

Cation Radicals as Intermediates in Aromatic Halogenation with Iodine Monochloride: Solvent and Salt Effects on the Competition between Chlorination and Iodination

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Three distinct classes of substitutional reactivity can be discerned in the halogenation of a series of methyl-substituted methoxybenzenes (ArH) with iodine monochloride (ICl), namely, exclusive iodination, exclusive chlorination, and mixed iodination/chlorination. Spectral studies establish the prior formation of the charge-transfer complex [ArH,ICl] which suffers electron transfer to afford the reactive triad [ArH^{•+}, I[•], Cl⁻] according to Scheme 1. Separate reactivity studies show that chlorination and iodination can result from the quenching of the aromatic cation radical by chloride and iodine (atom), respectively. Iodination *versus* chlorination thus represents the competition between radical-pair and ion-pair collapse from the reactive triad, and it is predictably modulated by solvent polarity and added salt.

Electrophilic aromatic substitution is generally considered to proceed *via* the rate-limiting collapse of the electrophile (E) and the aromatic substrate (ArH) to form the σ -complex (EArH) or Wheland intermediate.¹ Since many electrophiles are also oxidizing agents, an alternative mechanism involving an initial electron transfer to generate the aromatic cation radical (ArH^{•+}) as the reactive intermediate has been presented.² Symptomatic of the latter are the transient charge-transfer complexes [ArH, E] that are commonly observed in systems undergoing electrophilic substitution.³

Among the best and earliest examples of aromatic charge-transfer complexes is that originally observed in solution between benzene and diiodine (Benesi and Hildebrand),⁴ whose molecular structure has been established by X-ray crystallography (Hassel and Stromme)⁵ and whose electronic structure has been theoretically clarified (Mulliken).⁶ Aromatic charge-transfer complexes are also known for the other halogens, especially dibromine and dichlorine, relevant to aromatic bromination and chlorination, respectively.⁷ The interhalogens form analogous charge-transfer complexes with the same aromatic donors,⁸ and iodine monochloride (ICl) is known to iodinate (poly)methylbenzenes,⁹ anilines,^{9a,10} phenols,¹¹ haloaromatics,^{9b,12} and (poly)methoxybenzenes.^{9a,13} In most cases, polar solvents such as acetic acid have been

used, and a mechanism involving heterolytic cleavage of ICl followed by electrophilic attack of the iodine cations on the aromatic substrate has been proposed.^{11c} In some cases, chlorination has been observed as an undesired side reaction, especially in solvents of low dielectric constant such as carbon tetrachloride. For example, salicylic acid is exclusively iodinated in acetic acid^{11a} and nitrobenzene.^{11c} In carbon tetrachloride, both iodination and chlorination occur,^{11c} whereas a mixture with neat ICl leads to the chloro derivative as the major product.^{11c} On the basis of the rather unambiguous polarity of ICl (*viz.* partial positive charge on iodine and partial negative charge on the chlorine moiety), the chlorination path is not easily explained in terms of electrophilic attack. Thus, the homolytic cleavage of ICl to yield iodine and chlorine atoms has been invoked in less polar solvents.^{11c} Indeed, the dichotomy between heterolytic *versus* homolytic cleavages is supported by thermodynamic calculations¹⁴ that show heterolytic cleavage of ICl in the gas phase to require about 650 kJ/mol *more* energy than bond homolysis, for which a dissociation energy of 211 kJ/mol has been reported.¹⁵ Thus, in the absence of a solvent (to stabilize the ions by solvation), homolytic cleavage is expected, whereas ion formation is predicted in solvents with dielectric constant greater than 3.9.¹⁴ Significantly, solutions of iodine monochloride in polar solvents are electrically conducting,^{11c} and a weak conductivity is observed¹⁴ even in chlorobenzene ($\epsilon = 5.7$).¹⁶

O'Malley and co-workers¹⁷ have recently found that various anthracene and naphthalene derivatives are exclusively chlorinated in a polar solvent such as aceto-

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nitrile ($\epsilon = 36$),¹⁶ which is contrary to the arguments based on solvent polarity only. Thus, in analogy to earlier work¹⁸ on aromatic fluorination with I_2/AgF in acetonitrile, they propose a mechanism in which electron transfer from arene to ICl is followed by either radical-pair collapse between the aromatic cation radical and iodine atom in the case of iodination or ion-pair collapse between the aromatic cation radical and chloride ion in the case of chlorination.¹⁷ Based primarily on kinetic measurements, a charge-transfer complex undergoing electron transfer has been proposed as the initial step in the chlorination of isopropyl iodide with iodine monochloride in dichloromethane.¹⁹

Since methoxy substituents enhance aromatic donors, we have focused our attention in this study on the behavior of various methoxy and dimethoxybenzenes toward iodine monochloride, especially in a nonpolar solvent such as dichloromethane. In contrast to the earlier work on 1,4-dimethoxybenzene in acetic acid,¹³ we now find chlorination and iodination products in comparable amounts, the molar ratio of which is varied by the solvent or by added salt. For several substituted dimethoxybenzenes, chlorination products are obtained exclusively. Other methoxy and dimethoxy derivatives in the same solvent yield iodo products exclusively. Clearly, electronic and steric properties of the substrates must be systematically examined in view of a postulated¹⁷ electron-transfer step prior to halogenation. Accordingly, this study addresses the dual questions as to (a) whether electron transfer leading to aromatic cation radicals is a relevant pathway to halogenation with ICl and (b) how structural and environmental factors can control chlorination *versus* iodination.


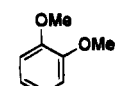

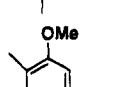

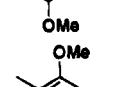

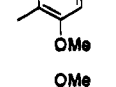

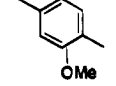

Results

1. Methoxybenzenes as Electron Donors. The initial positive-scan cyclic voltammetry (CV) of the methoxy and dimethoxybenzenes identified in Table 1 was carried out at a platinum electrode in 5 mM dichloromethane solutions containing 0.2 M tetra-*n*-butylammonium hexafluorophosphate as the supporting electrolyte. The dimethoxybenzenes 5–11 showed reversible cyclic voltammograms at scan rates of $\nu = 0.1 \text{ V s}^{-1}$ with current ratios between the anodic and cathodic peak of $i_a/i_c = 1.0$ (theoretical value). In the case of 5 and 7, the cathodic peak currents were somewhat less than theoretical even at a higher scan rate of $\nu = 0.5 \text{ V s}^{-1}$. Calibration of the CV peaks with ferrocene indicated a reversible one-electron oxidation of the aromatic donor to the cation radical, *i.e.*



In the case of the anisoles 1–4, the cyclic voltammogram was irreversible even at scan rates up to 2.0 V s^{-1} , and only the anodic peak potentials (E_p) are reported. In Table 1, the results clearly show that the donor strength of the arenes increased significantly on proceeding from the anisoles 1–4 to the dimethoxybenzenes 5–11. Bromine and iodine substituents in the anisoles increased

Table 1. Oxidation Potentials^a of Various Methoxy and Dimethoxybenzene Donors

Substrate	E_p ($E_{1/2}$) ^b	Substrate	E_p ($E_{1/2}$) ^b
1 	1.83 ^c	7 	1.33 (1.26)
2 	1.81 ^c	8 	1.25 (1.16) ^d
3 	1.78 ^c	9 	1.18 (1.14) ^d
4 	1.59 ^c	10 	1.09 (1.02) ^d
5 	1.47 (1.42)	11 	1.34 (1.26) ^d
6 	1.44 (1.35) ^d		

^a In dichloromethane under an argon atmosphere at 25°C.

^b $[V]$ vs. SCE at 25°C; F_p = anodic peak potential at $\nu = 100 \text{ mV/s}$; $E_{1/2}$ = average of anodic and cathodic peak potentials.

^c Irreversible cyclic voltammogram.

^d From ref. 27.

the oxidation potentials significantly in 2 and 1, respectively. A methyl substituent in the *para* position shifted the peak potential by roughly -200 mV . However, the oxidation potentials of the methyl-substituted dimethoxybenzenes followed an unusual trend. Thus, increasing the number of methyl groups decreased $E_{1/2}$ initially, and a minimum was passed at the 2,5-dimethyl analogue 10. The value for $E_{1/2}$ then increased on passing to the trimethyl compound 11. It follows that the substitution pattern played a more important role in determining the oxidation potential of methoxy and dimethoxybenzenes than the number of methyl substituents. This result is in strong contrast to previous observations with polymethylbenzenes, for which the oxidation potentials decreased monotonically with the increasing number of methyl groups.²⁰

2. Halogenation of Methoxy and Dimethoxybenzenes with Iodine Monochloride in Dichloromethane. The series of substituted methoxy and dimethoxybenzenes in Table 2 were exposed to iodine monochloride in dichloromethane solution under a uniform set of conditions to allow direct comparison of the chlorination and iodination processes. All reactions were carried out at room temperature and protected from any adventitious light to avoid complications from the photoactivation of iodine monochloride (which exhibits a broad absorption band centered around 445 nm).²¹ In order to avoid multiple halogenation, the methoxy compounds were

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Table 2. Halogenation of Methoxy and Dimethoxybenzenes with Iodine Monochloride^a

Aromatic donor	Products (%) ^b	conv. ^c (%)	time/temp (h)/(°C)	Aromatic donor	Products (%) ^b	conv. ^c (%)	time/temp (h)/(°C)
1	 (91) (9)	70	20/25	7	 (100)	65	4/25
2	 (77) (23)	61	45/25	8	 (76) (24) ^d	29	20/25
3	 (99)	93	1/25	9	 (100)	42	22/25
4	 (100)	99	1/25	10	 (100)	32	3/25
5	 (95) ^e	48	22/25	11	 (100)	37	18/25
6	 (60) (40)	47	21/25				

^a In dichloromethane solution in the dark. ^b Relative yield based on ICl. ^c Conversion based on ICl.

