



SOME CHEMISTRY OF AROMATIC FLUORINE CONTAINING RADICAL ANIONS

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Abstract: A review of the literature and ab initio calculations show that aromatic fluorine containing radical anions do not readily dissociate into aryl radicals and fluoride ions. © 1997 Elsevier Science Ltd.

In 1991 a paper appeared in which it was concluded that aromatic radical anions containing leaving groups can react with nucleophiles by a bimolecular displacement process.¹ Subsequently another paper appeared which supported this conclusion.²

Several papers have attacked the conclusions reached in the two publications and they have claimed that in fact the $S_{RN}1$ mechanism best fits the available data.^{3,4,5} This mechanism involves formation of a radical anion, $ArX^{\cdot-}$, by addition of an electron to ArX , followed by dissociation to Ar^{\cdot} and X^- . The aryl radical is then thought to attack on a nucleophile, Nu^- , to give $ArNu^{\cdot-}$ which then transfers an electron to ArX to regenerate $ArX^{\cdot-}$.

The bimolecular $S_{RN}2$ mechanism postulates that the nucleophile attacks on $ArX^{\cdot-}$ to give $ArNu^{\cdot-}$ and X^- .

One of the major reasons for invoking the $S_{RN}2$ mechanism is that the overall rates of the

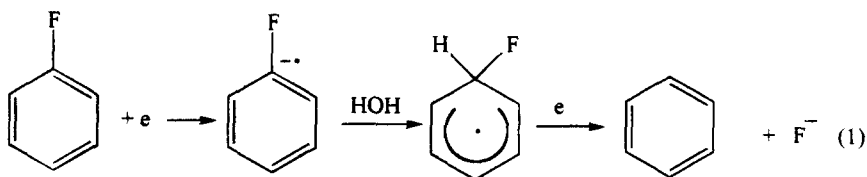
reactions are leaving group dependent. Within the halogen series the rates are $I > Br > Cl > F$. There are many other leaving groups that participate in these reactions as well and they also show characteristic rate behavior.⁶ Another reason for invoking the $S_{RN}2$ reaction mechanism is to explain the product composition which is also a function of the leaving groups. The $S_{RN}1$ mechanism postulates that the radical anion dissociates into Ar^{\cdot} and X^{-} . The aryl radical is then a common intermediate irrespective of the nature of X. In general it is found that a common intermediate leads to the same product composition when the intermediates are generated and react under identical conditions. Such a finding need not be observed with the $S_{RN}2$ mechanism where there is no common intermediate. The difficulties associated with the $S_{RN}1$ mechanism have been recognized and various explanations for the role of the leaving groups have been offered.^{3,6}

Of the four halobenzenes fluorobenzene reacts most slowly and shows the most deviated product composition from the other halobenzenes under S_{RN} conditions. This report will focus on various radical anions containing fluorine and the results of various experimental approaches will be correlated with ab initio calculations of fluorobenzene and its products of addition of electrons and nucleophiles.

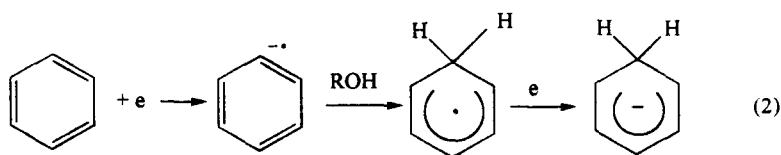
San Roman *et al.*⁷ prepared the fluorobenzene radical anion in ammonia-methanol solution. They showed that it either lost an electron to the solution or reacted with the methanol to give unidentified products. No evidence for dissociation was obtained.

Namiki⁸ has prepared the fluorobenzene radical anion in ethanol at 4° K. He observed its ESR spectrum. On warming to 77° K the fluorobenzene radical anion was no longer observed. It was suggested that dissociation did not occur but rather cyclohexafluorodienyl radicals were formed by reaction with the solvent.

