Notes

The Reaction of Hypochlorous Acid with Some Quinones and Related Compounds

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1,4-Naphthoquinone and 2-methyl-1,4-naphthoquinone react with hypochlorite ion[1] to give the corresponding epoxides. The epoxidation of these quinones by means of hypochlorous acid has been cited,[2] but these claims were considered somewhat dubious in light of the established mechanism[3] for the nucleophilic epoxidation of α,β-unsaturated carbonyl compounds. An investigation of the reaction of aqueous hypochlorous acid (free of chlorine) with quinones, described in this paper, revealed that the epoxide is not a significant product, and that an unexpected reaction does occur under appropriate conditions.

Stirring finely powdered 1,4-naphthoquinone (I) with aqueous hypochlorous acid for 20 hr. at 25° resulted in no reaction, and the organic starting material was recovered unchanged. The next logical step called for a reaction run under homogeneous conditions. The major product isolated from the reaction of I with aqueous hypochlorous acid in dioxane proved to be 2-chloro-1,4-naphthoquinone (II), obtained in 60–70% yield after recrystallization. Similarly, 2-methyl-1,4-naphthoquinone was converted to 2-methyl-3-chloro-1,4-naphthoquinone (56% yield), and 3-chloro-2,5-diphenylbenzoquinone was obtained in excellent yield from the reaction of hypochlorous acid with the quinone in dioxane.

The dioxane used as the solvent was not specially purified, except for a simple distillation. The results of the experiments indicated that the presence of peroxides in the solvent could be responsible for the observed substitution reactions. This was borne out by further experiments in which other solvents were used in place of the peroxide-containing dioxane. The reaction of chlorine-free hypochlorous acid with I in acetone or in peroxide-free dioxane under a nitrogen atmosphere and in the dark led to the formation of none or only small amounts (10% or less) of the 2-chloro derivative. Furthermore, reactions of HOCl with I in other solvents known to contain peroxides, such as tetrahydrofuran and isopropyl ether (used in combination with acetone to assure homogeneity), as well as acetone to which *t*-butyl hydroperoxide was added, resulted in the formation of II in yields ranging from 40 to 60%.

It was apparent that in the presence of peroxides the reaction of hypochlorous acid with quinones proceeds *via* a free-radical mechanism. Precedence for the free-radical attack on a quinone with ultimate replacement of hydrogen at the 2-position exists in the work of Fieser, *et al.* 2,3-Dimethyl-1,4-naphthoquinone was prepared from the monomethylquinone through reaction with lead tetraacetate[4] or with acetyl peroxide.[5] The reaction of 2-methyl-1,4-naphthoquinone with lead tetrapropionate to give 3-ethyl-2-methyl-1,4-naphthoquinone was also reported.[4] The interaction of hypochlorous acid with toluene, under the influence of light, to give benzyl chloride as the principal product is the only reported instance[6] of a possible free-radical reaction of hypochlorous acid with an organic compound. The possibility that the hypochlorous acid simply decomposes to free chlorine, which is then involved in the reaction with the quinone, is untenable. Elemental chlorine does react with 1,4-naphthoquinone[7] to form the expected stable addition product, 2,3-dichloro-2,3-dihydro-1,4-diketonaphthalene. Dehydrochlorination of the latter occurs when it is treated with base, resulting in the formation of the monochloroquinone.

A preliminary experiment to determine the effectiveness of an *in situ* reaction of HOCl with 1,4-naphthoquinone in aqueous dioxane gave promising results. Chlorine was slowly bubbled into an aqueous dioxane solution of the quinone and a mixture of products was ultimately obtained. Through processes of column chromatography and fractional crystallization 2-chloro-1,4-naphthoquinone (42% of the total product) and 2,3-dichloro-1,4-naphthoquinone (50.2%) were isolated.

A study of the reaction of hypochlorous acid with *cis*- and *trans*-1,4-diphenyl-2-butene-1,4-dione in dioxane containing peroxides was undertaken to determine the application of the reaction to compounds structurally similar to the quinones. The only product isolated from the reaction of the *trans* isomer was *meso*-2,3-dichloro-1,4-diphenyl-1,4-butanedione (53.8% after recrystallization). The direct addition of chlorine to the *trans*-unsaturated dione was described by Conant and Lutz,[8] who obtained only the *meso* addition product. The *cis* isomer reacted with HOCl in dioxane to give a mixture of *dl*-2,3-dichloro-1,4-diphenyl-1,4-butanedione (68.23%), the *meso*-dichloro compound (16.7%), and *trans*-1,4-diphenyl-2-butene-1,4-dione (15.0%), which was separated by silica gel chromatography. The direct addition of chlorine to the *cis*-unsaturated dione in chloroform at −20° resulted

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[1] S. Marmor, *J. Org. Chem.*, **28**, 250 (1963).

