RELATION BETWEEN THE OXIDATION-REDUCTION POTENTIALS OF QUINONES AND THEIR CHEMICAL STRUCTURE

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General Introduction

The problem of relating the oxidation–reduction potentials of quinones to their chemical structure can be divided into the following two parts : (*a*) A study of the factors which influence the potentials of the unsubstituted quinones. In such a discussion we shall be concerned with the nature of the quinonoid ring and the structure of the aromatic system(s) attached to this ring. (*b*) An investigation of the influence of substituents on the potential of one particular parent quinone. This study includes a consideration of the nature, the number and the position of the substituent groups.

It is interesting in this introduction to trace the development of ideas in the above connections. Before oxidation–reduction potentials of quinones were known, the effect of structure on their " oxidising strength " or their " stability " had already been discussed by organic chemists. The first " theory " was put forward by F. Kehrmann in 1898 : [1] " The oxidising strength of quinones decreases as the molecular weight increases and as there are more negative substituents in the molecule." No clear indication of what was meant by " negative substituents " was given ; the first part of the statement was based on the well-known sequence (I), (II), (III), in
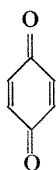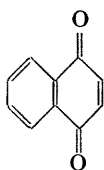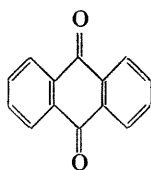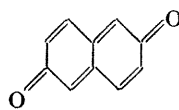

(I.)   (II.)   (III.)   (IV.)

which the stability increases from left to right, typical quinone properties being nearly absent in anthraquinone. R. Willstätter and J. Parnas in 1907,[2] however, pointed out that the problem could not be quite so simple ; for example, *amphi*naphthaquinone (IV) is extremely unstable, although it has, of course, exactly the same molecular weight as the isomeric α- and β-naphthaquinone. Willstätter and Parnas then suggested that it is not so much the simple increase in molecular weight that is decisive, but rather the stabilisation of the quinonoid system by linking an aromatic ring to its olefinic bonds. It was shown that even the extremely unstable *amphi*-
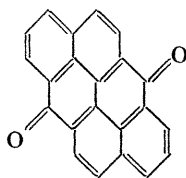
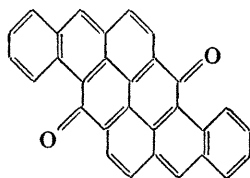[1] *Ber.*, 1898, **31**, 979.   [2] *Ibid.*, 1907, **40**, 1406.

naphthaquinone could be stabilised in this way, as one could prepare " *amphi*chrysoquinone " (V),[3] " anthanthrone " (VI),[4] and " *amphi-iso*-pyranthrone " (VII),[5] the stability again increasing from left to right.   This
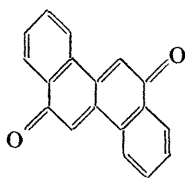
(V.)   (VI.)   (VII.)

rule of Willstätter and Parnas has guided organic chemists for many years. The influence of substituents on the stability and oxidising power of quinones was even in this qualitative way less clearly delineated.   Some general indications were apparent such as that by Kehrmann referred to above. O. Dimroth and V. Hilcken in 1921[6] showed that the *position* of a substituent was as important as its *nature*.

Real progress could only be made when qualitative considerations on oxidising power and stability could be replaced by quantitative determinations of oxidation–reduction potentials.   Although F. Haber and R. Russ determined the potential of *p*-benzoquinone as early as in 1904,[7] it was not until about 1920 that better and easier experimental techniques were developed (W. M. Clark, E. Biilmann, S. P. L. Sørensen).   This allowed a systematic investigation on a large scale.   Between 1920 and 1935 Fieser and his collaborators at Harvard prepared a very large number of quinones and quinols and determined their potentials.[8]   Although other measurements[9] had been reported and particular quinones had aroused interest in connection with special applications (as indicators, dyes, etc.), an entirely new point of view was stressed by Fieser and his collaborators.   They clearly recognised how our understanding of the particular problems might be of great importance for other and more general problems in organic chemistry. To quote J. B. Conant and L. F. Fieser :[10]

" The measurement of reduction potentials affords a new method of studying quantitatively the free energy of an addition reaction which can be brought about with a series of related substances.   By such quantitative studies the differences caused by substitution and by structural changes can be discovered, and when sufficient data have been obtained it should be possible to make many interesting and important generalisations in regard

[3] E. Beschke and F. Diehm, *Annalen*, 1911, **384**, 173.
[4] L. Kalb, *Ber.*, 1914, **47**, 1724.
[5] R. Scholl and C. Tänzer, *Annalen*, 1923, **433**, 163.
[6] *Ber.*, 1921, **54**, 3050.
[7] *Z. physikal. Chem.*, 1904, **47**, 257.
[8] See also refs. (10) and (11); full references given in subsequent paragraphs.   For a survey of this work see also L. F. Fieser and M. Fieser, " Organic Chemistry ", Boston, Heath, 1944.
[9] See, *e.g.*, V. K. LaMer and L. E. Baker, *J. Amer. Chem. Soc.*, 1922, **44**, 1954.
[10] *Ibid.*, 1923, **45**, 2194.

to the driving force of a given organic reaction and the structure of the organic compound concerned."

However, the important generalisations which were hoped for were not immediately apparent in terms of classical organic chemical ideas. In particular, the problem of the influence of substituents appeared to be very complicated, and even a comparison of the potentials of the unsubstituted " parent quinones " did not immediately yield results. Although the Willstätter–Parnas rule appeared to be of some guidance, one observed great irregularities. Clearly, as already pointed out by Conant and Fieser in 1924,[11] this is not surprising, as an adequate interpretation of the facts should not only take into account the stability of the quinone (to be denoted by Q), but also that stability of the quinol (to be denoted by QH_2) formed on reduction.

From the theoretical point of view the first important step forward was not made until 1941. Then G. E. K. Branch and M. Calvin [12] put forward the hypothesis that in a reaction of the type $Q + H_2 \rightarrow QH_2$, e.g.,
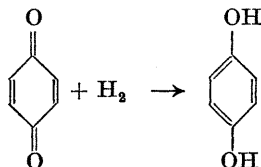
the driving force should be the gain in resonance energy of the aromatic QH_2-system over that of the quinonoid Q-molecule. The difficulty in testing this hypothesis was to evaluate R_{QH_2} and R_Q, the two resonance energies concerned. For the unsubstituted quinones, methods of approximating these quantities have been developed by Branch and Calvin themselves,[12] by M. G. Evans,[13] by M. Diatkina and J. Syrkin,[14] and recently with somewhat greater precision by M. G. Evans, J. Gergely, and J. de Heer.[15] As a result of these quantum-mechanical calculations we can now conclude that for a certain series of unsubstituted quinones the hypothesis of Branch and Calvin has been proved to be correct. A linear relationship is found between the oxidation–reduction potential, E^0, and the difference in resonance energy of Q and QH_2, i.e., $R_{QH_2} - R_Q$.

