Radical cation mechanism of aromatic halogenation by halogens or iodine chloride in 1,1,1,3,3,3-hexafluoropropan-2-ol

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The reaction between aromatic compounds ArH and halogenating agents, *viz.* iodine chloride, chlorine, bromine, iodine, *N*-bromosuccinimide and *N*-chlorosuccinimide, in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP) has been investigated. EPR spectroscopy established that these reagents produced persistent radical cations $ArH^{\cdot+}$ from ArH with $E_{rev}(ArH^{\cdot+}/ArH)$ up to 1.6, 1.3, 1.4, 1.1, 1.5 and 1.2 V *vs.* Ag/AgCl, respectively. Cyclic voltammetry of the halogenating species shows that no effect of complexation with halide ion is observed in HFP, as expected from its capacity to drastically attenuate nucleophilic reactivity, and that the cathodic peak potentials E_{pc} (referenced to the internal ferricinium/ferrocene redox couple) are significantly or remarkably higher in HFP than in acetonitrile. For *N*-bromosuccinimide, the difference amounts to almost 1 V.

The persistency of the radical cations in HFP is such that the kinetics of reactions between a halogenating agent, such as iodine chloride or bromine, and ArH, such as 1,4-dimethoxybenzene [$E_{rev}(ArH^{\cdot+}/ArH) = 1.50$ V *vs.* Ag/AgCl] or 1,4-dimethoxy-2,3-dimethylbenzene [$E_{rev}(ArH^{\cdot+}/ArH) = 1.16$ V], have been studied at room temperature over periods of hours. The initial concentration of the radical cation corresponds to yields in the range of 40–100%, depending on the reaction conditions. It is thus possible to establish that the radical cation decays *via* two pathways, one being the well known oxidative substitution reaction with halide ion. The second mechanism involves halogen atom transfer from the halogenating agent (Cl atom from ICl, Br atom from bromine). In the case of the radical cation of 1,4-dimethoxy-2,3-dimethylbenzene reacting with bromide ion or bromine, the latter reaction is $>10^2$ times faster.

Introduction

Some of the classical polar aromatic substitution mechanisms have been discussed in terms of ideas emanating from the electron transfer (ET) concept.[1] Two approaches have been pursued, namely (i) to regard the aromatic substitution transition state as a resonance hybrid between the initial state and one in which an electron has been shifted between the substrate ArH and the electrophile E^+ [eqn. (1)] [2] and (ii) to find evidence for

$$ArH + E^+ \longrightarrow [ArH\,E^+ \longleftrightarrow ArH^{\cdot+}\,E^{\cdot}]^{\ddagger} \longrightarrow Ar^+(H)E \quad (1)$$

an initial ET step leading to a radical cation $ArH^{\cdot+}$ which combines with $E^{\cdot}$ to give the Wheland intermediate [eqn. (2)].[3]

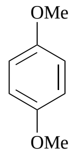
$$ArH + E^+ \longrightarrow ArH^{\cdot+} + E^{\cdot} \longrightarrow Ar^+(H)E \quad (2)$$

For some time we have been involved in work related to the second approach as applied to aromatic substitution by nitronium ion, NO_2^+, and have concluded that a mechanism of the type shown in eqn. (2) is not supported by available facts.[4] In principle, the same problem can be raised for many types of ArH, E^+ reactions, and it is likely that each electrophile will require an answer of its own. Recently we have found conditions which make aromatic halogenation according to eqn. (3)

$$ArH + X_2 \longrightarrow ArH^{\cdot+} + X^{\cdot} + X^- \longrightarrow\longrightarrow Ar^+(H)X \quad (3)$$

conveniently accessible to experimental study, as reported in a preliminary communication,[5] and we now report the results of a more complete study.

There is previous evidence that halogens can act as $1e^-$ oxidants towards reactive aromatics (ArH) and give persistent radical cations in solution or in the form of solid salts.[6] Mixed halogens react similarly; it was suggested recently [7] that the reaction of iodine chloride with reactive ArH in acetonitrile or dichloromethane to give ArCl and/or ArI would proceed according to an electron transfer mechanism [eqns. (4)–(6)]. In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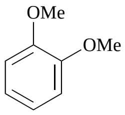
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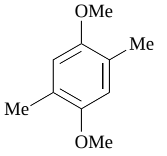
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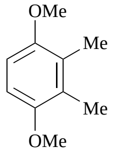
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$$ArH + ICl \longrightarrow ArH^{\cdot+} + I^{\cdot}\ (0.5\,I_2) + Cl^- \quad (4)$$

$$ArH^{\cdot+} + Cl^- \longrightarrow\longrightarrow Ar{-}Cl \quad (5)$$

$$ArH^{\cdot+} + I^{\cdot}\ (\text{or } I_2) \longrightarrow\longrightarrow Ar{-}I \quad (6)$$

some cases, namely 1,4- (**1**) and 1,2-dimethoxybenzene (**2**) and 1,4-dimethoxy-2,5-dimethylbenzene (**3**), it was possible[7c] to demonstrate the formation of $ArH^{\cdot+}$ by UV spectroscopy in dichloromethane at −78 °C. Addition of an excess of a chloride ion source led to the immediate disappearance of the radical cation and formation of the ring substituted chloro derivative. It was shown also that the reaction of $\mathbf{1}^{\cdot+}$ and iodine gave 2-iodo-1,4-dimethoxybenzene as the only product.

1,1,1,3,3,3-Hexafluoropropan-2-ol (HFP), a non-nucleophilic and strongly hydrogen bonding solvent,[8] increases the persistency of radical cations in an unprecedented manner. To a large extent, this effect must be due to the strong attenuation of reactivity experienced by many nucleophiles, as shown by a decrease of about 10^8 in the rate of reaction between a model radical cation, tris(4-bromophenyl)aminium ion, and acetate, chloride or bromide ion in going from acetonitrile to HFP.[9] In a preliminary communication,[5] we demonstrated that iodine

Table 1 Formation of radical cations $ArH^{\bullet +}$ from ArH and a deficit of ICl in HFP at 22 °C

ArH	$E°(ArH^{\bullet +}/ArH)/V$[a]	EPR spectrum[b]	$\tau_{\frac{1}{2}}$/min[c]
4,4′-Di-*tert*-butylbiphenyl	1.69	m	—
4-*tert*-Butylanisole	1.67	none	
1,4-Dimethylnaphthalene	1.63	none	
1,4-Dimethoxybenzene (**1**)	1.50	vs	36[d]
2,8-Dimethyldibenzothiophene	1.50	none	
1,2-Dimethoxybenzene (**2**)	1.49	w	<3
Pentamethylanisole	1.48	m	—
1-Methoxynaphthalene	1.47	s[e]	26
2,2′-Dimethoxy-5,5′-di-*tert*-butylbiphenyl	1.47	s	14
2,2′-Dimethoxy-5,5′-dimethylbiphenyl	1.46	s (9)	9
2,4,6,8-Tetramethyldibenzothiophene	1.42	none	
Anthracene	1.41	w	<1
3,3′,4,4′-Tetramethyl-1,1′-binaphthalene	1.40	s	3
1,4,5,8-Tetramethylnaphthalene	1.32	s	6.5
Thianthrene	1.32	vs	—
1,4-Dimethoxy-2-methylbenzene	1.29[f]	s	49
1,4-Dimethoxy-2,3-dimethylbenzene (**4**)	1.16[f,g]	vs	1600
1,4-Dimethoxy-2,5-dimethylbenzene (**3**)	1.13[f]	vs	—
9,10-Dimethylanthracene	1.11	vs	250
Perylene	1.10	vs (>5000)	>5000
1,4-Dimethoxy-2,5-di-*tert*-butylbenzene	1.03	s	141[h]
Hexamethoxytriphenylene	0.96	vs	—
4-*tert*-Butyl-*N*,*N*-dimethylaniline	0.74	s	—

[a] *Versus* the Ag/AgCl electrode in dichloromethane or acetonitrile. [b] vs = very strong, s = strong, m = medium, w = weak, vw = very weak. In all cases except one, the primary radical cation $ArH^{\bullet +}$ was the species detected. [c] The quantity $\tau_{\frac{1}{2}}$ was calculated from the first-order kinetic expression, which is an approximation for the $ArH^{\bullet +}$–halide ion reaction. However, since the reactions were run under closely similar conditions, $\tau_{\frac{1}{2}}$ provides a crude indication of the persistence of the radical cations. [d] In dichloromethane, $\tau_{\frac{1}{2}} < 1$ min. [e] The dehydro-dimer radical cation, $Ar–Ar^{\bullet +}$ (of 4,4′-dimethoxy-1,1′-binaphthalene), was formed. [f] Ref. 7*c* gives 1.22 V. [g] The $\mathbf{4}^{\bullet +}/\mathbf{4}$ potential was found to be 0.81 V in HFP. [h] In dichloromethane, $\tau_{\frac{1}{2}} \approx 10$ min.

chloride, bromine or chlorine reacted with ArH in HFP to give solutions of radical cations which could be conveniently characterized at room temperature by EPR and UV spectroscopy and studied with respect to their reactivity. Thus for example the reaction of bromine and an excess of **3** or its isomer 1,4-dimethoxy-2,3-dimethylbenzene (**4**) gave a solution of $\mathbf{3}^{\bullet +}$ (or $\mathbf{4}^{\bullet +}$) which reacted further with bromide ion with a second-order rate constant of 0.0057 (or 0.17) $dm^3 mol^{-1} s^{-1}$ at 22 °C.

Thus HFP holds promise as a suitable medium for the study of the radical cation mediated mechanism of aromatic halogenation and, in a wider perspective, electrophilic aromatic substitution in general. In what follows, we delineate some of the problems associated with the ET mechanism of aromatic halogenation.

Results

Oxidation of ArH by iodine chloride in HFP

The redox properties of ICl were first semiquantitatively probed by allowing it to react with an excess of a variety of ArH in HFP at 22 °C and recording the EPR spectral activity of the solution. As seen from Table 1, the borderline $E°(ArH^{\bullet +}/ArH)$ of those ArH which still give rise to $ArH^{\bullet +}$ was situated at 1.50–1.55 V (*vs.* Ag/AgCl in dichloromethane; all potentials given in this paper are referred to this reference electrode, unless otherwise stated). 4,4′-Di-*tert*-butylbiphenyl (1.69 V) was an exception, presumably because of the lower reactivity of its sterically hindered radical cation. Two dibenzothiophene derivatives, 2,8-dimethyl- and 2,4,6,8-tetramethyl-dibenzothiophene did not give detectable radical cations in spite of their favourable $E°(ArH^{\bullet +}/ArH)$.