^d Sum of two isomers. ^e Trace amounts of chloroproducts also detected.

present in 20 % excess relative to iodine monochloride. As anticipated from the bifunctional character of the halogenating agent, three halogenation patterns were observed (see Table 2):

Exclusive iodination was observed for aromatic donors ArH = 3, 4, and 7. Upon the addition of 0.36 mmol (0.072 M) of these donors to 0.30 mmol (0.06 M) of ICl in dichloromethane, the red-brown color of ICl started to fade immediately. In the case of 3 and 4, the reaction was nearly complete (conversion greater than 90 %) in less than 1 h to yield an almost colorless solution of the iodo product. By comparison, 7 reacted significantly slower (65% conversion in 4 h) in accord with the stoichiometry for iodination, *i.e.*



High selectivity was achieved, and each aromatic donor afforded only one iodo isomer. The position of the iodo group relative to the methoxy substituent depended on the substitution pattern. For example, iodination occurred at the *para* position relative to the methoxy group whenever an open *para* position was available (substrate 3 and 7). Otherwise, iodination occurred at the *ortho* position relative to the methoxy substituent (substrate 4).

(21) Photoinduced halogenations with iodine monochloride will be reported separately.

Exclusive chlorination was observed in dimethoxybenzenes 9–11. With these aromatic donors, the reaction mixtures turned very dark brown immediately after their addition to the solution of ICl in dichloromethane. As the reaction progressed, the solution became increasingly more purple. This color was identified as that of diiodine in dichloromethane (*vide infra*). Although the color change from dark brown to purple occurred rapidly at the beginning, the yields of chloro product never exceeded 50% (based on the amount of ICl). This result is in accord with the 2:1 stoichiometry between aromatic donor and ICl in eq 3:



Mixed halogenation was obtained with substrates 1, 2, 5, 6, and 8. With anisoles 1 and 2, only a single isomer of the iodo and chloro product was observed. Iodination and chlorination occurred at the same position on the aromatic ring. More than one chloro isomer was found in the other cases, and the products were not completely identified (see Experimental Section). Yields and molar ratios of the halogenated products varied with the substrate. For example, the molar ratio of the iodination and chlorination products from dimethoxybenzene 6 was found to depend strongly on the relative amounts of starting materials, as demonstrated in Table 3. In general, the intensity of the purple-colored reaction mixture was a reliable (visual) indicator for the relative

Table 3. Effect of Reactant Concentrations on the Halogenation of 1,4-Dimethoxybenzene (ArH) with Iodine Monochloride^a

[ArH]/[ICl]	[ArI]/[ArCl] ^b	[ArH]/[ICl]	[ArI]/[ArCl] ^b
0.5	1.1	4.0	3.4
1.0	1.4	30	9.0
2.0	2.8		

^a In dichloromethane solution in the dark at 25 °C. ^b ArI = 2-iodo-1,4-dimethoxybenzene; ArCl = 2-chloro-1,4-dimethoxybenzene.

amounts of chloro and iodo products (compare the stoichiometry in eqs 2 and 3).

Although no attempt was made to measure the kinetics of aromatic halogenation with ICl, the time/conversions in Table 2 provided an adequate (qualitative) guide to the reactivity of the various methoxy and dimethoxybenzenes. For example, the parent anisole (**3**) was the most reactive substrate, followed by its methyl derivative **4**, as judged by the high conversions (93 and 99%, respectively) that were achieved within 1 h at 25 °C. Among the dimethoxybenzenes, the methyl derivative **7** was similarly judged to be the most reactive toward ICl. By comparison, bromoanisole **2** reacted quite slowly (less than 20% conversion in 16 h), whereas the dimethoxybenzenes gave fair conversions (~50%) in the same time span. If the mixed halogenations were considered to derive from the sum of eqs 2 and 3 (each of which exhibited a different stoichiometry for ArH and ICl), the conversions in mixed halogenation reactions were difficult to compare since the theoretical maximum depended on the molar ratio of the reactants (see Table 3).

Since iodine monochloride is in thermodynamic equilibrium with its molecular components,²² diiodine was deliberately added to the solution of dimethoxybenzene and ICl in dichloromethane. It is significant that the iodination/chlorination ratio of 60:40 (see Table 2) did not change when excess I₂ (up to twice the amount of ICl) was present in solution. To investigate the question of whether iodo and chloro products were formed independently (or one from the other), we monitored the molar ratio in the reaction mixture of **6** and ICl in chloroform-*d* by ¹H NMR spectroscopy. No change in the ratio between the iodo and chloro products was observed over time. Moreover, when the iodo compounds **1** and **5** were exposed to ICl in dichloromethane, no iodine exchange with chlorine was observed (see Table 2).

3. Solvent and Salt Effects on Aromatic Halogenations with Iodine Monochloride. The halogenation of 1,4-dimethoxybenzene with iodine monochloride was carried out in four solvents of different polarity and in the presence of high concentrations of tetra-*n*-butylammonium hexafluorophosphate salt in dichloromethane. The results in Table 4 show that the distribution among iodo and chloro products was unaffected by the replacement of dichloromethane with carbon tetrachloride. However, there was a greater than 5-fold increase in the ratio of iodo and chloro products for halogenations carried out in acetonitrile and a 3-fold decrease in trifluoroacetic acid as compared to the results in dichloromethane. The presence of high concentrations (0.2 M) of tetra-*n*-butylammonium hexafluorophosphate in the dichlo-

Table 4. Solvent and Salt Effects on Aromatic Halogenation with Iodine Monochloride^a

solvent	ε ^b	[ArI]/[ArCl] ^c
acetonitrile	36	90/10
dichloromethane	8.9	60/40
dichloromethane with added salt ^d		40/60
carbon tetrachloride	2.2	60/40
trifluoroacetic acid	8.6	30/70

^a Of 1,4-dimethoxybenzene in the dark at 25 °C. ^b Dielectric constant from ref 16. ^c Molar ratio of iodination and chlorination products. ^d 0.2 M Bu₄N⁺PF₆⁻.

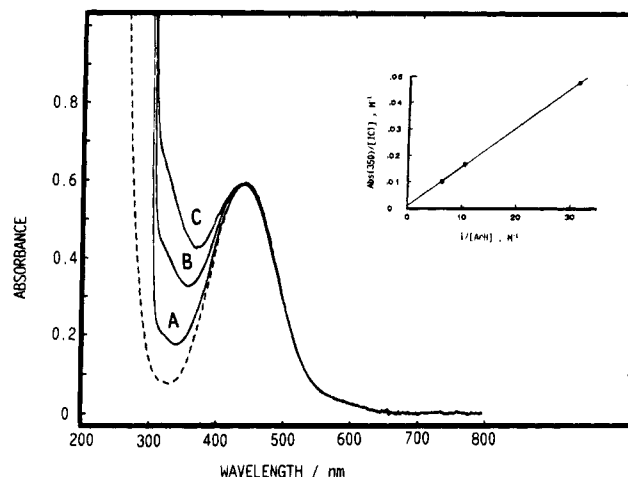


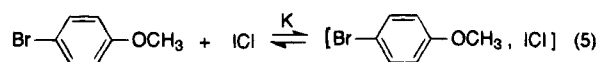
Figure 1. Charge-transfer absorption spectra from a solution of iodine monochloride (3.8 mM) and 0 (---), (A) 0.032, (B) 0.096, and (C) 0.160 M 4-bromoanisole in dichloromethane at 25 °C. Inset: Benesi-Hildebrand plot.

romethane solution of 1,4-dimethoxybenzene and ICl inverted the iodo/chloro ratio in comparison to the halogenation in the absence of the salt.

4. UV-vis Spectroscopic Studies of Aromatic Donors with Iodine Monochloride. The absorption spectrum of iodine monochloride in dichloromethane solution underwent the successive changes shown in Figure 1 upon the incremental addition of 4-bromoanisole (BA) at 25 °C. When the absorbance change at 350 nm (*A*₃₅₀) was monitored according to the Benesi-Hildebrand treatment,²³ *i.e.*

$$\frac{[ICl]}{A_{350}} = \frac{1}{K \epsilon_{350} [BA]} + \frac{1}{\epsilon_{350}} \quad (4)$$

the linear relationship shown in the inset yielded $K = 0.6 \text{ M}^{-1}$ and $\epsilon_{350} = 1090 \text{ M}^{-1} \text{ cm}^{-1}$. These values accorded with the formation constants and extinction coefficients of related aromatic charge-transfer complexes with iodine monochloride,⁸ *i.e.*



More generally, the spectral changes were complicated by the simultaneous halogenation of the other more reactive methoxy and dimethoxybenzenes by iodine monochloride. For example, the colorless solution of dimethoxybenzene in dichloromethane turned bright red immediately upon the addition of iodine monochloride, followed by a complex series of color changes to purple.

(22) A free energy of formation for liquid ICl has been reported to be $\Delta G_f^\circ = -13.8 \text{ kJ/mol}$ at 25 °C.¹⁶ This corresponds to an equilibrium constant of $K = 283 \text{ M}^{-1}$ for the formation of ICl from I₂ and Cl₂, and the amount of free I₂ in liquid iodine monochloride is estimated to be about 6 mol %.

