Anal. Calcd. for $C_8H_{12}N_4S_2$: C, 42.1; H, 5.3; N, 24.6. Found: C, 42.2; H, 5.4; N, 24.5.

To 4.4 g. of the above finely divided pyrimidyl thiourea in 20 ml. of dry chloroform was slowly added with shaking a solution of 1 ml. of bromine in 10 ml. of chloroform over a period of 15 minutes, the temperature being maintained below 30°. The solution was evaporated to dryness on the steam-bath. The dry, orange, solid residue was treated with a solution of 2 g. of sodium hydrosulfite in 50 ml. of water for ten minutes to remove excess bromine. The tan oil which formed was treated with excess ammonia and it crystallized upon scratching. After two hours the crystalline solid was filtered off and recrystallized from 50% alcohol to yield 4 g. (87%) of 2-amino-5-ethylmercapto-7-methylthiazolo[4,5-d]pyrimidine, m.p. 187–189 (Table I, No. 7).

Failure of 2-Amino-4-chloro-6-methylpyrimidine to React with Potassium Thiocyanate.—The refluxing of molecular equivalents of 2-amino-4-chloro-6-methylpyrimidine and potassium thiocyanate for six hours in either 95% ethanol, toluene or xylene gave only a quantitative recovery of the original chloropyrimidine.

2-Amino-4-hydroxy-6-phenyl-5-thiocyanopyrimidine.—A warm solution of 4.7 g. (0.025 mole) of 2-amino-4-hydroxy-6-phenylpyrimidine and 6.2 g. (0.076 mole) of sodium thiocyanate in 200 ml. of methanol (saturated with sodium bromide) and 50 ml. of glacial acetic acid was cooled to 5°. While stirring a solution of 1.8 ml. (0.035 mole) of bromine in 50 ml. of glacial acetic acid was added over a period of 20 minutes. The ice-bath was removed and stirring was continued for one hour. The solution was heated to boiling and 20 ml. of hot water was added. The hot solution was filtered, made to *p*H 6 with 10% ammonia, and most of the alcohol removed under vacuum. The yellow crystalline deposit was dried, yield 4.1 g. (66%). For purification the product was crystallized from alcohol, m.p. 287–289° with decomposition.

Anal. Calcd. for $C_{11}H_8ON_4S$: N, 23.0, S, 13.1. Found: N, 22.7; S, 13.2.

Bis-(2-amino-4-hydroxy-6-phenylpyrimidyl-5)-1-disulfide.—To 30 ml. of 10% sodium hydroxide solution was added 0.5 g. of 2-amino-4-hydroxy-6-phenyl-5-thiocyanopyrimidine. After standing overnight at room temperature the solution was made to 200 ml. with distilled water and filtered from a trace of residue. The filtrate was neutralized to *p*H 6 with 10% acetic acid. The pale yellow crystalline precipitate was filtered off, washed with water, then alcohol, and dried. The yield was quantitative, m.p. > 300°.

Anal. Calcd. for $(C_{10}H_8ON_3S-)_2$: N, 19.3; S, 14.7. Found: N, 19.3; S, 14.7.

Ultraviolet Absorption Spectra.—The spectra were determined with a Beckman model DU spectrophotometer using solutions containing 10 mg. per liter. For solutions of *p*H 1, 0.1 *N* hydrochloric acid was used and for *p*H 11, a glycine-sodium hydroxide buffer.

Acknowledgments.—The authors are indebted to S. W. Blackman, N. Martinez, Jr., and J. Tillmans for microanalyses and Phoebe Lee Graham for the measurement of ultraviolet absorption spectra.

