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Revisiting the mechanism of β -O-4 bond cleavage during acidolysis of lignin part 10: reactions of C₆-C₂-type non-phenolic syringyl model compounds and comparison of the reactions with those of the guaiacyl analogues

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Abstract

A C₆-C₂-type non-phenolic syringyl lignin model compound (**I**, 2-(2-methoxyphenoxy)-1-(3,4,5-trimethoxyphenyl)ethanol) as well as its derivatives was acidolyzed in aqueous 82vol% 1,4-dioxane containing 0.2 mol/L HBr, HCl, or H₂SO₄ at 85°C. The results were compared with those on the guaiacyl analogues (**V** as well as its derivatives) obtained in our previous reports. The acidolysis of compound **I** was slower than that of compound **V**, which is in accordance with our previous result on the formation rates of the benzyl cation intermediates (**BC**) from a syringyl compound and its guaiacyl analogue. The enol ether-type compound was primarily produced in the acidolysis of compound **I**, similar to that of compound **V**. The acidolysis using HBr or HCl was faster than that using H₂SO₄, indicating the participation of Br⁻ or Cl⁻, respectively, in the acidolysis. It was suggested that Br⁻ (as well as Cl⁻) adds to the cation center of the **BC** to afford the adduct in the acidolysis of compound **I**, similar to that of compound **V**, and hence, this adduct formation is a major bypass of the common route. The bypass activity in the acidolysis of compound **I** was about half in that of compound **V**.

Keywords Biorefinery, Hydrobromic acid, Hydrochloric acid, Sulfuric acid, Woody biomass conversion

Introduction

Acidic treatment is one of the most basic chemical methods and utilized in chemical conversion of woody biomass as acidolysis. Acidolysis is traditionally applied to isolation of lignin [1], despite being accompanied by structural alterations, and analysis of chemical structure

of lignin [2–6]. It is recently interested in its application as a pretreatment for biorefinery of woody biomass. Because all these applications are owing to the achievement of the acidolytic cleavage of β -O-4 bond, the most abundant type of linkage between lignin monomeric units, the cleavage mechanism was primarily examined in the 20th century [2, 7–16]. We quantitatively reinvestigated the mechanism in this century, using guaiacyl-type model compounds, and presented several important proposals in the series of this study [17–25].

However, because guaiacyl-type model compounds were applied in most previous studies including the above, the β -O-4 bond cleavage of syringyl-type lignin substructures

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has not yet been examined quantitatively but just done with qualitative bases only in a few studies [26–29]. This study thus employed a non-phenolic β -O-4-type lignin model compound consisting of a syringyl nucleus and C₆–C₂-type side chain, 2-(2-methoxyphenoxy)-1-(3,4,5-trimethoxyphenyl)ethanol (**I**, Fig. 1), and examined the mechanism under acidolytic conditions in detail. Derivatives of compound **I**, 1-(2-methoxyphenoxy)-2-(3,4,5-trimethoxyphenyl)ethene (**IIc** (the *cis*-isomer), **II t** (the *trans*-isomer), and **II** (used when these isomers are not distinguished), the enol ether compound that is presumed to be the primary product in an acidolysis of compound **I**, Fig. 1), 1-methoxy-2-(2-methoxyphenoxy)-1-(3,4,5-trimethoxyphenyl)ethane (**III**, the α -methyl-etherified derivative of compound **I**, Fig. 1), and 1-bromo-2-(2-methoxyphenoxy)-1-(3,4,5-trimethoxyphenyl)ethane (**IV**, the α -bromo-substituting derivative of compound **I**, Fig. 1), were also acidolyzed to help discuss the mechanism. The obtained results are compared with those reported in our previous studies in which the corresponding guaiacyl-type analogues, 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethanol (**V**, Fig. 1), 1-(2-methoxyphenoxy)-2-(3,4-dimethoxyphenyl)ethene (**VIc** (the *cis*-isomer), **VI t** (the *trans*-isomer), **VI** (used when these isomers are not distinguished), Fig. 1), 1-methoxy-2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethane (**VII**, Fig. 1), and 1-bromo-2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethane (**VIII**, Fig. 1), were acidolyzed [17, 18, 22, 23] to examine the difference in the acidolyses between these syringyl and guaiacyl model compounds. Although the C₆–C₂-type side chains of these compounds, the 2-phenoxyethanol types, are different from the C₆–C₃ type of native lignin, the 2-phenoxypropane-1,3-diol-type, its application can simplify discussion with maintaining significance in the primary report on acidolysis of the syringyl-type compound.

Materials and methods

Materials

All chemicals other than the synthesized or isolated compounds described below were purchased from FUJIFILM Wako Pure Chemical Industries Co. (Osaka, Japan), Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), or Sigma-Aldrich Japan K. K. (Tokyo, Japan), and used without further purification except for 4-chlorophenol, which was employed as the internal standard (IS) for quantification and purified by recrystallization from ethanol. Water (H₂O) and 1,4-dioxane were deionized and distilled, respectively, before use followed by degas using sonication under reduced pressure. Hydrochloric acid and sulfuric acid (H₂SO₄) solutions with certified concentrations were purchased. A purchased hydrobromic acid solution was titrated with a purchased sodium hydroxide solution with a certified concentration before use.

Compound **I** was synthesized from a commercially available 5-acetyl-1,2,3-trimethoxybenzene in accordance with the method of Adler et al. [30]. Compound **II** was isolated from the reaction solution obtained by an acidolytic treatment of compound **I** in accordance with the method described in our previous report [17]. Compound **III** or **IV** was synthesized from compound **I** in accordance with the methods described in our previous reports [18, 23]. Their structures and high purities were confirmed by a proton nuclear magnetic resonance spectrometer (¹H-NMR, JNM-A500, 500 MHz, JEOL Ltd., Tokyo, Japan) using chloroform-*d* as the solvent. The obtained spectral data are as follows (see the square in Fig. 1 for the carbon numbering and nomenclature of the aromatic nuclei): compound **I** δ 3.55 (s, 1H, C α -OH), 3.84 (s, 3H, Ar_AC4- or Ar_BC3-OCH₃), 3.87 (s, 6H, Ar_AC3-OCH₃ & Ar_AC5-OCH₃), 3.89 (s, 3H, the

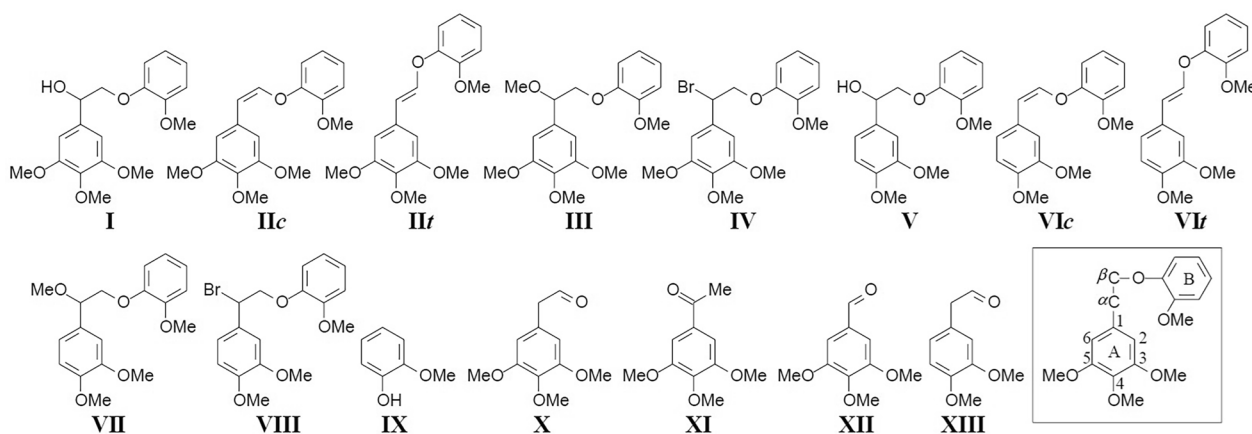


Fig. 1 Chemical structure of model compounds used and discussed in this study. The square shows the carbon numbering used in this study