Nearly all radical cations generated by ICl oxidation in HFP gave fully resolved EPR spectra of excellent quality which permitted unambiguous assignment of the species formed, either by comparison with known spectra or satisfactory simulation in cases where spectra were not known. Full documentation is provided in the Experimental section in order to counter further aspersions under the label of 'indiscriminate use of EPR spectroscopy'.[10]

In some cases, half-lives of the radical cations were calculated by the first-order kinetic expression in order to give an approximate idea of the observation times available in HFP. For two compounds, 1,4-dimethoxybenzene **1** and 1,4-dimethoxy-2,5-di-*tert*-butylbenzene, the radical cations were also generated at 22 °C in dichloromethane in which their half-lives decreased by a factor of >10. Previous studies[7c] of the reactivities of $\mathbf{1}^{\bullet +}$ and $\mathbf{3}^{\bullet +}$ against chloride ion or iodine in dichloromethane were performed at −78 °C in order to provide stable initial conditions.

Oxidation of ArH by chlorine, bromine and iodine in HFP

Table 2 gives the results of similar studies with chlorine, bromine and iodine to those reported for ICl in Table 1. The upper limits of $E°(ArH^{\bullet +}/ArH)$ which still allow for observation of $ArH^{\bullet +}$ were: Cl_2, 1.3 V; Br_2, 1.4 V; I_2 1.1 V. The quality of the EPR spectra again was excellent, allowing for unambiguous identification of nearly all radical cations observed. One exception was 4,4′-dimethoxystilbene,[11] with $E°(ArH^{\bullet +}/ArH) = 0.71$ V in HFP and 1.05 V in dichloromethane, which gave a weak, badly resolved EPR spectrum with Br_2, contrasting with the spectrum obtained with 4-tolyl-Tl^{III} bis(trifluoroacetate) as the oxidant.

Bromine could also be supplied in the form of tetrabutylammonium tribromide, the same results as with elemental bromine being obtained.

It was reported[12] earlier that hexamethylbenzene [HMB; $E°(HMB^{\bullet +}/HMB) = 1.61$ V] gave its radical cation, as demonstrated by EPR spectroscopy, on oxidation by Cl_2 in acetic acid at room temperature. When this reaction was performed in HFP, no EPR activity assignable to $HMB^{\bullet +}$ could be detected, in agreement with the considerably lower limit of oxidative capability of Cl_2 indicated in Table 2, 1.3 V. The experiment in acetic acid was repeated, but could not be reproduced, even on direct mixing of the reaction components within the sample tube.

Oxidation of ArH by other reagents containing 'positive halogen'

Two common reagents containing 'positive halogen' were also

Table 2 Radical cations $ArH^{\bullet +}$ from ArH and a deficit of Cl_2, Br_2 or I_2 in HFP at 22 °C

		EPR spectrum[b] ($\tau_{\frac{1}{2}}$/min[c]) with		
ArH	$E°(ArH^{\bullet +}/ArH)$/V[a]	Br_2	Cl_2	I_2
1,4-Dimethoxybenzene (**1**)	1.50	none	none	—
1-Methoxynaphthalene	1.47	none	—	—
2,2′-Dimethoxy-5,5′-dimethylbiphenyl	1.46	none	—	—
Anthracene	1.41	none	—	—
3,3′,4,4′-Tetramethyl-1,1′-binaphthalene	1.40	w	—	—
1,4,5,8-Tetramethylnaphthalene	1.32	vw	none	—
1,4-Dimethoxy-2-methylbenzene	1.29[d]	m	s (175)	—
1,4-Dimethoxy-2,3-dimethylbenzene (**4**)	1.16[d,e]	vs (16[f])	s (29)	—
Pyrene	1.20	w	—	—
1,4-Dimethoxy-2,5-dimethylbenzene (**3**)	1.13[d]	vs (>5000)	—	none
9,10-Dimethylanthracene	1.11	s (50)	vs	w
Perylene	1.10	—	vs (1340)	w
4,4′-Dimethoxystilbene	1.05[g]	vw[h]	—	—
1,4-Dimethoxy-2,5-di-*tert*-butylbenzene	1.03	m (>2000)	—	m
1,2,4,5,6,8-Hexamethylanthracene	1.00	—	—	s
1,2,4,5-Tetramethoxybenzene	0.84	—	—	vs
1,2,3,4,5,6,7,8-Octamethylanthracene	0.83	—	—	vs
4-*tert*-Butyl-*N*,*N*-dimethylaniline	0.74	—	—	s
N-Methylphenothiazine	0.73	s	—	s
Bis[4-(dimethylamino)phenyl]squaraine	0.35	—	—	vs

[a] *Versus* the Ag/AgCl electrode in dichloromethane or acetonitrile. [b] vs = very strong, s = strong, m = medium, w = weak, vw = very weak. [c] The quantity $\tau_{\frac{1}{2}}$ was calculated from the first-order kinetic expression, which is an approximation for the $ArH^{\bullet +}$–halide ion reaction. However, since the reactions were run under closely similar conditions, $\tau_{\frac{1}{2}}$ provides a crude indication of the persistence of the solutions. [d] Ref. 7*c* gives 1.22 V. [e] The $\mathbf{4}^{\bullet +}/\mathbf{4}$ potential was found to be 0.81 V in HFP. [f] In the presence of 4.0 mmol dm^{-3} Bu_4NBr. [g] In HFP, E_{rev} was 0.71 V (0.1 V s^{-1}); a second reversible couple was seen at E_{rev} = 1.01 V (5 V s^{-1}). [h] Less well resolved: very weak multiplet of *ca.* 15 lines with an hfs splitting of 0.10–0.11 mT.

Table 3 Radical cations $ArH^{\bullet +}$ from ArH and *N*-chlorosuccinimide or *N*-bromosuccinimide in HFP at 22 °C

ArH	$E°(ArH^{\bullet +}/ArH)$/ V[a]	EPR spectrum[b]
N-Chlorosuccinimide		
1,4-Dimethoxy-2,3-dimethylbenzene (**4**)	1.16[c,d]	m[e]
1,4-Dimethoxy-2,5-dimethylbenzene (**3**)	1.13[c]	s[f]
1,4-Dimethoxy-2,5-di-*tert*-butylbenzene	1.03	vs
N-Bromosuccinimide		
1,4-Dimethoxybenzene	1.50	m
2,2′-Dimethoxy-5,5′-dimethylbiphenyl	1.46	none
3,3′,4,4′-Tetramethyl-1,1′-binaphthalene	1.40	vw
1,4-Dimethoxy-2,3-dimethylbenzene (**4**)	1.16[c,d]	s
1,4-Dimethoxy-2,5-dimethylbenzene (**3**)	1.13[c]	s
1,4-Dimethoxy-2,5-di-*tert*-butylbenzene	1.03	vs

[a] *Versus* the Ag/AgCl electrode in dichloromethane or acetonitrile. [b] vs = very strong, s = strong, m = medium, w = weak, vw = very weak. [c] Ref. 7*c* gives 1.22 V. [d] The $\mathbf{4}^{\bullet +}/\mathbf{4}$ potential was found to be 0.81 V in HFP. [e] The formation of $\mathbf{4}^{\bullet +}$ showed an induction period of about 70 min, and $[\mathbf{4}^{\bullet +}]$ reached a maximum after about 20 h. [f] $[\mathbf{3}^{\bullet +}]$ reached a maximum after about 2 h.

examined in HFP, namely *N*-chloro- and *N*-bromo-succinimide. Table 3 shows that the upper limits of $E°(ArH^{\bullet +}/ArH)$ which still allowed for the observation of $ArH^{\bullet +}$ were 1.2 and 1.5 V, respectively. It should be noted that the listed reactions of *N*-chlorosuccinimide were relatively slow, and that the formation of, for example, $\mathbf{4}^{\bullet +}$ exhibited an induction period of about 70 min. It may be that even less reactive compounds can undergo electron transfer to *N*-chlorosuccinimide, but such a search was not pursued in view of the anomalous behaviour of this compound.

Cyclic voltammetry of halogenating reagents in HFP

The properties of HFP as a solvent for electrochemical studies have been little explored. So far it has been established that the increased persistency of radical cations in HFP leads to the observation of reversibility of $ArH^{\bullet +}/ArH$ couples at scan rates which are 100–1000 times slower than in dichloromethane.[13] This is presumably mostly due to the vastly decreased reactivity of nucleophiles in HFP and only to a lesser extent to any stabilizing effect of HFP upon cationic species.[8e]

The decreased reactivity of anionic nucleophiles in HFP is expected to influence strongly the electrochemistry of bromine and iodine in view of the well known tendency of bromine and iodine to associate with the corresponding anions to form trihalide ions, Br_3^- or I_3^-.[14] This is well illustrated by the cyclic voltammetry of tetrabutylammonium bromide in acetonitrile [Fig. 1(*a*)] which shows two anodic processes, one with E_{pa} at 0.76 V and one with E_{pa} at 1.06 V, assigned to the electrode reactions of eqns. (7) and (8). Clearly the first anodic process

$$6\,Br^- \longrightarrow 2\,Br_3^- + 4\,e^- \qquad (7)$$

$$2\,Br_3^- \longrightarrow 3\,Br_2 + 2\,e^- \qquad (8)$$

involves at some stage the association between Br_2 (or $Br^{\bullet}$) and Br^- to give eventually Br_3^- which is oxidized to bromine in the second anodic process. This can be seen by scanning a solution of Bu_4NBr_3 in the anodic direction, showing only one peak at E_{pa} = 1.07 V. In HFP, reaction (7) disappears entirely [Fig. 1(*b*)], and only the second wave at E_{pa} = 1.09 V and E_{pc} at 0.85 V remains. By calibration with the ferrocene (FcH) system, the anodic process of Fig. 1(*b*) was shown to be a 2e$^-$ oxidation. Similar results were obtained by cyclic voltammetry of bromine or tetrabutylammonium tribromide in AN or HFP. In HFP, no indication of any secondary involvement of bromide ion was seen. The CV results obtained for all bromine-based species are listed in Table 4.

On the first negative scan, *N*-bromosuccinimide displayed a reduction peak at E_{pc} = 0.63 V in HFP and on the first positive scan a peak at E_{pa} = 1.08 V (Fig. 2) which originates from the reoxidation of Br^- liberated in the reduction process together with succinimide anion as shown in eqn. (9).[15] The latter

$$\text{S–Br} + 2\,e^- \longrightarrow Br^- + S^- \qquad (9)$$
$$\text{S = succinimidyl}$$

becomes protonated by HFP[9] and thus is removed from reaction with bromine, and in subsequent cycles only the bromine-bromide couple is seen (Fig. 2).

Table 4 Cyclic voltammetry of bromide ion, bromine and tribromide ion in acetonitrile (AN) or 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP). Scan rate 200 mV s^{-1}. Reference electrode, Ag/AgCl.

