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A New Mechanism of Nucleophilic Substitution

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A new radical-anionic chain mechanism of nucleophilic substitution at aliphatic, aromatic, and unsaturated carbon atoms is examined (the $S_{RN}1$ mechanism of nucleophilic substitution).
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I. INTRODUCTION

According to the classification of Ingold and Hughes [1], nucleophilic substitution at a saturated carbon atom can take place via two mechanisms: the synchronous S_N2 mechanism and the two-stage S_N1 mechanism. However, in recent years it has become evident that between these limiting cases there is a possibility of a whole "spectrum" of mechanisms [2,3] and that different ionic intermediates can participate in each of these [4]. In nucleophilic aromatic substitution the specific features of the aromatic system are observed, being manifested primarily by the absence of the simple S_N2 mechanism. Nucleophilic aromatic substitution, which requires the presence of electron-accepting groups in the aromatic ring, usually takes place in stages and involves the formation of σ-anionic complexes. However, instances of S_N1 processes, leading to the formation of aryl cations, are also known.

A new type of nucleophilic substitution, involving a radical-anionic chain mechanism with formation of a substrate radical-anion and a nucleophilic radical, was discovered in 1966 in saturated systems and in 1970 in aromatic systems, and was called the $S_{RN}1$ mechanism (radical, nucleophilic, unimolecular substitution [5]). The term "radical" reflects the nature of the reaction and the term "nucleophilic" reflects its result. As regards the definition of the term "unimolecular", the authors see here an analogy (which, incidentally, is not supported by kinetic data) with S_N1 reactions, with the sole difference that the C–X bond is broken in a radical anion and not in a neutral molecule.

II. $S_{RN}1$ NUCLEOPHILIC SUBSTITUTION IN ALIPHATIC COMPOUNDS

The radical-anionic chain mechanism of nucleophilic substitution in aliphatic compounds was finally formulated in 1966 [6-9] (see the relevant reviews [10-12]) on the basis of previous (starting from the 1950s) vigorous studies on the chemistry of ambident ions. It was established that, although in principle the interaction of salts of aliphatic nitro-compounds with alkyl halides can involve alkylation

both at carbon and oxygen, the main result is the *O*-alkylation reaction[10,11]

$$RR'\bar{C}-NO_2 \leftrightarrow RR'C=NO_2^- \xrightarrow{R''CH_2X} \begin{cases} \longrightarrow RR'C(NO_2)CH_2R'' \\ \longrightarrow RR'C=N(O)OCH_2R'' \rightarrow (RR'C=NOH + R''CHO) \end{cases}.$$

The nitronic esters formed subsequently decompose with formation of an oxime and an aldehyde.

However, somewhat unexpectedly, considerable amounts of *C*-alkylation products are formed in this reaction from *o*- and *p*-nitrobenzyl chlorides and also from 2,4-dinitrobenzyl chloride; thus, on interaction with the sodium salt of 2-nitropropane, *o*-nitrobenzyl chloride gives rise to 46% of the *C*-alkylation product and to 30% of the *O*-alkylation product, while the corresponding proportions of the two products obtained from the *p*-isomer are 83% and 1% (in alcohol at 30°C):[13,14]

$$p\text{-}NO_2C_6H_4CH_2Cl + (CH_3)_2\bar{C}NO_2 \cdot Na^+ \rightarrow p\text{-}NO_2C_6H_4CH_2C(CH_3)_2NO_2 .$$

In contrast to this, benzyl chloride itself, *m*-nitrobenzyl chloride, and *p*-$RC_6H_4CH_2Cl$ [R = CN, CF_3, $\overset{+}{N}(CH_3)_3$, $COCH_3$, $COOCH_3$, CH_3, or Br] react only via oxygen[14].

Later it was found that the ratio of the *C*- and *O*-alkylation products depends also on the nature of the substituted group X in the *p*-nitrobenzyl system *p*-$NO_2C_6H_4CH_2X$ (Table 1).[15] It is noteworthy that this effect of the leaving group is not observed for the unsubstituted benzyl system: the tosylate, chloride, bromide, and iodide give an 82–84% yield of benzaldehyde.

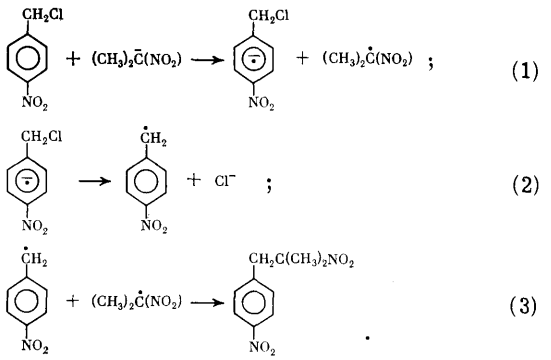
Table 1. Alkylation of the lithium salt of 2-nitropropane by the compounds *p*-$NO_2C_6H_4CH_2X$ in DMF at −16°C.[15]

X	Yield of product, %		Relative rate (unity for $C_6H_5CH_2X$)	X	Yield of product, %		Relative rate (unity for $C_6H_5CH_2X$)
	C-alkylation	*O*-alkylation			*C*-alkylation	*O*-alkylation	
$\overset{+}{N}(CH_3)_3Cl^-$	93	0	>100	*p*-$CH_3C_6H_4SO_2O$	40	32	8
C_6Cl_5COO	93	0	>100	Br	17	65	65
Cl	92	6	>100	I	7	81	3

Furthermore, the *p*-nitro-group has only a slight influence on the rate of *O*-alkylation; thus *p*-nitrobenzyl iodide, which reacts mainly via oxygen, interacts with the lithium salt of 2-nitropropane only three times as fast as benzyl iodide. On the other hand, the *p*-nitrobenzyl derivatives, which react mainly via the carbon atom [X = Cl, C_6Cl_5COO, or $\overset{+}{N}(CH_3)_3.Cl^-$], react much more vigorously than the corresponding benzyl derivatives.

It was observed that the rate of *O*-alkylation of *p*-nitrobenzyl systems *p*-$O_2NC_6H_4CH_2X$ (X = Cl, Br, or I) in dimethylformamide (DMF) at 0°C depends to a much greater extent on the nature of the halogen X than the rate of *C*-alkylation (Table 2).[16,17] On this basis, it was suggested that *O*-alkylation constitutes a usual S_N2-substitution, which is involved in competition with *C*-alkylation via another mechanism when groups difficult to eliminate are present.

In 1964, Kornblum and coworkers proposed for the first time a radical-ionic *C*-alkylation mechanism[16,17]:



(1)

(2)

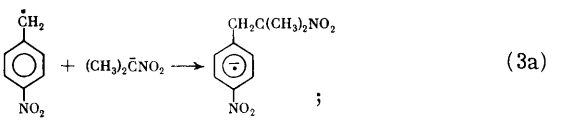
(3)

It is suggested that in the first stage an electron is transferred from the 2-nitropropane anion to *p*-nitrobenzyl chloride with formation of the radical-anion of *p*-nitrobenzyl chloride; next it decomposes with formation of the *p*-nitrobenzyl radical and the *p*-nitrobenzyl and 2-nitropropyl radicals recombine.

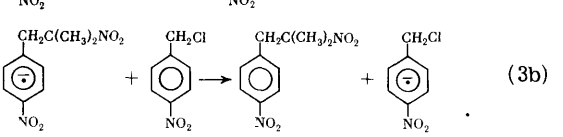
Table 2. Alkylation of the lithium salt of 2-nitropropane by nitrobenzyl halides in DMF at 0°C.[17]

X	Yield of product, %		Rate constant, litre $mole^{-1}$ s^{-1}		
	C-alkylation	*O*-alkylation	overall	*C*-alkylation	*O*-alkylation
			p-$NO_2C_6H_5CH_2X$		
Cl	92	6	0.023	0.021	0.002
Br	20	80	0.34	0.068	0.27
I	8	86	1.9	0.15	1.8
			o-$NO_2C_6H_4CH_2X$		
Cl	31	52	0.0052	0.0016	0.0036
Br	1	98	0.33	0.004	0.032

Finally, in 1966 Kornblum and coworkers and independently Russell and Danen postulated a chain *C*-alkylation mechanism[6-9] having introduced stages (3a) and (3b) instead of stage (3):



(3a)



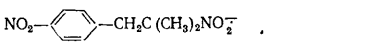
(3b)

The proposed mechanism was confirmed by a whole series of observations.

As already stated, the rate of *C*-alkylation is relatively insensitive to the nature of the leaving group, while the variation of the rates of *O*-alkylation in the Cl, Br, and I series is typical for substitution via the S_N2-mechanism[16,17].

Furthermore, it was known that aromatic nitro-compounds react with anions, including carbanions[18,19], to form radical-anions. Indeed, when the lithium salt of 2-nitropropane was added to a solution of nitrobenzene in DMF, a distinct EPR spectrum of the nitrobenzene radical-anion was produced. However, *p*-nitrobenzyl chloride at −50°C gave only an unresolved EPR signal with a width of 30 G.[16,17] Russell and Danen were able to generate *m*-nitrobenzyl chloride and *p*-nitrobenzyltrimethylammonium bromide radical-anions in ethylene by interaction with the 2-nitropropane anion under irradiation ($\lambda > 300$ nm); however, under these conditions *p*-nitrobenzyl chloride gave rise only to the EPR spectrum of the radical-anion of the reaction product—2-methyl-2-nitro-1-(*p*-nitrophenyl)propane[9].

The authors[6-9] of the proposed mechanism emphasised that stage (3a)—the interaction of the radical with the anion leading to the radical-anion—constitutes a fundamentally new type of reaction. In their discussion of the structure of the radical formed in this stage, Russell and Danen proposed an alternative structure with the localisation of the unpaired electron at the nitro-group of the side chain:



This radical-anion can isomerise rapidly to an aromatic radical-anion via an intramolecular or intermolecular mechanism, for example, as a result of the reversability of stage (3b), or it can enter stage (3b) directly before isomerising[9]. *o*-Nitrobenzyl chloride reacts via the radical-anionic mechanism with more difficulty; similarly, *o*-nitrotoluene undergoes one-elctron reduction with more difficulty than does *p*-nitrotoluene[20].

Table 3. The influence of added aromatic nitro-compounds on the interaction of *p*-nitrobenzyl chloride and the lithium salt of 2-nitropropylene in DMF at 0°C.[17]

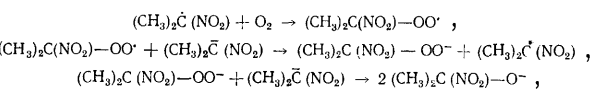
Inhibitor (equiv.)	Yield of product, %	
	C-alkylation	*O*-alkylation
—	92	6
$C_6H_5NO_2$ (4)	84	7
m-DNB (1)	61	29
m-DNB (2)	40	48
p-DNB (0, 2)	6	88
p-DNB (1)	2	72

An extremely important piece of evidence in support of the intermediate formation of the *p*-nitrobenzyl chloride radical-anion is the fact that the addition of aromatic nitro-compounds sharply inhibits *C*-alkylation, while the rate of *O*-alkylation hardly changes; thus the rate of reaction of *p*-nitrobenzyl chloride (0.01 M) with the lithium salt of 2-nitropropane (0.02 M) in DMF at 0°C diminishes after the addition of 0.01 M *p*-dinitrobenzene (*p*-DNB) by a factor of ten[17] (see also Table 3). This inhibiting influence can be explained by the fact that aromatic nitro-compounds react rapidly with *p*-nitrobenzyl chloride radical-anions, regenerating the initial *p*-nitrobenzyl chloride and thereby preventing *C*-alkylation. The inhibiting capacity varies in proportion to the electron affinity of the aromatic nitro-inhibitor (*p*-DNB > *m*-DNB > $C_6H_6NO_2$), which agrees with the series based on the relative reactivities of these compounds in electrochemical reduction: the polarographic reduction potentials in acetonitrile at 25°C are −0.69, −0.90, and −1.15 V for *p*-DNB, *m*-DNB, and nitrobenzene respectively[21].

Naturally, the inhibitors can react also with the radical-anions of the reaction products formed in stage (3a), blocking stage (3b) thereby and terminating the chain.

It is also known that aromatic nitro-compounds are effective inhibitors of free-radical chain processes[22,23] in which only neutral radicals participate, and, although the mechanism of such inhibition is not altogether clear, there is a possibility of the blocking of the proposed mechanism as a result of the interaction of the inhibitor with *p*-nitrobenzyl radicals. The inhibiting influence of hexaphenylethane is almost certainly due to the interaction of *p*-nitrobenzyl radicals with triphenylmethyl radicals[8,9].

C-Alkylation is fully inhibited in the presence of molecular oxygen; instead the 2-nitropropane anion is oxidised to acetone and the nitrite ion[24]:



In the absence of *p*-nitrobenzyl chloride the 2-nitropropane anion is resistant to the action of oxygen.

The finding that the alkylation of the anion of 2-ethoxycarbonyl-3-coumaranone, which usually proceeds via the S_N2-mechanism and gives rise to considerable amounts of *O*-alkylation products, takes place almost exclusively as *C*-alkylation when *p*-nitrobenzyl chloride is used[6,7]:

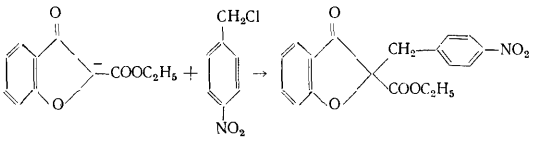


Table 4. Alkylation of the sodium salt of 2-ethoxycarbonyl-3-cumaranone by benzyl halides in DMF at 0°C.[6]

X	Yield of product, %		10^4k, litre mole^{-1} s^{-1}		
	C-alkylation	*O*-alkylation	overall	*C*-alkylation	*O*-alkylation
			$C_6H_5CH_2X$		
Cl	40	50	0.08	0.03	0.04
Br	64	29	13	8	4
I	72	18	200	144	36
			m-$NO_2C_6H_4CH_2X$		
Cl	40	52	0.19	0.06	0.10
Br	65	28	49	32	14
I	73	18	440	320	79
			p-$NO_2C_6H_4CH_2X$		
Cl	90	2	30	27	0.6
Br	66	24	53	35	13
I	74	19	440	325	75

The ratios of the rates of *C*-alkylation for $C_6H_5CH_2X$, m-$O_2NC_6H_4CH_2X$, and p-$O_2NC_6H_4CH_2X$ are 1 : 4 : 4 when X = Br and 1 : 2 : 2 when X = I. On the other hand, when X = Cl, the rate of reaction for the *p*-nitrobenzyl system increases sharply and the ratios become 1 : 2 : 900 (Table 4).[6] Only this last reaction is suppressed by the addition

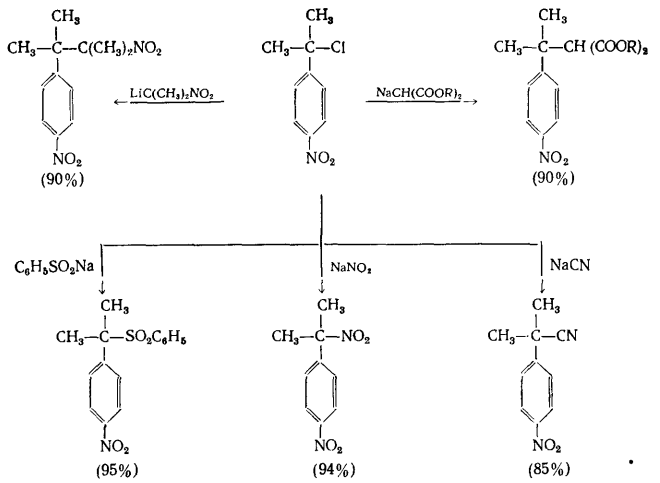
of *m*- and *p*-DNB (Table 5), while the addition of copper(II) chloride (6×10^{-6} mole) decreases the rate constant for alkylation by *p*-nitrobenzyl chloride from 3×10^{-3} to 5×10^{-5} litre mole^{-1} s^{-1} and alters the yield of the *C*- and *O*-alkylation products from 90 and 2% to 45 and 48% respectively[7].

