Scope and Mechanism of Aromatic Iodination with Electrochemically Generated Iodine(I)

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Abstract: Iodine(I) was anodically produced from I_2 at platinum in acetonitrile and in methylene chloride. This product was then used as an iodinating reagent for substituted benzenes. Compounds as unreactive in electrophilic substitutions as ethyl benzoate were monoiodinated in high yield on a scale as large as 10 g. Relative reaction rates for substituted benzenes were measured in acetonitrile by a competition method. A linear Hammett plot with $\rho^+ = -6.27$ was obtained. Deuterium isotope effects (k_H/k_D) were measured using 4-deuterioanisole (1.45), 4-deuteriotoluene (1.54), benzene-d_6 (2.25), 4-deuteriochlorobenzene (4.46), and ethyl 3-deuteriobenzoate (1.50). The data are interpreted in terms of electrophilic substitution via a σ-complex with rate-limiting deprotonation of this intermediate. The nonlinear variation of k_H/k_D as a function of substituent is discussed.

It has been previously shown that an iodine(I) species can be generated by the electrochemical oxidation of iodine in acetonitrile.[1] This product is stable in solution, and it was proposed that it is complexed with acetonitrile. It can, however, be used as a reagent.[1,2] The present paper discusses one aspect of its reactivity, the scope and mechanism of the iodination of aromatic compounds.

Results

Aromatic iodination with electrochemically generated iodinating agents was investigated for a variety of substituted benzenes. In a typical experiment, the oxidation of iodine was performed at a platinum sheet anode in acetonitrile-lithium perchlorate. A cell[1] divided into compartments for anode, cathode, and reference electrode was employed, and all oxidations were carried out potentiostatically at 1.9 V.[3] Passage of 2.4 faradays/mol of iodine resulted in a stable, pale-yellow solution, and the oxidation was terminated. A tenfold excess of the aromatic substrate was added to the stirring solution, and after workup a high yield of monoiodinated product(s) generally resulted (Table I). Analysis of isomeric mixtures was accomplished by GLC and/or NMR using comparisons with data from authentic samples or the literature.

The mechanism was explored by measuring product yields from experiments in which a known amount of iodinating agent was added to a mixture of two aromatic substrates. In this way the relative reactivities were evaluated. Competitive reactions of benzene and toluene where the initial molar ratios were varied from approximately 1:1 to 4:1 were performed (Table II). GLC analysis indicated a ratio of products directly proportional to the initial substrate concentration ratio.

The product composition was also found to be independent of the initial ratio of substrates to iodinating agent for the benzene–toluene competition. Reaction of the oxidized iodine solution with an equal molar mixture of anisole and toluene, however, resulted in a change in relative yields of the para-iodinated aromatics, depending on the ratio of substrates to iodinating agents (Table II). When equivalent amounts of each substrate and iodinating agent were used, analysis of the products indicated that toluene was preferentially iodinated. In contrast, reaction of a tenfold excess of each of the substrates to the iodinating agent gave preferential attack on anisole.

The relative rates of iodination were determined for a series of substituted benzenes (Table III). Equal molar mixtures of substrates, both in tenfold excess, were competitively iodinated. The relative product yields were determined by GLC after work up. The ratio of ortho to para products was determined by NMR in cases where the isomers were not separated by GLC. The ortho to para ratio for any substrate was independent of the presence of other substrates. Kinetic isotope effects were measured by iodinating para-deuterated substrates (Table IV). The change in the ortho to para ratio in comparison to the protio substrate was measured by NMR and MS to calculate the isotope effect.

Stability of the product was determined for anisole by reacting a mixture of anisole, 4-iodoanisole, and iodinating agent in a molar ratio of 1:10:1. The observed ortho to para product ratio of 19:81 indicated that the product is stable in the reaction mixture. It was also determined that the product ratio was unchanged if oxidation was terminated before all the iodine was consumed. Analysis of the products after reaction from a benzene–toluene competition with an iodine solution oxidized to 1 faraday/mol gave a product ratio of 20:1, the same as after passage of 2 faradays/mol.

