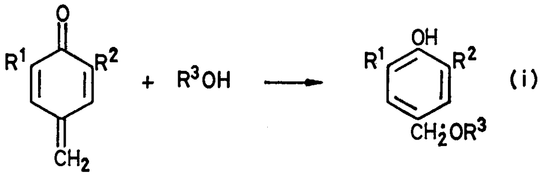
The Chemistry of Reactive Lignin Intermediates. Part 5.[1] Rates of Reactions of Quinone Methides with Water, Alcohols, Phenols, and Carboxylic Acids

By **Gordon Leary,* Ian J. Miller, Wayne Thomas,** and **Anthony D. Woolhouse,** Chemistry Division, D.S.I.R., Petone, New Zealand

The rates of reactions of the quinone methides 2-methoxy-4-methylene-6-t-butyl- and 2,6-dimethyl-4-methylene-cyclohexa-2,5-dienone with water, phenols, and a wide range of alcohols and carboxylic acids have been measured. The reactions are second-order in alcohol or acid and of the order 1.5 in water. The rate constants depend on the pK_a values of the acids and the degree of substitution of the alcohols.

QUINONE methides are formed as reactive intermediates during the polymerization of lignin,[2] and are thought to react by addition of hydroxy-compounds (water, alcohols, phenols, or acids) as in equation (i). Addition of carbohydrates or lignin phenols would form lignin–carbohydrate or lignin–lignin bonds, respectively. Thus studies of the reactions of quinone methides with hydroxy-compounds are of importance in understanding the bonding of lignin in plants.



(1) $R^1 = OMe$, $R^2 = Bu^t$
(2) $R^1 = R^2 = Me$

From the few [3-6] kinetic studies of quinone methide reactions it is known that in dilute solutions containing hydroxy-compounds the rate of disappearance of quinone methide is first-order in quinone methide and is qualitatively dependent on the pK_a of the hydroxy-compound.[2,6] At higher concentrations of quinone methide, particularly in the absence of hydroxy-compounds, the formation of dimers has been observed.[7,8] In previous papers [5,9] the effect of pH on the addition of water to vinyl-substituted quinone methides and the nature of the products formed by competitive addition of hydroxy-compounds to simple quinone methides were described. This paper reports the rates of disappearance of two quinone methides in the presence of selected hydroxy-compounds, including a wide range of alcohols and acids.

EXPERIMENTAL

Materials.—t-Butyl alcohol (B.D.H. reagent grade) was purified by prolonged storage over CaH_2 and then was distilled after several hours under reflux immediately prior to use. The hydroxy-compounds were recrystallized or distilled until satisfactory physical constants were obtained.[10] Water was purged with nitrogen to remove dissolved carbon dioxide.

2-Methoxy-4-methyl-6-t-butylphenol was prepared [11] and purified by vacuum distillation [b.p. 97—99° at 1 mmHg (lit.,[11] 86—88° at 0.6 mmHg)]. 2,4,6-Trimethylphenol (Aldrich) was recrystallized from ether–pentane to give needles, m.p. 69—71° (lit.,[12] 69°). The quinone methides (1) and (2) were prepared from these phenols by treating a solution of the phenol in n-heptane with aqueous alkaline potassium hexacyanoferrate(III) [0.7 g $K_3Fe(CN)_6$ and 0.1 g NaOH, in 10 ml H_2O].

Kinetic Runs.—Separate solutions of the hydroxy-compound in t-butyl alcohol and the quinone methide in heptane were prepared and brought to the temperature required. Samples of the quinone methide (5 ml) and the hydroxy-compound (35 ml) solutions were then mixed, and the absorbance of the mixture (*ca.* 10^{-5}M in quinone methide) was monitored at 310 nm in the thermostatically controlled cell holder of a Beckman Acta CV spectrophotometer. Hydroxy-compound concentrations in the final solutions were in the range 0.004—8M.

Pseudo-first-order rate constants (k) 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 usually *ca.* 2.5% of A_0. When duplicate runs did not give close agreement they were repeated until three or more satisfactory values for k were obtained (±2% for the acids, ±10% for the less reactive alcohols).

The activation parameters were calculated [13] from rate determinations at ten or more separate temperatures spread evenly over the range 15—60 °C.

RESULTS AND DISCUSSION

Reaction Medium.—Since the quinone methides are only stable in dilute aprotic solutions and were prepared in heptane, a solvent was required which did not react significantly with the quinone methides yet would dissolve heptane and hydroxylic compounds (including water), and if possible would also participate in hydrogen bonding, since this is said [6] to be important in the polymerization of lignin. t-Butyl alcohol satisfied these requirements for the quinone methide (1) and was

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used in all experiments with it. The quinone methide (2) appeared to react with t-butyl alcohol very slowly, but this had a negligible effect on the rate constants calculated for the other hydroxy-compounds in the t-butyl alcohol–heptane solvent mixture.

