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The Role of One-electron Transfer in Substitution Reactions

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The principal examples of substitution reactions which involve an intermediate one-electron transfer stage are examined. Attention is concentrated on the causes which make this stage important and its relations with other stages in the mechanism are analysed. It is noted that the application of the ideas of one-electron transfer to the mechanisms of all substitution reactions without exception is invalid. Cases of the activation of substitution reactions under conditions favouring electron transfer are discussed. The urgent need for studies in this field is demonstrated and certain tasks for the immediate future are formulated.
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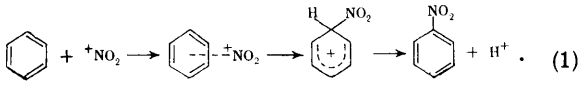
I. INTRODUCTION

The aim of the present review is to discuss the evidence supporting the presence of a one-electron transfer stage in the mechanisms of certain substitution reactions. Numerous studies in which the existence of such a stage explains the observed facts but is justified mainly by logical considerations have been left outside the scope of this review. Attention has been concentrated on reactions for which the existence of an electron transfer stage has been proved. The review includes fundamental examples. The causes which make the electron transfer stage real and the interrelations between this stage and others in the mechanism are discussed. Together with reactions which clearly proceed via a one-electron transfer stage, cases are considered where radical-ions are formed in a secondary reaction pathway and not the main pathway. It is shown that in certain reactions it is possible to increase the yield and rate of formation of the final products by creating conditions favouring the electron transfer stage.

II. THE CONCEPT OF THE ONE-ELECTRON TRANSFER STAGE IN A SUBSTITUTION REACTION

The concept of one-electron transfer as an intermediate stage in inorganic reactions has proved extremely fruitful and is supported by extensive experimental data obtained in the 1940s–1950s. The development of these ideas occurred simultaneously with the development of the foundations of nuclear chemistry and technology[1]. The problem of the role of one-electron transfer in organic reactions was considered during the last 15 years[2-8]. During this period, the development of new methods for the investigation of unstable or relatively unstable species, such as electron transfer products, led to the possibility of their wide-scale investigation. One may say that such species were extremely unfamiliar in organic chemistry during earlier periods.

After the first studies, which drew the attention of organic chemists to the important role of one-electron transfer in reactions, many investigators began to consider the mechanisms of virtually all reactions from the standpoint of oxidation-reduction processes. However, as experimental data accumulated, it was shown that the idea of the one-electron stage should be used in moderation (cf. Okhlobystin[9] and Beletskaya[10]). The hypothesis of one-electron transfer as an intermediate reaction stage presupposes that the reagent and the substrate are involved in an oxidation-reduction interaction. Subsequent stages involve the combination of the products arising as a result of the oxidation-reduction reaction. We shall consider as an example the nitration of benzene[11-13]. The substitution proceeds via the stages in the scheme below[14]:

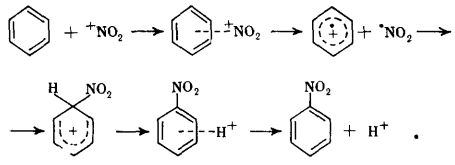


(1)

The process begins with the formation of a π-complex, which corresponds to partial charge transfer. Next the π-complex rearranges to a σ-complex with subsequent elimination of a low molecular weight species—a proton. Within the framework of perturbation theory[14], this is formulated as the formation of a transition state "from the perturbation of the π-system to the perturbation of a definite carbon atom". However, an isolated electron transfer stage is not considered in the perturbation theory[14]. At the same time, it follows from a theoretical study[15] that the approach of the reagent to the substrate bond subjected to attack alters the energy levels of the lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO). The intermolecular distance over which the one-electron stage can take place depends on the degree of perturbation. When the distance is large, the products formed in this stage can emerge into the bulk of the reaction solution and when it is small they can recombine in the solvent "cage"[15].

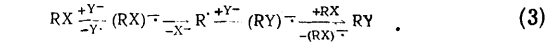
Quantum-chemical calculations[12] have shown that the LUMO of the nitronium cation has an energy of −11.0 eV, while the HOMO of benzene has an energy of −9.24 eV. This makes theoretically probable yet another nitration stage, namely the transfer of an electron (a single charge) from the benzene HOMO to the nitronium cation LUMO;

this stage is represented in the general scheme (2). The species constituting the biradical pair may combine to form a σ-complex:



(2)

Thus one-electron transfer consists in the transfer of a single charge and not of a partial charge as in a π-complex. Partial transfer leads to charge-transfer complexes (CTC), while complete transfer results in the formation of radical-ions, radicals, or ions. The final products may be formed as a result of the combination of radicals derived from the reagent and the substrate, as in scheme (2). Another pathway is also possible, namely the decomposition of the substrate radical-ion with formation of a new radical capable of reacting with a second reagent molecule. This pathway is indicated in relation to the nucleophilic substitution reaction (3).[8] Such reactions are observed among both aromatic and aliphatic compounds and are classified as $S_{RN}1$ reactions:



(3)

In reactions of the $S_{RN}1$ type the one-electron transfer stage also plays an important role, initiating the transformation and imparting to it a chain mechanism.

We shall consider in greater detail the theoretical postulates and then shall analyse the experimental data characterising the role of one-electron transfer in the mechanism of substitution reactions.

III. THEORETICAL PROBLEMS

1. Thermodynamic Conditions for One-Electron Transfer

Electron transfer can occur only when the difference between the ionisation potential of the donor (I_D) and the electron affinity of the acceptor (E_A) is greater than zero ($I_D - E_A > 0$). In order to determine the sign of this difference, it is possible to compare the HOMO and LUMO energy levels of the substrate and the reagent. For electrophilic and nucleophilic substitution reactions of aromatic compounds, such comparisons can be made using Fig. 1. Evidently the LUMO levels of electrophilic reagents are lower than the HOMO levels of aromatic substrates. In principle, this creates the possibility of electron transfer from the HOMO level of the substrate to the LUMO level of the reagent. For the benzene nitration reaction, this stage was in fact taken into account in scheme (2). Furthermore, Fig. 1 shows that the HOMO level of the hydroxide anion lies above the LUMO levels of substrate molecules, while the HOMO level of the chloride ion lies above the LUMO level of nitrobenzene. Hence it follows that, when an aromatic substrate reacts with a nucleophile, an electron transfer stage is probable.

The calculation whose results are illustrated in Fig. 1 was performed approximately 20 years ago. Naturally, it was necessary to have a later confirmation of these results. Recent calculations by Epiotis[16] showed that relations of the type illustrated in Fig. 1 are confirmed and that they are valid for a wider range of substrates and reagents. Epiotis' study was undertaken to discover the correspondences between the reactivities at individual positions of the substrate molecule and the spin valences of the radical-ion in the same positions. Epiotis based his calculations on the perturbation theory, which, as stated above, does not treat electron transfer as an isolated stage. At the same time the fundamental scheme of orbital interactions obtained by Epiotis for the transition states of electrophilic, nucleophilic, and radical substitutions in aromatic compounds is of great interest for further exposition of the subject (Fig. 2).

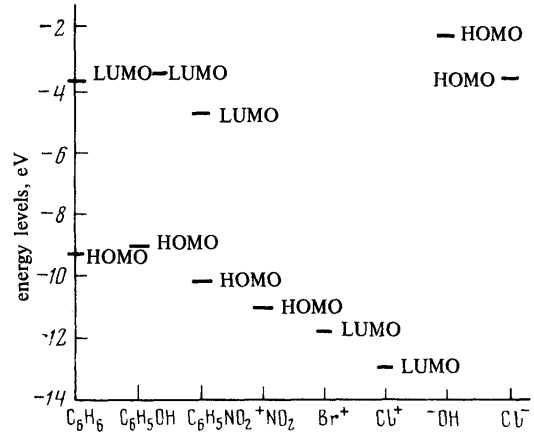


Figure 1. Energy level diagrams for some substrates and reagents in aromatic substitution[12].

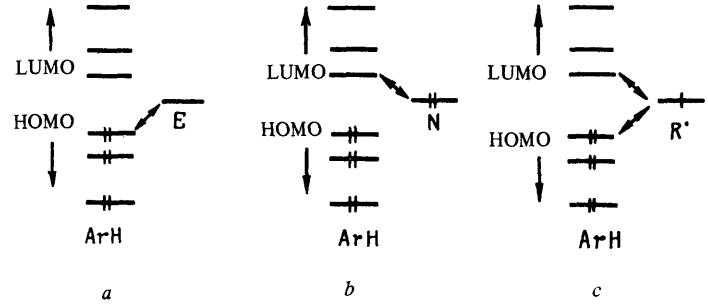


Figure 2. Schematic diagram of the orbital interactions of an aromatic molecule (ArH) with an electrophile (E), a nucleophile (N), and a radical (R·).[16]

Fig. 2 illustrates the types of orbital interactions which are analogous for nucleophilic and electrophilic substitution reactions to those discussed in connection with Fig. 1. For radical substitution, the type of interaction is determined by the nature of the radical R·. If the attacking radical is a nucleophile and has a low ionisation potential, the decisive factor for it is a donor type interaction (with LUMO). For an electrophilic radical with a high ionisation potential the decisive factor should be an acceptor type interaction (with HOMO).