TUCKAHOE, NEW YORK RECEIVED MARCH 30, 1951

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, BROOKHAVEN NATIONAL LABORATORY]

Quinone–Hydroquinone Exchange Reactions. I. Non-Exchange in Duroquinhydrone[1]

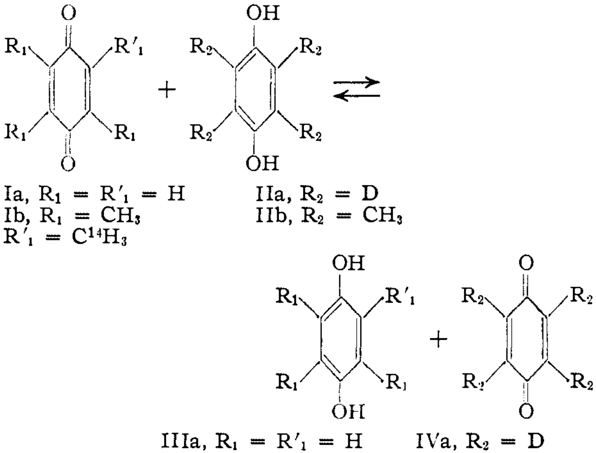
BY AKSEL A. BOTHNER-BY

Quinhydrone complexes have been prepared from duroquinone and durohydroquinone, one compound being labeled with carbon-14. Thermal decomposition *in vacuo* yielded the original compounds, no exchange of radioactive isotope having taken place after complex formation. The formulation of quinhydrones as symmetrical resonance hybrids is thus disproven.

It has been reported by Gragerov and Miklukhin[2] that the exchange reaction between benzoquinone (Ia) and hydroquinone-2,3,5,6-d_4 (IIa) in a quinhydrone complex does not occur to any appreciable extent in 24 hours at room temperature, or in 6 hours at 70°.

As part of a general program for the investigation of oxidation–reduction exchange reactions in organic systems, supplies of carbon-14 labeled duroquinone and durohydroquinone had been prepared, and it was therefore decided to determine whether this interesting observation could be repeated in the case of the quinhydrone complex between duroquinone and durohydroquinone. This complex, although unstable, can be prepared by the method of Michaelis and Granick.[3]

Durohydroquinone-α-C^{14} (IIIb) was prepared from trimethylhydroquinone diacetate (V) by chloromethylation according to the method of Smith and Carlin[4] with formaldehyde-C^{14} to give 2-chloromethyl-C^{14}-3,5,6-trimethyl-4-acetoxyphenol (VI) which was reduced with lithium aluminum hydride. The latter reagent simultaneously reduced the chloromethyl group to a methyl group and cleaved the acetoxy ester linkage to give the desired compound in good yield. The easy reduction of the chloromethyl group may perhaps be attributed to an intramolecular reduction by a phenoxyaluminohydride of the type suggested in a previous communication.[5] Oxidation with ferric sulfate in the usual manner gave duroquinone-α-C^{14}.



Ia, $R_1 = R'_1 = H$
Ib, $R_1 = CH_3$
$R'_1 = C^{14}H_3$

IIa, $R_2 = D$
IIb, $R_2 = CH_3$

IIIa, $R_1 = R'_1 = H$
IIIb, $R_1 = CH_3$
$R'_1 = C^{14}H_3$

IVa, $R_2 = D$
IVb, $R_2 = CH_3$

Two experiments were conducted. In the first the quinhydrone was prepared from radioactive

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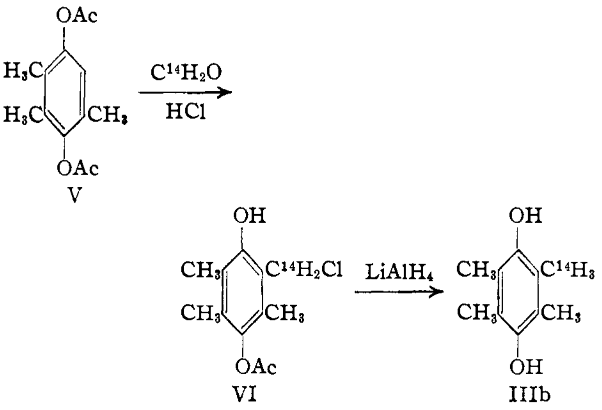
[1] Work carried out under the auspices of the U. S. Atomic Energy Commission.

