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CHARGE TRANSFER IN BIOLOGY

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November 1965

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INTRODUCTION

In the context of biochemistry, the topic of charge transfer has been most closely associated with the donor-acceptor complexes. The research activity on the chemical and physical aspects of donor-acceptor complexes has been impressively on the increase, and, quite like a dose-response curve, interest in the biological implications of the new results has closely followed. We have attempted to present the topic of transfer of charge from a somewhat wider frame of reference than complex formation. Yet, clearly this topic, which can span the entire range of possibilities from weak interactions to full-fledged redox reactions in organic, inorganic or mixed systems, is so large that it could not be completely covered in less than a monograph. As a result, the decision as to what aspects would be emphasized largely reflects current interests, mostly our own. In Part I we have presented solution properties of the donor-acceptor complexes. Two books and a review dealing with the general area of donor-acceptor complexes have recently appeared, covering the topic from the point of view of the physical chemist^{1,2} and from the point of view of the organic chemist.³ Another review,⁴ dealing mainly with reactions, is imminent. Despite the availability of these, it nevertheless seemed well for us to cover enough of the fundamental aspects of the topic to make this chapter more or less self-contained. However, particular emphasis has been placed on the more recent literature and those areas which seemed most germane to our purpose--a consideration of the biological aspects of the topic. Szent-Gyorgyi's recent book⁵ is also largely devoted to the possible role of donor-acceptor complexes in biology. Special aspects of charge-transfer interactions such as hydrogen bonding must here be totally neglected. Charge transfer in metal ion complexes, a large topic

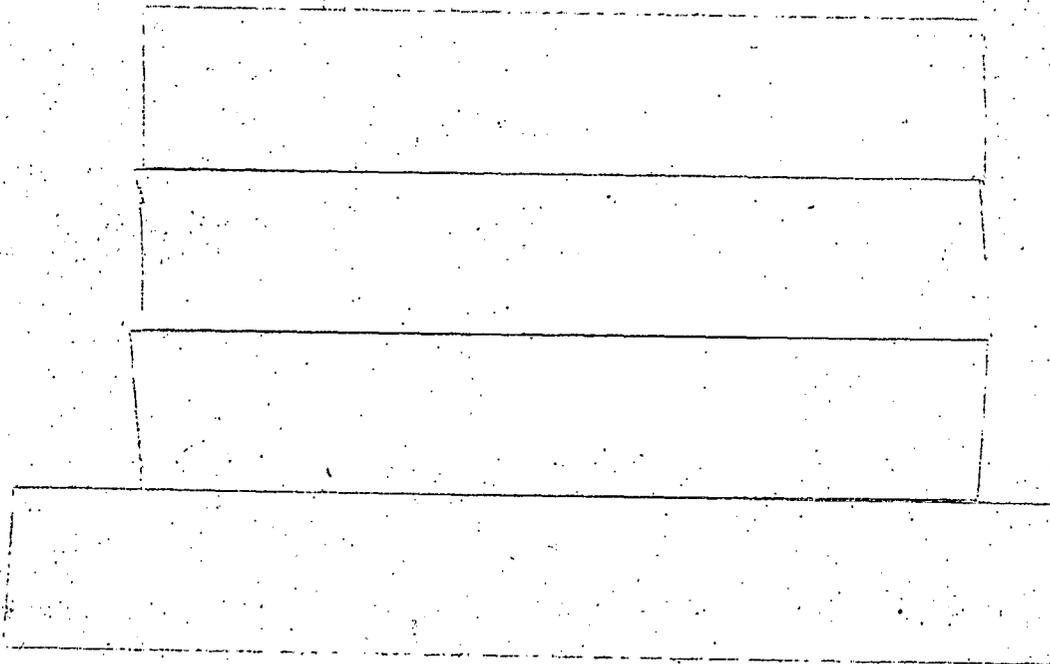
in its own right, is treated only superficially.

The second part of the chapter will attempt to survey transfer of charge from the point of view of semiconduction and, in particular, photoconduction. At present, the surge of interest in these fields stems more from the activities of the solid state chemists and physicists than from those of the biochemist. The situation insofar as biochemistry is concerned is not really well defined. Yet, as the important role of organized structures in living systems continues to emerge, it seems well that biochemists in general should have an awareness of the recent advances in these areas.

PART I. DONOR-ACCEPTOR COMPLEXES IN SOLUTION

Energetics

As confusion on occasion has arisen, we should first define our terms. For complexes of the sort to be considered here, resonance contributions of the type drawn in Fig. 1 will play a role in defining the energetics.



In accord with the distinction made by Mulliken and Person,⁶ the term "charge transfer complex" will be applied to those complexes where the resonance interaction, R_N , makes the predominant contribution to the overall stability of the complex in the ground state (see Fig. 2). The term "donor-acceptor complex" will be applied to those complexes where the resonance contribution to its overall stability is less than that due to other factors such as dispersion forces, dipole-dipole interactions, etc. In order that the concept of a donor-acceptor and charge transfer complex remain experimentally distinct from other possible types of complex, the donor-acceptor and charge transfer complexes should

exhibit a charge transfer absorption band. The origin and some characteristics of this absorption will be discussed below. This is a more restrictive definition than that adopted in a number of biochemical papers. In our view, the value of the donor-acceptor concept is in its being subject to an unambiguous experimental test. That test, in this case, is the appearance of a new absorption band and is, in fact, the only proper one. To those complexes experimentally demonstrable by any physical method, but not conforming to the above definitions by displaying a charge transfer band, we apply the general term "molecular complex".

In Mulliken's valence bond approach⁷ the donor-acceptor complex, DA, is considered to be described by a wave function which may be written

$$\Psi = a\psi(DA) + b\psi(D^+A^-)$$

As in Fig. 1, we are stating in this relation that the ground state of the complex is described by taking some combination of the wave function $\psi(DA)$ describing D ... A (formula I, Fig. 1) and $\psi(D^+A^-)$, describing D^+A^- (formula II, Fig. 1). In the term $\psi(DA)$, the "no bond" wave function, we include all the dipole-dipole, van der Waals-London and dipole-induced dipole forces. $\psi(D^+A^-)$ is termed the "dative bond" wave function. The value of the coefficient a may be greater or less than b, but generally $a \gg b$. For the case $b \gg a$, to which we shall return later, the complex is ionic in the ground state, since D^+A^- predominates. In the case of a complex between a weak Lewis acid and a weak Lewis base, a third term $\psi(D^-A^+)$ is added to the total ground state wave function. In such cases $D^+A^- \rightleftharpoons D \dots A \rightleftharpoons D^-A^+$ is a closer resonance description. The total wave function can then be taken as

$$\Psi = a\psi(DA) + b\psi(D^+A^-) + c\psi(D^-A^+)$$

The energetics of charge transfer complex formation are depicted in Fig. 2, but with neglect of possible solvation effects. The zero point of energy is taken as the energy of the separated donor and acceptor molecules. Bringing these molecules together to the normal equilibrium distance for the complex (about 3.5 \AA) without permitting resonance interaction forces to operate results, in the case depicted, in a lowering of the energy by an amount, W_0 . In practice this term could conceivably be a repulsive term. The resonance interaction with the charge transfer structure D^+A^- further lowers the energy of the pair by an amount R_N . The total intermolecular binding energy, $\Delta H = W_0 + R_N$. Typical experimental ΔH values range from a few hundred calories to about 7 or 8 Kcal mole⁻¹. A breakdown of the contributions of W_0 and R_N to the total ΔH is given in Table I for a few cases. These experimental values are obtained by an indirect method. It involves an experimental determination of the dipole moment of the excited state of the complex and working through a lengthy series of equations which have been derived by Briegleb (see footnote a of Table I for reference).

By addition of a proper sized quantum of light (the charge transfer energy $h\nu_{CT}$), a nearly complete transfer of an electron from donor to acceptor may be induced with formation of an excited state of greater polarity. An expression for the energy of the excited state is readily derived from Fig. 2, as follows: The ionization potential, I , of the donor corresponds to $D \longrightarrow D^+ + e$, and the electron affinity, E_a , to $e + A \longrightarrow A^-$. The coulomb energy term, E_C , and the resonance interaction, R_E , contribute as indicated in the figure, and the energy of the excited state becomes, by adding the individual contributions

$$W_E = I_D - E_a - E_C + R_E$$

The reader may question why the resonance interaction raises the energy of the excited state but lowers that of the ground state (cf. Fig. 3). A purely mechanical explanation lies in the fact that the selection rule for the charge transfer transition requires the wave function of the excited state to be an odd function (interchanging terms changes the sign of the function). The wave function must, therefore, be taken as

$$\Psi = a\psi(D^+A^-) - b\psi(DA)$$

where the negative sign assures oddness. In the standard variational calculation of the energy by the Ritz method,⁸ the negative sign in this wave function causes the second order perturbation term (resonance energy term) in the expression for the energy to be of opposite sign from the resonance energy term of the ground state. However, real understanding comes by considering electron repulsion effects. For the ground state, the perturbation is a delocalization of a donor electron into an empty acceptor orbital. The decrease in electron repulsion lowers the energy. For the ionic excited state, the perturbation is the introduction of a little ground state localization. The electron repulsion increases, and the energy is raised.

The energy of the charge transfer transition is then

$$W_E - W_N = h\nu_{CT} = I_D - E_a - E_c + R_E - W_0 - R_N = I_D - E_a + \Delta$$

where several factors have been absorbed in the term Δ , which is approximately constant for many complexes having a common donor or acceptor.

In the molecular orbital approach to the description of donor-acceptor complexes favored by Dewar,⁹ the orbitals are considered to extend over the entire complex. For weak complexes, the donor-acceptor interaction between the highest filled bonding orbitals of donor and the lowest empty orbitals of acceptor is considered as a perturbation. The new orbitals

for the weak complexes will be very similar to the orbitals of donor and acceptor separately, but with the energy levels of donor slightly lowered and those of acceptor slightly raised (Fig. 4). In molecular orbital theory the ionization potential of the donor is approximately equal to minus the energy of the highest occupied m.o. and the electron affinity of acceptor to the energy of the lowest unoccupied m.o. The energy of the first charge transfer transition (solid arrow in Fig. 4) is given as before by

$$\Delta E = h\nu_{CT} = I - E_a + \Delta_s$$

where Δ is a term resulting from the perturbation. The dashed arrows in Fig. 4 represent the spectroscopic transitions characteristic of the donor and the acceptor. It is important to realize the following points. Perturbations resulting from neighbor interactions can occur in complexes in the absence of a resonance interaction such as in Fig. 1 and can cause small shifts in the absorption maxima of the components. Hypochromic effects and band broadening can be explained without invoking an intermolecular donor-acceptor interaction.¹⁰

In the m.o. description the charge transfer interaction will be inversely proportional to the difference in energy between interacting orbitals. Extensive tabulations of the results of Hückel calculations for many molecules of interest in biochemistry have been published in the Pullman's' recent book,¹¹ and may serve as a guide for the experimentalist. But, if need be, one should not hesitate to resort to chemical considerations in predicting donor-acceptor compounds. Clearly, species capable of undergoing a facile oxidation (a measure of ease of electron loss) such as iodide ion, hydroquinones, amines and phenols should be donors. The donor strength of π -systems should be increased by electron

donating groups such as alkyl, $-NR_2$, $-OH$, and $-O-CH_3$. Species capable of undergoing a ready chemical reduction (electron gain) such as iodine, oxygen, quinones and riboflavin should be acceptors. Acceptor strength should be increased by electron withdrawing substituents such as $-CF_3$, $-CN$, $-SO_3H$ and $-C \begin{array}{l} \text{O} \\ \parallel \\ \text{OR} \end{array}$.

Using a given acceptor, the linear correlations anticipated above between the energy of the charge transfer transition and the ionization potential or calculated energy of the highest occupied molecular orbital of donor have been observed.^{12,13} Experimental values for electron affinities are accessible with difficulty. However, the expected relationships between the energy of the charge transition and first half wave reduction potential¹⁴ (Fig. 5) and/or the calculated energies of the lowest unoccupied molecular orbital of the acceptor¹⁶ have been observed.

An important concern in dealing with complexes is the matter of stability or trends in stabilities. The free energy of complex formation is not intimately related to such parameters as ionization potential, electron affinity, or charge transfer transition energy. The reasons are several. First, a considerable contribution to the enthalpy part of the free energy term is from van der Waals or other forces (cf. Fig. 2 and Table I). It is not expected that these forces will be related in any simple way to the above parameters. The entropy contribution to the free energy probably strongly reflects solvation differences and again no simple correlations are anticipated. The scatter of points in Figs. 6, 7 and 8 undoubtedly reflects such effects as we have described. Nevertheless, the rough correlations evident from the figures between ionization potential, electron affinity, or charge transfer energy, and complex

stability may be useful for predictive purposes.

Other Characteristics of the Charge Transfer Absorption Band

The charge transfer band is always broad, frequently asymmetric, and devoid of vibrational fine structure, even at low temperatures. The broadness and lack of fine structure are undoubtedly due to small variations in the equilibrium distance between partners. Because of the broad and asymmetric character of the charge transfer absorption, it may often be difficult to determine the position of the absorption maximum precisely. However, fine structure has on at least one occasion been observed in the charge transfer band. This is in the donor-acceptor complexes of menadione with 3,5-diiodotyrosine or 3,5-dibromotyrosine.¹⁸ (Fig. 9). This was attributed, in this atypical case, to a superposition of the singlet-triplet transition of the quinone which becomes increasingly allowed due to the fact that the halogen atoms cause a breakdown of the spin selection rules by spin-orbit coupling. The evidence in favor of assigning a very weak absorption at 535 m μ in p-benzoquinone to a singlet-triplet transition has recently been reviewed.¹⁹

Briegleb has noted²⁰ that a fairly good empirical correlation exists between ν maximum (cm^{-1}) and the position of half maximum height of the charge transfer absorption band, $\nu_{\text{max}} - \nu_{1/2} \approx .104 \nu_{\text{max}}$. For the few cases of complexes of biological molecules where sufficient data has been reported to enable comparison within a series, we find that the band shapes deviate from Briegleb's correlation. Whether this is attributable to the fact that the charge transfer bands, frequently reported as difference spectra, are not authentic or due to other reasons is not clear. Briegleb also reports²⁰ that within a series, the half width at half

height varies inversely with the heat of formation of the complex. Thus, weak complexes will show the broadest charge transfer absorption bands.

Some donor-acceptor complexes show two distinct maxima in the charge transfer band. Examples are the complexes of certain substituted benzenes and tetracyanoethylene (TCNE).²¹ The most likely explanation of the multiple maxima is as follows: In molecules of high symmetry such as benzene the highest occupied molecular orbitals are degenerate (Fig. 10). On substitution of the benzene ring, the degeneracy is removed, and the two orbitals now split to an extent depending on the number of substituents, their nature and relative position on the ring. The resulting two electronic levels have two different ionization energies, and the transitions from each are no longer equienergetic.

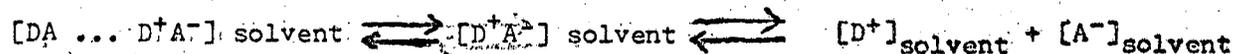
In crystals, where the orientation of the molecules of the donor-acceptor complex relative to the crystal axis is fixed, it is possible to determine the direction of polarization of the transition moment of the charge transfer absorption by using polarized light. The light absorption by the crystal is greatest when the electric vector of the incident polarized light is parallel to the direction of polarization of the transition moment of the absorption band (Fig. 11). Historically, such a study of the quinhydrone (p-benzoquinone-quinol) complex²² provided important support for Mulliken's theory which predicted that the direction of charge transfer should be from donor to acceptor ring. Recently a reinvestigation of this complex using a technique for obtaining polarized reflection spectra²³ rather than polarized absorption spectra has shown the old data to be somewhat in error. In the quinhydrone crystal it is known from X-ray studies that the molecules are

oriented with their planes parallel, and tilted 34° from the direction of the needle axis of the crystal (Fig. 12). The reflection spectra obtained from the prominent face of the crystal and the direction of the polarization of the light are reproduced in Fig. 13. From the essentially plane curve observed for light polarized along the b axis it was concluded that the charge transfer moment was exclusively along the needle (a) axis and therefore directed between the centers of the six-membered ring (Fig. 14). Nakamoto's study²² had indicated a small absorption component along the b axis and a direction of polarization of the transition moment perpendicular to the plane of the rings.

A result completely analogous to that of Anex and Parkhurst has been obtained for a complex of coronene and chloranil by Ilten and Sauer in this laboratory.^{23a}

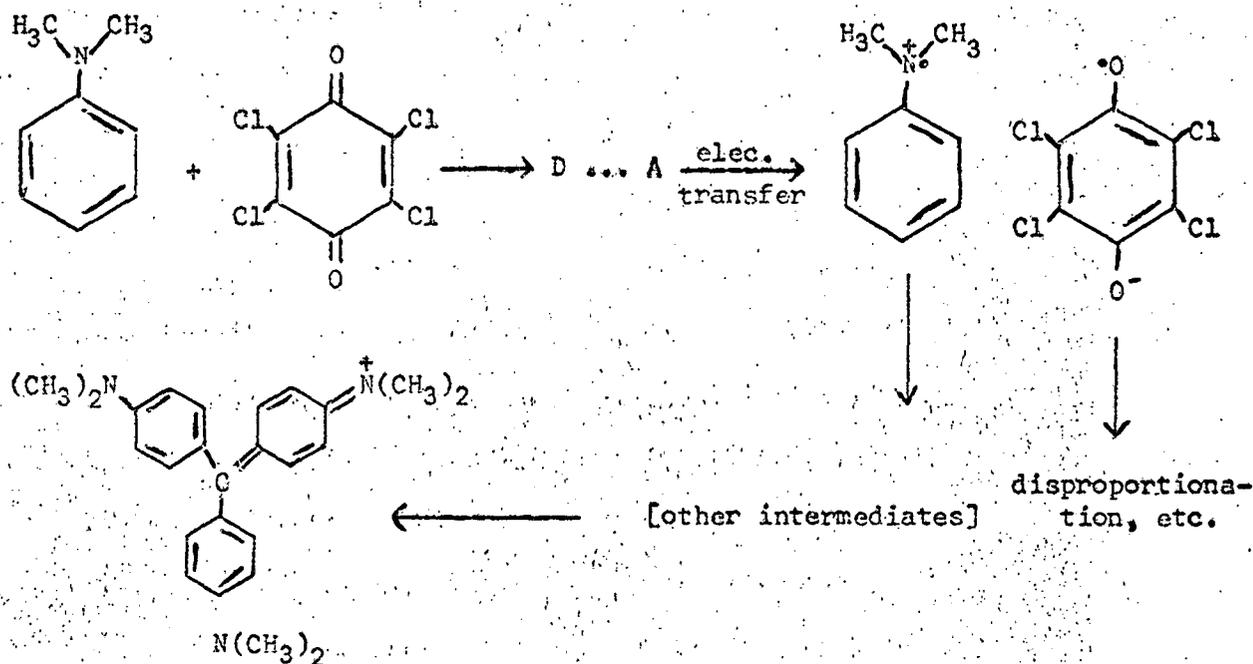
Paramagnetic Complexes and Electron Transfer Reactions

Complete transfer of an electron from donor to acceptor can occur thermally with formation of an ionic species. This corresponds to the $b \gg a$ case referred to on page 4. A potential energy diagram illustrating this situation is given in Fig. 15. In solution, the thermally induced electron transfer may go through a "tight" ion pair on the way to solvent separated ions.



The radical ions formed should show an ESR (electron spin resonance) signal, but frequently a signal characteristic of only one species is observed. This is presumably due to disproportionation of one radical. A further point of interest regarding these electron transfer reactions is that the activation energy for the thermal reaction may be lower than

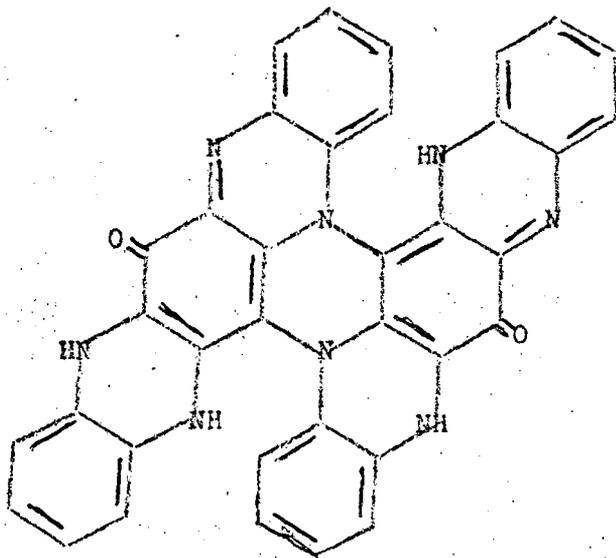
and semiquinone radical were identified as intermediates. The overall course of the reaction is apparently



The intermediate steps must involve an intermolecular methyl migration.

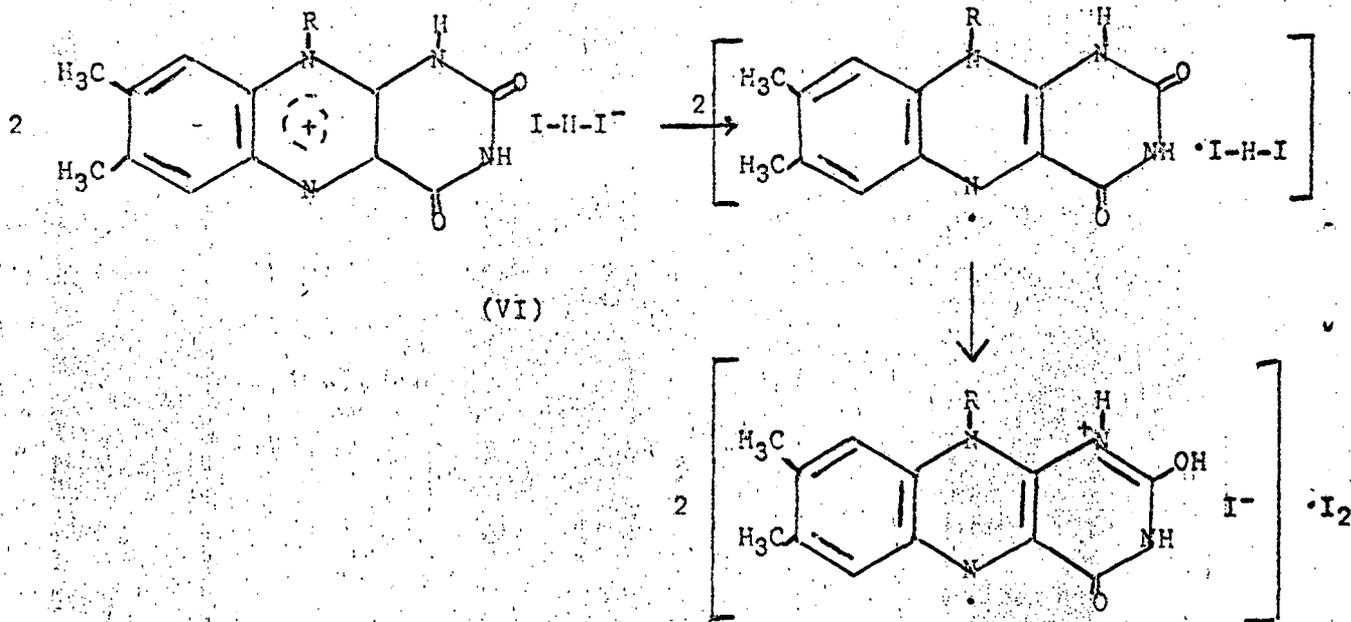
It is of interest that unsubstituted o-phenylenediamine and chloranil react²⁶ under nitrogen with displacement of halogen to yield a dimeric quinone amine of suggested structure (V) (four moles of amine, two of quinone). Therefore, in dealing with chloranil as an acceptor, one must also be cognizant of possible displacement reactions, particularly with amine donors. The displacement may occur subsequent to complex formation.

Recently a remarkable complex of riboflavin hydroiodide and HI has been reported by Fleishman and Tollin.²⁷ This material, obtained by evaporating a solution of riboflavin in 47% hydroiodic acid-ethanol mixtures occurs as pink platelets. The analytical data suggest the stoichiometric composition, riboflavin hydroiodide:HI (1:1). The visible absorption spectrum of the solution and solid corresponds to that of protonated



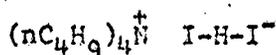
(V)

riboflavin semiquinone. The material shows an ESR signal characteristic of the semiquinone and of such intensity that the material must be 100% radical. It seems quite likely that this material is derived from the hydrogen diiodide salt of riboflavin (VI) by an electron transfer from the anion. This complex is then similar to the complex of p-phenylenediamine and chloranil in this respect. Hydrogen dibromide and dichloride

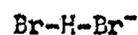


(VI)

salts of ammonium ions are known²⁸ and a tetra alkylammonium hydrogen diiodide (VII) has recently been prepared.²⁹ Hydrogen dibromide salts of carbonium ions (VIII) were also reported²⁹ and show a charge transfer absorption band.

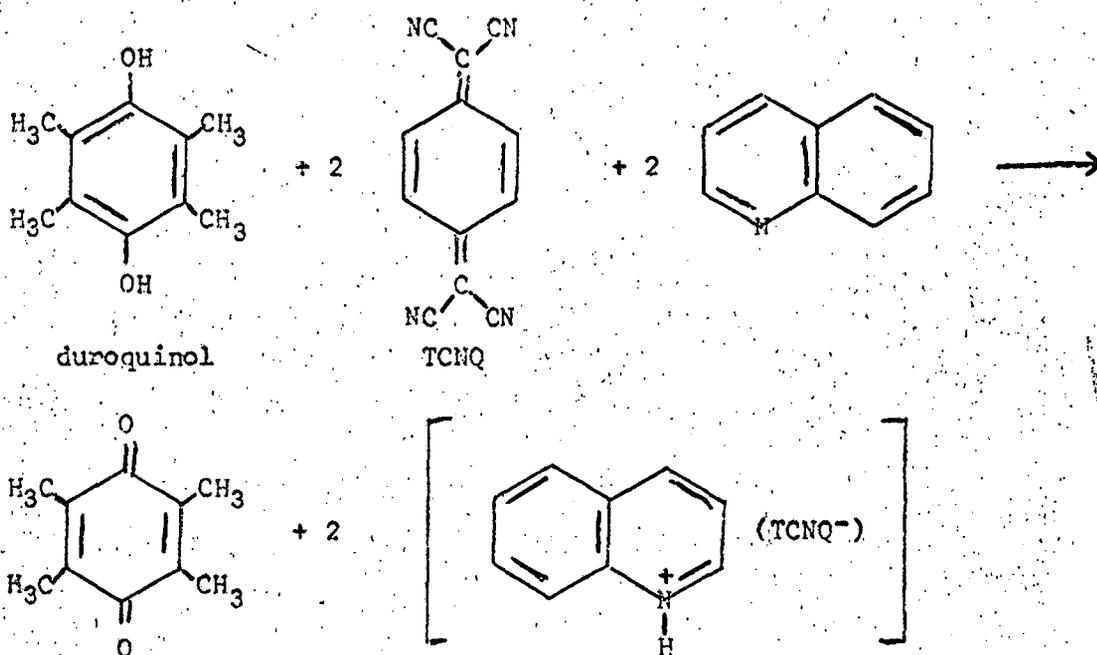


(VII)



(VIII)

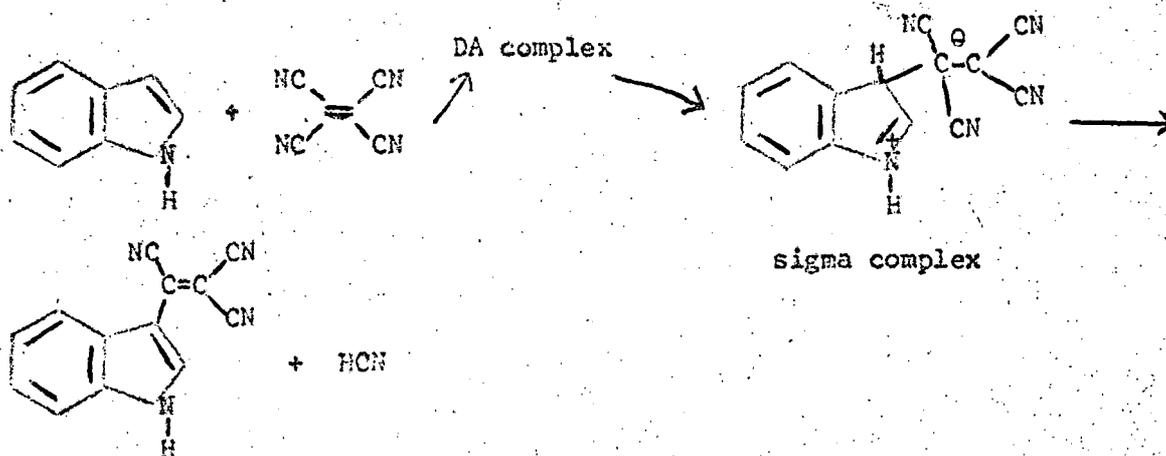
Some other oxidation reactions may follow the general course of complex



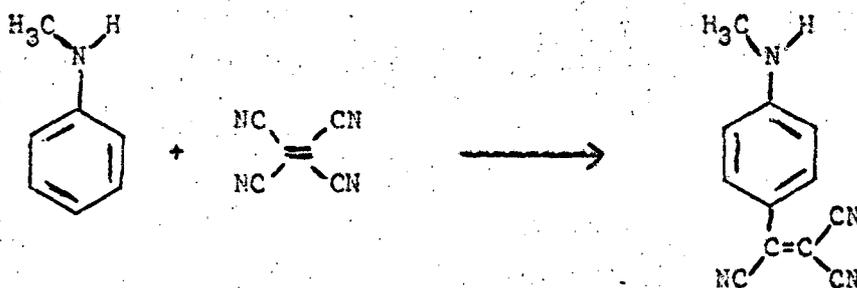
formation followed by electron transfer. The oxidation of duroquinol by 7,7,8,8-tetracyanoquinodimethide (TCNQ), an excellent electron acceptor, in the presence of a proton acceptor has been reported.³⁰

As with chloranil, one should be aware of the possibility of a displacement reaction with TCNQ or TCNE (tetracyanoethylene). Indole has been observed to react with TCNE³¹ in solution at ordinary temperatures.

