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NUCLEOPHILIC DISPLACEMENT REACTIONS ON FLUORINE. I. GENERAL PHENOMENON AND LONE-PAIR NUCLEOPHILES

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Summary

S_N2 displacement reactions involving halogen atoms are progressively more facile in going from F to I. Diverse and hitherto largely mechanistically uncorrelated examples of $S_N2(F)$ reactions are presented and it is suggested that they form part of a general phenomenon in fluorine chemistry.

Nucleophilic displacements on fluorine atoms, *i.e.*, of the type X—F + :Z → X: + F—Z, have been noted only rarely in comparison to the corresponding isoelectronic reactions involving Cl, Br and I atoms. (For example, see refs. 1 and 2 for a discussion of S_N2 displacement reactions involving the heavier halogens and the corresponding null results observed for fluorine.) In this article examples of S_N2 displacement reactions on fluorine atoms are pointed out and it is shown that such reactions are in fact quite common in fluorine chemistry, and as such constitute a general class of reactions. No attempt has been made to be encyclopaedic in the literature references but instead it is suggested that the interested reader consult Grakauskas'article [3] for more specific examples of the first class of $S_N2(F)$ reactions quoted. Mechanistic considerations are however given little emphasis in this article. Similarly, the reader will find Sheppard and Sharts' book [4] of relevance for it discusses some of the examples of $S_N2(F)$ reactions quoted here without being as general or as taxonomic as we shall be.

In this and future papers, four classes of reactions are considered that may be expected to proceed relatively unambiguously by nucleophilic displacement on fluorine. In the first class of reaction, X = F and Z is some "lone-pair nucleophile". For example, the nitroform anion, $C(NO_2)_3^-$, readily reacts with aqueous F_2 to form $FC(NO_2)_3$ [5]. The second class of reaction

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retains Z as a "lone-pair nucleophile" but now X is some other anionic leaving group. For example, *N*-fluoro-perfluoromorpholine, $O(CF_2CF_2)_2N{-}F$, reacts with I^- to form $O(CF_2COOH)_2$ through the intermediacy of the $O(CF_2CF_2)_2N$ anion [6]. The third class of reaction involves σ- and π-bond donation, *i.e.*,

$$X{-}F + Z{-}Y \rightarrow X^- + F{-}Z + Y^+$$

$$X{-}F + Z{=}Y \rightarrow X^- + F{-}Z{-}Y^+$$

The fluorination of cyclic ureas to form $NF_2(CH_2)_nNHCOF$ and $NF_2(CH_2)_nNCO$ [7] is an example of this third class where Z = N(F) and Y = C(O). The fourth class of reaction involves the cationic X—F species, *i.e.*, $[X{-}F]^+ + {:}Z \rightarrow X{:} + [F{-}Z]^+$. An example of such a reaction is that between iodine pentafluoride and the krypton fluoride ion [8],

$$KrF^+ + IF_5 \rightarrow Kr + IF_6^+$$

In the current paper we shall limit our discussion to the first two classes of reaction.

