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# THE $S_{ON}2$ MECHANISM

## A NON-OXIDATIVE REACTION THAT IS INITIATED BY ELECTRON TRANSFER OXIDATION

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**Abstract**—Under oxidizing conditions, aromatic chloro and fluoro compounds undergo what formally are typical nucleophilic substitution reactions with surprising ease. As an example, 4-fluoroanisole is converted to 4-acetoxyanisole by anodic or metal ion oxidative initiation, and the reaction is shown to be a chain process. It is proposed that a mechanism analogous to that of the reductively initiated $S_{RN}1$ mechanism operates: The substrate is oxidized to a radical cation by the initiator system, and the radical cation then undergoes *ipso* attack by the nucleophile. In the third step, the leaving group leaves as a *species at the same oxidation level as the nucleophile*, giving the radical cation of the product to be formed. A chain transfer step involving this ion and a new substrate molecule then completes the propagation sequence.

Previously reported cases of this phenomenon are discussed and the individual steps of the chain reaction are considered in terms of their thermochemistry. It is concluded that the $S_{ON}2$ mechanism should be more favoured with easily oxidizable substrates.

The prevailing paradigm of organic chemistry strongly emphasizes the concept of electrons being transferred *pairwise*, as expressed in the general acceptance of "curved arrow" mechanisms in almost all situations where even-electron species take part. Consequently, the role of single electron transfer (ET) is seldom adequately recognized in organic reaction mechanisms, contrary to the state in inorganic chemistry where ET processes have long occupied an important position.[1] Here Marcus' theory has been remarkably successful in guiding new experimentation and providing ideas for new developments. A recent analysis[2] has indicated that the same theoretical framework can incorporate organic ET reactions as well and is indeed very well suited for developing and discussing structure-reactivity relationships of organic ET reactions. In transferring these ideas from the realm of inorganic to organic chemistry, one can foresee a vigorous development of this important part of organic chemistry.

One class of ET mechanisms that has already been fairly well recognized among organic chemists is the electron transfer chain (ETC) mechanism in which an electron or a "positive hole" catalyzes a transformation that *does not involve a change of the oxidation level of the substrate.* In its most general form, this mechanism can be written as eqns (1)–(3) in which A and B are neutral reactant and product species, respectively. The initiation step is an oxidative or reductive ET step (eqn 1)

$$A \xrightarrow[+e^-]{-e^- \text{or}} A^{\pm} \quad (1)$$

$$A^{\pm} \xrightarrow[\text{ral steps}]{\text{one or seve-}} B^{\pm} \quad (2)$$

$$B^{\pm} + A \rightarrow B + A^{\pm} \quad (3)$$

which produces a radical ion. This species ($A^{\pm}$) then undergoes one or several associative or dissociative chemical steps (eqn 2), eventually giving a new radical ion ($B^{\pm}$) which corresponds to the product. The final chain transfer step (eqn 3) consists of an ET step between $B^{\pm}$ and A yielding the product (B) and $A^{\pm}$ which sets off a new sequence of reactions, etc. The above-mentioned characteristics of the ETC mechanism are clearly visible in this Scheme.

Best known among ETC reactions is the $S_{RN}1$ variety,[3] coined as such after its nature as a reductively initiated (eqn 4), formally nucleophilic substitution reaction involving a crucial monomolecular dissociative step (eqn 5). Here one capitalizes on the differing stabilities of the

$$RX \xrightarrow{+e^-} (RX)^{-\cdot} \quad (4)$$

$$(RX)^{-\cdot} \rightarrow R^{\cdot} + X^- \quad (5)$$

$$R^{\cdot} + Nu^- \rightarrow (RNu)^{-\cdot} \quad (6)$$

$$(RNu)^{-\cdot} + RX \rightarrow RNu + (RX)^{-\cdot} \quad (7)$$

radical anions $(RX)^{-\cdot}$ and $(RNu)^{-\cdot}$ to bring about an otherwise very slow reaction (eqn 8) at one and the same oxidation level via ETC catalysis. The initiation step, addition of an electron to RX,

$$RX + Nu^- \rightarrow RNu + X^- \quad (8)$$

can be achieved electrochemically, either via a cathode or a dissolving metal, or photochemically.

