

Predicting the Reactivity of Phenolic Compounds with Formaldehyde. II. Continuation of an *Ab Initio* Study

Tohru Mitsunaga,¹ Anthony H. Conner,² Charles G. Hill, Jr.³

¹ Faculty of Bioresources, Mie University, Tsu 514-8507, Japan

² USDA Forest Service, Forest Products Laboratory, Madison, Wisconsin 53705

³ Department of Chemical Engineering, University of Wisconsin, Madison, Wisconsin 53705

Received 20 March 2001; accepted 20 December 2001

ABSTRACT: Phenol–formaldehyde resins are important adhesives used by the forest products industry. The phenolic compounds in these resins are derived primarily from petrochemical sources. Alternate sources of phenolic compounds include tannins, lignins, biomass pyrolysis products, and coal gasification products. Because of variations in their chemical structures, the reactivities of these phenolic compounds with formaldehyde vary in quite subtle ways. Previously, it was demonstrated that the reactivity of a number of phenols with formaldehyde in nonaqueous conditions could be correlated with charges calculated for reactive sites on the aromatic ring (Conner, A. H. *J Appl Polym Sci* 2000, 78, 355–363). We studied the reactivity of a larger number of phenolic compounds with formaldehyde in an aqueous solution using sodium hydroxide as the catalyst. Reaction rates were determined from measurements of the concentrations of the phenolic compounds and formalde-

hyde as functions of time. The reaction rate constants varied over a wide range (approximately 10^{-2} to 10^4 L mol⁻¹ h⁻¹). An estimate of the reactivity per reactive site on the phenolic ring was determined by dividing the rate by the number of reactive sites. Atomic charges for each phenolic compound were calculated by *ab initio* methods at the RHF/6-31+G level of theory using the CHelpG method. The charge per reactive site was estimated by summing the charges at all the reactive sites on the phenolic ring and dividing by the number of reactive sites. A strong correlation was observed between the reactivity per reactive site and the average charge per reactive site. © 2002 Wiley Periodicals, Inc. *J Appl Polym Sci* 86: 135–140, 2002

Key words: chemical computation; *ab initio*; phenolics; formaldehyde; adhesives

INTRODUCTION

To utilize phenolic adhesive systems more effectively and to develop new phenolic adhesives, it is important to understand the reactions of phenolic compounds with formaldehyde. To date, analytical studies on phenolic adhesives have concentrated mainly on kinetic studies.^{1–5} These studies involve not only the calculation of reaction rates but also complex processes for isolation and identification of intermediates, as well as reaction products. Computational chemistry methods allow analysis of reaction mechanisms and prediction of the reactivities of chemical starting materials. Therefore, computational chemistry might be used to predict the reactivities of phenolic compounds with formaldehyde and thereby provide new insight into the reaction mechanisms. Such information would be useful in developing strategies for the formulation and cure of phenolic adhesives. This insight would also serve to decrease the time needed for development of new adhesive systems.

Sprung⁶ investigated the reactions of a series of methylphenols with formaldehyde. His kinetic measurements were based solely on the rate of the disappearance of formaldehyde. As expected, differences in the reactivities of this series of phenolic compounds depended on subtle differences in the chemical structure. Conner⁷ demonstrated that the relative rates of these reactions could be correlated with electrostatic charges at reactive positions in the phenolic ring calculated using *ab initio* methods. Because of limitations on the analytical instruments in use at the time Sprung conducted his study, it was not clear whether either formaldehyde or the phenolic compounds were undergoing reactions other than those involved in hydroxymethylation. Moreover, Sprung's kinetic data were collected in nonaqueous systems rather than in the aqueous-based systems typically encountered in industrial applications of phenolic adhesives. Because of these limitations on the earlier work and the industrial significance of phenol–formaldehyde adhesives, we employed aqueous-based systems to investigate the reactions of formaldehyde with a larger series of phenolic compounds (Table I). These phenolic compounds included most of the phenols investigated by Sprung.

