The Chemistry of Reactive Lignin Intermediates. Part II.[1] Addition Reactions of Vinyl-substituted Quinone Methides in Aqueous Solution

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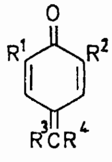
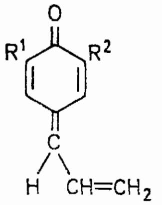
The rate equation describing the pH dependence of addition reactions of the quinone methide 4-allylidene-2-methoxycyclohexa-2,5-dienone (IIb) (QM) in aqueous solution has the form $v = \{k_0 + k_{OH^-}[OH^-] + k_{H_3O^+}[H_3O^+]\}[QM]$. The values of the individual rate constants are reported. Some data for the analogous 2,6-dimethoxy-compound (IIc) are also reported. Mechanisms of addition of hydroxy-compounds are discussed.

Benzyl ether linkages in lignin are thought to be formed by addition of hydroxy-compounds to quinone methides.[2,3] During lignification, a number of hydroxy-compounds (phenols, alcohols, carbohydrates, water, *etc.*) are present which may add to transient quinone methides.

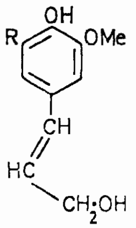
Rates of addition of hydroxy-compounds to quinone methides are reported to be pH-dependent [4] and dependent on the dissociation constants of the hydroxy-compounds.[3] However, quantitative data have been reported only for the rates of addition of methanol to the simple quinone methides (I) and the extended quinone methide (IIa),[5,6] and of water and acetic acid to the quinone methide (IIb),[1] the hydroxy-compound being both solvent and reactant in each case. Further studies are therefore necessary for an understanding of these reactions and their role in lignin biosynthesis.



(I)



(II)a; $R^1 = R^2 = Me$
b; $R^1 = H$, $R^2 = OMe$
c; $R^1 = R^2 = OMe$



(III)a; R = H
b; R = MeO

In this paper the effect of varying pH in the range 2.8—13.3 on the rate of reaction of the quinone methide (IIb) in aqueous solution is reported. Some data for the closely related quinone methide (IIc) are also given. Mechanisms of addition are discussed.

EXPERIMENTAL

Materials.—Coniferyl alcohol [3-(4-hydroxy-3-methoxyphenyl)prop-2-en-1-ol] (Fluka AG; Purum) was used without further purification. Sinapyl alcohol [3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-en-1-ol] was prepared by reducing ethyl sinapate with $LiAlH_4$.[7] It was purified by column chromatography.

AnalaR reagents were used to prepare buffers and solutions. Doubly distilled water was boiled or purged with nitrogen before use. The nitrogen was pretreated by passing it through a tube of soda-lime and a water scrubber.

Sodium perchlorate was used to prepare solutions of constant ionic strength (I 0.25).

Solutions used were as follows: (1) acetate buffers of constant ionic strength (I 0.25) in the pH range 2.8—4.8, (2) phosphate buffers with and without added salts in the pH range 6.7—8.1, (3) sodium hydroxide solutions in the pH range 12.2—13.3, and (4) pH 7 sodium acetate solutions.

Kinetic Runs.—The quinone methides (IIb and c) were obtained as transient species having $\lambda_{max.}$ *ca.* 350 nm by flash photolysis of the lignin precursors coniferyl alcohol (IIIa) and sinapyl alcohol (IIIb) in aqueous solution.[1] The

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[1] Part I, G. Leary, *J.C.S. Perkin II*, 1972, 640.

[2] J. M. Harkin, in 'Oxidative Coupling of Phenols,' eds. W. I. Taylor and A. R. Battersby, Dekker, New York, 1967, p. 285.

[3] K. Freudenberg and A. C. Neish, 'Constitution and Biosynthesis of Lignin,' Springer-Verlag, New York, 1968, p. 93.

[4] C. D. Cook and B. E. Norcross, *J. Amer. Chem. Soc.*, 1956, **78**, 3797.