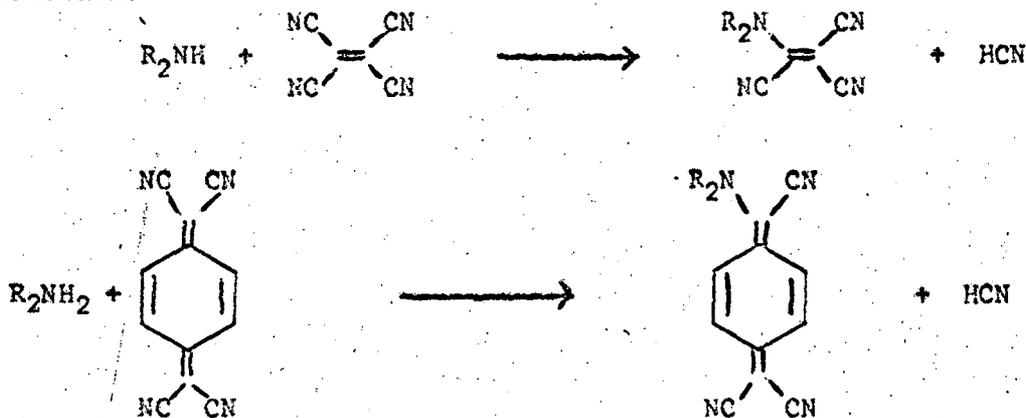
A reaction with N-alkylanilines is also observed.³² Displacement by amines of a



cyano group from TCNE³³ and TCNQ³⁴ has been observed. Formation of these

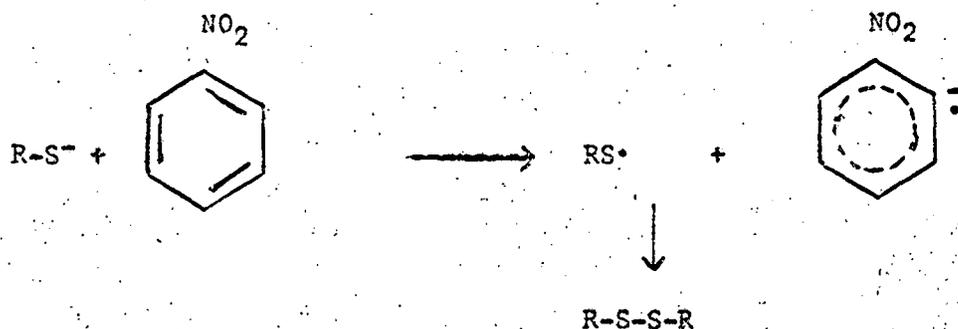


latter products is accompanied by a pronounced bathochromic shift in the absorption spectrum which should not be interpreted as due to complex formation.

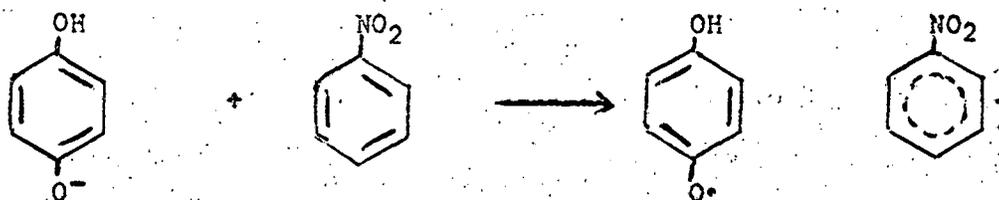


Mercaptide is oxidized anaerobically to disulfide in the presence of nitrobenzene³⁵ or other good electron acceptor.³⁶ The nitrobenzene

anion radical may be detected by ESR.

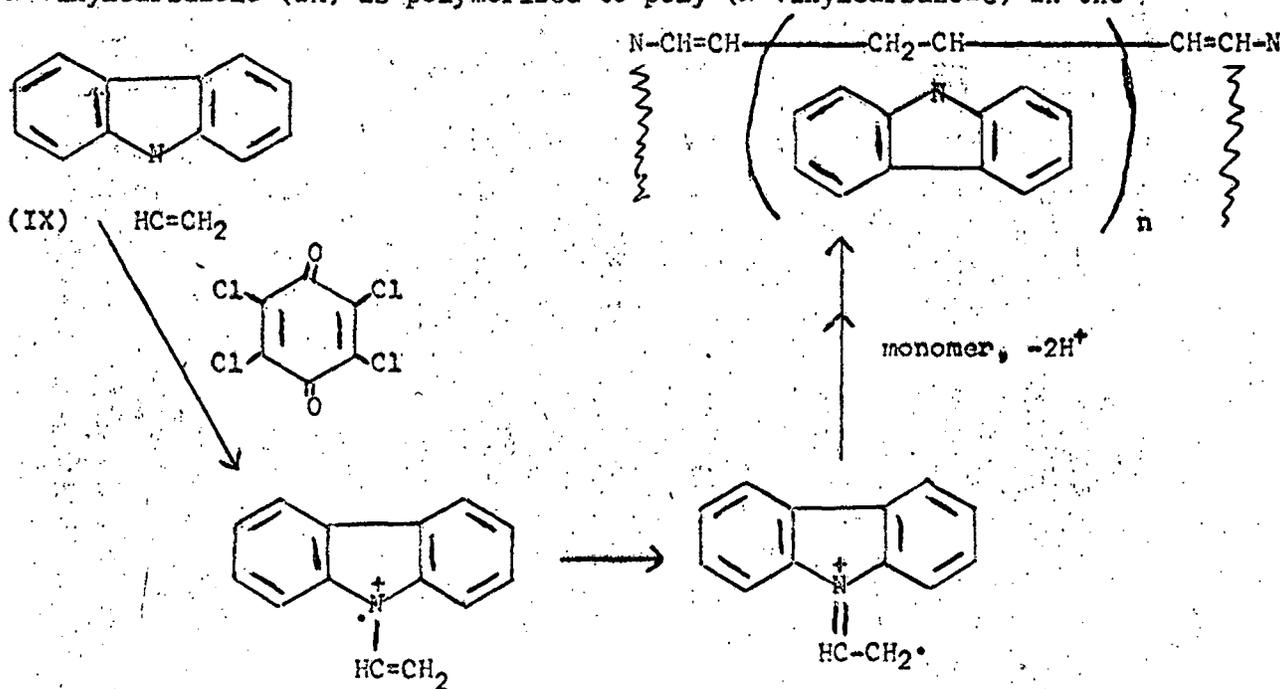


Russell and his coworkers³⁷ have noted a redox reaction between the monoanion of 1,4-quinol and nitrobenzene. Both product species were detected by ESR. They were also able to detect the nitrobenzene anion radical when carbanions were used as donors.

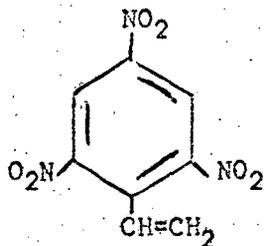


Charge transfer has also been used to initiate polymerizations.

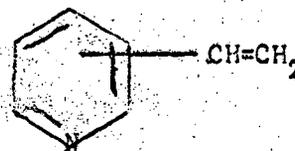
N-vinylcarbazole (IX) is polymerized to poly (N-vinylcarbazole) in the



presence of p-chloranil, tetracyanoethylene and tetracyanoquinodimethane, among others.³⁸ There is some evidence that complex formation precedes electron transfer as suggested above for the reaction leading to crystal violet. A mechanism such as that outlined is favored by the authors. It appears, however, that electron delocalization may be adequate to induce polymerization. Trinitrostyrene (X) copolymerizes exothermically with vinylpyridines (XI) on mixing solutions of the two.³⁹ Free radical formation as an initiating step appears less likely here.



(X)



(XI)

We cannot undertake here a systematic treatment of the many cases of electron transfer from zero valent metals to hydrocarbon acceptors capable of yielding anion radicals, although these processes involve transfer of charge in a broad sense.⁴⁰ Also beyond the somewhat arbitrary scope of this chapter is a detailed consideration of the mechanisms of electron transfer between inorganic metal ions via inorganic or organic bridging groups.⁴¹

For discussion of magnetic resonance methods for determining the rates of electron exchange between radicals of the type we have considered in this section, one may consult, among others, the recent book of Caldin⁴² or the chapter of Fraenkel.⁴³

Equilibrium Constants

It is not our purpose to review in detail here the numerous procedures available for determining equilibrium constants, as they have been amply treated elsewhere.^{44,45} As a number of authors have recently emphasized, the determination of an equilibrium constant and a molar extinction coefficient should be part of the characterization of any donor-acceptor complex. This is not an entirely trivial matter, however, and we will discuss a few recent papers in which some of the pitfalls have been exposed.

Person⁴⁶ has discussed the use of the Scott equation (1) in some detail.

$$(1) \frac{[D][A]\ell}{\Delta O.D._k} = \frac{1}{K\epsilon} + \frac{1}{\epsilon}[D]$$

$\Delta O.D._k$ is the absorption due to complex at wavelength k , K is the equilibrium constant, ϵ the molar extinction of complex, ℓ the optical pathlength and the remaining terms represent donor and acceptor concentrations. The absorption due only to complex ($\Delta O.D.$), which is the absorption of the mixture at wavelength k minus the sum of the absorption due to components, is determined for a series of donor concentrations. The left side of equation (1) is then plotted versus donor concentrations and extrapolated to the intercept to determine K . For weak complexes, since the concentration of complex is small, the points plotted as the left side of equation (1) may not be very different from the intercept. Difficulty is then experienced in obtaining a reliable non-zero initial slope in the plot of the data. This slope is obviously important since the determination of K involves an extrapolation. Person⁴⁶ has set the optimal concentration range for use of equation (1) (for the case of excess donor) at

$$.1 \left(\frac{1}{K} \right) < [D] < 9 \left(\frac{1}{K} \right)$$

where K is the equilibrium constant. These limits may be a little flexible,

but one should proceed by first obtaining a rough value for K, then planning optimum concentration ranges for final runs.

A different approach to a systematic study of the effects of experimental errors has also appeared.⁴⁷ A computer program was developed which enabled ready calculation of the equilibrium constant from input experimental data. Beginning with synthetic data (no errors) small errors were deliberately introduced into the input data--for example, amounting to a weighing error of 0.3 mg in 20-500 mg, or an instrumental error of $\pm .003$ absorbance units. Recalculation of the constant revealed that for certain concentration situations the determined equilibrium constant could be extremely sensitive to small experimental errors. The same conclusion was reached when K was determined by a graphical method with the same data. This again emphasizes the need for careful planning of experimental conditions.

In a second study,⁴⁸ again employing synthetic data, multiple equilibria were considered. The results indicate that the presence of some 1:2 complex may not be detected as a deviation of the data from a linear plot of the usual sort. Johnson and Bowen specifically considered the data plots obtained with equation (2) (the Benesi-Hildebrand equation), but the conclusions will presumably apply to all similar equations.

$$(2) \quad \frac{[A]}{\Delta \text{O.D.}} = \frac{1}{\epsilon} + \frac{1}{K\epsilon[D]}$$

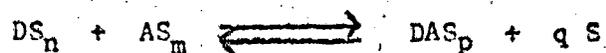
(The Benesi-Hildebrand equation where the terms are as described previously)

Experimentally, the presence of higher order complexes may be manifest as variations of the determined equilibrium constant with wavelength, or as a variation of the integrated intensity of the charge transfer

band with temperature. Practically speaking, the effects are often small and one could probably conclude that the major absorbing species is a 1:1 complex if the data fit a linear plot of the Benesi-Hildebrand type. Methods are available for an independent experimental determination of the stoichiometry of a complex (cf. references 44,45).

Contact Charge Transfer

Mulliken's theory of charge transfer spectra predicts that for weak complexes the molar extinction coefficient of the charge transfer band should be low. There have been many difficulties in demonstrating this expectation experimentally. For weak complexes, attempts to determine both the equilibrium constant and extinction coefficient experimentally [for example, using equation (1) or (2)] often gave the point of intercept in the extrapolation as zero. This indicated either that as $K \rightarrow 0$, $\epsilon \rightarrow \infty$, or vice versa, which was contrary to that anticipated from the theory. In an attempt to explain this difficulty Orgel and Mulliken⁴⁹ put forward the concept of contact charge transfer. In essence this theory stated that a charge transfer transition could occur between two molecules [D,A], which just happen to be together through chance collisions without forming a real complex. The observed extinction coefficient would then be the sum of the actual extinction and some contribution from chance contacts. It has now been shown⁵⁰ that a satisfactory theory for weak complexes can be based on the idea of competition between solvation and complexing by writing the equilibrium expression as



where S represents the solvent. By taking proper account of solvent, it was shown that the relationship between ϵ and K anticipated from Mulliken's early theory could be observed. The upshot is that it now seems unnecessary

to retain the concept of contact charge transfer.

Solvent Effects

The effects of solvent on charge transfer maxima have been reviewed by Murrell⁵¹ and Reichardt,⁵² the latter in connection with empirical measures of solvent polarity. The rules of thumb are as follows: For complexes of the non-ionic type, the charge transfer maximum should be red shifted in polar solvents, blue shifted in non-polar solvents. For ionic complexes, the opposite behavior is anticipated. However, a recent attempt⁵³ to correlate absorption maxima of complexes with solvent polarity has failed, and it appears there may be exceptions to the general rules.

Complex stability is also affected by solvent. Ionic complexes show a lower degree of association in polar solvents as Kosower⁵⁴ has observed for a series of pyridinium iodides. For complexes where little charge is transferred in the ground state, it is difficult to make a general statement concerning trends in stability. The situation varies from case to case, depending on the relative changes in solvation energies of components and complex. In cases where hydrogen bonding can play a role, the situation is further complicated.

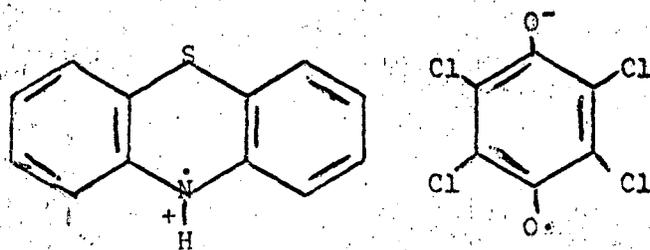
In certain cases--for example, the tetramethyl-p-phenylenediamine complex with chloranil--one may obtain an ionic or non-ionic complex by varying solvent polarity.²⁵

Other Useful Physical Methods for the Study of Complex Formation

Many physical methods are useful for studying complexes. We emphasize, however, that not all these methods are adequate in characterizing a complex as of the donor-acceptor type.

Infrared Spectroscopy. Shifts in bond stretching frequencies as a result of changes in bond strength can be anticipated in strong donor-

acceptor complexes. Intensities are generally decreased, and in certain cases vibrations which are ordinarily symmetry forbidden may appear. For weak complexes, the spectra hardly differ from a superposition of the spectra of the components, a difficulty common to all the spectroscopic tools. Many specific cases have been reviewed in references 1 and 3. We will note only the recently described⁵⁵ complex of phenothiazine and chloranil (XII) as it is illustrative of a common result. In a Nujol mull or KBr pellet the quinone carbonyl peak appears at 6.4 μ , shifted up from its usual 6.0 μ position. This immediately identifies the complex as of the ionic type.



(XII)

For complexes of donors with low ionization potential or acceptors of high electron affinity (or both) the charge transfer band may be found in the near infrared. For example, the p-phenylenediamine-chloranil complex²⁵ shows a new absorption at 942 μ in acetonitrile. In polar solvents the complex of β -carotene and iodine shows a new absorption at 1000 μ . This complex is a 1:2 complex, characterized as $[(C_{40}H_{56})I^+]I_3^-$. The charge transfer absorption is attributed to the moiety $(C_{40}H_{56} \rightarrow I^+)$ in which the I^+ is acting as a very powerful electron acceptor.⁵⁶ A band at 900 μ has been assigned to a donor acceptor complex of riboflavin and dihydroriboflavin.^{57,58}

Nuclear Magnetic Resonance Spectroscopy. Thus far only proton resonance appears to have been employed for the study of donor-acceptor complexes.

Attempts to determine equilibrium constants with NMR have met with varying degrees of success. A derivation similar to that of the Benesi-Hildebrand equation (2) readily leads to an equation suitable for use with NMR. Equation (3) is the form for donor in excess, the reciprocal of changes in observed chemical shifts of acceptor being plotted versus

$$(3) \quad \frac{1}{\Delta_{\text{obsd}}^A} = \frac{1}{K \Delta_{DA}^A [D]} + \frac{1}{\Delta_{DA}^A}$$

the reciprocal of donor concentration. The term Δ_{DA}^A is the chemical shift of pure complex and corresponds to the molar extinction coefficient in the usual form of this equation. Hanna and Ashbaugh⁵⁹ have studied a number of complexes of aromatic donors with TCNQ. They find equilibrium constants in agreement with those obtained by other methods when donor concentrations are expressed in terms of molality.

The reported failure of the method when concentrations are expressed as mole fractions is disconcerting. An attempt to determine with NMR the equilibrium constants for complexes of silver ions with a number of olefins has also failed.⁶⁰

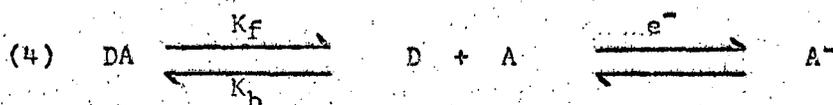
A successful attempt to obtain an equilibrium constant by NMR is reported for a complex of iodine and phenylmethylsulfide.⁶¹ In addition, the changes in chemical shift with temperature were sufficiently large in this case to enable determination of the thermodynamic parameters for complex formation. By using the relaxation times of the signals, Larsen and Allred deduce a lifetime of about 10^{-4} seconds for the complex, surprisingly long for a complex in solution.

Magnetic resonance should prove a useful tool in facilitating identification of coordination sites in complexes. For example,⁶² in

the aniline-iodine complex, a large selective downfield shift is observed for the N-H protons on complex formation. Such a large deshielding of these protons can only indicate that charge is indeed transferred from nitrogen and that this is the site of coordination with iodine.

Polarography. It has long been appreciated that complex formation can affect the observed reduction potential of molecules.⁶³ However, little systematic study seems to have been reported on these effects for donor-acceptor complexes in general. Recently a polarographic study of several complexes, known to be of the donor-acceptor type, has been carried out in non-aqueous solvents. An attempt was made to employ shifts in half-wave potentials for the determination of equilibrium constants.⁶⁴ The method is analogous to that commonly used for metal ion complexes.⁶⁵

For a 1:1 complex, the situation in the polarographic experiment is described by the equation (4)



Provided A^- , the product of the polarographic reduction, has a negligible ability to function as an acceptor with D, a study of the shift in half-wave reduction potential of the $A + e^- \rightarrow A^-$ system with donor concentration may be related to the free energy of formation of DA. The conditions which must be satisfied for successful use of the method are (i) chemical equilibrium for the formation of DA must be rapidly achieved; (ii) the rate of electron transfer to A or (DA) at the electrode must be high; and (iii) the solvation energy of A^- must be unchanged by addition of the donor. The fulfillment of these conditions may be tested experimentally.^{65,66}

When these conditions are fulfilled an expression of the form (5) may be derived. Here we have written activity coefficients equal to one for

$$(5) \quad F_0 = \text{antilog}_{10} \left[\frac{.4343F}{RT} \Delta E_{1/2} + \log_{10} \frac{I_S}{I_c} \right] =$$

$$1 + K_1[D] + K_2[D]^2 + \dots$$

simplicity. F is the Faraday, I_S and I_c are the limiting currents for uncomplexed and complexed species, respectively, and K_1 , K_2 , etc. are the equilibrium constants for 1:1 complex formation, 1:2 complex formation, etc. All terms on the left are obtained from polarographic data and a plot of $(F_0 - 1)/D$ versus $[D]$ yields a value for K_1 from the intercept (Fig. 16). A zero slope ($K_2 = 0$) is indicative of a 1:1 complex, the non-zero slope indicates 2:1 interactions. The constant K_2 may be obtained from this slope. Good agreement was observed between the constants obtained by this method and those obtained by the usual spectroscopic method for 1:1 complexes. It should be noted that the polarographic data indicated some 2:1 complex in certain instances where 1:1 complexes had been assumed in optical studies. This is especially interesting in view of the results obtained by Johnson and Bowen.⁴⁸

The polarographic technique gives no information on the nature of forces leading to complex formation.

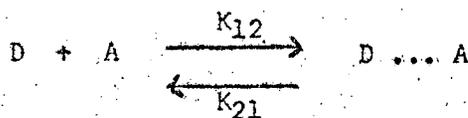
Fluorescence and Phosphorescence. Fluorescence techniques in particular are admirably suited for exploitation in biochemical research.^{67,68,69} Detailed kinetic information as well as equilibrium constants may be obtained. It seems worth emphasizing, however, that while demonstration of fluorescence quenching does indicate an interaction, this does not of itself demonstrate an interaction of the donor-acceptor type.

The energy absorbed in the charge transfer transition may be emitted

as a fluorescence. The spectrum of the fluorescence is quite generally a mirror image of the charge transfer absorption spectrum. In energy transfer studies the charge transfer emission may be of considerable interest, but for diagnostic purposes the absorption spectrum is infinitely superior.

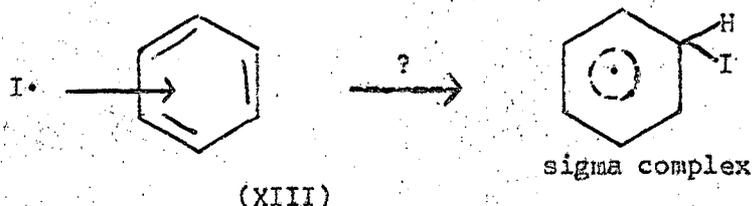
Phosphorescence from donor-acceptor complexes at low temperature is known, but the emission is invariably characteristic of the donor. Christodouleos and McGlynn⁷⁰ have reported a particularly interesting study. They observed a marked increase in the ratio of phosphorescence to fluorescence quantum yields with increasing concentration of acceptor in several complexes. The effects are particularly marked for poly-halogenated acceptors. This again demonstrates an enhanced intersystem crossing from singlet to triplet levels in donor-acceptor complexes of halogenated materials due to spin-orbit coupling.

Temperature Jump Relaxation and Flash Techniques. The rate constants K_{12} and K_{21} in an equilibrium



can often be determined by the temperature jump relaxation method.⁷¹ The method involves altering suddenly the temperature of a system in equilibrium (2 to 10 degree jumps in 10^{-6} seconds are common) and following the course of recovery to a new equilibrium by some rapid detection method. It is a general method for the study of complexes. The serotonin creatinine sulfate-riboflavin complex (entry 21, Table II) has been studied by this method.⁷² The constant K_{12} is greater than $8 \times 10^7 \text{ M}^{-1} \text{ sec}^{-1}$; K_{21} is greater than $2 \times 10^5 \text{ sec}^{-1}$. Accordingly, the lifetime of the complex in solution must be less than 5×10^{-6} seconds.

Flash spectroscopy has turned up the existence of donor-acceptor complexes of iodine atoms (produced by the flash) and benzenoid hydrocarbons (XIII).⁷³ The existence of some sigma complex in these systems

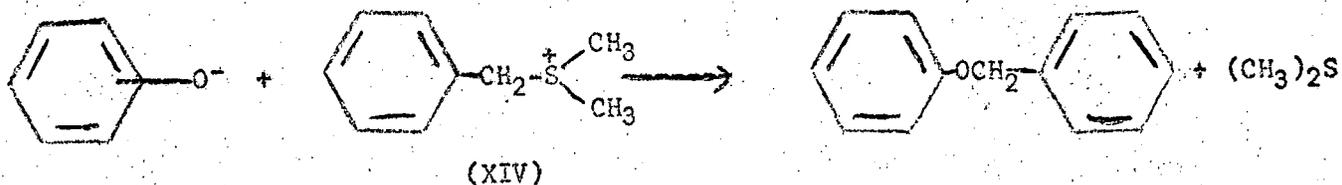


can probably not be ruled out with absolute confidence. For some of the hydrocarbons, complex formation was completely reversible, for others iodination occurred, implicating a sigma complex. In view of chemical similarities between the iodine atom and the mercaptyl radical $RS\cdot$ (e.g., both dimerize to a stable molecule, can be reduced to a stable anion, can be oxidized in the presence of water to an acid, are highly polarizable) one might anticipate similar complexes of the mercaptyl radical and biologically more interesting π systems. None has been identified thus far.

Effect of Complex Formation on Reaction Rates

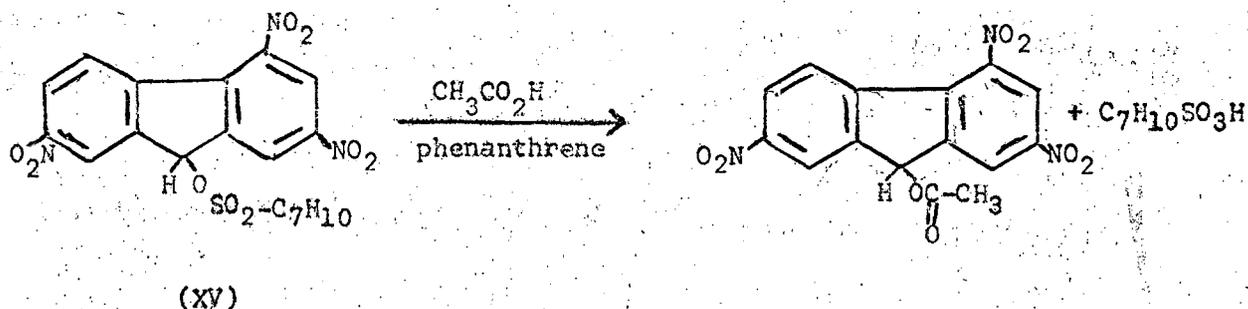
From the previous discussions it might well be anticipated that the chemical properties of a donor or acceptor may be affected by the donor-acceptor interaction. Indeed, a number of cases are known where specific catalysis due to complexing with a donor or acceptor is observed. In the following we give some recent examples.

Complex formation may be expected to produce a rate enhancement in a reaction in which the free energy of the transition state is lowered more than that of the ground state by the interaction. The solvolysis of dimethyl benzylsulfonium chloride (XIV) has been observed to proceed three times faster with phenoxide than with hydroxide, although the latter is a much stronger base.⁷⁴

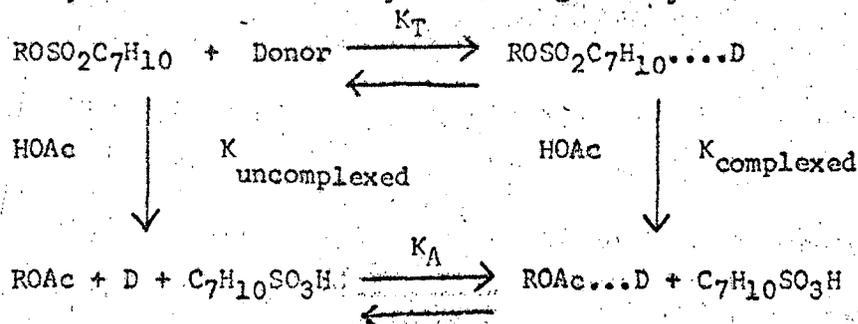


This rate enhancement appears to be due to π complexing in the transition state, such as in Fig. 17. In the solvolysis of trimethylsulfonium chloride, where π complexing is impossible, the rate is higher with hydroxide, as expected. This fact lends support to the complexing interpretation.