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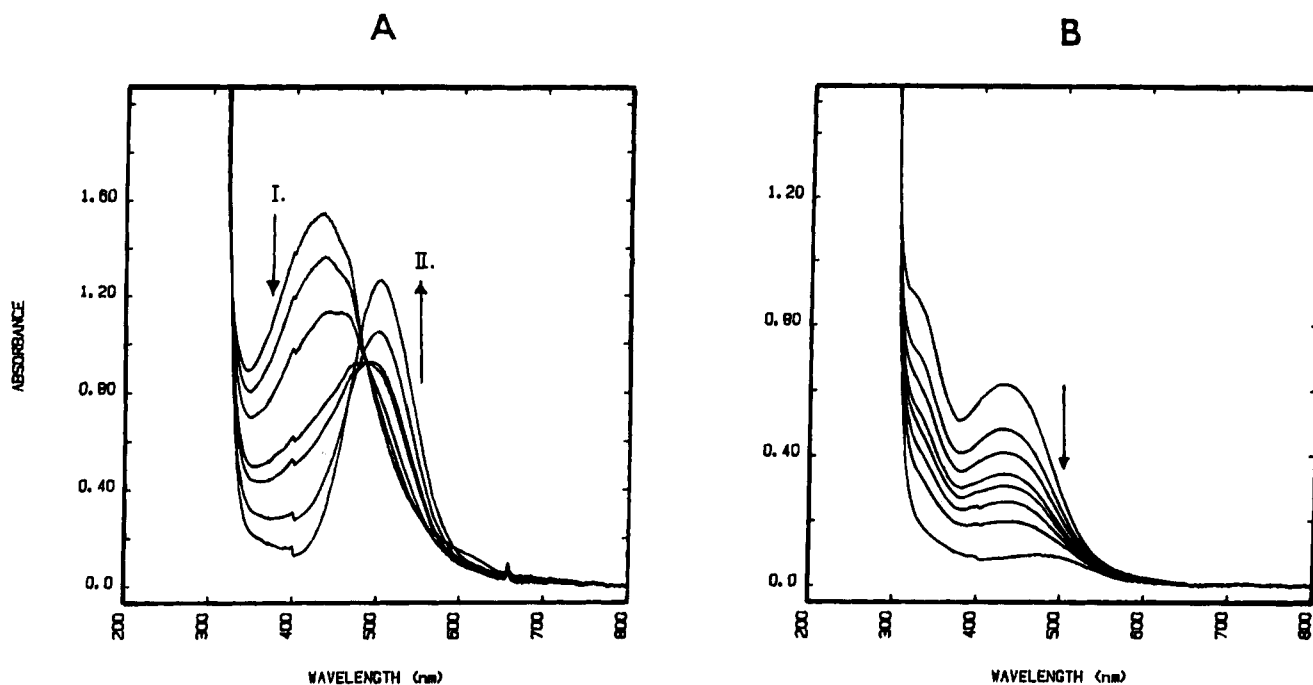
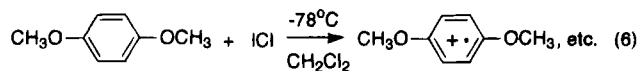


Figure 2. Spectral changes accompanying the reaction of (A) 1,4-dimethoxybenzene and (B) anisole with iodine monochloride in dichloromethane at 25 °C.

These dramatic color changes are manifested spectroscopically in Figure 2A by the monotonic diminution of the composite absorption band I (due to ICl absorption with $\lambda_{\text{max}} = 445$ nm and CT absorption with $\lambda_{\text{max}} = 350$ nm⁸) and concomitant growth of a new absorption band II ($\lambda_{\text{max}} = 505$ nm). Band II coincided with that obtained independently from a solution of diiodine in dichloromethane. Iodine absorption was only observed in those reaction mixtures that contained chlorination products (compare eq 3 and Table 2). Neither a purple coloration nor diiodine absorption was apparent in the halogenation of anisole which yielded iodoanisole without contamination by chloroanisole. The latter is confirmed in Figure 2B by the simultaneous disappearance of the ICl and charge-transfer absorptions at $\lambda_{\text{max}} = 445$ and 350 nm, respectively.

5. Direct Observation of Aromatic Cation Radicals at Low Temperature. The spectral change accompanying the exposure of 1,4-dimethoxybenzene (**6**, 1 μmol) to iodine monochloride (9.5 μmol) at low temperature (-78 °C) is illustrated in Figure 3. The characteristic twin peaks at 440 and 468 nm of the new absorption band was diagnostic of dimethoxybenzene cation radical (**6**^{•+}) that was unambiguously generated earlier by electron-pulse radiolytic²⁴ and laser-flash photolytic²⁵ techniques ($\lambda_{\text{max}} = 430, 460$ nm and $\epsilon = 9040, 9540$ M⁻¹ cm⁻¹ in water²⁴). Quantitative analysis of the cation radical **6**^{•+} produced with excess iodine monochloride indicated a spectral yield of ~50% based on the dimethoxybenzene added, *i.e.*



Similarly, the treatment of the more reactive 2,5-di-

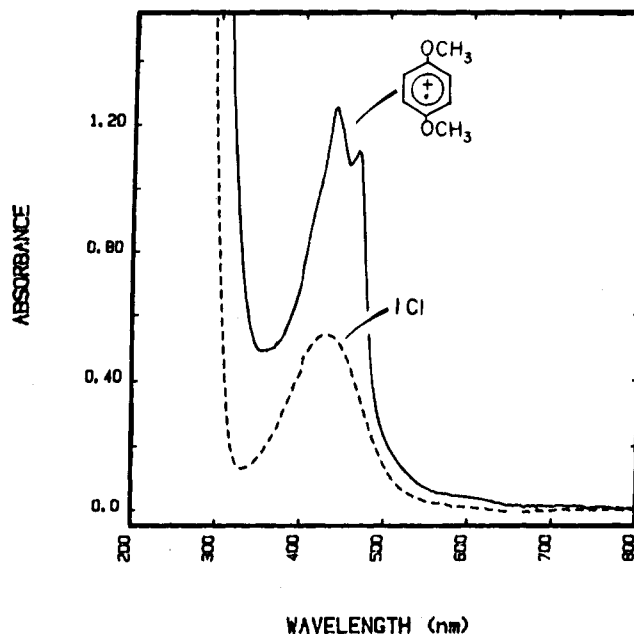


Figure 3. Absorption spectrum (---) of 2 mM iodine monochloride in dichloromethane at -78 °C. Spectrum (—) after addition of 0.2 mM 1,4-dimethoxybenzene. The solid line corresponds to the absorption spectrum of the cation radical **6**^{•+}.

methyl analogue **10** with ICl under comparable low-temperature conditions led to the absorption spectrum in Figure 4 with twin maxima at 432 and 460 nm. The authentic spectrum of the cation radical (**10**^{•+}) produced by the complete oxidation of 2,5-dimethyl-1,4-dimethoxybenzene²⁶ is shown in the inset for comparison. A quantitative yield of cation radical **10**^{•+} was evaluated from the absorbance of the 460-nm band in Figure 4 (based on $\epsilon_{460} = 8500$ M⁻¹ cm⁻¹²⁷). Similar experiments with *o*-dimethoxybenzene **7** at -78 °C led to a broad

(24) O'Neill, P.; Steenken, S.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1975**, *79*, 2773.

(25) Sankararaman, S.; Haney, W. A.; Kochi, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5235.

(26) Rathore, R.; Kochi, J. K. Manuscript in preparation.

(27) Rathore, R. Unpublished results.

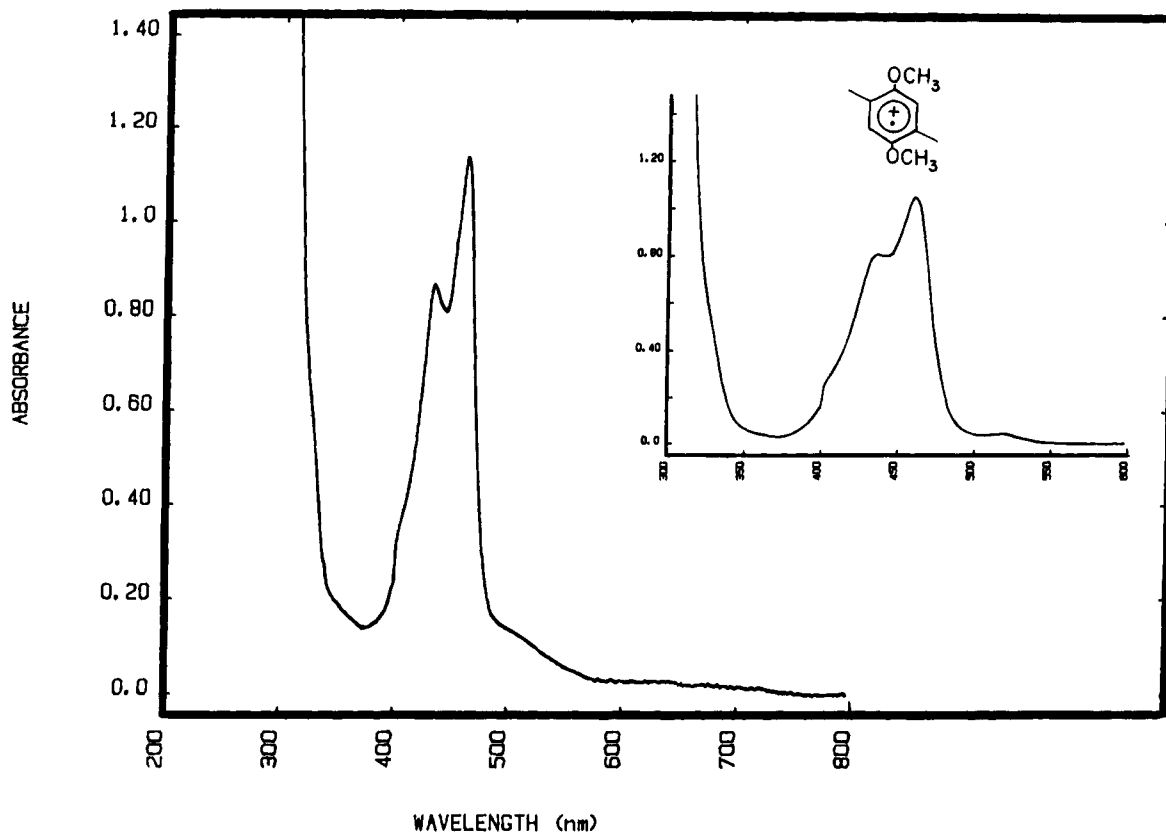
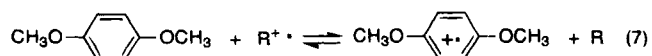