[5] L. J. Filar and S. Winstein, *Tetrahedron Letters*, 1960, 9.

[6] L. K. Dyall and S. Winstein, *J. Amer. Chem. Soc.*, 1972, **94**, 2196.

[7] K. Freudenberg and H. H. Hübner, *Chem. Ber.*, 1952, **85**, 1181.

concentration of coniferyl alcohol in solutions was in the range 5×10^{-5} to 10^{-4} mol dm^{-3} and of sinapyl alcohol *ca.* 1.5×10^{-5} mol dm^{-3}. Concentrations were determined spectrophotometrically at 260—290 nm.

Flash photolysis was carried out in a Northern Precision Co. type F.P. IP apparatus.[1] The 10 cm cell was placed in a 25 °C water-bath for *ca.* 10 min and then quickly transferred to the apparatus. The disappearance of the quinone methide was followed at a suitable wavelength in the 360—375 nm region and recorded (a) by a Tektronix type 549 storage oscilloscope or (b) by a Beckman Acta CV spectrophotometer, by rapidly transferring the cell to the temperature-controlled cell holder of the spectrophotometer. When recording was performed with the storage oscilloscope, the temperature of the solution in the cell was measured as soon as the reaction was nearing completion, to ensure that it had not changed significantly.

TABLE 1

Observed * rate constants at 25 °C for the reaction of the quinone methide (IIb) in aqueous solutions

	$10^2k_{obs}/s^{-1}$	pH_m	Solution composition (mol dm^{-3})		
			$10^2[HOAc]$	$10^2[NaOAc]$	$10[NaClO_4]$
1	51.3 ± 1.5	2.88	5.1		2.5
2	28.7 ± 0.9	3.20	5.1	0.17	2.5
3	7.30 ± 0.22	3.80	5.2	0.90	2.4
4	3.08 ± 0.12	4.25	5.2	2.8	2.2
5	1.18 ± 0.05	4.80	5.1	8.9	1.6
6	59.5 ± 1.8	2.80	45	0.80	2.4
7	14.5 ± 0.4	3.50	45	4.5	2.1
8	8.76 ± 0.26	3.80	45	8.0	1.7
			$10^4[NaH_2PO_4]$	$10^4[Na_2HPO_4]$	$10[NaClO_4]$
	0.36 ± 0.03	7.1	2.3—23	2.7—27	
	0.36 ± 0.03	8.1	4.0	46	
	0.33 ± 0.03	6.7	12	14	2.5
			$10^2[NaOH]$		
	99.3 ± 2.0		20.6		
	48.3 ± 1.0		10.2		
	22.1 ± 0.4		4.90		
	7.85 ± 0.16		1.55		

* Monitoring with quartz–halogen lamp and storage oscilloscope (see text).

Rate constants were determined from the equation $kt = 2.303 \log (A_0 - A_\infty)/(A_t - A_\infty)$ where A is the absorbance of the solution; A_∞ was essentially zero for runs with coniferyl alcohol and small ($<4\%$ of A_0) for runs with sinapyl alcohol. Kinetic plots were linear for at least two half-lives.

Rate constants in Table 1 are the mean values for six to eight runs having a temperature range not greater than 0.5 °C. Differences between the mean temperatures of sets of runs at different pH values were also not greater than 0.5 °C. Rate constants in Table 2 are the mean values for five to six runs and in Table 3 the mean values of duplicate runs.

Measurements of pH in the region 2.8—8.1 were made with a Beckmann Zeromatic pH meter. The glass electrode was calibrated with citrate–HCl and borate–HCl buffers of pH 3.00, 4.00, and 8.00 (± 0.02) (Merck ampoules).

In the pH region 12.2—13.3 sodium hydroxide concentration was determined by acid–base titration.

The anion of coniferyl alcohol was quite stable in these alkaline solutions, there being little change in its spectrum over 24 h.