Another well established, albeit less well recognized class of ETC reactions is cycloaddition[4] (or cycloreversion[5]) of so far only the $2\pi + 2\pi$ and $2\pi + 4\pi$ varieties; there is no reason why this phenomenon should not be extendable to all types of cycloadditions. Taking a $2\pi + 2\pi$ cycloaddition as an example, the following Scheme (eqns 9–11) has been proposed[6] to account for the ready occurrence of this reaction. Initiation

$$C{=}C \xrightarrow{-e^-} \overset{+}{C}{-}\dot{C} \quad (9)$$

$$\overset{+}{C}{-}\dot{C} + C{=}C \rightarrow \boxed{+\cdot} \quad (10)$$

$$\boxed{+\cdot} + C{=}C \rightarrow \square + \overset{+}{C}{-}\dot{C} \quad (11)$$

(eqn 9) can be achieved by high-valence metal ions,[6] radical cations,[7] or anodically.[8] This type of catalysis is very efficient, for example allowing a Diels–Alder reaction to be run at 0° in 15 min instead of 200° for 20 hr in its thermal version.[7]

Recently, Alder[9] drew the attention to the possibility of extending the ETC reaction concept to novel situations, among them the $S_{ON}2$ mechanism (for oxidatively initiated nucleophilic substitution) which is the subject of the discussion of this paper.[10] We had earlier expressed our puzzlement over an aromatic substitution reaction (eqn 12, Ar = 4-methoxyphenyl, X = F, Nu = OAc) which formally is not an oxidation process, yet demands oxidizing conditions (anodic or metal ion oxidation) to proceed.[11]

$$ArX + Nu^- \rightarrow ArNu + X^- \qquad (12)$$

It was immediately clear that Alder's proposal offered a satisfactory solution to this problem (hinted already in 1975 in connection with aromatic photosubstitution)[12] and that in fact a number of similar phenomena might be ordered neatly by this principle,[10] given in general terms below (eqns 13–16). Since the most commonly encountered substrates are aromatic halides (X = F, Cl, Br) we see that the $S_{ON}2$ mechanism provides a way to activate these otherwise notoriously unreactive compounds for nucleophilic substitution (eqn 12) via an associative step (eqn 14), involving *ipso* attack of $Nu^-$ on a radical cation of ArX. It is the purpose of this paper to summarize the experimental evidence for the $S_{ON}2$ mechanism and discuss its theoretical background.

$$ArX \xrightarrow{-e^-} (ArX)^{+\cdot} \qquad (13)$$

$$(ArX)^{+\cdot} + Nu^- \rightarrow \dot{A}r(Nu)X \qquad (14)$$

$$\dot{A}r(Nu)X \rightarrow (ArNu)^{+\cdot} + X^- \qquad (15)$$

$$(ArNu)^{+\cdot} + ArX \rightarrow ArNu + (ArX)^{+\cdot} \qquad (16)$$

## RESULTS AND DISCUSSION

In principle, many different combinations of X and Nu groups of eqn (12) are experimentally feasible. For an unambiguous mechanistic discussion—if we ever can conduct such!—it is, however, important to limit at least initially the scope of the reaction in two respects. Firstly, $Nu^-$ should be as difficulty oxidizable as possible in order to avoid the complication that an initial $Nu^-$ to $Nu^\cdot$ oxidation step can be invoked. In such case we would be dealing with a homolytic aromatic *ipso* substitution process by $Nu^\cdot$ which in principle, if not practise (see below), is a different concept.[13] Acetate ion, with an $E^0$ for $AcO^\cdot/AcO^-$ of 2.4 V (vs the normal hydrogen electrode: all potentials given in this paper refer to this scale) or other carboxylate ions fulfill this requirement reasonably well and besides, the extreme instability of aliphatic $RCOO^\cdot$ toward decarboxylation[14] makes substitution by $RCOO^\cdot$ unlikely.† Cyanide ion, with an $E^0$ of 1.9 V for $CN^\cdot/CN^-$, is less well suited in this respect but can be considered in photoinitiated reactions.[11] Secondly, also X should correspond to an $X^-$ which is as difficultly oxidizable as possible to avoid two complicating features, one of principal and one of practical importance. The latter is easily disposed of; an easily oxidized $X^-$ would strongly interfere with the initiation step (eqn 13) and very soon bring the chain reaction to a halt. The former one is connected with the step of eqn (15) where we cannot allow suspicions that X can leave as $X^\cdot$ (eqn 17) or as $X^+$ after a second ET step (eqn 18, followed by eqn 19) which is a common situation in anodic aromatic substitution chemistry.[15,16]

