Studies of Substrate Selectivity in Aromatic Iodination and Other Substitution Reactions Reinforce Previous Conclusions About the Nature of the Mechanism of Electrophilic Aromatic Substitutions

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We have investigated substrate selectivity as a probe to distinguish between electron-transfer (ET) and conventional polar mechanisms of electrophilic aromatic substitution. Selectivity toward mesitylene and durene, in competition experiments, has been determined for iodination, bromination, acetylation, mercuriation and thallation reactions under the same experimental conditions. In all cases mesitylene, *i.e.* the substrate with the higher σ-basicity, was more reactive than durene; a similar behaviour was shared by two other pairs of substrates, namely, mesitylene/naphthalene and m-$C_6H_4(OMe)_2$/p-$C_6H_4(OMe)_2$, where again the more reactive substrate within each pair was that with the higher σ-basicity. These findings suggest that the structure of the transition state of the above reactions resembles that of the σ-complex, and would therefore endorse the conventional polar mechanism of electrophilic aromatic substitution. Only for the nitration reactions were the experimental results too ambiguous to allow a definite mechanistic conclusion to be reached.

The mechanistic features of electrophilic aromatic substitution reactions are the object of continuous interest.[1] In a recent investigation,[2] a comparison of efficiency was attempted between four different experimental procedures, which activate the I_2 molecule to induce aromatic iodination ($S_2O_8^{2-}/I_2$, Ce^{IV}/I_2, NO^+/I_2, Ag^+/I_2). In the same medium, these procedures presented different efficiency, but they were found to proceed through the generation of the same intermediate, *i.e.* the 'I^+' ion, since the same relative reactivity for two diagnostic substrates was obtained. The two substrates, mesitylene (1,3,5-trimethylbenzene) and durene (1,2,4,5-tetramethylbenzene) were chosen as a significant pair because they show opposite trends in their σ-basicity and redox potential values and, consequently, their relative reactivity provides an indication about the nature of the mechanism, whether ionic or through electron transfer.[2] The result of this study was that, in agreement with its higher σ-basicity, mesitylene (MES) reacted better than durene (DUR), which instead would be the substrate more easily oxidized to a radical cation within an electron transfer substitution mechanism. In addition, the absence of a primary kinetic isotope effect was verified for these iodination reactions.[2] It was concluded that the attack of the 'I^+' electrophilic species on the aromatic compounds is rate-determining, and that the structure of the transition state resembles that of the σ-complex: the more stable is this intermediate, the more easily attainable is the transition state.[2]

These facts supported a conventional polar mechanism of electrophilic substitution. We report here on a generalized view of the electrophilic aromatic iodination, which emerges from the use of additional iodination procedures, also performed on other selected pairs of substrates. Furthermore, the study has been extended to include electrophilic substitutions other than iodination, such as nitration, to allow for a broader assessment of the reactivity features of this fundamental class of reactions.

Results and Discussion

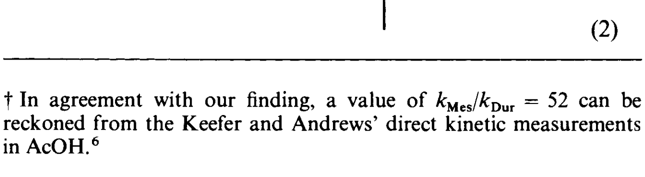
As has been noted in the previous paper,[2] in order to draw mechanistic information on a certain reaction type it is essential that different procedures are carried out in the same reaction medium. A meaningful comparison of the reactivity data concerning the iodination reaction has been obtained in the present study by using a mixed solvent [CH_3CO_2H/CF_3CO_2H (TFA)/$(CF_3CO)_2O$(TFAA)/CH_3CN 60:8:8:24 v/v; hereafter, 'mixed' solvent]. In other cases a 3:1 v/v mixture of CH_3CO_2H/CH_3CN was the reference solvent (hereafter, '3:1' solvent). The reactions were run at room temperature. The relative reactivity of the substrate in competition experiments was determined by GLC measurements of the amounts of products formed. For the sake of a meaningful comparison, the two substrates were both in considerable excess with respect to the reactive species (I^+, or others). In cases of high conversion into products, however, where this condition could no longer be fulfilled, the previous investigation[2] had shown that the relative substrate reactivity is, in general, affected by no more than 10%, *i.e.* within experimental uncertainty.

Iodination Reactions of Mesitylene and Durene.—Various procedures for the activation of the I_2 molecule[2] are reported in this work, and compared in efficiency toward mesitylene and durene. These procedures can be grouped into three fundamental classes, according to the kind of activation involved.

(*a*) *Iodination by Lewis acid* (*LA*) *catalysis.*[3] The reagents employed were Ag_2SO_4/I_2,[2] CF_3CO_2Ag/I_2,[4] $FeCl_3/I_2$ and $CuCl_2/I_2$.[5] Activation of I_2 occurs by electrophilic catalysis (eqn. 1).

$$I_2 + LA \longrightarrow I^{\delta+}\cdots I\cdots LA^{\delta-} \xrightarrow{ArH} ArI + HI + LA \quad (1)$$

As an example of this type of behaviour, the use of ICl as iodinating agent† is described within this group. In all cases reaction with an excess of the two substrates (mesitylene and durene) gave nuclear iodinated products only (see Table 1).