Figure 4. Absorption spectrum obtained from 2,5-dimethyl-1,4-dimethoxybenzene (3 mM) and 0.4 mM iodine monochloride in dichloromethane at $-78\text{ }^{\circ}\text{C}$. Inset: Absorption spectrum of the cation radical $10^{+\bullet}$.

absorption band ($\lambda_{\text{max}} = 405\text{ nm}$) with a distinctive shoulder at $\sim 430\text{ nm}$, both of which are strongly reminiscent of the absorption spectrum previously reported for the cation radical of *o*-dimethoxybenzene.²⁸

The spectral observation of cation radicals $6^{+\bullet}$ and $10^{+\bullet}$ required excess iodine monochloride to maximize their yield at $-78\text{ }^{\circ}\text{C}$. [For example, a 5-fold excess of ICl was required to convert 2,5-dimethyl-1,4-dimethoxybenzene to its cation radical ($10^{+\bullet}$) in quantitative yield.] The cation radicals generated in this manner were persistent at $-78\text{ }^{\circ}\text{C}$, as indicated by the invariant spectra (see Figures 3 and 4), for prolonged periods. Unfortunately, these were not optimum conditions to examine the separate reactivity of the cation radicals as reactive intermediates. Accordingly, the cation radicals $6^{+\bullet}$ and $10^{+\bullet}$ were also independently generated *in situ* by the oxidation of 1,4-dimethoxybenzene and 2,5-dimethyl-1,4-dimethoxybenzene, respectively, as given in eq 7

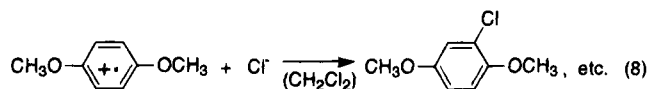


where $\text{R}^{\bullet} = 9,10\text{-dimethoxy-1,4:5,8-dimethano-1,2,3,4,5,6,7,8-octahydroanthracenium hexachloroantimonate}$.²⁶ [Spectral titration indicated that the electron transfer in eq 7 was complete for $10^{+\bullet}$.]

6. Reactivity of Aromatic Cation Radicals toward Iodine and Chloride. Since 1,4-dimethoxybenzene (**6**) suffered competitive iodination/chlorination by ICl, whereas the 2,5-dimethyl derivative (**10**) was exclusively chlorinated (see Table 2), the reactivities of the

corresponding cation radicals $6^{+\bullet}$ and $10^{+\bullet}$ were compared directly as follows.

Chloride. 1,4-Dimethoxybenzene (0.3 mmol) was added to a solution of iodine monochloride (0.3 mmol) in dichloromethane at $-78\text{ }^{\circ}\text{C}$ in the dark. To the red solution of the cation radical $6^{+\bullet}$ was added an excess of the soluble chloride salt PPN^+Cl^- [where PPN^+ = bis-(triphenylphosphoranylidene)ammonium] and the mixture kept in the dark at $-78\text{ }^{\circ}\text{C}$ for 2 h. Upon workup of the saline solution, 2-chloro-1,4-dimethoxybenzene was obtained in 19% yield as the sole halogenation product, *i.e.*



Similarly, a dilute ($9 \times 10^{-5}\text{ M}$) solution of cation radical $10^{+\bullet}$ was prepared from 2,5-dimethyl-1,4-dimethoxybenzene and ICl at $-78\text{ }^{\circ}\text{C}$, and its reaction with PPN^+Cl^- was directly monitored by UV-vis spectroscopy. In Figure 5, the diagnostic twin absorption band of $10^{+\bullet}$ is shown to vanish immediately upon the addition of the chloride salt at $-78\text{ }^{\circ}\text{C}$. In order to identify the products, the same experiment was carried out with higher amounts of reactants (see Experimental Section), and the 3-chloro derivative described in Table 2 was found to be the sole halogenation product.

Iodine. Owing to the overlapping absorption spectra of iodine monochloride ($\lambda_{\text{max}} = 445\text{ nm}$) and diiodine ($\lambda_{\text{max}} = 505\text{ nm}$), iodine atoms could not be selectively generated by I_2 photolysis.²⁹ Thus, in an alternative procedure,

(28) Shida, T. *Electronic Absorption Spectra of Radical Ions*; Elsevier: Oxford, 1988.

(29) Harris, A. L.; Brown, J. K.; Harris, C. B. *Ann. Rev. Phys. Chem.* 1988, 39, 341 and references cited therein.

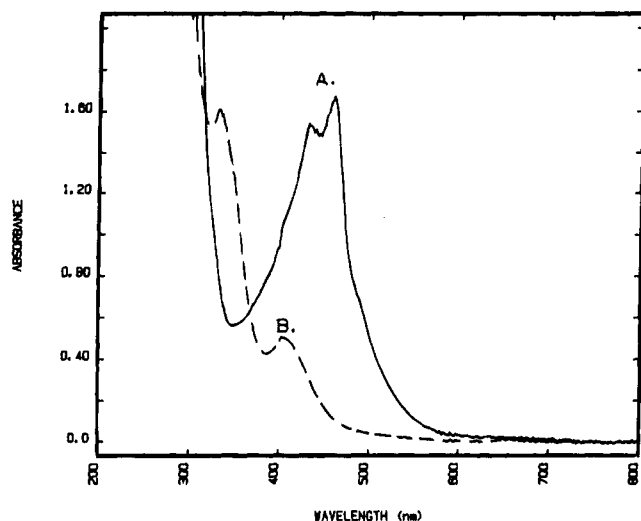
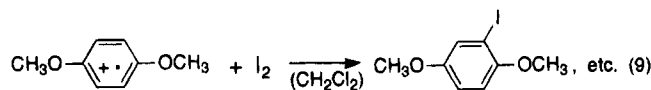


Figure 5. (A) Absorption spectrum of the cation radical of **10** generated from 0.1 mM 2,5-dimethyl-1,4-dimethoxybenzene and 7 mM iodine monochloride at $-78\text{ }^{\circ}\text{C}$. (B) Spectrum after addition of excess PPN^+Cl^- .

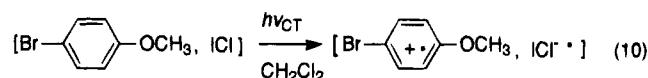
the cation radicals $\mathbf{6}^{++}$ and $\mathbf{10}^{++}$ were generated by electron transfer (eq 7) in the presence of molecular iodine. For example, a solution of diiodine (0.2 mmol) in dichloromethane was added to $\mathbf{6}^{++}$ prepared from a dichloromethane solution of 1,4-dimethoxybenzene (0.2 mmol) and 0.05 mmol of oxidant \mathbf{R}^{++} (see eq 7). After the reaction mixture was allowed to stand overnight in the dark, workup yielded the iodo derivative in 68% yield, *i.e.*



[The control experiment carried out in the absence of \mathbf{R}^{++} yielded no 2-iodo-1,4-dimethoxybenzene, and **6** was recovered completely.] In a second experiment, the cation radical $\mathbf{10}^{++}$ was generated from a solution of 2,5-dimethyl-1,4-dimethoxybenzene (0.13 mmol) and \mathbf{R}^{++} (0.05 mmol) (*vide supra*). The addition of diiodine (0.05 mmol) at $25\text{ }^{\circ}\text{C}$ led to no change. Furthermore, the prolonged (3 h) irradiation of the red solution with filtered light ($\lambda > 480\text{ nm}$) from a 450-W xenon lamp yielded no iodo product, and the dimethoxybenzene was recovered intact. Further attempts to iodinate the 2,5-dimethyl derivative **10** with the iodinating agent consisting of a mixture of silver trifluoroacetate and diiodine³⁰ afforded no iodination product. [Under the same conditions, good yields of 2-iodo-1,4-dimethoxybenzene were obtained from **6**.]

