Environ. Sci. Technol. **2004**, *38,* 5022−5029

Investigations of the Reactions of Monochloramine and Dichloramine with Selected Phenols: Examination of Humic Acid Models and Water Contaminants†

VICTOR L. HEASLEY,* AUDRA M. FISHER, ERICA E. HERMAN, FAITH E. JACOBSEN, EVAN W. MILLER, ASHLEY M. RAMIREZ, NICOLE R. ROYER, JOSH M. WHISENAND, DAVID L. ZOETEWEY, AND DALE F. SHELLHAMER

Department of Chemistry, Point Loma Nazarene University, 3900 Lomaland Drive, San Diego, California 92106

Our paper reports on the reactivities and orientations of two common phenols, phenol (**2**) and *m*-cresol (**3**), and some of their chlorinated intermediates with aqueous monochloramine, NH_2Cl, and dichloramine, $NHCl_2$. We also examined the further reactivity of 2,4,6-trichlorophenol (**4**) with the chloramines. The phenols are an important area of investigation because they are substituents in the humic acids and are common contaminants in water. *m*-Cresol (**3**) was found to be more reactive than phenol (**2**) with both chlorinating agents. Both NH_2Cl and $NHCl_2$ were sufficiently reactive to chlorinate all positions *ortho* and *para* to the hydroxyl groups. Mono- and dichloramine showed the same orientation with **2** but different orientations in their reactions with the substituent phenols. Indophenol (as its salt) was formed to a minor extent at high pH but not at pH 9. Both NH_2Cl and $NHCl_2$ rapidly replaced the *para*-chlorine in 2,4,6-trichlorophenol (**4**) to give a mixture of 2,6-dichloro-1,4-benzoquinone-4-(*N*-chloro) imine (**5**) and 2,6-dichloro-1,4-benzoquinone (**18**). Similar reactions occur with 2,4,6-trichloro-*m*-cresol (**17**) and 2,4,6-trichloro-3-methoxyphenol (**29**). The products for **17** were confirmed by mass spectrometry (EI and CI), ^{1}H NMR, ^{13}C NMR, and IR; the products for **29** were confirmed by mass spectrometry (EI and CI) and IR. An ion radical mechanism is suggested to account for the chlorine replacement by the chloramines. [No side chain oxidation of the methyl group in **17** in H_2O or ether occurred, with or without ultraviolet radiation.] Both **5** and **18** underwent further chlorination with NH_2Cl or $NHCl_2$. Imine **5** did not function as a chlorinated agent.

Introduction

Although chloramine (monochloramine, NH_2Cl, and dichloramine, $NHCl_2$, alone, or in mixtures of unknown proportions) has become a common water disinfectant (*1*−*6*), only one model compound of the humic acids, resorcinol (**1**), a reactive, diphenol, has been thoroughly investigated in its chlorination reaction with NH_2Cl in ether and in H_2O (*7*). Other organic compounds, some of which are models of the humic acids (*4*), contaminants in drinking H_2O (*4*), or compounds in saliva (*5*), have received narrow investigations with chloramine in order to determine the extent of formation of chloroform $CHCl_3$ (*4*) or speculation about products that may have formed (*5*). Formation of *N*-nitrosoamines from NH_2Cl and amine contaminants in drinking water has been reported recently (*2*). Some disinfection byproducts (DBP) have been identified (*8*−*11*) in the reactions of chloramine with the humic acids, but, in general, a clear picture has not been established of the relationship between DBP and the substituents of the humic acids. It is well-known that chloramine, unlike hypochlorite ion, OCl^-, or hypochlorous acid, HOCl, reacts with humic materials to form low amounts of trihalomethanes (*4*, *6*, *7*, *12*). The reactions of the other two common water treatment disinfectants, OCl^- and HOCl, have been investigated extensively with humic acid models (*13*−*20*).

Therefore, we chose to investigate the reactions of two simple phenols, phenol (**2**), *m*-cresol (**3**), and their chlorination intermediates with NH_2Cl and $NHCl_2$, determining the extent and orientation of ring-substitution. We also intended to study the reaction of 2,4,6-trichlorophenol (**4**) with the chloramines since **4** has been shown to be a serious contaminant in drinking water sources (*21*−*23*). The structures for all of the reactants and products involved in our study are shown in Figure 1. Phenol (**2**) is an obvious, important compound to study since it is a substituent in the humic acids (*24*) and is a common contaminant in drinking water and drinking water sources (*25*−*27*). *m*-Cresol (**3**) was chosen because it is likely a substituent in the humic acids (*28*) and because its particular electronic features were important to our study. A curious statement in the literature (*9*), involving a study of monochloramine with fulvic acid, also encouraged us to investigate the reaction of phenols with the chloramines. This statement, which expresses the ambiguity that exists concerning the reactivity of the chloramines with phenols, is as follows: "Monochloramine has previously been shown to be less reactive toward phenolic species and is thus not likely to cause either ring rupture or direct substitution. Instead, monochloramination probably results in primarily aromatic side-chain oxidation and substitution products." This statement about the reactivity of phenols and monochloramine is not referenced as a journal article but relates to a personal statement, not necessarily based on laboratory investigation. Furthermore, an article which appeared in 1987, and of which the authors (*9*) of the statement apparently were unaware, shows clearly that the *para*-chlorine of 2,4,6-trichlorophenol (**4**) is displaced by NH_2Cl to give 2,6-dichloro-1,4-benzoquinone-4-(*N*-chloro) imine (**5**) (*29*). The unreferenced statement (*9*) and the reaction of **4** with NH_2Cl to form **5**, in direct contradiction to this statement, made it clear to us that a thorough study of the reactivities of phenols **2**, **3**, and **4** with NH_2Cl and $NHCl_2$ might assist in clarifying this area. We intended to thoroughly investigate the reaction of **4** to give **5** since this reaction involves the unusual displacement of an aromatic chlorine by a weak nucleophile (chloramine).

The pH range for drinking water is reported to be 9 to 6, and, therefore, the predominant chloramine species, based on our observations and reported in the literature (*6*), is NH_2Cl at the higher level and $NHCl_2$ at the lower level with a

† Parts of this paper were presented at recent American Chemical Society (ACS) meetings: (E.E.H.) 227th National Meeting of the ACS, Anaheim, CA, March 29, 2004; (F.E.J.) 38th Western Regional Meeting of the ACS, Santa Barbara, CA, October 29, 2002; (D.L.Z.) 221st National Meeting of the ACS, San Diego, CA, April 2, 2001.

* Corresponding author phone: (619)849-2231; fax: (619)849-2598; e-mail: vheasley@ptloma.edu.

