Electron-transfer Chain Catalysis of Substitution Reactions. Experimental Evidence for the $S_{ON}2$ Mechanism

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Summary Two possible cases of an oxidative electron-transfer chain catalysis mechanism, the $S_{ON}2$ mechanism, are presented: the anodic 'oxidation' of 4-fluoroanisole in the presence of acetate ion to give 4-acetoxyanisole, and the Cu^{III} 'oxidation' of chloro- and fluoro-benzene in the presence of water to give phenol.

In the preceding communication,[1] Alder has introduced the concept of electron-transfer chain (E.T.C.) catalysis in which a non-redox process is catalysed or stimulated by an electron-transfer reagent. Foremost among such mechanisms is the $S_{RN}1$ reaction[2–4] where the key intermediates are radical anions.

Alder extended the E.T.C. concept to mechanisms involving radical cations as well, *e.g.*, the $S_{ON}2$ mechanism, a bimolecular mechanism for what is formally a nucleophilic substitution *via* one-electron oxidation of the substrate, equations (1)—(4). For such a reaction to take place a good leaving group is essential, and the obvious choice in the type of bond-breaking step (3) involved is fluoride ion. It is extremely difficult to oxidize and is very unlikely to leave as fluorine atom or, worse, fluorine cation from the radical in reaction (3) or from species resulting from its further oxidation. Moreover, the abstraction of fluoride ion from a cyclohexadienyl radical has been shown to be highly exothermic by thermochemical calculations.[5]

$$\text{Initiation:} \quad RX \xrightarrow{-e^-} RX^{\cdot+} \qquad (1)$$

$$\text{Propagation:} \left\{ \begin{array}{ll} RX^{\cdot+} + Nu^- \rightarrow [RXNu]^{\cdot} & (2) \\ [RXNu]^{\cdot} \rightarrow RNu^{\cdot+} + X^- & (3) \\ RNu^{\cdot+} + RX \rightarrow RNu + RX^{\cdot+} & (4) \end{array} \right.$$

One likely candidate for the $S_{ON}2$ mechanism is the substitution of fluorine for acetoxy that takes place upon anodic,[6] Ag^{II},[7] and 12-wolframocobalt(III)ate[8] 'oxidation' of 4-fluoroanisole [reaction (5), Ar = $4\text{-}MeOC_6H_4$)] in the presence of acetate ion. In the anodic case, coulometry indicated the consumption of one electron per mol of substrate.[6] We now report that reaction (5) (Ar = $4\text{-}MeOC_6H_4$) can be run catalytically under conditions of low conversion. Moreover, we show that Cu^{III} can induce $S_{ON}2$ type behaviour, in that Cu^{III} oxidation of chloro- and fluoro-benzene in trifluoroacetic acid–acetic acid–water gives phenol as the predominant product. Finally, a number of suspected cases of the $S_{ON}2$ mechanism have been spotted in the literature.

$$ArF + AcO^- \rightarrow ArOAc + F^- \qquad (5)$$

Anodic oxidation of 4-fluoroanisole in HOAc–KOAc at low conversions (higher conversions, up to 2 F mol^{-1} lowered the yields appreciably)[6] gave current yields of 4-acetoxyanisole in excess of 100% (Table 1), the best yield so far being obtained at 2% conversion and a relatively low substrate concentration. This experiment corresponds to a consumption of 0·37 e$^-$ per molecule of product formed. We are somewhat puzzled over the strong decrease in current yield as conversion is increased, but tentatively ascribe it to further oxidation of 4-acetoxyanisole, a substrate likely to undergo 'cascade' electron transfers under oxidizing conditions (at higher conversions, polymeric material is indeed very clearly visible).

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

[Substrate]/M	Conversion/ F mol^{-1}	Current yield[b]/%
2·0	0·2	84
2·0	0·1	99
2·0	0·02	128
1·0	0·02	212
0·5	0·02	270

[a] At a platinum anode at 25 °C; current density 5·0 mA cm^{-2}; [AcO$^-$] 0·5 M. [b] Calculated for 1 F mol^{-1}.

