[CONTRIBUTION FROM STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Electron Exchange-Polymers. I

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Introduction

This paper, and subsequent ones in this series, will describe experimental results and theoretical conclusions which had their inception in the author's idea that it should be possible to prepare polymeric substances capable of reversibly exchanging electrons with the molecules or ions of a contiguous phase.

Polymeric substances of this character have been prepared and this unusual exchange property has been successfully demonstrated. The behavior is thus analogous to that of the cation exchange-polymers, some of which are able to exchange protons for other cations in a contiguous phase. It can now be stated that two of the fundamental particles, the electron and the proton, can be reversibly exchanged between polymeric substances and contiguous phases in much the same manner.

The exchange of a cation may be considered, in the sense of the generalized theory of oxidation and reduction,[1] to involve an oxidation and reduction, though electrons are only displaced in the process. The exchange of electrons would be an extreme case, and would correspond to the classical oxidation and reduction.

Analogies have frequently been pointed out between the behaviors of protons and electrons. Clark[2] has referred to this. Schwarzenbach[3] has proposed that an acid–base equilibrium be described by a normal acidity potential E_{ac} defined by the equation

$$E = E_{ac} + \frac{RT}{F} \ln \frac{[\text{Acid}]}{[\text{Base}]}$$

in analogy to the oxidation–reduction equilibrium for which the normal oxidation potential of the system E_{ox} is defined by

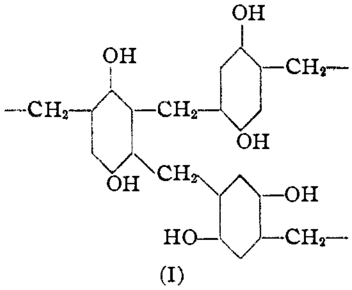
$$E = E_{ox} + \frac{RT}{F} \ln \frac{[\text{Ox.}]}{[\text{Red.}]}$$

Michaelis and Schubert[4] comment that in the field of ionization theory the acceptance of protons is the analog of the elementary reduction process. Schubert[5] has discussed the analogy between two-step ionization and two-step oxidation. There is thus ample background indicating the formal resemblance between proton exchange and electron exchange. However, the differences observed in working with the two phenomena has caused their theoretical treatments to proceed along different lines, as Schubert has pointed out.[5a]

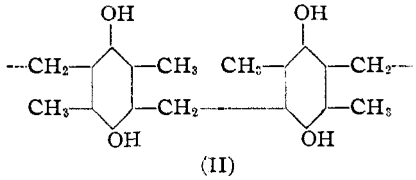
Proton exchange by cation exchange-polymers is conditioned in part by the hydrogen ion concentration of the phase contiguous to the exchanger. The electron exchange would be expected to be controlled in part by the availability of electrons to the exchanger, where availability involves potential, and the ability of the exchanger to accept them. It remained to be investigated how close the analogy would be between the two processes. The problem of constructing and establishing an electron exchanger turned out to be more difficult than had been at first anticipated. However, I am now able to report successful verification of the concept.

The electron exchange-polymer consists of given residues, capable of entering an oxidation–reduction system, which are bound together by linkages which do not necessarily interfere seriously with (though they may influence) the functional oxidizable or reducible groups. This permits building up a polymeric structure with many sites capable of accepting or donating electrons.

In setting up this problem, two classes of polymeric substances were considered: (1) those in which the active group forms a part of the backbone of the polymer chain, and (2) those in which the active group is a substituent on the chain. Class 1 consists of substances of the types hydroquinone–formaldehyde resins (I), substituted hy-



(I)



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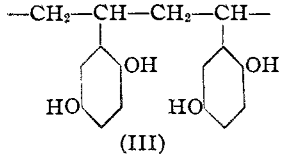

(III)

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(1) See A. E. Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, Chapter 4.

(2) W. M. Clark, "The Determination of Hydrogen Ions," Williams and Wilkins, Baltimore, Md., 1928, 3d ed., Chapter XVIII.

