3238 *J. Org. Chem.* 1991, *56*, 3238–3245

Research Council for partial financial support of this work. We thank Dr. W. Kitching (University of Queensland) for providing access to their high-field NMR facility (JEOL-GX-400 spectrometer).

Supplementary Material Available: ^{13}C NMR parameters (observed shifts (Tables IX and X) and calculated shifts (Tables XI and XII)) of (*E*)- and (*Z*)-5-substituted (X) adamant-2-yl fluorides 8 and 9 (respectively), photocopies of the ^{13}C NMR spectra of 8 (X = F, Cl, Br, I, and $Sn(CH_3)_3$) and 9 (X = F, Cl, Br, I, $Si(CH_3)_3$, and $Sn(CH_3)_3$) as well as the mixtures 8 and 9 (X = F, Cl, Br, I, C_6H_5, p-$NO_2C_6H_4$, p-$NH_2C_6H_4$, $Si(CH_3)_3$), and $Sn(CH_3)_3$) (24 pages). Ordering information is given on any current masthead page.

Aromatic Iodination: Evidence of Reaction Intermediate and of the σ-Complex Character of the Transition State

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The reactivity of four different procedures of aromatic iodination is compared under the same experimental conditions, and their selectivity toward two substrates in competition, i.e., mesitylene (1,3,5-trimethylbenzene, MES) and durene (1,2,4,5-tetramethylbenzene, DUR), is evaluated. Two of these procedures, namely, $S_2O_8^{2-}/I_2$ and Ce^{IV}/I_2, present strong oxidizing capacity. Since the same MES/DUR relative reactivity is obtained from the four procedures, it becomes possible to state that a common reactive intermediate, most likely the I^+ ion, is generated. The use of the MES/DUR mechanistic probe allows one to describe the reactivity picture of the iodination reaction as one of electrophilic substitution at the aromatic nucleous, with a transition state properly represented in terms of a σ-complex. The radical cation of durene also forms when the iodination is carried out by means of oxidizing agents, but it is solely responsible for the formation of side-chain substitution products and is not involved in the nuclear substitution process.

Due to the importance that the iodo derivatives, and in particular the aryl iodides, have under the form of valuable synthetic intermediates[1] and also in view of their wide medical or biochemical applications,[2] a host of experimental procedures have been developed to obtain them.[3]

$$\mathrm{ArH} + \mathrm{I_2} \rightarrow \mathrm{ArI} + \mathrm{HI} \qquad (1)$$

Since the iodine molecule is the least reactive among the halogens toward an electrophilic substitution process,[4] most of the synthetic effort has been placed in converting molecular iodine into a more active species. One way of achieving this employs a strong Lewis acid such as Ag^+, which polarizes the iodine molecule, making it more electrophilic and more reactive toward ArH.[3,5] Another way exploits mixed anhydrides such as acetyl (or trifluoroacetyl) hypoiodite, CH_3CO_2I, where a rather mobile electrophilic iodine atom is embedded.[6] An alternative approach requires oxidizing agents. These are suggested to transform I_2 (or even I^-) into a robust electrophilic species, possibly I^+. Several of these oxidants have been described, and their capabilities to drive the iodination to valuable conversion vary considerably.[3] Interestingly, some of these oxidants are strong enough that the oxidation of electron-rich aromatic substrates into a radical cation ($ArH^{\bullet+}$) becomes feasible as well.

Such a variety of experimental procedures could well conceal nonhomogeneous mechanistic pathways, such as electrophilic, atom-transfer or electron-transfer mechanisms, featuring different reactive intermediates. In addition, it is not clear from the literature how much the different efficiency of the various iodination procedures depends on the relative merits of the promoting agents, with the experimental conditions being so different from case to case. It seemed of interest to deepen the knowledge of these points.

A classical mechanistic test to ascertain whether different experimental procedures give rise to the same reactive intermediate is a competitive experiment toward two substrates. Whenever different procedures afford the same reaction products and the same relative reactivity of substrate, there is good reason to conclude that the same reactive intermediate was involved in all cases. In this paper the above mechanistic criterion has been applied to the iodination reaction, to verify if the same reactive intermediate was originated from a number of widely different iodinating agents. These were (a) I_2 with an Ag^+ salt,[3] (b) I_2 and $(NH_4)_2S_2O_8$,[7] (c) catalytic amounts of $NO^+BF_4^-$ (or $NaNO_3$) in combination with O_2 and I_2 (Radner method),[8] (d) I_2 with a Ce(IV) salt (Sugiyama method).[9] Mesitylene and durene were the two aromatic substrates competing for the iodinating species. The choice of these two substrates was not trivial, as it will appear later on. The experimental results of this study are reported herein.

Methods and Results

For a meaningful comparison of the reactivity among the above iodination methods, the same reaction medium had to be employed. This was a mixture 60:8:8:24 v/v of CH_3CO_2H/CF_3CO_2H (TFA)/$(CF_3CO)_2O$ (TFAA)/CH_3CN. The composition of this mixed solvent resulted from "averaging" those employed in the original a–d methods. The iodination reactions were run at room temperature. Typical concentrations were on the order of [DUR] 0.3,

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(1) (a) Fanta, P. E. *Synthesis* 1974, 9. (b) Heck, R. F. *Org. React.* 1982, *27*, 345.

(2) Seevers, R. H.; Counsell, R. E. *Chem. Rev.* 1982, *82*, 575.

(3) (a) Merkushev, E. B. *Russ. Chem. Rev. (Engl. Transl.)* 1984, *53*, 343. (b) *Synthesis* 1988, 923.

(4) De La Mare, P. B. D. *Electrophilic Halogenation*; Cambridge University Press: Cambridge, 1976; p 159.

(5) Derbyshire, D. H.; Waters, W. A. *J. Chem. Soc.* 1950, 3694.

(6) Barnett, J. R.; Andrews, L. J.; Keefer, R. M. *J. Am. Chem. Soc.* 1972, *94*, 6129.

(7) Wirth, H. O.; Königstein, O.; Kern, W. *Liebigs Ann. Chem.* 1960, *634*, 84.

(8) Radner, F. *J. Org. Chem.* 1988, *53*, 3548.

(9) Sugiyama, T. *Bull. Chem. Soc. Jpn.* 1981, *54*, 2847.