However, one should note that both the calculations of Nagakura and Tanaka[12] and those of Epiotis[16] were performed without taking into account the influence of external substitution factors: solvation and coordination of the species in solution, the formation of hydrogen bonds, steric hindrance, etc. Under certain conditions, these factors may become decisive and may drive the reaction via a different pathway. The nature of the reacting species is also important. Calculations have been made recently[17] in order to determine the tendency of particular reagents to interact with the substrate via ionic or radical-ion pathways. The difference between these pathways is evident from a comparison of schemes (1) and (2). For example, it was found that, when benzene interacts with a proton, the one-electron mechanism is favourable until the substrate and reagents approach one another to a distance of 1.5–2 Å. The reaction of benzene with the nitronium cation can proceed via scheme (2) only over a range of distances from 1.5 to 2.5 Å, while benzene and the extremely reactive methyl cation can interact only via the ionic mechanism whatever the distance.

Electron transfer is preceded by the formation of a charge-transfer complex: $D + A \rightarrow [D^{\delta+}, A^{\delta-}] \rightarrow [D^{\cdot}, A^{-}]$. When the CTC is subjected to additional polarisation under the influence of a third molecule (donor, acceptor, or solvent), electron transfer is facilitated[5].

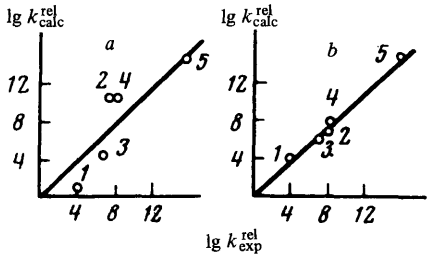


Figure 3. Relation between the experimental and calculated relative rate constants for the exchange of deuterium for protium in heteroaromatic compounds: 1) [3-D]thiophen; 2) [2-D]thiophen; 3) [3-D]furan; 4) [2-D]furan; 5) [2-D]pyrrole[19]; *a*) the values of k^{rel}_{calc} obtained taking into account only the localisation energy, which is proportional to the activation energy for electrophilic substitution; *b*) the values of k^{rel}_{calc} obtained taking into account not only the localisation energy but also the ionisation potential of the molecule involved in the deuterium–protium exchange.

Electron transfer in the reagent–substrate system can occur under the conditions of slight overlapping of the corresponding orbitals or when bridge groups (extraneous ions, solvent molecules) are involved. Electron transfer takes place over an extremely short period, amounting to 10^{-15} s. This is less than the time required for the alteration of the positions of the nuclei of the reacting molecules. Nuclei move over a period of 10^{-13} s or longer[5]. Consequently, the changes in the positions of nuclei take place approximately 100 times more slowly than the change in the electronic state. In conformity with the Franck–Condon principle[5], it is assumed that the positions of the nuclei remain unaltered during electron transfer. This implies that the electron transfer reaction can occur during the extremely short time intervals corresponding to a favourable disposition of the reagent, substrate, and the species present in solution.

2. The Donor–Acceptor Properties of the Reacting Species and the Kinetics of Substitution Reactions

It has been established[18] that the interaction of many heteroaromatic molecules with electrophiles is faster the lower the ionisation potential of the substrate. The calculated rate constants for these reactions agree with experimental values only when models taking into account the electron-donating properties of the heteroaromatic molecule are used[19] (Fig. 3).

The rate constants for the nitration of aromatic hydrocarbons by acetyl nitrate in acetic anhydride, calculated relative to benzene (k^{rel}), vary linearly (Fig. 4) with the ionisation potentials I of the hydrocarbons[20]. There is a similar relation between the ionisation potentials and the relative rate constants for the isotope exchange of hydrogen in an acid medium involving aromatic compounds (Fig. 5).[20]

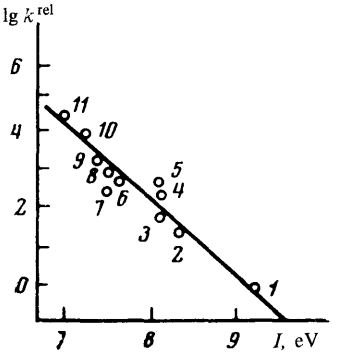
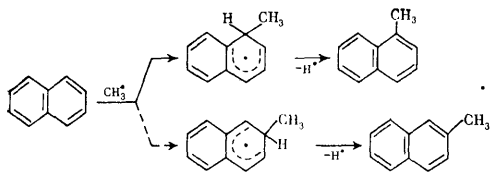


Figure 4. Relation between I and k^{rel} for the nitration of aromatic compounds: 1) benzene; 2) biphenyl; 3) naphthalene; 4) phenanthrene; 5) triphenylene; 6) chrysene; 7) fluorene; 8) fluoranthene; 9) coronene; 10) pyrene; 11) perylene[20].

For radical substitution, the kinetics and direction of the reaction must be determined by the degree of localisation of electron density in individual positions in the molecule and not by its ionisation potential or electron affinity. However, it has been found that the rate of radical substitution in the series of alkylbenzenes varies linearly with ionisation potential, as for other reactions involving states with charge separation[21]. This also confirms the dependence of the site of substitution in the methylation of naphthalene on the polarity of the solvent[22] (acetyl peroxide was used as a source of methyl radicals).

The π-electron density in the naphthalene molecule is distributed non-uniformly: it is greater in the α-position than in the β-position, which ensures the preferential binding of the methyl radical to the α-carbon atom of naphthalene. If the methylation of naphthalene proceeds in accordance with the homolytic substitution mechanism (4), then it is unrelated to the appearance of charged

intermediate states. This implies that the site of substitution should not depend on the polarity of the medium.



(4)

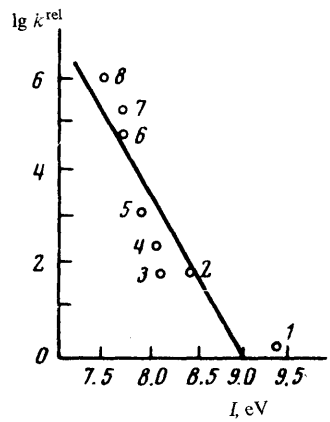


Figure 5. Relation between I and k^{rel} for hydrogen isotope exchange in an acid medium involving aromatic compounds: 1) benzene; 2) biphenyl; 3) terphenyl; 4) naphthalene; 5) chrysene; 6) pyrene; 7) 1,2-benzanthracene; 8) anthracene; 9) perylene[20].

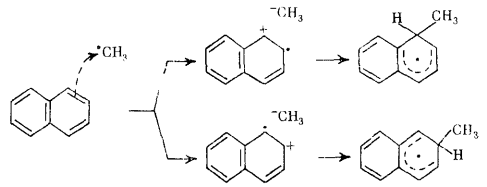
Table 1. The influence of solvent polarity on the selectivity of the homolytic methylation of naphthalene[22].

Solvent	ε*	Ratio of yields of α- and β-methylnaphthalenes	Solvent	ε*	Ratio of yields of α- and β-methylnaphthalenes
Benzene	2.3	7.0	o-Dichlorobenzene	9.9	5.8
Chlorobenzene	5.6	6.2	Pyridine	12.3	4.0

*The static dielectric constant ε was adopted as a characteristic of the polarity, which is valid when solvents belonging to a single series of aromatic compounds are compared[23].

In considering reactions (4), one must emphasise that neither the methyl radical nor the naphthalene molecule can themselves be in any way polarised in a polar solvent and give rise to states with separated charges. A dipolar structure is not characteristic of the methyl radical and naphthalene has an ionisation potential too high for this[22]. However, it follows clearly from Table 1 that the selectivity of the homolytic methylation of naphthalene decreases with increasing solvent polarity. The greater the solvent polarity, the more effective the stabilisation of the polar transition state which implies, according to Hammond[24], a greater decrease of the activation energy for the formation of charged species.

In the homolytic methylation of naphthalene the polarity of the solvent has such a significant effect on the reaction selectivity that the authors[22] explained this effect by the formation of species with a unit charge and not merely a fractional charge. Scheme (5) shows how naphthalene radical-cations arise in the interaction between the reagent and the substrate. Here it is important that the degree of stabilisation of the naphthalene radical-cation is independent of whether the positive charge is located at the α- or the β-carbon atom.



(5)

Owing to the stabilisation of the α- and β-"cations" by the polar solvent, the reactivities of the α- and β-position in naphthalene do not differ quite so much and the selectivity of the methylation reaction is accordingly reduced. Whereas in benzene (ε = 2.3) α-methylnaphthalene is formed seven times faster than β-methylnaphthalene, in pyridine (ε = 12.3) the rate of its formation is only four times greater[22].

3. The Site of Substitution and the Distribution of Spin Density in the Radical-Ion of the Reacting Molecule

If the interaction between the substrate and the reagent begins with one electron transfer, a biradical pair should be formed. The nature of the subsequent transformation should depend on the properties of the species involved in the biradical pair. In particular, the substrate radical-ion may be converted into a σ-electron radical with ejection of an ionogenic group. Such interaction of a σ-radical with the reagent leads to a radical-ion of the final product and these species should combine at the site of the radical free valence. If the substrate radical-ion does not show a tendency to eject the ionogenic group, its combination with the radical derived from the reagent is possible. The formation of a new bond is then most probable in the position where the spin density is a maximum. In other words, there should be a correspondence between the nature of the distribution of spin density in the radical-ion and the position which the substituent enters in the corresponding uncharged molecule.

The quantitative characteristics of the distribution of spin density can be obtained from the ESR spectrum of the radical-ion. The ESR spectrum makes it possible to determine the hyperfine interaction constant for the ith hydrogen atom a_i^H. This constant is directly proportional to the spin density of the ith carbon atom to which the ith hydrogen is linked[25].

Under these conditions, different degrees of delocalisation of the unpaired electron in radical-ions with charges of different signs is then possible for the same molecule[26]. Consequently, when electrophilic substitution is considered the site of substitution data must be referred to the properties of the radical-cation, while in nucleophilic substitution correlation with the properties of the radical-anion is required. We may note that the formation of radical-cations or radical-anions has been demonstrated experimentally in the substitution reactions of aromatic compounds[25].