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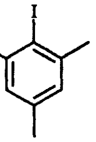
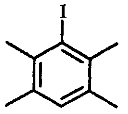
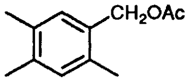
† In agreement with our finding, a value of $k_{Mes}/k_{Dur} = 52$ can be reckoned from the Keefer and Andrews' direct kinetic measurements in AcOH.[6]

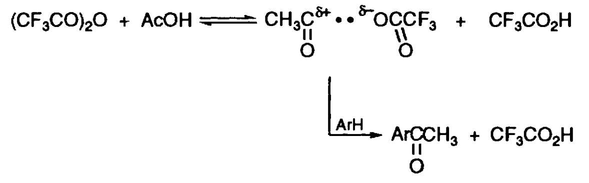
Table 1 Competition iodination experiments of mesitylene and durene by various procedures at room temperature[a]

Entry	Reagent	Solvent[b]	Reaction time[c]	Conversion (%)[d]	Products (mmol)				
								Others[e]	k_{Mes}/k_{Dur}[f]
1	Ag_2SO_4/I_2	mixed	8	99	0.49	1.8×10^{-2}	—	—	48 ± 1
2	Ag_2SO_4/I_2	3:1	3	48	0.23	7.6×10^{-3}	—	—	48 ± 2
3	CF_3CO_2Ag/I_2	3:1	8	87	0.42	1.5×10^{-2}	—	—	47 ± 4
4	$FeCl_3/I_2$	3:1	24 h	32	0.16	5.5×10^{-3}	—	—	46 ± 2
5	$CuCl_2/I_2$	3:1	65 h	11	0.054	2.1×10^{-3}	—	—	39 ± 5
6	ICl[g]	mixed	16	51	0.15	5.4×10^{-3}	—	—	43 ± 3
7	$S_2O_8^{2-}/Cu(OAc)_2/I^-$	3:1	24 h	11	0.057	1.9×10^{-3}	0.16	0.015	46 ± 2
8	IO_4^-/I_2	mixed	120	91	0.87	4.4×10^{-2}	—	0.020	39 ± 2
9	IO_4^-/I^-	mixed	120	30	0.15	4.4×10^{-3}	—	traces	53 ± 3
10	$H_2O_2/FeSO_4/I_2$	3:1	60	25	0.12	3.8×10^{-3}	0.05	—	49 ± 4
11	PCC[h]/I_2	mixed	17 h	50	0.48	2.0×10^{-2}	traces	0.060	41 ± 7
12	I_2 under anodic oxidation[i]	3:1	60	39[j]	0.27	9.6×10^{-3}	0.45	0.19	45 ± 2
13	$PhI(OCOCF_3)_2/I_2$	mixed	60	37	0.36	1.2×10^{-2}	—	—	48 ± 3
14	$(CF_3CO_2)_2Hg$[k]/I_2	mixed	16	98	0.47	1.8×10^{-2}	—	—	44 ± 2
15[l]	CF_3CO_2Ag/I_2	3:1	8	53	0.15	5.3×10^{-3}	—	—	46 ± 3

[a] Typically, Dur (4.5 mmol), Mes (2.0 mmol), promoter (1.0 mmol), I_2 (0.5 mmol), in the solvent mixture (13 cm^3). [b] 'Mixed' solvent stands for the mixture AcOH/TFA/TFAA/CH_3CN 60:8:8:24 v/v; '3:1' stands for AcOH/CH_3CN 10:3 v/v. [c] In minutes, unless otherwise stated. [d] Of iodination, as based on 0.5 mmol I_2, or on 1 mmol 'I^+' with an oxidizing promoter. [e] Compound **A**, see Scheme 2 and ref. 2. [f] From GC quantification of nuclear iodinated products. [g] On 0.30 mmol. [h] Pyridinium chlorochromate. [i] See Experimental section. [j] Faradic yield. [k] Mixed with I_2 prior to the addition to the substrates, to allow for formation of the mixed anhydride, eqn. (7). [l] In the solvent mixture (40 cm^3).

In order to get a homogeneous comparison with the previous results,* the reaction using Ag_2SO_4 as promoter[2] has been repeated here.

The conversion into iodinated products varies widely among the different procedures, being quantitative after 8 min with Ag_2SO_4, but only 11% after 65 h with $CuCl_2$. This is resonably linked to the different efficiency of the Lewis acids. In the case of the slowest reactions with the less efficient promoters, replacement of the 'mixed' solvent (containing TFAA) with the '3:1' solvent allows the suppression of the interference by a competing acetylation of the substrates, due to the *in situ* formation of an acetylating mixed anhydride from TFAA and AcOH.[7]



Scheme 1

In spite of the differences in conversion among the various procedures, the values of substrate selectivity obtained in the experiments of this group are found to be: (i) satisfactorily constant within experimental error ($k_{Mes}/k_{Dur} = 45 \pm 3$); (ii) unaffected by exchanging the two solvent mixtures (compare entries 1 and 2; Table 1); (iii) in agreement with previous determinations ($k_{Mes}/k_{Dur} = 50 \pm 2$).[2]

(*b*) *Iodination through oxidizing agents.*[3] The reagents employed were $S_2O_8^{2-}/Cu^{2+}/I^-$,[2] IO_4^-/I_2 (or I^-),[8] $H_2O_2/Fe^{2+}/I_2$, and pyridinium chlorochromate (PCC)/I_2 (Table 1). Oxidation of I_2 (or even of I^-) by these promoters was expected to produce an 'I^+' species.

$$\tfrac{1}{2}I_2 + \text{oxid} \longrightarrow \text{'}I^+\text{'} + \text{red} \qquad (3)$$

The system $S_2O_8^{2-}/Cu^{2+}$ (in entry 7) allows a homogeneous comparison with previous results,[2] Fenton's reagent, rarely used to induce aromatic iodination,[9] performed satisfactorily with mesitylene and durene (entry 10).