The present state of our quantum-mechanical methods does not allow us to calculate resonance energies of substituted quinols and quinones with any accuracy. However, for a number of compounds, E. Berliner [16] estimated these quantities from experimentally known heats of combustion and apparently proved that the resonance hypothesis can be extrapolated to substituted quinones. We will show in a subsequent paragraph that Berliner's ideas can be criticised and might lead to confusion as to the nature

[11] J. Amer. Chem. Soc., 1924, **46**, 1858.
[12] " The Theory of Organic Chemistry ", New York, Prentice Hall, **1941**.
[13] Trans. Faraday Soc., 1946, **42**, 113.
[14] Acta Physicochim. U.R.S.S., 1946, **21**, 921.
[15] Trans. Faraday Soc., 1949, **45**, 312.
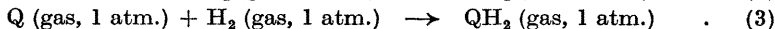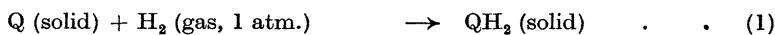[16] J. Amer. Chem. Soc., 1946, **68**, 49.

of the resonance phenomena.   As it is our conviction that here, as in other parts of organic chemistry, the resonance phenomenon is sometimes introduced too uncritically, we will confine part of this Review to elaborating some fundamental notions and definitions which are involved.   After that it will be clear that other intramolecular energetic factors will co-operate (or counteract) in the resonance stabilisation.   In addition, intermolecular and entropy influences will be involved in determining the free-energy change of the oxidation–reduction reaction under consideration, and it is this total free-energy change that determines the potential.

The entire problem is therefore seen to be a very complex one.   The recognition of this fact in itself is of great advantage as it now becomes clear that simple theories should not be expected to cover all facts.   Our task will be to analyse this complex problem into its different aspects and then to discuss several special topics within the framework thus outlined.

1. Experimental Data

In the scope of this paper it is not our intention to give any details about experimental methods.   The only idea underlying the inclusion of this section is to mention the sources of the experimental data and to comment on their exact meaning in connection with their comparison with theory. We can consider three different reactions :

$$Q \text{ (solid)} + H_2 \text{ (gas, 1 atm.)} \longrightarrow QH_2 \text{ (solid)} \qquad . \qquad . \quad (1)$$
$$Q \text{ (in solution)} + H_2 \text{ (gas, 1 atm.)} \longrightarrow QH_2 \text{ (in solution)} \qquad . \quad (2)$$
$$Q \text{ (gas, 1 atm.)} + H_2 \text{ (gas, 1 atm.)} \longrightarrow QH_2 \text{ (gas, 1 atm.)} \qquad . \quad (3)$$

If we divide the free-energy changes, ΔG^s, ΔG^l and ΔG^g, accompanying these reactions by $2F$ (F = Faraday's constant), we obtain the oxidation–reduction potentials referring to the solid, solvated, and gaseous state, respectively. These three quantities, all of which are mentioned in the literature, we denote by E_S^0, E_L^0 and E_G^0 ; each of these terms is a function of the temperature. E_S^0 and E_L^0 can be determined directly by means of the usual electrochemical methods.[17] E_G^0 can only be obtained indirectly and only if : (i) E_S^0 is known, (ii) P_Q and P_{QH_2}, the vapour pressures of the quinone and quinol at the temperature concerned, are known, and (iii) the quinone and quinol vapours behave as ideal gases or have approximately the same activity coefficients at that temperature.   We then obtain E_G^0 from [17e]

$$E_g^0 = E_s^0 - \frac{RT}{2F} \log P_Q / P_{QH_2}$$

The free-energy change expressed by E_S^0 will be dependent on the lattice energies of Q and QH_2 in their respective crystals.   As theoretical work is

[17] (a) J. B. Conant, H. M. Kahn, L. F. Fieser, and S. S. Kurtz, Jr., J. Amer. Chem. Soc., 1922, 44, 1382 ; (b) J. B. Conant and L. F. Fieser, ibid., p. 2480 ; (c) idem, ibid., 1923, 45, 2194 ; (d) idem, ibid., 1924, 46, 1858 ; (e) J. B. Conant, ibid., 1927, 49, 293 ; (f) L. F. Fieser, ibid., 1928, 50, 439 ; (g) idem, ibid., 1929, 51, 3101 ; (h) idem, ibid., 1930, 52, 4915 ; (i) idem, ibid., p. 5204 ; (j) L. F. Fieser and M. A. Peters, ibid., 1931, 53, 793 ; (k) L. F. Fieser and M. Fieser, ibid., 1934, 56, 1565 ; (l) idem, ibid., 1935, 57, 491.

usually performed on *isolated* molecules and the lattice energies concerned are unknown, E_S^0 is of little use to us.   It is evident that E_G^0 would be very suitable, but unfortunately the data required to determine this quantity with any accuracy are seldom available.   So one usually considers E_L^0 only ; in the rest of this paper we will refer to this quantity as E^0.   The disadvantage remains that in correlating E^0 with theoretical data, solvation and association phenomena may interfere ; in other words, we may expect E^0 to be dependent on the choice of the solvent.   As the usual, electrochemical, determinations must be made in polar, conducting, solvents, it became a matter of interest to find a method to determine E^0 in a non-polar solvent.   This problem was solved by Kvalnes [18] who developed an optical method, essentially based on the equilibrium set up in a system containing the Q–QH_2 pair to be investigated and a standard optically active Q'–QH_2' pair.

In a dissociating solvent E^0 is usually defined by the expression

$$E_h = E^0 + \frac{RT}{2F} \log \frac{[Q]}{[T]}$$

where [T] represents the total concentration of the reduced quinone.   In this reduced form the quinone may exist as undissociated molecules QH_2, in the first ionised state QH^-, and as fully ionised $Q^=$.   Thus :

$$[T] = [QH_2]\left\{1 + \frac{K_1}{[H^+]} + \frac{K_1 K_2}{[H^+]^2}\right\}$$

where K_1 and K_2 represent, respectively, the first and the second dissociation constant of the quinol.   Few second dissociation constants of quinols have been measured, but K_1 and K_2 are usually of the order 10^{-8} to 10^{-9} and 10^{-11} to 10^{-13}, respectively.   Hence at a hydrogen-ion activity of 10^{-1}, which is the standard at which E^0 is defined, the last two terms in the above expression are negligible compared with unity, and E^0 measures effectively the free-energy change involved in the reaction $Q + H_2 \rightarrow QH_2$. It would be of considerable theoretical interest if the free-energy change of the reaction $Q + 2e \rightarrow Q^=$ could be measured and compared with that for hydrogenation.   Unfortunately, as mentioned above, values of K_1 and K_2 which would be required for this measurement are rarely available and direct measurements in alkaline solution are nearly always impossible.