Table 5. The influence of added inhibitors on the reaction of *p*-nitrobenzyl chloride with the sodium salt of 2-ethoxycarbonyl-3-cumaranone in DMF at 20°C.[6]

Inhibitor (equiv.)	Yield of product, %		$\tau_{1/2}$, h
	C-alkylation	*O*-alkylation	
—	90	2	0.5
C_6Cl_6 (2)	67	24	2
$PhNO_2$ (2)	67	26	3
m-DNB (2)	58	36	3
p-DNB (0.1)	47	42	4
p-DNB (1)	46	49	6
p-DNB (2)	44	46	7

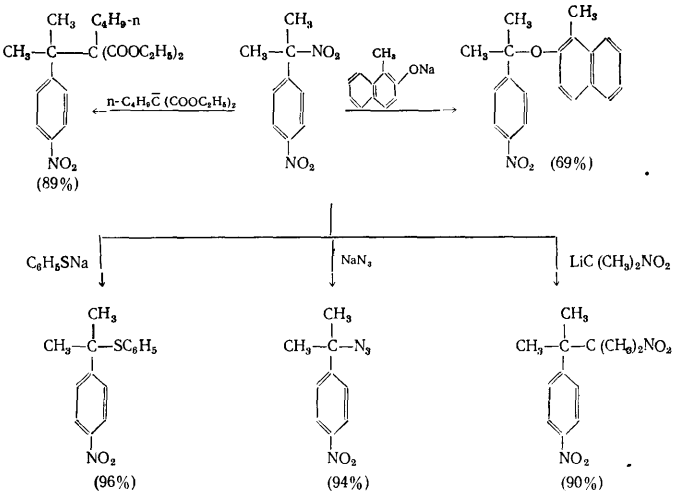
The successful study of the radical-anionic chain mechanism was continued by investigating substitution at a tertiary carbon atom in the *p*-nitrocumenyl system. This system has many advantages compared with the *p*-nitrobenzyl system. When tertiary halides are used, the competing S_N2-substitution mechanism is almost completely excluded. Also excluded is the side reaction of the bases with the fairly acidic products of the methylene group of the benzyl halide (for example, in the reaction of *p*-nitrobenzyl chloride with sodium 1-methyl-2-naphthoxide up to 40% of *p*,*p*′-dinitrostilbene is formed together with the *O*- and *C*-alkylation products).

It was found that *p*-nitrocumenyl chloride reacts exceptionally readily with various nucleophiles at room temperature in an inert gas atmosphere giving a high yield of the substitution product[25]:



Primary, secondary, and tertiary amines readily react with *p*-nitrocumenyl chloride to form alkylation products in high yields (Table 6)[26].

Such ease of substitution at a tertiary carbon atom is very striking. Even more surprising is the finding that α,*p*-dinitrocumene reacts easily with a wide variety of nucleophiles[27]:



Before Kornblum's investigation, no examples of the substitution of the nitro-group at a saturated carbon atom were known. Naturally, neither cumenyl chloride nor α-nitrocumene undergo these reactions.

Table 6. The reaction of *p*-nitrocumenyl chloride with amines (in DMSO, in the light, in N_2 atmosphere, ~35°C).[26]

Amine	Reaction time, h	Yield, %	Amine	Reaction time, h	Yield, %
Quinuclidine	10	90	Di-n-butylamine	88	34
Diazabicyclo-octane	36	85	Methylamine	5	91
Piperidine	18	91	Dimethylamine	5	96
Pyrrolidine	16	90	Trimethylamine	22	66
n-Butylamine	90	67	Ammonia	428	27

It is noteworthy that reactions of this type are relatively insensitive to steric hindrance and can be used successfully to synthesise sterically hindered compounds. In fact the first stage (electron transfer) involves only the aromatic nitro-component of the molecule. The second stage (conversion of the radical-anion into a radical as a result of the elimination of the leaving group) is also insensitive to the influence of steric factors. The third stage involves addition to the planar system of the radical; a combination of minimal steric requirements with a high reactivity of the radical ensures the ease of this stage also. Finally, the last stage (electron transfer from the aromatic nitro-radical-anion to the nitroarene) is very rapid and probably proceeds with minimal steric requirements[11].

Subsequent, detailed studies confirmed each stage of the proposed mechanism. At the beginning of these investigations the inhibiting influence of molecular oxygen was already noted[16-17,25-29] (Table 7). Thus the reaction of *p*-nitrocumenyl chloride with sodiomalonic ester in argon gives the *C*-alkylation product in 95% yield, while

in the presence of oxygen the alkylation is completely suppressed and *p*-nitrocumenyl alcohol is formed in 94% yield. Similarly the reaction of α,*p*-dinitrocumene with sodiobutylmalonic ester in argon gives a 98% yield of the *C*-alkylation product, while in the presence of oxygen *C*-alkylation proceeds to an extent of only 6% and *p*-nitrocumenyl alcohol is formed in 80% yield. In the absence of anions neither *p*-nitrocumenyl chloride nor α,*p*-dinitrocumene react with oxygen. Oxygen influences similarly the reaction of *p*-nitrocumenyl systems with amines[26].

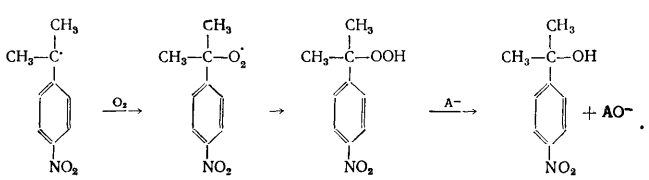
Table 7. The inhibiting influence of molecular oxygen on the reactions of *p*-nitrocumenyl chloride with nucleophiles (in DMSO).[29]

Anion	Atmosphere	Yield, %	
		substitution product	*p*-$NO_2C_6H_4C(CH_3)_2OH$
$C_4H_9\bar{C}(COOC_2H_5)_2$	N_2	89	0
$C_4H_9\bar{C}(COOC_2H_5)_2$	O_2	0	88
$\bar{C}H(COOC_2H_5)_2$	Ar	95	0
$\bar{C}H(COOC_2H_5)_2$	O_2	0	94
1-Methyl-2-naphthoxide	Ar	63	30*
1-Methyl-2-naphthoxide	O_2	0	66
$C_6H_5S^-$	Ar	95	0
$C_6H_5S^-$	O_2	4	83
$(CH_3)_2\bar{C}NO_2$	Ar	85	10
$(CH_3)_2\bar{C}NO_2$	O_2	20	70
N_3^- ***	N_2	97	0
N_3^- ***	O_2	63	20**
$C_6H_5SO_2^-$ ***	N_2	97	0
$C_6H_5SO_2^-$ ***	O_2	0	72

*p-$NO_2C_6H_4C(CH_3) = CH_2$.
**p-$NO_2C_6H_4C(CH_3)_2OOH$.
***In HMPA.

When the reactions with sodium azide and piperidine are carried out in hexamethylphosphoramide (HMPA), it is possible to isolate *p*-nitrocumenyl hydroperoxide and not *p*-nitrocumenyl alcohol; thus the hydroperoxide is formed in 76% yield in the reaction of sodium azide with α,*p*-dinitrocumene in the presence of oxygen.

The mechanism of the inhibiting action of oxygen now becomes clear. Oxygen reacts with *p*-nitrocumenyl radicals, forming peroxy-radicals, which abstract hydrogen from the solvent and are converted into *p*-nitrocumenyl hydroperoxide. The anions (with the exception of the azide ion) rapidly reduce the hydroperoxide to the alcohol:



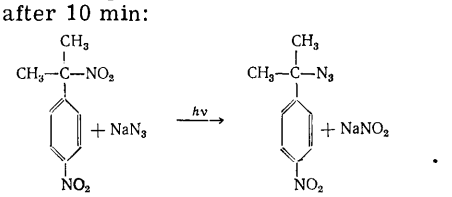
A^- represents an anion with reducing properties. In dimethylsulphoxide (DMSO) the solvent can also behave as the reducing agent[30].

The influence of the presence of traces of oxygen on the rate of reaction shows that it has a chain mechanism. Thus *p*-nitrocumenyl chloride reacts with sodium benzenesulphinate almost quantitatively with formation of the corresponding sulphone. In nitrogen at 25°C the reaction takes place over a period of 2 h, while in the presence of oxygen (1 mole %) only 10% of the substance reacts during this period. Analogous observations were made in the reactions with quinuclidine[26], sodiomalonic ester, the lithium salt of 2-nitropropane, and sodium azide[29].

As already stated above, the inhibiting influence of nitroarenes (*p*- and *m*-DNB) on the *C*-alkylation of the 2-nitropropane anion has been explained by the rapid electron transfer from the *p*-nitrobenzyl chloride radical-anion to the nitroarene, while the rate of *O*-alkylation via the S_N2-mechanism does not change under these conditions. *p*-Nitrocumenyl chloride cannot react via the S_N2 mechanism and the reaction is therefore simply retarded when nitroarenes are added. Thus the interactions of *p*-nitrocumenyl chloride with sodium azide, which takes place to an extent of 65% in 75 s, and with sodium nitrite, which is 93% complete after 20 min, are fully suppressed by the addition of *p*-DNB (10 mole %); the reaction with sodium benzene sulphinate, which takes place to an extent of 83% in 5 min, is only 19% complete after this period following the addition of *m*-DNB (10 mole %).[11] These results indicate the intermediate formation of radical-anions from the *p*-nitrocumenyl systems and a chain mechanism of the process.

Di-t-butylnitroxyl has also been used as a radical trap[31]. The reactions of *p*-nitrocumenyl chloride with the lithium salt of 2-nitropropane and quinuclidine, which proceed to an extent of 90% in 30 min and 61% in 5 h respectively, proceed to an extent of only 3–4% in the presence of 5 mole % of di-t-butylnitroxyl, while the reaction of α,*p*-dinitrocumene with sodium benzenesulphinate (20 min, 48%) is fully suppressed; galvinoxyl has a similar effect[11].

At the very beginning of studies on the radical-anionic chain mechanism the activating influence of illumination on the rate of the process was already established, diffuse daylight or the light of a fluorescent lamp being frequently sufficient[8,9,25–27]. Thus α,*p*-dinitrocumene does not react with sodium azide in the dark over a period of 2 days; under the influence of daylight, the extent of reaction after 30 min is 63% and under illumination by light from two 20-watt lamps at a distance of 15 cm the reaction is complete after 10 min:



The quantum yields of this reaction and the analogous reaction with *p*-nitrocumenyl chloride are 570 and 600, which undoubtedly indicates a chain mechanism of these processes. It is noteworthy that illumination is not always necessary for the reaction but frequently accelerates it. The study of the influence of the wavelength on the quantum yield shows that illumination promotes the formation of a charge-transfer complex of the nucleophile and the *p*-nitrocumenyl system [stage (1)].[11]

The hypothesis of the activating influence of light on stage (2) of the mechanism is less likely. Also unlikely is the following mechanism of stage (1): the nitro-compound undergoes $n \rightarrow \pi^*$ excitation under the influence of

light and abstracts hydrogen from the solvent, whereupon the base abstracts a proton with formation of a radical-anion [32-34]:

$$p\text{-}NO_2C_6H_4CR_2Cl \xrightarrow[\text{solvent}]{h\nu} [p\text{-}ClCR_2C_6H_4NO_2H^{\cdot}] \xrightarrow{B^-} p\text{-}ClCR_2C_6H_4NO_2^{\cdot-} .$$

The proposed reaction mechanism (see above) shows that the nucleophile plays a dual role in stages (1) and (3a) of the process. In stage (1) it plays the role of a one-electron reductant of the *p*-nitrobenzyl (*p*-nitrocumenyl) system. In stage (3a) the nucleophile, which propagates the reaction chain, adds to the *p*-nitrobenzyl (*p*-nitrocumenyl) radical. Presumably not only the anions which initiated the radical chain but also the anions which are not effective one-electron reductants of these systems react with radicals at this stage. In other words, the catalytic amount of the nucleophile capable of chain initiation is sufficient for the reaction between nucleophiles inactive in this respect and, for example, *p*-nitrocumenyl chloride or α,*p*-dinitrocumene. Indeed, this effect has been observed (Table 8). [35] Thus, whereas α,*p*-dinitrocumene does not react with sodium azide in the dark over a period of 48 h, the addition of 5 mole % of the lithium salt of 2-nitropropane leads to the formation of the corresponding azide in 97% yield after only 3 h. *p*-Nitrocumenyl chloride and sodium nitrite do not react in the dark over a period of 90 min; the addition of 5 mole % of the same initiator makes it possible to obtain 93% of α,*p*-dinitrocumene in 90 min. The reaction of *p*-nitrocumenyl chloride with quinuclidine is very slow in the dark, but the addition of 7 mole of the initiator makes it possible to obtained the corresponding salt in 63% yield after 36 h:

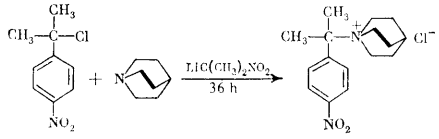


Table 8. Reactions of α,*p*-dinitrocumene with anions initiated by the lithium salt on 2-nitropropane (in HMPA in the dark) [35].

