Influence of Nucleophiles on the High Temperature Aqueous Isomerization of *cis*- to *trans*-Cinnamic Acid

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The rate of isomerization of *cis*- to *trans*-cinnamic acid in water at 195 °C was monitored as a function of added nucleophile. The expected nucleophile addition products were not observed but could be synthesized and, when subjected to the reaction conditions, rapidly converted to *trans*-cinnamic acid. Deuterium labeling studies indicated that proton abstraction was not the rate-determining step, that the α-deuterium of α,β-dideuterio-*cis*-cinnamic acid was rapidly exchanged for an α-hydrogen atom without loss of the cis geometry, and that some direct isomerization of *cis*- to *trans*-cinnamic acid occurred without the loss of vinyl deuterium atoms. The isomerization appears to involve an addition-elimination mechanism in the case of HO^- and HS^- ions, with the former more effective. Anthrahydroquinone ion was quite effective, meaning that it was a superior nucleophile or was promoting reactions by another mechanism (possibly electron transfer chemistry). The results have bearing on the rate-determining step in one of the delignification mechanisms occurring during the pulping of wood.

Introduction

Chemical pulping involves heating wood chips in aqueous sodium hydroxide at 170 °C with the goal being to free the carbohydrate fibers from the lignin component. Delignification is aided by the hydrosulfide ion (kraft process) and anthrahydroquinone ion (AQ process). These ions, together with hydroxide ion, have been proposed to promote pulping because of their nucleophilic character.[1] Yet, nucleophilicities of these species at 170 °C in water have not been systematically studied. This and the companion study[2] address nucleophilicities of these ions at high temperatures.

The relative effectiveness of ions to promote the rate of dissolution of lignin from wood follows the order anthrahydroquinone dianion (AHQ^{2-}) > hydrosulfide ion (HS^-) ≫ hydroxide ion (HO^-).[1] The research described here addresses the issue of whether this order follows the nucleophilicity of the ions toward a carbonyl-conjugated olefin, a hypothesized step in the delignification mechanism.[1] The carbonyl-conjugated olefin of lignin is a highly unstable quinone methide intermediate, a material which is not easy to study directly. The rate of addition of nucleophiles to *cis*-cinnamic acid, reflected by the rate of isomerization of *cis*- to *trans*-cinnamic acid, was therefore selected to model the reactions of nucleophiles with quinone methides. The research uncovered an unusual property of the isomerization reaction of cinnamic acids.

The nucleophilicity of an ion is not an intrinsic property but depends on the type of substrate under attack, the type of solvent used in the reaction, and the reaction temperature.[3] At room temperature, hydrosulfide ion is seven times more reactive than hydroxide ion in replacing the bromine of methyl bromide (saturated carbon).[4] However, hydroxide ion is a stronger nucleophile than hydrosulfide ion toward a carbonyl carbon (unsaturated carbon). Polarizability of the nucleophile is important during reactions at a saturated carbon center, while basicity is important during reactions at an unsaturated carbon center.[5-7]

Solvation of the nucleophile is a key factor in determining reactivity. Nucleophilic reactions typically proceed much faster in dipolar aprotic solvents than in polar solvents.[8] In the gas phase, where absolute reaction rates are very high, oxyanions are more nucleophilic than sulfur analogs toward saturated carbon centers[9,10] and unsaturated carbon centers.[11] In gas-phase reactions of methyl bromide, HO^- is 10 000 times more reactive than HO^- which is hydrated with three water molecules. There is a further difference of 10^{12} between the latter gas-phase hydrated ion and solution-phase cases.[12] The effects of solvation on nucleophilic properties of ions in water at high temperatures (170-200 °C) are not known but should be intermediate between room temperature water solutions and gas-phase conditions.

The conversion of *cis*- to *trans*-cinnamic acid by way of a nucleophile addition/elimination is shown in Scheme I. In order for this reaction to be a suitable model for investigating nucleophilic addition, the slow step should be the addition step. If either rearrangement or elimination is the slow step, the resulting rate constant will probably not reflect the nucleophilicity of the reagent.

Results

Product Studies. The isomerization of *cis*- to *trans*-cinnamic acid (1) was investigated in oxygen-free water solutions containing hydroxide, hydrosulfide, and anthrahydroquinone ions. Reagent concentrations were kept near or below 1 M to minimize byproduct formation and

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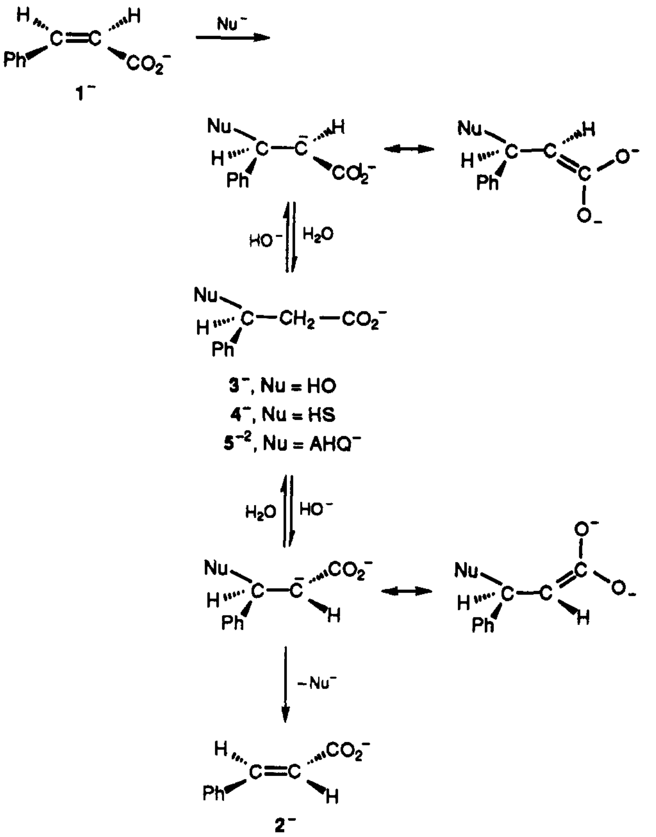
Scheme I



to more closely parallel that used in pulping systems. Temperatures of 195 °C were employed to get reasonable reaction rates. The reactions were followed by gas chromatographic (GC) techniques. The identity of each product was confirmed by comparing its GC and GC–mass spectrometric (GC-MS) properties to a synthesized or purchased sample.

Compound **1** was heated in aqueous sodium hydroxide at 195 °C. The major product after 8 h was *trans*-cinnamic acid (**2**). In a separate study, we observed less than 1% conversion of *trans*- to *cis*-cinnamic acid over an 8-h period at 195 °C in NaOH solutions. Obviously, the trans isomer is much more stable than the cis isomer; the cis-to-trans isomerization is not very reversible.