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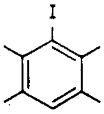
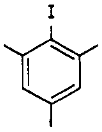
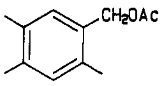
Table I. Competition Experiments of Iodination by Procedures a–c in the Mixed Solvent (AcOH/TFA/TFAA/CH_3CN) at Room Temperature

expt no.	[DUR], M	[MES], M	[I_2], M	promoter		reactn time[a]	products yield (%)			compd[b] A	k_{MES}[c] / k_{DUR}
				identity	concn, M						
						Procedure a					
1	0.416	0.150	0.040			24 h					
2	0.360	0.136	0.040			2.5 d		0.1			
3	0.357	0.143	0.040	Ag_2SO_4	0.079	8	3.9	96			48 ± 1
4	0.344	0.148	0.037	$AgClO_4$	0.159	30	2.9	88			52 ± 1
5	0.345	0.154	0.037	AcOAg	0.038	30	3.1	92			50 ± 2
6	0.348	0.156	0.036	Ag_2O	0.080	30	3.0	92			51 ± 1
											50 ± 2
7	0.351	0.153	0.041	Ag_2SO_4	0.080	80	3.4	90			46 ± 3
8[d]	0.353	0.142	(0.041	Ag_2SO_4	0.020)[i]	8	0.71	21			51 ± 1
9[d]	0.389	0.136	(0.035	Ag_2O	0.073)[i]	30	2.5	59			49 ± 1
						Procedure b					
10	0.354	0.139	0.035	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.077 0.042	60	0.12	3.5	10	1.1	48 ± 2
11[e]	0.358	0.146	0.035	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.078 0.042	60	0.14	4.1	10	1.4	49 ± 2
12	0.356	0.137	0.036	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.017 0.042	300	1.3	38	15	3.4	51 ± 2
13	0.352	0.130	0.035	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.017 0.043	24 h	2.6	71	22	6.0	53 ± 2
14	0.349	0.141	0.076[g]	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.077 0.042	24 h	1.2	35	18	1.2	51 ± 1
15	0.361	0.135	0.038	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.078 0.042	300	0.7	18	36	3.9	49 ± 1
16[f]	0.350	0.142	0.041	$(NH_4)_2S_2O_8$ $Cu(OAc)_2$	0.015 0.044	240	1.2	36	8	0.6	51 ± 3
17	0.354	0.142	0.034	$(NH_4)_2S_2O_8$	0.073	25 h	0.1	4.6	<0.1		52 ± 3
											51 ± 1
						Procedure c[h]					
18	0.355	0.135	0.037	$NO^+BF_4^-$	2.5×10^{-3}	8	4.3	92	0.7		48 ± 1
19	0.338	0.140	0.035	$NaNO_3$	2.7×10^{-3}	8	2.7	71	0.3		52 ± 2
20	0.343	0.145	0.037	$NaNO_3$	3.6×10^{-3}	60	3.7	88	5.0		49 ± 1
21	0.348	0.142	0.077[g]	$NaNO_3$	3.5×10^{-3}	60	4.2	94	4.3		50 ± 1
											50 ± 1

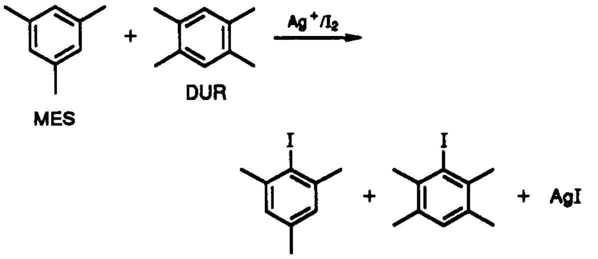
[a] In minutes, unless otherwise stated. [b] See text. [c] From nuclear iodinated products. [d] Preforming "I^+" and centrifuging: see text. [e] Run in air. [f] In the presence of AcONa, 0.17 M. [g] In this case the source of iodine was $Et_4N^+I^-$. [h] In the presence of oxygen. [i] Centrifuged.

[MES] 0.1, [I_2] 0.035, [promoter] 0.03 M.

The relative reactivity of mesitylene vs durene was determined from GLC measurement of the amounts of the nuclear iodinated products. The standard logarithmic expression for competitive processes was used, on the assumption that the reaction of each substrate with the reactive intermediate was first order in substrate.[10]

Blank experiments (expts 1 and 2, Table I) gave preliminary confirmation that iodine *alone* is not reactive toward the two aromatic substrates, under the experimental conditions chosen, for reaction times equal to or longer than those adopted when the promoting agents were present.

Iodination with an Ag(I) Salt (Method a). Iodination by I_2 promoted by a silver(I) salt is indeed an efficient process, as it is reported in the literature (eq 2).[3] Conversion of mesitylene and durene in the present mixed solvent into iodomesitylene and iododurene occurred in high yield after very short reaction times (expts 3–6). No other products appeared besides the aryl monoiodides. The yields reported in Table I, are based on the molar amount of iodine, which was the limiting reagent with respect to the substrates and to the promoter. Alternative use of Ag_2SO_4, $AgClO_4$, or AcOAg as the promoter salt had no major effect on reactivity. Use of Ag_2O leads to the formation of a silver salt in situ, due to the acidic nature of the mixed solvent employed: this procedure had reactivity comparable with those above. The iodinated products are stable under the experimental conditions for prolonged reaction times (see expt 7 vs expt 3), indicating that protodeiodination does not occur. A blank experiment (not reported here) showed that the silver(I) cation, a mild oxidant itself (ca. 0.8 V vs NHE),[11] is not capable of oxidation, or of any other reaction, with the two substrates when iodine is absent, irrespective of the reaction atmosphere (either argon or air).



(2)

Besides the high reactivity induced by the silver cation as a Lewis acid, another remarkable feature of these experiments is the MES/DUR reactivity ratio, which is large in value and constant in all cases, within experimental error (i.e., 50 ± 2).

Iodination with Peroxydisulfate (Method b). The system peroxydisulfate–$Cu(OAc)_2$ is a well-known oxidant,

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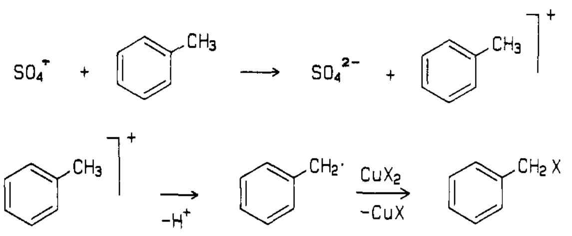
(10) Bunnett, J. F. *Investigation of Rates and Mechanisms of Reactions*, 3rd ed.; Lewis, E. S., Ed.; Wiley-Interscience: New York, 1974; Part I, p 159.

(11) *CRC Handbook of Chemistry and Physics*, 63rd ed.; CRC Press: Boca Raton, FL, 1982–1983.

easily conducive to the radical cations of aromatic substrates and, whenever possible, to their side-chain functionalization (Scheme I).[12]

Scheme I

$$S_2O_8^{2-} \xrightarrow{Cu(I)} 2SO_4^{\bullet-} \quad (3)$$



(4)

(5)

The redox potential of the $SO_4^{\bullet-}/SO_4^{2-}$ couple is in fact very high (at least 2.5 or even 3.1 V vs NHE).[13] It has been reported in a few cases[7,14] that use of I_2 with the $S_2O_8^{2-}$ oxidant, with or without a Cu(II) salt (eq 6), promotes

$$2SO_4^{\bullet-} + I_2 \rightarrow 2SO_4^{2-} + 2I^+ \quad (6)$$

aromatic iodination via the formation of a *positive halogen intermediate.* On the other hand, it has been shown[15] that the couple $S_2O_8^{2-}/Br^-$ gives benzylic bromination of toluene derivatives via a hydrogen atom abstraction reaction promoted by *bromine radical.* A competition of mechanistic pathways could be expected, therefore, to take place in the case of iodination.