The above results were obtained with acetonitrile-tetraethylammonium perchlorate. In acetonitrile–lithium perchlorate it was found that the coulometric n value was considerably greater than 2.0 faradays/mol of I_2. It has been previously determined that anhydrous lithium perchlorate contains sufficient water to result in a damp electrolyte solution. Oxidation of this solution always resulted in the formation of a small amount of white precipitate which was identified as N-iodoacetamide. If a tetraethylammonium perchlorate electrolyte solution was used, the current decayed to background after 2.3 faradays/mol, and no precipitate was found. The wet solution was effective in iodination, and an estimate of ρ was obtained (Table V).

It was found that the oxidation of I_2 in methylene chloride also generated an iodine(I) product. This species monoiodinated a variety of aromatics in high yield. An estimate of its selectivity was obtained by competition experiments (Table V).

The iodination of larger amounts of material was investigated. The following method proved practical. The oxidation was performed with a simple variable dc power supply. The cell was constructed by suspending a porous ceramic cup in a beaker containing acetonitrile–lithium perchlorate, a stirring bar, and a 150-cm^2 platinum sheet anode. A stainless steel spatula placed in the porous cup served as a cathode. This cell allowed oxidation of 8.0 g of I_2 in a period of 90 min. The cell was placed in an ice bath to prevent boiling of the solvent when currents of 1.5 A were passed. The potential was monitored using a Ag|$AgNO_3$ reference electrode and was not allowed to exceed 2.5 V during the course of the oxidation. The concentration of iodinating

Table I. Iodination Yields from Oxidized Iodine Solution[a]

Substrate[b]	Yield[c]	Isomers, % Ortho	Meta	Para
Anisole[d,e]	90	33	10	57
Biphenyl[d]	95	*f*	*f*	100
tert-Butylbenzene[d,g]	90	25	*f*	74
Phenyl ether[e,g]	75	17	*f*	82
Toluene[d]	93	48	4	48
Benzene	91			
Fluorobenzene[e]	85	10	*f*	90
Chlorobenzene[e]	80	20	*f*	80
Bromobenzene[e]	60	24	*f*	76
Iodobenzene[e]	70	33	*f*	67
Phenyl acetate[d]	55	36	*f*	64
Benzoic acid[d]	40	*f*	100	*f*
Ethyl benzoate[d,g]	65	*f*	100	*f*
Acetophenone[d]	15	α-Iodoacetophenone		
3,4-Dimethoxybenzoic acid[d]	20	3,4-Dimethoxy-5-iodobenzoic acid		
1,3-Dichlorobenzene[e]	21	1,3-Dichloro-4-iodobenzene (96%)		
p-Xylene[d]	90	2-Iodo-*p*-xylene		
m-Xylene[d,g]	84	4-Iodo-*m*-xylene (83%) 2-Iodo-*m*-xylene (17%)		
Ferrocene[d]	0[h]			
Nitrobenzene[e]	0			
Benzonitrile[d]	0			

[a] Oxidation of 0.5 g (1.95 mmol) of I_2 in lithium perchlorate–acetonitrile at 1.9 V vs. Ag|Ag$^+$ to 2.4 faradays/mol. [b] 35–50 mmol. [c] Based on 3.9 mmol iodinating agent. [d] Product analysis by NMR. [e] roduct analysis by GLC. [f] Less than detectable limit of analysis. [g] Oxidation of I_2 in tetraethylammonium perchlorate–acetonitrile. [h] Reaction resulted in oxidation to ferrocenium ion.

agent in the solution was assayed by reaction of 10 ml with an excess of benzene. The yield of iodinating agent was 75% by this method if the yield of iodobenzene was assumed to be 90%. The low yield of iodinating agent may be due to diffusion of some material into the cathode compartment. Iodination of toluene with this solution resulted in an 88% yield of iodotoluene.

Discussion

Scope. The scope of the electrochemical iodination has been explored, and it has been shown that aromatics as unreactive as ethyl benzoate can be iodinated in high yield. In acetonitrile there is an apparent cutoff point at $\sigma_m = 0.35$ since we have not been successful in iodinating compounds such as benzaldehyde and nitrobenzene. It has also been shown that methylene chloride is a suitable solvent for efficiently generating and reacting an iodine(I) species. The selectivity of this iodinating system is not as high as that of the acetonitrile system. From the viewpoint of synthesis, the wet acetonitrile system seems most attractive. The conductivity of this solution is somewhat higher than either dry acetonitrile or methylene chloride, and the yields are high. Although a major effort to develop large-scale synthesis was not pursued, we have prepared several grams of iodo aromatics in a divided cell (ion-exchange membrane or porous cup) using manually controlled potentials.

