

# A Reconsideration of the Mechanism for the Aromatic Version of Radical Nucleophile Displacement Reactions

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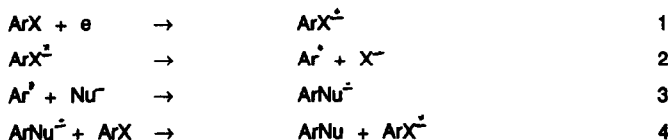
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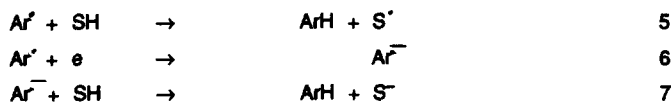
**Abstract:** A review of the literature and new experimental data indicate that aromatic radical anions containing leaving groups react with nucleophiles by a bimolecular displacement process.

## INTRODUCTION

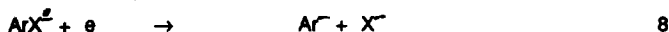
Since the initial investigation of Bunnett and Kim<sup>1</sup>, the reactions of a wide variety of aromatic substances containing leaving groups with an extensive number of nucleophiles have been studied. These studies have been reviewed<sup>2</sup>. The currently accepted mechanism for these reactions involves the steps 1-4. The major side reaction is reduction of the



starting material to form arene. The formation of the arene is usually ascribed to the processes 5-7. The sources of the electron, step 6, can be from dissolving metal, at an electrode, or from radical anions. In the early investigation it was

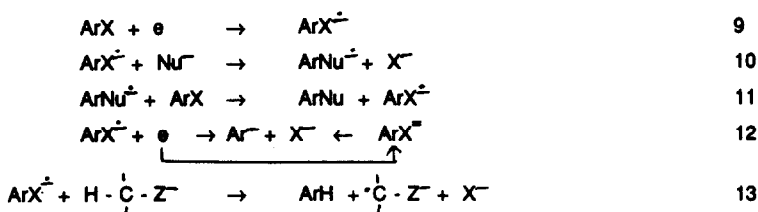


noted that arene could arise by electron transfer to the radical anion, equation 8<sup>3</sup>. It was not clear whether a dianion was an intermediate or whether expulsion occurs during the second electron transfer. There is general agreement that the



reduction is a two electron process. The open question has been the timing of the second electron transfer. Does it occur prior to the dissociation or as in step 2, followed by 5-7?

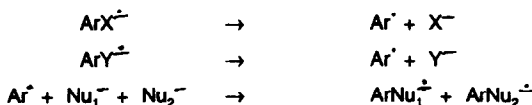
In the following discussion it will be argued that the existing data, and new experimental data, support the alternative mechanism outlined in equations 9-13. This mechanism proposes that the nucleophile reacts directly with the radical anion,  $\text{ArX}^{\cdot-}$ , derived from the starting material. The product radical anion,  $\text{ArNu}^{\cdot-}$ , transfers an electron to starting material to



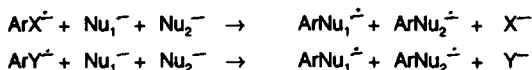
continue the chain. Arene is postulated to arise by addition of a second electron to the radical anion to give a dianion,  $\text{ArX}^{\cdot-}$ , or the carbanion,  $\text{Ar}^{\cdot}$  and  $\text{X}^-$  in a concerted manner, eq.12. The mechanism introduces a second route to arene, namely hydrogen transfer to the radical anion from anion,  $\text{H} - \overset{\cdot}{\underset{|}{\text{C}}} - \text{Z}^-$ , eq.13, or from alcohols<sup>4</sup>.

The accepted mechanism, hereinafter referred to as the radical mechanism<sup>5</sup>, is a chain process as is the presently proposed mechanism. Both mechanisms are chain reactions and thus both fit the experimental results which require a chain process.

How do these mechanisms differ and how can they be distinguished? The radical mechanism states that  $\text{ArX}^{\cdot-}$  dissociates into  $\text{Ar}^{\cdot}$  and  $\text{X}^-$ , step 2. Evidence should then be sought for the existence of such dissociation reactions as well as their rates. Step 3, involves reaction of the  $\text{Nu}^-$  with  $\text{Ar}^{\cdot}$  to give  $\text{ArNu}^{\cdot-}$ . Once again, evidence for such reactions should be provided. If  $\text{Ar}$  radicals are formed as intermediates it is very important to note that their origin should not affect the product ratios when they react competitively with a series of nucleophiles. There should be no leaving group effect in the following competition reactions.



On the other hand, the radical anion nucleophile mechanism may show such an effect. The relative amounts of the two products can be influenced by the leaving groups  $\text{X}^-$  and  $\text{Y}^-$ . It is also important to note that the radical anion



nucleophile mechanism nevertheless need not show a leaving group effect. For example, very fast displacement reactions will be expected to show negligible leaving group effects. Competing nucleophiles of equal nucleophilic power should react with different  $\text{ArX}^{\cdot-}$  reactants with equal relative reactivity. These kinds of statements relate to "The Reactivity-Selectivity Principle"<sup>6</sup> which will be discussed at the appropriate time.

The radical mechanism may show products of the reaction of the aryl radical with solvent, substrate and other reactants such as products and the intermediate radical anions. In the absence of such products, in particular such products derived from the solvent i.e. arene, then it is necessary to postulate that the reaction of the radical with the nucleophile is much faster than it is with the solvent. In some cases it has been necessary to postulate that the reactions of the radical with the anion are diffusion controlled.

Not much is known about the reactivity of radical anions,  $\text{ArX}^{\cdot-}$ , which contain leaving groups. In some instances, to be discussed later, it appears that they can abstract hydrogens from certain alkoxides and enolate ions. In a general way it is known that they are much less reactive than aryl radicals. For example, the radical anion from naphthalene is quite stable whereas the  $\alpha$ -naphthyl radical is very reactive.

In the case of the radical mechanism, the reactivity of the aryl radical should not be affected very much by a change

in structure. This is due to the fact that the unpaired electron is in an  $sp^2$  orbital which is orthogonal to the  $\pi$  system and thus substituent effects can only be transmitted to the orbital by induction<sup>7</sup>.

In the case of the radical anion nucleophile reaction the structure of the anion radical,  $ArX^{\cdot-}$ , may well influence the rate at which it is formed and the rate at which it reacts with the nucleophiles and thus changes in reactivity with substituent changes may become important. Just how changes in the anion radical,  $ArX^{\cdot-}$ , will affect the rate of production of radicals by the radical mechanism is not immediately obvious.

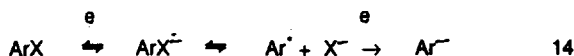
Similar problems arise when the nature of the counterion associated with  $Nu^-$  is considered with respect to the rate of the reaction of  $Nu^-$  with  $ArX^{\cdot-}$  in the anion radical nucleophile reaction or conversely with  $Ar^{\cdot}$  in the radical mechanism. Counterion effects are expected in the anion radical nucleophile reaction. A more loosely associated  $Nu^-$  should react more rapidly. On the other hand if the aromatic radical reacts with the nucleophile under diffusion control then one would not expect a counterion effect on the rate of reaction.

#### SOME CHEMISTRY OF AROMATIC RADICAL ANIONS CONTAINING LEAVING GROUPS

Stable aromatic radical anions containing suitable leaving groups should react with nucleophiles if the radical anion nucleophile mechanism is correct. Such ions should show no reaction if dissociation to an aryl radical is required.

