

PRESIDENTIAL ADDRESS.

Mechanism of the Benzidine Transformation and Some Allied Topics.

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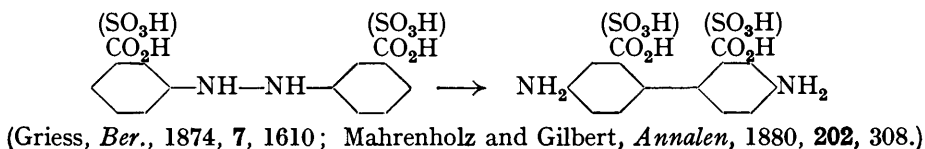
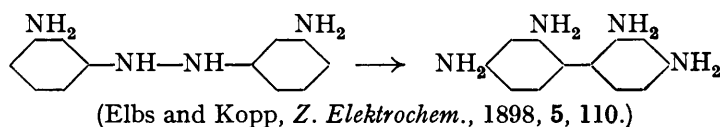
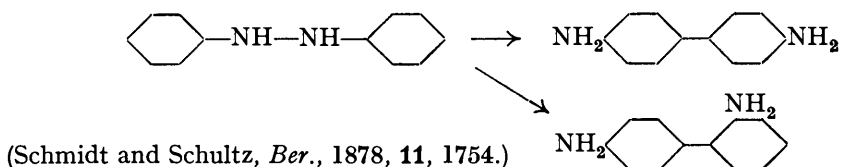
THIS subject has been selected in order to illustrate the thesis that electronic mechanisms should be related not only to all the known facts of a reaction but also to all the relevant analogies.

There are few processes that can be regarded from so many points of view as the benzidine conversion and it therefore provides suitable material for an attempt to develop a more comprehensive symbolisation. The purpose is much wider than appears from the title of this address, because it is hoped that the theory of small electron displacement swings will be found to confer real advantages and that more general use will be made of its resources.

Paul Jacobson, who devoted a large part of his experimental work to the study of the benzidine and semidine transformations of substituted hydrazobenzenes, has published a summary of everything known on the subject in 1922 (*Annalen*, **428**, 76) together with a discussion of the course of the reactions. In view of this it is unnecessary to repeat the historical account and Jacobson's paper should also be consulted for details of the cases examined up to its date. Here we need only the outlines of the chief results. It may, however, be recalled that the discovery of hydrazobenzene and of its rôle as the precursor of benzidine in the reduction of azobenzene (Zinin, 1845) in acid media was announced by A. W. Hoffmann in a communication to the Royal Society in 1863 (*Proc.*, **12**, 576).

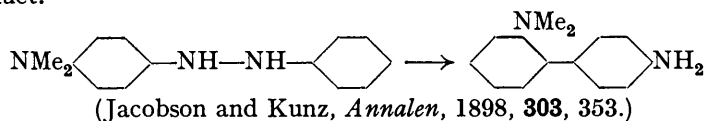
The Formation of Diaminodiaryl Derivatives from Hydrazodiaryls.

Hydrazobenzenes with free *p*-positions yield *pp'*-diaminodiphenyls and often *op'*-diaminodiphenyls (diphenylnes) as by-products :

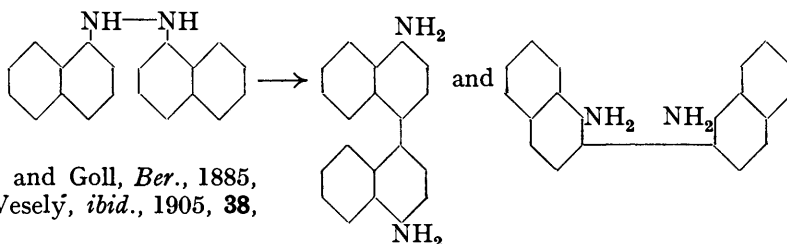


The dicarboxylic acid gives a little diphenylene derivative, the disulphonic acid none. 2 : 2'-Dimethylhydrazobenzene gives a little diphenylene derivative, relatively less than hydrazobenzene; 3 : 3'-dimethylhydrazobenzene affords dimethylbenzidine only (Schultz, *Ber.*, 1884, **17**, 467; Jacobson, *Ber.*, 1895, **28**, 2557). 3 : 5-Dimethylhydrazobenzene also yields a dimethylbenzidine and no diphenylene derivative or semidine (Hönigsberger, Huber, and Jacobson, *Annalen*, 1922, **427**, 204).

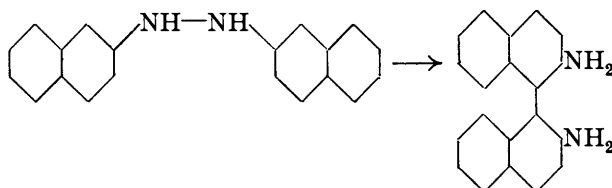
In certain cases when the hydrazobenzene bears one *p*-substituent the diphenylene is the chief product.



Hydrazonaphthalenes may yield 4 : 4'-diaminodi- α -naphthyls, *oo'*-diaminodinaphthyls, or the dibenzcarbazoles derived from these by elimination of ammonia :



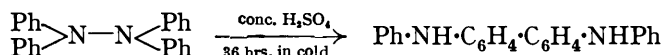
In view of the fact that the 2- and the 4-position show about equal reactivity, it is of interest that no mixed 2 : 4-derivative could be detected in the products.



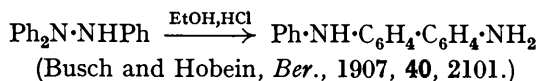
(Meisenheimer and Witte, *Ber.*, 1903, **36**, 4155; Boyd, Dissert., Heidelberg, 1896, mentions a possible *o*-benzidine change in the benzene series.)

There is no record of the formation of a *m*-aminodiphenyl derivative and the orientation of the reaction is exclusively *op*.

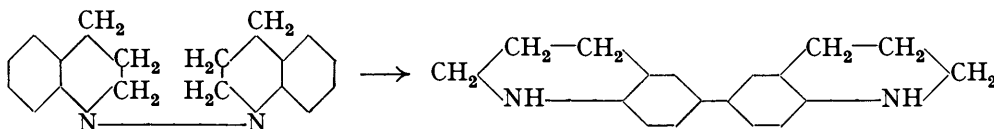
The hydrazobenzenes may be *N*-substituted and the reaction succeeds. The following are examples :



(cf. Gnehm and Werdenberg, *Z. angew. Chem.*, 1899, 1027; Kadeira, *Ber.*, 1905, **38**, 3575; Wieland and Gambarjan, *Ber.*, 1906, **39**, 1499). The main reaction, observed also when hydrochloric acid or acetic acid is employed, is hydrolysis to diphenylamine and the coloured salt of diphenylhydroxylamine.

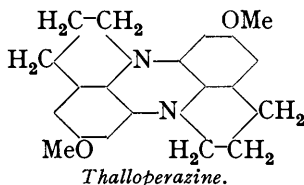


This reaction is much more facile than that with tetraphenylhydrazine, doubtless because the starting substance is a stronger base and exhibits *less* tendency to dissociate into free radicals.



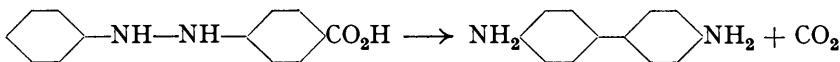
This transformation (Wieland and Haas, *Ber.*, 1920, **53**, 1336) proceeds smoothly when an ethereal solution of the hydrazine is shaken with 2*N*-hydrochloric acid. Under similar

conditions bis-6-methoxytetrahydroquinolyl (*idem, ibid.*) affords 6-methoxytetrahydroquinoline and a substance termed thallopazine.

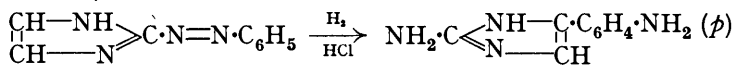


Here we must recognise the formation of an *o*-semidine and its oxidation by the hydrazine derivative.

Certain displacements of groups have been observed. For instance, hydrazobenzene-4-carboxylic acid is converted into benzidine with particular ease and in almost theoretical yield (Noelting and Werner, *Ber.*, 1890, **23**, 2356) :



Pyman and his collaborators have shown that a glyoxaline * nucleus may replace a benzene nucleus (Fargher and Pyman, *J.*, 1919, **115**, 222, 238, 244, 250, 257; Pyman and Ravald, *ibid.*, 1920, **117**, 1428) :



In this case, as in many others, an azo-compound was reduced in acid solution. We may at once dismiss the idea that there is any deep significance in the simultaneous presence of oxidising and reducing agents, other than the hydrazo-compound, in the system under such conditions. The reagent is always a strong acid and the intermediate is surely always a hydrazo-compound. So many clean reaction processes with pure hydrazo-compounds are known that there can be little doubt of this. Even when the azo-compound is the starting point, it is possible to select conditions which do not encourage the belief that we are witnessing an oxidation-reduction in which the reagents play the part of oxidisers and reducers. For example, azobenzene is smoothly converted into benzidine sulphate by sodium iodide and sulphur dioxide in aqueous solution (Bodenstein, German Patent, No. 172,569 of 1906). The effective reducing agent is hydriodic acid, which is continuously regenerated, and the presence of an oxidising agent, apart from the azobenzene in suspension, is excluded. The point is of some importance because the usual agent, namely, stannous chloride, is converted into stannic chloride, which has some oxidising properties. A case (β -hydrazonaphthalene) in which the benzidine transformation is brought about not only by acid but also by the agency of an alkali has been mentioned by Meisenheimer and Witte (*loc. cit.*). In one place these authors state that they obtain a mixture of products by the alkaline reduction of 2-nitronaphthalene, but they proceed to separate these by the use of hydrochloric acid. However, these authors state in another place that β -hydrazonaphthalene yields 1 : 1'-diaminodi- β -naphthyl on prolonged boiling with alkali. No benzidine or reduced benzidine is formed in the catalytic reduction of azobenzene or hydrazobenzene and this is perhaps an indication that hydrogen *atom* (as distinct from proton) interchange is not of chief importance in the reaction.

