Synthesis of and Assignment of Carbon-13 NMR Resonances to *m*-Cresol Novolak Dimers†

Leonard E. Bogan, Jr.,* and Steven K. Wolk

Rohm and Haas Company, 727 Norristown Road, Spring House, Pennsylvania 19477

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ABSTRACT: We have made conclusive assignments of the peaks in the ^{13}C NMR spectra of five of the six *m*-cresol novolak dimers (bis(hydroxymethylphenyl)methanes) with the information collected in 2D-INADEQUATE NMR experiments. The NMR experiments were carried out on mixtures of isomeric *m*-cresol novolak dimers, which were prepared by the stepwise condensation of formaldehyde with chloro-*m*-cresols, followed by hydrogenation. These assignments made possible the measurement of the relative reactivities of the three sites of attack on the ring by formaldehyde in acid-catalyzed condensations. The relative reactivities of the 2-, 4-, and 6-sites of *m*-cresol are 0.34 ± 0.06, 0.54 ± 0.07, and 0.12 ± 0.06, respectively. Knowledge of these reactivities allows a better understanding of the structure of *m*-cresol novolak resins, which is important in the optimization of photoresists for high-resolution microlithography.

Novolak resins are the products of the acid-catalyzed condensation of phenols with formaldehyde. Although the first commercial novolak resins appeared in 1910,[1] these materials continue to have significant commercial importance. Novolak resins are commonly characterized by melt or solution viscosity and (less frequently) by gel permeation chromatography. NMR spectroscopy for the analysis of these resins is a technique which has not yet been fully exploited. ^1H NMR has been used to determine the M_n of phenol novolak resins by taking the ratio of ring proton resonances to methylene proton resonances.[2] ^{13}C NMR has been used to determine the relative amounts of *o,o'*, *o,p'*, and *p,p'* methylene bridges in phenol novolak homopolymers. Two groups have published ^{13}C NMR chemical shift assignments for the isomeric phenol novolak dimers and trimers.[3] Other workers have reported the ^{13}C NMR spectra of phenol novolak polymers,[4] oligomers, and model compounds[4a,c,5] in solution and in the solid state.[6] One study reported the ^{13}C NMR spectra of Bisphenol A and *p-tert*-butylphenol novolak resins.[7] There are two reports on the use of 2D NMR techniques with phenolic resins.[8]

One of us has recently described the use of ^{13}C NMR to determine novolak copolymer compositions and site and comonomer reactivity ratios for the condensation of phenol and cresols with formaldehyde.[9] In order to measure site reactivity ratios, it was necessary to make peak assignments for all of the possible isomers of two phenolic rings linked by a methylene group. This had already been done for the three phenol–formaldehyde dimers,[3] and by analogy to them, we readily assigned peaks to the three *o*-cresol–formaldehyde dimers. The NMR spectrum obtained for the mixture of six isomers prepared by reaction of an excess of *m*-cresol with formaldehyde was too complex to assign in a similar manner.

Novolak dimers can be prepared by the reaction of formaldehyde with a large excess (≥50 equiv) of phenolic monomer under typical novolak synthesis conditions. In the case of *m*-cresol, three symmetric and three dissymmetric isomers can be formed (Figure 1), giving six possible resonances for the methylene carbons and nine possible resonances for both the phenolic and the methyl carbons. Unequivocal assignment of these resonances required the preparation of mixtures containing subsets of the set of six possible isomers together with the use of 2D-INADEQUATE NMR experiments. The details of these experiments are the subject of this report.

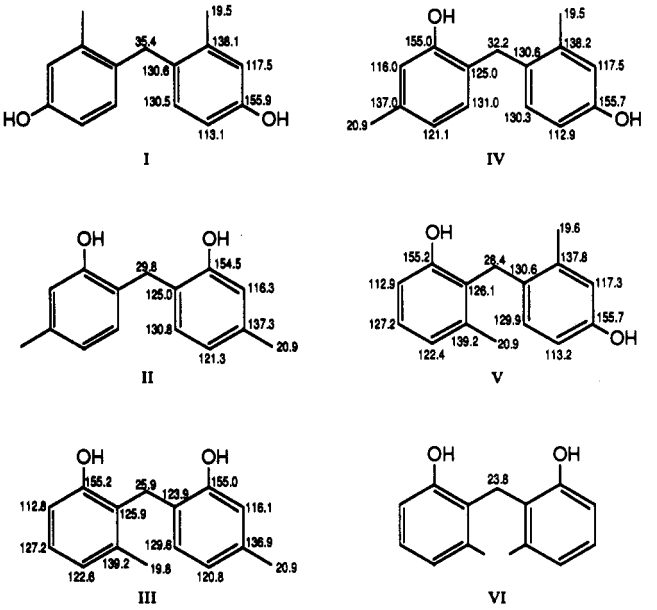

Figure 1. The six possible *m*-cresol novolak dimer isomers and their ^{13}C chemical shifts (dioxane-d_8 solutions, 0.2 g of dimer/0.4 mL of dioxane).

