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REACTIONS OF RESORCINOL AND ITS CHLORINATED DERIVATIVES WITH MONOCHLORAMINE: IDENTIFICATION OF INTERMEDIATES AND PRODUCTS

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Abstract—An investigation of the reaction of resorcinol (compound 1) and its chlorinated derivatives 4-chlororesorcinol (compound 4), 4,6-dichlororesorcinol (compound 5), and 2,4,6-trichlororesorcinol (compound 2) with monochloramine (NH_2Cl) in ether and aqueous solution (pH 7) is reported. NH_2Cl reacted with compounds 1, 2, 4, and 5 to give the pentachloro intermediate, 2,2,4,4,6-pentachloro-5-cyclohexen-1,3-dione (compound 3), which underwent ring opening with H_2O and loss of CO_2 in the presence of NH_2Cl to produce the following: 1,1,3,5,5-pentachloro-3-penten-2-one (compound 6), 1,1,1,3,5,5-hexachloro-3-penten-2-one (compound 7), and 1,1,3,5,5,5-hexachloro-3-penten-2-one (compound 8). Compound 6 reacted further with NH_2Cl to give compounds 7 and 8; in the presence of NH_2Cl, compound 7 rearranged to compound 8. Mechanisms for the preceding reactions are analyzed in detail. Another aspect of the investigation involved a determination of the amounts of chloroform, $CHCl_3$, which is produced from compound 3 with NH_2Cl (4%) and with NaOCl (50%). The low production of $CHCl_3$ from compound 3 and NH_2Cl is discussed in connection with the probable reactions of compounds 7 and 8 with NH_2Cl and H_2O.

Keywords—Resorcinol Monochloramine Chloroform Intermediates Mechanisms

INTRODUCTION

Resorcinol (compound 1) (Fig. 1) is an important model for examining the reactions of chlorinating agents on humic acids because it is postulated to be a substituent in the humic acids and is assumed to be partially responsible for the production of the chloroform ($CHCl_3$) that is formed when drinking water is chlorinated [1–3]. Recently, we reported on the reaction of resorcinol (compound 1) and its chlorinated derivatives with hypochlorite ion (OCl^-) in methanol, identifying the early generation products and the intermediate, which undergoes ring opening [4].

In the investigation described here, we examined the reaction of monochloramine, NH_2Cl, with resorcinol (compound 1) and its chlorinated derivatives, 2,4,6-trichlororesorcinol (compound 2), 4-chlororesorcinol (compound 4), and 4,6-dichlororesorcinol (compound 5) (Fig. 1), in ether and in H_2O. NH_2Cl is a chlorinating agent that is widely used for treating municipal drinking water because it does not react with humic acid contaminants to produce significant amounts of $CHCl_3$ and related halomethanes [5,6]. The reaction of the model compound resorcinol (compound 1) with NH_2Cl has not been investigated. It was our goal in this study to determine whether resorcinol (compound 1) and its chlorinated derivatives reacted with NH_2Cl and, if a reaction occurred, whether $CHCl_3$ was produced, the structure of the intermediate, and final products.

MATERIALS AND METHODS

Starting materials

Compounds 1, 4, and 5 and molecular sieves (8–12 mesh) were obtained from Aldrich (Milwaukee, WI, USA). Compound 2 was prepared as described previously [7]. The pentachloride (2,2,4,4,6-pentachloro-5-cyclohexen-1,3-dione, compound 3) (Fig. 1) preparation procedure has been described previously [4]; a modified, simpler procedure is reported here. Five grams (45 mmol) of compound 1 were dissolved in 30 ml of ether and 60 ml of methylene chloride. Chlorine gas (Cl_2) was passed slowly into the solution for 45 min to 1 h. At this point, GC analysis was performed to determine conversion to compound 3. Chlorine gas was passed into the solution until the conversion of compound 1 to compound 3 was approx. 95%. The solvent was then removed using a rotary evaporator, and the remaining liquid was cooled in ice until crystallization occurred. The crystals were isolated and washed with pentane. Purity, as determined by GC, was 98%. Monochloramine, NH_2Cl, was made as described previously [8]. Usually, the NH_2Cl/ether layer was isolated, dried over $MgSO_4$, titrated iodometrically (~0.3 M) according to the standard analytical chemistry procedure, and used directly in reactions. On one occasion, the NH_2Cl/ether layer was distilled to eliminate the possibility of impurities in the ether solution [8]. NCl_3 was made as described previously [9]. Hypochlorous acid (HOCl) was prepared by chlorination of aqueous $NaHCO_3$/ether. Hypochlorous acid in the ether layer was identified by its ultraviolet absorption at 298 nm.