remaining ArC-OCH₃), 3.97 (dd, 1H, $J=9.3$ & 10.0 Hz, C β -H_a), 4.18 (dd, 1H, $J=3.0$ & 10.0 Hz, C β -H_b), 5.03 (dd, 1H, $J=3.0$ & 9.3 Hz, C α -H), 6.67 (s, 2H, Ar_AC2-H & Ar_AC6-H), 6.89–6.97 (m, 3H, Ar_BC2-H & Ar_BC5-H & Ar_BC1- or Ar_BC6-H), 7.01 (ddd, 1H, $J=1.7$ & 7.2 & 8.8 Hz, the remaining Ar_BC-H); compound **IIc** δ 3.85 (s, 3H, Ar_AC4- or Ar_BC3-OCH₃), 3.88 (s, 3H, the remaining Ar_AC4- or Ar_BC3-OCH₃), 3.88 (s, 6H, Ar_AC3-OCH₃ & Ar_AC5-OCH₃), 5.53 (d, 1H, $J=6.9$ Hz, C β -H), 6.62 (d, 1H, $J=6.9$ Hz, C α -H), 6.94 (sext, 1H, $J=1.5$ & 7.8 Hz, Ar_BC1- or Ar_BC6-H), 6.98 (dd, 1H, $J=1.4$ & 7.8 Hz, Ar_BC2- or Ar_BC5-H), 7.06–7.10 (m, 2H, the remaining two Ar_BC-H), 7.07 (s, 2H, Ar_AC2-H & Ar_AC6-H); compound **II \mathbf{t}** δ 3.83 (s, 3H, Ar_AC4- or Ar_BC3-OCH₃), 3.86 (s, 6H, Ar_AC3-OCH₃ & Ar_AC5-OCH₃), 3.90 (s, 3H, the remaining ArC-OCH₃), 6.24 (d, 1H, $J=12.4$ Hz, C β -H), 6.49 (s, 2H, Ar_AC2-H & Ar_AC6-H), 6.95 (sext, 1H, $J=1.5$ & 6.4 Hz, Ar_BC1- or Ar_BC6-H), 6.98 (dd, 1H, $J=1.5$ & 8.3 Hz, Ar_BC2- or Ar_BC5-H), 7.04 (d, 1H, $J=12.4$ Hz, C α -H), 7.07–7.13 (m, 2H, the remaining two Ar_BC-H); compound **III** δ 3.39 (s, 3H, C α -OCH₃), 3.85 (s, 6H, Ar_AC3-OCH₃ & Ar_AC5-OCH₃ or Ar_AC4-OCH₃ & Ar_BC3-OCH₃), 3.87 (s, 6H, the remaining two ArC-OCH₃), 4.03 (dd, 1H, $J=3.8$ & 10.3 Hz, C β -H_a), 4.19 (dd, 1H, $J=7.8$ & 10.3 Hz, C β -H_b), 4.58 (dd, 1H, $J=3.8$ & 7.8 Hz, C α -H), 6.62 (s, 2H, Ar_AC2-H & Ar_AC6-H), 6.85–6.95 (m, 4H, the remaining four Ar_BC-H); compound **IV** δ 3.81 (s, 3H, Ar_AC4- or Ar_BC3-OCH₃), 3.84 (s, 3H, the remaining Ar_AC4- or Ar_BC3-OCH₃), 3.86 (s, 6H, Ar_AC3-OCH₃ & Ar_AC5-OCH₃), 4.48 (dd, 1H, $J=6.9$ & 10.9 Hz, C β -H_a), 4.53 (dd, 1H, $J=6.9$ & 10.9 Hz, C β -H_b), 5.22 (t, 1H, $J=6.9$ Hz, C α -H), 6.69 (s, 2H, Ar_AC2-H & Ar_AC6-H), 6.86–6.92 (m, 3H, Ar_BC2-H & Ar_BC5-H & Ar_BC1- or Ar_BC6-H), 6.98 (ddd, 1H, $J=2.2$ & 7.0 & 9.0 Hz, the remaining Ar_BC-H).

Four compounds, 2-methoxyphenol (**IX**, guaiacol, Fig. 1), (3,4,5-trimethoxyphenyl)acetaldehyde (**X**, a Hibbert's monomer, Fig. 1), 5-acetyl-3,4,5-trimethoxybenzene (**XI**, the methyl-etherified derivative of acetosyringone, Fig. 1), and 3,4,5-trimethoxybenzaldehyde (**XII**, the methyl-etherified derivative of syringaldehyde Fig. 1), were identified as reaction products by analyzing a reaction solution obtained in an acidolytic treatment of compound **I** under the conditions described below and other solutions of compounds **IX**, **XI**, and **XII** as the authentic compounds, using a gas chromatograph connected with a mass spectrometer (GC/MS, GC-2010/PURVUM2, Shimadzu Co., Kyoto, Japan). The MS spectral data are as follows (m/z (rel. int.)): compound **IX** 124 (M⁺, 87), 109 (100), 81 (61), 53 (14); compound **X** 210 (M⁺, 30), 182 (12), 181 (100), 148 (16), 79 (10), 53 (11); compound **XI** 210 (M⁺, 74), 195 (100), 152 (11), 139 (16); compound **XII**

197 (11), 196 (M⁺, 100), 181 (46), 125 (27), 110 (18), 95 (11), 93 (13).

Acidolytic treatment

The detailed method was described in our previous report [23], although 4-chlorophenol, the internal standard compound (IS), was always added in reaction solutions before the reactions were started. Typically, acidolysis reactions were conducted in an aqueous 82vol% 1,4-dioxane solution (30 mL) that was prepared to contain a starting compound (**I**, **II** (**IIc/II \mathbf{t}**)=52/48), or **III**), acid (hydrogen bromide (HBr), hydrogen chloride (HCl), or H₂SO₄), and IS with concentrations of 1.0 mmol/L, 0.20 mol/L, and 2.0 mmol/L, respectively, at 85 °C for specified periods.

To a chloroform-*d* solution of compound **I** was added bromotrimethylsilane to prepare the solution containing compound **IV**. An amount of the chloroform-*d* solution was added to the above-described acidolytic solution containing HBr or H₂SO₄ at 85 °C to initiate the reaction, and then the mixture was stirred at the same temperature for 10 s or 3 min. The detailed procedure was described in our previous report [23]. The concentration of compound **IV** in the acidolysis solution was not exactly specified, although compound **IV** contained in the chloroform-*d* solution seemed rather pure on the basis of the NMR spectrum.

Quantification

The detailed procedures for quantification were described in our previous report [23]. In the acidolyses of compound **IV**, the procedure was slightly modified as follows: a portion of the reaction solution withdrawn was primarily added to methanol (CH₃OH) containing sodium methoxide (NaOCH₃) in an ice-water bath, and stood for 10 min with stirring.

Quantification was done by a high-performance liquid chromatograph (HPLC) consisting of a system controller (SCL-10A, Shimadzu Co.), online degasser (DGU-12A, Shimadzu Co.), solvent delivery unit (LC-10AD & LC-20AD, Shimadzu Co.), column oven (CTO-10Avp, Shimadzu Co.), and photodiode array detector (SPD-M 20Avp, Shimadzu Co.), and based on the absorbances at 280 nm. Conditions for the HPLC analyses were as follows: a column for HPLC (Luna 5 u C18(2) 100Å length: 150 mm, inner diameter: 4.6 mm, particle size: 5.0 μm, Phenomenex, Inc., Torrance, CA, USA) was used at an oven temperature of 40 °C with a solvent flow rate of 1.0 mL/min; the solvent was CH₃OH/H₂O (v/v) and graduated from 25/75 to 75/25 for 20 min with maintaining 75/25 for 30 or 15 min (a total time of 50 or 35 min, respectively) in the acidolysis of compound **I** using H₂SO₄ or all the others, respectively.

Results and discussion

Prior information for the following contents

Figure 2 illustrates the rationally presumed acidolysis reactions of compounds **I** and **III** (syringyl type) under the employed acidolytic conditions on the basis of the knowledge on the acidolyses of compounds **V**, **VI**, **VII**, and **VIII** (guaiacyl type) obtained in our previous reports [17, 18, 22, 23, 25]. Compound **I** is primarily protonated at the oxygen of the α -hydroxy group to be the conjugate acid (**CA_I**). **CA_I** liberates the H₂O molecule to be the benzyl cation-type intermediate (**BC_I**). Either proton (H⁺) is abstracted from the β -carbon of **BC_I** not by the counter anions of the applied acids but by the solvents to afford compound **II**. Protonation at the double bond generates the β -oxycarbocation-type intermediate (**C β ⁺_{II}**). **C β ⁺_{II}** also forms via the transfer of either hydride (H⁻) from the β - to α -carbon of **BC_I** as a minor route. The protonation at the double bond must not afford **BC_I**, according to our previous report which showed that protonation at the double bond of compound **VI** exclusively generates **C β ⁺_{VI}** [18, 22]. A H₂O molecule adds to the cation center of **C β ⁺_{II}** to afford the conjugate acid of the hemiacetal compound that readily undergoes the β -O-4 bond cleavage to afford compounds **IX** and **X**.

Our previous reports showed the following important results in the acidolyses of compound **V** [18, 22]: (i) the rate-determining step with respect to the disappearance of compound **V** is the abstraction of either H⁺ from the

β -carbon of **BC_V** as well as minor transfer of either H⁻ from the β - to α -carbon of **BC_V**; (ii) pre-equilibria are established between compound **V** and **CA_V** and between **CA_V** and **BC_V** prior to the rate-determining step. Thus, the acidolysis reaction of a β -O-4-type substructure can be divided into the former and latter halves: the elementary reactions from the substructure to **BC**; those from **BC** to the final products including the rate-determining step and β -O-4 bond cleavage. The former half affects the whole reaction rate through regulating the concentration of **BC**, although it does not include the rate-determining step but consists of only the elementary reactions prior to the step. The fast formation of **BC** generally results in its high concentration in the pre-equilibria, and hence, being accompanied by the fast rate-determining step.

It was examined in our previous report how the types of aromatic nucleus affect the rate of the former half, viz. the formation of **BC**, using simple 6 C₆-C₁-type model compounds consisting of phenolic and non-phenolic *p*-hydroxyphenyl, guaiacyl, and syringyl nuclei [31]. The obtained results were as follows: (i) the **BC** formation from the phenolic compound is much faster than that from the corresponding non-phenolic compound regardless of the types of aromatic nucleus; (ii) the **BC** formation rates are in the order: *p*-hydroxyphenyl > guaiacyl > syringyl, regardless of being phenolic or non-phenolic; (iii) the **BC** formation from the phenolic syringyl compound, which is slowest among those from all the

