Scheme I

(*c* 2.5, EtOH) [lit.[5] [α]$_D$ 9.1° (*c* 2.2, EtOH)]; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.81 (1 H, dd, *J* = 6.1 and 16.4 Hz, CH$_3$OOCCH_aH$_b$CHOHCOOCH$_3$), 2.87 (1 H, dd, *J* = 4.4 and 16.4 Hz, CH$_3$OOCCH$_a$$H_b$CHOHCOOCH$_3$), 3.20 (1 H, d, *J* = 5.4 Hz, CH$_3$OOCH$_a$H$_b$CHO*H*COOCH$_3$), 3.72 and 3.82 (6 H, 2 s, CH$_3$OOCCH$_a$H$_b$CHOHCOOC*H*$_3$), 4.51 (1 H, m, CH$_3$OOCCH$_2$C*H*OHCOOCH$_3$).

Role of the *p*-Hydroxyl Group in the Nitrobenzene Oxidation of Hydroxybenzyl Alcohols

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For nearly half a century, the alkaline nitrobenzene oxidation of lignin[1,2] has been used to convert lignin to identifiable mixtures of aromatic aldehydes and, to a lesser extent, aromatic acids. The generally accepted mechanism for this oxidation is a heterolytic process involving a quinone methide intermediate.[3] Recent findings[4] suggest that a homolytic oxidative–cleavage mechanism better describes this reaction. This new mechanism is formally similar to that observed by Trahanovsky[5,6] in the ceric ammonium nitrate oxidation of 1,2-diarylethanols. Furthermore, Ashby[7] has found ESR evidence that the Cannizzaro reaction, which is a side reaction in the nitrobenzene oxidation, may also be homolytic in nature. Also, the hemoprotein ligninase of *Phanerochaete chrysosporium* has recently been found[8] to catalyze the one-electron oxidation of methoxybenzene lignin model compounds

forming cation radical intermediates that eventually demethylate to quinone products.

The claim has frequently been made[3,9] that a *p*-hydroxyl group is required on a lignin model compound for the nitrobenzene oxidation to work. The function of the *p*-hydroxyl group was believed to be threefold: (a) to impart aqueous alkali solubility to the compound, (b) to protect the aldehyde product from the Cannizzaro side reaction, and (c) to facilitate the formation of a quinone methide intermediate. We have reason to question the last function.

The necessary *p*-hydroxyl claims are based on some methylation studies. When a series of about a dozen C$_3$ arene compounds also containing either 4-hydroxy-3-methoxy or 3,4-dimethoxy substituents were subjected to the nitrobenzene oxidation reaction, only the compounds with the 4-hydroxy-3-methoxy substituents gave appreciable amounts of aldehydes.[9,10] Leopold[11] methylated various lignins with diazomethane (methylation of phenolic OH's) and found that the yield of vanillin from the nitrobenzene oxidation of these methylated lignins decreased by 15–20%. Further methylation by dimethyl sulfate[12] (all OH's methylated) resulted in a 70% decrease in vanillin product. These methylation studies clearly show that benzylic hydroxyl groups in lignin are more important in vanillin formation than are *p*-hydroxyl groups.

In this study the kinetics and activation parameters of the alkaline nitrobenzene oxidation of *p*-hydroxybenzyl alcohol (1), *m*-hydroxybenzyl alcohol (2), and 4-hydroxy-3-methoxybenzyl alcohol (3) were studied as lignin model compounds. The compounds were chosen to test the necessity of a *p*-hydroxyl group in its presumed role of acting as a precursor for the formation of a quinone methide intermediate.

Results and Discussion

Kinetics. In an earlier study,[4] the nitrobenzene oxidation of *o*-, *m*-, and *p*-hydroxybenzyl alcohols at 150 °C for 1 h was found to give the corresponding hydroxybenzaldehydes in 14, 47, and 51% yields, respectively. Compound 3, also called vanillyl alcohol, gives vanillin in 70% yield under the same conditions. The aldehyde yields can be improved by longer reaction times, but side reactions also become increasingly important with time. Under the conditions used in these kinetic runs, 1, 2, and 3 gave 60–75% oxidation to the corresponding benzaldehydes. *o*-Hydroxybenzyl alcohol was the only one of this series that gave a poor yield of aldehyde and, for this reason, its kinetics were not studied. The pseudo-first-order rate constants and activation parameters for the oxidations of 1, 2, and 3 are given in Table I.

