[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

An Optical Method for the Study of Reversible Organic Oxidation–Reduction Systems. V. *o*-Benzoquinones

BY D. E. KVALNES[1]

As a result of numerous investigations the effect of substitution upon the oxidation–reduction potential of the *p*-benzoquinone–hydroquinone system is well-known. However, very few potentiometric measurements have been made with *o*-benzoquinone systems. Conant and Fieser[2] determined the potentials of *o*-benzoquinone and of the tetrachloro and bromo compounds. Later Fieser and Peters,[3] by an improved method, obtained a better value for the potential of *o*-benzoquinone. Recently Ball and Chen[4] have determined the potentials of *o*-benzoquinone and of a few substituted compounds of physiological interest. All of the *o*-benzoquinones mentioned, with the exception of the tetrahalogen compounds, are very unstable in aqueous acid solutions and their potentials cannot be measured in the ordinary way. It was hoped that some of the simply substituted *o*-benzoquinones would be sufficiently stable to allow potential determinations in benzene. This was found to be the case; furthermore, the *o*-benzoquinones were fairly stable in aqueous solution so that electrometric measurements were made by the direct titration of the catechol with ceric sulfate solution.

Using the method described in previous papers,[5] and an optically active reference system of particularly high potential (0.815 v.), the results summarized in Table I were obtained. All of the *o*-benzoquinones studied appeared to be quite stable in benzene solution with the exception of *o*-benzoquinone and the 4-chloro- and 4-bromo-*o*-benzoquinones. These appeared to undergo decomposition after fifteen to thirty hours and consequently their potentials are not very accurate and represent minimum values.

It has been shown that the potential of *o*-benzoquinone in aqueous solution is about 100 mg. higher than that of *p*-benzoquinone. In benzene the difference is at least 120 mv. The effect of the first and second methyl groups upon the potential of *o*-benzoquinone is to lower the potential 37 and 31 mv., respectively, whereas the corresponding values for the para compounds are 58 and 48 mv. The replacement of the hydrogen atoms of the methyl group by phenyl groups results in a slight rise in the potential. This small change might be expected in light of earlier work.[5d] The change in potential brought about by the gradual replacement of hydrogen by chlorine is best shown by the determinations in aqueous solution; the rise in potential is 17, 8 and 8 mv., for the mono-, di- and tetrachloro compounds. No differences between the chloro and bromo compounds are apparent. The ability of the methoxy group to bring about a profound lowering of the potential of *o*-benzoquinone is to be noted. It is obvious that the changes in the potential of *o*-benzoquinone resulting from substitution are very similar to the corresponding changes for the para system, even though the groups are not adjacent to the carbonyl groups of the quinone or to the hydroxyl groups of the pyrocatechol.

TABLE I

OXIDATION–REDUCTION POTENTIALS AT 25°

System named as oxidant	Relative potential in benzene; benzoquinone = 0.711 v. E_0', v.	Normal potential in aqueous solution by e. m. f. measurement, E_0, v.	
o-Benzoquinone	0.833	0.794[a]	
4-Chloro-*o*-benzoquinone	.810	.811[b]	
4-Bromo-*o*-benzoquinone	.810	...	
4-Methyl-*o*-benzoquinone	.796	.744[b]	
4-Triphenylmethyl-*o*-benzoquinone	.804	...	
4-Methoxy-*o*-benzoquinone	...	.658[b]	
3,4-Dimethyl-*o*-benzoquinone	.765	...	
3,5-Dichloro-*o*-benzoquinone	...	.819[b]	
Tetrachloro-*o*-benzoquinone	.860	.827[c]	0.876[d]
Tetrabromo-*o*-benzoquinone	.860	.823[c]	.872[d]

[a] Fieser and Peters, THIS JOURNAL, **53**, 793 (1931); 0.5 *N* H_2SO_4 as solvent. Ball and Chen[4] give 0.792 for 30°.

[b] Kvalnes, using 0.2 *N* H_2SO_4 (experimental part).

[c] Conant and Fieser, THIS JOURNAL, **46**, 1858 (1924); 0.1 *N* H_2SO_4 as solvent.

