

MECHANISM OF ORGANIC CHEMICAL REACTIONS

by

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PREFACE...

IN the following pages the author has endeavoured to give a brief account of modern views of the mechanism by which some familiar reactions of organic chemistry take place. Such knowledge is now an essential part of the equipment of every organic chemist, and it is hoped that the book will be useful not only to students reading for a University degree or professional qualification of similar standing, but will also be of interest to the older generation of organic chemists who have got somewhat out of touch with modern academic work.

The rapid increase in knowledge in all branches of chemistry has placed an almost unbearable burden on present-day students, and in the hope of easing this burden somewhat the author has been at pains to confine himself to the more familiar reactions, to be as brief as is consistent with clarity, to avoid unnecessary detail, and, as far as possible, to illustrate each reaction by simple and familiar examples. The plan usually adopted has been to describe the reaction under consideration very briefly, outline the chief experimentally established facts which must be covered by any theory of the reaction, and finally to give the mechanism which is at present thought best to fulfil this condition. Since the book is not intended as a handbook for research workers no attempt has been made to give a full bibliography. The references given, which are often to review articles or to papers containing a summary, should amply meet the needs of any reader wishing to study a given reaction in greater detail, and from these references a chemist wishing to undertake research should have no difficulty in drawing up a full bibliography of previous work on any reaction dealt with in this volume. As a further help a bibliography of other books dealing with reaction mechanism and published during the past ten years has been appended.

The author's thanks are due to Dr. H. Mackle of the Queen's University, Belfast, and to his former students Drs. A. D. Jenkins, P. W. Ranby and A. G. Snow, and Messrs. R. F. Branch,

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REACTION CODINGS

- E1 Unimolecular elimination
- E2 Bimolecular elimination
- SE1 Unimolecular electrophilic substitution
- SE2 Bimolecular electrophilic substitution
- SE1' Unimolecular electrophilic substitution with allylic inversion
- SE2' Bimolecular electrophilic substitution with allylic inversion
- SN1 Unimolecular nucleophilic substitution
- SN2 Bimolecular nucleophilic substitution
- SN1' Unimolecular nucleophilic substitution with allylic inversion
- SN2' Bimolecular nucleophilic substitution with allylic inversion
- SNi Intramolecular nucleophilic substitution
- SNi' Intramolecular nucleophilic substitution with allylic inversion

ABBREVIATIONS

<i>Ann. Chim.</i>	Annales de Chimie
<i>Annalen</i>	Liebig's Annalen der Chemie
<i>Ber.</i>	Berichte der deutschen chemischen Gesellschaft. Now Chemische Berichte
<i>Bull. Soc. chim.</i>	Bulletin de la Société chimique de France
<i>Canad. J. Chem.</i>	Canadian Journal of Chemistry
<i>Canad. J. Res.</i>	Canadian Journal of Research
<i>Chem. and Ind.</i>	Chemistry and Industry
<i>Chem. Reviews</i>	Chemical Reviews
<i>Compt. rend.</i>	Comptes rendues de l'Académie des Sciences
<i>Experientia</i>	Experientia
<i>Helv. Chim. Acta</i>	Helvetica Chimica Acta
<i>J. Amer. Chem. Soc.</i>	Journal of the American Chemical Society
<i>J. Chem. Physics.</i>	Journal of Chemical Physics
<i>J. Phys. Chem.</i>	Journal of Physical Chemistry
<i>J. pr. Chem.</i>	Journal für praktische Chemie
<i>J. Roy. Inst. Chem.</i>	Journal of the Royal Institute of Chemistry
<i>Monatsh.</i>	Monatshefte für Chemie
<i>Naturwiss.</i>	Naturwissenschaften
<i>Quart. Reviews</i>	Quarterly Reviews
<i>Rec. Trav. chim.</i>	Recueil des Travaux chimiques des Pays-Bas
<i>Research</i>	Research
<i>Trans. Faraday Soc.</i>	Transactions of the Faraday Society
<i>Z. Naturforsch.</i>	Zeitschrift für Naturforschung

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CHAPTER I

Introduction

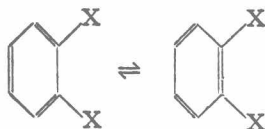
MESOMERISM.