A 16-fold excess of nitrobenzene over hydroxybenzyl alcohol was used in each reaction to simplify the kinetics by removing nitrobenzene dependence from the rate law and also to approximately duplicate the nitrobenzene excess normally used in the oxidation of lignin. The result was that both the disappearance of alcohol and the appearance of aldehyde followed pseudo-first-order kinetics. These kinetics were, however, further complicated by side reactions.

Benzyl alcohols 1 and 3, both of which contain a *p*-hydroxyl group, each undergo a competing self-condensation reaction under the strongly basic conditions of the reaction. The reaction of 1 with dilute NaOH has been

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Table I. Pseudo-First-Order Rate Constants and Activation Parameters for the Nitrobenzene Oxidation of X,Y-PhCH₂OH

X	Y	kinetic method	$10^5 k_1$ (s⁻¹)			$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)
			120 °C	135 °C	150 °C		
4-OH	H	I[a]	3.75	12.0	26.7	21.5 ± 1.8	−27 ± 4
		II[b]	4.74 ± 0.36	18.1 ± 1.2	35.4 ± 3.1	21.4 ± 2.5	−24 ± 6
		III[c]	5.95 ± 0.30	18.4 ± 1.1	59.8 ± 2.2	30.9 ± 4.8	0 ± 12
3-OH	H	I	2.75	7.42	23.5	22.8 ± 1.2	−22 ± 3
		II[d]	1.92 ± 0.14	5.22 ± 0.67	16.6 ± 2.6	22.8 ± 1.6	−23 ± 2
		III[d]	2.44 ± 0.44	9.1 ± 1.6	23.0 ± 4.0	23.9 ± 1.7	−19 ± 2
4-OH	3-OMe	I	4.20	18.3	48.3	26.9 ± 2.5	−13 ± 4
		II	6.86 ± 0.47	27.8 ± 1.0	78.2 ± 6.7	26.1 ± 1.2	−12 ± 3
		III[c]	6.86 ± 0.54	31.2 ± 1.7	80.0 ± 6.0	26.3 ± 1.6	−11 ± 4

[a] Computer model method (see Experimental Section). No error determination is possible with this method. [b] Pseudo-first-order k for appearance of aldehyde. [c] k for disappearance of alcohol. These k values are a composite of k_1 and k_2 for 1 and to a lesser extent for 3. [d] Initial rate for approximately 20–35% reaction.
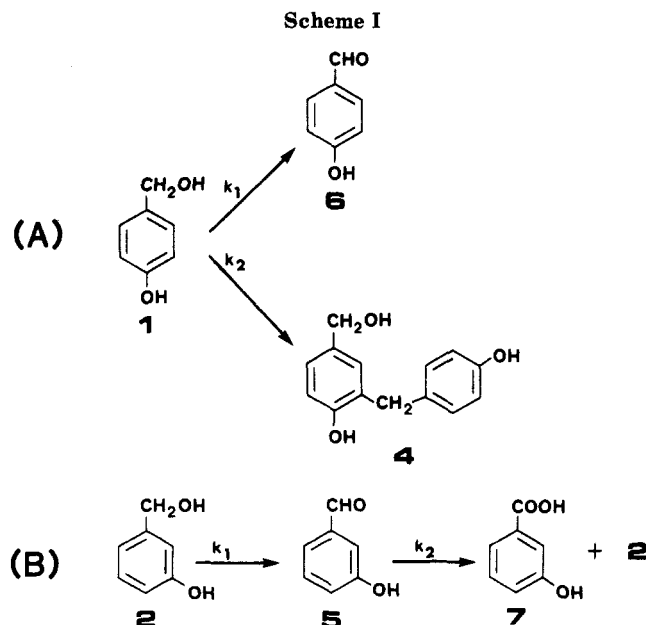
Scheme I

reported[13] to give mainly 5-(hydroxymethyl)-2,4′-dihydroxydiphenylmethane (4) (Scheme I). We have determined the second-order rate constants for the self-condensation of 1 and 3 in 2 N NaOH containing no nitrobenzene. The k_2 values for 1 at 135 °C and 150 °C were found to be $(7.1 \pm 0.9) \times 10^{-2}$ M⁻¹ min⁻¹ and 0.73 ± 0.03 M⁻¹ min⁻¹, respectively, while the corresponding k_2 values for 3 were $(7.0 \pm 0.5) \times 10^{-2}$ M⁻¹ min⁻¹ and 1.16 ± 0.15 M⁻¹ min⁻¹ at 120 °C and 150 °C, respectively.