7. Charge-Transfer Excitation of Methoxybenzene Complexes with Iodine Monochloride. In order to verify the charge-transfer character of the new absorption band in Figure 1, the solution of 4-bromoanisole (BA) and iodine monochloride in dichloromethane was deliberately irradiated at $\lambda_{\text{exc}} = 355\text{ nm}$ with a 25-ps (fwhm) laser pulse. Since this excitation wavelength was close to the minimum in the ICl absorbance, it was optimally suited to directly excite the charge-transfer complex in eq 5. The transient spectrum in Figure 6A ($\lambda_{\text{max}} = 510\text{ nm}$) obtained immediately following laser excitation corresponded to that of 4-bromoanisole cation

radical ($\text{BA}^{\cdot+}$),³¹ *i.e.*

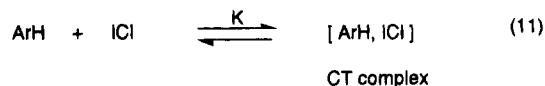


This charged species persisted unchanged over relatively long periods as shown in the transient spectrum in Figure 6B taken at $0.6\text{ }\mu\text{s}$ following the same 355-nm excitation of the charge-transfer complex but with a 10-ns laser pulse. It is noteworthy that the subsequent disappearance of $\text{BA}^{\cdot+}$ occurred by second-order kinetics with $k_2 = 6.6 \times 10^9\text{ M}^{-1}\text{ s}^{-1}$ as shown by the computer fit of the spectral decay (Figure 6B, inset).³²

Discussion

The series of methyl-substituted methoxy and dimethoxybenzenes are particularly useful aromatic donors to study halogenation with iodine monochloride since three distinct classes of substitutional reactivity can be discerned, namely, exclusive iodination, exclusive chlorination, and mixed iodination/chlorination. As a measure of aromatic donor strength, the one-electron oxidation potentials in Table 1 show that the value of $E_{1/2}$ decreases significantly with the number of methoxy groups. However, no clear trend with the number of methyl groups is found, and the oxidation potentials of the methyl-substituted dimethoxybenzenes **6–11** are more affected by the substitution pattern than by the number of methyl groups. This phenomenon is explicable by considering the degree of rotational freedom of the methoxy group in and out of the aromatic plane. Since the product of one-electron oxidation, *i.e.*, the cation radical, is optimally stabilized by locating the methoxy group in the plane of the aromatic ring,²⁶ steric hindrance of *ortho*-substituents plays a direct role in establishing the value of $E_{1/2}$.

Prior Formation of the Charge-Transfer Complex. The acceptor properties of iodine monochloride are manifested by its electron affinity of 2.84 eV,³³ as well as in its ability to form charge-transfer complexes with various electron donor molecules.^{8,9b} All substrates used in this study show, immediately upon mixing with ICl, a new absorption band around 350 nm where neither ICl nor the methoxybenzene donor absorb (see Figure 1). This new absorption band (in some cases transient and obscured by the high rate of the halogenation reaction) is ascribed to the charge-transfer (CT) complex⁸ depicted in eq 11



where ArH represents the methoxy and dimethoxy donor and K is the formation constant of the charge-transfer complex.

Electron Transfer in the $[\text{ArH}, \text{ICl}]$ Complex. As predicted from Mulliken theory,³⁴ the degree of charge

(31) Sankararaman, S.; Haney, W. A.; Kochi, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7824.

(32) The rate constant was calculated using an extinction coefficient of $\epsilon_{500} = 8200\text{ M}^{-1}\text{ cm}^{-1}$ for $\text{BA}^{\cdot+}$. See: Bockman, T. M.; Lee, K. Y.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1581.

(33) Ross, U.; Schulze, T.; Meyer, H.-J. *Chem. Phys. Lett.* **1985**, *121*, 174.

(34) (a) Mulliken, R. S.; Person, W. B. *Molecular Complexes*; Wiley: New York, 1969. (b) Foster, R. *Organic Charge Transfer Complexes*; Academic Press: New York, 1969.

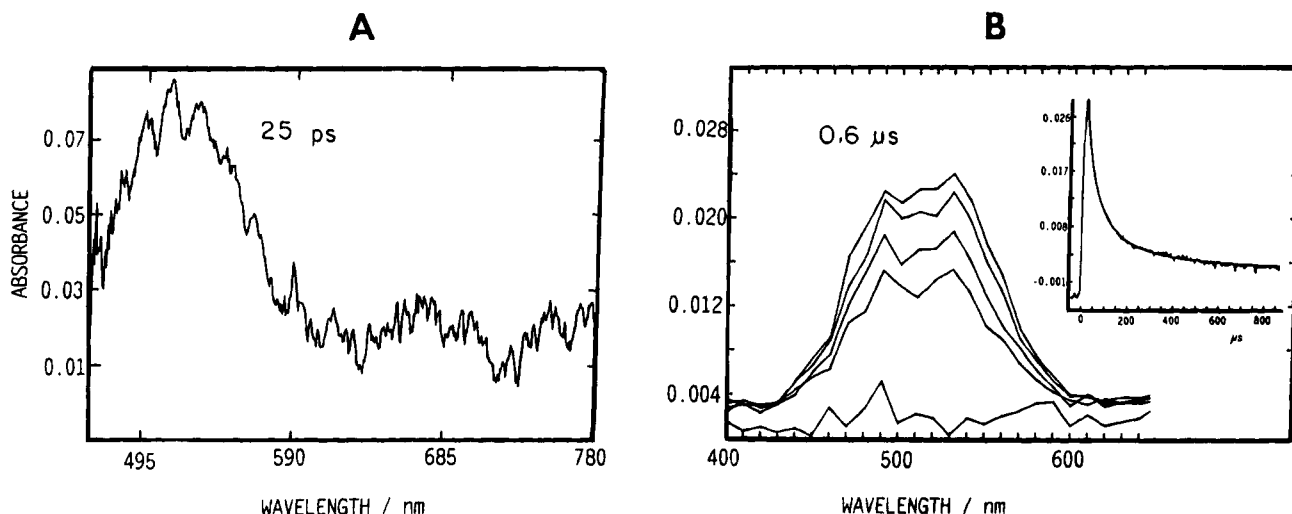
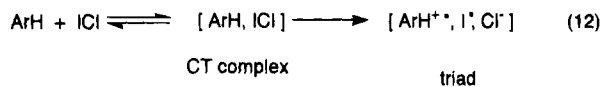


Figure 6. (A) Transient spectrum of the bromoanisole cation radical generated by the photoexcitation of the CT complex [2, ICl] in dichloromethane with a 25-ps laser pulse at 355 nm. (B) Similar to A with a 10-ns laser pulse at (top-to-bottom) 0.6, 0.8, 1.0, 1.4, and 3.2 μ s following excitation. Inset: Spectral decay at $\lambda = 510$ nm showing second-order kinetics.

transfer in CT complexes depends on the ionization potential of the donor and electron affinity of the acceptor. For the [ArH, ICl] complexes, complete one-electron transfer from ArH to ICl will lead to the donor cation radical and reduced acceptor species.³⁵ Indeed, we observe the spontaneous formation of the cation radical from several dimethoxybenzenes even at the low temperature of -78 °C (see Figures 3 and 4). The corresponding reduced ICl species could not be detected in the same steady-state spectroscopic experiment. Even on the picosecond time scale, no spectroscopic evidence³⁶ for a short-lived ICl⁻ transient is found in the laser-flash photolysis experiment (see Figure 6). Whereas reduced molecular iodine, I₂⁻, is quite stable and can be readily detected using time-resolved spectroscopic techniques ($\lambda_{\text{max}} = 750$ nm),³⁸ we believe the corresponding reduced species of iodine monochloride, ICl⁻, is quite metastable owing to the large difference in electronegativity of the two halogen moieties. A spontaneous cleavage of ICl⁻ into chloride and iodine atoms is proposed, and complete electron transfer from the dimethoxybenzene donor to the ICl within the CT complex will lead to the triad depicted in Scheme 1. [Note that the adiabatic electron transfer

Scheme 1



in eq 12 bears a formal resemblance with the charge-transfer activation in eq 10.^{39]}

(35) The driving force ($-\Delta G^\circ$) for such an electron transfer, *i.e.*, [ArH, ICl] \rightarrow [ArH⁺, ICl⁻] is evaluated in solution by the (reversible) oxidation potential of ArH in Table 1 and the reduction potential of iodine monochloride (which is unknown). Although the latter precludes a reliable estimate of the electron transfer rates, the short lifetime of ICl⁻ (as described in Scheme 1) will drive the electron transfer despite moderately positive values of ΔG° . See: Andrieux, C. P.; Gorande, A.; Savéant, J.-M. *J. Am. Chem. Soc.* **1992**, *114*, 6892 for a detailed discussion of this important point.

(36) The spectral window of the experimental detection in picosecond flash photolysis experiments is limited to 400–800 nm.³⁷

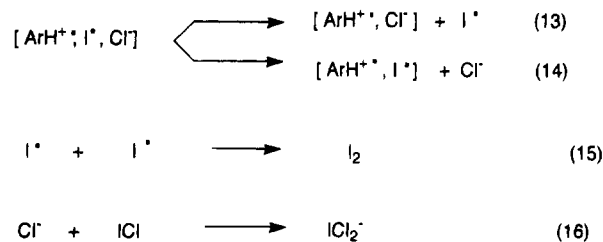
(37) Hubig, S. M.; Rodgers, M. A. J. In *CRC Handbook of Organic Photochemistry*; Scaiano, J. C., Ed.; CRC Press: Boca Raton, 1989; Vol. 1, p 315.

(38) Kliner, D. A. V.; Alfano, J. C.; Barbara, P. F. *J. Chem. Phys.* **1993**, *98*, 5375 and references therein.

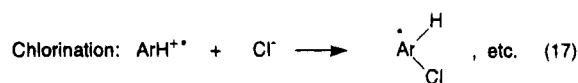
(39) Kim, E. K.; Bockman, T. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1993**, *115*, 3091.

The escape of the iodine atoms from the solvent cage in eq 13 followed by I₂ formation with another iodine atom (eq 15), and the diffusive separation of chloride (eq 14) to form ICl₂⁻ aggregates with ICl^{9c,40} (eq 16), represent additional steps in the mechanism (see Scheme 2).