10.1021/es030644h CCC: $27.50
Published on Web 08/28/2004

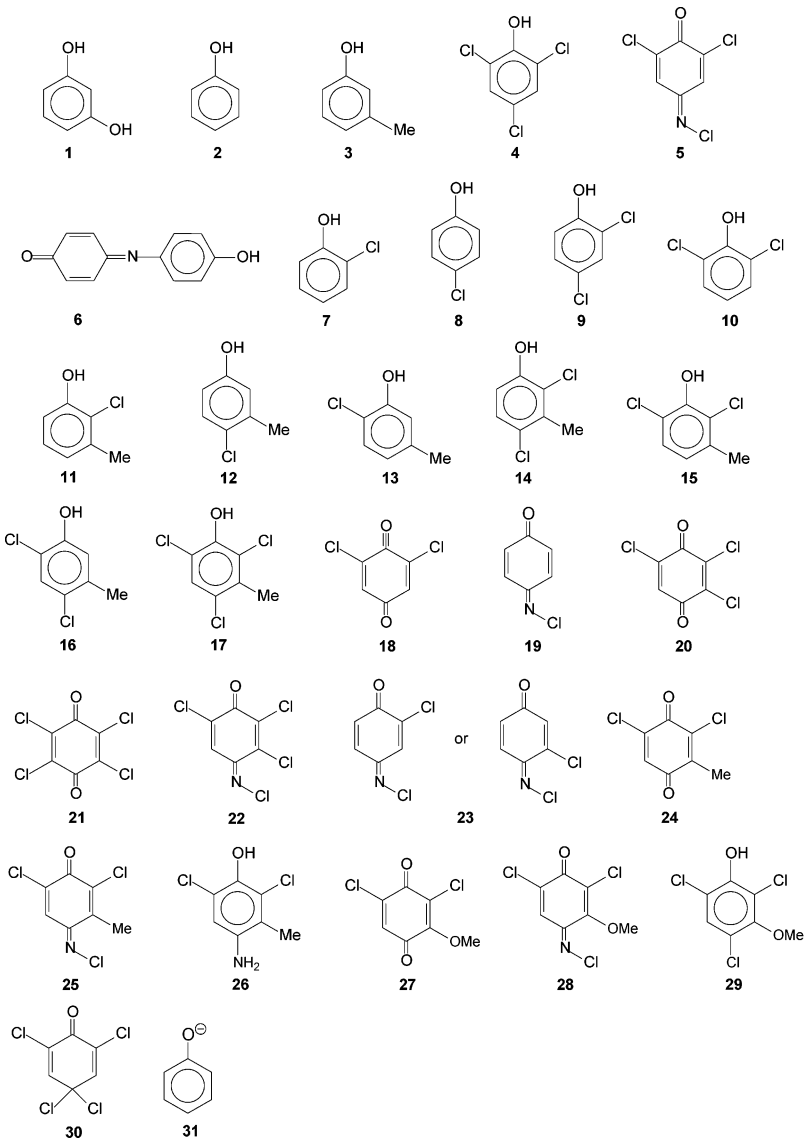


FIGURE 1. Structures of phenols and related compounds involved in the study.

mixture of the two at intermediate pH ranges. Therefore it was our goal to examine the reactivities of phenols **2** and **3** with both chlorinating agents. Our assumption was that chlorination of the ring, if it occurred, would proceed via the basic electrophilic substitution mechanism.

Another factor to consider in our study was the possible formation of indophenol (**6**) (its salt at high pH) from **2** and NH_2Cl and the chloro-substituted indophenols from phenols **7**, **8**, and **9**, if the phenols came in contact with NH_2Cl at strongly basic pH levels. Since no indophenol (**6**) was formed with **2** at pH 9, we concluded not to investigate *m*-cresol at a high pH. Formation of indophenols between NH_2Cl and phenols at high pH is a well-investigated reaction (*30*−*32*) and comes under the titles of the Berthelot and Gibbs reactions. Indophenol contaminants would be particularly likely to form during the initial mixing process when the strongly basic NH_2Cl solution and phenols could come in contact with each other.

Experimental Section

Sources of the Reagents and Some of the Products. Phenol (**2**), *m*-cresol (**3**), and the following chlorination products of phenol (**2**) are available commercially (Aldrich): 2,4,6-trichlorophenol (**4**); 2-chlorophenol (**7**); 4-chlorophenol (**8**); 2,4-dichlorophenol (**9**); 2,6-dichlorophenol (**10**). The products of *m*-cresol (**3**) were obtained as follows: 2-chloro-*m*-cresol (**11**) (synthesized as described below); 4-chloro-*m*-cresol (**12**), and 6-chloro-*m*-cresol (**13**) were commercially available; 2,4-dichloro-*m*-cresol (**14**), 2,6-dichloro-*m*-cresol (**15**), and 4,6-dichloro-*m*-cresol (**16**) were identified from published information (*33*); we have recently reported on the synthesis of 2,4,6-trichloro-*m*-cresol (**17**) (*34*). 2,6-Dichloro-1,4-benzoquinone-4-(*N*-chloro) imine (**5**), 2,6-dichloro-1,4-benzoquinone (**18**), 1,4-benzoquinone-4-(*N*-chloro) imine (**19**), 2,3,6-trichloro-1,4-benzoquinone (**20**), and 2,3,5,6-tetrachloro-1,4-benzoquinone (chloranil, **21**) were available commercially (Aldrich). Compound **19** was synthesized as reported in the literature (*35*). Compound **22** was identified from its mass spectrum. It was present in a sustained chlorination reaction and could be prepared independently by the chlorination (NH_2Cl or $NHCl_2$) of **5**. The mass spectrum *m*/*z* (EI) of **22** is as follows: M^+: 251 (0.01), 249 (0.11), 247 (0.52), 245 (1.0), 243 (0.73); $M-Cl^+$: 214 (0.07), 212 (0.36), 210 (1.0), 208 (0.99); $M-Cl-CO^+$: 186 (0.06), 184 (0.39), 182 (1.0), 180 (0.94). The mass spectrum *m*/*z* (EI) of **23** is as follows: M^+: 179 (0.11), 177 (0.68), 175 (1.0), $M-Cl^+$: 142 (0.39), 140 (1.0).

Compound **24** was identified in the reaction mixture by comparison of the mass spectrum to the independently synthesized compound (*36*). The mass spectrum, *m*/*z* (EI)