A mass balance, obtained by adding the observed amounts of *cis*- and *trans*-cinnamic acids and comparing the amount to the starting levels of each, was quite good—about 92% recovery after 8 h (Figure 1). Small amounts (~3%) of benzaldehyde and benzoic acid, identified by GC-MS, account for some of the lost material balance at longer reaction times. Both byproducts were also formed by heating *trans*-cinnamic acid in aqueous sodium hydroxide. The intermediate adduct **3**, corresponding to the addition of water to cinnamic acid, was not detected. In the 15 min that it takes to heat from room temperature to 195 °C, a synthesized sample of **3** was completely converted to *trans*-cinnamic acid in aqueous NaOH; therefore, adduct **3** could be an unstable intermediate in the isomerization reaction.

cis-Cinnamic acid (**1**) was also isomerized to *trans*-cinnamic acid (**2**) in aqueous sodium sulfide at 195 °C. Under the conditions employed, sodium sulfide is effectively hydrolyzed to one molecule of sodium hydrosulfide and one molecule of sodium hydroxide (eq 1).[13,14]

$$Na_2S + H_2O \rightleftarrows NaSH + NaOH \qquad (1)$$

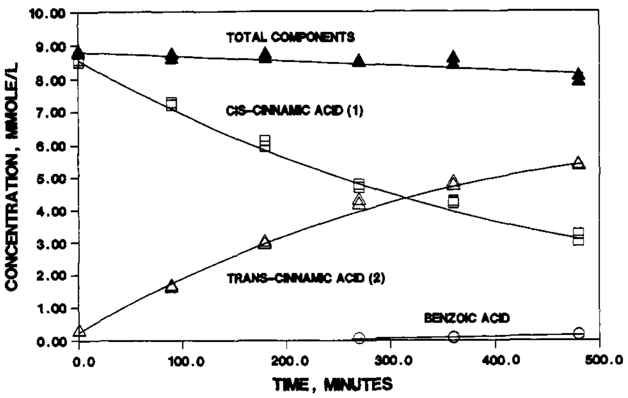
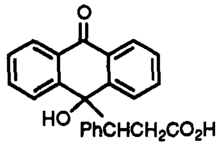


Figure 1. Mass balance for the reaction of **1** in 0.787 M NaOH at 195 °C.

If an addition/elimination mechanism is operating, the hydrosulfide adduct **4** (Scheme I) would be an intermediate. Adduct **4** was not detected by GC-MS; an authentic sample of **4** was found to rapidly degrade to **2** under the employed reaction conditions. The material balance was nearly constant (similar to that shown in Figure 1); benzaldehyde and benzoic acid were again present in small amounts.

Compound **1** was heated in solutions containing hydroxide and anthrahydroquinone ions at 195 °C. The major product of the reaction was *trans*-cinnamic acid (**2**). The material balance for *cis*- and *trans*-cinnamic acid was ~85% after 8 h; some of the incomplete balance was a result of increases in benzaldehydes and benzoic acid to ~6% at long reaction times. The anticipated addition/elimination mechanism (Scheme I) should produce an intermediate adduct (**5**), which was not observed in the reaction mixture. An authentic sample of the lactone of **5** was not stable under the employed reaction conditions and was rapidly converted to **2** and ~25% undetectable products.



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Isomerization of Deuterium-Labeled Cinnamic Acids. At 195 °C proton abstraction of the olefinic hydrogen atoms may occur; hydroxide ion has been shown to be a very strong base at 170 °C.[13] Scheme II presents a possible base-induced isomerization mechanism, via intermediates or transition states 6^{-2} and 7^{-2}. The role of proton abstraction in promoting isomerization was investigated by examining the reactions of α,β-dideuterio-*cis*- and -*trans*-cinnamic acid (**1**- and **2**-α,β-d_2).

If proton abstraction was the rate-determining step for the isomerization of **1** to **2**, then the ratio of the reaction for the nondeuterated compound to that of a vinyl deuterated analog would be approximately 3–8 (primary

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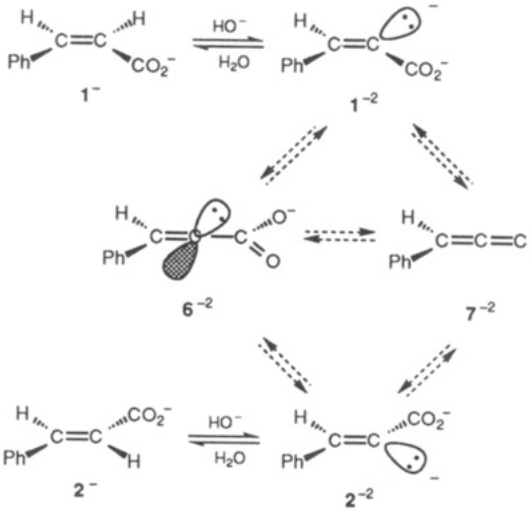
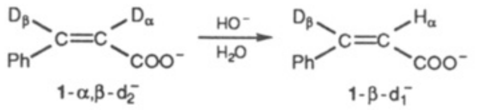
Scheme II



isotope effect).[3] If, however, nucleophilic addition was the rate-determining step, then a ratio of 0.8–1.2 would be expected (secondary isotope effect).[3] Isotope effects often do not change drastically with changes in temperature;[3] however, an expected range of values cannot be predicted with certainty since a close analogy to the system was not available. Finally, detection of α,β-dideuterio-*trans*-cinnamic acid during the degradation of α,β-dideuterio-*cis*-cinnamic acid would indicate that proton abstraction is not the pathway which caused cis–trans isomerization.

The rate of disappearance of **1**-α,β-d$_2$ with NaOH at 195 °C was only slightly slower than that of the nondeuterated analog; the observed k_H/k_D was 1.07 over an 8-h reaction period. This result agrees with a secondary isotope effect, indicative of an addition–elimination mechanism. A rapid exchange of one deuterium atom was also observed (mass spectroscopy). Proton NMR techniques showed that the α-deuterium atom was exchanged (eq 2). These two results seemed contradictory to each other, unless proton abstraction is occurring but is not responsible for cis-to-trans isomerization.



