[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

ADDITION OF HYDROGEN CHLORIDE TO *p*-BENZOQUINONES. FAILURE OF ACETYL CHLORIDE TO REACT WITH *p*-BENZOQUINONE

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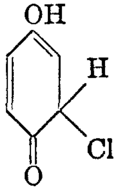
There have appeared numerous reports (1) of the preparation of halogenated *p*-benzoquinones by oxidation of halohydroquinones obtained from the reaction of halogen acid with *p*-benzoquinones. These reports are conflicting in several respects, especially as regards the ease with which a pure haloquinone may be isolated. There is also an uncertainty as to whether the reaction is best carried out with aqueous halogen acid or with anhydrous hydrogen halide in dry chloroform or other solvent. In addition, no structures have been assigned to some of the products obtained (1). The present investigation was undertaken in an effort to clarify this situation and to determine the general utility of this method of preparation of halogenated *p*-benzoquinones.

Clark (2) has suggested that the reaction of a halogen acid with quinone proceeds by way of initial oxidation of the halogen acid, to give hydroquinone and halogen, followed by substitution of halogen in the hydroquinone; however, his data appear not to support this suggestion. It seems more reasonable to assume that halogen acid adds in a 1,4-manner to quinones, as has been demonstrated (3, 4) to be the mechanism of the reaction of numerous other reagents with quinones. Tautomerism of the addition product (I) gives the halohydroquinone, which may be oxidized by the starting quinone. The resultant haloquinone may add halogen acid, thus giving rise to dihalohydroquinone. Although numerous investigators (5–8) have reported preparation of haloquinones by oxidation of hydroquinones obtained in this manner, and have mentioned no difficulty with separation of more highly halogenated products, others (9-11) have reported that separation of the more highly halogenated quinones was difficult. Since it has been reported (8) that the reduction potential of hydroquinone is just slightly higher than that of chlorohydroquinone, some dihalohydroquinone would be expected.



I

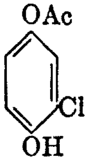
In the present work, there has been studied the addition of hydrogen chloride to *p*-benzoquinone, *p*-toluquinone, 3-chloro-, 5-chloro-, and 6-chloro-toluquinone, and addition of hydrogen bromide to 6-bromotoluquinone. From the results obtained, it seems safe to state that polyhalogenated quinones are always obtained and that the separation of these less-soluble compounds from the monohalogenated products is usually exceedingly difficult, if at all possible. The structures tentatively assigned (1) to certain of the compounds obtained by addition of halogen acids to halotoluquinones should be disregarded, for most of the compounds in question were probably not pure. Work is now in progress on synthesis, by unequivocal methods, of the dichlorotoluquinones.

The only satisfactory preparation which has been encountered by us is that which we first investigated, 5-chlorotoluquinone (12). In contrast with the report of Clark (2), we were not able to isolate pure chlorohydroquinone from the addition of hydrogen chloride to quinone. The best sample obtainable by us from this reaction melted at 100.9–101.9°, which is in agreement with the value of 101–102° reported by Conant and Fieser (8), but well below the melting point of 106.0–106.8° which was obtained by us for chlorohydroquinone prepared by reduction of an authentic sample of chloroquinone. For this purpose, chloroquinone was prepared by electrolytic reduction of *o*-nitrochlorobenzene and oxidation of the resultant 2-chloro-4-hydroxyaniline. It was also possible to isolate pure chloroquinone after oxidation of the impure chlorohydroquinone.

It has been frequently reported (1) that when halogen acid is added to a quinone already substituted with an *ortho*, *para*-director the hydroquinone obtained bears the substituents in the 2,5-relationship. It is also a fact that numerous similar reactions (13) have always yielded 2,5-disubstituted hydroquinones. It should be mentioned, however, that a few investigators (2, 14–16) have claimed the presence of small amounts of the 2,6-isomer. One report (14) of the isolation of 2,3-dichlorohydroquinone from the reaction of hydrogen chloride with chloroquinone could not be confirmed by Hollander (15). It seems generally agreed that the 2,5-isomer is the chief product, and difficulty with separating other isomers is definitely minor in comparison with separating more highly halogenated products.