$$\dot{A}r(Nu)X \rightarrow ArNu + X^\cdot \qquad (17)$$

$$\dot{A}r(Nu)X \xrightarrow{-e^-} \overset{+}{A}r(Nu)X \qquad (18)$$

$$\overset{+}{A}r(Nu)X \rightarrow ArNu + X^+ \qquad (19)$$

Fluorine is here the most satisfactory and unambiguous choice since a proposal of $F^\cdot$ acting as a leaving entity in eqn (15) amounts to saying that it should be possible to oxidize $F^-$ (with an $E^0 = 3.6$ V for $F^\cdot/F^-$) to fluorine by a chemical oxidant! One cannot, however, escape the possibility that fluorine atom transfer can take place from $\dot{A}r(Nu)F$ (eqn 20) to a suitable radical acceptor.[17] Such a bimolecular step is rather unlikely in view of the extremely low radical concentrations in the systems at hand.

$$\dot{A}r(Nu)F + R^\cdot \rightarrow RF + ArNu \qquad (20)$$

The intervention of such a step would moreover mean that the chain reaction cannot be sustained and lead to stoichiometric or less than such use of the initiator. Chlorine ($E^0$ for $Cl^\cdot/Cl^- = 2.6$ V) is presumably a borderline case with different behaviour in different situations; for oxidants of weak or medium power it can be tolerated as X in eqn 12, but even so its choice might be open for criticism for the above-mentioned reasons. Thus our scrutiny of the experimental evidence for the $S_{ON}2$ mechanism will initially be limited to aromatic fluoro compounds, with occasional mentioning of chloro derivatives.

Having thus rather drastically curtailed the choice of leaving groups and nucleophiles for the discussion of the $S_{ON}2$ reaction we finally face a common situation in oxidative substitution chemistry, namely that the product of such a reaction often is more easily oxidized than the substrate. This constitutes another experimental limitation since after a certain period of reaction the product will start to consume the initiator and thus lower the catalytic efficiency. Mechanistic studies must therefore be confined to runs at low conversion to minimize this effect.

Table 1 shows results from the anodically initiated fluorine/acetoxyl exchange of 4-fluoroanisole in HOAc/KOAc. In agreement with the above reasoning the current yield (equal to the catalytic efficiency) increases with decreasing degree of conversion, reaching 270% at 2% conversion. In other words, in this run each "hole" generated by ET to the anode produces almost

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† It may be necessary to modify this assumption in view of the experimental finding that two types of acetoxy radical exist,[18] one with an extremely high rate of decarboxylation and a more stable one with the ability to act as an H atom abstracting species. So far it is not known if the latter type of $AcO^\cdot$ will add to aromatic rings; should this be the case, a lot of oxidative acetoxylation chemistry will have to be reevaluated.[14] It would also complicate, but not invalidate, the present discussion of the $S_{ON}2$ mechanism in the case of Nu=AcO (eqn 12).

Table 1. Current yields of 4-acetoxyanisole from the anodic oxidation of 4-fluoroanisole in HOAc/KOAc[a]

| [$\mathrm{AcO}^-$]/M | [Substrate]/M | Current density/mA cm$^{-2}$ | Conversion/ F mol$^{-1}$ | Current yield[b]/% |
|---|---|---|---|---|
| 0.5 | 2.0 | [c] | 1.0 | 40[d] |
| 0.5 | 2.0 | [c] | 0.5 | 75[d] |
| 0.5 | 2.0 | 5.0 | 0.2 | 84 |
| 0.5 | 2.0 | 5.0 | 0.1 | 99 |
| 0.5 | 2.0 | 5.0 | 0.02 | 128 |
| 0.5 | 1.0 | 5.0 | 0.02 | 212 |
| 0.1 | 2.0 | 3.5[c] | 0.02 | 91 |
| 0.5 | 0.5 | 5.0 | 0.02 | 270 |

[a] Conditions, see experimental part. [b] Calculated for 1 F mol$^{-1}$. [c] Run at a constant potential of 1.7 V. [d] Ref. 10. [e] This value could not be exceeded due to the limited capacity of the potentiostat used (100 V).

three molecules of the acetate, thus demonstrating the chain reaction characteristics expected of an $S_{ON}2$ mechanism. Both Ag(II)[19] and Co(III),[20] the latter as the wolframocobalt(III)ate ion, bring about the same transformation, albeit not so far with catalytic efficiency (yields 100 and 24%, respectively).

