Reaction of Formaldehyde at the *Ortho-* and Para-Positions of Phenol: Exploration of Mechanisms Using Computational Chemistry

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Abstract

Computational chemistry methods can be used to explore the theoretical chemistry behind reactive systems, to compare the relative chemical reactivity of different systems, and, by extension, to predict the reactivity of new systems. Ongoing research has focused on the reactivity of a wide variety of phenolic compounds with formaldehyde using semi-empirical and ab initio computational chemistry methods. This research has been expanded to study theoretical transition states formed on reacting phenol with formaldehyde. According to transition state theory, the energy of a transition state is related to the reaction rate. Transition states for reaction of formaldehyde at the *ortho-* and *para-*positions of phenol were determined by computational means. These theoretical calculations predict that formaldehyde reacts faster at the para-position of phenol than at the ortho-position, in agreement with experimental data.

Introduction

The reaction of phenolic compounds with formaldehyde forms the basis for synthesis of an important class of adhesives used to manufacture bonded wood products. Better understanding of the fundamental chemistry behind the synthesis and cure of phenolic adhesive systems would make it possible to utilize these systems more effectively to bond wood, to modify these systems for use under a wider set of bonding conditions, and to develop new systems based upon the same general chemistry. Newer computational chemistry methods can be used to explore the theoretical chemistry behind reactive systems, to compare the relative chemical reactivity of different systems, and, by extension, to predict the reactivity of new systems. Research on the reactivity of a wide variety of phenolic compounds with formaldehyde using semi-empirical and *ab initio* computational chemistry methods has been expanded to study theoretical transition states formed on reacting phenol with formaldehyde. Preliminary results are reported in this paper.

Results and Discussion

Previous research showed that the reactivity of a large number of phenolic compounds toward formaldehyde could be correlated with atomic charges at reactive sites on the aromatic nucleus (2). These charges were calculated using ab initio computational chemistry methods. Calculations at a relatively high level of theory (i.e., RHF/6-31+G) showed that for a given phenolic compound the sum of the atomic charges at those carbon atoms of the phenolic nucleus on which the highest occupied molecular orbital resides can be correlated with the experimental reactivity of that compound (Fig. 1). In addition, it was shown that the correlated data could be used to calculate the relative reactivity of formaldehyde at the various aromatic positions on the phenolic nuclei (Fig. 2).

Data in the literature for the reactivity of the phenolic compounds with formaldehyde (1l) used in these calculations were collected prior to the availability of modern analytical techniques, such as nuclear magnetic resonance (NMR) and HPLC. Instead, the data were calculated from the disappearance of formaldehyde. The formaldehyde consumption reactions were not necessarily limited to the formation of monomeric hydroxymethyl derivatives of the phenols, although

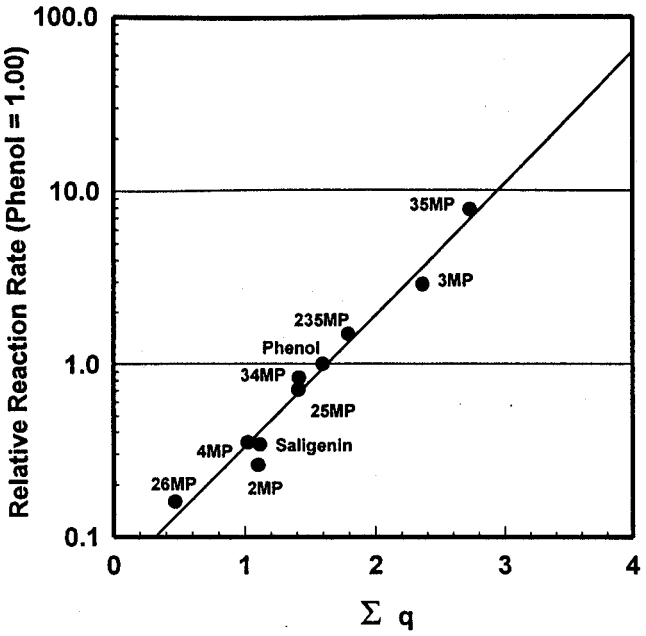

Figure 1.—*Correlation of relative reaction rate for series of phenolic compounds with formaldehyde with sum of charges (Σq) calculated at RHF/6 31 +G level of theory (2). For explanation of compound abbreviations see Figure 2.*