(3) G. Schwarzenbach, *Helv. Chim. Acta*, **13**, 870 (1930).

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

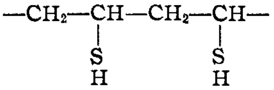
(5) M. Schubert, *Ann. New York Acad. Sci.*, **40**, 111 (1940).

(5a) Reference 4, p. 113

droquinone-formaldehyde resins (II), and similar substances. To Class 2 belong substances like polyvinylhydroquinone (III).

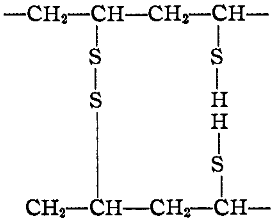
The substances belonging to Class 1 would be expected to exhibit effects due to the constraints of linking and cross-linking; distortions of the ring so produced might be reflected in the observed potentials of half-reduction, or in the propensity toward semiquinone formation,[4,7] and the effects might be expected to be more marked than those exhibited for the same reason by compounds of the second class. The change from oxidized to reduced form might, in the first case (Class 1), be reflected in a marked change in polymer dimensions, since the longer diameter of the quinone ring is about 0.26 Å. longer than the diameter of the hydroquinine ring.[8] Changes in polymer dimensions and other physical properties with reduction or oxidation might also be expected in compounds of Class 2 if there were, for example, a dimerization of adjacent semiquinoid forms, or if resins of the type IV were on mild oxidation to cross-link (V) or form rings (VI).

A further classification of exchange-polymers in terms of charge-type of the oxidized form may be made: (a) the oxidized form carries no charge (*e. g.*, of III or IV), and (b) the oxidized form carries a positive charge, as would be the case with a polymer such as butyl polyvinylpyridinium halide (VII).[9] These charge-types might be found in polymers of Class 1 or Class 2. An example of a polymer belonging to Class 1b would be polyvinylpyridinium bromide cross-linked with the ethylene bridge (VIII).[10]



$-CH_2-\underset{SH}{CH}-CH_2-\underset{SH}{CH}-$

(IV)



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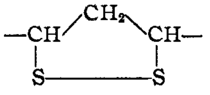

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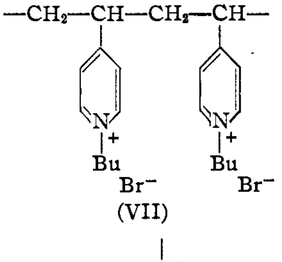
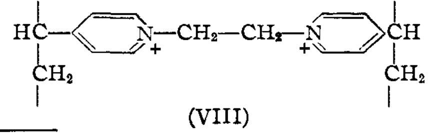


(VII)



(VIII)

The idea of electron exchangers and the hypothesis based upon it have been illustrated with specific structures (I to VIII) but naturally many other chemical examples could have been chosen. These would differ in oxidizable groups, *e. g.*, indophenols might be used, or other groupings found in oxidation–reduction indicators and similar but colorless substances. They might differ in methods of linking of monomers, *e. g.*, instead of the illustrated type of linking, polyesters, ethers, polyamides, might be produced.

Experimental

It seemed desirable to make an initial test of this hypothesis against a relatively simple polymeric substance, and for this reason polymerized vinylhydroquinone was chosen. This substance was prepared (see the following paper) from vinylhydroquinone, a new compound, prepared by decarboxylation of dihydroxycinnamic acid. This substance was prepared from *o*-hydroxycinnamic acid by the method of Neubauer and Flatow.[11] The resin was a pale yellow, polystyrene-like material, not very soluble in benzene, soluble in some organic liquids such as glacial acetic acid, and becoming tacky in water. It was extracted with benzene to remove monomer.