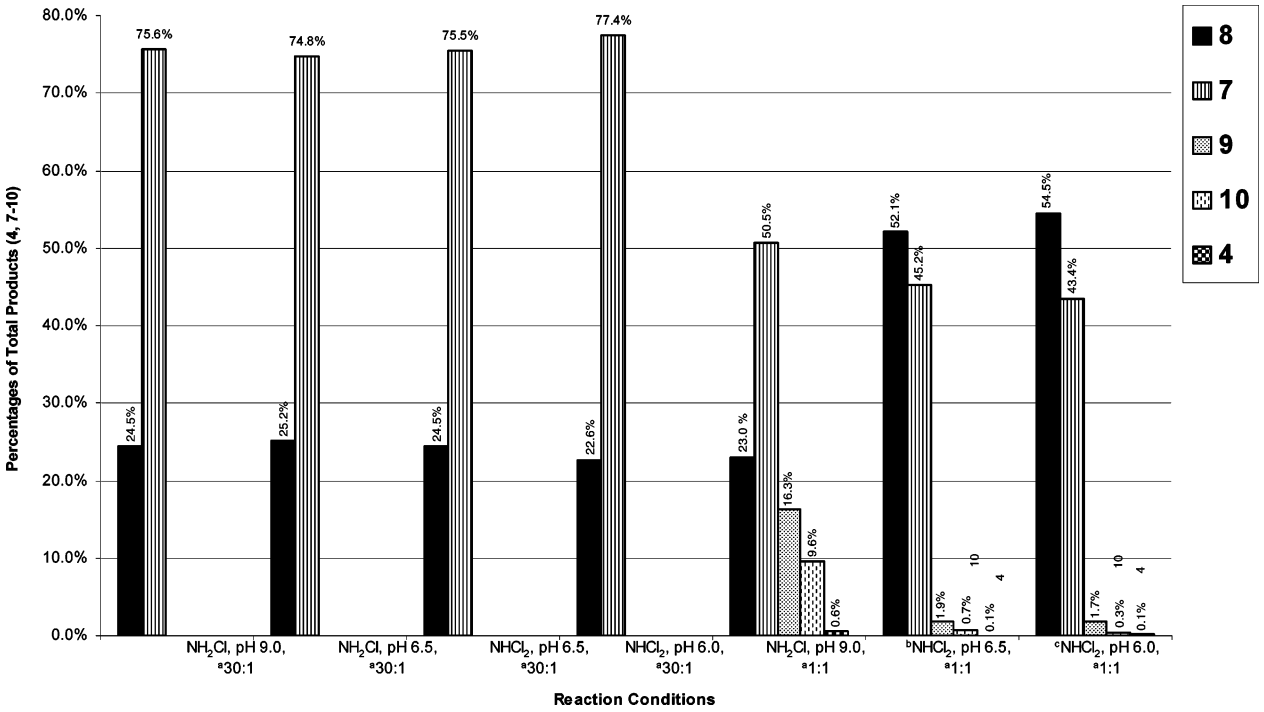


FIGURE 2. Percentages of products from the reactions of phenol with NH_2Cl and $NHCl_2$. [a]Molar ratio of phenol to chloramine. [b]A few percent of 5 and 21. [c]A few percent of 5.

of **24** is M^+: 194 (0.34), 192 (0.81), 190 (1.0); $M-CO^+$: 164 (0.51), 162 (1.0); $M-CO-Cl^+$: 129 (0.41), 127 (1.0).

We report compound **25** for the first time. According to Pattan, chloroimines can be synthesized by the action of sodium hypochlorite and HCl on the corresponding aminophenol (*32*). We used the procedure of Cason et al. to synthesize 4-amino-2,6-dichloro-*m*-cresol (**26**) as a precursor to **25** (*37*, *38*). The mass spectrum *m*/*z* (EI) of **25** is as follows: M^+: 229 (0.04), 227 (0.32), 225 (0.98), 223 (1.0); $M-CO^+$: 199 (0.31), 197 (0.95), 195 (1.0); $M-CO-Cl^+$: 164 (0.13), 162 (0.67), 160 (1.0). The mass spectrum *m*/*z* (CI) of **25** confirms the parent ion at 229: MH^+: 230 (0.04), 228 (0.31), 226 (0.95), 224 (1.0). IR (cm^{-1}): C═O, 1698; C═N, 1569. ^1H NMR (300 MHz): δ 8.03 (s,3H) and 2.44 (s,3H). ^{13}C NMR (75.4 MHz): 172.7, 165.3, 143.3, 140.7, 134.8, 124.8, and 15.1. Compound **25** melted at 75−78 °C.

The EI mass spectrum *m*/*z* (EI) of **27** is as follows: M^+: 210 (0.13), 208 (0.69), 206 (1.0); $M-CO^+$: 182 (0.08), 180 (0.59), 178 (1.0); $M-CO-Cl^+$: 173 (0.38), 171 (1.0). The mass spectrum *m*/*z* (CI) is as follows: MH^+: 213 (0.04), 211 (0.36), 209 (1.0), 207 (0.94). IR (cm^{-1}) GC−FTIR of **27** shows C═O at 1743 and 1714 cm^{-1}. High-resolution mass spectrum (HRMS−EI) for **27**, calculated for $C_7H_4Cl_3NO$, 222.935847, found 222.935897.

The mass spectrum *m*/*z* (EI) of **28** is as follows: M^+: 243 (0.33), 241 (1.0), 239 (0.81); $M-CO^+$: 215 (0.48), 213 (0.81), 211 (1.0); $M-Cl^+$: 208 (0.11), 206 (0.65), 204 (1.0); $M-O-Cl^+$: 180 (0.10), 178 (0.61), 176 (1.0). The mass spectrum *m*/*z* (CI) confirms the parent ion: MH^+: 242 (0.96), 240 (1.0). IR (cm^{-1}): C═O, 1695; C═N; 1573.

Synthesis of 2-Chloro-*m*-cresol (11). 2-Chloro-*m*-cresol (**11**) was not commercially available and was synthesized independently using cuprous chloride (CuCl) and the diazonium ion from 2-amino-*m*-cresol. Fresh CuCl was prepared by adding 0.252 g of hot sodium bisulfite ($NaHSO_3$) in 2.7 mL of H_2O to 3.15 g of cupric sulfate ($CuSO_4$) and 0.252 g of sodium chloride (NaCl). This hot solution was allowed to drop to room temperature, and the white precipitate of CuCl was filtered and mixed with 5.1 mL of concentrated hydrochloric acid (HCl). The CuCl solution was placed on ice until needed. The diazonium ion of 2-amino-*m*-cresol was prepared as follows: 1.22 g of 2-amino-*m*-cresol was dissolved in 2.55 mL of concentrated HCl and 2.55 mL of H_2O, and the solution was brought to ice temperature in an ice bath. Sodium nitrite ($NaNO_2$) (0.72 g) in 1.5 mL of H_2O at ice temperature was then added to the solution of 2-amino-*m*-cresol to give the diazonium ion. The CuCl solution and the diazonium ion salt solution were stirred vigorously for several minutes. The reaction product was extracted with dichloromethane (CH_2Cl_2) and dried over magnesium sulfate ($MgSO_4$). Removal of the solvent yielded a reddish oil which was purified by column chromatography (Si), beginning with hexane and followed by ether. 2-Chloro-*m*-cresol (**11**) eluted in the 7% ether/hexane fraction, melting at 48−49 °C; reported (*33*) 49−50 °C. Compound **11** was confirmed by its mass spectrum.

Synthesis and Studies of the Chloramines. Both NH_2Cl and $NHCl_2$ were identified by their UV spectral maxima at 244 and 296 nm, respectively (*6*). NH_2Cl at ca. pH 13 was prepared from 6 M ammonia, NH_3, and sodium hypochlorite, NaOCl, as described previously (*7*, *39*). NH_2Cl at pH 9 was obtained by dropwise addition of 1 M H_2SO_4 to the stirred pH 13 solution monitored with a pH meter until the pH reached ca. 12 and then was continued with dropwise addition of 0.25 M H_2SO_4 to pH 9. Stable solutions (steady pH) of the chloramines could be made at pH 9, 8, 7, 6.5, and 6 by this procedure. (The pH changed by only 0.3 pH units in 45 min; the concentration of the chloramines, in the absence of the phenol, did not change during the 45 min period at their respective pHs.) The pH 9 solution showed exclusively NH_2Cl; pH 6 solutions showed only $NHCl_2$. At no time were buffers used to control pH levels because of our previous observation that the phosphate ion in the buffer interfered by reacting as a nucleophile displacing chloride from the various chlorine species (*35*).

We discovered that it was possible to prepare a NH_2Cl solution in the acidic range at pH 6.5, containing only a small amount of $NHCl_2$, by dropwise addition of 0.25 M H_2SO_4 to the pH 9 solution. NH_2Cl lasted for approximately 10 min at pH 6.5 before slowly converting NH_2Cl entirely into $NHCl_2$.