One of the major problems associated with obtaining an understanding of the mechanism of these substitution reactions is the fact that they are chain reactions and thus many of the conventional means of studying the reactions cannot be applied. In fact, the various methods of initiating the chains, such as by dissolving metal, photochemically and electrochemically, often lead to different ratios of products or in some instances no reaction at all is observed under some initiating conditions.

What evidence is there for dissociation of aromatic radical anions,  $ArX^{\cdot-}$ ? The various X groups which have been shown to be leaving groups in the substitution process include F, Cl, Br, I,  $C_6H_5I$ ,  $OP(OR)_2$ ,  $OP(OAr)_2$ ,  $C_6H_5S^-$  ( $C_6H_5$ )<sub>2</sub>S,  $C_6H_5Se^-$ ,  $N(CH_3)_3$  and  $N_2$ . Most of the studies have focused on halogens as the leaving groups. Pulse radiolysis and electrochemical techniques have been used to generate halide ion presumably via radical anion formation. The results obtained from these studies are often very different. This may be due to the very different conditions that are used. A further complication arises in the electrochemical experiments in that two electrons are transferred. Two mechanisms for the two electron reductions have been postulated. The first, 14, suggests that the substrate,  $ArX$ , accepts an electron to give the

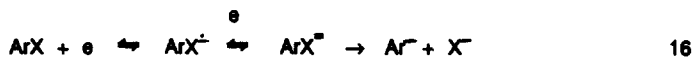


radical anion which then dissociates to the radical. The radical either reacts with a nucleophile, solvent or adds another electron to give  $Ar^{\cdot-}$  which then reacts with solvent to give  $ArH$ . This is a two electron process and when water is present the reductions are quantitative<sup>8</sup>. This pathway places significant limitations on the various rate constants. It has also been suggested that  $Ar^{\cdot-}$  can arise by reaction 15. This is a termination reaction. It is also interesting to note that only electron



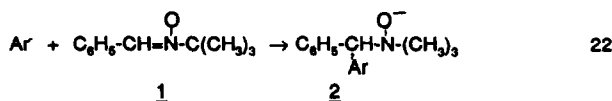
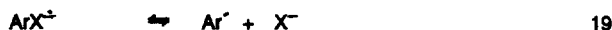
transfer is allowed even though it is well known that radicals and radical anions couple. No coupling products between  $Ar^{\cdot}$  and  $ArX^{\cdot-}$  or  $ArNu^{\cdot-}$  have ever been observed. When alkyl halides are allowed to react with sodium naphthenide coupling products are formed in significant quantities<sup>9</sup>.

Another mechanism for the two electron process involves electron transfer to  $ArX$ , eq.16 to give the radical anion  $ArX^{\cdot-}$  which then accepts another electron to give the dianion  $ArX^{2-}$ . This dianion then dissociates to  $Ar^{\cdot-}$  and  $X^-$ . There



is strong evidence that this is the correct mechanism for the electrochemical reduction of halonitrobenzenes in liquid ammonia. Teherani and Bard<sup>10</sup> have prepared the radical anions from *o*, *m*, *p*-chloronitrobenzenes, *m*-bromonitrobenzene and *o*, *m*, *p*-iodonitrobenzenes in liquid ammonia. The radical anions did not dissociate under these conditions but rather accepted another electron to give the dianions which did dissociate. The dianion from *m*-chloronitrobenzene did not dissociate. Savéant and Thiebault<sup>11</sup> have studied the electrochemical reduction of halobenzophenones in liquid ammonia. They found that the dianion of *m*-fluorobenzophenone did not dissociate. The dianions of *p*-chloro, *m*-bromo and *p*-bromobenzophenones did. The reduction of *m*-chlorobenzophenone gave different products depending on the conditions. There was no dissociation of the radical anion.

Recently Simonet, Chaquiq el Nadre and Mabon<sup>12</sup> have studied the electrochemical reduction of bromobenzene and 2-chloropyridine in benzonitrile. Under these conditions reduction of benzonitrile occurs to give its radical



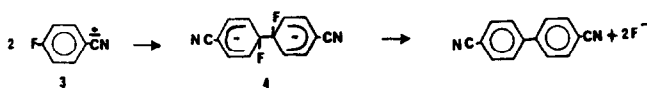
anion, eq.17, which transfers an electron to the substrate, ArX, eq.18. It was suggested that ArX<sup>•-</sup> dissociates to Ar<sup>•</sup> and X<sup>-</sup>. When the reductions were conducted in the presence of *t*-butylphenylnitron, 1, the product in solution was 2. This is the product of the addition of an aryl anion to 1. The product of aryl radical addition was not detected. The proposed mechanism requires that step 20 be faster than trapping by 1 and further that the aryl radical does not react with the benzonitrile. Furthermore step 20 represents combination of two species whose concentrations are quite low. These are rather remarkable requirements. If the ArX<sup>•-</sup> accepts another electron, 21, to give the anions Ar<sup>-</sup> and X<sup>-</sup> it can then be trapped by 1. This mechanism does not require any special features. Clearly all of the electrochemical data require a two electron reduction via the radical anion. These data also support a second electron addition to give a dianion which in some cases can be observed. In other cases it must dissociate rapidly to an aryl anion. Alternatively the second electron transfer can occur with concerted loss of the leaving group. There is no direct evidence that arene radical anions that have been generated electrochemically dissociate into aryl radicals.

Radical anions have also been generated by addition of electrons primarily through pulse radiolysis<sup>13</sup>. The results often differ widely from those obtained by electrochemical generation. Dorfman<sup>14</sup> has commented on the difference between aromatic radical ions generated by pulse radiolysis and those produced by reduction with sodium in THF. There are wide differences in various reports on the courses of these reactions and attempts to compare results from electrochemical experiments as mentioned earlier are often not meaningful.

Behar and Neta<sup>15</sup> formed the radical anions from 4-chloro, 3-bromo, 4-iodo and 2-iodonitrobenzenes. They decayed by second order process. They<sup>16</sup> also prepared the 4-bromobromobenzophenone radical anion which decayed

with a rate constant  $k < 7s^{-1}$ . This result is to be contrasted to the report of Saévant and Thiebaut<sup>11</sup> who generated the radical anion from *p*-bromobenzophenone electrochemically and reported decay rates of  $8 \times 10^4 \pm 2 \times 10^4 s^{-1}$  in DMF,  $2400 \pm 700$  in acetonitrile and  $590 \pm 35$  in ammonia. An explanation for this apparently wide difference in behavior is that the 4-bromobenzophenone radical anion is quite stable but it does add a second electron under electrochemical conditions and the dianion then dissociates to the anion and bromide ion.

The pulse radiolyses of 4-fluorobenzonitrile, fluorobenzene, 4-fluoroanisole, 4-fluoronitrobenzene and 2,4-dinitrofluorobenzene in water have been investigated<sup>17</sup>. The only radical anion observed was that from 4-fluorobenzonitrile. This radical anion had a lifetime of  $1.1 \pm 0.3 \mu s$  at 19°C. In alkaline solutions decay appears as a loss of fluoride ion whereas in acid solution protonation occurs at a diffusion controlled rate. These results are to be contrasted to those of Rieger *et al.*<sup>18</sup> and Houser *et al.*<sup>19</sup>. They prepared the radical anion electrochemically from 4-fluorobenzonitrile and showed that it dimerized and expelled fluoride to give 4,4'-dicyanobiphenyl. Very clearly the radical anion prepared under these conditions



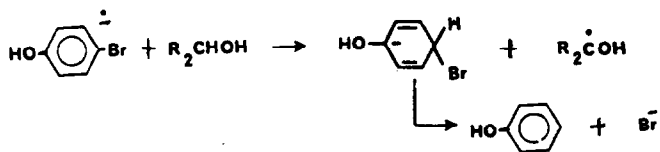
is different from the one prepared by pulse radiolysis.