(2)

The exchange rates of **1**-α,β-d$_2$ and **2**-α,β-d$_2$ at 195 °C were then investigated in more detail (Figure 2). After 30 min, nearly all of α,β-dideuterio-*cis*-cinnamic acid (**1**-α,β-d$_2$) was converted to β-deuterio-*cis*-cinnamic acid (**1**-β-d). The rate of deuterium loss from α,β-dideuterio-*trans*-cinnamic acid (**2**-α,β-d$_2$) was considerably slower. The site of exchange in the trans isomer was the same (α-deuterium) as that in the cis isomer. Since the trans exchanged more slowly than the cis, it should be possible to observe production of **2**-α,β-d$_2$ during the reactions of **1**-α,β-d$_2$ if addition–elimination was the mode of isomerization.

The concentrations of both mono- and dideuterio species of the cis and trans isomers were determined during the reaction of **1**-α,β-d$_2$ in aqueous NaOH at 195 °C (Figures 3 and 4). It should be noted that the sample of **1**-α,β-d$_2$ contained a small amount of **2**-α,β-d$_2$ impurity. During the initial phase of *cis*- to *trans*-cinnamic acid isomerization at 195 °C of the deuterated substrate, the level of **2**-α,β-d$_2$ increased slightly (Figure 4). The isomerization was done several times, with the same initial increase in **2**-α,β-d$_2$ observed in each case.

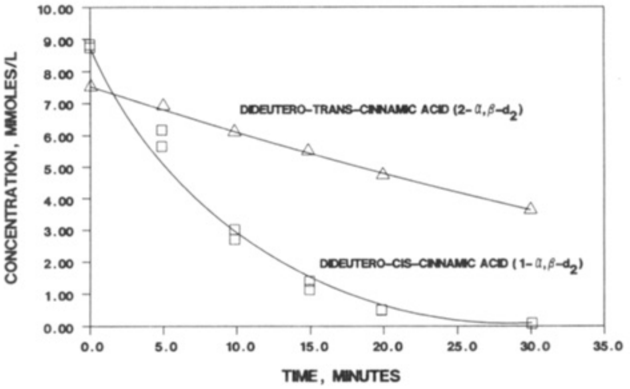


Figure 2. Comparison of the rate of exchange of the α-deuterium atom in **1**-α,β-d$_2$ and **2**-α,β-d$_2$ in 1.19 M NaOH at 195 °C.

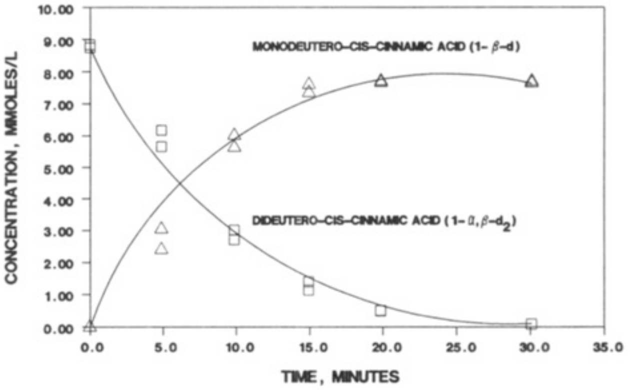


Figure 3. Analysis of *cis* components from the reaction of **1**-α,β-d$_2$ in 1.19 M NaOH at 195 °C.

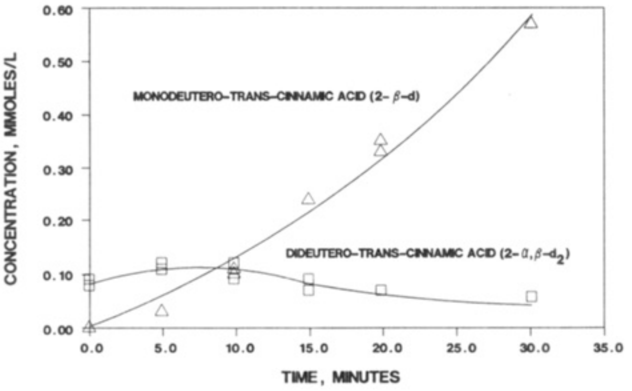


Figure 4. Analysis of *trans* components from the reaction of **1**-α,β-d$_2$ in 1.19 M NaOH at 195 °C.

The production of **2**-α,β-d$_2$ leveled off and decreased as the isomerization proceeded. There are two reasons why the concentration of **2**-α,β-d$_2$ does not continually increase. First, the starting material (**1**-α,β-d$_2$) leading to the **2**-α,β-d$_2$ is rapidly disappearing; it is undergoing rapid C_α-D,H exchange to give 1-β-d$_1$ (Figure 3), which then limits the amount of **1**-α,β-d$_2$ available for isomerization to 2-α,β-d$_2$. Second, once formed, **2**-α,β-d$_2$ also loses one deuterium, via an alkali-induced solvent exchange reaction, giving rise to 2-β-d. Using the data in Figure 1 and the rate data developed below, we were able to model the expected reaction profile for the formation of **2**-α,β-d$_2$ from **1**-α,β-

d_2 and found quite close agreement between the calculated and observed (Figure 4) profile.

The observed steady increase in the levels of 2-β-d (Figure 3) can be explained by (a) an increased level of β-deuterio-*cis*-cinnamic acid undergoing isomerization to β-deuterio-*trans*-cinnamic acid and (b) the slow conversion of 2-α,β-d_2 to 2-β-d. If proton abstraction was the mechanism of the cis–trans isomerization, there would have been an immediate decrease in concentration of 2-α,β-d_2, similar to that seen in Figure 2.

Relative Reaction Rates. 1. Qualitative Assessment. Compound 1 was heated at 194 °C in oxygen-free aqueous solutions which had constant ionic strengths and contained hydroxide, hydrosulfide, and anthrahydroquinone ions. Examples of four kinetic runs are given in Figure 5. In general, duplicate samples were collected at five reaction times.

The isomerization of *cis*- to *trans*-cinnamic acid was fastest in the presence of AHQ, even though the concentration of AHQ was much less than that of the other ions. The isomerization in 0.8 M NaOH was more rapid than for the combination of 0.4 M NaOH and 0.4 M NaSH. Clearly, the order of reactivity was $AHQ^{-2} > HO^- > HS^-$.

2. Detailed Kinetic Treatment. The concentrations of the nucleophiles (10–100 equiv) essentially remained constant throughout the reaction period, which allowed use of pseudo-first-order rate expressions.[15] The second-order rate constants for the disappearance of reactant were calculated from eq 3, where $[HO^-]$ = concentration of

$$k_r = k_{HO}[HO^-] + k_{HO'}[HO^-]^2 + k_{Add}[Add] + k_{Add'}[Add]^2 + k_{Add/HO}[Add][HO^-] \quad (3)$$

hydroxide ion (M), [Add] = concentration of additive (M), k_r = rate constant for the disappearance of reactant (s^{-1}), k_{HO} = rate constant associated with hydroxide ion (M^{-1} s^{-1}), and k_{Add} = rate constant associated with the additive (M^{-1} s^{-1}).

