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# HIGH TEMPERATURE ISOMERIZATION OF cis-CINNAMIC ACID IN AQUEOUS ALKALI

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## ABSTRACT

The mechanism by which cis-cinnamic acid isomerized to trans-cinnamic acid in aqueous sodium hydroxide at 195°C was investigated to determine the role of proton abstraction. The isomerization rate of  $\alpha,\beta$ -dideutero-cis-cinnamic acid was 1.07 times slower than that of the nondeuterated compound, indicating proton abstraction is not the rate-determining step. The  $\alpha$ -deuterium of  $\alpha,\beta$ -dideutero-cis-cinnamic acid, however, was rapidly exchanged for an  $\alpha$ -hydrogen atom in alkali at 195°C without loss of the cis geometry. It was concluded that isomerization resulted from addition-elimination rather than proton abstraction.

## INTRODUCTION

The ability of a pulping reagent to act as a nucleophile is important to the delignification of wood.<sup>1</sup> Relative nucleophilicities could explain the effectiveness of different pulping reagents. An apparent critical step in the fragmentation of lignin macromolecular structure involves the addition of a nucleophile to a conjugated carbonyl structure (a quinonemethide) - formally a Michael reaction.<sup>1</sup>

In order to determine the relative nucleophilicities of various ions toward conjugated carbon centers, we have investigated the relative rates of conversion of cis-cinnamic acid (1) to trans-cinnamic acid (2) in the presence of these ions at high temperatures in water.<sup>2</sup> The selection of cis-cinnamic acid as a model for lignin Michael reactions was based on the anticipated simplicity of the isomerization reaction and on solubility in aqueous alkali.

The conversion of 1 to 2 in aqueous alkali was studied at 195°C in order to have reasonable reaction rates. Under these conditions, however, proton abstraction of the olefinic hydrogen atoms may occur; hydroxide ion has been shown<sup>3</sup> to be a very strong base at pulping temperatures, namely 170°C. Therefore, before proceeding with a study of nucleophilicities, we needed to demonstrate that the isomerization of 1 to 2 was of an addition-elimination type and not simply an acid-base type (Fig. 1).

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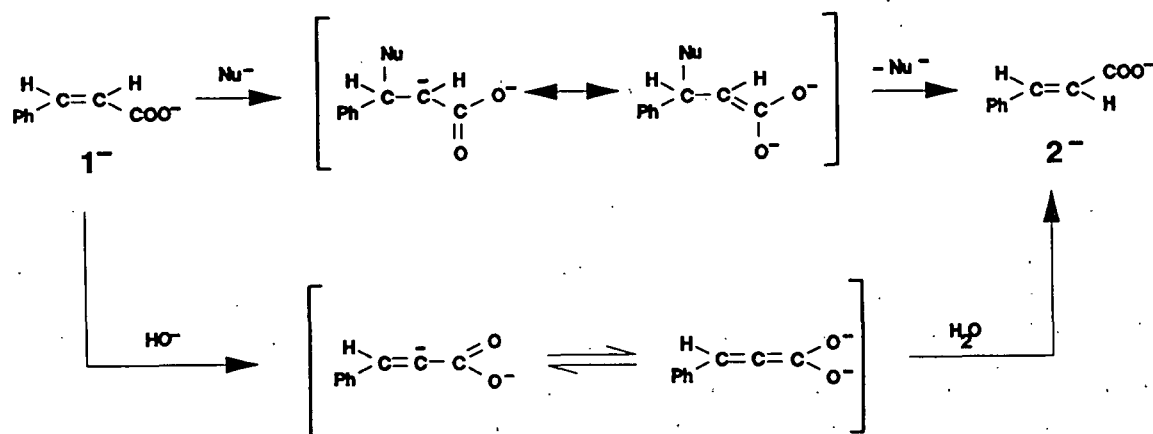


Figure 1. Comparison of isomerization of 1 by a nucleophilic addition-elimination (top) to a proton abstraction mechanism (bottom).

The role of proton abstraction in promoting isomerization was investigated by examining the reactions of  $\alpha,\beta$ -dideutero-cis-cinnamic acid (1- $\alpha,\beta$ -d<sub>2</sub>) and  $\alpha,\beta$ -dideutero-trans-cinnamic acid (2- $\alpha,\beta$ -d<sub>2</sub>). If proton abstraction was the rate-determining step for the isomerization of 1 to 2, then the ratio of the reaction rates for the nondeuterated compound to that of a vinyl deuterated analog would be approximately 3-8 (primary isotope effect).<sup>4</sup> If, however, nucleophilic addition was the rate-determining step, then a ratio of 0.8-1.2 would be expected (secondary isotope effect).<sup>4</sup> Finally, detection of  $\alpha,\beta$ -dideutero-trans-cinnamic acid during the degradation of  $\alpha,\beta$ -dideutero-cis-cinnamic acid would indicate that proton abstraction is not the pathway which caused cis-trans isomerization.