The kinetics of the oxidation of 2 presented a different problem. No self-condensation side reaction was observed, but the oxidation product *m*-hydroxybenzaldehyde (5) undergoes a Cannizzaro reaction. Several experiments were done to assess the importance of the Cannizzaro side reaction in these oxidations. When *p*-hydroxybenzaldehyde (6) was heated at 155 °C in 2 N NaOH, 97.6% of 6 was recovered unreacted after 1 h and 91.3% was unreacted after 5 h. In contrast, under the same conditions 5 was completely converted into 56.2% *m*-hydroxybenzoic acid (7) and 43.8% 2 after 1 h. These two control reactions clearly show that a *p*-hydroxyl group on benzaldehyde protects it from the Cannizzaro reaction at 155 °C, but a *m*-hydroxyl group does not provide any such protection. At lower temperatures 5 is much less reactive to the Cannizzaro reaction. In another control experiment, the concentrations of 2, 5, and 7 were determined for each kinetic point by a HPLC method, since the GC method

used did not give yields of benzoic acid products. At 275 min, the last point of the kinetic run at 135 °C, 50.6% 2, 47.3% 5 and 2.2% 7 was found. Because the products of the Cannizzaro reaction of 5 are both 2 and 7, the numbers indicate that when 2 is about half oxidized at 135 °C, 92% of the product is aldehyde 5 and only 8% of the Cannizzaro reaction has occurred.

Three different kinetic approaches were used to determine the pseudo-first-order rate constants for the oxidation of 1, 2, and 3 in the presence of the side reactions mentioned above. Kinetic method I involved an iterative computer program[14,15] using the model systems shown in Scheme I. The computer program determined the values of k_1 and k_2 that gave the best fit of model reaction concentrations to actual experimental values found for the concentrations of alcohol and aldehyde. The computer-determined values of k_2 for the self-condensation reactions of 1 and 3 were within 30% of their experimentally determined values for three of the four values studied and less than a factor of 2 in all cases. Kinetic method II followed the first-order appearance of benzaldehyde product. This method is probably the best kinetic approach for 1 and 3 because the self-condensation side reaction does not directly affect the appearance of benzaldehyde product. Kinetic method III followed the disappearance of benzyl alcohol. The rate constants determined by method III are invariably larger than those determined by method II because the former contains a contribution from the self-condensation reaction. The most obvious example of this effect is that the k_1 for 1 at 150 °C is 70% larger by method III than by method II because under these conditions 40–45% of 1 follows the self-condensation reaction. At the same temperature less than half this amount of 3 goes into the self-condensation reaction. The kinetics of 2 followed by both methods II and III used initial rates (20–35% reaction) because the first-order linearity found in this initial region was lost by the end of 1 half-life.

The pseudo-first-order rate constants for the nitrobenzene oxidation of 1 (with a *p*-OH) and 2 (with a *m*-OH) are very similar. The average values of k_1 from all three kinetic methods for 1 are about a factor of 2 greater than those of 2. The average values of k_1 for 3 differ from those of 1 by less than a factor of 2. The lack of a significant substituent effect for the k_1 of 3 vs. 1 is consistent with a homolytic process, since homolytic processes are normally less sensitive to substituent effects than are heterolytic processes. The similarity of the products and pseudo-first-order rate constants for the nitrobenzene oxidations

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of 1, 2, and 3 is consistent with a common mechanism being followed in each case. Whatever the nature of the mechanism, a quinone methide intermediate cannot be formed from 2 because of the meta relationship of its substituents.

Activation Parameters. The activation parameters for 1 by method III should be ignored because, as discussed earlier, the value of k determined by method III is too large due to the appreciable contribution of the self-condensation reaction. The remaining values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for both 1 and 2 are the same within experimental error. The large negative values of $\Delta S^{\ddagger}$ indicate the presence of an ordered transition state in the slow step of this oxidation and are consistent with the homolytic oxidative–cleavage mechanism postulated earlier[4] for this oxidation with the first step being the slow step. The $\Delta H^{\ddagger}$ values of 3 are 4–5 kcal/mol larger than those of 1 and 2, and the $\Delta S^{\ddagger}$ values are less negative. The rate similarities of 1 and 3 are partly due to a favorable $\Delta S^{\ddagger}$ change balancing the unfavorable $\Delta H^{\ddagger}$ change.

Summary. The fact that the oxidation of both 1 and 2 give good yields of aldehydes at rates that differ by less than a factor of 2.5 and with activation parameters that are the same within experimental error is consistent with both oxidations going through a common mechanism. This mechanism cannot involve a quinone methide intermediate because such an intermediate is not physically possible from 2. To the extent that our compounds are adequate models of the lignin structure, the presence of a quinone methide intermediate in the nitrobenzene oxidation of lignin is also seriously questioned.