Nuclear iodination of mesitylene and durene was obtained under the experimental conditions of the present work (expts 10–17) by employing $(NH_4)_2S_2O_8$ and $Cu(OAc)_2$. The conversion was however much lower than that obtained from method a. No major difference was observed when using I^- instead of I_2, apart from a lower reactivity with the former (cf. expts. 13 and 14). The MES/DUR reactivity ratio came out 51 ± 1, in very good agreement with the reactivity ratio obtained from the nonoxidizing method a, and the value of this ratio was independent of the extent of the conversion and of the reaction atmosphere (argon or air). The presence of *side-chain iodinated* products was excluded by subjecting the reaction mixture to exhaustive acetoxylation or to basic hydrolysis.

In addition to the nuclear iodinated products, side-chain acetoxylated durene was also formed. Its yield increased on increasing the amount of $S_2O_8^{2-}$ (cf. expts. 12 and 15), while this variation did not affect the I-MES/I-DUR ratio. Side-chain acetoxylated mesitylene was in all cases absent, or too low to be detected. Addition of AcONa (expt 16), as it is sometimes the practice,[15] increased somewhat the extent of the iodination pathway at the expenses of side-chain acetoxylation. Oxidation *without* the Cu(II) salt gave a poorer conversion (expt 17) into iodinated products and only a trace of side-chain acetoxylated durene. In both these cases the value of the MES/DUR ratio in the nuclear iodination did not change. The yields in Table I were calculated on the basis of limiting the reagent, either $S_2O_8^{2-}$ or I_2, according to the conditions.

Iodination by NO^+/O_2 (Method c). Iodination of aromatic substrates with I_2, promoted by *catalytic* amounts of $NO^+BF_4^+$ in an oxygen atmosphere, has recently been reported by Radner.[8] The catalytic cycle suggested is shown in Scheme II. The oxidation of iodine

Scheme II

$$I_2 + NO^+ \rightarrow [I\text{-}I/NO]^+ \rightarrow I^+ + INO \quad (7)$$

$$I^+ + ArH \rightarrow ArI + H^+ \quad (8)$$

$$INO \rightarrow 0.5I_2 + NO \quad (9)$$

$$NO \xrightarrow{\text{oxid. } (O_2)} NO^+ \quad (10)$$

to I^+ would be carried out by NO^+ in an inner-sphere electron transfer step, eq 7, (E^0 of NO^+ is 1.51 V vs NHE in CH_3CN).[16] Indeed, a very efficient nuclear iodination of mesitylene and durene takes place by Radner's method in the present solvent (expts 18–21), with conversions approaching those of method a, and the measured MES/DUR reactivity ratio is 48 ± 1. Only small amounts of side-chain acetoxylated durene were recovered.

As Radner himself discovered,[8] $NaNO_3$ can conveniently replace $NO^+BF_4^-$ as the catalytic promoter. In fact, it was almost as effective as $NO^+BF_4^-$ toward MES and DUR, both with I_2 and I^-, affording a substrate relative reactivity of 50 ± 1. A precise explanation of the reason why NO_3^-, a modest oxidant, is as effective as the much stronger oxidant NO^+ toward I_2 was not offered by Radner.[8] Some experiments reported in the following section may provide a rationale for this fact.

Iodination with Cerium(IV) (Method d). Ammonium hexanitrocerate(IV) (CAN) is a good one-electron oxidant (E^0 = 1.4 V vs NHE in AcOH),[13] capable of oxidation and of functionalization of electron-rich aromatic substrates in a way similar to that indicated in Scheme I. However, CAN has also been reported[9] to promote iodination of alkyl aromatics via the formation of a *cationic halogen species* by an oxidative electron transfer step (as in eq 6) both on I_2 and on I^-. Conversely, Baciocchi and Crescenzi have recently demonstrated[17] that halogenation of alkyl aromatics with CAN/Br^- or with CAN/Cl^- proceeds via the formation of a *radical halogen* as the intermediate (Scheme III). Again, a competition of mechanistic pathways could be expected here.

Scheme III

$$Ce^{IV}ONO_2 + X^- \rightarrow Ce^{IV}X + NO_3^- \quad (11)$$

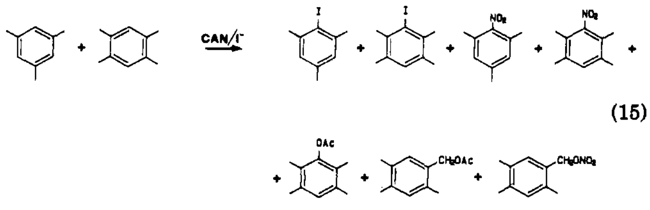
$$Ce^{IV}X \rightarrow Ce^{III} + X^\bullet \quad (12)$$

$$X^\bullet + ArCH_3 \rightarrow HX + ArCH_2^\bullet \quad (13)$$

$$ArCH_2^\bullet + Ce^{IV}X \rightarrow ArCH_2X + Ce^{III} \quad (14)$$

$$X = Br \text{ or } Cl$$

Treatment of mesitylene and durene in the present solvent with CAN (limiting reagent) and I^- gave rise to extensive nuclear iodination in a short time, accompanied by considerable amounts of other products (expt 22, Table II) (eq 15). The nature of these products suggested that



(15)

nuclear nitration and *side-chain oxidation* were pathways competing with iodination, but the amount of Ce(IV)

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[12] (a) Walling, C.; Zhao, Ch.; El-Taliawi, G. M. *J. Org. Chem.* **1983**, *48*, 4910.

[13] Eberson, L. *Adv. Phys. Org. Chem.* **1982**, *18*, 79.

[14] Marko, D. M.; Belyaev, Yu. A. *Khim. Referat. Zhur.* **1941**, *4*, 49; *Chem. Abstr.* **1943**, *37*, 6250.

[15] Citterio, A.; Santi, R.; Pagani, A. *J. Org. Chem.* **1987**, *52*, 4925.

[16] Eberson, L.; Radner, F. *Acc. Chem. Res.* **1987**, *20*, 53.

[17] Baciocchi, E.; Crescenzi, M. *Tetrahedron* **1988**, *44*, 6525.

present was not enough to account for the observed high conversion of substrates into products (210%). Substitution of I_2 for I^- produced no major changes. Exhaustive acetoxylation (as above) showed that benzyl-type iodides were not present and that only nuclear iodination had occurred. Hence, the operation of the radical intermediate $I^\bullet$, according to Scheme III, can be excluded.