The accuracy of the E^0 determinations differs somewhat for different quinones according to the specific experimental difficulties encountered. Fortunately, nearly all data, which are important to us, have been obtained by the same school [17] and should be very reliable for mutual *comparison*, in which we are interested in the first place.   In 1900 A. Valeur [19] determined thermochemically the heats of reduction of several quinones.   His results could be compared with the E_L^{0}'s and E_S^{0}'s obtained electrochemically as one also knew the temperature coefficients of the last two quantities. E. Biilmann [20] and Conant and Fieser [17b, c] thus found " fairly concordant

[18] W. H. Hunter and D. E. Kvalnes, *J. Amer. Chem. Soc.*, 1932, **54**, 2869 ; D. E. Kvalnes, *ibid.*, 1934, **56**, 676, 670, 2478, 2487.
[19] *Ann. Chim.*, 1900, **21**, 470.   [20] *Ibid.*, 1921, **15**, 109.

results " and discrepancies have to be ascribed very probably to the uncertainties and approximations involved in the thermochemical method.   An uncertainty in E^0 amounting to 10 mv. (which according to Fieser et $al.$ is exceptionally high) would mean an uncertainty in free-energy change of about 0·5 k.-cal.   As the accuracy of our theoretically obtained data will certainly not be of a smaller order, these divergencies need not worry us. Finally, one can say that very few of the values reported by Fieser et $al.$ have been criticised (see, however, K. Wallenfels and W. Möhle [21] for a critical discussion of some data).   Summarising, we may conclude that the data communicated by Fieser et $al.$ seem to offer an adequate basis for comparison with our theoretical ideas.

2. An Analysis of the Factors Influencing E^0

As stated in the previous section, E^0 will be a measure of the $free$-$energy$ $change$ ΔG^l accompanying reaction (2) as it occurs in solution.   In analysing the various factors which contribute to this free-energy change, it will be useful to relate ΔG^l to ΔG^g, the free-energy change of reaction (3) under ideal conditions in the gas phase.   Thus

$$\Delta G^l = \Delta G^g + \Delta G^{solv.}_{QH_2} - \Delta G^{solv.}_{Q}.$$

where $\Delta G^{solv.}$ is the free-energy change accompanying the solvation process of the species Q and QH_2.   The free-energy change in the ideal gas phase can be expressed by

$$\Delta G^g = G_{QH_2} - G_Q - G_{H_2}$$

G_{H_2} is the free energy of a molecule of hydrogen under the ideal standard conditions chosen and will be a constant term throughout any sequence of quinones we consider.

On the basis of the above analysis we can construct the following table, in which H denotes heat content and S entropy :

| (Intra)molecular properties. | Environment (intermolecular) properties. |
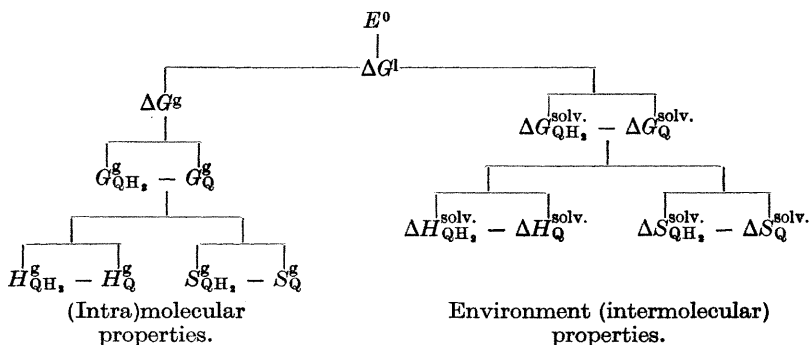
A slight simplification can be made by noting that $S^g_{QH_2}$ will differ very little from S^g_Q because these molecules differ little in mass and moments of inertia, and internal vibrations will contribute little to the entropy.   On the other hand, the term $\Delta S^{solv.}_{QH_2} - \Delta S^{solv.}_Q$ may not always be negligible and will be

dependent on the nature of the solvent. In fact, Conant and Fieser's observations [17b] show that the temperature coefficients in aqueous and alcoholic media are different, which emphasises this point. It is reasonable to suppose, however, that in a sequence of quinones containing the same number of polar groupings of the same configuration, solvation effects, influencing both $\Delta H^{\text{solv.}}$ and $\Delta S^{\text{solv.}}$, will remain constant throughout the series if all E^0's are measured in the same solution. We can, however, not expect this simplification always to hold, and especially will it fail in a sequence in which the number and nature of substituents are changed appreciably. This complication, as we will see, will make it difficult to analyse the effect of substituents on the intramolecular properties.

Summarising the position, we would say that in a series of closely related quinones the environmental energy and entropy terms, while not being entirely negligible, may reasonably be expected to remain constant. This, together with the slight simplification with regard to the intramolecular entropy change (see above), justifies us in attempting to relate the changes in free energy and hence the changes in E^0 to the changes in intramolecular energy of such related compounds. It is necessary therefore to analyse the various molecular factors influencing H_{QH_2} and H_Q (the superscripts g now having been dropped).

In an unsaturated molecule we have to distinguish :

(a) A framework of atomic nuclei.

(b) A number of electrons not involved in chemical bonding, *i.e.*, inner-shell electrons and those valence-shell electrons that are localised at particular nuclei.

(c) The so-called " σ-electrons ", which in pairs form localised " σ-bonds " between two particular centres, each centre consisting of an atomic nucleus plus a number of electrons of type (b).

(d) A system of " unsaturation-", " conjugation-", " mobile-", or " π "-electrons, being capable of moving through a larger part (" unsaturation- " or " conjugation-path ") of the molecule.

This division is more or less artificial, and interaction between different types of electrons might very well occur. Usually we are incapable of considering this interaction in any detail. In fact, in most cases only the energies of the π-electrons can be estimated quantitatively ; here two *approximation* methods are available : (i) the " valence bond " approach ; (ii) the " molecular orbital " approach.
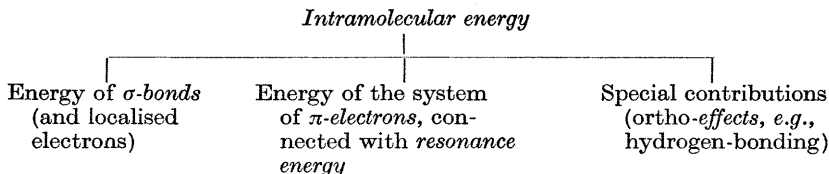
In this survey we do not want to discuss the criticism to which both these two methods are open or to analyse their merits relative to each other. However, we do want to stress that, although inner-shell electrons may possibly not interfere with chemical phenomena, this is certainly not the case with σ-electrons. In other words, in discussing the energetic aspects of an unsaturated molecule, σ-bond energies must be taken into account. In this connection it is very unfortunate that we usually have to confine ourselves to some qualitative remarks here, as our present-day quantum-mechanical theories are inadequate to deal quantitatively with the characteristics of σ-electrons and σ-bonds.

The total π-electronic energy, which thus can be calculated with the aid of one of the two approximation methods mentioned above, is closely connected to the " resonance-energy " or " delocalisation-energy " of the molecule under consideration. However, the two are not identical, as the resonance or delocalisation energy is equal to the total π-electronic energy minus the sum of the energies of these π-electrons in a hypothetical, localised bond-structure. This is true of both methods (i) and (ii) above. Whether a difference in total π-electronic energy of two molecules (*e.g.*, Q and QH_2) is accurately reflected by their difference in resonance energies is a question which cannot be answered in general but has to be considered in every particular case.