Correspondence to: T. Mitsunaga.

TABLE I
Phenolic Compounds, Their Reaction Rates with Formaldehyde, and the Charges at the Reactive Aromatic Sites
as Calculated at the RHF/6-31+G Level of Theory Using CHelpG

Compound	Abbreviation	k (L mol ⁻¹ h ⁻¹ ± SE)	Total charge (<i>e</i>)	Average k (L mol ⁻¹ h ⁻¹)	Average charge (<i>e</i>)
2-Methylphenol anion	2MP	0.21 ± 0.04	-0.853	1.10E - 01	-0.427
3-Methylphenol anion	3MP	1.80 ± 0.36	-1.844	6.00E - 01	-0.615
4-Methylphenol anion	4MP	0.15 ± 0.02	-0.936	7.70E - 02	-0.468
2,3-Dimethylphenol anion	23MP	1.28 ± 0.21	-1.025	6.39E - 01	-0.513
2,4-Dimethylphenol anion	24MP	0.39 ± 0.02	-0.412	3.91E - 01	-0.412
2,5-Dimethylphenol anion	25MP	1.51 ± 0.29	-1.136	7.54E - 01	-0.568
2,6-Dimethylphenol anion	26MP	0.12	-0.359	1.18E - 01	-0.359
3,4-Dimethylphenol anion	34MP	0.61 ± 0.30	-1.149	3.07E - 01	-0.575
3,5-Dimethylphenol anion	35MP	6.94 ± 1.80	-2.229	2.31E + 00	-0.743
2,3,5-Trimethylphenol anion	235MP	4.00 ± 0.66	-1.345	2.00E + 00	-0.673
2-Hydroxymethylphenol anion	2HMP	0.22 ± 0.04	-0.954	1.12E - 01	-0.477
3-Hydroxymethylphenol anion	3HMP	0.23 ± 0.07	-1.688	7.78E - 02	-0.563
Phenol anion	P	0.15 ± 0.03	-1.445	5.13E - 02	-0.482
Resorcinol anion	R	423 ± 106	-2.118	1.41E + 02	-0.706
Resorcinol dianion	RD		-2.496		-0.832
5-Methylresorcinol anion	5MR	6907 ± 1632	-2.457	2.30E + 03	-0.819
5-Methylresorcinol dianion	5MRD		-2.885		-0.962
3-Methoxyphenol anion	3OMP	16.77 ± 1.20	-2.091	5.59E + 00	-0.697
Phloroglucinol anion	Ph	18,369 ± 2655	-2.827	6.12E + 03	-0.942
Phloroglucinol dianion	PhD		-3.141		-1.047
5-Methoxyresorcinol anion	5OMR	3069 ± 670	-2.694	1.02E + 03	-0.898
5-Methoxyresorcinol dianion	5OMRD		-3.048		-1.016
3,5-Dimethoxyphenol anion	35OMP	1668 ± 286	-2.746	5.56E + 02	-0.915

EXPERIMENTAL

Reaction of phenols with formaldehyde

Reactions of the phenolic compounds with formaldehyde were conducted in a three-necked flask fitted with a condenser and a thermometer. The reactions were conducted at 30°C. The phenols, 2 mmol, and formaldehyde, 2 mmol, were dissolved in a 20% aqueous dimethylformamide (DMF) solution with stirring. A sufficient 10% sodium hydroxide solution was added such that the pH equaled the pK_a of the phenolic compound. The solvent volume was adjusted to give a solids concentration of 1%.