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + OH^\bullet \qquad (4)$$

$$OH^\bullet + \tfrac{1}{2}I_2 \longrightarrow OH^- + \text{'}I^+\text{'} \qquad (5)$$

In the case of PCC (entry 11), it is likely that the oxidation of I_2 is due to Cr^{VI}.[10] In agreement with the findings of the preceding group, while the extent of conversion into iodinated products varies, substrate selectivity is the same ($k_{Mes}/k_{Dur} = 46 \pm 4$) for all reagents. Once again,[2] this points to the formation of a common reactive intermediate.

A suitable model for this group of oxidizing promoters is represented by the aromatic iodination with electrolytically generated iodine(I), as described in the literature.[11]

$$\tfrac{1}{2}I_2 \xrightarrow[\text{anode}]{-e^-} \text{'}I^+\text{'} \xrightarrow{ArH} ArI + H^+ \qquad (6)$$

Using this electrochemical method for the iodination of the mixture of mesitylene and durene in our reference solvent, a k_{Mes}/k_{Dur} ratio (45 ± 2, entry 12) perfectly in line with those obtained from the 'chemical' promoters was obtained. Such agreement provides further support to the intermediacy of the

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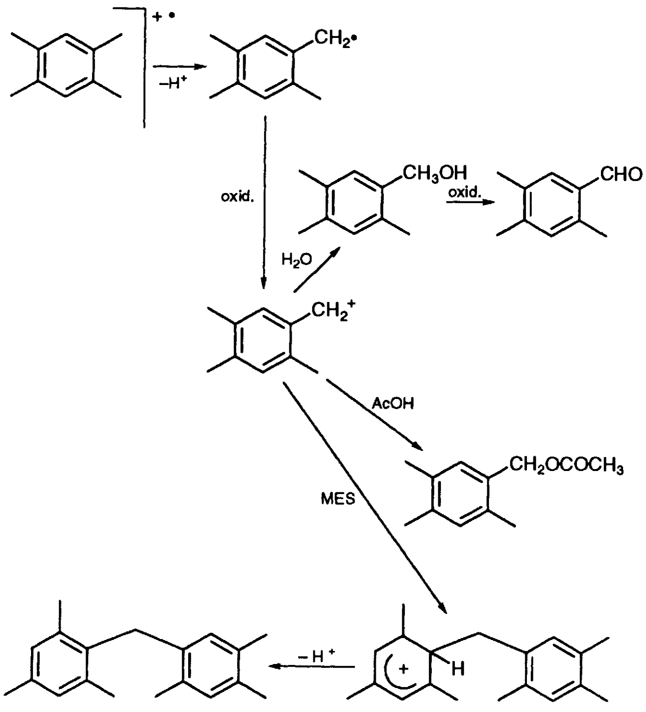
* In this investigation we used different GC columns and integrators than in previous work.[2] This may be the origin of a value of the k_{Mes}/k_{Dur} substrate selectivity being slightly lower (*ca.* 10%) than before.[2]

'I^+' species with all the procedures reported in Table 1. It is important to stress that with the oxidizing promoters (and also under electrochemical induction, entry 12), but not with the LA promoters, side-chain functionalization of durene (but not of mesitylene) was observed to varying extents. As already noted,[2] this is due to concurrent oxidation of durene to the radical cation, and its subsequent reaction(s) (Scheme 2).[12]



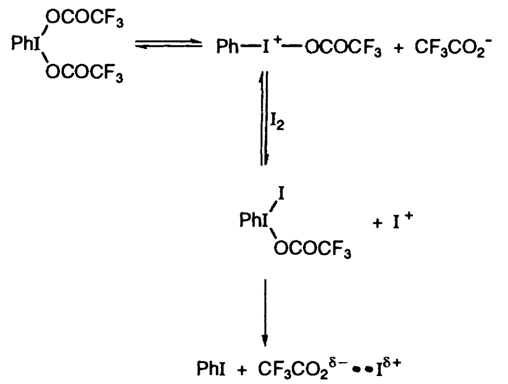
A

Scheme 2

Mesitylene, presenting a higher oxidation potential than durene, resists this competing pathway. However, it is noteworthy that the k_{Mes}/k_{Dur} ratios, which are assessed from the nuclear iodinated products are not affected by the concurrent formation of $Dur^{\bullet +}$, and remain comparable to the k_{Mes}/k_{Dur} values obtained from LA catalysis.

(*c*) *Iodination by mixed anhydrides.* The reagents employed were $PhI(OCOCF_3)_2/I_2$[13] and $(CF_3CO_2)_2Hg/I_2$.[14] Only nuclear iodinated products were obtained. A mixed anhydride (*i.e.* trifluoroacetylhypoiodite), containing a rather mobile electrophilic iodine atom, is likely to be formed from the hypervalent iodine compound *via* ligand exchange.[15]

Trifluoroacetylhypoiodite is similarly suggested[14] to result from equilibration of I_2 with mercury(II) trifluoroacetate.

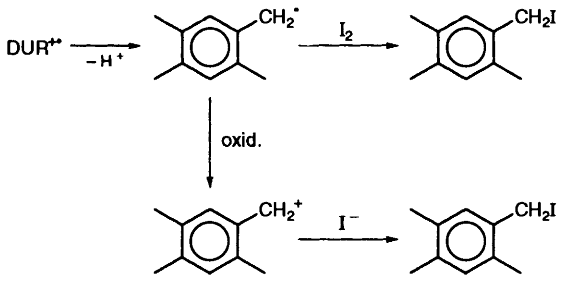


Scheme 3

$$(CF_3CO_2)_2Hg + I_2 \rightleftharpoons Hg(OCOCF_3)I + CF_3CO_2^{\delta -} \cdots I^{\delta +} \quad (7)$$

Generation of the mixed anhydride *in situ* in the presence of the mixture of mesitylene and durene, led to iodinated products. The substrate selectivity obtained in these two cases ($k_{Mes}/k_{Dur} = 46 \pm 2$) is again comparable to the values reported for the other two groups, supporting the formation of the 'I^+' species also from the mixed anhydrides. It therefore becomes possible to conclude that the results collected in Table 1 offer the unique possibility to compare the relative merits of a conspicuous number of procedures of aromatic iodination under the same conditions. Due to the importance that aryl iodides have in organic synthesis,[16] or in medical and biochemical applications,[17] the above information may have relevant practical use.