More recently Kariv-Miller and Vajtner⁹ have studied the electroreductive dehalogenation of fluorobenzenes. They found that fluorobenzene and 1,3-difluorobenzene could be reduced to benzene and fluorobenzene. These reductions only occurred if water was present; 5 % was found to be optimal. They did not provide a rationale for the need to have water present. An interesting possibility is that the radical anion is formed and it reacts with water to give the fluorocyclohexadienyl radical which then reacts with a second electron to give product and the fluoride ion. No dissociation of the



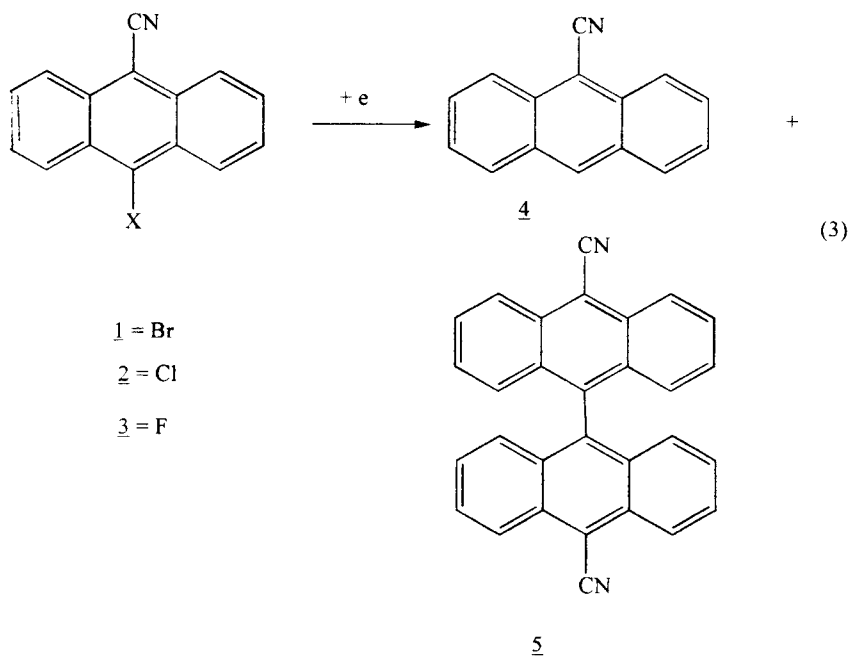
radical anion is required. This conclusion is strongly supported by the work of Mortensen and Heinze¹⁰, They have reduced benzene electrochemically. They have found that the benzene radical anion is the first product formed followed by protonation to give the cyclohexadienyl radical. This radical then accepts another electron to give the cyclohexadienide anion which is the observed product.



Various workers have studied the reduction of 4-fluorobenzonitrile.^{11,12,13,14} In nonaqueous media p,p'-dicyanobiphenyl is found as the major product. This can arise if two p-fluorobenzonitrile radical anions couple at the para positions to give dianions that then expel fluoride ion. The alternate mode of formation would be coupling of two p-cyanophenyl radicals. This seems very unreasonable indeed. Phenyl radicals lead to very little or no biphenyl when generated by various means.

More recently Ettayeb et al.¹⁵ have studied the electrochemical reduction of 4-chlorobenzonitrile, 4-iodobenzonitrile, 4-bromobenzonitrile and 4-chloropyridine in liquid ammonia and in the presence of 2-pyridinethiolate ions. Two products were formed, the dimer from the starting aryl halide and the product of substitution by the thiolate ion. The authors suggest that aryl radicals were formed and they more or less reacted equally with themselves or with the nucleophile. The postulate that they react with themselves represents a chain termination reaction. Yields of dimer up to 39% are certainly not in consonance with a termination reaction. An alternate mechanism suggests that the radical anions dimerize and expel halide ion or they react with the nucleophile. Dimerization of aromatic radical anions is well documented.

Of considerable importance to our understanding of the chemistry of these radical anions is the work of Hammerich and Parker¹⁶ and that of Heinze¹⁷. They report that 9-cyano-10-bromoanthracene, 1, undergoes electrochemical reduction to 9-cyanoanthracene, 4. Reductive cleavage of the chloro compound, 2, yields a small amount of 9-cyanoanthracene, 4, and mostly dimer, 5. Reductive cleavage of the fluoro compound, 3, yields only dimer, 5. Very clearly production of a common intermediate radical i.e. the 9-cyanoanthranlyl radical is hard pressed to account for the different product ratios. If such a radical was formed it could only be reduced when 1 was the substrate and could only dimerize when 3 was the substrate. A much more satisfactory explanation



for the production of 4 and 5 involves transfer of a second electron to the radical anion to give halide ion and the 9-anthranlyl carbanion which reacts with the solvent, acetonitrile, to give the reduced product. This process is in competition with the dimerization process. It is evident then that ease of reduction is Br > Cl > F.