It may be assumed with confidence that the transformations are prototropic and occur in a proton-acceptor medium as the result of the action of an acid on a hydrazo-compound.

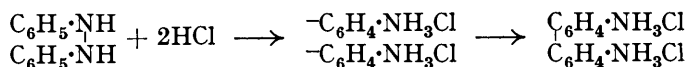
Tichwinsky (*J. Russ. Phys. Chem. Soc.*, 1903, **35**, 667) was the first to draw attention to the fact that an acid converts a weak base into the salt of a strong base in the course of the migration, which, he stated, does not occur in benzene solution in the presence of hydrogen chloride. In accordance with a well-known principle he perceived in this fact the driving force of the change and it may be recalled that a similar case is the conversion of neutral benzil into a salt of benzilic acid under the influence of basic reagents.

Another feature of obvious importance was stressed by Jones and Kenner (*J.*, 1931,

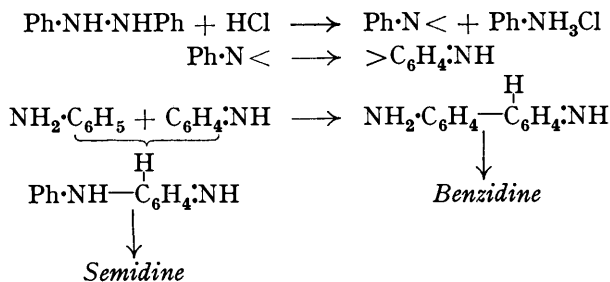
* Michaelis and Schäfer (*Annalen*, 1915, **407**, 229) have shown that the reduction of 4-benzeneazo-1-phenyl-3-methylpyrazole yields an *o*-semidine (migration of anilino-group) and a *p*-semidine (migration of phenylmethylpyrazolylamino-group).

1848; 1932, 711), who dwelt on the "heterogeneity" of the nitrogen-to-nitrogen link and its tendency to seek relief in dissociation.

The views of A. V. Weinberg ("Kinetische Stereochemie," Brunswick, 1914, p. 70) and of Jones and Kenner are not very different in that they both postulate dissociation of the *salt* of hydrazobenzene into radicals and their subsequent recombination. Tichwinsky, on the other hand, gave the scheme :



A similar theory is that of Stieglitz (*J. Amer. Chem. Soc.*, 1903, **25**, 62), which is represented as follows :



The powerful argument advanced by Jacobson (*loc. cit.*) against this "dissociation" theory in any of its forms is that in 63 examples of benzidine and semidine rearrangements of unsymmetrical hydrazo-compounds, he did not encounter a single case where A-B furnished any A-A or B-B. This proves conclusively that no "mixture" occurs of the aromatic residues contained in a single molecule and it should be noted that the circumstances in some examples are favourable for the recognition of by-products. Thus no benzidine is obtained in the reduction of azobenzene-2-carboxylic acid (Paal, *Ber.*, 1891, **24**, 3060; Jacobson, *Annalen*, 1909, **367**, 328). This was later reinforced by Ingold and Kidd (*J.*, 1933, 984), who made the somewhat similar point that a mixture of 2:2'-dimethoxy- and 2:2'-diethoxy-hydrazobenzidines gave on conversion a product that behaved thermally as if it contained only the two symmetrical benzidines in the anticipated proportion. The two hydrazo-compounds were found to undergo conversion at comparable rates, the transformation of the dimethoxyhydrazobenzene being very roughly six times as rapid as that of the diethoxyhydrazobenzene.

The transformations of hydrazobenzenecarboxylic acid and benzeneazoglyoxaline (*v. supra*) are difficult to reconcile with any form of a free-radical hypothesis.

Wieland (*Ber.*, 1915, **48**, 1098) also rejected this type of view for the oxidation-reduction of hydrazobenzene with formation of aniline and azobenzene, again because he noted no "mixing" of the radicals in the products.

A further point is that tetraphenylhydrazine dissociates into stable radicals which do not, so far as is known, pass into diphenylbenzidine, even in the presence of hydrochloric acid and yet it undergoes the benzidine change to some extent in sulphuric acid solution (*v. supra*). The plea (Jones and Kenner) that the radicals set free from a single molecule may not escape from the sphere of each other's reactivity does not seem valid here. The weight of evidence is clearly in favour of the true intramolecular character of the migration, because this supplies the only satisfying explanation of the fact that the two nuclei invariably hold together.

Indeed, Jacobson actually investigated a claim by Hirsch (*Ber.*, 1890, **23**, 3222) that he was able to isolate a monomethylbenzidine by conversion of a mixture of hydrazo-compounds prepared by joint reduction of nitrobenzene and *o*-nitrotoluene. It was found (*Ber.*, 1895, **28**, 2545) that even under these conditions benzidine and tolidine only are obtained.

Dr. W. A. Waters has kindly contributed (private communication) a discussion of the

limiting conditions for thermal dissociation in solution. He concludes that dissociation into free radicals is possible if $2\alpha/D\tau^3f^2 > 1$, where α is the bond polarisability, D is the dielectric constant, τ is the sum of the atomic radii, and f is the covalent bond force constant (cf. Sidgwick, "Chemistry of the Covalent Link," 1933, p. 123). D is clearly the limiting experiment variable. For example, for C-Cl, free radical dissociation requires that $D < 24$, and such dissociation in water is therefore excluded.

Solvents of low dielectric constant are requisite for free-radical dissociation in most cases and this theoretical deduction is in good agreement with experiment.

The obvious features* of the transformation may be summarised as follows :

The hydrazobenzene-benzidine conversion is an intramolecular process of oxidation-reduction, because, as pointed out by Jacobson, the hydrazo-group is reduced and the *o*- or *p*-positions of the aromatic nuclei are oxidised. It is brought about by strong acids in a proton-acceptor medium and is therefore probably prototropic. The "heterogeneity" of the hydrazo-group must be recognised in any satisfactory description of the mechanism.

From time to time hypotheses involving intermediate stages have been advanced. *p*-Aminodiphenylamine is certainly not an intermediate, because this base is unchanged by hot mineral acids (Robinson and Robinson, J., 1918, 113, 643). Lapworth (J., 1898, 73, 451) suggested that interchange of the anilino-group and hydrogen gives successively the *o*-semidine and *p*-semidine, and that wandering of aminophenyl then gives the diphenylene and the benzidine. The qualification of this hypothesis is best quoted. "The two changes thus represented, however, must probably be regarded as simultaneous and not successive, and it is not suggested that paramidodiphenylamine is actually an intermediate compound, although the latter would probably yield benzidine under suitable treatment." Presumably this difficult passage means that the stages occur in such rapid succession that they are effectively simultaneous. Chattaway (*P.*, 1902, 18, 176) and Fry (*Z. physikal. Chem.*, 1911, 76, 397) have also contemplated the semidines as intermediates in the benzidine conversion, and van 't Hoff ("Ansichten," II, 258) thought the intermediate might be 4-hydrazinodiphenyl. These suggestions are not supported by experiments on the supposed intermediates and the value of such experiments was sometimes discounted in advance; they offer no advantages at the present time in the generalisation of the phenomena.

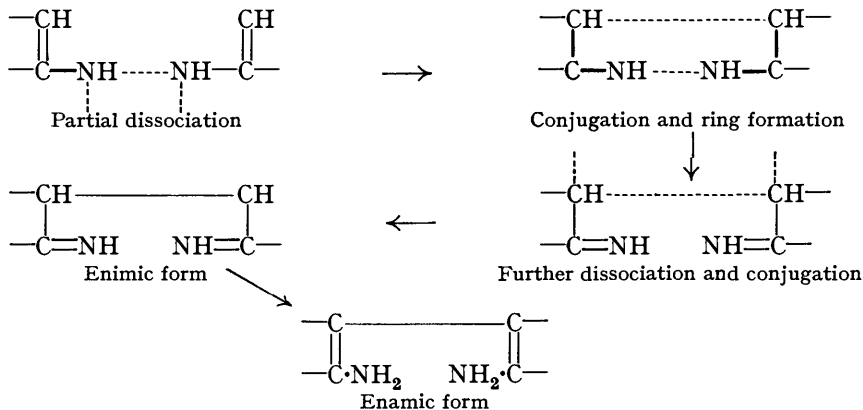
The modern tendency is to avoid the postulation of definite intermediates and to take as direct a view of each change as is possible. The development from this standpoint may now be considered. Employing the symbolism of partial polar dissociation of valency bonds, Robinson and Robinson in 1918 (*loc. cit.*) represented the intramolecular mechanism as a regrouping of polar valencies and a citation from the paper will best serve to make the views of that period clear. "The following brief statement expresses the form in which this and related reactions may be generalised. In a molecular complex A-b-c-D, b or c or both represent atoms capable of assuming a higher valency by salt-formation. The