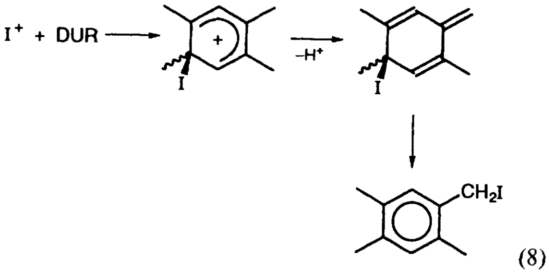
Another point to be stressed with regards to the meaningfulness of these competition experiments, is that the reaction crudes were occasionally subjected to exhaustive acetoxylation[2] to remove any side-chain iodinated product. Relative reactivity (k_{Mes}/k_{Dur}) determined before and after this treatment gave strictly consistent results in the case of the promoters of groups *a* and *c*, while the oxidizing promoters gave different values of k_{Mes}/k_{Dur}, which were larger by *ca.* 10–30%, after solvolysis: this was essentially due to a lower content of iododurene after solvolysis. The relative reactivities given in Table 1 are those after solvolysis. We interpret this as being due to concurrent production of side-chain iododurene (which co-elutes with nuclear iododurene in the GLC analyses) by interaction of the benzyl radical (or benzyl cation, see Scheme 2) of DUR with either I_2 or I^-, according to the experiment.



Scheme 4

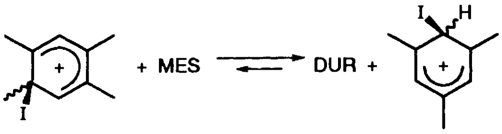
Generation of a significant fraction of $DUR^{\bullet +}$ with the oxidizing promoters would make possible this side-chain process, while there is no way it can take place with the promoters of groups *a* and *c*. Such evidence (along with other evidence, *vide infra*) renders unlikely the possibility of *ipso*-attack of I^+ on durene. In fact, a typical outcome of *ipso*-adducts is side-chain functionalization (mostly in the *para* position, when available).[18]

Side-chain iodinated durene is instead not observed with promoters *a* and *c* and therefore, when it is involved (with



(8)

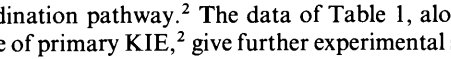
promoters *b*), it must arise from a different route (as shown in Scheme 4). This is relevant because one could be concerned that formation of the *ipso*-adduct from durene, and subsequent equilibration of it with unchanged mesitylene in a sort of *trans*-halogenation,[19] could affect the value of the relative reactivity and so undermine the validity of the competition experiments.



(9)

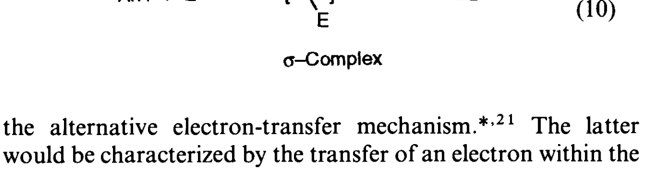
Lack of side-chain iodination (or of solvolysis products therefrom) with promoters *a* and *c*, is clearly against such an objection. Further evidence against the occurrence of the equilibration shown in eqn. (9) comes from the invariance of the $k_{\mathrm{Mes}}/k_{\mathrm{Dur}}$ ratio on a three-fold increase of the volume of the reaction solvent. Since the *trans*-halogenation of eqn. (9) is bimolecular, it had to be affected (and retarded) by dilution: the fact that it is not, indicates that it does not occur (entry 15).

Iodination of other pairs of substrates. The intermediate 'I^+' species invariably reacts better with mesitylene than with durene, in agreement with the higher σ-basicity of the former substrate: this confirms the electrophilic character of the iodination reaction.[2] The concurrent formation of $\mathrm{Dur}^{\bullet +}$ under oxidizing conditions does not cause a change in the mesitylene *vs.* durene selectivity: thus, $\mathrm{Dur}^{\bullet +}$ has nothing to do with the nuclear iodination pathway.[2] The data of Table 1, along with the absence of primary KIE,[2] give further experimental support to the suggestion[2] of a 'conventional' electrophilic mechanism[18b,20] for the iodination reaction ($E^+ = I^+$), as opposed to



(10)

the alternative electron-transfer mechanism.*,[21] The latter would be characterized by the transfer of an electron within the π-complex, giving rise to a charge-transfer (CT) complex (a radical-ion pair; k_{ET}), which later collapses (k_c) to the σ-complex. According to this scheme, and on the assumption of a rate-determining CT-complex (k_{ET}) formation, durene ought to



(11)

react better than mesitylene, in agreement with its lower oxidation potential and consequently higher ease of formation of the radical cation. This is not experimentally observed. The value of the mesitylene : durene reactivity ratio has indeed been proposed[24a,b] as a significant probe to distinguish between the two mechanistic formulations, owing to the fortuitous inversion between $\mathrm{p}K_{\mathrm{B}}$ and E° values (*vide infra*) of these two substrates. That ratio is larger than 1 in the case of our iodination reaction, in agreement with the polar mechanism of eqn. (10). The same result was found for the acetylation reaction (both in solution and in the gas-phase)[25] and for other electrophilic substitutions.[24a] The correlation between reactivity and ionization potentials occasionally observed in electrophilic aromatic substitution[21] is inconclusive in general, in resolving the mechanistic dichotomy, since there is also correlation between reactivity and σ-basicity for the same substrates.[24a] Only the substrates for which specific effects lead to opposite predictions by means of the two parameters are mechanistically significant.[24a,c]