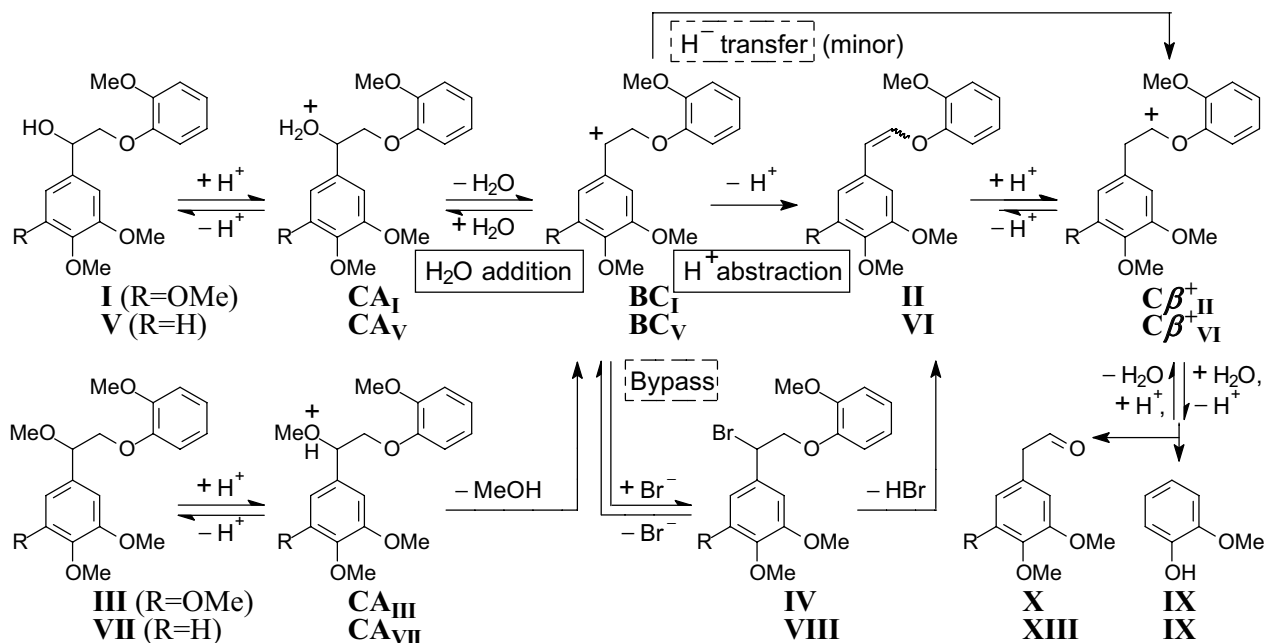


Fig. 2 Acidolysis reaction of compound **I** or **III** rationally presumed on the basis of the knowledge obtained in earlier and our previous reports [2, 7–23], including the characteristic action of HBr as a bypass proposed in our previous reports [23]. All the reaction modes of **BC_I** or **BC_{III}**, the H₂O addition and H⁺ abstraction as well as the bypass with minor H⁻ transfer, are surrounded by solid as well as dotted squares, respectively

phenolic compounds, is still faster than that from the non-phenolic *p*-hydroxyphenyl compound, which is fastest among those from all the non-phenolic compounds. These results suggest that the equilibrated concentration of BC_I , which is generated from compound **I**, the non-phenolic syringyl type, is lower than that of BC_V , which is generated from compound **V**, the non-phenolic guaiacyl type. It can thus be predicted that the disappearance and β -*O*-4 bond cleavage of compound **I** are slower than those of compound **V**. However, because this prediction is based only on the difference in the rates of the former halves between the acidolyses of compounds **I** and **V**, the purpose of this study is to quantitatively confirm whether the entire acidolysis reaction of compound **I** is actually slower than that of compound **V**.

It has been shown in our previous report that the three aqueous 82vol% 1,4-dioxane solutions containing HBr, HCl, and H_2SO_4 at a concentration of 0.2 mol/L show their proton activities close to one another [25], using the method employed in another of our previous reports [32]. A different method has been employed for measuring their proton activities to suggest the similarity in another of our previous reports [33]. Therefore, differences in the rates between acidolyses using the three acids observed in this study do not originate from those between their proton activities but from nucleophilic participation of the counter anions of HBr and HCl, bromide anion (Br^-) and chloride anion (Cl^-), respectively, owing to their high nucleophilicities. In contrast, the counter anion of H_2SO_4 , hydrogensulfate anion (HSO_4^-), is an inert nucleophile in the aqueous solutions employed in this study, and hence, does not participate at all. All the counter anions hardly abstract any H^+ in the aqueous solutions, because they are bases weaker than the solvents, whose amounts are extremely larger than those of the counter anions. Thus, it is not rational at all to consider that the counter anions directly regulate the rate of the rate-determining step, the H^+ abstraction from BC_I or BC_V to generate compound **II** or **VI**, respectively. Because proton activity exclusively regulates the rates in acidolyses using H_2SO_4 without any participation of the counter anion, HSO_4^- , the acidolyses are often treated as the reference in discussion on those using HBr and HCl in the following content.

Starting substrates, compounds **I**, **II**, and **III**, and a major reaction product, compound **IX**, were quantified in this study, although the other starting substrate, compound **IV**, was not quantified. Compounds **X**, **XI**, and **XII** were not quantified but identified as reaction products. These four compounds were not quantified because of the following facts: (i) compound **IV** is not stable enough in the post-treatment to be quantitatively analyzed; (ii) isolation of compound **X** must be accompanied

by the difficulty, which is presumed on the basis of that found in the isolation processes of the guaiacyl analogue of compound **X**, (3,4-dimethoxyphenyl)acetaldehyde (**XIII**, Fig. 1), in previous reports [16, 17]; (iii) the acidolysis rate of compound **I**, **II**, or **III** is independent of the types of final products, because it is confirmed in the following content that elementary reactions after the rate-determining step determine the types.

Fair amounts of compound **XI** were produced in the acidolyses of compounds **I** and **II** using HBr as well as H_2SO_4 at least on the basis of the peak areas in the HPLC analyses despite its large absorptivity. Instead, the peaks of compound **X** seemed rather small. Thus, compound **XI** may not have formed via the isomerization of compound **X** but an unknown mechanism, such as the migration of the syringyl nucleus from the α - to β -carbon of $\text{C}\beta^+_{II}$. This will be examined in our future work.

Table 1 lists the pseudo-first-order reaction rate constants (k_{obs}) with respect to the disappearances of compounds **I**, **II** (total of **IIc** and **IIt**), and **III** when these compounds were individually acidolyzed in this study, squared correlation coefficients (R^2) in all their acidolytic runs, and k_{obs} 's with respect to those of compounds **V**, **VI**, and **VII** when they had individually been acidolyzed in our previous report under the same conditions as this study [23]. All the k_{obs} values obtained in the acidolyses using HBr and HCl conducted in this study were based on all data points observed before the starting compounds reached a recovery yield of 20 mol%.

Acidolysis of compound **I**

Figure 3 shows the time-course changes in the recovery yields of compound **I** and yields of compounds **II** (sum of **IIc** and **IIt**) and **IX** as well as **IIc** and **IIt** in the acidolyses of compound **I** using HBr, HCl, and H_2SO_4 . The yield of compound **II** in the acidolysis using H_2SO_4 was quite low and did not exceed 0.5% throughout the entire reaction. The sum of the recovery yield of compound **I** and yields of compounds **II** and **IX** was almost 100% throughout the entire reaction in the acidolysis using HBr or HCl. It gradually decreased in the acidolysis using H_2SO_4 and became lower than 90% at the end (48 h) when the recovery yield of compound **I** was still about 80%. Thus, some amounts of unknown substances including condensation products were generated in the acidolysis using H_2SO_4 . The HPLC chromatogram showed peaks at retention times when condensation products should appear.

The disappearance rates of compound **I** in the acidolyses using the three acids were in the order: $\text{HBr} > \text{HCl} > \text{H}_2\text{SO}_4$. This order is the same as that in the acidolyses of compound **V** using these acids observed in our previous report [23] and suggests that Br^- or Cl^-

Table 1 Pseudo-first-order reaction rate constants (k_{obs}) and squared correlation coefficients (R^2) in each run observed in the acidolyses of compounds **I**, **II**, and **III** conducted in this study, and those obtained for compounds **V**, **VI**, and **VII** in our previous reports [23]

Comp	Acid	k_{obs} (h^{-1}) ^a	R^2
I	HBr	0.0418 ± 0.0026	0.998 1.00
	HCl	0.0178 ± 0.0001	0.997 0.988
	H ₂ SO ₄	0.00458 ± 0.00055	0.983 0.995
II	HBr	0.470 ± 0.048	0.999 1.00
	HCl	0.337 ± 0.039	0.930 0.998
	H ₂ SO ₄	0.169 ± 0.010	0.980 0.989
III	HBr	0.127 ± 0.003	0.981 0.999
	HCl	0.0705 ± 0.0006	0.995 0.991
V	H ₂ SO ₄	0.0719 ± 0.0015	0.999 0.998
	HBr	0.637	–
VI	HCl	0.310	–
	H ₂ SO ₄	0.0154	–
	HBr	0.552	–
VII	HCl	0.395	–
	H ₂ SO ₄	0.191	–
	HBr	2.88	–
	HCl	1.72	–
	H ₂ SO ₄	1.50	–

^a The values after the '±' marks are standard deviations obtained by repetitive runs

participates in the acidolysis of compound **I**, similarly to the report. For visualizing the participation activity, the ratio of the k_{obs} values between the acidolyses using HBr and H₂SO₄ ($k_{\text{I-HBr}}/k_{\text{I-H}_2\text{SO}_4}$) or between those using HCl and H₂SO₄ ($k_{\text{I-HCl}}/k_{\text{I-H}_2\text{SO}_4}$) is calculated to be 9.1 or 3.9, respectively. The participation of Br[−] is thus greater than that of Cl[−]. In the acidolyses of compound **V**, the corresponding ratio is 41.4 ($k_{\text{V-HBr}}/k_{\text{V-H}_2\text{SO}_4}$) or 20.1 ($k_{\text{V-HCl}}/k_{\text{V-H}_2\text{SO}_4}$), respectively. The participation is thus less active in the acidolysis of compound **I** than in that of compound **V**. The participation mode is discussed in a later section.

The disappearance of compound **I** was slower than that of compound **V** in its acidolysis regardless of the acid types. The slower disappearance was accompanied by the slower β-O-4 bond cleavage, viz. the slower formation of compound **IX**. This is in accordance with our prediction described in the previous section. For visualizing how much slower the acidolysis of compound **I** was than that of compound **V**, the ratio of the k_{obs} values between

compounds **I** and **V** is calculated to be 1/15.2, 1/17.4, or 1/3.4 in the acidolyses using HBr, HCl, or H₂SO₄, respectively ($k_{\text{I-HBr}}/k_{\text{V-HBr}}$, $k_{\text{I-HCl}}/k_{\text{V-HCl}}$, or $k_{\text{I-H}_2\text{SO}_4}/k_{\text{V-H}_2\text{SO}_4}$, respectively). These ratios indicate that the acidolysis of compound **I** is essentially 3.4 times slower than that of compound **V** without any participation and the participation of Br[−] or Cl[−] is less active in the acidolysis of compound **I** than in that of compound **V**, as already suggested in the former paragraph. The less active participation is discussed in detail later.