Results and Discussion

Dimer Synthesis. The reaction of 25 equiv of *m*-cresol with 1 equiv of formaldehyde yields, after distillation of water, catalyst, and unreacted cresol, a mixture of the six possible isomers of bis(3-hydroxytolyl)methane (*m*-cresol novolak dimer, Figure 1). A small quantity of compound I can be isolated from the mixture by careful distillation, but we were unable to isolate any of the other isomers in this way. Godfrey et al. reported the isolation of pure *m*-cresol novolak dimers by the stepwise reaction of dichloro-*m*-cresols with formaldehyde followed by hydrogenation[10] (Figure 2). Our attempts to repeat this work were unsuccessful, so we modified this strategy. We previously reported that [(dimethylamino)methyl]phenols are stable synthons for hydroxymethylphenols.[9] We prepared the (dimethylamino)methyl derivatives of 4- and 6-chloro-*m*-cresol. These alkylate chloro-*m*-cresol at oxygen, rather than at the ring. When the phenolic group

† For Shipley Company, 2300 Washington Street, Newton, MA 02162.

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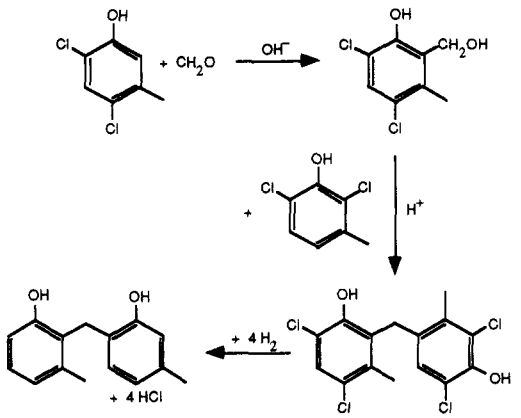

Figure 2. Godfrey et al. method for the synthesis of dissymmetric *m*-cresol novolak dimer.

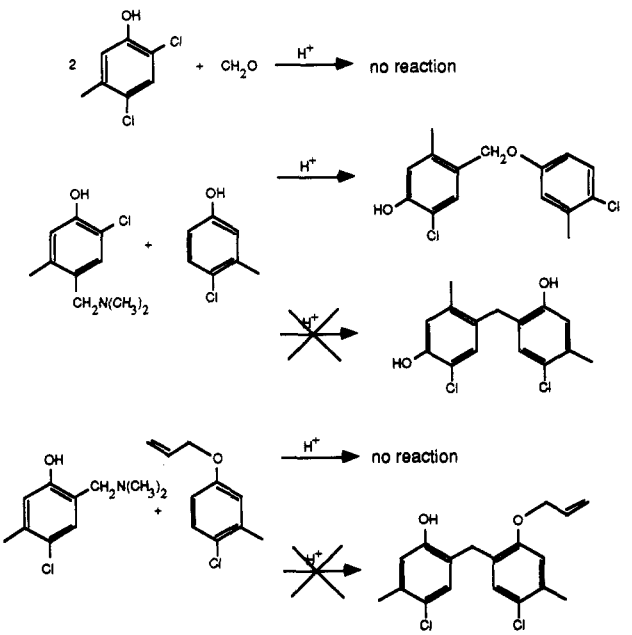

Figure 3. Failed attempts at the synthesis of *m*-cresol novolak dimers.

was protected as an allyl ether, we observed no reaction with the [(dimethylamino)methyl]cresol (Figure 3).

The direct reaction of formaldehyde with *mono*chloro *m*-cresols was more successful. The acid-catalyzed reaction of 2 equiv of 2-chloro-5-methylphenol with formaldehyde gave the 4,4′ dimer as the only product. Hydrogenation over a Pd catalyst yielded dimer I as a pure material. Similarly, the condensation of 4-chloro-3-methylphenol with formaldehyde gave a nearly equimolar mixture of the unhindered, symmetric isomer and the dissymmetric isomer, from which II and III were prepared by hydrogenation (Figure 4).