An objection[23] to the choice of mesitylene and durene as a meaningful mechanistic probe has been based on the suggestion that the collapse (k_c) of the pair $[\mathrm{Dur}^{\bullet +}, \mathrm{E}^{\bullet}]$ to the σ-complex would be retarded by lack of spin density at the unsubstituted nuclear positions of $\mathrm{Dur}^{\bullet +}$. This could affect its overall reactivity to such an extent as to make it comparable to mesitylene, for which the collapse at the three unsubstituted nuclear positions is unimpeded.[23] In support of this point, the levelling of the reactivity of mesitylene and durene in the mercuriation reaction has been stressed.[26]

Even though the value of the $k_{\mathrm{Mes}}/k_{\mathrm{Dur}}$ ratio obtained for the iodination reaction is significantly greater that 1, in rebutting the above point, we have nevertheless tried to reinforce the relevance of substrate selectivity as a mechanistic probe, by looking for other substrate pairs whose σ-basicity and E° values would again present opposite trends, as occurs for mesitylene ($\mathrm{p}K_{\mathrm{B}}$ 0.4;[27] E° 2.35 V[28] *vs.* NHE) and durene ($\mathrm{p}K_{\mathrm{B}}$ 2.2;[27] E° 2.07 V[28]). Naphthalene ($\mathrm{p}K_{\mathrm{B}}$ 4;[29] E° 2.08 V[30]) and mesitylene are one such pair. *m*-Dimethoxybenzene (E_{p} 1.7 V[21b]) and *p*-dimethoxybenzene (E_{p} 1.5 V[21b]) are another.[31] The σ-basicity of the latter two compounds is not available, but the *meta*-isomer is described[32] as much more reactive than the *para* toward the bromination reaction, taken as a typical electrophilic process.† The advantage of these two new pairs of substrates is that their radical cations have significant spin density at the unsubstituted nuclear positions[33] and, according to the mechanism shown in eqn. (11), they would have favourable chances for fast-pair collapse (k_c) of the respective CT-complexes to the σ-complexes.

Table 2 shows the results of an iodination reaction of these substrate pairs by means of an efficient LA promoter (entries 16 and 18). With the mesitylene/naphthalene pair, the iodination was also carried out with a good oxidizing promoter such as ammonium hexanitrocerate(IV)[2] (CAN; entry 17). Although the uncertainty associated with these determinations is larger than those reported in Table 1, due to the wider reactivity difference, it clearly emerges that the more reactive substrate within each pair is always the one with the more favourable σ-basicity; this is verified both under oxidizing and non-oxidizing conditions. The E° value of durene and of naphthalene being equal the latter has a much lower σ-basicity: this would explain the larger reactivity difference of *ca.* 2100 between mesitylene and naphthalene *vs.* that of 45 between mesitylene and durene. In the experiment with CAN, but not with the silver salt, modest amounts of naphthalene acetate and nitronaphthalene were also detected. This indicates that cerium(IV) ion is able to oxidize naphthalene to $\mathrm{Naph}^{\bullet +}$, which then reacts with the solvent or with the counter-ions of the oxidant at the ring position(s); however, iodonaphthalene must arise from a pathway which does not require $\mathrm{Naph}^{\bullet +}$, since the $k_{\mathrm{Mes}}/k_{\mathrm{Naph}}$ ratios with CAN and with Ag^+ are the same (entries 16 and 17).

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* Claims in favour of an electron-transfer mechanism for electrophilic substitution are now restricted to the nitration and nitrosation reactions,[22] although a much wider generality was implied in the original formulation,[21b,23] in particular even for halogenation.

† An analogy can be drawn with *meta*- and *para*-xylenes, whose $\mathrm{p}K_{\mathrm{b}}$ values[27] are 3.2 and 5.7, respectively, and the E° values,[28] although closer than those of the two dimethoxybenzenes, are again in the opposite direction and, are, respectively, 2.38 and 2.30 V.

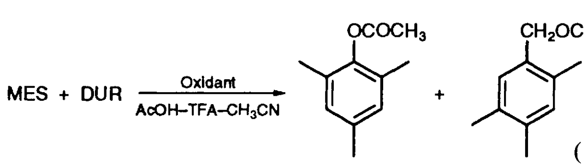
Table 2 Iodination of other substrate pairs in the 3 : 1 AcOH/CH_3CN solvent at room temperature[a]

Entry	Reagent	Pair[b]	Reaction time (min)	Conversion[c] (%)	Selectivity
16	CF_3CO_2Ag/I_2	Mes/Naph	30	99	$k_{Mes}/k_{Naph} = 2000 \pm 200$
17	CAN/I_2	Mes/Naph	180	99	$k_{Mes}/k_{Naph} = 2200 \pm 200$[d]
18	CF_3CO_2Ag/I_2	*m*-MeO/*p*-MeO	15	94	$k_m/k_p = 1100 \pm 150$

[a] Typically, 4.5 mmol for naphthalene and *p*-dimethoxybenzene, 2.0 mmol Mes, 1.0 mmol *m*-dimethoxybenzene, 0.9 mmol promoter, 0.45 mmol I_2. [b] Naph = naphthalene, *m*-MeO and *p*-MeO are *meta*- and *para*-dimethoxybenzene, respectively. [c] With respect to 0.45 mmol I_2 with Ag^+, or 0.90 mmol 'I^+' with CAN. [d] Accompanied by small amounts of naphthalene acetate and nitronaphthalene.