Table 2 shows that the site of electrophilic substitution of aromatic compounds is clearly related to the values of a_i^H for the corresponding radical-cations.

Table 2. Comparison of the properties of a series of aromatic compounds and the corresponding radical-cations.

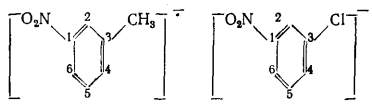
Compound	Reaction	Reactivity in different positions	Order of variation of a_i^H for different positions
NN-Dimethylaniline	Bromination	4 > 2 > 3 (Ref.27)	4 > 2 > 3 (Ref.28)
Naphthalene	Nitration	1 > 2 (Ref.29)	1 > 2 (Ref.30)
Naphthalene	T-H exchange	1 > 2 (Ref.31)	1 > 2 (Ref.30)
Anthracene	Acylation	9 > 1 > 2 (Ref.25)	9 > 1 > 2 (Ref.30
Biphenylene	Nitration	2 > 1 (Ref.32)	2 > 1 (Ref.33)
Azulene	Nitration	1 > others (Ref.34)	1 > others (Ref.35)

When azulene is nitrated, the 1-position is the most reactive[34] and the electron density is a maximum in the same position in the radical-cation[35]. However, in the azulene radical-anion the maximum density is concentrated in the 6-position[36,37].

Table 3. Comparison of the values of a_i^H and E_{act} for the substitution of chlorine by an ethoxy-group on treatment of chloronitrobenzenes and chlorodinitrobenzenes with an ethanol–piperidine mixture.

Compound	a_i^H in ESR spectrum of radical-anion G, (Refs.38 and 39)	E_{act}, kcal mole^{-1} (Ref.40)
Nitrobenzene	$a_2^H = a_6^H = 3.30$; $a_4^H = 3.82$	—
2-Chloronitrobenzene	$a_6^H = 3.30$; $a_4^H = 3.92$	18.1
4-Chloronitrobenzene	$a_2^H = a_6^H = 3.42$	17.1
1,3-Dinitrobenzene	$a_2^H = 2.77$; $a_4^H = a_6^H = 4.49$	—
2-Chloro-1,3-dinitrobenzene		12.2
4-Chloro-1,3-dinitrobenzene		10.7

Interesting correspondences have also been formed for nucleophilic reactions. The relative rates of substitution of chlorine in chloronitrobenzene under the influence of various nucleophiles agree satisfactorily with the constants a_i^H for the radical-anions. However, the treatment must be based on the values of a_i^H for the radical-anions of nitro-derivatives without chlorine. (The hyperfine interaction constants of the radical-anions of chloronitrobenzene and nitrobenzene are virtually the same.) Table 3 shows that the constant a_2^H (a_6^H)† of the radical-anion of 4-chloronitrobenzene is close to a_2^H (a_6^H) of the nitrobenzene radical-anion; exactly the same correspondence between the constants a_6^H and a_4^H is observed for the 2-chloronitrobenzene–nitrobenzene pair. Here $a_4^H > a_2^H$ in the nitrobenzene radical-anion. The substitution of the chlorine in 4-chloronitrobenzene by an ethoxy-group is easier and requires a smaller activation energy than the corresponding substitution in 2-chloronitrobenzene. The spin density in the 4-position of the 1,3-dinitrobenzene radical-anion is higher than in the 2-position ($a_4^H > a_2^H$). The reactivity of 4-chloro-1,3-dinitrobenzene in nucleophilic substitution is correspondingly greater than that of 2-chloro-1,3-dinitrobenzene. The displacement of chlorine by the methoxide ion[16] in 4-chloro-3-methylnitrobenzene is faster than in 6-chloro-3-methylnitrobenzene (Table 4, Nos. 1 and 2) which agrees with the finding that the spin density in the 4-position of the 3-methylnitrobenzene radical-anion is greater than the 2-position[41] [cf. scheme (6)]. The same correspondence may be noted between the values of a_i^H for the 3-chloronitrobenzene radical-anion[39] [see scheme (6)] and the relative rate constants for the substitution by the methoxide ion[16] of the chlorine atoms at the ith carbon atoms (Table 4, Nos. 3 and 4).

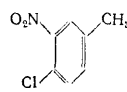
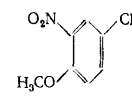
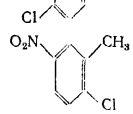
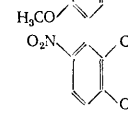
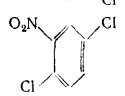
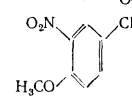
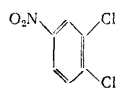
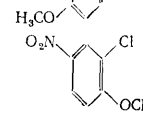


(6)

$a_6^H = 3.30$ G $\quad a_4^H = 4.07$ G

$a_4^H = 3.88$ G $\quad a_6^H = 3.20$ G

Table 4. The relative rate constants for the substitution of chlorine by a methoxide ion in certain chloronitrobenzenes in methanol at 25 °C.[16]

No.	Initial compound	Reaction product	k^{rel}
1			1
2			3.6
3			1
4			2.6

Thus the theoretical postulates described above support the possibility of the formation of substrate radical-ions and reagent radicals at the initial stage of the substitution reaction. There is evidence in support of a further combination of the radical-ion with the reagent radical or ion. The decomposition of the substrate radical-ion with formation of a secondary radical capable of interacting with another reagent molecule is also likely. Naturally, the agreement between the results of calculations and particular experimental data cannot by itself serve as proof that the one-electron transfer stage really occurs. For this, it is necessary to analyse the results of studies on the mechanisms of many specific reactions. Our discussion of theoretical problems was based on data for aromatic

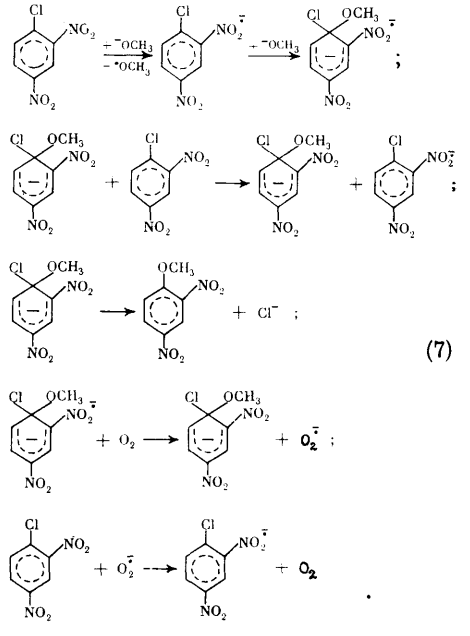
† The numbering of the positions in substituted nitrobenzenes begins with the atom linked to the nitro-group.

compounds: since the stability of aromatic radical-ions is high, they have been detected more frequently and more fully characterised. Thus, in considering specific reactions, we shall deal primarily with substitution in aromatic compounds.

IV. THE ROLE OF ONE-ELECTRON TRANSFER IN AROMATIC SUBSTITUTION REACTIONS

1. Nucleophilic Substitution

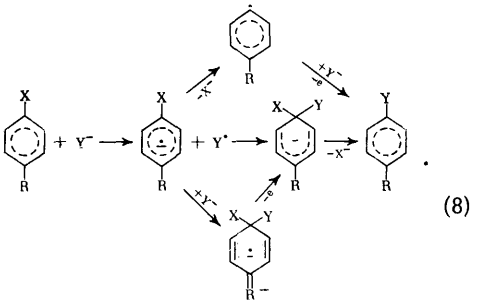
When 1-chloro-2,4-dinitrobenzene is treated with sodium methoxide, 2,4-dinitroanisole is formed. It has been established[42] that the reaction mixture contains the radical-anions of the starting material and the final product. Mechanism (7), which includes chain transfer steps involving electron exchange with participation of organic molecules and oxygen, has been put forward on the basis of ESR data for the accumulation and consumption of radical-anions[42]:



(7)

The catalytic effect of oxygen indicated by mechanism (7) agrees with the finding that nucleophilic reactions of aromatic nitro-compounds are an order of magnitude slower in nitrogen than in air. Benzoquinone or tetracyanoethylene inhibits such reaction; they are accelerated under the influence of light and are faster in glass apparatus than in cast iron apparatus[42]. All these findings support a radical mechanism of the reaction. An important feature of the mechanism of aromatic substitution reactions [mechanism (7)] is that it constitutes a harmonious combination of newly formulated concepts with earlier ideas, leading ultimately to a σ-complex as the usual precursor of the substitution product.

The radical-anion may not be converted into the substitution product solely via a radical-dianion as in scheme (7). The radical-anion may be converted into a free radical and then into the final product, bypassing the σ-complex. These possibilities are described in the scheme[42]



(8)

All the pathways taken into account in scheme (8) are based on the hypothesis of one-electron transfer with formation of a radical-ion. Apart from the data quoted above, the formation of the radical-anion is indicated by numerous kinetic studies[42]. The σ-complex obtained in the reaction exhibits the effect of chemically induced nuclear polarisation[43] (the CINP effect).