Triplet runs were performed for each of the principal reagents (NaOH, NaOH/NaSH, and NaOH/AHQ) and the results averaged. The R^2 value, which measures the goodness of the fit between data and the calculated regression line, was 0.99 for all of the triplet kinetic runs. Also, 95% confidence limits were determined in each case and are incorporated into the rate constant values.

To get adequate temperature control and to insure safety, we followed the reactions closely and restricted reaction times to 8 h or less. Depending on the additive, only about 45–65% isomerization had occurred in 8 h. We observed kinetic orders between 1.0 and 1.2 for NaOH and the additives and assumed a tentative order of 1 in each case; however, the accuracy suffers when determining a kinetic order for only 1 half-life.[15] Reactant concentrations were corrected for thermal expansion of the solutions.

The observed rate constants varied with the level of NaOH present in the reaction mixture; a fact which complicated the calculations of the individual rate constants of each reactant.

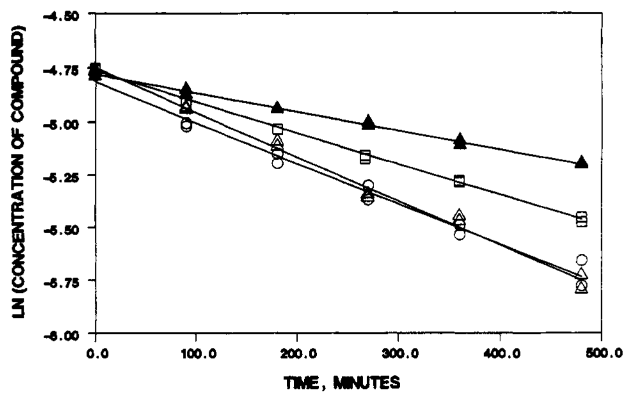


Figure 5. Concentration vs time profiles for reactions of 1 at 195 °C in water with 0.79 M NaOH, △; 0.39 M NaOH and 0.39 M NaCl, ▲; 0.39 M NaOH and 0.39 M NaSH, □; 0.44 M NaOH and 0.12 M AHQ, ○.

3. Hydroxide Reactions. Two NaOH concentrations at constant ionic strength (Figure 5) and another at 1.03 M NaOH (as part of the kinetic isotope study) were examined. The k_{HO} rate constant increased with increasing NaOH concentration. Plotting $k_r/[HO^-]$ vs $[HO^-]$ gave a straight line (Figure 6), from which k_{HO} and $k_{HO'}$ were obtained from the intercept and slope, respectively, according to eq 4. Equation 4 comes from dividing eq 3 by $[HO^-]$ and dropping the additive terms. This analysis

$$k_r/[HO^-] = k_{HO} + k_{HO'}[HO^-] \quad (4)$$

$$k_{HO} = 2.7 \times 10^{-5}\ M^{-1}\ s^{-1};\ k_{HO'} = 2.3 \times 10^{-5}\ M^{-2}\ s^{-1}$$

implies that there are two mechanisms of base-promoted isomerization: a dominant mechanism, first order in HO^-, and a minor mechanism, second order in HO^-. The reaction order for the NaOH-promoted isomerization was determined to be 1.2.

4. Hydrosulfide and Related Sulfur Compound Reactions. Isomerizations were performed at 195 °C in the presence of sodium sulfide. An analysis similar to that described above was performed. For three of the kinetic runs, $[HS^-] = [HO^-]$. Setting $[X^-] = [HS^-] = [HO^-]$ and dividing eq 3 by $[X^-]$ gives eq 5. A plot of $k_r/[X^-]$ vs $[X^-]$ gives a straight line (Figure 6), from which k_{HS} and $k_{HS'} + k_{HS/HO}$ were obtained from the intercept and slope, respectively.

The rate constants obtained in this way were then used to calculate the rate of a reaction in which $[HO^-] > [HS^-]$. This was done in two ways, since the data analysis does not provide individual values for $k_{HS'}$ and $k_{HS/HO}$; therefore,

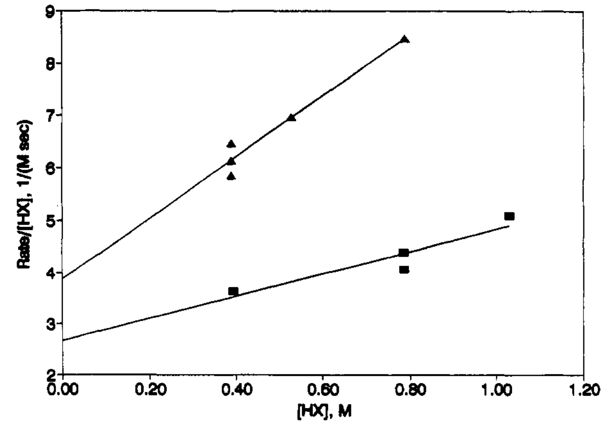


Figure 6. Data analysis to examine interactive reactant effects for the isomerization of 1 at 195 °C: NaOH, □; NaOH/NaSH, ○.

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[15] Moore, J. W.; Pearson, R. G. *Kinetics and Mechanism*, 3rd ed.; John Wiley and Sons: New York, 1981; pp 37–82.

$$k_r/[X^-] = k_{HO} + k_{HS} + (k_{HO'} + k_{HS'} + k_{HS/HO})[X^-] \quad (5)$$

$$k_{HS} = 1.3 \times 10^{-5}\ M^{-1}\ s^{-1};\ k_{HS'} + k_{HS/HO} = 3.3 \times 10^{-5}\ M^{-2}\ s^{-1}$$

one calculation assumed no $k_{HS'}$ term and the other no $k_{HS/HO}$ term. The calculation predicted isomerization rates in the case of 1.06 M HO^-/0.18 M HS^- of 6.3 and 5.8 × 10^{-5} s^{-1}, respectively; the observed value isomerization rate for was 5.6 (±0.8) × 10^{-5} s^{-1}. It is not possible to determine which (if not both) interactive terms apply; however, inclusion of such terms leads to a significantly better fit to the observed data.

Analysis of the sulfide solution used in these reactions showed the presence of 6% sodium sulfite, 2% sodium thiosulfate, and 0.6% sodium sulfate impurities. Of prime importance was the level of sulfite and thiosulfate ions. These ions are known to have nucleophilicities similar to that of hydrosulfide ion.[4] Separate 195 °C reactions of 1 with sodium sulfite and sodium thiosulfate, in the presence of excess of sodium hydroxide, were then investigated at ionic strengths comparable to the previous runs; only two reaction times and a zero time were examined. Both sulfite and thiosulfate ions were reactive.