salt absorbs energy and passes into an activated condition,† represented by $\overset{\cdot\cdot}{\text{A}}-\overset{\cdot\cdot}{\text{b}}-\overset{\cdot\cdot}{\text{c}}-\overset{\cdot\cdot}{\text{D}}$, omitting the acid for reasons of convenience. If the partial valencies become conjugated

with unsaturated groups in A or D, we obtain $\overset{\cdot\cdot}{\text{A}}-\overset{\cdot\cdot}{\text{b}}-\overset{\cdot\cdot}{\text{c}}-\overset{\cdot\cdot}{\text{D}}$ and $\overset{\cdot\cdot}{\text{A}}-\overset{\cdot\cdot}{\text{b}}-\overset{\cdot\cdot}{\text{c}}-\overset{\cdot\cdot}{\text{D}}$. Ring-formation by the partial valencies, followed by a second similar complete process, leads in the first case to $\overset{\cdot\cdot}{\text{b}}-\overset{\cdot\cdot}{\text{A}}-\overset{\cdot\cdot}{\text{c}}-\overset{\cdot\cdot}{\text{D}}$ and in the second to $\overset{\cdot\cdot}{\text{b}}-\overset{\cdot\cdot}{\text{A}}-\overset{\cdot\cdot}{\text{D}}-\overset{\cdot\cdot}{\text{c}}$. The products are obtained in the keto-, enamic, or thioketo-modifications, according as the atoms b and c are oxygen, nitrogen, or sulphur. The less extensive change is represented by the semidine transformation, the conversion of phenylhydrazine into *p*-phenylenediamine, of phenylnitroamine into nitroaniline, and by many other reactions. The full change resulting from conjugation of the partial valencies with both unsaturated groups A and D is represented by the benzidine rearrangement, and it is obvious that even within the four corners of the general scheme the nature of the products may be considerably varied according as the conjugated chains in A and D are long or short. The type of rearrangement assumed

* Stereochemical problems are not discussed here, though doubtless of great interest. It seems that the various reactive centres must in any case be near enough to enable the new bonds to be produced. If we are surprised by this, the only course open is to accommodate our ideas to the facts.

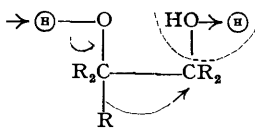
to occur in the synthesis of indole derivatives is represented below, and the thickened lines stand for a normal valency plus a partial valency.



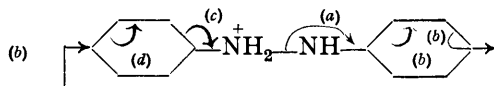
† The activated molecules are said to be 'partially dissociated' because the phenomenon appears to be a stage towards complete ionic dissociation, but the physical basis of the process is not quite clear. It may be that the energy change causes the movement of an electron from one atom to another (polarisation of the molecule) or a mere change in the position of one or more electrons within the sphere of the atom itself. In this case the evidence shows that the change is repeated in the same sense in alternate atoms forming part of a conjugated chain and in the opposite sense in the other atoms of the chain. Several further suggestions might be made, especially that a part use may be made of the field surrounding a single electron."

It must be emphasised that our dissociated valencies were from the first definitely assumed to be of opposite polarity: $\text{A---B} \longrightarrow \overset{+}{\text{A}} \cdots \overset{-}{\text{B}}$ and when an electronic basis was more clearly defined the translation $\text{A} \cdots \text{B}$ was suggested* (Kermack and Robinson, J., 1922, 121, 440) and stated to be applicable to migration mechanisms previously represented with the aid of partial valencies.

* The curved arrow symbol for an electron displacement was first given in this paper of 1922 (p. 433); it was adopted in teaching from that time on and partial valency representations were abandoned in 1923—1924. Publications in which the system was clearly explained and consistently used appeared in 1925 (*J. Soc. Chem. Ind.*, 44, 456; J., 1610, 1619; also letters to *Chemistry and Industry* in 1923—1925; Rapport Institut International Solvay, 1925). These earlier papers contained many of the suggestions collected and amplified by Allan, Oxford, Robinson, and Smith (J., 1926, 401). The statement of Wallis ("Organic Chemistry," Gilman, 1938, p. 789) that the present writer "prefers" partial valencies to electronic displacements for the representation of the mechanism of migrations is therefore not correct for the time since 1922—1924. In particular Kermack and Robinson (*loc. cit.*, 1922) mentioned the general form of the pinacol-pinacolin and Wagner-Meerwein changes as examples of reactions which must be represented by electronic displacements equivalent to the polar partial valency symbols previously used. The translations were not published in all cases because they were deemed to be unambiguous. They were, however, given in lectures in several centres in this country, including London, Cambridge, Oxford, and Manchester. The cases chosen always included the pinacol-pinacolin change and, for example, before the Cambridge University Physical and Chemical Society (Jan. 28th, 1926) the representation given was that annexed. The idea that, instead of water being split off from H and OH inside the molecule, a proton comes in from outside and is ejected from another place was adopted at the suggestion of Professor Lapworth in 1924. Lapworth had long since developed similar views in connexion with tautomerism. This modification is the only one that needed to be made in the literal translation of the polar partial valency symbols of 1920. A further point worthy of mention is that the gradualness of migrations and indeed of all bond changes was emphasised by the writer in 1920 (*Mem. Manchester Lit. Phil. Soc.*, 1920, 54, 4). The words used were: ". . . all the alterations of valency are progressive . . . and a similar gradual change will be found to be true of all the valency rearrangements . . . all these reactions could be regarded as being almost continuous and with many intermediate phases."



Thus the translation of the above scheme in electronic symbolism became the following for the benzidine rearrangement, and this was given by Ingold and Kidd (*loc. cit.*) :



We may now examine this scheme in a little more detail and attempt some small refinements and perhaps modifications.

It will be found that it already embraces the main features of the process to which attention has been drawn. The function of the acid catalyst is to increase the nitrogen-from-nitrogen dissociation tendency represented by the displacement (a). This is in line

with one aspect of the views of Tichwinsky and of Jones and Kenner $\text{—}\overset{+}{\text{N}}\text{H}_2\text{—}\overset{+}{\text{N}}\text{H—}$. It may seem at first sight unlikely that a positive charge on a nitrogen atom should facilitate the relinquishment of electrons, but it must be remembered that there is by hypothesis a compensating gain of electrons from the benzene nucleus, so that the total electron atmosphere, all shared, remains unaltered.

It is probable that the process (a) should be sub-divided as in the expression : $\text{—}\overset{+}{\text{N}}\text{H}_2\text{—}\overset{+}{\text{N}}\text{H—}$, but these two displacements may always be combined in a single symbol.

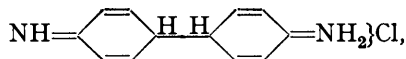
The displacements (b) are the usually assumed consequences of the increase of covalency between the nitrogen atom and the nucleus, conferring anionoid* reactivity on the *p*-carbon atom and controlling the orientation of the process. In this part it is merely a normal *p*-substitution of an aniline derivative (hetero-enoid system) by a cationoid reagent (Hamilton and Robinson, J., 1916, 109, 1029; Robinson, *ibid.*, p. 1038; Robinson and Robinson, J., 1917, 111, 958; Robinson, *J. Soc. Chem. Ind.*, 1925, 44, 456; Allan, Oxford, Robinson, and Smith, *loc. cit.* and later papers).

The displacements (c), (d) require more justification because they are not familiar in hetero-enoid systems and aniline derivatives, even as salts, do not in general display cationoid reactivity. However, the circumstances are sufficiently exceptional and there is a close analogy with nitrobenzene which goes far to justify the assumption made.



It will be observed that in both cases the nitrogen is positively charged and, still more significant, in both cases the nitrogen atom is represented as relinquishing a part of its electron atmosphere. It is hardly necessary to recall the instances of *p*-attack of nitrobenzene by anionoid reagents, because attention has frequently been directed to the examples (*loc. cit.*, 1925, 1926; cf. Bradley and Robinson, J., 1932, 1254). Examination of the details shows, therefore, that the electronic translation of our theory of 1918 is in accord with analogies and expresses many of the features of the benzidine transformation in an acceptable manner. This does not mean that it is necessarily correct or that there is nothing more to say.

We stated, for example, that the product would be obtained in the enimic modification,



and implied a subsequent tautomeric (prototropic) change in order to reach the benzidine

* The terms "anionoid" and "cationoid" were employed by Lapworth (1925) to denote reagents or reactive centres exhibiting reactivity analogous to that of anions and cations respectively. From the first they had nothing to do with ionic charges and implied "electron donor" and "electron acceptor" respectively. Ingold's terms "nucleophilic" and "electrophilic" are very acceptable alternatives, but the meaning is precisely the same.

salt. This is indeed a necessary consequence of the above electronic scheme if it is taken to the end. Against this idea two strong arguments may be advanced.

In the first place such imine salts are known to be extremely prone to hydrolysis to ketones (later phenols) and yet the production of ammonia or phenols has not been observed even as small by-products.