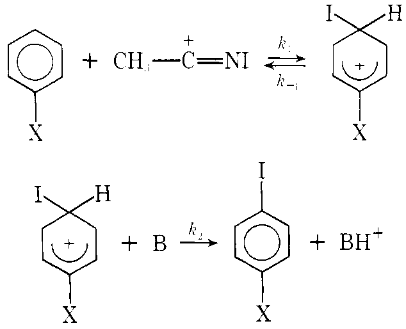
There are, of course, a number of other methods for performing iodinations.[4] These all involve electrophilic attack, and the more reactive systems have selectivities and scope similar to those described here. The present technique is advantageous in that it gives excellent yields, employs mild conditions, and is extremely rapid. Indeed, low temperatures could be used.

Mechanism. The substituent and isotopic effects can be interpreted in terms of the classical mechanism of electrophilic substitutions. The high positional and substrate selectivity point toward rate-determining formation (k_1) or destruction (k_2) of the σ complex via transition states with considerable positive charge localized in the ring.

Table II. Product Dependence on Reagent Concentrations

Substrates (mmol)		Iodinating agent,[a] mmol	Obsd product ratio[b]	Rel rate para[c]
Toluene (0.47)	Benzene (0.56)	0.39	17.7	63.0
Toluene (0.47)	Benzene (1.12)	0.39	9.02	63.9
Toluene (0.47)	Benzene (1.68)	0.39	5.96	64.5
Toluene (0.47)	Benzene (2.24)	0.39	4.41	63.3
Toluene (4.7)	Benzene (5.6)	0.99	17.8	63.2
Anisole (0.46)	Toluene (0.47)	0.39	*d*	*d*
Anisole (2.30)	Toluene (2.35)	0.39	168	208
Anisole (4.60)	Toluene (4.70)	0.39	452	558

[a] Oxidation of 0.5 g of I_2 in 160 ml of acetonitrile–tetraethylammonium perchlorate. Reaction of each pair with 16 ml of oxidized solution. [b] GLC analysis of product mixture: (mmol of isomeric iodotoluenes)/(mmol of iodobenzene) or (mmol of isomeric iodoanisoles)/(mmol of isomeric iodotoluenes). [c] [mmol of *p*-$IC_6H_4CH_3$ × (init mmol of C_6H_6) × 6]/[mmol of C_6H_5I × (init mmol of $C_6H_5CH_3$)]; [mmol of *p*-$IC_6H_4OCH_3$ × (init mmol of $C_6H_5CH_3$)]/[mmol of *p*-$IC_6H_4CH_3$ × (init mmol of $C_6H_5OCH_3$)]. [d] Analysis of products indicated quantitative iodination of toluene and less than 5% iodoanisole.



The nature of the iodinating agent or the base, B, are not defined. It is, however, suggested that in acetonitrile the *N*-iodonitrilium ion or protonated *N*-iodoacetamide are most reasonable possibilities for the former.[1]

The relative rate data from the acetonitrile–tetraethylammonium fluoroborate system were treated according to the method introduced by Brown.[5] A plot of log k_{rel} vs. σ^+ was linear with a value of $\rho = -6.27 \pm 0.34$ (Figure 1) with a correlation coefficient of 0.99.

The observed isotope effects strongly indicated that the carbon-hydrogen bond is broken in the rate-limiting step. Therefore, k_2 is suggested to be partially or totally rate limiting in all cases. The variation in isotope effect with substituent is extremely interesting in that a plot of k_H/k_D vs. σ^+ goes through a maximum of $k_H/k_D = 4.45$ for chlorobenzene.