A detailed study of the acetolysis of 2,4,7-trinitro-9-fluorenyl-p-toluenesulfonate (XV) has been carried out in the presence of phenanthrene.^{75,76}



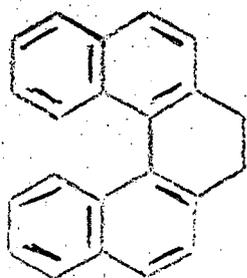
The 2,4,7-trinitrofluorenyl ring system is a good acceptor and was chosen in an attempt to maximize possible catalytic effects. The kinetic data is successfully interpreted in terms of the simplest mechanisms involving 1:1 complex formation (below). The ratio of the rate constants, $K_{\text{complexed}}/K_{\text{uncomplexed}}$, was found to be 21, indicating a very effective catalysis.



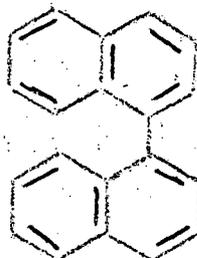
The equilibrium constant K_T derived from the kinetic data is in good

agreement with the result of an independent spectroscopic determination. Detailed analysis of the thermodynamics of the solvolysis suggests the catalytic effect can be attributed to an increase in the entropy of activation (less negative ΔS^\ddagger) by complex formation.

Catalysis of the racemization of optically active binaphthyl donors by organic acceptors has also been observed.⁷⁷ The donors were (+)-9,10-dihydro-3,4,5,6-dibenzophenanthrene (XVI) and (+)-1,1'-binaphthyl (XVII).

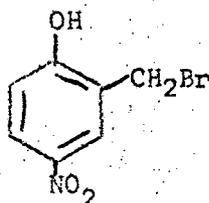


(XVI)



(XVII)

Catalytic effects parallel to acceptor strength are observed for the acceptors 1,3,5-trinitrobenzene, picryl chloride and 2,4,7-trinitrofluorene.



(XVIII)

The intermediacy of a complex has been proposed to account for the high specificity of 2-hydroxy-5-nitrobenzyl bromide (XVIII) for tryptophan in a reaction with proteins.⁷⁸ There is no spectroscopic evidence for this complex at present.

Complexes of Biological Materials

In Table II are collected all the literature data on molecular complexes of small biological molecules which we have been able to locate.

It would be superfluous to discuss in detail every case, since the table has been made fairly detailed. In particular, the wavelength at which the association constant was determined, or the maximum of new absorption is given, and compared with the absorption maximum of uncomplexed material. In a very large number of the cases listed in Table II a charge transfer band is not observed and a donor-acceptor interaction is therefore questionable.

Flavins. A great number of complexes of the flavin cofactors have been studied. The desire to implicate a donor-acceptor interaction in enzyme-cofactor binding is behind most of this work. This also holds true for the complexes of the NAD type molecules to be considered in the next section. The topic of cofactor binding has been reviewed in detail by Shifrin and Kaplan.⁷⁹

Insofar as the flavin complexes are concerned, the work in this field may be summarized as follows. About ten years ago, Theorell and Nygaard⁸⁰ proposed a scheme for the binding of FMN to the old yellow enzyme which envisioned hydrogen bonding at the isoalloxazine nucleus, as in Fig. 18. Tyrosine was implicated at the binding site by iodination studies.

Harbury and co-workers^{81,82} attempted to test this suggestion by examining in detail a number of phenol complexes of riboflavin and 3-methyl-riboflavin, where hydrogen bonding at position 3, as in Fig. 18, would be impossible. Finding that complexes formed equally well with both methylated and unmethylated flavin they were inclined to believe that charge transfer forces, not hydrogen binding, might be more predominant in these interactions.

It perhaps adds perspective to recall what the situation regarding such interactions was at that time. The "hydrophobic" bond concept,⁸³ which gave to water an important role in such interactions, was not well established. Mulliken, in an early classic paper on charge transfer, had suggested (in one sentence) that charge transfer "might afford new possibilities for understanding intermolecular interactions in biological systems." Kosower^{84,85} had already observed the charge transfer absorption of several pyridinium salts in the nicotinamide series and had suggested that a donor-acceptor complex could account for the 360 m μ absorption in NAD triosephosphate dehydrogenase. In this context Harbury's suggestion and (see below) that of Isenberg and Szent-Gyorgyi was completely reasonable.

There is no doubt that many of the complexes studied by Harbury and co-workers exist, but there is serious question as to whether they are of the donor-acceptor type. The spectrum of one of the complexes, typical of them all, is reproduced in Fig. 19. Naphthoate was one of the strongest complexes of the series. The effect of phenol is less pronounced, as is that of tyrosine. It seems certain that the hypochromicity and small red shift are not due to charge transfer absorption. Compare the spectrum in Fig. 19 with the situation encountered by Benesi and Hildebrand⁸⁶ and which prompted Mulliken to undertake a theoretical study (Fig. 20). The charge transfer band in Fig. 20 is definite and unmistakable.

At about the same time as Harbury's work appeared, Isenberg and Szent-Gyorgyi⁸⁷ reported a study of the red complexes of FMN with tryptophan and serotonin (Table II, entries 7, 21). The difference spectrum of complexed versus uncomplexed FMN showed a maximum at 503 m μ , comparable to the maximum at 500 m μ known for riboflavin semiquinone in acid solution. On this spectral evidence, it was proposed that an electron transfer had occurred

to give riboflavin semiquinone. That semiquinone formation had occurred was questioned almost immediately,⁸² but theoretical calculations⁸⁹ indicated that riboflavin could indeed be a good acceptor. Later⁹⁶ an ESR signal characteristic of flavin semiquinone was observed in an acidic solution of the complexes of FMN with serotonin and tryptophan. This indicated that electron transfer could occur under appropriate conditions, but no signal was observed in neutral solutions. The weak signal observed in acid solution with tryptophan as donor now appears to have been due to the influence of light, however.⁸⁸

Here the matter has rested, but recently Kosower⁹⁰ has raised a cogent point. He notes that the charge transfer transition from indole to riboflavin should appear at about 330 m μ , not at 500 m μ in the visible region of the spectrum. The basis of this suggestion lies in an estimate of the relative electron affinity of riboflavin in the series in Table III. The details of Professor Kosower's analysis are not available to us at present. One can, however, use the molecular orbital energies calculated by the Pullmans to make a rough estimate of $I_p - E_a$ which, as we have already noted, differs from the charge transfer energy only by a perturbation term which may be reasonably constant. These estimates, made using the orbital energies given in the Pullmans' book,¹¹ are given in Table IV with the experimentally known charge transfer energies. The calculated $I_p - E_a$ in units of β , the resonance integral of m.o. theory, (a negative energy quantity) reproduce the trends in experimental energy values quite well. A plot of $\Delta E_{C.T.}$ versus $I_p - I_a$ shows some scattering of points but does support an estimate of 80-90 Kcal for the charge transfer energy from indole to FMN. This is also quite evident from examination of the $I_p - E_a$ entries in Table IV for the indole-NAD⁺ and indole-FMN

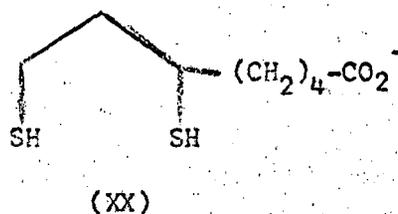
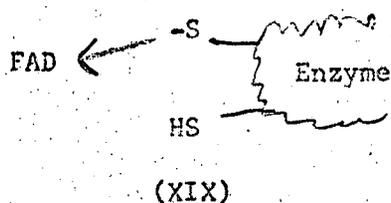
complexes. While the estimate is rough, it seems unlikely to be in error by the 25 or so Kcal needed to save the former 500 m μ assignment for the charge transfer band of the tryptophan-FMN complex. As no ESR signal is observed in a neutral solution of riboflavin and tryptophan,^{88,96} it now appears that the long wavelength absorption is due to broadening or splitting of the riboflavin absorption band located at 447 m μ .

Massey and co-workers have recently assigned certain absorption maxima in a number of flavoproteins (entries 78-88, Table II) to charge transfer transitions.⁹¹ Conditions favoring reduced enzyme favor the appearance of the 720 m μ absorption in lipoyl dehydrogenase (entry 78). The appearance of this peak is attributed to formation of a complex involving FADH₂ and NAD. In this connection complexes of reduced riboflavin, N-methyl-3-nicotinamide and N-methyl-4-nicotinamide have been studied (entries 76, 77, Table II).⁹² The difference spectrum of one of these complexes is given in Fig. 21. The peak at 510 m μ is assigned to the charge transfer band.

The green color of these complexes of reduced riboflavin, attributable to the long absorption tail, is reminiscent of the complex reported by Mahler and Brand.⁹³ This latter complex is prepared by grinding together solid riboflavin and NADH₂. An ESR signal is observed in the complex and its green color is likely attributable, in this instance, to riboflavin semiquinone. A relationship between the two series of FMN-NAD complexes such as that shown in Fig. 22 seems possible. A charge transfer transition NADH₂ \longrightarrow FMN is energetically reasonable, but chemical reaction between the materials would make it difficult to study and it has not been observed thus far.

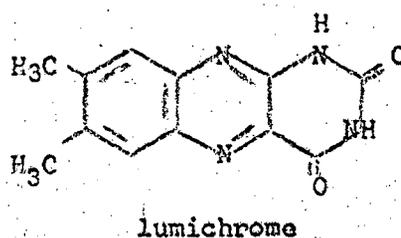
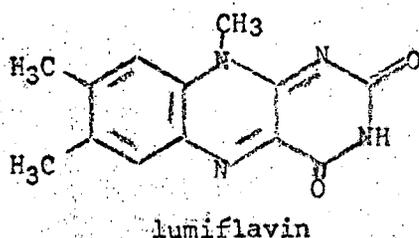
Concerning lipoyl dehydrogenase, Kosower⁴ has recently suggested

that the red intermediate observed during the reduction of this enzyme is a complex of thiol anion and FAD (XIX). Searls and Sanadi⁹⁴ claimed to have detected a similar complex in a reaction between dihydrothioatate (XX) and FMN. An intensification of the orange tinge of the solution was



observed immediately after mixing the reagents. The difference spectrum of this solution versus FMN showed a maximum at 535 m μ which was assigned to a charge transfer complex between thiol and FMN. With time the solution turned olive green and an ESR signal appeared. Massey and Atherton⁹⁵ were unable to reproduce this result under anaerobic conditions, although a reduction of FMN apparently did occur. They concluded that the 535 m μ absorption appeared only in the presence of light and some hydrogen peroxide which had been generated by air oxidation of reduced flavin.

In the following we consider some of the more recent reports of complexes involving riboflavin. Fleishman and Tollin^{88,97} have attempted to determine whether the acceptor strength of riboflavin can be increased by protonation of the isoalloxazine nucleus. They report complex formation between a number of phenols and riboflavin, and a few with lumiflavin and lumichrome, in 6-12 N acid (entries 27-42, Table II). In some cases highly colored complexes were isolated from solution. Discrete new

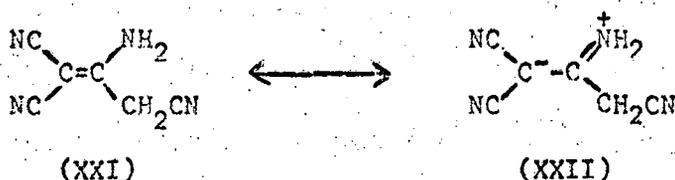


absorption maxima, assigned to charge transfer transitions, appear with naphthalenediols and trimethylquinol as donor (Fig. 23). With other phenols color changes are observed, since the riboflavin absorption broadens considerably out towards the green, but no discrete new maxima appear. Phenols substituted with electron-withdrawing groups (i.e., tetrachloroquinol) show no color reaction. Interestingly, no color change is observed with 2,6-ditertiarybutylphenol. In answer to their original question, they find the stabilities of the complexes are actually lower in strong acid, but they are unable to correlate stabilities with any donor parameters. Surprisingly, an ESR signal, characteristic of riboflavin semiquinone and increasing in intensity with increasing acid concentration, is observed.⁹⁷ No signal attributable to phenol radical is detected, presumably because of its disproportionation. From the results it seems that although complex stability decreases in acid solutions, electron transfer reactions occur only in acid solution, presumably due to the added stability of the flavin radicals under these conditions. Fleishman and Tollin also report²⁷ that their riboflavin hydroiodide complex forms stable highly colored complexes with phenols.

It is also interesting to recall, in connection with flavin complexes in acid solution, another result of Isenberg and Szent-Gyorgyi.¹⁰⁹ In 1% aqueous HCl, solutions of serotonin and indole with FMN show a new absorption at 570 m μ and a shoulder at 620 m μ when the spectra are observed at low temperatures. This absorption is at considerably longer wavelength than they observed in neutral solutions.

A complex of 1,1,3-tricyano-3-aminopropene (XXI) and riboflavin (entry 74, Table II) has been suggested to be of the charge transfer

type.⁹⁸ Such a complex would be of interest in that (XXI) has been reported to block oxidative phosphorylation.⁹⁹ A hypochromic effect is observed for the riboflavin maxima, but no new peak appears. The same note refers to charge transfer complexes of tryptophan (a weak donor) and picric acid (a strong acceptor) with riboflavin. As one would anticipate a healthy contribution from dipolar structure (XXII) in the tri-cyanoaminopropene it is not clear whether this compound should be a donor or acceptor (or alkylating agent). A donor-acceptor interpretation for the complex of (XXI) and riboflavin seems questionable.



A proposal has been put forward¹⁰⁰ that "electrostatic" forces can play a role in complexes of a number of purines and pyrimidines (entries 50-69, Table II) with riboflavin. The interaction is suggested to be favored by the complementarity of charge (obtained as charge densities in Huckel calculations) in the regions C₆ to N₉ in the purines and N₁ to N₁₀ of the flavin (Fig. 24). These fractional charges are manifestations of the slight polarity of the individual bonds and arise from slight polarization of the bond due to the different electronegativities of the component atoms. The interaction is to a good approximation equivalent to interaction between oriented dipoles. Partial transfer of an electron from donor to acceptor is viewed as enhancing the interaction by increasing the charge on oppositely paired atoms. This proposal is along the lines previously suggested by Karreman¹⁰¹ for the tryptophan-riboflavin complex. No charge transfer band is observed in any of the above complexes, only the usual hypochromic effect in the riboflavin absorption. In dimethyl-

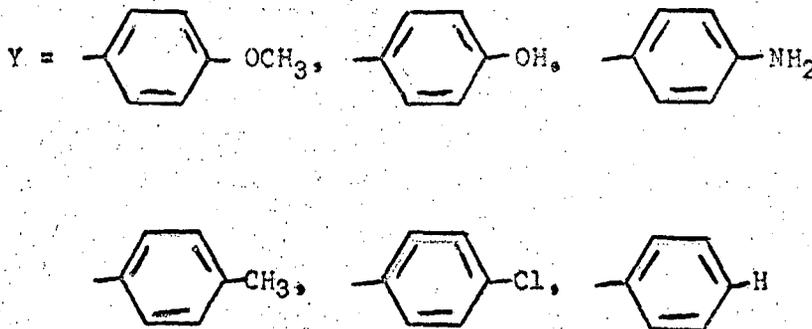
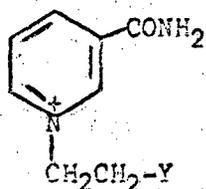
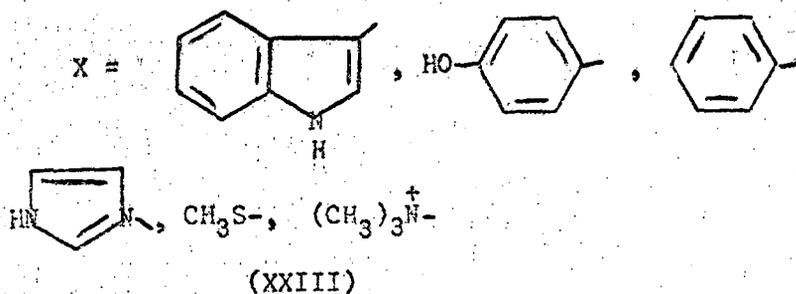
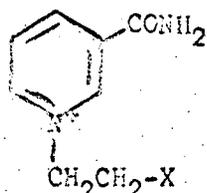
formamide, the complexes are barely demonstrable even by fluorescence techniques, which leads one to suspect a contribution from water in stabilizing the complexes. Straightforward calculation of charge densities in this way probably overestimates the effects, if there are any, in that contributions from sigma electrons are neglected. Polarization of sigma electrons would be opposite to the π electron polarization.

Finally, we call attention to the remarkable stability of the complexes of nitrophenols¹⁰⁶ and FAD (entries 48-51, Table II). This stability may be due to protonation of the adenine moiety of FAD by the phenols. Briegleb and Delle^{106a} have detected salt formation in complexes of aromatic amines and picric acid ($pK_a 1.8 \times 10^{-1}$). They used infrared spectroscopy and detected a typical salt band at 3.4μ .

Pyridine Nucleotides. The overall course of development of work in this area parallels that of the flavin series.

Following the lead of Kosower who had established the identity of the charge transfer bands in the pyridinium iodides, Cilento and Guisti¹⁰² sought complexes of a number of indoles with NAD^+ and its analogues as possible models for enzyme binding. Similar studies have been reported by Alivasitos, et al.¹²⁵ The broad new absorption appearing in the spectrum of the tryptophan- NAD^+ mixture is shown in Fig. 25. It should be noted that the small association constants reported in this series (entries 89-96, Table II) are in the range of uncertain reliability of the Benesi-Hildebrand method.

Shifrin¹⁰³ has tried a novel approach to the problem. He has synthesized two series of molecules in which the potential donor and acceptor sites are in the same molecule (see XXIII and XXIV). Both absorption



(XXIV)

and emission spectra were studied for the series (XXIII) in an attempt to reproduce the spectral behavior of bound NAD^+ . The enhanced fluorescence of enzyme-bound NAD^+ was not reproduced in these models. The absorption spectra of all the above compounds show absorption tails on the long wavelength side of the maxima (cf. Fig. 26). These absorption tails are assigned to a charge transfer transition, but a case such as that in trace C of the figure may be questionable. For the series (XXIV)

the maxima, taken from difference spectra, can be correlated with Hammett sigmas for the substituent.^{103a}

Other Complexes. We now turn to a consideration of complexes of other biological materials which have on occasion been linked with the topic of charge transfer. We defer a critical discussion of the possible physiological significance of the various complexes to specialists, and consider only the physical aspects of complex formation.

Complexes of various carcinogenic hydrocarbons with purines have long been of interest in the study of chemical carcinogenesis. From time to time theories have been proposed which invoke charge transfer or electron transfer. These various theories have recently been discussed by Mme. Pullman.¹²⁷ That purines can increase the solubility of polycyclic aromatic hydrocarbons has been appreciated for many years¹²⁸ and quantitative studies have been reported.^{129,130} An X-ray crystallographic study¹³¹ of a 1:1 crystalline complex between tetramethyluric acid and pyrene shows a face to face alternate stacking of the purine and hydrocarbon molecules. The interactions in solution similarly appear to involve a stacking type association between partners, but for DNA-hydrocarbon association the intercalation versus adsorption question is still not settled.^{131a} Some time ago⁸⁹ it was noted that the relative solubilizing power of the purines could be correlated with the energy of the highest occupied molecular orbital. This type correlation has often suggested a charge transfer contribution to the intermolecular binding forces. However, no charge transfer band is observed in these complexes and there has always remained a question as to the relative contribution of the charge transfer energy to the overall binding. We note with interest a recent theoretical study of the intermolecular forces between purines and 3,4-benzpyrene.¹³² By

considering only classical dipole-induced dipole and London forces it was shown that the relative solubilizing power of the purines toward this hydrocarbon could be accounted for. An approximate expression for estimating London forces is obtained from a second order perturbation treatment¹³³ and is:

$$W'' = \frac{-3}{2} \frac{\alpha_1 \alpha_2}{R^6} \frac{I_1 I_2}{I_1 + I_2}$$

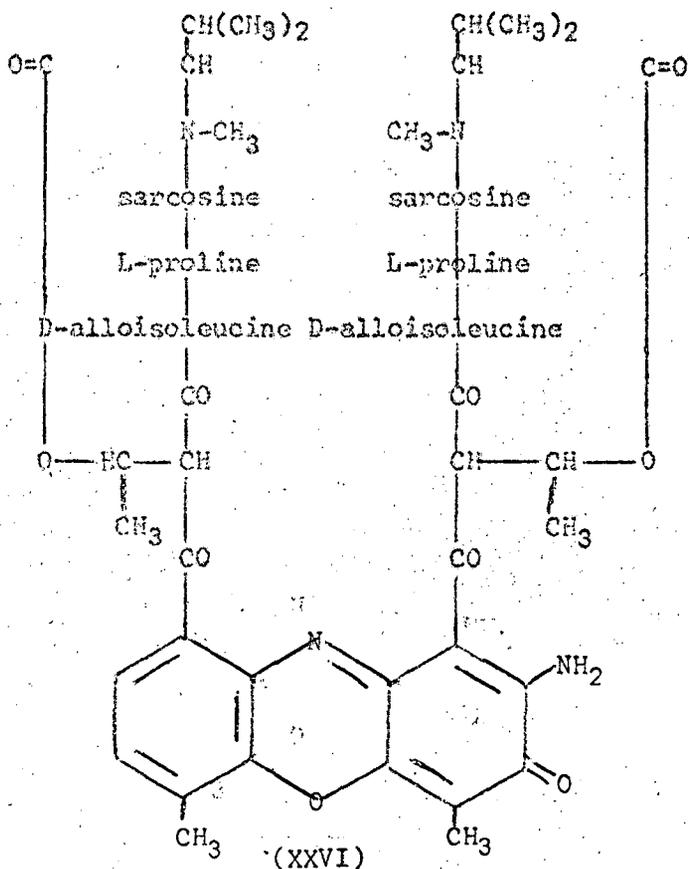
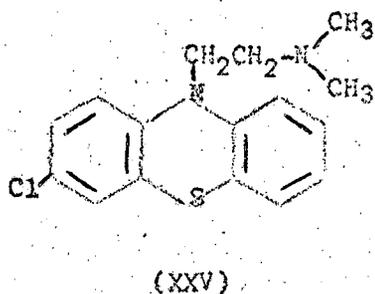
where α_1, α_2 are the respective molecular polarizabilities, I_1, I_2 are the ionization potentials of the partners, and R is the intermolecular distance. The calculations are preliminary and have incorporated a number of approximations but show that a very large contribution from London forces is to be anticipated. The relative contribution from charge transfer forces remains to be assessed, but one wonders if any contribution is to be found, particularly in the absence of charge transfer band.

A problem somewhat related to the above involves the binding of the mutagenic acridine dyes to nucleic acids. Considerable experimental effort has been devoted to distinguishing between an ionic association at the phosphate groups of the polymeric chain¹³⁴ and an intercalation of dye between base pairs of the chain.¹³⁵ Lerman¹³⁶ has recently reported a study of the chemical reactivity (diazotization) of the amino group in bound and unbound 5-aminoacridine. He finds the rate of reaction significantly decreased when the dye is bound to DNA and interprets this as due to an increased shielding of the amino group on intercalation of the dye between base pairs. An attempt to settle the matter by absorption spectroscopy has also been reported.¹²¹ The reasoning was that if the dye were intercalated between bases there would be a considerable interaction with the π systems of the bases since the interannular

distance would be about 3.5 \AA . Under such circumstances one might find a charge transfer absorption. For acriflavin bound to DNA, and proflavin to guanylic acid and thymidylic acid, a new shoulder appears in the dye absorption band which is assigned to a charge transfer transition with dye as acceptor (entries 123-125, Table II). This is offered as support for Lerman's intercalation mechanism. We note, however, that for the moderate donor thymine (highest occupied m.o. $.510 \beta$) and moderate acceptor proflavin (lowest empty m.o. $-.408 \beta$) a charge transfer energy as low as 50-55 Kcal is quite surprising as is the fact that a similar complex of guanine (highest occupied m.o. $.307 \beta$) shows virtually the same maximum.

Calculations have recently revealed a correlation between the highest occupied molecular orbital and the hallucinogenic activity of a series of drugs of the LSD type.¹³⁷ This has caused some further speculation as to a possible role for charge transfer in the mode of action of these drugs. The anticipated donor properties of LSD (a substituted indole) and chlorpromazine¹³⁸ (XXV) have been noted previously and a possible role for charge transfer in their mode of action has been considered. Actinomycin C₃ (XXVI), a highly toxic antibiotic, is expected to have good acceptor properties.¹³⁹

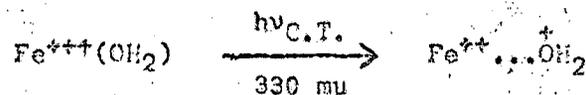
Polycyclic aromatic hydrocarbons inhibit various flavin containing enzymes.^{140,124} This has been attributed to formation of donor-acceptor complexes. It is of interest that the absorption maximum reported for the complex of 3,4-benzpyrene (energy highest occupied m.o. $.371 \beta$) and FMN¹²⁴ (entry 158, Table II) corresponds roughly with that expected from the results of Table IV. The existence of complexes of polycyclic aromatic hydrocarbons with FMN and quinones (cf. entry 159, Table II) has led to



speculation that such complexes may play a role in certain aspects of chemical carcinogenesis,¹⁴¹ but this is a controversial point.

Complexes of Metal Cations

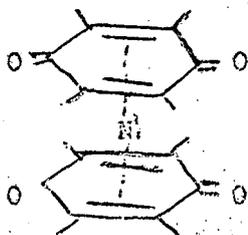
Charge transfer transitions in complexed metal ions have been well documented.^{142,143} An example is the case of the hydrated ferric ion, where a new absorption corresponding to a "metal reduction spectrum" occurs at 330 m μ . Another is the 227.5 m μ absorption in the complex $[\text{Co}(\text{NH}_3)_5\text{Cl}]^{++}$ attributed to electron transfer from chloride to metal ion. At low temperatures,



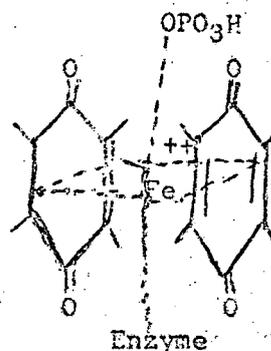
charge transfer to a frozen matrix can be made to reverse quite slowly. For example, ultraviolet irradiation of a frozen aqueous matrix of Fe^{++} or I^- at 77° K gives an ESR signal characteristic of the hydrogen atom

(a doublet with 500 gauss splitting), arising from electron transfer to the matrix.¹⁴⁴

An intense new absorption band occurs in a number of nickel-quinone complexes¹⁴⁵ such as (XXVII). This has been characterized as a charge transfer band. It might be noted that an iron complex of Coenzyme Q (XXVIII) has been proposed¹⁴⁶ as an intermediate in oxidative phosphory-



(XXVII)



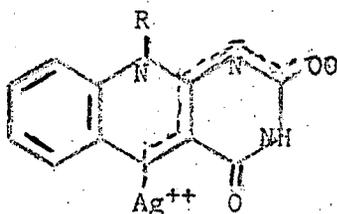
(XXVIII)

lation. As there is no biochemical evidence bearing on this proposal as yet, it seems premature to comment on the possible spectroscopic properties of such a complex.

Good evidence for charge transfer transitions involving metal ions complexed to biological molecules seems to be rare. Orgel¹⁴⁷ has pointed out that the larger than ordinary extinction for the 575 m μ band of oxygenated hemocyanin may be due to a band of Cu⁺⁺ modified by a charge transfer component. The copper containing enzyme laccase has an unusually intense absorption in the vicinity of 600 m μ , possibly due to charge transfer to oxygen or enzyme.¹⁴⁸ Similarly, the blue color of ascorbic acid oxidase in the presence of oxygen¹⁴⁹ may be due to a charge transfer transition. Charge transfer contributions may also be involved in the long wavelength absorption of some metal containing porphyrins.¹⁵⁰

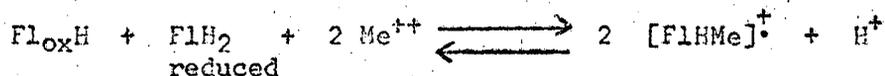
The increased absorption above 500 m μ observed for riboflavin in the presence of a number of transition metals¹⁵¹ has been confirmed and extended by Radda and Calvin¹¹⁰ who also noted a similar effect with sodium and magnesium ions. This is likely the result of a perturbation of molecular orbital energies by the electrostatic effects of a coordinated metal ion, rather than a charge transfer phenomenon. The shift of the long wavelength absorption maximum of riboflavin from 447 m μ to 430 m μ in the presence of ferrous ion in a pyrophosphate, but not a phosphate or maleate buffer,¹⁵² is unexplained.