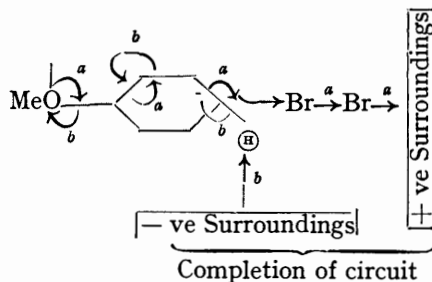
Secondly, this mechanism should operate with *pp*-disubstituted hydrazobenzenes, perhaps as indicated below :



In practice this never occurs; if the *o*-positions are free, a semidine is produced, and hydrazomesitylene, in which there are no free *o*- or *p*-positions, undergoes no rearrangement. Hence it seems certain that the protons in the *p*-positions of the benzene nuclei are removed in the course of the rearrangement, and it is probable also that the nuclei at no time depart far from their aromatic character and never so far that they could be described as hydroaromatic.

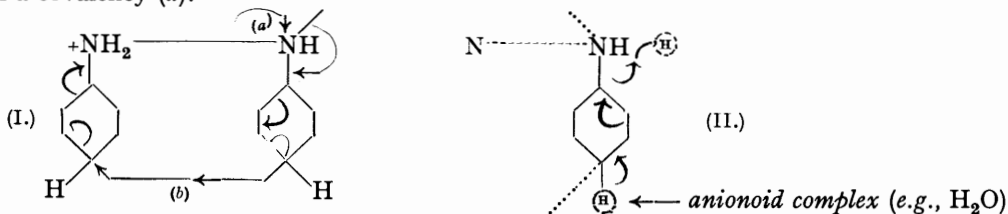
In order to cope with this type of difficulty in similar cases the writer has suggested that many electronic mechanisms are brought to completion by a number of displacement swings or oscillations in different directions, and that each of these may have a very small amplitude. Thus the original activating and orienting displacements are regarded as creating a strain which is relieved by a reversal of only a part of them, the formation of certain new bonds and the breaking of others being progressive though not necessarily unidirectional.*

In aromatic substitution the outcome is that "reaction at a point" which was first regarded as a desideratum by Flürscheim. An example already given is the bromination of anisole [*Chem. News*, 1926, 133, 3455, 7; "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry Brochure, 1932, p. 39] and this may be reproduced here, but it must be emphasised that analogous schemes are postulated in all cases of aromatic substitution whether by anionoid or cationoid reagents and in many other types of reactions.



The arrows (*a*) represent a forward process of substitution or addition, whilst the displacements (*b*) relieve the strain in the electromeric system without reversing the effective substitution or addition, accomplished in the first phases.

Applying this to the above electronic mechanism for the benzidine change, we have as the first phase the following (I), in which the arrows represent displacements of unknown and possibly very small extent compared with a full one-electron make or break of a covalency (*a*).

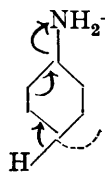


* Because the electrons participating in a new covalency may come first from one side and then from the other, and similarly for the destination of electrons in the breaking of a bond.

Here the changes not to be reversed are (a) and (b), for these represent respectively a link broken and a new one formed in the process.

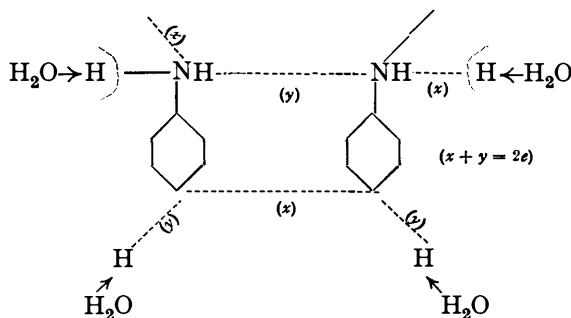
In the next phase the reversal in the right hand nucleus is just the same as that assumed above in the bromination of anisole. It is represented by (II). It is obvious that because of its accumulation of unshared electrons the nitrogen atom will presently take up a proton, and later still one more proton to give the neutral salt of the di-acid base. Furthermore, the proton in the *p*-position, having given up a part of its shared electron atmosphere to the aromatic nucleus, will begin to attach itself to an anion or anionoid complex such as water. The need for the presence of proton donors *and* acceptors is thus clear, exactly as in Lowry's example of mutarotation.

In the left-hand nucleus the displacements are of the same type and are not properly reversals, although by virtue of their occurrence this aromatic nucleus also recovers its original condition.



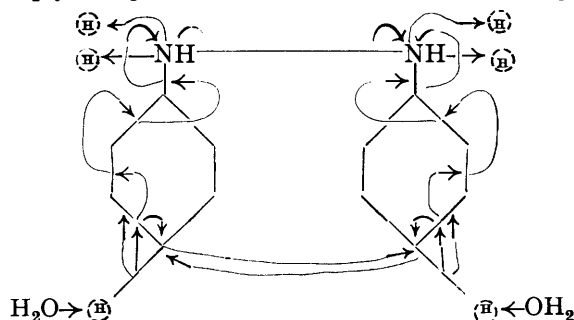
They are expressed in the inset. The same consequences follow, that is, at some stage the nitrogen will acquire a third proton and the proton in the *p*-position will be detached.

Now if we examine the position after these two phases, which it must be reiterated may be assumed to be of extremely small magnitude relative to an electron link, it is noticed that there is no difference between the two nuclei. We have such a condition as :



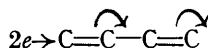
in which (*x*) may be small compared with (*y*). The only possible lack of symmetry concerns the attachment of protons to the nitrogen atoms and here there may well be interchange or resonance levelling up the position. This being so, the next displacement phase, the third we have assumed, need not take place in the clockwise direction represented on paper for the first. It might do so or be anti-clockwise and thus the theory of small successive displacements allows emphasis to be laid on the overall symmetry and gradualness of the change.

In order to avoid any possible misapprehension it must be very clearly stated that it is maintained that each of the phases occurs in detail as already described. The treatment that follows is a simplification that brings out a further aspect of the mechanism. Let it be assumed that clockwise and anti-clockwise displacements alternate with those necessary for *p*-proton removal; then, omitting the displacements which are reversed, that is, those that simply swing to and fro, we arrive at the following representation :

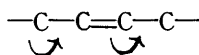


Now this expresses very clearly the intramolecular oxidation-reduction stressed by Jacobson (*loc. cit.*). The hydrazo-group is here seen to be reduced by electrons that pass through * the conducting aromatic nuclei and the *p*-positions are oxidised at the same time, since they lose not two protons merely but a total of two electrons also, that is, two hydrogen atoms. The theory of small displacement swings has thus given us a picture of a symmetrical process which has the closest resemblance to the most direct representation that could be devised.

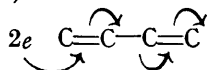
A similar treatment can be applied to the case of graphitic conduction, or conduction in any unbroken unsaturated chain (conjugated double bonds). The mechanism here is



followed by



and, if we sum these displacements,



Thus electrons can enter and leave an unsaturated chain at any point without disturbance of the structure and we avoid awkward assumptions of oxidised or otherwise modified terminal groups. Dr. L. E. Sutton has kindly drawn the writer's attention to the evidence that the benzene ring is a super-conductor and the relation of this idea to its abnormal diamagnetic susceptibility.

Having reached this stage, we are in a position to collate with our view of the benzidine transformation another group of reactions, namely, the oxidative couplings of aromatic nuclei, especially such as occur in the *op*-positions to a hetero-atom (N, O, S). Familiar examples are the oxidation of the naphthols to dinaphthols, the oxidation of dimethylaniline to *N*-tetramethylbenzidine, and the action of bromine on ethyl sodioacetoacetate (which is an oxidation and not an alkylation). It is first necessary to discuss the constitutional factors that make such oxidative couplings possible. In particular we must enquire whether the hetero-atom must bear a hydrogen atom. In the case of the phenols this structural condition certainly must be satisfied, at least when the normal oxidising agents are employed. The phenol ethers are not, for example, oxidatively coupled by chromic acid or ferric salts. On the other hand the disubstituted anilines do undergo the reaction and there is evidence available that it does not occur as the result of salt-formation. Thus strychnidine and many similar bases give intense colour reactions with ferric chloride, due in the first instance to oxidative coupling *para* to the tertiary nitrogen. The reaction occurs in dilute acid solution, but as the concentration of acid is increased the speed of colour formation is diminished and in some cases no colour is developed unless the acid concentration is low. The strychnidine derivative can then be recovered unchanged.

If the analogy of all these processes is conceded, the conclusion must be that the hydrogen atom is *not* an essential structural feature. Had we reached the contrary view, the oxidative couplings might have been formulated as benzidine-type transformations of intermediate hydrazo-compounds and peroxides, and such a mechanism cannot be certainly excluded; it is probably rare but remains a possibility. The rôle of the hydrogen atoms of the phenols is therefore, probably, as in many substitution reactions, to be found in potential or actual ionic dissociation, thereby greatly enhancing the anionoid reactivity of the hetero-enoid system.

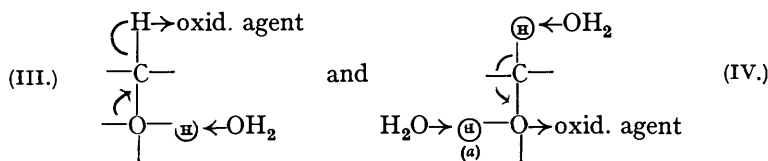
A similar phenomenon among nitrogen compounds is perhaps the oxidation of benzene-azonaphthionic acid to Congo-red (German Patents, Nos. 84,893, 88,595 of 1896; cf. Brass, *Ber.*, 1912, 45, 2529).