RESULTS AND DISCUSSION

Effect of Varying pH *on the Rate of Reaction of the Quinone Methide* (IIb).—The kinetics were pseudo-first-order in all the buffers and solutions studied. Rate constants (k_{obs}) at 25 °C, the compositions of the buffers and solutions, and measured pH values (pH_m) are shown in Table 1. The data suggested a rate equation of the form (i), where [QM] is the concentration of (IIb) and k_0 the rate constant at neutral pH (see below).

$$v/[QM] = k_{obs} = k_0 + k_{OH^-} [OH^-] + k_{H_3O^+} [H_3O^+] \quad (i)$$

Neutral pH *region* (*reaction monitored in flash photolysis apparatus*). Measurements of k_{obs} in dilute phosphate buffers at pH_m 7.1 and 8.1 gave values of $3.6 \pm 0.3 \times 10^{-3}$ s^{-1} at both pH values (Table 1). A ten-fold variation in the concentrations of the buffer components had no effect on the value of k_{obs}. In solutions of ionic strength 0.25, the value of k_{obs} was $3.3 \pm 0.3 \times 10^{-3}$ s^{-1}. In this pH region (6.7—8.1) contributions to k_{obs} from the acid and base terms in equation (i) were negligible and $k_{obs} = k_0$.

Region of pH 12.2—13.3. A plot of log ($k_{obs} - k_0$) *versus* log [OH$^-$] for sodium hydroxide solutions (1.6×10^{-2}—2.1×10^{-1} mol dm^{-3}) was linear with slope 1.00 (r 0.999) in good agreement with equation (i). A plot of k_{obs} *versus* [OH$^-$] gave the value 4.85 mol^{-1} dm^3 s^{-1} for k_{OH^-}.

Region of pH 2.8—4.8. A plot of log ($k_{obs} - k_0$) *versus* $-pH_m$ for acetate buffers 1—5 having pH_m 2.88—4.80 (see Table 1) was linear with slope 0.94 (r 0.999), in fair agreement with equation (i). The values of log ($k_{obs} - k_0$) for the more concentrated buffers 6—8 having pH_m 2.80—3.80, when superimposed on the above plot, deviated significantly from it only at pH 3.80. This deviation and the low slope of the order plot were possibly due to a contribution to the rate equation from a term involving acetic acid becoming significant as the pH values of the buffers increased.

At pH_m 2.88, the only significant contribution to the value of k_{obs} was from the term $k_{H_3O^+}$ [H$_3$O$^+$]. As it is not possible to relate quantitatively measured pH values of concentrated solutions to the oxonium ion concentration of the solution,[8] $[H_3O^+]$ was calculated by simply assuming the relationship $pH_m = -\log [H_3O^+]$. The experimental value of k_{obs} at pH_m 2.88 was then used to calculate $k_{H_3O^+}$. The value obtained was 3.89×10^2 mol^{-1} dm^3 s^{-1}.

Neutral pH *region* (*reaction monitored in spectrophotometer*). In the region of neutral pH, the rate at 25 °C was slow enough for the reaction to be followed in a conventional u.v.–visible spectrophotometer with a temperature-controlled cell holder. Rates were measured in unbuffered water, and in dilute phosphate buffers (pH_m 6.7—7.2) containing (a) no added salt, (b) 0.25 mol dm^{-3} sodium perchlorate, and (c) 0.25 mol dm^{-3} sodium chloride. The results are shown in Table 2. The value of k_{obs} was independent of initial quinone methide concentration over a 5.5-fold change in concentration and of initial coniferyl alcohol concentration over at least a 2.5-fold change. The rate also showed essentially no dependence on ionic strength.