One interpretation of these data would assume that k_2 is rate limiting in all cases and that the secondary isotope effect on the equilibrium (k_1/k_{-1}) is negligible. These are rational assumptions in that a number of aromatic iodination reactions are proposed on the basis of isotope effects to have k_2 rate limiting,[6] and the equilibrium secondary isotope effect should be on the order of $k_H/k_D = 0.9$.[7] The variable primary isotope effect would then result from the varying structure of the transition state as a function of substituent.[8] The chlorobenzene transition state would be relatively symmetrical (nearly equal force constants f_1, f_2) and all others less symmetrical. Most reasonably the least stable σ

$$\mathrm{C{-}H{-}B}$$

$$f_1 \quad f_2$$

complex from ethyl benzoate would have $f_1 > f_2$, and reactants like toluene and anisole would have $f_1 < f_2$. If the base were, for example, an oxygen which forms strong O-H bonds compared to C-H bonds, this could be interpreted in

Table III. Competitive Iodination[a]

Substrates[b]		Rel yield[c] (% para)		Rel rate para iodination
Benzene	Chlorobenzene	15.72	1 (80)	3.82
Fluorobenzene	Chlorobenzene	8.24 (90)	1 (80)	9.29
Chlorobenzene	Bromobenzene	2.66 (80)	1 (75)	2.84
Chlorobenzene	Iodobenzene	1.29 (80)	1 (67)	1.54
Biphenyl	Benzene	2.61 (95)	1	14.86
tert-Butylbenzene	Benzene	7.07 (74)	1	31.38
Toluene	Benzene	21.10 (50)	1	63.24
Toluene	Biphenyl	8.08 (50)	1 (95)	4.26
Toluene	*tert*-Butylbenzene	2.98 (50)	1 (74)	2.02
Phenyl ether	Toluene	10.50 (83)	1 (50)	17.44
Anisole	Phenyl ether	48.20 (62)	1 (83)	36.06
Anisole	Toluene	407.00 (62)	1 (50)	504.0[d]
Bromobenzene	Benzoic acid[e]	15.9 (80)	1 (100)[f]	25.44
Bromobenzene	Ethyl benzoate	18.8 (80)	1 (100)[f]	30.08
Bromobenzene	Methyl benzoate	20.1 (80)	1 (100)[f]	32.16

[a] Oxidation of 2.0 g of I_2 in 160 ml of acetonitrile-tetraethylammonium perchlorate at 1.9 V vs. Ag|Ag^+ to 2.2 faradays/mol. Reaction of each pair with 10 ml of the oxidized solution. [b] 7-10 mmol. [c] GLC analysis of product mixture. [d] This value not used in calculation of ρ. [e] GLC analysis as the trimethylsilyl ester. [f] Only the meta isomer was formed, and the relative rate is calculated for para iodination of bromobenzene vs. iodination of one meta position of the benzoate ester.

Table IV. Kinetic Isotope Effect[a]

Substrate[b]	% ortho	% para	k_H/k_D
Anisole[c]	37.8	62.2	
Anisole-*4-d*[c]	54.7	45.3	1.45[d]
Toluene[c]	50.5	49.5	
Toluene-*4-d*[c]	77.2	22.8	1.54[d]
Chlorobenzene[e]	26.1	73.9	
Chlorobenzene-*4-d*[e]	83.4	16.6	4.46
Benzene-d_6[f]			2.25
Ethyl benzoate-*3-d*[g]			1.50

[a] Oxidation of 0.5 g of I_2 in acetonitrile-tetraethylammonium perchlorate to 2.4 faradays/mol. Reaction of each substrate with 0.39 mmol of iodinating agent. [b] 0.46-0.56 mmol. [c] Analysis by NMR. [d] Average of two trials. [e] Analysis by GLC. [f] GLC analysis of competitive iodination of benzene and benzene-d_6 vs. chlorobenzene. [g] Mass spectral analysis of peaks (*m/e*) 277 and 276 of the product from iodination of ethyl benzoate-*3-d*.

Table V. Effect of Solvent on Competitive Iodination

	Relative yield (% para)[b]			
Substrates[a]	CH_2Cl_2-TBAF[c]		CH_3CN-$LiClO_4$[d]	
Benzene-chlorobenzene	11.0	1 (87)	24.8	1 (80)
Fluorobenzene-chlorobenzene	3.11 (95)	1 (87)	13.1 (90)	1 (80)
Chlorobenzene-bromobenzene	1.30 (87)	1 (88)	1.59 (80)	1 (75)
Chlorobenzene-iodobenzene	1.15 (87)	1 (95)	1.10 (80)	1 (67)
Toluene-benzene	2.83 (45)	1	7.33 (50)	1
Rho (ρ)	2.85 ± 0.15		6.25 ± 0.42	

[a] 4.7-5.7 mmol of each substrate. [b] Analysis by GLC after work-up. [c] Oxidation of 0.5 g of I_2 in methylene chloride-tetrabutylammonium tetrafluoroborate to 2.0 faradays/mol. [d] Oxidation of 0.5 g of I_2 in acetonitrile-lithium perchlorate to 2.4 faradays/mol.