Analysis of the reaction mixtures by high-performance liquid chromatography (HPLC)

Samples of the reaction mixture were taken at various times after the reaction was initiated. The amount of the phenolic compound in the sample was analyzed using a Hewlett-Packard 1050 series chromatograph containing an Inertsil ODS-3 column (25 × 0.46 cm). The mobile phase consisted of acetonitrile/0.01% aqueous trifluoroacetic acid (TFA). An elution gradient of 5–45% acetonitrile in 30 min was used for the analyses of the products of the reactions of formaldehyde with phloroglucinol, resorcinol, 5-methylresorcinol, and 5-methoxyresorcinol; corresponding gradients of 10–45% acetonitrile in 25 min and 30% to 60%

acetonitrile in 30 min were used for the reaction of phenol and the reactions of methylphenols and methoxyphenols, respectively. The eluants were detected by UV absorbance at 273 nm. The amount of each phenolic compound present was calculated using calibration curves describing the relation between the concentration and peak area for that compound. Each phenolic compound formed during the reaction was assumed to be characterized by the same relative response as that of the starting phenolic compound.

Determining formaldehyde by the hydroxylamine hydrochloride method

The concentration of formaldehyde remaining in the reaction mixture was determined by the hydroxylamine hydrochloride method.⁸ One milliliter of the sample was taken from the reaction mixture and poured into a weighing jar containing 3 mL of a 0.02N hydrochloric acid solution. The solution was adjusted to pH 4 with a 0.02N sodium hydroxide solution, and 3 mL of a 0.5N hydroxylamine hydrochloride solution was added to form hydrochloride. After stirring the solution for 10 min, the sample was then back-titrated to pH 4 with a 0.02N sodium hydroxide solution using an autotitrator FMS-201 (Fluid Management Systems, Inc.).

TABLE II
p*K_a* Values and Dissociation Constants
of the Phenolic Compounds

Phenolic compound	p <i>K_a</i>		<i>K_a</i>
	Literature ¹²	This study	
Phenol	10.0	10.3	4.9E – 11
Resorcinol	9.4	9.7	1.9E – 10
Phloroglucinol		9.2	6.0E – 10
2MP	10.2	10.6	2.5E – 11
3MP		10.4	4.3E – 11
4MP	10.2	10.6	2.5E – 11
23MP		10.9	1.1E – 11
24MP		10.9	1.1E – 11
25MP		10.7	2.0E – 11
26MP	10.2	10.9	1.1E – 11
34MP		10.7	2.0E – 11
35MP		10.5	3.0E – 11
235MP		11.1	7.9E – 12
2HMP		10.1	7.9E – 11
3HMP		10.1	7.9E – 11
5MR		9.9	1.2E – 10
30MP		9.9	1.2E – 10
50MR		9.4	4.3E – 10
35OMP		9.6	2.5E – 10

Computational method

Optimized starting structures for each of the phenolic compounds were obtained using HyperChem⁹ at RHF/PM3. The structures were further optimized at the RHF/6-31+G level of theory using Gaussian 98.¹⁰ The final, optimized structures were used to calculate ChelpG (ref. 11)-based charges obtained using Gaussian 98.

RESULTS AND DISCUSSION

The reaction between phenol and formaldehyde in an alkaline solution leads to the introduction of a hydroxymethyl group onto the aromatic nucleus at positions *ortho* and *para* to the phenolic group. The reaction corresponds to an electrophilic aromatic substitution. Under alkaline conditions, phenol forms a phenoxyanion. A phenoxyanion is generally considered to be the phenolic form that reacts with electrophilic compounds like formaldehyde. Consequently, the reactions of the phenolic compounds (Table I) with formaldehyde were conducted at conditions such that each phenolic compound studied was characterized by the same concentration of its corresponding anion, that is, at a pH equivalent to the p*K_a* of that individual phenolic compound.

An aqueous solution containing 20 % (w/w) DMF was needed for completely dissolving the methylphenols and phloroglucinol. Hence, this solvent system was used in all our studies. The p*K_a* values of the phenolic compounds determined in the indicated aqueous DMF solution are shown in Table II. The p*K_a* determined in a solution containing an organic solvent

is generally higher than is the corresponding p*K_a* in water. The p*K_a* values for phenol measured in water¹² and a 20% DMF solution were 9.98 and 10.31, respectively. These results indicate that DMF has only a small effect on the extent of ionization of phenol and, by inference, is presumed to have a minimal effect on the extent of ionization of the other phenols.