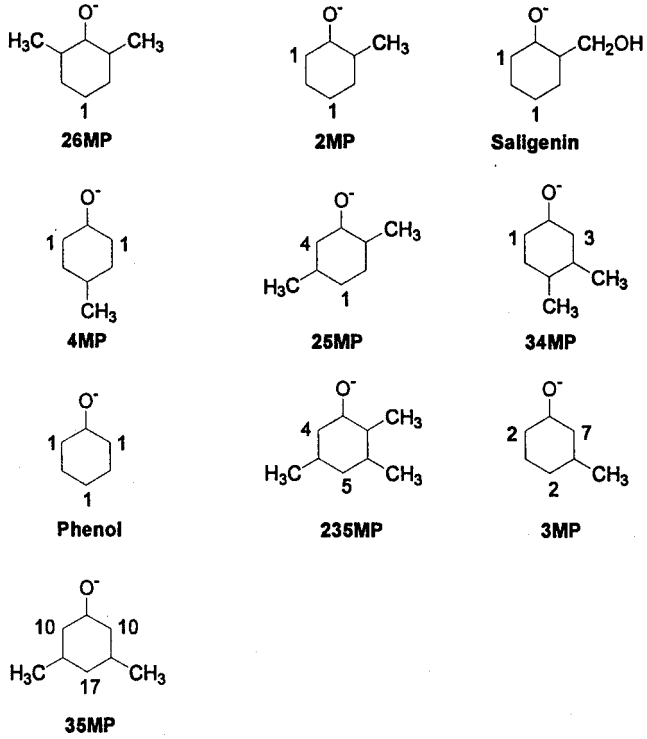

Figure 2.– *Calculated relative positional rate constants for reactions of series of phenolic compounds with formaldehyde (2). Relative reactivity of para-position of phenol is defined as unity.*

only the initial reaction times were considered in calculating the kinetic data. Thus, the correlations of charge with reactivity were considered to be qualitative. In some cases, inconsistencies were noted with other data in the literature. Specifically, it is generally recognized that the *para*-position of phenol is more reactive than the *ortho*-position (1,3,5,7,9,10, 13) (Table 1, Fig. 3). Yet, the charge calculations predicted that the *ortho*-position was slightly more reactive than the *para*-position. This inconsistency was probably due to the inadequate accounting of steric interactions at the *ortho*-position. Other computational methods need to be explored to overcome this limitation.

As a reaction proceeds, it goes through an activated complex (transition state) in which the reactants assume proper relational positions that allow the reaction to take place. According to transition-state theory, the energy barrier for the formation of the transition state is directly related to the reaction rate. Computational chemistry methods are available for calculating the energies of reactants, the products, and a theoretical transition state. In the study reported here, semi-empirical PM3 coupled with RHF/STO-3G methods were used to calculate energy profiles for the reaction of formaldehyde with phenol.

Formaldehyde does not occur as free formaldehyde in water solution. Instead, it occurs predominately as methylene glycol (methanediol) and higher polymeric addition products, $HO(CH_2O)_xH$ (where x on average equals approx. 3). For the purposes of our calculations, we considered formaldehyde to exist in solution as methylene glycol. Because the reaction occurs under basic conditions, phenol was assumed to exist as the phenolate anion.

We considered two possible mechanisms for the reaction of formaldehyde (i.e., methanediol) with phenol. The first was a 4-centered reaction mechanism, illustrated in Figure 4 for the reaction of methanediol at the para-position of phenol. The second was an S_n2-like reaction mechanism, illustrated in Figure 5. The S_n2-like reaction mechanism necessitates two transition states: one for the reaction of methanediol at the aromatic nucleus to form an intermediate with the loss of a hydroxyl anion, and the second for the abstraction of a hydrogen ion from the intermediate. The latter should be a very facile reaction; its transition state was not calculated. Both reaction mechanisms result in the same products, namely hydroxymethylphenol and water.

The results of our transition state calculations are shown graphically in Figure 6. The energies were determined from single-point calculations at the RHF/STO-3G level of theory using the IPCM solvation

Table 1.—*Comparison of rates for reaction of formaldehyde with phenol under basic conditions.*[a]

Rate constant	Freeman & Lewis 1954 (5)	Minami & Ando 1956 (9)	Peer 1959 (10)	Zavitsas 1968 (13)	Eapen & Yeddanapalli 1968 (3)	Aldersley & Hope 1972 (1)	Higuchi et al. 1999 (7)
K02	0.82	0.48	0.55	0.70	0.71	0.76	0.68
K04	1.00	1.00	1.00	1.00	1.00	1.00	1.00
K26	1.35	0.60		1.76	1.24	1.25	1.28
K24	1.18	1.24		1.27	2.12	0.63	2.29
K42	0.59	0.40		0.76	0.59	1.06	0.63
K264	6.53	1.56		3.75	3.00	1.01	3.23
K246	1.41	0.60		0.89	1.41	2.05	1.20

[a] Mnemonics used for rate constants are defined in Figure 3.