[d] Conant and Fieser, reference *c*; 50% alcoholic solution, 0.5 *N* in HCl.

Experimental Part

1. Preparation of Materials.—*d*-Camphor-10-sulfonyl chloride was converted to the sulfinic acid, in good yield,

(1) National Research Fellow in Chemistry.

(2) Conant and Fieser, THIS JOURNAL, **46**, 1858 (1924).

(3) Fieser and Peters, *ibid.*, **53**, 793 (1931).

(4) Ball and Chen, *J. Biol. Chem.*, **102**, 691 (1933).

(5) (a) Hunter and Kvalnes, THIS JOURNAL, **54**, 2869 (1932); (b) Kvalnes, *ibid.*, **56**, 667 (1934); (c) **56**, 670 (1934); (d) Kvalnes, *ibid.*, **56**, 2478 (1934).

according to the general directions of Krishna and Singh.[6] The reaction between *p*-benzoquinone and the sulfinic acid gave *d*-camphor-10-sulfonyl hydroquinone.[5a] A better sample of *d*-camphor-10-sulfonyl-benzoquinone than that previously recorded[5a] was prepared by treating a dry ethereal solution of the hydroquinone with excess dry lead tetraacetate and shaking the suspension for ten minutes. The mixture was filtered and concentrated under diminished pressure. The dark yellow crystalline residue thus formed was filtered off and exposed to the air to decompose the unchanged lead tetraacetate. It was then treated with dry ether, filtered from lead dioxide, and concentrated under diminished pressure. The bright yellow crystalline quinone melted at 139–140°; $[\alpha]^{25}_{5461}$ +345°; c = 0.1580 in benzene; α = +1.09°; l = 2.

For a source of several of the substituted pyrocatechols use was made of the reaction discovered by Dakin:[7] oxidation of a salicylaldehyde with alkaline hydrogen peroxide. 4-Chloro-,[8] 3,5-dichloro-[8] and 4-bromo-salicylaldehyde[9] and 2-hydroxy-5-methoxybenzaldehyde were converted to the pyrocatechols in this manner. Tetrachloro-[10] and tetrabromo-[11] pyrocatechol were prepared by halogenation of pyrocatechol and were oxidized to the quinones with fuming nitric acid in acetic acid.[10,12] Triphenylcarbinol was condensed with pyrocatechol and oxidized to the quinone according to the directions of Zincke and Wugk.[13] Perhaps a better method of preparing the quinone involves oxidizing the pyrocatechol, dissolved in benzene, by shaking with lead dioxide and precipitating the quinone from the filtrate by the addition of ligroin.

Vanillin (20 g.) was reduced by the method of Clemmensen to give creosol (2-methoxy-4-methylphenol). This product was demethylated with hydrobromic acid in acetic acid[14] to give 4-methylpyrocatechol (6 g.). 3,4-dimethylphenol was converted into 3,4-dimethyl-*o*-benzoquinone by the series of reactions given by Diepolder.[15]

Hydroquinone monomethyl ether[16] was converted by the Reimer–Tiemann reaction[17] into 2-hydroxy-5-methoxybenzaldehyde.

4-Methoxypyrocatechol.—Oxidation of the above compound with hydrogen peroxide gave the pyrocatechol in good yield; recrystallized from benzene in small white crystals which melted at 48–50°.

Anal. Calcd. for $C_7H_8O_3$: C, 60.00; H, 5.71. Found: C, 59.93; H, 5.56.

4-Methoxypyrocatechol Diacetate.—White plates from benzene-ligroin which melted at 69–70°.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.93; H, 5.36. Found: C, 5926; H, 5.33.

Pyrocatechol, 4-chloro-, 4-bromo-, 4-methyl- and 4-methoxypyrocatechol were oxidized to the *o*-benzoquinones by treatment of a dry ethereal solution of each with specially prepared silver oxide[18] and anhydrous sodium sulfate. The silver oxide suspensions in the ether solutions were shaken from three to five minutes, filtered and concentrated under diminished pressure. The crystalline *o*-benzoquinones were filtered off, washed with a little cold dry ether and used directly since their instability made it inadvisable to attempt recrystallization.

4-Bromo-*o*-benzoquinone came out of an ether solution in the form of reddish-brown plates which melted at 74–75°.