The bright red complex of silver ion and riboflavin¹⁰⁴ has been considered to involve charge transfer from metal ion to flavin (XXIX).¹⁵³



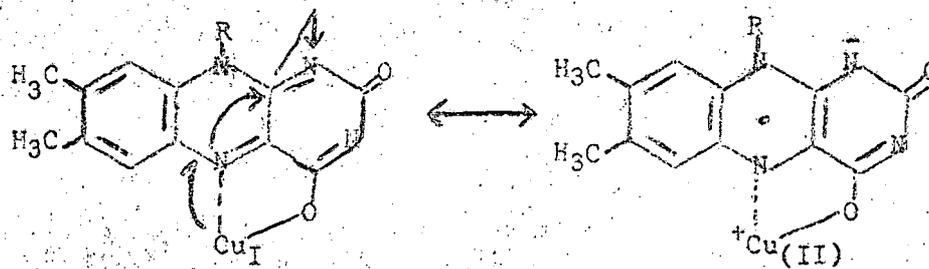
(XXIX)

This silver-riboflavin complex was the first of a remarkable series of "charge transfer chelates" of riboflavin semiquinone which have been studied in some detail by Hemmerich and his co-workers.¹⁵⁴ With valence stable d metal ions at physiological pH, the equilibrium between oxidized and reduced flavin can be shifted toward chelated radical semiquinone (termed a "comproportionation"). With coordinated metals such as Mo^V, Fe⁺⁺ and Cu^I (and Ag^I already referred to above) in acetonitrile solution,



one can observe a redox reaction and formation of the chelates (XXX).

Redox processes of this type may play a role in redox catalysis in metal containing flavoproteins.¹⁵⁵



(XXX)

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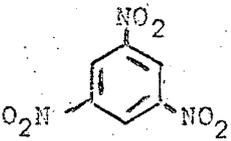
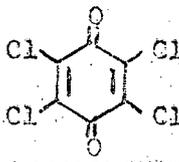
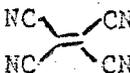
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153. P. Bamberg and P. Hemmerich, Helv. Chim. Acta, 44 (1961) 1001.
154. P. Hemmerich, paper presented at the Symposium on Flavins, Amsterdam, June 1965.
155. P. Hemmerich, Mosbacher 14th/Colloquium der Gesellschaft für physiologische Chemie, Springer-Verlag, Heidelberg, 1964.

Table I
 Experimental Breakdown of the Energy of Formation in Some
 Donor-Acceptor Complexes^a

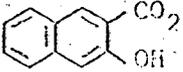
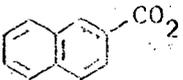
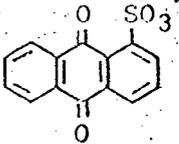
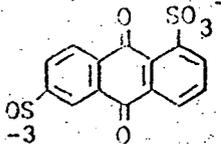
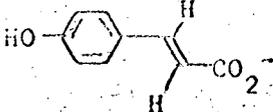
Acceptor						
	Hexamethyl- benzene	2,3,5,6-Tetra- methylquinol ^b	Hexamethyl- benzene	Durol	Hexamethyl- benzene	Durol
H	-4.7	-4.0	-5.35	-4.4	-7.75	-5.5
W ₀	-2.5	-2.65	-3.4	-2.5	-5.1	-2.8
R _N	-2.2	-1.35	-1.95	-1.9	-2.7	-2.7

a. Energies are in Kcal, data is from reference 1, p. 25, where experimental details and further examples may be found

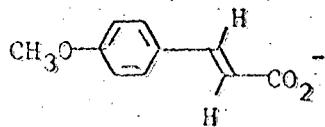
b. Durol

Table II

Molecular Complexes of Biological Materials

Entry No.	Complex	Reference	Association Constant ^a	Molar Extinction Coefficient ^b	Method ^c	λ , m μ	Other
1	 - FMN	81	200-1000	Not Reported	B.H. eqn.	445, 373	λ_{\max} FMN 447, 375
	" - Riboflavin	81	200-1000	"	"	"	
	" - 3-Methyl-Riboflavin	81	200-1000	"	"	"	λ_{\max} 3-Methyl- riboflavin 445, 373
2	 - FMN	81	100-200	"	"	"	
	" - Riboflavin	81	100-200	"	"	"	
	" - 3-Methyl-Riboflavin	81	100-200	"	"	"	
3	 - FMN	81	100-200	"	"	"	
4	 - FMN	81	100-200	"	"	"	
5	 - FMN	81	20-100	"	"	"	

6



- FMN

81

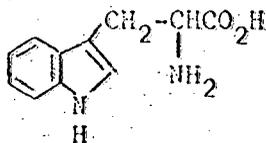
20-100

"

"

"

7



(tryptophan)

- FMN

81

20-100

"

"

"

"

- FMN

87

60

"

"

500

See text,
page 000

"

- 3-Methyl-
Riboflavin

81

20-100

"

"

445,373

"

- Riboflavin^d

81

"

- "

109

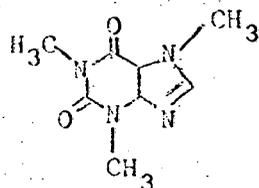
Not de-
terminedNot re-
ported

B.H.

570,620

1% HCl, ice,
-70°C

8



(caffeine)

- FMN

81

20-100

"

"

445,373

"

- FMN^e

104

90

Fluores-
cence

17°C, pH 7.5

"

- FMN

104

103

Fluores-
cence

5°C

"

- FMN

105

53

Fluores-
cence

"

- Riboflavin

81

20-100

Not Re-
ported

B.H.

445 or
373

"

- 3-Methyl-
Riboflavin

81

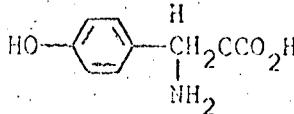
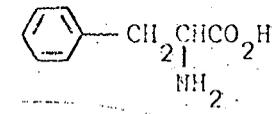
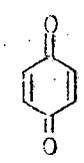
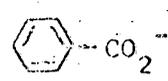
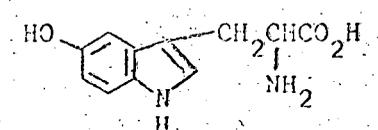
20-100

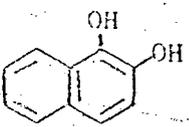
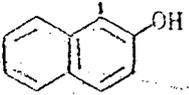
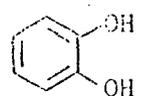
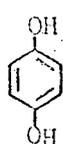
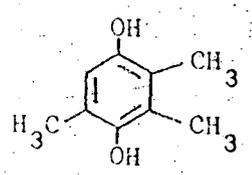
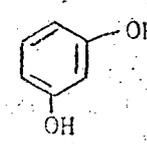
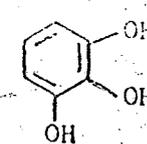
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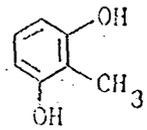
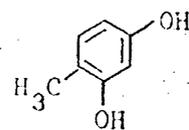
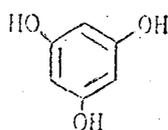
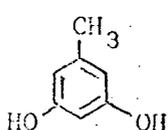
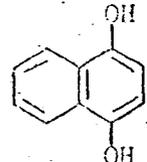
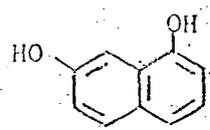
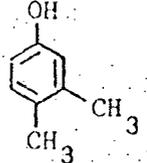
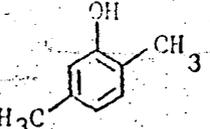
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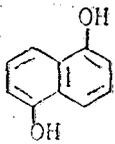
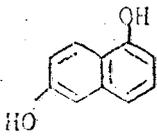
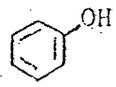
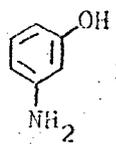
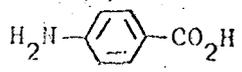
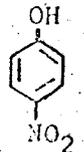
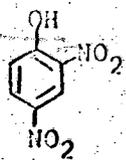
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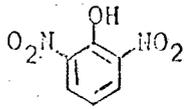
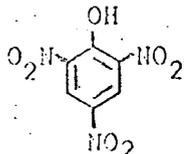
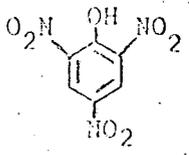
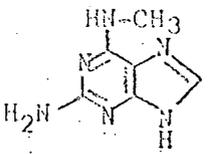
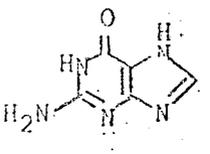
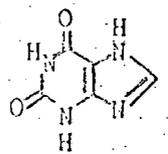
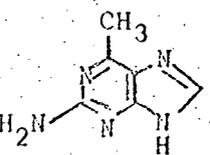
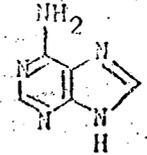
9	<chem>COc1ccc(cc1)C(=O)[O-]</chem>	- FMN	81	20	"	"	"
	"	- Riboflavin	81	<20	"	"	"
	"	- 3-Methyl Riboflavin	81	<20	"	"	"
10	<chem>Oc1ccc(cc1)C(=O)[O-]</chem>	- FMN	81	<20	"	"	"
	"	- Riboflavin	81	<20	"	"	"
	"	- 3-Methyl Riboflavin	81	<20	"	"	"
11	<chem>Oc1ccccc1C(=O)[O-]</chem>	- FMN	81	<20	"	"	"
12	<chem>Oc1ccccc1C(=O)[O-]</chem>	- FAD	106	1.54×10^3 (!)		Fluorescence	
13	<chem>Oc1ccccc1</chem>	- FMN	81	<20	Not Reported	B.H.	445 or 375
	"	- Riboflavin	107	5		"	"
14	<chem>Oc1ccc(Cl)cc1</chem>	- FMN	81	<20	Not Reported	"	"
15	<chem>Clc1c(Cl)c(Cl)c(Cl)c1C(=O)[O-]</chem>	- Riboflavin ^F	82	455(15°C)	"	"	"
16	<chem>Oc1ccc(cc1)CC(N)C(=O)OCC</chem>	- 3-Methyl Riboflavin	81	<20	"	"	"
	(tyrosine ethyl ester)						

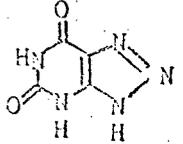
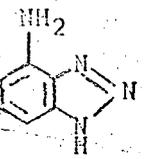
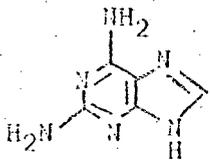
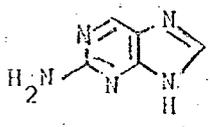
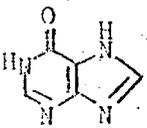
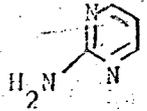
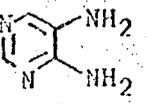
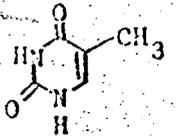
17	 (tyrosine)	- Riboflavin	97	"no significant spectral changes"				
18	 (phenylalanine)	- 3-Methyl Riboflavin	81	<20	Not Reported	B.H.	445 or 373	
	"	- FMN	97	"no significant spectral changes"				
	"	- Riboflavin	118	Not determined	Not determined	Difference spectrum		
19		- FMN	81	<20	Not reported	B.H.	445 or 373	
20		- FMN	81	<20	"	"	"	
	"	- 3-Methyl Riboflavin	81	<20	"	"	"	
	"	- Riboflavin	81	<20	"	"	"	
21	 (serotonin)	- FMN ^g	87	400	~4500	"	500	
	"	- FMN	109	Not determined	Not determined		570, 620	1% HCl, ice, -70°C
22	Leucine	- Riboflavin	118	"	"	difference spectrum		no C.T. band
23	Glycine	- Riboflavin	118	"	"	"		"
24	FMNH ₂	- FMN	57	18	680(900)	Indirect	900	

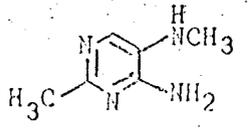
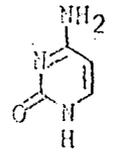
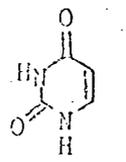
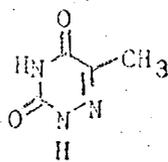
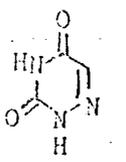
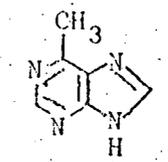
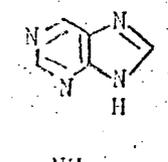
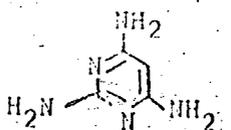
25	TPNH ₂	- FMN	109	Not determined	Not determined	Increased long λ Absorption		in ice at -70°C
26	NADH ₂	- FMN	109	"	"	"		"
27	" 	- FMN	110	No evidence	for complex	Fluorescence		water, room temp.
27	" 	- FMN	97 ^h	242	Not reported	Modified Scott eqn.	<500	pH 6.8
27	"	- FMN	97	68	"	"	"	12 N HCl
28		- FMN	97	10.4	"	"	?	pH 6.8
28	"	- FMN	97	0.68	"	"	"	12 N HCl
28	"	- Lumiflavin	97	2.9	"	"	"	12 N HCl
28	"	- Riboflavin	97	3.2	"	"	"	12 N HCl
28	"	- Riboflavin	97	3.9	"	"	"	6 N HCl
29		- Riboflavin	97	2.9	"	"	"	"
30		- Riboflavin	97	.10	"	"	"	"
31		- Riboflavin	97	3.3	"	"	"	"
32		- Riboflavin	97	6.2	"	"	"	"

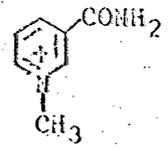
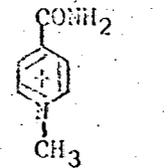
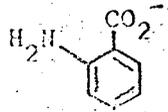
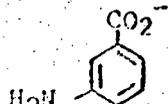
33		- Riboflavin	97	5.5	"	"	"	"
34		- Riboflavin	97	6.2	"	"	"	"
35		- Riboflavin	97	7.4	"	"	"	"
36		- Riboflavin	97	9.2	"	"	"	"
37		- Riboflavin	97	55	750	"	625	"
38		- Riboflavin	97	98	Not re-ported	"	550	"
39		- Riboflavin	97	55	"	"	?	"
40		- Riboflavin	97	88	"	"	"	"

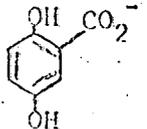
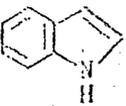
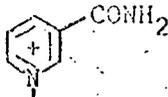
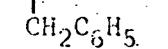
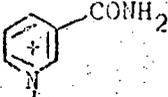
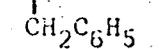
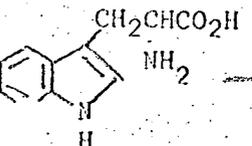
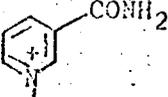
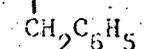
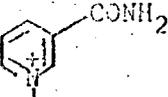
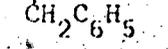
41		- Riboflavin	97	111	"	"	590	"
42		- Riboflavin	97	102	"	"	<500	"
43	Adenosine	- Riboflavin	104	140		Fluorescence		5°C
	"	- Riboflavin	104	120		"		17°C
44	FAD (internal complex)		104	Not determined		"		λ_{max} FMN 447 m μ λ_{max} FAD ~450 m μ
	"		100	80% folded		"		
45		- FAD	106	31	Not reported	B.H.	450	λ_{max} FAD ~450 m μ
46		- FAD	106	9	"	"	"	
47		- FAD	107	13	"	"	"	
48		- FAD	106	2×10^3		Fluorescence		
49		- FAD	106	5×10^4		"		

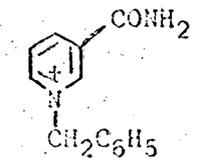
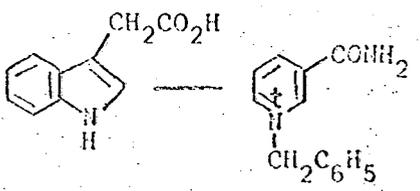
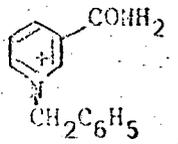
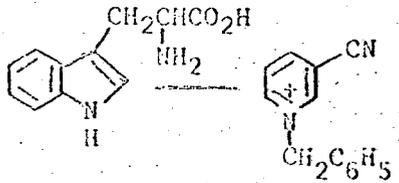
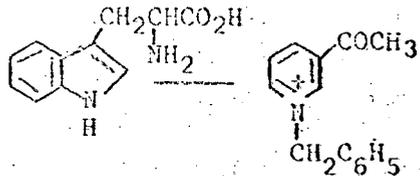
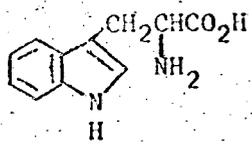
50		- FAD	106	2.5×10^4		Fluorescence	
51	 (picric acid)	- FAD	106	8.3×10^4		"	
52		- FMN	98	Not determined	Not determined	Hypochromic effect	200-300
53		- Riboflavin	100	17.2		Fluorescence	
54		- Riboflavin	100	14.1		"	
55		- Riboflavin	100	13		"	
56		- Riboflavin	100	8.8		"	
57		- Riboflavin	100	7.6		"	

58		- Riboflavin	100	7.6	Fluorescence
59		- Riboflavin	100	7.9	"
60		- Riboflavin	100	6.5	"
61	 · HNO ₃	- Riboflavin	100	6.4	"
62		- Riboflavin	100	3.9	"
63		- Riboflavin	100	2.8	"
64		- Riboflavin	100	4.8	"
65		- Riboflavin	100	2.4	"

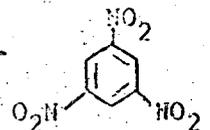
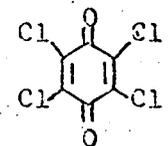
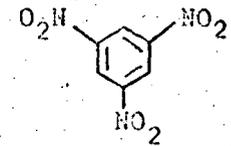
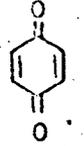
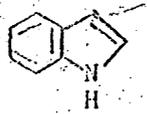
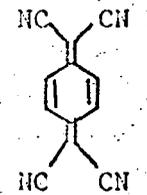
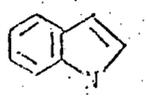
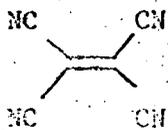
66		- Riboflavin	100	2.0	Fluorescence
67		- Riboflavin	100	1.8	"
68		- Riboflavin	100	0.53	"
69		- Riboflavin	100	0.50	"
70		- Riboflavin	100	0.14	"
71		- Riboflavin	100	0.5	"
72		- Riboflavin	100	0.18	"
73		- Riboflavin	100	5.6	"

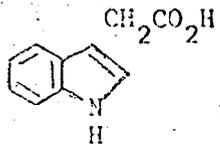
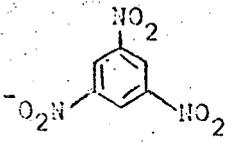
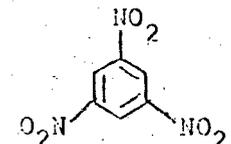
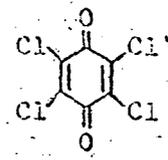
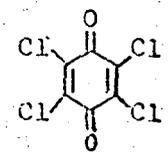
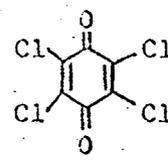
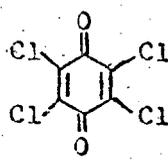
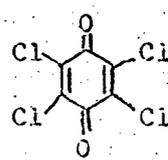
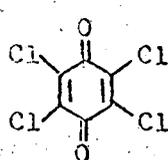
74	$\begin{array}{c} \text{NC} \quad \text{NH}_2 \\ \quad \\ \text{---} \quad \text{---} \\ \quad \\ \text{NC} \quad \text{CH}_2\text{CN} \end{array}$	- Riboflavin	98	Not de- termined	Not de- termined	Hypochromic effect	200-300
75	FMNH ₂ -		92	"	"	Difference spectrum	~510
76	FMNH ₂ -		92	"	"	"	~510
77	FMNH ₂ -	NAD ⁺	92	"	"	"	~580
78	Lipoyl dehydrogenase -	FADH ₂ - NAD	91,92	"	"	"	720
79	D-amino acid oxidase -	FAD - Δ ^{1,2} - pyrrolidine-2-carboxylate ^l	91	"	"	"	615
80	D-amino acid oxidase -	FAD - Δ ^{1,2} - piperidine-2-carboxylate ^m	91	"	"	"	640
81	D-amino acid oxidase -	FAD - indole-2-carboxylate	91	"	"	"	530
82	D-amino acid oxidase -	FAD -	91	"	"	"	565
							
83	D-amino acid oxidase -	FAD -	91	"	"	"	530
							

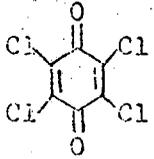
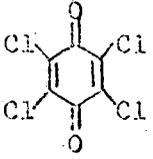
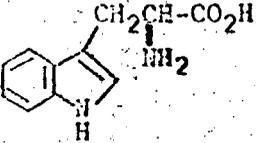
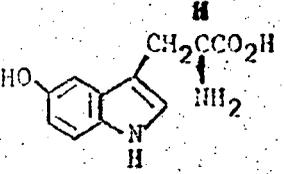
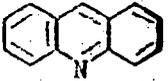
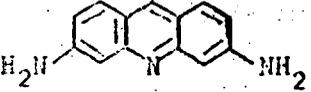
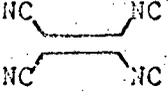
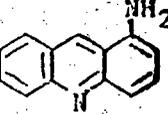
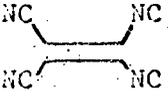
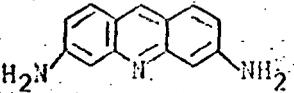
84	D-amino acid oxidase - FAD 	91	"	"	"	<530
85	D-amino acid oxidase - FADH ₂ - Δ ^{1,2} - piperidina-2-carboxylate ^{2m}	91	"	"	"	
86	Butyryl Co A dehydrogenase (green) - FAD - unknown group	91	"	"	"	720
87	NADH ₂ - cytochrome b ₅ reductase - FADH ₂ - NAD	91	"	"	"	flat long wavelength absorption
88	Glutathione reductase - FADH ₂ - TPN	91	"	"	"	720
89	 —————  	102	2.5 2.2 2.47	540(370) 890(380) 560(370) 640(400)	B.H.	pH 6,6
90	Glycyl-L-tryptophan -  	102	2.9 2.98 2.92	500(400)	B.H.	pH 6,6-6,1
91	 —————  	102	2.2 2.52 2.20	860(370) 540(390) 430(400)	B.H.	
92	Serotonin creatinine sulfate -  	102	1.8 1.81 2.07	1410(380)	B.H.	pH 6,4-6,6

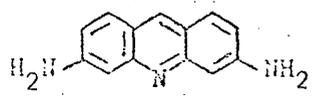
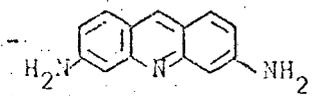
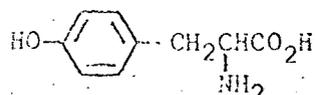
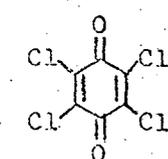
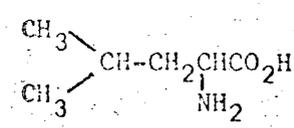
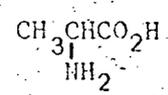
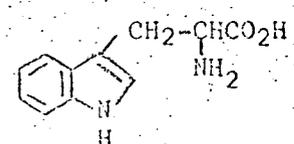
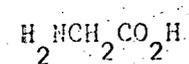
3	Acetyl tryptophan		102	4.0 5.0 4.73	510(400)	B.H.	pH 6.5
4			102	4.1 4.09 4.41	1220(370)	B.H.	pH 6.3-6.7
5	Yohimbine		102	1.42 1.41	"	"	pH 2.2-4.0
6			102	4.9	890	"	
7			102	no reproducible results			
8			109	Not reported	Not reported		ice, -70°C
9	NAD (internal complex)		111	"	"	Fluorescence	
00	NADH ₂ (internal complex)		112	20-25	"	"	

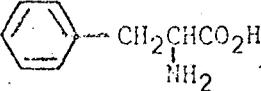
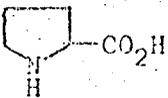
Other internal complexes (?)

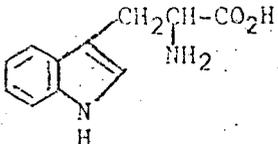
01	Deamino - NAD, Deamino - NADH ₂ , 3-acetylpyridine - NAD, 3-pyridinaldehyde - NAD, 3-pyridinaldehyde - deamino - NAD		113				
02	NADH ₂ - 		114	Not determined	Not determined	New absorption	
03	Phenothiazine - 		114	"	"	"	in chloroform
	Phenothiazine - "		55	"	"	Infrared	material isolated as solid from benzene
04	Phenothiazine - 		114	"	"	New absorption	in chloroform
05	Phenothiazine - 		114	"	"	"	in chloroform
06	 — 		114	"	"	"	chloroform, observed two maxima (reaction ?)
07	 — 		31	"	"	"	CH ₂ Cl ₂ , complex formation followed by reaction

08			114	"	"		
09	Adenine, Caffeine		114	"	"		
10	Adenosine		115	"	"	Color change	480 ⁱ Intensity reaches maximum after 15 minutes
11	Guanosine		115	"	"	"	610 ⁱ Intensity reaches maximum after 8 hours
12	Desoxycytidine · HCl		115	"	"	"	badly ⁱ defined maximum
13	Thymidine		115	"	"	"	"
14	Adenylic acid		115	"	"	"	500 ⁱ Intensity reaches maximum after 2 hours
15	Guanylic acid		115	"	"	"	570 ⁱ Intensity reaches maximum after 6 hours

116	Desoxycytosine-5'-phosphate -		115	"	"	"	badly defined maximum ⁱ
117	Thymidine-5'-phosphate -		115	"	"	"	550 ⁱ
118	 -	Acridine	117	23	6.7×10^2 (390) ^P	B.H.	390
119	 -	Acridine	117	100	-1.1×10^3 (390) ^P	B.H.	390
120	 (acridine) -		116	Not determined	weak	New Absorption	~460 ^j
121	 -		116	"	strong	New Absorption	~529 ^j
122	 -		116	"	weak	New Absorption	~470 ^j
123	Guanylic acid -		121	"	Not determined	New peak	565 ^k Progressive color change during 3 days

24	Thymidilic acid -		121	"	"	New peak	560 ^k	Progressive color change during 3 days
25	Desoxyribonucleic acid -		121	"	"	"	506 ^k	Opacity of solution increases during 2 days, but no detectable color change
26	β-Carotene -	I ₂	56	"	Not determined		1000	
27	Numerous carcinogenic hydrocarbons -	I ₂	120	"	"			
28	Tryptophan, Proline, Glycine, Alanine -	O ₂	108	"	"	New absorption	350-410 ⁿ	
29			119 ⁿ	"	"		360	λ _{max} chloranil 285, 380
30		"	119	224	"	B.H.	360	pH 7
31		"	119	318	"	"	350	pH 8
32		"	119	176	"	"	355	k ~ 0 at pH 12
33		"	119	298	"	"	390	

134		-	"	119	Not determined	"	360	pH 7.4	
135		-	"	119	"	"	360	pH 8	
136	Amethopterin	-	Tryptophan	117	45	1.6×10^2 P	B.H.	420	Pteridines as a class have a maximum in the vicinity of 380m μ
137	Amethopterin	-	Serotonin	117	60	1.6×10^2 P	B.H.	420	
138	Aminopterin	-	Tryptophan	117	25	5.2×10^2 P	B.H.	430	
139	Aminopterin	-	Serotonin	117	45	5.2×10^2 P	B.H.	430	
140	N ¹⁰ -Methylfolic acid	-	Tryptophan	117	22	3.6×10^2 P	B.H.	420	
141	N ¹⁰ -Methylfolic acid	-	Serotonin	117	34	3.6×10^2 P	B.H.	420	
142	Folic acid	-	Tryptophan	117	13	1.1×10^3 P	B.H.	400	
143	Folic acid	-	Serotonin	117	30	1.1×10^3 P	B.H.	400	
144	N ¹⁰ -Formylfolic acid	-	Tryptophan	117	15	7.1×10^2 P	B.H.	400	
145	N ¹⁰ -Formylfolic acid	-	Serotonin	117	23	7.1×10^2 P	B.H.	400	
146	9-Methylfolic acid	-	Tryptophan	117	9	8.5×10^2 P	B.H.	400	
147	9-Methylfolic acid	-	Serotonin	117	20	8.5×10^2 P	B.H.	400	

148	2,4-Diamino-6,7-dimethylpteridine - Tryptophan	117	7	-1.2×10^3 P	B.H.	370	
149	2,4-Diamino-6,7-dimethylpteridine - Serotonin	117	18	-1.2×10^3 P	B.H.	370	
150	2-Amino-4-hydroxypteridine-6-carboxylic acid - Tryptophan	117	5	2.2×10^3 P	B.H.	410	
151	2-Amino-4-hydroxypteridine-6-carboxylic acid - Serotonin	117	15	2.2×10^3 P	B.H.	410	
152	Xanthopterin - Tryptophan	117	2	5.0×10^3 P	B.H.	410	
153	Xanthopterin - Serotonin	117	15	-7.7×10^3 P	B.H.	410	
154	 - I ₂	122	Not de-termined	Not de-termined			Black complex, shows sharp EPR signal
155	 - I ₂	122	"	"			"
156	3-Methylcholanthrene - Vitamin k ₃	123	"	"		480-490 ^j	Red complex, in CH ₂ Cl ₂ . λ _{max} in Vit. k ₃ 325 mμ
157	1,2-Dibenzanthracene - Vitamin k ₃	123	"	"		"	
158	3,4-Benzpyrene - FMN	124	"	"		490 ^j	
159	Several carcinogenic hydrocarbons - Substituted benzoquinones	126	"	"		fusion ^q point of mixture	
160	Chlorpromazine - FMN	138	"	"		color change	ice, -70°C

Footnotes to Table II

- a. For uniformity, all equilibrium data is presented as an association constant. If originally reported as a dissociation constant, the reciprocal is given here. Units are liter/mole.
- b. Units are liter/mole cm. Numbers in brackets following the constant indicate the wavelength.
- c. B.S. refers to the Benesi-Hildebrand equation (II). We use this designation if the equation in the original paper is of this form, although the authors may not have designated it as such.
- d. ΔH of complex formation reported as $-5.1 \text{ Kcal mole}^{-1}$ at pH 5.9. Shifts in riboflavin redox potential in presence of interactant also noted.
- e. ΔH of complex formation reported as $-1.6 \pm 0.6 \text{ Kcal mole}^{-1}$.
- f. ΔH of complex formation reported as $-3.3 \text{ Kcal mole}^{-1}$ at pH 9.2.
- g. The comments in the text concerning the tryptophan-TMN complex presumably apply also to this complex.
- h. All experiments reported in Reference 97 where 6 N HCl is indicated,
- i. the solvent was also 50% in ethanol.
- i. Maximum of new absorption, considerable absorption on long wavelength side of maximum, solvent is dimethylsulfoxide.
- j. Maximum of new absorption.
- k. Maximum of new peak appearing as a shoulder.
- l. Product of enzymic oxidation of D-proline.
- m. Product of enzymic oxidation of D-pipecolic acid.
- n. All experiments reported in Reference 119 are in 50% aqueous ethanol.
- p. Extinction reported as $\epsilon_{\text{mixture}} - \epsilon_{\text{components}}$ at the indicated wavelength.
- q. No correlation between quinone reduction potential or hydrocarbon ionization potential and complex stability.
- r. Fine structure observed in the C.T. band with tryptophan attributed to tryptophan singlet to triplet transition.