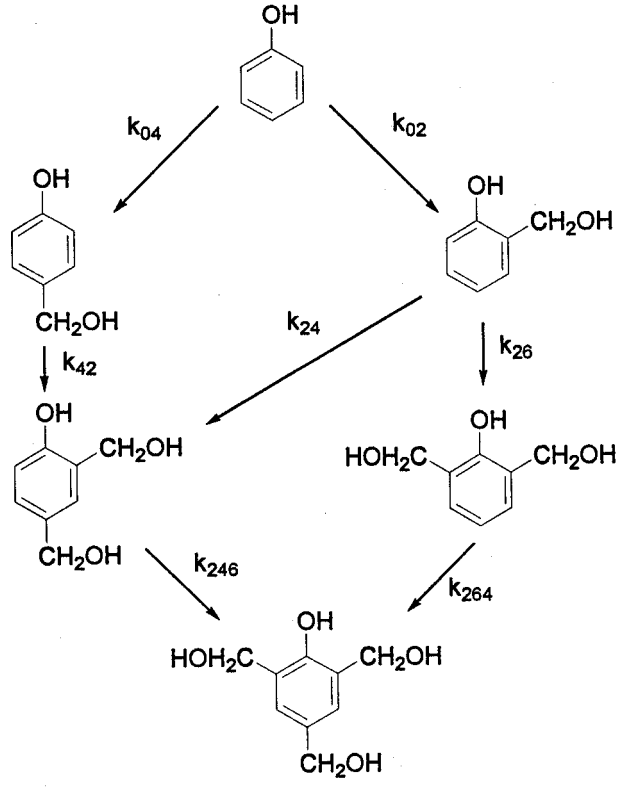

Figure 3.—*Reaction scheme for formation of hydroxymethylphenols on reacting formaldehyde with phenol. Relative rates for each reaction are listed in Table 1. Note from Table 1 that the reaction of formaldehyde at the para-position (kO_4) of phenol is faster than that at the ortho-position (kO_2), as predicted from the calculations.*

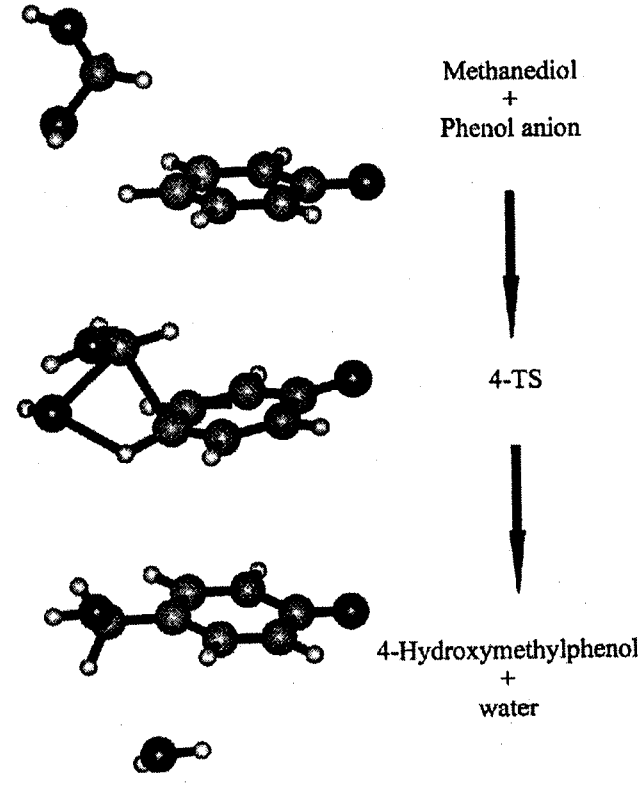

Figure 4.—*Illustration of 4-centered reaction mechanism for reaction of formaldehyde (i.e., methanediol) at para-position of phenol.*

model to simulate reaction in water. The single-point calculations were made on the PM3-optimized structures for the reactants, transition state, products, and intermediate. Reactants (phenol and formaldehyde [methyleneglycol]) occur on the left side of the reaction coordinate and products (hydroxymethylphenol and water) on the right. The calculations show that both the *para*- and *ortho*-transition states for the 4-centered mechanism occur at higher energy than the para- and *ortho*-transition states of the S_n2-like mechanism. Thus the calculations suggest that the S_n2-like mechanism is favored over the 4-centered mechanism. In addition, the calculations suggest that in both reaction mechanisms, the *para*-transition states occur at a lower energy than do the *ortho*-transition states. Therefore, the calculations suggest that reaction of formaldehyde at the *para*-position of phenol is favored over reaction at the *ortho*-position. This is in agreement with experimental data (Table 1).