Two of the remaining three isomers were prepared by stepwise reactions analogous to those of Godfrey: first the (dimethylamino)methyl derivative of a cholorocresol was prepared; then that derivative was reacted with excess *m*-cresol to form a mixture of three isomers. These schemes are shown in Figure 5.

The last isomer, compound VI, was observed only in the mixture obtained from the reaction of 50 equiv of *m*-cresol with 1 equiv of formaldehyde. Compound VI was identified in the NMR spectrum of this mixture by elimination after assignments had been made for the other five isomers.

Peak Assignments. The similarity of compounds I–VI made it impossible, in the absence of additional experiments, to assign peaks to each of the isomers without

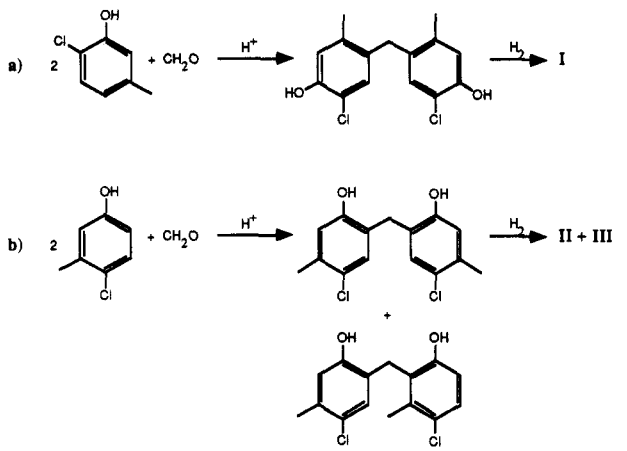

Figure 4. Synthesis of *m*-cresol novolak dimers from chlorocresols and formaldehyde.

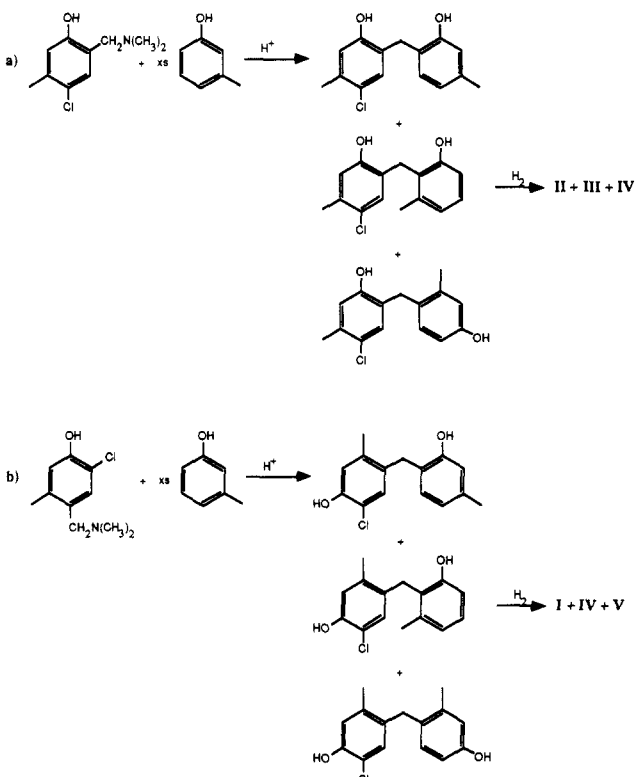

Figure 5. Synthesis of *m*-cresol novolak dimers from chlorocresols and formaldehyde.

making assumptions about relative site reactivities. Since we wanted to make the assignments in order to measure site reactivities, we carried out 2D-INADEQUATE NMR experiments to make unambiguous assignments.