The oxidation titrations reported in this and the following paper were carried out in the conventional manner,[12] using a bright platinum electrode referred to a saturated calomel electrode. The potentials were read with an L. & N. Student Potentiometer. Equilibrium was taken to have been reached when the same potential was read at the end of each of three successive minutes following 30 sec. mechanical stirring and 30 sec. without stirring. The data were recorded to the nearest tenth of a millivolt and calculated to the standard of the normal hydrogen half-cell. The temperature was that of the room. In common with the observations of other workers,[13] the greatest variations in mid-point potential were found with changes in solvent systems.

The oxidation of polymerized vinylhydroquinone could be carried out in solution in 90% acetic acid according to the method of Michaelis and Hill.[14] In the experiment reported here 90 parts of glacial acetic acid was made up to 100 by adding water, and the *p*H (glass electrode) found was −0.45. Polymerized vinylhydroquinone (12.094 mg., 0.1777 me.) was dissolved in 10 ml. of acetic acid solution and titrated with 0.0359 *N* bromine solution in the same solvent. Room temperature was 23°. During the course of the titration the solution developed a pinkish-orange coloration. The system came to equilibrium slowly, but stable potentials were obtained except at the beginning and very end of the titration, when there was evident a tendency to a slow drift of the potential downwards. The course of the titration is shown in Fig. 1. The mid-point potential was −0.713 v.; the final *p*H approximately −0.6. . The end-point, if all the hydroquinone residues had been available, should have come at 4.95 ml. bromine solution; found, a little over 4.90 ml. The abscissa of the curve in Fig. 1 is calculated on 4.95 ml. as 100% oxidation. Included in Fig. 1 for reference purposes are the titration data for hydroquinone and ethylhydroquinone. 10.043 mg. of recrystallized hydroquinone

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(7) L. Michaelis, *Chem. Revs.*, **16**, 243 (1935); *Ann. New York Acad. Sci.*, **40**, 39 (1940).

(8) Determined graphically from data given by J. M. Robertson, *Chem. Revs.*, **16**, 417 (1935); *Proc. Roy. Soc.* (*London*), **A150**, 106 (1935).

(9) G. I. Cathers, Dissertation, Yale University, 1948; R. M. Fuoss and U. P. Strauss, *J. Polymer Sci.*, **3**, 246 (1948).

(10) G. I. Cathers, Dissertation, Yale University, 1948.

(11) O. Neubauer and L. Flatow, *Z. physiol. Chem.*, **52**, 375 (1907).

(12) L. Michaelis, "Potentiometry," in "Physical Methods of Organic Chemistry," A. Weissberger, ed., Interscience Publishers, New York, N. Y., 1946, p. 1051.

(13) H. Gilman, Editor, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 812.

(14) L. Michaelis and E. S. Hill, THIS JOURNAL, **55**, 1481 (1933).

in 10 ml. 90% acetic acid (pH 0.0) was titrated with bromine in the same solvent; final pH *ca.* −0.4; room temperature 24°. For the latter, 12.918 mg. of ethylhydroquinone in 10 ml. of acetic acid–water, pH −0.45, was titrated with bromine in the same solvent. The final pH was *ca.* −0.6. In Fig. 1, a curve is drawn through the points for the polymerized vinylhydroquinone for increased ease of visualization.