Several other aromatic fluorine compounds (4-fluorotoluene, 4-t-butylfluorobenzene, 2-chlorofluorobenzene, 4-bromofluorobenzene, 1-fluoronaphtalene, 4-fluorophenyl acetate, 4-dimethylaminofluorobenzene and 2-fluoroanisole) were anodically oxidized under the same conditions, but fluorine/acetoxyl exchange took place with 2-fluoroanisole only. In the other cases normal acetoxylation occurred with displacement of hydrogen in ring or $\alpha$ positions. Since current yields in most cases were low due to high oxidation resistancy of the substrates relative to $\mathrm{AcO}^-$, one compound, 4-bromofluorobenzene was instead oxidized in trifluoroacetic acid (TFA), 0.5 M in its sodium salt. This system is known to be considerably more resistant toward oxidation than HOAc/KOAc, allowing for anodic trifluoroacetoxylation of even deactivated aromatics.[21] After anodic oxidation in this system and hydrolysis of the trifluoroacetates formed, 4-bromofluorobenzene gave a 10% yield of 4-bromo- and 4-fluorophenol in a ratio of 1.8:1 in addition to ring acetoxylated 4-bromofluorobenzenes (30%).

We next studied a metal ion promoted $S_{ON}2$ type reaction, the Cu(III) promoted fluorine/hydroxyl and chlorine/hydroxyl exchange of fluoro- and chlorobenzene in TFA, 0.2 M in water. Cu(III) was added as its biuret complex and the reaction was run at reflux temperature. In both cases halogen/hydroxyl exchange took place, giving a 35–45% yield of phenol in addition to ring hydroxylated halogenobenzenes (3–10%). Under the same conditions 4-bromofluorobenzene gave a 10% yield of 4-bromo- and 4-fluorophenol in a ratio of 1.8:1, the same as was obtained anodically.

The $S_{ON}2$ mechanism can in principle be entered from a different angle, namely to form the acetoxyfluorocyclohexadienyl radical radical of eqn (14) (Nu=AcO, X=F) *via* acetoxyl radical attack on the parent compound (eqn 21). Because of the instability of the acetoxyl radical ($E_a$ for decarboxylation *ca.* 7.5 kcal mol$^{-1}$) it was instead

$$\mathrm{Ac\dot{O}} + \mathrm{ArF} \rightarrow \mathrm{\dot{A}r(OAc)F} \qquad (21)$$

deemed experimentally more favourable to use the benzoyloxyl radical (from decomposing benzoyl peroxide); this has the additional advantage that the chain length can be estimated from the ratio between 4-methoxyphenyl benzoate (formed in the first cycle) and acetate (formed in subsequent cycles).

Table 2 shows results from the decomposition of benzoyl peroxide in the presence of 4-fluoroanisole in HOAc with or without acetate present. In the latter case the predominant products are those of fluorine/acyloxyl exchange in an acetate:benzoate ratio of 2.6–9.5. In addition, small amounts of products expected from normal benzoyloxyl radical chemistry[22] (fluoromethoxybiphenyls and fluoromethoxyphenyl benzoates) are formed. Total yields, based on $\mathrm{PhCOO}^{\cdot}$, in excess of 100% demonstrate the chain character of the process. In the absence of $\mathrm{AcO}^-$ and with suppression of the autoionization of HOAc by adding a minute amount of TFA, the benzoate yield remains constant while that of the acetate decreases strongly. 4-Methoxyphenyl benzoate is completely stable under the conditions used.

These results are best interpreted in terms of an $S_{ON}2$ mechanism with addition of $\mathrm{PhCOO}^{\cdot}$ at the fluorine-bonded C atom as the initiation step. The first cycle produces one molecule of the benzoate and then the reaction proceeds through maximally ten cycles, each producing one molecule of the acetate. Without acetate ion present, the chain reaction cannot be sustained by the considerably weaker nucleophile, acetic acid.