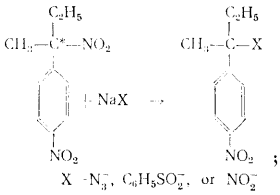
Anion	Amount of initiator, mole %	Reaction time, h	Degree of reaction, %	Product*	Yield, %
$(CH_3)_2\bar{C}NO_2$	—	3	37	$RC(CH_3)_2NO_2$	71
N_3^-	—	48	0	RN_3	0
N_3^-	5	3	100	RN_3	97
$C_6H_5SO_2^-$	—	96	8	$RSO_2C_6H_5$	8
$C_6H_5SO_2^-$	0.8	4	77	$RSO_2C_6H_5$	75
$C_6H_5SO_2^-$	5	4	100	$RSO_2C_6H_5$	95
$\bar{C}H(COOC_2H_5)_2$	—	12	26	$RCH(COOC_2H_5)_2$	26
$\bar{C}H(COOC_2H_5)_2$	5	12	53	$RCH(COOC_2H_5)_2$	51

*R = *p*-nitrocumenyl.

Although the 2-nitropropane anion is a fairly effective initiator, other anions also have this capacity and the azide ion, which does not react with α,*p*-dinitrocumene in the dark, initiates the reaction with sodium benzenesulphinate in the light [35]. The observed series of induced reactions confirms the proposed mechanism and extends the synthetic scope of reactions via this mechanism.

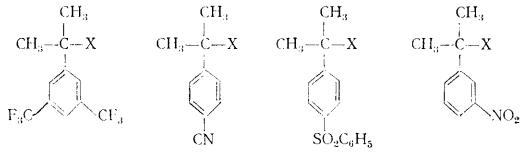
It is quite natural that not only reducing nucleophiles, but also typical one-electron transferring agents can induce reactions with relatively inactive nucleophiles [11]. Thus the reaction between α,*p*-dinitrocumene and sodium azide in the dark is initiated by the addition of 5 mole % of sodionaphthalene, 3 mole % of sodium-trimesitylboron, and 4 mole % of a solution of sodium in HMPA (the yields of *p*-nitrocumenyl azide after 30 min are 97, 92, and 87% respectively). *p*-Nitrocumenyl chloride, which reacts slowly with sodium nitrite in the dark in HMPA (6% after 90 min), is converted into α,*p*-dinitrocumene during this period in yields of 89 and 85% after the addition of 12 mole % of sodionaphthalene and 20 mole % of a solution of sodium in HMPA ("solvated electron") respectively.

The radical mechanism of the reaction was confirmed in a study of the stereochemistry of the substitution: when optically active α-methylpropyl-α,*p*-dinitrobenzene reacts with sodium azide, benzenesulphinate, or thiophenoxide in HMPA, the racemic azide, sulphone, or thioether are formed. Naturally the interaction with sodium nitrite also leads to the racemisation of the initial compound [11]:

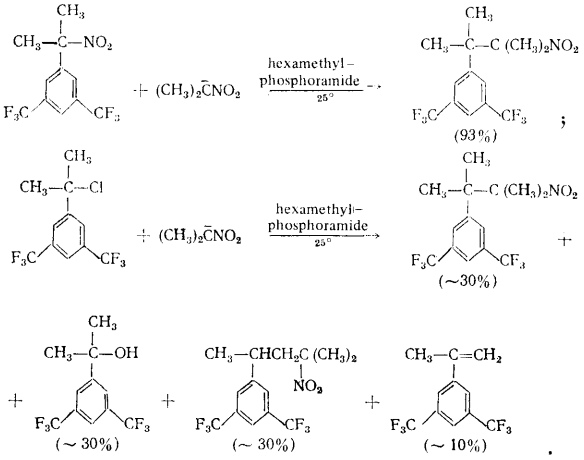


X = N_3^-, $C_6H_5SO_2^-$, or NO_2^-.

Vigorous attempts have now been made to extend the range of organic compounds capable of involvement in radical-anionic chain substitution reactions. Several cumenyl systems containing electron-accepting substituents in the benzene ring have been found [11]:



Although a whole series of synthetically valuable reactions have been observed for these systems, they are fairly frequently accompanied by side processes which do not occur with *p*-nitrocumenyl systems and this can be undoubtedly accounted for by the different stabilities of the corresponding radical-anions and radicals. This hinders routine applications of the radical-anionic chain substitution reactions for synthetic purposes:



Thus, whereas α-nitro-3,5-bis(trifluoromethyl)cumene smoothly alkylates the 2-nitropropane anion at a carbon atom with a yield of 93%, 3,5-bis(trifluoromethyl)cumenyl chloride gives the same product with a yield of only 30%. Two competing side reactions takes place: (a) *O*-alkylation via the S_N2 mechanism with subsequent formation of 3,5-bis(trifluoromethyl)cumenyl alcohol; (b) dehydrochlorination with formation of α-methyl-3,5-bis(trifluoromethyl)styrene and subsequent Michael addition to the latter of the 2-nitropropane anion [11].

Like the *p*-nitrocumenyl system, the *m*-nitrocumenyl system gives high yields of *C*-alkylation products in the reactions with sodium thiophenoxide, sodiomalonic ester, and sodiobutylmalonic ester, but in the reaction of *m*-nitrocumenyl chloride with ambident ions the formation of considerable amounts of *O*-alkylation products (S_N2 reaction) is observed [28]. Thus the reaction of *m*-nitrocumenyl chloride with sodium nitrite gives 52% of α,*m*-dinitrocumene and 27% of *m*-nitrocumenyl alcohol; under the same conditions, the *p*-isomer is converted to an extent of 92–95% into α,*p*-dinitrocumene. The reaction of the lithium salt of 2-nitropropane with *m*-nitrocumenyl chloride in HMPA leads to the formation of 33% of the *C*-alkylation product, 35% of *m*-nitrocumenyl alcohol, and 15% of *m*-nitromethylstyrene; the reaction with sodium benzenesulphinate gives 59% of the sulphone and 11% of *m*-nitrocumenyl alcohol, while *p*-nitrocumenyl chloride or α,*p*-dinitrocumene give rise only to the corresponding sulphone in 97% yield. Oxygen almost completely inhibits substitution via the radical-anionic mechanism in *p*-nitrocumenyl systems and leads to the formation of *p*-nitrocumenyl alcohol, whereas such inhibition of the reaction of *m*-nitrocumenyl chloride is not so pronounced and *m*-nitrocumenyl alcohol is formed in small amounts (Table 9) [28]. On the basis of these observations, it is suggested [28] that a non-chain radical "cage" mechanism can play an important role for *m*-nitrocumenyl chloride:

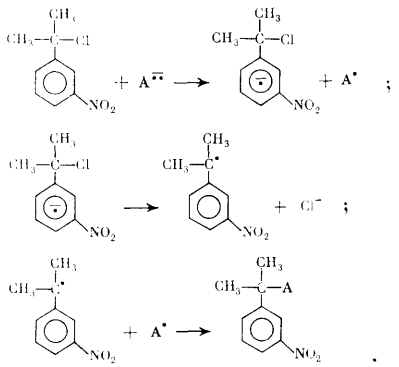


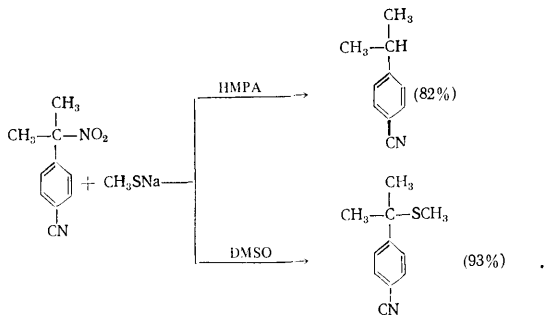
Table 9. The inhibiting influence of oxygen on the reaction of *m*-nitrocumenyl chloride with anions (in DMSO). [28]

Anion	Atmosphere	Yield of products, %		
		substitution product	*m*-$NO_2C_6H_4C(CH_3)_2OH$	initial substance
$\bar{C}H(COOC_2H_5)_2$	Ar	92	0	—
$\bar{C}H(COOC_2H_5)_2$	O_2	70	3	22
$C_6H_5S^-$	N_2	94	0	—
$C_6H_5S^-$	O_2	82	2	12
N_3^- *	N_2	79	0	6
N_3^- *	O_2	76	0	14

* In HMPA.

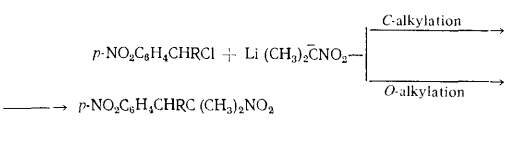
Incidentally, the absence of selectivity in the alkylation of ambident anions by *m*-nitrocumenyl chloride can be explained with the aid of this mechanism.

The reaction of *p*-cyano-α-nitrocumene with sodium methanethiolate in DMSO gives the corresponding sulphide in 93% yield, while in HMPA the product is *p*-cyanocumene in 82% yield [11]:



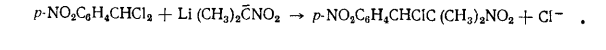
In view of the similarity of the electron-accepting properties of the *p*-nitrophenyl and γ-pyridyl residues, 2-nitro-γ-pyridylpropane evidently interacts with the 2-nitropropane anion via a radical-anionic mechanism [11]. Light accelerates the reaction, while the addition of 5 mole % of *m*-DNB or di-t-butyl nitroxide fully inhibits it.

Although Kornblum [11] frequently emphasised and demonstrated the relative insensitivity of the *C*-alkylation via the radical-anionic mechanism to steric requirements (say in relation to *p*-nitrocumenyl systems), in 1976 Norris and Randles [36] showed that this is not always the case. By studying the interaction of α-alkyl-*p*-nitrobenzyl chlorides (R = CH_3, C_2H_5, iso-C_3H_7, or t-C_4H_9) with the lithium salt of 2-nitropropane, they showed, that, when R = CH_3 or C_2H_5, competing $S_{RN}1$ and S_N2 processes, leading to *C*- and *O*-alkylation products, take place. For more sterically hindered chlorides (R = iso-C_3H_7 or t-C_4H_9), the reaction proceeds exclusively as *O*-alkylation despite the clear $S_{RN}1$ mechanism and only the corresponding ketones *p*-$NC_2C_6H_4COR$ are formed as a result of the decomposition of nitronic esters (Table 10):



The hypothesis that in the last two cases the S_N2 mechanism operates is disproved by a whole series of observations: the reaction in the dark is much slower than in the light, oxygen and *p*-DNB have an inhibiting effect and, finally, α-isopropyl- and α-t-butyl-benzyl chlorides do not react under the conditions indicated. According to the authors [36], steric hindrance in stage (3a) of the radical-anionic chain mechanism provides the best explanation of the results. It also explains the decrease of the rate of interaction with increasing bulk of the group R (Table 10).

p-Nitrobenzylidene chloride also reacts with the lithium salt of 2-nitropropane via the radical-anionic chain mechanism with formation of 1-chloro-2-methyl-2-nitro-1-(*p*-nitrophenyl)propane [37–39]:



The reaction is inhibited by oxygen and *p*-DNB and is accelerated under illumination (Table 11).

Table 10. The interaction of α-alkyl-*p*-nitrobenzyl chlorides with the lithium salt of 2-nitropropane in DMSO at 20°C. [36]

Alkyl	Reaction conditions	Reaction time, h	Yield of products, %		
			C-alkylation	O-alkylation	initial substance
CH_3	N_2	20	66	34	0
CH_3	N_2, *hν*	20	82	18	0
CH_3	O_2	20	36	57	7
CH_3	N_2 *	7	18	13	69
CH_3	N_2, *hν* *	7	33	11	56
CH_3	N_2 *	23	45	19	36
CH_3	N_2, *hν* *	23	81	19	0
CH_3	O_2 *	23	0	71	29
C_2H_5	N_2	30	71	29	0
C_2H_5	N_2, *hν*	30	80	20	0
C_2H_5	O_2	30	24	71	5
iso-C_3H_7	N_2, *hν*	45	0	100	0
iso-C_3H_7	N_2	24	0	56	44
iso-C_3H_7	N_2, *hν*	24	0	81	19
iso-C_3H_7	O_2	24	0	57	43
iso-C_3H_7	N_2 **	24	0	35	65
t-C_4H_9	N_2, *hν*	96	0	100	0
t-C_4H_9	N_2	54	0	64	36
t-C_4H_9	N_2, *hν*	54	0	88	12
t-C_4H_9	O_2	54	0	9	91
t-C_4H_9	N_2 **	54	0	27	73

*In DMF.
**In the presence of 100 mole % *p*-DNB.

Table 11. The interaction of *p*-nitrobenzylidene chloride with the lithium salt of 2-nitropropane in DMSO at 20°C. [39]

Amount of $(CH_3)_2CLiNO_2$, (equiv.)	Reaction conditions	Reaction time, min	Yield, %*		
			initial substance	A	B
2	N_2	40	11	51	16
2	N_2, *hν*	40	3	55	24
2	O_2	40	26	37	8
1	N_2	60	50	31	6
1	N_2 **	60	68	10	2
4	N_2, 30°	3	3	50	36
4	N_2, 30°	60	0	0	88

*Notation: A = 1-chloro-2-methyl-2-nitro-1-(*p*-nitrophenyl)propane; B = β,β-dimethyl-*p*-nitrostyrene.
**After the addition of 10 mole % *p*-DNB.

However, perhaps the most interesting fact in this connection is that the authors [38,39] observed in their study of the reaction in the presence of an excess of the nucleophile a new type of elimination reaction with participation of a radical-anion—an $E_{RC}1$ reaction (radical-chain unimolecular elimination). The secondary interaction between the reaction product and the nucleophile leads to the formation of β,β-dimethyl-*p*-nitrostyrene and 2,3-dimethyl-2,3-dinitrobutane via the mechanism

$$p\text{-}NO_2C_6H_4CHClC(CH_3)_2NO_2 + 2(CH_3)_2\bar{C}NO_2 \rightarrow$$
$$\rightarrow p\text{-}NO_2C_6H_4CH{=}C(CH_3)_2 + (CH_3)_2C(NO_2){-}C(NO_2)(CH_3)_2 + Cl^- + NO_2^-$$

and not to double substitution. The reaction is initiated by light (in DMF in the dark at 5°C it proceeds to an extent of only 8%, while under illumination its extent is 96%) and is inhibited by *p*-DNB: in DMSO in the dark at 20°C the yield of β,β-dimethyl-*p*-nitrostyrene after 150 min is 90%, while in the presence of 20 mole % of *p*-DNB the yield falls to 18%. Benzylidene chloride itself does not undergo this reaction. The authors [38,39] proposed the following mechanism for this interaction:

$$ArCHClC(CH_3)_2NO_2 + (CH_3)_2\bar{C}NO_2 \rightarrow [ArCHClC(CH_3)_2NO_2]^{\cdot-} + (CH_3)_2\dot{C}NO_2 ;$$
$$[ArCHClC(CH_3)_2NO_2]^{\cdot-} \xrightarrow{slow} Ar\dot{C}HC(CH_3)_2NO_2 + Cl^- ;$$
$$Ar\dot{C}HC(CH_3)_2NO_2 + (CH_3)_2\bar{C}NO_2 \rightarrow ArCH{=}C(CH_3)_2 + (CH_3)_2\dot{C}NO_2 + NO_2^- ;$$

or

$$Ar\dot{C}HC(CH_3)_2NO_2 + A^- \rightarrow ArCH{=}C(CH_3)_2 + NO_2^- + A\cdot ;$$
$$(CH_3)_2\bar{C}NO_2 + (CH_3)_2\dot{C}NO_2 \rightarrow [(CH_3)_2C(NO_2){-}C(CH_3)_2NO_2]^{\cdot-} ;$$
$$[(CH_3)_2C(NO_2){-}C(CH_3)_2NO_2]^{\cdot-} + ArCHClC(CH_3)_2NO_2 \rightarrow ;$$
$$\rightarrow (CH_3)_2C(NO_2){-}C(NO_2)(CH_3)_2 + [ArCHClC(CH_3)_2NO_2]^{\cdot-} .$$

It is of interest to note that *p*-nitrobenzylidene acetate also interacts with the lithium salt of *p*-nitropropane, forming 2-methyl-2-nitro-1-(*p*-nitrophenyl)propyl acetate:

$$p\text{-}NO_2C_6H_4CH(OCOCH_3)_2 + (CH_3)_2\bar{C}NO_2 \rightarrow p\text{-}NO_2C_6H_4CH(OCOCH_3)C(CH_3)_2NO_2 .$$

However, a completely different, ionic-chain (and not radical-chain) mechanism operates here: in the first stage the diacetate undergoes nucleophilic cleavage with formation of the free aldehyde [37,40]. The reaction is insensitive to light, oxygen, and *p*-DNB, and both benzylidene acetate itself and other $ArCH(OCOCH_3)_2$ undergo this reaction.