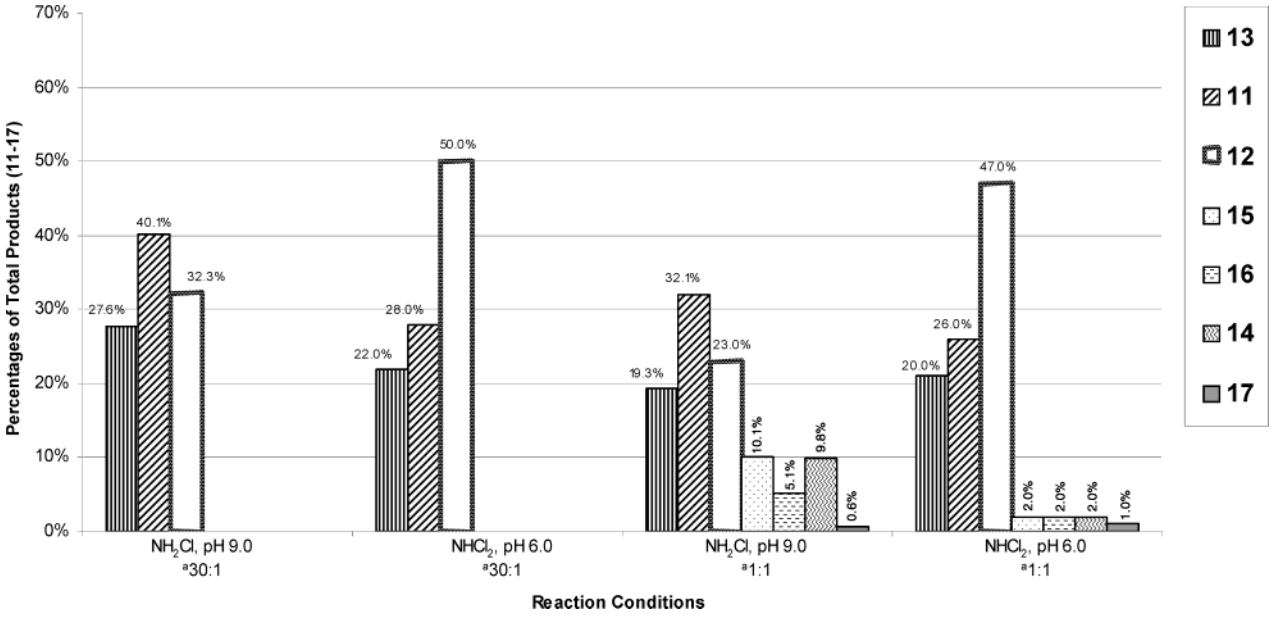


FIGURE 3. Percentages of products from the reactions of *m*-cresol (3) with NH_2Cl and $NHCl_2$. [a]Molar ratio of phenol to chloramine.

We present data in Figure 2 on the reaction of phenols **1** and **2** with NH_2Cl in the acidic range (pH 6.5), but the products are almost certainly mainly the result of the reaction of $NHCl_2$ since the reactions of the chloramines with the phenols are not very rapid, and in 10 min only a small amount of NH_2Cl would remain.

$NHCl_2$ at pH 6 can also be made by dropwise addition of dilute NaOH to a $NHCl_2$ solution at pH 4 or 5.

Conditions for Reaction of the Phenols 2 and 3 with the Chloramines. All phenol reactions were run at approximately 0.1 M in deionized water except for the monochloro-*m*-cresol reactions which were 0.05 M because of their lower solubilities; at these concentrations complete solubilities were attained. Molarities of the chloramines were ca. 0.1 or higher if the goal of the experiment was to ensure multiple chlorinations of **2** or **3** leading eventually to trichlorophenols **4** and **17**, respectively. If the goal of the experiment was to ensure monochlorination, the concentration of the chloramine was ca. 0.003 M; at this concentration no multichlorination occurred. In general the phenol solution was adjusted to the appropriate pH, and the chloramine solution at that pH was mixed in the phenol solution with stirring. When the reaction of the phenol and the chloramine was complete (as indicated by the absence of chloramine), the solution was extracted with dichloromethane, CH_2Cl_2, dried over anhydrous $MgSO_4$, and analyzed by gas chromatography (GC) under the following conditions: GC column: a 25-mm Agilent Technologies ultraperformance column with an internal diameter of 0.20 mm and methyl silicone stationary phase of 0.33 micrometer film thickness with the following temperatures: Compounds **1**, **2**, **7**, **8**, **9**, **10**, **24**, **25**, **27**, **28**, **29**: programming from 120 to 220 °C at 10 °C/min.; compounds **3**, **11**, **12**, **13**, **14**, **15**, **16**, **17**: programming from 75 to 220 °C at 3 °C/min.; compounds **4**, **5**, **18**, **19**, **20**, **21**, **22**, **23**, **30**: programming 75−220 °C at 10 °C/min. The structures of reactants and products are shown in Figure 1. The retention times (min) of all reactants and products in the GC under the conditions indicated above are as follows: (**2**), 4.7; (**3**), 7.9; (**4**), 8.7; (**5**), 10.3; (**7**), 5.1; (**8**), 9.2; (**9**), 8.7; (**10**), 9.4; (**11**), 8.7; (**12**), 15.4; (**13**), 8.6; (**14**), 15.1; (**15**), 16.1; (**16**), 14.8; (**17**), 22.6; (**18**), 6.2; (**19**), 9.0; (**20**) 8.9; (**21**) 10.9; (**22**) 12.4; (**23**) 8.3; (**24**) 6.1; (**25**) 9.3; (**27**) 7.3; (**28**) 10.5; (**29**) 8.7; (**30**), 9.0; (**31**), 6.7. The products were all identified in the respective reaction mixtures using gas chromatography−mass spectrometry (GC−MS) based on authentic materials. The GC−MS conditions were the same as those described for GC. The chlorination products and their percentages are shown in Figures 2−5. A few percent of 2,6-dichloro-1,4-benzoquinone-4-(*N*-chloro) imine (**5**) and 1,4-benzoquinone-4-(*N*-chloro) imine (**18**) were also observed in the reactions of **2** with $NHCl_2$ in a molar ratio of 1:1.

Determination of the Half-Lives of the Chloramines in Their Reactions with Phenols (2 and 3). The half-lives of monochloramine and dichloramine in solution with **2** or **3** were determined by monitoring the concentration of chloramine over time. These data are shown in Table 1. The chloramines and **2** or **3** were added together in a 1:30 molar excess of phenol.

The concentrations of the chloramines were monitored by iodometric titiration at regular intervals, and a plot of the concentration (M) versus time gave a straight line. From this regression line we calculated the half-life of each chloramine under reaction conditions.

Reactions were conducted in the following manner: 100 mL of 0.1 M **2** or **3** were placed in a flask and adjusted to pH 6 or 9 using dilute NaOH. Enough chloramine at the corresponding pH was added to give a 30:1 molar ratio of phenol to chloramine. Aliquots of 10 mL were withdrawn and titrated with 0.1 M Na_2SO_4.