The 2D-INADEQUATE experiment reveals carbon–carbon *J*-coupling interactions via double-quantum coherence.[12,16] The resulting two-dimensional frequency map shows ^{13}C chemical shifts along one axis and sums of chemical shifts (or, more precisely, sums of offsets from the carrier frequency) along the second axis. Only carbons which are coupled can show identical sums of frequency, and thus resonances corresponding to adjacent carbons can be assigned. By observation of a complete set of cross-peaks, the carbon skeletons of molecules can be traced out. This experiment has been used to obtain ^{13}C chemical shift assignments in phenol–acetaldehyde oligomers,[8b] to obtain structural proof of nonadienes produced by hydroboration,[13] and for structural determinations in alkaloids.[14]

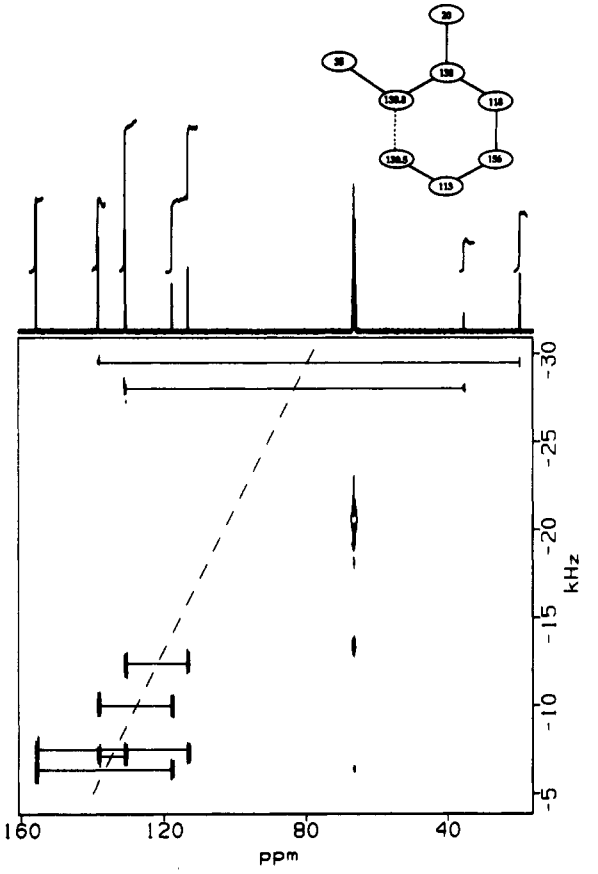

Figure 6. 2D-INADEQUATE spectrum of compound I. The one-dimensional ^{13}C NMR spectrum, with integrals, is shown along the ^{13}C chemical shift axis. The dashed line represents the pseudodiagonal. The stick figure represents the observed connectivities (marked by horizontal lines), which confirm the assignments. The connectivity represented by the dashed line was not observed. (See text.)

For the 2D-INADEQUATE spectra, samples were made as concentrated as possible due to the inherent insensitivity of the experiment. However, it was discovered empirically that the chemical shifts were slightly concentration dependent, presumably due to ring current/stacking interactions. Thus, each sample was also prepared at a standard concentration (200 mg total dimer concentration/0.4 mL of dioxane-d_8). The chemical shifts summarized in Figure 1 are those observed at this standard concentration.

Figure 6 shows the 2D-INADEQUATE spectrum of compound I. The one-dimensional ^{13}C NMR spectrum of the sample is shown along the ^{13}C chemical shift axis of the two-dimensional spectrum. Integration of the one-dimensional spectrum suggests that the compound is symmetric, because the methylene intensity is half of the other resonances. The observed connectivities in the 2D-INADEQUATE spectrum are depicted by the diagram in the figure. One expected coupling, represented by a dashed line in the diagram, is not observed. However, it is known that AB-type J-coupling systems can result in greatly diminished signals in 2D-INADEQUATE spectra,[15] and such a signal would probably be absent from the spectrum. Assuming that this is true, these results confirm that the sample is indeed compound I.

The product mixture of the reaction shown in Figure 4b was analyzed by this same method. The presence of only two methylene resonances, roughly equal in intensity, in the one-dimensional spectrum (29.8 and 25.9 ppm; Figure 7) supports the presence of two of the isomers. The 2D-INADEQUATE spectrum of the sample, expansions of

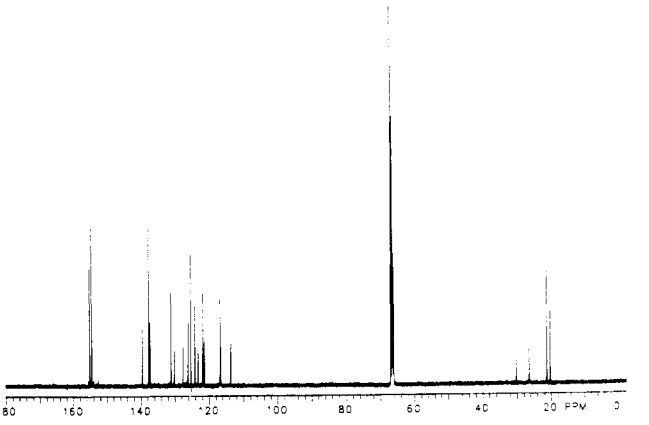

Figure 7. ^{13}C NMR spectrum of a mixture of compounds II and III. The observation of only two methylene peaks (29.8 and 25.9 ppm) supports the presence of two isomers.