Solvent	Species (scan direction)	E_{pa}/V	E_{pc}/V	E'_{pa}/V	E'_{pc}/V
AN	Bu_4NBr (+)	0.76	0.3	1.06	0.97
HFP	Bu_4NBr (+)	—	—	1.09	0.85
AN	Br_2 (−)	0.70	0.1	1.05	0.96
HFP	Br_2 (−)	—	—	1.03	0.82
AN	Bu_4NBr_3 (−)	0.76	0.1	1.07	0.94
HFP	Bu_4NBr_3 (−)	—	—	1.03	0.82
AN	*N*-Bromosuccinimide (−)[a]	—	0.07	1.23	—
HFP	*N*-Bromosuccinimide (−)	—	0.63	1.08	0.74

[a] Ref. 15.

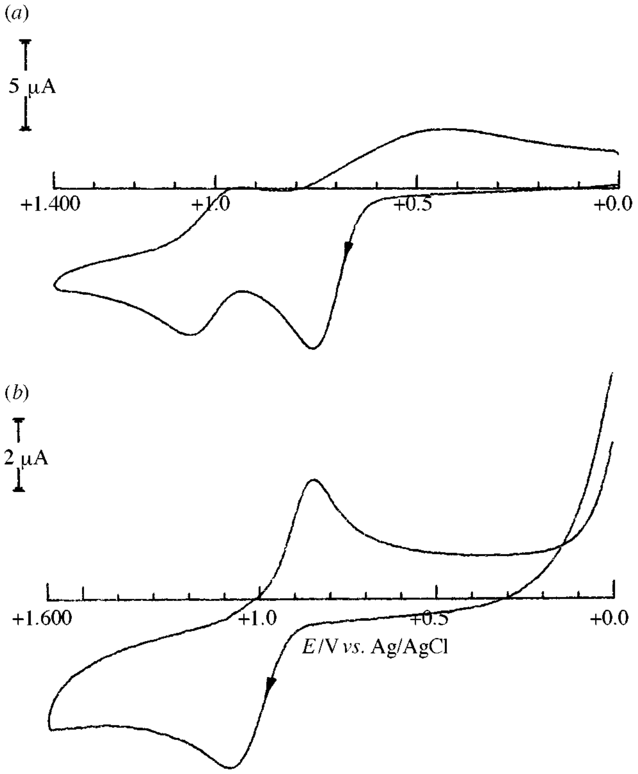

Fig. 1 Cyclic voltammetry of a solution of tetrabutylammonium bromide (1.4 mmol dm^{-3}) at a scan rate of 200 mV s^{-1} in the positive direction from 0.0 V in (*a*) acetonitrile and (*b*) 1,1,1,3,3,3-hexafluoropropan-2-ol. Supporting electrolyte: tetrabutylammonium hexafluorophosphate (0.15 mol dm^{-3}).

Cyclic voltammetry of iodine chloride in HFP showed two redox couples upon scanning in the negative direction, one at E_{pc}, E_{pa} = 1.03, 1.24 V and one at 0.50, 0.56 V, the latter coinciding with the iodine reduction process, separately established to occur in the same potential range [Fig. 3(*a*) and (*b*), Table 5] by cyclic voltammetry of iodine or tetrabutylammonium iodide solutions.

In acetonitrile, anodic oxidation of iodide ion showed two redox couples, one at E_{pa}, E_{pc} = 0.36, 0.13 V due to formation/reduction of I_3^- and one at E_{pa}, E_{pc} = 0.62, 0.55 V due to formation/reduction of I_2,[14c] analogously to the behaviour of bromide ion in acetonitrile except for the peak positions (Fig. 1). Cyclic voltammetry of ICl in acetonitrile displayed four cathodic peaks (best detectable by Osteryoung square wave voltammetry), the nature of which was not further analysed, except for noting that the two peaks at lower potentials presumably belonged to iodine.

Cyclic voltammetry of Et_4NCl in HFP showed an elongated oxidation peak at 1.50 V and a reduction peak at 0.95 V, in principle the same behaviour as in acetonitrile, except for the positions of the peaks (1.07 and 0.87 V, respectively). *N*-Chlorosuccinimide showed a reduction peak at E_{pc} = −0.17 V and an oxidation peak at E_{pa} = 1.5 V, the latter originating from Cl^- generated in the reduction process.[16]

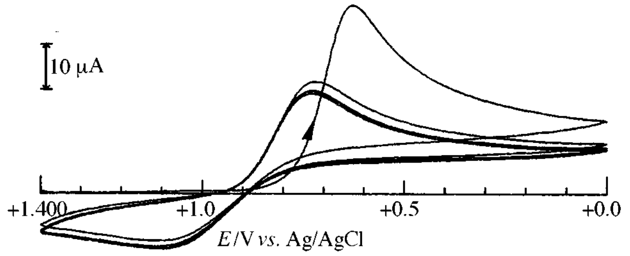

Fig. 2 Cyclic voltammetry of a solution of *N*-bromosuccinimide (6.0 mmol dm^{-3}) at a scan rate of 200 mV s^{-1} in the negative direction from 1.4 V in 1,1,1,3,3,3-hexafluoropropan-2-ol. The first cycle shows the reduction of the substrate at E_{pc} = 0.63 V and reoxidation of bromide ion at E_{pa} = 1.08 V, whereas subsequent cycles reflect the electrochemistry of the Br_2/Br^- couple. Supporting electrolyte: tetrabutylammonium hexafluorophosphate (0.15 mol dm^{-3}).

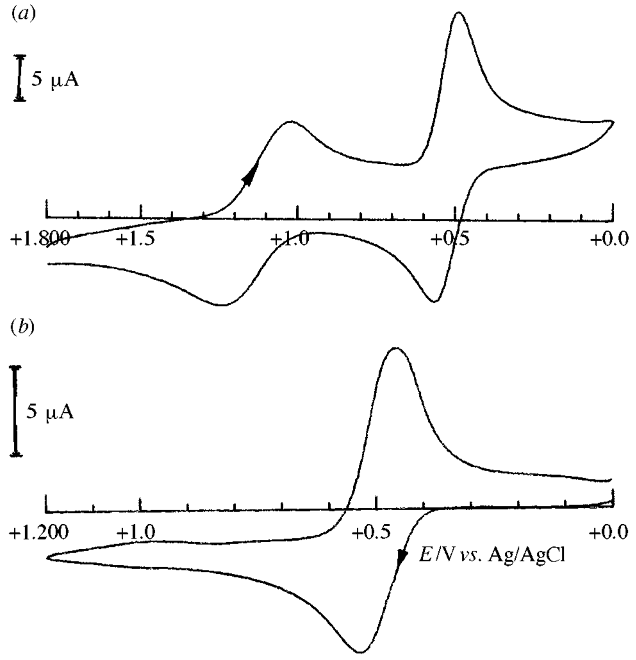

Fig. 3 Cyclic voltammetry at a scan rate of 200 mV s^{-1} in (*a*) the negative direction from 1.8 V of a solution of iodine chloride (satd.) and (*b*) the positive direction from 0.0 V of a solution of tetrabutylammonium iodide (3.9 mmol dm^{-3}) in 1,1,1,3,3,3-hexafluoropropan-2-ol. Supporting electrolyte: tetrabutylammonium hexafluorophosphate (0.15 mol dm^{-3}).

In all cases, the potentials were standardized against the FcH^+/FcH couple in both acetonitrile and HFP in order to make possible a comparison between potentials obtained in the two solvents. The E_{pc} values are summarized in Table 6, together with the 'upper limits' of oxidative power determined by the EPR spectral method (Tables 1–3).

Products of reaction between ICl and 1 or 4

Product studies of halogenation by ICl in HFP were limited to two substrates, one representing cases where both iodination and chlorination occurs (**1**) and one in which only chlorination takes place (**4**) according to a previous study.[7c] The differences with respect to reactions carried out in dichloromethane[7c] were rather small (see below), and thus no extended study was carried out.

The reaction of 1,4-dimethoxybenzene **1** with a slight deficit of ICl in HFP after 20 h at room temperature gave a 29% conversion of **1** into its iodo (82%) and chloro substitution products (18%), somewhat different from the results obtained in

Table 5 Cyclic or square wave voltammetry of iodine chloride or iodide ion in acetonitrile (AN) or 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP). Scan rate 200 mV s^{-1}. All potentials are given in V *vs.* the Ag/AgCl electrode.

Solvent	Species (scan direction); method[a]	E_{pa}	E_{pc}	E'_{pa}	E'_{pc}	E''_{pa}	E''_{pc}	E'''_{pa}	E'''_{pc}
AN	ICl (−); CV	1.14	0.87	0.70	0.62	ns	ns	ns	0.02
AN	ICl (−); OSWV	—	0.93	—	0.65	—	0.30	—	0.06
HFP	ICl (−); CV	1.24	1.03	—	—	0.56	0.50	—	—
AN	Bu_4NI (+); CV					0.62	0.53	0.26	0.03
HFP	Bu_4NI (+); CV	—	—	—	—	0.51	0.42	—	—

[a] CV = cyclic voltammetry, OSWV = Osteryoung square wave voltammetry, ns = not seen.

Table 6 Peak potentials for the cathodic reduction of halogen species in acetonitrile or 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP), referenced to the internal ferrocinium/ferrocene couple (FcH^+/FcH)

	Peak potential (E_{pc}) in			
Halogen species	HFP	Acetonitrile	ΔE_{pc}/V	E_{lim}^{EPR}/V
Br_2	0.77	0.53	0.24	1.0
Br_3^-	0.77	0.51	0.26	
Cl_2	0.90	0.44[a]	0.46	0.9
I_2	0.39	0.12	0.27	0.7
ICl	0.98	0.44	0.54	1.2
N-Bromosuccinimide	0.58	−0.36	0.94	1.1
N-Chlorosuccinimide	−0.26	−0.75[b]	0.49	
Cl–C(CN)$_3$	0.47	−0.02[a]	0.49	1.1

[a] Ref. 46. [b] Ref. 25.

Table 7 Products from the reaction of ICl (0.15 mol dm^{-3}) and ArH (0.14 mol dm^{-3}) in dichloromethane (DCM) or HFP in the dark at room temperature

ArH	Solvent	*t*/h	Conversion (%)	ArI (rel. %)	ArCl (rel. %)
1	DCM	20	49	49	51
1[a,b]	DCM	21	47	60	40
1	HFP	20	29	82	18
4	DCM	60	72	0	100
4[a,b]	DCM	22	42	0	100
4	HFP	24	47	0.2	98[c]

[a] $[ArH]_0 = 0.072$, $[ICl]_0 = 0.060$ mol dm^{-3}. [b] Ref. 7*c*. [c] The dichloro derivative (0.9%) was also formed.

