Fig. 2—The pKa' of 5,5-diphenylhydantoin in hydroalcoholic medium plotted against the concentration of ethyl alcohol.

ionized and unionized forms of diphenylhydantoin was determined. The absorbance values were also obtained for a series of solutions varying in pH, but still in the general region where the pH approximates the pKa' value, at which point the ionized and unionized species are equal in concentration. The pKa' was calculated by the expression,

$$pKa' = pH + \log \frac{A - B}{B - C}$$

where A = absorbance of diphenylhydantoin in 0.01 N NaOH, B = absorbance of diphenylhydantoin in buffered solution, C = absorbance of diphenylhydantoin in 0.01 N HCl. For the 7 buffers used in this study an average pKa' of 8.31 ± 0.04 (*SD*) was obtained.

The pKa' was also determined potentiometrically by titrating sodium diphenylhydantoin with standard hydrochloric acid. Since diphenylhydantoin is soluble in alcohol but not in water, and the reverse is true for the sodium salt, a series of titrations was performed in solvent mixtures containing varying concentrations of alcohol in water. The average

pKa' value was determined at each alcohol level from the data obtained for at least five points in each titration curve using the expression,

$$pKa' = pH - \log \frac{(salt)}{(acid)}$$

The pKa' in water (0% alcohol) was obtained by plotting the average pKa' values *versus* alcohol concentration. This procedure was first reported by Mizutani (4). Figure 2 shows a plot of pKa' *versus* alcohol concentration. Extrapolation to 0% alcohol content yields a pKa' value of 8.33 which is in good agreement with the spectrophotometric value.

The pKa' values for hydantoin and 5,5-dimethylhydantoin have been reported (5) as 9.12 and 9.19, respectively. Butler (6) reported a pKa' value of 8.5 for 5-ethyl-5-phenylhydantoin. One would expect the 5,5-diphenyl derivative to be more acidic (lower pKa) than the 5-ethyl-5-phenyl derivative. This was demonstrated in the present report by spectrophotometric and potentiometric methods.

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⊙⤳ *Keyphrases*

5,5-Diphenylhydantoin—pKa' value determination

UV spectrophotometry—procedure
Potentiometric titration—procedure

Chemistry and Biochemistry of Polyvalent Iodine Compounds VII. The ARP (Apparent Reduction Potential) of 1,3-Dihydro-1-hydroxo-3-oxo-1,2-benziodoxole

By A. EISENMANN* and W. WOLF

Iodoso compounds are strong oxidizing agents. In order to define an order of magnitude for this oxidizing action, the ARP (apparent reduction potential) of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole has been measured using the method of Conant and Lutz. At pH 7.4, the ARP of benziodoxole was 0.327 ± 0.005 v., indicating that this heterocyclic iodine derivative, under the conditions used, is approximately as strong an oxidizing agent as ceric ion. The usefulness of this technique is discussed.

THE KINETICS (1) and the mechanism (2) of the reduction of 1,3-dihydro-1-hydroxy-3-oxo-1,2-

benziodoxole (*I*) to *o*-iodobenzoic acid have been studied in this laboratory. This process is irreversible, and thus, a normal oxidation-reduction potential cannot be measured. As it had been suggested that the difference between the two classes of trivalent iodine (iodoso, iodonium) is more one of degree and rate of reaction than of nature (3), it was of

interest to see if a value could be assigned to the "oxidizing power" of such compounds.

One method that is appropriate for a study of irreversible systems is that of Conant and Lutz (4). Instead of a normal potential, Conant (5) has defined an "apparent reduction potential" (ARP) as a pseudo-redox potential. The ARP is the potential of a reversible redox system which will cause 20–30% reduction within 30 min. of the oxidized form of the irreversible system. A more precise definition is derived from the use of the rate equation for a monomolecular reaction:

$$\frac{ds}{dt} = kx(c - s) \qquad \text{(Eq. 1)}$$

where c is the initial concentration of the compound studied, s is the amount which has been irreversibly reduced at any given time, and $x(c - s)$ is the concentration of the substance undergoing the irreversible change. If the system contains a large excess of a reversible redox system, with an equimolar amount in the reduced and oxidized form, x (fraction of compound reduced irreversibly by the reaction) will be essentially constant during the reaction. Then, integration of Eq. 1 yields Eq. 2:

$$k_1 = kx = \frac{2.3}{t} \log \frac{1}{1 - s} \qquad \text{(Eq. 2)}$$

where t is the time in min. for the reaction and s is the fraction which has been reduced of the irreversible substance. If, according to Conant, t is set at 30 min., use a $k_1 = 0.01$, then, by inserting these values of t and k_1 in Eq. 2 one defines a value of 25.9% reduction for s, instead of the vague 20–30% previously suggested. Using this value, a more accurate ARP could be determined; as shown by Conant (4), the ARP is a general concept and is not restricted to monomolecular reactions.

EXPERIMENTAL METHOD

The apparatus consisted of a glass cell with an i.d. of 65 mm. and a capacity of 125 ml., closed with a loose-fitting rubber top with openings for two electrodes, a gas bubbler, and admittance of the irreversible agent. A platinum electrode and a saturated calomel reference electrode (both Beckman) formed the cell circuit; both were located a few centimeters above the bottom of the cell.

Nitrogen gas from a commercial tank was bubbled through using a Corning gas-dispersion fixture. The entire cell was mounted on a magnetic stirrer with adjustable rotational speeds. The potential was measured by a Corning 10 pH meter and also recorded constantly on a Texas Instruments recorder.

A solution of 0.05 M phosphate buffer (pH = 7.4 ± 0.1), 90 ml., was placed in the glass cell at the beginning of each trial. Equimolar amounts of the reducing agent and its oxidized form (each being about 0.001 M in the buffer solution) were then added, thus forming the reversible reference system. The stirring speed was adjusted and nitrogen bubbled in. When a steady potential had been recorded for about 5 min., 10.5 ml. of a solution of I was rapidly introduced into the redox cell. This solution was prepared by dissolving the weighed sample of I in 0.6 M NaOH with 10.0 ml. distilled water. The change in potential was followed for 30 min. As I was approximately 0.002 M in the buffer solution, it was in about 100% excess of the reducing agent.

Not all reversible systems are equally well suited for these experiments. The systems used formed a graded series of potentials, going in steps of about 50 mv. or so. This gave a good range for a quick determination of an approximate ARP. Since the measured change in cell potential was really the change in potential of the reversible redox system, these systems also had to come quickly to equilibrium. A sluggish system would not accurately reflect the amount of reduction which had taken place at any given moment. However, the 30-min. observation period compensated for this, as well as for the different rates of reaction.

RESULTS AND DISCUSSION

The data obtained are summarized in Table I.

The E.M.F. values of the reference systems used ranged from 77.2–599 mv. A redox system with a normal potential higher than the ARP did not appreciably reduce I, while one with a lower potential reduced it almost completely and very rapidly.

After the cell E.M.F. values were corrected for the calomel electrode to a hydrogen standard (E_h), a plot of these E_h values against the change in cell potential after 30 min. showed a linear relationship (Fig. 1). Points 1 and 4 represent two trials of the

TABLE I—SUMMARY OF DATA

Run No.	E.M.F.,[a] mv.	E_h, mv.	1	5	10	15	20	30	% Reduction[b]
					mv. (min. After)				
6	77.2	−164.0	63.9	136.8	166.8	179.8	193.8	200.8	99+
8	82.2	−160.6	138.3	203.8		(after 8 min.)			99+
9	134.9	−107.9	111.9	153.1	164.1	171.1	174.1	179.1	99+
3	172.0	−71.3	3	37.8	76.2	115.9			99+
4	176.8	−67.1	0.2	0.3	0.3	0.4	0.7	1.4	5
1	185.5	−58.9	0	0	−0.6	−1			0
10	211	−31.8	45	98	122	135	143	150	99+
5	354	110.1	13	50	57	62	69	75	99+
12	366	123.2	3	17	25	30	34	39	91
7	403	160.2	24	53	66	68	68	68	99+
11	534	290.1	−10	−5	0	5	12	21	67
14	575	333.8	−9	−6	−5	−4	−3	−1	0
13	577	334.8	−8	−3	−1	0	2	5	19
16	586	344.8	−3	−2	−2	−1	1	2	8
17	591	348.8	−5	−3	−2	−1	−1	0	0
15	599	356.8	−6	−4	−3	−3	−2	0	0