Compound **II** gradually accumulated, showed the maximum amount, and then decreased regardless of the acid types, although even the maximum yields were only 7%, 4%, and lower than 0.5% in the acidolyses using HBr, HCl, and H₂SO₄, respectively. This is the same tendency as the yields of compound **VI** in the acidolyses of compound **V** conducted in our previous report, although the maximum yields, 48%, 33%, and 17%, respectively, were much higher [22]. These phenomena are discussed in the next section.

Compound **IIc** formed more preferably than compound **IIt** at the initial stages in the acidolyses using HBr and HCl, followed by the gradual decreases in the differences between their amounts. The acidolysis using H₂SO₄ is not covered in this paragraph, because compound **II** was detected with a yield of no more than 0.5% at any data point. The ratio of the detected amounts between compounds **IIc** and **IIt** (**IIc/IIt**) is calculated to be 1.9 or 2.4 in the acidolysis of compound **I** using HBr or HCl, respectively, at the first data point (1 h). It gradually decreases during either acidolysis, and reaches 1.3 or 1.5, respectively, at the end (24 h). These ratios show that the formation of compound **IIc** is kinetically more favorable than that of compound **IIt**. This is the same tendency as our previous reports which showed that the formation of compound **VIc** is kinetically more favorable than that of compound **VIt** in the acidolyses of compound **V** using the acids [18, 22, 23]. The **IIc/IIt** ratio in the acidolysis using HBr, 1.9, is smaller than the real kinetic selectivity that should be equal to or slightly larger than 2.4, owing to the fast acidolysis in using HBr. The **IIc/IIt** ratio would further decrease in an extended acidolysis and reach a bottom that is independent of the acid types and smaller than unity due to the thermodynamic stability of compound **IIc** lower than that of **IIt**. Compound **IIt** should form more preferably than compound **IIc** when compound **II** exclusively forms from **BC_I**, which carries two conformers suitable for the formation of compound **II**. This preferable formation of compound **IIt** is because it forms from the sterically smaller and thermodynamically more stable conformer. Thus, the kinetically more preferable formation of compound **IIc** suggests that compound **II** additionally or exclusively forms from a

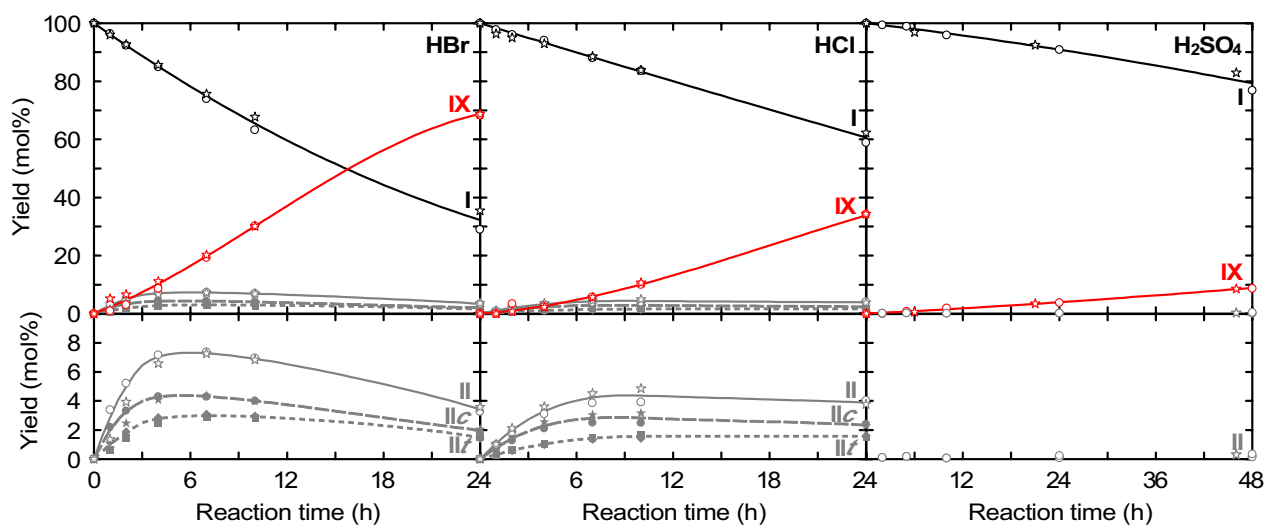


Fig. 3 Time-course changes in the recovery yield of compound I (black solid line with black contouring white marks) and yields of compounds II (gray solid line with gray contouring white marks) and IX (red solid line with red contouring white marks) as well as IIc (gray long broken line with gray marks) and IIt (gray dotted line with gray marks) in the acidolyses of compound I using HBr (left), HCl (middle), or H₂SO₄ (right). Circles and diamonds represent the 1st trial. Stars and squares represent the 2nd trial. The vertical axes in the lower figures are magnified by a factor of 5 for clearly showing the yields of compound II

compound or intermediate other than BC₁, which is discussed in a latter section.

Acidolysis of compound II with the results obtained in the previous section

Figure 4 shows the time-course changes in the recovery yields of compound II as well as IIc and IIt and yields of compound IX in the acidolyses of compound II using HBr, HCl, and H₂SO₄. The sum of the recovery yield of compound II and yield of compound IX slightly decreased to about 85–90% at the end of the reaction (6 h) regardless of the acid types, suggesting the

formation of unknown substances including condensation products. Compound I was not detected at all during the entire reactions regardless of the acid types. This confirms that protonation at the double bond of compound II does not generate BC₁ at all but exclusively Cβ⁺_{II}. This is the same observation as our previous report in which protonation at the double bond of compound VI does not afford compound V at all but exclusively Cβ⁺_{VI} [17, 18, 22, 23]. The rate-determining step with respect to the disappearance of compound II must be the primary protonation because of the following two confirmations in our previous reports [18, 22]: (i) Cβ⁺_{VI}

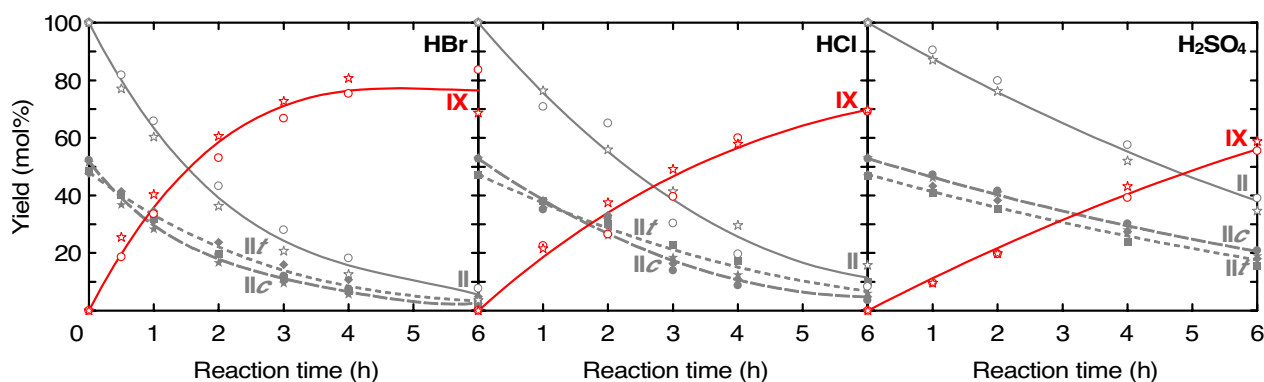


Fig. 4 Time-course changes in the recovery yield of compound II (gray solid line with gray contouring white marks) as well as IIc (gray long broken line with gray marks) and IIt (gray dotted line with gray marks) and yield of compound IX (red solid line with red contouring white marks) in the acidolyses of compound II using HBr (left), HCl (middle), or H₂SO₄ (right). Circles and diamonds represent the 1st trial. Stars and squares represent the 2nd trial

does not frequently progress to the reverse deprotonation but further H₂O addition followed by the β -O-4 bond cleavage; (ii) The relatively fast interconversion between compounds **VIc** and **VI_t** is a process isolated from the protonation to afford **C β ⁺_{VI}**.

The disappearance rates of compound **II** in the acidolyses using the three acids were in the order: HBr > HCl > H₂SO₄. This order is the same as that observed in the acidolyses of compound **VI** as shown in our previous report [23]. These orders suggest that Br⁻ or Cl⁻ also participates in the acidolysis of compound **II** or **VI**. The $k_{\text{II-HBr}}/k_{\text{II-H}_2\text{SO}_4}$ or $k_{\text{II-HCl}}/k_{\text{II-H}_2\text{SO}_4}$ ratio is calculated to be 2.8 or 2.0, respectively, suggesting that the participation of Br⁻ is more active than that of Cl⁻. The $k_{\text{VI-HBr}}/k_{\text{VI-H}_2\text{SO}_4}$ or $k_{\text{VI-HCl}}/k_{\text{VI-H}_2\text{SO}_4}$ ratio is 2.9 or 2.1, respectively, which is close to the $k_{\text{II-HBr}}/k_{\text{II-H}_2\text{SO}_4}$ or $k_{\text{II-HCl}}/k_{\text{II-H}_2\text{SO}_4}$ ratio, respectively. Thus, Br⁻ or Cl⁻ participates in the acidolysis of compound **II** with an activity similar to that in the acidolysis of compound **VI**. This is contrast to the acidolysis of compound **I**, in which the participation is less active than that in the acidolysis of compound **V**. A possible participation mode in the acidolysis of compound **II** or **VI** is that protonation at the double bond is concertedly assisted by the anti-attack of Br⁻ or Cl⁻ to the β -carbon without as well as with affording the discrete Br⁻ or Cl⁻ adduct.