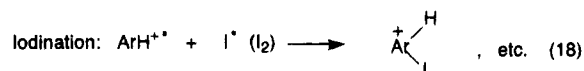
Scheme 2



Aromatic Cation Radicals as Intermediates in Chlorination and Iodination. The triad of reactive intermediates is sufficient to account for aromatic chlorination and iodination *via* ion-pair and radical-pair collapse, respectively. Thus, ion-pair collapse of the aromatic cation radical with chloride (as experimentally observed in Figure 5 and eq 8) constitutes a viable pathway for aromatic chlorination with ICl, *i.e.*⁴¹



The radical-pair collapse of ArH⁺ with iodine atoms must compete with the diffusion-controlled rate at which iodine atoms combine in eq 15. However, the efficient iodination of ArH⁺ with diiodine (see eq 9) establishes the lower limit for the fast rate of the homolytic combination⁴² to afford the Wheland intermediate according to eq 18



which is subsequently followed by a fast deprotonation.⁴³

(40) Wang, Y. L.; Nagy, J. C.; Margerum, D. W. *J. Am. Chem. Soc.* **1989**, *111*, 7838 and references therein.

(41) The further (oxidative) conversion of the homolytic adduct to the substitution product *via* the Wheland intermediate has been discussed by Kim et al. in ref 39.

The previously proposed¹⁷ mechanism for aromatic chlorination with iodine monochloride is confirmed experimentally in this work for dimethoxybenzene (**6**) and the dimethyl analogue **10**. In the former case, a reaction with ICl leads to a mixture of chloro and iodo product arising from the competition between ion-pair and radical-pair collapse. However, the addition of excess chloride to a solution of the cation radical at $-78\text{ }^\circ\text{C}$ results in exclusive chlorination. Similarly, the cation radical of **10** generated from ICl is quenched by chloride (see Figure 5) leading exclusively to the chloro product. Interesting is the fact that, before excess chloride is added, the cation radicals of both **6** and **10** are stable for hours at $-78\text{ }^\circ\text{C}$, indicating that (i) either there is no free Cl^- present in the solution or the release of Cl^- from ICl_2^- is very slow and (ii) at low temperature the cation radicals do not react with I_2 formed by recombination of two iodine atoms (see eq 15). The radical-pair collapse leading to iodo product is more difficult to demonstrate experimentally owing to the transient character of iodine atoms. Attempts to generate iodine atoms photolytically from molecular iodine²⁹ and then to react I^\cdot with the cation radicals of **6** generated from ICl at low temperature do not give unambiguous results because of the interfering photolysis of ICl. However, an efficient (68%) reaction between cation radical $\mathbf{6}^{+\cdot}$ (generated by electron transfer) and molecular iodine at room temperature in dichloromethane is observed under conditions in which the parent donor **6** is not iodinated. However, the fact that $\mathbf{6}^{+\cdot}$ reacts rapidly with diiodine at room temperature suggests the radical-pair collapse of iodine atoms and aromatic cation radicals to be a viable pathway for iodination.⁴²

Competition between Ion-Pair and Radical-Pair Collapse. Having established that both chlorination and iodination can evolve from the cation radical as the common intermediate, let us now consider the factors that govern the competition between ion-pair and radical-pair collapse. Solvent and general salt effects, as well as the structure and reactivity of cation radicals (including steric and electronic effects) are important factors to be considered. On the other hand, the donor properties of the methoxy and dimethoxybenzenes mainly contribute to cation radical production and apparently play only a limited role in the follow up reactions.

The solvent effect in Table 4 supports the competition between the radical-pair and ion-pair collapse described above, since the effect of solvent polarity is evident in the comparative results in tetrachloromethane, dichloromethane, and acetonitrile.⁴⁴ Thus, in nonpolar solvents (CCl_4 and CH_2Cl_2), the collapse of the destabilized ion pair is enhanced⁴⁵ and leads to a higher proportion of chloro product. Contrariwise, in polar solvents such as CH_3CN , the ions are readily separated and stabilized by

solvation to allow the radical collapse for iodination to be competitive. How trifluoroacetic acid enhances ion-pair collapse is not fully understood at this juncture, and other solvent properties (such as hydrogen bonding and proton transfer) must be explicitly considered.

The general salt effect observed with tetra-*n*-butylammonium hexafluorophosphate in dichloromethane seems, at first sight, not to be in line with the solvent effect.⁴⁶ However, the unexpected enhancement of chlorination in the presence of salt can be accommodated, if the equilibrium between Cl^- , ICl , and ICl_2^- is taken into account. Thus, tetrabutylammonium hexafluorophosphate can liberate chloride from the complex ion by preferential ion pairing, e.g.



The proposed ion exchange, although speculative, is in line with observations reported earlier⁴⁶ that ICl_2^- aggregates dissociate completely into ICl and Cl^- in a polar environment. Thus, upon the addition of salt more free chloride⁴⁷ will be available for ion-pair collapse, and as a result, the competition with iodination will be shifted toward chlorination.

Steric Effects on the Reactivity of Methoxybenzene Cation Radicals. In order to address the question as to why the ratio of iodination and chlorination varies with the methoxy and dimethoxybenzenes (see Table 2), let us consider structure and reactivity of the aromatic donor in terms of the electronic and steric effects of the substituents. Otherwise, there is no clear trend with the strength of the aromatic donor as expected from the proposed mechanism in which iodination and chlorination both evolve from a common (cation-radical) intermediate. Moreover, there is no selectivity based on free *para*-positions, since iodination and chlorination have both been observed at free *para*-positions.

We suggest that the competition between iodination and chlorination can be influenced by steric effects in the approach of iodine to the aromatic cation radical to be ultimately bound in the σ -complex (eq 18). The optimum conformation of the methoxy group in the cation radical places it in the plane of the aromatic ring to allow maximum overlap of the oxygen p-orbitals with the aromatic π -system and extensive delocalization of the positive charge.²⁶ In this conformation, an *o*-methyl substituent will force the methoxy group to adopt the preferred position shown in Scheme 3.

As a result, the *ortho* position is somewhat hindered for the approach of a relatively large iodine with a van der Waals radius of 2.15 Å.¹⁶ By comparison, chloride with a significantly smaller ionic radius of 1.81 Å¹⁶ is less subject to steric hindrance. When the methoxy group is not forced to favor a particular orientation, iodination in the *ortho* position may occur and comparable amounts

(42) Coupling of a pair of radicals generally occurs at diffusion-controlled rates. See: Ingold, K. U. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 1, p 37ff.

(43) See: Melander, L. *Arkiv Kemi* **1950**, 2, 211. See also: Melander, L. *Isotope Effects on Reaction Rates*; Ronald: New York, 1960.

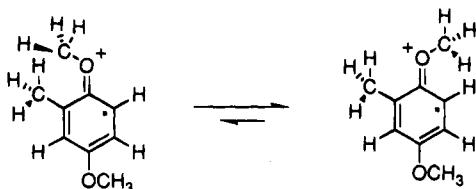
(44) To probe the salt effect on the competition between iodination and chlorination, we chose 1,4-dimethoxybenzene (**6**) as substrate and dichloromethane as solvent for the following reasons: First, **6** exhibits almost equal preference for iodination and chlorination in dichloromethane. Thus, this system is expected to be most sensitive to environmental changes and allows variation in the product ratio to favor either iodination or chlorination. Secondly, significant salt effects have been observed in solvents of medium polarity—such as dichloromethane—in which most of the ionic species are solubilized in form of ion pairs.⁴⁵

(45) For solvent effects on ion-pair dynamics, see: Yabe, T.; Kochi, J. K. *J. Am. Chem. Soc.* **1992**, *114*, 4491. For the relative rates of ion-pair and radical-pair collapse, see: Masnovi, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1985**, *107*, 7880.

(46) (a) We expected the added salt to show the same effect as the use of a more polar solvent, i.e., stabilization of the $[\text{ArH}^+, \text{Cl}^-]$ ion pair, and thus decrease of the rate of ion-pair collapse,⁴⁵ which allows the radical collapse yielding iodination to become competitive. (b) We used salt concentrations as high as 0.2 M, since dramatic salt effects were observed at this concentration in earlier experiments.⁴⁵ As only a minor effect was achieved even at this high concentration (see Table 4), we did not vary the salt concentration.

(47) Studies of common salt effects were not performed because the addition of excess chloride would have attenuated the reactivity of ICl (due to ICl_2^- formation).

Scheme 3



of iodination and chlorination are expected. This general formulation is consistent with the iodination of the 2-methyl derivative **8** at the 5- rather than the 6-position. Furthermore, the 2,5-dimethyl derivative **10** has both free positions blocked by a pair of methoxy groups that rotate away from the neighboring methyl groups. The same is true for the 2,3-dimethyl derivative **9**; *i.e.*, no iodination is observed despite the two open positions which are activated by methyl groups in the *para* position. Moreover, 2-iodo derivative **5** is exclusively iodinated at the 5-position, not at the 6-position which is equally favored in terms of electronic effects. Presumably, the iodo substituent of the substrate forces the neighboring methoxy group to rotate toward the 6-position and allow iodination to occur at the 5-position only. On the basis of this qualitative picture, the following generalization may be made: Methoxy groups in *neutral* donors are less sterically hindering than methyl groups because they can be readily rotated out of the aromatic plane. On the other hand, the steric effect of methoxy groups in the cation radical or positively charged σ -complex is greater on a neighboring position than that of a methyl group when the methoxy group is forced into a preferred (planar) conformation (*e.g.*, by another substituent).