Instrumentation and analysis

The 300-MHz ^1H nuclear magnetic resonance (NMR) and 75.4-MHz ^{13}C NMR spectra were obtained using a Varian Unity 300 instrument (Varian, Walnut Creek, CA, USA) and are reported relative to Me_4Si or $CDCl_3$. Mass spectral analyses were obtained at 70 eV using a Hewlett-Packard gas chromatograph (model 5890, Hewlett-Packard, Avondale, PA, USA) interfaced with a Hewlett-Packard mass selective detector (model 5970B). Results are expressed as electron impact (m/z) and as relative intensity (%). Products were analyzed using a Hewlett-Packard gas chromatograph (model 5890).

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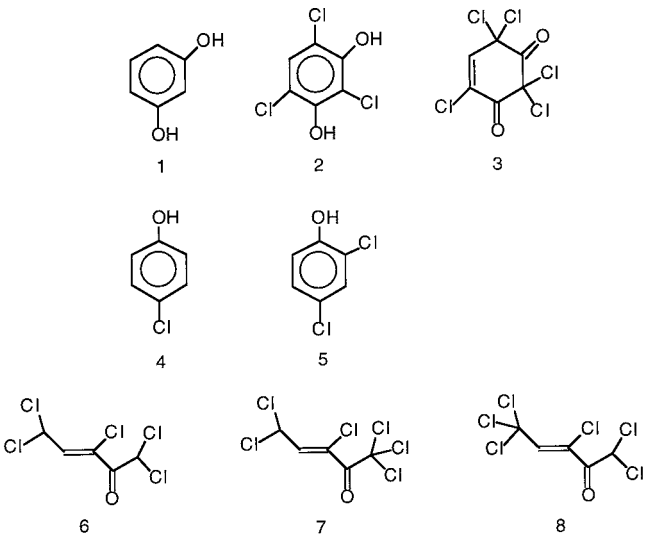

Fig. 1. Structures of reactants 1, 2, and 3 and products 6, 7, and 8.

The GC and GC–MS analyses were performed using a 25-m Hewlett-Packard ultraperformance column with an internal diameter of 0.20 mm and a methyl silicone stationary phase of 0.33 μm film thickness. Liquid infrared spectra were recorded with a Nicolet 610 Fourier transform spectrometer (Nicolet Instruments, Madison, WI, USA). Gas-phase infrared spectra were obtained with a Nicolet 610 interfaced with a Hewlett-Packard gas chromatograph (model 5890).

Starting compounds and products were analyzed by GC at 120 to 220°C at a rate of 10°C/min and showed the following retention times (min): 1, 5.5; 2, 9.8; 3, 7.8; 4, 6.0; 5, 6.2; 6, 5.5; 7, 6.8; and 8, 7.2.

Reaction of the pentachloride with NH_2Cl

General reaction conditions: to a stirred solution of NH_2Cl in ether (~0.3 M) was added 0.21 g (0.75 mmol) of the pentachloride (compound 3). Usually, the reaction was run in a molar ratio of 1:3 (compound 3:NH_2Cl; 2.5 ml of NH_2Cl/ether) to speed up the conversion of compound 3 to the mixture of compounds 6 (1,1,3,5,5-pentachloro-3-penten-2-one), 7 (1,1,1,3,5,5-hexachloro-3-penten-2-one), and 8 (1,1,3,5,5,5-hexachloro-3-penten-2-one) (Fig. 1). The yield under these conditions was 88%. The stoichiometry in the reaction of compound 3:NH_2Cl was 1:1 because 1 Meq of NH_2Cl and compound 3 reacted completely.