Table III
Charge Transfer Bands of Indole Complexes^a

	Max. (m μ)	E _{C.T.} (Kcal mole ⁻¹)
1) FMNH ₂ :FMN	900	31.8
2) FMNH ₂ :NAD ⁺	700	40.8
3) Indole:chloranil	ca. 500	53.0
4) Indole:FMN	330 (estimate)	86.3 (estimate)
5) Indole:NAD ⁺	ca. 300	95.3

^aData from Kosower, ref. 90

Table IV
 Estimate of Charge Transfer Energy from Molecular Orbital
 Parameters

	I_p	E_a	$I_p - E_a^a$	E.C.T.
FMNH ₂ FMN	+ .105 β	- .344 β	\sim - .24 β	31.8 Kcal
FMNH ₂ NAD ⁺	+ .105 β	- .356 β	\sim - .25 β	40.8 Kcal
Indole Chloranil	- .534 β	- .1 \pm .05 β^b	- .63 \pm .05 β	53.0 Kcal ^c
Indole FMN	- .534 β	- .344 β	\sim - .88 β	80-90 Kcal (estimate)
Indole NAD ⁺	- .534 β	- .356 β	\sim - .89 β	86-95 Kcal ^d

^aThe algebraic signs here are tricky. This is ΔH . Since by definition $\Delta H = I_p$, but $\Delta H = -E_a$, algebraic addition of the terms in the table gives the correct result. Since β is negative, the total ΔH is positive, as expected.

^bThe Pullmans quote - .23 β for benzoquinone, - .18 β for cyanoquinone. As chloranil is a much better acceptor than either, an estimate of - .1 \pm .05 is reasonable and conservative.

^c λ_{max} 355 m μ quoted in Table II (entry 132) for tryptophan-chloranil is for donation from the amino group, not the indole nucleus.

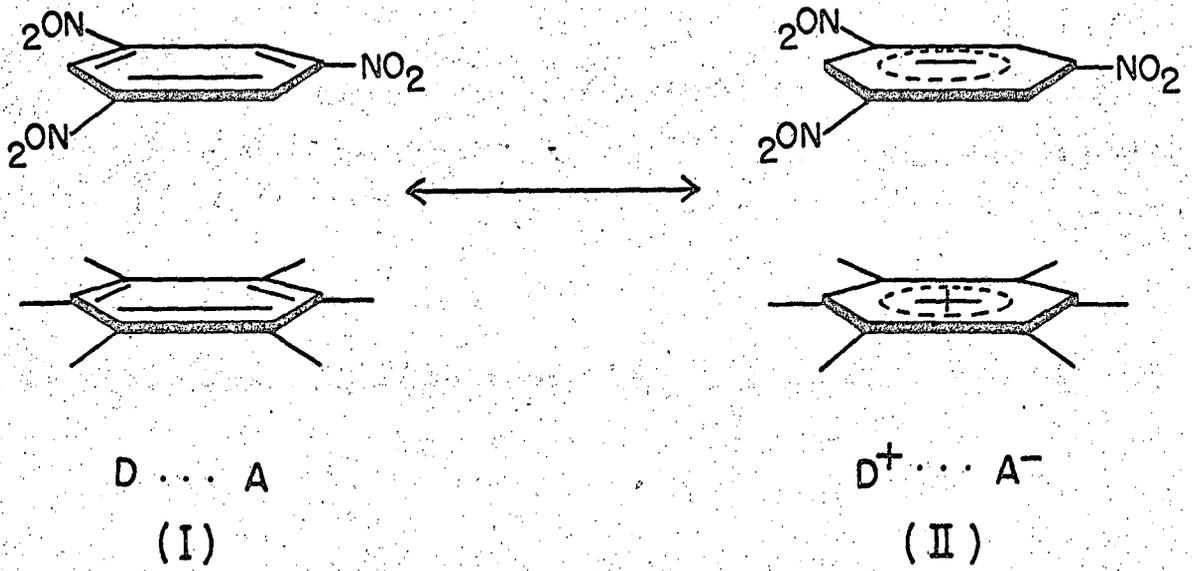
^dUsing Kosower's estimate of ca. 300 m μ or calculating from Fig. 26, using λ_{max} C.T. 320 m μ .

Part I.

FIGURE CAPTIONS

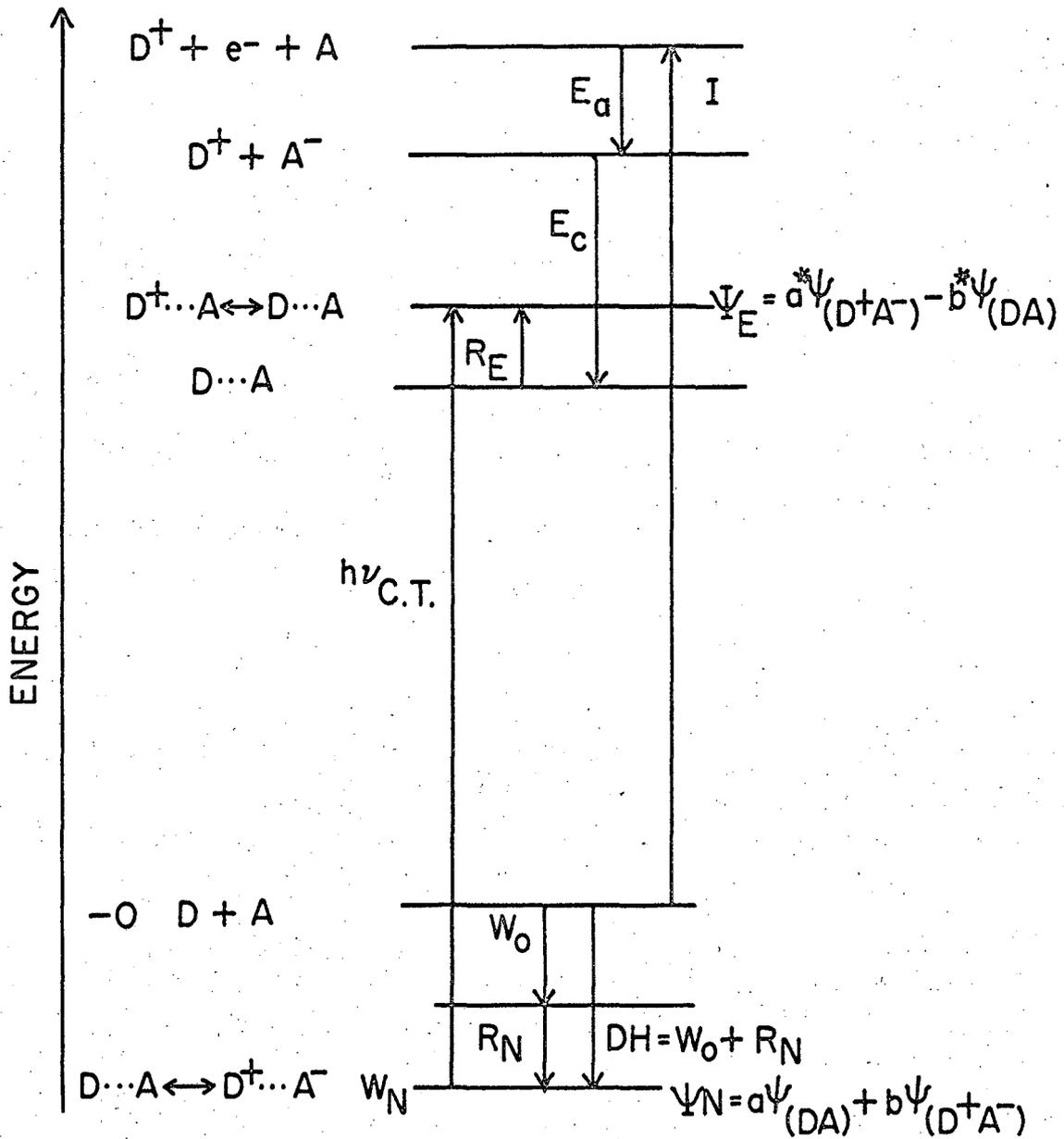
- Fig. 1. Resonance description of the donor-acceptor complex of hexamethylbenzene and S-trinitrobenzene.
- Fig. 2. Diagram of energy relationships in a donor-acceptor complex.
- Fig. 3. Effect of resonance interaction on the energies of the ground and excited states.
- Fig. 4. Schematic diagram of energy relationships in a donor-acceptor pair according to the molecular orbital description (perturbation effects exaggerated).
- Fig. 5. Dependence of the energy (a v c. t.) on the first half wave reduction potential (in acetonitrile) of acceptor for complexes with A, hexamethylbenzene and B, pyrene (from reference 14).
- Fig. 6. Free energy of formation, ΔF , in relation to the ionization potential of donor for donor-acceptor complexes of iodine. 0 = aromatic and aliphatic hydrocarbon donors; Δ = amine donors (data from reference 1).
- | | | | |
|-----------------------|-------------------------|--------------------------|-----------------------|
| 1. benzene | 10. naphthalene | 19. 1-bromobutane | 27. $nC_4H_{12}-NH_2$ |
| 2. toluene | 11. 1-methylnaphthalene | 20. anisole | 28. $(CH_3)_2NH$ |
| 3. o-xylene | 12. styrene | 21. N, N-dimethylaniline | 29. $(C_2H_5)_2NH$ |
| 4. m-xylene | 13. stilbene | 22. pyridine | 31. $(C_2H_5)_3N$ |
| 5. p-xylene | 14. biphenyl | 23. α -picoline | 32. $(nC_3H_7)_3N$ |
| 6. mesitylene | 15. chlorobenzene | 24. NH_3 | |
| 7. durol | 16. bromobenzene | 25. CH_3NH_2 | |
| 8. pentamethylbenzene | 17. cyclohexene | 26. $C_2H_5NH_2$ | |
| 9. hexamethylbenzene | 18. 2, 3-dimethylbutane | | |
- Fig. 7. Free energy of formation, ΔF , in relation to first half wave potential of acceptor in donor-acceptor complexes with hexamethylbenzene as donor. Thermodynamic data from reference 15; polarographic data, reference 17.
- Fig. 8. Free energy of formation, ΔF , in relation to charge transfer energy, $h\nu_{ct}$, of a series of complexes with trinitrobenzene (data from reference 1).
- Fig. 9. Charge transfer band of complexes of 3, 5-diiodotyrosine and 3, 5-dibromotyrosine with menadione. Use of phenolate and menadione alone gave no absorption in this region. Dotted line indicates anticipated featureless band (from reference 18).
- Fig. 10. Schematic representation of the energy levels of a substituted benzene and unsubstituted benzene.
- Fig. 11. Schematic diagram of incident light with electric vector polarized parallel to charge transfer transition moment.

- Fig. 12. Morphology and molecular orientation in a quinhydrone crystal. — · —, benzoquinone; —, hydroquinone.
- Fig. 13. Reflection spectra obtained on the prominent (001) face of the quinhydrone crystal. a) light polarized parallel to axis a; b) light polarized parallel to b. (From reference 23).
- Fig. 14. Direction of polarization of the charge transfer transition in quinhydrone. New assignment is arrow number one.
- Fig. 15. Potential energy diagram illustrating possible thermal and photo-induced electron transfer from donor to acceptor.
- Fig. 16. Polarographic data for complex formation as a function of donor concentration (in CH_2Cl_2 at 25°). Hexamethylbenzene complexes of: A, tetracyanoethylene; B, tetracyanobenzene. Pyrene complexes of: C, chloranil; D, tetracyanobenzene; E, tetracyanoquinodimethane (data from Reference 64).
- Fig. 17. Possible pi complexing in the transition state during the solvolysis of benzyldimethylsulfonium ion by phenoxide.
- Fig. 18. Scheme for binding FMN to Old Yellow Enzyme proposed by Theorell and Nygaard.
- Fig. 19. Absorption spectra of 3-methylriboflavin plus -----, .21 molar benzoate; ————, .02 M naphthoate.
- Fig. 20. Charge transfer band of donor-acceptor complexes of iodine with various solvent molecules.
- Fig. 21. Difference spectrum of FMNH_2 and NAD^+ relative to FMNH_2 , (from Reference 95).
- Fig. 22. Possible equilibrium relationships between oxidized and reduced forms of flavin and pyridine nucleotide coenzymes.
- Fig. 23. 9-Methylisoalloxazine with phenols. Solvent is 50% ethanol. Flavin is 0.1 M, phenol 0.2 M. 1, 1,4-naphthalenediol; 2, 1,2-naphthalenediol; 3, trimethylquinol (from Reference 88).
- Fig. 24. Supposed pairing of charges in overlap of adenine and isoalloxazine.
- Fig. 25. Absorption spectrum of L-tryptophan in the presence of NAD^+ . 1.71×10^{-2} M tryptophan + 56.5 mg. NAD^+ /ml. (from Reference 102). Dashed line is tryptophan absorption.
- Fig. 26. Trace A, absorption spectrum of a methanolic solution of indolylethylnicotinamide. Comparison with Fig. 25 reveals similarities in the 320 to 420 $\text{m}\mu$ region. Trace B, spectrum of N-(β -p-hydroxyphenylethyl)-3-carbamoylpyridinium chloride in water (solid curve) and that of an equimolar mixture of tyramine hydrochloride and N-methylnicotinamide perchlorate in water (dashed curve). Trace C, spectrum of N-(β -4'-imidazolylethyl)-3-carbamoylpyridinium chloride in methanol (solid curve). Dashed curve is the spectrum obtained subtracting absorption of N-methylnicotinamide perchlorate (from Reference 103).



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Fig. 1



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Fig. 2

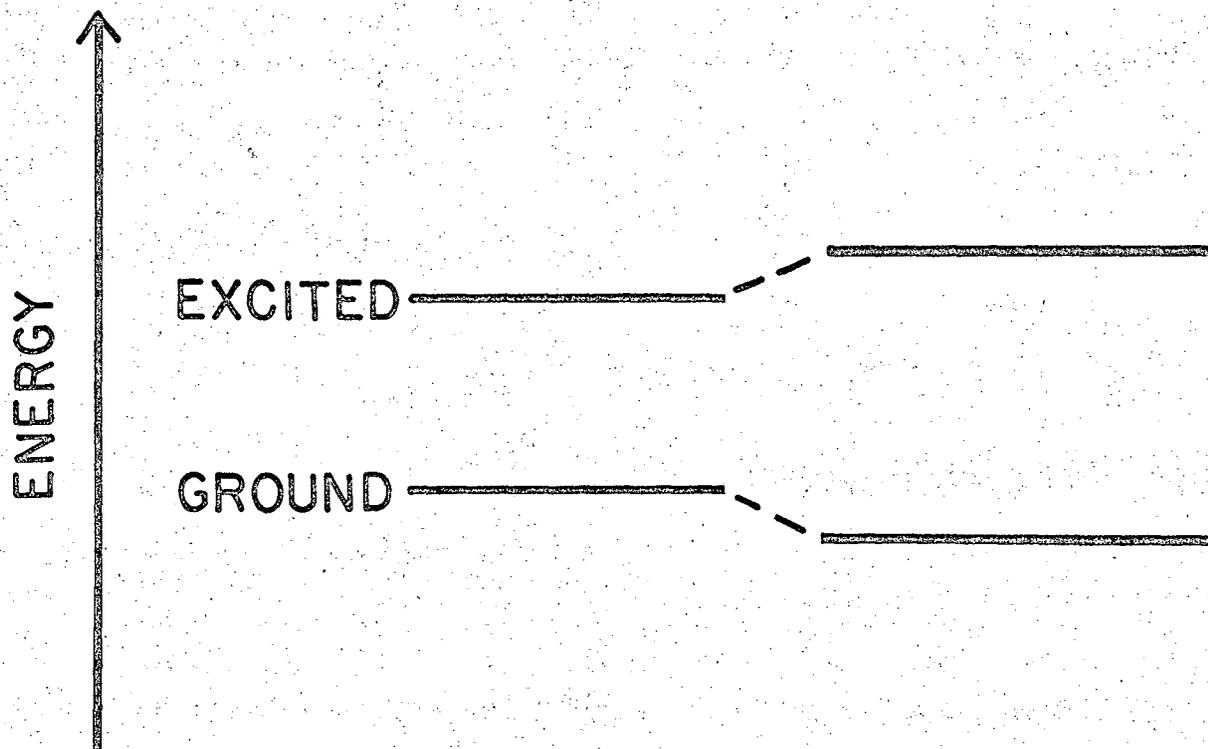
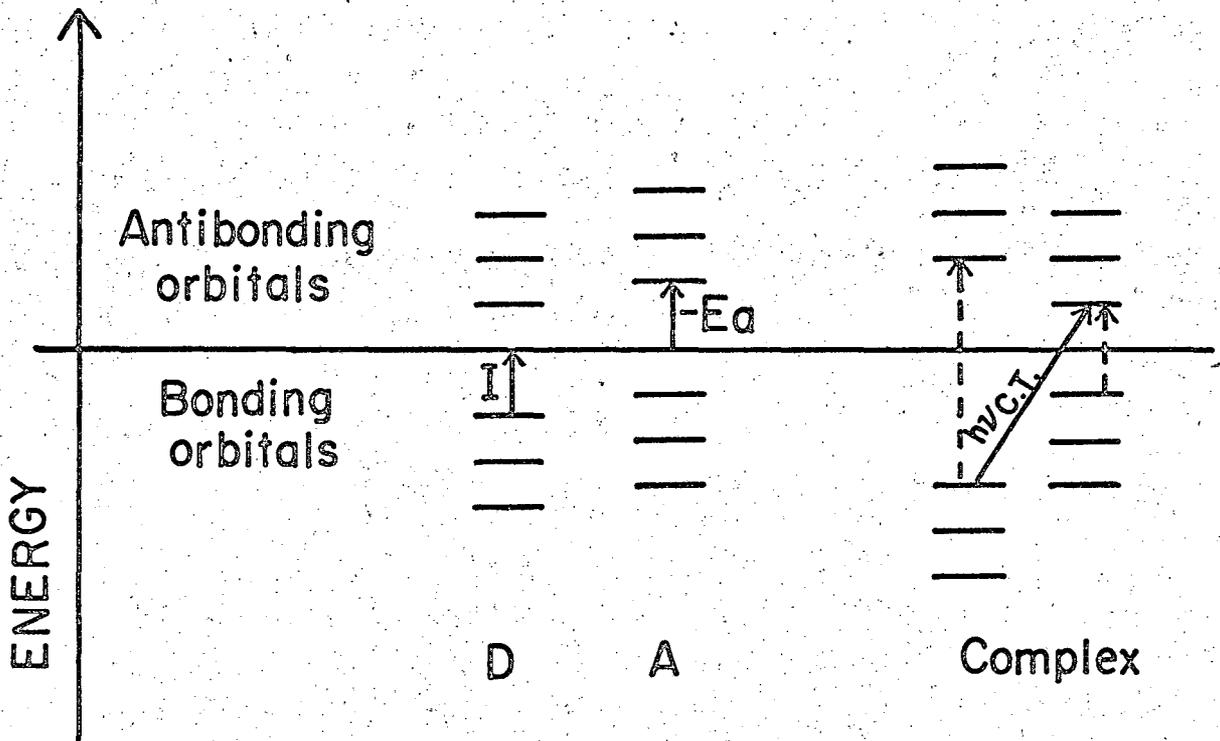


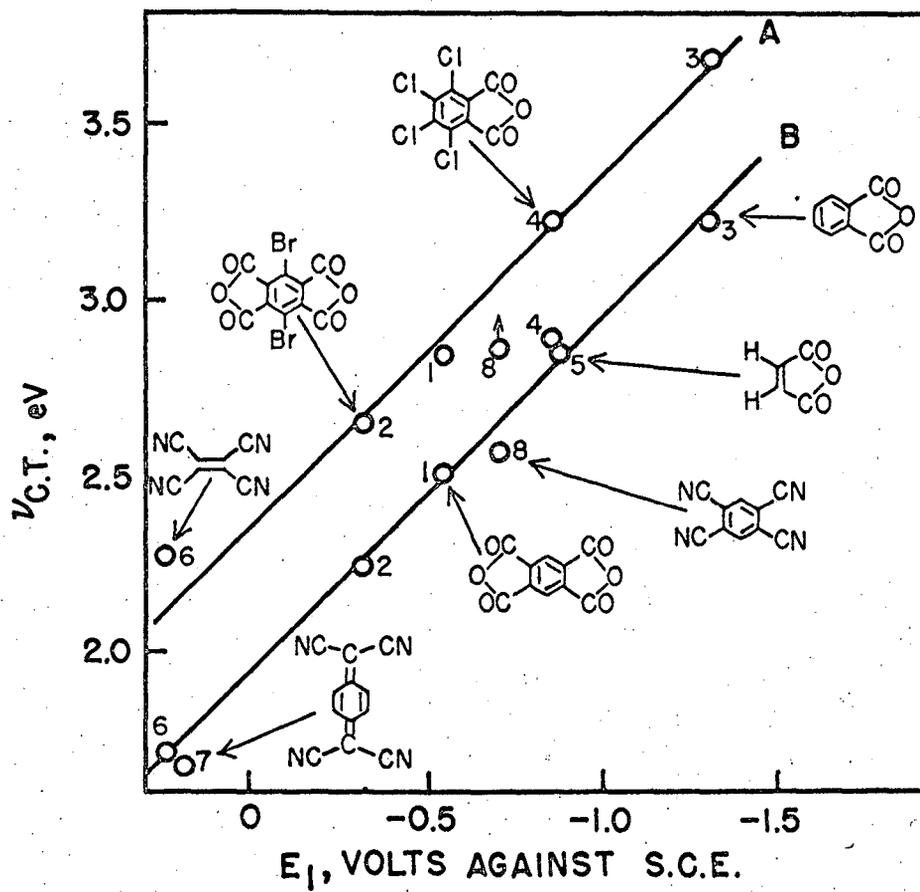
Fig. 3

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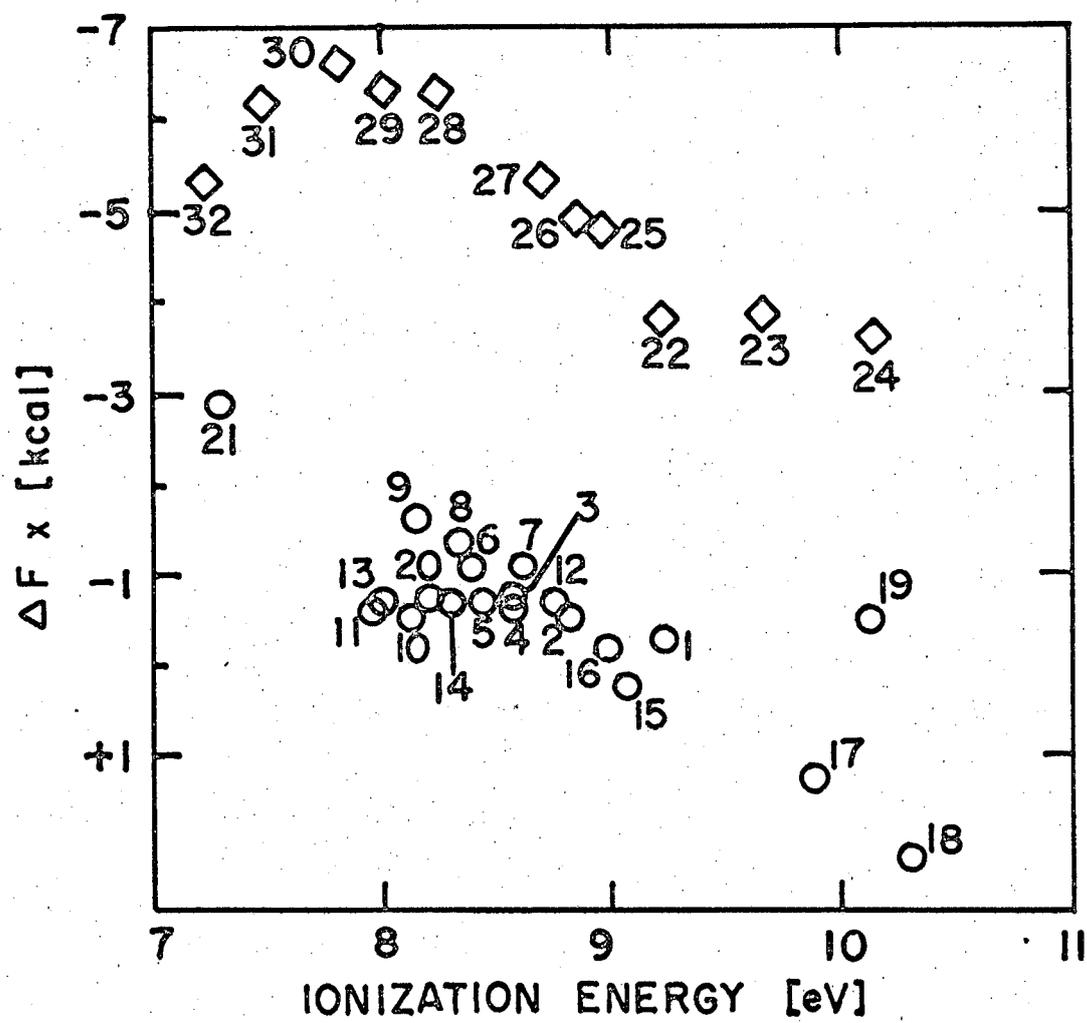
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Fig. 4