The rate constant for SO_3^{2-} from four runs (one of which also contained HS^-) were 20, 22, 24, and 25 (±8) × 10^{-5} M^{-1} s^{-1}; the rate constant for $S_2O_3^{2-}$ from one run was 7.2 (±5.7) × 10^{-5} M^{-1} s^{-1}. These values were calculated from eq 3, assuming no additive interactive terms, except those of HO^- and HS^-. The large errors associated with the k values are due to having only 1 degree of freedom to determine the standard error. Also, propagation of errors in additive runs increases the confidence intervals around the k_{Add} values.[16] The contributions of SO_3^{2-} and $S_2O_3^{2-}$ to the overall rate constant observed for NaSH solutions are small (since their concentrations are small) and thus were ignored. The apparent reactivity of sulfite and thiosulfate toward unsaturated carbon centers has not been previously reported.

5. Anthrahydroquinone Reactions. Data from four degradations of 1 in solutions containing 0.435–0.451 M sodium hydroxide and 0.110–0.118 M anthrahydroquinone gave an average rate constant k_{AHQ} of 12.3 (±3.1) × 10^{-5} M^{-1} s^{-1} from values of 9.5, 12.2, 13.5, and 14.0 (±2.1–3.1) × 10^{-5} M^{-1} s^{-1}. The k_{AHQ} values were calculated from eq 3, using no AHQ/AHQ or AHQ/HO^- interactive terms. The AHQ/AHQ term, which contains $[AHQ]^2$, will be a small contributor to the overall rate at our low AHQ concentrations. An AHQ/HO^- interactive term probably exists in this system, since a kinetic run performed at a higher HO^- concentration had a rate in excess of the predicted k_{HO}, $k_{HO'}$, and k_{AHQ} values. An appropriate value for $k_{AHQ/HO}$ could not be determined from the limited data.

6. Relative Rates. Simple (noninteractive) rate constants of the reaction of 1 with hydroxide, hydrosulfide, and anthrahydroquinone ions, at a constant ionic strength and constant NaOH concentration, are shown in Table I.

Table I. Second-Order Reaction Rate Constants of 1 at 195 °C

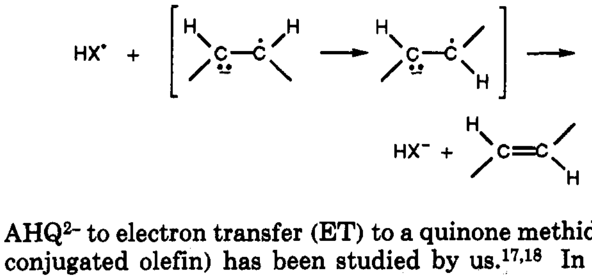
nucleophile	10^5k, M^{-1} s^{-1}	k_{rel}
NaOH	2.6 ± 0.3	1.0
NaSH	1.3 ± 0.5	0.5
Na_2AHQ	12.3 ± 3.1	4.7

Discussion and Conclusions

General Mechanistic Arguments. Reasonable candidate mechanisms for the isomerization of *cis*- to *trans*-cinnamic acid by NaOH and other nucleophiles at high temperature are (1) nucleophilic addition/elimination, (2) proton removal/inversion/reprotonation, and (3) electron transfer. Even though nucleophile addition products were not observed, our data best support a nucleophilic addition/elimination mechanism. The adducts were shown to be highly reactive under the conditions employed and to give the observed products. The addition/elimination mechanism can account for (1) the increase in isomerization rates when *nonbasic* nucleophiles were added to the highly alkaline system, (2) the secondary isotope effect in the isomerization of α,β-dideuterio-*cis*-cinnamic acid, and (3) the conversion of some α,β-dideuterio-*cis*- to α,β-dideuterio-*trans*-cinnamic acid by NaOH.

The proton removal/inversion/reprotonation isomerization mechanism can be discounted for several reasons. The observed secondary deuterium isotope effect and rapid D/H exchange (in comparison to the slow *cis*-to-*trans* isomerization) with a vinyl-labeled starting material indicates that proton removal, a logical slow step, cannot be the slow step. The rate of the inversion step should be the same when nonbasic nucleophiles are present, yet nucleophiles (HS^-, AHQ^{-2}, SO_3^{-2}, and $S_2O_3^{-2}$) promote the rate of isomerization; therefore, the inversion step cannot be the slow step. For this mechanism to apply, a dideuteriovinyl starting material would give a monodeuterio product, yet we observed some alkali-promoted conversion of *cis*- to *trans*-cinnamic acid with retention of vinyl deuterium labels. More label retention would have occurred if the nonproductive proton exchange reaction had been slower than isomerization.

In the third mechanism under consideration, the reagent ion transfers an electron to the double bond of *cis*-cinnamic acid to give a radical anion, which then inverts to the trans isomer, followed by transferring the extra electron back to a reagent radical (eq 6). The ability of HS^-, SO_3^{2-}, and AHQ^{2-} to electron transfer (ET) to a quinone methide (a conjugated olefin) has been studied by us.[17,18] In this regard, AHQ^{2-} showed the existence of ET reactions, while HO^-, HS^-, and SO_3^{2-} showed little or no tendency to electron transfer at 150 °C in aqueous alkali; SO_3^{2-} does in isopropyl alcohol at high temperatures. The relatively rapid isomerization of *cis*- to *trans*-cinnamic acid with AHQ^{2-} may be reflecting the ion's ability to electron



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[16] Meyer, S. L. *Data Analysis for Scientists and engineers*; John Wiley and Sons: New York, 1977; pp 39–48.

[17] Smith, D. A.; Dimmel, D. R. *J. Org. Chem.* **1988**, *53*, 5428.

[18] Kuroda, K.; Dimmel, D. R. *J. Wood Chem. Technol.*, **1992**, *12*, 313.

transfer; the rate differences observed for HO^-, HS^-, and SO_3^{2-} cannot be accounted for by ET chemistry under the studied conditions.

Providing there is no radical change in the mechanism with each added reagent, the nucleophilic addition/elimination mechanism is the obvious choice to explain the aqueous alkali, high temperature isomerization of *cis*- to *trans*-cinnamic acid (Scheme I). Under acidic conditions, isomerization of *cis*- to *trans*-cinnamic acid occurs through an addition–elimination mechanism.[19]

In an addition/elimination mechanism, the slow step must be the addition step; the intervening proton-transfer steps should be rapid in comparison. The fact that the synthesized adducts underwent rapid conversion to *trans*-cinnamic acid indicates that the elimination step is not the slow step. Thus, the relative rates of *cis*-to-*trans* isomerization reported in Table I should reflect the rates of the nucleophilic addition of the various nucleophiles to the double bond of *cis*-cinnamic acid. If the mechanism is constant with each reagent, anthrahydroquinone ion is the most reactive species at adding to the conjugated double bond, followed by hydroxide and hydrosulfide ions.