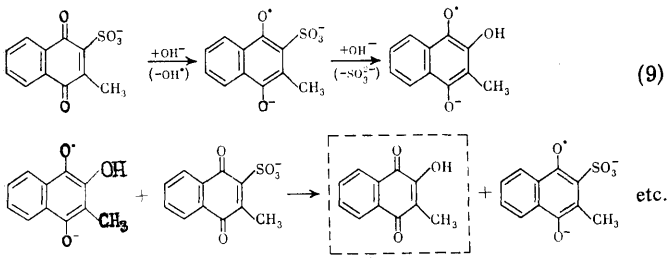
At the same time scheme (8) emphasises that the reactions of aromatic compounds with nucleophiles can proceed via different mechanisms with participation of various intermediate species. The contribution of each mechanism depends on the reaction conditions, including the effect of the structure and the medium. The same initial compounds may give rise to final products with identical structures via different mechanisms. This leads to the problem of estimating the contribution of a particular mechanism and the criterion should be the type of the rate-determining intermediate species rather than the reaction order. According to Shein[42], the classification of the mechanisms of the nucleophilic substitution reactions of aromatic compounds based on the reaction order, generally accepted at the present time, is inadequate. He suggested[42] that the mechanisms be classified in terms of the type of intermediate species: radical-ion, free-radical, carbanionic, etc. mechanisms. Reactions involving several species are also possible, for example, the process with a mechanism of the radical-ion–radical-dianion–σ-complex type indicated in scheme (7). The fundamental characteristics of scheme (7) have been attributed[42] to many other nucleophilic substitution reactions of aromatic compounds, including the substitution of chlorine by a methoxy-group in 4-chloronitrobenzene. In the latter case the formation of the main product is accompanied by that of a side product—4-nitrophenol (yield up to 15%). The ambiguity in the treatment of the pathways leading to the side product is striking. According to Shein's data[42], the main product (4-nitroanisole) is oxidised. Solodovnikov[44] justified a fundamentally different pathway—the oxidation of the radical-anions of the initial compound. The ambiguity of the treatment becomes of fundamental importance, because, according to Solodovnikov[44], virtually all 4-chloronitrobenzene radical-anions are converted into 4-nitrophenol. It was concluded on this basis that the "formation of 4-chloronitrobenzene radical-anions is a reaction taking place simultaneously with the substitution reaction"[44]. If this conclusion is accepted, one must assume that the substitution reaction itself proceeds either via a non-radical mechanism or via cryptoradical mechanism, where radical species are formed and combined in a solvent "cage" without emerging into the solution. It is so far difficult to make a

choice between Shein's[42] and Solodovnikov's[44] treatments.

There is a greater unanimity in the treatment of the mechanism of another nucleophilic reaction—the substitution of a nitro-group in 1,2-dinitrobenzene (DNB) by a hydroxy-group. Various investigators have established the following facts: (1) that the reaction of DNB with OH^- ion in aqueous dimethyl sulphoxide results in the formation of 2-nitrophenoxide and nitrite only[45]; (2) that a long-lived DNB radical-anion is formed on mixing the reactants[45,46]; (3) that in the system considered the electron donor is indeed the OH^- ion, which is converted into the short-lived $OH^{\cdot}$ radical[46]; (4) that a σ-complex containing an OH group at the tetrahedral carbon atom is formed in the pathway to 2-nitrophenoxide[45]; (5) that the initial DNB and the σ-complex are not involved in electron exchange with one another[45]; (6) that the reaction of DNB with O_2^- also leads to the substitution of the nitro-group by a hydroxyl and that DNB forms a radical-anion[47]; (7) that in the interaction of DNB with OH^- the one-electron transfer leading to the formation of the radical-anion takes place in the first stage with participation of uncharged DNB;[45] (8) that the kinetic curve for the accumulation and consumption of the DNB radical-anion is S-shaped and that the curve for the accumulation of 2-nitrophenoxide is parabolic (the start of the descending branch of the curve for the radical-anion corresponds to an inflection in the curve for the final product)[45]; (9) that kinetic calculations agree with experimental data only when the DNB radical-anion is regarded as the starting material in the substitution of a nitro-group by an OH^- ion[45].

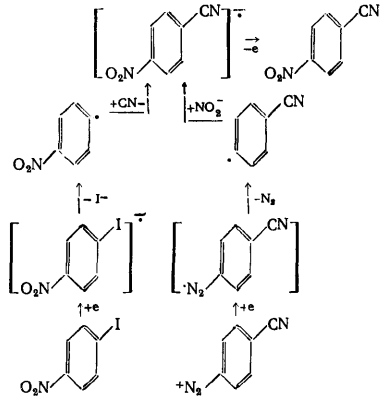
A radical-ion mechanism has also been adopted[48] for the substitution of chlorine in 2-chloro-9,10-anthraquinone by a methoxy-group under the influence of sodium methoxide. The reaction represents a typical instance of substitution; during its course, 2-chloroanthraquinone radical-anions are formed, their number initially increasing to a maximum and then falling sharply. The addition of an inhibitor (benzo-1,4-quinone) lowers the rate of formation of radical-anions, which entails also a decrease of the rate of formation of 2-methoxyanthraquinone. If the radical-anions were obtained via a secondary pathway, the rate of formation of the final product should not have increased following the introduction of an inhibitor. It should have actually increased, since the oxidation of the radical-anions involves the regeneration of uncharged substrate molecules, which implies that the radical-ion mechanism is decisive in the given instance. Other nucleophilic reactions of anthraquinones are also associated with the formation of radical-anions: hydroxylation of 9,10-anthraquinone-2-sulphonic acid[48]; hydroxylation, alkoxylation or cyanation of the homoaromatic ring of 9,10-anthraquinone condensed in the 1,2-positions with the 2,1,5-oxadiazole ring[49]. However, the authors[48,49] adduce arguments according to which the one-electron reduction of the quinone takes place simultaneously with the main nucleophilic reaction. For example, it has been found that the concentration of anthraquinone-2-sulphonate radical-anions ceases to depend on the duration of the reaction with the alkali after a certain time interval and the overall yield of the radical-anion does not exceed 10%.[48] The introduction of inhibitors [oxygen, potassium hexacyanoferrate(III)] prevents the formation of radical-anions and the yield of 2-hydroxyanthraquinone actually increases somewhat[48]. In this case the radical-ion pathway in the process is not the main one.

This example shows that the inclusion of the electron transfer stage in the reaction mechanism must be justified in each individual case. It is of interest that another representative of the class of quinone sulphonates—sodium 3-methyl-1,4-naphthoquinone-2-sulphonate—also gives rise to a radical-anion on reaction with alkali. The final product is 2-hydroxy-3-methyl-1,4-naphthoquinone. As the reaction proceeds, the number of radical-anions reaches a maximum and then falls immediately and at this instant the concentration of the final product begins to increase[48]. When inhibitors [oxygen, potassium hexacyanoferrate(III)] are introduced, neither the accumulation of radical-anions nor the formation of the final product is observed[48], which shows that the hydroxylation of 3-methyl-1,4-naphthoquinone-2-sulphonic acid proceeds via a radical-ion salt in accordance with the chain mechanism



(9)

The results concerning the "reconstruction" stages in the nucleophilic substitution of 4-iodonitrobenzene by a cyanide ion, quoted by Russell et al.[8], are of interest. One-electron reduction at an electrode in the presence of cyanide leads to the 4-iodonitrobenzene radical-anion. Like other halogeno-derivatives, 4-iodonitrobenzene readily splits off a halide ion in the radical-anionic state and is converted into a 4-nitrophenyl radical (a radical of the σ-electron type). The latter reacts with a cyanide ion and gives rise to a 4-cyanonitrobenzene radical-anion. The same radical-anion may be arrived at by reducing a 4-cyanobenzenediazonium salt with dithionite in the presence of nitrite. One-electron oxidation by the initial substrate converts the radical-anion into neutral 4-cyanonitrobenzene:



(10)

Singh and Kumar[50] obtained data showing that the substitution of a diazo-group linked to an aromatic compound by iodine also proceeds via an electron transfer stage. When arenediazonium fluoroborates are treated with potassium iodide in methanol (under nitrogen), iodobenzenes are formed:

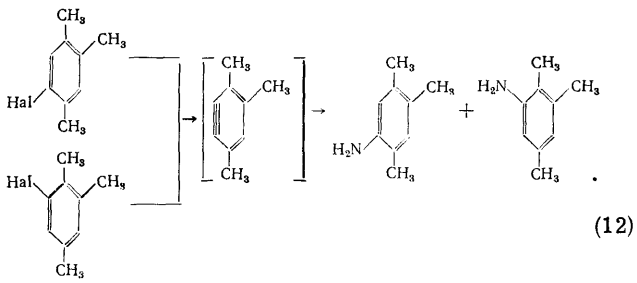
$$ArN_2^+ + I^- \longrightarrow ArN_2^{\cdot} + I^{\cdot};\quad I^{\cdot} \longrightarrow \tfrac{1}{2}I_2;$$

$$ArN_2^{\cdot} \xrightarrow{-N_2} Ar^{\cdot};\quad Ar^{\cdot} + I^- \longrightarrow Ar{-}I^{\cdot -};\qquad (11)$$

$$ArI^{\cdot -} + ArN_2^+ \longrightarrow [ArI]^{+} + ArN_2^{\cdot}\ \text{etc.}$$

Mechanism (11) is consistent with the known ability of the iodide ion to transfer one electron and also with the fact that the reaction is accelerated on irradiation with light and is inhibited in the presence of oxygen. In the presence of electron-accepting substituents in the benzene ring, the reaction rate increases, falling if electron-donating substituents are present. In the reaction involving 4-nitrobenzenediazonium, nitrobenzene, elemental iodine, and formaldehyde were found together with 4-iodonitrobenzene[50]. Formaldehyde is formed when 4-nitrophenyl radicals abstract hydrogen atoms from the solvent—methanol ($CH_3OH \rightarrow CH_2O$). Despite a careful search, neither 3-iodonitrobenzene nor 4-nitroanisole could be found among the products. This disproves another possible mechanism—cine-substitution involving the formation of dehydrobenzene.