[2] I. P. Gragerov and G. P. Miklukhin, *Doklady Akad. Nauk., S. S. S. R.*, **62**, 79 (1948).

[3] L. Michaelis and S. Granick, THIS JOURNAL, **66**, 1023 (1944).

[4] L. I. Smith and R. B. Carlin, *ibid.*, **64**, 524 (1942).

[5] A. Bothner-By, *ibid.*, **73**, 846 (1951).



durohydroquinone and inactive duroquinone. In the second, inactive durohydroquinone and active duroquinone were used. Portions of the quinhydrone in each case were decomposed thermally *in vacuo* and the quinone separated from the hydroquinone by means of its greater volatility. One-half of the quinhydrone was analyzed in this manner immediately; one-half after 24 hours standing at 25°. The samples so obtained were converted to barium carbonate and radioactivity determinations were made. The results are shown in Table I.

TABLE I

	Activities c./m./cm.^{2} $BaCO_3$ Duroquinone	Durohydroquinone
Expt. 1		
Before preparation of complex	0	1950
Immediately after preparation of complex	209	1513
24 hours after preparation of complex	190	1550
Expt. 2		
Before preparation of complex	1950	0
Immediately after preparation of complex	834	321
24 hours after preparation of complex	833	301

An examination of these figures leads to two conclusions. (1) There is a rather rapid exchange between the quinone and hydroquinone in solution prior to precipitation of the complex. (2) There is no detectable exchange in the solid complex in a period of 24 hours. That the sums of the activities of the components in the complex are not equal to the activity of the initially active species is due to exchange in solutions with the inactive species which was present in excess in the preparation of the complexes.

Experimental[6]

2-Chloromethyl-C^{14}-3,5,6-trimethyl-4-acetoxyphenol.—The procedure of Smith and Carlin[3] was used. From 2.00 g. of trimethylhydroquinone diacetate and 6.1 ml. of formaldehyde-C^{14} having a calculated activity of 175 μc[7] there was obtained 1.85 g. of crude product, used directly in the next step. The unused formaldehyde was recovered as a dilute aqueous solution by combining the liquors from the filtrate and traps, making alkaline, and steam distilling in an apparatus well protected with cold traps.

Durohydroquinone-α-C^{14}.—Crude 2-chloromethyl-C^{14}-3,-5,6-trimethyl-4-acetoxyphenol (1.82 g.) was dissolved in 50 ml. of dry ether and added dropwise to a stirred solution of 2.0 g. of lithium aluminum hydride in 100 ml. of ether. Stirring was continued for 0.5 hour after addition was complete, 100 ml. of 10% hydrochloric acid was added carefully, and stirring was continued until clear layers resulted. A little additional ether was required to dissolve all the durohydroquinone. The ether layer was separated, dried, and concentrated until durohydroquinone began crystallizing out. An equal volume of light petroleum ether was added, and the solution cooled for several hours in the ice-box. The durohydroquinone so obtained melted at 220–223° and was analytically pure. The yield was 1.10 g. or 89%.

Duroquinone-α-C^{14}.—The filtrate from the crystallization of the durohydroquinone-α-C^{14} was evaporated to dryness in a stream of nitrogen. The residue was added to the aqueous layer from the lithium aluminum hydride reduction, and an additional 0.50 g. of durohydroquinone-α-C^{14} was added. Ten grams of ferric sulfate was dissolved in the mixture and it was steam distilled in an apparatus protected with cold traps. Some of the duroquinone-α-C^{14} crystallized in the distillate. The rest was extracted with ether. After evaporation of the ether through a helix packed column, a total yield of 0.50 g. of crude duroquinone-α-C^{14} melting at 107–110° was obtained. One recrystallization from methanol gave 0.43 g. of quinone, melting at 110–111°.

Preparation of Quinhydrone Complexes.—Twenty mg. of the radioactive and 40 mg. of the non-radioactive component were placed in a 15-ml. centrifuge tube. One-half ml. of absolute acetone was pipetted in, and distilled water was added dropwise to incipient cloudiness. The tube was then chilled in an ice-bath, when a black precipitate of the quinhydrone appeared. Excess liquid was quickly removed through a capillary pipet, and the quinhydrone was dried on a porous tile.