The rate constants associated with HO^-, HS^-, and AHQ^{2-}-promoted isomerization of *cis*-cinnamic acid increased with increasing hydroxide concentration. One explanation is that the solutions' ionic strength changed; ionic reactions are strongly influenced by the ionic strength of the medium.[20] Another explanation is that there is another mechanism of isomerization which is promoted by a second HO^- ion. The kinetic analysis supported this conclusion.

We have no firm explanation for the role of a second HO^- ion. The equilibrium constant for the hydrolysis of sodium sulfide (eq 1) is not well understood under these conditions,[21] although studies indicate that Na_2S is largely dissociated to NaSH and NaOH in water at 150–170 °C.[13,14] A 0.5 M NaSH solution could have 0.5% Na_2S present; the amount of the latter would increase at high base concentrations. Possibly, S^{2-} is effective at promoting *cis*- to *trans*-cinnamic acid isomerization. The AHQ^-/AHQ^{2-} equilibrium, which presumably lies largely on the AHQ^{2-} side at high pHs, could also be influenced by HO^- in a positive way. This same argument does not apply well to a HO^-/O^{2-} case.

Proton Exchange with Retention of Configuration. Proton abstraction is occurring with the cinnamic acids but appears not to be responsible for *cis*-to-*trans* isomerization. A specific exchange of an α-deuterium atom with retention of the configuration about the double bond was observed. The simplest, and most likely, sequence for the exchange is α-deuterium atom abstraction by hydroxide ion to form a vinyl carbanion intermediate, which is then protonated by water to produce β-deuterio-*cis*- and *trans*-cinnamic acid, respectively. These steps correspond to the first and last set of equilibria shown in Scheme II.

The exchange rate of the trans isomer (2-α,β-d_2) is slower than that of the *cis* isomer (1-α,β-d_2), meaning that $2^- \rightarrow 2^{-2}$ occurs more slowly than $1^- \rightarrow 1^{-2}$ (Scheme II). This rate difference may be related to the α-deuterium atom being more sterically hindered for *trans*-cinnamic acid than for *cis*-cinnamic acid; it is protected by the phenyl ring if all of the π-orbitals are in the same plane for maximum conjugation. Also, HO^- might be repelled at C_α by the high electron density of the neighboring phenyl ring in *trans*-cinnamic acid.

The proposed *cis*- and *trans*-vinyl carbanions could theoretically convert by way of common linear intermediates in which the CO_2^- group is either in conjugation with the C_α–C_β double bond (6^{-2}, Scheme II) or, by rotating the CO_2^- group 90°, in conjugation with the C_α-negative charge (allenic intermediate 7^{-2}). In the process, the hybridization of the α-carbon atom changes from sp^2 to sp. However, our evidence suggests such a process did not occur, since protonation of the allenic intermediate should be rapid and given isomerized product, rather than retained geometry. The linear intermediates would probably be protonated preferentially by water from the less hindered backside of C_α to form *cis*-cinnamic acid, yet dideuterio-*trans-cinnamic* acid did not give monodeuterio-*cis*-cinnamic acid.

The behavior of vinyllithium compounds with respect to their geometry has been the subject of several investigations. The isomers *cis*- and *trans*-propenyllithium have been reported to hold their respective geometries during derivatization.[22] On the other hand, (1-silyl-1-alkenyl)lithium compounds readily isomerize to the trans form, while (1-alkoxy-1-alkenyl)lithium compounds slowly isomerize.[23] The silicon atom is thought to assist in the ionization of the carbon–lithium bond to provide a linear intermediate which then isomerizes to the more stable form.[24] Corresponding studies of vinylsodium compounds have not been reported.

Proton abstraction clearly occured for both cinnamic acid isomers, but the event did not cause a change in geometry. The vinyl carbanions which are formed appear to hold their geometry long enough to be protonated rather than convert to a linear allenic intermediate. This is the first case, to our knowledge, of a vinyl carbanion holding its geometry in a conjugated carbonyl system.

Implications to Pulping Chemistry. The results of this study can be related to our understanding of pulping reactions. Quinone methides are key intermediates in the reactions of lignin. The addition of a nucleophile to C_α of the quinone methide starts a set of reactions which can lead to C_β–O bond cleavage and fragmentation of the lignin to water-soluble material (eq 7). There are, however, several competing reactions which stabilize the lignin end units; one such reaction is an enolization to give a vinyl ether (eq 8). The ability of additives, such as HS^- and $AHQ,^{2-}$ to promote pulping is probably related to the relative effectiveness of the additive to add to or electron transfer to quinone methides and promote the C_β-O bond cleavage before undesirable competing reactions take place.[25]

The relative rates, $AHQ^{2-} > OH^- > SH^-$, for the isomerization of *cis*- to *trans*-cinnamic acid do not match the relative effective of these ions to promote lignin fragmentation. The latter order is $AHQ^{2-} \approx SH^- \gg OH^-$. On a relative basis, hydroxide ion was much better at the

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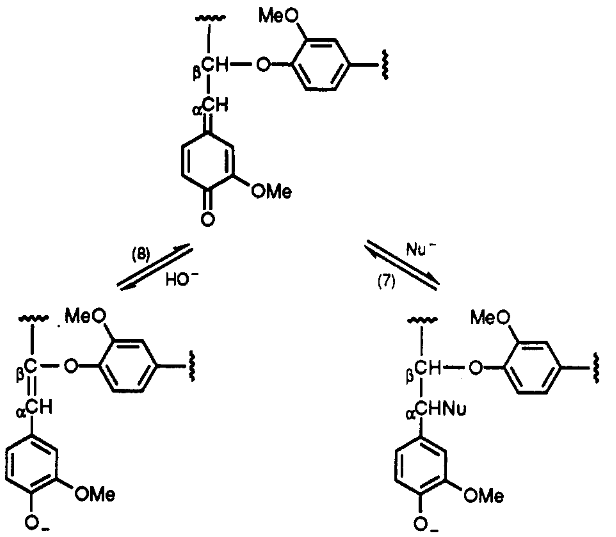

isomerization reaction than at the delignification of wood. Assuming there is a parallel between nucleophile additions to *cis*-cinnamic acid and that of additions to reactions at C_α of a quinone methide, we are left to conclude that the reactions *following* nucleophilic addition to a quinone methide play a more significant role. A key latter reaction in the proposed set of delignification reactions is neighboring group displacement of a C_β ether by a C_α substituent. The following paper considers cleavage of C_β ethers by nucleophiles. The effect of SO_3^{2-} and $S_2O_3^{2-}$ (which would be present in pulping liquors) on the degradation of quinone methides may be of some importance.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Infrared (IR) spectra, referenced against polystyrene, were obtained using sodium chloride disks on a Perkin-Elmer 700 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were obtained on a Jeol FX100 Fourier transform spectrometer at normal probe temperature. Electron impact (EI) mass spectroscopy (MS) was performed on a Hewlett-Packard 5985 instrument interfaced to a gas chromatograph, using helium as the carrier gas (30 mL min^{-1}), a source temperature of 200 °C, an ionizing voltage of 70 eV, and a GC-MS interface of 250 °C.