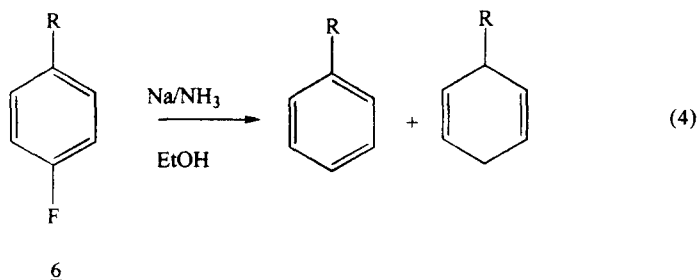
Cheng *et al.*¹⁸ have reduced the four halobenzenes with sodium naphthenide. The major products were benzene and biphenyl. Fluorobenzene yielded 72% benzene and 17% biphenyl. The

other halobenzenes gave similar amounts of benzene, 82 - 90 % and similar amounts of biphenyl 6 10 %. The results were discussed in terms of a mechanism involving phenyl radicals. No explanation was provided for the different behavior of fluorobenzene.

Sargent¹⁹ suggested a different mechanism and provided some experimental results. His mechanism still has the phenyl radical as a common intermediate. He also did not comment on the fluorobenzene results. He did show that the biphenyl yield was not a function of the benzene present. He also showed that the biphenyl had to arise by the coupling of the carbons that bonded the original halo substituent. Very clearly this will be the case if the radical anions dimerize and then eject halide ions. It is not surprising that fluorobenzene gave more biphenyl than the other halides. Its radical anion should be more difficult to reduce than the others.

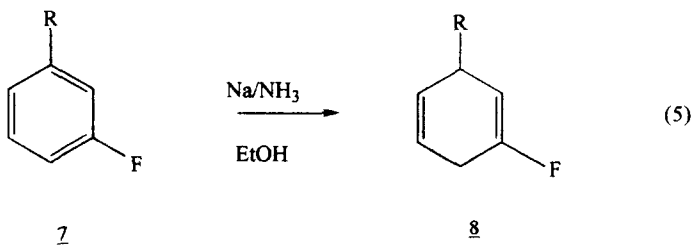
Komin and Wolfe²⁰ have studied the reactions of 2-bromo, 2-chloro and 2-fluoropyridines with the potassium salt of acetone in liquid ammonia. They found the usual rate order, Br > Cl > F for the substitution process. The interesting thing about these observations is the finding of Buick et al.¹¹ that the radical anion of 2-fluoropyridine is readily detected by ESR spectroscopy. The other halo pyridines gave only the spectrum of the pyridine radical anion. None of this anion was observed in the case of the 2-fluoropyridine. Very clearly the S_{RN}2 mechanism is indicated for the reaction of 2-fluoropyridine radical anion with the acetone enolate ion.

Jessup et al.²¹ have studied the Birch reduction of a variety of fluoroaromatics. They find that para fluoro substituted compounds, 6, are reduced with the loss of fluoride ion. The meta substituted compounds, 7, were reduced to the dihydro compounds, 8, without loss of fluoride ion. These results can be understood in the context of forming the radical anion from the aromatic fluorine containing ring of the compounds, 6. Protonation of the radical anion in the para position yields a cyclohexadienyl radical which can accept an electron with loss of fluoride ion to give the parent aromatic system which can be reduced to the dihydro compound.



R = CO₂⁻, Ph., 4-FPh

CH₃, OCH₃



R = CO₂⁻, Ph, 3-FPh

(CH₃)₃Si

In the case of compounds, **7**, formation of the radical anion followed by protonation in the para position yields ultimately compounds **8**, without fluoride ion loss. In none of these reactions is fluoride ion loss from the radical anion a requirement for the production of the observed products.

In another series of experiments²² the four 4-halobiphenyls were treated with potassium. In the case of the fluoro compound the formation of quaterphenyl was observed. This can arise if the radical anions dimerize and then eject fluoride ions.

All of the data cited so far are supportive of the concept that fluorine containing radical anions are relatively stable and they exhibit a unique chemistry. It would of course be of considerable value to have other evidence which would support these conclusions.