Formation and Detection of the Indophenol (6) of Phenol (2) at High pH (the Salt at This pH). An experiment involving **2** and NH_2Cl was run at pH 13 to determine the amount of indophenol (**6**) that was formed in comparison to chlorinated phenols. Phenol **2** (0.217 mg, 2.3 mmols) in 5 mL of aqueous NH_2Cl (2.25 mmols) reacted to give a mixture of 96% chlorinated phenols (**4**, **7**, **8**, **9**, **10**) and 4% **6** (the salt at this pH). The percentages of chlorinated phenols were determined by GC analysis using decane as an internal standard. The percent of **6** (as its salt) was determined using Beers Law, the absorption maximum (λ_{max}, 635), and corresponding molar absorptivity (log ϵ_{max}, 3.95) (both values for the salt) (*32*). At pH 13, the presence of other indophenols from the chlorinated and dichlorinated phenols (**7**, **8**, **9**, **10**) were detected using their absorption maxima and molar absorptivities (*32*). When the reaction was run at pH 9, no **6** was detected.

Reaction of 2,4,6-Trichlorophenol (4) with NH_2Cl and $NHCl_2$ in H_2O. The reactions of **4** with $NHCl_2$ (pH 6) and NH_2Cl (pH 9) were conducted under the following conditions: a 0.002 M solution of **4** was obtained by dissolving 0.1

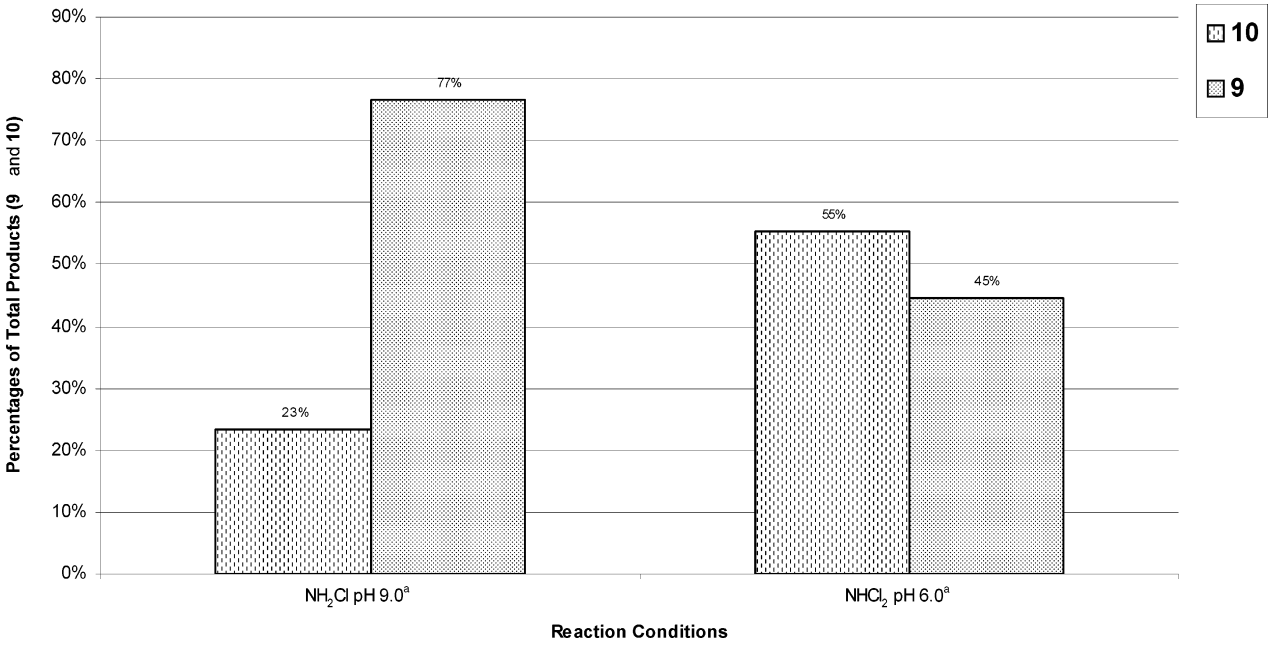


FIGURE 4. Percentage of products from the reactions of 2-chlorophenol (7) with NH_2Cl and $NHCl_2$. [a]All reactions were done at a 1.0:0.05 molar ratio of 2-chloro-*m*-cresol to chloramine.

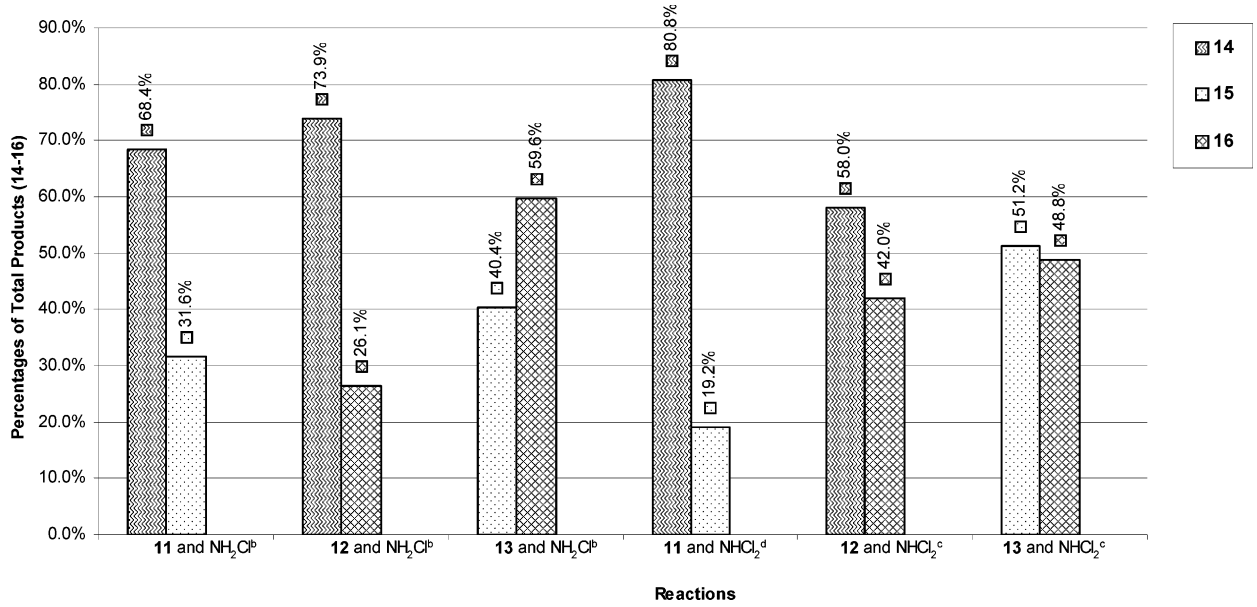


FIGURE 5. Percentages of products from the reaction of 2-, 4-, or 6-monochloro-*m*-cresol (11, 12, 13) with NH_2Cl and $NHCl_2$. [a]All reactions done at a 1.0:0.05 molar ratio of chloro *m*-cresol:chloramine. [b]pH 9.0. [c]pH 6.0. [d]pH 6.5. Reaction of 11 and $NHCl_2$ was conducted only at 6.5. The results for 12 and 13 with $NHCl_2$ were the same at pH 6.5 and 6.0.