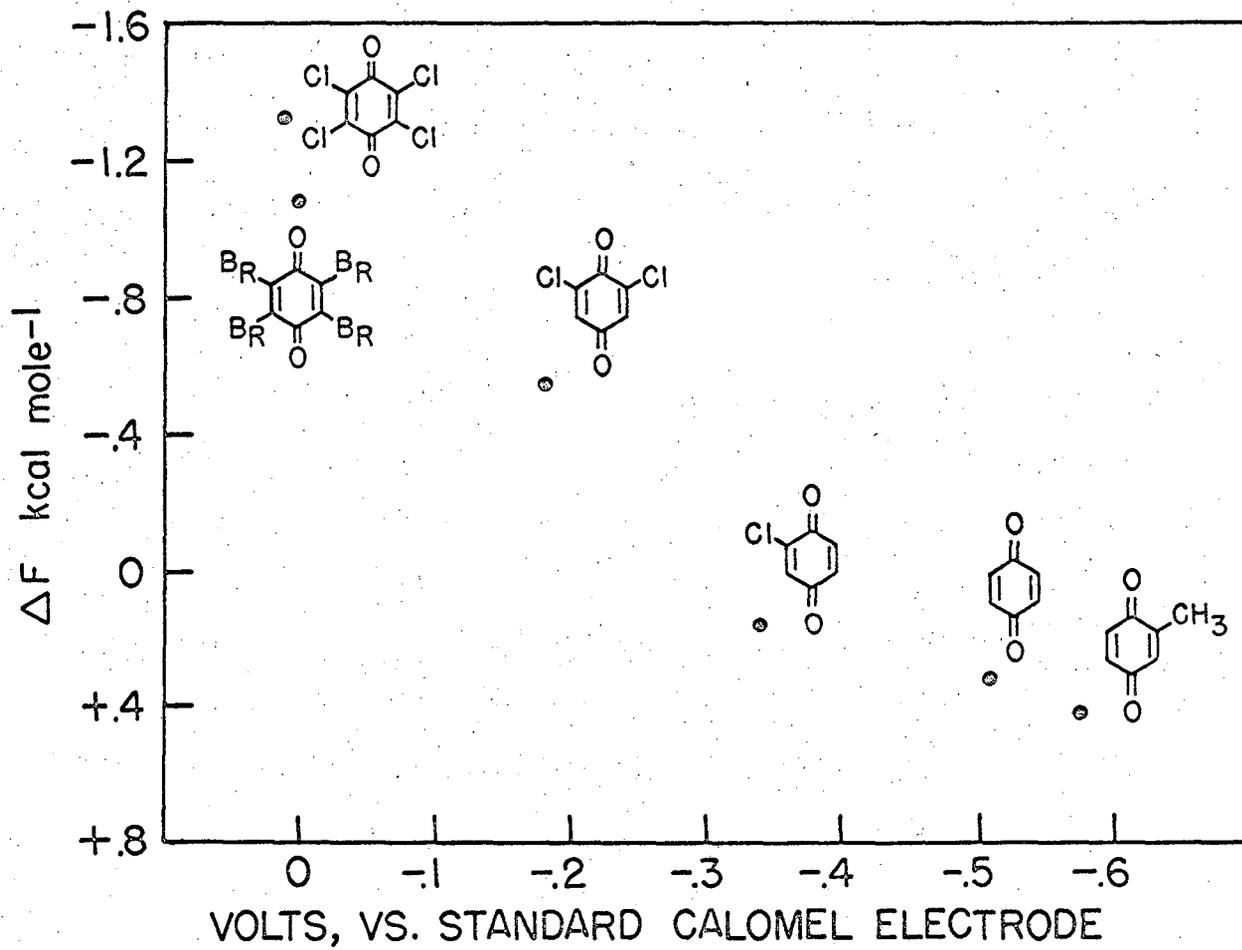
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Fig. 5



MUB-8193

Fig. 6



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Fig. 7

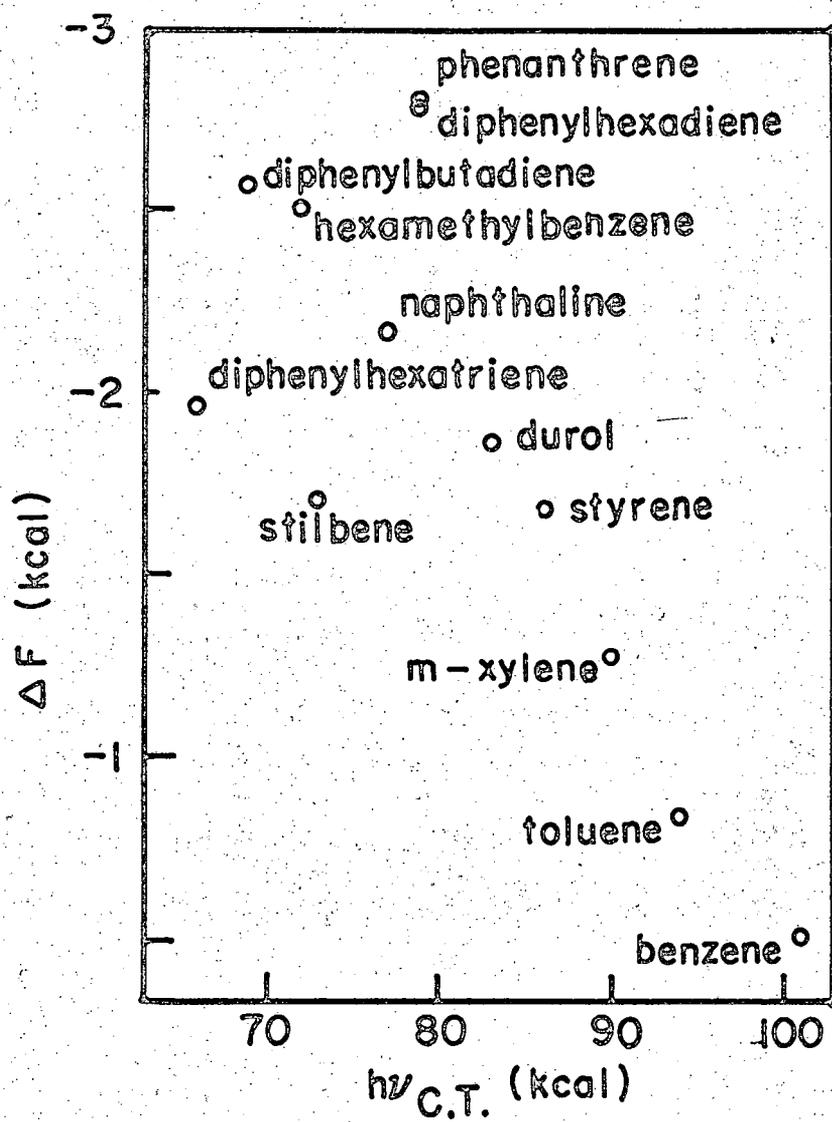


Fig. 8

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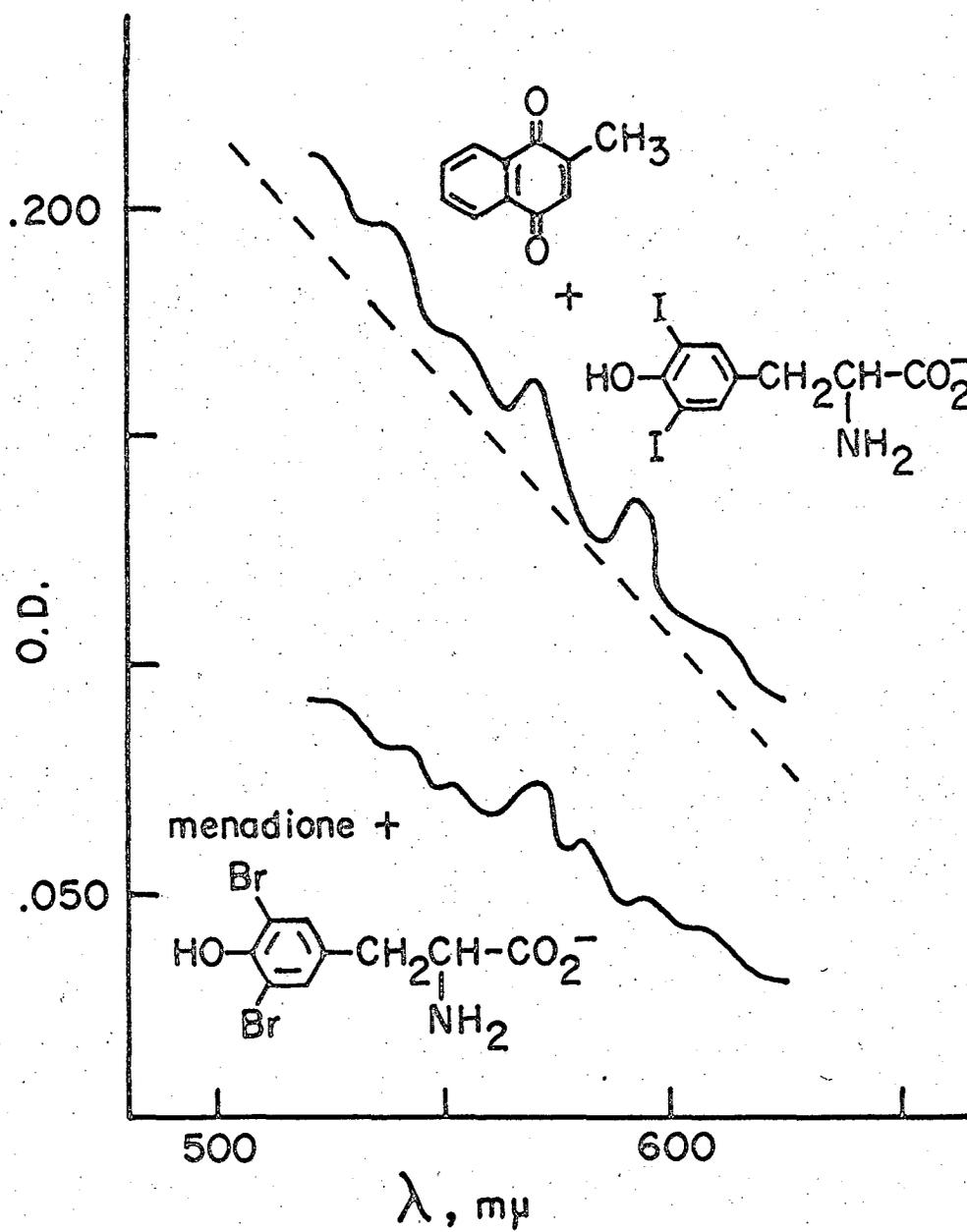
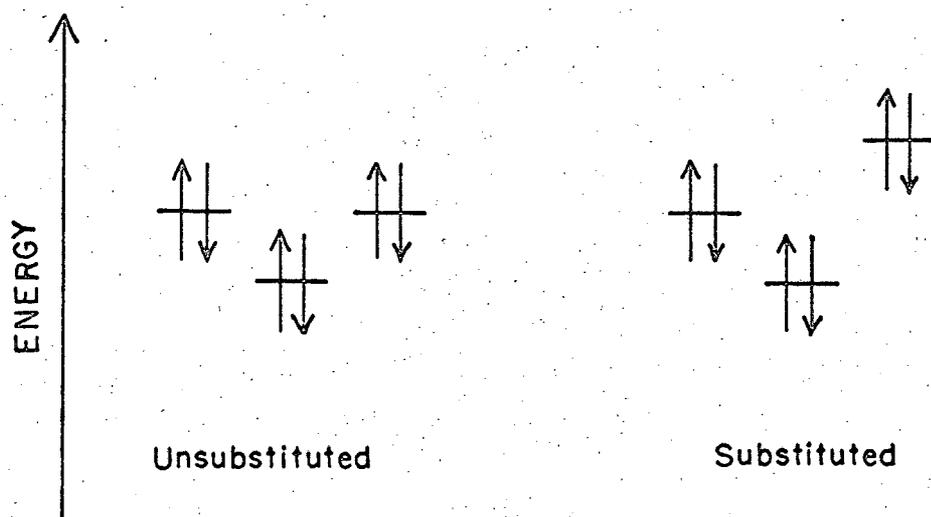


Fig. 9

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Fig. 10

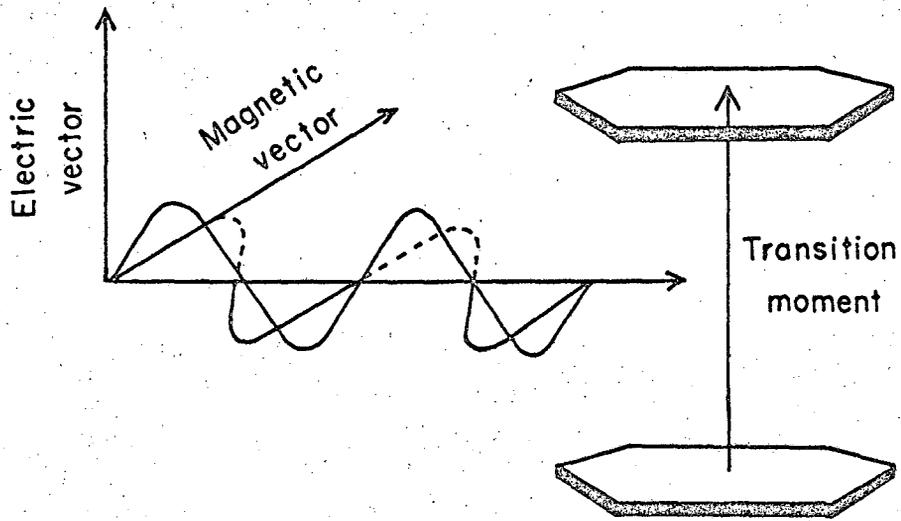


Fig. 11

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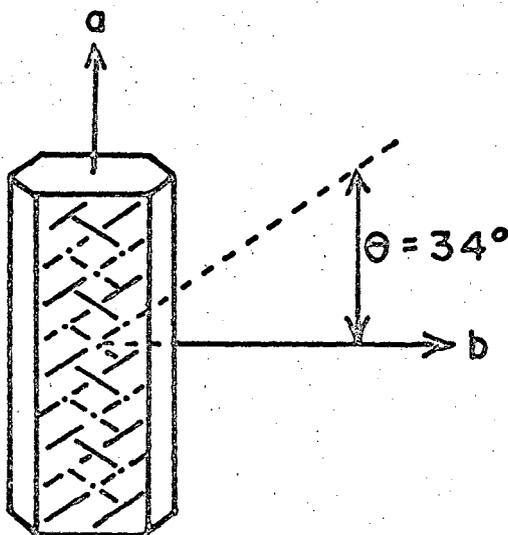
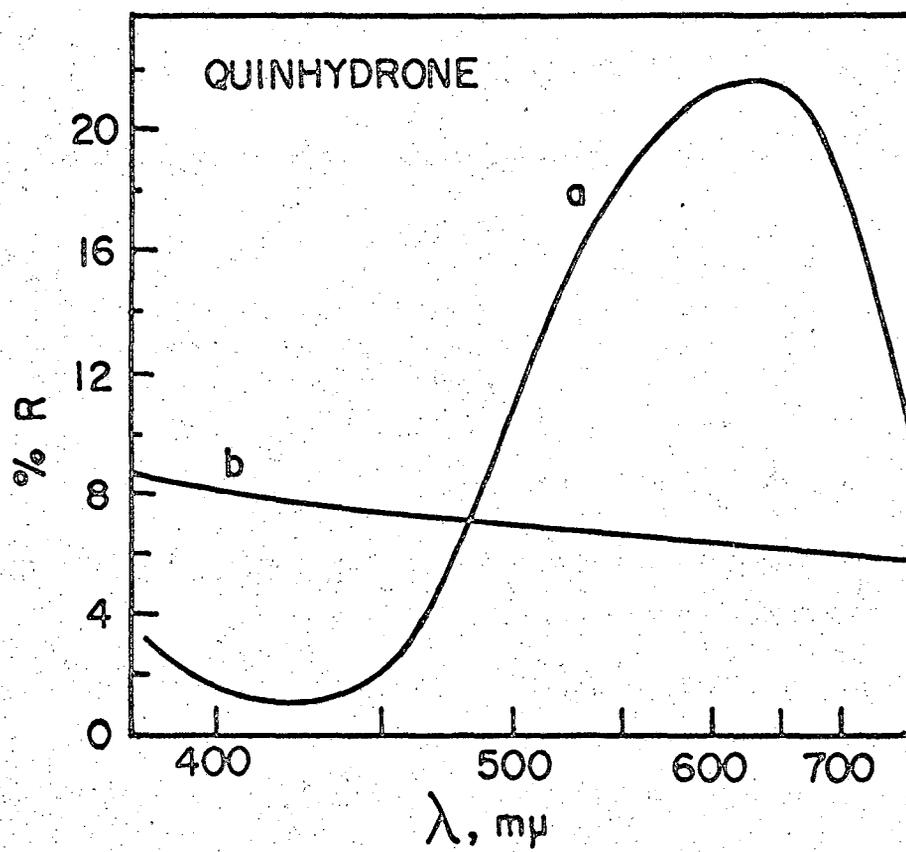


Fig. 12

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Fig. 13

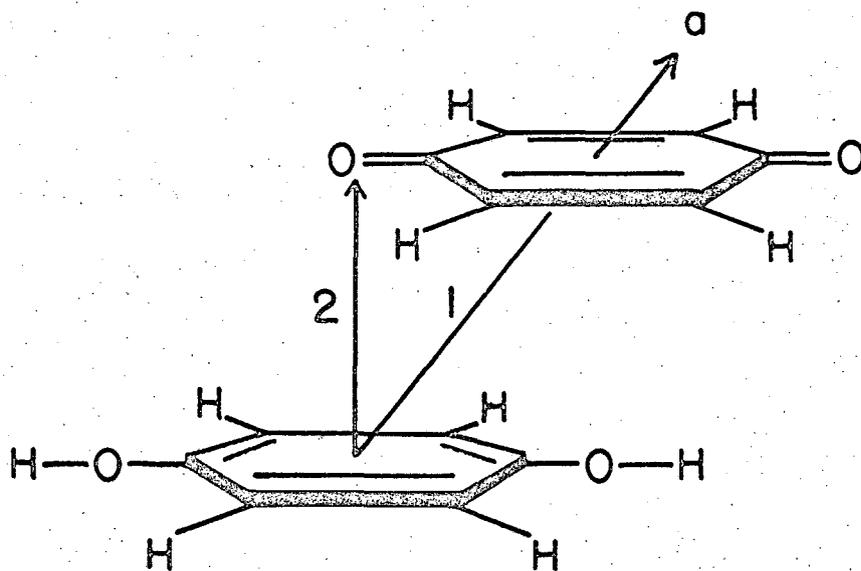
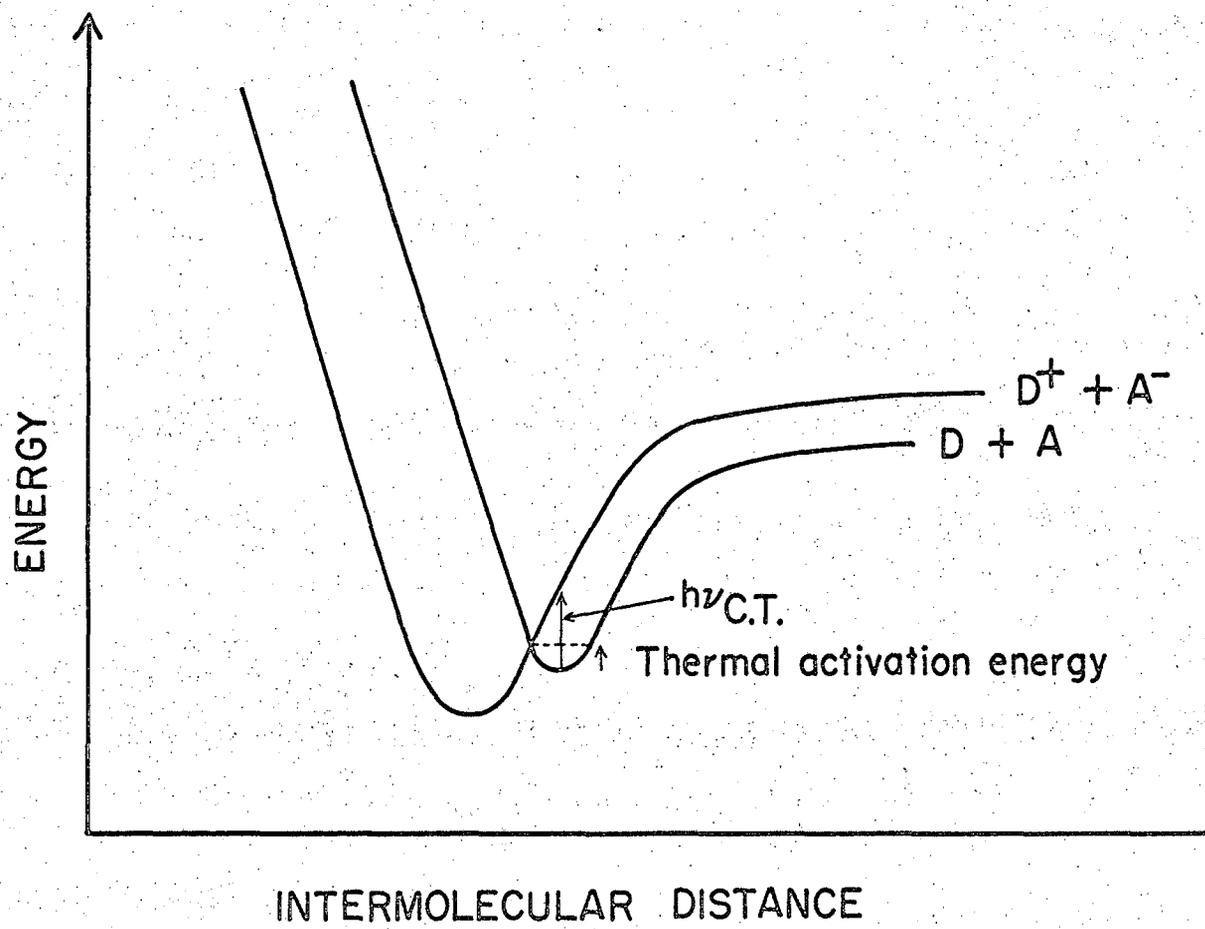


Fig. 14

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Fig. 15

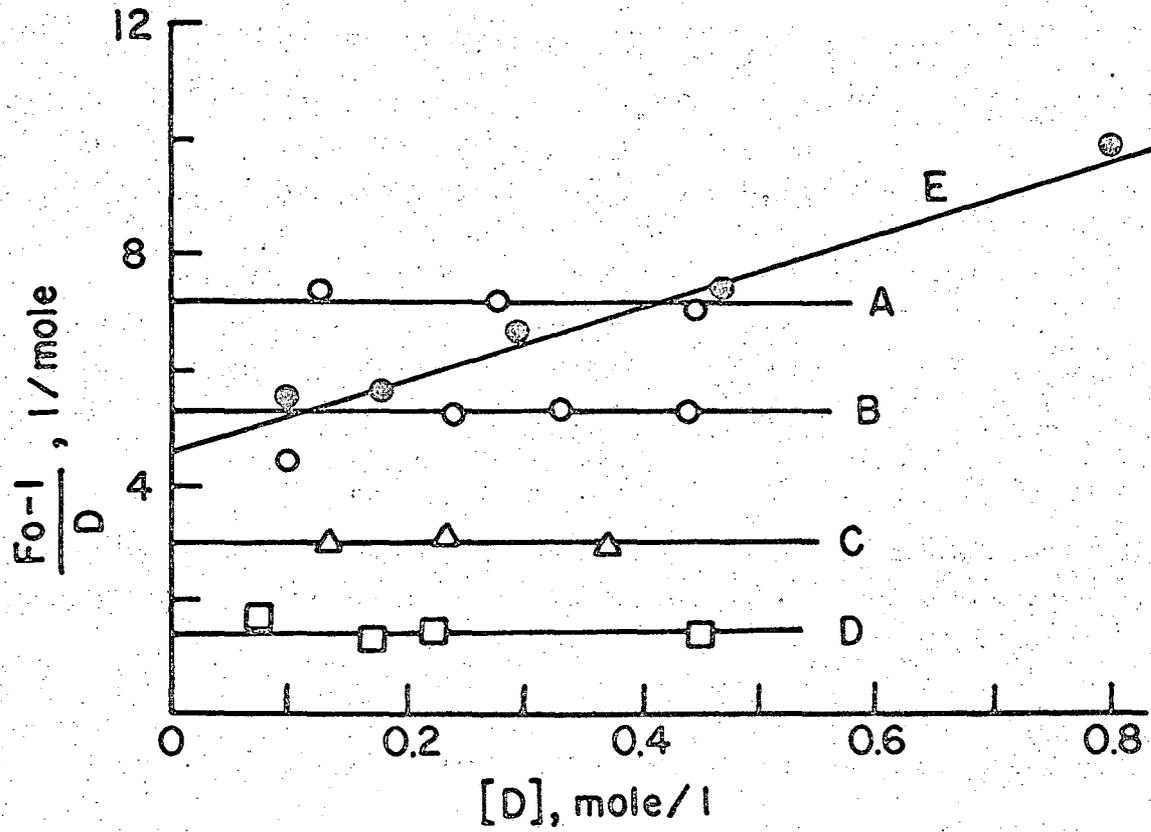
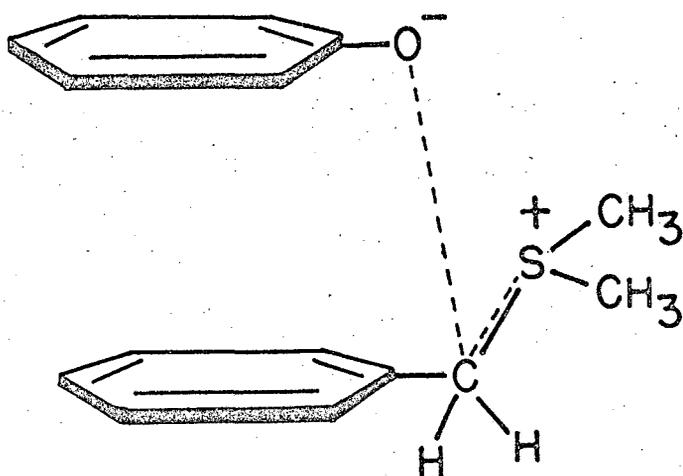


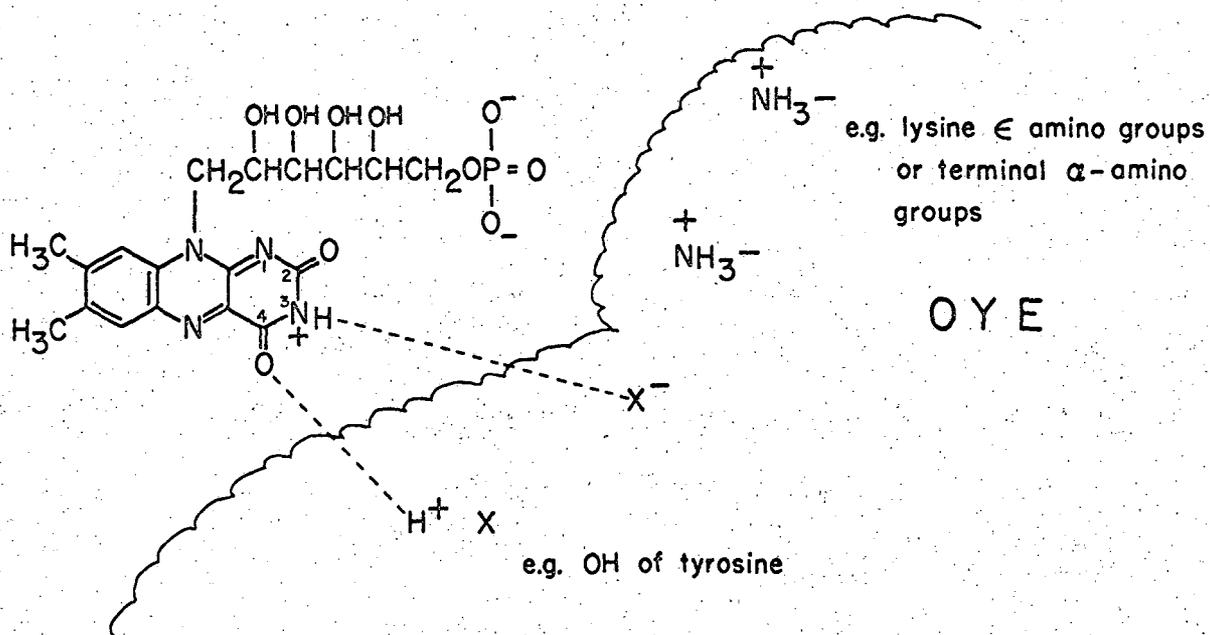
Fig. 16

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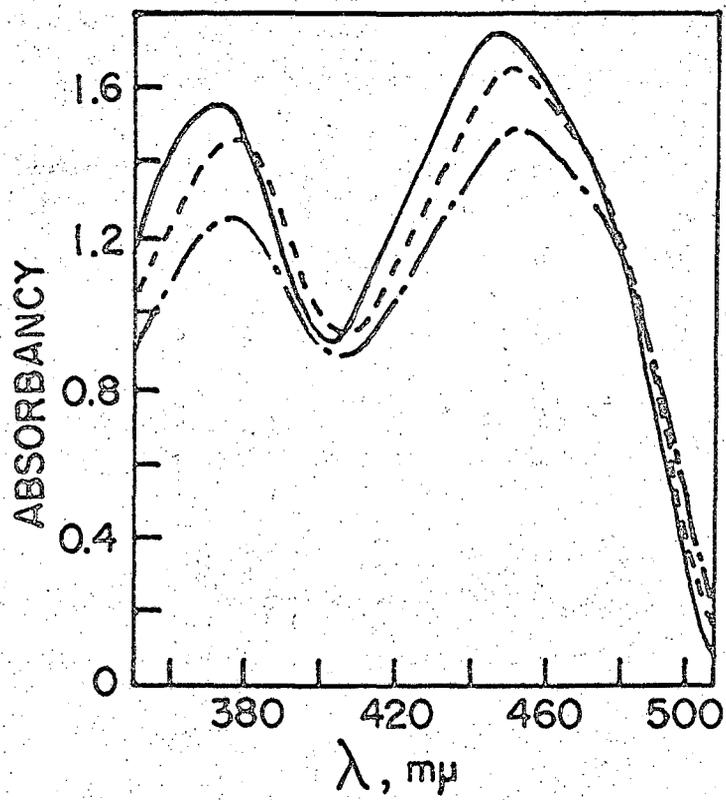
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Fig. 17