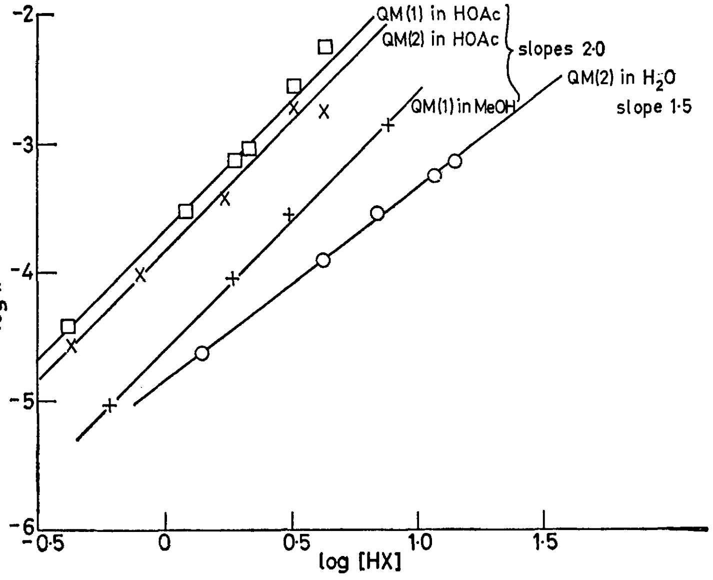

FIGURE 1 Plot of log k *versus* log [ROH]

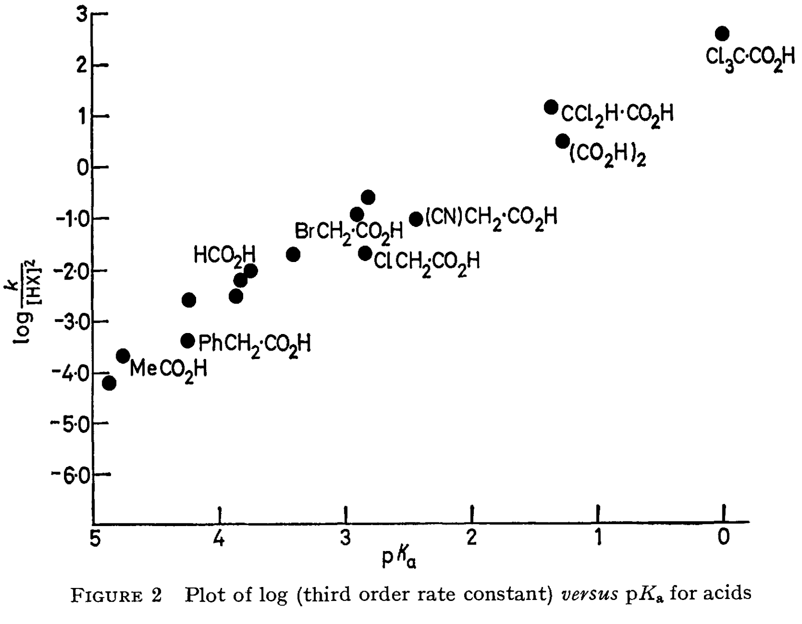

FIGURE 2 Plot of log (third order rate constant) *versus* pK_a for acids

The products of the reactions of quinone methides have been found [3,9] to be of the type outlined in equation (i). In acid–alcohol mixtures it appeared [9] that only the alcohol added, to form benzyl ethers. An exception was when t-butyl alcohol was the alcohol, in which case only the ester was formed.

Order of Reaction.—Kinetic plots used to calculate pseudo-first-order rate constants were linear for reactions with all the hydroxy-compounds over at least three half lives. Pseudo-first-order rate constants for reactions of the quinone methide (1) with acetic acid and the quinone methide (2) with acetic acid, water, and methanol were determined over at least a ten-fold change in hydroxy-compound concentration; Figure 1 shows plots of log k *vs.* log [hydroxy-compound]. The data show reasonable fits to lines of slopes 2.0 and 1.5, indicating that the reaction is second-order in methanol and in acetic acid but of the order 1.5 in water.

Runs for all other hydroxy-compounds except t-butyl and isopropyl alcohols were carried out on at least two concentrations; the results were in accord with the reaction being second-order in hydroxy-compound. The rate data for water did not fit an equation of the type $k = k_1[H_2O] + k_2[H_2O]^2$.