TABLE 1. Reaction Rates (Half-Reaction Times)

reactant	pH	time (min)	chlorinating agent
2	9.0	93	NH_2Cl
2	6.0	140	$NHCl_2$
3	9.0	56	NH_2Cl
3	6.0	77	$NHCl_2$

g (ca. 0.50 mmol) in a 250 volumetric flask using small amounts of NaOH. Five milliliters (0.010 mmol) of this solution of **4** was added to a reaction flask, and the pH was adjusted to 6 or 9 with H_2SO_4. No precipitation of **4** was observed. To the stirred solution of **4** was added 15 mL of ca. 0.1 M (1.5 mmol) NH_2Cl or $NHCl_2$. After 45 min. the reaction solution was extracted with dichloromethane, dried over $MgSO_4$, and analyzed by GC. The major products with either NH_2Cl or $NHCl_2$ were 2,6-dichloro-1,4-benzoquinone-4-(*N*-chloro) imine (**5**) (35%) and 2,6-dichloro-1,4-benzoquione (**18**) (55%). 10% of the products were unidentified minor products. We established that **5** was not derived from the reaction of **4** and aqueous NH_3. Also, **5** was not converted to **18** in either aqueous NH_2Cl or $NHCl_2$ at concentrations of the chloramines used in the reactions of **4** with the chloramines. The presence of the radical inhibitor TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, free radical) had no affect on the composition of the products from **4** and the chloramines under aqueous conditions. Although Maeda et al. (*29*) synthesized their $NHCl_2$ in situ from NH_4Cl and OCl^-, with phosphate as buffer (pH 6), when we repeated their synthetic procedure we obtained essentially the same results as ours. They (*29*) did not report the formation of **18**.

Under identical conditions, aqueous NH_2Cl and $NHCl_2$ reacted with 2,4,6-trichlo-*m*-cresol (**17**) and 2,4,6-trichloro-3-methoxyphenol (**29**) to yield analogous products, 2,6-dichloro-3-methyl-1,4-benzoquinone-4-(*N*-chloro)imine (**25**) (40%) and 2,6-dichloro-3-methoxy-1,4-benzoquinone-4-(*N*-chloro)imine (**28**) (60%), respectively, and 2,6-dichloro-3-methyl-1,4-benzoquione (**24**) (60%) and 2,6-dichloro-3-methoxy-1,4-benzoquinone (**27**) (30%), respectively. There were no minor products in the reaction with **17**. The reaction of **29** had about 10% minor products.

Reaction of 2,4,6-Trichlorophenol (4) with NH_2Cl and $NHCl_2$ in H_2O/Glyme. To 0.3 g (1.5 mmol) of **4** dissolved in 15 mL of glyme (1,2-dimethoxyethane) in a flask equipped with a stirrer was added 15 mL of 0.1 M $NHCl_2$ (1.5 mmol) at pH 6. Following extraction with dichloromethane as described previously, GC analysis showed **5** (32%), **18** (20%), and an additional product 2,4,4,6-tetrachloro-2,5-cyclohexadienone **30** (48%) (*39*). When this reaction was conducted in the presence of TEMPO, only **5** and **18** were formed.

Results and Discussion

Reaction of Phenols 2 and 3 with the Chloramines at 1:1 Molar Ratios. Figures 2 and 3 show that **2** and **3**, in a 1:1 molar ratio with the chloramines (NH_2Cl at pH 9, the mixture of $NH_2Cl/NHCl_2$ at pH 6.5 and $NHCl_2$ at pH 6.0), have the chlorinating capacity to chlorinate all the activated positions (*ortho* and *para*) to the hydroxyl groups, producing mono-, di-, and trichlorophenols leading ultimately to trichlorinated phenols **4** and **17**, respectively. We established that an excess of NH_2Cl and/or NH_2Cl with **2** and **3** converted all of the chlorinated intermediates to trichlorophenols **4** and **17**, respectively. These data indicate that both NH_2Cl and $NHCl_2$ show extensive reactivity toward the phenols, even the partially chlorinated less reactive intermediates would be expected to fully chlorinate the activated positions in phenolic substituents in the humic acids. As shown in Table 1, the rates would be slow since the reactions of **2** and **3** with the chloramines are not rapid. The concentrations of both the humic acids and the chloramines would be low, but relatively long reaction times would favor chlorination.

Reaction of Phenols 2 and 3 To Give Monochloro Products. The data in Figure 2 give the ratios of monochloro isomers that are formed under the conditions of (**2**): chloramine of 30:1, respectively. Some of the data in this figure deserves comment. With phenol (**2**), both NH_2Cl (pH 9) and $NHCl_2$ (pH6) and the mixtures of chloramines (pH 6.5) show the same ratio of isomers within experimental error, with 2-chlorophenol (**7**) being the predominant product. This result is surprising since **2** at pH 9 (NH_2Cl), which exists in a 1/0.14 ratio with its phenoxide ion (**31**), might be expected to exhibit different orientation than chlorination at pH 6 ($NHCl_2$) where molecular **2** is essentially the sole reactant (ratio of **2** to **31** is 1:0.00014). Also the anions in the intermediate ion-pairs following the electrophilic attack, NH_2^- and $NHCl^-$, are quite different from NH_2Cl and $NHCl_2$, respectively, and the orientation in the products could have been affected; apparently this is not the case. The predominance of the *ortho* isomer (**7**) over the *para* isomer (**8**) may result from interactions (complex formation) between the oxygen of **2** and the hydrogen of the chloramines, resulting in greater delivery of the chlorine to the *ortho* position.

The data in Figure 3 indicate that *m*-cresol (**3**), in contrast to **2**, reacts differently with the two chlorinating agents NH_2Cl and $NHCl_2$. NH_2Cl and **3** continue to give nearly the same amount of *ortho* product (**11** and **13**−68%) as was the case with **2**, but $NHCl_2$ shows a significant increase in *para* product (**12**). Perhaps this is the result of steric hindrance in the formation of the complex between $NHCl_2$, the oxygen, and the hydrogen of the hydroxyl group, since the two large chlorine atoms in the $NHCl_2$ molecule could interact with the methyl group.

Chlorination of Monochlorinated Phenols with the Chloramines. The data in Figure 4 show significant differences in the position of attack for NH_2Cl and $NHCl_2$ toward 2-chlorophenol (**7**), with NH_2Cl attacking primarily at the 4-position to give **9** (77%) and $NHCl_2$ reacting slightly more rapidly at the 6-position to yield 55% of **10**. Similarly, the results from the chlorination of the monochloro isomers (**11**, **12**, and **13**) of **3** (Figure 5) indicate differences in the reactivities of NH_2Cl and $NHCl_2$. The data in Figures 4 and 5 are in line with those in Figure 3 which indicate that the substituted phenols show differences in the reactivities of NH_2Cl and $NHCl_2$; phenol (**2**), an unsubstituted phenol, as has already been stated did not show differences in reactivities. These results could have important implications in the reactions of the humic acids where phenolic substituents, and perhaps other substituents, could show differences in reactivities between the two chloramines.