We can now conclude with more confidence and generality that the structure of the transition state of the iodination reaction does resemble that of the σ-complex, since all the structural factors enhancing the 'basicity' of the substrate, and consequently the stability of the positively charged Wheland intermediate, do favour nuclear iodination.

As an example of a reaction where the ease of formation of the radical cation of the substrates is instead significant to the relative amount of products formed, we selected the oxidative acetoxylation[34] of mesitylene and durene. We employed both



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CAN and $S_2O_8^{2-}/Cu^{2+}$ as oxidants in this process, in a mixed solvent (AcOH/TFA/CH_3CN, 60 : 16 : 24 v/v) where TFA replaced TFAA to prevent unwanted side-reactions such as acetylation (Scheme 1) or nitration (*vide infra*). The reaction mixtures were then subjected to exhaustive acetoxylation, to convert the accompanying trifluoroacetoxylated products[35] into acetoxylated ones. We also detected small amounts of a diarylmethane derivative[2] (compound **A** in Scheme 2) of 2,4,5-trimethylbenzaldehyde and (only with CAN) of a side-chain nitro derivative of durene.[36] The alternative formation of side-chain acetoxylated mesitylene or of nuclear acetoxylated durene was checked and could be excluded (see Experimental section): nuclear rather than side-chain acetoxylation is a typical[36,37] (although not exclusive)[38] outcome of the reaction of $Mes^{\bullet +}$ produced by various one-electron oxidants or by anodic oxidation, the opposite being true for $Dur^{\bullet +}$. In our experiments, the relative reactivities were calculated by summing up the amount of all the side-chain products from durene and comparing them with the amount of 2-acetoxymesitylene.

With both oxidants, durene was found to be more reactive than mesitylene, the stronger oxidant $S_2O_8^{2-}$ being slightly less selective than CAN (Table 3); the reaction with CAN (entry 19) led to higher conversion perhaps for solubility reasons.[2] The k_{Mes}/k_{Dur} ratio from the latter oxidant (*i.e.* 5.7×10^{-3}) compares very well with the ratio of the absolute rate constants of direct reaction of durene and of mesitylene with CAN in neat AcOH (*i.e.* 4.8×10^{-3}).[39]

A similar oxidation by CAN of the mesitylene/naphthalene pair (entry 21) gave nuclear acetoxylated products; despite using the '3 : 1' solvent mixture, these products were accompanied by small amounts of nitro derivatives, arising from an unwanted competing reaction of NO_2^+, possibly deriving from the ligands of Ce^{IV} ion.[2] If the relative reactivity is calculated from the acetoxylated products only, a k_{Mes}/k_{Naph} ratio of 0.024 is obtained.

It clearly appears that the substrate selectivity values of the oxidative acetoxylation experiments with the two pairs reflect the relative ease of ionization, and are therefore 'inverted' with respect to those obtained from the substitution reactions of Tables 1 and 2. Since the acetoxylation experiments necessarily involve the intermediacy of the radical cation of the substrates in the kinetically significant step,[34] by virtue of contrast we can exclude the intermediacy of the $ArH^{\bullet +}$ species [see eqn. (11)] as responsible for the selectivity ratios of all the iodination reactions examined.

Due to the low reactivity of the unactivated I_2 molecule, the iodination reaction offers the unique possibility of a distinction between ease of formation of the π-complex and the σ-complex. In reaction with 'unactivated' I_2, durene shows a larger formation constant than mesitylene for the unproductive complexation of eqn. (13),[40] in agreement with the higher electronic

$$ArH + I_2 \overset{K}{\rightleftharpoons} \pi\text{-complex} \qquad (13)$$

density conferred by the larger number of methyl groups. However, on addition of a promoter a more powerful electrophile is produced from I_2 [see for example eqn. (1)] and an electrophilic iodination takes place, where mesitylene is more reactive than durene. This means that the factors dominating nuclear electrophilic substitution are other than those affecting the extent of π-complex formation[41] [see eqn. (11)]. Certainly,

$$ArH, E^+ \longleftrightarrow ArH^{\bullet +}, E^{\bullet} \qquad (14)$$

stabilization of the ground-state π-complex may be due to some resonance contribution [eqn. (14)] from the CT-state;[22c,42] but the existence (and energy) of this CT-structure does not appear to be a necessary requirement for the nuclear substitution process to occur. Were it so, were k_{ET} rate-determining, an 'inverted' mesitylene/durene reactivity ratio such as that of the acetoxylation (Table 3) would be obtained. In addition, even when $Dur^{\bullet +}$ is present in the reacting mixture (as with the oxidizing promoters), since side-chain functionalized products are also detected (see Scheme 2), no effect on the intermolecular selectivity of the nuclear iodination emerges. Finally, no sign of side-chain derivatives of durene is obtained under LA catalysis, but only nuclear iododurene.

We have tried to increase the extent of the CT contribution [$DUR^{\bullet +}, I_2^{\bullet -}$] to the iodination reaction, by irradiating with UV light a reacting mixture of mesitylene, durene and I_2 without promoter in the '3 : 1' solvent; according to eqn. (11) we expected to enhance the production of iododurene by the ET pathway. There were no major effects; as with the 'blank' experiment of iodination of mesitylene and durene by I_2 alone,[2] we obtained only a small amount of iodomesitylene (*ca.* 0.1%) but no traces of iododurene or of any durene derivative.

The possibility that k_c in eqn. (11) is rate determining, with $k_{-ET} \gg k_c$, would lead to a kinetic expression indistinguishable from that of eqn. (10):* anyhow the σ-complex formation

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* In fact, one obtains $v = k_{obs}[ArH][E^+]$, with k_{obs} being the slow step of eqn. (10), or being $= K_{ET}k_c$ for eqn. (11).