* The electron does not, of course, really pass through such a chain of atoms. A simple mechanical analogy is a row of billiard balls in contact against a cushion where the impact of a ball at one end causes a ball from the other end to move away.

This interesting type of oxidation does not occur with azobenzene but only with those amino- or hydroxy-azo-compounds that are, or may be, formulated for other reasons as arylhydrazones. Here we may be dealing with proton-removal or with the appearance of the more reactive aniline derivative in the form $\text{Ph}\cdot\text{NH}\cdot\text{N}^-$.

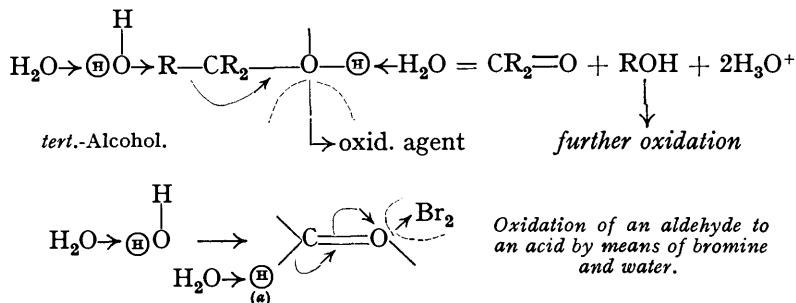
There remains for consideration the question of the position of attack of the oxidising agent. Do the electrons leave the molecule from carbon or oxygen (or nitrogen)? An answer can only be obtained after a study of oxidation mechanisms generally and a digression must be made for this purpose.

If we take one of the simplest cases, $-\text{CH}\cdot\text{OH}- \longrightarrow -\text{CO}-$, two mechanisms are theoretically possible :

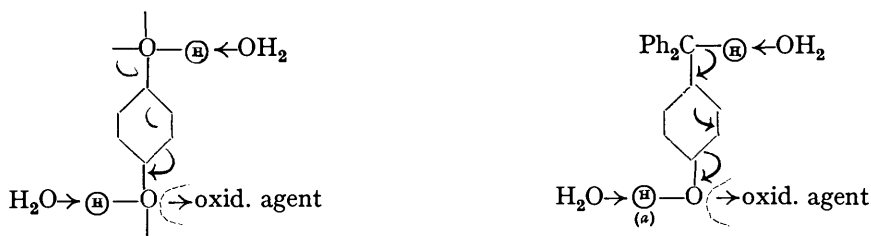


The second alternative is the more natural because the unshared electrons are at once available and because the term "anionoid complex" connotes "reducing agent." The importance of the "consequent process" is clear here, for the reaction succeeds because a condensation of the electrons is possible in the double bond. (The hydroxyl radical has no such convenience and water is not readily oxidised for this reason. On the other hand, water may serve to transmit an oxidation process by the formation of hydroxyl and reduction to water again.) Again it is only the mechanism (IV) which enables a large number of oxidations of organic compounds to be viewed from a single standpoint. If the proton marked (a) displays a tendency to ionise, the reducing potential of the oxygen atom is naturally greatly enhanced (hydroxyl ion is a stronger reducing agent than water).

The following is a mixed batch of suggested mechanisms, in all of which the electron leak is from the oxygen atom and there are obvious analogies among nitrogen and sulphur compounds.

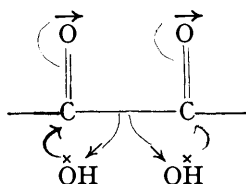


Mechanism (III) would be very unsatisfactory here. The oxidation of a ketone is more difficult than that of an aldehyde because the proton (a) is not available for ready detachment. When it occurs, it will be similar to the oxidation of a *tert.*-alcohol. Although every student of organic chemistry knows these facts, the relation between them, so far as the writer is aware, has not previously been discussed.

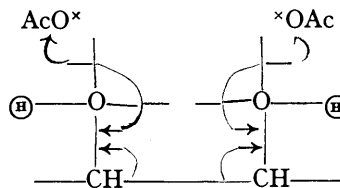


In the oxidation of quinol to benzoquinone one electron may be derived from each oxygen atom and this is probable when the oxidising agent is an acceptor of one electron, e.g., $\text{Fe}^{+++} \rightarrow \text{Fe}^{++}$. In the second figure we have a type represented by the direct oxidation of leucoaurin to aurin and again one electron may be derived from each of two centres. The greater the resonance energy of the product, the more facile is the oxidation process and in the nitrogen analogues the proton (*a*) is not detached but instead a distributed positive charge is assumed by the nitrogen atoms.

Quite a different class of oxidations is that by hydrogen peroxide, lead tetra-acetate, and the like. In agreement with Haber these reagents are best regarded as sources of hydroxyl (acetoxy, etc.) radicals.

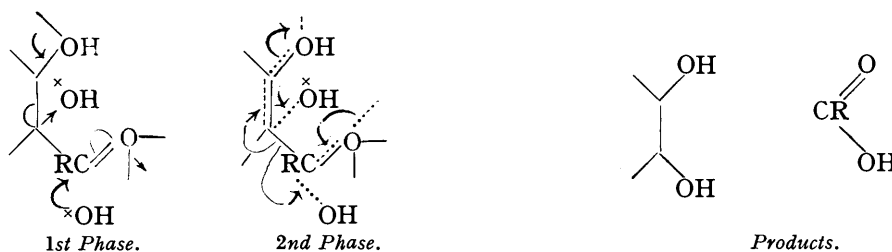


Oxidation of an α -diketone by hydrogen peroxide.

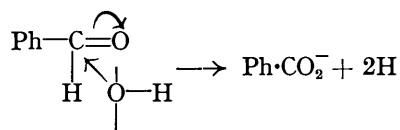


Oxidation of a glycol by lead tetra-acetate.

In Dakin's reaction we see the attack of a cationoid centre as above and also an anionoid centre. The latter functions alone in the *o**p*-hydroxylation of phenols by means of persulphates.

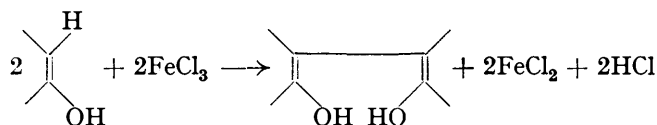


In this representation of Dakin's reaction the phases are for simplicity transfers of one electron. The use which it is found necessary to make of both unshared electrons and electron defect on different carbon atoms is strong evidence of the free-radical character of the oxidising agent. A third class of oxidation-reductions may be briefly mentioned in passing :

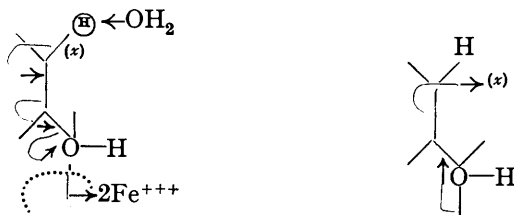


The initial product in the Cannizarro reaction loses two hydrogen atoms in order to become the ion of a carboxylic acid. The benzil-benzilic acid conversion has been discussed by the writer from the same point of view (*Ann. Reports*, 1923, 20, 118). In the Pondorff and Oppenauer reactions, which resemble the Cannizarro reaction formally, it is possible that both ketone and alkoxy (or even alcohol) are co-ordinated with the aluminium atom and that intramolecular oxidation-reduction occurs in the complex.

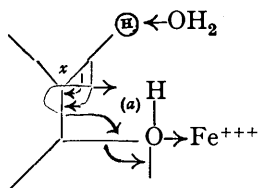
Returning to the case of oxidative coupling of phenols and amines, we take as an example the oxidation of β -naphthol by means of ferric chloride :



It will be agreed that the process is most likely to be symmetrical and that the new bond connecting the aromatic nuclei is not completed as a co-ordinate link. Supposing for the sake of argument that it were so formed, it would be necessary to denude the *o*-position to the hydroxyl of electrons (loss of H^-). The natural scheme for this would be :—



Such a molecule would be strongly cationoid at x and would attack a normal β -naphthol molecule (on the right) in the usual manner. The more acceptable symmetrical process combines these two types of displacement in a single molecule; they may occur in successive phases. Omitting the displacements that are reversed we get the following :

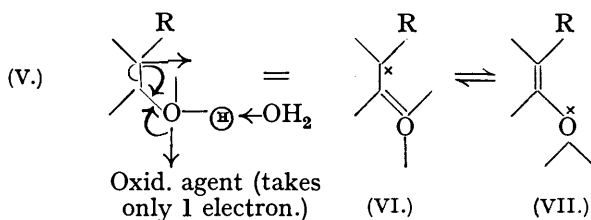


The arrows represent the eventual transfer of one electron each and the two at (a) belong to different phases.

Coupling of two x positions is possible, due to electrons unshared and in defect.

If two such figures are combined, we get an expression almost identical in principle with that developed for the benzidine conversion. All that is necessary for the combination is of course to connect two x positions by the arrows left free, the usual process of radical coupling.

When position 1 in a β -naphthol is substituted, oxidation affords the interesting dehydro- β -naphthols extensively studied by Pummerer. These are dimerides of radicals, into which some of them undoubtedly dissociate on heating in solution or in reactions. The simplest scheme for their formation is perhaps :



(VII) is derived from the naphthol by the simple processes of oxidation and removal of proton; the remaining arrows in (V) show the displacements required to pass from (VII) to (VI). Coupling of the electromerides (VI) and (VII) gives Pummerer's preferred constitution, for example, for dehydro-1-methyl-2-naphthol (*Ber.*, 1919, 52, 1403).