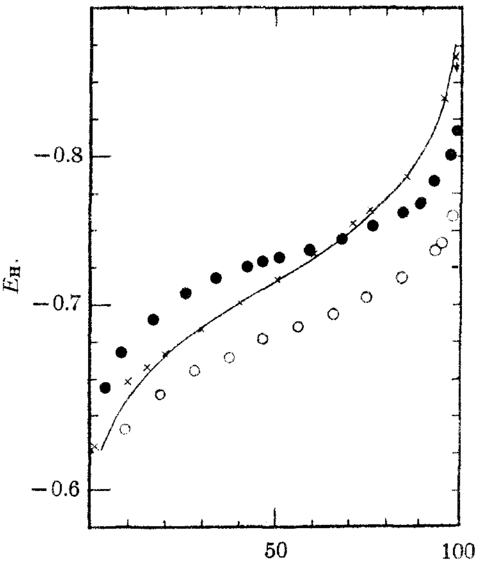

Fig. 1.—Oxidation of polymerized vinylhydroquinone, of hydroquinone and of ethylhydroquinone in solution in aqueous acetic acid with bromine in the same solvent: E_H potential in volts referred to the normal hydrogen electrode: ×, polymerized vinylhydroquinone; pH, −0.45 to −0.6; temperature 23°. The line is drawn through the points to improve visualization of the curve. $\overset{\times}{\downarrow}$, this point showed a slight downward drift. ●, hydroquinone, pH 0.0 to −0.4, temperature 24°; ○, ethylhydroquinone, pH −0.45 to −0.6, temperature 23°.

The oxidation of polymer in solution was thus shown to be possible. It was found difficult to show stoichiometric electron exchange when the polymer was in the solid form in bulk. When the polymer was dispersed by dissolving *ca.* 10 mg. in 0.1 ml. glacial acetic acid and adding 10 ml. of buffer in which the polymer was insoluble, milky-white suspensions were formed which with the first drop of oxidant became orange-opalescent, and which on further oxidation threw down a curdy, orange precipitate. The oxidized form of the resin is orange-yellow in color.

It was decided to disperse the polymer with a carrier or stabilizer. It then became possible to obtain more nearly quantitative oxidation and to obtain clear evidence of the reversible oxidation of the polymer. Polymerized vinylhydroquinone (14.871 mg., 0.2185 me.) was dissolved in 0.15 ml. of glacial acetic acid and treated with 10 ml. of buffer (sulfuric acid–potassium sulfate) containing 2.44 mg. (3.5 × 10^{-5} millimole) of bovine plasma albumin (Armour, crystalline). A milky suspension formed. This was titrated under nitrogen with ceric sulfate, pH 0.54, 0.0279 *N*. At the first drop of oxidant the suspension began to flocculate and a pinkish-orange color developed. The color became somewhat more intense as the titration progressed, and the precipitate, now brick-red, became dispersed. As the mid-point was passed the color of the precipitate became gradually less red until it was quite noticeably paler at the end-point. The potential changed quite suddenly, between 6.10 and 6.25 ml. cerate, from −0.466 to −0.72 v. (against the saturated calomel electrode). The calculated end-point for equivalence was 7.83 ml. assuming all hydroquinone residues available. The difference between the calculated and found volumes of ceric sulfate is ascribable to polymer inside the particles of precipitate and thus inaccessible to oxidant. At this point the titration was stopped, purified hydrogen gas led in, and 0.5 ml. palladium catalyst added[15] with stirring.

A platinized electrode came to a stable potential of −0.2730 v. against the calomel half cell (pH 0.46) after one and one-quarter hours. The vessel was then flushed with nitrogen for two and one-half hours, until the potential had fallen −0.13 v.[14] The suspension was now grayish (*i. e.*, polymer reduced) and there was a small amount of granular orange precipitate (unreduced polymer) present. Titration with ceric sulfate was again carried out, an orange color and flocculation of the precipitate appearing with the first drops of oxidant. The course of this titration followed closely that of the first one. The pH of the final solution was 0.50. The amount of cerate used at the end-point was 5.1 ml., indicating again that some polymer was unavailable. The potential data, calculated for per cent. oxidation based on the amount of oxidant actually used, are shown in Fig. 2 and indicate good agreement between the two experiments. A separate test of the albumin solution showed the amount of oxidant used to be inconsequential.