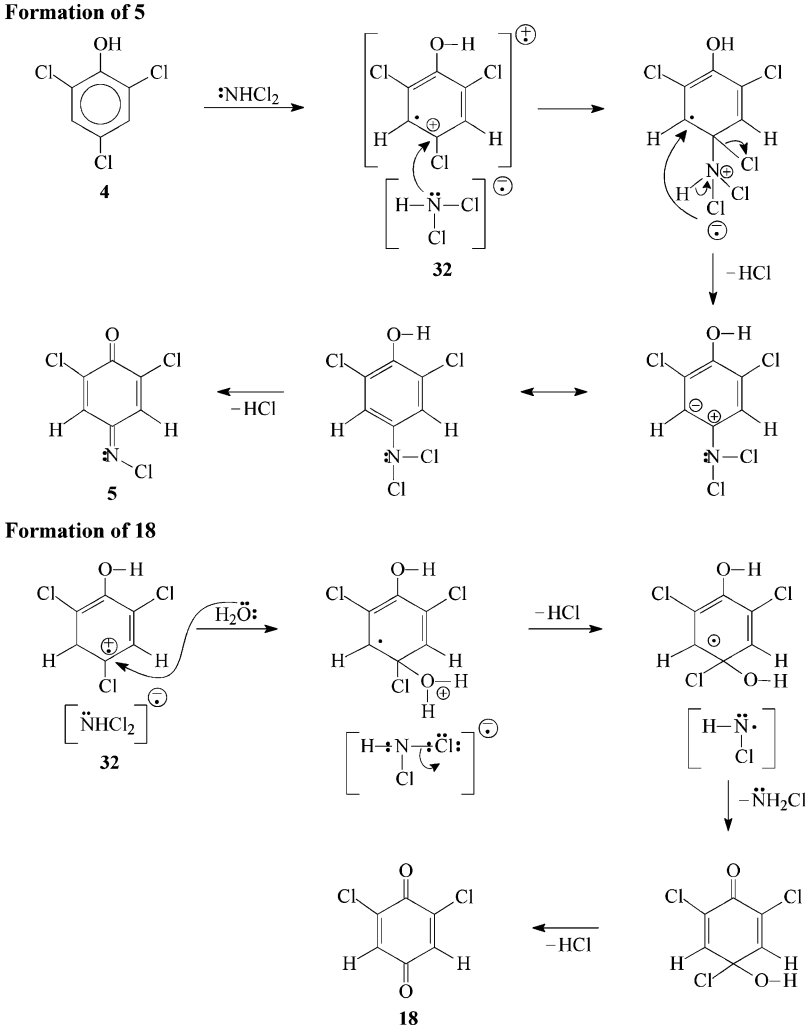
A possible explanation for the differences in the positions of attack by the chloramines on **7** (Figure 4) may arise from NH_2Cl, as an electrophile, reacting at the more electron rich *para*-position in **7** (chlorine withdraws electrons from the *ortho*(6-)-position), while the reactivity of $NHCl_2$ is still controlled by complexing with hydrogens with oxygen, leading to *ortho* attack. The differences in the reactivities of the chloramines with the monochlorocresols containing two substituents (Figure 5), which show different results for NH_2Cl and $NHCl_2$, probably involve multiple complexities that defy explanations.

Differences in the Reactivities of Phenols 2 and 3 with the Chloramines. The data in Table 1 show that *m*-cresol (**3**) is more reactive than phenol (**2**) with both NH_2Cl and $NHCl_2$. The greater reactivity of **3** is reasonable since the methyl group increases the electron density of the aromatic ring and, therefore, its reactivity toward the chloramines (chlorine electrophiles).

Considerations on the Formation of Indophenol (6) During the Chlorination Process. Our data show that a small amount of **6**, probably present as its salt, was formed when phenol (**2**) was chlorinated with NH_2Cl at pH 13. (Indophenols from the substituted phenols were also detected by UV analysis at this pH, but their amounts were not determined.) No **6** was detected when **2** and monochloramine reacted at pH 9. The implications of these results are that **6** might be present as a contaminant in drinking water, if **6** were formed during the mixing process where the pH potentially rises because of hydroxide ion (OH^-) formation during the reaction of ammonia (NH_3) and hypochlorite ion to give the chloramines.

Considerations of the Mechanism of the Displacement of the *para*-Chloride in 4 Resulting in the Formation of 5 and 18. Direct displacement of the *para*-chloride in an aromatic compound like **4** by strong nucleophiles such as NH_3 is without precedent in organic chemistry. Therefore we were not surprised that aqueous NH_3 did not react with **4** to give 2,6-dichloro-4-aminophenol, which is known to react further with the chloramines to give **5** (*32*). Since NH_2Cl is significantly less basic than NH_3 (10^{-10} less basic) (*40*) a direct, nucleophilic displacement of chloride (either SN^2 or SN^1) by the chloramines is inconceivable. We also established that **5** was not converted directly to **18** under any of our reaction conditions. Maeda et al. (*29*) did not address the mechanism of the displacement of chloride in **4** leading to **5**, but Pallagi, Toro, and Farkas (*30*) have clearly established that *para*-substituted phenols (some substituted with chloride in the *para* position) react with N-chloro imines by either an ion radical or a radical mechanism to give indophenols. They determined that a radical mechanism was inhibited by TEMPO but that an ion radical reaction was

SCHEME 1. Ion Radical Mechanism for the Reaction of 4 with $NHCl_2$



unaffected by the radical inhibitor TEMPO. Because of the similarities of the N-chloro imines and the chloramines, we are suggesting an ion radical mechanism in the reactions leading to **5** and **18** (see Scheme 1) and not a radical mechanism because the reactions of **4** with NH_2Cl or $NHCl_2$ were unaffected by TEMPO. The first step in the mechanism involves the transfer of an electron from the phenol (**4**) to the chloramines to give a cation/radical-anion/radical pair (**32**). The cation radical of the ion radical pair **32** can undergo attack by $NHCl_2$ anion radical leading ultimately to **5**, or radical pair **32** can react with H_2O to give **18**. A similar set of mechanistic equations can be developed for the reaction of NH_2Cl with **4**. Radical inhibitors, such as TEMPO, do not affect ion radical reactions (*30*) so it is difficult to obtain direct proof for this mechanism. In our case, however, TEMPO did prevent the formation of tetrachloride **30** in the reaction of **4** and the chloramines in a mixture of H_2O and glyme. This result suggests to us that **30** is formed by a radical mechanism, and the presence of TEMPO prevents this radical mechanism. This result is similar to an observation by Pallagi, Toro, and Farkas (*30*) where they found that the organic solvent acetonitrile greatly altered the kinetics of the reaction of their phenols and chloro imines (which in the absence of acetonitrile were known to react by ion radical mechanisms) but that TEMPO restored the original kinetics. They interpreted the role of the organic solvent as follows: the organic solvent allowed one of the radicals from the ion radical pair to get outside of the solvent cage before collapsing to give the "regular" indophenol product and, once outside the solvent cage, initiated a fast radical chain mechanism which could be inhibited by TEMPO. In our case the process has definite similarities. We observed the formation of an entirely different product (**30**) when glyme was present, probably formed by a radical mechanism, whose formation was inhibited by TEMPO. In other words, glyme probably permits one of the ion radicals to escape the solvent cage before collapsing, leading to tetrachloride **30** by a radical chain mechanism.

The radical ion mechanism is undoubtedly responsible for the formation of the imines (**25** and **28**) and quinones (**24** and **27**) from starting compounds **17** and **29**.

Considerations on the Further Chlorination of 5 and 18 by the Chloramines. Continued chlorination of the reaction mixture of **5** and **18** led to **20**, **21**, and **22** and many other minor, unidentified products, confirming that extensive chlorination of **4** with the chloramines can result in many contaminants in drinking water. We established that N-chloro imine **5** itself is almost certainly not a chlorinating agent since it did not chlorinate the very reactive resorcinol (**1**).