[2] American Cyanamid Co., Organic Chemicals Division, Technical Bulletin, 1,4-Naphthoquinone, p. 13, cites a reaction of the quinone with 4% HOCl to give the epoxide. The literature sources referred to were T. Zincke and Wiegand, *Ann. Chem.*, **286**, 71 (1895); T. Zincke, *Chem. Ber.*, **25**, 3602 (1892); A. Mandinaveitia, *et al.*, *Anales soc. espan. fis. quim.*, **27**, 647 (1929); *Chem. Abstr.*, **24**, 359 (1930). These references actually described the reaction of aqueous calcium hypochlorite solutions, whose concentrations were equivalent to 4% HOCl. The abstract referred to contains the error of specifying HOCl as the reactant.

[3] C. Bunton and G. Minkoff, *J. Chem. Soc.*, 665 (1949).

[4] L. F. Fieser and F. C. Chang, *J. Am. Chem. Soc.*, **64**, 2043 (1942).

[5] L. F. Fieser and A. E. Oxford, *ibid.*, **64**, 2060 (1942).

[6] B. F. Clark, Jr., *Chem. News*, **143**, 265 (1931); *Chem. Abstr.*, **26**, 1591 (1932).

[7] L. F. Fieser, *J. Am. Chem. Soc.*, **70**, 3170 (1948).

[8] (a) J. B. Conant and R. E. Lutz, *ibid.*, **47**, 881 (1925); (b) R. E. Lutz, *ibid.*, **49**, 1108 (1927).

in the formation of a mixture of the *dl*- and *meso*-dichloro derivatives,[8] with the former predominating.

Experimental Section

All melting points are uncorrected.

Materials.—Hypochlorous acid was prepared by the reaction of chlorine with an aqueous suspension of mercuric oxide, followed by distillation under reduced pressure.[9] The resulting approximately 1 *M* solutions were analyzed[10] and found to be free of chlorine. Solutions of HOCl were analyzed prior to each use to ascertain the absence of free chlorine. All other reagents were obtained from standard sources.

Reaction of Hypochlorous Acid with Quinones. General Procedure.—To a solution of 0.01 mole of the quinone in 80 ml. of dioxane (containing peroxides) was added a solution of chlorine-free hypochlorous acid (0.04 mole)[11] over a period of 15 min. The temperature of the stirred reaction mixture was maintained at 20–25° by means of an ice–water bath applied as needed. The reaction mixture was then stirred at room temperature until analysis of 1-ml. samples of HOCl indicated that the reaction was complete (usually about 2 hr.).

The solution was evaporated to at least half its original volume and then saturated with water. The solid that separated was filtered and the filter cake was washed thoroughly with water. After air drying, the product was recrystallized from a suitable solvent.

In a typical run 2-chloro-1,4-naphthoquinone, m.p. 115–115.5°, was obtained in 63.8% yield, after recrystallization from ethanol. The infrared spectrum of this product was identical with that of an authentic sample prepared according to Fieser[7]; no depression was observed in a mixture melting point determination. A 56% yield of 3-chloro-2-methyl-1,4-naphthoquinone (recrystallized from acetic acid–water, m.p. 152–153°) was obtained. The infrared spectra of this product and an authentic sample[7] were identical.

In general, reactions of 1,4-naphthoquinone and hypochlorous acid in other solvents were carried out under the same conditions as described above. The reaction in peroxide-free dioxane[12] was run in a nitrogen atmosphere.

In those cases where only small amounts of 2-chloro-1,4-naphthoquinone were formed, the following column chromatography procedure was used to separate the product from unreacted naphthoquinone. About 0.5 g. of the crude material was deposited on a silica gel (J. T. Baker 3405) column and then eluted with benzene–cyclohexane (60:40 v./v.). A distinct separation of yellow bands appeared on the column. When the eluate became colorless, 100% benzene was used to elute the next fraction. The chloroquinone was contained in the first fraction, while the unreacted starting material was found in the second. A small amount of dark red material remained adsorbed at the top of the column, but could be removed by elution with methanol. The identity of the latter material was not determined, but appeared to be a mixture of several substances.

Reaction of 2,5-Diphenyl-1,4-benzoquinone with Hypochlorous Acid.—Hypochlorous acid solution (25 ml., 1.6 *M*) was added to a stirred solution of 1.0 g. of 2,5-diphenyl-1,4-benzoquinone (0.0038 mole) in 150 ml. of dioxane containing peroxides. The temperature was maintained at 20–21° during the addition, which required 10 min. After the mixture was stirred for 1 hr. at 20–25°, another 15 ml. of HOCl solution was added. The mixture was stirred at room temperature for 6 hr. and was then evaporated to about one-fourth its original volume. Water (50 ml.) was added and the orange-yellow solid was filtered and washed thoroughly with water. The solid weighed 1.1 g. and melted at 185–188°. The crude product was recrystallized from acetone, and 0.95 g. (84.8% yield) of 3-chloro-2,5-diphenyl-1,4-benzoquinone, m.p. 187–189°, was obtained.

Anal. Calcd. for $C_{18}H_{11}ClO_2$: C, 73.35; H, 3.76; Cl, 12.03. Found: C, 73.26; H, 3.76; Cl, 11.96.