In a similar vein San Roman *et al.*<sup>19</sup> treated fluorobenzene with solvated electrons generated by photoionization of sodium methylate. The radical anion generated under these conditions did not dissociate. It was in equilibrium with the solvated electron and it reacted with the methanol. This is to be contrasted to the report<sup>17</sup> that the radical anion from fluorobenzene could not be observed.

The above discussion serves to illustrate that the chemistry of radical anions is extremely complex and it is generally not prudent to consider results from a particular system as being generally applicable. The results certainly show that aromatic radical anions can accept a second electron to give a dianion which can then dissociate to the aryl anion and the leaving group. Having established this mechanism it is difficult to rationalize dissociation rate constants that have been reported<sup>2</sup> for radical anions of  $k=10^{10}s^{-1}$ . All of these rate measurements depend on certain assumptions as to the mechanism of the dissociation process, i.e. it is assumed that it is the radical anion that is dissociating.

#### REACTIONS OF RADICAL ANIONS WITH HYDROGEN SOURCES

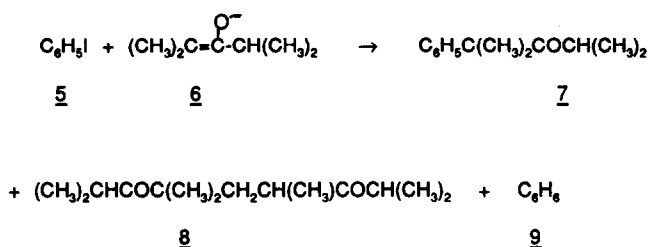
Arai and Dorfman<sup>4</sup> have shown that aromatic radical anions are reduced by alcohols. The radical anion from fluorobenzene reacts with methanol<sup>19</sup>. It has also been shown that *p*-bromophenol is reduced in the presence of hydrated electrons and isopropanol<sup>20</sup>. This observation was taken as evidence for dissociation of the *p*-bromophenol radical anion to bromide ion and the *p*-hydroxyphenyl radical. Alternatively hydrogen transfer can occur from the alpha carbon of the alcohol to the radical anion to give the anion which then expels bromide ion. Similar reductions have been observed in



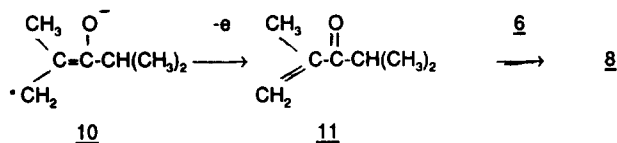
other systems<sup>18,21</sup>. The reaction of the radical anion from fluorobenzene has been already noted<sup>19</sup>.

The reaction of the radical anion with certain hydrogen sources such as alkoxide ion explains some early observation of Rossi and Bunnett<sup>22</sup>. They found that when isopropoxide ion and acetone enolate ion were allowed to react with halobenzenes that the isopropoxide ion was consumed with the production of benzene at a rate that competed effectively with the substitution process i.e. all of the isopropoxide was consumed. The radical mechanism requires that the phenyl radical show a special reactivity towards isopropoxide ion and that it selectively attacks on the isopropoxide ion to the exclusion of other hydrogen sources. This is, of course, at variance with what is known about the reactivity of the phenyl radical which is one of the more reactive radicals known<sup>23</sup>. If the radical anion attacks on the isopropoxide ion with hydrogen transfer then a new, more stable, radical anion is generated. Such reactions are well known<sup>4</sup>.

The reaction of an aromatic radical anion with hydrogen transfer also accounts for the different products observed from the reactions of iodobenzene, 2-bromopyridine and 2-chloroquinoline and various enolate ions containing  $\beta$ -hydrogens<sup>24</sup>. Iodobenzene, 5, gave with the enolate ion, 6, the products 7, 8, and benzene, 9, in 32, 20 and 20% yields



respectively. If the radical anion abstracts an hydrogen from the enolate ion in competition with substitution then benzene and the new radical anion, 10, are formed. The ion, 10, can give up an electron to give 11 which adds to 6 to give ultimately



8. 2-Chloroquinoline and 2-bromopyridine gave the expected substitution products unaccompanied by significant amounts of dimer, 8. The radical mechanism requires then that the phenyl radical abstract hydrogen from the enolate ion whereas the pyridyl and quinolyl radicals do not. In view of the fact that these are all sigma radicals such a reaction pattern is not expected<sup>7</sup>. The radical anion mechanism easily accommodates the results. There are three different radical anions undergoing competing abstraction and substitution reactions. The heteroaromatic ions are undoubtedly more stable than the iodobenzene radical anion and thus they are more selective in the reactions they undergo and thus substitution becomes the major reaction path.

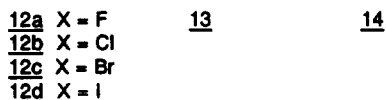
One might argue that hydrogen transfer to the radical anion is a route to arene and that at the same time dissociation to the aryl radical followed by attack on the nucleophile is the path to substitution products. Such a postulate is not in keeping with the results. It requires that the 2-chloroquinoline and 2-bromopyridine radical anions dissociate more rapidly than the iodobenzene radical anion. Although the relative stabilities of these three radical anions is not known, increased delocalization and the presence of the nitrogen in the ring are both stabilizing factors<sup>25</sup> and thus the radical anion mechanism is in accordance with the results.

## REACTIONS OF STABLE AROMATIC RADICAL ANIONS WITH NUCLEOPHILES

There is very positive evidence for the reaction with various nucleophiles of aromatic radical anions that do not dissociate. Chambers and Adams<sup>26</sup> showed that the p-dinitrobenzene radical anion generated electrochemically reacted with the water in dimethylformamide to give p-nitrophenol. Shein has suggested that substitution reactions of p-dinitrobenzene<sup>27</sup>, p-nitrochlorobenzene<sup>28</sup> and 2,4-dinitrochlorobenzene<sup>29</sup> involve reaction of nucleophiles with various radical anions. It has been demonstrated by Abe and Ikegami<sup>30</sup> that displacement of nitrite ion by hydroxide ion from o- or p-dinitrobenzene is kinetically controlled by the attack of hydroxide ion on the dinitrobenzene radical anion. More recently Russell et al.<sup>31</sup> have called attention to this work and they have issued the following caution "it seems appropriate to be cautious in assigning the S<sub>RN</sub>1 mechanism to all aromatic processes proceeding via a radical chain sequence".

In a recent report<sup>32</sup>, it was shown that the reactions of p-nitrobenzonitrile and 4-nitrophthalonitrile with the lithium salts of 2-R-5-nitro-1,3-dioxanes led to the expulsion of the nitrite ion and formation of a carbon-carbon bond. It was also shown that the radical anions of 4-nitrophthalonitrile and p-nitrobenzonitrile were formed during the reactions. These radical anions are stable towards dissociation of nitrite ion. It was found that oxygen lowered the rates of the reactions. These observations are precisely those that have been found for substitutions on aromatic radical anions. Since the radical anions do not dissociate and since the reactions are inhibited by oxygen there is no viable alternative to direct reaction between the radical anion and the nucleophile.

It has now been found that para substituted halonitrobenzenes, 12a-d, react, in the dark and under illumination,  $p\text{-XC}_6\text{H}_4\text{NO}_2 + \text{C}_6\text{H}_5\text{SO}_2^-\text{Na}^+ \rightarrow p\text{-O}_2\text{NC}_6\text{H}_4\text{SO}_2\text{C}_6\text{H}_5$



in both DMSO and HMPA, with sodium benzenesulfinate, 13, to give the sulfone, 14. Sodium benzenesulfinate was chosen as the nucleophile because it is one of the most easily handled nucleophiles and thus studies of its reactions are conducted without difficulty.