The relation between cine-substitution and radical-ion mechanisms has been examined[51]. The reactions of 5- and 6-halogenopseudocumenes with potassium amide in liquid ammonia lead to 5- and 6-pseudocumidines, both isomeric amines being obtained regardless of whether the 5- or 6-position in the initial molecule contains a halogen atom. The nature of the halogen atom does not affect the ratio of the amino-derivatives obtained in the reaction of chloro- and bromo-derivatives; the ratio is constant and close to 1.5. The isomer ratio is not constant only for iodo-derivatives, being 0.63 and 5.86 when 5-iodopseudocumene and 6-iodopseudocumene are used respectively as starting materials. According to the authors[48], the cine-substitution mechanism is the only one in the reactions of chloro- and bromo-derivatives,



(12)

The reaction of iodopseudocumenes ArI proceeds not only via mechanism (12) but also via one-electron transfer:

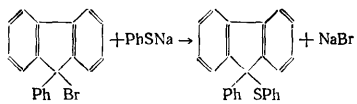
$$ArI \longrightarrow (ArI)^{\cdot -} \longrightarrow Ar^{\cdot} + I^{-};$$

$$Ar^{\cdot} + NH_2^{-} \longrightarrow (ArNH_2)^{\cdot -}; \qquad (13)$$

$$(ArNH_2)^{\cdot -} + ArI \longrightarrow [ArNH_2] + (ArI)^{\cdot -} \text{ etc.}$$

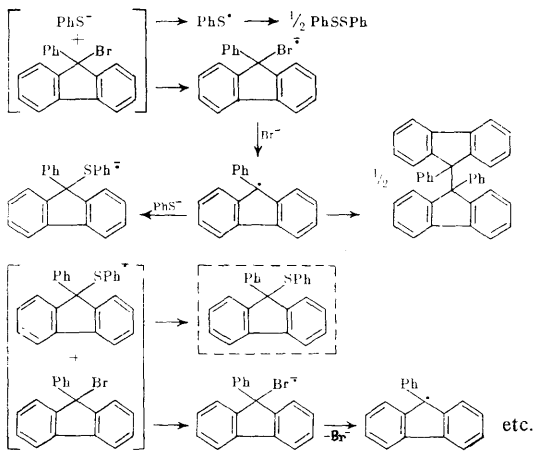
The hypothesis that mechanisms (12) and (13) operate simultaneously has been confirmed by experiments in the presence of radical-trapping agents: the introduction of 2-methyl-2-nitrosopropane or tetraphenylhydrazine alters the ratio of the pseudocumidines and makes it equal to 1.5 (for both 5- and 6-iodopseudocumenes). A characteristic feature of the iodopseudocumene radical-anions is that they split off a halide anion more readily than other halogeno-derivatives. As a result pathway (13), involving an electron transfer stage, becomes important.

The necessity to take into account the radical stage in nucleophilic substitution is also indicated by the results of a study of the mechanism of the introduction of an arylthio-group into 9-bromo-9-phenylfluorene[52]. When this bromo-derivative is treated with sodium thiophenoxide in dimethylformamide (DMF) in an atmosphere of nitrogen (30°C, 4 h), the formation of sodium bromide and 9-phenyl-9-phenylthiofluorene is observed:



(14)

Sodium bromide is obtained quantitatively and the yield of the nucleophilic substitution product is only 42% of the theoretical value. The substrate and the nucleophile are also involved in other reactions which lead to 9,9-diphenylbifluorenyl (in 38% yield) and diphenyl disulphide (in 30% yield). The formation of these substances, which are indicated in scheme (15), conflicts with the usual ideas concerning nucleophilic substitution. Attention should be drawn to the fact that, in the presence of radical traps (oxygen and tetrabromo-*o*-benzoquinone), the formation of both the side products enumerated above and of the products resulting from the introduction of the arylthio-group is retarded[52]. Consequently the stage involving electron transfer from the nucleophile to the substrate occurs in the main reaction pathway, as in scheme (15). A phenylthiyl radical and a substrate radical-anion are formed in this stage. Both radical products are involved in further reactions: the phenylthiyl radical gives rise to diphenyl disulphide, while the substrate radical-anion is converted into a 9-fluorenyl radical. The latter reacts in two ways. It dimerises to bifluorenyl and, on reacting with a nucleophile, gives rise to a radical-anion of the "nucleophilic substitution product". Chain propagation is ensured by electron transfer from the above radical-anion to an unreacted substrate molecule, which loses a bromine atom and then reacts with the nucleophile, etc.

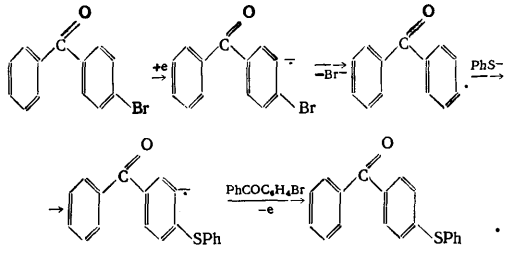


(15)

Mechanism (15) differs from mechanisms of the S_N1 or S_N2 type precisely by the inclusion of the one-electron oxidation-reduction stage. The driving force in this stage may be the ease of elimination of a bromide anion and the formation of a fluorenyl radical unsaturated in the 9-position, next to the stabilising benzene rings.

It has been shown[53] that the introduction of arylthio-groups into bromo-derivatives may be "stimulated" by creating conditions which promote the primary formation of radical-anions. Nucleophilic substitution of bromine by the thiophenoxide ion in 4-bromobenzophenone requires extremely severe conditions. When potentials are applied, the reaction proceeds readily and with a high yield (80%). It is sufficient to employ potentials which ensure solely the formation of substrate radical-anions (the potential and the

amount of current passed through the system are strictly controlled). Next comes the chemical reaction in the bulk of the solution with formation of 4-phenylthiobenzophenone[53]:

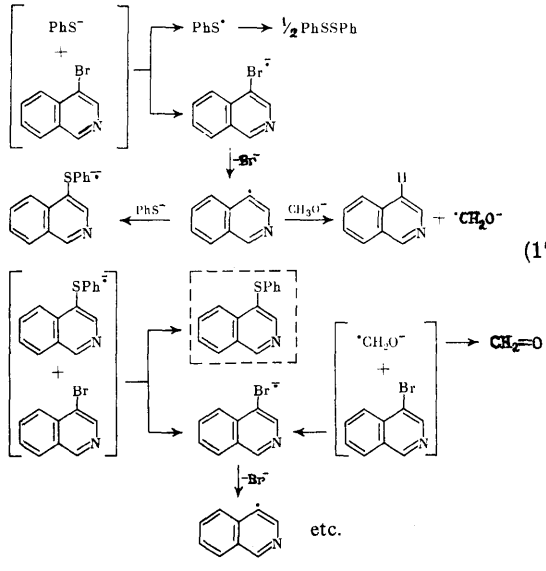


(16)

Nucleophilic substitution may be accelerated also without applying potentials, by introducing into the reaction mass substances which can behave as powerful electron donors. Thus sodium methoxide catalyses the introduction of an arylthio-group into 4-bromoisoquinoline by sodium thiophenoxide [scheme (17)].[54]

The introduction of sodium methoxide constitutes together with the introduction of thiophenoxide, yet another electron source for the generation of substrate radical-anions. However, if the thiophenoxide is converted into a phenylthiyl radical, as a result of electron transfer to the substrate, and then into the disulphide and is thus removed from the reaction sphere, substrate radical-ions are generated in the presence of methoxide ions with retention of a major proportion of the thiophenoxide. The overall rate of introduction of the arylthio-group in the presence of sodium methoxide increases and the yield of 4-phenylthioisoquinoline rises. However, the yield of side product—an unsubstituted isoquinoline—also increases with formation of only traces of the product of a competing substitution reaction—4-methoxyisoquinoline.

The introduction of azobenzene suppresses the effect of sodium methoxide, which confirms the radical-chain mechanism of the reactions via the scheme[54]:



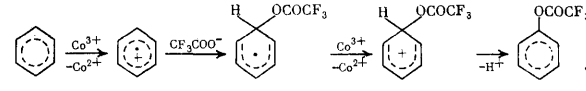
(17)

The formation of the phenylthiyl radical in reactions (15) and (16) was inferred from the isolation of diphenyl disulphide[52,64]. Bank and Noyd showed directly[55] that the phenylthioxide ion is involved in nucleophilic substitution and gives rise to a phenylthiyl radical. If styrene is added to a reaction mass containing 2-butyl nosylate (2-butyl 4-nitrobenzenesulphonate) as the substrate and sodium thiophenoxide as the reagent‡, the styrene polymerises with incorporation of phenylthiyl radicals. The corresponding sulphur-containing oligomer was isolated and characterised. When the thiophenoxide is mixed with styrene in the absence of the nosylate, the oligomer is not formed. When a radical trap (t-butyl phenyl nitrone) was introduced into the reaction mass, the reaction of 2-butyl nosylate with lithium thiophenoxide was retarded and the product of the addition of the phenylthiyl radical to the nitrone was detected by ESR. This indicates the formation of phenylthiyl radicals in the main pathway of the nucleophilic reaction.

2. Electrophilic Substitution

The study of the mechanisms of electrophilic substitution is extremely difficult, because aromatic radical-cations are much less stable than the radical-anions. Much less information has therefore been obtained about the role of one electron oxidation in the mechanisms of these reactions than for nucleophilic substitution in aromatic compounds.