A safe deduction from the fact of the oxidisability of the 1-substituted α -naphthols is that the removal of the proton in position 1 does not occur in the first stages of the oxidation process.

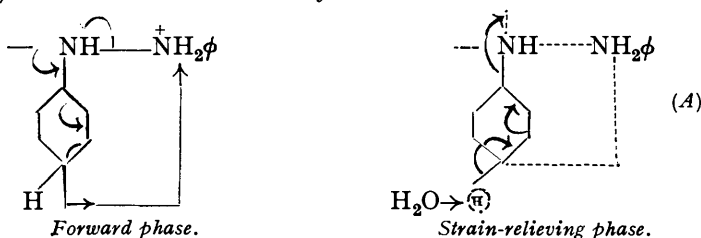
If we have correctly interpreted the facts, the close analogy of these oxidations of the *o*-position in phenols by an external agent with the intramolecular oxidation of the *p*-positions in hydrazobenzene is evident.

It would be an example of over-generalisation to attempt the inclusion of all couplings of aromatic nuclei in this framework; some of them are doubtless dimerisations, followed by decomposition, and the formation of diphenyl from benzene may be so regarded.

*Analogous Theories of the Semidine Rearrangement.**

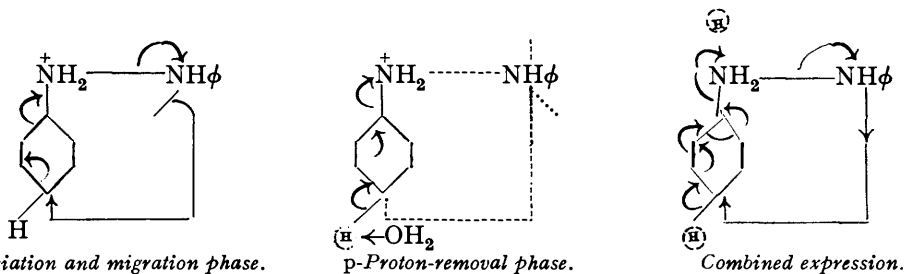
The semidine rearrangement, like the formation of benzidine, is clearly intramolecular and the arguments mentioned above are relevant to this case also. The conditions of the reactions are like those of the hydrazobenzene to benzidine change and we would expect it to be expressed by a half, or little more than half, of the scheme developed for the full migration. There are, however, several ways in which this can be done.

(A) Representation as a migration analogous to substitution in which the *p*-position (or *o*-position) exhibits anionoid reactivity.



Alternation of these phases completes the reaction and in addition the left-hand nitrogen picks up two protons and the right-hand nitrogen loses one proton.

(B) A substitution in which the nucleus exhibits cationoid reactivity.



These symbolisations represent the two possible mechanisms in which bonds are eventually broken and new bonds formed unidirectionally. That is, in which two electrons pass from an atom to a neighbour or in which a new covalency is formed by a pair of electrons on one atom becoming associated with the nucleus of another atom.

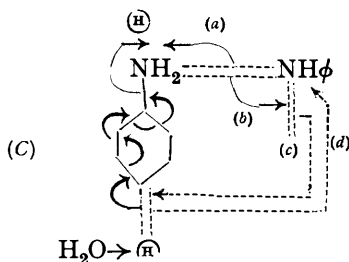
Scheme (A) has the advantage that it closely resembles the most acceptable theory of ordinary substitutions of aniline derivatives by means of cationoid reagents (halogenation, nitration, diazo-coupling, etc.). Indeed, if we pursue the obvious analogies of the semidine rearrangement, we are led through the stages: phenylhydrazine to *p*-phenylenediamine, phenylhydroxylamine to *p*-aminophenol, *N*-chloroanilines to nuclear-chlorinated anilines, and perhaps to the migration of diazo-groups in diazo-amino-compounds and to the migration of nitroso- and nitro-groups from nitrogen to the nucleus. These reactions exhibit a close formal resemblance and why should the intramolecular nitration by $\cdot\text{NH}\cdot\text{NO}_2$ in the side chain differ fundamentally from the nitration by $\text{HO}\cdot\text{NO}_2$?

On the other hand we cannot possibly apply scheme (A) to *both* nuclei in the benzidine transformation and (A) does not neatly accommodate the function of a strong acid in the semidine change. Although it is hard to allow for the compensating effect of the break of the nitrogen-to-nitrogen bond, we would not expect the appearance of a positive charge in the side chain to enhance anionoid reactivity of the nucleus. Here the *m*-substitution of benzylammonium salts may be recalled.

Scheme (B) gives a clear picture of the function of the acid catalyst and it is analogous to one side of the benzidine change (first phase), but the pursuit of the analogies, as detailed above, leads us into conflict with present ideas of aromatic substitutions.

* A *p*-semidine rearrangement is represented, although the *o*-semidine change is much the more common event. This has been done to facilitate ready comparison with the figures in the benzidine section. The group ϕ must be *p*-substituted and might, for example, be *p*-NHAc·C₆H₄.

It is possible to combine schemes (A) and (B) and the result is a symbolisation in which the bonds are not broken or formed unidirectionally but are dissociated and produced in a homopolar fashion. As the electrons of a covalency bond do not have the same destination, we represent some of the bonds, not by a line as usual but by two dotted lines; the unshared electrons on one of the nitrogen atoms are similarly represented. Omitting as before the displacements that cancel out in different phases of (A), we arrive at the representation below.



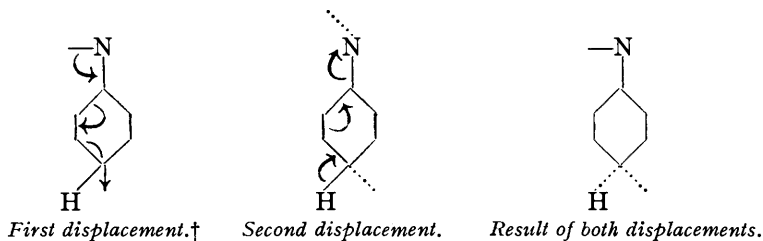
(A) and (B) combined.

Oxidation-Reduction Mechanism.

(a), (b) represent the homopolar dissociation of a bond and also regrouping of unshared electrons.
(c), (d) represent the formation of a bond by coupling of two electrons.*

This expression as it stands supplies no explanation of orientation; a migration to the *m*-position could be represented in the same way. But it is a synthesis of small successive displacements and the first, third, fifth, and so on, of these, of either (A) or (B) type, control the orientation, since it is not possible to secure the necessary unshared electrons or electron defect in positions other than those *o*- or *p*- to the nitrogen.

It should be noticed that the contribution of (A) to the combined and summarised scheme (C) is in effect nothing more than the dissociation of the bond binding the *p*-substituent (or *o*-substituent) to the nucleus.

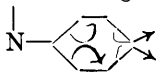


This will proceed in (C) until the dotted lines in the third figure represent one electron each. Every reversible, activating displacement process can be similarly summarised as a dissociating mechanism and, provided the underlying principles are recognised, there is a useful gain in simplification of the figures.

The Orientation Phenomena.

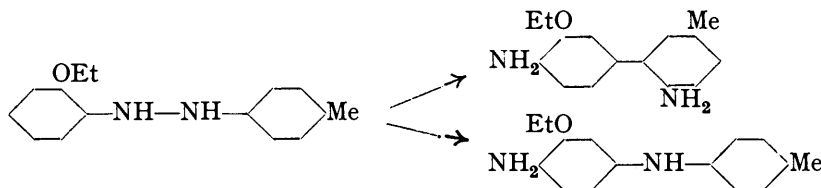
In considering these it must be remembered that a large number of the cases refer to the products of reduction of azo-compounds in acid media, usually by means of stannous

* The contributions of (c) and (d) to the bond must eventually be equal, one electron each, provided the corpuscular character of the electron persists at this range from the atomic nuclei. It seems just within the bounds of possibility that the conception of the electron corpuscle in the atom, necessarily based on observations of relations with matter and energy outside the atom, may have its origin in a more fundamental quantum property. On the other hand the validity of what we now conceive as a part of a full electron displacement may be denied by physical theory and we should need to replace the conception by one of an equivalent time-variable resonance in the bonds in the course of their making and breaking.

† In this and all similar schemes the displacement through one chain only in the nucleus is represented. This is held to include the possibility  in which the contributions of the two routes may be equal or unequal.

chloride and hydrochloric acid in alcoholic solution. The only exception to the rule that benzidines are formed if the *p*-positions are free appears to be *o*-aminoazobenzene, which gives *p*-phenylenediamine and aniline only (Witt, *Ber.*, 1912, **45**, 2383) and is therefore no real exception. The substituents in the *o*- and *m*-positions may be numerous and varied in nature; they may be neutral, basic, or acidic groups. This fact suggests that the mechanism is of a compelling character and is again hard to reconcile with a free-radical hypothesis—so many different kinds of free radicals have to be postulated and they all need to behave in the same way.