which are shown in Figure 8A,B, yields unambiguous assignments of all the resonances and confirms the presence of compounds II and III. The symmetric isomer (II), which has signals from the ring carbons of twice the intensity, displays the stronger cross-peaks (Figure 8A). The dissymmetric isomer (III), has one ring identical to the symmetric isomer. A set of weaker cross-peaks is observed slightly resolved from the symmetric isomer at a lower contour level (Figure 8B), as well as a set for the unique ring. Though considerable noise is observed at this lower contour level, cross-peaks can still be readily identified by their doublet nature,[16] and from knowledge of the shifts in the 1D spectra.

The next sample analyzed was the product of the synthetic route outlined in Figure 5b. Three methylene resonances were observed, indicating the presence of three isomers. The two most concentrated compounds were identified using these same techniques (data not shown). A symmetric isomer, compound I, was identified, which had been observed in one of the previous samples. In addition, isomer IV was confirmed as the second most prominent isomer.

Thus, the complete chemical shift assignments have been obtained unambiguously for four out of the six isomers. Assignments were made for compound V by elimination of the peaks assigned to compounds I and IV from the spectrum of the product mixture from the reaction shown in Figure 5b. Due to overlap, we were unable to assign peaks to compound VI in the same way from the spectrum of the grand mixture of dimers; only the peak due to the methylene carbon of this compound could be unambiguously assigned.

Determination of Relative Site Reactivities. Relative site reactivities were determined using a competition experiment like the ones described previously.[9] Fifty equivalents of m-cresol was reacted with 1 equiv of formaldehyde, and the volatiles were removed by distillation. The methylene carbon peaks in the ^{13}C NMR spectrum (dioxane-d_8 solution, inverse-gated pulse sequence, 300-s delay) of the resulting mixture were integrated to determine the composition of the mixture (Table I). Relative site reactivities were calculated by dividing the number of substitutions at each site by the total number of substitutions. The measurement uncertainty for each type of substitution was incorporated to give worst case reactivities; these were averaged and reported with ranges which span those worst cases.

We have previously observed that full relaxation of the methylene carbons in an experiment like this is not seen even with a 60-s delay.[9] In order to test the accuracy of