Similar reactions, although not as clean, have been reported before, e.g. in the attack of pentafluorobenzoyloxyl radical on chloro- and fluorobenzene to give 40–50% yields of phenyl pentafluorobenzoate,[23] in the radical aroyloxylation of perfluoroaromatics.[24] and in the thermally[25] or photochemically[26] generated benzoyloxyl

Table 2. Products from 4-fluoroanisole (ArF) in HOAc/KOAc in the presence of decomposing benzoyl peroxide at 78°C[a]

| $(PhCOO)_2$/ mmol | Yield of products/%[b] ArOAc | ArOCOPh | Others[c] | Acetate/benzoate ratio |
|---|---|---|---|---|
| 0.25 | 41 | 16 | 12 | 2.6 |
| 0.5 | 65 | 20 | 10 | 3.3 |
| 1.0 | 88 | 12 | 11 | 7.3 |
| 1.0[d] | 65 | 18 | 14 | 3.6 |
| 1.0[e] | 78 | 12 | 12 | 6.5 |
| 2.0 | 54 | 10 | 9 | 5.4 |
| 1.0[f] | 10 | 12 | 10 | 0.8 |
| 1.0[g] | 6 | 10 | 8 | 0.6 |
| 1.0[h] | 57 | 6 | 7 | 9.5 |

[a] Conditions, see experimental part. [b] GLC yield, based on PhCOO·. [c] Fluoromethoxybiphenyls and fluoromethoxyphenyl benzoates. [d] [ArF] = 2 M. [e] [KOAc] = 1 M. [f] No acetate ion added. [g] No acetate ion present and TFA (50 μl) added. [h] KF (2 mmol) added.

radical attack on chlorobenzene to give phenyl benzoate in low yield.

Once the possibility of an $S_{ON}2$ mechanism had been verified, a literature search revealed a number of reactions of similar type. Again limiting ourselves to chloro- and fluoroaromatics as substrates, a list of such reactions is given in Table 3 (Nos. 1–8); in addition, our attention was drawn to a case involving $=N_2$ as a leaving group in a very efficient chain reaction (No. 9).

Reactions 1–3 give low yields and actually appear as side-reactions to other processes. The remarkable reaction 4 is indeed a strong attest to the power of "hole" catalysis: Fluorobenzene is hydrolyzed in neutral aqueous solution at room temperature with a half-life of < 30 min. Reaction 5, hydroxydehalogenation of 4-halogenotoluenes by hydroxide ion at temperatures around and above 300°, displays a behaviour characteristic of an aryne mechanism in the absence of any catalyst and air (*p*/*m* ratio of cresols formed = 0.82 in all cases). In the presence of air and Cu(II) in catalytic amount a switch to an *ipso* hydroxydehalogenation process was noticed. In view of the properties of Cu(III) described above it is reasonable to propose that this species plays a catalytic role here, air functioning as the ultimate oxidant in the system.

Reactions 6–8 are taken from a large list of similar photosubstitutions, assumed to occur *via* initial photoionization of the substrate (excitation to the triplet

Table 3. Possible cases of the $S_{ON}2$ mechanism, reported in the literature

| Reaction No | Compound | Initiator/$Nu^-$ | Product (%) | Ref. |
|---|---|---|---|---|
| 1 | PhCl | Anode/$CF_3COO^-$ | $PhOCOCF_3$ (2) | 27 |
| 2 | PhCl | Co(III)/$CF_3COO^-$ | $PhOCOCF_3$ (6) | 28 |
| 3 | PhCl | Pb(IV)/$CF_3COO^-$ | $PhOCOCF_3$ (trace) | 29 |
| 4 | PhF | $S_2O_8^{2-}$/Cu(II)Fe(II)/$H_2O$ | PhOH (~ 30) | 30 |
| 5 | $4\text{-}MeC_6H_4$ | Cu(II)/$O_2$/$OH^-$ | $4\text{-}MeC_6H_4OH$[a] | 31 |
| 6 | $4\text{-}MeOC_6H_4F$ | hν/$CN^-$ or anodic | $4\text{-}MeOC_6H_4CN$ (95) | 12 |
| 7 | $4\text{-}MeOC_6H_4F$ | hν/$AcO^-$ | $4\text{-}MeOC_6H_4OAc$ (20) | 12 |
| 8 | $4\text{-}MeOC_6H_4Cl$ | hν/$CN^-$ | $4\text{-}MeOC_6H_4CN$ (89)[b] | 12 |
| 9 | $Ph_2CN_2$ | Cu(II) or $(4\text{-}BrC_6H_4)_3N^{+\cdot}$ | $Ph_2C{=}CPh_2$ (~ 80)[c] | 32 |