The base-catalyzed hydroxymethylation of phenol by formaldehyde in a dilute aqueous solution is generally considered a second-order reaction.¹⁴ Thus, the reaction follows the general rate expression

$$dP/dt = -k[P][F] \quad (1)$$

where *P* is the concentration of the phenolic compound, and *F*, the concentration of formaldehyde at any time *t*. Equation (1) can be rearranged as shown:

$$dP/[P][F] = -k dt \quad (2)$$

By plotting the data in the form of the left-hand side of eq. (2) versus *dt*, one obtains a linear plot with slope *k*. This method was used to determine the rate constants (*k*) for reactions of phenolic compounds with formaldehyde. It should be noted that the rate constant determined in this fashion represents the sum of the rate constants for each of the reactive sites on the aromatic ring. The average rate constant per reactive site (*k_{ave}*) was calculated by dividing the value of *k* by the number of reactive sites. This procedure gives an estimate of the reactivity of the phenolic compound with formaldehyde on an individual reactive-site basis. Values of *k_{ave}* for each of the phenolic compounds used in this study are shown in Table I.

In terms of frontier molecular orbital theory,¹³ the reaction between phenol and formaldehyde is envisioned as involving the highest occupied molecular orbital (HOMO) of the phenoxyanion and the lowest unoccupied molecular orbital (LUMO) of formaldehyde. The HOMO of the phenoxyanion is distributed at the *o*- and *p*-positions of the aromatic ring. The LUMO of formaldehyde is located on the carbon atom. In addition, chemical computational methods predict that the carbon atom of formaldehyde bears a positive charge, while the *o*- and *p*-positions of the aromatic ring bear negative charges. Because there are no apparent steric factors to prevent a reaction, one predicts that formaldehyde will react with phenol at the *o*- and *p*-positions, as was observed experimentally. Thus, the electrons in the HOMO orbital of the phenoxyanion are in effect shared with the LUMO orbital of formaldehyde to form a bond, giving the *o*- and *p*-hydroxymethylphenol derivatives.

The reaction of formaldehyde with other phenolic compounds can be envisioned as taking place in a similar fashion. By establishing a correlation between the average reactivity (*k_{ave}*) for each compound in a