Reactions in ether establishing that compounds 4 and 5 were on the reaction pathway used the general reaction conditions described above: Sufficient tetrahydrofuran (~50:50 with water) was added to water to bring the reactants into solution at a final volume of 2.5 ml.

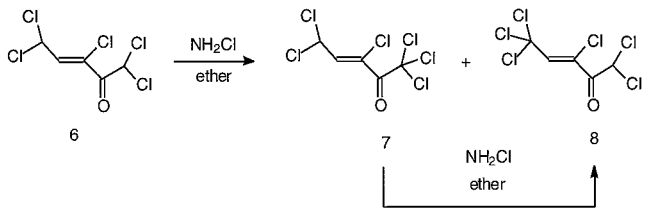

Fig. 2. In the presence of NH_2Cl, compound 6 gives compounds 7 and 8; compound 7 rearranges to compound 8.

Rate study on the reactions of compounds 3 and 6 with NH_2Cl

We added 0.64 mg (2.25 mmol) of compound 3 to 1 ml of 0.22 M (0.22 mmol) monochloramine (10:1 molar ratio). Gas chromatography analysis showed essentially no reaction at the end of 1 min; little reaction had occurred even by 10 min: compound 3, 95.5%; compound 6, 1.4%; compound 7, 1.1%; and compound 8, 2.0%. In a similar manner, 0.57 mg (0.22 mmol) of compound 6 was added to 1 ml of 0.225 M (0.22 mmol) chloramine (1:1 molar ratio). Compound 6 reacted rapidly with NH_2Cl. In 1 min, the analysis showed the following: compound 6, 82.5%; compound 7, 3.0%; and compound 8, 14.5%.

Synthesis and structure confirmation of the products

The structure of compound 6 was reported previously [4]. It was synthesized as follows: 0.15 g (0.53 mmol) of compound 3 was suspended in H_2O (25 ml) and stirred overnight. The resulting compound, formed by ring opening by water and decarboxylation of the intermediate acid, was extracted with ether and dried over $MgSO_4$. The solvent was removed on a rotary evaporator, and the liquid was distilled under vacuum (72–76°C at 1 torr) to give compound 6 with 90% purity.

The structure of compound 7 was established by ^1H NMR, ^{13}C NMR, GC-MS, and infrared spectrometry. ^1H NMR (300 MHz): δ5.90 (d, 1 H, J = 1.8 Hz) and 6.28 (d, 1 H, J = 1.8 Hz). ^{13}C NMR (75.4 MHz): 50.8, 123.3, 129.1, 139.4, and 182.4. GC-MS: M^+: 290 (1.4) and 288 (0.86); M-Cl^+: 261 (0.11), 259 (0.59), 257 (1.8), 255 (2.9), and 253 (1.8); M-Cl-CO^+: 233 (0.40), 231 (2.1), 229 (6.4), 227 (9.3), and 225 (6.4); M-CCl_3-CO: 149 (3.4), 147 (32), 145 (97), and 143 (100); CCl_3: 123 (1.2), 121 (5.9), 119 (18), and 117 (14); and $CHCl_2$: 87 (3.2), 85 (14), and 83 (20). Infrared spectrometry, gas phase (cm^{-1}): CO, 1774; C = C, 1614. Compound 7 was synthesized as follows: 0.15 g (0.53 mmol) of compound 3 was stirred into 11 ml of aqueous 0.2 M NH_2Cl (2.2 mmol of NH_2Cl) at ice temperature and pH 6.15. (NH_2Cl solution at pH 6.15 was obtained by titration of aqueous NH_2Cl [pH = ~11] with 0.1 M HCl.) The reaction was stirred at ice temperature for 45 min and then extracted with ether. After drying over $MgSO_4$ and removal of the solvent under vacuum with a rotary evaporator, the remaining liquid was distilled (80°C at 1 torr) to give compound 7 with 69% purity. The major impurity was isomer 6. Perhaps at pH 6.15, dichloramine ($NHCl_2$) is the chlorinating agent because NH_2Cl is known to disproportion to NH_4^+ and $NHCl_2$ at acidic pH.