The structural formulæ of classical organic chemistry are, in many cases, no longer a satisfactory representation of the properties of a molecule, and it is now realized that the actual structure may be a hybrid derived from two or more classical or canonical formulæ. Such hybridization is known as mesomerism or resonance. Although the doctrine of mesomerism is of comparatively recent origin, the basic idea in a somewhat different form was introduced by Kekulé, who explained the non-existence of isomeric ortho-disubstitution products of benzene by postulating that the double bonds in the ring were not localized, but were continually changing places. This idea of non-localized double bonds was also used to explain the non-existence of other isomers predicted by classical organic chemistry, such as the non-existence of isomeric pairs of anthracene derivatives, for example



In such cases the isomers were deemed to be in dynamic equilibrium with one another, and since the isomeric change did not involve the migration of any atom or group but merely a rearrangement of the double bonds, the phenomenon was at a later date named "valency tautomerism". In recent years the postulated dynamic nature of the phenomenon has been abandoned, and a substance showing valency tautomerism is no longer regarded as consisting of two molecular species in equilibrium with one another. On the contrary it is regarded as a single molecular species to the structure of which two or more canonical extremes have contributed—but not necessarily, or even usually,

equally. Thus the Kekulé conception of an ortho-disubstitution product of benzene as an equilibrium mixture:



is no longer acceptable, and has been replaced by the postulate of a single molecular species with a structure lying somewhere between the above two "canonical extremes".

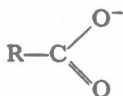
Unfortunately a mesomeric molecule cannot be given a written structure, all that is possible being to write the various possible canonical extremes, indicating that they are mesomeric, or "in resonance", by means of a double-headed arrow, \longleftrightarrow which must not be confused with the double arrow \rightleftharpoons used to indicate a reversible reaction. The double-headed arrow represents a static state; the double arrow a change taking place in both directions.

In order that a molecule may exist in a mesomeric form the following three conditions must be fulfilled:

1. The atoms in the canonical extremes must occupy positions which are almost identical.
2. The canonical extremes must have almost the same free energy.
3. With a few exceptions the number of unpaired electrons (not lone-electrons) must be the same in each canonical extreme.

If these conditions are fulfilled the actual molecular species will not be that of any of the canonical extremes, but will be a hybrid to which each canonical formula has contributed. It will have a lower free energy than any of the canonical extremes, i.e. will be thermodynamically more stable than any of them, and there will be a shortening of some of the bonds.

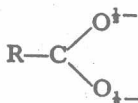
A simple and familiar example of mesomerism is the ion of a carboxylic acid. According to classical organic chemistry such an ion is written as



i.e. the two oxygen atoms are shown as being different, with the whole negative charge localized on one of them. Although such formulæ are still used as a matter of convenience, there is no evidence whatsoever of any difference in the two oxygen atoms, and according to modern views the negative charge is not localized but is distributed over both of them, i.e. the actual ion is a mesomeric hybrid of the two identical canonical extremes:



Since in this case the two canonical extremes are identical in every way they will contribute equally to the mesomeric structure, and it can be safely assumed that there is the equivalent of a half negative charge on each oxygen atom:



The ion of a monothio-carboxylic acid is a mesomeric hybrid of two non-identical canonical forms:



and in this case it is extremely unlikely that both contribute equally to the mesomeric hybrid. On the contrary, oxygen being more electronegative than sulphur, the oxygen atom almost certainly carries a higher portion of the negative charge than does the sulphur atom.

EFFECTS.

By an "effect" is understood some influence which alters the distribution of electrons in a molecule from what may be described as the normal or "canonical" positions.

Inductive and Inductomeric Effects. The inductive effect is a permanent displacement of electrons, present even in an isolated molecule, and brought about by electrostatic attraction or repulsion. It is often symbolized by *I* preceded by a plus or minus sign to indicate the direction in which it acts; but since there is no agreed sign convention, and what is a $+I$ effect to one school is

a —I effect to another, it is better to describe the effect of any atom or group as being an attractive or repulsive inductive effect.