For reactions of the first class, *i.e.*, $F{-}F + {:}Z^- \rightarrow F^- + F{-}Z$, the logical sites for the nucleophilic center in $:Z^-$ are the atoms C, N and O. For Z = C we have already cited the reaction of the nitroform anion [5]. Related reactions occur for other nitronates and nitroanions [9, 10]. Experiments on the analogous fluorination of sulfonyl-stabilized carbanions are in progress [11]. Admittedly, initial fluorination of an oxygen of the nitroanion or sulfonyl carbanion to form a hypofluorite is possible, and the subsequent reaction of the hypofluorite with another molecule or anion would then be an example of the second class of reaction with X = O and Z = C. Analogous fluorination reactions occur for the case when Z = N in class 1 reactions involving nitroanilines [12], amides [13 - 15], urea and its derivatives [5, 13 - 17], urethanes (carbamates) [12, 13, 18, 19], cyanamide [20], dicyanamide [21], sulfamides [22], phosphamides [23], nitramines [24], perfluoroimine anions [25] and guanidines [21, 26]. These reactions have been performed, in general, using water, HF or CH_3CN as the solvent. Generalizing Sheppard and Sharts' suggestion [27], we propose that the solvent may be necessary in order to hydrogen bond the incipient fluoride ion. Additionally, we note that $Solv{-}H + F - F + {}^-NRR' \rightarrow (Solv\cdots H\cdots F)^- + FNRR'$ (where Solv = solvent) constitutes an interesting case of "simultaneous" S_N2 and S_E2 (proton-polarized X—F) [28] displacements on fluorine. (The possibility of aqueous fluorination proceeding through OF_2 or HOF, as proposed in ref. 6, cannot be summarily dismissed and these represent examples of class 2 reactions with X = O.) In formal analogy to the above nitrogen compounds, aliphatic amines dissolved in an aqueous $NaHCO_3$ buffer are also fluorinated by aqueous fluorine [29] in an exactly similar manner to their chlorination by aqueous chlorine [30]. The optimum pH for reaction in this buffered solution is *ca.* 7.5 which excludes the possibility of any negatively charged nitrogen species being present.

In fact, since most primary amines have pK_b values around 10 - 11, both the amine and the ammonium ion should be present in reasonable concentrations. Hence this reaction is also suggestive of simultaneous S_N2 and S_E2 displacements on the fluorine atom.

Let us now consider class 1 reactions with Z = O. Fluorine has long been known to react with aqueous basic solutions to form OF_2 in a reaction which is extremely pOH-dependent [31]. The mechanism for this reaction is still not completely understood and intermediates such as HOF and OF^- have been invoked. However, the reactions of OF_2 do not correspond to that expected of an "anhydride of HOF" [32] nor does HOF behave like ordinary "hypohalous" acids [33, 34]. HOF may be formed from fluorine and water but its interconversion with OF_2 has not been observed. These complications no doubt arise in part from the kinetic instability of HOF, for although it is stable with respect to unimolecular decomposition [35], it decomposes in both aqueous acid and aqueous base solutions [34]. The former reaction yields H_2O_2 [36] while the latter reaction yields O_2, but in both cases the corresponding mechanisms are obscure. We may also note that no unequivocal experimental data exist on protonated or deprotonated HOF although quantum chemical studies have been made involving H_2OF^+ and $HOFH^+$ [37], and OF^- [38 - 40]. These complexities make it virtually impossible to evaluate the role of OF_2 or HOF in the aqueous fluorination of organic compounds cited earlier. Intuitively, however, we do not believe that these intermediates are necessary to explain the observed results.

Much more definite examples of class 1 reactions with Z = O exist than those mentioned above. Thus, carbonyl fluoride, carbon dioxide, perfluoroalkanoyl fluorides and perfluoroketones readily react with molecular fluorine to form hypofluorites provided an ionic metal fluoride is present [41 - 45]. Compounds synthesized in this manner include CF_3OF, $CF_2(OF)_2$, $FO(CF_2)_4OF$ and $(CF_3)_2C(OF)_2$. The F^- ion adds across the C=O bond to form the fluoroalkoxide [46, 47] *, which in turn reacts with F_2 to form the hypofluorite and F^-. Water has been shown to be necessary for the synthesis of CF_3COOF [48]. This may be attributed to the water-assisted ionization $CF_3COOH + H_2O \rightarrow CF_3COO^- + H_3O^+$. The trifluoroacetate ion is then fluorinated to form the hypofluorite and F^- while proton transfer between CF_3COOH and F^- generates further CF_3COO^-. A similar situation occurs during the fluorination of aliphatic carboxylic acids which in water leads to the formation of CO_2 and the alkyl fluoride containing one less carbon atom [49]. The formation of these products has been explained in terms of the generation of an acyl hypofluorite which then decarboxylates. In nonpolar solvents, where the acid is most probably dimerized, C-fluorinated products are formed [50]. Analogous C-fluorinated products are observed for acyl chlorides and anhydrides [50]. Addition to doubly-bonded oxygen