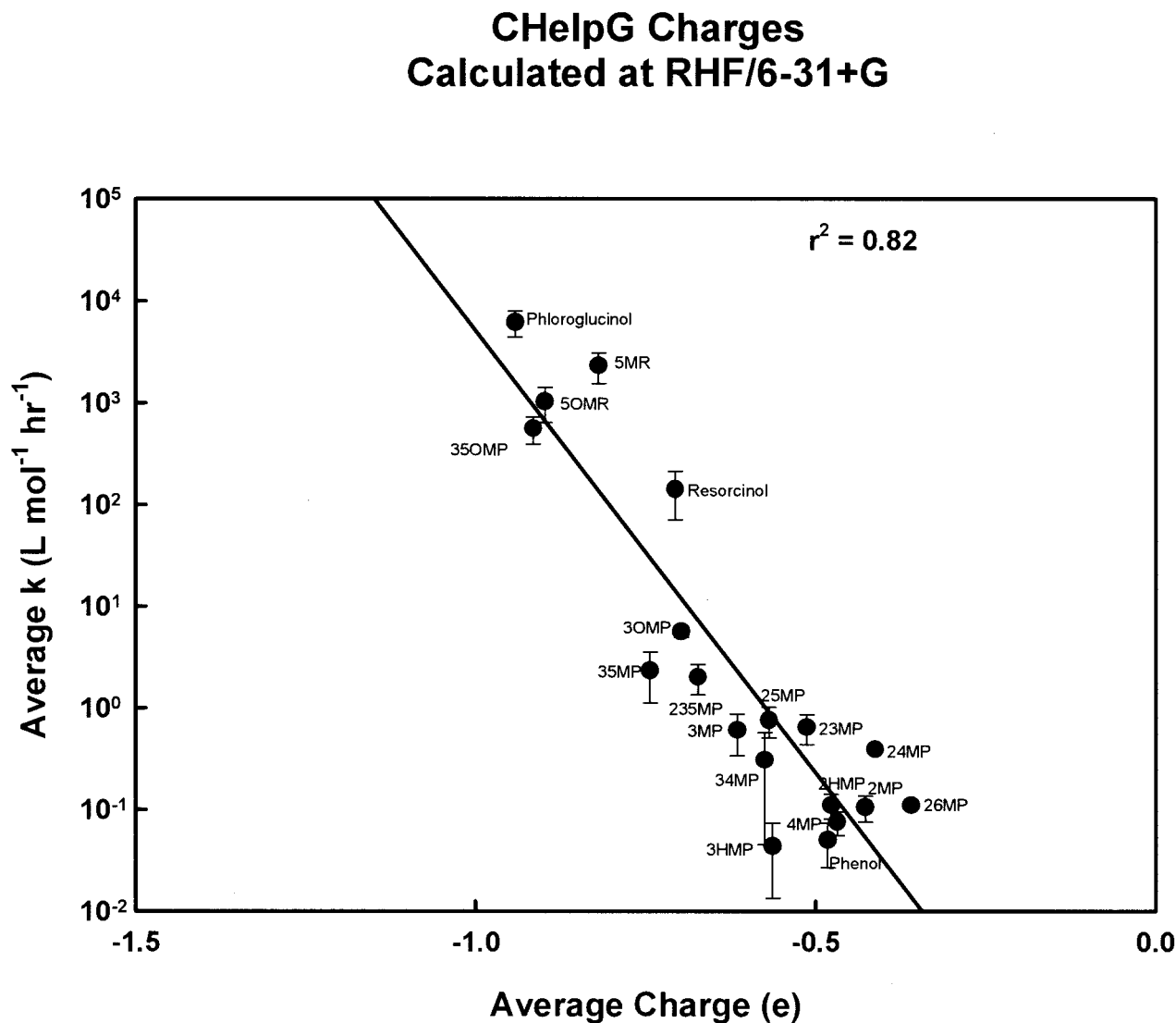


Figure 1 Semilog plot of the average rate constant versus average CHelpG charge calculated at the RHF/6-31+G level of theory for the reactions of formaldehyde with various phenolic compounds. The compounds containing two and three phenolic groups are assumed to exist in solution as monoanions.

series of phenolic compounds with their respective calculated average-charge per reactive site (q_{ave}), a method can be devised to predict the reactivity of formaldehyde with a wide variety of phenolic compounds.

The general method used to determine the number of reactive sites, to estimate the average charge per reactive site, and to account for gross steric hindrance can be illustrated from calculations at RHF/6-31+G on the 2,5-dimethylphenol anion (25MP) using the CHelpG method for calculation of the charges. The total of all the atomic charges equals -1 , as required for an anion bearing a net charge equal to that of a single electron. Large negative charges are located at the C2 (-0.209), C4 (-0.482), and C6 (-0.654) positions of the aromatic ring. The HOMO orbital is also distributed on these same sites. Consequently, one

expects the positively charged carbon of formaldehyde to be capable of reacting at these three sites. However, because a methyl group is attached at C2, access of formaldehyde to this site is more sterically hindered than is its access to the C4 and C6 positions. As a result, it is assumed that reaction of 25MP is possible only at two reactive sites, namely, at C4 and C6. The average charge per reactive site (q_{ave}) for 25MP can be calculated by summing the charges at the unsubstituted carbons on which the HOMO orbital is located and dividing by the number of reactive sites. In the present case, the average charge is thus $[(-0.482) + (-0.654)]/2 = -0.568$.