## RESULTS

During the initial reactions of 1- $\alpha,\beta$ -d<sub>2</sub> with hydroxide ions at 195°C, two important findings were noted. First, a secondary isotope effect, indicative of an addition-elimination mechanism, was observed. The ratio of the rate constants for isomerization of non-isotopic labeled 1 to deuterium label 1,  $k_H/k_D$ , was 1.07 (Fig. 2). A rapid exchange of one deuterium atom, however, was detected by mass spectroscopy. Proton NMR techniques showed that the  $\alpha$ -deuterium atom was exchanged (Eq. 1). These two results seemed contradictory to each other, unless proton abstraction is occurring but is not responsible for cis to trans isomerization.

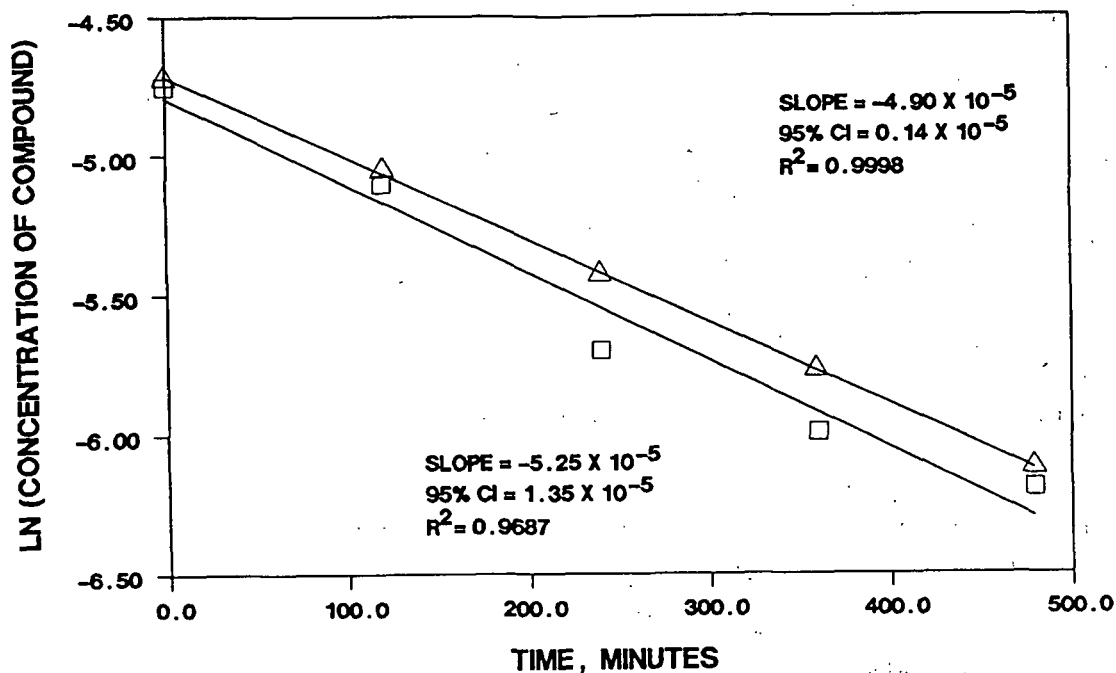
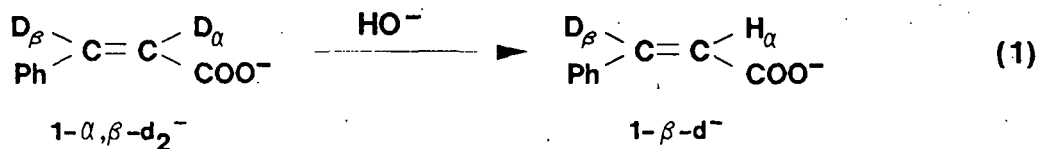


Figure 2. Comparison of isomerization rates of cis-cinnamic acid (□), and 1- $\alpha,\beta$ -d<sub>2</sub> (Δ), at 195°C in 1.03 M NaOH.