From our data, no conclusion may be reached as to whether addition is best carried out in aqueous medium or in a dry organic solvent such as chloroform. For example, addition to toluquinone is best carried out in aqueous hydrochloric acid, whereas with benzoquinone best results are obtained in chloroform solvent.

Since preparation of halogenated hydroquinones by addition of halogen acids to quinones is of such limited and uncertain scope, the reported (17–20) addition of acetyl chloride to quinones appears an attractive route to the same compounds. If such an addition to benzoquinone should occur, the initial addition product



II

would be the monoacetyl chlorohydroquinone, II, which would not be oxidized, in anhydrous medium, to the quinone; hence, there would be no difficulty with introduction of additional halogen atoms. This course of the reaction seems inconsistent with one report (20) that both mono- and di-chloro derivatives of diacetyl hydroquinone were obtained. Actually, we have found that carefully purified acetyl chloride in dry equipment does not react with quinone, but vigorous reaction ensues on addition of acetic acid. Thus, initial attack is by hydrogen ion on the quinone oxygen, and this reaction is no different from a normal addition of hydrogen chloride to quinone except that the hydroquinone is acetylated in the reaction medium. The latter reaction furnishes adequate hydrogen chloride so that only catalytic amounts of acid are necessary to initiate the addition reaction by establishing equilibrium with acetic anhydride and hydrogen chloride. A mixture of the mono- and di-halogenated derivatives was obtained.

EXPERIMENTAL

All melting points are corrected. Analyses are by the Microanalytical Division of the Department of Chemistry and Chemical Engineering of the University of California.

6-Bromotoluquinone was prepared by the general procedure described for 6-chlorotoluquinone (12) except that the oxidation in a 1-mole run was carried out in two liters of 70% aqueous acetic acid. The yield of steam-distilled quinone was 127 g. (63%), which after one crystallization from 60% aqueous alcohol melted at 91–93.5°. The best sample obtained by further crystallization melted at 93.6–93.9°.

3-, 5-, and 6-chlorotoluquinones were the samples previously described (12).

Chloroquinone. *o*-Chloronitrobenzene (11.2 g., 0.07 mole) was reduced electrolytically by the procedure previously described (12), using a current density of 0.8 amp./sq. dec. and 1.5 equivs. of current, but a nickel cathode was used instead of platinum. The aminophenol was oxidized with dichromate as previously described, and steam-distillation gave 4.1 g. (40%) of chloroquinone, m.p. 54–56°. After two crystallizations from 75% aqueous ethanol, the m.p. became constant at 55.3–56.3° [literature (22), m.p. 56–56.5°]. Reduction with sodium hydrosulfite in aqueous solution, followed by ether extraction and two crystallizations from chloroform gave *chlorohydroquinone* of the constant m.p. 106.0–106.8°. Reductive acetylation (21), followed by four crystallizations from hexane, gave *diacetyl chlorohydroquinone* of the constant m.p. 70.7–71.5° [literature (22), m.p. 70.5°].

Additions of halogen acid in aqueous medium were carried out essentially as described (12) for the addition of hydrogen chloride to toluquinone, except that longer periods of standing were required in some cases before the solution became light-colored.

For the reactions in chloroform, hydrogen chloride from a cylinder was passed into a 7% solution of dry quinone in chloroform (dried over phosphorus pentoxide) until the black quinhydrone had changed to nearly white hydroquinone. Time of reaction was usually 1–2 hours. Similar results were obtained on cooling the reaction in an ice-bath or allowing it to warm to about 35°. The product was obtained either by filtration of the cold solution or evaporation of the solvent.

Oxidation of the hydroquinones was with ferric ion, as previously described (12), and the steam-distilled quinones were crystallized from hexane or 50% aqueous ethanol.

Since similar procedures were used in all instances, only the results are cited below.

Quinone plus hydrogen chloride in chloroform. Repeated crystallization of the hydroquinone from chloroform failed to yield material melting above 100.9–101.9°. Chloroquinone was obtained in 69% over-all yield, m.p. 52–55°, raised by two crystallizations to 55.3–56.3°, not depressed on mixing with the authentic sample described above. Reduction of this sample of chloroquinone with sodium hydrosulfite yielded chlorohydroquinone of m.p. 105.5–106.3°.