A plot of the log of k_{ave} versus the average charge on a reactive site q_{ave} is shown in Figure 1. The correlation coefficient (R^2) for this plot is 0.82. In light of the fact that values of k_{ave} cover a range of six orders of

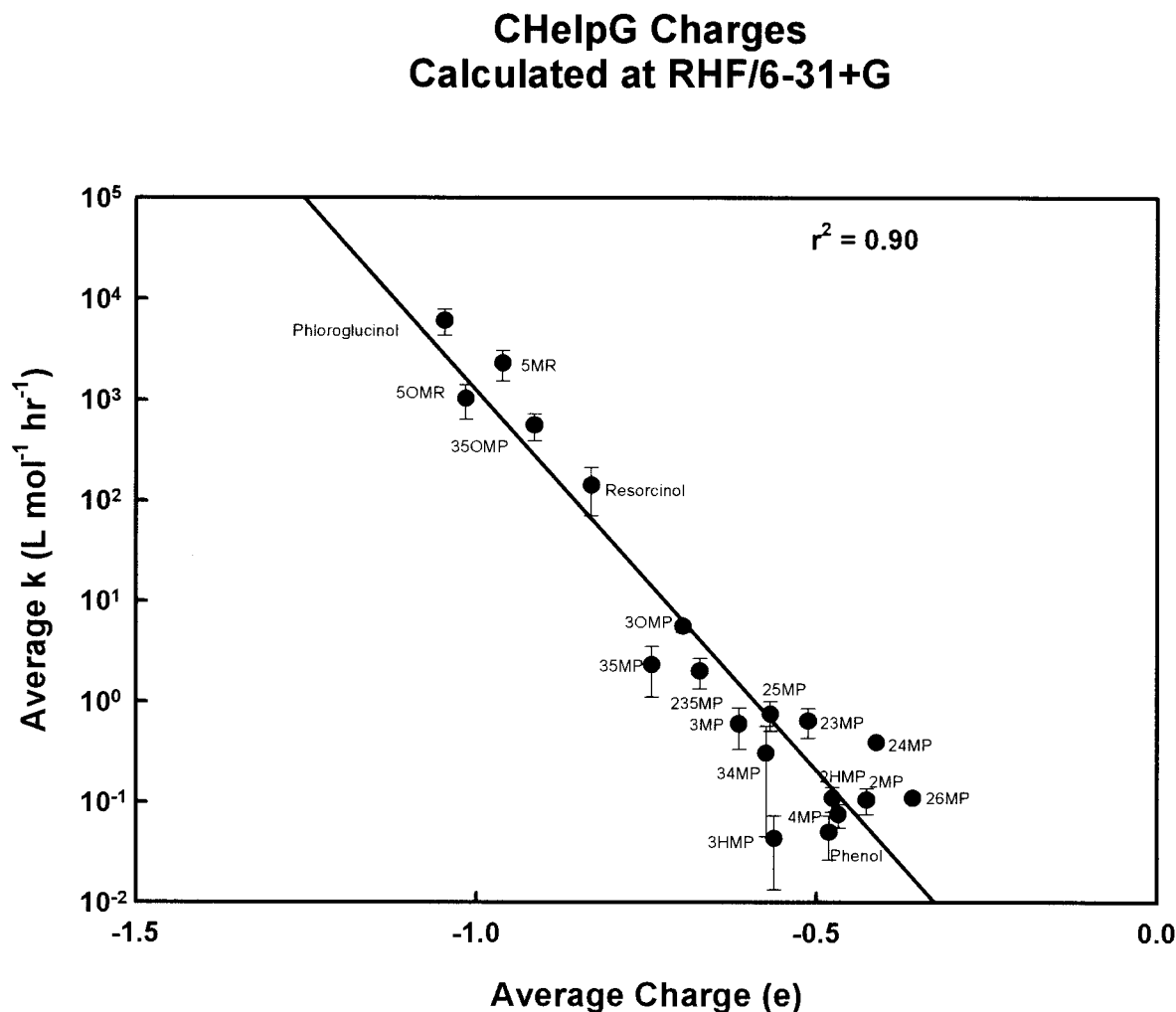


Figure 2 Semilog plot of the average rate constant versus average CHelpG charge calculated at the RHF/6-31+G level of theory for the reactions of formaldehyde with various phenolic compounds. The compounds containing two and three phenolic groups are assumed to exist in solution as dianions.

magnitude (10^{-2} to 10^4), this represents a good correlation between k_{ave} and q_{ave} .