Finally, the energy of an isolated molecule may still be influenced by factors which are usually described under the heading " *ortho-* effects ". In a molecule of the type (VIII), where X and Y may be complicated groups, interactions between X and Y may give rise to special energetic terms (*e.g.*, stabilisation through hydrogen-bridge formation). Electrons, " localised " in the valence shells of atoms constituting X and Y, often participate here. Again, the *ortho*-effects are in many cases not tractable quantitatively and even their nature is not always completely clear. Here, too, we usually have to make rather rough guesses.

Summarising, the important part of the intramolecular energy of an unsaturated molecule has been sub-divided as is indicated below :

Intramolecular energy

Energy of *σ-bonds* (and localised electrons)	Energy of the system of *π-electrons*, connected with *resonance energy*	Special contributions (ortho-*effects*, *e.g.*, hydrogen-bonding)

We want to stress that this sub-division is not at all of a fundamental or of a more or less " unique " character as is the main division given at the beginning of this section. On the contrary, it is immediately connected with the quantum-mechanical approximation methods which are available at present for determining the energy of an unsaturated molecule.

3. Detailed Discussion of *o*- and *p*-Unsubstituted Quinones

In this section we wish to discuss the changes in oxidation–reduction potential, E^0, measured in a particular solvent, in a series of related compounds in terms of the behaviour of the electronic energies of the molecules concerned.

We again emphasise that changes in solvation energy and entropy changes will be very closely the same throughout such a series. Fieser and Conant [17b] have shown that the temperature coefficient of the E^0 is in aqueous solution of the order of 0·7 mv. per degree for a number of substituted and unsubstituted quinones. This value corresponds to an entropy change, accompanying the reaction, of about − 32 cals. per degree, a change which

corresponds roughly to the entropy of hydrogen under the standard conditions of pressure and temperature. According to the arguments given in section 2, this is what we should expect on theoretical grounds. We are aware that there are small but significant differences in this entropy change for the same reaction in different solvents, but these are small compared with the energy changes that we shall have to discuss. Indeed, the influence of environment on the total free-energy change, which as we pointed out may include solvation, association, salt-effects, etc., is small compared with the value of the internal (intramolecular) free-energy change. It may, however, be of the same order as the differences between one quinone and another in which we are interested. Therefore we feel it important that any comparisons which are to be discussed in terms of electronic energy should be made between systems measured under the same environmental conditions and in as dilute a solution as possible. It seems to us that the equilibrium we are discussing, which for a compound such as p-benzoquinone can be measured with great accuracy, affords a very good system in which to make an extensive systematic study on the influence of intermolecular factors on a simple well-defined chemical process. For comparison with theoretical work, we have chosen the E^0's in alcoholic solution, since these are the most adequate for our purpose. The above arguments make it plausible that we may find a relation between E^0 and the intramolecular energy of unsubstituted o- and p-quinones and if such a relation exists it will provide the best justification for this procedure.

We now have to consider the electronic energies in the molecules Q and QH$_2$ (*cf.* section 2). As an example, take :
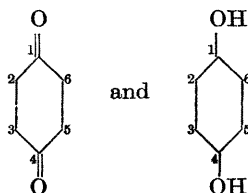
Following Evans, Gergely, and de Heer,[15] we can analyse the energy, E_1, of Q + H$_2$, apart from the energy of inner-shell electrons, into the following terms :

$$E_1 = 2D_{C_2-C_3} + 4D_{C_1-C_2} + 4D_{C-H} + 2D_{C-O} + D_{H-H} + 4E_{p0} + E_{8\pi} \quad . \quad (1)$$

where all D's refer to σ-bond energies between the atoms indicated in the subscripts. Fig. 1a shows diagrammatically the assignment of p-electrons to the carbon–oxygen skeleton. On each of the oxygens there is a doubly occupied p_y orbital, whose symmetry-axis is in the plane of the ring. The energy of an electron in such an orbital is denoted by E_{p0}. The energy of the system of 8 mobile electrons originating from p_z orbitals is denoted by $E_{8\pi}$.

Similarly, the relevant part of the energy of the quinol E_2, can be expressed as

$$E_2 = 2D'_{C_2-C_3} + 4D'_{C_1-C_2} + 4D'_{C-H} + 2D'_{C-O} + 2D_{O-H} + E_{10\pi} \quad . \quad (2)$$

where the D'''s have the same significance as the D's in equation (1), and reference to Fig. 1b shows that we now have to consider the energy of 10 mobile electrons, $E_{10\pi}$, originating from 8 p_z orbitals.
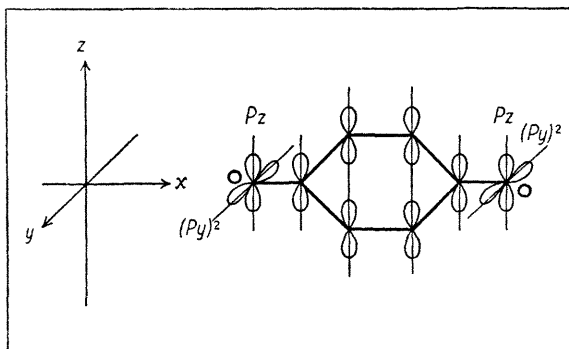

FIG. 1a

Thus, for the energy-change in the reaction p-benzoquinone $+ H_2$ $\longrightarrow$ quinol, we have

$$E_2 - E_1 = \Delta E = \Delta D_\sigma - D_{\text{H-H}} + 2D_{\text{O-H}} - 4E_{p0} + E_{10\pi} - E_{8\pi} \quad . \quad (3)$$

where ΔD_σ denotes the total change in σ-bond energy resulting from the changes in the bond lengths concerned. Strictly speaking, ΔD_σ may be different for different quinones (in the reduction of naphthaquinones, for example, changes in ten, not six, C–C σ-bonds are involved). However, in the reduction of o- and p-unsubstituted quinones we may assume the changes in bond lengths as essentially taking place in the " quinonoid nucleus " only, and consequently the change in energy ΔD_σ may be taken as a constant throughout a series of quinones. Thus if we change from one quinone to another the energy change ΔE in equation (3) will be governed by changes in
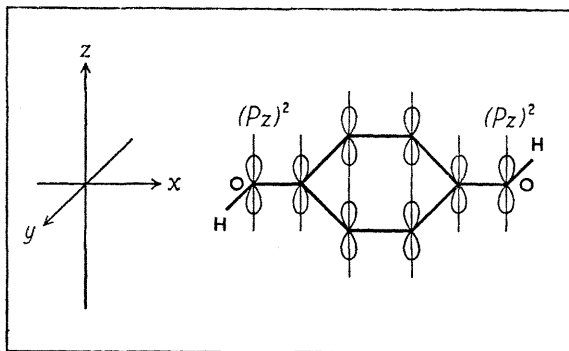

FIG. 1b

$(E_{10\pi} - E_{8\pi})$, the difference between the total binding energy of 10 and 8 mobile π-electrons in QH_2 and Q, respectively.