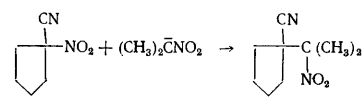
The reactions of (4-nitrobenzyl)- and (4-nitrophenyl)-methyl halides with the t-butoxide ion in t-butyl alcohol, which lead to high yields of 4,4′-dinitrostilbene and 4,4′-dinitrotetraphenylethylene respectively, also proceed via the radical-ionic chain mechanism [41]:

$$ArCH_2X + t\text{-}C_4H_9O^- \rightleftarrows Ar\dot{C}HX + t\text{-}C_4H_9OH;$$
$$ArCH_2X + t\text{-}C_4H_9O^- \rightarrow ArCH_2X^{\cdot-} + t\text{-}C_4H_9O\cdot ;$$
$$ArCH_2X^{\cdot-} \rightarrow ArCH_2^{\cdot} + X^-$$
$$ArCH_2^{\cdot} + Ar\bar{C}HX \rightarrow [ArCH_2CHXAr]^{\cdot-}$$
$$[ArCH_2CHXAr]^{\cdot-} + ArCH_2X \rightleftarrows ArCH_2X^{\cdot-} + ArCH_2CHXAr$$
$$ArCH_2CHXAr + t\text{-}C_4H_9O^- \rightarrow ArCH{=}CHAr + t\text{-}C_4H_9OH + X^-.$$

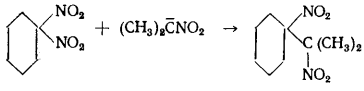
The radical-ionic chain mechanism has been considered as one of the possibilities for the reaction of benzyl halides with sodium thiolates in which the formation of benzyl and thiyl radicals was demonstrated [42].

The range of substitution reactions involving radical-anions was extended in 1970 when Kornblum and coworkers found that the anions of nitro-compounds can react with α-nitrocarbonyl compounds (esters and ketones), α-nitronitriles, and α,α-dinitro-compounds, displacing the nitro-group [43,44]:

$$(CH_3)_2C(NO_2)COOC_2H_5 + (CH_3)_2\bar{C}(NO_2) \xrightarrow[\sim 20°]{DMSO} (CH_3)_2C(COOC_2H_5){-}C(NO_2)(CH_3)_2 \quad (95\%);$$
$$(CH_3)_2C(NO_2)COC_6H_5 + (CH_3)_2\bar{C}NO_2 \rightarrow (CH_3)_2C(COC_6H_5){-}C(NO_2)(CH_3)_2 \quad (82\%);$$



(84%);



(91%).

Further studies confirmed the radical-anionic chain mechanism of these reactions†. Thus light accelerates the reaction and, when the wavelength of the initiating

† It is of interest to note that the nitro-group can be substituted under the influence of the *p*-thiocresolate ion in primary and secondary nitro-compounds under the conditions of the usual S_N2 mechanism [45].

light is 400 nm, the quantum yield of ethyl α-nitroisobutyrate is 220; ethyl α-chloroisobutyrate does not react with the lithium salt of 2-nitropropane, while the α-bromoester gives rise to a complex range of products, from which the *C*-alkylation product was isolated in a yield of only 9%.[43,44]

Sodionaphthalene is an effective catalyst of the reaction of 2,2-dinitropropane with the anion of 2-nitropropane[46]:

$$(CH_3)_2C(NO_2)_2 + (CH_3)_2\bar{C}NO_2 \xrightarrow{C_{10}H_8Na} (CH_3)_2C(NO_2)-C(NO_2)(CH_3)_2 .$$

Inhibitors of radical processes strongly retard the reaction of ethyl α-nitroisobutyrate, α-nitroisobutyrophenone, and α,α-dinitrocyclohexane with the lithium salt of 2-nitropropane[44]. A complete analogy is observed in this case between the first two stages of the mechanism of the above reactions (one-electron reduction of α-nitrocompounds with subsequent decomposition of the resulting radical-anion into a radical and a nitrite ion) and the previously investigated behaviour of aliphatic nitro-compounds under the influence of more vigorous reductants, such as metallic sodium and the electric current[47,48].

The anions of nitroalkanes are not the only species which can displace the nitro-group from α,α-dinitrocompounds. Thus, 2,2-dinitropropane reacts at 25°C, albeit fairly slowly, with sodium benzenesulphinate to give the corresponding sulphone in 81% yield[49]:

$$(CH_3)_2C(NO_2)_2 + C_6H_5SO_2^- \xrightarrow[25^\circ]{3\ days} (CH_3)_2C(NO_2)SO_2C_6H_5 .$$

The reaction is accelerated under illumination and is fully inhibited by the addition of 10 mole % of di-t-butylnitroxyl.

The reaction between 2,2-dinitropropane and sodioethylmalonic ester is accelerated by irradiation with light or by the addition of 15 mole % of the potassium derivative of nitrobenzene:

$$(CH_3)_2C(NO_2)_2 + C_2H_5\bar{C}(COOC_2H_5)_2 \xrightarrow{DMF} (CH_3)_2C(NO_2)-C(C_2H_5)(COOC_2H_5)_2 .$$

Irradiation also accelerates the reaction between 2,2-dinitropropane and sodioethylacetoacetic ester or sodiomethylacetylacetone[46].

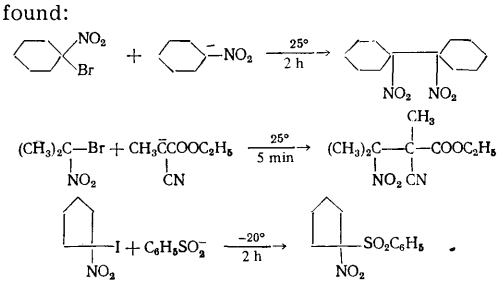
The mechanism of certain reactions between α-halogeno-α-nitro-compounds and nucleophiles, discovered previously, became understood in the light of these investigations. Thus, as early as 1940, Seigle and Hass[50] found that 2-halogeno-2-nitropropanes react with the sodium salt of 2-nitropropane to form 2,3-dimethyl-2,3-dinitrobutane:

$$(CH_3)_2C(NO_2)X + (CH_3)_2\bar{C}NO_2 \rightarrow (CH_3)_2C(NO_2)-C(NO_2)(CH_3)_2 ;$$
$$X = Cl, Br \text{ or } I.$$

The reaction between 2-chloro-2-nitropropane and sodioethylmalonic ester proceeds with a 68% yield[51]:

$$(CH_3)_2C(NO_2)Cl + C_2H_5\bar{C}(COOC_2H_5)_2 \rightarrow (CH_3)_2C(NO_2)-C(C_2H_5)(COOC_2H_5)_2 .$$

In recent years, mainly as a result of the efforts of Kornblum's[49,52] and Russell's[46] groups, new examples of the substitution of the halogen in α-halogen-α-nitro-derivatives via the radical-anionic chain mechanism have been found:



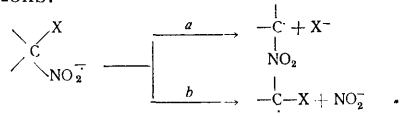
The reactions are catalysed by light and are inhibited by di-t-butylnitroxyl, *p*-dinitrobenzene, or triphenylmethyl radicals.

Reactions of this kind constitute the basis of the synthesis of α,β-unsaturated nitriles, ketones, and esters, where the first stage is the interaction of the sodium salts of $RCHYCOOC_2H_5$ (Y = CN, $COCH_3$, $COOC_2H_5$, or SO_2Ar) with α-halogeno-α-nitro-derivatives $R^1R^2CHalNO_2$ or the α,α-dinitro-derivatives $R^1R^2C(NO_2)_2$ in HMPA or DMF; subsequent heating of $R^1R^2C(NO_2)-CRYCOOC_2H_5$ in HMPA at 120°C leads to the formation of $R^1R^2C=CRY$;[53,54] the reduction of $R^1R^2C(NO_2)-CR(SO_2Ar)COOC_2H_5$ with sodium sulphide in DMF at room temperature yields $R^1R^2C=CRCOOC_2H_5$.[55]

Substitution of a sterically hindered nitro-group by hydrogen, including compounds synthesised via the $S_{RN}1$ mechanism, can be achieved by treatment with sodium methanethiolate in DMSO via the following mechanism[56]:

$$R_3C-NO_2 + CH_3S^- \rightarrow R_3C-NO_2^{\cdot-} + CH_3S^{\cdot} ;$$
$$R_3C-NO_2 \rightarrow R_3C^{\cdot} + NO_2^- ;$$
$$R_3C^{\cdot} + CH_3S^- \rightarrow R_3C-H + H_2\dot{C}-S^- ;$$
$$H_2\dot{C}-S^- + R_3C-NO_2 \rightarrow H_2C=S + R_3C-NO_2 .$$

Thus the decomposition of the intermediate radical-anions of the α-nitro-compounds can proceed, in principle, in two directions:



Pathway *a* obtains for X = Cl, Br, or I and pathway *b* obtains for X = COOR, COR, CN, or NO_2.

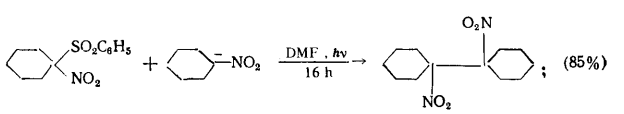
Owing to their instability the 2-nitropropane[57,58] and 2,2-dinitropropane[59] radical-anions are not revealed by EPR spectroscopy. The driving force of the decomposition of the radical-anions via pathway *a* is the presence of a readily eliminated group X and the formation of a resonance-stabilised nitroalkyl radical. The radical-anions derived from nitroalkanes[60] and α-fluoronitroalkanes[58] are fairly unstable but can be detected by EPR spectroscopy.

Yet another example of pathway *a* is provided by α-nitrosulphones. In the reaction of α-nitroisopropyl-*p*-tolyl sulphone with the potassium[61] or lithium[31] salts of 2-nitropropane in DMSO at 20°C the product was 2,3-dimethyl-2,3-dinitropropane in 80% (15 min) or 96% (2.5 h) yields:

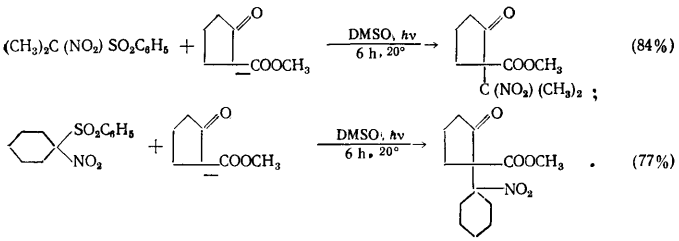
$$(CH_3)_2C(NO_2)SO_2C_6H_4CH_3\text{-}n + (CH_3)_2\bar{C}NO_2 \rightarrow (CH_3)_2C(NO_2)-C(NO_2)(CH_3)_2 .$$

Although the intermediate radical-anion of the initial sulphone was not detected in electrolysis in DMF or acetonitrile, all the results support the radical-anionic chain mechanism. The reaction is slower in the dark; when 5% of *p*-DNB is added it takes place to an extent of only 7% in 15 min, while in the presence of 5 mole % of di-t-butyl nitroxide its extent is only 1% after 4 h.

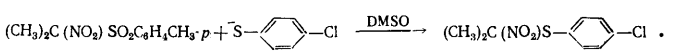
The reactions of α-nitrosulphones with other anions have also been studied[31]:



$$(CH_3)_2C(NO_2)SO_2C_6H_4CH_3\text{-}p + CH_3\bar{C}(COOC_2H_5)_2 \xrightarrow[2\ h]{DMSO,\ h\nu} (CH_3)_2C(NO_2)-C(CH_3)(COOC_2H_5)_2 ; \quad (82\%)$$



The reaction between α-nitroisopropyl-*p*-tolyl sulphone and the *p*-chlorothiophenoxide ion does not occur in the dark (DMSO, 2 h); under illumination by two 20-watt fluorescent lamps during the same period, the extent of the reaction is 95% and the corresponding sulphide is formed in 59% yield:



After 6 min, the extent of the reaction is 54%, while after the addition of 10 mole % of *m*-DNB it is only 13%; di-t-butylnitroxyl fully inhibits the reaction.

When α-nitroisopropyl phenyl sulphone is treated with six equivalents of sodium toluene-*p*-sulphinate in HMPA in the dark (20°C, 22 h) the reaction is not observed, while under illumination 25% of α-nitroisopropyl-*p*-tolyl sulphone is formed; the reaction is inhibited by the addition of 5 mole % of di-t-butylnitroxyl. The reverse reaction exhibits the same features:

$$(CH_3)_2C(NO_2)SO_2C_6H_5 + p\text{-}CH_3C_6H_4SO_2^- \rightleftarrows$$
$$\rightleftarrows (CH_3)_2C(NO_2)SO_2C_6H_4CH_3\text{-}p + C_6H_5SO_2^- .$$

For the perfluoroalkylation of thiophenols [62,63], selenophenols [64], and sulphinic acids [65] by perfluoroalkyl iodides under illumination with ultraviolet light in liquid ammonia in accordance with the scheme:

$$ArXH + R_FI \xrightarrow[\text{liq. } NH_3]{h\nu} ArXR_F \ (X=S, Se, SO_2)$$

the authors propose the following radical-anionic chain mechanism:

$$ArS^- + R_FI \xrightarrow{h\nu} ArS^{\cdot} + R_FI^{\cdot-} ;$$
$$R_FI^{\cdot-} \rightarrow R_F^{\cdot} + I^- ;$$
$$ArS^- + R_F^{\cdot} \rightarrow [ArSR_F]^{\cdot-} ;$$
$$[ArSR_F]^{\cdot-} + R_FI \rightarrow ArSR_F + R_FI^{\cdot-} .$$

III. $S_{RN}1$ NUCLEOPHILIC SUBSTITUTION IN AROMATIC COMPOUNDS

Nucleophilic substitution in non-activated halogenobenzenes is known to proceed with much difficulty (if it occurs at all). The substitution of the halogen with a high yield can be achieved only in isolated reactions, for example, under the influence of lithium cuprates [66].