Both the reactions in DMSO of 12a-c and 12a-d in HMPA showed that the yield of product, 14, was always greater for the illuminated samples. In DMSO, after 24 hr at room temperature, 12a gave 64% 14 in the light and 54% in the dark. The light reaction of 12b gave 16% 14 and the dark yielded 11%. With 12c the yields were 29 and 22%.

The results obtained in HMPA are much more significant in that the yield differences were greater. After 24 hr the illuminated sample of 12a gave 78% of 14 and the dark reaction yielded 70%. In the case of 12b the yields were 67% for the illuminated reaction and 42% for the dark reaction. The illuminated reaction of 12c gave 72% of 14 and the dark reaction 50% of 14. The p-iodonitro compound, 12d, yielded 63% in the light and 36% of 14 in the dark. When the dark reactions in HMPA were repeated with the addition of 10 mole% of galvinoxyl, the yields of sulfone from 12a dropped from 70 to 53%. In the case of the reaction of 12b the ratio of sulfone to starting material dropped from 0.69 to 0.58. A yield could not be calculated because of contamination. The reaction of 12c in the dark and in the presence of 10 mole% galvinoxyl led to a decrease in yield of sulfone from 50 to 42%. Galvinoxyl did not appreciably alter the yield of sulfone from 12d.

These results are exactly the same as those that have been used to establish that radical nucleophile substitution reaction are chain reactions which involve radical anions. The important difference between these observations and earlier ones is that the radical anions from 12a-d have been shown to be stable towards dissociation<sup>10,33</sup>. They have been prepared electrochemically and by pulse radiolysis. They react with themselves in bimolecular reactions to give various

products. They do not expel halogen in a unimolecular process. Although the earlier studies did not address themselves to the mechanism of these reactions, it has been more or less assumed that they follow a well-recognized addition-elimination sequence<sup>24</sup>. This reaction mechanism would not show catalysis by light nor inhibition by galvinoxyl. The results demonstrate that an addition-elimination reaction is not able to account for the findings. Direct reaction of the nucleophile with the radical anions from 12a-d accounts in all regards with the experimental results.

These findings are supported by the recent results of Sammes et al.<sup>35</sup> They studied the displacement of nitro groups from *p*-nitrobenzaldehyde, methyl-*p*-nitrobenzoate, trifluoromethyl-*p*-nitrobenzene, *p*-nitrobenzonitrile and *p*-dinitrobenzene by various phenoxide ions. These reactions yielded substituted diphenyl ethers. They showed that the reaction of *p*-dinitrobenzene with 2,6-dibromo-4-methylphenoxide ion was completely inhibited by adding one equivalent of 1,1-diphenyl-2-picrylhydrazyl. They concluded that the reaction was radical in nature. They did not elaborate on this conclusion.

As was mentioned earlier, the fluorobenzene radical anion does not dissociate to a phenyl radical and fluoride ion. In fact, fluorobenzene reacts with a variety of nucleophiles<sup>2</sup> under the conditions used for radical anion nucleophile substitution reactions. Since dissociation does not occur, it seems that direct reaction between the nucleophile and the radical anion is the process by which products are formed.

All of these results show that observable aromatic radical anions with suitable leaving groups react with nucleophiles in a bimolecular process to give the products of substitution.

#### REACTIONS OF ARYL RADICALS WITH NUCLEOPHILES

It is now established that aromatic radical anions containing leaving groups can react with nucleophiles to give the products of substitution. It might be argued that apparently less stable radical anions do dissociate in a unimolecular process to give aryl radicals which then attack on the nucleophiles. It is important to reiterate that this pathway imposes stringent requirements on the rates of the reactions of the nucleophile with the aryl radicals. The phenyl radical has been shown to be extremely reactive towards a variety of substrates<sup>23</sup>. It is characteristic of the radical anion nucleophile substitution reactions that they proceed to give, in general, two products, those of substitution and those of reduction. Other typical radical products have never been found. There have been a few tests of the reactions of aryl radicals with nucleophiles. Bartak, Danen and Hawley<sup>28</sup> have decomposed phenylazotriphenylmethane (PAT) in DMSO in the presence of 0.1M sodium nitrite. The products were shown to be ca. 5% of nitrobenzene and 75% benzene. This result is to be contrasted to the finding that electrolysis of *p*-iodonitrobenzene in DMSO in the presence of nitrite ion "nearly eliminates hydrogen abstraction as a reaction pathway, as evidenced by the absence of a nitrobenzene wave"<sup>36</sup>. The product was *p*-dinitrobenzene. Clearly these results are at variance with each other. The radical mechanism is hard pressed to explain the great differences in yields of substitution products. If one considers that the PAT decomposition involves phenyl radicals and the electrochemical experiment involves attack by nitrite ion on the *p*-iodonitrobenzene radical anion then there is no problem in understanding the large yield changes.

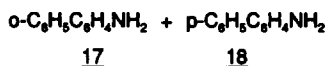
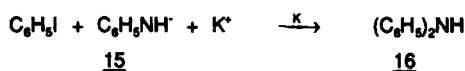
In another series of experiments Helgee and Parker<sup>37</sup> measured absolute rate constants for the reactions of the reduction products of  $\alpha$ -naphthylidiazonium salts with DMSO and DMSO containing thiophenoxide ion. They assumed that they were observing the reactions of  $\alpha$ -naphthyl radicals. They find "the rate constant that we observe for the reaction between  $\alpha$ -naphthyl radical and  $C_6H_5S^-$ ,  $1.7 \times 10^9 M^{-1} s^{-1}$  suggests that the data reported by Pinson and Saveant<sup>38</sup> for the reduction of 1-bromonaphthalene in the presence of  $C_6H_5S^-$  are inconsistent with the involvement of the  $S_{RN}1$  mechanism in the reaction which resulted in 100% yield of  $\alpha$ -naphthylthiophenyl ether". The results of Helgee and Parker<sup>37</sup> show that



attack on the solvent competes with substitution whereas Pinson and Saveant<sup>38</sup> only found substitution. Once again it is difficult to rationalize the results on the basis of a common intermediate, i.e. the  $\alpha$ -naphthyl radical.

#### REACTIONS OF PHENOXIDE IONS AND ANILIDE IONS WITH AROMATIC SUBSTRATES

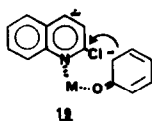
When potassium anilide ion, 15, was allowed to react with iodobenzene, in the presence of potassium, the substitution products 16, 17, and 18 were formed in 19, 11 and 11% yields respectively<sup>1</sup>. The production of these products



without the formation of any meta substituted product is not in accord with other phenylation reactions by phenyl radicals<sup>39</sup>. Invariably phenyl radicals react to give all three substitution products, ortho, meta and para. Direct displacement by the anilide ion on the radical anion accounts for the regiochemistry. There are partial negative charges on nitrogen and the ortho and para carbons. These observations will be discussed in more detail in the summary.

