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NUCLEOPHILIC DISPLACEMENT REACTIONS ON FLUORINE. II. THE ROLE OF σ- and π-BOND NUCLEOPHILES

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Summary

S_N2 displacement reactions on fluorine by σ- and π-bond nucleophiles are discussed and shown to constitute a general class of reaction. Mechanisms are suggested for reactions mentioned in the literature which are consistent with this generalization.

In the first paper in this series [1], we discussed the general phenomenon of S_N2 displacements on fluorine. All of the examples presented in that paper were of the general type, $\underset{\curvearrowleft}{X}\!-\!F + :Z \rightarrow X: + F\!-\!Z$, and were labelled class 1 if X = F or class 2 if X ≠ F. We now consider examples of class 3, *i.e.*

$$\sigma, \underset{\curvearrowleft}{X}\!-\!F + \overset{\curvearrowleft}{Z}\!-\!Y \rightarrow X^- + F\!-\!Z + Y^+$$

$$\pi, \underset{\curvearrowleft}{X}\!-\!F + \overset{\curvearrowleft}{Z}\!=\!Y \rightarrow X^- + F\!-\!Z\!-\!Y^+$$

Examples of the first sub-class, "σ", reaction are rare. We may cite the aqueous fluorination of cyclic ureas, $\overline{\lfloor(CH_2)_nNHCONH}$, to form $NF_2(CH_2)_nNCO$ and $NF_2(CH_2)_nNHCOF$ [2] as an example where X = N, Y = C(O) and Z = N(F). Similar reactions occur for both cyclic and acyclic carbamates [3]. We may describe these reactions as fragmentations of acyl difluoroammonium ions:

$$-X-C(O)-NF_2^+- \rightarrow -X-CO^+ + F_2N-$$

where X = NH or O. These reactions are precedented by the formation and subsequent fragmentation of acylammonium ions [4]:

$$R_3N + R'CO^+ \rightarrow [R_3NCOR']^+ \rightarrow R_2NCOR' + R^+$$

In the particular case under discussion, the acylium ion is resonance-stabilized, *i.e.* $-X-C{\equiv}O^+ \leftrightarrow -X^+{=}C{=}O$, and thus this type of fragmentation is much more likely. The electrophilic alkylation and protodealkylation of difluoroamines, RNF_2, which are similar reactions, have also been reported [5]. Another probable example of this class of reaction involves the reduction of SF_6 by $LiAlH_4$ [6] where it is suggested that X = S, Y = Al and Z = H. Since SF_4 [7] and SF_2 [8] are highly reactive, it is not surprising that the reduction of SF_6 does not yield these species but leads instead to S^{2-} and F^- ions. As 7-coordinate sulfur neither exists nor has been suggested as an intermediate in any mechanism, it is highly probable that the initial reduction of S^{VI} to S^{IV} proceeds *via* the process

$$H_3Al^-{-}H + F{-}SF_5 \rightarrow H_3Al + HF + SF_5^-$$

Simultaneous S—F polarization [9] by some nucleophile such as $AlCl_3$ or AlH_3 cannot be excluded however. This would lead to the direct formation of SF_4 and the appearance of $FAlX_3^-$ would add to the exothermicity of the reaction. Comparison with LiH would be most instructive.

Let us now turn to the π sub-class of reaction. The low-temperature fluorination of alkenes [10], alkynes [11] and imines [12] has been shown to proceed through ionic, *not* radical, intermediates. The analogous polar fluorination of alkenes [13], arenes [14] and imines [15] by CF_3OF and other hypofluorites has also been reported. Apparently there is no corresponding reaction between *N*-fluoroamines and alkenes, alkynes or imines. Perchloryl fluoride reacts only with activated alkenes, C=C—X, such as enol acetates [16] enamines [17] and substituted styrenes [18] to form α-fluoroketones. We favor an initial $S_N2(F)$ reaction forming $[F{-}C{-}C^+{-}X \leftrightarrow F{-}C{-}C{=}X^+] [ClO_3]^-$. In the case of enol acetates or enamines, this species may hydrolyze *in situ* to form the product or lead to the "organyl" chlorate which then hydrolyzes on addition of water. In the substituted styrenes, a hydrogen atom exists on the same carbon atom as the chlorato group. Ready loss of HOClO then leads to the observed product. It may be noted that direct "allowed" cyclo-addition [19] to form $F{-}C{-}C(X){-}O{-}ClO_2$ is also possible, but we feel that its inclusion is erroneous for four different reasons. First of all, we note that polar alkenes are needed. This is unusual unless the reaction is "forbidden" [20, 21]. In addition we note that since the dipole moment of ClO_3F is only 0.023 ± 0.01 D [22], polar effects are unlikely. Measurements of the relative rates of reaction of ClO_3F with a series of substituted styrenes or stilbenes, a process similar to acid-catalyzed hydration [23] [$S_N2(H)$], would be useful*. Secondly, alkenes do not react with a periodate (which is isoelectronic with ClO_3F [24, 25]) in the absence of catalytic amounts of MnO_4^-, RuO_4 or OsO_4 [26, 27]. These metal oxide catalysts oxidize the olefin and are themselves re-oxidized by the IO_4^- ion. Thirdly, the by-products formed from these reactions are those which would be expected from a polar reaction. Finally, the mechanism proposed above is consistent with that suggested [1] for the reaction of ClO_3F with substituted enolates such as $C_2H_5OOCCH{=}C(OC_2H_5)O^-$. If X = O^- in C=C—X,

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* The addition of fluoride ion to trap any carbonium ion formed should also be investigated.

we would expect it to be an extremely activating substituent to electrophilic attack by analogy to Ar—O^- [28]. In the case of the reaction involving enolates, it is unlikely that the ClO_3^- ion adds to the newly formed C=O group and thus the α-fluoroketone is formed directly.