Considerations on the Oxidation of Side Chains. The statement (*9*) mentions the likely oxidation of side chains in phenols by the chloramines. The term "side chain" in organic chemistry is used to refer to alkyl groups such as the methyl group in *m*-cresol (**3**). Since side chain is not defined in the statement (*9*), perhaps it is used to refer to the hydroxyl group (phenol) which is oxidized to a carbonyl group in the reactions with the chloramines. We made a detailed study of the oxidation of the methyl group in **17** with the chloramines in aqueous solution, with and without UV radiation, observing whether benzylic chlorinated products or the complete oxidation product, a carboxylic acid, was formed. No

oxidation of the methyl group was detected under these conditions. Even reaction of **17** with the chloramines with UV irradiation in ether did not lead to chlorination of the methyl side chain. Only products **5** and **18** were formed in aqueous solution, and no products were detected in ether.

Acknowledgments

We recognize, with pleasure, support from the following sources: NSF-RUI (CHE-013224); NSF-RUI (CHE-9902718); and The Research Associates of Point Loma Nazarene University. We also thank Dr. Rich Kondratt at the Mass Spectroscopy Center, University of California, Riverside, for high-resolution mass spectral data.

Literature Cited

(1) Maier, S. H.; Powell R. S.; Woodward, C. A. *Water Res.* **2000**, *34*, 2301−2309.
(2) Mitch W. A.; Sedlak, D. L. *Environ. Sci. Technol.* **2002**, *36*, 588−595.
(3) Betts, K. S. *Environ. Sci. Technol.* **2002**, *36*, 92A−93A.
(4) Chaidou, C. I.; Georgakilas, V. I.; Stalikas, C.; Saraci, M.; Lahaniatis, E. S. *Chemosphere* **1999**, *39*, 587−594.
(5) Scully, F. E., Jr.; White, W. N. *Environ. Sci. Technol.* **1991**, *25*, 820−828.
(6) Wolfe, R. L.; Ward, N. R.; Olson, B. H. *J. AWWA* **1984**, *76*, 74−88.
(7) Heasley, V. H.; Alexander, M. B.; DeBoard, R. H.; Hanley, J. C., Jr.; McKee, T. C.; Wadley, B. D.; Shellhamer, D. F. *Environ. Toxicol. Chem.* **1999**, *18*, 2406−2409.
(8) Ginwalla, A. S.; Mikita, M. A. *Environ. Sci. Technol.* **1992**, *26*, 1148−1150.
(9) Kanniganti, R.; Johnson, J. D.; Ball, L. M.; Charles, M. J. *Environ. Sci. Technol.* **1992**, *26*, 1998−2004.
(10) Cozzie D. A.; Kanniganti R.; Charles M. J.; Johnson, J. D.; Ball L. M. *Environ. Mol. Mutagen.* **1993**, *21*, 237−246.
(11) Singer, P. C.; Shi, J.; Weinberg, H. S. *Proc. Water Qual. Technol. Conf.* **1998**, 554−578.
(12) Norman, T. S.; Harms, L. L.; Looyenga, R. W. *J. AWWA* **1980**, *72*, 176−180.
(13) Gallard, H.; Von Gunter, U. *Environ. Sci. Technol.* **2002**, *36*, 884−890.
(14) Rebenne, L. M.; Gonzalez, A. C.; Olson, T. M. *Environ. Sci. Technol.* **1996**, *30*, 2235−2242.
(15) Tretyakova, N.; Lebedev, A. T.; Petrosyan, V. *Environ. Sci. Technol.* **1994**, *28*, 606−613.
(16) Boyce, S. D.; Hornig, J. F. *Environ. Sci. Technol.* **1983**, *17*, 202−211.
(17) Norwood, D. L.; Johnson, J. D.; Christman, R. F.; Hass, J. R.; Bobenrieth, M. J. *Environ. Sci. Technol.* **1980**, *14*, 187−189.
(18) Rook J. J. Possible Pathways for the Formation of Chlorinated Degradation Products During Chlorination of Humic Acids and Resorcinol. In *Water Chlorination: Environmental Impact and Health Effects*; Jolly, R. L., Ed.; Ann Arbor Science Publishers: Ann Arbor, MI, 1979; Vol. 3, pp 85−98.
(19) Smith, J. G.; Lee, S. F.; Netzer, A. *Water Res.* **1976**, *10*, 985−990.
(20) Singer, P. C. *Water Sci. Technol.* **1999**, *40*, 25−30.
(21) Patnaik, P.; Yang, M.; Powers, E. *American Laboratory-News Edition*; Wham, W. N., Ed.; 2000; Vol. 332, p 16.
(22) Karlsson, S.; Kaugare, S.; Grimvall, A.; Boren, H.; Savenhed, R. *Water Sci. Technol.* **1995**, *31*, 99−103.
(23) Hodin, F.; Boren, H.; Grimvall, A.; Karlsson, S. *Water Sci. Technol.* **1991**, *24*, 403−410.
(24) Burttschell, H.; Rosen, A.; Middleton, F.; Ettinger, M. *J. AWWA* **1959**, *51*, 205−214.
(25) Ahlborg, U.; Thunberg, T. *CRC Crit. Rev. Toxicol.* **1980**, *7*, 1−35.
(26) Fam, S.; Stenstrom, M. *J. Water Pollut. Control Fed.* **1987**, *59*, 969−978.
(27) Dean-Ross, D.; Rahimi, M. *Bull. Environ. Contam. Toxicol.* **1995**, *55*, 245−250.
(28) Hejzlar, J.; Boren, H.; Grimvall, A. In *Naturally-Produced Organohalogens*; Grimvall, A., de Leer, E., Eds.; Kluwer Academic Publishers: Dordrecht/Boston/London, 1995; p 201.
(29) Maeda, N.; Ohya, T.; Nojima, K.; Kanno, S. *Chemosphere* **1987**, *16*, 2249−2258.
(30) Pallagi, I.; Toro, A.; Farkas, O. *J. Org. Chem.* **1994**, *59*, 6543−6557.
(31) Harfmann, R.; Crouch, S. *Talanta* **1989**, *36*, 261−269.
(32) Pattan, C. A Thesis: Kinetics and Mechanism of the Berthelot Reaction with Particular Reference to Ammonia Analysis, Michigan State University, 1975, pp 1−63.
(33) Huston, R.; Chen, P. *J. Am. Chem. Soc.* **1933**, *55*, 4214−4217.
(34) Heasley, V.; Anderson, J.; Bowman, Z.; Hanley, J., Jr.; Sigmund, G.; Van Horn, D.; Shellhamer, D. *J. Org. Chem.* **2002**, *67*, 6827−6830.
(35) Heasley, V.; Burns, M.; Kemalyan, N.; McKee, T.; Schroeter, H.; Teegarden, B.; Whitney, S.; Wershaw, R. *Environ. Toxicol. Chem.* **1989**, *8*, 1159−1163.
(36) Norris, R.; Sternhell, S. *Aust. J. Chem.* **1973**, *26*, 333−43.
(37) Cason, J.; Harman, R.; Adams, P.; Goodwin, S. *J. Org. Chem.* **1951**, *16*, 328.
(38) Cason J.; Allen, C.; Goodwin, S. *J. Org. Chem.* **1948**, *13*, 403.
(39) Svec, P.; Zberovsky, M. *Org. Chem. Technol.* **1974**, *21*, 23−27.
(40) Sisler, H. *J. Chem. Ed.* **1983**, *60*, 1002−1004.

Received for review September 26, 2003. Revised manuscript received June 26, 2004. Accepted July 9, 2004.

ES030644H