However, Bunnett and coworkers [67] showed that nucleophilic substitution in aryl halides or other aromatic compounds containing a group suitable for nucleophilic substitution can be readily achieved when metallic potassium (or sodium), which is an electron donor, is used as the catalyst, or under the influence of light. Naturally, activation by a metal in liquid ammonia is due to the solvated electron [68]. The amide ion, the thiophenoxide ion, carbanions such as the fluorenyl and cyanomethyl anions, and ketone enolates such as the acetonyl anion can function as nucleophiles [67].

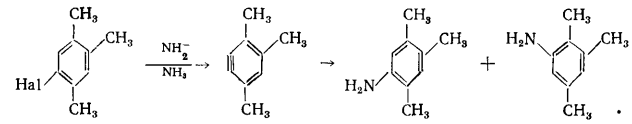
A different mechanism was proposed for these reactions: the substrate is reduced with formation of the aryl radical, which can interact subsequently with the nucleophile (anion), forming a radical-anion; the latter gives up an electron to the initial molecule and is converted into the reaction product [5]:

$$ArX + e \rightarrow [ArX]^{\cdot-} \text{ (chain initiation)}$$
$$\left.\begin{array}{l} [ArX]^{\cdot-} \rightarrow Ar^{\cdot} + X^- \\ Ar^{\cdot} + Y^- \rightarrow [ArY]^{\cdot-} \\ [ArY]^{\cdot-} + ArX \rightarrow [ArX]^{\cdot-} + ArY \end{array}\right\} \text{ (chain propagation)}$$
$$Ar^{\cdot} + RH \rightarrow ArH + R^{\cdot} \text{ (chain termination).}$$

Thus the new mechanism is based on the possibility of generating aryl radicals from ArX and on the hypothesis that a reaction takes place between Ar· and the anion. In other words, it is suggested that the anion behaves as "trap" for the aryl radical.

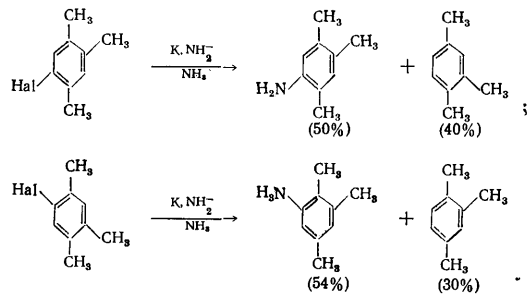
Liquid ammonia is usually employed as the solvent. The results depend on the experimental conditions, for example, on the way in which the carbanions are formed—by the action of KNH_2 or metallic potassium (whether or not the system contains an excess of electrons capable of reducing the aryl radical to the anion, i.e. $Ar^{\cdot} \rightarrow Ar^-$, depends on this). However, in most cases it is possible to select conditions ensuring a high yield of the nucleophilic substitution product.

The $S_{RN}1$ mechanism for reactions involving aromatic compounds was postulated for the first time in order to account for the results of the reaction of aryl halides (Hal = Cl, Br, or I) with the amide ion in liquid ammonia [5,69]. This reaction, involving 5- or 6-halogenopseudocumenes, proceeds via the aryne mechanism and leads to a mixture of isomers, whose composition is independent of the nature of the halogen for Hal = Cl or Br:

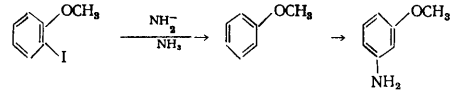


In the case of the more readily reducible ArI this mechanism is accompanied by another substitution reaction pathway, which leads to a different ratio of the isomers.

In the presence of metallic potassium, the aryne mechanism is suppressed, and the substitution proceeds wholly at the carbon atom linked to the halogen [69]:



o-Anisidine was obtained in 68% yield from *o*-iodoanisole, together with *m*-anisidine (17%) and anisole (8%). [69] The formation of *m*-anisidine is characteristic of the aryne mechanism:



The products of the substitution of the halogen for hydrogen (anisole or pseudocumene) are probably formed in the chain termination stage owing to the interaction of the aryl radical with the solvent.

In the presence of potassium reactions take place in the complete absence of the catalyst; thus iodobenzene reacts with potassium amide to form diphenylamine (19%) and *o*- and *p*-aminobiphenyls (11% of each) [69]. In acetonitrile, in the presence of potassium, chlorobenzene reacts with the cyanomethyl ion to form benzyl cyanide (36%) as well as benzene (26%) and toluene (18%). The latter might have been formed as a result of the decomposition of the radical-anion:

$$[C_6H_5CH_2CN]^{\cdot-} \rightarrow CN^- + C_6H_5\dot{C}H_2 \xrightarrow{RH} C_6H_5CH_3 .$$

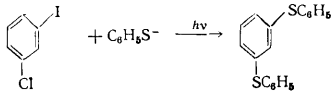
Subsequently it was shown that the $S_{RN}1$ reactions are initiated also by radiation. Under these conditions, aryl iodides react with the anion Ar'S' with formation of asymmetric sulphides in 70–95% yield [70]:

$$ArI + e \xrightarrow{h\nu} [ArI]^{\cdot-} ;$$
$$[ArI]^{\cdot-} \rightarrow Ar^{\cdot} + I^- ;$$
$$Ar^{\cdot} + Ar'S^- \rightarrow [ArSAr']^{\cdot-} ;$$
$$[ArSAr']^{\cdot-} + ArI \rightarrow [ArI]^{\cdot-} + ArSAr' .$$

The reaction constitutes a convenient method for the synthesis of diaryl sulphide, since for its occurrence it is sufficient to irradiate a solution of the reactants in liquid ammonia with light having $\lambda_{max} = 350$ nm. It has been noted that bromobenzene reacts much more slowly than iodobenzene. The absence of symmetrical sulphides from the reaction mixture implies that electron transfer is faster than the fragmentation of the radical-anion $[ArSAr']^{\cdot-}$ into an aryl radical and an arenethiolate anion. This conclusion is confirmed by the formation of the same sulphide (in 73–76% yield) in reactions of *p*-iodoanisole with $C_6H_5S^-$ and of iodobenzene with *p*-$CH_3OC_6H_4S^-$. [71]

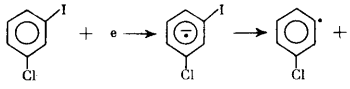
However, the problem of the mechanism of the initiation stage still remains open; it is not clear whether irradiation promotes electron transfer from the anion to the aromatic substrate or whether the C–X bond undergoes homolysis under the influence of radiation. The first version appears more probable, although in the case of iodobenzene one cannot rule out the possibility that the activation in certain reactions proceeds as a result of the photolysis of the C–I bond.

When the *m*-dihalogeno-derivative is introduced into the reaction with $C_6H_5S^-$, then, apart from fluoro-derivatives, the product of the substitution of both halogens—di(thiophenoxy)benzene [72] (only traces of the monosubstituted compounds are obtained)—is formed in a high yield in all cases:

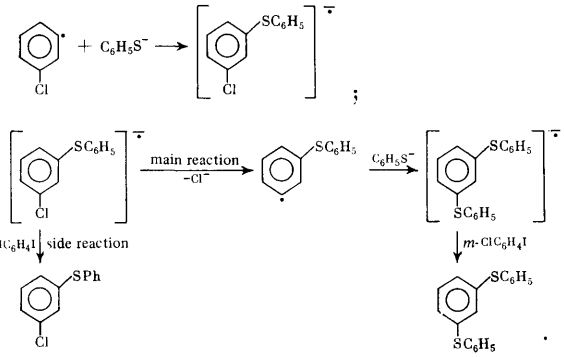


(91%)

The reaction of *m*-fluoroiodobenzene results in the formation of *m*-$FC_6H_4SC_6H_5$ (96%) only. The authors [72] believe that this result confirms the mechanism in which the rate of fragmentation of the radical-anion $[m\text{-}ClC_6H_4SC_6H_5]^{\cdot-}$ is higher than that of electron transfer:



;



;

Naturally, the only exception should be the radical-anion $[m\text{-}FC_6H_4SC_6H_5]^{\cdot-}$, since the carbon–fluorine bond is ruptured with difficulty and electron transfer predominates.

The photostimulated reaction with $C_2H_5S^-$ is much slower than that with ArS^-:

$$C_6H_5I + C_2H_5S^- \xrightarrow[NH_3]{h\nu} \underset{(30\%)}{C_6H_5SC_2H_5} + \underset{(44\%)}{C_6H_5S^-} + \underset{(3\%)}{(C_6H_5)_2S} .$$

The composition of the products of this reaction shows that radical-anion $[C_6H_5SC_2H_5]^{\cdot-}$ only partly gives up its electron to iodobenzene; most of it is able to fragment with formation of $C_2H_5^{\cdot}$ and $C_5H_5S^-$. Precisely this fragmentation pathway is observed in reduction with ArSAlk. The $C_6H_5S^-$ formed can interact with iodobenzene to give diphenyl sulphide (via the same $S_{RN}1$ mechanism).

Together with the C–N and C–S bonds, photostimulated aromatic nucleophilic substitution makes it possible to obtain the C–P bond. Thus the reactions of various aryl iodides with potassium dialkyl phosphites lead to the formation of arylphosphonates in a high yield (87–96%): [73, 74]

$$(RO)_2POK + ArI \xrightarrow[NH_3]{h\nu} ArP\underset{\underset{O}{\|}}{(OR)_2} .$$

1-Iodonaphthalene is converted after 2 h into the corresponding phosphonate in 93% yield (4% in the absence of radiation) [73]. The radical-anion of the aryl halide and the dialkyl phosphite radical are formed initially:

$$ArX + (RO)_2PO^- \xrightarrow[NH_3]{h\nu} [ArX]^{\cdot-} + (RO)_2PO^{\cdot} .$$

Next the reaction proceeds via the usual pathway involving the formation of $[ArPO(OR)_2]^{\cdot-}$. It is suggested that this radical-anion is more stable than $[ArSAr]^{\cdot-}$ owing to the more pronounced electron-accepting properties of the $OP(OR)_2$ group and for this reason it interacts with aryl halide instead of decomposing.

The ratio of the products of mono- and di-substitution was investigated as a function of the nature of the halogen in a series of studies on the substitution of halogens under the influence of $(RO)_2PO^-$ in dihalogenobenzenes under irradiation [75–77]. The authors of these studies state that the results agree solely with the $S_{RN}1$ mechanism.

The possibility of employing this reaction for the synthesis of aryl phenyl selenides in high yields has been demonstrated:

$$ArX + C_6H_5Se^- \xrightarrow[liq.\ NH_3]{h\nu} ArSeC_6H_5 .$$

This reaction proceeds only with halogeno-derivatives of phenanthrene, naphthalene, and biphenyl, but not benzene [78].

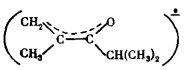
The new reaction involving the arylation of nucleophiles can be used to form carbon–carbon bonds. After initiation by an alkali metal or irradiation, various carbanions,

including ketone enolates, are arylated under the influence of ArX. Thus it has been shown that bromobenzene does not react with the potassium enolate of acetone in the dark, but, under illumination with near ultraviolet light (150 W), phenylacetone is formed in a high yield [79] with a small admixture of 1,1-diphenyl-2-propanone—the double phenylation product. In contrast to bromobenzene, iodobenzene undergoes this reaction also in the dark, but under irradiation it is appreciably accelerated (5–15% of the product is formed in the dark after 3 h, while the yield under irradiation is 67%). 3-Pentanone and 4-heptanone are phenylated in the α-position in 80% yield [80]. The radical chain mechanism is confirmed by the inhibiting effect of radical traps of the type of di-t-butylnitroxyl and also oxygen. Although the yield of the ketone phenylation products does not in general exceed the yields obtained by other methods (for example, in the phenylation of enolates by means of iodonium salts [81]), the proposed reaction is preparatively more convenient.

In the presence of sodium or potassium the reactions of aryl halides with acetone enolate give rise to a mixture of the ketone $ArCH_2COCH_3$ and the alcohol $ArCH_2CH(OH).CH_3$, with an overall yield up to 89%, as well as a certain amount of 1,1-diarylacetone [82]. Since the ketone is not reduced to the alcohol under these conditions but forms a ketyl, it is suggested that the radical-anion $[ArCH_2.COCH_3]^{\cdot-}$ is reduced and that this reaction proceeds simultaneously with its "oxidation" under the influence of ArX.

Bromo- and iodo-benzenes react similarly with the enolate ion derived from 2-butanone and 3-methyl-2-butanone [83]. Regardless of the method of initiation (by potassium or by illumination with light), 2-butanone gives rise to a mixture of phenylated ketones—$C_6H_5CH_2COCH_2.CH_3$ and $CH_3COCH(C_6H_5)CH_3$; the reaction of 3-methyl-2-butanone also results in a mixture of isomers, but the isomer $C_6H_5CH_2COCH(CH_3)_2$ predominates (81% yield).

When enolate ions derived from ketones such as di-isopropyl ketone are used as the anion in a photostimulated reaction with iodobenzene, benzene and a dimeric product (A) are formed together with the ketone arylation product. It is suggested that, apart from the usual reaction involving the radical-anion formed, the phenyl radical abstracts a β-hydrogen atom from the radical-anion. Since the radical-anion



formed is fairly stable, it is not involved in electron transfer, but is stabilised with formation of (A) or disproportionates to form a dianion and an unsaturated ketone [84]:

$$(CH_3)_2{-}\underset{\underset{O}{\|}}{C}{-}C(CH_3)_2{-}CH_2{-}C(CH_3)_2{-}\underset{\underset{O}{\|}}{C}{-}C(CH_3)_2 \quad (A)$$

The $S_{RN}1$ mechanism has also been resorted to in order to account for the causes of the formation of the dimeric product

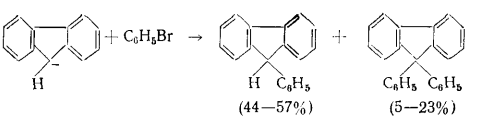
$$(C_6H_5)_2C(CONR_2){-}C_6H_4{-}C(C_6H_5)CONR_2$$

when 2-bromo-*N*,*N*-dimethyl-2-diphenylacetamide is acted upon by an excess of sodium methoxide in 2,2-dimethoxypropane [85].