Experimental Section

Benzyl alcohols 1–3 were obtained commercially and purified by recrystallization.

The general reaction conditions used here were similar to those used in the nitrobenzene oxidation of lignin.[16] Typically a reaction mixture consisted of 0.484 mmol of benzyl alcohol, 7.8 mmol of nitrobenzene, and 10 mL of 2 N sodium hydroxide. For a kinetic run a series of eight identical mixtures of the same benzyl alcohol solution was sealed in eight 22-mL mini Parr reactors and heated in a fluidized sand bath. Analysis of each sample consisted of the addition of the internal standard benzophenone, continuous chloroform extraction to remove the excess nitrobenzene, acidification, another chloroform extraction to remove the phenols, acylation, and analysis on a PE 900 gas chromatograph with FID detector using a $^1/_8$ in. × 6 ft OV-17 column.[17] The products of one kinetic run on 2 were also analyzed on a HP-1090A liquid chromatograph using a 5-μm C-18 column with a programmed mix of methanol/water.

An iterative computer model method[14,15] was used to estimate the best values of the pseudo-first-order oxidation rate constants and the second-order rate constants for the side reactions shown in Scheme I. The average values of the correlation coefficients (r) for the determinations of the pseudo-first-order rate constants for 1 and 3 were 0.986 (14 runs) by method II and 0.990 (14 runs) by method III. The average r values for the determinations of the k_1's of 2 were 0.983 (6 runs) by method II and 0.943 (6 runs) by method III. No error estimation was possible for method I.

Registry No. 1, 623-05-2; 2, 620-24-6; 3, 498-00-0; nitrobenzene, 98-95-3; lignin, 9005-53-2.

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A Cerium(III) Modification of the Peterson Reaction: Methylenation of Readily Enolizable Carbonyl Compounds

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The Peterson methylenation procedure[1] (e.g., eq 1) has many redeeming points, yet its utility in synthesis is often limited by high basicity and lack of chemoselectivity of the lithium reagent. We envisioned circumventing these problems by using Imamoto's cerium trichloride methodology. Imamoto has fond that alkyllithium reagents interact with anhydrous cerium trichloride presumably to form a "$RCeCl_2$" species.[2] These cerium reagents show remarkable nucleophilic properties in additions to aldehydes and ketones and can be selectively added to these groups in the presence of esters, amides, and halides.[2]
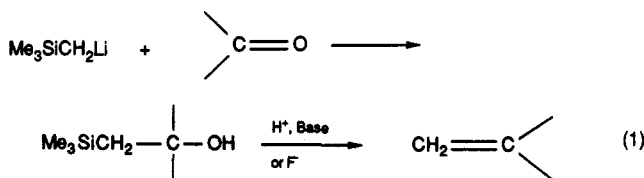
[(Trimethylsilyl)methyl]lithium in tetrahydrofuran (prepared from (chloromethyl)trimethylsilane) or in pentane (purchased)[3] was added to anhydrous $CeCl_3$ at –78 °C. Addition of aldehydes and ketones to the reagent solution followed by aqueous workup under various acidic or basic conditions resulted in complex mixtures largely of allylic silanes and alkenes. This situation was markedly improved by the addition of 1 equiv of N,N,N',N'-tetramethylethylenediamine (TMEDA) per equiv of $CeCl_3$ just prior to workup with aqueous $NaHCO_3$. The procedure resulted in excellent yields of the desired 2-hydroxy silanes. In all cases involving enolizable aldehydes and ketones the Li/Ce reagents gave yields of addition products superior to those obtained by use of Mg/Ce reagents, Mg reagents, or Li reagents. A comparison of the yields of adducts obtained from $(CH_3)_3SiCH_2Li$ with and without $CeCl_3$ is given in Table I.

The 2-hydroxy silanes were converted to the corresponding methylene compounds[4] by treatment with aqueous HF (with or without pyridine) or potassium hydride (see table). The latter was found to cause double-bond isomerization in sensitive cases.

Experimental Section

Procedure B: Addition of [(Trimethylsilyl)methyl]lithium/Cerium Trichloride. Anhydrous cerium trichloride[2] was prepared as follows: To a 25-mL flask was added (0.652 g, 1.75 mmol) cerium trichloride heptahydrate. The temperature was raised to 140 °C over 1 h under high vacuum (0.10 >mm Hg). After 1 h at 140 °C, a spin bar was added, and the cerium tri-

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(4) For a review of reagents useful for the conversion of 2-hydroxy silanes into alkenes, see ref 1d.