Now, if we wish, we can replace $(E_{10\pi} - E_{8\pi})$ by $(R_{QH_2} - R_Q)$, the differ-

ence in resonance energy of the compounds concerned.   This is allowed here, because one takes as datum line for the definition of resonance energy (essentially delocalisation energy) the total energy $E_{\text{loc.}}$ of the π-electrons in hypothetical localised bond structures of the type (IX) and (X).

:OH   O

(IX.)   (X.)
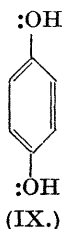
Then

$$R_{\text{QH}_2} = E_{10\pi} - E_{\text{loc.}}^{\text{QH}_2} \quad \text{and} \quad R_{\text{Q}} = E_{8\pi} - E_{\text{loc.}}^{\text{Q}}$$

Thus

$$E_{10\pi} - E_{8\pi} = R_{\text{QH}_2} - R_{\text{Q}} + (E_{\text{loc.}}^{\text{Q}} - E_{\text{loc.}}^{\text{QH}_2})$$
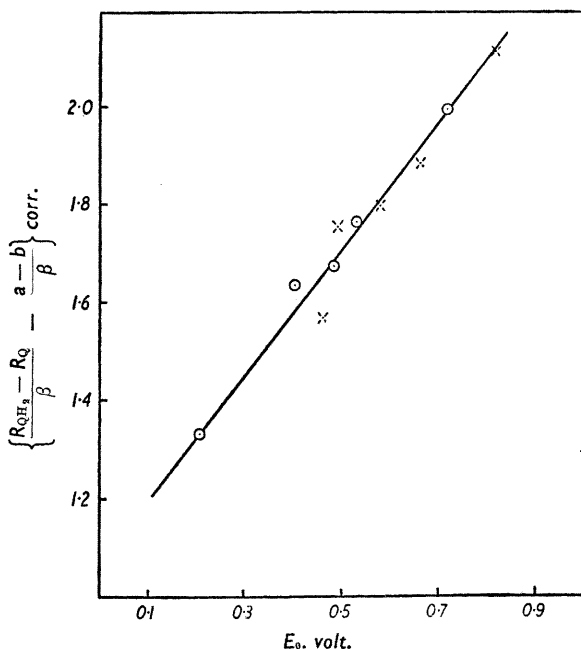

FIG. 2

As the last term is the same throughout a series of unsubstituted o- and p-quinones, we can essentially deal with $R_{\text{QH}_2} - R_{\text{Q}}$.   By molecular-orbital calculations, Evans, Gergely, and de Heer [15] have shown that R_{QH_2} and R_{Q} can be expressed adequately by means of certain additivity rules, the value of which will be further discussed by Coulson, Evans, and de Heer (in preparation).   These calculations follow the earlier crude approximations

made by Branch and Calvin [12] [see also ref. (22)], Evans,[13] and Diatkina and Syrkin,[14] approximations which can be severely criticised.[15] In Fig. 2 we show the linear relationship obtained by plotting the E^0's of a series of unsubstituted o- and p-quinones against $(R_{QH_2} - R_Q)$, expressed in units of β (the " resonance integral " in benzene) and only known apart from an additive constant $(a - b)/\beta$, as reported by Evans, Gergely, and de Heer. These values have been corrected empirically for the hydrogen-bonding in the o-dihydroxy-compounds, which will stabilise these by an amount 0.12β ($\pm$ 2.4 k. cals.). Any other small differences between o- and p-compounds [e.g., in D_{O-H}, see equations (2) and (3) above] might be included in this correction term, but the hydrogen-bonding will probably be the largest specific ortho-effect.

As a result of these recent investigations the resonance theory is well established for the compounds under consideration. In the light of the analysis of section 2 and this section, this can only mean that several other factors have the same influence throughout this series of quinones or cancel out by coincidence. We should not be surprised, therefore, if the situation with substituted quinones turns out not to be so simple.

4. The Influence of Substituents

(a) Influence of Entropy and Environment.—From the evidence reported by Conant and Fieser, quoted several times in this Review, we again seem to be justified in assuming that the entropy change is of the order of 30 entropy units and will be constant in a series of substituted quinones, provided the measurements are made in the same solvent. However, no very extensive experimental study of this subject has been made, and we understand from Dr. Guptar [23] that in certain solvents ΔS may be very different from the above value.

As we pointed out in section 2, the energetic considerations of isolated molecules really apply to the gaseous state, and whereas in the case of unsubstituted quinones the same polar groups are present throughout the series, this is no longer true if we consider now a series based on the same parent quinone but involving a change in the number or/and nature of substituents. This effect is amply illustrated in Fig. 3, in which we show the effect of chlorine substituents, on the E^0 of p-benzoquinone.[17c, e, 18] It is seen that, whereas in the gaseous state the free-energy change increases progressively and regularly with the number of chlorine atoms, yet in alcoholic and benzene solutions E^0 shows variations which can only be due to specific environmental effects. The difference of the trend in alcoholic solution and in benzene would indicate that the influence of solvent is very sensitive to its polarity and approaches closest to the ideal gaseous state in the non-polar solvent benzene. As far as we know, this is the only series in which it has been shown definitely, by comparison of the ΔG's in the gaseous state and in a solvent, that the environment gives rise to such

[22] P. G. Carter, Trans. Faraday Soc., 1949, 45, 597.
[23] Imperial Chemical Industries Limited Laboratories, Blackley ; private communication.

important changes as to obscure the intrinsic, intramolecular variation. This alone, however, illustrates how careful one must be in drawing conclusions on the influence of substituents in terms of intramolecular, electronic considerations.

   (b) **Influence on Intermolecular Energies : Inductive and Conjugation Effects.**—If a substituent X is linked to an aromatic molecule (Fig. 4), in general the entire electronic structure will change.   As mentioned before,
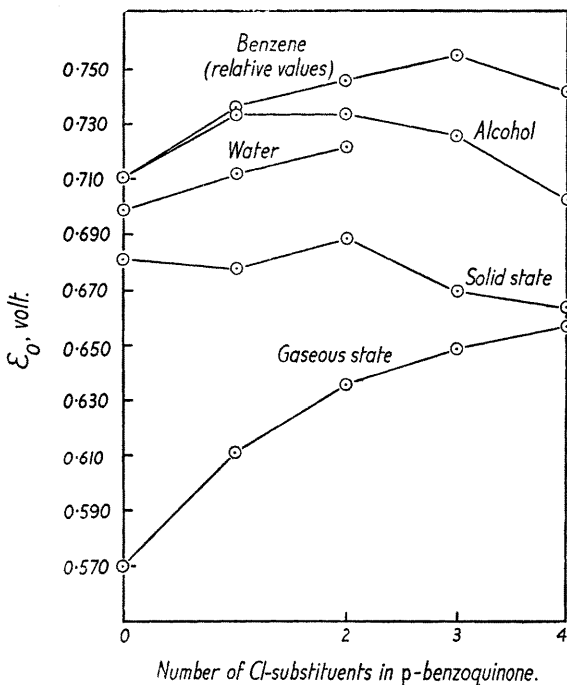

Benzene (relative values)
Water
Alcohol
Solid state
Gaseous state

$\mathcal{E}_0$, volt.