The arylation of cyclic ketones (cyclobutanone, cyclopentanone, cyclohexanone, cyclo-octanone, and 2-indanone), initiated by radiation, takes place with excellent yields [80]. However, it has been shown in the same study that the reaction is not undergone by the monoanions of β-dicarbonyl compounds, although as can be seen from the first part of the review, alkyl radicals do react with these anions. It is suggested that arylation in such cases involves ready chain termination, although the true cause has not yet been established.

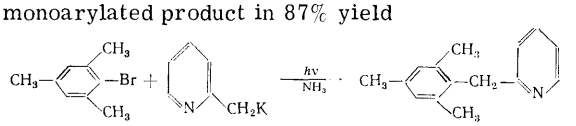
The influence of the nature of Ar in ArX on the yield of the product $ArCH_2COCH_3$ has been studied in relation to the photochemically initiated arylation of the acetone enolate ion [86]. The reactions of $2,4\text{-}(CH_3O)_2C_6H_3Br$, $2,4,6\text{-}(CH_3O)_3.C_6H_2I$, $2\text{-}\bar{O}OCC_6H_4Br$, and $2,5,6\text{-}(CH_3)_3C_6H_2I$ take place with with satisfactory yields. The reactions of compounds in which the benzene ring contains several bulky alkyl substituents take place much less effectively. After 1.5 h, the compounds $4\text{-}(C_2H_5)_2NC_6H_4Br$, $4\text{-}\bar{O}C_6H_4Br$, and $3\text{-}NO_2C_6.H_4Br$, i.e. compounds with any strong electron-donating or electron-accepting substituents, altogether failed to give an arylation product. 1- and 2-Iodonaphthalenes, 9-bromoanthracene, and 9-bromophenanthrene proved to be effective arylating agents.

The possibility of arylating "purely carbon" carbanions has also been demonstrated [86]. For example, the anion of penta-1,3-diene reacts with bromobenzene in the presence of potassium (NH_3, −78 °C) to give a mixture of phenylated mono- and di-olefins. 3-Phenylindene (32%), 1-phenylindene (3%), diphenylindene (11%), and triphenylindene (4%) were obtained by the reaction of the indene anion with bromobenzene. The fluorene anion reacts similarly in the presence of potassium or sodium:



(44–57%) (5–23%)

In those cases where the reaction of the carbanion with ArX proceeds also without a catalyst, for example, the interaction of α- and γ-picolinyl anions with bromo- or iodo-benzene [83], the yield can be increased by adding potassium or by irradiation. For example, the yield in the reaction with bromobenzene is 57% in the dark and 73% under irradiation, while the yield in the reaction with iodobenzene alone is 14% and 63% in the presence of potassium (the overall yield of the products of mono- and di-arylation is indicated); on the other hand, the reaction with chlorobenzene does not take place at all without initiation. The aryne mechanism has been proposed for the dark reaction, which has been confirmed by the absence of arylation in the case of bromomesitylene; however, the $S_{RN}1$ process takes place readily under the influence of irradiation and leads to the formation, in the case of the α-picolinyl anion, of a monoarylated product in 87% yield



The phenylation of α-cyano-carbanions in the presence of potassium is more complex [5,87]. Thus chlorobenzene reacts with the cyanomethyl anion in the presence of potassium in liquid ammonia to form phenylacetonitrile, toluene, benzene, and aniline. Significant amounts of 1,2-diphenylethane were obtained in the analogous reaction with iodobenzene together with the product already enumerated. It is noteworthy that the process itself takes place readily, in contrast to the photochemical reaction,

‡ It has been shown specially that benzyl radicals do not interact with anions.

which takes place appreciably less effectively than the reaction with the acetone enolate ion:

$$C_6H_5X + \bar{C}H_2CN \rightarrow [C_6H_5X]^{\cdot-} + {}^{\cdot}CH_2CN \quad ;$$

$$[C_6H_5X]^{\cdot-} \rightarrow C_6H_5^{\cdot} + X^- \quad ;$$

$$C_6H_5^{\cdot} + \bar{C}H_2CN \rightarrow [C_6H_5CH_2CN]^{\cdot-} \quad ;$$

$$CN^- + {}^{\cdot}CH_2C_6H_5^{\bullet} \leftarrow [C_6H_5CH_2CN]^{\cdot-} \xrightarrow{C_6H_5X} [C_6H_5X]^{\cdot-} + C_6H_5CH_2CN \quad ;$$

$$\downarrow +e_s$$

$$C_6H_5CH_2CH_2C_6H_5 \quad C_6H_5CH_2^- \xrightarrow{NH_3} C_6H_5CH_3 + NH_2^- \quad ;$$

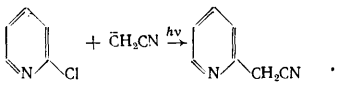
$$C_6H_5^{\cdot} + e_s \rightarrow C_6H_5^- \xrightarrow{NH_3} C_6H_6 + NH_2^- \quad ;$$

$$C_6H_5^{\cdot} + NH_2^- \rightarrow [C_6H_5NH_2]^{\cdot-} \xrightarrow{C_6H_5X} [C_6H_5X]^{\cdot-} + C_6H_5NH_2 \ .$$

The formation of all the products can be explained by a scheme postulating the ready interaction of $C_6H_5^{\cdot}$ with $\bar{C}H_2CN$ as well as the fragmentation of the resulting radical-anion. It is noteworthy that the elimination of the cyano-group from the benzyl cyanide formed can take place similarly under the influence of potassium [88]. The formation of hydrocarbons even in solvents from which the radical cannot abstract a hydrogen atom can be explained by the reduction of the radicals to the anions. Thus the reaction of $C_6H_5^{\cdot}$ with NH_3 is ruled out in view of the absence of benzene from the products of the reaction with acetone enolate ions, although the reaction was carried out in the presence of an effective hydrogen donor—the isopropoxide anion. The fraction of toluene and diphenylethane in the reaction product increases for fluorobenzene, which is reduced with difficulty under the influence of the radical-anion. The corresponding reaction with the anions obtained from other nitriles leads to the formation of different alkylbenzenes.

It has been shown recently [89] that, when a number of aryl halides other than C_6H_5X are used, the above reaction leads to the formation of α-aryl- or α-heteroaryl-acetonitriles in very satisfactory yields, and can therefore be of synthetic interest.

The arylation of the anion $\bar{C}H_2CN$ in liquid ammonia under irradiation, leading to $ArCH_2CN$ in nearly quantitative yields, has been achieved for 1- and 2-chloronaphthalene, 4-chlorobiphenyl, 4-bromobenzophenone, and 2-chloropyridine, for example:



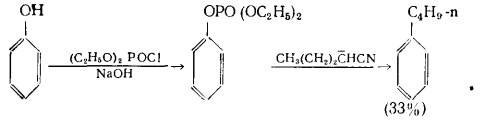
(98%)

9-Bromophenanthrene reacts similarly (the yield of the arylation product is 60–70%). It is of interest to note that the reactivity of the anion $\bar{C}H_2CN$ in these reactions is approximately the same as that of the acetone enolate, i.e. the differences between the rates of these reactions with bromobenzene are determined by other stages.

The results were explained by examining the distribution of electrons in the resulting radical-anion using the molecular orbital perturbation theory [99]. However, in practice we are dealing with the greater stability of the radical-anion $[ArCH_2CN]^{\cdot-}$ compared with $[C_6H_5CH_2N]^{\cdot-}$.

It is of interest that, together with halogeno-derivatives of aromatic compounds, other aromatic compounds, containing groups capable of being fairly readily eliminated as anions, can be used in this reaction [91]. Thus $ArSC_6H_5$ (but not $C_6H_5SC_2H_5$) reacts under the influence of irradiation with the acetone enolate ion to form $ArCH_2COCH_3$, but the extent of the fragmentation of the radical-anion can be very great, depending on the nature of Ar. The relative contributions of the processes can be inferred from the ratio of the yields of the two ketones $C_6H_5CH_2COCH_3$ and $ArCH_2COCH_3$. An approximate estimate of the reactivities of ArX gives the following sequence: $I \simeq Br > SC_6H_5 \gg Cl > F \gg OC_6H_5$. [71,79] The sulphonium and ammonium salts $(C_6H_5)_3^{\ddagger}SCl^-$ and $C_6H_5^{\ddagger}N(CH_3)_3I^-$ are fairly reactive. Thus the reaction of $C_6H_5^{\ddagger}N(CH_3)_3I^-$ with the α-picolinyl anion leads to the arylation products in 88% yield (3% of the diarylated derivative is also formed) [92].

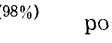
In some cases the $OPO(OC_2H_5)_2$ group proved to be particularly convenient for preparative purposes. The corresponding ester can be obtained in a high yield (87%) from phenol under the influence of $(C_2H_5O)_2POCL$ in the presence of alkali. Treatment of the resulting ester with, for example, the anion $CH_3(CH_2)_2\bar{C}HCN$ leads to n-butylbenzene in 38% yield. Thus the overall yield in this process is 33%; this reaction is of synthetic value, because it makes it possible to introduce an alkyl group into a specific position in the benzene ring and, in contrast to the Friedel–Crafts reaction, only the non-rearranged product can be obtained. Furthermore, in those cases where a nitrile is formed in the reaction, the cyano-group can be readily removed from the latter with formation of the same alkyl derivative:



The use of a phosphate ester for the conversion of phenols into anilines is of particular interest [93]. The yield of anilines in the reaction of aryl diethyl phosphate with potassium amide in liquid ammonia in the presence of potassium is 56–78%:

$$ArOPO(OC_2H_5)_2 + KNH_2 \xrightarrow[NH_3]{K} ArNH_2 \ .$$

(Ar = phenyl, 2,6-dimethylphenyl, or 2-methoxy-4-methylphenyl).

The $S_{RN}1$ mechanism has been proposed for the non-catalysed reaction of arenediazonium salts $ArN_2^{\ddagger}X^-$ with potassium iodide in methanol [94,95], whose products are ArI, ArH, and formaldehyde. It is suggested that the first stage involves the reduction of the diazonium cation by the iodide ion with formation of $[ArN_2]^{\cdot}$, which decomposes to Ar$^{\cdot}$ (or R ). The radical interacts with the iodide ion to form $ArI^{\cdot-}$, which reduces the initial cation.

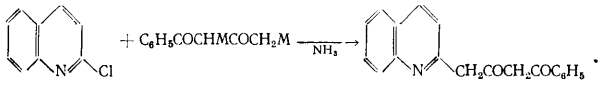
It has been shown that DMSO can be used successfully in the $S_{RN}1$ reaction instead of ammonia [96–98]. The reactions of iodobenzene with diethyl phosphite, the thiophenoxide ion, and ketone enolate ions have been achieved in this solvent in high yields under the influence of irradiation. It is of interest that in the last case the $S_{RN}1$ process can be thermally induced. However, the authors [92,98] note difficulties in the interpretation of the kinetics observed in DMSO. The dimsyl ion is phenylated with high yields in DMSO under the influence of bromobenzene (80%) and iodobenzene (87%). [99] The authors of this study, who live in Madras, note that under their climatic conditions the reaction takes place simply under the influence of sunlight. An important advantage of DMSO compared with other solvents is its low reactivity as a donor of hydrogen atoms compared with phenyl radicals, although the reaction products can be more conveniently isolated from ammonia. Other promising solvents are DMF and acetonitrile, where the reaction of iodobenzene with $(C_2H_5O)_2POK$ has been shown to take place with high yields [96].

The possibility of $S_{RN}1$ processes in 50% aqueous t-butyl alcohol has been demonstrated in relation to the reaction of C_6H_5X (X = Cl, Br, or I) with sodium phenoxide catalysed by sodium amalgam [100]. The reaction leads to the formation of diphenyl ether and benzene, the former being the main product of the reaction with iodobenzene and the latter that of the reaction with chlorobenzene, which can be accounted for by the different rates of reduction of these halogenobenzenes. It is suggested that in the reaction with C_6H_5Cl, phenyl radicals are formed at a low rate but are able to diffuse into the solution and are reduced on the surface of the amalgam to anions. In conformity with the $S_{RN}1$ mechanism, the reaction does not occur in the absence of Na/Hg and is inhibited by oxygen.

Extremely fruitful results were obtained by carrying out $S_{RN}1$ reactions as well as other anionic processes under the conditions of interfacial catalysis [101-103]. Norris and coworkers [101] showed that, under these conditions, which make it possible to reduce the amount of the aprotic dipolar solvent, the reactions of nitroalkane anions take place with *p*- or *o*-nitro-substituted benzyl or benzylidene chlorides and also with *p*-dinitrobenzene to given excellent yields of products. 2-Nitro-2-(*p*-nitrophenyl)propane is formed in the reaction of the tetrabutylammonium salt of 2-nitropropane with *p*-dinitrobenzene in acetone or benzene in yields up to 76% after only 5 min, i.e. much faster than in the usual procedure in DMSO. [101,104]

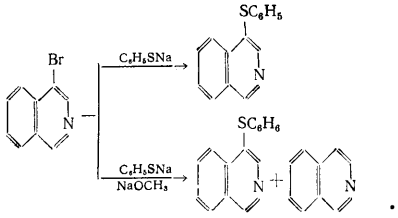
It has been shown recently for reactions of halogeno-derivatives of naphthalene, benzophenone, and benzonitrile with the thiophenoxide ion that substitution via the $S_{RN}1$ mechanism can be initiated electrochemically [105].

The $S_{RN}1$ mechanism was postulated for the first time for nucleophilic substitution in heterocyclic compounds in the reaction of the benzoylacetone dianion with 2-chloroquinoline [106]:



Since the reaction occurred without irradiation and in the absence of an alkali metal, the authors suggested that the reduction proceeds under the influence of the ambident anion itself. The radical chain mechanism was indicated by the powerful influence of inhibitors of the type of *p*-dinitrobenzene. The same workers showed that the interaction of 2-chloroquinoline with $LiCH_2COR$ (R = CH_3 or C_6H_5) in liquid ammonia (−33 °C) is sharply accelerated on irradiation with near ultraviolet light or in the presence of a small amount of added $C_6H_5COCH(Li)COCH_2Li$. [107] The reactions of potassium enolates of various ketones take place readily under the influence of irradiation; the ketone $R^1R^2CHCOCH_3$ then reacts not only with the primary but also with the tertiary carbon atom [108]. Under these conditions, 2-chloroquinoline exhibits a higher reactivity than iodobenzene. It is of interest that, as in the case of halogenobenzenes, the reaction does not take place with the monoanions of β-dicarbonyl compounds. The authors postulate the $S_{RN}1$ mechanism [109] for the reaction of 3-bromoquinoline with the superoxide ion, because bromine in the 3-position is usually relatively unreactive in nucleophilic aromatic substitution reactions.