[a] The presence of Cu(II)/$O_2$ causes a switch from an aryne to an $S_{ON}2$-like mechanism, involving ipso substitution. [b] A quantum yield > 1.0 was observed. [c] Catalytic efficiencies of ca 4000 % were reached.

state, followed by loss of an electron). The "curious phenomenon that at higher concentration of para chloroanisole ($10^{-3}$ M) the quantum yield becomes higher than 1 (1.2)" was interpreted in terms of the sequence of eqns. 13–16. Thus den Heijer *et al.*[12] must be given credit for being first to recognize the possibility of a chain transfer step (eqn 16) in this type of reactions. Photochemical and anodic initiation give identical product compositions in the cases tested.

Reaction 9, ET initiated decomposition of diphenyldiazomethane to give mainly tetraphenylethylene, is formally of the $S_{ON}2$ type, although the associative step (eqn 23) presumably is of greater complexity. The

$$Ph_2CN_2 \xrightarrow{-e^-} (Ph_2CN_2)^{+\cdot} \qquad (22)$$

$$(Ph_2CN_2)^{+\cdot} + Ph_2CN_2 \rightarrow Ph_2\overset{+}{C}\text{–}\dot{C}Ph_2 + 2N_2 \qquad (23)$$

$$Ph_2\overset{+}{C}\text{–}\dot{C}Ph_2 + Ph_2CN_2 \rightarrow Ph_2C{=}CPh_2 + (Ph_2CN_2)^{+\cdot} \qquad (24)$$

initiators, Cu(II) or tris(4-bromophenyl)aminium perchlorate are very efficient, allowing for "catalytic yields" of up to *ca.* 4000%.

Taking for granted that the oxidant is capable of extracting an electron from the substrate (eqn 13; this step is easily analyzed in terms of Marcus' theory),[2] the feasibility of the two subsequent steps (eqns 14 and 15) can be inferred from a thermodynamic treatment. To start with, we put ArF equal to PhF and Nu=AcO, and consider Scheme 1:

$$\begin{tikzcd}
PhOAc + F^{\cdot} \arrow[rr, shift left] \arrow[d, shift left] & & PhF + AcO^{\cdot} \arrow[ll, shift left] \arrow[d, shift left] \\
(PhOAc)^{+\cdot} + F^{-} \arrow[u, shift left] \arrow[r, shift left] & (\dot{P}h(OAc)F \arrow[l, shift left] \arrow[r, shift left] & (PhF)^{+\cdot} + AcO^{-} \arrow[l, shift left] \arrow[u, shift left]
\end{tikzcd}$$

Scheme 1.

The lower part of Scheme 1 is our main target, but we cannot directly assess values to the energy levels involved because of the lack of thermodynamic data for ionic species, especially radical cations, in solution. However, following the reasoning developed in earlier work,[33] we can instead easily find thermodynamic data for the upper part of the Scheme where only an electron has shifted position within each pair of reactants. Then one can use $E^\circ$ data for the half-reactions involved to construct a complete energy diagram. Thus we find the following gas phase standard heats of formation (in kcal $mol^{-1}$) for eqn (25), and hence $\Delta H^\circ = -24.7 \approx -25$ kcal $mol^{-1}$. Making the reasonable assumption that the $S^\circ$

$$\begin{array}{ccccccc} PhOAc & + & F^{\cdot} & \rightarrow & PhF & + & AcO^{\cdot} \\ -66.8 & & 18.9 & & -27.7 & & -45 \end{array} \qquad (25)$$

terms cancel and hence $\Delta G^\circ = \Delta H^\circ$, and that likewise differences in heats of solution of these neutral species cancel, we can put $\Delta G^\circ$ in acetic acid for eqn (25) equal to $-25$ kcal $mol^{-1}$.