Anal. Calcd. for $C_6H_3O_2Br$: C, 38.52; H, 1.62. Found: C, 38.87; H, 1.89.

4-Methoxy-*o*-benzoquinone appeared as small scarlet needles by the concentration of an ether solution. It darkened at 85° and decomposed at 88–90°.

Anal. Calcd. for $C_7H_6O_3$: C, 60.87; H, 4.35. Found: C, 60.66; H, 4.46.

2. Potential Determinations. (a) **Polarimetric Measurements.**—The relative potentials in benzene, (E_0'), were determined by dissolving freshly prepared and weighed samples of the quinone, together with weighed samples of the proper optically active hydroquinone, in benzene. The solutions were shaken for one-half to one hour to effect complete solution of the optically active hydroquinone, and polarimetric readings were taken from time to time to determine the attainment of equilibria. Most of the solutions were pale green or reddish-green in color. In the case of *o*-benzoquinone and 4-chloro- and 4-bromo-*o*-benzoquinone the solutions turned dark in about twenty-four hours; in a few instances a small amount of black precipitate formed and these determinations were discarded. The solutions of tetrachloro- and tetrabromo-*o*-benzoquinone were quite red in color and polarimetric measurements were less accurate. It was impossible to make any readings with solutions of 4-methoxy-*o*-benzoquinone because of the intense red color of the quinone and because of the sparing solubility of the pyrocatechol in benzene. An attempt was made to study 2,3-dicyano-*p*-benzoquinone[19] which Rideal[20] has shown to possess a particularly high potential (0.917 v.) but the hydroquinone is so slightly soluble in benzene that it was precipitated as soon as it was formed.

The relative potential in benzene of the new optically active reference system, *d*-camphor-10-sulfonylhydroquinone and the corresponding quinone, is 0.815 v. It was possible to calculate this value because the potential range of the new and of the 0.739 v., reference system overlap so that equilibria data between 4-methyl-*o*-benzoquinone and each reference system were obtained.

(b) **Electrometric Measurements.**—In contrast to pyrocatechol most of the compounds given in Table I can be titrated directly with ceric sulfate solution. Equilibrium was attained very quickly after each addition of the oxidizing agent and it was only at the very end of the titration that the quinone appeared to be attacked. Good agreement was observed among the titration curves for

(6) Krishna and Singh, THIS JOURNAL, **50**, 792 (1928).
(7) Dakin, *Am. Chem. J.*, **42**, 488 (1909).
(8) Biltz and Stepf, *Ber.*, **37**, 4022 (1904).
(9) Brewster and Millam, THIS JOURNAL, **55**, 763 (1933).
(10) Jackson and MacLaurin, *Am. Chem. J.*, **37**, 7 (1907).
(11) Jackson and Shaffer, *ibid.*, **34**, 460 (1905).
(12) (a) Jackson and Flint, *ibid.*, **39**, 80 (1908); (b) Jackson and Carleton, *ibid.*, **39**, 496 (1908).
(13) Zincke and Wugk, *Ann.*, **363**, 299 (1908).
(14) N. O. De Vries, *Rec. trav. chim.*, **28**, 276 (1909).
(15) Diepolder, *Ber.*, **42**, 2916 (1909); *ibid.*, **44**, 2498 (1911); *cf.* Hinkel, Collins and Ayling, *J. Chem. Soc.*, **123**, 2968 (1923).
(16) R. Robinson and J. C. Smith, *ibid.*, 392 (1926).
(17) (a) Tiemann and Muller, *Ber.*, **14**, 1990 (1881); (b) Leon Rubenstein, *J. Chem. Soc.*, **127**, 1998 (1925).
(18) (a) Willstätter and Pfannenstiel, *Ber.*, **37**, 4744 (1904); (b) Willstätter and Müller, *ibid.*, **44**, 2171 (1911).
(19) Thiele and Günther, *Ann.*, **349**, 59 (1906).
(20) E. K. Rideal, *Trans. Faraday Soc.*, **21**, 143 (1925).

each substance and the figures given in Table I are average values.

The author appreciates the interest and advice of Professor L. F. Fieser during the course of this research.