A second $S_{ON}2$ type reaction was found during exploratory studies of the oxidative properties of Cu^{III} complexes *vs.* aromatic compounds. Copper(III) compounds have been used previously for the oxidation of organic compounds,[9–12] but so far such studies have been confined to aqueous media. Table 2 shows that benzene, alkyl-aromatic compounds, and chloro- and fluoro-benzene are oxidized to the usual range of oxidative-substitution and coupling products,[13] expected for stoicheiometric electron transfer mechanisms, by the copper(III) complex of biuret[14] in trifluoroacetic acid (TFA) or TFA–AcOH mixtures. However, in the presence of small amounts of water, the formation of phenol from the halogenobenzenes becomes predominant. While we have not yet succeeded in obtaining catalytic yields of phenols, compounds that can be very easily oxidized further, the reaction is certainly a non-redox process which, according to control experiments, does not take place in the absence of Cu^{III}. It does not take place either with the much weaker oxidant, Cu^{II}, present.[15]

A survey of the recent literature on anodic and metal-ion oxidation of chloro- and fluoro-aromatic compounds† showed the following suspected cases. Anodic[16] and cobalt(III) trifluoroacetate[17] oxidation of chlorobenzene gave 2 and 6% of phenyl trifluoroacetate, respectively, lead tetra-acetate

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† We have restricted ourselves to chloro- and fluoro-derivatives because of the requirement of having a leaving group which is difficult to oxidize; naturally, several other types of $S_{ON}2$ behaviour can be envisaged, such as the 'oxidative' substitution of the methoxy-group by cyanide ion in certain polymethoxyaromatic compounds either anodically (S. Andreades and E. W. Zahnow, *J. Am. Chem. Soc.*, 1969, **91**, 4181; L. Eberson and B. Helgée, *Acta Chem. Scand., Ser. B*, 1975, **29**, 451; 1977, **31**, 813) or photochemically (J. den Heijer, O. B. Shadid, J. Cornelisse, and E. Havinga, *Tetrahedron*, 1977, **33**, 779).

TABLE 2. Oxidation of some aromatic compounds by the Cu^{III} complex of biuret.[a]

		Yield/%[c]						
Reaction[b] medium		Acetate		Phenols				
(expt. no.)	Compound	Nuclear	α	*o*	*m*	*p*	Dimers	Other products
HOAc–TFA (1)	Mesitylene	0·2	28				Trace	3,5-Dimethylbenzyl trifluoroacetate, 2 3,5-Dimethylbenzaldehyde, 0·7
TFA (2)	Mesitylene						5[d]	
TFA (3)	Mesitylene						31[d]	
HOAc–TFA (4)	Toluene	0·2	2					Benzaldehyde, 0·3
TFA–H_2O (5)	Benzene							Phenol, 11
TFA–H_2O (6)	Chlorobenzene			6	$<0·1$	7		Phenol, 33
TFA–H_2O (7)	Fluorobenzene			1	$<0·1$	1		Phenol, 44

[a] Conditions used in all experiments, unless otherwise noted: substrate (5 mmol), $KCu(biuret)_2$ (10 mmol), glacial acetic acid (25 ml), TFA (2·5 ml), reflux temperature, reaction period 2 h. [b] Reaction medium in experiment 2 was TFA (25 ml), in experiments 5—7 TFA (25 ml) and water (5 mmol), and experiment 3 TFA (25 ml) and mesitylene (12·5 ml). [c] G.l.c. yield based on Cu^{III}. [d] Experiment 2: 3,5,2′,4′,6′-pentamethyldiphenylmethane, 5%, and bimesitylene, 0·1%. Experiment 3: 3,5,2′,4′,6′-pentamethyldiphenylmethane, 24%, and bimesitylene, 7%.

oxidation of chlorobenzene in TFA gave traces of phenol,[18] and oxidation of fluorobenzene in aqueous solution by peroxydisulphate in the presence of Cu^{II} and Fe^{II} salts gave phenol in yields of up to 96% at room temperature.[19] We also draw attention to the *ipso* hydroxydehalogenation process observed with *p*-halogenotoluenes in aqueous alkali at high temperatures;[20] it is catalysed by copper salts and with air present as an oxidant the product pattern changes from a *m*/*p* cresol mixture (characteristic of a benzyne mechanism) to predominantly *p*-cresol, indicating a switch to an $S_{ON}2$ mechanism. If this is so, it would seem to be possible to find more efficient ways of catalysing this industrially important process. Finally, another entry into the $S_{ON}2$ mechanism should also be possible *via ipso*-radical attack,[21] the initiation step then being $RX + Nu^{\bullet} \rightarrow [RXNu]^{\bullet}$ [*cf.* equation (2)]. One possible case is the attack of pentafluorobenzoyloxyl radical on chloro- and bromo-benzene to give relatively high yields (40—50% based on the amount of $ArCO_2^{\bullet}$) of phenyl pentafluorobenzoate,[22] in spite of the fact that the reaction conditions employed were far from ideal for the $S_{ON}2$ sequence to occur. In other words, it should be possible to induce or even catalyse nucleophilic aromatic substitution of halogenobenzenes by decomposing diacyl peroxides.

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