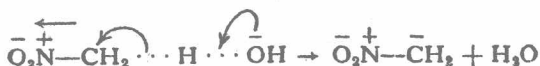
An inductive effect may be due to an integral positive or negative charge on an atom. Thus a quaternary nitrogen atom carries a full positive charge, and hence exerts an attractive inductive effect. The oxygen atom of the alkoxide ion, RO^- , carries a full negative charge, and hence exerts a repulsive inductive effect. The positive nucleus of an atom, e.g. a halogen atom, exerts an attractive inductive effect, and hence at first sight it would seem that the halogens would exert an increasing attractive inductive effect with increasing atomic number, i.e. with increasing nuclear charge. This is not the case, however, since allowance has to be made for distance from the nucleus and for screening by the orbital electrons. Hence of the halogens the fluorine atom exerts the largest inductive effect and the iodine atom the smallest.

An alkyl group, particularly a methyl group, exerts a repulsive inductive effect, probably because the nuclear positive charge of a carbon atom is much greater than the nuclear positive charge of a hydrogen atom. Consequently the electrons forming a carbon-hydrogen covalency are nearer to the carbon atom than to the hydrogen atom so that the carbon atom in, say, the methyl group has a fractional negative charge.

The inductive effect is indicated by a straight arrow pointing in the direction in which the valency electrons have been displaced. It is transmitted through a chain of saturated carbon atoms but, since a saturated carbon atom is a fairly effective screen, the effect soon dies away.

The inductive effect can be assisted by the approach of an ion carrying a positive or negative charge, and is then sometimes called the inductomeric effect. In nitromethane, for example, the positive charge on the nitrogen atom exerts an attractive inductive effect, and draws the electrons forming the carbon-hydrogen bonds away from the hydrogen atoms. Hence it makes these hydrogen atoms more inclined to leave the molecule as protons, but nitromethane itself is still an un-ionized covalent compound. If a powerful electron-repelling group such as a hydroxyl ion approaches a hydrogen atom of a nitromethane molecule, its electron-repelling properties are added to the inductive effect of the nitrogen atom, and the resulting inductomeric effect is so great that a hydrogen atom is completely

protonized and becomes covalently bound to the hydroxyl ion. The process is represented thus:

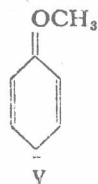
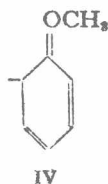
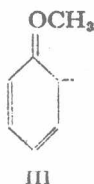
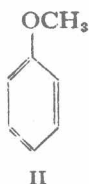
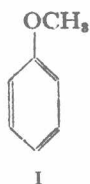


in which the dotted bonds are bonds being built up or broken, and the curved arrows represent the shift of electron pairs. (If it is desired to indicate the shift of single electrons it is customary to use dotted curved arrows, $\cdot\cdot\cdot$.)

Mesomeric or Tautomeric and Electromeric Effects. The mesomeric (formerly tautomeric) effect is also a displacement of electrons but differs somewhat in origin from the inductive effect. It is best explained by some simple examples.

If a carbonyl compound is considered, $\text{R}_2\text{C}=\text{O}$, the oxygen atom has a greater tendency to acquire a negative charge than has the carbon atom. Hence there will be a tendency for one pair of electrons forming the double bond to become associated solely with the oxygen atom, i.e. there will be a tendency for the molecule to take the dipolar form $\text{R}_2\text{C}^+-\text{O}^-$. This change does not go even approximately to completion, but neither the double-bonded formula nor the dipolar formula is a true representation of the molecule, which must be regarded as a mesomeric hybrid to which both structures contribute (p. 1). Hence the term "mesomeric effect".