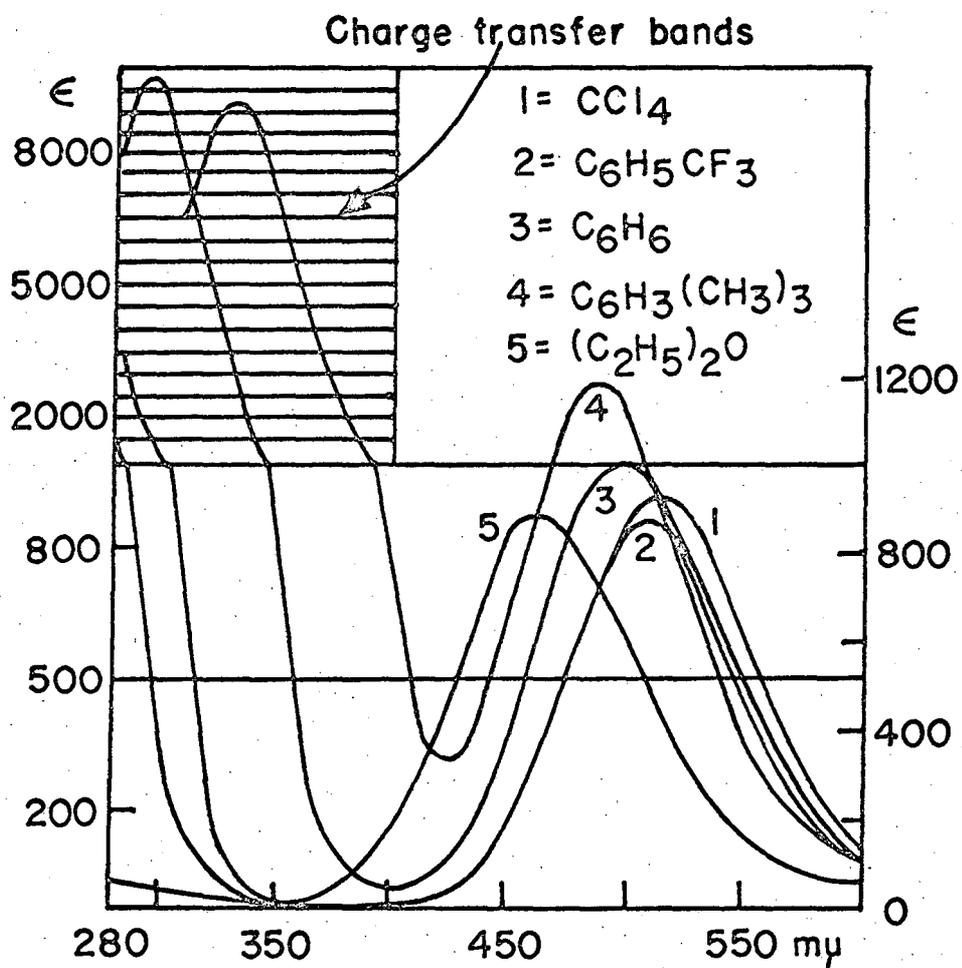
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Fig. 18



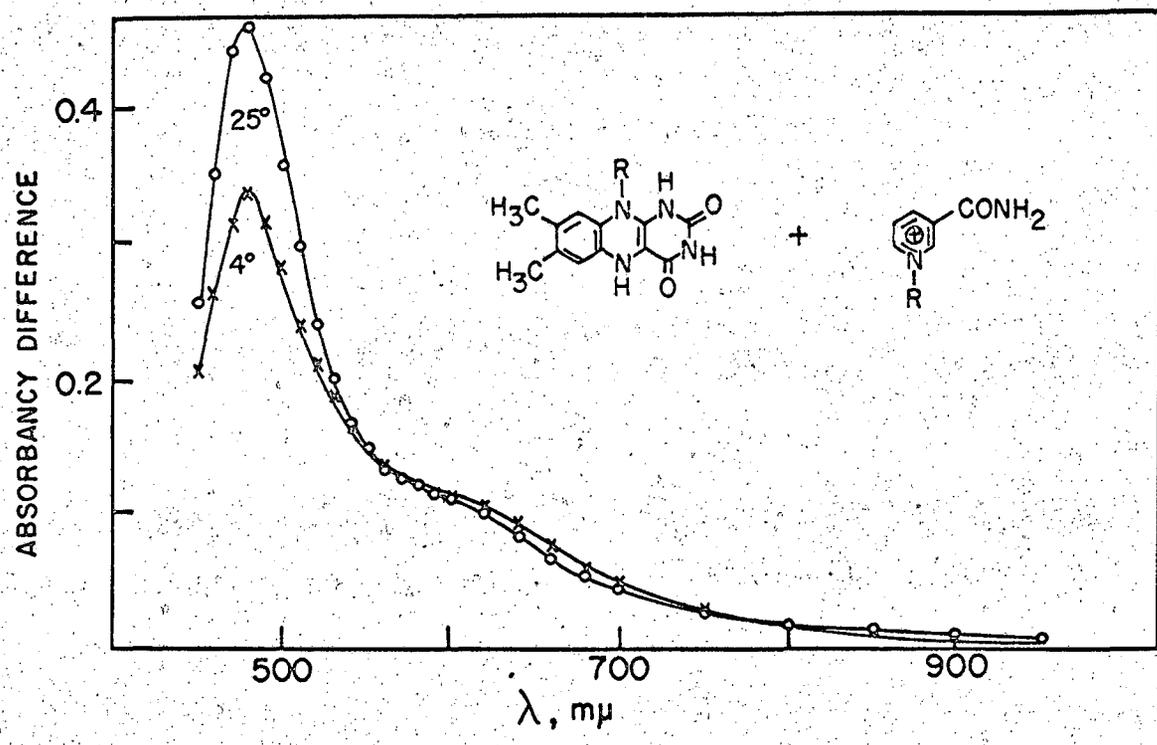
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Fig. 19



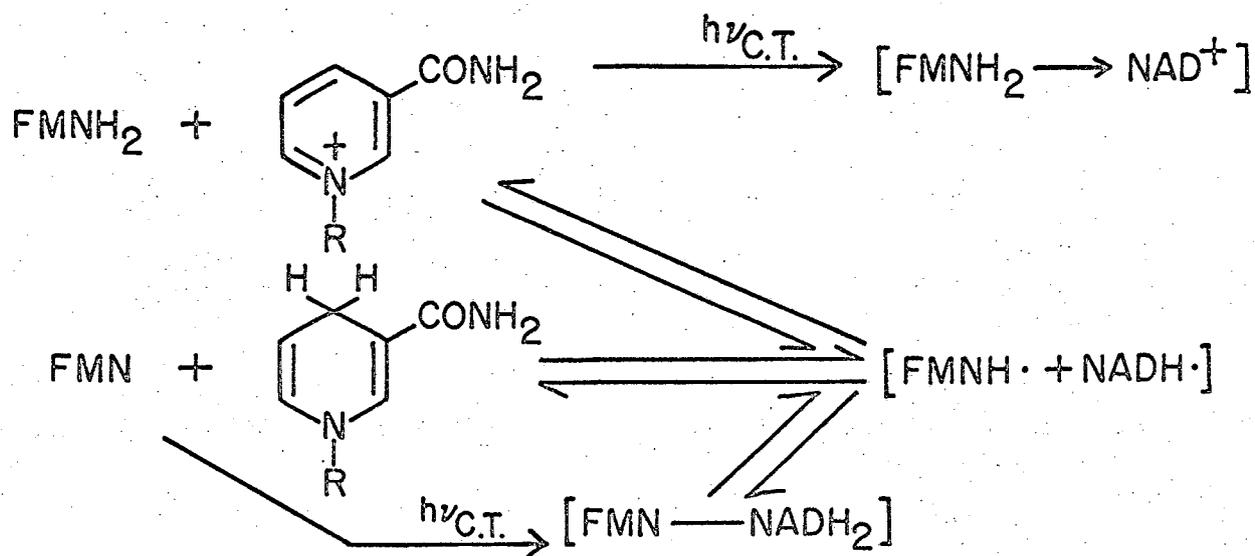
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Fig. 20



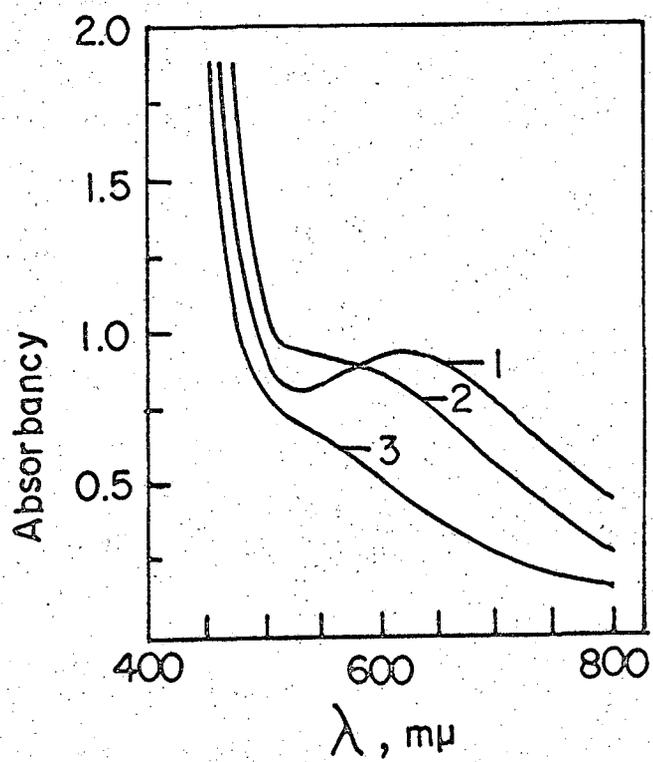
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Fig. 21



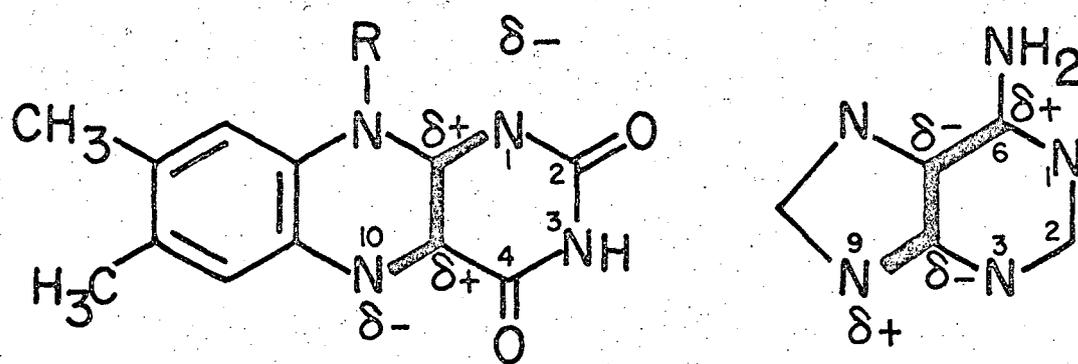
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Fig. 22



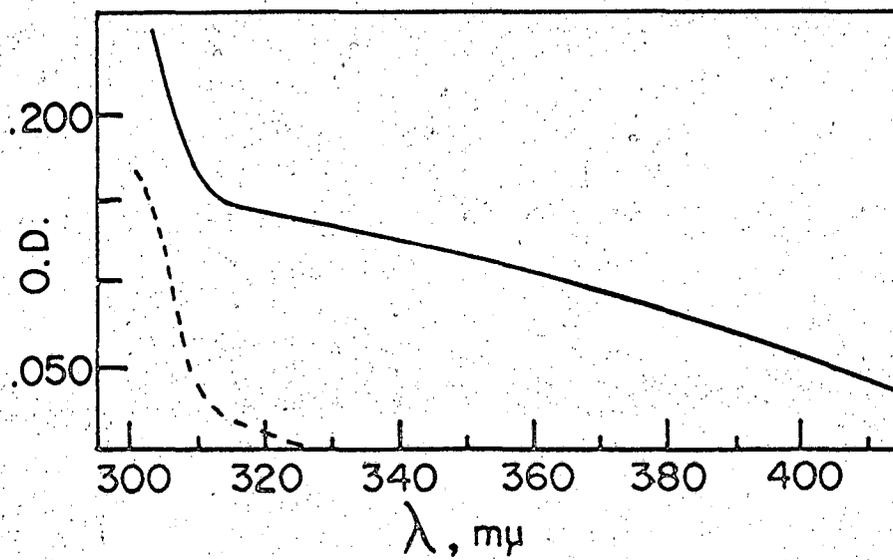
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Fig. 23



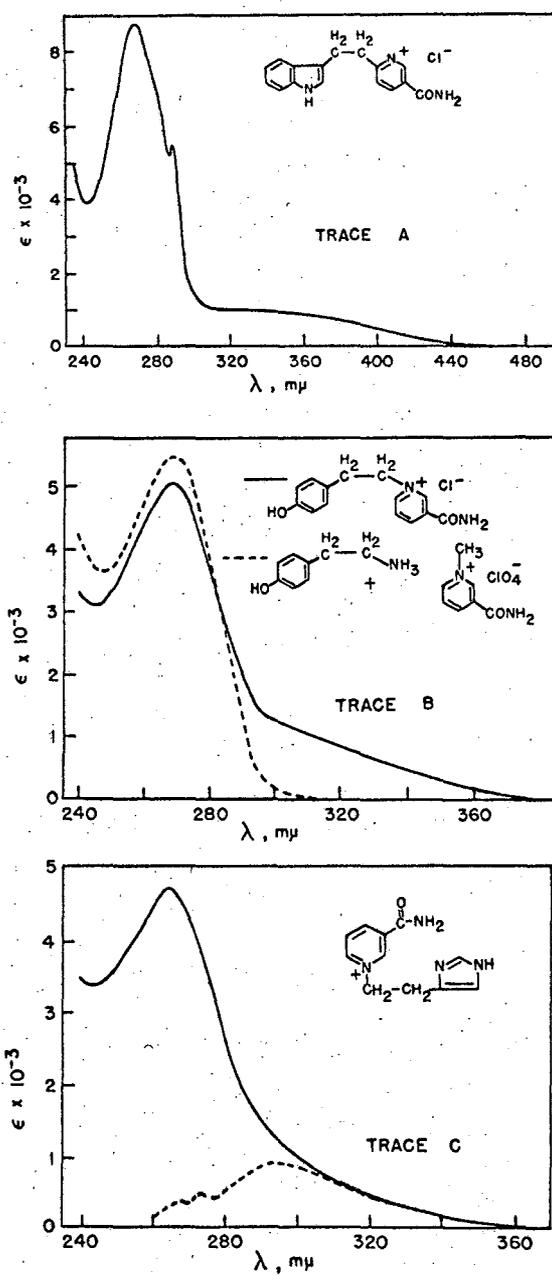
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Fig. 24



MUB-8211

Fig. 25



MUB-8688

Fig. 26

PART II. TRANSFER OF CHARGE IN THE ORGANIC SOLID STATE

Processes involving transfer of charge through condensed organic matrices are not only of intrinsic interest but may also have an important bearing on many areas of biochemistry. Twenty years have now passed since Szent-Gyorgyi¹ proposed that the solid state might play a role in biological processes. The flurry of research and speculation on the role of semiconduction in biology which this suggestion eventually precipitated has already been reviewed, in whole or in part, several times.²⁻⁵ Very recently a critical treatment of conductivity in organic crystals, proteins and donor-acceptor complexes, including some of the biological aspects, has appeared.⁶ This chapter also has a good historical perspective. The same volume⁷ contains a comprehensive review of the organic polymers which conduct electricity, presenting well over two-hundred references to the original literature.

Our plan in this second part will be (1) to summarize the current situation regarding transfer of charge in biological molecules via semiconduction; (2) to consider some of the recent results in the organic semiconductor field which seem of interest to us; and (3) to consider the photochemical processes which can result in generation of charge carriers and transfer of charge, an area currently yielding some very interesting results.

Transfer of Charge by Semiconduction

In this section, electrical conductivity is considered in the context of a charge transfer process. Semiconductors are somewhat arbitrarily defined as materials having electrical properties somewhere between those of conductors and insulators. Their conductivity varies exponentially

with temperature according to the relationship

$$\sigma = \sigma_0 e^{-E/kT}$$

where σ is the conductivity and E is best considered as the activation energy for conduction. Conductivity in the organics has often been considered in terms of an excitation of a valence electron to a conduction band, a picture taken over from the inorganics. Whether it is at all applicable to organic materials or whether the activation energy is in truth related to a band gap is a matter of current debate among the experts. This is a highly non-trivial topic and in the ensuing discussion we will restrict ourselves to phenomenology.

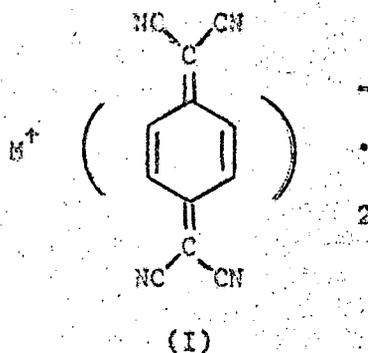
For dry proteins and nucleic acids the activation energy for conduction is large and the conductivity is accordingly very low. Hydrated proteins and nucleic acids are better conductors, but the increased conductivity is thought to be due to protons from the water which act as charge carriers. Rosenberg,⁸ however, feels he has shown that proteins can show electronic conduction which is intrinsic. With 7.5% water adsorbed on protein, no electrolysis of the water occurs during the conductivity experiments. This is felt to be incompatible with a conduction mechanism involving water protons.

Oxygen adsorbed on the surface of the conducting material can increase surface conduction, presumably by trapping electrons as O_2^- , facilitating conduction by the resultant positive "holes". A recent study⁹ shows that conduction in purines and pyrimidines is increased by adsorbed oxygen. The conductivities are still low, however.

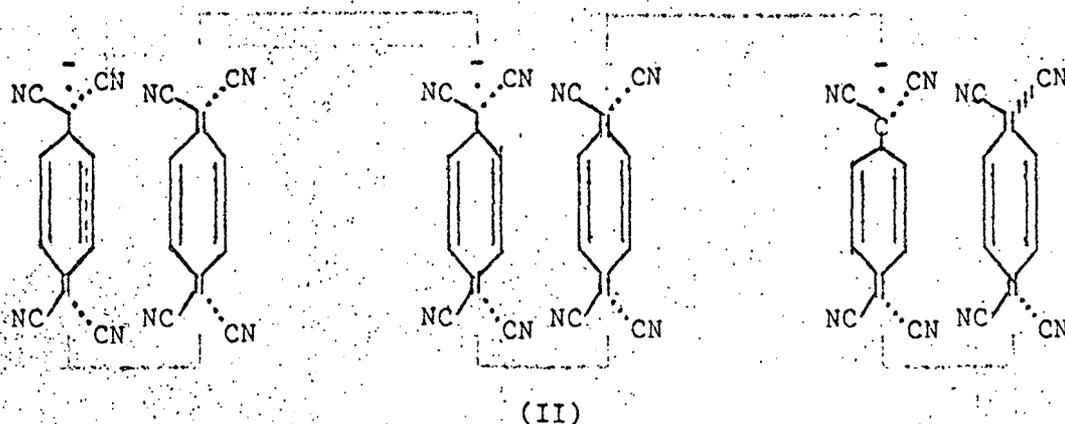
Direct transmission of electrons through the π -systems of proteins or nucleic acids now seems a rather unlikely possibility in living sys-

tems. Propagation of electronic excitation in biopolymers will be considered in another chapter of this volume. Recalling the phenomenon of bioluminescence which involves generation of electronic excitation from stored chemical energy, one realizes the physical feasibility of such a process in a living system.

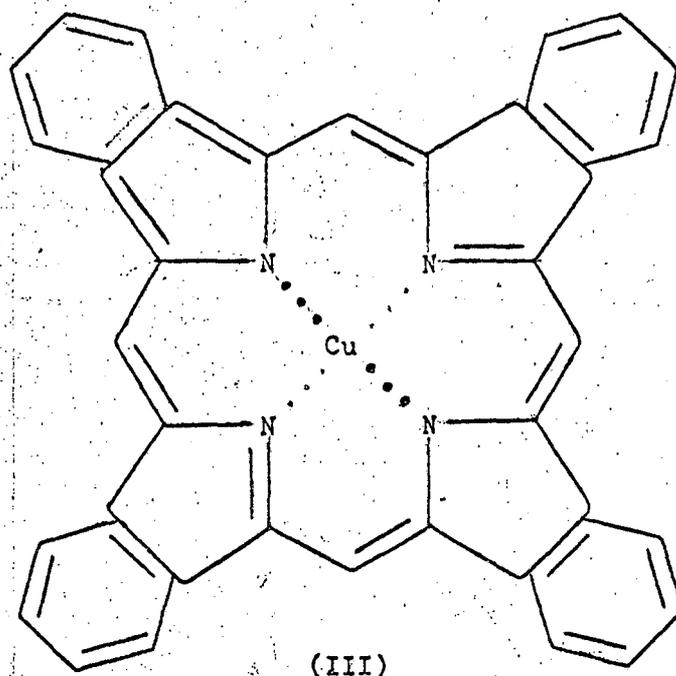
The highest conductivities thus far observed in organic molecules are found among the donor-acceptor complexes. The activation energies for conduction are small, on the order of 0.1 electron volt (~ 2 Kcal.) or less. Examples are the complexes of aromatic hydrocarbons with iodine and complexes of amines with chloranil or related quinones. The best conductors have a high free radical content and are usually not of simple stoichiometry. The complex salts of TCNQ¹⁰ (I) are the best of the known



organic conductors. The cation may be a metal ion such as cesium, the quinolinium ion, or *N*-alkylated poly-2-vinylpyridine.¹¹ Magnetic susceptibility studies¹² indicate that the odd electrons, which are presumably the charge carriers, are degenerate, the same situation one finds in a metal. These salts are considered to have a superposition of TCNQ molecules with the free electrons on alternate molecules (II).

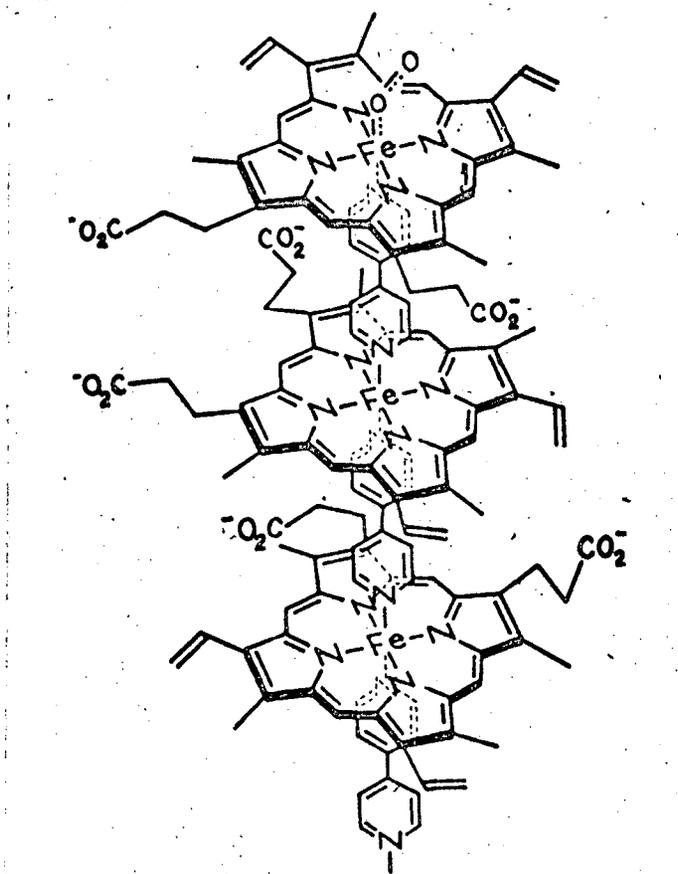


A semiconduction mechanism has, on occasion been considered as a possibility for electron transfer through the cytochrome system. It is interesting that the charge carrier mobility in copper phthalocyanine (III), an often used model for metal porphyrins, is, in fact, among the highest (about $400 \text{ cm}^2/\text{volt}/\text{sec}$ at 400° K.) thus far observed in organic materials.¹³ Introduction of the copper increases the carrier mobility by two orders of magnitude over that observed in phthalocyanine itself. This has been attributed to a metal interaction which permits the molecular orbitals to be delocalized over more than one molecule. There is support for this suggestion in an ESR study of copper phthalocyanine where a metal-metal interaction can be demonstrated.¹⁴ Other metal ion



bridging groups could presumably function in a similar way in a variety of oxidation-reduction processes. Green¹⁵ has described mitochondrial electron transport in terms reminiscent of semiconduction.

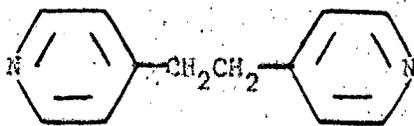
It is worth recalling here, in connection with models involving porphyrin-like molecules, the interesting system reported several years ago by Wang and Brinigar.¹⁶ They prepared a polymeric material (IV) which



(IV)

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could coordinate with oxygen at a terminal iron atom. Salt formation with poly-L-lysine permitted aqueous solutions of polymer to be prepared. The rate of oxidation of cytochrome c by molecular oxygen was enhanced ten-fold by the presence of polymer. When the unconjugated dipyriddy ethane (V)



(V)

Ferredoxin is an electron transport protein which participates in photo-reduction reactions catalyzed by chloroplasts.

Photoconductivity

The photoprocesses involved in photosynthesis and vision have been capriciously referred to by some as "dark areas." Insofar as our understanding is concerned, this is still essentially true. When the electron microscope began revealing a number of years ago the highly organized lamellar structures in chloroplasts and the layered organization of rhodopsin in the rods of the eye it became apparent that new concepts and techniques would be required before an understanding of the function of such structures would be reached. It is very fortunate that solid state phenomena are of such great concern to many whose major interests are outside the sphere of biology. These workers are continuing to provide both techniques and insights.

Of major concern to us here is the means by which charge carriers may be produced in organic solids by light which is energetically insufficient to cause a direct ionization. These will be the most significant for biological photoprocesses. It will be useful to first consider some of the spectroscopic consequences of forming molecular aggregates.

For crystals, one cannot consider a single molecule as the light absorbing unit. Because the molecules are only a few Angstroms apart and the van der Waals' interactions between molecules non-negligible, the absorption of light leads to an energy level characteristic of the assembly as a whole. The excitation is delocalized over many molecules in the crystal. This delocalized excited state, produced by a sort of excited state resonance, is called an exciton. One "resonance state" in which the excitation is localized on a single molecule is pictured in Fig. 2. In trying to get a mental picture of what an exciton really is

one must cope with a wave-particle dualism. In some circumstances it is best considered as a particle of excitation energy hopping in a random way from molecule to molecule; in other circumstances it must be considered as a wave of excitation energy propagating through the solid.

The interaction between the transition dipoles of excited molecules in the crystal splits the original energy level into a band of levels. This is the exciton band. Strong interactions produce a greater splitting and lead to wider exciton bands. The lowest exciton level may be lowered with respect to the excited state of the isolated molecule. As a result, the lowest energy absorption band of the crystal may be considerably red-shifted relative to the isolated molecule. The selection rules for transitions into the exciton levels depend on the relative orientation of the transition dipole moments in the assembly. Kasha has discussed the selection rules using simple vector diagrams.¹⁹

By a simple extension of the above ideas, it is evident that triplet excitation in crystals leads to triplet excitons and triplet-exciton bands. The energy level diagram for crystals is then that given in Fig. 3.