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* For the isolation of CF_3OK, CF_3ORb and CF_3OCs see ref. 46, and for the isolation of $(CF_3)_2CFOK$ see ref. 47.

is not limited however to carbonyl compounds. Thus thionyl fluoride is readily fluorinated to SOF_4 irrespective of the presence of a metal fluoride catalyst. However, further fluorination to SF_5OF will only occur in the presence of this catalyst [51]. In principle, additional reactions are also possible for the other chalcogens, S, Se and Te. One such apparent reaction is the formation of $C_2F_5SeF_5$ from $[Cs]^+[C_2F_5SeF_4]^-$ and F_2 [52].

Let us now turn to the case where Z = halogen. Alkali metal fluorides are known to catalyze the formation of ClF_5 from ClF_3 and F_2 [53], an $S_N2(F)$ displacement reaction involving ClF_4^- on molecular fluorine appearing to be the simplest mechanism for this reaction. Similarly, ClO_3^- reacts with F_2 to form perchloryl fluoride [54]. However, the isoelectronic reaction involving BrO_3^- and F_2 does not lead to BrO_3F [55] despite the inherent stability of the final products [34]. These results may be explained when the fact that the electronegativities of Cl and O are comparable but considerably higher than that of Br is taken into account. Thus it is possible that the positive charge on Cl is less than that on Br even though both oxyanions formally contain pentavalent halogen. Hence the nucleophilicity of Cl is probably greater than that of Br. In those cases where the halate ion is fluorinated on a peripheral oxygen, a highly reactive and unstable halyl hypofluorite is probably formed.

Now consider the second class of reaction, *i.e.* $X{-}F + :Z^- \rightarrow X:^- + F{-}Z$, but where X is not F. We will catalog these reactions first in terms of X and then in terms of Z. The reaction of *N*-fluoro-perfluoromorpholine with the iodide ion [6] mentioned above is an example where X = N and Z = I. However, this class of reaction has only been observed rarely when X = C. Removal of fluorine from a saturated carbon atom by the action of $LiAlH_4$ ($Z = H^-$) is a much more difficult process than the corresponding removal of the other halogens [56]. The process is however greatly facilitated by the addition of $AlCl_3$ [57], but now the reaction undoubtedly proceeds through polarization of the C—F bond [28] by the Lewis acid and subsequent S_N2 attack on the carbon atom. Hence this reaction cannot be considered a member of the second class of $S_N2(F)$ reactions. Reducing of perfluoroalkenes with $LiAlH_4$ occurs much more readily and may be attributed to replacement of a vinylic fluoride by hydrogen through attack by the hydride on the C=C bond, thereby forming a stabilized carbanion which eliminates F^- [56]. This mechanistic interpretation is supported by the existence of similar reactions with other nucleophiles [58, 59], and for this reason these reactions are also not examples of $S_N2(F)$ processes.

No example appears to exist where X = Z = C. In contrast to the heavier halogens, alkyl groups are not displaced as typified by the non-reaction of alkyl fluorides with organolithium reagents *via* (F, Li) exchange [60, 61]. In addition, no example appears to exist where Z = N or O when X = C. For example, in contrast to the chloro and bromo analogs, reaction of $FC(NO_2)_3$ with OH^-, OOH^- or $OC_2H_5^-$ results in the abstraction of a nitro group [10]. Loss of a nitro group from fluorinated, as well as non-fluorinated, polynitromethanes is quite common upon reaction with nucleophiles [62]. In many cases an EPR signal has been observed [62, 63] and has been attributed to the radical anion of the nitro compound [63]. For example, $CF_2(NO_2)_2$ reacts with alkoxides and OH^-, but not with I^- or $(CH_3)_2CNO_2^-$, to form the radical anion $CF_2(NO_2)_2^{-}\cdot$ [63].