Experimental Section

1. Materials and Instrumental Methods. Anisole (Aldrich), 4-bromoanisole (Aldrich), 2-iodoanisole (J. T. Baker), 4-methylanisole (Aldrich), and 1,4-dimethoxybenzene (Aldrich) were used as received. 1,2-Dimethoxy-4-methylbenzene, 1,4-dimethoxy-2-methylbenzene, 1,4-dimethoxy-2,3-dimethylbenzene, 1,4-dimethoxy-2,5-dimethylbenzene, and 1,4-dimethoxy-2,3,5-trimethylbenzene were prepared by alkylation of the corresponding readily available hydroquinones.⁴⁸ All solvents were purified by standard procedures.⁴⁹ Iodine monochloride (ICl, Aldrich) was purified by distillation under an argon atmosphere. It was stored in a Schlenk flask (under argon) and kept in the freezer. Samples were extracted with the aid of an all-glass syringe equipped with a platinum needle.

Melting points were uncorrected. ¹H and ¹³C NMR spectra were measured in CDCl₃ solution on a General Electric QE-300 spectrometer. Chemical shifts are reported in ppm units downfield from tetramethylsilane (¹H) and chloroform (¹³C). Gas chromatography was performed on a Hewlett-Packard 5790A series gas chromatograph with a HP 3390A integrator. GC-MS analyses were obtained with a Hewlett-Packard 5890 chromatograph interfaced to a HP 5970 mass spectrometer (EI, 70 eV). UV-vis spectra were recorded on a Hewlett-Packard 8450A dual diode array spectrophotometer. The picosecond and nanosecond flash photolysis instrumentation have been described elsewhere.⁵⁰

Cyclic voltammetry (CV) was carried out on a BAS 100A electrochemical analyzer. The CV cell was of an air-tight design with high-vacuum Teflon valves and Viton O-rings to allow an inert atmosphere to be maintained without contamination by grease. The working electrode consisted of an adjustable platinum disk embedded in a glass seal to allow periodic polishing (with a fine emery cloth) without changing the surface area ($\sim 1 \text{ mm}^2$) significantly. The SCE reference electrode and its salt bridge was separated from the catholyte by a sintered glass frit. The counter electrode consisted of an platinum gauze that was separated from the working electrode by $\sim 3 \text{ mm}$. The CV measurements were carried out in a solution of 0.2 M supporting electrolyte (tetra-*n*-butylammonium hexafluorophosphate) and 5 mM substrate in dry dichloromethane under an argon atmosphere. All cyclic voltammograms were recorded at a sweep rate of 0.1 V s^{-1} and were IR compensated. The potentials were referenced to SCE which was calibrated with added ferrocene (5 mM). The $E_{1/2}$ values were calculated by taking the average of anodic and cathodic peak potentials.

2. General Procedure for Aromatic Halogenation with Iodine Monochloride. The aromatic donor (0.36 mmol, 0.072 M) was added to a solution of ICl (0.30 mmol, 0.06 M) in dichloromethane under argon at room temperature. The reaction mixture was kept in the dark for several hours depending on the rate of the reaction (see Table 2). After evaporation of the solvent, the residue was extracted with ether, washed with aqueous sodium thiosulfate solution, water, and brine, and dried over MgSO₄. Known halogenation products were identified by GC/MS, comparison of the melting points with literature values, and/or comparison of the ¹H NMR spectra with authentic samples synthesized by known methods. New compounds were identified by GC/MS and ¹H and ¹³C NMR spectra. The yields reported in Table 2 were determined by ¹H NMR spectroscopy using nitromethane as internal standard. Since iodine monochloride was the limiting reagent in all cases, the yields are based on the amount of ICl used.

4-Iodoanisole: mp 52–53 °C (lit.⁵¹ mp 53–54 °C); *m/z* 234 (M⁺). **4-Bromo-2-iodoanisole:** ¹H NMR 3.86 (s, 3H), 6.69 (d, *J* = 8.7 Hz, 1H), 7.41 (d, d, *J* = 8.7, 2.4 Hz, 1H), 7.87 (d, *J* = 2.2 Hz, 1H); *m/z* 314, 312 (M⁺). The product was identified by comparison of the spectral data with those of an authentic sample synthesized by treating 4-bromoanisole with diiodine, mercury(II) oxide, and sulfuric acid according to a literature procedure.⁵² **4-Bromo-2-chloroanisole:** ¹H NMR 3.88 (s, 3H), 6.80 (d, *J* = 8.8 Hz, 1H), 7.33 (d, d, *J* = 8.7, 2.4 Hz, 1H), 7.49 (d, *J* = 2.3 Hz, 1H); *m/z* 220, 222, 224 (M⁺). An authentic sample of this product was prepared from 4-bromo-2-chlorophenol using a modified method by Faith et al.⁵³ 4-Bromo-2-chlorophenol (1.04 g, 5 mmol) was refluxed for 2.5 h in 8 mL of dry acetone with 0.59 g of potassium carbonate and 0.8 mL of dimethyl sulfate. After filtration, the solution was concentrated in vacuo, treated with dilute sodium hydroxide, and extracted with ether. The ¹H NMR spectrum of this authentic sample coincided with the chloro compound obtained with ICl. **2,4-Diiodoanisole:** mp 66–68 °C (lit.⁵⁴ mp 68–69 °C); ¹H NMR 3.84 (s, 3H), 6.56 (d, *J* = 8.7 Hz, 1H), 7.55 (d, d, *J* = 8.7, 2.1 Hz, 1H), 8.02 (d, *J* = 2.0 Hz, 1H); *m/z* 360 (M⁺). **1-Iodo-2-methoxy-5-methylbenzene:** ¹H NMR 2.34 (s, 3H), 3.82 (s, 3H), 6.69 (d, *J* = 8.2 Hz, 1H), 7.07 (d, d, *J* = 8.5, 1.0 Hz, 1H); *m/z* 248 (M⁺). An authentic sample of this compound was prepared from 2-methoxy-5-methylaniline by reacting it with sodium nitrite and HCl and then treating the diazonium salt with potassium iodide using a modified method by Citterio.⁵⁵ The ¹H NMR spectrum of this authentic sample coincided with the iodo compound obtained with ICl.⁵⁶

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1-Iodo-4,5-dimethoxy-2-methylbenzene: $^1\text{H NMR}$ 2.37 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 6.76 (s, 1H), 7.21 (s, 1H); $^{13}\text{C NMR}$ 27.28, 55.68, 55.98, 88.29, 112.54, 121.18, 133.38, 147.35, 148.97; HRMS calcd for $\text{C}_9\text{H}_{11}\text{IO}_2$ (M^+) 277.9804, found 277.9812. **2-Iodo-1,4-dimethoxybenzene:** $^1\text{H NMR}$ 3.74 (s, 3H), 3.81 (s, 3H), 6.80 (m, 2H), 7.33 (d, $J = 2.9$ Hz, 1H); m/z 264 (M^+). An authentic sample was prepared from 2,5-dimethoxyaniline by treating it with sodium nitrite and HCl, followed by potassium iodide using a modified method by Citterio.⁵⁵ The $^1\text{H NMR}$ spectrum of this authentic sample matched the iodo compound obtained with ICl.⁵⁷ **2-Chloro-1,4-dimethoxybenzene:** $^1\text{H NMR}$ 3.76 (s, 3H), 3.85 (s, 3H), 6.81 (m, 2H), 6.96 (d, $J = 2.9$ Hz, 1H); m/z 172, 174 (M^+).⁵⁷ **1-Iodo-2,5-dimethoxy-4-methylbenzene:** mp 77–78.5 °C; $^1\text{H NMR}$ 2.19 (s, 3H), 3.77 (s, 3H), 3.82 (s, 3H), 6.67 (s, 1H), 7.17 (s, 1H); $^{13}\text{C NMR}$ 16.42, 56.04, 57.04, 81.30, 114.04, 121.05, 127.94, 152.23, 152.56; HRMS calcd for $\text{C}_9\text{H}_{11}\text{IO}_2$ (M^+) 277.9804, found 277.9807. **1-Chloro-2,5-dimethoxy-3,4-dimethylbenzene:** $^1\text{H NMR}$ 2.10 (s, 3H), 2.22 (s, 3H), 3.74 (s, 3H), 3.77 (s, 3H), 6.71 (s, 1H); $^{13}\text{C NMR}$ 11.92, 12.89, 55.12, 60.36, 109.38, 124.25, 125.10, 132.28, 147.86, 153.79; HRMS calcd for $\text{C}_{10}\text{H}_{13}\text{ClO}_2$ (M^+) 200.0604, found 200.0600. **1-Chloro-2,5-dimethoxy-3,6-dimethylbenzene:** $^1\text{H NMR}$ 2.24 (s, 3H), 2.30 (s, 3H), 3.76 (s, 3H), 3.79 (s, 3H), 6.56 (s, 1H); $^{13}\text{C NMR}$ 12.76, 16.39, 56.08, 60.15, 110.83, 123.64, 128.85, 129.14, 147.93, 153.88; HRMS calcd for $\text{C}_{10}\text{H}_{13}\text{ClO}_2$ (M^+) 200.0604, found 200.0591. **1-Chloro-2,5-dimethoxy-3,4,6-trimethylbenzene:** $^1\text{H NMR}$ 2.18 (s, 3H), 2.20 (s, 3H), 2.31 (s, 3H), 3.66 (s, 3H), 3.75 (s, 3H); $^{13}\text{C NMR}$ 12.67, 12.87, 13.44, 60.15, 60.25, 123.67, 125.81, 127.65, 129.04, 129.24, 153.17; HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{ClO}_2$ (M^+) 214.0761, found 214.0763. **1,4-Diiodo-2,5-dimethoxybenzene:** mp 164–167 °C (lit.⁵⁸ mp 167–168 °C); m/z 390 (M^+).