The exchange rates of 1- $\alpha,\beta$ -d<sub>2</sub> and 2- $\alpha,\beta$ -d<sub>2</sub> at 195°C were then investigated in more detail (Fig. 3). After 30 minutes, nearly all of  $\alpha,\beta$ -dideutero-cis-cinnamic acid (1- $\alpha,\beta$ -d<sub>2</sub>) was converted to  $\beta$ -deutero-cis-cinnamic acid (1- $\beta$ -d). The rate of deuterium loss from  $\alpha,\beta$ -dideutero-trans-cinnamic acid (2- $\alpha,\beta$ -d<sub>2</sub>) was considerably slower. The site of exchange in trans isomer was the same ( $\alpha$ -deuterium) as that in cis isomer. The exchange rate of the trans isomer is presumably slower due to steric effects. The  $\alpha$ -deuterium atom in 2- $\alpha,\beta$ -d<sub>2</sub> is protected by the phenyl ring if all of the  $\pi$ -orbitals are in the same plane for maximum conjugation. Since the exchange rate of 2- $\alpha,\beta$ -d<sub>2</sub> was much slower than that of 1- $\alpha,\beta$ -d<sub>2</sub>, it should be possible to observe production of 2- $\alpha,\beta$ -d<sub>2</sub> during the reactions of 1- $\alpha,\beta$ -d<sub>2</sub> if addition-elimination was the mode of isomerization.

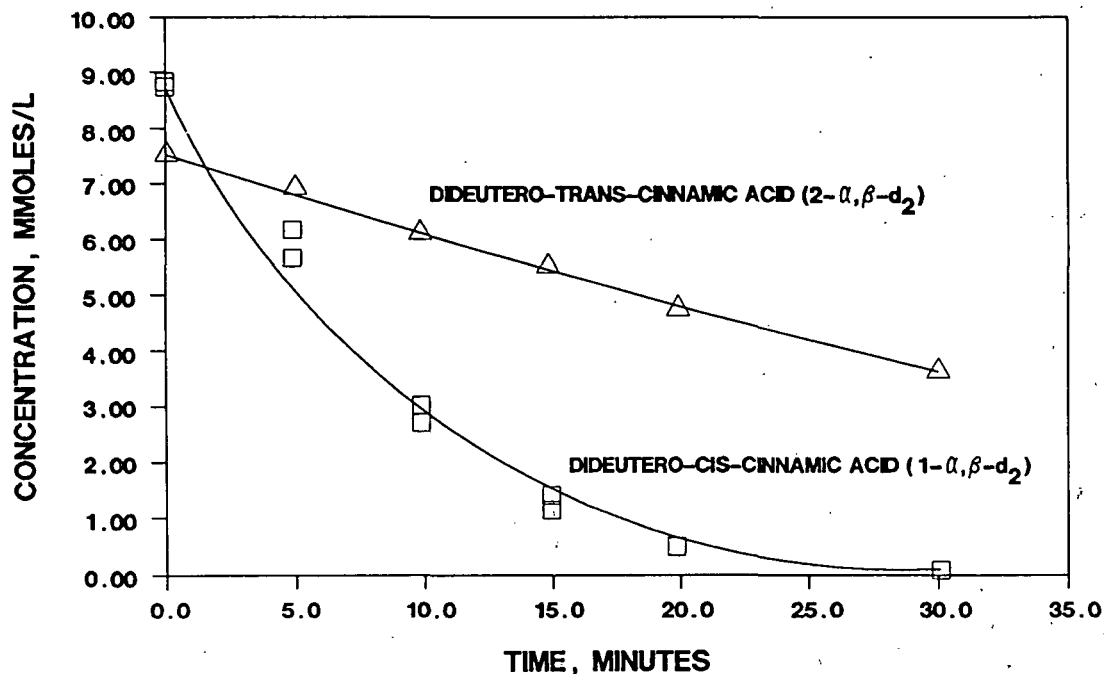


Figure 3. Comparison of the rate of exchange of the  $\alpha$ -deuterium atom in 1- $\alpha,\beta$ -d<sub>2</sub>,  $\square$ , and 2- $\alpha,\beta$ -d<sub>2</sub>,  $\Delta$ , in 1.20 M NaOH at 195°C.

The concentrations of both mono and dideutero species of the cis and trans isomers were determined during the reaction of 1- $\alpha,\beta$ -d<sub>2</sub> in aqueous sodium hydroxide (Fig. 4 and 5). It should be noted that the sample of 1- $\alpha,\beta$ -d<sub>2</sub> contained a small amount of 2- $\alpha,\beta$ -d<sub>2</sub> impurity. During the initial phase of cis to trans-cinnamic acid isomerization at 195°C of the deuterated substrate, the level of 2- $\alpha,\beta$ -d<sub>2</sub> increased slightly. The isomerization was done several times, with the same initial increase in 2- $\alpha,\beta$ -d<sub>2</sub> observed in each case.