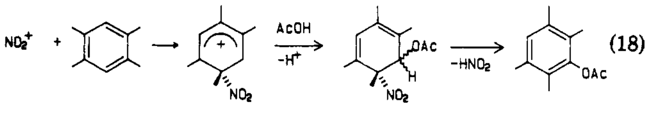
An explanation of what had occurred in expt 22 may be found along this line. CAN, i.e., $(NH_4)_2Ce(NO_3)_6$, contains six NO_3^- ligands. By analogy with the solvent employed by Radner,[8] the present mixed solvent contained 8% trifluoroacetic anhydride (TFAA), for variable water content quenching. Hence, under these conditions a mixed anhydride (i.e., trifluoroacetyl nitrate) could easily form, according to a well-documented pathway (eq 16).[18] Trifluoroacetyl nitrate is a strong nitrating agent, which in polar solvents releases the NO_2^+ species (eq 17),[19] i.e., a

$$NO_3^- + (CF_3CO)_2O \rightleftharpoons O_2NOC(O)CF_3 + CF_3CO_2^- \quad (16)$$

$$O_2NOC(O)CF_3 \rightleftharpoons NO_2^+ + CF_3CO_2^- \quad (17)$$

species with both an electrophilic and an oxidant (E^0 1.56 V vs NHE)[16] nature. This was likely to be responsible for some of the products formed in expt 22 and for the higher than stoichiometric conversion. For such an hypothesis to be tested, MES and DUR were treated in the mixed solvent (containing TFAA) with $Bu_4N^+NO_3^-$ *without* I_2 and *without* CAN (expt 23). The amount of $Bu_4N^+NO_3^-$ was comparable to that of the NO_3^- counterions that were introduced in the experiment run with CAN. A product mixture of nitromesitylene, nitrodurene, and nuclear-acetoxylated durene and of side-chain oxidation of durene resulted. On the other hand, reaction of $Bu_4N^+NO_3^-$ *and* I_2 with MES and DUR (expt 24) gave a product distribution similar to that observed in expt 22 from CAN.

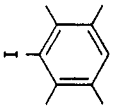
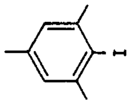
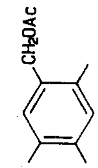
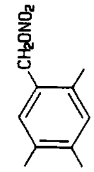
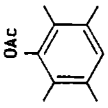
These results explain, first of all, why $NaNO_3$ can replace $NO^+BF_4^-$ in the iodination of aromatic substrates (method c).[8] The oxidizing species NO_2^+ is formed from eqs 16 + 17 and then may produce the positive halogen ion by an inner-sphere electron transfer step analogous to that (eq 7) reported in Scheme II for the NO^+ ion. Since $NaNO_3$ is used in catalytic amounts in Radner's iodination method, no nitration products appeared in his hands.[8] On the contrary, when the amount of NO_3^- ions is increased, either because it was added purposely or because it was added under the form of the counterions of CAN, nuclear nitration products show up as well. Besides, the NO_2^+ ion is capable of inner-sphere oxidation of durene (but not of mesitylene, and electron-poorer substrate),[16] concurring to the side-chain functionalization of that substrate along with the Ce(IV) ion. Finally, *nuclear* acetoxylated durene is likely to result from an ipso attack of NO_2^+ on durene, as already described by Suzuki (eq 18).[20] The conversion into products, higher that expected on the molar basis of the Ce(IV) cation alone, could therefore be due to the concomitant formation of the other reactive species NO_2^+.



(18)

For removal of the interference by the NO_2^+ species, the mixed solvent was replaced by a 3:1 $AcOH/CH_3CN$ mixture. Under these new conditions (expts 26 and 27), the

Table II. Competition Experiments of Iodination by Procedure d at Room Temperature

expt no.	[DUR], M	[MES], M	$[I_2]$, M	promoter		solvent[a]	reactn time, min	product yield (%)						
				identity	concn, M								other	$\frac{k_{MES}{}^b}{k_{DUR}}$
22	0.355	0.135	0.043[c]	CAN[d]	0.078	mixed	8	4.1	120	42	5.9	31	*e*	*k*
23	0.358	0.139		$Bu_4N^+NO_3^-$[d]	0.355	mixed	8			17		10	*f*	
24	0.360	0.137	0.036[d]	$Bu_4N^+NO_3^-$	0.388	mixed	8	4.4	96	34		28	*g*	48 ± 1
25	0.360	0.171	0.040[d]	$NaNO_3$[j]	3.6×10^{-3}	two	60		<0.2					
26	0.352	0.136	0.037[d]	CAN	0.077	two	8	0.17	5.2	5.1	0.9		*h*	53 ± 2
27	0.349	0.137	0.038	CAN	0.035[d]	two	60	0.66	19	7.8	2.1		*i*	49 ± 1

[a] "Mixed" solvent stands for the mixture $AcOH/TFA/TFAA/CH_3CN$, 60:8:8:24 v/v; "two" solvent stands for the mixture $AcOH/CH_3CN$, 10:3 v/v. [b] From nuclear iodinated products. [c] In this case $[Et_4N^+I^-]$. [d] Taken as yield determining. [e] Plus: 3.7% 2,4,6-trimethylnitrobenzene; 4.4% 2,3,5,6-tetramethylnitrobenzene; ca. 1.2% compound A (see text). [f] Plus: 3.0% 2,4,6-trimethylnitrobenzene; 1.7% 2,3,5,6-tetramethylnitrobenzene; ca. 0.5% compound A. [g] Plus: 3.2% 2,4,6-trimethylnitrobenzene; 3.2% 2,3,5,6-tetramethylnitrobenzene; ca. 1.3% compound A. [h] Plus ca. 0.2% compound A. [i] Plus ca. 0.4% compound A. [j] Radner method, in the presence of oxygen. [k] Not evaluated.

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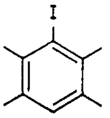
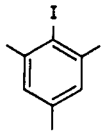
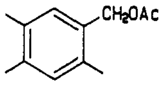
(18) (a) Crivello, J. V. *J. Org. Chem.* **1981**, *46*, 3056. (b) Masci, B. *Ibid.* **1985**, *50*, 4081. (c) Galli, C. *J. Chem. Res.* **1984**, 272.

(19) Masci, B. *Tetrahedron* **1989**, *45*, 2719.

(20) Suzuki, H. *Synthesis* **1977**, 217.

Table III. Comparison of the Reactivity of the Four Procedures in 3:1 AcOH/CH$_3$CN at Room Temperature

				promoter			product yield (%)			
expt no.	[DUR], M	[MES], M	[I$_2$], M	identity	concn, M	reactn time, min				$\frac{k_{MES}}{k_{DUR}}$[a]
28	0.348	0.147	0.039	Ag$_2$SO$_4$	0.019	2.5	1.5	44		50 ± 1
29	0.351	0.158	0.038	NO$^+$BF$_4^-$	2.5 × 10^{-3}	2.5	0.04	1.4		48 ± 2
30	0.344	0.141	0.040	CAN	0.039	300	2.9	79	12[b]	49 ± 2
31	0.358	0.135	0.038	(NH$_4$)$_2$S$_2$O$_8$ Cu(OAc)$_2$	0.016 0.046	300	0.15	4.2	0.8	50 ± 3

[a] From nuclear iodinated products. [b] Plus: 3.0% 2,4,5-trimethylbenzylnitrate; ca. 0.8% compound A (see text).

formation of trifluoroacetyl nitrate from CAN was suppressed, and the Ce(IV) ion remained the only promoter of the iodination of MES and DUR, as in the Sugiyama original method.[9] Nuclear nitration products disappeared, in fact, with respect to expt 22, as also did nuclear-acetoxylated durene (arising from eq 18). From the nuclear-iodinated products, a MES/DUR reactivity ratio of 50 ± 2 could be reckoned. *Side-chain* acetoxylated and nitrated durene were still observed, although on a much smaller scale, but these are common products of the oxidation of electron-rich aromatic substrates by Ce(IV) ion,[21] which derive from the radical cation of the substrate (see eqs 5 and 14).