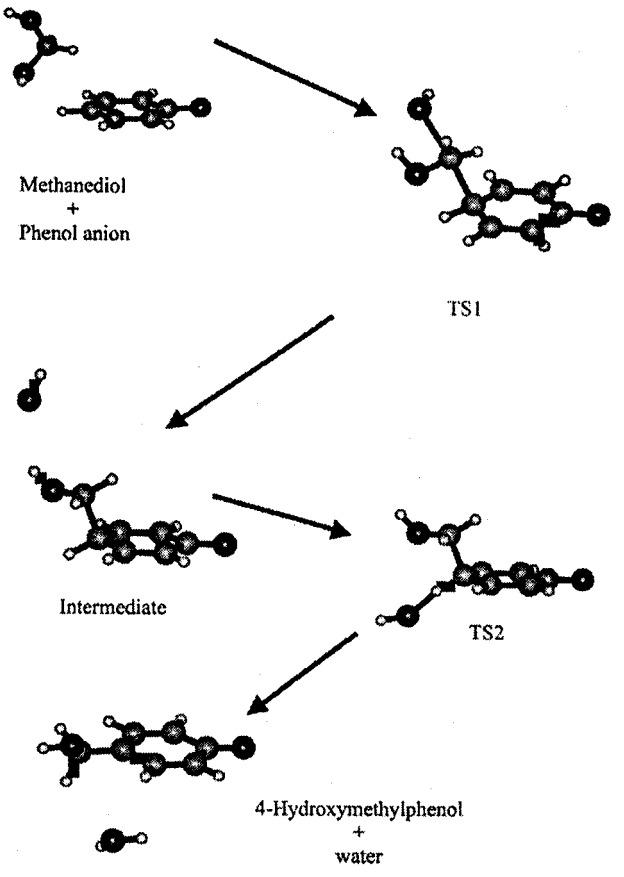

Figure 5.—*Illustration of Sn2-like reaction mechanism for reaction of formaldehyde (i.e., methanediol) at para-position of phenol.*

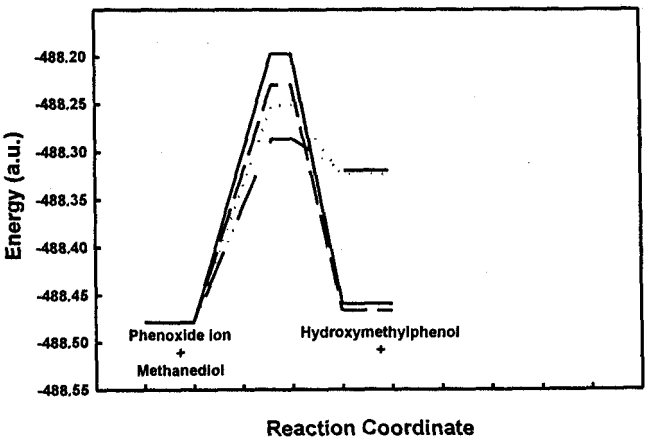

Figure 6.—*Energy profile for reaction of formaldehyde at* ortho- *and* para-*positions of phenol. Energies were determined from single-point calculations at RHF/STO-3G level of theory using IPCM solvation model to simulate reaction in water. Single-point calculations were made on PM3-optimized structures for the reactants, transition state, products, and; in the case of the S_n2-like reaction mechanism, the intermedzate.*

Computational Methods

Structure optimizations and energies of the reactants (phenol and methylene glycol), products (water and *p*- and *o*-hydroxymethylphenol), intermediates, and the hydroxyl anion were calculated at RHF/PM3 using HyperChem 4.5 (8) or MOPAC (version 6) (12). The optimized structures and energies were then refined with Gaussian 98 (6). Transition states were calculated using the Berny algorithm (TS) and the synchronous transit-guided quasi-Newton (STQN) methods. Transition states were confirmed by the presence of one and only one imaginary (negative) vibration in the IR spectra calculated with HyperChem or Gaussian 98. The reactions were simulated as occurring in water by conducting single-point calculations on the PM3-optimized reactants, products, intermediates, and transition states at RHF/STO-3G using the IPCM solvation model (4) as implemented in Gaussian 98.

Conclusions

Transition state theory seems to be better than charge calculations as a means of comparing positional reactivity of formaldehyde with phenol. Calculations of the transition state automatically account for electronic interactions, steric interactions, and overlap between orbitals to form bonds during the course of a reaction. However, transition state calculations are much more difficult and require more computational time than do charge calculations. Further work is needed to fully assess the usefulness of these methods for explaining and predicting reaction of other phenolic compounds with formaldehyde.

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