Again in the case of a phenolic ether such as anisole, the usual canonical formula is not a true representation of the molecule since the oxygen atom has lone electrons which can be used for forming a double bond with the carbon atom to which it is attached. This becomes possible without exceeding the octet since the ring contains conjugated double bonds (according to the Kekulé formula), so that in addition to two identical canonical benzenoid formulæ (I and II below), two identical ortho-quinonoid formulæ (III and IV) and one para-quinonoid formula (V) are possible:

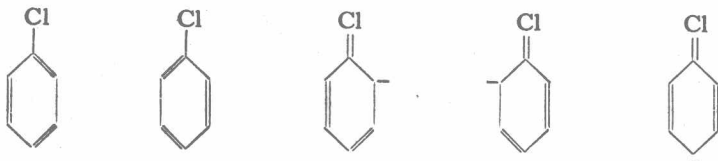


None of these truly represents the molecule of anisole, which must be regarded as a mesomeric hybrid of all five, but the result is that there is a fractional negative charge on the carbon atoms in the ortho and para positions to the methoxyl group.

The mesomeric effect is represented by curved arrows pointing in the direction of the electron shift:



A halogen atom, which exerts an attractive inductive effect, can also exert a mesomeric effect in the opposite direction owing to its ability to use its lone electrons for valency purposes. Thus chlorobenzene must be regarded as a mesomeric hybrid to which the five canonical structures contribute:



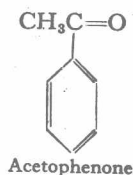
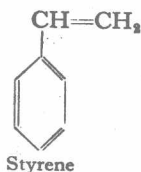
Consequently the molecule itself has fractional negative charges in the positions ortho and para to the chlorine atom. At the same time the chlorine atom is exerting an attractive inductive effect which tends to draw the electrons away from these positions. The result of these opposing effects is discussed in Chapter III.

Since most atoms of which the more common organic compounds are composed cannot accommodate more than eight electrons in the outer quantum group, the mesomeric effect can only be transmitted through conjugated double bonds. The effect can be enhanced by the approach of a positive ion towards the seat of the fractional negative charges, the term "electromeric effect" then being used.

CONJUGATION.

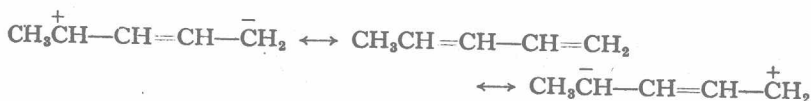
Two or more multiple bonds are said to be "conjugated" when each is separated from the next by one single bond, e.g. butadiene, $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$; acrolein, $\text{CH}_2=\text{CH}-\text{CH}=\text{O}$;

and acrylonitrile, $\text{CH}_2=\text{CH}-\text{C}\equiv\text{N}$. The double bonds of the Kekulé benzene rings are conjugated with one another, and can conjugate with multiple bonds external to the ring, e.g.

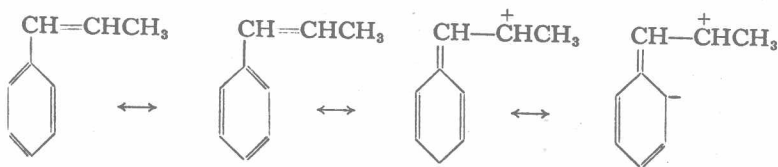


The term "phenyl-vinyl conjugation" is often used to describe the conjugation of an aromatic ring with a lateral olefine bond.

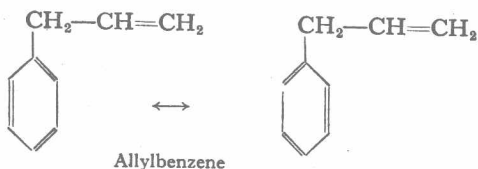
A conjugated system is capable of mesomerism, and hence a compound in which multiple bonds are conjugated has less free energy, and hence is more stable, than an isomer of similar nature in which the multiple bonds are "isolated". Thus α -methylbutadiene must be regarded as being a mesomeric hybrid to which the canonical forms



contribute. In the same way propenylbenzene is a mesomeric hybrid to which a number of canonical forms such as