The average charges used in the construction of Figure 1 were based on the assumption that all the phenolic compounds existed in solution as monoanions. However, in the case of the di- and triphenolic compounds, one should also consider that dianionic forms of these compounds probably also exist under the reaction conditions used in this study. An alternative plot of the data in the form of k_{ave} versus q_{ave} (calculated using average charge values for the dianions of the di- and triphenols) is shown in Figure 2. This approach results in a slightly stronger correlation ($R^2 = 0.90$) between the experimental data and the calculated charges.

These correlations of the experimental data with the calculated value are not perfect because several other factors can also affect reactivity (e.g., steric hindrance). These other factors have not been adequately accounted for in the present study. However, the strong

correlation that was observed indicates the predominate role that charge considerations play in determining the reactivity of formaldehyde with phenolic compounds. In addition, the method indicated above can be used to predict the relative reactivities of phenolic compounds with a variety of different chemical structures. Thus, the rates of reaction of resorcinol and phloroglucinol relative to phenol are on the order of 4000 and 180,000, respectively. These relative reactivities are consistent with the experimental observations that a phenol-formaldehyde resin must be cured at elevated temperatures while a resorcinol-formaldehyde resin cures at room temperature and that resins made from compounds containing a phloroglucinolic substructure (e.g., pine tannins) cure almost instantaneously.

CONCLUSIONS

1. Rate constants for the reactions of a variety of phenolic compounds with formaldehyde in an

aqueous solution under alkaline conditions were obtained from experimental measurements. These data represent the largest available database for the reactivities of different phenolic compounds with formaldehyde.

2. A strong correlation was obtained between k_{ave} determined experimentally for the reactions of phenolic compounds with formaldehyde and q_{ave} determined by calculations at the RHF/6-31+G level using CHelpG.
3. The best correlation between k_{ave} and q_{ave} was obtained when di- and triphenols were assumed to exist in solution as their respective dianions.

REFERENCES

1. Aldersley, J. W.; Hope, P. *Angew Makromol Chem* 1972, 24, 137–153.
2. Astarloa-Aierbe, G.; Echeverria, J. M.; Egiburu, J. L.; Ormaetxea, M.; Mondragon, L. *Polymer* 1998, 39, 3147–3153.
3. Dijkstra, R.; DeJonge, J.; Lammers, M. F. *Trav Chim* 1962, 81, 285–296.
4. Grenier-Loustalot, M. F.; Larroque, S.; Grenier, P.; Leca, J.-P.; Bedel, D. *Polymer* 1994, 35, 3046–3054.
5. Grenier-Loustalot, M. F.; Larroque, S.; Grande, D.; Grenier, P. *Polymer* 1996, 37, 1363–1369.
6. Sprung, M. M. *J Am Chem Soc* 1941, 63, 334–343.
7. Conner, A. H. *J Appl Polym Sci* 2000, 78, 355.
8. Meyer, B. *Urea-Formaldehyde Resins*; Addison-Wesley: Reading, MA, 1979; pp 123–126.
9. HyperChem 5.1; Hypercube, Inc., Gainesville, FL.
10. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98, Revision A.7*; Gaussian, Inc.: Pittsburgh, PA, 1998.
11. Breneman, C. M.; Wiberg, K. B. *J Comp Chem* 1990, 11, 361–373.
12. Abe, I.; Ono, H. *Mokuzai Gakkaishi* 1980, 26, 686–692.
13. Clark, T. *A Handbook of Computational Chemistry*; Wiley: New York, 1985; pp 133–138.
14. Zavitsas, A. A.; Beaulieu, R. D.; Leblanc, J. R. *J Polym Sci Part A-1* 1968, 6, 2533–2540.