The disappearance of compound **II** was slightly slower than that of compound **VI** in its acidolysis regardless of the acid types. For visualization, the ratio of the k_{obs} values between the acidolyses of compounds **II** and **VI** using HBr ($k_{\text{II-HBr}}/k_{\text{VI-HBr}}$), HCl ($k_{\text{II-HCl}}/k_{\text{VI-HCl}}$), or H₂SO₄ ($k_{\text{II-H}_2\text{SO}_4}/k_{\text{VI-H}_2\text{SO}_4}$) is calculated to be 1/1.2, 1/1.2, or 1/1.1, respectively. This slightly slower disappearance should be owing to the electron-withdrawal effect of the excess methoxy group in the syringyl nucleus of compound **II** substituting at the *meta*-position of the side chain (the Hammett substituent σ value: +0.115). When this relatively small effect is considered together with the above-described exclusive formation of **C β ⁺_{II}** or **C β ⁺_{VI}** in protonation at the double bond of compound **II** or **VI**, respectively, the double bond is considered to mesomerize with the lone pairs of the phenoxy oxygen more greatly than with the π -electron system of the 3,4,5-trimethoxyphenyl nucleus in compound **II** or 3,4-dimethoxyphenyl nucleus in compound **VI**. The relatively small effect should also be owing to another factor that the stability of **C β ⁺_{II}** or **C β ⁺_{VI}** is not largely affected by the types of aromatic nucleus in the backbone due to the absence of the delocalization of the cation to the aromatic nucleus. The three ratios close to one another suggest that the participation activity of Br⁻ or Cl⁻ is not different between the acidolyses of compounds **II** and **VI**, as

suggested in the previous paragraph. This is contrast to largely different participation activities in the acidolyses between compounds **I** and **V** ($k_{\text{I-HBr}}/k_{\text{V-HBr}}$: 1/15.2, $k_{\text{I-HCl}}/k_{\text{V-HCl}}$: 1/17.4, $k_{\text{I-H}_2\text{SO}_4}/k_{\text{V-H}_2\text{SO}_4}$: 1/3.4). Because the $k_{\text{II-H}_2\text{SO}_4}/k_{\text{VI-H}_2\text{SO}_4}$ ratio (1/1.1) is smaller than unity and larger than the $k_{\text{I-H}_2\text{SO}_4}/k_{\text{V-H}_2\text{SO}_4}$ ratio (1/3.4), the type of aromatic nucleus in the backbone can essentially have an effect on the acidolysis of compound **II** or **VI** as well as its analogues less great than that of compound **I** or **V** as well as its analogues.

The disappearance of compound **II** was much faster than that of compound **I** in its acidolysis regardless of the acid types, which is visualized by calculating the $k_{\text{II-HBr}}/k_{\text{I-HBr}}$, $k_{\text{II-HCl}}/k_{\text{I-HCl}}$, or $k_{\text{II-H}_2\text{SO}_4}/k_{\text{I-H}_2\text{SO}_4}$ ratio to be 11.2, 18.9, or 36.9, respectively. The ratios also show that the participation of Br⁻ or Cl⁻ accelerates the disappearance of compound **II** with an activity less great than that in the disappearance of compound **I** in its acidolysis, as described above. This ratio is much larger than the $k_{\text{VI-HBr}}/k_{\text{V-HBr}}$, $k_{\text{VI-HCl}}/k_{\text{V-HCl}}$, or $k_{\text{VI-H}_2\text{SO}_4}/k_{\text{V-H}_2\text{SO}_4}$ ratio (0.9, 1.3, or 12.4, respectively), regardless of the acid types. Thus, the difference in the disappearance rates between compounds **II** and **I** is much larger than that between compounds **VI** and **V**. This larger difference results in the observation described in the previous section that the accumulation of compound **II** in the acidolyses of compound **I** was smaller than that of compound **VI** in those of compound **V**. However, the former small accumulations may have also resulted from another possibility that compound **II** did not form as the primary product in the acidolyses of compound **I**, although our previous reports confirmed that almost all molecules of compound **V** primarily convert to compound **VI** [17, 22, 23]. This possibility can be evaluated on the basis of the k_{obs} values observed in the acidolyses of compounds **I** and **II**. In the acidolyses of compound **I**, the formation rate of compound **II** as a primary product is expressed by Eqs. (1) and (2) owing to the absence of the reconversion to compound **I**:

$$d[\text{II}]_t/dt = k_{\text{I(i)}}[\text{I}]_t - k_{\text{II}}[\text{II}]_t \quad (1)$$

$$k_{\text{I(i)}} + k_{\text{I(ii)}} = k_{\text{I}} \quad (2)$$

where $[\text{I}]_t$ or $[\text{II}]_t$ shows the concentration of each compound at a reaction time of t , k_{I} or k_{II} is the k_{obs} value of compound **I** or **II**, respectively, and $k_{\text{I(i)}}$ or $k_{\text{I(ii)}}$ corresponds to the rate constant for the reaction route of compound **I** via compound **II** or for the sum of all other routes, respectively. The solution of Eq. (1) draws a simulational curve for the formation of compound **II** in

the acidolysis of compound **I**. Figure 5 shows the simulational curves obtained by assuming $k_{I(i)}/k_{II(i)}$ ratios of 1.0, 0.75, 0.5, and 0.25 in the acidolyses of compound **I** using HBr and HCl with the experimental curves. The simulational curves are clearly closest to the corresponding experimental curves in a $k_{I(i)}/k_{II(i)}$ ratio of 1.0 in both acidolyses. Thus, almost all molecules of compound **I** primarily convert to compound **II** in the acidolyses of compound **I** using HBr and HCl. This is in accordance with the result in our previous reports as described above [17, 22, 23]. It is also suggested that the H^- transfer converting BC_I to $C\beta^+_{II}$ is just a minor route for BC_I in the acidolysis, similarly to the minority of the H^- transfer converting BC_V to $C\beta^+_{VI}$ shown in our previous reports [17, 18, 22, 23]. The simulational curve even in a ratio of 0.25 for the acidolysis of compound **I** using H_2SO_4 seemed to exceed the experimental curve (not shown in Fig. 5), possibly suggesting the existence of reaction routes in which compound **II** is not generated, although the reliability is quite low due to the tiny yield of compound **II**.

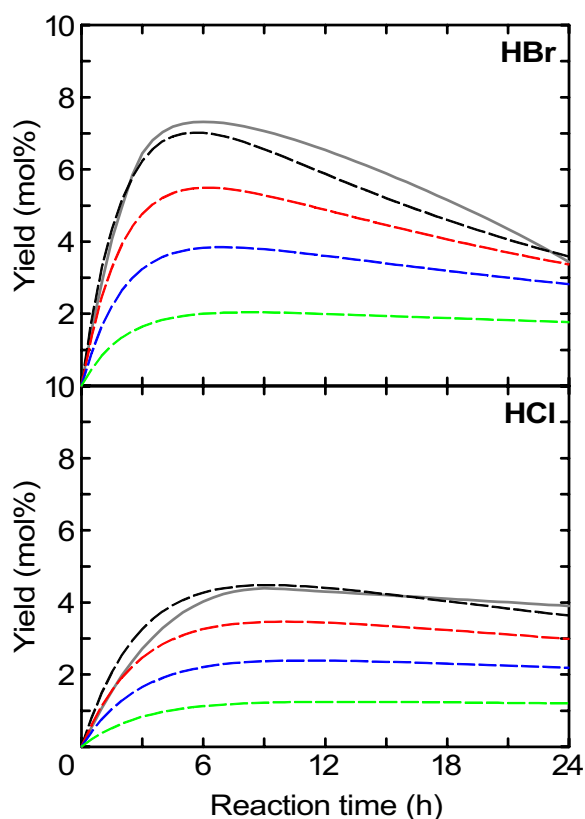


Fig. 5 Simulational curves for time-course changes in the yield of compound **II** as the primary product in the acidolysis of compound **I** using HBr (upper) or HCl (lower) when the ratios of $k_{I(i)}/k_{II(i)}$ are assumed to be 1.0 (black long broken line), 0.75 (red long broken line), 0.5 (blue long broken line), and 0.25 (green long broken line) with the experimentally obtained curve (gray solid line)

The ratio of the detected amounts between compounds **IIc** and **IIt** (IIc/IIt) decreases from 1.1 at a reaction time of 0 h to about 0.7 at the end of the reaction (6 h) in the acidolysis of compound **II** using HBr or HCl. This is the same tendency as the decrease of this ratio in the acidolyses of compound **I** using these acids, as described in the previous section. Thus, the decrease of the IIc/IIt ratio can be discussed similar to the content described in the previous section. The decrease is also the same tendency as our previous report which showed that the same type ratio, $VIc/VI t$, decreases during the acidolyses of compound **V** using these acids [23]. The $IIc/II t$ ratio at the initial, 1.1, seems to be maintained during the entire reaction when H_2SO_4 was used.

Acidolysis of compound **III** with the results obtained in the previous sections

Figure 6 shows the time-course changes in the recovery yields of compound **III** and yields of compounds **I**, **II**, and **IX** as well as **IIc** and **II t** in the acidolyses of compound **III**. The yield of compound **II** (as well as **IIc** and **II t**) in that using H_2SO_4 is not shown, because it was absent at most data points and sometimes detected with tiny amounts ($\leq 0.1\%$). The sum of the recovery yield of compound **III** and yields of compounds **I**, **II**, and **IX** was not largely deviated from 100% during the entire reaction in any acidolysis, suggesting that any acidolysis reaction was mostly quantitatively followed. The rate-determining step with respect to the disappearance of compound **III** is the CH_3OH liberation from CA_{III} to generated BC_I , because compound **III** is not naturally reproduced from BC_I .

Because BC_I primarily forms from compound **III**, which is not reproduced from BC_I , the acidolysis of compound **III** contributes to analyzing to which reaction mode BC_I preponderantly progresses. This cannot be examined in the acidolysis of compound **I** due to the reconversion of once-produced BC_I to compound **I**. These are reasons for employing the acidolysis of compound **III** in this study, although native lignin does not have any α -methoxy group.