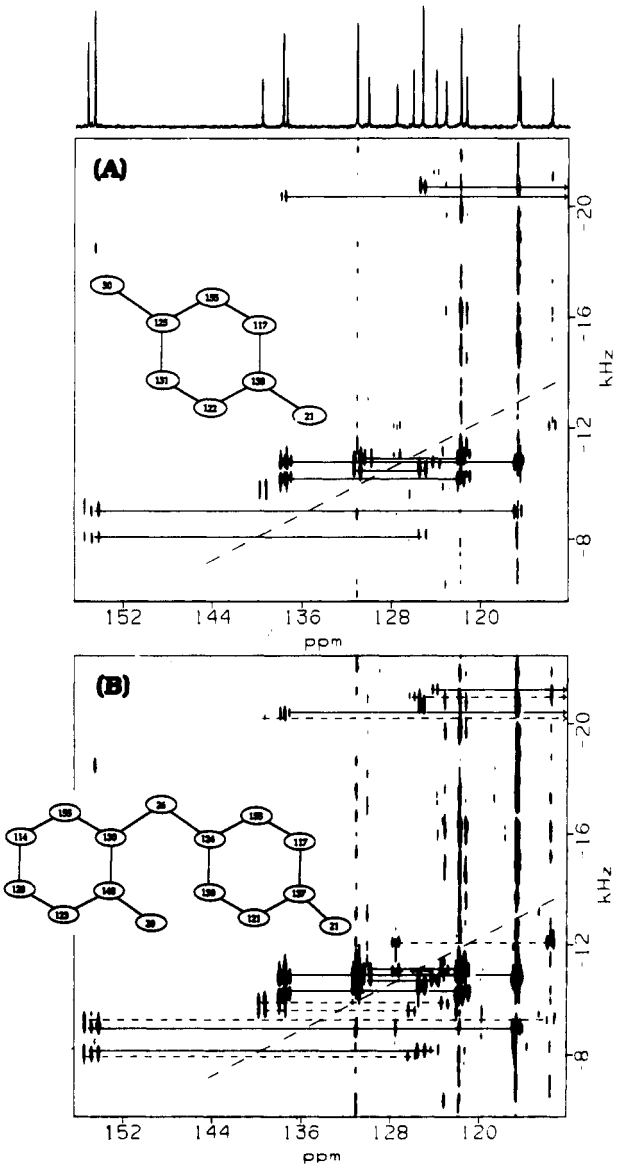

Figure 8. Expansion of the 2D-INADEQUATE spectrum of a mixture of compounds II and III. The one-dimensional ^{13}C spectrum is shown in Figure 7. (A) A higher contour level, showing only the connectivity in the symmetric isomer (II). (B) A lower contour level, showing the connectivity in the asymmetric isomer. The solid and dashed horizontal lines show the connectivities of the two separate rings. The lines which end in arrows at the edge of the contour plots represent connectivities to the methylenes, not seen in this expansion. The dashed, angled lines represented the pseudodiagonal. The stick figures represent the observed connectivities, which confirm the assignments.

this measurement, we prepared a reference sample from known amounts of solid I and a II and III mixture (prepared as shown in Figure 4). For a sample which contained 50.4% I, we measured 51.8% I using this method.

Conclusions

We have made conclusive assignments of the peaks in the ^{13}C NMR spectra of five of the six *m*-cresol novolak dimers with the information collected in 2D-INADEQUATE NMR experiments. These assignments made possible the measurement of the relative reactivities of the three sites of attack on the ring by formaldehyde in acid-catalyzed condensations. Knowledge of these reactivities allows a better understanding of the structure of *m*-cresol novolak resins, which is important in the optimization of photoresists for high-resolution microlithography.

Table I
Results of Two ^{13}C NMR Analyses of the Product Mixture from the Reaction of 50 equiv of *m*-Cresol with 1 equiv of Formaldehyde, and the Relative Site Reactivities Calculated from These Distributions

compd	amount, %	
I	32.5 ± 1.3	31.7 ± 1.1
II	15.5 ± 1.1	15.3 ± 3.2
III	8.0 ± 1.9	7.4 ± 3.2
IV	28.7 ± 1.1	28.6 ± 1.1
V	14.2 ± 1.3	14.8 ± 3.2
VI	1.1 ± 0.6	2.1 ± 2.1
site	**relative reactivity**	
2	0.339 ± 0.033	0.34 ± 0.06
4	0.541 ± 0.038	0.54 ± 0.07
6	0.122 ± 0.026	0.13 ± 0.06

Experimental Section

Monomers and solvents were obtained from commercial sources. Formaldehyde solutions were titrated before use and formaldehyde was charged on the basis of this titer.

Grand Mixture of Dimers. *m*-Cresol (74.7 g, 0.69 mol), water (34.6 g), and oxalic acid dihydrate (0.5 g) were combined in a 500-mL flask under N_2 and heated to reflux. To this mixture was added 37% $CH_2O_{(aq)}$ (1.1 mL, 1.0 g, 0.012 mol) in one portion. The mixture was held at reflux for 90 min; then the unreacted materials were removed by distillation under a N_2 sweep at a maximum temperature of 205 °C.

Bis(5-chloro-4-hydroxy-3-methylphenyl)methane. 2-Chloro-5-methylphenol (50.0 g, 0.351 mol), 36.8% aqueous formaldehyde (14.3 g, 0.175 mol), and concentrated aqueous HCl (6 mL) were stirred at reflux in 100-mL of water until the precipitate formed balls. The precipitate was collected by filtration and extracted with CH_2Cl_2. The remaining solid was recrystallized from acetone–xylenes to yield an oil from which white crystals separated upon standing overnight.

Chloro[(dimethylamino)methyl]cresols. 2-Chloro-5-methylphenol (47.3 g, 0.331 mol) and dimethylamine (31.4 g, 0.696 mol) were dissolved in 90 mL of water, at room temperature. Over a 10-min period, 36.3% aqueous formaldehyde (27.4 g, 0.331 mol) was added, and the temperature rose to 30 °C. After about one-third of the formaldehyde had been added, a yellow oil separated from the solution. Upon being stirred for 0.5 h after the addition was completed, the second phase became a white solid. Water was added to make 600 mL total, and the mixture was stirred an additional 2 h. The white precipitate was collected by filtration, washed with 3 × 200 mL water, and dried in vacuo; yield 65 g. An analogous procedure was used to prepare the (dimethylamino)methyl derivative of 4-chloro-3-methylphenol.