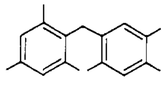
Determination of the Kinetic Isotope Effect (KIE). The determination of the KIE for the aromatic iodination reaction has been reported in a few instances in the literature. Values in the range of 1.4 to 4.0 have been found with various substrates and under different experimental conditions.[8,22] A measure of KIE has been obtained here, by mass spectrometric technique, from competition experiments between mesitylene or durene, and their fully deuteriated analogues, by employing a silver salt as the promoter of the iodination (see Experimental Section for details). Mesitylene gave a $k_H/k_D = 1.06 \pm 0.02$ and durene gave 1.15 ± 0.03. It can be safely concluded that under the experimental conditions of this work, and with the two employed substrates, the C–H bond rupture is *not* rate-determining in the iododehydrogenation process.

Discussion

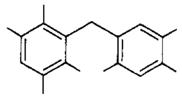
From the gathered results some points can be established.

Relative Efficiency of the Promoters. The reactivity of the four iodinating systems is intrinsically higher in the TFA-containing mixed solvent. This had already been observed for method b.[8] The comparison among the methods has, however, to be done in the TFA-free mixed solvent (Table III), due to the above problems of method d. This trend of decreasing relative efficiency of the promoter results in method a > method c > method d > method b. Silver ion is a remarkable promoter, but it is expensive. The Radner method, particularly the one exploiting NaNO$_3$ (provided that TFAA is present! See expt 25), stands out for simplicity of the procedure and for the cheapness of the reagent. Concerning methods d and b, there appears to be an inverse correlation of efficiency vs strength of the oxidant. However, both CAN and (NH$_4$)$_2$S$_2$O$_8$ are partially insoluble in the organic solvents, including those here employed, and this may affect the reactivity in an unpredictable way.

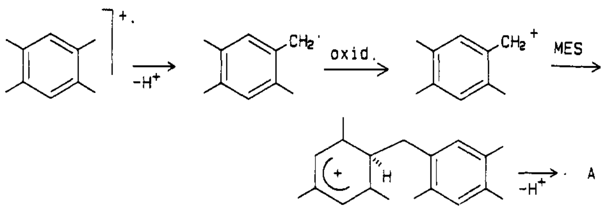
A further point is worth noting. In the reactions promoted by S$_2$O$_8$$^{2-}$, the strongest oxidant in the lot, the product mixture also contained significant amounts[23] of a compound whose mass spectrum was in agreement with structure A. No attempts were made to isolate and further characterize this compound. However, a similar observation was made by McKillop et al.[24] They isolated the hexamethyldiphenylmethane A from the reaction of DUR and MES with thallium trifluoroacetate (TTFA), while the heptamethyldiphenylmethane B was isolated from the reaction of DUR alone with TTFA. Compound B is also one of the products arising from the radical cation of durene produced by electrochemical oxidation.[25] TTFA was suggested by the authors[24] to give rise to the radical cation of durene by oxidative electron transfer. It is likely that compound A could arise from the following pathway:



A



B



(19)

The attack of the electrophilic benzyl cation derived from durene would occur preferentially on the more reactive mesitylene. This is found to be the case both in McKillop's experiment[24] and in the present experiments with S$_2$O$_8$$^{2-}$. The amount of A detected in the experiments promoted by CAN, a less powerful oxidant, was accordingly smaller.[26]

Nature of the Reactive Intermediate of the Iodination. The MES/DUR relative reactivity in the iodination reaction is strictly the same for the four methods (i.e., 50 ± 1), that is, under both *oxidizing* and *non-oxidizing* conditions. The formation, under the former conditions, of moderate amounts of side-chain acetoxylated durene does not affect the MES/DUR relative reactivity.[27] This was true even for method d in the TFAA-containing mixed solvent (expt 22), even though the MES/DUR relative reactivity was not given there, due to the large amount of side products formed from durene, which would

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[21] Baciocchi, E.; Rol, C.; Mandolini, L. *J. Org. Chem.* **1977**, *42*, 3682.

[22] (a) Miller, L. L.; Watkins, B. F. *J. Am. Chem. Soc.* **1976**, *98*, 1515. (b) Grovenstein, E.; Aprahamian, N. S. *Ibid.* **1962**, *84*, 212. (c) Berliner, E. *Ibid.* **1960**, *82*, 5435.

[23] In the range of 1–3%, with a maximum of 6% for expt 13.

[24] McKillop, A.; Turrell, A. G.; Young, D. W.; Taylor, E. C. *J. Am. Chem. Soc.* **1980**, *102*, 6504.

[25] Nyberg, K. *Acta Chem. Scand.* **1970**, *24*, 1609.

[26] In the order of 0.8% or less.

[27] The initial amount of durene was corrected for the amount of side-chain acetoxylated durene formed, before reckoning the k_{MES}/k_{DUR} for nuclear iodination. See Experimental Section.

make unreliable the use of the standard equation for competitive reactions.

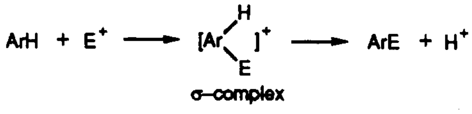
The absence of any significant primary KIE, as obtained under the iodination conditions of method a, indicates that, with reference to the conventional mechanism of electrophilic aromatic substitution, a σ-complex intermediate is formed: it loses the proton in a step kinetically fast as compared to the step of its formation, which is rate-determining and essentially irreversible. The constant MES/DUR reactivity ratios strongly suggest (i) that this mechanistic picture applies also to methods b, c, and d, and (ii) that the four iodinating procedures give rise to the *same* reactive intermediate, although by different ways and with different efficiencies. From this common reactive intermediate originates the same substrate selectivity in the rate-determining step.

What is the nature of this intermediate? Clearly, it has to be an electrophilic species. In fact, mesitylene, which stabilizes the positive charge of a σ-complex better than durene, owing to the ortho–para arrangement of the methyl groups, reacts faster and by a conspicuous value, i.e., fifty. Even more specifically, it can be stated that the reactive intermediate of these iodination reactions is the I^+ ion.[28] Two experiments (expts 8 and 9, Table I) run under silver ion catalysis support such a statement. Iodine and a silver salt (in one case Ag_2SO_4, in the other the silver salt formed in situ from Ag_2O) were mixed together in 1:1 CH_3CN/AcOH. A yellowish precipitate of AgI was observed. The suspension was centrifuged and the clear supernatant solution was withdrawn by syringe. It was injected into the solution of mesitylene and durene, with care being taken to reproduce the "normal" mixed-solvent composition. A MES/DUR reactivity ratio of 51 and 49 resulted, respectively,[29] from the iodinated products that were formed. One concludes from these two experiments that the I^+ species had to form in the preliminary step (eq 20).