An example of the second class of reaction where Z = P has been invoked in the reaction of $(CF_3)_2CFSSCF(CF_3)_2$ with $(C_6H_5)_3P$ to form $[(CF_3)_2CS]_2$ and $(C_6H_5)_3PF_2$ [64]. An initial $S_N2(F)$ reaction would yield $(C_6H_5)_3PF^+$ and $(CF_3)_2CFS^-$ and $(CF_3)_2C{=}S$ or $(CF_3)_2CFSS\overset{-}{C}(CF_3)_2$, the latter readily fragmenting to yield the two preceeding products. The loss of F^- by the fluorothiolate ion to form the thioketone, phosphine-catalyzed thioketone dimerization, and acquisition of the F^- ion by the fluorophosphonium ion would then account for the observed products. However, by analogy with other disulfides [65], it is possible to suggest phosphine attack on a sulfur atom to form $(C_6H_5)_3P^+SCF(CF_3)_2$ and the same fluorothiolate ion as before. The new thiolatophosphonium ion picks up an F^- ion and loses the $(CF_3)_2CFS^-$ entity by subsequent heterolysis of the P—S bond. Loss of the F^- ion from the fluorothiolate ion and its subsequent gain by the fluorophosphonium ion yields the same products as before. (The $(CF_3)_2CFS^-$ ion, formed from $CF_3CF{=}CF_2$, together with elemental sulfur and KF yields the thioketone dimer and the disulfide [66].) Intuitively, the $[C_6H_5SO_2CHC_6H_5]^-$ and $[C_6H_5SO_2CHC_6H_4NO_2\text{-}p]^-$ anions might have been expected to be good leaving groups. However, neither $(C_6H_5)_3P$ nor the stronger "halophiles" $[(CH_3)_2N]_3P$ and $C_6H_5S^-$ (*i.e.* Z = S) remove fluorine from the corresponding fluorosulfones to form the above anions [2]. The reactions of these halophiles with $FC(NO_2)_3$ have not been investigated but an investigation of the reaction with the disulfone $(C_6H_5SO_2)_2CHF$ is at present in progress.

Let us now turn to X = N. The primary compounds of interest in this case are *N*-fluoro-perfluoromorpholine, $O(CF_2CF_2)_2NF$, and *N*-fluoro-perfluoropiperidine, $(CF_2)_5NF$. Fluorination of 2-nitropropane and malonic ester anions has been reported [67]. It has been suggested that these reactions are not examples where Z = C, but instead proceed through attack on the oxygen to form an unstable hydroxylamine, *e.g.* $(CH_3)_2C{=}N(O)ON(CF_2)_5$. Subsequent attack on the carbon atom then leads to the formation of the observed compound. The resulting $(CF_2)_5N^-$ ion decomposes by loss of F^- and subsequent hydrolysis. It is not possible to prove that this mechanism is incorrect; however, $(CF_3)_2CF^-$ synthesized *in situ* (*i.e.* $CF_3CF{=}CF_2$ + CsF) reacts with *N*-fluoro-perfluoropiperidine to yield $CF_3CF_2CF_3$ [68]. This is clearly an example of an $S_N2(F)$ reaction where Z = C and no such ambident (Z = O) behavior is possible here. For this reason, it is probably unnecessary in general to invoke a Z = O pathway as suggested in the examples quoted above.

One example where X = Z = N has been reported, *i.e.* the reaction of *N*-fluoro-perfluoropiperidine with the all-hydrogen piperidine to form

N-fluoropiperidine in low yield [69]. The perfluoropiperide anion loses F^- and the resulting $\Delta^{1:2}$-piperideine rapidly adds piperidine.