Thermal Decomposition of the Samples.—A piece of 12 mm. Pyrex tubing 50 cm. long was sealed at one end and clamped in a vertical position. A sample of the complex weighing about 20 mg. was placed in the bottom of the tube, and the tube was evacuated to a pressure of 10^{-5} mm. The lower end was immersed to a depth of three inches in a water-bath and brought to a temperature of 90°. The complex thereupon decomposed and the quinone sublimed on to the cold upper portion of the tube. The tube was cooled, air was admitted slowly, and a separation effected by cutting the tube apart.

Radioactivity Measurements.—The samples were converted to barium carbonate by the procedure of Steele,[8] as modified by Anderson.[9] It was counted as an "infinitely thick" layer with a surface area of 2 cm.,^{2} in a standard geometry sample holder using a Nucleometer. The counts were all corrected for background, which ran around 50 c./m. The analyses and determinations were carried out by Miss Yvette Delabarre.

Discussion

The interaction of a quinone and a hydroquinone may produce any or all of several products, depending on steric and electrical properties. Among the products may be listed solid quinhydrones, 1:1 complexes in solution[10] and semiquinones.[11]

The solid quinhydrones are now generally conceded to be held together by hydrogen bonding, and the structures VII, VIII and IX have been proposed for them.

The older formula VII, proposed by Willstätter and Piccard[12] implies that the two components of the complex have lost identity through the formation of a symmetrical resonance hydrid, the isocyclic rings being so oriented that the π-orbitals overlap and a ready transfer of electrons from one to the other takes place. The structure is incompatible

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(6) Melting points uncorrected.

(7) The formaldehyde-C^{14} was most generously supplied to me by Dr. M. Gibbs, Biology Department, Brookhaven National Laboratory.

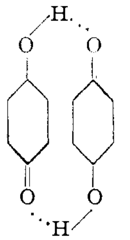
(8) R. Steele, BNL-T-6, Brookhaven National Laboratory Report.

(9) R. C. Anderson, to be published.

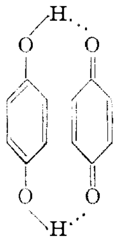
(10) L. Michaelis and S. Granick, THIS JOURNAL, **66**, 1023 (1944).

(11) L. Michaelis and M. P. Schubert, *Chem. Revs.*, **22**, 437 (1938).

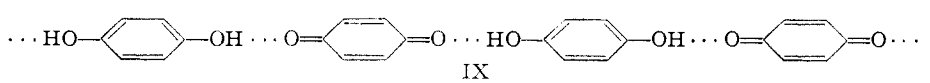
(12) R. Willstätter and J. Piccard, *Ber.*, **41**, 1463 (1908).



VII



VIII



IX

with the results reported by Gragerov and Miklukhin[2] and here.

Formula VIII, proposed by Michaelis, permits each moiety to retain its identity when the complex is decomposed. The deep color of the quinhydrone complexes may better be explained on the basis of this formula than of formula IX, since the highly polarizable hydroquinone ring is acted upon at close range by the positive charge centered in the quinone ring. A parallel case may be cited in naphacene picrate, which is red. The strong dipole–dipole interaction implied by this formulation would help to stabilize the complex.

Formula IX has been proposed by Palacios and Foz[13] on the basis of X-ray diffraction patterns from solid quinhydrone. The complex is held together by hydrogen bonding alone, and it is difficult to account for the development of an intense color. Evidence supporting this formula is available in the paper of Wagner and Grunewald[14] reporting measurements of light absorption due to complex formation in moderately concentrated quinone–hydroquinone solutions. Their results indicated that there were deviations from the simple mass action law in the direction implying formation of complexes containing more than two components.

