because compound VIII was stable enough to judge that the E2 elimination can be excluded from a plausible mechanism even in the THF system.

KOtBu Treatment of Compounds VIII and IX, and Treatment of Compound III with Other Bases

Because the presence of the α-hydroxyl group of compound III must be important in its β-*O*-4 bond cleavage, a non-phenolic β-*O*-4 type dimeric lignin model compound with functional groups at the α-position, compound VIII or 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethanone (IX in Fig. 1), was treated in the KO*t*Bu/*t*BuOH or KO*t*Bu/THF system. Compound VIII was significantly stable in the KO*t*Bu/*t*BuOH system, and its yield was 100% even at a reaction time of 48h. A small amount of compound II was detected when compound VIII was treated in the KO*t*Bu/THF system. The formation mechanism of compound II from compound VIII may be E2 type elimination, which is shown by the dotted line in Fig. 3. When a compound, 2-(2-methoxyphenoxy)propane (X in Fig. 1), was treated in the KO*t*Bu/THF system, no reaction occurred. This result suggests that the formation of compound II from compound VIII does not result from an S_N2-type substitution reaction of the B-ring of compound VIII with *tert*-butoxide.

The disappearance of compound IX was much more rapid than that of compound III in the KO*t*Bu/*t*BuOH system (Fig. 7). Compound II was quantitatively detected accompanying the disappearance of compound IX. Compound V was obtained as a reaction product from the A-ring of compound IX, and the yield was about 50% on the basis of the disappearance of compound IX. There was only one unidentified peak in the HPLC chromatogram other than the identified compounds when a reaction solution of the KO*t*Bu/*t*BuOH treatment of compound IX was analyzed. The mechanism of the quantitative formation of compound II from compound IX is not yet clear. A possible explanation is an S_N2-type substitution reaction of the B-ring of compound IX resulting from *tert*-butoxide. It is known that a carbonyl group accelerates an S_N2-type substitution reaction at an α-carbon (Kirby 1996). It may also be possible that the addition of *tert*-butoxide to the α-carbonyl group of compound IX affords the oxo-anion at the α-position and the anion intramolecularly attacks the neighboring β-carbon.

When compound III was treated in different base systems, potassium ethoxide in ethanol and potassium methoxide in methanol, under conditions identical to those employed in the KO*t*Bu treatments of this study, no reactions occurred. The stability of compound III in sodium hydroxide in an aqueous Diox system at 30°C is estimated to be quite high on the basis of the data obtained by Gierer *et al.* (1987). Those data indicated that the β-*O*-4 bond of compound III is cleaved at 30°C only when KO*t*Bu is applied as a base. This is a unique characteristic of KO*t*Bu. As another peculiar attribute of KO*t*Bu, it was reported that treatment of Klason lignin with KO*t*Bu releases a phenolic lignin moiety from the complex structure of Klason lignin (Yasuda *et al.* 1981).

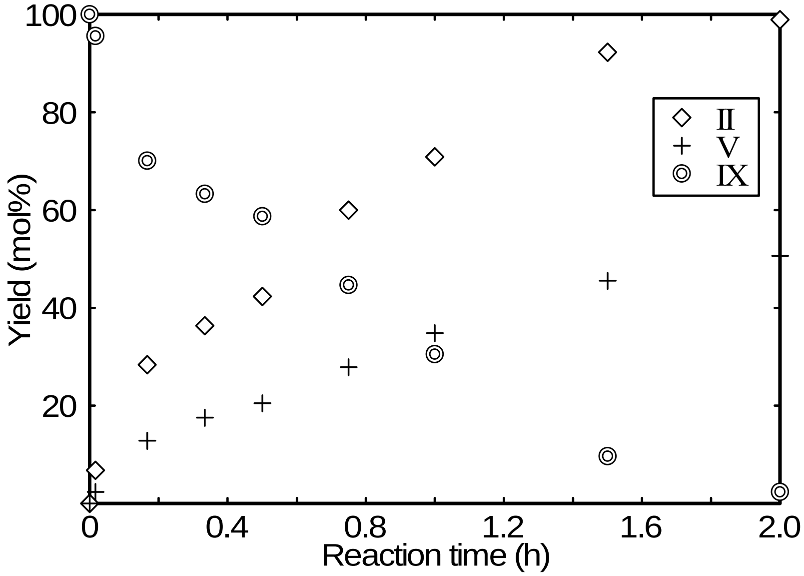

Fig. 7. Change in the yields of compounds II, V, and IX when compound IX was treated in the KO*t*Bu/*t*BuOH system.

CONCLUSIONS

1. The β-*O*-4 bond of compound III was cleaved in any system under conditions that were remarkably milder than those in a common alkaline delignification process.

2. The *β*-*O*-4 bond of compound III seemed to be cleaved more rapidly with the decrease of the solvent polarity.
3. The cleavage of the *β*-*O*-4 bond of compound III was notably rapid in the THF system. The half-life was as short as 12min.
4. A peculiar reaction product (compound VI), which is apparently a reduction product, was formed in a fairly large quantity, when Diox or THF was used as solvent.

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