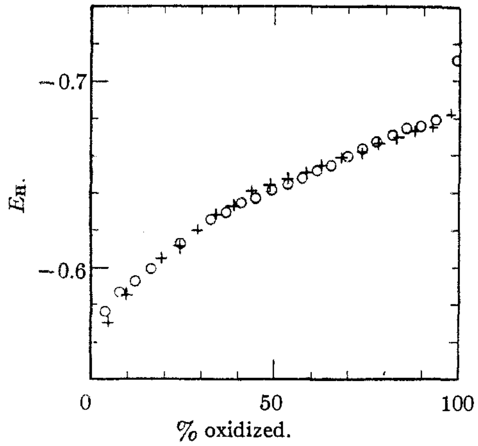

Fig. 2.—Oxidation, and reoxidation following reduction, of polymerized vinylhydroquinone suspended in the presence of albumin: E_H potential in volts referred to the normal hydrogen electrode: ○, oxidation with ceric sulfate, pH 0.54; +, repetition of above after reduction with hydrogen and removal of excess hydrogen; final pH 0.50.

A titration of polymerized vinylhydroquinone dispersed at another pH is given in the following paper, together with reference titrations of other substances and a summary of pertinent data. A large number of titrations of the polymer have been made under a variety of conditions. Some of the curves obtained have shown unusual features difficult as yet to interpret. The curves given in this and the following paper are quite reproducible on repetition of the given experiments.

Discussion

The slopes of the curves which can be drawn for hydroquinone and ethylhydroquinone speak for a bivalent oxidation, while the slopes of the polymerized vinylhydroquinone curves are near that of a monovalent oxidation (see Figs. 1 and 2).

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[15] 0.05 g. $PdCl_2 \cdot 2H_2O$ dissolved with 0.05 g. of gum arabic in 50 ml. of water. See J. Houben, "Die Methoden der organischen Chemie," 3rd ed., 2, p. 325 (method of Paal and Skita).

The interpretation of these curves is of interest, especially in connection with the use of these polymers as models of more complicated systems. Michaelis and his co-workers[16] have already formulated the theory for the slopes of the potentiometric titration curves. According to their analysis the rather flat curves are obtained when there is no appreciable semiquinone formation, and no appreciable dimerization; that is, when there is no appreciable formation of an intermediate compound during the oxidation of the reduced form of the substance or the reduction of the oxidized form.

For substances which form no intermediate the slope (δ) at the mid-point of the curve is 0.026 volts per unit of μ, where μ has the following meaning: at 0% oxidation $\mu = -1$; at 50% oxidation $\mu = 0$; at 100% oxidation $\mu = +1$. At the midpoint the index potential E_i, which is defined as the potential difference between 50% oxidation and 25% (or 75%) oxidation, is 0.0143 v. at 30°. If appreciable intermediate compound formation occurs it is recognized from the slope of the titration curve. With increase in intermediate formation δ increases and E_i increases, and when the amount of intermediate formation becomes great enough points of inflection appear in the curves below and above the midpoint. The formation of semiquinone intermediate is increased if the *p*H of the medium is such that ionization of the substance is aided, for the increased number of resonance forms of the semiquinoid ion stabilize it as compared with the un-ionized semiquinone form. Thus the shapes of these curves will vary with *p*H.

Under the acid conditions employed in these experiments hydroquinone and ethylhydroquinone show no appreciable semiquinone formation. The semiquinone form of hydroquinone, and presumably of the other compound, is not stable in aqueous solution. In solution the rate of its dismutation is so great that little semiquinone can accumulate. Thus when quinhydrone is dissolved in acid a pale yellow solution is obtained rather than the highly colored solution which would be expected of this greenish-brown substance. Accordingly in the titrations (Fig. 1) hydroquinone showed E_i 20, 14 mv.; δ, 27 mv. per unit of μ. Ethylhydroquinone showed E_i 22, 22 mv.; δ *ca.* 42 mv. per unit of μ.