Table 3 Relative reactivity of substrate with various reagents at room temperature[a]

Entry	Reaction	Reagent	Solvent	Selectivity
19	Acetoxylation	CAN	*b*	k_{Mes}/k_{Dur} (5.7 ± 0.4) × 10^{-3}[c]
20	Acetoxylation	$S_2O_8^{2-}/Cu(OAc)_2$	*b*	k_{Mes}/k_{Dur} (8.7 ± 0.4) × 10^{-3}[c]
21	Acetoxylation[d]	CAN	3:1	k_{Mes}/k_{Naph} (2.4 ± 0.1) × 10^{-2}[e]
22	Bromination	Br_2	3:1	k_{Mes}/k_{Dur} 57 ± 5
23	Bromination	CAN/Br^-	3:1	k_{Mes}/k_{Dur} 28 ± 1[f]
24	Bromination	$S_2O_8^{2-}/Br^-/Cu(OAc)_2$	mixed	k_{Mes}/k_{Dur} 26 ± 3[f]
25	Acetylation	$AcOH/TFAA/H_3PO_4$	*g*	k_{Mes}/k_{Dur} 14 ± 1
26	Mercuriation	$(CF_3CO_2)_2Hg$	mixed	k_{Mes}/k_{Dur} 12 ± 2
27	Thallation	$(CF_3CO_2)_3Tl$[h]	*i*	k_{Mes}/k_{Dur} 4.6 ± 0.3
28	Nitration	$NO_3^-/TFAA$	*j*	k_{Mes}/k_{Dur} 2.8 ± 0.1[k] (but k_{Mes}/k_{Dur} 0.19 ± 0.01)[l]
29	Nitration[d]	$NO_3^-/TFAA$	*j*	k_{Mes}/k_{Naph} 20 ± 1[k]

[a] See Experimental section for amount of reagents. [b] In $AcOH/TFA/CH_3CN$ 60:16:24 v/v. [c] See eqn. (12); accompanied by 2,4,5-trimethylbenzaldehyde and compound **A** in smaller amounts. [d] With Mes and Naph as substrates. [e] Accompanied by the nitro derivatives in small amounts. [f] Accompanied by side-chain acetoxylated Dur. [g] In $TFA/TFAA/CH_3CN$ 54:8:38 v/v. [h] Formed *in situ* from Tl_2O with the solvent. [i] In $TFA/TFAA/CH_3CN$ 62:15:23 v/v. [j] In $AcOH/TFAA/CH_3CN$ 72:5:23 v/v. [k] From nuclear nitro derivatives only, and corrected for statistical factors. [l] Overall reactivity (see text); uncorrected for statistical factors.

would be kinetically significant, and one could only imply (at will!) the CT-complex formation, without any experimental support for it from reactivity considerations. In compliance with Eyring theory, it appears sound to conclude that the reactivity of the aromatic iodination reaction is uniquely determined by the relative energy levels of the structures of the reagent and of the TS of the rate-determining step, the latter being structurally similar to the σ-complex. The question whether or not a CT-complex [and therefore an ET step, eqn. (11)], which would be produced from the reagent in a fast pre-equilibrium step as compared to the kinetically significant σ-complex formation, is along the reaction coordinate of the nuclear iodination reaction, and has or has not relevance to the overall reactivity, is '. . . irrelevant if not inherently meaningless' according to L. P. Hammett.[43]

Other Electrophilic Reactions with the Mesitylene/Durene Pair.—The iodination reaction is probably not the most representative halogenation reaction and the above conclusions, although based on the study of different substrate pairs, might appear inadequate for a safe generalization of the reactivity features of all the S_EAr reactions. Thus, we chose to extend the investigation to other electrophiles, generated in our reference solvent and treated with mesitylene and durene.

The bromination reaction (Table 3) was effected with both molecular Br_2 and with two oxidizing agents of Br^-. The two methods yield somewhat different k_{Mes}/k_{Dur} ratios (entry 22 *vs.* 23 and 24), and we take this as evidence of a polarized $Br^{\delta+} \cdots Br^{\delta-}$ species as the reactive intermediate in the first case,* while with the two oxidants a significant amount of the more strongly electrophilic 'Br^+' would be produced: the substrate selectivity would accordingly be higher for the weaker electrophilic species. The acetylation reaction (entry 25) was carried out by inducing the formation of the mixed anhydride acetyl-trifluoroacetate (see Scheme 1) under catalysis with H_3PO_4.[7,25] The mercuriation reaction (entry 26) was effected by treating $(CF_3CO_2)_2Hg$ with mesitylene and durene, and then subjecting the mercuriated products to iododemercuriation with I_2.[1] Similarly, thallation (entry 27) was effected by means of $(CF_3CO_2)_3Tl$ (formed *in situ*), followed by iododethallation.[3] Thus, the substrate selectivity of both the metallation reactions was evaluated from the resulting nuclear iodinated products. Our substrate selectivities compare very well with k_{Mes}/k_{Dur} ratios of 7.3 and 4.4, respectively, from the direct kinetic constants in TFA.[26]

These four substitution reactions afforded nuclear functionalized compounds whose relative amounts allowed the determination of the reported k_{Mes}/k_{Dur} ratios (Table 3). Invariably, mesitylene was shown to be more reactive than durene, by extents that reasonably depend on the strength of the electrophilic species. Interestingly, both in the brominations induced by oxidants (entries 23 and 24) and in the thallation reaction (entry 27) side-chain derivatives of durene were also detected, suggesting concurrent formation of $Dur^{\bullet+}$. Once again, and analogously to the iodination case, the intermolecular selectivity remained the opposite (*i.e.*, $k_{Mes}/k_{Dur} > 1$) to the relative ease of formation of the $ArH^{\bullet+}$ species from the two substrates. One concludes that the $ArH^{\bullet+}$ species is not responsible for the formation of the nuclear products. The various electrophilic substitutions reported here proceed in agreement with the relative σ-basicity of the two substrates as required by the operation of the 'conventional' ionic mechanism [eqn. (10)].