Reaction of [(Dimethylamino)methyl]cresol with *m*-Cresol. In 150 g of propionic acid were mixed 2-[(dimethylamino)methyl]-4-chloro-5-methylphenol (20.0 g, 0.100 mol), *m*-cresol (270.9 g, 2.50 mol), and *p*-toluenesulfonic acid hydrate (1.00 g, 0.005 mol). The mixture, which became a solution at ca. 65 °C, was heated to 100 °C and held at that temperature for 18 h. The unreacted materials were removed by distillation at a maximum temperature of 205 °C and minimum pressure of 8 mmHg.

Hydrogenation of Chlorinated Dimers. In a typical procedure, 8 g of bis(5-chloro-4-hydroxy-3-methylphenyl)methane and 0.5 g of NaOH were dissolved in 100 mL of 0.1 N methanolic KOH in a 500-mL pressure bottle. After 10 g of 50% (w/w) wet Pd on charcoal (5% Pd) was added, the mixture was shaken with an initial 50 psi hydrogen. After consumption of 20 psi, the bottle was refilled with hydrogen to 50 psi and shaken for 16 h, during which time 10 psi hydrogen was consumed. The mixture was filtered into 1 kg of 4% (w/w) aqueous HCl. The product was collected by filtration, washed with water, and dried in vacuo; yield 4.6 g.

NMR. NMR spectra were recorded at 62.896 MHz on a Bruker AM-250 or at 100.6 MHz on a Varian XL-400 NMR spectrometer. Samples were dissolved in dioxane-d_8 (0.2 g of polymer/0.4 mL

of solvent) and spectra were referenced to TMS at 0 ppm. One-dimensional spectra were obtained using an inverse-gated ^1H decoupling pulse sequence with a 30° pulse width and a 300-s delay.

Two-dimensional incredible natural-abundance double-quantum transfer experiment (2D INADEQUATE) spectra were obtained using the pulse sequence described by Bax,[11,12] using quadrature detection in both frequency domains. The sweep width used in the t_1 time domain was chosen to be twice the sweep width in t_2, yielding a spectrum with cross-peaks symmetric about a pseudodiagonal.[16] A total of 256 scans were collected in 4096 complex points for each of 128 t_1 values, and 4 dummy scans were used to establish a pseudo steady state. A relaxation delay of 5 s was used between scans. The total time for each experiment was about 47 h.

Two separate experiments were done for each sample, with τ delays of 4 or 6 ms, corresponding to J_{CC} values of 62.5 ($sp^2 - sp^2$) and 43 Hz ($sp - sp^3$), respectively.[8b] The first value was used to maximize the intensity of the signals from within the aromatic rings, while the latter was used to optimize the signals from the bridging carbons.

Data were transferred via ethernet to a microVax computer and processed using FTNMR (Hare Research, Inc.). In the t_2 domain, FIDs were apodized with a skewed, 80° phase-shifted, sine bell that decayed to zero at the end of the data points and were zero-filled once prior to Fourier transformation. In the t_1 dimension, a 90° phase-shifted, sine bell that decayed to zero at the end of the data points was used in combination with an exponentially decaying apodization function (line broadening, 40 Hz), and the matrix was zero-filled to obtain a final size of 4096 × 256.

References and Notes

(1) Knop A.; Pilato, L. A. *Phenolic Resins*; Springer-Verlag: Berlin, 1985; p 48.

(2) (a) Szymanski, H. A.; Bluemle, A. *J. Polym. Sci. A* **1965**, *3*, 63. (b) Dankelman, W.; de Wit, J. *Angew. Makromol. Chem.* **1977**, *62*, 101.

(3) (a) Sojka, S. A.; Wolfe, R. A.; Dietz, E. A., Jr.; Dannels, B. F. *Macromolecules* **1979**, *12*, 767. (b) Walker, L. E.; Dietz, E. A., Jr.; Wolfe, R. A.; Dannels, B. F.; Sojka, S. A. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1983**, *24*, 177. (c) Mackey, J. H.; Tiede, M. L.; Sojka, S. A.; Wolfe, R. A. **1983**, *24*, 179. Pethrick, R. A.; Thomson, B. *Br. Polym. J.* **1986**, *18*, 171. (e) Pethrick, R. A.; Thomson, B. *Br. Polym. J.* **1986**, *18*, 380.