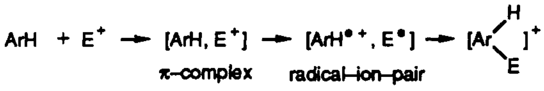
$$I_2 + Ag^+ \rightleftharpoons I^+ + AgI \qquad (20)$$

Secondly, with the MES/DUR relative reactivity of these two experiments being coincident with those reported in Tables I–III, there is compelling evidence that the I^+ ion is the reactive intermediate in all the methods a–d as well. Lines and Parker had suggested the $I_2^{\bullet+}$ species as the reactive intermediate in an electrochemically induced iodination.[30] Such a possibility is excluded here since the non-oxidizing method a, which cannot form $I_2^{\bullet+}$, behaves as the oxidizing methods b, d, and c that could form it.

Comments upon the Nature of the Transition State of an Electrophilic Aromatic Substitution. The nature of the mechanism of electrophilic aromatic substitution is the object of continuous attention. Along with the traditional pathway via the σ-complex intermediate (eq 21),[31] an alternative stepwise pathway has in fact been proposed,[32] initiated by an electron transfer within a π-complex to give a radical-ion-pair intermediate and/or a transition state (TS) with similar structure, which then collapses to the σ-complex (eq 22). There is a problem of a clear distinction in the description of the experimental reactivity in terms of the first or of the second pathway, because the structural factors that increase the electronic density on the aromatic molecule, thereby enhancing its reactivity toward electrophilic species, increase as well the ease of oxidation of the molecule, favoring the formation of $ArH^{\bullet+}$. Baciocchi and Mandolini have pointed out,[33] however, that in the series of the polyalkylbenzenes there are some pairs of substrates for which specific effects lead to significant differences in the prediction of reactivity by the two transition-state models.[34] Mesitylene and durene represent one such pair. The higher reactivity of mesitylene toward an electrophilic species, with respect to durene, is indicated by its stronger σ-basicity (pK_b 0.4 and 2.2, respectively).[35] On the other hand, durene is more easily oxidized into a radical cation than mesitylene ($E°$ 2.07 and 2.35 V, respectively, in CF_3CO_2H vs NHE).[36] As a consequence, a MES/DUR reactivity ratio larger than 1 would become evidence of a σ-complex character of the transition state of the rate-determining step. Conversely, a transition state with a charge-transfer component would be manifested by a MES/DUR ratio <1. Hence, the value of the MES/DUR reactivity ratio may become a mechanistic tool to distinguish between the operation of the two transition-state models.[33]

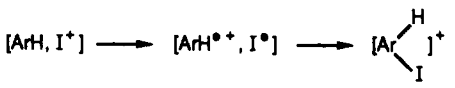


$$ArH + E^+ \longrightarrow \underset{\sigma\text{-complex}}{[Ar\overset{H}{\underset{E}{<}}]^+} \longrightarrow ArE + H^+ \qquad (21)$$

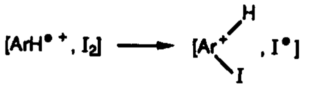


$$ArH + E^+ \longrightarrow \underset{\pi\text{-complex}}{[ArH, E^+]} \longrightarrow \underset{\text{radical-ion-pair}}{[ArH^{\bullet+}, E^{\bullet}]} \longrightarrow [Ar\overset{H}{\underset{E}{<}}]^+ \qquad (22)$$

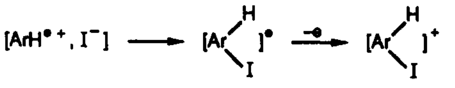
The MES/DUR ratio of 50 obtained in the present iodination study belongs to the former mechanistic case and is perfectly in line with other values reported for bona fide *electrophilic* aromatic processes.[33] While the structure of the transition state, according to pathway 21, is obvious when $E^+ = I^+$, a transition-state picture with a radical-ion-pair character for iodination would be as shown in eq 23 or 24 or 25 if one implies an electron-transfer step from the intermediate I^+ (23) or implies that the radical cation of the substrate is formed independently and then reacts with what is available (24 or 25).[37] In any event, the $ArH^{\bullet+}$ species must play a major role according to the mechanistic pathway 22.



$$[ArH, I^+] \longrightarrow [ArH^{\bullet+}, I^{\bullet}] \longrightarrow [Ar\overset{H}{\underset{I}{<}}]^+ \qquad (23)$$



$$[ArH^{\bullet+}, I_2] \longrightarrow [Ar^+\overset{H}{\underset{I}{<}}, I^{\bullet}] \qquad (24)$$



$$[ArH^{\bullet+}, I^-] \longrightarrow [Ar\overset{H}{\underset{I}{<}}]^{\bullet} \xrightarrow{-e} [Ar\overset{H}{\underset{I}{<}}]^+ \qquad (25)$$

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[28] Whether this I^+ ion is indeed a "free" ion cannot be stated. Certainly, it is strongly solvated by the reaction medium, which is, however, the same in all the four procedures here compared. The absence of any effect upon the k_{MES}/k_{DUR} ratio exerted by the nature of the gegenions, which vary considerably among the four procedures, does suggest that the electrophilic species is not covalently bound: see ref 4.

[29] The lower yields of these experiments are due in general to possible losses of the electrophile during the removal of the supernatant solution and its transfer to the reaction vessel. Besides that, the modest solubility of Ag_2SO_4 in CH_3CN would account for the lower yield of iodinated products in expt 8 with respect to expt 9.

[30] Lines, R.; Parker, V. D. *Acta Chem. Scand.* **1980**, *B34*, 47.

[31] (a) Brown, H. C.; Stock, L. M. *Adv. Phys. Org. Chem.* **1963**, *1*, 35. (b) Baciocchi, E.; Illuminati, G. *Progr. Phys. Org. Chem.* **1967**, *5*, 1. (c) Olah, G. A. *Acc. Chem. Res.* **1971**, *4*, 240.

[32] (a) Perrin, C. L. *J. Am. Chem. Soc.* **1977**, *99*, 5516. (b) Fukuzumi, S.; Kochi, J. K. *Ibid.* **1981**, *103*, 7240.

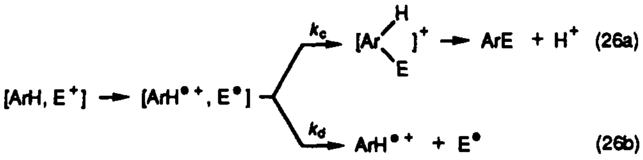
[33] Baciocchi, E.; Mandolini, L. *Tetrahedron* **1987**, *43*, 4035.

[34] For similar thoughts, see: (a) Perrin, C. L. *J. Phys. Chem.* **1984**, *88*, 3612. (b) Reference 24, p 6508.

[35] Brower, D. M.; Mackor, E. L.; MacLean, C. *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1970, Vol. II, p 851.

[36] Howell, J. O.; Goncalves, J. M.; Amatore, C.; Klasinc, L.; Wightman, R. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 3968.