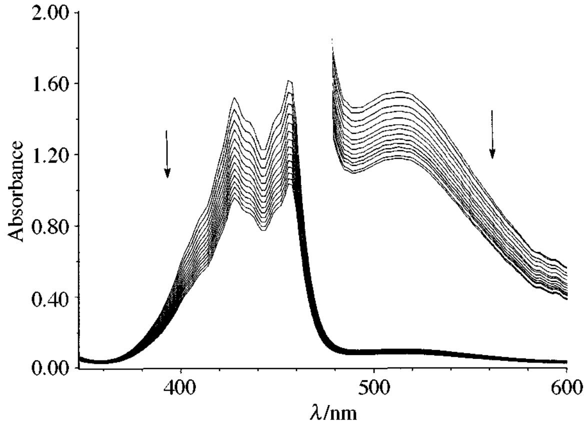

Fig. 4 Monitoring the UV–VIS absorption of $\mathbf{1}^{\cdot+}$ and iodine, formed by addition of ICl in an initial concentration of 1.58 mmol dm^{-3} to a 38 mmol dm^{-3} solution of **1** in HFP. The inset shows the I_2 maximum at 510 nm on a scale magnified by a factor of 14.3. The time between spectra was 200 s.

dichloromethane (49% conversion into 49 and 51% yields of iodo and chloro products, respectively). Similar reaction of **4** with ICl ($[ICl]_0/[\mathbf{4}]_0 = 2$) in HFP gave after 20 h remaining starting material (9%), the 5-chloro substitution product (90%), the dichloro derivative (0.8%), and the iodo product (0.2%). In dichloromethane, only the chloro product was obtained from **4** (Table 7).

In order to demonstrate the formation of radical cation $\mathbf{1}^{\cdot+}$ and iodine in eqn. (3), a deficit of ICl (1.58 mmol dm^{-3}) was added to a solution of **1** (38 mmol dm^{-3}) in HFP and the UV–VIS absorption monitored with time (Fig. 4). The formation of intermediate products according to eqn. (4) was rapid (<20 s) under these conditions, but at a lower $[\mathbf{1}]_0$ of *ca.* 3 mmol dm^{-3} the initial phase of formation of $\mathbf{1}^{\cdot+}$ could also be recorded, $[\mathbf{1}^{\cdot+}]$ reaching a maximum of 0.77 mmol dm^{-3} (see next paragraph) after *ca.* 7 min (Fig. 5).

The absorption maximum of iodine in HFP was independently found to be located at 510 nm, meaning that the iodine maximum can be well distinguished from the radical cation maxima at 428 and 456 nm. The extinction coefficient of I_2 at 510 nm in HFP was evaluated to be 713 M^{-1} cm^{-1}. The extinction coefficient of the 456 nm maximum of $\mathbf{1}^{\cdot+}$ could not be reliably determined in HFP due to the reactivity of $\mathbf{1}^{\cdot+}$ and was therefore taken to be the same as that of $\mathbf{3}^{\cdot+}$, 9280 M^{-1} cm^{-1} (see Experimental section). With these values, $[\mathbf{1}^{\cdot+}]_0$ and $[I_2]_0$ of Fig. 4 were approximately 0.87 (55% yield) and 0.71 mmol dm^{-3} (90% yield).

Products of reaction between Br_2 and 4

The reaction of **4** and a deficit (50 mol%) of bromine in HFP gave a green solution, exhibiting an intense EPR spectrum of $\mathbf{4}^{\cdot+}$. Workup after 20 h then showed a 35% conversion into the 5-bromo compound. With an equivalent amount of bromine, the initially green solution had turned yellow after 1 h and then showed a 91% conversion into the 5-bromo derivative. No other compound was formed and only unchanged substrate remained. In order to get a more detailed picture of this reaction, a preparative experiment in which a slight deficit of bromine (0.018 mol dm^{-3}) was allowed to react with **4** (0.020 mol dm^{-3}) in HFP was performed. In 60 s after mixing, the reaction had proceeded to give the 5-bromo compound in 65% yield, corresponding to a second-order rate constant of >1 dm^3 mol^{-1} s^{-1}. In 150 s after mixing, monitoring of the decay of the EPR spectrum of $\mathbf{4}^{\cdot+}$ was commenced and continued for about 3 h (Fig. 6). The rate constant for the disappearance of $\mathbf{4}^{\cdot+}$ was evaluated according to the expression $1/\mathrm{Int} - 1/\mathrm{Int}_0 = kt$ (Int = EPR spectral intensity), giving $k = 7.7 \times 10^{-7}$ Int^{-1} s^{-1} (the solid curve in Fig. 6 represents the best fit to the data). At the end of this experiment (5 h), the yield of the bromo product was nearly quantitative.

A comparison with reactions of **4** and bromine in acetic acid, a common solvent for aromatic bromination, showed that these reactions were essentially over in 1–10 min, giving a 47% (50 mol% bromine) or 97% (equivalent amount of bromine) yield of the 5-bromo derivative (Table 8).

Kinetics of the slow phase of the reaction between ICl and 4

The kinetic study had the goal of demonstrating the scope of using HFP as a medium for mechanistic studies of electron transfer mediated halogenation, proceeding *via* a fast initial electron transfer reaction, followed by a slow phase in which the

Table 8 Products from the reaction of bromine and **4** in acetic acid or HFP in the dark at room temperature

Solvent	t/h	Conversion (%)	ArBr (rel. %)
HOAc (50 mol% Br_2)	0.01	47	100
HOAc (100 mol% Br_2)	0.16	97	100
HFP (50 mol% Br_2)[a]	20	35	100
HFP (100 mol% Br_2)[b]	1.5	94	100

[a] The green colour persisted for >2 h. [b] The initially green colour became yellow within 1 h.

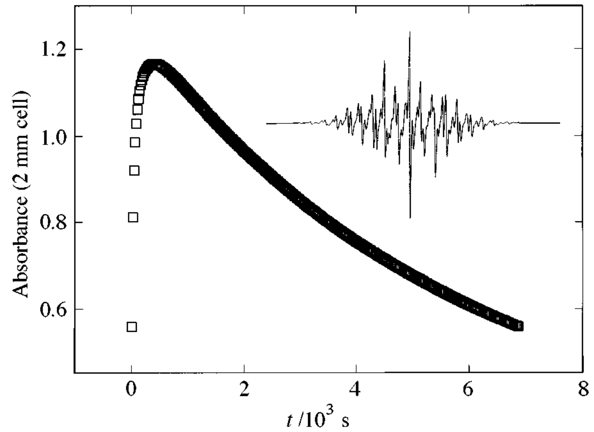

Fig. 5 Monitoring the UV–VIS absorption of $\mathbf{1}^{\cdot +}$ at 456 nm, formed by addition of ICl in an initial concentration of 1.58 mmol dm^{-3} to a *ca.* 3 mmol dm^{-3} solution of **1** in HFP. $[\mathbf{1}^{\cdot +}]_{max} = 0.63$ mmol dm^{-3} was reached after 7 min, and the EPR spectrum was recorded at $t = 60$ min.

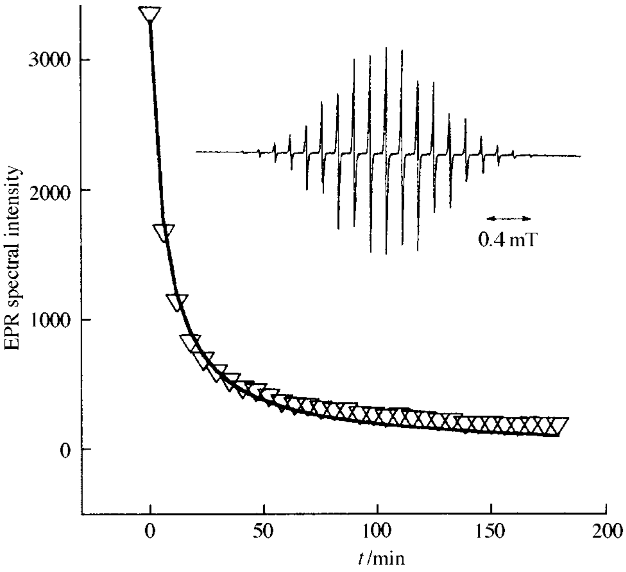

Fig. 6 Decay of the EPR spectrum of $\mathbf{4}^{\cdot +}$, obtained by adding bromine ($[Br_2]_0 = 0.018$ mol dm^{-3}) to a solution of **4** ($[\mathbf{4}]_0 = 0.020$ mol dm^{-3}) in HFP. The first point was recorded 150 s after mixing. The solid curve represents the best fit to the data, using the expression Int = $1/(kt + 1/\text{Int}_0)$ with $k = 7.7 \times 10^{-7}$ Int^{-1} s^{-1}.

radical cation undergoes follow-up reactions with the halide ion formed and/or an excess of the halogenating species. Thus reactions between a halogen or interhalogen and ArH like **3** or **4** were carried out in order to establish the kinetics of disappearance of the radical cation formed. Generally, the electron transfer reaction between these reaction components occurred 'instantaneously'[17] on mixing, providing a solution of the radical cation the disappearance of which could be monitored either by UV or EPR spectroscopy.

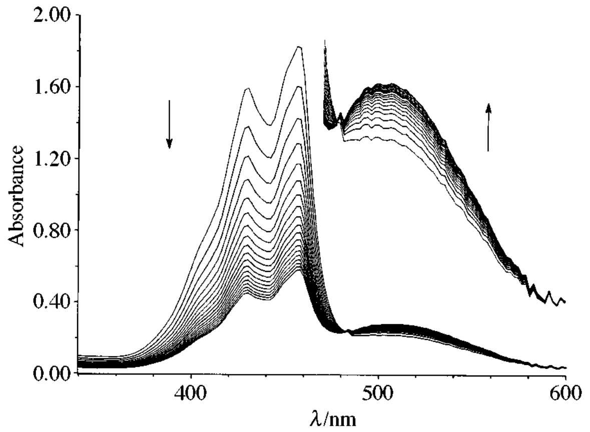

Fig. 7 Monitoring the UV–VIS absorption of $\mathbf{4}^{\cdot +}$ and iodine, formed by addition of an excess of ICl (3.35 mmol dm^{-3}) to **4** (1.68 mmol dm^{-3}) in HFP. $[\mathbf{4}^{\cdot +}]_0$ was calculated to be 1.55 mmol dm^{-3}. The first and last spectrum corresponds to a decrease in $[\mathbf{4}^{\cdot +}]$ of 1.17 mmol dm^{-3} and an increase in $[I_2]$ of 0.44 mmol dm^{-3}. The inset shows the I_2 maximum at 510 nm on a scale magnified by a factor of 5. The time between spectra was 200 s.