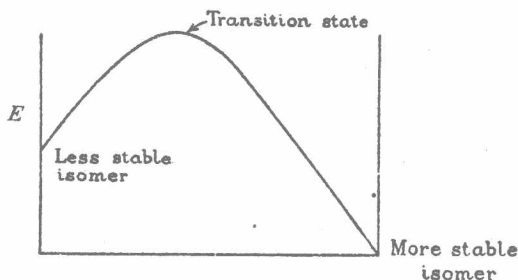


contribute. Owing to the phenyl-vinyl conjugation it is more stable than allyl benzene, in which the lateral olefinic bond is isolated from the benzene ring:



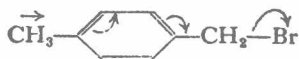
The usual aromatic mesomerism in the ring is present, but there is no conjugation with the exocyclic olefine bond.

The fact that one isomer has less free energy than another, and hence is thermodynamically the more stable, does not necessarily imply that it will be formed preferentially in a reaction which might lead to either isomer, since control is often kinetic rather than thermodynamic, i.e. the product contains that isomer in greatest amount which is formed by the quickest reaction (see p. 38 for examples). If this is the isomer with the higher free energy the system will be metastable, and may remain so almost indefinitely if the two isomers are separated by a high-energy barrier, that is, if the less stable must take up a considerable amount of energy in order to reach a transition state from which it can lose energy to form the more stable isomer. The more stable isomer is, of course, the one formed from the transition state with the greatest loss of energy:



There is often a marked tendency for the less stable isomer to be formed first, and Ostwald's Law of Successive Reactions (which applies more to physical than to chemical changes, and is a useful generalization rather than a law of nature) postulates that when more than one product is possible the least stable is formed first, and then passes into the next more stable, and so on until the most stable isomer is reached.

Hyperconjugation.¹ A methyl group exerts a repulsive inductive effect, and if this can be transmitted through a conjugated chain it will facilitate the ionization of a halogen atom. In accord with prediction it is found that *p*-methylbenzyl bromide ionizes more easily than does benzyl bromide:



¹ CRAWFORD: *Quart. Rev.* 3 (1949), 226; BAKER, NATHAN *et al.*: *J.* (1935), 1840, 1847; (1942), 191; BAKER: "Hyperconjugation" (Clarendon Press, Oxford, 1952).

If the methylic hydrogen atoms are replaced one by one by methyl groups, i.e. if the methyl group is converted successively into ethyl, *iso*-propyl and *tert.*-butyl, there should be a continuous increase in the ease with which the bromine atom is ionized, since the inductive effect increases in the order methyl, ethyl, *iso*-propyl, *tert.*-butyl. This, however, does not agree with experimental fact, since the tendency for the bromine atom to ionize decreases as the methyl group in the para-position is successively exchanged for ethyl, *iso*-propyl and *tert.*-butyl, although in the last two cases the difference is very slight. This result shows that some influence other than the repulsive inductive effect must operate. The generally accepted explanation is that in the struc-

ture $\text{H}-\overset{\textstyle |}{\underset{\textstyle |}{\text{C}}}-\overset{\textstyle |}{\underset{\textstyle |}{\text{C}}}=\overset{\textstyle |}{\underset{\textstyle |}{\text{C}}}$, the valency electrons forming the carbon

hydrogen bond are not completely localized, but to some extent are to be found between the terminal carbon atom and the carbon atom to which this is attached, thus conferring some double-bond character on the carbon-carbon bond. This would imply exceeding the octet of the second carbon atom, which to accommodate temporarily the electrons from the carbon-hydrogen bond must temporarily get rid of some of the electrons of the double bond. The electromeric change is shown in the accompanying formula:



and can be described by saying that the ionic form contributes to the mesomeric structure. Both hydrogen atoms of a methylene group, and all three hydrogens of a methyl group, can behave in this way, and it is this electromeric change which is called hyperconjugation. A halogen atom can probably participate in hyperconjugation:¹



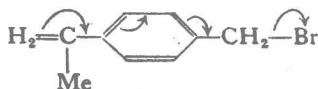
If the idea of hyperconjugation is applied to the *p*-alkylbenzyl bromides it will at once be seen that as we pass from methyl to ethyl, *iso*-propyl and *tert.*-butyl, although the inductive effect is

¹ J. (1948), 17.

increasing, electron release by hyperconjugation is decreasing:



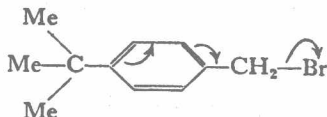
Inductive effect of methyl.
Hyperconjugation of three hydrogen atoms.