#### DISCUSSION

The formation of  $\alpha,\beta$ -dideutero-trans-cinnamic acid (2- $\alpha,\beta$ -d<sub>2</sub>) indicates that isomerization of cis- to trans-cinnamic acid occurred via addition-elimination and not proton abstraction. The production of 2- $\alpha,\beta$ -d<sub>2</sub> rose initially and then decreased slowly as the isomerization proceeded. There are two reasons why 2- $\alpha,\beta$ -d<sub>2</sub> does not continually increase. First,  $\alpha,\beta$ -dideutero-trans-cinnamic acid is derived from  $\alpha,\beta$ -dideutero-cis-cinnamic acid, and the concentration of the latter drops rapidly at 195°C in alkali (Fig. 4). Second,  $\alpha,\beta$ -dideutero-trans-cinnamic acid is slowly converted to  $\beta$ -deutero-trans-cinnamic acid (2- $\beta$ -d). The observed steady increase in the levels of 2- $\beta$ -d

acid. If a water molecule attacks the central carbon atom from the front side to form the trans product 2- $\beta$ -d<sup>-</sup>, it must contend with the large phenyl ring. If water attacks from the back side to form the cis product 1- $\beta$ -d<sup>-</sup>, it will find a smaller deuterium atom. Protonation on the back side should therefore be favored.

A change in the hybridization of the  $\alpha$ -carbon atom from sp to sp<sup>2</sup>, which places the negative charge back onto the carbon atom, can lead to a trans intermediate (2- $\beta$ -d<sup>-2</sup>). This intermediate may then be protonated by water to form 2- $\beta$ -d<sup>-</sup>.

According to reactions outlined in Fig. 6, intermediate 3 would be a common intermediate for both 1- $\alpha,\beta$ -d<sub>2</sub> and 2- $\alpha,\beta$ -d<sub>2</sub> exchange reactions. If 3 is the most stable intermediate, the exchange of the  $\alpha$ -deuterium in  $\alpha,\beta$ -dideutero-trans-cinnamic acid (2- $\alpha,\beta$ -d<sub>2</sub>) should, because of steric reasons, result in the formation of  $\beta$ -deutero-cis-cinnamic acid (1- $\beta$ -d). Since the isomerization rate from trans- to cis-cinnamic acid was found to be very low, this would suggest that 3 is not an important form.

The geometry of vinylolithium compounds has been the subject of several investigations. The isomers, cis- and trans-propenyllithium, have been reported to hold their respective geometries during derivatization.<sup>5</sup> On the other hand, 1-silyl-1-alkenyllithium compounds readily isomerize to the trans form, while 1-alkoxy-1-alkenyllithium compounds slowly isomerize.<sup>6</sup> The silicon atom is thought to assist in the ionization of the carbon-lithium bond, providing a linear intermediate, which then isomerizes to the more stable form.<sup>7</sup> Corresponding studies of vinylsodium compounds have not been reported.

#### CONCLUSIONS

The high temperature, alkali-promoted isomerization of cis-cinnamic acid appears to be a result of an addition-elimination mechanism involving hydroxide ion. Proton abstraction was not the rate-determining step since a secondary, rather than a primary, isotope effect was observed. The observation of  $\alpha,\beta$ -dideutero-trans-cinnamic acid production in the isomerization of  $\alpha,\beta$ -dideutero-cis-cinnamic acid is conclusive evidence that proton abstraction is not the principal mechanism of the isomerization. Proton abstraction clearly

occurred for both cinnamic acid isomers but did not cause a change in geometry. It appears that vinyl carbanions are formed, that these hold their geometry long enough to be protonated, and that a linear allenic intermediate is not formed. This is the first case, to our knowledge, of a vinyl carbanion holding its geometry in a conjugated carbonyl system.

#### EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary melting point apparatus. Infrared (IR) spectra, referenced against polystyrene, were obtained using sodium chloride discs on a Perkin-Elmer 700 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were obtained on a Jeol FX100 Fourier transform spectrometer at normal probe temperature. Mass spectroscopy (MS) was performed on a Hewlett-Packard 5985 instrument interfaced to a gas chromatograph. Separation by GC was typically performed on OV-17 (3%) on Chromosorb W HP (100-120 mesh) in glass tubing (6 ft x 2 mm) rigged for on-column injection. Electron impact (EI) MS used helium as the carrier gas (30 mL min<sup>-1</sup>), a source temperature of 200°C, an ionizing voltage of 70 eV, and a GC-MS interface temperature of 250°C.