In order to estimate the energy level of $\dot{P}h(OAc)F$ we use a modification of the method developed by Dorrepaal and Louw.[34] They put $\Delta H^\circ$ for eqn 26 equal to that of $PhH + H^{\cdot} \rightarrow \dot{P}hH_2$ ($= -22$ kcal $mol^{-1}$ according to the most

$$PhF + H^{\cdot} \rightarrow \dot{P}h(H)F \qquad (26)$$

recent data compilation)[35] in order to estimate the standard heat of formation of the fluorocyclohexadienyl radical. We now actually want to estimate $\Delta H^\circ$ for eqn (27), and this is done by simply adding to $-22$ kcal $mol^{-1}$ the average difference in bond energy between a C–H and C–O bond (taken to be 10 kcal $mol^{-1}$), assuming that the important energy parameters of eqns (26) and (27) are connected with breaking of the aromatic sextet (the same energy change in both reactions) and formation of the new bond (assumed to

$$PhF + AcO^{\cdot} \rightarrow \dot{P}h(OAc)F \qquad (27)$$

differ by 10 kcal $mol^{-1}$, as described above). We thus can put $\Delta H^\circ$ of eqn (27) at $-12$ kcal $mol^{-1}$. With the same assumptions as above–except that we have to include a $T\Delta S^\circ$ term of *ca.* 7 kcal $mol^{-1}$—we obtain $\Delta G^\circ$ for eqn (27) equal to $-5$ kcal $mol^{-1}$ in acetic acid. Using the following $E^\circ$ values (for oxidation), PhOAc, 2.8 V; PhF, 3.1 V; $F^-$, 3.6 V; $AcO^-$, 2.4 V, we obtain the free energy diagram of Fig. 1 where the energy levels are indicated in parentheses.

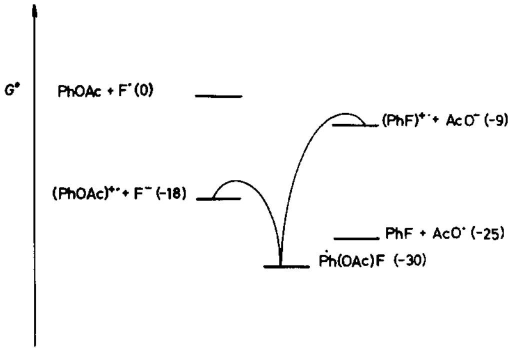

Fig. 1. Free energy diagram involving the reactions of Scheme 1.

Although the approximate nature of these calculations must be kept in mind, we can be reasonably sure that the *ipso* substitution intermediate, $\dot{P}h(OAc)F$, is formed in an exergonic step from $(PhF)^{+\cdot}$ and $AcO^-$ and thus eqn (14) represents a feasible step in this case. It is also obvious that loss of $F^-$ from the intermediate is favoured over that of $AcO^-$, so that also eqn. 15 is a feasible step relative to the reverse of eqn (14). We cannot, however, use the diagram for a *quantitative* estimate of the energy of activation for loss of $F^-$ due to the uncertainty of the data, but we can nevertheless get an idea of how it is influenced by the nature of the substrate and product, most importantly by their oxidation potentials.

We now lower these potentials by changing Ar from Ph to $4\text{-}MeOC_6H_4$ (the very system for which we have good experimental evidence for the $S_{ON}2$ mechanism) and assume that the differences between the energy levels of $(ArOAc + F^{\cdot})$, $(ArF + AcO^{\cdot})$, and $\dot{A}r(OAc)F$ are the same as for Ar=Ph. With $E^\circ$ for oxidation of ArF and ArOAc equal to 2.10 and 1.6 V, respectively, we can draw the energy diagram of Fig. 2. We now see that eqn (14) still is a feasible step and that loss of $F^-$ from the intermediate is still favoured over that of $AcO^-$. This reaction is moreover exergonic, showing that this step will tend to

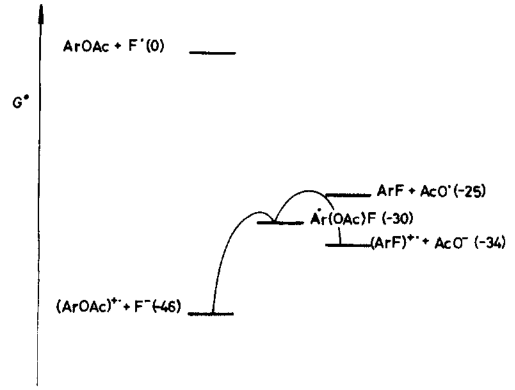

Fig. 2. Free energy diagram involving the reactions of Scheme 1, with Ph exchanged for 4-$MeOC_6H_4$.

be faster as the substrate is more easily oxidized. One would therefore predict that the $S_{ON}2$ mechanism will be favoured for easily oxidized substrates.