Rate Constants for Acids.—Mean values for the third-order rate constants determined for the acids are given in Table 1. A plot of the logarithm of the third-order rate constants *vs.* pK_a values [14] for the acids in water (Figure 2) confirms [2,6] that the rate constants are roughly proportional to acidity. Glycolic acid and the dicarboxylic acids show no marked deviations, *i.e.* the second hydroxy-group shows no significant effect other than that which affects the pK_a value.

TABLE 1

Rate constants for reactions with acids

	$(k/\text{Acid}]^2)/\text{dm}^6\ \text{mol}^{-2}\ \text{s}^{-1}$
Quinone methide (1)	
Trichloroacetic	3.71×10^2
Dichloroacetic	1.27×10^1
Oxalic	3.00
Malonic	2.47×10^{-1}
Bromoacetic	1.16×10^{-1}
Cyanoacetic	8.64×10^{-2}
Chloroacetic	2.03×10^{-2}
Mandelic	1.82×10^{-2}
Formic	9.43×10^{-3}
Glycolic	6.05×10^{-3}
Lactic	2.83×10^{-3}
Succinic	2.62×10^{-3}
Phenylacetic	4.06×10^{-4}
Acetic	1.96×10^{-4}
Propionic	6.37×10^{-5}
Quinone methide (2)	
Acetic	1.35×10^{-4}

Rate Constants for Alcohols and Phenols.—The mean values for the third-order rate constants for the reactions of alcohols and phenols are given in Table 2. For the simple alcohols studied there is an order of reactivity tertiary < secondary < primary < methanol. This appears to be a consequence of steric rather than acidity effects, since if the alcohol or phenol results are plotted in the Brønsted plot of Figure 2, there is no fit. This agrees with recent observations by Higuchi,[6] and also with the report that steric effects significantly slow the reactions of various quinone methides with methanol.[3]

TABLE 2

Rate constants for reactions with alcohols and phenols (25 °C)

	$(k/\text{ROH}]^2)/\text{dm}^6\ \text{mol}^{-2}\ \text{s}^{-1}$
Quinone methide (1)	
Guaiacol	1.4×10^{-5}
Phenol	1.4×10^{-5}
Glycerol	5.0×10^{-6}
Ethylene glycol	3.5×10^{-6}
Propane-1,2-diol	1.8×10^{-6}
Methanol	1.8×10^{-6}
Ethanol	1.1×10^{-7}
Allyl alcohol	5.1×10^{-7}
2-Methoxyethanol	4.0×10^{-7}
Benzyl alcohol	2.4×10^{-7}
Propan-2-ol	5.5×10^{-8}
Quinone methide (2)	
Methanol	3.0×10^{-5}
Ethanol	1.5×10^{-5}
t-Butyl alcohol	1.2×10^{-8}

The rates of addition of polyols are greater than those expected from the additive effects of the separate hydroxy-groups. For example, propane-1,2-diol has a rate constant significantly greater than the sum of the rate constants for ethanol and propan-2-ol.

Rate Constants for Water.—The value of $k/[\text{H}_2\text{O}]^{3/2}$ for the disappearance of the quinone methide (1) at 25 °C was $5.5 \pm 1.0 \times 10^{-7}$; for the quinone methide (2) it was $1.51 \pm 0.11 \times 10^{-5}\ \text{dm}^{9/2}\ \text{mol}^{-3/2}\ \text{s}^{-1}$.

Mechanism.—The activation parameters for the reactions of the quinone methide (2) with water and methanol and the quinone methide (1) with glycolic acid are shown in Table 3. The entropies of activation have exceedingly high negative values and the enthalpies of activation for the acid and the alcohol are very similar. Thus the rate difference for the overall third-order reactions depends almost entirely on entropy effects.

The high negative entropy of activation and the overall third-order reaction suggest that hydroxy-compounds react with the quinone methides *via* a termolecular complex, possibly with a different hydroxylic group associated with both the carbonyl group and the benzylic carbon atom. This could allow concerted protonation of the carbonyl group and nucleophilic attack on the benzylic carbon atom. The wide separation of these two functional groups would explain why hydroxy-acids, dicarboxylic acids, and glycols retain their overall third-order dependence, as the second function on the reagent cannot cover the required distance. The greater rates of reaction with polyhydroxy-compounds could be due to some assistance from hydrogen bonding in forming the termolecular complex.

If this interpretation is correct, then a dihydroxy-molecule that had the two groups separated sufficiently to allow the quinone methide to ' fit ' between the two groups would be expected to react more readily.

The order of 1.5 for water could arise from an intermediate complex consisting of water attacking the benzylic carbon atom while the carbonyl group is protonated. The half order would then arise through $[\text{H}^+] = [\text{OH}^-] \propto \text{H}_2\text{O}$. The rates of reaction of quinone methides have been found [5] to be pH-dependent in dilute aqueous acid.

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