Bunnett⁵ in particular has criticized the $S_{RN}2$ mechanism. He states "Having found no transition state or intermediate for the postulated $S_{RN}2$ steps that is both acceptable in respect to quantum mechanical theory and in accord with experimental facts, I conclude that the $S_{RN}2$ mechanism is most unlikely for radical-chain electron transfer nucleophilic substitution".

In the case of fluorobenzene radical anion there have been at least two ab initio calculations concerning its structure etc.^{23,24} These have led to the conclusion that all of the electron density of the SOMO is centered on the ortho and meta positions of the benzenoid ring. There is no electron density on the ipso or para carbons. These computations are in total agreement with the ESR spectrum recorded by Namiki⁹ at 4° K.

These computations have now been redone with much larger basis sets. Fluorobenzene has been investigated using the RHF/6-31G^{**} and the RHF/6-31G^{*} programs.^{25,26} The results of these computations are recorded in Table 1 and Table 2.

Table 1

C_6H_5F RHF 6-31G ^{**}	E_{HOMO}	E_{LUMO}	E_{LUMO+1}
$E_T = -329.5636599$	-0.33360	0.13357	0.15125
Point Group C_{2v}			
C - F	1.33 Å		

Table 2

C_6H_5F RHF 6-31G [*]	E_{HOMO}	E_{LUMO}	E_{LUMO+1}
$E_T = -329.5546697$	-0.33363	0.13420	0.15164
Point Group C_{2v}			
C - F	1.33 Å		

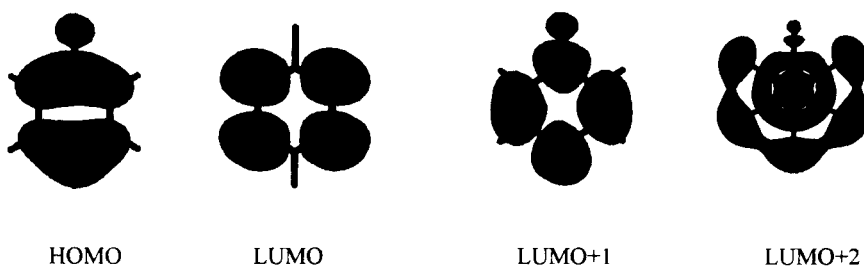
The energies obtained from the 6-31G^{**} calculation are slightly lower than those generated by application of the 6-31G^{*} model. These results are in keeping with the variational principle.

As postulated by Hehre²⁵, the 6-31G^{*} basis set provides a reasonable balance between accuracy and computer resource. Most of the computations were conducted using the 6-31G^{*} basis set with full geometry optimization.

The bond distances for fluorobenzene as computed are C - F 1.33 Å and C - C 1.38 Å. The HOMO - LUMO gap is 0.46783 Hartree, 293.6 Kcal/mole.

The HOMO is a π orbital and the LUMO is a π^* . The LUMO+1 is also a π^* orbital and it is separated from the LUMO by 10.9 kcal/mole. The profiles of the frontier orbitals are illustrated in Figure 1. It is interesting to note that the HOMO, the LUMO and the LUMO + 1 are all π orbitals. The first σ^* orbital is the LUMO + 2.

Figure 1



Addition of an electron to fluorobenzene leads to the radical anion which is 55.8 Kcal/mole higher in energy than that of fluorobenzene itself. The results of both the UHF/6-31G^{**} and UHF/6-31G^{*} calculations are summarized in Tables 3 and 4.

Table 3

C_6H_5F 6-31G ^{**}	$E_{\alpha HOMO-1}$	$E_{\alpha HOMO}$	$E_{\alpha LUMO}$
$E_T = -329.4791533$	-0.15559	0.04074	0.38485
Point Group C_{2v}			
$\langle s^2 \rangle = 0.85$	C - F 1.36Å		

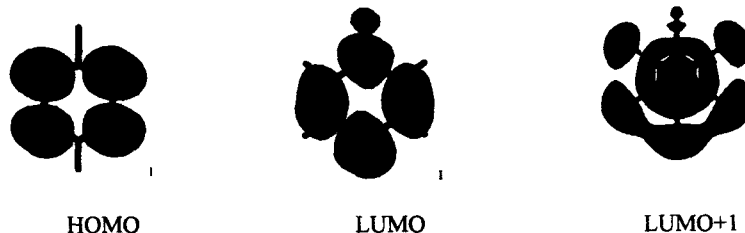
Table 4

C_6H_5F 6-31G [*]	$E_{\alpha HOMO-1}$	$E_{\alpha HOMO}$	$E_{\alpha LUMO}$
$E_T = -329.4655350$	-0.15531	0.04142	0.38573
Point Group C_{2v}			
$\langle s^2 \rangle = 0.85$	C - F 1.36Å		