When polymerized vinylhydroquinone is titrated in the dissolved state the initially colorless solution becomes pink-orange with the first drop of oxidant. With further addition of oxidant the pink-orange color becomes more intense, the pinkness becoming more marked. After the titration has proceeded some distance the solution begins to lose its pinkness and a yellow color supervenes. This sequence of colors could be produced if the polymer were in colloidal suspension and were to pass through a sequence of particle-size changes with its oxidation. This possibility has not been experimentally ruled out. The effective particle size might change if a thread-like molecule were to bunch up, or to become extended; or if many molecules were to clump together reversibly; and such behavior might occur under the influence of the added electrolyte or through a dimerization of semiquinoid forms within a molecule or between molecules, or through mechanisms such as discussed by Rabinowitch and Epstein.[17]

Against this interpretation of the color change are the observations that the same color sequence appears whether the oxidizing agent is bromine, cerate (or dichromate—see paper II), and whether the titration is carried out in a solution of a given concentration or in a solution one-tenth as concentrated. The same sequence of colors with these different oxidizing agents argues against a particle-size change due to the influence of added electrolyte, because the charge-type changes are so different. The lack of influence of dilution, the same shape of curve being obtained experimentally with a ten-fold difference in concentration, argues against an association of molecules. However, when the dispersed polymer is titrated with cerate the particles have been observed to flocculate, to be peptized, and to reflocculate at different stages during the titration (see above) when the stirring is stopped to enable a reading, but this behavior does not seem to influence the color of the solution and suspended matter. These present arguments are admittedly qualitative, and further pursuit of this phase of the problem is of course contemplated.

A more likely explanation of the color change seems to lie in semiquinone formation, with or without accompanying dimerization. In the polymeric molecules large numbers of oxidizable groups are held in a more or less constrained relation to each other. If some of these groups were to be oxidized to the semiquinone stage (the first step[16] in the oxidation) then even though the semiquinone were inherently easily dismutable (as judged by analogy with hydroquinone itself) yet since it requires the *conjunction* of two semiquinoid forms for dismutation to occur the constraints of the linkage might well hamper the dismutation. While this would not stabilize the semiquinone it would certainly allow it to accumulate. If optical examination of the polymer during the oxidation showed not a peak of color formation at 50% oxidation, but a plateau over a range of added oxidant, this supposition would receive support.

It seems to us, therefore, that the color change observed during the course of the titration can best be explained on the basis of the formation of some semiquinone. The formation of semiquinone would account for the appearance of the pink color, the yellow being attributable to the fully quinoid residues.

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(16) L. Michaelis, *Chem. Revs.*, **16**, 243 (1935); L. Michaelis and M. P. Schubert, *ibid.*, **22**, 437 (1938); L. Michaelis, *Ann. New York Acad. Sci.*, **40**, 39 (1940).

(17) E. Rabinowitch and L. F. Epstein, THIS JOURNAL, **63**, 69 (1941).

There is in this interpretation a possible explanation of an observation by Haas[18] that the combination of the active group of yellow ferment with its specific protein in the presence of a large excess of triphosphopyridine nucleotide allows on reduction at *p*H 7 (0°) the appearance of an amount of the red free-radical form which is otherwise observed with the *free* active group only in strongly acid solution, where the increased ionization of the free substance allows increased resonance stabilization. It was inferred from this observation that the Michaelis relation of radical dismutation[16] was displaced toward the radical. The mechanism which our observations suggest is that the active group when combined with the specific protein into the ferment complex is so isolated from other active groups that accumulation of radical is favored by the hampering of dismutation, and not *necessarily* by a stabilizing of the radical form.

The formation of semiquinone would also account satisfactorily for the increased slope of the curve for polymerized vinylhydroquinone (Fig. 1). Here E_i was found to be 32 and 35 mv., and δ *ca.* 70 mv. per unit of μ. It has seemed to us, however, that there is another phenomenon which might and probably does contribute to the shape of the curve, and which would be adequate of itself to account for the slope were not the special color change observed during the titration. This other phenomenon is treated in the following paper.