Arenes, like alkenes, have been studied more extensively with respect to their fluorination by ClO_3F than by *N*-fluoroamines. However, the fluorination of activated arenes has been reported with both reagents. Thus *N*-fluoro-perfluoropiperidine has been reported as reacting with phenoxides [29] and *N*,*N*-dialkylanilines [30]. In both cases, *ortho* substitution occurs in contrast to the reaction with ClO_3F where no such regiospecificity has been observed [31 - 33]. This preference for *ortho* substitution by *N*-fluoro-perfluoropiperidine but not by ClO_3F may be explained in three different ways. First of all, the reaction may involve a cyclic transition state as suggested by Polischuk *et al.* [29, 30]. The oxygen atom attached to the Cl in ClO_3F occupies the same steric position as the lone pair in R_2NF. Hence this oxygen atom may contribute considerable steric hindrance towards the formation of the desired intermediate. Alternatively, but admittedly less convincingly, the nitrogen lone pair may be required in the transition state in a similar manner to that proposed recently for the α effect [34]. Finally, we may invoke the rule that a reaction is only "allowed" [26] if the highest occupied molecular orbital (HOMO) of one reactant is of the same symmetry as the lowest unoccupied molecular orbital (LUMO) of the other reactant [35]. For phenoxides and anilines the HOMO is the same, and in any case, does not change in passing from one fluorinating agent to the other. If the LUMO for $(CF_2)_5N$—F is compared with that for O_3Cl—F, at first glance both would appear to be of σ^* symmetry, *i.e.* X  F. However, on closer study the LUMO for O_3Cl—F may be shown to be of σ symmetry. Now the LUMO of a molecule M is the HOMO of the ions M^- and M^{2-}. Let us assume that the molecular orbital orderings are constant throughout an isoelectronic series as has been assumed elsewhere [36, 37]*. If there is some isoelectronic analog M′ for M^- and/or a similar isoelectronic analog M″ for M^{2-}, we may derive the LUMO for M from the properties of M′ and/or M″. ClO_3F^- is unknown, but PF_4 [38] and PCl_4 [39], which are isoelectronic to it, possess an unpaired electron in the equatorial position of a pseudo-trigonal-bipyramid**. Interpolating back to ClO_3F, it therefore follows that the LUMO is a σ-symmetry orbital. We may thus conclude that if *ortho*-fluorination is "allowed" with *N*-fluoro-perfluoropiperidine, it is "forbidden" with perchloryl fluoride. We note that phenoxyl radicals give *para*-substituted products [29] with the former reagent, but the possibility of $S_H2(F)$ reactions [41] cannot be dismissed.

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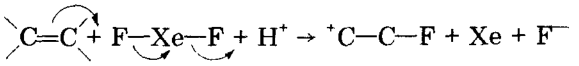
[*] It appear sufficient but not necessary that the molecules should be isoelectronic in the sense of ref. 25 for this "if" clause to be true.

[**] These results have been explained qualitatively in ref. 40 where ref. 38 mentioned above has unfortunately been wrongly cited.

Let us now consider the reactions of the binary xenon fluorides, XeF_2, XeF_4 and XeF_6, with organic compounds. The reaction of alkenes in CCl_4 [42] yields both *gem*- and *vic*-difluorides as well as products derived from chain cleavage and oxidative degradation. No mechanistic studies have been described, however, for these reactions. More recently, the reaction of 2-substituted 1,1-diphenylethylenes with XeF_2 has been reported [43]. The observed catalysis of this reaction by HF and CF_3COOH is strongly suggestive of a simultaneous class 3 $S_N2(F)$ and $S_E2(F)$ reaction [9], *i.e.*



$$>C{=}C< + F{-}Xe{-}F + H^+ \rightarrow {}^+C{-}C{-}F + Xe + F^-$$

The formation of rearranged products such as the *gem*-difluoride may occur through a concerted reaction or by a ready H^- shift from the β-fluorocarbonium ion [44]. Such a process is related mechanistically to the reaction of alkenes with fluorine in polar media [10] or with aryl-iodo-difluorides [45] Arenes may be fluorinated similarly by XeF_2 in both the gaseous phase [46] and in solution [47]. For the former reaction, a free-radical process has been suggested, and for the latter, strong evidence exists for electrophilic fluorination of the arene by a weak F—Xe—F···H—F complex. An equivalent process would involve S_N2 displacement of the fluorine atom by the arene in a class 3 reaction.

In conclusion, therefore, we find that nucleophilic displacement reactions on fluorine with σ- or π-bond nucleophiles are reasonably common and well-defined, and so constitute a general class of reaction.

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