(4) (a) Pethrick, R. A.; Thomson, B. *Br. Polym. J.* **1986**, *18*, 380. Pethrick, R. A.; Thomson, B. *Br. Polym. J.* **1986**, *18*, 171. (b) Sojka, S. A.; Wolfe, R. A.; Guenther, G. D. *Macromolecules* **1981**, *14*, 1539. (c) Kim, M. G.; Tiedeman, G. T.; Amos, L. W. *Weyerhauser Sci. Symp.* **1979**, *2*, 263. (d) Siling, M. I.; Urman, Ya. G.; Adorova, I. V.; Alekseyeva, S. G.; Matyukhina, O. S.; Slonim, I. Ya. *Vysokomol. Soedin., Ser. A* **1977**, *19*, 309. (e) Tsuge, M.; Miyabayashi, T.; Tanaka, S. *Bunseki Kagaku* **1974**, *23*, 520; *Chem. Abstr.* **1974**, *81*, 136852j. (f) Mukoyama, Y.; Tanno, T.; Yokokawa, H.; Fleming, J. *J. Poly. Sci.* **1973**, *11*, 3193.

(5) (a) Dradi, E.; Casiraghi, G.; Casnati, G. *Chem. Ind.* **1978**, 627. (b) de Breet, A. J. J.; Dankelman, W.; Huysmans, W. G. B.; de Wit, J. *Angew. Makromol. Chem.* **1977**, *62*, 7.

(6) (a) Hatfield, G. R.; Maciel, G. E. *Macromolecules* **1987**, *20*, 608. (b) Bryson, R. L.; Hatfield, G. R.; Early, T. A.; Palmer, A. R.; Maciel, G. E. *Macromolecules* **1983**, *16*, 1669. (c) Fyfe, C. A.; McKinnon, M. S.; Rudin, A.; Tchir, W. J. *Macromolecules* **1983**, *16*, 1216. (d) Fyfe, C. A.; McKinnon, M. S.; Rudin, A.; Tchir, W. J. *J. Polym. Sci., Polym. Lett. Ed.* **1983**, *21*, 249. (e) Fyfe, C. A.; Rudin, A.; Tchir, W. *Macromolecules* **1980**, *13*, 1320.

(7) Novikov, N. A.; Mozoleva, A. P.; Uvarov, A. V.; Alekseyeva, S. G.; Slonim, I. Ya. *Vysokomol. Soedin., Ser. A* **1986**, *28*, 1064; *Chem. Abstr.* **1987**, *106*, 8531s.

(8) (a) Duff, A. J.; Kemp, W.; Steedman, W.; Boyd, A. S. F. *Br. Polym. J.* **1989**, *21*, 407. (b) Zetta, L.; DeMarco, A.; Cornia, M.; Casiraghi, G. *Macromolecules* **1988**, *21*, 1170.

(9) Bogan, L. E., Jr. *Macromolecules* **1991**, *24*, 4807.

(10) Godfrey, L. E. A.; Hawkins, E. G. E.; Jenkins, P. A. *J. Appl. Chem.* **1957**, *7*, 440.

(11) Bax, A.; Freeman, R.; Frenkiel, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 2102.

(12) Bax, A.; Freeman, R.; Frenkiel, T. A.; Levitt, M. H. *J. Magn. Reson.* **1981**, *43*, 478.

(13) Brown, H. C.; Pai, G. G.; Naik, R. G. *J. Org. Chem.* **1984**, *49*, 1072.

(14) Bhacca, N. S.; Balandrin, M. F.; Kinghorn, A. D.; Frenkiel, T. A.; Freeman, R.; Morris, G. A. *J. Am. Chem. Soc.* **1983**, *105*, 2538.

(15) Bax, A.; Freeman, R. *J. Magn. Reson.* **1980**, *41*, 507.

(16) Martin, G. E.; Zektzer, A. S. *Two-Dimensional Methods for Establishing Molecular Connectivity*; VCH Publishers, Inc.: New York, Chapter 5.

Registry No. I, 15534-74-4; II, 57693-38-6; III, 103272-88-4; IV, 103272-89-5; V, 103272-87-3; VI, 137203-82-8; CH_2O, 50-00-0; 2-chloro-5-methylphenol, 615-74-7.