One can make similar estimates using chloride as the leaving group and arrives at similar conclusions: Loss of chloride is much favoured over loss of acetate from the intermediate, and easily oxidized substrates should give an intermediate which loses chloride in an exergonic process. With cyanide ion as the nucleophile, the situation is qualitatively the same, so from this point of view cyanide ion is a suitable nucleophile in the $S_{ON}2$ mechanism.

The chain transfer step (eqn 16), ET between $(ArOAc)^{+\cdot}$ and ArF (ArCl), does not present any particular difficulties. It can be analyzed in terms of Marcus' theory,[2] and in view of the slight endergonicity to be expected for this step ($\Delta G^\circ \leq 10\,\mathrm{kcal\,mol^{-1}}$) both kinetic and equilibrium conditions make it a feasible proposition. For an $(ArOAc)^{+\cdot}$ of high oxidation potential, e.g. $(PhOAc)^{+\cdot}$, there is always the complication that ET may take place also from $AcO^-$ which leads to termination of the chain process. This is presumably the reason for the stoicheiometric requirement of oxidant in reactions with substrates that are difficult to oxidize, and leads to the prediction that the chain reaction should be more efficient with easily oxidizable substrates for this reason too.

Summarizing, we have demonstrated that the oxidatively initiated, non-oxidative substitution of chloro- and fluoroaromatics by certain nucleophiles is best described by the $S_{ON}2$ mechanism (eqns 13–16). Predictions based on simple thermochemical considerations and the Marcus theory so far are in agreement with experimental findings.

## EXPERIMENTAL

*Anodic initiation.* The anodic initiation of the $S_{ON}2$ mechanism was carried out at room temp. in a non-divided micro-cell (volume of electrolyte, 5.0 ml), equipped with two Pt foil electrodes, each of 2 $cm^2$ effective surface area. The reactions were run in a constant current mode (an AMEL model 552 potentiostat was used as a current source) and the charge passed was monitored by a home-built electronic integrator. The mixture was worked up by pouring it into $NaHCO_3$aq, followed by ether extraction and gas chromatographic analysis (reference compound, 3-*t*-butylphenyl acetate; 2 m × 0.3 mm 5% neophentylglycol succinate on Chromosorb P column). Compounds were identified by comparison with authentic specimen (glc/MS; Finnigan 4021 instrument) in most cases.

*Potassium* Cu(III)($H_{-4}$)(*biuret*)$_2$ *initiation.* A soln of the Cu(III) complex of biuret[36] (10 mmol), substrate (5 mmol) and water (5 mmol) in TFA (25 ml) was refluxed for 2 hr. After evaporation of the solvent workup and analysis was performed as described above.

*Benzoyl peroxide initiation.* Unless otherwise stated (Table 2), a soln of substrate (1.0 M), benzoyl peroxide (Table 2), and KOAc (0.5 M) AcOH (5.0 ml) was kept at 78° for 20 hr (equiv to *ca.* 10 half-lives for decomposition of benzoyl peroxide).[37] Workup and analysis, see above.

*Thermodynamic data.* Standard heats of formation were taken from recent compilations.[35,38] Standard potentials for $AcO^\cdot/AcO^-$, $F^\cdot/F^-$ and $CN^\cdot/CN^-$ in aqueous and acetonitrile soln have been calculated (for a list of these and other $E^\circ$ values, see Ref. 2). The AcOH values were taken to be equal to those pertaining to aqueous medium. In view of the powerful H-bonding properties of HOAc *vs* $AcO^-$ and $F^-$, this approximation probably does not introduce any significant errors.

The standard potentials of $(PhF)^{+\cdot}/PhF$ and $(PhCl)^{+\cdot}/PhCl$ were estimated at values slightly above that of benzene by methods discussed in Ref. 2. For PhOAc, the gas phase ionization potential has been estimated at 9.1 eV,[39] and this value was converted to an $E^\circ$ value of $(PhOAc)^{+\cdot}/PhOAc$, 2.8 V. The $E^\circ$ value for oxidation of 4-methoxyphenyl acetate as estimated from its $E_{1/2}$ value, whereas that of 4-methoxyfluorobenzene was measured to be 2.10 V in dichloromethane-TFA (20:1)/$Bu_4NBF_4$ (0.2 M) by cyclic voltammetry at 100 $Vs^{-1}$.

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