An alternative to the tightly bound molecular exciton pictured in Fig. 2 is a more loosely bound exciton in which the electron resides on an adjacent or nearby molecule (Fig. 4). This bound electron-hole pair is variously referred to in the literature as a Wannier exciton, a charge transfer exciton, or an ionic exciton. It moves through the crystal as a unit and is not a charge carrying state. The energy of this exciton state is given by

$$E_{C.T.} = I - EA + C + P.$$

I is the ionization potential and EA the electron affinity of the molecule; C is the coulomb interaction between electron and hole, and P is the interaction (mainly dipole-dipole) due to polarizations of the lattice. This state is quite near a conducting state. It differs mainly by the energy needed to overcome the coulombic forces between the electron-hole pair, allowing them to move independently. It is therefore of interest to consider it here.

The ionic exciton concept, introduced first by Wannier,²⁰ has been most successfully used in the inorganic semiconductor field. The first application to organic crystals is apparently that of Lyons,²¹ but it has also been considered by Merrifield.²² More recently the effects of configuration interaction (mixing) between ionic and neutral excitons has been considered in some detail by Jortner, Rice and co-workers,^{23,24} for organic crystals, and by Azumi and McGlynn,^{25,26} for excited dimers. The results of the crystal work are mainly of interest here.

The theoretical prediction for aromatic hydrocarbons (the only ones now available) are as follows.^{23,24,27} Ionic exciton states will contribute mainly to neutral excitons of small band width; that is, singlet excitons which correspond to weak transitions and triplet excitons. Ionic contributions may broaden the exciton band widths and may be particularly important in enhancing the rates of triplet energy migration. A spectroscopic study of anthracene²⁸ indicates the ionic exciton lies energetically above the first singlet level. No undisputed direct experimental detection of an ionic exciton level in a one component organic crystal has yet been made.

The principal macroscopic effect of exciton dissociation is photoconductivity. There are several pathways by which an exciton may become

dissociated to yield a conducting state. One is by interaction with a quantum of lattice vibrational energy. The vibrational energy of the lattice and the kinetic energy of the exciton supply the dissociation energy. Another pathway may be by interaction of the exciton with a defect or impurity in the crystal. Provided sufficient energy becomes available at these sites, dissociation will occur. An exciton-crystal surface interaction has also been observed to lead to conducting states. On energy conservation grounds, a static imperfection cannot readily dissociate an exciton which lies below all conducting states.

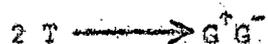
The recent discoveries of exciton-exciton interactions leading to charge carriers in the bulk of crystals are the most significant recent advances in this field, and we will present them in somewhat greater detail. The significance lies in the fact that the interaction of two excitons, a process energetically capable of yielding an equivalent of twice the excitation energy, can provide ample energy for reaching a conducting state. The advent of the laser, in particular, has signaled many of these recent advances.

All the studies of exciton interactions which we will discuss have been performed on anthracene which is, in effect, the E. coli of workers in the field. Choi and Rice²⁹ attempted to explain the fact that the response of photoconductivity with wavelength of exciting light generally parallels the absorption spectrum by invoking interaction of two singlet excitons. They demonstrated theoretically that two singlet excitons could lead to a pair of charge carriers and an unexcited molecule with adequate efficiency to account for photoconductivity. At about the same time³⁰ it was reported that for weakly absorbed light (4150-4550 Å) the photoconductivity of anthracene varied as the square of incident light

intensity, offering support for a singlet biexciton process. Hasegawa and Schneider³¹ then reported that photoconductivity could be induced in anthracene with the red (6943 Å) light from a ruby laser. Almost simultaneously it was observed³² that the ruby laser light (an approximately 40 Kcal quantum of light) could elicit a delayed (milliseconds) fluorescence in anthracene. The characteristic blue fluorescence of anthracene corresponds to the emission of a 79 Kcal photon. It was proposed that the triplet state of anthracene had been directly populated by the intense laser light. Interaction of two triplet excitons then in a (comparatively) slow process yielded an excited singlet from which fluorescence occurred. The direct population of a triplet level from the ground state is of course the reverse of a phosphorescence. The intense light beam partially compensates for the intrinsically low probability of such a transition. By studying the intensity of the delayed fluorescence as a function of exciting light in the region 5000 Å to 7000 Å they indirectly determined the spectrum of the ground state singlet to first excited triplet transition.³³ (See Fig. 5.) Quite recently it has been reported³⁴ that the photoresponse of conduction in anthracene in the 5000 Å to 7000 Å region parallels quite well (Fig. 6) this singlet-triplet spectrum. Equally interesting, a study of the quantum efficiency of the production of charge carriers revealed that the triplet exciton yields charge carriers 40 times more efficiently than the singlet exciton.

Although the exact details are not known at present, evidence is available, then, that the triplet level in addition to the singlet level can yield charge carriers efficiently. In a recent detailed theoretical

consideration of triplet excitons in aromatic molecular crystals,²⁷ Jortner, Rice and Katz have again pointed out that the most favored triplet-triplet annihilation process should lead to a charge transfer state. For indirect evidence in support of this contention they refer



to a flash spectroscopic study of Lindquist's.³⁵ Lindquist reports that the kinetics of decay of triplet fluorescein in solution cannot be understood unless the decay mechanism includes a reaction between two fluorescein triplets to yield a molecule each of oxidized and reduced fluorescein.

We should note here in passing that a detailed study of ruby laser generation of excitons in anthracene crystals³⁶ indicates a somewhat more complicated picture than we presented above. Using a giant pulse ruby laser (capable of delivering up to 10 megawatts of power in a single 30 nanosecond pulse) two photon direct excitation to a vibrationally excited singlet exciton level was demonstrated to occur, as well as a singlet to two triplet process (the reverse of a triplet-triplet annihilation).

Photoconductivity in copper phthalocyanine (III) now has been observed to occur with near infrared light.³⁷ Weak absorption of light in the near infrared by copper phthalocyanine has previously been observed.³⁸ Although the ratio of extinction coefficients for visible and infrared light is 100:1, the ratio of the photoreponse peak heights (Fig. 7) is 3:1. This suggests that the quantum yield ratio is about 30:1 in favor of the long wavelength absorption peak. This is similar to the 40:1 ratio observed previously for charge carrier production from triplet and

singlet levels in anthracene.³⁴ The implication that the near infrared absorption of copper phthalocyanine is a singlet to triplet transition has not been confirmed at present.

Donor-Acceptor Complexes

Since the charge transfer transition may be considered as a first step in the production of charge carriers, it is natural that the photoconductivity of donor-acceptor complexes be investigated. The conductivity of some complexes which are relatively good conductors in the dark and show strong ESR signals can indeed be enhanced by light. We focus here, however, on recent attempts to produce by light improved conductivity in low conductivity complexes. These complexes show no ESR signal or at best only a very weak signal. Examples are the complexes of anthracene and trinitrobenzene,³⁹ or the pyrene-TCNE complex.⁴⁰ Photoconductivity in this class of low conductivity complexes has been inadequately investigated, but it is evident from the cases thus far reported that the photoconductivities of the solids are low. The study of Akamoto and Kuroda⁴⁰ offers some interesting features. The spectral dependence of photoconduction for several complexes did not follow the absorption spectrum (Fig. 8) and excitation in the charge transfer band elicited no photoresponse. This is true for both conduction in the bulk of the crystal and along its surface which can be studied separately by different electrode arrangements. The weak photocurrent peak elicited by the low energy light showed a different temperature dependence from the main response peak and was considered to be secondary to the main peak. It was proposed that the secondary photocurrent resulted from excitation to a charge transfer exciton state which was dissociated at a crystal imperfection.

A study of energy transfer in crystalline donor-acceptor complexes of several aromatic hydrocarbons with trinitrobenzene⁴¹ indicates no transport of excitation energy and a rapid (10^{-8} sec) relaxation of the excited state to the ground state. This may, in fact, be responsible for the lack of photoresponse in the charge transfer band in solid donor-acceptor complexes.

By way of contrast, the donor-acceptor complex of tetrahydrofuran and TCNE in solution shows a reversible photoresponse and ESR signal on irradiation in the charge transfer band.⁴² This is attributed to a reversible electron transfer.

Models of Lamellar Systems

One of us has already reviewed this laboratory's interest in such systems.^{43,44} In essence, it is as follows: In working from the dark reactions involving the path of carbon in photosynthesis back toward the primary light reaction, attention next fixed on the process by which electromagnetic energy is stored as chemical energy. This is the so-called quantum conversion step. It involves, on the one hand, a chemical reduction, the conversion of pyridine nucleotide to reduced pyridine nucleotide, and on the other the oxidation of water to oxygen. The process is a very complicated one, involving two different pigment systems; but it was felt, more or less intuitively, that whatever the final details proved to be, a charge separation step would be necessary. This was suggested by the fact that nearly all the energy of a 40 Kcal. quantum of light is stored as chemical energy. Under these conditions, the energy barrier preventing the products from going back to starting materials is so small that a physical separation of the oxidizing and reducing sites is necessary. Ionization of a donor-acceptor complex,

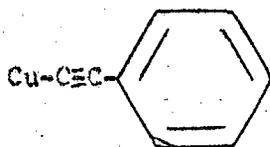
involving, for example, a quinone at a trapping site, could lead to a charge separation.

Indeed, it is proved⁴⁵ that evaporating a layer of ortho-chloranil onto a film of phthalocyanine enhanced the dark conductivity of the phthalocyanine by a factor of 10^7 and the photoconductivity by 10^5 . Similar observations were made using other hydrocarbons.⁴⁶

In a somewhat similarly conceived experiment,⁴⁷ carried out by painting the components (aromatic amines and various dyes) onto opposite electrodes and then clamping them together, a photovoltage of up to three volts in room light is claimed. This is attributed to a dye-induced photo-oxidation of the amine as a first step.

Dye Sensitized Photoconductivity

We cannot really do justice to this exceedingly interesting topic here. The technical applications of sensitized photoconductivity in photocopying methods and photographic processes are tremendous. We will refer to only one recent report as an example of this phenomenon.⁴⁸ Coating copper phenylacetylenide (VIII) powder with a dye, chlorophyll is a particularly good one, by dipping the powder in an ethanolic solution of the dye gives the material a good conductivity photoresponse with visible light. Chlorophyll itself shows a very low photocurrent.⁴⁹



(VIII)

The above result is one more manifestation of the remarkable effects which can be elicited from a suitably contrived inhomogeneous solid. Needless to say, Nature's contrivances are even more remarkable, although she has worked at it a little longer.

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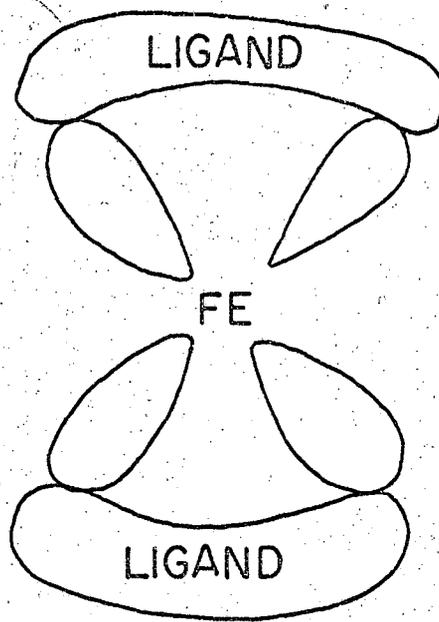
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Part II.

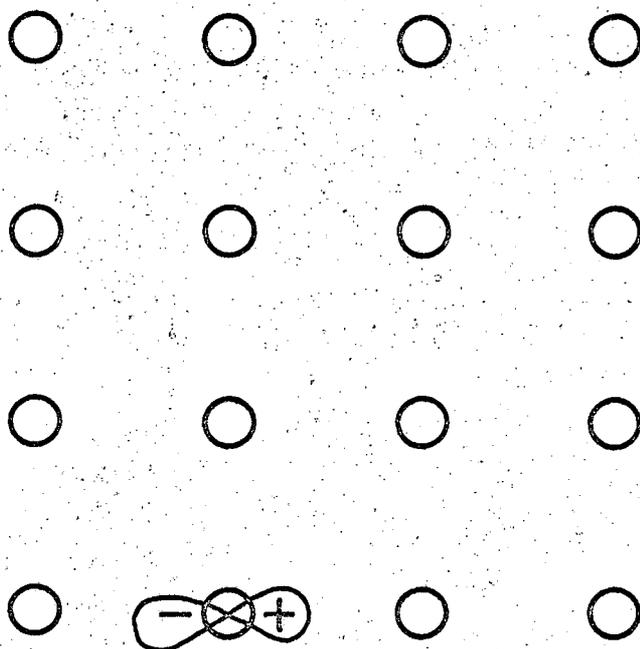
FIGURE CAPTIONS

- Fig. 1. Orbitals of a square planar complex formed by two conjugated chellating ligands.
- Fig. 2. Excitation localized on a single molecule of an array.
- Fig. 3. Crystal energy levels. Arrows indicate orientation of electron spin in excited and ground states.
- Fig. 4. An ionic exciton.
- Fig. 5. Triplet excitation spectrum of single crystal anthracene as measured by observing the intensity of the blue fluorescence as a function of the wavelength of exciting light (from Reference 151).
- Fig. 6. Photocurrent and the triplet absorption spectrum as a function of the exciting wavelength (from Reference 152).
- Fig. 7. Photoresponse of copper phthalocyanine. Photocurrent units are arbitrary; left scale refers to lower curve, which is the absorption spectrum (from Reference 155).
- Fig. 8. Spectral dependence of photoconduction in pyrene-TCNE complex. A, sandwich cell; B, surface cell; C, absorption spectrum (from Reference 158).



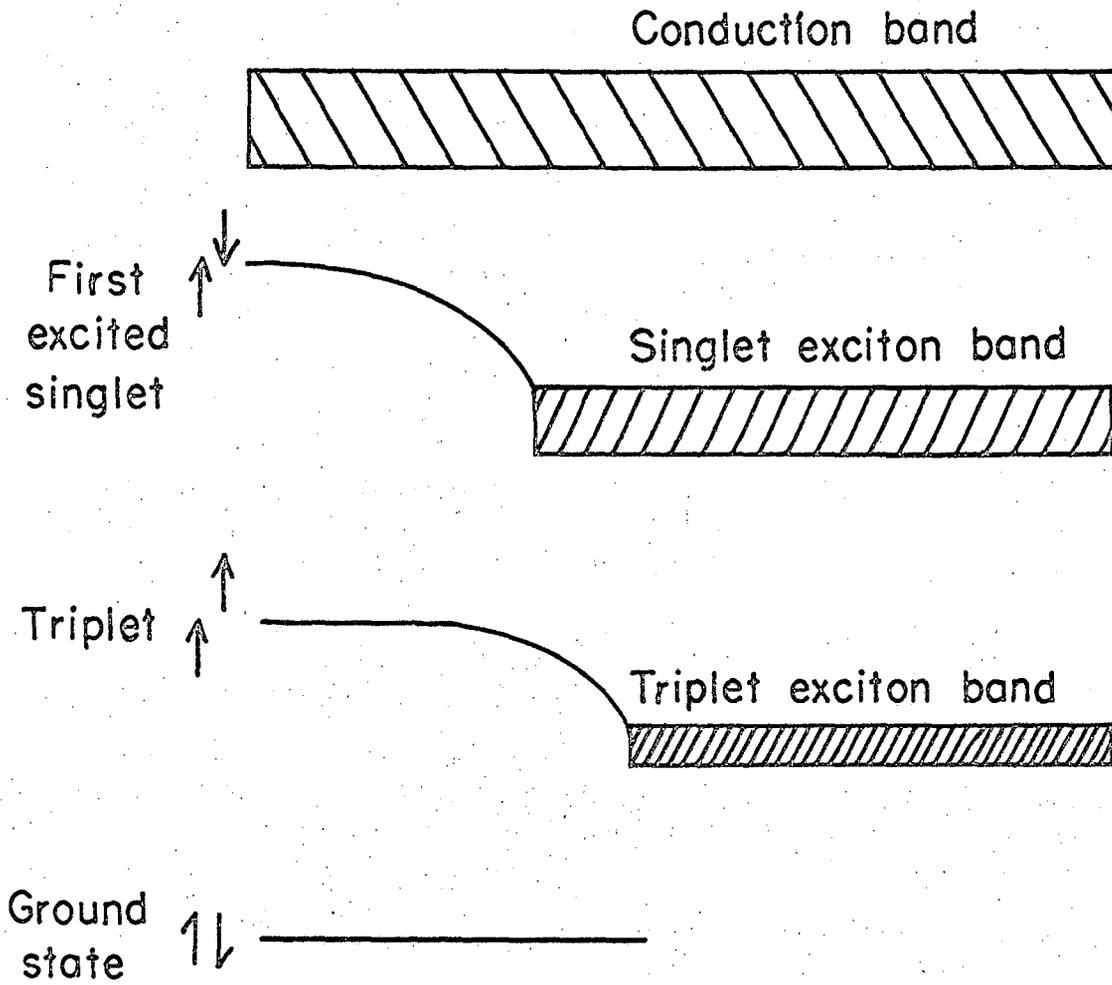
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Fig. 1



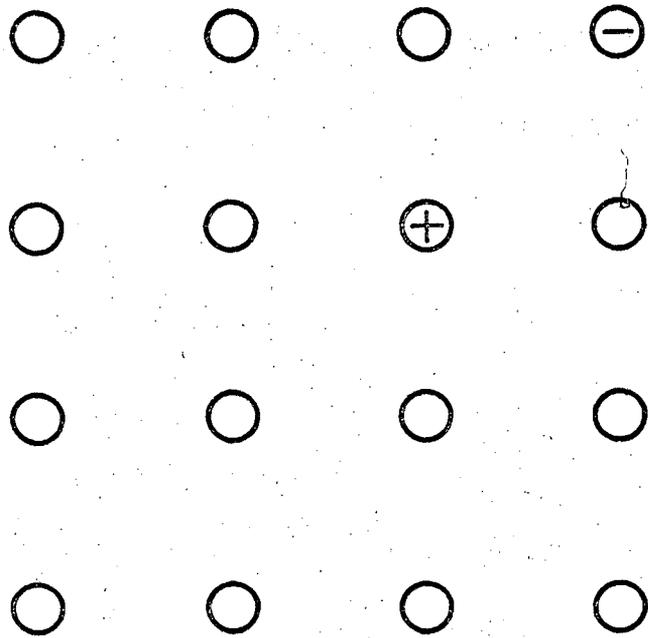
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Fig. 2



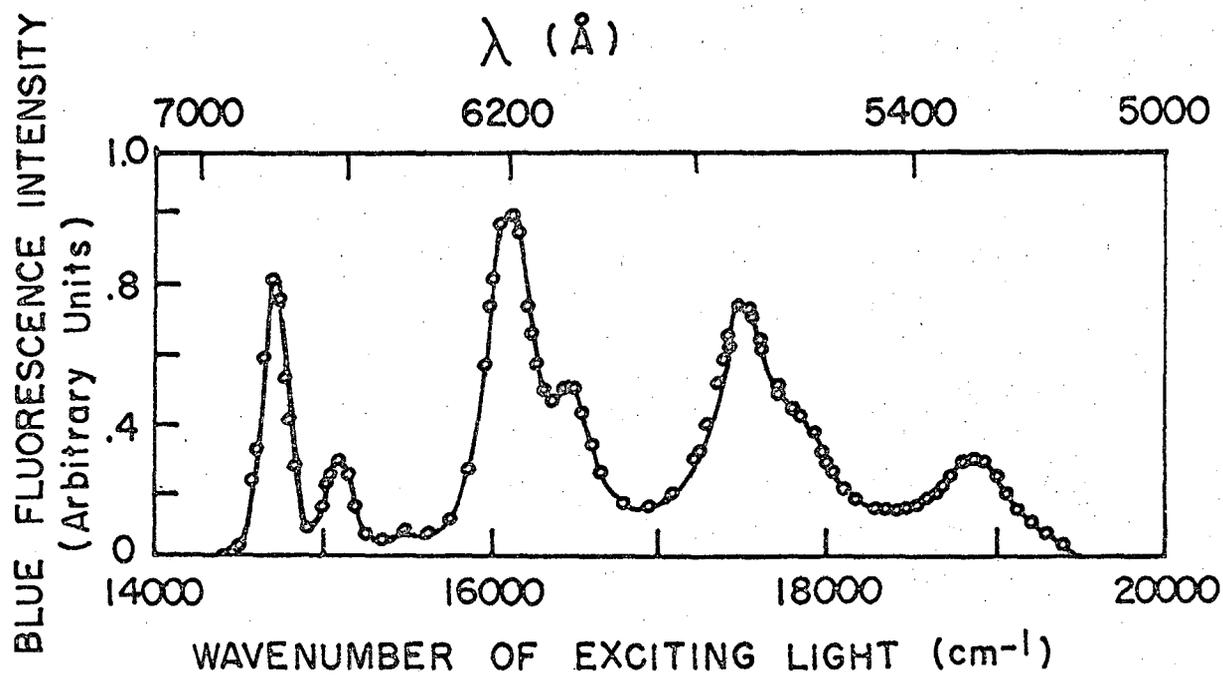
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Fig. 3



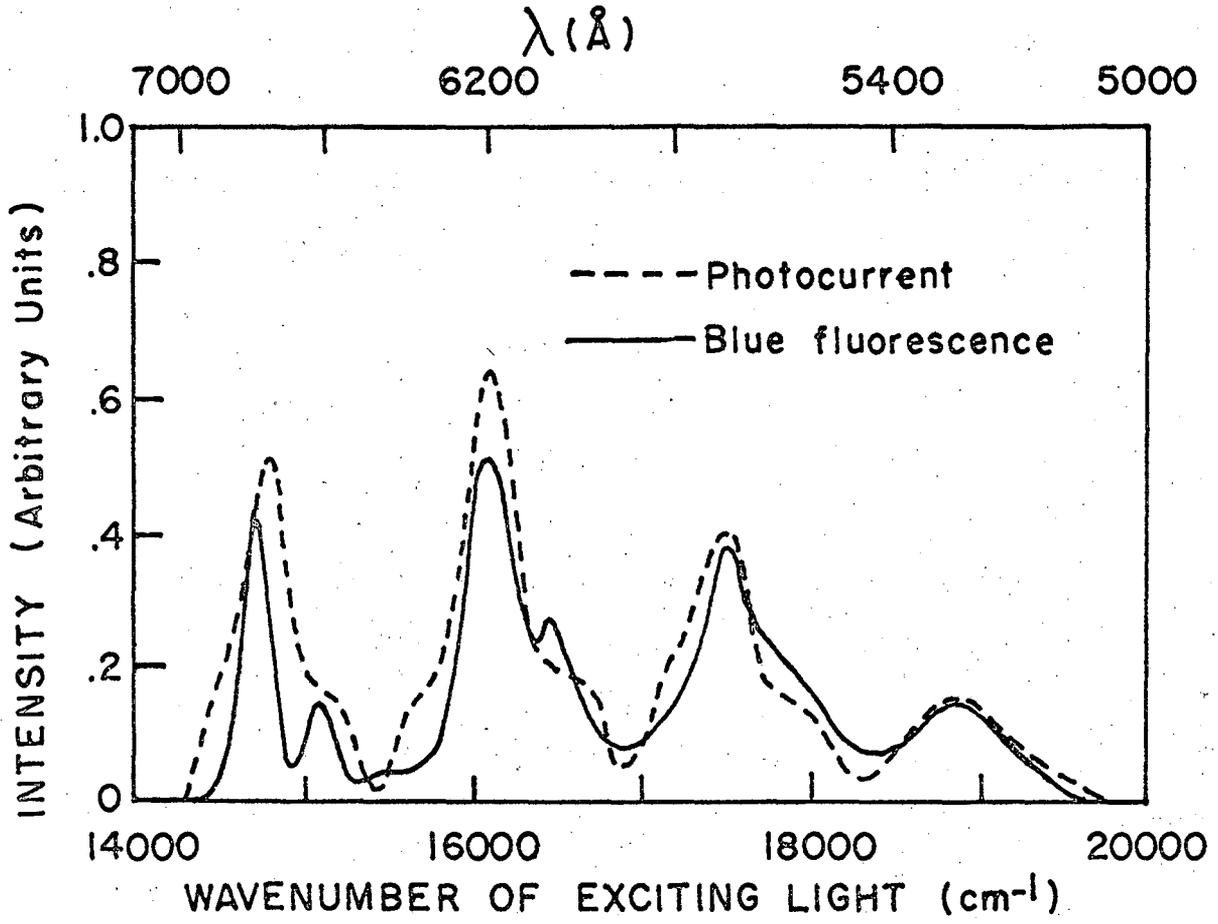
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Fig. 4



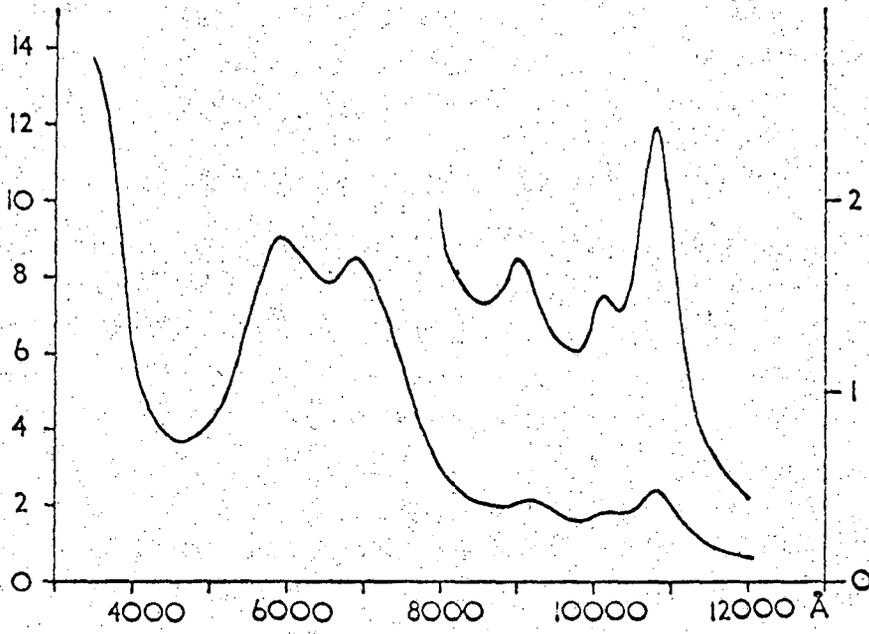
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Fig. 5



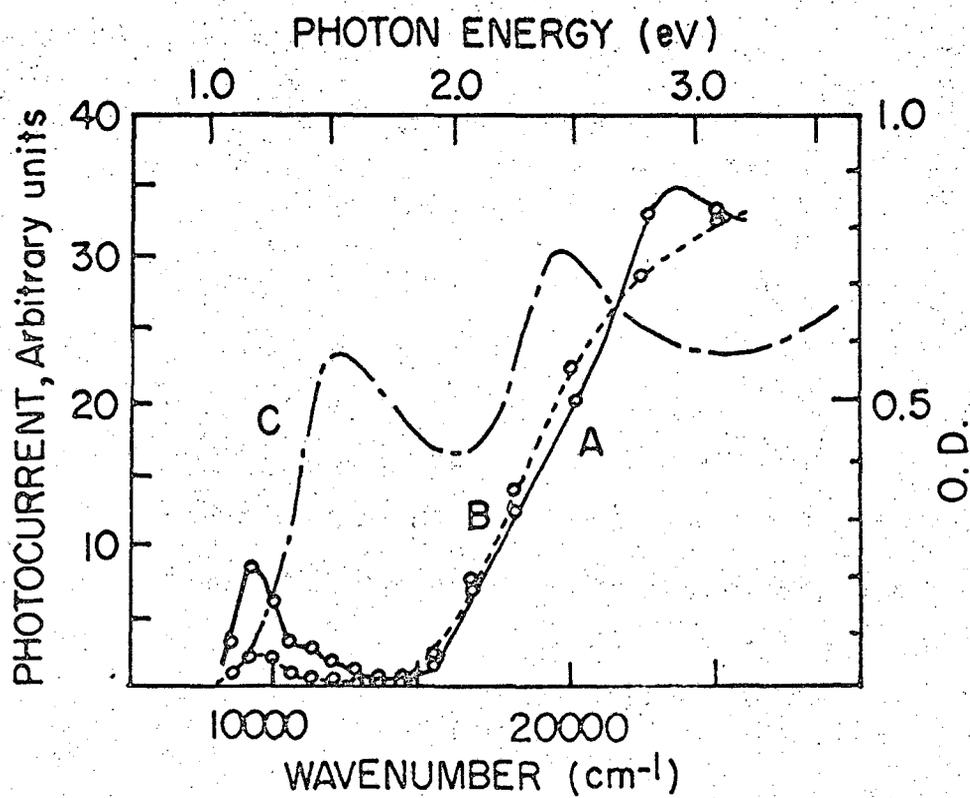
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Fig. 6



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Fig. 7



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Fig. 8

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