Compound **I** was exclusively the major product regardless of the acid types, which shows that BC_I progresses much more preponderantly to the H_2O addition than to the other H^+ abstraction. All other minor routes are disregarded in the following discussion in this paragraph. The ratio of the initial formation rates between compounds **I** and **II** in the acidolysis of compound **III** can show how preponderant the H_2O addition is as a reaction mode of BC_I over the other H^+ abstraction. Their initial formation rates correspond to the slopes of the tangential lines to their formation curves drawn in Fig. 6 at the origin. The initial formation rate of compound **I** or **II** in the

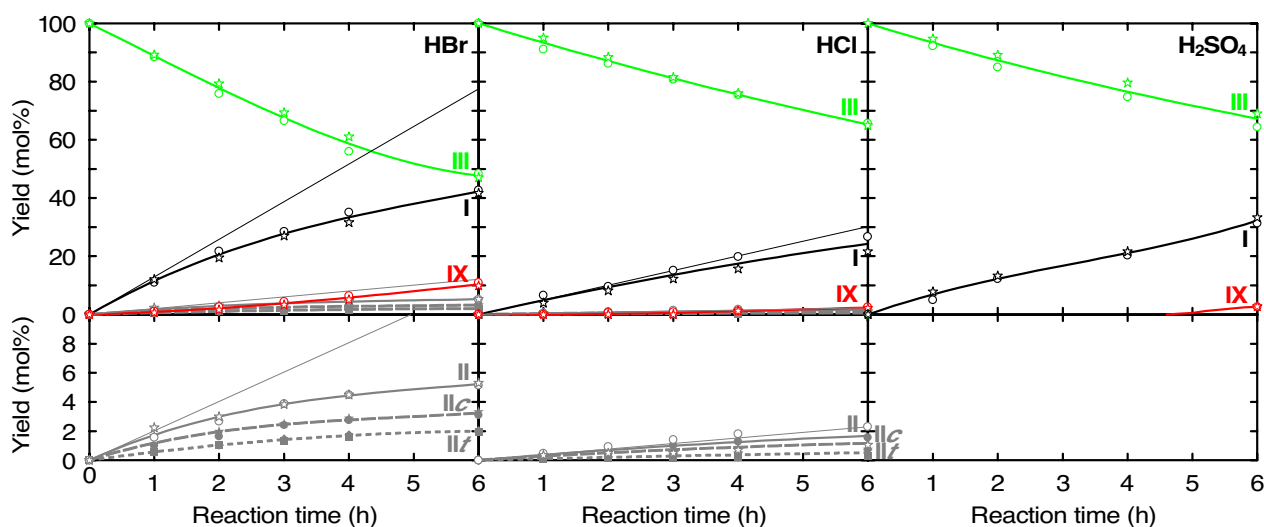


Fig. 6 Time-course changes in the recovery yield of compound **III** (green solid line with green contouring white marks) and yields of compound **I** (black solid line with black contouring white marks), **II** (gray solid line with gray contouring white marks), and **IX** (red solid line with red contouring white marks) as well as **IIc** (gray long broken line with gray marks) and **IIc** (gray dotted line with gray marks) in the acidolysis of compound **III** using HBr (left), HCl (middle), or H₂SO₄ (right). Circles and diamonds represent the 1st trial. Stars and squares represent the 2nd trial. The vertical axes in the lower figures are magnified by a factor of 5 for clearly showing the yields of compound **II**. The black and gray thin solid lines are tangents at the origin

acidolysis of compound **III** using HBr is 12.9 or 2.0%/h, respectively, with a ratio of 6.5 (**I/II**), although the formation curves may not completely follow the experimental data points for the entire reaction. This ratio is 13.2 or almost infinity in the acidolysis using HCl or H₂SO₄, respectively. The infinity is because compounds **II** and **IX** were not detected at all during the entire reaction in the acidolysis of compound **III** using H₂SO₄ except for the final data point. The preponderant degrees of the H₂O addition are thus in the order of the acidolyses using: HBr < HCl < H₂SO₄. The participation of Br⁻ or Cl⁻ leads **BC**₁ to the H⁺ abstraction mode, which is discussed in detail in the next section.

The ratio of the initial formation rates is 5.6, 11.9, or almost infinity when the same type ratio is calculated between compounds **V** and **VI** (**V/VI**) in the acidolysis of compound **VII** using HBr, HCl, or H₂SO₄, respectively, on the basis of the tangential lines drawn in the figure in our previous report showing the formations of compound **V** and **VI** in the acidolyses of compound **VII** [23]. The preponderance of the H₂O addition is thus greater in **BC**₁ than in **BC**_V in the acidolyses using HBr or HCl, whereas the H⁺ abstraction is almost inactive as a reaction mode of both **BC**₁ and **BC**_V in those using H₂SO₄. Because of this inactivity, the H⁻ transfer or another unknown reaction may be a major route in the acidolysis of compound **I** or **V** using H₂SO₄. In fact, the acidolysis of compound **I** using H₂SO₄ afforded compound **II** via **BC**₁ and the successive H⁺ abstraction with the amount that

seemed smaller than that even when only 25% of compound **I** was assumed to convert to compound **II** as the primary product, as described in the previous section, despite the quite low yield of compound **II** and hence its low reliability.

The disappearance rates of compound **III** in its acidolyses using the three acids, which correspond to the formation rates of **BC**₁ from it, were in the order: HBr > HCl ≈ H₂SO₄. For visualization, the $k_{\text{III-HBr}}/k_{\text{III-H}_2\text{SO}_4}$ or $k_{\text{III-HCl}}/k_{\text{III-H}_2\text{SO}_4}$ ratio is calculated to be 1.8 or 1.0, respectively, which confirms that Br⁻ participates in the CH₃OH liberation step, but the participation of Cl⁻ is not visible. In the acidolyses of compound **VII**, the $k_{\text{VII-HBr}}/k_{\text{VII-H}_2\text{SO}_4}$ or $k_{\text{VII-HCl}}/k_{\text{VII-H}_2\text{SO}_4}$ ratio is 1.9 or 1.1, respectively, which shows that the participation activity of Br⁻ or Cl⁻ is not largely different in the CH₃OH liberations between the acidolyses of compounds **III** and **VII**. A possible participation mode of Br⁻ is an assist in the CH₃OH liberation from **CA**_{III} or **CA**_{VII}, following the S_N2-type mechanism, with or without the discrete formation of the Br⁻ adduct. This participation should also contribute to the H₂O liberation from **CA**_I or **CA**_V in the acidolysis of compound **I** or **V**, respectively, with a similar activity, so that the $k_{\text{III-HBr}}/k_{\text{III-H}_2\text{SO}_4}$ (or $k_{\text{III-HCl}}/k_{\text{III-H}_2\text{SO}_4}$) ratio can be applied to the ratio of the presumptive rate constants with respect to the former halves (H₂O liberation from **CA**_I) in the acidolyses of compound **I** between HBr and H₂SO₄. The $k_{\text{VII-HBr}}/k_{\text{VII-H}_2\text{SO}_4}$ (or $k_{\text{VII-HCl}}/k_{\text{VII-H}_2\text{SO}_4}$) ratio can similarly be applied to

the acidolyses of compound **V**. When these presumptive ratios are considered with the $k_{\text{I-HBr}}/k_{\text{I-H}_2\text{SO}_4}$ (or $k_{\text{I-HCl}}/k_{\text{I-H}_2\text{SO}_4}$) and $k_{\text{V-HCl}}/k_{\text{V-H}_2\text{SO}_4}$ (or $k_{\text{V-HCl}}/k_{\text{V-H}_2\text{SO}_4}$) ratios, which correspond to the latter halves of the acidolyses of compounds **I** and **V**, the participation of Br^- (or Cl^-) is suggested to be less great in the former halves of the acidolyses of compounds **I** and **V** than in the latter halves. Because the participation in the CH_3OH or H_2O liberation must catalytically accelerate the formation of BC_I or BC_V , the equilibrated concentrations of BC_I or BC_V in the acidolyses of compound **I** or **V**, respectively, are not different between the acidolyses using the three acids.

The disappearance of compound **III** was faster than that of compound **I** in its acidolysis regardless of the acid types. For visualization, the $k_{\text{III-HBr}}/k_{\text{I-HBr}}$, $k_{\text{III-HCl}}/k_{\text{I-HCl}}$ or $k_{\text{III-H}_2\text{SO}_4}/k_{\text{I-H}_2\text{SO}_4}$ ratio is calculated to be 3.0, 4.0, or 15.7, respectively. Because it was shown in our previous report that the formation of the **BC** from a non-phenolic lignin model compound carrying an α -hydroxy group is about 7 times as fast as that from its α -methyl-etherified derivative regardless of solvent types [34], about the sevenfold of the $k_{\text{III-HBr}}/k_{\text{I-HBr}}$, $k_{\text{III-HCl}}/k_{\text{I-HCl}}$ or $k_{\text{III-H}_2\text{SO}_4}/k_{\text{I-H}_2\text{SO}_4}$ ratio (about 20, 30, or 110, respectively) can correspond to how faster the former half, the formation of BC_I , is than the latter half, the rate-determining step, in the acidolysis of compound **I**. These ratios suggest, similarly to the previous paragraph, that Br^- or Cl^- participates in the latter half of the acidolysis of compound **I** more greatly than in the former half to decrease the ratio from the essential, about 110, to about 20 or 30, respectively. The participation in the latter half is further discussed in detail in the next section.