No unambiguous examples where X = N and Z = O appear to exist. *N*-Fluoro-perfluoropiperidine is stable to alkaline hydrolysis [70], but absolute ethanol reacts to form acetaldehyde. The formation of an intermediate such as ethyl hypofluorite ($S_N2(F)$ type reaction or *N*-ethoxy-perfluoropiperidine ($S_N2(N)$ type reaction) appears to be most unlikely in view of the inert behavior of *N*-fluoro-perfluoropiperidine towards aqueous base. (A study of the corresponding reaction with $C_2H_5O^-/C_2H_5OH$ would be interesting.) The available data on the reaction with ethanol are consistent with a cyclic transition state yielding two molecules of HF, acetaldehyde and the $\Delta^{1:2}$-piperideine, but no supporting evidence exists. In contrast to the case where Z = O, clear examples where Z = P, As and Sb have been noted. Triphenylphosphine, -arsine and -stibine all react with *N*-fluoro-perfluoropiperidine to yield the Group V dihalide and the $\Delta^{1:2}$-piperideine [69]. The analogous defluorination reaction of NF_3 to form N_2 has been reported and mechanistically interpreted [69] as:

$$NF_3 \xrightarrow[-F^-]{S_N2(F)} NF \xrightarrow{\text{dimerize}} N_2F_2 \xrightarrow[-F^-]{S_N2(F)} N_2$$

In addition, reactions where Z = I involving HI or I^- and essentially any *N*-fluoroamine including the above *N*-fluoro-perfluoropiperidine [69, 70], NF_3 [69] and HNF_2 [71] have been reported.

Turning now to the case where X = Z = O. One possible example of such a reaction is that between OF_2 and aqueous OH^- to form O_2. Unfortunately the formation of HOF and OF^- as intermediates has not as yet been demonstrated. (An alternative mechanism involving an $S_N2(O)$ reaction has been suggested [28], but no definitive evidence is available.) In a similar manner, CF_3OF forms CO_3^{2-}, F^- and O_2 [72], and in general R_fCF_2OF forms R_fCOO^- [44]; mechanisms similar to those invoked in the chemistry of OF_2 may be written. More definitively, CF_3OCs reacts with $CF_2(OF)_2$ to form CF_3OF and FCOOF, which further reacts to form CF_3OOCOF [73, 74]. Another example of a reaction where X = Z = O is the formation of SF_5OF and FSO_3^- from SF_5O^- and FSO_2OF [75]. In principle, it should be possible to define relative "F^+ affinities"* for a series of anions, but insufficient data exist to date.

Examples of reactions where X = O and Z = halogen exist for Cl, Br and I, Z = F being merely the unobserved reverse of the X = F, Z = O case described above. From the earliest investigations on hypofluorites [72, 77], their reaction with I^- to form I_2 or I_3^- has been noted. In almost all cases this is a two-electron oxidation [78], although the reaction of $(CF_3)_3COF$ with I^- appears to be a one-electron oxidation [79]. Reactions involving Cl^-

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* The notion of "F^+ affinities" is formally analogous to proton and methyl cation affinities (ref. 76) although the corresponding experiments would be considerably more difficult to undertake.

and Br^- have also been noted [44, 78, 79]. As with the two-electron reactions involving I^-, the intermediate halogen fluoride should readily react with another X^- ion to form the diatomic X_2 molecule.

We now consider X = halogen, and in particular X = ClO_3. We do not believe that *all* [80, 81] fluorination reactions of ClO_3F proceed *via* initial nucleophilic attack on the Cl atom; examples will be presented first and the reasons for the mechanistic choice given afterwards. The following classes of compounds with Z = C have been fluorinated using this reagent: diethyl malonates [82, 83], cyanoacetates [84], β-keto-esters [85], malononitriles [86], 1,3-diketones [87], esters [88], nitronates [89 - 91] and diethyl nitromalonate [92]. Examples where Z = N are much less common. Thus piperidine reacts with ClO_3F to form the *N*-perchlorylamine but piperidines which are sterically hindered yield the *N*-fluoro derivative [93]. Reactions of other amines and/or their *N*-lithio derivatives to form the *N*-fluoro compound have also been noted [94, 95].