Recently Alam et al.<sup>40</sup> have studied the electrochemically stimulated reactions of various phenoxide ions with *p*-bromobenzophenone, *p*-chlorobenzonitrile and 2-chloroquinoline. The results of these experiments were quite remarkable<sup>41</sup>. *p*-Bromobenzophenone coupled only at the ortho and para positions of the phenoxide ion in the ratio 2:1. A similar result was obtained with *p*-chlorobenzonitrile. 2-Chloroquinoline gave only the product of ortho coupling! Beugelmans and Bois-Choussey<sup>42</sup> have studied the photostimulated reactions of a variety of aromatic compounds containing bromine, which functions as the leaving group, with phenoxides and naphthoxides. Once again remarkable regiospecificity was found. For example,  $\beta$ -naphthoxide reacted with *p*-bromobenzonitrile to give an 85% yield of the  $\alpha$ -substituted product. When the two ortho positions of the phenoxide were blocked, coupling occurred exclusively at the para position.

These reactions show the characteristics of ionic processes rather than free radical substitutions. A mechanism analogous to that for substitution by anilide ion is entirely compatible with the experimental observations. The coupling of the 2-chloroquinoline can be understood in terms of an intermediate complex, 19.



In no case has such regiospecificity been found for free radical arylation reactions<sup>39</sup>.

#### LEAVING GROUP, SOLVENT AND COUNTER ION EFFECTS IN ELECTROCHEMICALLY STIMULATED RADICAL ANION SUBSTITUTION REACTIONS

Electrochemical stimulation of these substitution reactions is remarkably efficient and subject to quantitative control. Most of the substrates that have been used are those that form radical anions readily. They include chloroquinolines, halobenzonitriles, halobenzophenones, halonitrobenzenes and in at least one instance iodobenzene. There have been no reports of reactions of the other halobenzenes.

The chemistry of the benzonitriles is of particular interest to our understanding of the mechanism of these substitution reactions. In early work<sup>18a</sup> a variety of aromatic nitriles were reduced to stable anion radicals which were observed by EPR. *p*-Aminobenzonitrile and *p*-fluorobenzonitrile gave *p,p'*-dicyanobiphenyl. The formation of this material was attributed to loss of amide ion and fluoride ion from the radical anion to give *p*-cyanophenyl radicals which were thought to dimerize. Very clearly the high reactivity of the phenyl radicals precludes such a mechanism. Dimerization of the radical anions followed by expulsion of either amide ion or fluoride ion accounts for the results.

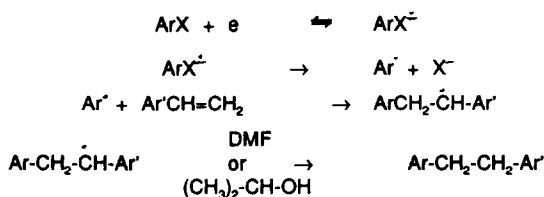
More recently Bartak et al.<sup>43</sup> and Buick et al.<sup>44</sup> studied the electrochemistry of a number of halobenzonitriles in DMF. Of particular interest was the study of *p*-chlorobenzonitrile. It was concluded that the radical anion from this substance dissociated to the *p*-cyanophenyl radical which then was further reduced to the anion which reacted with the solvent or with adventitious water to give benzonitrile. An attempt was made to trap the *p*-cyanophenyl radical with cyanide ion. Very little terephthalonitrile was formed. This result was compared to earlier work<sup>45</sup> in which *p*-chloronitrobenzene was reduced in the presence of nitrite and cyanide ion to give the substitution products in quantitative yields.

These observations were explained by postulating that the *p*-cyanophenyl radical was formed very rapidly and thus close to the electrode surface which led to its rapid reduction. The authors further postulated that the loss of halogen from the chloro, bromo, and iodobenzonitrile anions must have rate constants of at least  $10^{10}\text{s}^{-1}$ .

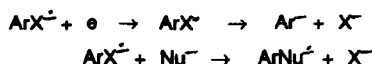
An alternate and more viable explanation is that the reaction of the *p*-chlorobenzonitrile anion with cyanide ion is relatively slow and that the radical anion is thus reduced. This explanation is in accord with other reactions of *p*-chlorobenzonitrile under electrochemical stimulation in the presence of nucleophiles. Reduction of *p*-chlorobenzonitrile in the presence of diethyl phosphite anion in ammonia gave 100% yield of the substitution product<sup>46</sup>. Similarly<sup>47</sup> it was found that reduction of *p*-chlorobenzonitrile in the presence of the anion of ethyl cyanoacetate in ammonia yielded 48% of the substitution product. The reaction of *p*-chlorobenzonitrile with phenoxide ion in ammonia under electrochemical stimulation yielded ca. 10% of the ortho and para substituted coupling products<sup>40</sup>.

In another study<sup>48</sup> *p*-chlorobenzonitrile and various styrenes were reduced in ammonia in the presence and absence of isopropanol. The reactions were also conducted in the presence and absence of redox catalysts. In DMF only a redox catalyst was used. The DMF served as a hydrogen source. In ammonia the addition-reduction product, 4-(2-phenylethyl)benzonitrile was formed in 90% yield under the best conditions. In DMF an 80% yield of the same product was obtained.

The authors suggested the following mechanism for the overall reaction. This reaction sequence and the others which invoke the *p*-cyanophenyl radical as a key intermediate are hard pressed to explain the very low yield in the presence



of cyanide ion to the varying yields of other substitution products up to 100% with diethyl phosphite anion. If the radical anion is formed and decomposes so rapidly why is it trapped so readily by the phosphite ion but not by cyanide? The alternate mechanism is much more able to explain the results. The radical anion is formed and there is competition



between reduction and nucleophilic substitution. The yields of the substitution product will vary with the nucleophilicity of a particular nucleophile and the solvent. Thus the formation of no product to 100% yield is accounted for.

The reactions of the various styrenes is also explained in terms of addition of the radical anion onto the styrene to give the benzylic radical which abstracts an hydrogen from DMF or isopropanol. This latter mechanism does not require that the very reactive phenyl radical seek out the styrene and react with it to the exclusion of all other hydrogen sources. This requirement is particularly telling when the mechanism also requires that the intermediate benzylic radical reacts readily with DMF or isopropanol.

There are other experiments in which the radical anion mechanism explains the results without any assumptions. Pinson and Saveant<sup>46</sup> studied the electrochemically stimulated reaction of p-bromobenzophenone with thiophenoxide ion in acetonitrile. When the counter ion was tetrabutylammonium the substitution product was formed in 95% yield with 3% of benzophenone. When the counter ion was sodium complexed with 18-crown-6-ether the yield of substitution product dropped to 38% and 17% of benzophenone was produced. Any mechanism requires then that the nature of the counter ion must play an important role in determining the product ratios. There does not appear to be any evidence for implicating the counter ion if the reaction involves attack by an aryl radical on the nucleophile. On the other hand, if the mechanism involves nucleophilic attack on the radical anion then the nature of the counter ion can play an important role in modifying the nucleophilicity of the nucleophile. Thus one can understand the change in the product ratios.

In another series of experiments, the tetrabutylammonium salt of thiophenol was allowed to react with p-bromobenzophenone in DMSO. The yield of substitution product was 60% and no benzophenone was produced. When sodium ion complexed with 18-crown-6-ether was the counter ion 40% of the substitution product was obtained along with 29% of benzophenone. Competition between substitution and reduction of the intermediate radical anion provides an explanation for these results.

In the same paper it is reported that p-bromobenzonitrile and p-iodobenzonitrile were allowed to react with benzenethiolate ion in acetonitrile under electrochemical stimulation. p-Bromobenzonitrile yielded 80% of the substitution product, 4% recovered starting material and 10% of benzonitrile. p-Iodobenzonitrile yielded 20% of the substitution product and 80% of benzonitrile. Very clearly, the same radical cannot be an intermediate. The authors suggest that the radical is formed in both cases but with the iodo compound it is formed very near to the electrode and it is thus rapidly reduced. This is the same argument that was used in the case of the p-chlorobenzonitrile. It is not reasonable to conclude that reduction of a particular substrate is fast in one case and slow in another. The alternate explanation is that the p-iodobenzonitrile radical anion accepts an electron more readily than does the p-bromobenzonitrile radical anion.