Quinone plus aqueous hydrochloric acid. After oxidation and fractional steam-distillation, followed by repeated crystallization, the best material from two runs melted respectively at 51–65° and 52–56°. Top fractions from the crystallizations melted up to 110° and higher.

Toluquinone plus hydrogen chloride in chloroform. After oxidation, steam-distillation, and repeated crystallization, the best samples from three runs melted respectively at 94–104°, 95–105.5°, and 101–103.7°.

Toluquinone plus aqueous hydrochloric acid. Use of the procedure previously described (12) gave a 75% yield of steam-distilled 5-chlorotoluquinone, m.p. 101–104°, raised by one crystallization to 103.7–104.8°.

3-Chlorotoluquinone plus aqueous hydrochloric acid. Systematic crystallization of the hydroquinone from water yielded only fractions with melting points such as 145–156°. From several runs, after fractional steam-distillation and systematic crystallizations (8–12 times), there were obtained fractions of quinone melting at 98.5–100° or near there. Analysis showed: Cl, 37.08, 36.80. (Calc'd for dichlorotoluquinone, $C_7H_4Cl_2O_2$: Cl, 37.12. This sample showed a depressed m.p. of 97.7–98.9° when mixed with an authentic sample of 3,5-dichlorotoluquinone of m.p. 103.3–103.8°. Classification of this substance as a mixture of isomers or as 3,6-dichlorotoluquinone must await synthesis of the latter compound by an unequivocal method.

5-Chlorotoluquinone plus aqueous hydrochloric acid. After oxidation, steam-distillation, and repeated crystallizations, the best samples from two runs melted respectively at 85–89° and 84–88.7°. Top fractions melting as high as 200–225° were obtained. A combination of several fractions melting in the range, 85–120°, was fractionally steam-distilled through a 65-cm. Vigreux column with heated jacket and partial reflux head, to yield four fractions, the last melting at 83–136° and the first melting at 85–95° and giving a chlorine analysis of 39.48, 38.81 %. Kehrmann, Silva, and Keleti (11) reported a quinone melting at 85–86° as obtainable from this reaction.

6-Chlorotoluquinone plus aqueous hydrochloric acid. From one run there was obtained a best fraction of quinone of m.p. 85–97°, chlorine content, 39.48, 39.77%. From another run in which the hydroquinone was repeatedly crystallized before oxidation, a quinone sample was obtained which melted at 78.2–78.6°, chlorine content, 39.85, 40.21%. Previously (11) there has been reported as isolated from this reaction a quinone of m.p. 76°.

6-Bromotoluquinone plus aqueous hydrobromic acid, followed by oxidation, steam-distillation, and repeated crystallization, gave material of m.p. 87–97°.

Reaction of acetyl chloride with quinone. Acetyl chloride (8 g.), purified by distillation from dimethylaniline, was mixed at 25° with 5.4 g. of dry quinone in a carefully dried apparatus. The mixture darkened slowly, but with no evolution of heat or hydrogen chloride, even after heating under reflux for two hours, and insoluble quinone remained. On addition of 1 ml. of glacial acetic acid at 25°, there immediately ensued a vigorous exothermic reaction with evolution of hydrogen chloride, and during about 10 minutes the color changed through red to light yellow. After removal of solvent and one crystallization from 75% aqueous ethanol, material of m.p. 62–65° was obtained, and further crystallization from ethanol, hexane or aqueous acetic acid gave the same material. Several runs gave similar results. Hydrolysis and oxidation yielded a quinone mixture of m.p. 52–95°. Fractional steam-distillation, followed by recrystallization, gave a quinone of m.p. 159–161°, the m.p. reported by Ling (23) for 2,5-dichloroquinone.

Slow evaporation of a hexane solution of the mixed diacetyl hydroquinones gave a mixture of large flat tablets and fine needles. Hand-picking of the tablets, followed by recrystallization, gave diacetyl chlorohydroquinone of m.p. 68.3–69.3°, no depression on mixing with the authentic sample described above.

SUMMARY

In contrast with numerous previous reports, it has been shown that addition of halogen acids to *p*-benzoquinones is not a satisfactory general preparation of pure halogenated hydroquinones.

It has been shown that *p*-benzoquinone does not react with acetyl chloride, but that reaction with hydrogen chloride occurs on addition of small amounts of acid to the reaction mixture.

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