Number of Cl-substituents in p-benzoquinone.

FIG. 3

the present quantum-mechanical treatment of such molecules does not allow us to treat these electronic changes as a whole, but, in accordance with the considerations of section 2, we have to analyse the influence of a substituent into the following effects :

(i) As the group X will in general not have the same electronegativity as the centre A to which it is linked, a polar A–X σ-bond will be formed. This bond, in turn, will polarise adjacent σ-bonds in the aromatic molecule and so the effect is passed on, becoming smaller and smaller, the greater the distance from the bond A–X.   This effect is usually called the " inductive effect " although in our opinion " inductive effect on the σ-electrons " would indicate more explicitly what it amounts to.   As mentioned in section 2, it is impossible at present to treat any effect on σ-bonds and σ-electrons quantitatively, and we have to limit the discussion to qualitative considerations.

(ii) As the " σ-framework " (nuclei, inner-shell and σ-electrons) of the

original aromatic molecule has been distorted by the effect mentioned under (i), the field in which the mobile π-electrons move will change also. Consequently, all the π-electronic energies (and hence the resonance energy) will change. We suggest calling this effect the " inductive effect on the π-electrons ".

(iii) The substituent X may provide a p_z-orbital (Fig 4) which will extend the conjugation path (unsaturation path) of the π-electrons of the aromatic molecule. As this p_z-orbital will in general be occupied by one or two electrons, the number of π-electrons is also increased by this substitution. Resulting changes in π-electronic energies, charge shifts, etc., will be denoted by the term " conjugation effects ". These effects, together with the one mentioned under (ii), can in principle be taken into account quantitatively by introducing the
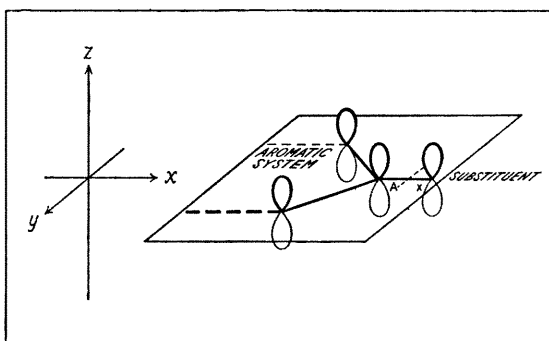

Fig. 4

appropriate parameters in the secular equations concerned. However, the choice of such parameters is very ambiguous, and if we are not dealing with the simplest kind of substituted molecule, calculations become very laborious. So here, too, one often has to fall back on qualitative considerations.

(iv) The substituent X may be in the *o*-position to a group already present in the aromatic molecule. This may give rise to effects which may be of different origin, but which we group together under " *ortho-* effects ".

To mention a few examples, —OH, —OAlkyl, halogens and —NH₂ all provide, if linked to an aromatic molecule, a doubly occupied p_z-orbital. With slightly more complicated substituents the situation is completely analogous ; e.g., if we link a carboxyl group, then the carbon and the two oxygen atoms each provide a p_z orbital, thus extending the conjugated system, while together they contribute four π-electrons. The same (three extra orbitals, four extra electrons) holds for —NO₂. In all these examples all the effects mentioned under (i), (ii) and (iii) are present. With substituents such as —NH₃⁺ and —CH₃ only the inductive effects are effective, unless we take into account " hyperconjugation ",[24] which allows for all the

[24] R. S. Mulliken, C. A. Rieke, and W. G. Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 41

conjugation effects mentioned above although, compared with " ordinary " conjugation, these are of a smaller order. As for the *ortho*-effects, it is clear that, *e.g.*, in (XI) hydrogen bridges will be formed in both the quinone and the quinol while in compounds such as (XII) there can only be a (weak) hydrogen bond in the quinol. *o*-Substituted groups may also through steric effects affect the conjugation.[25]
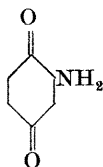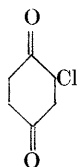
(XI.)   (XII.)

This long theoretical introduction was necessary to show clearly the complexity of the situation. In fact " simple theories, covering all experimental results " must always be looked upon with great suspicion. With this in mind we now direct attention to Tables I and II, which reproduce some of the results obtained by Fieser and Fieser [17g, l] [see also (12)].

TABLE I

Effect of substituents in the 1- or 3-position on the E^0 of 9 : 10-phenanthraquinone (alcoholic solution)

Substituent.	ΔE^0 (mv.).	Substituent.	ΔE^0 (mv.).	Substituent.	ΔE^0 (mv.).
NH_2 . .	− 98	OAc . .	+ 9	CO_2Me .	+ 58
CH_3 . .	− 64	SO_3H .	+ 23(1), + 30(3)	COPh .	+ 59
OH . .	− 50(1), − 53(3)	Br . .	+ 28	CN . .	+ 76
OCH_3 .	− 39	CO_2H .	+ 49	NO_2 . .	+ 91

TABLE II

Effect of substituents in the 2-position on the E^0 of 1 : 4-naphthaquinone (alcoholic solution)

Substituent.	ΔE^0 (mv.).	Substituent.	ΔE^0 (mv.).	Substituent.	ΔE^0 (mv.).
NHMe . .	− 252	OMe . .	− 131	C_6H_5 . .	− 32
NH_2 . .	− 210	OH . .	− 128	CO_2Me . .	− 9
NHPh . .	− 198	CH_3 . .	− 76	Cl . .	+ 24
NMe_2 . .	− 181 (aqueous)	NHAc . .	− 67	SO_3Na . .	+ 69
$OC_4H_9(n\text{-})$.	− 133	$CHPh_2$ . .	− 51	$SO_2 \cdot C_6H_4Me$	+ 121

Summarising their work, Fieser and Fieser [8] remark that " although there are minor irregularities in the order, it is seen that the groups that lower the potential of a quinone facilitate substitution in the benzene ring, whereas the groups that increase the potential retard benzene substitutions ". Thus

[25] See, *e.g.*, B. M. Webster and P. E. Verkade, *Rec. Trav. chim.*, 1948, **67**, 411.

there apparently is a correlation between the influence of substituents on different properties of the same molecules (see also section c, below), but this correlation does not offer us an explanation, for, e.g., benzene substitution constitutes a very complex problem itself.

Branch and Calvin [12] conclude that " those substituents which, through either resonance or induction, can assist the ring to accommodate a positive charge will stabilize the quinone while reducing the stability of the hydroquinone and thus reduce E^0. Similarly those groups which can assist in the accommodation of negative charge will raise the potential."