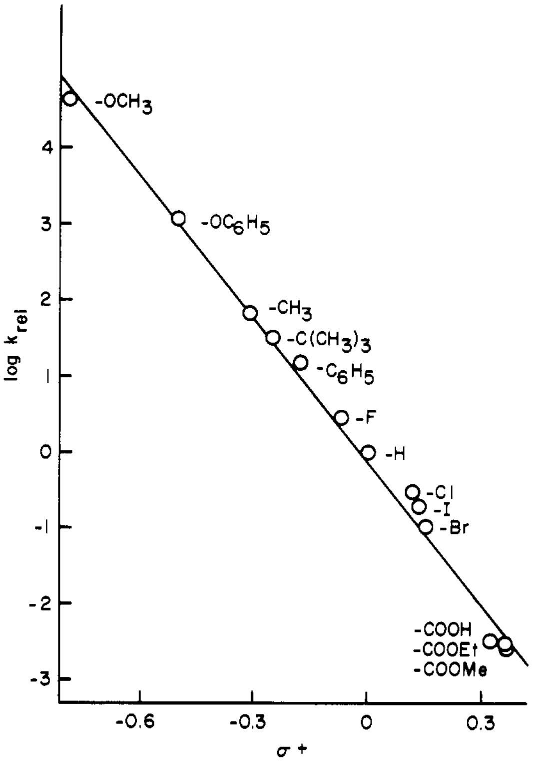


Figure 1. Hammett plot for iodination.

terms of transition states in which the hydrogen was still near the carbon in all cases.[9] All transition states would then resemble the σ complex, and a linear Hammett plot with a high negative ρ^+ value would be reasonable. Indeed, such an explanation abrogates an apparent dichotomy concerning linear Hammett plots and variable transition-state structures. If one considers wide variations in transition-state structure, e.g., hydrogen much less and much more than half transferred, a linear Hammett plot should not result. Similar problems have been treated by several authors.[14-16]

The nature of the proton acceptor is of course very important in this scheme. Unfortunately, it is not simple to vary this independently. Changing the medium does affect the selectivity of the reaction. The ρ value determined for a few points using methylene chloride is -2.85. This solvent is less basic than acetonitrile, should complex the iodine(I) differently, and should have different bases for proton abstraction. Interpretation of the differences is, however, impossible because the observed rate ratios are determined by six rate constants, and we cannot dissect the solvent effect on each of these components.

Although the data from reactions in acetonitrile seem to provide an example of the predicted maximum isotope effect for "symmetrical" transition states,[7,12,15] we have sought an alternative explanation involving a change in the rate-limiting step. More explicitly, this argument assumes that chlorobenzene and ethyl benzoate have $k_2 < k_{-1}$ (Figure 2b) and reflect a full isotope effect. Toluene and anisole would, however, have $k_2 > k_{-1}$ (Figure 2a) so that a sizable isotope effect on k_2 would show up as a relatively small observed isotope effect, $k_H{}^o/k_D{}^o$.

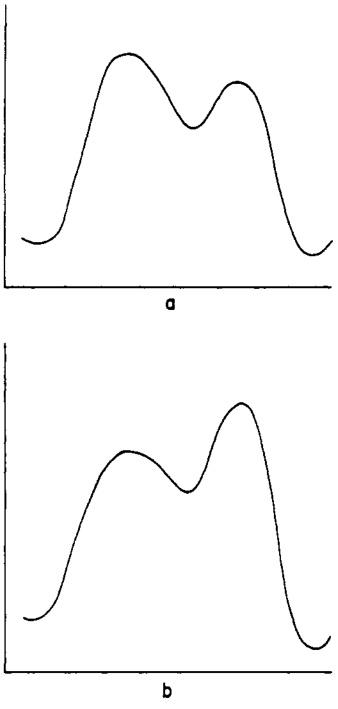


Figure 2. Reaction coordinate and energy plots; (a) k_1 rate limiting, e.g., toluene; (b) k_2 rate limiting, e.g., chlorobenzene.