The behaviors of all the polymers so far investigated indicate a certain instability toward very strong oxidizing agents, and tendency toward some further reactions. Thus in strong acid (hydrochloric, etc.) with ceric sulfate some oxidation of the quinones might be expected, as well as addition of the acid to the unsaturated system. Or, with the reduced polyvinylpyridinium compounds further reduction might be anticipated, or addition of reactants from the medium, as observed by, for example, Karrer, *et al.*,[19] when the dihydropyridinium products of hydrosulfite reduction were found to contain sulfur. These problems will be discussed in succeeding papers. It need only be mentioned here that strong oxidizing agents slowly destroy hydroquinone–formaldehyde resins, and a strong reducing agent seems to carry the reduction of polyvinylpyridinium polymer beyond the dihydro stage.

These results, together with those reported in the paper which follows, indicate quite conclusively that electron exchange-polymers can be and have been prepared. It will no doubt be possible by appropriate variations in structure, reaction medium and *p*H, to run the gamut of reduction potentials with these substances. Some control of *p*H is to be expected if ion exchange monomer were copolymerized with an electron exchanger.

Apart from the very interesting theoretical problems opened up by the development of these substances their production makes possible a systematic attack from a new direction on a number of important biochemical problems. Early in this work it was suggested to me by Dr. G. J. de Suto-Nagy that these polymers might serve as models for certain biological systems. It might be possible to investigate some of the problems stated by, for example, Korr,[20] for here one could work with a heterogeneous system in which structurally-known constraining arrangements (as in Class 1 polymers) might be introduced, or constraints of other kinds such as those due to copolymerization with basic or acidic monomer. The activating or deactivating effects of such constraints, reflected in the semiquinone formation constants, for example, might well find analogies in biological systems. It might be supposed,[21] for example, that the reduction–oxidation polymers might serve as catalysts in organic and other oxidations through their ability to take up electrons and pass them on to other molecules, in a function which has been laid to the coenzyme.[22]

We have in these electron exchange-polymers a new chemical instrument by means of which many interesting chemical and biochemical problems may be attacked. Emphasis should probably be laid on the value of these polymers as substances by means of which convenient, simplified models of much more complicated systems may be contrived.

Acknowledgment.—I would like to acknowledge the stimulating discussions of this problem held with Dr. Charles S. Cleaver, Dr. G. J. de Suto-Nagy, Dr. Joseph Fleischer, Mr. Robert A. Hardy, Mr. Harold K. Inskip, Dr. F. H. M. Nestler, Mr. Ivor H. Updegraff and Mr. Vincent Verplanck.

Summary

The hypothesis that electron exchange-polymers could be produced has been advanced and tested by oxidation studies made on a polymerized vinylhydroquinone. Analogies to the proton exchange-resins have been pointed out. During the oxidation of the polymer, whether in solution or in a dispersed solid form, a pink color develops. This is interpreted to indicate the accumulation of semiquinoid residues the dismutation of which is hampered by the constraints of the polymer structure. An observation of E. Haas on the effect of the combination of yellow ferment with its specific protein on free-radical formation has been reinterpreted. The possible usefulness of electron exchange-polymers in attacking certain biochemical problems has been mentioned.

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(18) E. Haas, *Biochem. Z.*, **290**, 291 (1937).

(19) P. Karrer, F. W. Kahnt, R. Epstein, W. Jaffe and T. Ishii *Helv. Chim. Acta*, **21**, 223 (1938).

(20) I. M. Korr, *Cold Spring Harbor Symposium on Quantitative Biology*, **7**, 74 (1939).

(21) See, for example, H. A. Abramson and I. R. Taylor, *J. Phys. Chem.*, **40**, 519 (1936); L. Michaelis and M. P. Schubert, *J. Biol. Chem.*, **119**, 133 (1937); and E. S. G. Barron, *Physiol. Revs.*, **19**, 184 (1939).

(22) See, for review, L. Michaelis and C. V. Smythe, *Ann. Rev. Biochem.*, **7**, 1 (1938).