M. J. S. Dewar [26] says something similar : " Since a quinone is a cationoid ring system passing over into the anionoid hydroquinone by the uptake of two electrons it will be stabilized more by negative substituents than will be its reduction product while positive substituents will stabilize the reduction product more than the quinone."
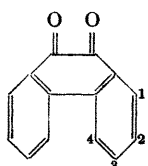
But surely the uptake of two electrons is not a simple electrostatic process, but is essentially the adding of two electrons to an available molecular π-orbital. Moreover this only constitutes the first part of the reaction $Q + 2e + 2H^+ \rightarrow QH_2$, as it will be followed immediately by the association of two protons (two OH σ-bonds being formed) as the reduction is nearly always carried out in an acid medium (compare section 2).

Inductive and conjugation effects most certainly both play their part and it is difficult to understand the overall result theoretically.

In some cases we can come to a better understanding, for evidently one or the other effect predominates. A good test for tracing conjugation effects is given by changing the position of a substituent group in the molecule. If we do this and thus vary its distance from the essential group(s) in the aromatic compound ("essential" with respect to the property we are studying), then the inductive effect on the σ-electrons should decrease with this distance while conjugation effects (together with the inductive effect on π-electrons) very often alternate (compare the o-p-activation of benzene substitutions). Such an alternation effect was reported by Fieser [17g] for the E^0's of several substituted 9 : 10-phenanthraquinones. This effect was most pronounced with OH substituents ; the results, reproduced in Table III,

TABLE III

Effect of the position of the OH *group on the* E^0 *of* 9 : 10-*phenanthraquinones*

|	Position of OH—	1.	2.	3.	4.
O O structure	ΔE^0 (mv.) (relative to the parent quinone) .	— 50	— 1	— 53	0

imply that for the 1- and 3-substituted compounds there must be a stabilisation of the quinone which (to the same extent) has no analogy in the case

[26] " The Electronic Theory of Organic Chemistry ", Oxford Univ. Press, 1949.
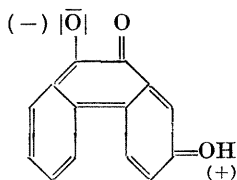
of the corresponding dihydric phenol.   Fieser himself pointed out that this is a resonance (conjugation) phenomena.   The extra conjugation stabilisation can be expressed qualitatively by the inclusion of canonical structures such as (XIII) and (XIV).   Similar structures cannot be written for the
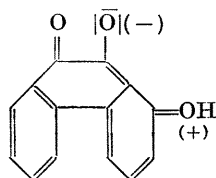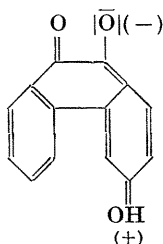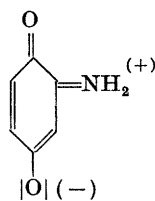

(XIII.)   (XIV.)

(XV.)   (XVI.)

2- and 4-substituted molecules unless we break the benzenoid configuration of every nucleus, as, *e.g.*, in (XV), and hence these canonical forms do not contribute much to the stability of these compounds.   The fact that the influence of an OH group in the 2- or 4-position is practically nil must be ascribed to a small inductive effect (on the σ-electrons) of the OH group.

It is clear from this discussion that the OH group affects E^0 by the stabilisation of the quinone owing to this conjugation effect.   We might now enquire what other groups we should expect on this basis to exert a similar influence.   Such will be —NH_2, acting in a way illustrated in (XVI), OAlkyl, acting in a way similar to OH by virtue of its O-$2p_z$-electrons, halogens, and finally CH_3 by virtue of its hyperconjugation.[24]   The sequence of the stabilisation of the quinone would be given by the degree of conjugation, which in its turn will be dependent on two factors : (*a*) the electronegativity of the attached centre, and (*b*) the magnitude of the resonance integral between the p_z orbital on this centre and the corresponding orbital of the carbon atom to which this centre is attached.

Little is known about the values of these quantities [organic chemists often entirely neglect the factor mentioned under (*b*) in qualitative discussions], and it is difficult therefore to arrange these groups in order.   We would however suggest tentatively the following sequence :

$$NH_2 \;>\; \genfrac{}{}{0pt}{}{OH}{OCH_3} \;>\; Cl \;>\; CH_3$$
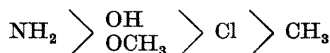
Stabilisation of the quinol on the other hand will be given by groups AB which can contribute canonical forms of the type (XVII) and (XVIII).

Such groups are CO, CO_2H, CN, NO_2. Here again the question of sequence depends upon factors of which we have no precise knowledge.

Comparing our expectations on the basis of this discussion with the numerical results listed in Tables I and II, we note that there are two important discrepancies, namely, that the apparent conjugation effect of CH_3 is much greater than what one would expect on the basis of hyperconjugation, whereas with Cl and Br the results are in complete disaccordance with our ideas.

These discrepancies only emphasise the point that we have already made, namely, that inductive effects operating on the σ-bonds must be taken into consideration in any complete theoretical treatment. In general, in organic chemistry opposite influences of CH_3 and halogens, as they often occur, have been ascribed to inductive effects, and we feel that a quantitative treatment of this phenomena is one of the greatest needs of molecular electronic theory at present.

OH   OH(+)   O
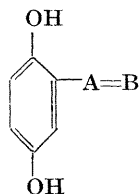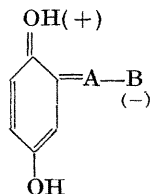
[structures]
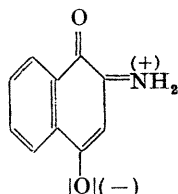
(XVII.)   (XVIII.)   (XIX.)

Two remaining points appear from Tables I and II : (1) We cannot always speak of *the* influence of a substituent group on the E^0, as this influence may depend upon the structure of the parent quinone to which it is attached. This is most marked in ·the exceptional case of the carbomethoxy-group, which causes a slight increase in the potential of 9 : 10-phenanthraquinone, but lowers that of 1 : 4-naphthaquinone. (2) In general, the influence on E^0 is more pronounced in the case of naphthaquinone. We can understand this, for (i) inductive effects on the σ-electrons will be greater (shorter distances to the important groups), and (ii) conjugation-stabilisation, which is reflected by the consideration of structures such as (XIX), need not break the benzenoid structure of any nucleus.

ortho-Effects will certainly play their part in determining the E^0 of many of the quinones of Tables I and II, but it is difficult to separate their influence from other factors. Prelog *et al.*,[27] however, have shown that *ortho*-effects are predominant in determining differences in E^0 between quinones of the type (XX), n varying from 9 to 19. For large values of n the potential

$$[CH_2]_{n-3} \qquad O=\!\!\!<\!\!\!>\!\!\!=O$$
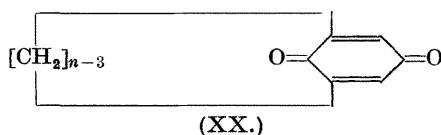
(XX.)