The reaction between an excess of **4** (*ca.* 40 mmol dm^{-3}) and ICl (1.58 mmol dm^{-3}) proceeded within <1 s to give a yellow-green solution of $\mathbf{4}^{\cdot +}$, iodine and chloride ion [eqn. (10)]. At the

$$ArH + ICl \longrightarrow ArH^{\cdot +} + 0.5\, I_2 + Cl^- \qquad (10)$$

beginning of the kinetic run (*ca.* 15 s after mixing), $[\mathbf{4}^{\cdot +}]$ was 1.02 mmol dm^{-3} (yield 64 ± 8%; average of four runs), using $\varepsilon = 5340$ dm^3 mol^{-1} cm^{-1} at λ_{max} of $\mathbf{4}^{\cdot +}$ in HFP (see Experimental section). The radical cation decayed slowly, the time dependence being monitored at λ_{max} of the radical cation = 456 nm. Assuming that the initial state of the decay period corresponds to the right side of eqn. (10), the radical cation and chloride ion were present initially in equal concentrations. The Abs/t data were accordingly first treated by the second-order expression Abs = $a + 1(k_2t + 1/\text{Abs}_0)$, where the a term reflects the fact that there was residual absorbance of $\mathbf{4}^{\cdot +}$ at 458 nm at the end of the reaction (independently, it was verified by EPR spectroscopy that $\mathbf{4}^{\cdot +}$ was present at the appropriate concentration level at the end of the run) and Abs and Abs_0 are the absorbances at time t and 0, respectively. The k_2 values were converted into concentration units by multiplying with $\varepsilon_{max} =$ 5340 dm^3 mol^{-1} cm^{-1} (see Experimental section). The average rate constant calculated for the disappearance of $\mathbf{4}^{\cdot +}$ in the runs where chloride ion had not been added was 1.7 ± 0.3 dm^3 mol^{-1} s^{-1}. At the end of the reaction, $[I_2]_\infty$ was on average 0.73 mmol dm^{-3} (92 ± 9% yield).

By addition of an excess of tetraphenylphosphonium chloride, the reaction with chloride ion was evaluated under pseudo-first-order conditions. There was some scatter in the second-order rate constants obtained, the average being 0.40 ± 0.12 dm^3 mol^{-1} s^{-1}. The difference between the k_2 values obtained with and without added chloride ion is too large to be reconciled with any possible errors. An earlier study of the reaction between the radical cation of 9,10-diphenylanthracene and chloride ion[18] showed this reaction to be second-order in radical cation and first order in Cl^-. Evaluation of the rate constants by the third-order expression[19] $0.5(1/\text{Abs}^2 - 1/\text{Abs}_0^2) = kt$ for runs without chloride ion added and as pseudo-second-order reactions with excess chloride ion added gave average rate constants of $(2.4 \pm 0.5) \times 10^3$ and $(2.2 \pm 0.9) \times 10^3$ dm^6 mol^{-2} s^{-1}, respectively (Table 9).

The reaction was also performed under conditions in which $[ICl]_0/[\mathbf{4}]_0$ was kept ⩾2 in order to see if a reaction between $\mathbf{4}^{\cdot +}$ and ICl might occur. A repetitive UV spectroscopic run scan with $[ICl]_0/[\mathbf{4}]_0 = 2$ showed that $\mathbf{4}^{\cdot +}$ was consumed and that additional iodine was formed in this reaction (Fig. 7). The total increase in $[I_2]$ over the whole reaction period was 38% of the

Table 9 Kinetics of the slow phase ($4^{\bullet+} + Cl^-$) of the reaction between ICl and **4** in HFP at 22 °C, monitored by UV spectroscopy at 458 nm. $[ArH]_0$ *ca.* 40, $[ICl]_0 = 1.58$ mmol dm^{-3}.

$[ArH^{\bullet+}]_0$/mmol dm^{-3} (% Yield)	$[I_2]_\infty$/mmol dm^{-3} (% Yield)	Added $[Cl^-]$/ mmol dm^{-3} [a]	k_2/Abs^{-1} s^{-1}	k_3/Abs^{-2} s^{-1}	k_2/dm^6 mol^{-2} s^{-1}
0.81 (51)	0.82 (104)	—		9.93×10^{-5}	2.8×10^3
1.04 (66)	0.76 (96)	—		1.01×10^{-4}	2.9×10^3
1.05 (66)	0.64 (81)	—		6.76×10^{-5}	1.9×10^3
1.17 (74)	0.71 (90)	—		6.76×10^{-5}	1.9×10^3
(64 ± 8)	(92 ± 9)				$(2.4 \pm 0.5) \times 10^3$
0.73 (46)		18.8	0.013 3		3.5×10^3
0.75 (47)		25.5	0.006 78		1.3×10^3
0.56 (35)		43.6	0.011 4		1.4×10^3
0.67 (42)		50.3	0.018 9		1.9×10^3
0.70 (44)		60.3	0.040 5		3.5×10^3
0.62 (39)		79.0	0.024 6		1.7×10^3
					$(2.2 \pm 0.9) \times 10^3$

[a] This concentration was corrected by adding 1.6 mmol dm^{-3} of $[Cl^-]$ formed in the initial electron transfer step.

Table 10 Kinetics of the slow phase ($4^{\bullet+}$ + I–Cl) of the reaction between ICl and **4** in HFP at 22 °C, monitored by UV spectroscopy at 458 nm. $[ArH]_0 = 1.68$ mmol dm^{-3}.

$[ICl]_0$/mmol dm^{-3}	$[ArH^{\bullet+}]_0$/mmol dm^{-3} (% Yield)	$[I_2]_\infty$/mmol dm^{-3} (% Yield)	k_2/Abs^{-1} s^{-1}	k_2/dm^3 mol^{-1} s^{-1}
3.11	1.68 (100)	1.43 (85)	1.46×10^{-4}	0.78
3.56	1.69 (100)	1.88 (111)	1.19×10^{-4}	0.64
4.33	1.68 (100)	*a*	—	0.54
6.73	1.60 (95)	*a*	—	0.79
9.66	1.45 (86)	*a*	—	0.94
				0.74 ± 0.14[b]

[a] Not recorded. [b] Average ± standard deviation.

decrease in $[4^{\bullet+}]$, compared to 50% required by eqn. (11). This

$$ArH^{\bullet+} + ICl \longrightarrow Ar^+(H)Cl + I^\bullet\ (0.5\ I_2) \qquad (11)$$

indicated that the reaction of eqn. (11) plays a role when ICl is present in sufficient excess. Kinetic experiments showed that the second-order rate constant of the reaction of eqn. (11) was 0.74 ± 0.14 dm^3 mol^{-1} s^{-1} (Table 10).

Kinetics of the reaction between Br_2 and 4

Table 10 shows results from measurements of the kinetics of reactions between bromine and **4** in HFP. The first five runs were performed with a large excess of **4** and without any added source of bromide ion, assuming that the electron transfer reaction between bromine and **4** ideally would result in equimolar concentrations of $4^{\bullet+}$ and bromide ion. The second-order rate constants k_2 were again calculated by the second-order expression $Abs = a + 1(k_2t + 1/Abs_0)$, where the a term reflects the fact that there is residual absorbance at 458 nm at the end of the reaction and where Abs and Abs_0 are the absorbances at time t and 0, respectively. The k values were converted into concentration units by multiplying with $\varepsilon_{max} = 5340$ dm^3 mol^{-1} cm^{-1} (see Experimental section). The k_2 values varied over a factor of 5, the average value being 0.11 ± 0.06 dm^3 mol^{-1} s^{-1}.[20] In the presence of added bromide ion, rate constants could be calculated by the first-order expression, but k_2 still showed considerable scatter, the average value from five runs at different $[Br^-]$ being 0.17 ± 0.09.

With **4** and bromine in a molar ratio of $\geqslant 1$, it was expected in view of the preparative experiments that the reaction of eqn. (12) would become important as a product-forming step. The

$$ArH^{\bullet+} + Br{-}Br \longrightarrow Ar^+(H)Br + Br^\bullet \qquad (12)$$

lower part of Table 11 shows results from runs performed with bromine present in excess or in equivalent concentration. The second-order rate constant obtained was 17.3 ± 1.7 dm^3 mol^{-1} s^{-1}.

Kinetics of the reaction between Br_2 and 3 and the effect of adding dichloromethane

In order to study the effect of adding dichloromethane to HFP in a typical ET bromination, a slower-reacting substrate than **4** was needed. 2,5-Dimethyl-1,4-dimethoxybenzene (**3**) filled this requirement; it reacted within <1 s with bromine in HFP to give a solution of its radical cation $3^{\bullet+}$ which reacted *ca.* 20 times slower with bromide ion (added in excess, since otherwise the reaction was too slow for reliable measurements to be done) than $4^{\bullet+}$, k_2 being 0.0057 dm^3 mol^{-1} s^{-1}. The rate constant increased upon addition of dichloromethane to the medium, until no radical cation was detectable on the time-scale employed at an 81 : 19 ratio (v/v) of dichloromethane–HFP (Table 12).

Discussion

General

Our earlier experience with HFP has shown it to stabilize radical cations in an unprecedented manner;[8,9] others have shown similar stabilization of carbocations.[21] The reason for this behaviour of HFP, apart from its lack of nucleophilicity, seems to reside mainly with the extraordinary capability of HFP to engage in hydrogen bonding to nucleophiles, thus strongly decreasing their reactivity. It was therefore possible to demonstrate the formation of persistent radical cations in HFP at 22 °C from reactions where earlier studies had relied on either indirect evidence or experimental studies under extreme conditions of temperature and time-scales, as for example in the ICl halogenation of polycyclic aromatic hydrocarbons in acetonitrile[7b] and of dimethoxyaromatics in dichloromethane.[7c]

Table 11 Kinetics of the slow phase ($4^{\cdot+}$ + Br^- or Br_2) of the reaction between bromine and **4** in HFP at 22 °C, monitored at 458 nm by UV spectroscopy

[**4**]/mmol dm^{-3}	$[Br_2]_0$/mmol dm^{-3}	$[ArH^{\cdot+}]_0$/mmol dm^{-3} (% Yield)	Added $[Br^-]$/ mmol dm^{-3}	k/s^{-1}	$k_2/Abs^{-1}\ s^{-1}$	$k_2/dm^3\ mol^{-1}\ s^{-1}$
55	4.0	2.4 (60)	0	—	8.7×10^{-6}	0.046
15	2.8	2.1 (75)	0	—	1.34×10^{-5}	0.071
8.6	2.8	1.7 (61)	0	—	9.5×10^{-6}	0.051
21	2.8	1.3 (46)	0	—	2.8×10^{-5}	0.15
17	2.7[a]	1.8 (67)	0	—	4.2×10^{-5}	0.22
		(62 ± 9)[b]				0.11 ± 0.06[b]
19	2.8	0.81	18.6	8.2×10^{-3}		0.34
15	2.8	—	32.3	6.1×10^{-3}		0.16
16	2.8	1.08	33.6	6.3×10^{-3}		0.16
13	2.8	0.65	55	7.7×10^{-3}		0.13
12	2.7[a]	0.61	74	4.5×10^{-3}		0.057
						0.17 ± 0.09[b]
1.68	3.02	1.27 (76)	0		—	15.1
1.68	2.41	1.31 (78)	0		—	18.5
1.68	1.80	1.24 (74)	0		3.91×10^{-3}	20.9
1.68	1.66	1.37 (83)	0		3.01×10^{-3}	16.1
1.68	1.66	1.28 (77)	0		3.12×10^{-3}	16.7
1.68	1.72	1.32 (79)	0		3.30×10^{-3}	17.6
1.68	1.80	1.28 (76)	0		3.21×10^{-3}	17.1
1.68	1.89	1.26 (75)	0		3.04×10^{-3}	16.2
						17.3 ± 1.7[b]

[a] Bu_4NBr_3 was used as the bromine source. [b] Average ± standard deviation.