Let us now return to the question of initial fluorination or perchlorylation. First of all, displacement of ClO_3^- by F^- in perchlorylamines seems unlikely and is an unnecessary mechanistic step if fluorination occurs initially. Secondly, the cyclic transition state [80, 81] quoted in the literature seems untenable for both the fluorination of malononitriles [86] and the *para*-fluorination of phenolic steroids [96] (an example of a class 3, $S_N2(F)$ reaction). Admittedly, the absence of an intramolecular cyclic transition state in these cases does not preclude it elsewhere, but it does make it more conceptually superfluous. Finally, the dipole moment of ClO_3F is negligibly small (0.023 ± 0.01 D [97]), and this allows the possibility of essentially neutral Cl and F atoms existing in ClO_3F with the latter atoms being more sterically accessible. (Experiments have been reported which claim that ClF possesses a positive fluorine atom [98, 99], but these results have been questioned [100]. If ClF does possess a positive fluorine atom, *a fortiori*, a positive fluorine atom should also occur in ClO_3F.)

Admittedly many of the chemical reactions of fluorine presented here are not paralleled in the behavior of the other halogens, and for this reason the relative rates of $S_N2(F)$ reactions and the corresponding reaction for the heavier halogens cannot be determined. However, where comparisons do exist, $S_N2(F)$ reactions do appear to be relatively slow. We will now attempt to explain this phenomenon.

The suggestion [1, 2] that the ease of displacement on halogen atoms may be correlated with the bond energy/thermochemical data is of limited value. First, only in rare cases are there sufficient data to enable a comparison of the reaction $X{-}Hal + :Z \rightarrow X: + Hal{-}Z$ for all four halogens. Secondly, there is no underlying reason why changes in activation energies must parallel corresponding changes in the free energies of reaction. Although such relationships are common, they consistently occur only in closely related systems*. To illustrate the dilemma that can result when one attempts to correlate the ease of displacement on halogen atoms with the relevant bond energies, consider the case of X—Hal + H^- (or H^+) → X^- (or X^+) + Hal—H. For X—Hal + H^- → X^- + Hal—H, the relationship $\Delta\Delta H^-$(Hal) = ΔH^-(X—F + H^- → X^- + F—H) — ΔH^-(X—Hal + H^- → X^- + Hal—H) applies. Whatever the nature of X, the analogous value of $\Delta\Delta H^+$(Hal) (for the reaction X—Hal + H^+ → X^+ + Hal—H) is always equal to $\Delta\Delta H^-$(Hal). This means that regardless of the type of displacement of Hal by H, (whether it is S_N2 or S_E2) the trend in reactivity based solely on the $\Delta\Delta H$ values should run parallel for both S_N2(Hal) and S_E2(Hal) reactions. This is clearly not the case, since X—F is most reactive in S_E2(F) reactions [28] but least reactive in S_N2(F) reactions.

It may be argued that d orbitals are important in explaining the bonding, energetics and structures of such species as the noble gas dihalides and trihalide ions. Hence fluorine, which lacks energetically accessible d orbitals, should in general form the weakest bound "triatomic complex" of the species X—Hal—Z. However, no definitive conclusion may be reached since, according to recent *ab initio* quantum chemical calculations, d orbitals are important in classical second row compounds such as CH_2 [102] and NH_3 [103] in contrast to "hypervalent" [104] compounds such as PH_5 [105]. Furthermore, contrary to intuition, the 3d orbitals of F are as important in understanding the bonding in KrF_2 [106] as are the 4d orbitals of Kr. The results of this calculation on KrF_2 reproduce many of the features of the simpler three-center/four-electron bonding and ionic/covalent resonance models**. However, quantum chemical calculations which more closely mimic these particular models lead to no such correspondence***.