The findings of Davies[15] anent the infrared absorption spectrum of quinhydrone, and of Coryell,[16] Palacios and Foz,[13] and Sunder Lal and Nur-ul-Haq Khan[17] on the diamagnetism of the complex fit equally well with formulas VIII and IX.

Gragerov and Miklukhin[2] have stated that the hydrogen bonds in quinhydrone are not stabilized by resonance of the type

$$=O\cdots H{-}O{-} \longleftrightarrow {-}O{-}H\cdots O=$$

since the easy transfer of a proton pair would, contrary to findings, convert a quinone to a hydroquinone nucleus. They have neglected the fact that transfer of an electron pair is also necessary, and that the two hydrogen bonded atoms are not connected by a conducting network of bonds, as they are in such classical cases as *o*-nitrophenol or salicyl aldehyde. Thus non-exchange in the quinhydrone complex cannot be rigorously interpreted as refuting or supporting the statement that both forms contribute to a resonance hybrid structure in quinhydrones.

[13] Palacios and Foz, *Anal. Fis. Quim.*, **34**, 779 (1936).

[14] C. Wagner and K. Grunewald, *Z. Elektrochem.*, **46**, 265 (1940).

[15] M. M. Davies, *J. Chem. Phys.*, **8**, 557 (1940).

[16] C. D. Coryell, as quoted in Pauling, "Nature of Chemical Bond," Cornell University Press, Ithaca, N. Y., 1945, p. 278.

[17] Sunder Lal and Nur-ul-Haq Khan, *Current Sci.*, **13**, 312 (1944).

UPTON, L. I., N. Y.

RECEIVED APRIL 7, 1951

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY]

Reactions of Diazoketones. IV. Kinetics of the Decomposition of Some *p*-Substituted-α-diazoacetophenones in Acetic Acid[1]

BY JOHN F. LANE AND ROBERT L. FELLER[2]

The rates of decomposition of five *p*-substituted-α-diazoacetophenones in acetic acid have been studied under a variety of conditions and have been found to be of the first order with respect to diazoketone. The logarithms of the rates at 40° and 60°, plotted against appropriate values of Hammett's parameter σ, give straight lines of negative slope (ρ). The rate of decomposition of *p*-nitro-α-diazoacetophenone is slightly decreased by addition of sodium acetate. Addition of lithium chloride, however, causes a rapid reaction, leading to the formation of *p*-nitrophenacyl chloride, the kinetics of which are of the first order in diazoketone and in chloride ion. These results are discussed in terms of a mechanism involving preliminary reversible proton transfer from solvent to diazoketone followed by bimolecular reaction between the diazonium ion so produced and the acetate (or chloride) ion.

The aliphatic diazoketones, $RCOCHN_2$, which are readily obtained[3] by interaction of acyl chlorides with diazomethane, undergo two reactions of considerable synthetic interest

$$RCOCHN_2 + HB \longrightarrow RCH_2COB + N_2 \ (B = OAlk, OH, NH_2, NHR') \quad (1)$$

$$RCOCHN_2 + HA \longrightarrow RCOCH_2A + N_2 \ (A = OAlk, OH, O_2CR', Hal) \quad (2)$$

The first of these, known as Wolff's rearrangement,[4] occurs in slightly basic media and is frequently aided by traces of colloidal metals such as silver; the second occurs in acidic media and serves as a convenient path to the α-ketols, $RCOCH_2OH$,

[1] For detailed material supplementary to this article order Document 3296 from American Documentation Institute, 1719 N Street, N. W., Washington 6, D. C., remitting $1.00 for microfilm (images one inch high on standard 35 mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

[2] The Mellon Institute, Pittsburgh, Penna.

[3] (a) F. Arndt, *et alii*, *Ber.*, **60**, 1364 (1927); **61**, 1122, 1949 (1928); (b) W. Bradley and R. Robinson, *J. Chem. Soc.*, 1310 (1928); (c) W. Bradley and G. Schwarzenbach, *ibid.*, 2904 (1928).

[4] L. Wolff, *Ann.*, **394**, 25 (1912). *Cf.* R. Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1942, Volume I, Chapter 2.