These data show that the energy differences between the two basis sets is negligible. Introduction of the electron leads to a change in the C - F bond length from 1.33Å to 1.36Å. The major change is elongation of the C - C ortho meta bond from 1.38Å to 1.45Å. The reason for this is that the electron density is localized and shared nearly equally between the ortho and meta carbons which is in excellent agreement with the ESR spectrum of the radical anion.³

The electron densities of the frontier orbitals are illustrated in Figure 2. It is important to note that both the HOMO and the LUMO orbitals are π orbitals whereas the LUMO+1 is a σ^* orbital. It was first pointed out by Clarke and Coulson²⁷ that for dissociation of a radical anion, such as the fluorobenzene radical anion, to occur the electron must shift from the π^* orbital to a σ^* orbital. There does not appear to be any driving force for such an electron shift. Clarke and Coulson²⁷ also argued that a third body was required for this shift to occur. The importance of this will be discussed.

Figure 2



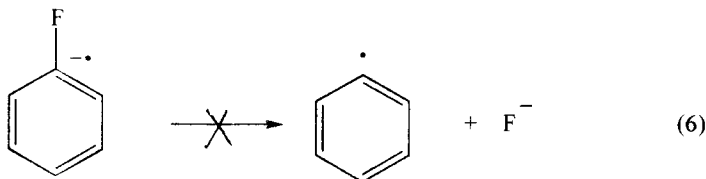
For open shelled substances an alternative mode of calculation is the ROHF formalization which has been employed for the sake of thoroughness. The most important point to be made here is that the electronic state and isosurfaces are unchanged from the corresponding UHF calculation.

The results presented above combined with that which is known on the basis of ESR experiments clearly establish the delocalized π -electronic structure of the fluorobenzene radical anion. In recognition of this, the postulate that fluorobenzene radical anion undergoes dehalogenation by unimolecular fragmentation requires the added step of π^* to σ^* orbital crossing.

In order to test the π^* to σ^* postulate a series of optimizations were carried out in which the carbon - fluorine bond length was incrementally increased by 0.01Å from 1.36Å to 1.40Å. These computations were calculated without any symmetry constraints. There was no change from a π^* to a σ^* state.

In order to assure that the fluorobenzene radical anion is a true intermediate a frequency calculation was carried out and only positive frequencies were found. These results show that the radical anion is a true minimum along the potential surface.

Finally the thermodynamics of the dissociation process (6) have been calculated using the ROMP2 formalism which takes into account electron correlation effects. The value found for this process is 52 kcal/mole which strongly supports the contention that the fluorobenzene radical anion is stable toward dissociation.²⁸



Reduction of fluorobenzene to the phenyl carbanion and fluoride ion is then a two electron process and it does not proceed through the intermediacy of the phenyl radical. Similarly attack by a nucleophile on the radical anion can yield a new radical anion and fluoride ion. It is interesting to note that the nucleophiles that are most efficient in S_{RN} chemistry are "soft" nucleophiles and good electron donors and they all have a negative charge.

Why does the radical anion react so readily with an electron or a nucleophile? It has been argued that this should be a high energy process because of the electrostatic effect of bringing two negatively charged species together.

If one considers the postulate of Clarke and Coulson that a third body is required for the π^* to σ^* transformation to occur then it seems reasonable that an approaching electron or nucleophile can perturb the orbitals so that the crossing over can occur and expulsion of X^- is facilitated. Such a process can yield the phenyl carbanion and fluoride ion. This is what is found when an electron was brought into contact with the radical anion with no symmetry constraints. The products were the phenyl carbanion and fluoride ion.

If one considers approach by a nucleophile, a similar perturbation can occur but now as the fluoride ion is leaving bonding can occur to the nucleophile with the formation of a new radical anion.

In essence then the formation of the radical anion followed by approach of a third body results

in what is basically an intramolecular displacement reaction and thus the formation of the radical anion prepares the system for further reaction.

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