The disappearance of compound **III** was slower than that of compound **VII** in its acidolysis examined in our previous report [23] regardless of the acid types. This shows that the formation of BC_I from compound **III** is slower than that of BC_V from compound **VII**. This is the same tendency as our previous report in which it was shown that the **BC** formation from a non-phenolic $\text{C}_6\text{-C}_1$ -type syringyl compound, 5-(2-hydroxyethoxymethyl)-1,2,3-trimethoxybenzene, is slower than that from the corresponding guaiacyl compound, 4-(2-hydroxyethoxymethyl)-1,2-dimethoxybenzene [31]. This slower degree in the report can be estimated to be 48.5 times at 85 °C. The formation of BC_I from compound **III** slower than that of BC_V from compound **VII** also suggests that the formation of BC_I from compound **I**, the former half of the acidolysis of compound **I**, is slower than that of BC_V from compound **V**, the former half of the acidolysis of compound **V**. These observations are rationally explained by the electron-withdrawal effect of the additional methoxy group

substituting at the *meta*-position of the side chain of compound **III** or **I** (Hammett substituent σ value: +0.115) on the α -carbon, the cation center of BC_I . For visualization, the $k_{\text{III-HBr}}/k_{\text{VII-HBr}}$, $k_{\text{III-HCl}}/k_{\text{VII-HCl}}$ or $k_{\text{III-H}_2\text{SO}_4}/k_{\text{VII-H}_2\text{SO}_4}$ is calculated to be 1/22.7, 1/24.4, or 1/20.9, respectively. These ratios can also be applied to that of the former halves, H_2O liberation, between the acidolyses of compounds **I** and **V**, similarly to the content of the previous paragraph. These ratios are not largely different, which indicates that the participation activities of Br^- as well as Cl^- are not largely different in the acidolyses between compounds **III** and **VII** and also in the former halves of those between compounds **I** and **V**. No large difference between these ratios is contrast to the large differences between the $k_{\text{I-HBr}}/k_{\text{V-HBr}}$, $k_{\text{I-HCl}}/k_{\text{V-HCl}}$ and $k_{\text{I-H}_2\text{SO}_4}/k_{\text{V-H}_2\text{SO}_4}$ ratios (1/15.2, 1/17.4, and 1/3.4, respectively), which are with respect to the latter halves in the acidolyses of compounds **I** and **V**. These ratios suggest, similarly to the previous paragraph, that the participation of Br^- (or Cl^-) in the former half is less great than in the latter half in the acidolyses of **I** or **V**. Because the $k_{\text{III-HBr}}/k_{\text{VII-HBr}}$, $k_{\text{III-HCl}}/k_{\text{VII-HCl}}$ or $k_{\text{III-H}_2\text{SO}_4}/k_{\text{VII-H}_2\text{SO}_4}$ ratio is larger than the above-described estimated ratio, 1/48.5, for the $\text{C}_6\text{-C}_1$ -type non-phenolic syringyl and guaiacyl compounds, the presence of the β -position, guaiacoxymethyl group, in compound **III** or **I** counteracts the electron-withdrawal effect from the syringyl nucleus.

Acidolysis of compound **IV** with the results in previous sections

Because the initial concentration of compound **IV** in the acidolysis solution was not completely clear due to the procedures described in the “Acidolytic treatment” section, ratios of detected amounts between compounds **I** and **II** (**I/II**) are targeted in this section and listed in Table 2. Because the acidolysis was conducted for the short period (3 min), once-generated compounds **I** and **II** remained unreacted. Compound **IV** seemed to still remain with roughly less than or more than the half of the initial amount in the acidolysis using HBr or H_2SO_4 , respectively, at a reaction time of 10 s. Compound **III** was generated from remaining compound **IV**

Table 2 Ratios of the detected amounts of compound **I** to **II** in the acidolyses of compound **IV** using HBr and H_2SO_4 obtained in this report and those of compound **V** to **VI** in the acidolyses of compound **VIII** using HBr and H_2SO_4 shown in our previous report [23]

I/II	V/VI	
	HBr	H_2SO_4
5.7	31.9	10.4

in the post-treatment in the CH_3OH solution containing NaOCH_3 at 0°C , and detected in the HPLC analysis instead of compound **IV**. Because our previous report showed that compound **VIII** has already disappeared completely at a reaction time of 10 s [23], compound **IV** is more stable than compound **VIII** owing to the formation of BC_1 slower than that of BC_V , as frequently discussed above. Although the post-treatment was conducted, compound **III** was not detected after the reaction for 3 min.

As shown in Fig. 7, compound **IV** undergoes two reaction modes: “the HBr elimination” to convert to compound **II**; “the Br^- liberation” to be BC_1 . BC_1 further undergoes three reaction modes: “the H^+ abstraction” from the β -carbon to convert to compound **II**; “the H_2O addition” to convert to compound **I** via CA_1 ; “the Br^- addition” to revert to compound **IV** with repetitively undergoing “the HBr elimination” and “the Br^- liberation”, which is more preferable in the acidolysis using HBr than in that using H_2SO_4 . The application of HBr directly promotes only “the Br^- addition” among all the 5 modes when compared with that of H_2SO_4 , but consequently and indirectly “the HBr elimination” rather than “the Br^- liberation”. The only direct promotion of “the Br^- addition” in the acidolysis using HBr is because of the following facts: among the other 4 modes, “the Br^- liberation” and “the H_2O addition” are competitively suppressed by the application of HBr; the other “the HBr elimination”

and “the H^+ abstraction” are sensitive to the basicity of the acidolysis system; the basicities are not different between the acidolyses using HBr and H_2SO_4 , because the counter anions, Br^- and HSO_4^- , are weaker bases than the solvents, whose amounts are huge in the acidolysis solutions.

The ratio of the detected amounts between compounds **I** and **II** (**I/II**) was 5.7 or 31.9 in the acidolysis of compound **IV** using HBr or H_2SO_4 , respectively (Table 2). These ratios indicate that compound **IV** undergoes both “the HBr elimination” and “the Br^- liberation”, because these ratios would be 0 or infinity when compound **IV** progresses only to either “the HBr elimination” or “the Br^- liberation”, respectively, on the basis of the discussion described in the previous paragraph. The ratio, 31.9, shows that the most preferable route for compound **IV** is exclusively “the Br^- liberation” followed by “the H_2O addition” to convert to compound **I**. The presence of the large amount of Br^- in the acidolysis using HBr enhances “the Br^- addition”, resulting in the indirect activation of “the HBr elimination” to afford compound **II** and the relatively small ratio, 5.7 (Table 2). Because compound **IV** certainly progresses to “the HBr elimination”, the route from BC_1 to compound **II** via compound **IV** in the acidolysis of compound **I** using HBr at least partly functions as a bypass of the direct route from BC_1 to compound **II**, the rate-determining step of the acidolysis. However, because the **V/VI** ratio is 4.5 or 10.4 in

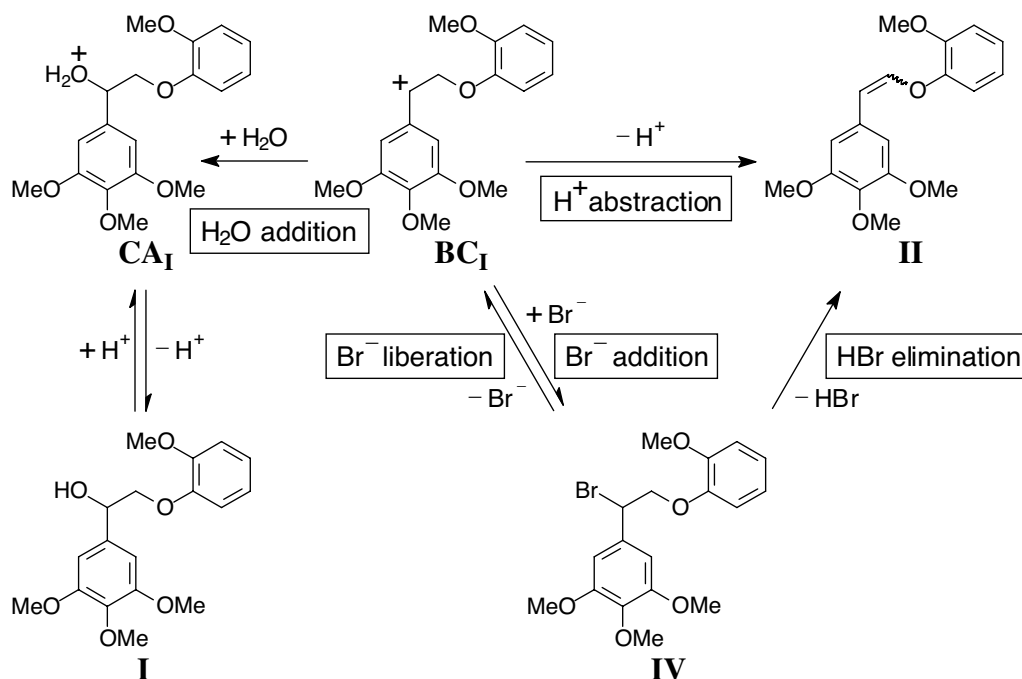
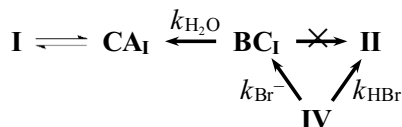


Fig. 7 Two reaction modes of compound **IV**, “the HBr elimination” and “the Br^- liberation”, and three reaction modes of BC_1 , “the H^+ abstraction”, “the H_2O addition”, and “the Br^- addition”, in the acidolysis of compound **IV**

the acidolysis of compound **VIII** using HBr or H₂SO₄, respectively (Table 2), as shown in our previous report [23], the bypass functions less actively in the acidolysis of compound **I** using HBr than in that of compound **V** using HBr. The bypass activities are further discussed in the next paragraphs.

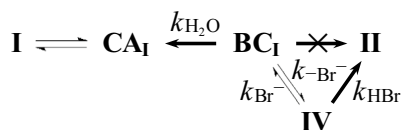
As shown in the previous section, compound **II** was not detected at all mostly during the entire reaction in the acidolysis of compound **III** using H₂SO₄. This indicates that the progress of **BC_I** to “the H⁺ abstraction” is invisible due to its relatively extreme slowness. It is thus presumed that **BC_I** generated from compound **IV** via “the Br⁻ liberation” hardly progresses to “the H⁺ abstraction” to be compound **II** also in the acidolysis of compound **IV** using H₂SO₄. This presumption suggests that the **I/II** ratio in this acidolysis, 31.9, mostly corresponds to the ratio of the rate constants between “the Br⁻ liberation” (k_{Br^-}) and “the HBr elimination” (k_{HBr}). On the basis of this suggestion, the acidolysis is schematically illustrated in the following formula, in which the “ $k_{\text{H}_2\text{O}}$ ” shows the rate constant with respect to “the H₂O addition.” Equation (3) is established from the above described **I/II** ratio, 31.9.