The isotope effect and rate data can be used to test the validity of this explanation. If a steady-state concentration of σ complex is assumed, the dependence of k_H°/k_D° on k_2^H/k_2^D and k_2/k_{-1} can be expressed as follows:

$$k^\circ = k_1k_2/(k_{-1} + k_2)$$

$$\frac{k_H^\circ}{k_D^\circ} = \frac{k_1^Hk_2^H}{k_1^Dk_2^D}\frac{(k_{-1}^D + k_2^D)}{(k_{-1}^H + k_2^H)}$$

Assume $k_1^H = k_1^D$, i.e., no secondary isotope effect on k_1 or k_{-1}.

$$\frac{k_H^\circ}{k_D^\circ} = \frac{k_2^H}{k_2^D}\frac{(1 + k_2^D/k_{-1}^D)}{(1 + k_2^H/k_{-1}^H)}$$

Solving these equations for two examples, toluene with k_1 rate limiting, $k_2^H/k_2^D = Y$, $k_2^H/k_{-1}^H = k_2^Y/k_{-1}^Y$, and chlorobenzene, $k_2^H/k_2^D = Z$, $k_2^H/k_{-1}^H = k_2^Z/k_{-1}^Z$ (Y = concentration to toluene; Z = concentration of chlorobenzene), leads to

Toluene:

$$1.6 = \frac{Y(1 + k_2^Y)/k_{-1}^YY}{1 + k_2^Y/k_{-1}^Y}$$

$$Y - 1.6 = 0.6k_2^Y/k_{-1}^Y$$

Chlorobenzene:

$$Z - 4.5 = 3.5k_2^Z/k_{-1}^Z$$

Then

$$\frac{Y - 1.6}{Z - 4.5} = \frac{0.6k_2^Y/k_{-1}^Y}{3.5k_2^Z/k_{-1}^Z} \tag{1}$$

It is also true, however, that a change in rate-limiting step as a function of substituent requires a nonlinear Hammett plot reflecting the different ρ values for reactions in which k_1 is rate limiting and reactions in which k_2 is rate limiting. In Figure 3 we have constructed a two-line plot consistent with the proposed change in the rate-limiting step.

In this plot, line a is determined by all substituents with $\sigma^+ > 0$. The $\rho = -8.1 \pm 1.3$ is assumed to be the value for reactions with k_1 rate limiting (Figure 2a). Line b for substituents with $\sigma^+ \leq 0$ has $\rho = -5.9 \pm 0.2$ and is assumed to be the value for reactions with k_2 rate limiting (Figure 2b). It can be shown that the difference, $\Delta\rho = 2.2$ can be taken as $\Delta\rho_{k_{-1}k_2}$ for the reactions k_{-1} and k_2.

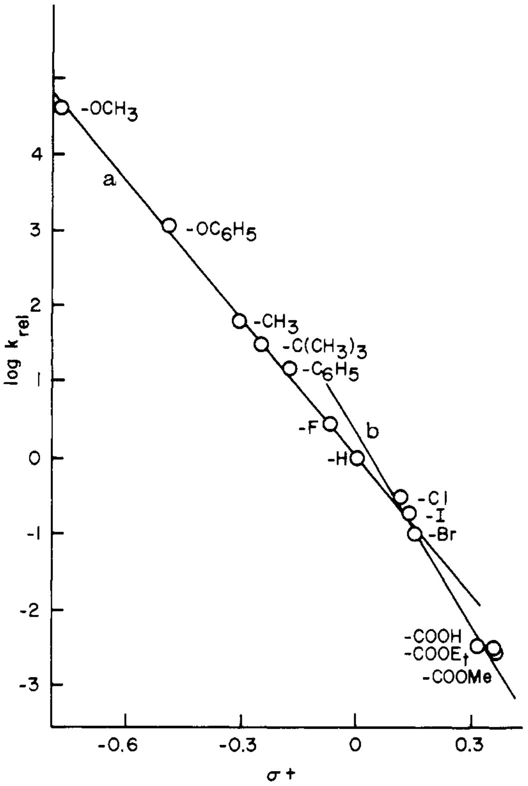


Figure 3. Hammett plot for iodination.