Kochi et al. recently found a method of synthesising and stabilising radical-cations in trifluoroacetic acid, which consists in rapid mixing and freezing of solutions of the aromatic compound and thallium(III) or cobalt(III) trifluoroacetate[56]. When frozen solutions are heated, it is possible to observe well resolved ESR spectra of aromatic radical-cations. The latter are converted into aryl trifluoroacetates. It has been shown[56] that two oxidant molecules are consumed per molecule of the aromatic compound; the rate-limiting stage is one-electron oxidation with formation of a radical-cation. The reactions involving benzene can be represented as follows[56]:

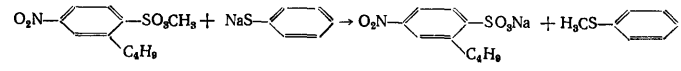


(18)

The anodic acetoxylation of aromatic compounds in acetic acid solutions containing alkali metal or tetraalkylammonium acetates proceeds quite analogously to oxidative substitution [reaction (19)]. Investigations have shown[57] that the process begins with one-electron oxidation at the anode and is followed by the stages indicated in scheme (18). The reaction proceeds very readily also at potentials very remote from the oxidation potential of the acetate ion (+2.00 V relative to sat. c. e.)§. For example, the lowest anodic potential at which ring acetoxylation of anisole can be observed is 1.20 V.[57] The acetate ion in the final product originates from the acetate salt and not from acetic acid: when the acetate is replaced by tosylate or perchlorate with the same cation, the acetoxylation of anisole does not occur even when acetic acid is used as the solvent[57].

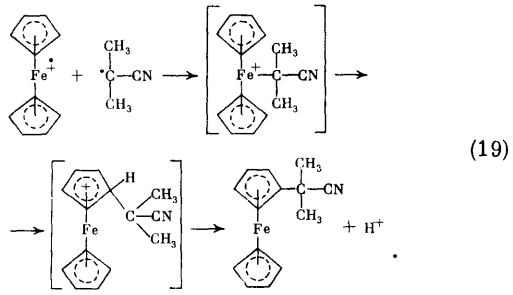
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‡ The final result of this reaction can be represented schematically as follows:



§ sat. c. e. = aqueous saturated calomel electrode.

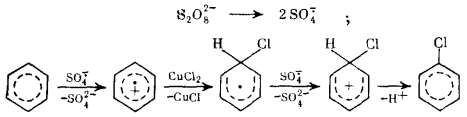
The radical-cation pathway in the substitution reaction is also illustrated in scheme (19).[58] In contrast to reaction (18), the radical-cation of the substrate interacts with a radical and not with an anion and the second one-electron oxidation stage is therefore not required in reaction (19):



(19)

The substitution product (α-cyanoisopropylferrocene) is formed in a yield up to 50% from ferrocene, copper fluoroborate, and azobisisobutyronitrile in acetonitrile at 80°C. In the absence of copper fluoroborate, which oxidises ferrocene to ferrocenium, the reaction does not occur, which implies that cyanopropyl radicals interact solely with ferrocenium and not with ferrocene. The product does not contain an unpaired electron and is therefore inert in relation to further substitution. This is an advantage of reaction (19) over Friedel–Crafts alkylation, in which products with an alkyl substituent undergo further substitution more readily than the initial ferrocene[58].

Copper(II) salts combine the properties of a one-electron oxidant[58] and a radical source[58,59]. An interesting version of a radical-cation process is illustrated in the following scheme[59]:

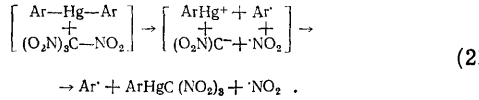


(20)

The reactions examined hitherto constitute instances of somewhat unusual substitution. They all proceed via a radical-ion pathway, because the substrate is introduced into the reaction after deliberate preliminary oxidation to the corresponding radical-cation. Studies on the mechanisms of the reactions which proceed as "typical" substitution processes without oxidation by an extraneous reagent are of interest. An example of "typical" substitution is the dark chlorination of benzene derivatives. In his study of the chlorination of toluene in acetic acid, Kochi[60] concluded that a toluene radical-cation is formed at an intermediate stage and that it reacts further with chlorine to give a chloro-derivative. The author bases this conclusion on the appearance of a well resolved ESR signal due to the radical-cation when acetic acid solutions of the substrate and chlorine are mixed directly in the spectrometer cell. Unfortunately, no data are quoted in his communication[60] concerning the kinetics of the accumulation and consumption of the radical-cation during the chlorination process and it is therefore impossible to decide whether the radical is formed in the main or a secondary reaction pathway.

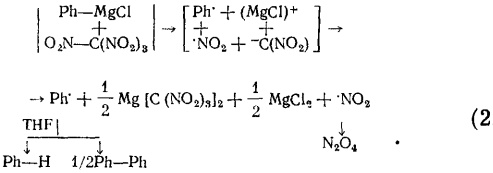
However, one must emphasise that electrophilic substitution via electron transfer is promoted by two important factors[60]: aromatic molecules are oxidised at fairly low potentials; the electrophile (for example, a halogen) readily undergoes one-electron reduction. Similarly the nitronium ion, which is directly or indirectly involved in aromatic nitration, can be readily reduced to nitrogen dioxide[60].

In our discussion of the nitration of benzene within the framework of scheme (2), we noted that, apart from the stage involving the formation of π- and σ-complexes, the interaction of benzene with the nitronium cation can also include an electron transfer stage. The σ-complex should then be obtained as a result of the combination of the benzene radical-cation and the $^{\cdot}NO_2$ radical. The decomposition of the σ-complex leads to nitrobenzene. If the decomposition is rapid, occurring over a period up to 10 s, the resulting nitrobenzene should give rise to a CINP effect. However, the effect could not be observed[61], although according to ^{1}H NMR data the reaction was not arrested appreciably in the σ-complex formation stage. Thus the electron transfer stage in reaction (2) was not confirmed experimentally. However, one should note that this stage may be unfavourable precisely for the nitration reaction owing to the low reactivity of the $^{\cdot}NO_2$ radical in the liquid phase. This idea is suggested by the results of a study of the interaction of aryl derivatives of tin, magnesium, and mercury with tetranitromethane in sulpholane[62]. For example, in the reaction of diarylmercury with tetranitromethane[62], the aryl and $^{\cdot}NO_2$ radicals are formed in an intermediate stage [see scheme (21)]. Despite the high reactivity of the aryl radical, it is scarcely attacked by the $^{\cdot}NO_2$ radical and gives rise mainly to an aromatic hydro-carbon as a result of reaction with the solvent. The trinitromethyl anion combines with the arylmercury cation, while the $^{\cdot}NO_2$ radical is probably stabilised in the form of nitrogen tetroxide and is subsequently consumed in secondary oxidation reactions:



(21)

The amount of ionic character of the carbon–metal bond affects the ease of the electron transfer reaction. Whereas tetranitromethane reacts with aryl derivatives of mercury and tin only after heating for many hours at 80°C, the reaction with phenylmagnesium chloride occurs after mixing the reactants and requires a reduced temperature (−50°C). However, the overall result of the reaction is independent of the nature of the carbon–metal bond: in each of the instances considered, tetranitromethane does not play its characteristic role of a nitrating agent. Only traces of nitrobenzene are formed and the main organic product is benzene. In the reaction with phenylmagnesium chloride, biphenyl (in 20% yield) is formed together with benzene (in 55% yield); tetranitromethane gives rise to the magnesium salt of trinitromethane under these conditions (in 80% yield):

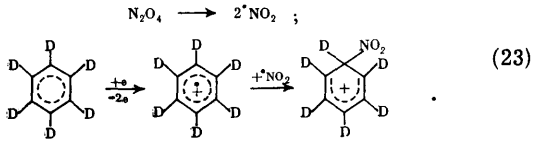


(22)

Nitrogen tetroxide is known to react with phenyl magnesium chloride[62]. However, reaction (22) is so rapid that the nitrogen tetroxide evolved has insufficient time to react with the initial phenylmagnesium chloride and impair the agreement, noted above, between the yields of the

electron donor and acceptor conversion products. The authors[62] attribute the formation of biphenyl in reaction (22) to the oxidation of the dimeric form of phenylmagnesium chloride. The possibility of the recombination of phenyl radicals after their emergence from the cage is rejected[62] on the grounds that biphenyl is not formed in the reactions with Ph_2Hg and Ph_4Sn. The main result of the reaction of tetranitromethane with aryl derivatives of mercury, tin, and magnesium is the generation of Ar$^\cdot$ and $^\cdot NO_2$ radicals, which hardly interact with one another in the liquid phase.

In the gas phase the $^\cdot NO_2$ radical may acquire the needed reactivity. This is indicated by the ion–cyclotron resonance data analysed below[63]. Perdeuterobenzene and nitrogen tetroxide were admitted into the mass spectrometer chamber, whereupon the $(C_6D_6NO_2)^+$ ion, corresponding to the product of the addition of the nitro-group to perdeuterobenzene without the displacement of deuterium, i.e. a σ-complex, was detected. The authors[63] used double resonance in order to determine the species on the energy of which depends the rate of formation of the σ-complex. It was found that the rate depends unambiguously on the energy of the $C_6D_6^+$ radical-cations and is independent of the energy of the $^+NO_2$ cations[63]. This implies that the $C_6D_6^+$ and $^\cdot NO_2$ species, and not C_6D_6 and $^+NO_2$, are the precursors of the σ-complex:



(23)

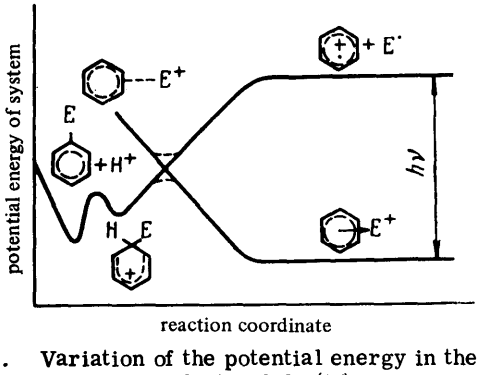


Figure 6. Variation of the potential energy in the substitution of benzene by an electrophile (E^+).