It was also reported that when 1-bromonaphthalene was allowed to react with benzenethiolate ion in DMSO under electrochemical stimulation, there was obtained an 100% yield of the substitution product. Under identical conditions in acetonitrile, 32% of the substitution product and 40% of naphthalene are formed. Clearly there is a solvent effect on the ratio of products. The authors explained this solvent effect on the basis that the naphthyl radical reacted more rapidly with acetonitrile than with DMSO. This argument is not supported by the finding that p-bromobenzonitrile reacted in acetonitrile with benzenethiolate ion to give 80% of the substitution product and 10% of benzonitrile. The radical mechanism requires that the 1-naphthyl radical and the p-cyanophenyl radical show significant differences in their reactivities towards these two solvents. Such a difference is not supported by what is known about the reactivities of aryl sigma radicals<sup>7</sup>.





The major thrust of their work involved competitive photostimulated reactions competing diethyl phosphite anion and pinacolone enolate ion with various substrates. These were fluorobenzene, chlorobenzene, bromobenzene, iodobenzene, diphenyl sulfide and phenyltrimethylammonium ion. The relative rate ratio for the two nucleophiles was found to be  $1.37 \pm 0.11$  with the phosphite anion being the more reactive. These results indicate that there is a constant difference in leaving group ability in these competitive experiments. They do not, of course provide any information in the variation in absolute rates. It was noted that fluorobenzene reacted more slowly than the other substrates. These experiments take as their central assumption that there should be reactivity-selectivity observations if the radical anion and nucleophile react<sup>6</sup>. This assumption has been shown not to apply in many bimolecular substitution processes<sup>8,54</sup>. The absence of reactivity-selectivity effects cannot be used to rule out the radical anion nucleophile mechanism.

When thiophenoxide ion was allowed to compete with pinacolone enolate ion with iodobenzene as the substrate, the rate ratio was  $0.079 \pm 0.006$  with the enolate ion being the more reactive. When the diethyl phosphite anion was used the rate ratio was  $0.061 \pm 0.007$  with the phosphite anion being the more reactive. These results are clearly explained by the anion radical nucleophile mechanism where the enolate ion and phosphite anion are more nucleophilic than the thiophenoxide ion. The results are in agreement with those of Halgee and Parker<sup>27</sup> which were discussed earlier. Galli and Bunnett in the same paper<sup>53</sup> reported so called "deviant results". They found that when chlorobenzene was allowed to react with diphenylphosphide ion and pinacolone enolate ion in competition the ratio of products was  $10.1 \pm 1.3$  with the phosphide ion being the more reactive. This result is to be compared to the same two reactants reacting with iodobenzene in the dark. Under these conditions the ratio of products was 5.2. p-Iodotoluene was allowed to react with these reagents in the dark and under illumination. The ratios of products was found to be 6.0 and 5.7 respectively. Clearly the radical nucleophile mechanism cannot account for these results. There should be no change in the ratio of products with a change in leaving group. The radical anion nucleophile mechanism provides an easy understanding of these results in that it allows for a leaving group effect.

In another series of experiments diphenylphosphide ion and diethyl phosphite anion were allowed to react with bromobenzene under illumination. The ratio of products was found to be  $15.8 \pm 0.4$  with the phosphide being the more reactive. When the same reactants were allowed to react with p-tolyl iodide in the dark the product ratio was  $4.39 \pm 0.18$ . Once again a leaving group effect is evident. In both cases the poorer leaving group, chlorine in the first and bromine in the second, led to larger competitive rate ratios. This behavior is precisely that predicted if a leaving group effect is operating.

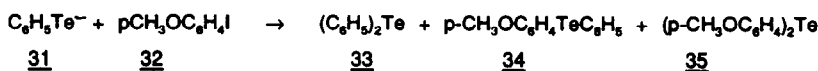
In another series of experiments Bunnett and co-workers<sup>50,55</sup> studied the reactions of acetone enolate ion with halobenzenes, phenyltrimethylammonium iodide, diphenyl ether, diphenyl sulfide and diphenyl selenide under potassium stimulation. They measured the yields of benzene, phenylacetone and 1-phenyl-2-propanol. They found them to be substrate dependent. The yields of benzene increased from 4% with iodobenzene as the reactant to 29% with fluorobenzene as the reactant. Diphenyl ether yielded 41% benzene. These results are not in accord with the radical nucleophile mechanism. They are in accord with competing substitution and reduction. A poor leaving group such as phenoxide ion slows the substitution process and allows reduction to compete more effectively.

A similar behavior was reported by Tremelling and Bunnett<sup>56</sup>. They studied the competitive reactions of potassium acetone enolate ion and potassium amide with mesityl iodide, bromide, chloride and fluoride under potassium stimulation. The products were mesitylene, mesitylamine, mesityl acetone and its reduction product, 1-mesityl-2-propanol. Once again the amount of arene produced varied as a function of the leaving group. The maximum was 80% from the fluoro compound and the smallest amount was 17% from the iodo compound. The ratio of enolate products to amide product was relatively constant. The ratio was 0.46 for fluoromesitylene and 0.57 for bromomesitylene. The wide variation in arene yield is once

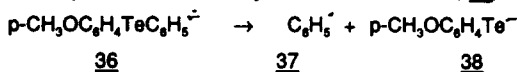
again easily understood in terms of reduction in competition with substitution.

#### ARYL GROUP SCRAMBLING REACTIONS

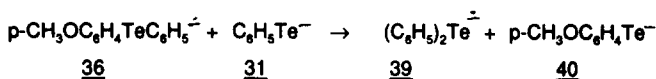
When the arsenic containing nucleophiles,  $Ar_2As^-$ , the antimony containing nucleophiles,  $Ar_2Sb^-$ , and tellurium containing nucleophiles,  $ArTe^-$ , were allowed to react with various substrates products of aryl group scrambling were obtained<sup>f</sup>.



So for example, reaction of  $C_6H_5Te^-$ , 31, with anisyl iodide, 32, yielded all three tellurides, 33, 34 and 35. The radical mechanism requires that the initially formed radical anion, 36, dissociates into a phenyl radical, 37, and the telluride, 38.



The anisyl radical would then react with 38 to give ultimately 35 and the phenyl radical would react with 31 to give 33. The scrambling of the aryl radicals has to take place without any competition from other known reactions of these radicals. The radical anion nucleophile mechanism postulates that 36 once formed can react with 31 to generate 39 and 40 which ultimately lead to 33 and 35.



Rossi and Bunnett<sup>3</sup> treated  $Ph_3As$  and  $Ph_3Sb$  in liquid ammonia in the presence of acetone enolate ion with potassium. The thrust of this study was to trap phenyl radicals with the acetone enolate ion. The idea was that intermediate aromatic radical anions could dissociate and add to the enolate ions. Those substances which only gave benzene were postulated to be cleaved by addition of a second electron with expulsion of the phenyl anion which reacted with the solvent to give benzene. The compounds  $Ph_3As$  and  $Ph_3Sb$  gave only benzene. No phenyl acetone was obtained and thus it was concluded that the two radical anions did not dissociate. If this is the case then the observed aryl group scrambling cannot involve dissociation. Scrambling via attack of the nucleophile on the radical anion is of course a viable alternative.