The structure of compound 8 was established by ^1H NMR, ^{13}C NMR, GC-MS, and infrared spectrometry. ^1H NMR (300 MHz): δ6.81 (s, 1 H) and 6.92 (s, 1 H). ^{13}C NMR (75.4 MHz): 62.8, 78.0, 124.9, 133.6, and 182.8. GC-MS: M-Cl^+: 261 (0.2), 259 (1.1), 257 (3.6), 255 (5.7), and 253 (3.1); M-Cl-CO^+: 233 (0.1), 231 (0.9), 229 (3.4), 227 (5.3), and 225 (3.6); M-$CHCl_2$-CO^+: 183 (12), 181 (43), 179 (100), and 177 (79); $CHCl_2CO$: 113 (4.5) and 111 (9.9); $CHCl_2$: 87 (6.7), 85 (33), and 83 (47). Infrared spectrometry, liquid phase (cm^{-1}): CO, 1763; C = C, 1610. Compound 8 was synthesized as follows: 0.21 g (0.75 mmol) of compound 3 was stirred into 10 ml of 0.3 M NH_2Cl in ether (3 mmol of NH_2Cl). After 6 h, the ether was removed under vacuum with a rotary evaporator, and the liquid was distilled (80°C at 1 torr) to give compound 8 with 85% purity.

Compounds 6, 7, and 8 were stable under distillation conditions and were stored indefinitely in the freezer.

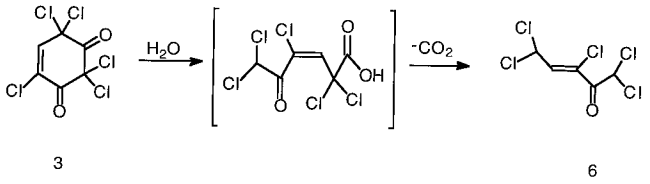

Fig. 3. Conversion of compound 3 to compound 6 by hydrolysis and decarboxylation.

RESULTS

We observed that compounds 1, 2, 4, and 5 reacted with NH_2Cl in ether or H_2O to give compound 3, confirming that resorcinol (compound 1) and its derivatives (compounds 2, 4, and 5) are all on the reaction pathway from compound 1 to compound 3. Furthermore, we established that the pentachloride (compound 3), prepared by independent synthesis, reacted with NH_2Cl in ether or in H_2O (pH 7) to give a mixture of ring-opened products (compounds 6, 7, and 8), as shown in Figure 1. We also observed that compound 6 reacted with NH_2Cl to give compounds 7 and 8. Subsequently, compound 7 in the presence of NH_2Cl rearranged to compound 8 (Fig. 2).

Therefore, compound 8 becomes the major product (85%) if compounds 6, 7, and 8 are allowed to stand in solution with excess NH_2Cl. If a stoichiometric amount of compound 3 and NH_2Cl (1:1 molar ratio) are reacted, the percentages of products are as follows: compound 6, 51%; compound 7, 25%; and compound 8, 24%.

The reaction of compound 3 with NH_2Cl in ether to give compound 6 definitely depended on the presence of trace amounts of H_2O. When the trace amounts of H_2O were removed with molecular sieves from ether solutions of compound 3 and NH_2Cl, the reaction rate decreased proportionally to the drying time. Additions of small amounts of H_2O to sieve-dried solutions of compound 3 and NH_2Cl restored the reaction rate.

Without NH_2Cl, ring opening of compound 3 by H_2O followed by decarboxylation is too slow to be on the reaction pathway, as we previously confirmed [4] (Fig. 3).

We established that the reaction of the pentachloride (compound 3) and NH_2Cl does not depend on catalysis by an unknown component in the NH_2Cl/ether solution. After careful purification by distillation under vacuum, NH_2Cl/ether also reacted at the same rate with compound 3 in ether to give the expected products. Ring opening of compound 3 in ether saturated with H_2O, $NH_3 \cdot H_2O$, $NaOH \cdot H_2O$, and $HCl \cdot H_2O$ did not occur (no NH_2Cl was present).

In a rate study, we determined that the reaction of compound 6 with NH_2Cl to give compounds 7 and 8 is much more rapid than the ring-opening reaction of the compound 3 with NH_2Cl and trace amounts of H_2O to give compound 6.