**$\alpha,\beta$ -Dideutero-cis-cinnamic Acid (1- $\alpha,\beta$ -d<sub>2</sub>).** 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 gas was added to the closed system. After 7 hr and continued replacement of spent deuterium, the mixture was filtered to remove the catalyst, and the resulting yellow filtrate was extracted with 5% hydrochloric acid solution to remove the quinoline. The hexane solution was dried (anhydrous sodium sulfate) and evaporated to yield a yellow liquid which was then refluxed in a mixture of 10 mL of 95% ethanol and 50 mL of 10% sodium hydroxide solution for 2 hours. The solution was acidified and extracted into diethyl ether. The combined ether extracts were dried, and evaporated to yield a solid which was recrystallized three times from hexane to give 2.2 g (50%) of 1- $\alpha,\beta$ -d<sub>2</sub> as a white crystalline solid: m.p. 64-65°C; IR (mull) cm<sup>-1</sup> 3750 (H-O), 1950, 1890 and 1820 (aryl-H overtones), 1690 (C=O), and 1610 (C=C); <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$  7.23-7.71 (m, 5, aryl-H), and 12.41 (s, 0.7, COOH); <sup>13</sup>C-NMR ppm 127.6, 128.3,

129.1, 134.5 (s, C<sub>1</sub>), and 166.9 (s, COOH); MS  $m/z$ : (rel. intensity) 150 (75, M<sup>+</sup>), 149 (100), 133 (10), and 105 (26).

**Benzaldehyde-formyl-d.** The procedure previously described by Burgstahler and co-workers<sup>8</sup> 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: <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ 7.47–8.00 (m, aryl-H).

**α,β-Dideutero-trans-cinnamic Acid (2-α,β-d<sub>2</sub>).** The procedure of Johnson<sup>9</sup> was modified as follows. Benzaldehyde-formyl-d (1.01 g, 9.4 mmol), acetic anhydride-d<sub>6</sub> (1.54 g, 14 mmol), and potassium acetate (0.55 g, 5.6 mmol) were combined and refluxed under nitrogen for four hours, at which time only a solid remained. The solid was dissolved in diethyl ether and the resulting solution extracted with 1 M sodium hydroxide. The combined alkaline extracts were acidified with 6 M hydrochloric acid and extracted with diethyl ether. The combined ether extracts were dried and evaporated. The resulting solid residue was recrystallized from a 20% ethanol-water solution to yield 0.53 g (37%) of 2-α,β-d<sub>2</sub> as white-yellow platelets: m.p. 132.5–133°C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ 6.52 (s, 0.19, Ar-CD=CH-COOH), 7.33–7.76 (m, 5, aryl-H) and 12.30 (br s, 0.8, COOH). Based on the NMR data, approximately 19% of the product was monodeuterated and the remainder, dideuterated. The product was sufficiently deuterated for further experiments.

**cis-Cinnamic acid Isomerization.** The isomerization experiments were carried out in 4-mL capacity, 316 stainless steel pressure vessels (bombs).<sup>10</sup> The bombs were filled with an appropriate amount of the reactants and sealed in a nitrogen atmosphere. Sodium hydroxide solutions used in degradation studies were prepared from ultrapure sodium hydroxide (30% solution) (Alfa Products) with oxygen-free water. The appropriate cinnamic acid isomer was dissolved in either 1.03 M or 1.20 M NaOH to achieve a concentration of 0.01 mol L<sup>-1</sup>. The oil bath was preheated to the desired temperature. The sealed bombs were placed in the oil bath for various 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 hydrochloric acid and extracted with diethyl ether. The combined ether extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and

diluted with 1 mL of methanol and 2 mL of 0.5 M diazomethane in ether (roughly a 25 fold excess). After 30-90 minutes, 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<sup>-1</sup>), a 6 ft x 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 minute, 10°C/min to 200°C, 30°C/min to 300°C, and held at 300°C. The retention times, as methyl esters, were phenylacetic acid (internal standard) 4.4 min, cis-cinnamic acid 6.3 min, and trans-cinnamic acid 7.4 min.

The level of deuterium atoms in the cis- and trans-cinnamic acids was determined by analyzing the EI mass spectrum of each material; the known M, M+1, M+2, pattern of the non-isotopically labeled cinnamic acid served to establish the patterns of molecular ions associated with the labeled acids.

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