#### STEREOCHEMICAL STUDIES

Aguar and his co-workers<sup>57</sup> have studied the reactions of lithium diphenylarsenide ion with cis and trans-1,2-dichloroethylene and cis and trans- $\beta$ -bromostyrene. The reactions of lithium diphenylphosphide anion were also investigated. In all cases the substitution products were obtained with complete retention of configuration. Although these reactions were not studied mechanistically, it is known that vinyl halides undergo nucleophilic substitution with acetone enolate ion under illumination and with potassium stimulation. If the reactions studied by Aguar and his co-workers involved vinylic radicals, they would have to be captured before they lost their stereochemistry. The barrier for loss of stereochemistry is ca. 2 k.cal/mole which leads to a life time of individual isomers of  $10^{-8}$ - $10^{-10}$  sec<sup>58</sup>. This rate requires that combination of the radical and anion be diffusion controlled if the radical mechanism is operating. Reaction of the radical anion with the nucleophile imposes no such restrictions.

### SOLVENT EFFECTS, FRAGMENTATION PATTERNS AND COUNTER IONS AS EVIDENCE FOR MECHANISM

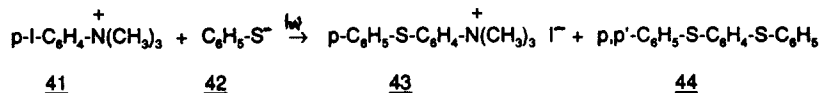
One of the major difficulties with accepting the idea that aryl radicals are formed in these reactions and that they then attack the nucleophiles is the lack of attack by these radicals on other substrates present in the reaction media. The photochemical initiated reactions are quite remarkable in that they often yield substitution products to the exclusion of reduction products, i.e. arenes. For example Moon and Wolfe<sup>59</sup> have studied the photochemically stimulated reactions of a number of enolate ions with 2-chloroquinoline in a variety of solvents. In ammonia they obtained a 90% yield of the substitution product when the potassium salt of acetone was allowed to react with the substrate. The same reactants in THF gave 81% of the substitution product and 13% recovered starting material. 1,2-Dimethoxyethane yielded 28% of the substitution product and 59% of recovered starting material. DMF as solvent resulted in 74% of the substitution product and 3% recovered starting material. The poorer material balance than was obtained in the other solvents was attributed to losses during isolation.

In another series of experiments DMSO was found to yield varying amounts of substitution products with the highest yield being 69% in a dark reaction. The formation of quinoline was not noted. Other workers have found DMSO to be an excellent solvent for these substitution reactions<sup>2</sup>.

Bunnett, Scamehorn and Traber<sup>60</sup> studied the photochemical stimulated reaction of potassium diethyl phosphite with iodobenzene in a variety of solvents. They found that iodide ion release was in excess of 90% in ammonia, DMSO, DMF and acetonitrile. The yields of the substitution product in DMSO and DMF were 68 and 63%. The authors suggested that the yields were actually much higher and that losses occurred during the isolation of the products. The yields in ammonia and acetonitrile were 96 and 94%. The formation of benzene was not reported. Arene is often found when the reactions are stimulated by metal or electrochemically. Rossi and de Rossi<sup>61</sup> state that the photostimulated reactions of the potassium ion of acetone lead to low yields of benzene.

The lack of attack on solvent has been questioned by Helgee and Parker<sup>37</sup>. They calculated that, from their results, to achieve a 99.9% yield of substitution product the rate of capture of the aryl radical in DMSO would have to be  $4.5 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ , in acetonitrile  $4.8 \times 10^{10}$  and in DMF  $1 \times 10^{12}$ . It is known that hydrogen abstraction by a phenyl radical from THF is three times faster than from DMF<sup>62</sup> and thus in order to obtain high degrees of substitution reactions the phenyl radical would have to capture the nucleophile extremely rapidly. In fact the rates in DMF and THF exceed the diffusion rate<sup>63</sup>. The reactions in DMF, THF etc. which lead to high yields of products of substitution are not in accord with the radical mechanism. This mechanism requires that the aryl radicals react with the solvents rather than the nucleophiles. Since this does not occur the conclusion must be that aryl radicals were not present during the reactions.

In another series of experiments Bunnett et al.<sup>60</sup> studied the reactions of p-iodophenyltrimethylammonium ion, 41, with thiophenoxide ion, 42. In ammonia the product, 44, was formed in 95% yield. In water iodide ion was released



quantitatively. The product, 44, was formed in only 5% yield along with 38% of 43. Much tar was formed, ca. 20% of the mass of 41 used.

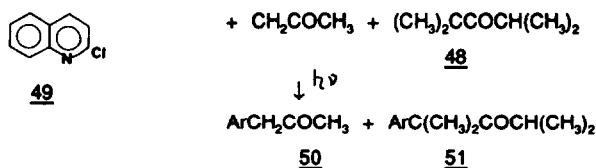




Komin and Wolfe<sup>68</sup> have studied the reactions of the potassium, sodium and lithium salts of acetone with 2-bromopyridine in ammonia and under photostimulation. They found that the potassium salt yielded 95% of the substitution product, the sodium salt gave 74% and the lithium salt gave only 6% with 58% of recovered starting material. These results clearly indicate that the nature of the cation can play an important role in governing the rate of the substitution process. These results are certainly in agreement with a change in nucleophilicity with changes in the counter ion and they thus support the radical anion nucleophile mechanism. It is not quite clear how a change in counter ion would affect the rate of attack of the aryl radical on the nucleophile. One might think that if the reaction is slowed the radical would react in some other fashion.

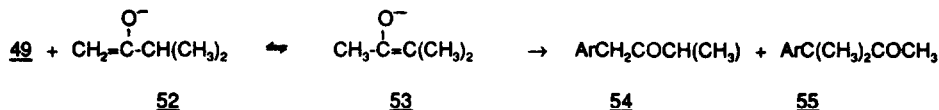
#### SELECTIVITY IN THE REACTIONS OF ENOLATE IONS

Hay and Wolfe<sup>69</sup> studied the competitive reactions of the potassium salt of acetone and the potassium salt of 2,4-dimethyl-3-pentanone, 48, with 2-chloroquinoline, 49. The products were the ketones, 51 and 50, in the ratio of 3.2:1.



Clearly attack on the tertiary carbon is favored.

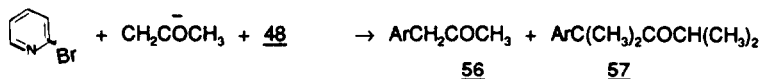
In another series of experiments 2-chloroquinoline was allowed to react with the mixture of enolates, 52 and 53.



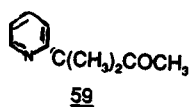
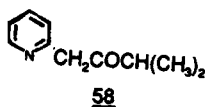
After 1hr the crude reaction mixture was found to contain 62% of 54, 13% of 55, 5% of quinoline and 6% of starting material. It was noted that the product ratio, 4.75:1, of 54 to 55 was significantly different from the reported 9:1 ratio obtained on phenylation of the same mixture of enolate ions<sup>70</sup>.

The authors concluded that there was a high selectivity towards the tertiary enolate ion, 53. The equilibrium mixture of 52  $\rightleftharpoons$  53 contains ca. 98% of 52.

More recently Komin and Wolfe<sup>68</sup> have studied competitive reactions of 2-bromopyridine with acetone enolate ion



and 48. The yields of products were 21% of 56 and 77% of 57. The product ratio, 57:56 was found to be 3.7:1 which is very nearly the same 3.2:1 as was found for the 2-chloroquinoline reaction. They also allowed 2-bromopyridine to react with the enolates 52 and 53. The products, 58 and 59 were formed in the ratio 7:1.