3. Stoichiometry for Aromatic Halogenation with Iodine Monochloride. An attempt was made to determine the stoichiometry for the hydrogen chloride generated in aromatic halogenation with ICl. In both cases, the yields of HCl were determined to be much lower than expected from eqs 2 and 3. Thus, in a typical experiment, dimethoxybenzene **11** (29 μmol in 3 mL) was treated with ICl (60 μmol in 5 mL) in dichloromethane for 18 h to yield 25.5 μmol (88% based on **11**) of the 3-chloro product. The HCl generated during the chlorination was entrained into 10 mL of distilled water with the aid of an argon flow for 5 min. The acidic aqueous solution was titrated with 0.02 N NaOH. [The NaOH solution was standardized with standard acidic potassium phthalate (KHP, Thorn Smith) which was dried for 1 h at 100 °C *in vacuo*.] The titration yielded 6 μmol of acidic protons, which corresponded to a relative yield of 24% based on the amount of chloro compound produced. In a second attempt, two solutions of methylanisole **4** (0.6 mmol) were treated with ICl (0.43 mmol) in 5 mL of dichloromethane for 3 h under identical conditions. In one reaction mixture, the yield of iodination products was determined after usual workup to be 98% (0.42 mmol). The second reaction mixture was poured into 10 mL of distilled water, the water layer separated from the dichloromethane layer, and the mixture titrated with 0.02 N NaOH solution which was standardized as described above. The titration yielded 0.18 mmol of acidic protons, which corresponded to a relative yield of 43% based on the amount of iodoanisole produced.

4. Generation of Cation Radicals with Iodine Monochloride at Low Temperature. The cation radicals of **6**, **7**, and **10** were generated in dichloromethane at -78 °C in quartz cuvettes fitted with a side arm and a Schlenk adaptor. For spectroscopic purposes, a dilute solution of cation radical $6^{+\bullet}$ was generated by adding 9.5 μmol of ICl to 5 mL of dichloromethane, cooling this solution in an acetone/dry ice bath, and adding 1 μmol (2×10^{-4} M) of **6** (20 μL of 0.049 M stock solution in dichloromethane). A spectrum featuring the characteristic twin peaks of $6^{+\bullet}$ at 440 and 468 nm was

recorded (see Figure 3), and an absorbance at 468 nm of 1.0 was measured. From an extinction coefficient of 9540 $\text{M}^{-1}\text{cm}^{-1}$ at 460 nm in water,²⁴ a cation radical concentration of $\sim 1 \times 10^{-4}$ M was computed. The latter corresponded to a cation radical yield of $\sim 50\%$ based on the initial concentration of **6**.

A dilute solution of cation radical $10^{+\bullet}$ was generated in two ways: (i) by adding **10** to a dichloromethane solution containing excess ICl at -78 °C and (ii) by stepwise addition of ICl to a solution of excess **10** in dichloromethane at -78 °C. In the first experiment, 30 μmol of ICl was dissolved in 5 mL of dichloromethane, the solution cooled to -78 °C in an acetone/dry ice bath, and then 0.54 μmol of **10** (1.08×10^{-4} M, 10 μL of a 0.054 M stock solution in dichloromethane) added. A spectrum showing the characteristic twin absorption bands of $10^{+\bullet}$ at 432 and 460 nm was recorded, and an absorbance of 0.920 at 460 nm was measured. From an extinction coefficient of 8500 $\text{M}^{-1}\text{cm}^{-1}$ at 460 nm,²⁷ a cation radical concentration of 1.08×10^{-4} M was computed. The latter indicated a quantitative conversion of **10** to its cation radical. In a second experiment, a 0.003 M (12 $\mu\text{mol}/4$ mL) solution of **10** in dichloromethane was prepared and cooled to -78 °C, and ICl was added in several increments of 0.36 μmol (20 μL of a 0.018 M stock solution in dichloromethane). The spectrum of the cation radical $10^{+\bullet}$ was recorded after each addition and the concentration of $10^{+\bullet}$ determined from an extinction coefficient of 8500 $\text{M}^{-1}\text{cm}^{-1}$ at 460 nm.²⁷ Figure 4 shows the spectrum obtained upon the addition of 1.44 μmol of ICl. Comparison of the incremental increase in the concentration of $10^{+\bullet}$ with the corresponding concentrations of ICl added indicated a ratio of $R = [\text{ICl}]/[10^{+\bullet}] = 4.5 \pm 0.5$.

5. Reactivities of the Cation Radicals $6^{+\bullet}$ and $10^{+\bullet}$ With Chloride and Iodine. Reaction of 1,4-Dimethoxybenzene Cation Radical with Chloride Ions. 1,4-Dimethoxybenzene (**6**, 0.3 mmol) was added to a solution of iodine monochloride (0.3 mmol) in dichloromethane at -78 °C in the dark. To the red solution of $6^{+\bullet}$ was added an excess (0.4 mmol) of PPN^+Cl^- [PPN^+ = bis(triphenylphosphoranylidene)ammonium] and the solution kept in the dark for 2 h at -78 °C. The solvent was removed at -78 °C, an aqueous sodium thiosulfate solution added, and the solution allowed to warm to room temperature. The products were extracted with ether, and analysis indicated unreacted starting material (81%) and 2-chloro derivative (19%).

Reaction of 2,5-Dimethyl-1,4-dimethoxybenzene Cation Radical with Chloride Ions. This reaction was carried out in two ways: (i) using low concentrations for spectroscopic purposes and (ii) using higher concentrations for product analysis. In the first experiment, a 9×10^{-5} M solution of cation radical $10^{+\bullet}$ was generated from **10** (0.44 μmol) and ICl (36 μmol) in dichloromethane (5 mL) at -78 °C. PPN^+Cl^- was added in two portions (first 30 μmol then 23 μmol) and the spectrum of $10^{+\bullet}$ recorded. After the addition of the first portion of PPN^+Cl^- most of the cation radical of **10** vanished. Upon the addition of the second portion of PPN^+Cl^- (which led to an excess of chloride salt relative to the amount of ICl in solution), the twin absorption band of $10^{+\bullet}$ disappeared completely (see Figure 5). In a second experiment, larger amounts of reactants were used to identify the products. Thus, 0.15 mmol of **10** was added to a solution of ICl (0.15 mmol) in dichloromethane at -78 °C; PPN^+Cl^- (0.19 mmol) was then added and the reaction mixture kept in the dark at -78 °C for 2 h. The solvent was removed at -78 °C, an aqueous thiosulfate solution added, and the mixture allowed to warm to room temperature. The organic components were extracted with ether, and they were identified as the starting material (89%) and 2-chloro derivative (11%).

Reactions of 1,4-Dimethoxybenzene Cation Radical with Diiodine. To a solution of ICl (11 μmol) in dichloromethane at -78 °C was added 1.6 μmol of **6**, and the spectrum of the cation radical $6^{+\bullet}$ was recorded. After the addition of diiodine (5 μmol), the solution was irradiated with filtered light ($\lambda > 530$ nm) at -78 °C for several hours until the characteristic twin absorption of $6^{+\bullet}$ at 440 and 468 nm disappeared, and only the absorption spectrum of diiodine (peaking at 505 nm) remained. In a second experiment, a

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solution of ICl (0.3 mmol), dimethoxybenzene (0.3 mmol), and diiodine (0.2 mmol) was irradiated with filtered light ($\lambda > 530$ nm) at -78 °C for 2 h. After workup (as described for the reaction with chloride), the 2-iodo and the 2-chloro product of **6** were identified by GC/MS analysis and found to exist in a molar ratio of 1:10. In similar experiments, in which the concentrations of the starting materials and the irradiation conditions (cutoff filter, irradiation time) were varied, the ratio of chloro and iodo derivatives was found to strongly depend on the reaction conditions. The dimethoxybenzene cation radical $6^{+\bullet}$ was also generated by electron transfer from $R^{+\bullet}$ [$R^{+\bullet} = 9,10$ -dimethoxy-1,4:5,8-dimethano-1,2,3,4,5,6,7,8-octahydroanthracenium hexachloroantimonate]²⁶ in dichloromethane at room temperature. To a solution of $R^{+\bullet}$ (56 μ mol) in dichloromethane was added dimethoxybenzene **6** (0.25 mmol) at room temperature. The spectra taken before and after addition of **6** indicated that the electron-transfer equilibrium between $R^{+\bullet}$ and $6^{+\bullet}$ (as described in eq 7) lay far on the side of $R^{+\bullet}$ and very little $6^{+\bullet}$ was produced. Nonetheless, diiodine (0.22 mmol) was added at room temperature and the reaction mixture stirred overnight. After usual workup [removal of dichloromethane, quenching with aqueous sodium thiosulfate solution, and extraction by ether], the 2-iodo derivative was obtained in 68% yield based on the amount of

$R^{+\bullet}$ used. In a control experiment, dimethoxybenzene (0.25 mmol) and diiodine (0.25 mmol) were dissolved in dichloromethane and the mixture stirred overnight at room temperature. After identical workup, no iodo product was found, and dimethoxybenzene was recovered quantitatively.

Reaction of 2,5-Dimethyl-1,4-dimethoxybenzene Cation Radical with Diiodine. The cation radical of **10** was generated by adding 0.13 mmol of **10** to a solution of $R^{+\bullet}$ (0.05 mmol) in dichloromethane at room temperature. Diiodine (0.05 mmol) was added at room temperature and the solution irradiated at $\lambda > 480$ nm for 3 h. No iodo product was found after usual workup, and the dimethoxybenzene **10** was recovered quantitatively.

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