Summary

A study has been made of substituted pyrocatechol-*o*-benzoquinone systems in regard to their potentials in aqueous and benzene solutions. For the latter it was necessary to use a new optically active hydroquinone–quinone pair of high oxidation–reduction level. The three optically active systems which have been used serve adequately for the interval between 0.590 and 0.870 v.

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Mixed Melting Point Curves of Some Dialkylbarbituric Acids[1]

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Mixed melting point studies were made of the following three pairs of barbituric acids: (a) diethylcarbinylethyl and propylmethylcarbinylethyl barbituric acids; (b) diethylcarbinylallyl and propylmethylcarbinylallyl barbituric acids; and (c) isoamylethyl and active amylethyl[2] barbituric acids. The general procedure is given by Caldwell and MacLean.[3] Definite mixtures

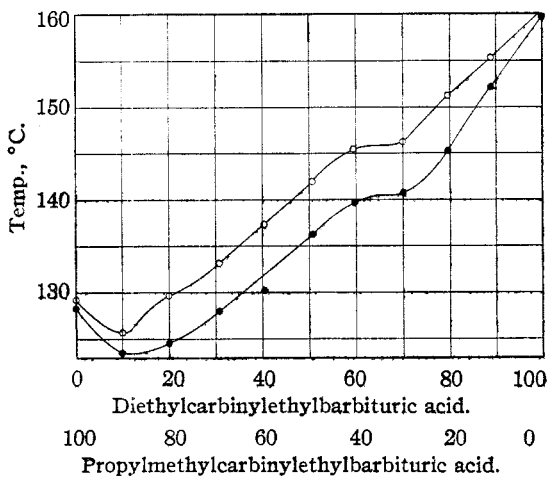

Fig. 1.

of the barbituric acids were weighed out, dissolved in acetone, evaporated to dryness and held in a desiccator until they were either hardened or crystallized. The total weights of samples of propylmethylcarbinylethylbarbituric acid and diethylcarbinylethylbarbituric acid, and propylmethylcarbinylallylbarbituric acid and diethylcarbinylallylbarbituric acid were 30 mg. in each determination. The total weights of samples of active amylethylbarbituric acid and isoamylethylbarbituric acid were 0.5 g. in each determination. Some of those mixtures which exhibited a minimum melting point required many weeks to harden and even then were only wax-like solids. It

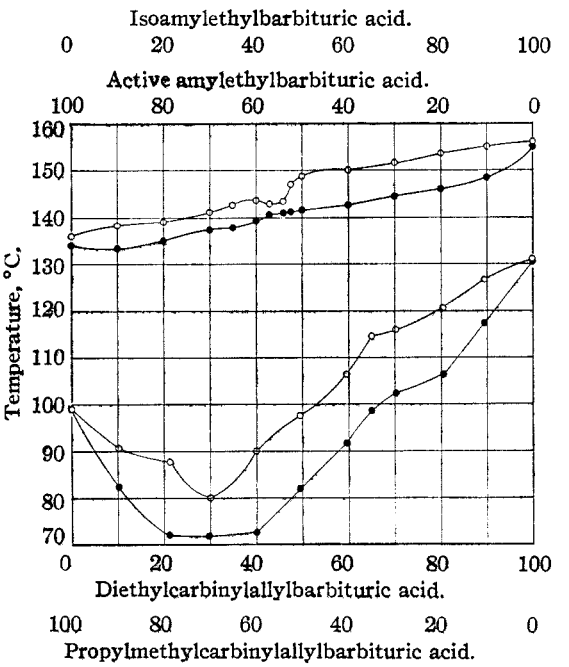

Fig. 2.

was found that a more intimate mixture could be obtained by dissolving the samples in acetone than by merely grinding them together in an agate mortar.

Melting point tubes of the usual size were filled with the solid pulverized mixture and the temperatures recorded were those of the first appear-

(1) Presented in part before the Division of Medicinal Chemistry at the Chicago Meeting of the American Chemical Society, September, 1933.

(2) *dl*-2-Methylbutylethylbarbituric acid.

(3) Caldwell and MacLean, THIS JOURNAL, **55**, 3458 (1933).