4-Phenylthioisoquinoline is formed in the reaction of 4-bromoisoquinoline with sodium thiophenoxide in methanol via the usual ionic mechanism (addition-elimination). However, it has been shown [110,111] that in the presence of sodium methoxide the reaction mechanism changes to a radical chain mechanism, which leads to the formation of a reduction product (isoquinoline) together with the substitution product; according to the authors, isoquinoline is formed as a result of the interaction of Ar˙ with the solvent:



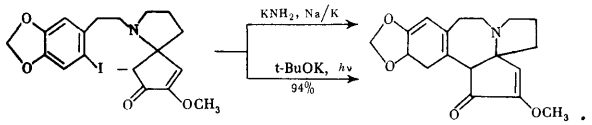
The remaining step is to postulate that, in contrast to the thiophenoxide ion, the methoxide ion behaves as an electron donor in this reaction. The possibility of the reduction of aryl halides under the influence of the methoxide ions is known. Thus it has been shown [111] that, in solution in CH_3OH-CH_3ONa (165 °C), 3-iodopyridine and 4-bromoquinoline give rise mainly to reductive dehalogenation products. The reaction proceeds via radicals, since deuterium is scarcely incorporated in the reaction product when CH_3OD is used. Although this is in fact a radical chain process, it does not have the $S_{RN}1$ mechanism, since there is no stage involving the addition of the anion to the radical. On the other hand, chain propagation proceeds in accordance with the following scheme:

$$CH_3O^- + ArX \rightarrow CH_3O^{\cdot} + ArX^{\cdot -} ;$$
$$ArX^{\cdot -} \rightarrow Ar^{\cdot} + X^- ;$$
$$Ar^{\cdot} + CH_3OH \rightarrow ArH + {}^{\cdot}CH_2OH ;$$
$$^{\cdot}CH_2OH + CH_3O^- \rightarrow CH_2O^{\cdot -} + CH_3OH ;$$
$$Ar^{\cdot} + CH_3O^- \rightarrow ArH + CH_2O^{\cdot -} ;$$
$$ArX + {}^{\cdot -}CH_2O \rightarrow ArX^{\cdot -} + CH_2{=}O .$$

It has been shown recently that, under the classical conditions of the $S_{RN}1$ reaction (ammonia, irradiation), 2-bromo-, 3-bromo-, and 2,6-dibromo-pyridines readily interact with potassium enolates derived from ketones; thus 2-acetonylpyridine is obtained after 15 min in 95% yield [112]. It has been noted that promotion with a metal in the case of heteroaromatic compounds is much less successful than in the case of carboaromatic systems.

The substitution of the halogen in 2- and 3-halogeno-thiophens under the influence of the acetone enolate ion and the amide ion has been achieved in both versions, i.e. under the influence of sodium and irradiation [113].

The $S_{RN}1$ reaction has found a remarkable application in intramolecular cyclisation with formation of the cyclic system of cephalotaxine—the starting material for the synthesis of the anticancer antibiotic cephalotazinone [114, 115]—and also in other similar cyclic systems [116]:



After the addition of the base and the formation of the carbonium ion, the reaction is initiated by an alkali metal or irradiation.

IV. $S_{RN}1$ NUCLEOPHILIC SUBSTITUTION AT AN OLEFINIC CARBON ATOM

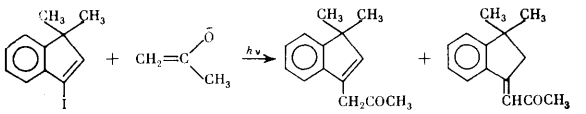
In 1976 the $S_{RN}1$ mechanism was extended to the reaction of vinyl halides [117]. It was found that β-bromostyrene reacts with potassium enolate of acetone under

irradiation (λ = 350 nm, 5 h) to form two isomeric unsaturated ketones (overall yield 82%) and a small amount of styrene (7%):

$$C_6H_5CH{=}CHBr + \bar{C}H_2COCH_3 \xrightarrow{h\nu} \underset{(48\%)}{C_6H_5CH{=}CHCH_2COCH_3} + \underset{(34\%)}{C_6H_5CH_2CH{=}CHCOCH_3} .$$

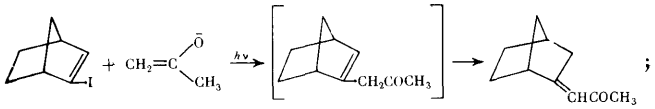
The reaction, initiated by metallic potassium, is accompanied by reduction, the saturated ketone $C_6H_5CH_2CH_2CH_2.COCH_3$ (63%) and the alcohol $C_6H_5(CH_2)_3CH(OH)CH_3$ (15%) being obtained.

The reactions with 1-iodo-3-dimethylindene§, 2-iodonorborn-2-ene, and 1-iodocyclopentene[117] take place similarly:

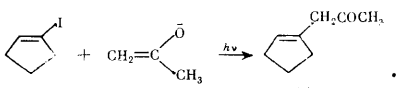


(main product)

;

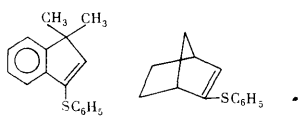


;



(72%) .

The reaction of the first two compounds with $C_6H_5S^-NH_4^+$ is slow, but also leads to substitution products:



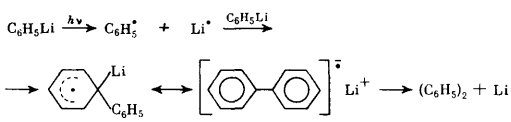
.

It is noteworthy that the authors do not regard the $S_{RN}1$ mechanism as rigorously proved in the reaction described.

V. GENERAL CONSIDERATIONS CONCERNING THE MECHANISM

The usual reactions of radicals are known to involve dimerisation, disproportionation, or the abstraction of an atom, usually a hydrogen atom, from the solvent[118,119]. The $S_{RN}1$ mechanism under consideration postulates that under certain conditions the radical can interact with the anion to form a radical-anion. There exist data confirming the possibility of this type of radical reaction.

The hypothesis that the phenyl radical adds to the phenyl anion was put forward to account for the formation of biphenyl in the photolysis of phenyl-lithium in ethereal solution[120]:



.

The direct detection of the radical-anions formed is of greatest interest. Such data have been obtained, although their number is extremely small. Thus it has been shown by EPR that certain aryl radicals (obtained by the reduction of ArN_2^+ under the influence of Ti^{3+}) add to the nitrite ion in aqueous solution with formation of radical-anions[133]. The occurrence of this stage demonstrates the reality of the subsequent chain mechanism of the substitution of the diazonium group by a nitro-group via the Sandmeyer reaction:

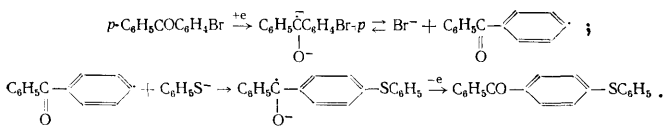
$$ArN_2^+ + Cu \rightarrow Ar^\bullet + N_2 + Cu^+ \ ;$$
$$Ar^\bullet + NO_2^- \rightarrow [ArNO_2]^{-\bullet} \ ;$$
$$[ArNO_2]^{-\bullet} + Cu^+ \rightarrow ArNO_2 + Cu \ .$$

The addition of the nitrophenyl radical to the iodide ion has been reported[123], but, according to other data[112], the radical-anion formed readily dissociates into the initial components. The radical-anions are not formed by the reaction with chloride and bromide ions[123].

Another example involves the interaction of the cyanide ion with the *p*-nitrophenyl radical, which is generated by the electrochemical reduction of *p*-iodonitrobenzene in DMSO.[123] The formation of the *p*-nitrobenzonitrile radical-anion (in a yield greater than 90%) was established by cyclic volt-amperometric and EPR methods:

$$p\text{-}NO_2C_6H_4^\bullet + CN^- \rightarrow [p\text{-}NO_2C_6H_4CN]^{-\bullet} \ .$$

Analogous radical-anions have been obtained from *o*- and *m*-nitrophenyl radicals. The reaction of $NO_2C_6H_4^\bullet$ with $C_6H_5S^-$ could not be investigated by these methods owing to the rapid interaction of $NO_2C_6H_4I$ with $C_6H_5S^-$. However, the hypothesis of the possible addition of the phenyl radical to the thiophenoxide anion was confirmed in a study[124] of the electrochemical reduction of *p*-bromobenzophenone in the presence of $C_6H_5S^-$; as a result of the oxidation-reduction cycle, the authors obtained the nucleophilic substitution product[124]:



.

However, it has been shown recently[125] that the product of this reaction may be formed by the usual $S_{RN}1$ mechanism in which the initial compound abstracts an electron from the radical anion; the only difference is that in the given instance the electron in the radical-anion is localised in the side chain and not in the aromatic ring.

The problem of the structure of the radical-anion obtained by the interaction of aryl radicals with the cyanomethyl anion has been considered in a study[90] using the method of the molecular orbital perturbation theory; the relative stabilities of the radical-anions were estimated as a function of the distribution of their electron density:

$$[Ar]^{-\bullet} CH_2Z \rightleftarrows ArCH_2 [Z]^{-\bullet} \ .$$

The hypothesis that the alkyl radical can interact with the nitrite ion to form a radical-anion was put forward by the authors of a monograph[119] to account for experimental data[126] having observed that *gem*.-dinitro-compounds are formed in the electrolysis of aliphatic nitro-compound in an alkaline medium in the presence of nitrite ions.

Thus the possibility of a stage involving the addition of the radical to the anion in the $S_{RN}1$ mechanism gives rise to no doubts.

Another fundamental problem arising when the $S_{RN}1$ mechanism is considered concerns the source of electrons This applies particularly to reactions where no catalyst is introduced and to processes initiated by irradiation. When metallic potassium is introduced into the reaction, there

§ The reaction does not take place in the dark even in the presence of an excess of the enolate.

is no doubt about the possibility of the formation of $[ArX]^{\cdot-}$, since it is known that all aryl halides are capable of being reduced by the solvated electron or electrochemically[127]. In principle, it is possible to envisage the reduction of ArX under the influence of certain anions (or nucleophiles). Thus a one-electron transfer stage has been observed for certain nucleophilic substitution reactions using a fairly readily reducible substrate. For example, the reactions of iodonitrobenzenes (but not the chloro- and bromo-derivatives) with bulky amines give rise to a nitrobenzene together with substitution products and sometimes as the main product, i.e. reductive dehalogenation via a radical mechanism takes place[128]. Analogous reduction processes under the influence of CH_3O^- [110,111] were examined above.

However, the problem remains how irradiation promotes this process. In some instances one cannot rule out the possibility that irradiation leads to the rupture of the Ar–X bond, particularly in the case of aryl iodides[129-131]. The possibility of this reaction pathway (together with the photostimulated electron transfer) was rejected by Bunnett and coworkers[80], because the reactivities of bromo- and iodo-benzenes differ insignificantly.

Hoz and Bunnett[132] recently made a detailed study of the reaction of iodobenzene with the diethyl phosphite ion initiated by irradiation. They showed that the reaction is preceded by the formation of a charge-transfer complex. It was found that the reaction is inhibited by nitroxy-radicals but is insensitive to the presence of oxygen and copper chloride. Kinetic measurements showed that the quantum yield of the reaction is greater than unity and that chain termination is a first-order process, which is confirmed by the virtually complete absence of biphenyl from the reaction products. On the basis of these results, the authors concluded that the radical-anion propagating the chain in the $S_{RN}1$ mechanism is formed by one of the following pathways:

$$\text{I (a) } PhI \overset{h\nu}{\rightleftarrows} (PhI)^*\ ,$$

$$(PhI)^* + (EtO)_2PO^- \rightarrow [PhPO(OEt)_2]^{\cdot-} + I^\cdot\ ;$$

$$\text{(b) } (PhI)^* + (EtO)_2PO^- \rightarrow Ph^\cdot + I^- + (EtO)_2PO^\cdot\ ;$$

$$Ph^\cdot + (EtO)_2PO^- \rightarrow [PhPO(OEt)_2]^{\cdot-}\ ;$$

$$\text{II } PhI + (EtO)_2PO^- \rightleftarrows PhI\cdot(EtO)_2PO^-\ ;$$

$$PhI\cdot(EtO)_2PO^- \overset{h\nu}{\rightarrow} [Ph\cdot I^-\cdot OP(OEt)_2]^* \rightarrow PhPO(OEt)_2 + I^-\ ;$$

$$[Ph\cdot I^{\cdot-} OP(OEt)_2]^* + (EtO)_2PO^- \rightarrow [PhPO(OEt)_2]^{\cdot-} + I^- + (EtO)_2PO^\cdot\ .$$

Virtually no kinetic studies on the $S_{RN}1$ mechanism have been described in the literature hitherto. The first attempt at such an investigation was undertaken by Perez de Marquez et al.[133], who used a flow technique involving very rapid contact between a p-$XC_6H_4-C_6H_5$ solution (X = F, Cl, Br, or I) in a 2 : 1 tetrahydrofuran–dimethoxyethane mixture and the surface of a potassium mirror (at −135°C) and detected the radical-anion $[ArH]^{\cdot-}$ in the EPR spectrum. They showed that the rate of its disappearance in an excess of ArX is consistent with first-order kinetics. However, we believe that this study has no direct bearing on the $S_{RN}1$ mechanism.

It is quite evident that the new mechanism of nucleophilic substitution at the carbon atom under consideration is still in its formulation stage, and that its further development in both theoretical and practical respects will be achieved in the immediate future.