Table 12 Kinetics of the slow phase ($3^{\cdot+}$ + Br^-) of the reaction between bromine and **3** in HFP and HFP–dichloromethane mixtures at 22 °C, monitored at 452 nm by UV spectroscopy

[**3**]/mmol dm^{-3}	Added $[Br^-]$/mmol dm^{-3}	k/s^{-1}	$k_2/Abs^{-1}\ s^{-1}$	$k_2/dm^3\ mol^{-1}\ s^{-1}$	[DCM]/vol%
22	78	5.0×10^{-4}		0.0064	0
22	115	5.9×10^{-4}		0.0050	0
34	—		2.2×10^{-6}	0.020	43
34	—		5.5×10^{-4}	5.1	57
34	—		9×10^{-4}	8.4	70
34	—		*a*	*a*	81

[a] Radical cation not seen.

One such case was the reaction between ArH and ICl, bromine or chlorine where we demonstrated in a preliminary communication[5] that persistent solutions of radical cations were formed in HFP. The radical cations could be identified by EPR and UV spectroscopy and the follow-up reactions with the halide ion formed in the ET step [eqn. (3)] could be monitored. This phenomenology raises some important questions regarding the aromatic halogenation mechanism, above all how the solvent affects the mechanistic problem common to many ArH–electrophile reactions: at what stage of reactivity will the competition between the classical polar mechanism and the electron transfer mechanism be weighted in favour of the latter [as exemplified for bromination in eqns. (13) and (14)]? Why is

$$ArH + Br{-}Br \longrightarrow Ar^+(H)Br + Br^- \qquad (13)$$

$$ArH + Br{-}Br \longrightarrow ArH^{\cdot+} + Br^- + Br^{\cdot} \longrightarrow \longrightarrow Ar^+(H)Br \qquad (14)$$

HFP so effective in promoting the ET mechanism? Or does the ET mechanism also prevail in other solvents, only that the reactions are too fast for proper observation of the intermediates?

Formation of $ArH^{\cdot+}$ by reaction of ArH and ICl, bromine, chlorine, iodine or *N*-haloimides with ArH in HFP

Tables 1–3 demonstrate that ICl, halogens and *N*-haloimides produce persistent solutions of radical cations from ArH in HFP and that each species has an approximate but characteristic potential limit of $E°(ArH^{\cdot+}/ArH)$ above which $ArH^{\cdot+}$ is not detectable by EPR spectroscopy (denoted E_{lim}^{EPR}). These potentials are collected in Table 6, together with cathodic peak potentials E_{pc} and the differences in E_{pc} between HFP and acetonitrile, all potentials in Table 6 being given *vs.* internal FcH^+/FcH. The E_{lim}^{EPR} is determined by both the oxidizing power of the halogenating species and by the nature of the follow-up reactions, so that for example *N*-bromosuccinimide with a lower $E_{pc} = 0.58$ V has an E_{lim}^{EPR} which is almost the same as that of ICl, with $E_{pc} = 0.98$ V, presumably because (i) the nucleophile formed from *N*-bromosuccinimide, succinimide anion, is protonated in HFP and (ii) ICl operates near the upper limit of radical cations possible to detect HFP in fast generation mechanisms.

In spite of possessing favourable redox potentials, the two dibenzothiophenes of Table 1 did not give detectable radical cation concentrations. This might be due to a high radical reactivity at the sulfur atom of these radical cations which according to CASSCF calculations on the parent heterocycle carries *ca.* 30% of the spin population.[22] The reactivity of the sulfur atom toward nucleophiles was predicted to be low.

The failure of hexamethylbenzene to give its radical cation under the conditions of the reactions described in Tables 1–3, let alone in the reaction between hexamethylbenzene and chlorine in acetic acid,[12] is not surprising in view of conclusions regarding the intrinsic half-life of $HMB^{\cdot+}$ reported previously: 'very short lived' when generated by anodic oxidation in trifluoroacetic acid at room temperature,[23a] half-life *ca.* 1.5 s in trifluoroacetic acid when generated by photolysis of HMB–Hg^{II} trifluoroacetate at 25 °C,[23b] and half-life *ca.* 20 ms when generated by anodic oxidation in dichloromethane at −70 °C.[23c] The hexamethylbenzene radical cation can only be observed on a min–h time-scale when slow reactions of generation are employed, as for example in the oxidation of HMB by Tl^{III} trifluoroacetate.[24]

Electrochemistry of halogenating species in HFP

Several important features are noticeable from the cyclic voltammetry experiments in HFP. In the first place, the electrochemistry of the halogen species which are prone to associate with halide ions is considerably simplified in HFP, in all probability due to the low nucleophilicity of the latter (Figs. 1 and 3; Tables 4 and 5) and accompanying much weaker tendency to associate with halogens. Secondly, as summarized in Table 6, when potentials referenced to the internal $\mathrm{FcH}^+/\mathrm{FcH}$ redox system are compared between HFP and acetonitrile, it is seen that the halogenating agents have consistently higher E_{pc} values in HFP, particularly for ICl ($\Delta E_{\mathrm{pc}} = 0.54$ V) and *N*-bromosuccinimide ($\Delta E_{\mathrm{pc}} = 0.94$ V). For the latter compound, an approximate $E°$ value $= -0.4$ V was determined from a kinetic study of the reactions between *N*-bromosuccinimide and various ferrocene derivatives in acetonitrile.[25] One-electron potentials have been estimated for the halogens in water and were: $E°(\mathrm{Cl_2/Cl_2^{\bullet -}})$ 0.0, $E°(\mathrm{Br_2/Br_2^{\bullet -}})$ -0.3 and $E°(\mathrm{I_2/I_2^{\bullet -}})$ -0.5 V.[26]

Thus one important finding is that halogen species are uniformly stronger oxidants in HFP than in acetonitrile and, by inference, presumably than in most other ‘normal’ solvents. This means that not only are radical cations more persistent in HFP but also is the borderline between the mechanisms of eqn. (13) and (14) moved to significantly higher potentials.

Kinetics of the slow phase of halogenation of 4 by ICl in HFP

The first step in the reaction between ICl and **4** in HFP is a fast electron transfer [eqn. (15)] which leads to the formation of the triad $\mathbf{4}^{\bullet +}\ \mathrm{Cl}^-\ \mathrm{I}^\bullet$, from which either the chloro product can develop directly or diffusion can take place followed by second-order recombination of the components. Table 9 shows that $[\mathbf{4}^{\bullet +}]_0$ was formed in 64% yield (measured *ca.* 15 s after mixing) from the reaction between ICl and a 25-fold excess of **4**, indicating that the extent of the intra-triad reaction is maximally 36%. Radical cation $\mathbf{4}^{\bullet +}$ then decayed by reaction with chloride ion in a third-order process[18] with a rate constant of 2.4×10^3 dm^6 mol^{-2} s^{-1}. Since very little (0.2%) of the iodo product was formed in preparative runs, the predominant further reaction of the iodine atoms must be recombination to give iodine, as also substantiated by a yield of iodine at infinite time of 92%.

$$\begin{tikzcd} \mathbf{4} + \mathrm{ICl} \arrow[r] & \mathbf{4}^{\bullet +}\ \mathrm{Cl}^-\ \mathrm{I}^\bullet \arrow[r] \arrow[d, "\text{diffusion}"] & \mathbf{4}\text{–}\mathrm{Cl}^\bullet \arrow[r] & {} \arrow[r] & {} \\ & \mathbf{4}^{\bullet +} + \mathrm{Cl}^- + \tfrac{1}{2}\mathrm{I}_2 & & \text{chloro product} & \end{tikzcd} \qquad (15)$$

Addition of an external source of chloride ion in excess decreased $[\mathbf{4}^{\bullet +}]_0$ (yield 35–47%), presumably an effect of the inevitable delay between mixing and recording (*ca.* 15 s). Kinetics performed under pseudo-second-order conditions provided the third-order rate constant between $\mathbf{4}^{\bullet +}$ and Cl^- at 2.2×10^3 dm^6 mol^{-2} s^{-1}, in agreement with the value obtained without added chloride ion.