***cis*-Cinnamic Acid (1).** Ethyl phenylpropiolate (10.0 g, 57.4 mmol) was dissolved in hexane (100 mL). Lindlar catalyst (Aldrich Chemical Co.) (1.0 g) and quinoline (1.0 g) were added, and the mixture was warmed to 50 °C. The vessel was flushed with hydrogen three times and pressurized with hydrogen from a balloon. Hydrogen was added as needed and the reaction monitored by TLC and GC. After 7 h the mixture was filtered to remove the catalyst, and the resulting yellow filtrate was extracted with 5% HCl to remove the quinoline. The hexane layer was dried over anhydrous sodium sulfate and the solvent evaporated. The resulting liquid was distilled to yield 6.8 g (67%) of ethyl cinnamate. The ester was then refluxed in a mixture of 30 mL of 95% ethanol and 120 mL of 10% sodium hydroxide solution for 2 h. The product mixture was acidified, extracted into diethyl ether, dried, and evaporated to yield a solid which was recrystallized three times from hexane to give 8.2 g (44%) of *cis*-cinnamic acid: mp 58–60.5 °C (lit.[26,27] mp 54–56 °C, 67.5–68.0 °C); IR (mull) cm^{-1} 3750 (O—O), 1950, 1880, 1810 (Ar—H overtones), 1690 (C═O), and 1630 (C═C); ^{1}H NMR 5.96 (d, *J* = 12.8 Hz, 1, PhC*H*═CHCOOH), 6.89 (d, *J* = 12.8 Hz, 1, PhCH═C*H*COOH), 7.26–7.64 (m, 5, aryl-*H*), and 12.41 (br s, 0.7, COO*H*); ^{13}C NMR δ 120.9 (d, PhCH═*C*HCOOH), 127.8, 128.5, 129.3 (aryl-*C*), 134.7 (s, C_1), 140.1 (d, Ph*C*H═CHCOOH), and 167.1 (s, COOH); MS *m/e* (rel intensity) 148 (65, M$^+$), 147 (100), 131 (16), 103 (40), 102 (19), 91 (20), 77 (31), and 51 (15).

3-Hydroxy-3-phenylpropionic Acid (3). A mixture of ethyl 3-hydroxy-3-phenylpropionate[28] (5.0 g, 26 mmol) in 5% KOH was refluxed for 4.5 h, acidified with 6 M HCl, extracted into diethyl ether, dried, and evaporated. The resulting solid was recrystallized from water to yield 3.3 g (77%) of white solid: mp 89.5–91.0 °C (lit.[29,30] mp 92–93 °C, 93–94 °C); IR (mull) cm^{-1} 3300 (O—H) and 1700 (C═O); ^{1}H NMR δ 2.55 (d, *J* = 7.0 Hz, 2, CH_2), 4.96 (t, *J* = 6.8 Hz, 1, C*H*), 5.30 (br, s, 0.6, O*H*), 7.1–7.4 (m, 5, aryl-*H*), and 11.95 (s, 0.7, COO*H*); ^{13}C NMR δ 44.5 (t, CH_2), 69.5 (d, *C*H), 125.6, 126.7, 127.9 (aryl-*C*), 144.7 (s, C_1), and 171.9 (s, *C*OOH); MS *m/e* (rel intensity) 166 (43, M$^+$), 107 (100), 79 (70), 77 (53), and 51 (14).

3-Mercapto-3-phenylpropionic Acid (4). The procedure of Apfeld and Dimmel[31] was modified to produce the title compound. Ethyl 3-hydroxy-3-phenylpropionate (4.0 g, 21 mmol), thiourea (1.7 g, 23 mmol), and concentrated hydrochloric acid (10 mL) in water (100 mL) were refluxed with stirring for 49 h. The mixture was then refluxed for an additional 6 h following the addition of 10 mL of 50% NaOH. After cooling, the mixture was acidified, extracted into diethyl ether, dried, and evaporated to yield an odorous white solid. The solid was recrystallized from water to give 1.81 g (45% yield) of 4: mp 90–100 °C (lit.[32] mp 109 °C); IR (mull) cm^{-1} 1710 (C═O); ^{1}H NMR and ^{13}C NMR showed the presence of some minor impurities; MS *m/e* (rel intensity) 182 (27, M$^+$), 183 (3, M + 1), 184 (1, M + 2), 149 (31), 107 (100), 79 (24), 77 (30), 51 (12), 45 (11). GC-MS of a diazomethane-treated sample showed the presence of the desired dimethylated product. No attempt was made to further purify the solid.

10-Hydroxy-10-(1-phenyl-3-carboxypropyl)-9-(10*H*)-anthracenone Lactone (Cyclized 5). 10-Hydroxy-10-(1-phenyl-3-oxopropyl)-9(10*H*)-anthracenone hemiacetal[33] (252 mg, 0.737 mmol) was dissolved in 10 mL of acetone. A chromic acid solution was prepared by dissolving sodium dichromate dihydrate (242 mg, 0.814 mmol) in water (5 mL) containing concd H_2SO_4 (0.15 mL, 2.7 mmol). This solution was added to the acetone solution over a period of 15 min and then stirred for an additonal 21 h. The resulting mixture was diluted with water, extracted into diethyl ether, dried, and evaporated to yield the desired product as a tan solid: mp 206–209 °C; IR (mull) cm^{-1} 1780 (lactone carbonyl), 1660 (carbonyl), 1600 (aromatic); ^{1}H NMR (DMSO-d_6) δ 3.06 (dd, *J* = 8, 17 Hz, 1, CHC$H_{cis}H_{trans}$), 3.56 (dd, *J* = 13, 17 Hz, 1, CHC$H_{cis}H_{trans}$), 4.03 (dd, *J* = 8, 13 Hz, 1, C*H*C$H_{cis}H_{trans}$), 6.22 (d, *J* = 7 Hz, 2, C_2'- and C_6'-*H*), 6.89 (t, *J* = 7 Hz, 2, C_3'- and C_5'-*H*), 7.05 (t, *J* = 7 Hz, 1, C_4'-*H*), 7.4–8.2 (m, 8, aryl-*H*); ^{13}C NMR δ 32.1 (*C*H_2), 57.4 (*C*H), 85.4 (C_{10}), 124.7, 125.8, 126.4, 126.7, 127.5, 127.7, 128.8, 128.9, 130.2, 130.7, 132.7, 132.9, 133.1, 134.3, 134.4, 139.3, 143.0 (aryl-*C*), 175.4 (lactone *C*), 181.0 (anthracenone *C*);[34] MS *m/e* (rel intensity) 340 (10, M$^+$), 341 (2, M + 1), 104 (100).