Scheme IV



In spite of the approach of Baciocchi and Mandolini,[33] the electron-transfer model has recently been reinforced by Kochi.[38] He believes that that the [ArH$^{•+}$, E$^•$] pair (Scheme IV) is an *ubiquitous* intermediate that gives rise by branching either to collapse (k_c) toward a *concerted* substitution process or to diffusive separation (k_d) to free species (in particular ArH$^{•+}$), susceptible to side-chain functionalization and/or spectroscopic observation, for instance by ESR.[39] Modulation in the value of those two rate constants would be responsible, for diverse electrophilic reactions, for a shift of the reactivity picture from the σ-complex to the electron-transfer behavior. A crucial point of Kochi's unifying rationalization is that the collapse to the σ-complex would readily occur with mesitylene ($k_c \gg k_d$), while diffusion and hence a slower *stepwise* substitution would occur with durene, due to difference in the spin density at the nuclear positions.[38a] From the variation of importance of these two reactive steps, which would decrease the significance of the Baciocchi and Mandolini mechanistic probe,[33] a leveling effect in the MES/DUR relative reactivity might even appear, as indeed shown by the reactivity data of the mercuriation.[38b]

Some considerations on this argument become possible on the basis of the present work: (a) The averaged value of the MES/DUR ratios from the four iodination methods, i.e., 50 ± 1, which is larger than 1 and is large enough to warrant against possible leveling effects due to a diffusion-controlled competition, in addition to the observed absence of primary KIE, suggest a mechanism of substitution with a rate-limiting σ-complex formation that reflects to a significant extent the relative σ-basicity of the two compounds. (b) Under oxidizing conditions, but *not* under Lewis acid catalysis (i.e., method a), side-chain oxidation products of durene appear, detected as benzyl acetate or nitrate (eq 27). Consistently, previous work on

$$\mathrm{ArCH_3}^{•+} \xrightarrow[-\mathrm{H}^+]{} \mathrm{ArCH_2}^{•} \xrightarrow{\text{oxid.}} \xrightarrow{\mathrm{X}^-} \mathrm{ArCH_2X} \quad (27)$$

$$\mathrm{X = OAc\ or\ ONO_2}$$

the reactivity determination of the durene/mesitylene pair under *oxidative* conditions had afforded ratios of 150 or higher.[40] Hence, the presence of the [durene]$^{•+}$ species in the iodination processes performed under oxidizing conditions, but *not* under Ag$^+$ catalysis, is granted. (c) In spite of the presence of the ArCH$_3^{•+}$ species under the oxidizing conditions here reported, a substrate selectivity equal to that obtained under Ag$^+$ catalysis is obtained. This suggests that the ArCH$_3^{•+}$ species has nothing to do with the iodination pathway.[41] (d) A recent determination of the equilibrium constants for the π-complex formation between iodine and several polyalkylbenzenes[42] is of some relevance to the present iodination study (eq 28). Durene,

$$\mathrm{ArH + I_2} \rightleftharpoons \pi\text{-complex} \quad (28)$$

in agreement with the higher electronic density conferred by the larger number of methyl groups, shows a larger formation constant with respect to mesitylene in this simple, unproductive process. Comparison with expt 2, run without any promoter, where 0.1% of 2-iodomesitylene could be detected vs *no traces* of 3-iododurene, is immediate: the factors dominating nuclear substitution by the electrophile I$_2$ are *other* than those affecting the extent of π-complexes formation between I$_2$ and the same two substrates.

It is difficult to conceive a shift of the reactivity behavior according to Scheme IV as due to the modulation of k_c and k_d among the four present iodinating systems where the *same* iodinating intermediate, i.e., I$^+$, reacts with the *same* pair of substrates in the *same* reaction medium. It is difficult to reconcile the ubiquitous intermediacy of [ArCH$_3^{•+}$, E$^•$], implied by Scheme IV, along the reaction coordinate of a process of nuclear substitution displaying a reactivity pattern just *opposite* to the one ascribable to the ease of formation of the [ArCH$_3^{•+}$] species. As a matter of fact, whenever the presence of the latter is warranted, side-chain products of durene do emerge. The product composition changes from a situation where iodomesitylene is largely prevalent over iodourene (under Ag$^+$ catalysis), to a situation where the benzyl acetate of durene appears in comparable, or prevalent, yield with respect to iododurene or even to iodomesitylene. The graduality in this shift is possibly related to the strength of the oxidizing agent.

These findings suggest that the iodination is an electrophilic aromatic substitution with a transition state better describable in terms of a σ-complex. The possible occurrence of a substitution pathway with a charge-transfer component is by no means excluded, in general, with more powerful electrophiles, such as NO$_2^+$ or NO$^+$,[43] or with substrates more electron-rich than the polyalkylbenzenes (e.g., polycyclic aromatic hydrocarbons),[16] or under harsher conditions (e.g., in the gas phase).[44] However, eqs 21 and 22 do appear as *two separate* competing mechanistic formulations, with their own domain of existence, and the wider generality of the conventional electrophilic behavior, already suggested,[33] is once more confirmed here.

Experimental Section

^{1}H NMR spectra were taken at 80.13 MHz on a Bruker WP 80 SY spectrometer. GLC analyses were performed on two columns, namely, a 50 m × 0.32 mm OV-17 capillary column and a 15 m × 0.53 mm SE-30 wide bore capillary column. GC-MS analyses were performed on a HP 5890 gas chromatograph equipped with a 12 m × 0.2 mm methyl silicone gum capillary column, coupled with a HP 5970 mass selective detector.

Materials. All the reagents and the solvents were reagent-grade commercial samples. CAN was dried at 90 °C for 3 h. 3-Iododurene, 3-nitrodurene, and 2-nitromesitylene were available

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(37) See: Jönsson, L.; Wistrand, L. G. *J. Chem. Soc., Perkin Trans. I* **1979**, 669 and references therein.

(38) (a) Kochi, J. K. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1227. (b) Lau, W.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 6720.

(39) (a) Kochi, J. K. *Tetrahedron Lett.* **1974**, 4305. (b) Lau, W.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7100. (c) Masnovi, J. M.; Kochi, J. K. *Ibid.* **1985**, *107*, 7880. (d) Elson, I. H.; Kochi, J. K. *Ibid.* **1973**, *95*, 5060. (e) Cozzens, R. F. *J. Phys. Chem.* **1975**, *79*, 18. (f) Clemens, A. H.; Ridd, J. H.; Sandall, J. P. B. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1227. (g) Johnston, J. F.; Ridd, J. H.; Sandall, J. P. B. *J. Chem. Soc., Chem. Commun.* **1989**, 244.

(40) Baciocchi, E.; Mandolini, L.; Rol, C. *Tetrahedron Lett.* **1976**, 3343.

(41) This argument is strongly reminiscent of the one by Ridd in the case of the nitration of mesitylene: Draper, M. R.; Ridd, J. H. *J. Chem. Soc., Chem. Commun.* **1978**, 445.

(42) Joens, J. A. *J. Org. Chem.* **1989**, *54*, 1126.

(43) (a) Masnovi, J. M.; Sankararaman, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 2263. (b) Kim, E. K.; Kochi, J. K. *J. Org. Chem.* **1989**, *54*, 1692. (c) Morkovnik, A. S. *Russ. Chem. Rev. (Engl. Transl.)* **1988**, *57*, 144.