Alternatively, the low rate of the S_N2 displacement reaction on fluorine may be associated with the high negative charge which exists on this atom in most molecules, and hence the attacking nucleophile and the F atom undergo a long-range repulsion which is greater than that for Cl, Br and I****. There are, however, several problems associated with this interpretation. First of all, such an explanation would suggest that amongst compounds containing the C—Hal bond (Hal = F, Cl, Br and I) the ease of displacement *of* the halogen would be F > Cl > Br > I, since long-range attraction would exist

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* Examples can be found in acid—base chemistry where the kinetic acidity or catalytic activity of an acid (or base) closely parallels the thermodynamic acidity (or basicity) for a given family of acids (or bases). However, the relationship breaks down if one tests this relationship between members of different classes of acids (or bases), *e.g.* oxygen-containing acids versus carbon-containing acids [101].

** See ref. 8 for a semi-quantitative application of this latter model to KrF_2 and related species.

*** Calculations at this lower level of accuracy were also performed by Bagus, Liu and Schaeffer [106].

**** See refs. 60 and 61 where this is expressed in terms of I being most positive.

between the nucleophile and the positive carbon. This, however, is contrary to the experimental results obtained for displacement from aliphatic carbon atoms [107].

A qualitative interpretation of the relative tendencies of S_N2 displacements on halogens in terms of halogen polarizabilities [108] (hard and soft acids and bases [109, 110]) has been offered. In this paper we have included both hard and soft bases as we believe that no firm conclusion may be drawn from this approach. Polarizability effects involving halogen atoms have been invoked to explain the surprising observation in the gas phase that the order of decreasing acidity for the haloacetic acids, $HalCH_2COOH$, is Hal = Br > Cl > F > H [111]. In principle, the long-range (> 6 Å) interactions between two atoms (or molecules) may be expressed in terms of the relation

$$V(R) = V_{\text{repulsion}}(R) + \sum_{m=1}^{\infty} a_m/R^m$$

where R is the interatomic separation [112, 113]. However, at interatomic distances corresponding to direct bond formation (*ca.* 1 - 2 Å) this expression is rarely used [114] and quantum correction terms must be included [115]. It certainly seems ill-advised to consider the ion-induced dipole (polarizability) term $V_4 = \alpha e^2/R^4$. For highly ionic compounds, ion pairs or zwitterions, just the use of the repulsion term and the now-dominant Coulombic attraction [116] or even just the latter [117 - 119] is sufficient to give meaningful results. Hence the use of polarizabilities to explain relative S_N2(Hal) rates for the four halogens is probably inappropriate.

We may also consider the variation of the central halogen in intermediates of the type X—Hal—Z in relation to Politzer's [120] study of Hal^-, Hal_2, H—Hal, CH_3—Hal and M^+ Hal^-. He showed that, regardless of the precise environment, fluorine atoms with eight valence electrons are destabilized relative to those with seven as far as the predicted linear extrapolation from the values for the other (isoelectronic, heavier) halogens is concerned. This destabilization amounts to *ca.* 25 kcal mol^{-1} for F. Unfortunately there are no data which enable direct comparison of the species under discussion. However, we note that the intermediate concerned formally contains 10 electrons around the central halogen rather than the original eight, and hence on a qualitative basis it would appear that when X = F the intermediate is relatively destabilized. Some quantitative measure of this destabilization may be obtained by considering the electron affinities (EA) of the eight-electron ^1S X^- ions to form the ^2S state of the nine-electron X^{2-} ions*.

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* The formation of F^{2-} and Cl^{2-} ions has been claimed in the negative-ion mass spectra of polyhalomethanes [121], but the result for the latter ion has been disputed recently [122]. The EPR spectra of γ-irradiated halide-doped $BaSO_4$ have been interpreted in terms of the formation of Br^{2-} and I^{2-} ions [123]. However, in all of the above cases, there are insufficient data to derive any quantitative measurements of the stability or even the electronic states of these doubly-charged anions.