Inductive effect of ethyl.
Hyperconjugation of two hydrogen atoms.



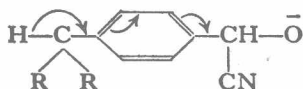
Inductive effect of *iso*-propyl.
Hyperconjugation of one hydrogen atom.



Inductive effect of *tert.*-butyl.
No hyperconjugation.

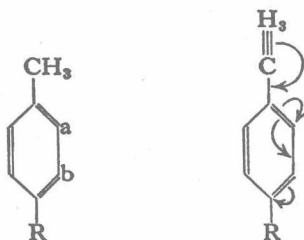
From the above it will be seen that the increasing inductive effect is countered by a decrease in hyperconjugation, and the very similar ease of ionization of the *iso*-propyl and *tert.*-butyl compounds shows that with this last pair of compounds the increase in inductive effect is almost exactly offset by the loss of hyperconjugation with the last hydrogen atom. (When more than one hydrogen atom undergoes hyperconjugation the total effect is not the sum of the individual effects.)

Hyperconjugation also influences the ease with which a *p*-alkyl benzaldehyde undergoes cyanohydrin formation. Thus if the alkyl group in the para position contains hydrogen atoms capable of hyperconjugation, conjugation will extend from them to the oxygen atom of the carbonyl group, but in the cyanohydrin participation of this oxygen is no longer possible:



Hydrogen atoms capable of hyperconjugation will increase the stability both of the aldehyde and of the cyanohydrin since in both cases more resonance energy can be lost, but owing to the greater length of the conjugated system the effect will be greater in the case of the aldehyde than in the case of the cyanohydrin. Hence the doctrine of hyperconjugation predicts that the stability of the *p*-alkylbenzaldehydes relative to the stability of their cyanohydrins will be greatest when the alkyl group is methyl (three hydrogen atoms capable of hyperconjugation), and will become progressively less in the ethyl, *iso*-propyl and *tert.*-butyl compounds. This is in agreement with experimental fact.

A further simple example of the effect of hyperconjugation is seen in the behaviour of the *p*-alkyl toluenes when they undergo nuclear substitution by electrophilic attack, e.g. nitration, halogenation and sulphonation:



Both nuclear positions, marked a and b in the formula on the left, have high electron density owing to the repulsive inductive effect of the alkyl group in the ortho position. Hence in the absence of hyperconjugation, substitution should take place mainly at b if R is an alkyl group (ethyl, *iso*-propyl or *tert.*-butyl) which exerts a greater inductive effect than does methyl. This, however, does not agree with experimental fact since in all three compounds substitution by electrophilic attack is mainly at a, where high electron density is to be expected owing to the inductive effect re-enforced by hyperconjugation with three hydrogen atoms.

Caution is necessary in interpreting results such as these since steric hindrance, i.e. resistance to the crowding together of bulky groups, may hinder access to the position ortho to the *tert.*-butyl group. Thus although both toluene and ethylbenzene on nitration give 50–55 per cent of the *o*-nitro-compound, with *tert.*-butylbenzene only about 15 per cent of the ortho-isomer is formed. (The figures available for *iso*-propyl benzene are too unreliable to be worth quoting.) This decrease in the amount of ortho-isomer formed has been attributed to steric hindrance by the bulky *tert.*-butyl group, but it is difficult with the data available to separate the influence of steric hindrance from the inductive effect and hyperconjugation.

As a last example of hyperconjugation the relative stability of the isomeric azomethines