In the acidolysis of compound **IV** using H₂SO₄

$$k_{\text{Br}^-}/k_{\text{HBr}} = 31.9 \quad (3)$$

In the acidolysis of compound **IV** using HBr, “the Br⁻ addition” is activated, which is schematically illustrated in the following formula. The **I/II** ratio in the acidolysis, 5.7, is expressed by Eq. (4). Because a steady-state can be presumed for the formation of **BC_I**, Eq. (5) with respect to the steady-state can be described. In these equations, k_{Br^-} , $[\text{BC}_\text{I}]$, and $[\text{IV}]$ show the rate constant with respect to “the Br⁻ addition”, concentration of **BC_I**, and that of compound **IV**, respectively.



In the acidolysis of compound **IV** using HBr

$$k_{\text{H}_2\text{O}}[\text{BC}_\text{I}]/k_{\text{HBr}}[\text{IV}] = 5.7 \quad (4)$$

$$d[\text{BC}_\text{I}]/dt = k_{\text{Br}^-}[\text{IV}] - k_{\text{H}_2\text{O}}[\text{BC}_\text{I}] - k_{\text{Br}^-}[\text{BC}_\text{I}] = 0 \quad (5)$$

When Eqs. (3), (4), and (5) are arranged, Eq. (6) is obtained as the correlation between $k_{\text{H}_2\text{O}}$ and k_{Br^-} .

$$k_{\text{Br}^-}/k_{\text{H}_2\text{O}} = 4.6 \quad (6)$$

When the same discussion is applied to the acidolysis of compound **VIII** using H₂SO₄ and HBr, the correlations between the rate constants are shown as Eqs. (7) and (8).

$$k_{\text{Br}^-}/k_{\text{HBr}} = 10.4 \quad (7)$$

$$k_{\text{Br}^-}/k_{\text{H}_2\text{O}} = 1.3 \quad (8)$$

On the basis of Eqs. 3), (6), (7), and (8), the following bypass activity can be presented when a specific amount of **BC_I** or **BC_V** is assumed to be the starting substrate in the acidolysis using HBr: 2.5% or 5.0%, respectively, converts to compound **II** or **VI**, respectively, via the bypass, while 97.5% or 95.0%, respectively, progresses to “the H₂O addition” to afford compound **I** or **V**, respectively. Thus, the bypass activity in the acidolysis of compound **I** using HBr is the half of that in the acidolysis of com-

pound **V** using HBr.

The relative bypass activity corresponds to the ratio of the rate constants in the latter halves between the acidolyses of compounds **I** and **V** using HBr without any influence from the former halves. On the other hand, the $k_{\text{I-HBr}}/k_{\text{V-HBr}}$ ratio, 1/15.2, includes the effects of the former halves on the latter halves, viz. the different equilibrated concentrations between **BC_I** or **BC_V**. Therefore, in considering the relative bypass activity with the $k_{\text{I-HBr}}$

$k_{\text{V-HBr}}$ ratio (1/15.2), the equilibrated concentration of **BC_I** in the acidolysis of compound **I** can be estimated to be 1/7.6 times of that of **BC_V** in the acidolysis of compound **V**. The $k_{\text{I-HCl}}/k_{\text{V-HCl}}$ ratio, 1/17.4, possibly suggests that the bypass activity in the acidolysis of compound **I**

using HCl is 2.3 times lower than that in the acidolysis of compound **V** using HCl. Incidentally, the equilibrated concentration of **BC_I** or **BC_V** is independent of the acid types.

Because the progress of **BC_I** or **BC_V** to “the H⁺ abstraction” is invisible in the acidolysis of compound **I** or **V** using H₂SO₄, respectively, as described in the previous section, the H⁻ transfer or another unknown reaction may be a major mode for **BC_I** or **BC_V**. Because the $k_{I-H_2SO_4}/k_{V-H_2SO_4}$ ratio, 1/3.4, is larger than the estimated ratio of the equilibrated concentrations between the acidolyses of compounds **I** and **V** (1/7.6), the H⁻ transfer or another unknown mode in the acidolysis of compound **I** using H₂SO₄ may possibly be 2.2 times faster than in that of compound **I** using H₂SO₄.

Compound **IIc** formed more preferably than compound **IIt** in the acidolysis of compound **I** using HBr or HCl, as shown and discussed in the “Acidolysis of compound **I**” section, although the more preferable formation of the latter should be observed when compound **II** forms directly from **BC_I** via “the H⁺ abstraction”. Thus, the more preferable formation of compound **IIc** suggests, as also described above, that compound **II** forms mostly via the bypass in which “the HBr elimination” occurs from compound **IV** following the E2 mechanism, which always prefers the anti-orientation. Two staggered conformers among three with respect to the covalent bond between the α - and β -carbons are suitable for this anti-elimination, as illustrated in Fig. 8. One of these two is the precursor of compound **IIc** and thermodynamically more stable owing to a stereoelectronic effect, the gauche effect. This effect originates both from the delocalizations of two electron pairs: the pair present in the bonding orbital of the bond between the β -carbon and hydrogen present at the antiperiplanar of the bromine to the empty anti-bonding orbital of the bond between the α -carbon and bromine; that present in the bonding orbital of the bond between the α -carbon and hydrogen present at the antiperiplanar of the phenoxy group to the empty

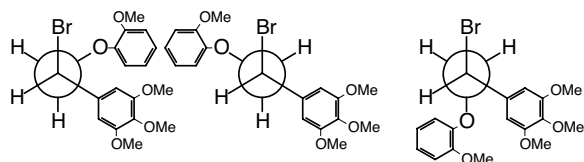


Fig. 8 Three staggered conformations with respect to the covalent bond between the α - and β -carbons of compound **IV**, among which the leftmost and middle exclusively progress to “the HBr elimination” to convert to compounds **IIc** and **IIt**, respectively. Although the steric factor is larger in the leftmost conformation than the middle, the leftmost is thermodynamically more stable owing to a stereoelectronic effect, the gauche effect, described in the text

anti-bonding orbital of the bond between the β -carbon and phenoxy oxygen. Only the former delocalization exists in the other conformation that is the precursor of compound **IIt**. The existence of the above-described two delocalizations thermodynamically stabilizes the former conformation, although its steric factor is larger than the latter.

Conclusions

Compound **I**, a non-phenolic syringyl-type compound, as well as its derivatives was acidolyzed for quantitatively analysis. The results were compared with those obtained from the same acidolysis of compound **V**, the guaiacyl analogue of compound **I**, as well as its derivatives conducted in our previous reports [17–25].

The disappearance of compound **I** in its acidolysis was slower than that of compound **V** in its acidolysis regardless of the acid types. It was thus confirmed that syringyl β -O-4-type substructures are acidolyzed more slowly than the guaiacyl analogues. The disappearance rates of compound **I** were dependent on the acid types and in the order: HBr > HCl > H₂SO₄, which shows the participation of Br⁻ or Cl⁻ in the acidolysis, similarly to the acidolysis of compound **V**. However, the participation activity was less great than that in the acidolysis of compound **V**.

The disappearance of compound **II** in its acidolysis was slower than that of compound **VI**, the guaiacyl analogue of compound **II**, in its acidolysis. The difference in the rates between compounds **II** and **VI** was smaller than that between compounds **I** and **V**, which resulted in the accumulation of compound **II** in the acidolysis of compound **I** smaller than that of compound **VI** in the acidolysis of compound **V**. It was confirmed that compound **II** exclusively forms as the primary product in the acidolysis of compound **I** using HBr or HCl, similarly to the exclusive formation of compound **VI** as the primary product in the acidolysis of compound **V** using these acids shown in our previous report.

The disappearance of compound **III** in its acidolysis, viz. the formation rate of **BC_I** from compound **III**, was slower than that of compound **VII**, the guaiacyl analogue of compound **III**, in its acidolysis, viz. the formation rate of **BC_V** from compound **VII**. The H₂O addition was the most preponderant reaction mode for **BC_I**, similarly to **BC_V** regardless of the acid types. Because **BC_I** or **BC_V** did not seem to progress to the route to afford compound **II** or **VI**, respectively, in the acidolysis of compound **I** or **V** using H₂SO₄, respectively, due to the extreme preponderance, the H⁻ transfer or an unknown reaction may be a major route. The participation of Br⁻ was confirmed in the formation of **BC_I** from compound **III**, although that of Cl⁻ was invisible.

The acidolysis of compound **IV** using HBr or H₂SO₄ confirmed that Br⁻ adds to the cation center of BC₁ to be compound **IV** that progresses to the HBr elimination to be compound **II** as the bypass of the direct route from BC₁ to compound **II** in the acidolysis of compound **I** using HBr, similarly to the acidolysis of compound **VIII** conducted in our previous report. The presence of the bypass accelerates the acidolysis of compound **I** using HBr as well as HCl relatively to that using H₂SO₄. It was also suggested that the bypass activity in the acidolysis of compound **I** is the half in that of compound **V**.

Acidolysis of syringyl lignin has thus been confirmed to be fairly slower than that of guaiacyl lignin. This slower acidolysis should be considered when reaction conditions are specified in acidolysis of hardwood.

Abbreviations

BC _x	Benzyl cation intermediate derived from compound x
BC	Benzyl cation intermediate without specifying the origin
CA _x	Conjugate acid generated by protonation at the oxygen of the α -hydroxy group of compound x
C β^+ _x	Oxycarbocation at the β -position generated by protonation at the double bond of compound x

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Author contributions

RM and KK conducted the experiments. RM, KK, and TK analyzed the obtained data and wrote the draft of this manuscript under the supervision of TY. TY completed the final manuscript. All the authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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