REFERENCES

1. C.K. Ingold, "Structure and Mechanism in Organic Chemistry" (Translated into Russian), Izd. Mir, Moscow, 1973.
2. T.W. Bentley and P.v.R. Schleyer, J.Amer.Chem. Soc., **98**, 7658 (1976).
3. F.L. Schadt, T.W. Bentley, and P.v.R. Schleyer, J.Amer.Chem.Soc., **98**, 7667 (1976).
4. I.P. Beletskaya, Uspekhi Khim., **44**, 2205 (1975) [Russ.Chem.Rev., No.12 (1975)].
5. J.K. Kim and J.F. Bunnett, J.Amer.Chem.Soc., 92, 7463 (1970).
6. N. Kornblum, R.E. Michel, and R.C. Kerber, J.Amer.Chem.Soc., 88, 5660 (1966).
7. N. Kornblum, R.E. Michel, and R.C. Kerber, J.Amer.Chem.Soc., 88, 5662 (1966).
8. G.A. Russell and W.C. Danen, J.Amer.Chem.Soc., 88, 5663 (1966).
9. G.A. Russell and W.C. Danen, J.Amer.Chem.Soc., 90, 347 (1968).
10. N.L. Holy and J.D. Marcum, Angew.Chem., 83, 132 (1971).
11. N. Kornblum, Angew.Chem., 87, 797 (1975).
12. N. Ono and A. Kaji, J.Synth.Org.Chem.(Japan), 35, 165 (1977).
13. L. Weisler and R.W. Helmkamp, J.Amer.Chem. Soc., 67, 1167 (1945).
14. H.B. Hass and M.L. Bender, J.Amer.Chem.Soc., 71, 1767 (1949).
15. N. Kornblum, P. Pink, and K.V. Yorka, J.Amer. Chem.Soc., 83, 2779 (1961).
16. R.C. Kerber, G.W. Urry, and N. Kornblum, J.Amer.Chem.Soc., 86, 3904 (1964).
17. R.C. Kerber, G.W. Urry, and N. Kornblum, J.Amer.Chem.Soc., 87, 4520 (1965).
18. G.A. Russell, E.G. Janzen, and E.T. Strom, J.Amer.Chem.Soc., 86, 1807 (1964).
19. M. Szwarc, Accounts Chem.Res., 5, 169 (1972).
20. D.H. Geske, J.L. Ragle, M.A. Bambenek, and A.L. Balch, J.Amer.Chem.Soc., 86, 987 (1964).
21. A.H. Maki and D.H. Geske, J.Amer.Chem.Soc., 83, 1852 (1961).
22. P.D. Bartett and H. Kwart, J.Amer.Chem.Soc., 74, 3969 (1952).
23. R.A. Jackson and W.A. Waters, J.Chem.Soc., 1653 (1960).
24. G.A. Russell, J.Amer.Chem.Soc., 76, 1595 (1954).
25. N. Kornblum, T.M. Davies, G.W. Earl, N.L. Holy, R.C. Kerber, M.T. Musser, and D.H. Snow, J.Amer.Chem.Soc., 89, 725 (1967).
26. N. Kornblum and F.W. Stuchal, J.Amer.Chem.Soc., 92, 1804 (1970).
27. N. Kornblum, T.M. Davies, G.W. Earl, G.S. Greene, N.L. Holy, R.C. Kerber, J.W. Manthey, M.T. Musser, and D.H. Snow, J.Amer.Chem.Soc., 89, 5714 (1967).
28. N. Kornblum, G.W. Earl, N.L. Holy, J.W. Manthey, M.T. Musser, D.H. Snow, and R.T. Swiger, J.Amer.Chem.Soc., 90, 6219 (1968).
29. N. Kornblum, G.W. Earl, N.L. Holy, J.W. Manthey, M.T. Musser, D.H. Snow, and R.T. Swiger, J.Amer.Chem.Soc., 90, 6221 (1968).
30. G.A. Russell and A.G. Bemis, J.Amer.Chem.Soc., 88, 5492 (1966).
31. N. Kornblum, S.D. Boyd, and N. Ono, J.Amer. Chem.Soc., 96, 2580 (1974).
32. G.A. Russell and E.J. Geels, Tetrahedron Letters, 1333 (1963).
33. H.J.S. Winkler, H. Winkler, and R. Bolling, Chem. Comm., 70 (1966).
34. R. Hurtley and A.C. Testa, J.Amer.Chem.Soc., 88, 4330 (1966).

35. N.Kornblum, R.T.Swiger, G.W.Earl, H.W.Pinnick, and F.W.Stuchal, J.Amer.Chem.Soc., 92, 5513 (1970).
36. R.K.Norris and D.Randles, Austral.J.Chem., 29, 2621 (1976).
37. D.J.Girdler and R.K.Norris, Tetrahedron Letters, 431 (1975).
38. D.J.Girdler and R.K.Norris, Tetrahedron Letters, 2375 (1975).
39. D.J.Freeman and R.K.Norris, Austral.J.Chem., 29, 2631 (1976).
40. D.J.Freeman, P.J.Newcombe, and R.K.Norris, Austral.J.Chem., 29, 327 (1976).
41. D.Bethell and R.Bird, J.Chem.Soc., Perkin Trans. II, 1856 (1977).
42. E.Flesia, M.P.Crozet, J.M.Surzur, R.Jauffred, and C.Ghiglione, Tetrahedron, 34, 1699 (1978).
43. N.Kornblum, S.D.Boyd, and F.W.Stuchal, J.Amer. Chem.Soc., 92, 5783 (1970).
44. N.Kornblum and S.D.Boyd, J.Amer.Chem.Soc., 92, 5784 (1970).
45. B.M.Benn and C.M.Meesters, Chem.Comm., 597 (1977).
46. G.A.Russell, R.K.Norris, and E.J.Panek, J.Amer.Chem.Soc., 93, 5839 (1971).
47. A.K.Hoffmann, W.G.Hodgson, D.L.Maricle, and W.H.Jura, J.Amer.Chem.Soc., 86, 631 (1964).
48. H.Sayo, Y.Tsukitani, and M.Masui, Tetrahedron, 24, 1717 (1968).
49. N.Kornblum, M.M.Kestner, S.D.Boyd, and L.C.Cattran, J.Amer.Chem.Soc., 95, 3356 (1973).
50. L.W.Seigle and H.B.Hass, J.Org.Chem., 5, 100 (1940).
51. E.E.Van Tamelen and G.Van Zyl, J.Amer.Chem. Soc., 71, 4316 (1949).
52. N.Kornblum, S.D.Boyd, H.W.Pinnick, and R.G.Smith, J.Amer.Chem.Soc., 93, 4316 (1971).
53. N.Ono, H.Eto, R.Tamura, J.Hayami, and A.Kaji, Chem.Letters, 757 (1976).
54. N.Ono, R.Tamura, J.Hayami, and A.Kaji, Chem. Letters, 187 (1977).
55. N.Ono, R.Tamura, J.Hayami, and A.Kaji, Tetrahedron Letters, 763 (1978).
56. N.Kornblum, S.C.Carlson, and R.G.Smith, J.Amer.Chem.Soc., 100, 289 (1978).
57. M.McMillan and R.O.C.Norman, J.Chem.Soc.B, 590 (1968).
58. N.H.Anderson, M.McMillan, and R.O.C.Norman, J.Chem.Soc.B, 1075 (1970).
59. L.H.Piette, P.Ludwig, and R.N.Adams, J.Amer. Chem.Soc., 84, 4212 (1962).
60. R.H.Gibson and J.C.Crosthwaite, J.Amer.Chem. Soc., 90, 7373 (1968).
61. J.J.Zeilstra and J.B.N.Endberts, Rec.Trav. chim., 92, 954 (1973).
62. V.N.Boiko, G.M.Shchupak, and L.M.Yagupol'skii, Zhur.Org.Khim., 13, 1057 (1977).
63. V.I.Popov, V.N.Boiko, N.V.Kondratenko, V.P.Sambur, and L.M.Yagupol'skii, Zhur.Org. Khim., 13, 2135 (1977).
64. V.G.Voloshchuk, V.N.Boiko, and L.M.Yagupol'skii, Zhur.Org.Khim., 13, 2008 (1977).
65. N.V.Kondratenko, V.I.Popov, V.N.Boiko, and L.M.Yagupol'skii, Zhur.Org.Khim., 13, 2235 (1977).
66. E.J.Corey and G.H.Posner, J.Amer.Chem.Soc., 89, 3911 (1967).
67. J.F.Bunnett, J.Chem.Ed., 51, 312 (1974).
68. J.L.Dye, Accounts Chem.Res., 1, 306 (1968).
69. J.K.Kim and J.F.Bunnett, J.Amer.Chem.Soc., 92, 7463 (1970).
70. J.F.Bunnett and X.Creary, J.Org.Chem., 39, 3173 (1974).
71. J.F.Bunnett and X.Creary, J.Org.Chem., 40, 3740 (1975).
72. J.F.Bunnett and X.Creary, J.Org.Chem., 39, 3611 (1974).
73. J.F.Bunnett and X.Creary, J.Org.Chem., 39, 3612 (1974).
74. K.Issleib, R.Vollmer, H.Oehme, and H.Meyer, Tetrahedron Letters, 441 (1978).
75. J.F.Bunnett and R.P.Traber, J.Org.Chem., 43, 1867 (1978).
76. J.F.Bunnett and S.J.Shafer, J.Org.Chem., 43, 1873 (1978).
77. J.F.Bunnett and S.J.Shafer, J.Org.Chem., 43, 1877 (1978).
78. A.B.Petrini and R.A.Rossi, J.Organometallic Chem., 144, C12 (1978).
79. R.A.Rossi and J.F.Bunnett, J.Org.Chem., 38, 1407 (1973).
80. J.F.Bunnett and J.E.Sundberg, J.Org.Chem., 41, 1702 (1976).
81. F.M.Beringer and S.A.Galton, J.Org.Chem., 28, 3417 (1963).
82. R.A.Rossi and J.F.Bunnett, J.Amer.Chem.Soc., 94, 683 (1972).
83. R.A.Rossi and J.F.Bunnett, J.Org.Chem., 38, 3020 (1973).
84. J.F.Wolfe, M.P.Moon, M.C.Sleevi, J.F.Bunnett, and R.R.Bard, J.Org.Chem., 43, 1019 (1978).
85. G.Simig, K.Lempert, Z.Vali, G.Toth, and J.Tamas, Tetrahedron, 34, 2371 (1978).
86. J.F.Bunnett and J.E.Sundberg, Chem.Pharm.Bull. (Japan), 23, 2620 (1975).
87. J.F.Bunnett and B.F.Gloor, J.Org.Chem., 38, 4156 (1973).
88. P.G.Arapakos, M.K.Scott, and F.E.Huber, J.Amer.Chem.Soc., 91, 2059 (1969).
89. R.A.Rossi, R.H.de Rossi, and A.F.Lopez, J.Org.Chem., 41, 3371 (1976).
90. R.A.Rossi, R.H.de Rossi, and A.F.Lopez, J.Org.Chem., 41, 3367 (1976).
91. R.A.Rossi and J.F.Bunnett, J.Amer.Chem.Soc., 96, 112 (1974).
92. J.F.Bunnett and B.F.Gloor, J.Org.Chem., 39, 382 (1974).
93. R.A.Rossi and J.F.Bunnett, J.Org.Chem., 37, 3570 (1972).
94. P.R.Singh and R.Kumar, Austral.J.Chem., 25, 2133 (1972).
95. R.Kumar and P.R.Singh, Tetrahedron Letters, 613 (1972).
96. J.F.Bunnett, R.G.Scamehorn, and R.P.Traber, J.Org.Chem., 41, 3677 (1976).
97. R.G.Scamehorn and J.F.Bunnett, J.Org.Chem., 42, 1449 (1977).
98. R.G.Scamehorn and J.F.Bunnett, J.Org.Chem., 42, 1457 (1977).
99. S.Rajan and K.Muralimohan, Tetrahedron Letters, 483 (1978).
100. S.Rajan and P.Sridaran, Tetrahedron Letters, 2177 (1977).
101. B.L.Burt, D.J.Freeman, P.G.Gray, R.K.Norris, and D.Randles, Tetrahedron Letters, 3063 (1977).

102. M. Borreau and M. Julia, Tetrahedron Letters, 1537 (1973).
103. M. Makosza and J. M. Jagusztyn-Grochowska, Roczniki Chem., 50, 1859 (1977).
104. N. Kornblum, L. Cheng, R. C. Kerber, M. M. Kestner, B. N. Newton, N. W. Pinnick, R. G. Smith, and P. A. Wage, J. Org. Chem., **41**, 1560 (1976).
105. J. Pinson and J. M. Saveant, J. Amer. Chem. Soc., **100**, 1506 (1978).
106. J. F. Wolfe, J. C. Greene, and T. Hudlicky, J. Org. Chem., **37**, 3199 (1972).
107. J. V. Hay, T. Hudlicky, and J. F. Wolfe, J. Amer. Chem. Soc., **97**, 374 (1975).
108. J. V. Hay and J. F. Wolfe, J. Amer. Chem. Soc., **97**, 3702 (1975).
109. T. Yamaguchi and H. C. van der Plas, Rec. Trav. chim., **96**, 89 (1978).
110. J. A. Zoltewicz and T. M. Oestreich, J. Amer. Chem. Soc., **95**, 6863 (1973).
111. J. A. Zoltewicz, T. M. Oestreich, and A. A. Sale, J. Amer. Chem. Soc., **97**, 5889 (1975).
112. A. P. Komin and J. F. Wolfe, J. Org. Chem., **42**, 2481 (1977).
113. J. F. Bunnett and B. F. Gloor, Heterocycles, **5**, 377 (1976).
114. M. F. Semmelhack, R. D. Stauffer, and T. D. Rogerson, Tetrahedron Letters, 4519 (1973).
115. M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, and L. D. Jones, J. Amer. Chem. Soc., **97**, 2507 (1975).
116. M. F. Semmelhack and T. B. M. Bargar, J. Org. Chem., **42**, 1481 (1977).
117. J. F. Bunnett, X. Creary, and J. E. Sundberg, J. Org. Chem., **41**, 1707 (1977).
118. W. A. Pryor, Free Radicals, McGraw-Hill, New York, 1966.
119. D. C. Nonhebel and J. C. Walton, "Free-Radical Chemistry: Structure and Mechanism" (Translated into Russian), Izd. Mir, Moscow, 1977.
120. E. E. van Tamelen, J. I. Brauman, and L. E. Ellis, J. Amer. Chem. Soc., **87**, 4964 (1965).
121. A. L. J. Beckwith and R. O. C. Norman, J. Chem. Soc. B, 403 (1969).
122. J. G. Lawless and M. D. Hawley, J. Electroanalyt. Chem., **21**, 365 (1969).
123. D. E. Bartak, W. C. Danen, and M. D. Hawley, J. Org. Chem., **35**, 1206 (1970).
124. J. Pinson and J. M. Saveant, Chem. Comm., 933 (1974).
125. W. J. M. van Tilborg, C. J. Smith, and J. J. Scheele, Tetrahedron Letters, 2113 (1977).
126. C. T. Bahner, Ind. Eng. Chem., **44**, 317 (1952).
127. A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, J. Chem. Soc. A, 666 (1969).
128. F. Pietra, M. Bartolozzi, and F. Del Cima, Chem. Comm., 1232 (1971).
129. A. Levy, D. Meyerstein, and M. Ottolerghi, J. Phys. Chem., **75**, 3350 (1971).
130. A. Levy, D. Meyerstein, and M. Ottolerghi, J. Phys. Chem., **77**, 3044 (1973).
131. N. Kharasch, R. K. Sharma, and H. B. Lewis, Chem. Comm., 418 (1966).
132. S. Hoz and J. F. Bunnett, J. Amer. Chem. Soc., **99**, 4690 (1977).
133. O. Perez de Marquez, J. Giulianelli, T. C. Wallace, and D. H. Eargle, J. Org. Chem., **41**, 839 (1976).

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