[a] Experimental value. The experimental E.M.F. values for mixtures of the same ions are not exactly identical, since no system was exactly equimolar. [b] As calculated graphically.
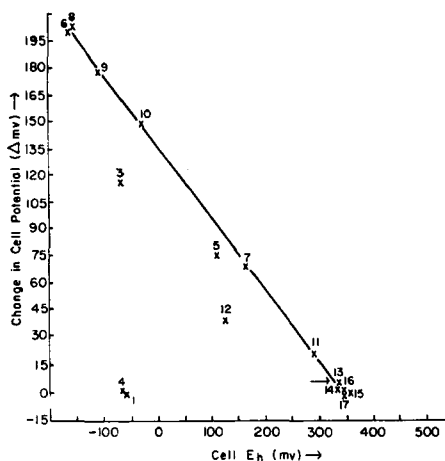
Fig. 1—Change in cell potential (Δmv.) as a function of the corrected E.M.F. (E_h).

Fig. 2—Percent reduction of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole as a function of cell E_h.

ferricyanide/ferrocyanide system; the values are seen to agree well with each other. This apparently anomalous result suggests that the ferricyanide ion is somehow hindered in reacting with I, and raises the interesting possibility that I may be a sterically selective oxidizing agent.

Some systems were used in one ratio, and the ceric/cerous system was used in different ratios (runs 8, 9, 12). Using a linear least-squares program on a Mathatron 848 computer, the equation of this line was found to be:

$$Y = 136.79 - 0.397X$$

where Y is the change in potential and X is E_h. Using a theoretical Δmv. of 6.85 for 25.9% reduction, the apparent reduction potential of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole under the conditions of these experiments was found to be 327 ± 5 mv. (Room temperature, pH 7.4, concentrations given.)

The linear relation shows that the amount of benziodoxole which is irreversibly reduced is a function of the electromotive force of the reversible system tested. This, of course, is the basis for the quantitative study employed here. The graph of percentage reduction *versus* E_h (Fig. 2) shows resemblance to a log curve, which is not surprising since the change of cell potential is logarithmically related to the percentage reduction. Values of E_h much greater than the ARP would show a 0% reduction on Fig. 2.

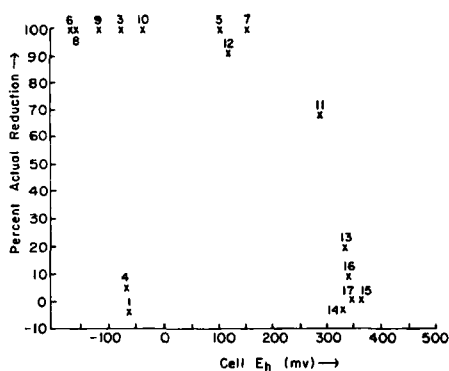Extension of this method to other iodoso and iodonium compounds is indicated, in order to verify Beringer's suggestions and to determine if a real difference exists or not between these two types of polyvalent iodine compounds.

It would also be advantageous to devise some new method for the determination of the ARP. Although this method has been updated and is relatively simple, a faster method is desirable. Polarography shows some hints of being applicable to the problem, but potentiometric titration seems to be possibly the most promising direction.

The authors consider that the present modification of the method of Conant and Lutz allows for an easy and accurate determination of the ARP of organic compounds suffering irreversible reduction. This method should also be adequate for the determination of the apparent oxidation potential.

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⊙⟋ *Keyphrases*

Iodine compounds, polyvalent—oxidizing agent

1,3-Dihydro-1-hydroxy-3-oxo-1,2-benziodoxole—apparent reduction potential

Potentiometric measurements—reduction potential