Since

$$\rho = \frac{\log k^Y - \log k^Z}{\sigma^Y - \sigma^Z}$$

then

$$\Delta\rho_{ab} = \frac{\log k_2^Y/k_2^Z - \log k_{-1}^Y/k_{-1}^Z}{\sigma^Y - \sigma^Z}$$

Identifying Y as toluene, Z as chlorobenzene, and $\Delta\rho_{ab}$ = 2.2 (Figure 3)

$$k_2^Yk_{-1}^Z/k_1^Yk_2^Z = 8.3$$

Therefore, from eq 1:

$$\frac{Y - 1.6}{Z - 4.5} = \frac{0.6(8.3)}{3.5}$$

$$1.4Z - 4.7 = Y$$

In order to have $Y > Z$

$$1.4Y - 4.7 > Y \qquad Y > 12$$

This indicates that in order to have k_H^2/k_D^2 larger for toluene than for chlorobenzene (avoiding the maximum), k_2^H/k_2^D for toluene must be greater than 12. In the absence of tunneling, this is an unrealistically large number. The proposition that the rate-limiting step is changing with substituent, therefore, is ruled out, and we conclude that k_2 is primarily rate limiting in all cases.

Experimental Section

General. All oxidations were carried out in a three-compartment cell.[1] All electrochemical potentials are reported vs. Ag|0.1 M $AgNO_3$ in acetonitrile. A Model 70 HV 1/90 Wenking potentiostat was employed. Coulometry was performed with an Acromag Model 212-LX-1 current integrator. The acetonitrile (Fisher Reagent Grade) was distilled twice from P_2O_5 and stored over Fisher 4A molecular sieves. Methylene chloride (Fisher Reagent) was passed through a column containing alumina (Woelm, super activity grade, 20 g/100 ml) directly into the cell. Tetraethylammonium perchlorate and anhydrous lithium perchlorate (0.1 M, G. F. Smith Chemical Co.) and tetrabutylammonium fluoroborate (0.1 M, Southwestern Analytical Chemicals, Inc.) were used as electrolytes without purification after drying in vacuo at 80° for 48 h. Dry nitrogen presaturated with solvent was continuously bubbled through the anode and cathode compartments. The cell was thermostated by a water bath at room temperature during the electrolysis. Rapid stirring of the anolyte during the electrolysis was achieved by a magnetic stirring bar.

GLC analyses were performed on a Model 720 F & M gas chromatograph equipped with thermal conductivity detectors. A 12 ft × 0.25 in. aluminum column packed with 15% Carbowax 20M on Chromosorb W was used. The oven temperature was generally programmed from 150 to 230° at 10°/min. Products collected were analyzed as $CDCl_3$ solutions by NMR on a Varian T-60 instrument, and chemical shifts are reported in δ units. Mass spectral analysis were recorded with an A.E.I. Model MS-12 spectrometer.

The following examples are representative of the general technique for oxidation of iodine and subsequent reaction with aromatic substrate. The two examples selected are representative of the preparative iodination of one activated and one deactivated aromatic substrate in each of the two solvent-electrolyte systems.

The procedure for determining the rates of competition iodination is given for iodine oxidized in acetonitrile-tetraethylammonium perchlorate only, because the same technique was used for the other solvent-electrolyte systems.

The procedure for determining the isotope effects is described for 4-deuteriochlorobenzene and is analogous to the technique for preparation of 4-deuterioanisole and 4-deuteriotoluene and their subsequent reaction with iodinating agent.

Iodoanisole. Oxidation of iodine (0.487 g, 1.91 mmol) at 1.90 V in acetonitrile-lithium perchlorate over a period of 49 min (2.30 faradays/mol) resulted in a slightly cloudy pale-yellow solution. The current decreased smoothly from 245 to 25 mA before the oxidation was terminated. Anisole (995 mg, 9.2 mmol) was added to the stirring anolyte solution. The solution color remained yellow but the precipitate disappeared. After 10 min of additional stirring, the solution was reduced to about 15 ml on a rotary evaporator. The residue was taken up in water, and the organic products were extracted into ether. The extracts were washed with 10% $NaHSO_3$ and 15% $NaHCO_3$ solutions before drying over anhydrous magnesium sulfate. The solution was filtered and evaporated to give a pale-yellow viscous oil (822 mg, 90%). GLC analysis of the oil indicated the presence of only the monoiodinated product. NMR gave an isomer ratio of 33% ortho (OCH_3, δ 3.80), 10% meta (OCH_3, δ 3.72), and 57% para (OCH_3, δ 3.70) after comparison with authentic samples.