It has been noted[64] that one-electron transfer is a possible but not necessarily a discrete stage of the reaction involving substitution in aromatic compounds. We shall now consider how the potential energy of the system varies during the substitution. Fig. 6 illustrates such variation for electrophilic substitution in an aromatic compound[20]. Before the start of the reaction, the potential energy of the system is a maximum; a decrease of this energy is observed when a π-complex is formed. The separation (transfer) of the single charge in the π-complex leads to a readical-cation of the aromatic compound and an electrophile radical. The energy increases by $h\nu$, and the system acquires a different energy profile. The quantity $h\nu$ determines the probability of the electron transfer stage. The radical-ion–radical pair $(C_6H_6^+ + E^\cdot)$ can rearrange into a σ-complex, which corresponds to a well in the new energy profile. The further decrease of energy is attributed to the formation of an electrophilic substitution product and the elimination of a proton. The energy curves cannot intersect. A gap, bounded by dashed semicircles, arises. It is small, which ensures the possibility of a transition from one curve to the other. In other words, the reaction may proceed via the pathway involving reverse electron transfer from $E^\cdot$ to $C_6H_6^+$ with return to the initial state. The initial compounds (benzene and the electrophile) then give rise to π- and σ-complexes along the pathway to the final product without forming radical species in the intervening stages.

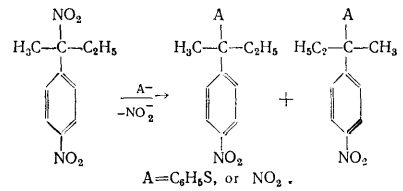
The radical stage becomes more probable when the energy gap $h\nu$ becomes sufficiently narrow to be overcome as a result of collision energy or under the conditions of a more favourable organisation of the solvation shell. The gap $h\nu$ is more easily overcome in interactions which lead to relatively stable electron transfer products or when these products decompose into rapidly and irreversibly reacting species. The gap can be easily overcome when there is a considerable difference between the oxidation-reduction potentials of the substrate and the reagent (in other words, between their LUMO and HOMO levels). In certain cases the distance $h\nu$ can be crossed with the aid of external influences: by the application of potentials, by the introduction of a stronger donor or acceptor, by irradiation, and by initiation with participation of a third molecule (a donor, or an acceptor, or a solvent).

Naturally, the above factors should promote the electron transfer stage not only in substitution reactions of aromatic compounds but also in substitution reactions involving a series of aliphatic compounds.

V. ONE-ELECTRON TRANSFER IN ALIPHATIC SUBSTITUTION REACTIONS

Among the first studies dealing with the radical stages in the mechanism of substitution reactions of aliphatic compounds, those of Kornblum's school[7] occupy an important place. In his studies of substitution at a saturated tertiary carbon atom Kornblum compared the behaviour of α-cumenyl chloride, α-nitrocumene, and their 4-nitro-derivatives in relation to anions. It was found that only the cumenyl compounds containing the nitro-group in the 4-position undergo substitution in the α-position. The reaction proceeds equally well with small and bulky anions. Such insensitivity to steric hindrance makes it possible to obtain highly branched products. When 4-nitrocumenyl chloride is treated with sodium thiophenoxide in argon or in nitrogen, two products are formed: 4-nitro-α-phenylthiocumene and 4,4′-dinitrobicumenyl. It is remarkable that, on reacting with sodium thiophenoxide, the optically active substrate gives rise to a racemic substitution product. Racemisation is observed also on treatment with sodium nitrite [scheme (24)]. In the presence of nitroxy-radicals or aromatic nitro-compounds, the substitution reaction is suppressed. Oxygen sharply retards the formation of substitution products,

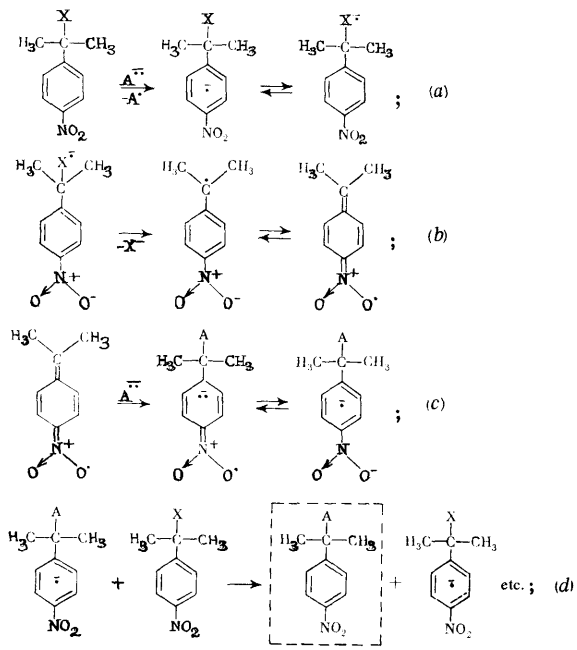
but promotes the formation of 4-nitrocumenyl hydroperoxide. Illumination has a marked initiating influence:



; (24)

A=C_6H_5S, or NO_2 .

The above findings fit logically within scheme (25), where a dual role is attributed to the anion A^-: that of an electron donor [stage (*a*)] and of the species undergoing addition [stage (*c*)]:



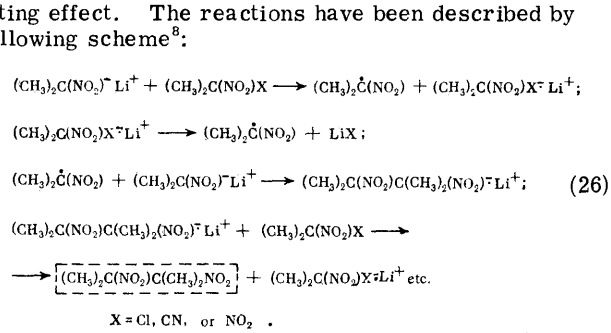
(25)

A = C_6H_5S or NO_2; X = Cl, N_3, $C_6H_5SO_2$, NO_2, or OAr .

Scheme (25) explains two characteristics of the reaction: its applicability to 4-nitro-substituted substrates alone and its insensitivity to steric factors. The presence of the nitro-group in the 4-position ensures the delocalisation of the excess electron and thus promotes the formation of the radical-anion [stage (*a*)]. Stage (*a*) involves the unhindered aromatic nitro-fragment of the 4-nitrocumenyl system. Stage (*b*) consists of intramolecular elimination and is likewise not controlled by steric factors. Stage (*c*) includes the addition of the anion A^- to the planar system of the free radical. The free radical exhibits a high reactivity and is susceptible to attack by the anion. Consequently stage (*c*) may be rapid; this is important, because stage (*c*) propagates the chain of reactions (25). Chain branching takes place in stage (*d*), where the radical-anion of the substitution product transfers one electron to an uncharged substrate molecule. The one-electron transfer at this stage proceeds as in other cases, rapidly and independently of steric factors[7]. As a result, substitution at the strongly hindered carbon atom involves a sequence of stages which is as a whole distinguished by a low sensitivity to steric effects. The ease of reaction (25) depends on the ease with which the anion A^- gives up an electron to the 4-nitrocumenyl system and thereby initiates the chain of stages (*a*)–(*d*).

If the above sequence of transformations takes place and stage (*c*) is indeed rapid and irreversible, such behaviour can be used to extend the limits of applicability of the reaction. The possibility arises of obtaining substitution products also with anions which do not enter into the reaction or react extremely slowly. The point is that the nitrocumenyl radical can be captured not only by the anions some of which have been used to generate this radical but also by other anions. A catalytic amount of a reactive nucleophile may induce the reaction of a less reactive (or completely inert) nucleophile with 4-nitrocumenyl chloride and α,4-dinitrocumene. This prediction, made by Kornblum, proved to be fully justified[7]. In the absence of elimination, sodium azide and α,4-dinitrocumene do not react (control time—48 h). In contrast to sodium azide, the lithium salt of 2-nitropropane reacts with α,4-dinitrocumene in the dark and after three hours gives the α-substitution product in 87% yield. If α,4-dinitrocumene (1 mole) is treated with sodium azide (2 moles) in the presence of the lithium salt of 2-nitropropane (0.1 mole), the entire initial α,4-dinitrocumene is converted in the absence of illumination over a period of 3 h into pure 4-nitrocumenyl azide in 97% yield. Such "stimulation" of the reaction has been observed also for the nitrocumenylchloride–sodium nitrite pair. Typical one-electron donors such as sodionaphthalene have been used successfully as "stimulating" agents[7].

According to Russell et al.[8] the substitution reactions in the series of α-*x*-α-nitroalkanes also involve a stage in which nitro-radical-anions are formed. The lithium salt of 2-nitropropane has also been used in this reaction as an electron donor. The formation of 2,3-dimethyl-2,3-dinitrobutane is accelerated under the influence of light; oxygen, dinitrobenzene, and free radicals have an inhibiting effect. The reactions have been described by the following scheme[8]:

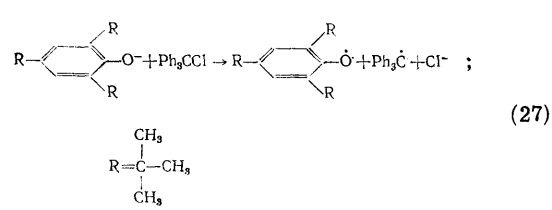


(26)

X = Cl, CN, or NO_2 .