TABLE 1

Electron affinities of Hal and Hal^-

	EA(Hal) exptl.[a] (eV)	EA(Hal) calcd.[b] (eV)	EA(Hal^-) calcd.[b] (eV)	EA(Hal^-) calcd.—corr.[c] (eV)
F	3.448	2.997	−4.07	−3.6
Cl	3.613	3.310	−3.19	−2.9
Br	3.363	3.7	−4.01	−4.3
I	3.063	4	−4.19	−5.1

[a] See ref. 120.

[b] Calculated using Glocker's method [124] and the data in refs. 125 and 126.

[c] Calculated using Glocker's method [124], the data in refs. 125 and 126, and the assumption that the error in predicting EA(Hal) is the same as in EA(Hal^-) for a given halogen.

Although such a measure may be inaccurate (usually to the extent of ±0.5 eV or *ca.* 11 kcal mol^{-1}), nevertheless Glocker's method [124] of constant second differences may be used to predict EA (Hal^-). Table 1 gives the experimental values of EA(Hal), its predicted value and the predicted and corrected values of EA(Hal^-). Whereas EA(F) is only 4 kcal mol^{-1} less than EA(Cl), EA(F^-) is *ca.* 18 kcal mol^{-1} less than EA(Cl^-). We may therefore deduce that fluorine, despite its high electronegativity, does not add additional electrons beyond F^-. It therefore follows that the S_N2(F) intermediate X—F—Z is destabilized relative to the other halogen intermediates, and accordingly S_N2(F) reactions are not favored. A partial quantitative measure of this destabilization may be obtained by an extension of Politzer's analysis of EA(Hal). In this case we should compare EA(Hal^-) and IP(Hal), where IP is the ionization potential. The value of EA(F^-) when Hal = F may then be predicted from a least-squares fit of the data for the other halogens and compared with the above value. On this basis, it is possible to predict that EA(F^-) = 0.9 eV corresponding to a net destabilization of 105 kcal mol^{-1}.

This approach may now be used to show why S_E2(F) reactions are particularly favored [28]. For this class of reaction the calculation proceeds from an eight-electron species X—Hal to another 8-electron species $[X—Hal—H]^+$. On a qualitative basis, no destabilization would be expected for Hal = F. By analogy with Politzer's [118] analysis of H—X bond strengths, the proton affinity, PA, of X—Hal (and the hydrogen affinity, HA, of $XHal^+$) may be plotted against $1/R$(H—Hal). The value of HA and PA for Hal = F may then be predicted from a least-squares fit to the other halogen data and compared with the experimental value. As the H—Hal bond distances in cations of the type $[X—Hal—H]^+$ are unknown, we will assume that these quantities are the same for the H—Hal diatomic molecule [118] and the $[X—Hal—H]^+$ "triatomic" ions. PA and HA data for all halogens are absent for most X—Hal series with the important exception of methyl and ethyl halides [127, 128].

For the proton affinities, there is an apparent 11 kcal mol^{-1} "stabilization" for fluorine protonation. It may be argued that this effect is meaningless and that no special anomaly exists for fluorine. However, the "conventional" 25 kcal mol^{-1} destabilization has not been taken into account in this case and its absence accounts for the somewhat surprising reactivity of the fluorine compound. When the hydrogen affinity data are considered and the seven-electron X—Hal^+ species inter-related with the eight-electron $[X—Hal—H]^+$ species, a destabilization of 37 kcal mol^{-1} is observed when Hal = F. This latter finding, although *not* relating to the initial or mechanistically relevant step in S_E2(Hal) reactions, nevertheless provides further support for the application of bond energy "fluorine anomaly" analyses to this problem.

In conclusion, although nucleophilic displacement on fluorine has been little noted in comparison to the analogous isoelectronic reactions for the heavier halogens, as shown by examples and comparisons, we believe that S_N2(F) reactions are sufficiently common to constitute a general class of reaction. Comparison with the related S_N2 reactions of the heavier halogens has also been made.

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