The finding that the radical cation of 1,4-dimethoxybenzene ($\mathbf{1}^{\bullet +}$) reacts slowly with iodine in dichloromethane to give the iodo compound,[7c] indicates that ICl (or in general, halogens; see below) also should act as a halogen (chlorine) atom donor toward radical cations [eqn. (16)]. Thus, when the reaction between ICl and **4** is carried out with an $[\mathrm{ICl}]_0/[\mathbf{4}]_0$ ratio $\geqslant 1$, the reaction of $\mathbf{4}^{\bullet +}$ with chloride ion [eqn. (15)] should experience competition from reaction with ICl. This reaction is demonstrated in Fig. 7 at a ratio of $[\mathrm{ICl}]_0/[\mathbf{4}]_0 = 2.0$ where a decrease in $[\mathbf{4}^{\bullet +}]$ of 1.17 mmol dm^{-3} is matched by an increase in $[\mathrm{I_2}]$ of 0.44 mmol dm^{-3}. Eqn. (16) shows that each $\mathrm{I_2}$ formed should require two $\mathrm{ArH}^{\bullet +}$, *i.e.*, the yield of iodine was 75%. The reaction between $\mathbf{4}^{\bullet +}$ and ICl had a rate constant of 0.74 dm^3 mol^{-1} s^{-1} (Table 10).

$$\mathrm{ArH}^{\bullet +} + \mathrm{Cl{-}I} \longrightarrow \mathrm{Ar^+(H)Cl} + \mathrm{I}^\bullet \qquad (16)$$

Kinetics of the slow phase of bromination of 4 by Br$_2$ in HFP

The kinetics of the reaction between **4** and $\mathrm{Br_2}$ is similar to that discussed above for the **4**–ICl reaction: a fast electron transfer step to give a triad of reactive species, where either reaction within the triad can take place or the components diffuse apart to react further in bimolecular encounters [eqn. (17)]. At low $[\mathrm{Br_2}]_0/[\mathbf{4}]_0$ ratios the yield of $[\mathbf{4}^{\bullet +}]$ was 62 ± 9% and the radical cation decayed in a second-order process, rate constants of 0.11 ± 0.6[20] and 0.17 ± 0.9 dm^3 mol^{-1} s^{-1} being obtained without and with bromide ion added, respectively. At $[\mathrm{Br_2}]_0/[\mathbf{4}]_0$ ratios $\geqslant 1$, the rate constant of the reaction between bromine and $\mathbf{4}^{\bullet +}$ [eqn. (18)] could be determined to be 17.3 ± 0.17 dm^3 mol^{-1} s^{-1}, $\geqslant 100$ times faster than reaction with bromide ion.

$$\begin{tikzcd} \mathbf{4} + \mathrm{Br{-}Br} \arrow[r] & \mathbf{4}^{\bullet +}\ \mathrm{Br}^-\ \mathrm{Br}^\bullet \arrow[r] \arrow[d, "\text{diffusion}"] & \mathbf{4}\text{-}\mathrm{Br}^\bullet \arrow[r] & {} \arrow[r] & {} \\ & \mathbf{4}^{\bullet +} + \mathrm{Br}^- + \tfrac{1}{2}\mathrm{Br}_2 & & \text{bromo product} & \end{tikzcd} \qquad (17)$$

$$\mathrm{ArH}^{\bullet +} + \mathrm{Br{-}Br} \longrightarrow \mathrm{Ar^+(H)Br} + \mathrm{Br}^\bullet \qquad (18)$$

Kinetics of the slow phase of bromination of 3 by Br$_2$ in HFP or HFP–dichloromethane

The reaction between $\mathbf{3}^{\bullet +}$ and bromide ion in neat HFP, as formed in the initial ET step, was too slow for convenient monitoring by UV or EPR spectroscopy. The second-order rate constant was hence determined with added bromide ion and found to be 5.7×10^{-3} dm^3 mol^{-1} s^{-1}. This is *ca.* 20 times slower than the $\mathbf{4}^{\bullet +}$–bromide ion reaction, presumably partly due to the larger steric effect of substitution into $\mathbf{3}^{\bullet +}$ where the nuclear position is flanked by two substituents.[7c] Another effect working in the same direction is the significant difference in spin density at the ring positions, as reflected in the coupling constants: 0.29 mT in $\mathbf{4}^{\bullet +}$ *vs.* 0.044 mT in $\mathbf{3}^{\bullet +}$. The effect of adding dichloromethane upon the rate of disappearance of the radical cation is relatively small up to about 50% (v/v) dichloromethane, a factor of 3.5, but *ca.* 1500 at 70% dichloromethane.

Product formation in the reaction between ICl and ArH

The reaction between **4** and ICl gave practically only the chloro product, the yield of iodo compound being 0.2%. Thus the radical cation pathway must by far be the predominant one, since only reactions between $\mathbf{4}^{\bullet +}$ and Cl^- and/or $\mathbf{4}^{\bullet +}$ and ICl will lead to the chloro product.[27] The yield of $[\mathbf{4}^{\bullet +}]_0$ shortly after mixing was generally in accord with the ET mechanism (Tables 9 and 10), taking into account that reactions within the triad take place during the mixing process. It is also obvious that the latter cannot be perfect. It is likely that the $\mathbf{4}^{\bullet +}$–ICl pathway is the more important one when ICl is present in excess over **4**, as shown in Fig. 7.

On the other hand the reaction between **1** and ICl gave predominantly iodo product (82%), the chloro product being formed in 18% yield. In dichloromethane, the corresponding yields were 49 and 51%, respectively. The latter distribution was considered to be the result of the competition between the $\mathbf{1}^{\bullet +}$–$(\mathrm{I}^\bullet)$ $\mathrm{I_2}$ and $\mathbf{1}^{\bullet +}$–Cl^- reactions. In HFP, the $\mathbf{1}^{\bullet +}$–$\mathrm{I_2}$ reaction was directly observed (Fig. 4) in that a decrease of 1.4 mmol dm^{-3} in $[\mathbf{1}^{\bullet +}]$ was matched by a decrease in $[\mathrm{I_2}]$ of 0.80 mmol dm^{-3}. The reaction of $\mathbf{1}^{\bullet +}$ with chloride ion is slowed down by the vastly decreased nucleophilicity of the latter[8,9] in HFP and it is therefore expected that the $\mathbf{1}^{\bullet +}$–ICl reaction is partly involved in the formation of the chloro product.

Iodine chloride is an important synthetic reagent, extensively used in the large-scale preparation of X-ray contrast agents *via* aromatic iodination reactions.[28] Generally it is assumed that a mechanism involving ‘I$^+$’ is valid. A frequently encountered side-reaction is the formation of chloro compounds which presumably is the result of the competing electron transfer mechanism. The results described above suggest that for a given substrate the ET mechanism mainly will be controlled by the nature of the solvent. HFP represents one extreme: it increases strongly the oxidation potential of ICl—presumably to a large extent by blocking the formation of ICl–halide ion complexes—and therefore extends the upper redox potential limit of substrates which will undergo ET oxidation. The other extreme should involve complexation of ICl with a donor molecule which reduces its redox potential. The favourable iodinating properties of the pyridine–ICl complex[29] might originate from this effect. In any given solvent, the iodination reaction will also be favoured by choice of a substrate which has as high an $E°(\mathrm{ArH^{\bullet+}/ArH})$ as possible.

Conclusions

The results presented above show that halogenation of ArH by common halogenating agents in HFP follows an ET mechanism, where an initial fast ET step gives a mixture of $\mathrm{ArH^{\bullet+}}$ and halide ion which react slowly to give halogenated product(s). It is also shown that $\mathrm{ArH^{\bullet+}}$ can abstract a halogen atom from ICl or $\mathrm{Br_2}$, a reaction earlier demonstrated only for iodine.[7c] The role of HFP in favouring the ET mechanism appears to be at least two-fold: it increases significantly the oxidative power of halogens and deactivates nucleophiles drastically, thus providing conditions for convenient observation of the intermediate $\mathrm{ArH^{\bullet+}}$ of a wide range of substrates. The initial ET step should also be amenable for study, for example by stopped-flow techniques.

Experimental

Methods

NMR spectra were recorded on a Varian XL-300 or Bruker 400 spectrometer. Mass spectrometry was performed on a JEOL JMS SX-102 instrument. GLC analyses (HP5892 series II) were made on a fused silica column (OV-1701, 25 m).

EPR spectra were recorded by the Upgrade Version ESP 3220-200SH of a Bruker ER-200D spectrometer. Spectral simulations were carried out by either the public domain programme WINSIM[30] or Simfonia® (Bruker AG). Cyclic voltammetry was performed by the BAS-100 instrument, using $\mathrm{Bu_4NPF_6}$ (0.15 mol $\mathrm{dm^{-3}}$) as the supporting electrolyte and an Ag/AgCl electrode as the reference, with *iR* compensation. All potentials were calibrated against the internal ferricinium/ferrocene couple (0.43–0.44 and 0.05 V *vs.* Ag/AgCl in acetonitrile and HFP, respectively). UV spectroscopy was performed by the HP-8452A UV–VIS diode array spectrophotometer, the kinetics being monitored by the HP89532K software package. All evaluations of rate constants were made by the SigmaPlot® programme.

Materials

1,1,1,3,3,3-Hexafluoropropan-2-ol (HFP) and acetonitrile were of Uvasol® quality from Merck AG[31] while dichloromethane was of Suprasolv® quality from the same source. Most compounds used were either purchased in highest quality available or available from earlier work. 1,4-Dimethoxy-2,5-dimethylbenzene (**3**) and 1,4-dimethoxy-2,3-dimethylbenzene (**4**), were available from earlier work.[5]