(44) (a) Schmitt, R. J.; Buttrill, S. E.; Ross, D. S. *J. Am. Chem. Soc.* **1984**, *106*, 926. (b) Morrison, J. D.; Stanney, K.; Tedder, J. M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 967.

Table IV. Kinetic Isotope Effect for the Iodination of Mesitylene and Durene[a]

	time		
	35 s	90 s	8 min
A. MES vs MES-d_3			
conversion (%)	11	28	90
k_H/k_D from 123 vs 120 ions	1.03	1.09	1.18
k_H/k_D from 108 vs 105 ions	1.04	1.07	1.17
	time		
	8 min	20 min	30 min
B. DUR vs DUR-d_2			
conversion (%)	8	10	12
k_H/k_D from 136 vs 134 ions	1.13	1.17	1.11
k_H/k_D from 121 vs 119 ions	1.12	1.17	1.18

[a] By method a from GC/MS measurements (see Experimental Section).

from previous investigations. 2-Iodomesitylene was synthesized according to method a: mp (from EtOH) 30.0–30.5 °C (lit.[45] mp 31 °C). 3-Acetoxydurene was obtained from esterification with acetic anhydride of 2,3,5,6-tetramethylphenol (Aldrich). 2,4,5-Trimethylbenzyl acetate and 2,4,5-trimethylbenzyl nitrate were obtained from column chromatography of the reaction crude of the oxidation of durene with CAN in AcOH at 50 °C.[21]

General Procedure for Iodination Experiments. The reaction products were identified by GC-MS and by comparison of the GLC retention times with those of authentic samples. The molar amount of products was determined from GLC areas with respect to hexadecane (internal standard). The MES/DUR reactivity ratios of the iodination were calculated from the amounts of nuclear iodinated products by the use of the standard equation for competitive reactions,[10] taking into account the 3 to 2 statistical factor of the two substrates. The amount of 2,4,5-trimethylbenzyl acetate, when formed, was subtracted from the initial amount of durene. Typical examples of the four methods are given below.

Method a (Expt 3). Durene (0.623 g, 4.64 mmol) and mesitylene (0.223 g, 1.86 mmol) were weighed in the reaction flask. Acetic acid (8 mL), TFA (1 mL), TFAA (1 mL), and CH_3CN (3 mL) were added, and the mixture was magnetically stirred to cause complete dissolution, while being kept under argon. Silver sulfate (0.323 g, 1.03 mmol) was added. Finally, I_2 (0.131 g, 0.516 mmol) was added, and the purple solution was stirred for 8 min at room temperature. The final pale yellow solution was added to internal standard (0.040 mmol), poured into water, extracted three times with $CHCl_3$, washed, and dried. Production of 2-iodomesitylene (0.495 mmol, 96%) and 3-iododurene (0.0203 mmol, 3.9%) was determined from GLC areas on averaging at least three injections on two different columns.

Method b (Expt 10). Durene (0.621 g, 4.63 mmol) and mesitylene (0.214 g, 1.78 mmol) were dissolved as above. Cupric acetate (0.108 g, 0.54 mmol) and I_2 (0.120 g, 0.47 mmol) were added. Finally, $(NH_4)_2S_2O_8$ (0.050 g, 0.22 mmol) was added, and the purple mixture was stirred under argon for 5 h at room temperature. After addition of the internal standard (6.4 × 10^{-3} mmol), the red solution was worked up as above, with a sodium thiosulfate wash to remove unreacted iodine. 2-Iodomesitylene (0.166 mmol, 38%), 3-iododurene (5.86 × 10^{-3} mmol, 1.3%), 2,4,5-trimethylbenzyl acetate (6.51 × 10^{-2} mmol, 15%), and compound A (ca. 3%, the response factor being extrapolated arbitrarily from compounds of comparable structure, such as 1,2-bis(4-methylphenyl)ethane) were obtained.

Method c (Expt 19). Durene (0.608 g, 4.53 mmol) and mesitylene (0.221 g, 1.84 mmol) were dissolved as above. Tetraethylammonium iodide (0.260 g, 0.996 mmol) was added, and the solution was flushed with O_2 for 2 min. Sodium nitrate (5 mg, 0.059 mmol) was quickly added, and the solution was stirred at room temperature for 60 min, with a small overpressure of O_2 being maintained. The final pale yellow solution was worked up as in method a after the addition of 0.042 mmol of internal standard. 2-Iodomesitylene (0.936 mmol, 94%), 3-iododurene (4.18 × 10^{-2} mmol, 4.2%), and 2,4,5-trimethylbenzyl acetate (4.29 × 10^{-2} mmol, 4.3% with respect to I^- or 0.95% with respect to DUR) were obtained.

Method d (Expt 25). Durene (0.609 g, 4.54 mmol) and mesitylene (0.214 g, 1.78 mmol) were dissolved in 10 mL of AcOH and 3 mL of CH_3CN. Iodine (0.127 g, 0.50 mmol) and CAN (0.252 g, 0.46 mmol) were added, with the mixture being then stirred under argon at room temperature for 60 min. The reddish final mixture was worked up as in method b. 2-Iodomesitylene (0.088 mmol, 19%), 3-iododurene (3.05 × 10^{-3} mmol, 0.66%), 2,4,5-trimethylbenzyl acetate (3.6 × 10^{-2} mmol, 7.8%), 2,4,5-trimethylbenzyl nitrate (9.7 × 10^{-3} mmol, 2.1%), and ca. 0.4% of compound A were obtained.

Kinetic Isotope Effect Measurements. The ring deuteriated mesitylene-*2,4,6*-d_3 and durene-*2,5*-d_2 were prepared by proton exchange in trifluoroacetic acid exactly as described by Lau and Kochi.[38b] In a competitive experiment, the relative amount of mesitylene and mesitylene-d_3 consumed under the conditions of method a were determined by GC/MS analysis, following both the molecular ions (M^+) and the base peaks ($M^+ - 15$), *m/z* 120 vs 123 and 105 vs 108, respectively. For example, a mixture of 1.06 mmol of MES-d_3 and 0.84 mmol of MES was prepared in the normal mixed solvent and iodinated with 0.33 mmol of I_2 and 0.30 mmol of Ag_2SO_4 at room temperature. An aliquot was removed before adding the promoter ("zero time"), and others were removed afters its addition at 35 s, 90 s, and 8 min and worked up as usual. GC/MS analysis of the recovered mesitylene allowed the determination of the k_H/k_D values reported in Table IV.[38b] The approximate relationship for the competition, i.e., $k_H/k_D = [MES]_0[MES\text{-}d_3]_t/[MES]_t[MES\text{-}d_3]_0$, which is correct for limited conversions, was used.[10] The point at 8 min, corresponding to a 90% conversion, was not included in the averaged k_H/k_D ratio reported in the text, but its k_H/k_D value shows that the approximate relationship gives a reasonably consistent ratio even in the nonlinear part of the exponential consumption of the substrates.

A similar competitive reaction was run for durene and durene-d_2, exactly as described above for mesitylene, following the ions *m/z* 134 vs 136 and 119 vs 121, respectively, and removing aliquots at proper times (Table IV).

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