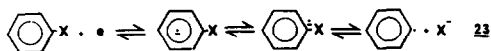
The results indicate that the nature of the substrate has a large influence on the ratio of products obtained. The radical mechanism cannot account for this variation. The aryl radicals are produced prior to their interaction with the nucleophiles and thus the only discrimination that could arise would be if they were themselves capable of selectivity. This concept has no experimental support.

The interactions of the radical anion with the nucleophile provides an explanation for the observed selectivity. The order of stability of the radical anions is 2-chloroquinoline most stable followed by the 2-bromopyridine ion and least stable bromobenzene. The rate of attack on the radical anion will be controlled by their reactivity and the slower the reaction the more selective it will be. The reason for favoring the tertiary site will be discussed in the summary.

#### SUMMARY

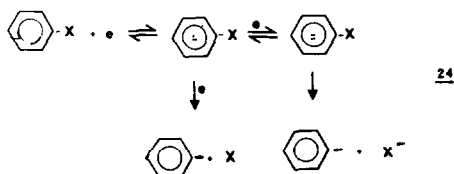
Although the various experimental results that have been discussed in this paper are not exhaustive, the discussion has touched upon essentially every area of mechanistic investigation. The results are all explained by the radical anion nucleophile mechanism competing with two electron reduction.

The reduction sequence involves initial addition of an electron to the  $\pi$  system. If loss of the leaving group is going to occur at this stage then the electron must leave the  $\pi$  orbital and enter the  $\sigma^*$  orbital of the carbon leaving group bond. Subsequent to this electron shift, dissociation to the aryl radical and the anion X can occur, eq. 23<sup>71</sup>.



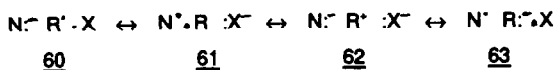
Some calculations<sup>72</sup> have indicated that in polychloro aromatic systems, the electron adds directly to the  $\sigma^*$  orbital. These calculations do not include the role of the solvent or the presence of and the nature of the counter ion.

Alternatively the electron adds to the  $\pi$  system, eq. 24, to give the radical anion which in some cases accepts another electron to give the dianion which then dissociates. This reaction undoubtedly involves one of the electrons of the dianion entering the  $\sigma^*$  orbital of the C-X bond.

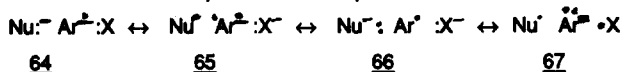


When the  $\pi$  system does not possess a group that can substantially delocalize the electron, the nitro group is an example, then direct addition of the second electron to the  $\sigma^*$  orbital with expulsion of X can occur.

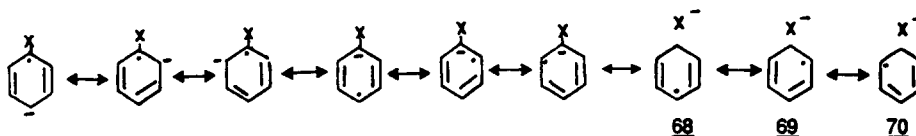
How does the nucleophile interact with the radical anion and why is the displacement process so facile? The Pross-Shaik<sup>73</sup> model for the  $S_N2$  reaction provides an understanding of the factors which control the radical anion nucleophile reaction. They consider the contributors to the transition state for the  $S_N2$  reaction to be 60-63. The importance of their approach is that it emphasizes that the initial interaction involves a single electron shift.



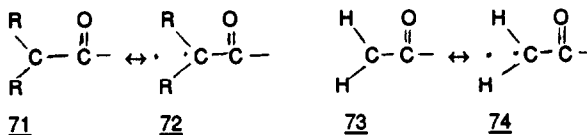
The same concept applied to the systems under investigation here lead to 64-67. Approach of the nucleophile to ArX will occur with an early electron shift if the nucleophile is soft and polarizable. The ease with which ArX can accept



the electron will be a factor in the determination of the rate of the reaction i.e. contributor 67 can stabilize the system. So for example, a nitro substituent can delocalize the electron in the initial radical anion and in essence lower the energy of the transition state by a greater contribution of 73 than when it is not present. Clearly, the bond strength, C-X, will also be reflected in the overall rate. It may not be as important as in a conventional S<sub>N</sub>2 reaction. The reason for this is that introduction of the electron into the π system raises the energy of the HOMO of the σ bond, i.e. weakens it, and lowers the energy of the σ\*. A valence bond approach illustrates this via contributors 68-70.



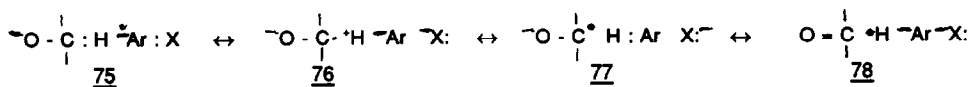
Are these concepts born out by the experimental results? A review of those nucleophiles that participate in the reactions where substitution is occurring on simple aryl halides and substances such as diphenyl sulfide, phenyltrimethylammonium salts and diphenyl ether reveals that the nucleophiles are soft, i.e. highly polarizable<sup>74</sup>. They do not have to approach closely to the C-X bond to begin to transfer the electron and thus Coulombic and steric interactions are minimized. This concept is further supported by the observations that tertiary enolate ions are significantly more reactive than primary ones. Loss of an electron from 71 gives the tertiary radical, 72, whereas loss from 73 yields 74 a primary



radical. The order of radical stability is 3° > 2° > 1°<sup>75</sup>. The primary C-H bond is ca. 7 kcal/mole stronger than the tertiary C-H bond which is a reflection of radical stability.

This analysis provides an explanation for substitution on carbon when phenoxide ion and anilide ion participate in these reactions. The more polarizable carbon sites react with the radical anion.

Another feature of this overall mechanistic scheme is that it explains the high reactivity towards transfer of α-hydrogens of alkoxides relative to other hydrogen sources. The important contributors to the transition state, using the Press-Shaik model, are 75-78. Electron transfer from 75 gives the contributor 76 which is stabilized by the negative charge



on oxygen. Contributor 78 illustrates this stabilization. Initial electron transfer is thus more facile than when the negative charge is not present. Polar contributors to the transition state for hydrogen abstraction by electronegative atoms and radicals have been well recognized for many years.<sup>62</sup> The overall process illustrated by 75-78 leads from one radical anion to another one with regeneration of the  $\pi$  system of the aromatic moiety.

In conclusion it is important to reiterate that these substitution reactions are chain reactions and in order for them to proceed efficient initiation is required. From a practical point of view lack of reaction should be viewed in the context of the chain mechanism. In some cases alternative modes of initiation, solvent and counter ion structure may be altered to achieve reaction.

## EXPERIMENTAL

The reactants were mixed in 0.01 mole quantities and then dissolved in 20 ml of solvent. In the reactions conducted in the presence of Galvinoxyl 10 mole percent of this material was added. The HMPA reaction mixtures were irradiated for 24 hr with two 40 watt fluorescent lights. The DMSO reaction mixtures were irradiated for 48 hr with a 20 watt fluorescent light. After the appropriate times, 10 ml of the reaction mixture was added to 75 ml of water. The mixtures were filtered and the products were air dried to constant weight. The product from p-fluoronitrobenzene was shown to be the sulfone by <sup>13</sup>C NMR spectroscopy. All of the other products consisted of sulfone and starting material. Carbon-13 NMR spectroscopy was used to determine the relative amounts of these materials and the yield of sulfone was then calculated.

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