Ethyl *m*-Iodobenzoate. Oxidation of iodine (0.502 g, 1.97 mmol) at 1.90 V in tetraethylammonium perchlorate-acetonitrile over a period of 68 min (2.08 faradays/mol) resulted in a clear pale-yellow solution. The current decayed smoothly from 210 to 4 mA while the color went from dark purple to pale yellow. To the stirring anolyte solution was added ethyl benzoate (1.052 g, 7.0 mmol). After 20 min of additional stirring, the mixture was worked up as previously and resulted in 2.50 g of a pale-yellow liquid. Distillation yielded 0.693 g (2.5 mmol, 65%) of ethyl *m*-iodobenzoate: bp 97-99° (2.0 mmHg) [lit. 153.5° (14 mmHg)];[17] NMR, 8.36 (t, 1 H), 8.00 (m, 2 H), 7.20 (t, 1 H), 4.46 (q, 2 H), 1.43 (t, 3 H).

Competitive Iodination. Oxidation of 2.0 g of iodine (7.9 mmol) in 160 ml of tetraethylammonium perchlorate at 1.90 V for a period of 190 min (2.2 faradays/mol) yielded a pale-yellow anolyte solution. A 10-ml aliquot of the anolyte (0.99 mmol of iodinating agent) was added dropwise to a stirring solution of 1 ml of acetonitrile containing toluene (0.433 g, 4.7 mmol) and benzene (0.437 g, 5.6 mmol). After stirring for 10 min, the solution was light-orange in color. Work-up and analysis by GLC indicated a product ratio (iodotoluenes/iodobenzene) of 17.8. NMR analysis of the product indicated that the iodotoluenes contained 46% ortho (methyl, δ 2.43), 6% meta (methyl, δ 2.30), and 48% para (methyl, δ 2.26).

Partial Oxidation. Iodine (0.5 g, 1.9 mmol) was oxidized in 160 ml of tetraethylammonium perchlorate-acetonitrile at 1.90 V for 20 min (1.18 faradays/mol) and a 10-ml aliquot of the anolyte (0.12 mmol of iodinating agent) was removed and added to a stirring solution containing 1 ml of acetonitrile, toluene (0.433 g, 4.7 mmol), and benzene (0.437 g, 5.6 mmol). The remaining anolyte was oxidized for an additional 50 min (2.15 faraday/mol), and a second 10-ml aliquot (0.21 mmol) of the anolyte was removed and added to the toluene-benzene mixture. Both reaction mixtures were worked up by the standard procedure and analyzed by GLC. The first mixture gave a product ratio (iodotoluenes/iodobenzene) of 17.3 and the second mixture a ratio of 18.0.

4-Deuteriochlorobenzene. To a stirring solution of *n*-butyllithium (1.28 g, 20 mmol) in 100 ml of ether was added dropwise 4-iodochlorobenzene (2.18 g, 10 mmol). The reaction was carried out in a dry nitrogen atmosphere over a period of 15 min. Excess D_2O was added dropwise to the reaction, and the mixture was stirred for an additional 15 min. The ether solution was washed with water and dried over anhydrous $MgSO_4$. Fractional distillation yielded 0.95 g (8.2 mmol, 82%) of 4-deuteriochlorobenzene: bp 120-124 °C. Mass spectral analysis indicated that the product was 94% deuterated.

Iodination of 4-Deuteriochlorobenzene. Iodine (0.5 g, 1.9 mmol) was oxidized at 1.90 V in 160 ml of tetraethylammonium perchlorate-acetonitrile for 75 min (2.4 faradays/mol). A 10-ml aliquot of the anolyte (0.24 mmol iodinating agent) was added to a stirring solution of 1 ml of acetonitrile and 4-deuteriochlorobenzene (545 mg, 4.8 mmol). GLC analysis after workup indicated a product ratio (2-iodo-4-deuteriochlorobenzene/4-iodochlorobenzene) of 5.02. A second 10-ml aliquot of the anolyte was added to a stirring solution of 1 ml of acetonitrile and chlorobenzene (553 mg, 4.9 mmol). GLC analysis after workup indicated a product ratio (2-iodochlorobenzene/4-iodochlorobenzene) of 0.353.

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