TABLE 2

Observed * rate constants at 25 °C for the reaction of the quinone methide (IIb) in neutral aqueous solutions

$10^3k_{obs}/s^{-1}$	pH_m	Solution composition (mol dm^{-3})	
1.30 ± 0.04		Unbuffered water	
1.28 ± 0.03	7.2	Phosphate buffer (B)	
1.23 ± 0.02	6.7	B + $NaClO_4$ (0.251 mol dm^{-3})	
1.38 ± 0.03	6.7	B + NaCl (0.250 mol dm^{-3})	
		10[NaOAc]	10^3[HOAc]
2.38 ± 0.12	6.9	2.50	1.42
3.36 ± 0.17	6.9	4.86	2.76

B = 1.2×10^{-3} mol dm^{-3} NaH_2PO_4 + 1.4×10^{-3} mol dm^{-3} Na_2HPO_4.

* Monitoring with Acta CV spectrophotometer (see text).

The values of k_{obs} (= k_0) obtained by this method of monitoring the reaction were markedly lower than the values obtained when the reaction was monitored in the flash photolysis apparatus. This difference was found to be caused by a photochemical reaction of the quinone methide induced by the quartz–halogen monitoring lamp of the flash photolysis apparatus. The reaction cell was sited between this source and the monochromator, the intensity of the monitoring beam was much higher than that of a conventional spectrophotometer, and the exposure time was comparatively long owing to the slowness of reaction in this pH region. Chopping the monitoring beam so that the cell was irradiated for only *ca.* one-sixtieth of the time reduced k_{obs} to a value close to that obtained by spectrophotometer monitoring of the reaction.

The values of $k_{H_3O^+}$ and k_{OH^-} are so much higher than that of k_0 (Table 4) that photochemical reactions are not thought to be significant outside the region of neutral pH.

Sodium acetate solutions. Measurements of k_{obs} in sodium acetate solutions (2.5×10^{-1} and 4.9×10^{-1} mol dm^{-3}; pH 7) were also made by using the spectrophotometer to monitor the reaction. Reaction mixtures were prepared by flash photolysis of an aqueous solution of coniferyl alcohol and then adding it to a solution of sodium acetate. A reaction dependent on sodium acetate concentration was observed (Table 2) and a value for k_{OAc^-} of $4.13 \pm 0.36 \times 10^{-3}$ mol^{-1} dm^3 s^{-1} was obtained by assuming the rate equation $k_{obs} = k_0 + k_{OAc^-}[OAc^-]$.

Reactions of the Quinone Methide (IIc).—The rates of reaction of the less reactive quinone methide (IIc) were also measured in neutral aqueous solutions at 25 °C by using the spectrophotometer to monitor the reaction. Measurements were carried out in unbuffered water, in dilute phosphate buffers (pH_m 6.7—7.2) containing (a) no added salt, (b) 0.25 mol dm^{-3} sodium perchlorate, and (c) 0.25 mol dm^{-3} sodium chloride, and in 0.25 and 0.50 mol dm^{-3} sodium acetate solutions adjusted to pH 7 with acetic acid. For the sodium acetate runs, the reactants were mixed after flash photolysis of the sinapyl alcohol solution. The results are shown in Table 3.

TABLE 3

Observed rate constants at 25 °C for the reaction of the quinone methide (IIc) in neutral aqueous solutions

$10^5k_{obs}/s^{-1}$	pH_m	Solution composition (mol dm^{-3})	
8.13 ± 0.16		Unbuffered water	
8.62 ± 0.17	7.2	Phosphate buffer (B)	
7.96 ± 0.16	6.7	B + $NaClO_4$ (0.252 mol dm^{-3})	
8.80 ± 0.18	6.7	B + NaCl (0.250 mol dm^{-3})	
		10[NaOAc]	10^3[HOAc]
8.63 ± 0.17	6.9	2.50	1.42
8.80 ± 0.18	6.9	4.88	2.76

B = 1.2×10^{-3} mol dm^{-3} NaH_2PO_4 + 1.4×10^{-3} mol dm^{-3} Na_2HPO_4.