EPR spectra

The substrate ArH was dissolved in HFP in a concentration of 2–40 mmol $\mathrm{dm^{-3}}$ in a sample tube and the solution bubbled by Ar, all operations being performed under dimmed light conditions. A deficit of the halogenating agent, dissolved in HFP or dichloromethane, was added. After bubbling with Ar for 100–150 s, the sample tube was sealed and transferred to the cavity. In general, the spectra were resolved to the same extent as or better than published spectra in HFP or in other solvents. In most cases, except for ArH with the highest $E°(\mathrm{ArH^{\bullet+}/ArH})$ values, the spectral intensity was high and the persistency of the radical cations high enough for spectra of very good quality to be obtained. The following compounds either produced EPR spectra identical to those previously recorded by generation from $\mathrm{Tl^{III}}$ reagents and ArH in HFP or their EPR spectra were analysed and shown to give hfs constants in satisfactory agreement with previous observations: 4,4′-di-*tert*-butylbiphenyl,[8b] 1,2-dimethoxybenzene (**2**),[8b] 1,4-dimethoxybenzene (**1**),[8d] pentamethylanisole,[8b] 1-methoxynaphthalene (forms the radical cation of 4,4′-dimethoxy-1,1′-binaphthalene[8d]), 2,2′-dimethoxy-5,5′-di-*tert*-butylbiphenyl,[32] 2,2′-dimethoxy-5,5′-dimethylbiphenyl,[8b] anthracene,[13] 3,3′,4,4′-tetramethyl-1,1′-binaphthalene [a^{H} 0.590 (6 H), 0.209 (2 H), 0.105 (6 H), 0.0352 (2 H), 0.0176 (4 H) mT; the spectrum was identical to that published from the 4-tolyl-$\mathrm{Tl^{III}}$ trifluoroacetate oxidation of this substrate[8b,33]], 1,4,5,8-tetramethylnaphthalene [a^{H} 0.782 (12 H), 0.176 (4 H); lit.[34] in TFA: a^{H} 0.781 (12 H), 0.182 (4 H) mT], thianthrene [HFP, $a^{2,3,6,7\text{-H}}$ 0.128 (4 H), $a^{33\mathrm{S}}$ 0.892 mT; the coupling of 0.012 mT to 1,4,5,8-H was not seen due to line-broadening; lit.[35] in nitromethane: $a^{2,3,6,7\text{-H}}$ 0.128 (4 H), $a^{33\mathrm{S}}$ 0.892 mT], 1,4-dimethoxy-2-methylbenzene [a^{H} 0.45 (1 H), 0.334 (6 H), 0.305 (3 H), 0.111 (1 H), 0.076 (1 H) mT], 1,4-dimethoxy-2,3-dimethylbenzene (**4**) [a^{H} 0.298 (6 H), 0.290 (2 H), 0.139 (6 H); lit.[36] in nitromethane at −25 °C: a^{H} 0.307 (6 H), 0.290 (2 H), 0.148 (6 H) mT], 1,4-dimethoxy-2,5-dimethylbenzene (**3**) [a^{H} 0.450 (6 H), 0.044 (2 H), 0.312 (6 H); lit.[36] in nitromethane at −25 °C: a^{H} 0.421 (6 H), 0.057 (2 H), 0.315 (6 H) mT], 9,10-dimethylanthracene [a^{H} 0.791 (6 H), 0.252 (4 H), 0.117 (4 H); lit.[37]: a^{H} 0.800 (6 H), 0.254 (4 H), 0.119 (4 H) mT], perylene [a^{H} 0.408 (4 H), 0.308 (4 H), 0.044 (4 H); lit.[37]: a^{H} 0.404 (4 H), 0.303 (4 H), 0.044 (4 H) mT], 1,4-dimethoxy-2,5-di-*tert*-butylbenzene [a^{H} 0.308 (6 H), 0.076 (2 H), 0.013 (18 H); lit.[36] a^{H} 0.324 (6 H), 0.103 (2 H), 0.0103 (18 H) mT], hexamethoxytriphenylene [a^{H} 0.069 (6 H), 0.018 (18 H) mT], 4-*tert*-butyl-*N*,*N*-dimethylaniline [a^{H} 1.10 (6 H), 0.501 (2 H), 0.156 (2 H), 0.039 (9 H), a^{N} 1.12; lit.[38] in acetonitrile: a^{H} 1.22 (6 H), 0.520 (2 H), 0.130 (2 H), 0.040 (9 H), a^{N} 1.13 mT], pyrene [a^{H} 0.618 (4 H), 0.246 (4 H), 0.130 (2 H); lit.[39]: a^{H} 0.539 (4 H), 0.217 (4 H), 0.120 (2 H) mT], 1,2,4,5,6,8-hexamethylanthracene [a^{H} 0.537 (2 H), 0.341 (12 H), 0.226 (6 H), 0.079 (2 H); lit.[40]: 0.543 (2 H), 0.348 (12 H), 0.237 (6 H), 0.079 (2 H) mT], 1,2,4,5-tetramethoxybenzene [a^{H} 0.220 (12 H), 0.088 (2 H); lit.[41] in nitromethane: a^{H} 0.225 (12 H), 0.088 (2 H) mT], 1,2,3,4,5,6,7,8-octamethylanthracene [0.540 (2 H), 0.330 (12 H), 0.165 (12 H); lit.[42] in TFA: 0.545 (2 H), 0.334 (12 H), 0.164 (12 H) mT], *N*-methylphenothiazine [a^{H} 0.723 (6 H), 0.210 (2 H), 0.082 (4 H), a^{N} 0.750, the smallest a^{H} of 0.022 mT was not seen with ICl, $\mathrm{I_2}$ or $\mathrm{Br_2}$ as the oxidant (it was seen in a spectrum from a sample made by 4-tolyl-$\mathrm{Tl^{III}}$ trifluoroacetate oxidation); lit.[43]: a^{H} 0.723 (6 H), 0.220 (2 H), 0.076 (4 H), 0.029 (2 H), a^{N} 0.750 mT]; bis[4-(dimethylamino)phenyl]squaraine [a^{H} 0.451 (12 H), 0.223 (4 H), 0.050 (4 H), a^{N} 0.451 (2 N); lit.[44] in dichloromethane: a^{H} 0.454 (12 H), 0.227 (4 H), 0.047 (4 H), a^{N} 0.454 (2 N) mT], 4,4′-dimethoxystilbene [shortlived, not resolved: multiplet of *ca.* 15 lines with an hfs splitting of 0.10–0.11 mT; a resolved spectrum was obtained by oxidation with 4-tolyl-$\mathrm{Tl^{III}}$ trifluoroacetate in HFP–trifluoroacetic acid (2%): a^{H} 0.38 (2 H), 0.169 (4 H), 0.114 (6 H), 0.0175 (4 H) mT; with high modulation amplitude, the simulated spectrum appears as a multiplet with a splitting of 0.10–0.11 mT].

Reactions with hexamethylbenzene were performed either as above or by injecting 10–50 µl of a fresh, saturated solution of chlorine in HFP *via* a plastic tube into 0.70 ml of a solution of hexamethylbenzene in HFP kept in the sample tube with the cavity tuned. With this arrangement, the time delay between mixing and start of spectral recording was 4–5 s. Reactions in acetic acid were performed in the same way.

Kinetics

UV spectrally monitored kinetics were performed in a darkened room at 23 °C with 0.70 ml samples of a solution of the substrate in HFP in 2 mm cells. The reaction was initiated by the addition of 5 µl of a dichloromethane solution of the appropriate halogenating reagent to the cell. The period between mixing and start of the kinetic run was *ca.* 15 s. Generally 100–200 data points were collected and the rate constants were evaluated using the SigmaPlot® programme (Jandel Scientific, Germany).

Calibration of extinction coefficients

The calibration of the extinction coefficients of the radical cations $\mathbf{3}^{\cdot +}$ and $\mathbf{4}^{\cdot +}$ was done by reacting a 20-fold excess of **3** or **4** in HFP with a solution of a known concentration of an inorganic redox reagent and recording the absorbance at the characteristic maxima in the region of 400–500 nm. As the latter, tetrabutylammonium hexachlororhenate(v)[45] was employed, since it had the required redox potential ($E_{\mathrm{rev}} = 1.24$ V *vs.* Ag/AgCl in acetonitrile) and exhibited no absorption above 400 nm in the reduced form, $\mathrm{Re^{IV}Cl_6}^{2-}$. The spectra obtained were unchanged over at least 20 min. The following data were obtained in HFP: $\mathbf{3}^{\cdot +}$, $\lambda_{\mathrm{max}} = 452$ nm, $\varepsilon = 9280$ dm^3 mol^{-1} cm^{-1} and $\mathbf{4}^{\cdot +}$, $\lambda_{\mathrm{max}} = 458$ nm, $\varepsilon = 5340$ dm^3 mol^{-1} cm^{-1}.

Reaction of 1,4-dimethoxybenzene (1) with ICl in CH_2Cl_2

1,4-Dimethoxybenzene (303 mg, 2.2 mmol) and ICl (340 mg, 2.1 mmol) were dissolved in 15 ml of dichloromethane and kept in the dark for 20 h. Workup as above according to GLC gave a mixture of **1** (51%), the chloro compound (25%) and the iodo compound (24%).

Reaction of 1,4-dimethoxybenzene (1) with ICl in HFP

1,4-Dimethoxybenzene (63 mg, 0.46 mmol) and ICl (70 mg, 0.43 mmol) were dissolved in 4 ml of HFP and kept in the dark for 20 h. Workup as above according to GLC gave a mixture of **1** (71%), the chloro compound (5%) and the iodo compound (24%).

Reaction of 1,4-dimethoxy-2,3-dimethylbenzene (4) with ICl in HFP

To a stirred solution of 4.18 mg (2.52×10^{-5} mol) of **4** in 3.0 ml of HFP was added dropwise 175 µl of a 0.29 mol dm^{-3} solution of ICl in dichloromethane (5.08×10^{-5} mol). The solution was stirred overnight in the dark and evaporated and analyzed by GLC. The product mixture consisted of **4** (9%), 5-chloro-1,4-dimethoxy-2,3-dimethylbenzene (90%), 5,6-dichloro-1,4-dimethoxy-2,3-dimethylbenzene [0.8%; identified by its mass spectrum (MS): *m*/*z* (GLC inlet, EI, 70 eV) 238 (7%), 236 (45), 234 (70), 223 (9), 221 (64), 219 (100)] and 5-iodo-1,4-dimethoxy-2,3-dimethylbenzene (0.2%; identified by its MS).

Reaction of 1,4-dimethoxy-2,3-dimethylbenzene (4) with ICl in CH_2Cl_2

1,4-Dimethoxy-2,3-dimethylbenzene (76 mg, 0.46 mmol) and ICl (70 mg, 0.43 mmol) were dissolved in 4 ml of dichloromethane and kept in the dark for 20 h. Workup as above according to GLC gave a mixture of **4** (28%) and the chloro compound (72%), no trace of the iodo compound (24%) being detectable.

5-Iodo-1,4-dimethoxy-2,3-dimethylbenzene

This compound was prepared by reaction of **4** and iodine in acetic acid with some periodic acid added. $\delta_{\mathrm{H}}(\mathrm{CDCl_3})$: 2.10 (s, 3 H), 2.25 (s, 3 H), 3.70 (s, 3 H), 3.77 (s, 3 H), 7.07 (s, 1 H); *m*/*z*-(GLC inlet, EI, 70 eV) 292 (100%), 277 (81).

Reaction of 1,4-dimethoxy-2,3-dimethylbenzene (4) with bromine in HFP

To a vigorously stirred solution of **4** (10 mg, 5.9×10^{-5} mol, 20 mmol dm^{-3}) in HFP (3.0 ml) was added bromine (8.7 mg, 5.4×10^{-5} mol, 18 mmol dm^{-3}) dissolved in HFP (*ca.* 1 ml). Samples were withdrawn at intervals, quenched in water–bisulfite and analysed by GLC. The following concentrations (**4**, bromo product, in mmol dm^{-3}) were obtained at: $t = 1$ min, 4.5, 11.7; 10 min, 4.3, 15.3; 30 min, 3.8, 14.2 and 300 min, 4.5, 18.5. At $t = 2.5$ min, EPR spectral monitoring of an aliquot was commenced (Fig. 6).

In a similar experiment, **4** (20 mg, 0.12 mmol) and bromine (10 mg, 0.062 mmol) were mixed in HFP (3 ml) to give a solution with the characteristically green colour of $\mathbf{4}^{\cdot +}$. The colour persisted for >2 h. After 20 h, the conversion into the bromo product was 35%. An experiment with a molar ratio of **4** to bromine of 1:1 initially gave a green solution of $\mathbf{4}^{\cdot +}$. The colour changed to yellow in <1 h, and the conversion into the bromo product was 91% after 1.5 h.

Reaction of 1,4-dimethoxy-2,3-dimethylbenzene (4) with bromine in HOAc

Compound **4** (22 mg, 0.132 mmol) and bromine (10 mg, 0.062 mmol) were mixed in 2 ml of acetic acid. Workup as above after 1 min showed 47% conversion into the 5-bromo product. A similar experiment with one molar equivalent of bromine after 10 min gave 97% conversion into the bromo product.

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