The *op*-coupling to a diphenyl derivative occurs as a side reaction with hydrazobenzene itself (production of diphenylene) and as the main process where one of the *p*-positions is occupied by Cl, Br, I, NMe₂, OAc, NHAc (with CH₃ substituent); NHAc alone leads to *p*-semidine and reduction to simple amines). In other similar cases the *op'*-diaminodiphenyls represent one of the main products and *o*-semidines are also obtained in substantial amount. For example (Jacobson and Huber, *Annalen*, 1909, **369**, 7) :

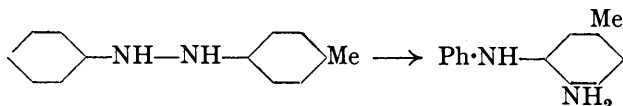


A curious anomaly is that 4-methylhydrazobenzene does not appear to yield a methyl-diphenylene but only an *o*-semidine. 4-Hydroxyazobenzene splits up on reduction. The general conclusion is that diphenyl formation is favoured, the benzidine type if possible and if not, with the exceptions noted, a diphenylene type is obtained. The tendency is clearly apparent to bring into play the longer conjugated systems first. This is connected in the writer's view with the question of duration and intensity of activations in the different positions. Attention has already been drawn to the example of diazo-coupling with 1-naphthol-3-sulphonic acid (Lapworth and Robinson, *Mem. Manchester Lit. Phil. Soc.*, 1927—1928, **72**, 45; Institute of Chemistry Brochure, 1932, 42). Here the diazo-salts of lower reactivity attack the *o*-position to hydroxyl, diazo-salts of medium reactivity attack both *o*- and *p*-positions, and diazo-salts of high reactivity (*e.g.*, 2:4-dinitrobenzenediazonium chloride) attack the *p*-positions only. The deduction was that the *p*-positions are less strongly activated than the *o*-positions and so can be attacked only by a reagent reaching a certain high chemical potential. But in order to accommodate the results the stronger activations in the *o*-positions which can make use of reagents of lower chemical potential must be of lower frequency than those in the *p*-positions. Otherwise the product should always be an *o*-hydroxy-azo-compound. Applying this idea to the hydrazobenzenes, it is only necessary to assume that the degree of frequent activation (value of unshared electrons or electron defect) in the longer conjugated systems reaches the level necessary for initiation of new bonding in order to explain the results. A steric factor may operate in addition, particularly if a powerful activation on one side of the hydrazo-group has a high frequency or duration. This is supposed to measure itself against the other side and there induces a reactivity which is not normally exhibited. This consideration may explain the success of Fischer's indole synthesis (*cf.* Robinson and Robinson, *loc. cit.*) and the interesting fact that α -hydrazonaphthalene affords 1:1'-diamino-di- β -naphthyl and 4:4'-diamino-di- α -naphthyl but not a mixed *op*- $\alpha\beta$ -derivative (*v. supra*).

The orientation phenomena among the semidine formation reactions are more varied and give answers to two questions. Which of the anilino-groups of an unsymmetrical substituted hydrazobenzene will migrate, and will it take up the *o*- or the *p*-position in the other nucleus?

The question as to whether *o*- or *p*-semidine formation is preferred is often impossible to answer because the issue is confused by the effect of migratory aptitude. For example, as the anilino-group has a greater migratory aptitude than the *p*-tolylamino-group

(Jacobson, *loc. cit.*), we are here debarred from a comparison of *o*- versus *p*-semidine formation.

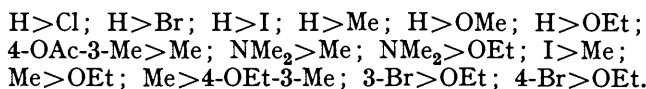


This is a case suited better by mechanism (B) or (C) than by (A), because the general electron displacement produced by the methyl group is from right to left and because *p*-toluidine is a stronger base than aniline.

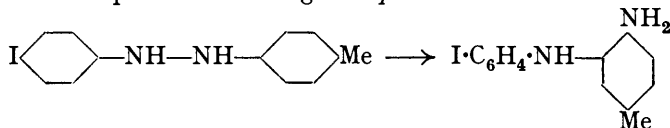
When the single substituent is a *p*-methoxyl or ethoxyl group, we again get as chief product an *o*-semidine in which the anilino-group has migrated. Here the general electrical effect of the OR group is opposite to that of a methyl group, but this is balanced by the electromeric displacement, $\phi \xrightarrow{\ominus} \text{OR}$.

However, in these cases the alkoxyphenylamino-group does migrate to some extent and it takes up the *p*-position in the anilino-nucleus. There are several further examples of this kind in which the alkoxyhydrazobenzene is further substituted by methyl groups. A few similar results are to be gleaned from the by-products in other examples, such as the mono-*p*-halogenated hydrazobenzenes. Hence, other things being equal, it appears that, where both possibilities exist, a *p*-semidine is produced in preference to an *o*-semidine and this is in line with the observations among the benzidine formations.

It is among the 4 : 4'-disubstituted hydrazobenzenes, which can only yield *o*-semidines (or the *o*-benzidines observed in the naphthalene but not in the benzene series), that we have the clearest comparisons, but here again the discussion is difficult because the orientations are analogous to those in the substitution reactions of disubstituted benzene derivatives. From individual cases we find the following migratory aptitudes; a few of these do not relate to 4 : 4'-disubstituted hydrazo-compounds. The substituents alone are indicated (for references, see Jacobson, *loc. cit.*) :

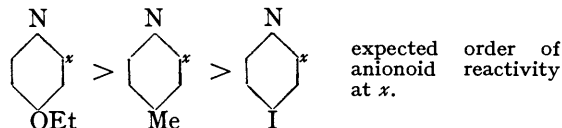


To take one example of the interpretation of this list, $\text{I} > \text{Me}$ means that the *p*-iodoanilino-group migrates into the *o*-position to nitrogen in *p*-toluidine.



The results do not exactly fit a simple scheme of anionoid or cationoid reactivity of the nucleus and disclose the operation of a complex of factors. If we exclude for a time the case of the anilino-group, there is a short series that can be placed in order : $\text{I} > \text{Me} > \text{OEt}$, with confirmatory evidence in the case of groups that cannot be included because of the lack of certain direct comparisons.

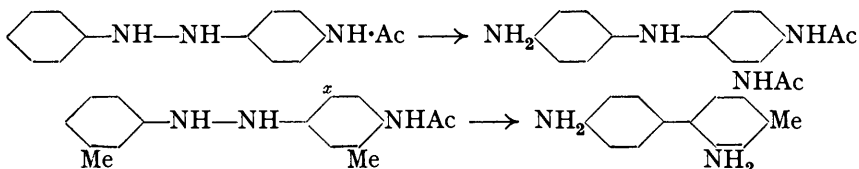
Here we certainly find that the accepting nucleus is that which possesses the greater anionoid reactivity as judged by known substitution reactions and by general theoretical considerations.



The cases $\text{NMe}_2 > \text{Me}$ and $\text{NMe}_2 > \text{OEt}$ may appear to contradict this, but in a strongly acid solution we have the salt NMe_2H^+ , and the expected effect is reversed when we pass from such a base to its salts.

Hence these results are in agreement with *initiation* by mechanism (A). Returning now to the anilino-group, the observations $\text{H} > \text{Me}$ and $\text{H} > \text{OR}$ are in harmony with the

above but $H > hal.$ seems anomalous. We are justified to a large extent in excluding these cases because of the complexity of the experimental results. Thus 4-chloroazobenzene on reduction in acid solution gives benzidine (by elimination of chlorine), chlorodiphenylene as the main product, anilinochloroaniline (the *o*-semidine), some chloroanilinoaniline (the *p*-semidine), and a part is reduced to *p*-chloroaniline and aniline. In view of the difficulties of the separations it is not possible to give the yields of these products exactly, but it is evidently illogical to concentrate attention on the contrast in the *o*-semidines. The benzidine, chlorodiphenylene and *p*-semidine may be credited to initial anionoid reactivity of the anilino-group. What does appear is that the reactivity of an anilino-group is preferentially displayed in the *p*-position to nitrogen. A special contrast is afforded by the cases



(Jacobson, Jaenicke, and Lockemann, *Annalen*, 1922, 427, 200.)

Here the directive effect of the methyl group is strong evidence of anionoid reactivity exhibited in the *p*-position to it (*x*).

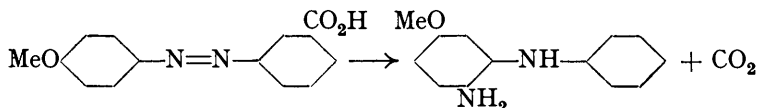
The results as a whole favour the view that the initiation is by mechanism (A). This, as implied above, is the orienting process. The value of its combination with (B) to give (C) is the advantage of closer accord with the benzidine conversion itself, the accommodation of more analogies, and the removal of certain disadvantages of a pure (A)-type mechanism.

The Displacements accompanying the Formation of Benzidines and Semidines.

Azobenzene-4-carboxylic acid (Jacobson, *Annalen*, 1898, 303, 384) and azobenzene-4-sulphonic acid give almost quantitative yields of benzidine on reduction in acid solution under the usual conditions. This is not unexpected, because these groups are frequently displaced quite readily in aromatic substitutions by cationoid agents. Wherever a proton is detachable by a water molecule, the cationoid CO_2H and SO_3H groups may equally be

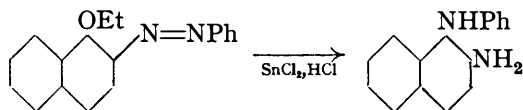
removed, *e.g.*, $\text{C} \leftarrow \text{O} \leftarrow \text{O}_2\text{H} \text{H} \oplus \leftarrow \text{OH}_2$, the products being carbonic acid and a hydrated hydrogen ion. The direct formation of carbon dioxide might also be postulated, but such a scheme would not apply to the elimination of the sulphonic group.