TABLE 4

Values for the individual rate constants of equation (i); reactions of (IIb)

$10^{-2}k_{H_3O^+}$/mol^{-1} dm^3 s^{-1}	3.89
k_{OH^-}/mol^{-1} dm^3 s^{-1}	4.85
$10^3k_0/s^{-1}$	1.29
$10^3k_{OAc^-}$/mol^{-1} dm^3 s^{-1}	4.13

The reactions of the quinone methide (IIc), like those of (IIb), obeyed first-order kinetics and were essentially independent of ionic strength. Unlike (IIb), (IIc) does not appear to react with sodium acetate at a significant rate at concentrations up to 0.50 mol dm^{-3}.

Products.—With these reactive quinone methides, which are made by photolysis,† it is difficult to demonstrate that the measured rates of reaction are actually rates of addition, as (a) one of the possible products is the parent substituted hydroxyphenylpropenol, which is always present in considerable excess, and (b) concentrations of the transient quinone methide are low. However, with (IIc) in unbuffered water, dilute phosphate buffers, and dilute hydrochloric acid solutions of pH *ca.* 4, the absorbance at the absorption maximum of sinapyl

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† Product studies with allylidenecyclohexadienones prepared by other methods are under way.

[8] R. G. Bates, ' Determination of pH. Theory and Practice,' Wiley, New York, 1964.

alcohol was observed to increase as the reaction proceeded. In the presence of the 0.25 mol dm^{-3} salts, sinapyl alcohol itself underwent a slow reaction with a decrease in absorbance, which prevented the above method of detecting products from being used.

Two products of addition are possible with these extended quinone methides. The product of terminal (1,8-) addition is the thermodynamically more stable, fully conjugated 3-phenylallyl compound and the product of addition to the benzylic position (1,6-addition) is the less stable 1-phenylallyl compound. In the case of addition of water the former product would be the precursor alcohol. The lower extinction coefficient of the product of addition to the benzyl position prevents spectrophotometric detection of this product in these reaction systems.

Mechanisms of Addition.—The pH dependence of the rate of reaction of the quinone methide (IIb) suggests that at least two, and possibly three mechanisms of addition are being observed (see Scheme). In the region of linear dependence on oxonium ion concentration the rate-determining step is likely to be the addition of a proton to form a resonance-stabilized allylic carbocation which would then react with available nucleophilic species.

In the region of linear dependence on hydroxide ion concentration nucleophilic addition of the hydroxide ion appears to be taking place. Of the other anionic nucleophiles included in this paper, namely the weak nucleophiles chloride and acetate ion, only the reaction of acetate ion with (IIb) is significant.

(1) $\mathrm{QM} + \mathrm{H_3O^+} \rightleftharpoons \mathrm{QMH^+} \begin{cases} \xrightarrow{+\mathrm{H_2O},\ -\mathrm{H^+}} \mathrm{QMHOH} \\ \xrightarrow{+\mathrm{N^-}} \mathrm{QMHN} \end{cases}$

(2) $\mathrm{QM} + \mathrm{Nu^-} \longrightarrow \mathrm{QMNu^-}$ (where $\mathrm{Nu^-} = \mathrm{OH^-}, \mathrm{OAc^-}$, *etc.*)

(3) $\mathrm{QM} + 2\mathrm{H_2O} \longrightarrow \mathrm{QMHOH} + \mathrm{H_2O}$

In the region of neutral pH, $k_{\mathrm{obs}} = k_0$ (determined with spectrophotometer monitoring of the reaction) is thought to be $k_{\mathrm{H_2O}}$, the rate constant for addition of H_2O. This is essentially independent of ionic strength and concerted nucleophilic and electrophilic attack by water molecules may be occurring.

The quinone methide (IIb) reacts 15—16 times faster than quinone methide (IIc) and this difference probably reflects the stabilizing electronic (and possibly steric) effects of the additional conjugated methoxy-group, which would oppose the requirements of the addition reaction.

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