Mechanism (26) has been extended to a large series of practically important reactions of 2,2-dinitropropane and 2-bromo-2-nitropropane with other carbanions[8].

The kinetics of the electron transfer stage in nucleophilic substitution at a saturated carbon atom have been investigated[65,66] and model systems in which stable free radicals are formed in the reactions have been examined. This enabled the author to investigate the kinetics of electron transfer on the basis of the accumulation of the radicals. The interaction of triphenylmethyl chloride with a sterically hindered phenoxide in accordance with the scheme



(27)

was chosen as a model of nucleophilic substitution. The model was justified in the following way.

"Since nucleophilic substitution involves the replacement of one anion by another and the electron may be regarded as the simplest nucleophile, the very formation of radicals in reaction (27) constitutes in essence the simplest type of nucleophilic substitution of a halogen by an electron"[66]. The initial rate of accumulation of phenoxy-radicals is related to the phenoxide and triphenylmethyl chloride concentrations by the equation

$$w_0 = \frac{d[ArO^{\cdot}]}{dt}\Big|_{t\to 0} = k_1[Ph_3CCl] + k_2[Ph_3CCl][ArOK]^2 \qquad (28)$$

where the constant k_1 describes the rate of dissociation of Ph_3CCl into ions, the first term of the equation being independent of the concentration [ArOK]. The authors[9, 65, 66] believe that this term corresponds to the reaction of the ionised triphenylmethyl chloride or the free triphenylmethyl cation with the phenoxide:

$$Ph_3CCl \rightleftarrows Ph_3C^+ + Cl^- \quad ; \qquad Ph_3C^+ + {}^{-}OAr \rightarrow Ph_3C^{\cdot} + {}^{\cdot}OAr \quad . \qquad (29)$$

The second term of Eqn. (28), which is quadratic in the phenoxide concentration, corresponds to electron transfer on collision of three molecules when the reaction involves undissociated triphenylmethyl chloride:

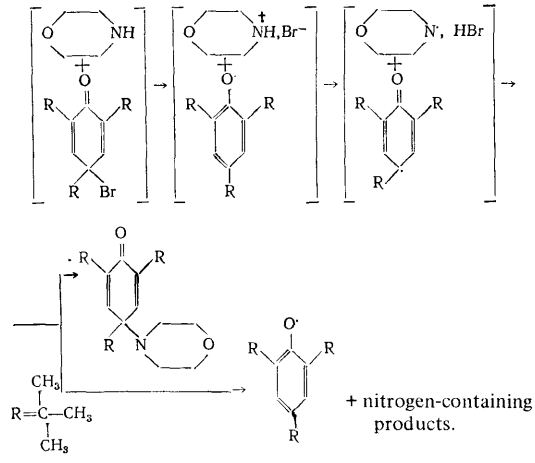
$$ArO^- \ldots\ldots Ph_3CCl \ldots\ldots MOAr \rightarrow ArO^{\cdot} + Ph_3C^{\cdot} + Cl^- \ldots\ldots MOAr \quad . \qquad (30)$$

The contribution of reactions (29) and (30) is determined by the solvating capacity of the solvent. When tetrahydrofuran (THF) is replaced by dimethoxyethane (DME), the contribution of reaction (29) increases almost by a factor of 2. In DMF only reaction (29) takes place, while in heptane reaction (30) occurs exclusively. The kinetic characteristics of the above model reaction have also been observed in the "typical" nucleophilic substitution of the halogen in alkyl halides by an alkoxy-group. In solvents of low polarity such reactions are frequently of third order overall (of first order with respect to the alkyl halide and of second order with respect to the alkoxide), but in highly polar solvents the reaction may be of first order with respect to the alkyl halide and of zero order with respect to the alkoxide. In solvents of moderate polarity there is a possibility of the simultaneous occurrence of the first- and third-order reactions[9, 65, 66]. On the basis of the kinetic study of electron transfer from the phenoxide to triphenylmethyl chloride, the authors[9, 66] suggest that the alcoholysis of alkyl halides be regarded as an oxidation-reduction reaction in accordance with the schemes below:

$$RX \rightleftarrows R^+ + X^-; \; R'O^- + R^+ \rightarrow [R'O^{\cdot} + R^{\cdot}] \rightarrow R'OR;$$
$$R'O^- \ldots\ldots R{-}X \ldots\ldots MOR \rightarrow [R'O^{\cdot} + R^{\cdot}] + X^- \ldots\ldots MOR; \qquad (31)$$

$$[R'O^{\cdot} + R^{\cdot}] \rightarrow R'OR \quad . \qquad (32)$$

These schemes represent a generalisation based on the results of studies of the model reaction which stops at the stage involving the formation of radical species incapable of combining with one another¶. The study of the amination of quinobromides undertaken by Bubnov[66], in which the liberation of radicals from the cage is accompanied by their combination with formation of the final S_N2 substitution products, is therefore of fundamental importance. When morpholine is used as the amine, the degree of liberation of the radicals from the cage is ~10% (according to ESR data). This implies that 90% remains as the contribution of the substitution process. Indeed the yield of quinamines in the syntheses proved to be 85%. The entirely satisfactory agreement between the yield of the reaction product estimated from kinetic ESR data and from independent chemical data may be regarded as part of the evidence in support of the following scheme:



(33)

The electrophilic substitution reaction[67]

$$AlkHgBr + NO_2BF_4 \rightarrow AlkNO_2 + Hg(BF_4)Br \qquad (34)$$

also proceeds as an oxidation-reduction process. The yield of the nitro-derivative in this process is low; in addition, an aliphatic hydrocarbon and an aldehyde are obtained. The authors explain these features of the process by mechanism (35), which involves the intermediate formation of a radical-cation from alkylmercury bromide. The latter gives rise to a highly reactive alkyl radical. The nitronium cation captures an electron and is converted into the $^{\cdot}NO$ radical. The latter is relatively inactive [cf. schemes (22) and (23)]. For this reason, the reaction of alkyl radicals with nitrogen dioxide proceeds to only a slight extent, a considerable proportion of the radical emerging from the cage into the bulk of the solution. Nitrogen dioxide radicals are probably consumed in secondary oxidation reactions and alkyl radicals either split off hydrogen from the solvent and form a hydrocarbon or are oxidised and give rise to an aldehyde[67]:

$$AlkHgBr + NO_2BF_4 \rightarrow \left[\begin{matrix} Alk^{\cdot} + (HgBr)^+ \\ + \quad + \\ {}^{\cdot}NO_2 + (BF_4)^- \end{matrix}\right] \begin{matrix} \rightarrow AlkNO_2 + Hg(BF_4)Br \\ \rightarrow Alk^{\cdot} + Hg(BF_4)Br + {}^{\cdot}NO_2 \end{matrix}$$
$$\begin{matrix} [O] \downarrow \\ RCHO \end{matrix} \qquad \begin{matrix} \downarrow [H^{\cdot}] \\ AlkH \end{matrix} \quad . \qquad (35)$$

---o0o---

The above data show that the one-electron transfer stage is both possible and frequently observed in the mechanisms of substitution reactions. At the same time it is evident that there is no justification for applying the hypothesis of one-electron transfer to all cases without exception. In each specific reaction the one-electron

¶ The question of the validity of this generalisation gave rise to a controversy. It was emphasised that the formation of radicals only as the final products makes the reaction too different from other nucleophilic substitution reactions and actually necessitates "its classification as not an S_N reaction, but as an oxidation-reduction process"[10].

transfer stage requires experimental proof. The development of such studies is urgently required because it leads to the synthesis of the required final products or to an increase of their yield and of the rate of their formation. The main problem is to determine the subsequent fate of the species arising after the one-electron transfer. These species may undergo transformations of the $S_{RN}1$ or S_N2 type along the pathway to the final product. Transformations which take place via complexes containing a tetrahedral carbon atom belong to reactions of the S_N2 type. The complexes may be obtained both as a result of recombination in the biradical pair and after emergence from the solvent "cage" with subsequent attack by a further molecule of the reagent. Reactions of the $S_{RN}1$ type involve the elimination of the ionogenic group from the primary radical-ion and the subsequent addition of the reagent at the site of the free valence.

The possibility of recombination in the biradical pair is difficult to test and data characterising reactions of this type are still ambiguous. This has given rise to a sceptical[10] and sometimes extremely negative[68] assessment of the one-electron transfer hypothesis. Reactions involving the liberation of a radical-ion from the solvent "cage" or the formation of secondary radicals are more readily susceptible to investigation. This field is now attracting much attention and has already yielded results which are of both theoretical and practical importance.

Further development of such research requires, however, the solution of many more fundamental problems. It is necessary to know the difference between the oxidation-reduction potentials of the reagent and the substrate established under reaction conditions. It is necessary to discover the features which determine the state of equilibrium in electron transfer reactions. An important factor is the stability of the species formed on electron transfer. It is therefore essential to discover what factors promote the stabilisation and destabilisation of such species and what general changes in reactivity accompany the transition of the substance to the radical-ion state. All these problems are new to organic chemistry. The principal obscurities are associated with the insufficiency of information about the nature of the chemical behaviour of radical-ions. At the present stage the development of studies devoted to the role of the oxidation-reduction stages in the reaction mechanism depends on the level of our knowledge concerning the transformation of a given substance as a result of electron transfer.

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