The n.m.r. spectrum shows a multiplet at 7.21 p.p.m. (phenyl H), and a singlet at 6.71 p.p.m. (quinoid H). The area ratio of the phenyl hydrogens bands to quinoid hydrogen band is 9.8:1.2, in good agreement with the theoretical value of 10:1.

Reaction of 1,4-Naphthoquinone with Chlorine in Aqueous Dioxane.—Chlorine (5 g., 0.07 mole) was slowly bubbled into a solution of 2.0 g. of 1,4-naphthoquinone in 150 ml. of dioxane (containing peroxides) and 10 ml. of water. The temperature was maintained at 15–20° during the addition of the chlorine, which required 1 hr. The reaction mixture was stirred at 15° for 30 min. more. The yellow solution was transferred to a beaker and allowed to evaporate in a hood overnight. The brown solid that separated was filtered, washed with water, and air dried. The crude product was recrystallized twice from ethanol giving 1 g. of light tan crystals, melting range 112–170°. A portion (0.207 g.) of the mixture was chromatographed on a silica gel column, using benzene–cyclohexane (60:40 v./v.) as first eluting solvent. The bright yellow solid (0.192 g.) obtained from the eluate was recrystallized twice from ethanol to give a product, m.p. 190–192°, whose infrared spectrum was the same as that of an authentic sample of 2,3-dichloro-1,4-naphthoquinone (Aldrich Chemical Co.); no depression was observed in a mixture melting point determination.

The mother liquors from the recrystallizations were combined and evaporated to dryness. The residual bright yellow solid (0.087 g.) was recrystallized once from ethanol. The identity of the product, m.p. 115–116°, as 2-chloro-1,4-naphthoquinone was verified from its infrared spectrum.

Reaction of *trans*-1,4-Diphenyl-2-butene-1,4-dione with Hypochlorous Acid in Dioxane.—To a stirred solution of 1.0 g. of *trans*-1,4-diphenyl-2-butene-1,4-dione (Eastman, recrystallized from ethanol) in 50 ml. of dioxane (containing peroxides) was added 25 ml. of 1.6 *M* HOCl over a period of 5 min. The temperature of the reaction mixture was maintained at 25° during the addition and for 4 hr. thereafter. The mixture was evaporated to half its volume and the white solid that separated was filtered. Recrystallization of the crude product (1.3 g.) from acetone afforded 0.7 g. (53.8%) of pure *meso*-1,4-diphenyl-2,3-dichloro-1,4-butanedione, m.p. 166–167° (lit.[8] m.p. 167°).

Reaction of *cis*-1,4-Diphenyl-2-butene-1,4-dione with Hypochlorous Acid in Dioxane.—To a solution of 4.7 g. (0.02 mole) of *cis*-1,4-diphenyl-2-butene-1,4-dione[13] in 200 ml. of dioxane (containing peroxides) was added 25 ml. of 1.6 *M* HOCl over a period of 10 min. The temperature was maintained at 25–30° during the addition and for 30 min. afterwards. Another 5 ml. of hypochlorous acid was then added and the mixture was stirred for 2.5 hr. more. The reaction mixture, which had become yellow, was evaporated to half its volume, and 50 ml. of water was added, causing the separation of a yellow oil. The organic phase was extracted with 100 ml. of ethyl ether and the ether solution was washed once with 100 ml. of water. After drying over anhydrous magnesium sulfate, the ether solution was filtered and the solvent was stripped on a rotating evaporator. The residual yellow oil was chilled in an ice–water bath, whereupon it solidified. The solid was recrystallized once from ethanol, but the product had a melting range of 83–140°.

The recrystallized solid and mother liquor residue were recombined and the components of the mixture were separated by column chromatography, using Baker silica gel as adsorbent. The mixture (4.60 g.) was deposited on the column and then eluted with 630 ml. of a benzene–hexane (25:75 v./v.) mixture. The residue from the first eluates weighed 3.14 g. and melted at 87–90°. After one recrystallization from ethanol, the product, *dl*-2,3-dichloro-1,4-diphenyl-1,4-butanedione, melted at 87–88° (lit.[8] m.p. 86°).

The column was then eluted with 75% benzene–hexane (75:25 v./v.) to give 0.77 g. of colorless solid, m.p. 165–167°. The solid was recrystallized from acetone, and the purified product, m.p. 166–167°, proved to be the *meso*-dichloro derivative, as determined by mixture melting point. Finally, elution of the column with 100% benzene afforded 0.69 g. of yellow solid, which, after recrystallization from ethanol, melted at 110–111°. A mixture melting point determination with an authentic sample of the *trans*-unsaturated dione gave no depression.

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(9) A. Chung and C. G. Israel, *J. Chem. Soc.*, 2667 (1955).

(10) "Scott's Standard Methods of Analysis," Vol. I, N. H. Furman, Ed., D. Van Nostrand Co., New York, N. Y., 1939, p. 274.

(11) When only small excesses of HOCl were used yields were considerably lower.

(12) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 284.

(13) J. B. Conant and R. E. Lutz, *J. Am. Chem. Soc.*, **45**, 1304 (1923).