[27] V. Prelog, O. Häfliger, and K. Wiesner, *Helv. Chim. Acta*, 1948, **31**, 878 ; V. Prelog, K. Wiesner, W. Ingold, and O. Häfliger, *ibid.*, p. 1325 ; see also *J.*, 1950, 420.

approaches that for 2 : 6-dimethyl(or diethyl)-*p*-benzoquinone, but from $n = 13$ the potential rapidly decreases with a further decrease in n. By a careful analysis, Prelog *et al.* conclude that the lowering of the potential has to be ascribed to hydrogen-bridge formation between the methylene groups and the oxygen atom. Evidently this will stabilise the quinone more than the corresponding quinol, as the oxygen atom is more negative in the former case. It is admitted that the tension caused by the quinonoid or benzenoid ring system by the smaller polymethylene rings might also be of importance.
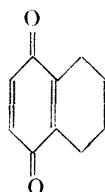
In this connection we refer to the work of R. T. Arnold and H. E. Zaug,[28] who showed that the potential of indane-4 : 7-quinone (XXI) is much larger than that of 2 : 3-dimethylbenzoquinone (XXII) or 5 : 6 : 7 : 8-tetrahydronaphtha-1 : 4-quinone (XXIII), the last two compounds differing but little in
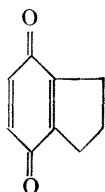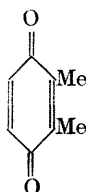

(XXI.)   (XXII.)   (XXIII.)
(641 mv.)   (588 mv.)   (585 mv.)

potential. Hydrogen bridges will not be of much influence in (XXI), so the tension caused by the presence of the five-membered ring which, according to Arnold and Zaug, will reduce the stability of the quinone more than that of the more flexible quinol system, must be the predominant factor. We might consider these experiments as a support to Prelog's hydrogen-bond theory, though, strictly speaking, the two cases cannot be compared directly.

(c) **The Influence of Substituents and Hammett's σ-Constants.**—P. G. Carter [29] has discovered a linear relationship between the E^0 of many substituted quinones and the σ_p-constants used by L. P. Hammett.[30] Admittedly, there are exceptions and the linearity is often approximate but there appears to exist an underlying relationship. We find this relationship surprising in its simplicity for the following reasons : (i) Hammett's σ-constants have been applied with great success to the reactivity of single groups attached
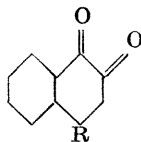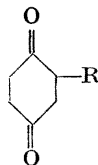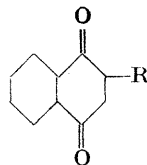
(XXIV.)   (XXV.)   (XXVI.)

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[28] *J. Amer. Chem. Soc.*, 1941, **63**, 1317.
[29] I.C.I. Laboratories, Blackley ; private communication.
[30] See, *e.g.*, " Physical Organic Chemistry ", New York, McGraw-Hill, 1940.

to the benzenoid ring. Here we are considering, however, the quinonoid nucleus, and moreover, the E^0's are related to the behaviour of two centres. (ii) Only in 3-substituted phenanthraquinones is the substituent in the p-position (or in a position equivalent to that) to one of the two important centres, and at the same time it is so far away from the other that it might have no influence ; but in all other cases mentioned by Carter the situation is ambiguous ; $e.g.$, in (XXIV) we would expect a relation between E^0 and the average of σ_m and σ_p and not with σ_p as such, while in (XXV) and (XXVI) the linear relationship is even more surprising as R is in an m-position to one important group and in an o-position to the other.

We would conclude from these remarks that Carter's relationship, simple though it appears, cannot have the same weight as the σ-constant relationship has in the systems to which Hammett originally applied his ideas.

5. Special Topics

(a) **Berliner's Empirical Relation between Resonance Energies and the Oxidation–Reduction Potentials.**—Berliner[16] has obtained, by subtracting from the known heats of combustion a standard energy based on a set of standard bond energies, what he called " empirical resonance energies " for a number of very different types of quinones and dihydric phenols. He found a linear relationship between $(R_{QH_2} - R_Q)$, thus determined, and E^0.

That such a relationship was obtained for a series of such different compounds, including substituted quinones, is entirely understandable since, apart from a constant term, Berliner's $(R_{QH_2} - R_Q)$ measures the difference in total electronic energy. His " resonance energy " is different therefore from that defined by us in this Review. We have confined it to the " delocalisation energy " of the mobile system of π-electrons, whereas Berliner's method must include as well the differences in energy of certain σ-bonds, expressed in terms of ionic–homopolar resonance in these particular bonds. We would suggest that in speaking of resonance energy one should be careful to define exactly what one means and if possible to confine oneself to one type of electronic system. Neglecting entropy, solvation, and $ortho$-effects, it would have been strange had Berliner not obtained a linear relationship, and it seems to us, that, while we have shown that the π-electronic system is of predominant importance in the case of certain unsubstituted quinones, Berliner's treatment does not bring us any further in understanding the E^0's of more complicated systems.

(b) **Pullman's Quinodimethane Treatment for Unsubstituted Quinones.**—A. Pullman, G. Berthier, and B. Pullman [31] have recently made an extensive study of the π-electronic structure of several quinodimethanes such as p-benzoquinodimethane (XXVII). One has often considered these molecules as prototypes for quinones,[32] as it is easier in theoretical work to

[31] $Bull.\ Soc.\ chim.$, 1948, **15**, 450.
[32] C. A. Coulson, D. P. Craig, A. Maccoll, and Mme. A. Pullman, " The Labile Molecule ", $Faraday\ Soc.\ Discussions$, 1947, 36 ; Diatkina and Syrkin, $loc.\ cit.$, ref. (14) ; M. Diatkina, A. J. Namiot, and J. Syrkin, $Compt.\ rend.\ Acad.\ Sci.\ U.R.S.S.$, 1945, **48**, 233 ; M. G. Evans, J. Gergely, and J. de Heer, $Proc.\ Physical\ Soc.$, 1949, **62**, A, 505.

perform calculations on the former type of molecule. Pullman *et al.* have calculated the " free valencies " [33] of the end carbon atoms (equivalent to the oxygen atoms in the corresponding quinones) and the

$CH_2 =$ $= CH_2$

(XXVII.)

" bond-orders " [33] of the $C=CH_2$ bond (equivalent to the $C=O$ bond). Obviously, both quantities are inter-dependent ; the greater the free valency of the carbon atoms concerned, the smaller the double-bond character in those bonds.

Pullman *et al.* discovered a linear relationship between the bond orders in the $C=CH_2$ bonds and the E^0 of the corresponding unsubstituted quinone. It is difficult to see what meaning is to be attached to these results, for certainly the E^0's should be determined by the structure of the quinols formed on reduction as well as by the structure and reactivity of the quinones. We believe that both in equilibrium and reactivity problems it is necessary to consider not only the initial state of the system involved but also the structure which is being formed.

As Pullman's method is just another way of dealing approximately with π-electronic systems, it can add no more to our understanding of the influence of substituents than we have been able to discuss in the foregoing pages.

[33] For a definition of these quantities, see, *e.g.*, C. A. Coulson, "The Labile Molecule", *Faraday Soc. Discussion*, 1947, 9.