NH_2Cl and compound 3 in ether saturated with NH_3 gas reacted to give the normal products (compounds 6, 7, and 8), proving that NH_3 did not interfere with the normal reaction. In the absence of NH_2Cl, compound 3 and NH_3 reacted to give trace amounts of compounds 6, 7, and 8; other products were not detected by GC. No amides from the reaction of compound 3 and NH_3 were observed in the GC analysis, although an amide of comparable molecular weight (4-chlorobenzanilide) did emerge.

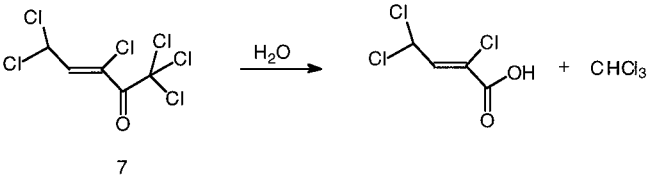

Fig. 4. Hydrolysis of compound 7 to give chloroform and a carboxylic acid.

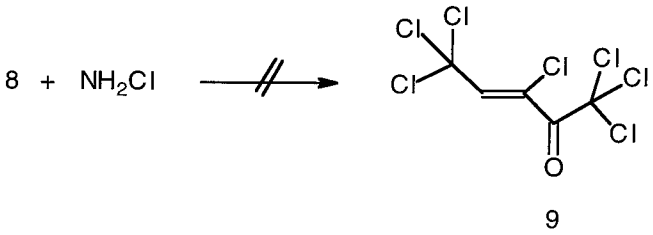

Fig. 5. Chlorination of compound 8 to give compound 9 does not occur.

We assumed that our chlorinating agent was monochloramine (NH_2Cl) and not dichloramine ($NHCl_2$) or trichloramine (NCl_3). We based this assumption on the following facts: NCl_3 in ether, by our own investigation, does not react with compound 3; NH_2Cl is confirmed in the ether solution by its maximum absorbance at 243 nm [6]; and reaction of compound 3 with aqueous monochloramine solutions that had been titrated with dilute HCl to pH values of 6.4 and 4 gave primarily compound 7. (This is, in fact, the procedure used to make compound 7.) At pH 4, $NHCl_2$ is known to be the major component, with NH_2Cl and NCl_3 also being present [6]. Therefore, $NHCl_2$ may be the reacting species at lower pH, but we have no proof that it is not NH_2Cl.

Our investigations show that hypochlorous acid (HOCl) does not react with compound 3 in ether.

Only a small amount of $CHCl_3$ (4%) by internal standard was formed when resorcinol (compound 1) and the pentachloride were reacted in H_2O at pH 7 with NH_2Cl to 700% (compound 1:NH_2Cl/1 mol:7 mol) and 200% (compound 3: NH_2Cl/1 mol:2 mol), respectively. Under the same reaction conditions, reaction of compound 1 with NaOCl to 700% gave approx. 50% $CHCl_3$ (by internal standard).

DISCUSSION

Our data show that resorcinol (compound 1) and its chlorinated derivatives (compounds 2, 3, 4, and 5) all react with NH_2Cl in H_2O and ether. The reaction pathway involves the intermediate pentachloride (compound 3), which undergoes ring opening with NH_2Cl/H_2O to give compound 6, which

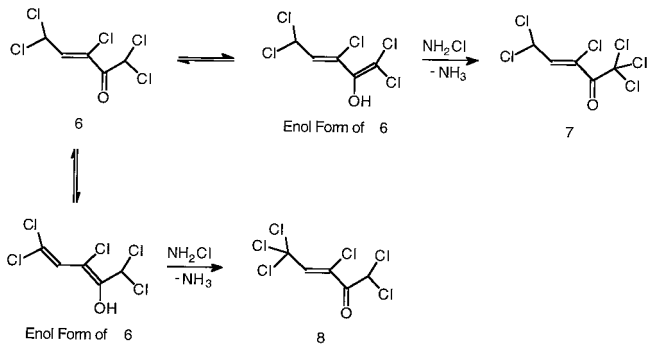

Fig. 6. Mechanisms for the formation of compounds 7 and 8 from compound 6 and NH_2Cl.