Anal. Calcd for $C_{23}H_{16}O_3$: C, 81.18; H, 4.71. Found: C, 80.68; H, 4.79.

α,β-Dideuterio-*cis-cinnamic* Acid (1-α,β-d_2). Ethyl phenylpropiolate (5.1 g, 29.2 mmol) was dissolved in hexane (40 mL). Lindlar catalyst (Aldrich Chemical Co.) (0.5 g) and quinoline (0.5 g) were added, and the mixture was warmed to 50 °C. Deuterium was added and the solution was allowed to react with the mixture for 7 h. The mixture was filtered to remove the catalyst, and the resulting yellow filtrate was extracted with 5% HCl to remove the quinoline. The hexane layer was dried over anhydrous sodium sulfate and evaporated to yield a yellow liquid (the ester) which was then refluxed in a mixture of 10 mL of 95% ethanol and 50 mL of 10% sodium hydroxide solution for 2 h. The product mixture was acidified, extracted into diethyl ether,

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dried, and evaporated to yield a solid which was recrystallized three times from hexane to give 2.2 g (50%) of the desired product as a white crystalline solid: mp 64–65 °C; IR (mull) cm^{-1} 3750 (H—O), 1950, 1890 and 1820 (aryl-H overtones), 1690 (C=O), and 1610 (C=C); ^{1}H NMR (DMSO-d_6) δ 7.23–7.71 (m, 5, aryl-*H*) and 12.41 (s, 0.7, COO*H*); ^{13}C NMR δ 127.6, 128.3, 129.1, 134.5 (s, C$_1$), and 166.9 (s, *C*OOH); MS *m/e* (rel intensity) 150 (75, M$^+$), 149 (100), 133 (10), and 105 (26).

Benzaldehyde-*formyl-d*. The procedure, previously described by Burgstahler and co-workers,[35] yielded a yellow liquid which was distilled (65-67 °C, 3–5 mm) to give 2.11 g (39%) of the desired product as a liquid: ^{1}H NMR (DMSO-d_6) δ 7.47–8.00 (*m*, aryl-*H*).

α,β-Dideuterio-*trans*-cinnamic Acid (2-α,β-d$_2$). The procedure of Johnson[36] was modified as follows. Benzaldehyde-*formyl-d* (1.01 g, 9.4 mmol), acetic anhydride-d_6 (1.54 g, 14 mmol), and potassium acetate (0.55 g, 5.6 mmol) were refluxed under nitrogen for 4 h, at which time only a solid remained. The solid was dissolved in diethyl ether and extracted into 1 M sodium hydroxide. The basic solution was acidified with 6 M hydrochloric acid and extracted into diethyl ether. The resulting product was recrystallized from a 20% ethanol–water solution to yield 0.53 g (37%) of the desired product as white-yellow platelets: mp 132.5–133 °C; ^{1}H NMR (DMSO-d_6) δ 6.52 (s, 0.19, ArCD=C*H*COOH), 7.33–7.76 (m, 5, aryl-*H*), and 12.30 (br s, 0.8, COO*H*). On the basis of the NMR data, approximately 19% of the product was monodeuterated and the remainder dideuterated.

***cis*-Cinnamic Acid Isomerization.** The isomerization experiments were carried out in 4-mL capacity, 316 stainless steel, pressure vessels (bombs).[37] The bombs were filled with an appropriate amount of the reactants and sealed in a nitrogen atmosphere. Solutions of NaOH and NaSH were prepared with oxygen-free water and stored under nitrogen; the one employed 30% ultrapure NaOH (Alfa Products), the other reagent grade Na$_2$S·9H$_2$O. Anthrahydroquinone solutions were prepared by reducing anthraquinone in a nitrogen atmsophere using sodium dithionite.[38] The resulting product was dissolved in aqueous sodium hydroxide, filtered, and stored under nitrogen. Aqueous NaOH solutions of *cis*-cinnamic acid were prepared such that, after dilution in the bombs, the solution contained 0.01 M compound.

[When *cis*-cinnamic acid was reacted in solutions containing high concentrations (>1 M) of sodium hydroxide or sulfide, hydrocinnamic acid was also observed as a product. Lower base concentrations were, thus, employed to minimize byproduct formation and maximize conversion to *trans*-cinnamic acid. The mechanism of hydrocinnamic acid formation was not investigated.]

The bombs were placed in a preheated oil bath and then removed after desired reaction times. The bombs were immediately cooled in an ice–water bath upon removal from the oil bath. The bomb contents were removed and combined with two aqueous sodium hydroxide rinsings, the first one containing a GC internal standard. The reaction samples were then acidified with HCl and extracted with diethyl ether. The combined ether extract was dried (Na$_2$SO$_4$), filtered, and treated with methanol and an ether solution of diazomethane. After 30–90 min, the excess diazomethane and ether were evaporated off to reduce the volume. The samples were then refrigerated until GC analysis.

Gas chromatography analyses employed a Hewlett-Packard 5890A instrument, helium as the carrier gas (20 mL min^{-1}), a 6 ft × 2 mm glass column containing OV-17 (3%) on Chromosorb W HP (100–120 mesh), an injector temperature of 300 °C, a detector temperature of 310 °C, and column temperature program of 100 °C for 1 min, 10° min^{-1} to 200 °C, 30° min^{-1} to 300 °C, and held at 300 °C. The GC retention times were benzaldehyde, 1.9 min; benzoic acid, 3.2 min; phenylacetic acid (internal standard), 4.4 min; hydrocinnamic acid, 5.7 min; *cis*-cinnamic acid, 6.3 min; and *trans*-cinnamic acid, 7.4 min. The levels of deuterium atoms in the *cis*- and *trans*-cinnamic acids were determined by mass spectral analyses.

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