It is stated (Jacobson, Jaenicke, and Lockemann, *loc. cit.*) that 4-methoxyazobenzene-3-carboxylic acid on reduction in acid solution under the usual conditions affords fission products and 2-amino-5-methoxydiphenylamine :



This, if confirmed, indicates a remarkable ease of decarboxylation of the primary product. The elimination occurs in the migrating anilino-group and hence has little bearing on the theory.

Displacements of halogens have been observed in benzidine conversions, of acetoxy groups in *p*-semidine formations (and in one case in the formation of an *o*-semidine), and of alkoxy-groups in the formation of *o*-semidines. *E.g.*,



(Nölting, Grandmougin, and Freimann, *Ber.*, 1909, 42, 1378.)

These reactions underline the very great tendency for the occurrence of the migrations; they are overall reductions of the hydrazo-stage and may be compared with the reduction of *o*- and *p*-halogenated amines and phenols and of α -halogenated ketones. The reducing agent is evidently the stannous chloride employed, but, as the reduction of 2-amino-1-ethoxynaphthalene cannot be effected under similar conditions, it is clear that the reaction mechanism facilitates the process. The mechanisms already suggested necessitate the progressive detachment of the OR^+ , in which the oxygen atom has only a sextet of electrons. The group will gradually become a powerful oxidising centre as the conversion proceeds and eventually take up two electrons from the stannous ion. It is the converse of the attack of nitrobenzene in the *p*-position by anionoid reagents. Here the hydrogen atom is displaced plus an extra electron (H^-) and this reduces some substance present in the system.

The suggestion may be hazarded that in the example given above the related hydrazo-compound would be decomposed by acid alone with the production of the semidine and acetaldehyde. The analogy in mind is the decomposition of ethoxytrialkylammonium hydroxides (Meisenheimer) to tertiary bases and acetaldehyde. These displacements present no obstacles to the acceptance of the intramolecular mechanisms, but they are very serious difficulties for the free-radical theories.

Possible Repercussion on the Theory of Aromatic Substitution.

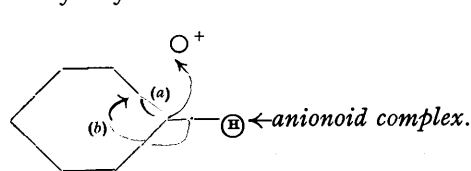
It has been shown that the hypothesis of successive small displacements allows us to combine two mechanisms (*A*) and (*B*) which control orientation (in the same sense) and that in the result (*C*) we achieve virtually non-polar reaction as the consequence of the alternate appearance of unshared electrons and electron defect at one and the same carbon atom. The possibility existed because there was a dissociable and reducible bond ($N-N$) in the system considered.

On general grounds we would expect a similar process for substitution by an external agent replacing the electron transfer through the nucleus to the reducible bond by a direct transfer of electrons from the site of substitution to a part of the reagent.

There is nothing novel in the results to which this suggestion leads, but the point is included because of its relation with the preceding discussion.

When a hydrogen atom attached to an aromatic nucleus is substituted as the result of attack by a cationoid reagent, the aromatic compound is oxidised and the cationoid reagent reduced; electrons pass from the aromatic substance to the substituting agent. If the cationoid agent is effective as a cation, then it cannot contribute electrons to the new bond binding it to the nucleus and we get a unidirectional process [analogous to (*A*) above]. The cause of the displacement in the nucleus is not specified; only the final result is indicated.

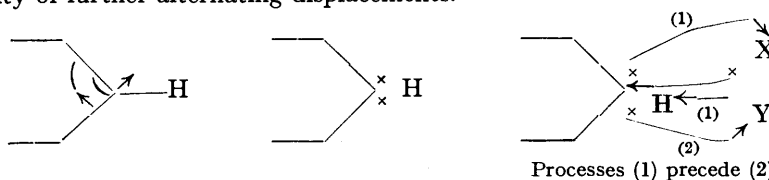
Displacements (*a*) and (*b*) alternate until the substitution is complete. A familiar example is the formation of azo-compounds from amines or phenols and diazonium salts.



Many oxy-acids are known to be bases and form ionisable salts with other strong acids (cf. Hammett, "Physical Organic Chemistry," 1940, pp. 46, 271 *et seq.*, for the evidence). Nitration in sulphuric acid is probably, therefore, at least in part, a direct attack on the nitroxy cation. This consideration explains the remarkable catalytic effect of perchloric acid in sulphonations and nitrations which has been observed in the Dyson Perrins Laboratory by Mr. G. Müller. A mixture of absolute nitric and perchloric acids is capable of effecting difficult nitrations far more quickly and at a lower temperature than one of nitric and sulphuric acids. The process is, however, too dangerous to have any practical application. Professor J. Kenner (private communication) has made use of similar considerations in his explanation of the course of diazotisation in strong acid media (Lecture to the Sheffield Section of the Chemical Society, Feb. 28th, 1941).

But if the reagent is dissociable, *per se*, or in course of reaction, into radicals or atoms

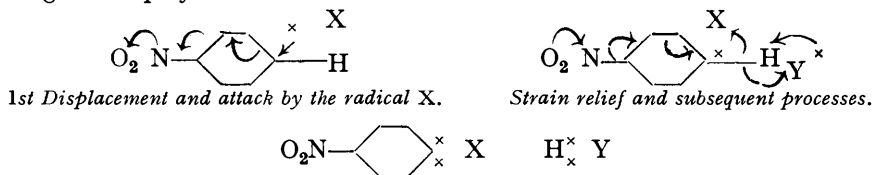
with both unshared electrons and electron defect, the course of the process is perhaps more likely to be (a) orienting loosening of the hydrogen to be displaced in accordance with principles already discussed and (b) direct oxidation of the substituted position without the necessity of further alternating displacements.



If at any stage the hydrogen is detached as a proton, it is clear that the electron previously binding it to the aromatic nucleus is at once available to reduce an atom or radical to an anion.

The radicals X, Y may be replaced by a molecule XY, which suffers homopolar disruption in the course of the reaction, or X, Y may be derived from different molecules or from different parts of the same molecule. For example, the radicals may be produced by photochemical or thermal activation, from a molecule such as Br_2 or HNO_3 (NO_2, OH) in the course of reaction, or from the decomposition of a substance such as SbCl_5 into SbCl_3 and 2Cl . The essential point is that the orienting polar displacement may be, and probably is, very small in relation to a full bond formation, and the substitution process may then be completed by homopolar coupling.* The latter is the equivalent with an external reagent of the later phases envisaged for the internal oxidation-reduction characteristic of the benzidine and semidine conversions. This idea fits in with the fact that the efficiency of control of orientation by the directing group in aromatic substitution has no kind of relation with the extent of electromeric displacements in the average resting phase that can be roughly estimated by dipole measurements. Chlorobenzene is nitrated in the *op*-positions as exclusively as phenol. However, when two different electromeric displacements can occur in one and the same molecule, their amplitude will naturally be one factor in control of relative reaction speeds. This may be brought about by the simultaneous appearance of different values of unshared electrons at the two possible sites of reaction or by a time-variability resulting in the more frequent appearance of unshared electrons (or of course electron defect) at the one site or at the other.

Finally, in agreement with Hey (Grieve and Hey, J., 1934, 1797; 1938, 108; Hey, J., 1934, 1966, and later papers), what is called amphoteric substitution is evidence of the operation of free radicals (cf. Hey and Waters, *Chem. Reviews*, 1937, No. 21). In these cases one and the same agent applied under similar conditions introduces a substituent *op* to either an anionoid group such as NMe_2 or a cationoid group such as NO_2 . In a cationoid system it is evidently the electron defect of a carbon atom of the nucleus which is first brought into play:



* Ingold and Ingold (J., 1926, 1313) have already proposed a "directive process," followed by a "subsequent change." The directive process for *op*-substitution was identical with that previously suggested by the writer. The "subsequent change" envisaged was a polar mechanism in which the proton from the position nitrated (for example) combined with hydroxyl ion from the nitric acid. This is a limiting case of the unidirectional mechanism (A) in which we assume that the proton is extracted by some neighbouring anion or anionoid complex. Ingold and Ingold proposed a quite different mode of *m*-substitution, which was regarded as an attack in the first instance on the hydrogen displaced. The writer has never concurred in this view and regards the mechanisms of *op*- and *m*-substitutions as identical in so far as the attack by the reagent is concerned. The orientation phenomena and other circumstances have been frequently discussed.

The suggestion made above is that a substitution oriented and initiated by polar displacement may be completed by a homopolar process. Just as the energy required to separate ionic charges is recovered in a complete cycle, so that required to separate duplets is compensated by the recombination of electrons to form other duplets.

This discussion may be summarised by the assertion that the electronic representation of the benzidine transformation, combined with the theory of small successive displacements, expresses and symbolises the meaning of all the ascertained facts and interprets acceptably the analogies to which attention has been drawn. We are able to harmonise the apparently disconnected views of authors who have dwelt on the rôle of the acid, the medium, the heterogeneity of the hydrazo-group, and the aspect of an oxidation-reduction process. We note also new analogies with orientation in other benzene substitutions and with the oxidative couplings of aromatic amines, phenols, and enols generally.