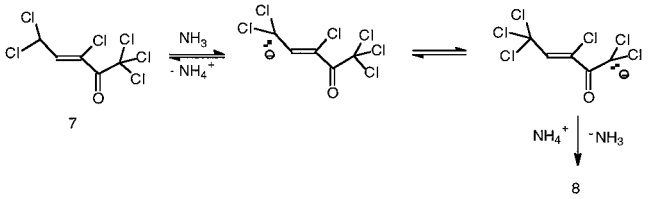

Fig. 7. Mechanisms for base-catalyzed rearrangement of compound 7 to compound 8.

chlorinates further to compounds 7 and 8. Compound 7 in the presence of NH_2Cl rearranges rapidly to compound 8.

The mechanism of ring opening of the pentachloride is not clear. Our data show that NH_2Cl and H_2O are involved in the ring opening to give compound 6 and, we presume, CO_2. Perhaps NH_2Cl, via a NH_2Cl-H_2O complex, assists as a catalyst in the nucleophilic attack of H_2O on the carbonyl group between the two CCl_2 groups, providing two protons for the terminal carbons and an oxygen for the formation of CO_2. The NH_2Cl molecule is now left to chlorinate compound 6. This type of mechanism requires the formation of compound 6 before compounds 7 and/or 8. We could not prove this point, however, because the rate study showed that the ring opening of compound 3 is slow compared to the reaction of NH_2Cl with compound 6. Consequently, GC analysis in the very early stages of the reaction of compound 3 and NH_2Cl indicated only mixtures of compounds 6, 7, and 8.

Our data show that little $CHCl_3$ is formed in the reaction of compounds 1 and 3 with NH_2Cl and H_2O. The small amount of $CHCl_3$ formed probably arises from nucleophilic displacement of the weak leaving group CCl_3 by H_2O, as shown in Figure 4. Absence of significant $CHCl_3$ formation probably arises from the fact that compound 7 is present in a relatively low percentage, hydrolyzes extremely slowly with H_2O, and rearranges quite rapidly to compound 8 in the presence of NH_2Cl. We established that compound 8 does not chlorinate further with NH_2Cl to give compound 9 (Fig. 5), which could hydrolyze to give $CHCl_3$ (Fig. 5). The pentachloride (compound 3) and OCl^- probably produced a large amount of $CHCl_3$, because most of the degradation intermediates and products contain the $-C(O)CCl_3$ leaving group [4]. Because rearrangement pathways are impossible for these intermediates and products (because of the absence of an α, β-carbon, carbon double bond as exists for compounds 7 and 8), hydrolysis leading to $CHCl_3$ becomes a major pathway.

The mechanisms for the reactions of compound 6 with NH_2Cl to form compounds 7 and 8 probably involve attack of the two enol forms of compound 6 on the chlorine of NH_2Cl, as shown in Figure 6. The mechanism for the conversion of compound 7 to 8 in the presence of NH_2Cl is not clear. We know that the mechanism does not involve a base-catalyzed

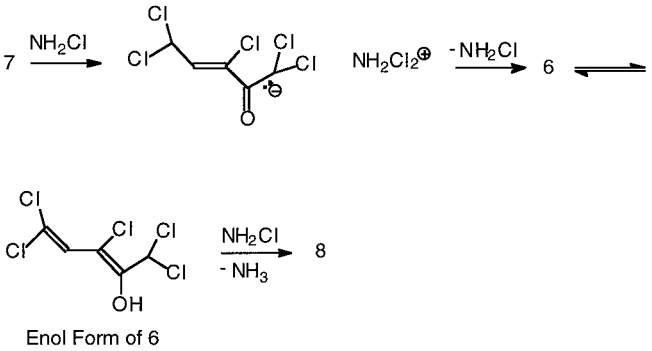

Fig. 8. Mechanism for the rearrangement of compound 7 to compound 8.

rearrangement of chlorine by NH_3, as shown in Figure 7, because compound 7 and NH_3 in ether do not give compound 8. Perhaps the rearrangement of compound 7 to compound 8 involves compound 6 and dichloramine ($NHCl_2$) as intermediates, as shown in Figure 8.

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