The Nitration Reaction.—This is the most studied[1] and the most controversial[22,30,44] of electrophilic aromatic substitutions. Evidence in favour of an ET pathway appears to be the strongest in this case,[22,45] due to the relevant oxidizing power of NO_2^+ (or also of NO^+).[30,44] We do not presume to be able to give here the solution to this mechanistic problem: we only tried the approach of substrate selectivity in this case, for comparison with the previous reactions.

The nitrating species was generated by the mixed anhydride

$$NO_3^- + (CF_3CO)_2O \rightleftharpoons O_2N^{\delta+} \cdots {}^{\delta-}OCOCF_3 + CF_3CO_2^- \quad (15)$$

method,[7b,46] in the solvent mixture $AcOH/TFAA/CH_3CN$ 72:5:23 v/v. Reaction with the mesitylene/durene pair (entry 28) gave a very complex mixture [eqn. (16)].

If one considers the nuclear nitrated products only, a k_{Mes}/k_{Dur} ratio of 2.8 is obtained. However, other products are formed,[2] which derive from durene or, better, from $Dur^{\bullet+}$ (see Scheme 2 and Experimental section). In particular, nuclear acetoxydurene was observed, which originates from *ipso*-attack by NO_2^+, followed by attack of AcOH and elimination of HNO_2:[2] this is the only evidence we have of *ipso* attack in the reactions of this work. Taking into account all the durene derivatives, a k_{Mes}/k_{Dur} ratio of 0.19 would be estimated. As far as mesitylene is concerned, the absence of side-chain nitro derivatives from it is reported to be against the involvement of the $Mes^{\bullet+}$,[47] and would appear to be in favour of nuclear attack by the nitronium ion. As far as durene is concerned

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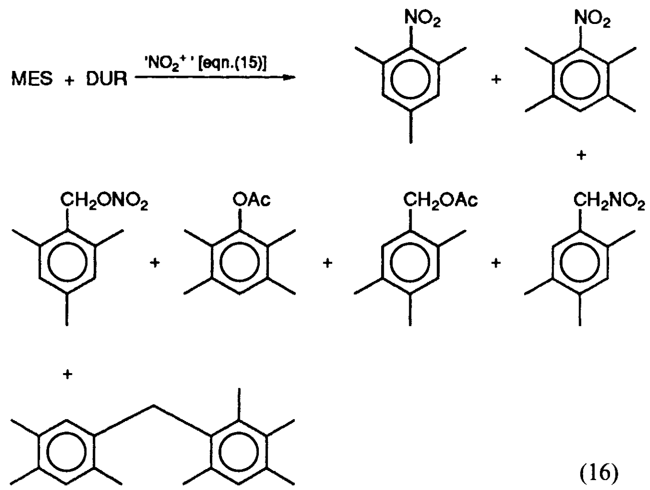
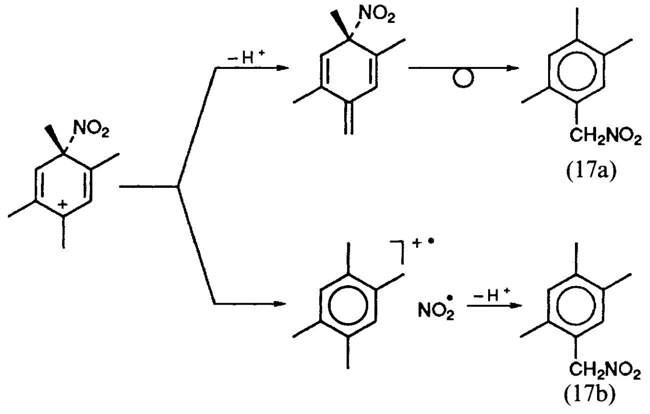
* Compare with a k_{Mes}/k_{Dur} = 66 in AcOH.[18b]



(16)

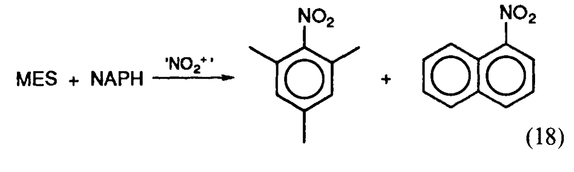
the formation of side-chain derivatives from it could be due both to the intermediacy of $Dur^{\bullet +}$ and reaction from it according to Scheme 2, and also to *ipso*-attack of NO_2^+ and subsequent side-chain functionalization; the latter step could be either ionic[18] [eqn. (17a)] or by ET[44b] [eqn. (17b)].



(17a)

(17b)

Finally, we found no difference in product distribution nor in substrate selectivity when the reaction of eqn. (16) was run in the presence of NaN_3 as a scavenger[48] of NO^+ ions possibly formed. From the mesitylene/naphthalene pair, the product pattern is less complex (entry 29), only the two nitro derivatives were found (see Experimental section).



(18)

Mesitylene was found to be more reactive than naphthalene: this is in agreement with the σ-basicity trend and confirms the result of the iodination (entries 16 and 17: $k_{Mes}/k_{Naph} \approx 2100$), although the value of the relative reactivity is much smaller here. One could suspect a polar mechanism by nitronium ion, accompanied by part of the reaction[45b] proceeding *via* the radical cation of naphthalene. However, reaction of nitronium ion with these substrates is likely to occur at, or close to, the encounter limit,[44c] adding a complication to the evaluation (and meaning) of substrate reactivity for this reaction. Certainly, the nitration reaction is too complex to presume to have given an unambiguous rationalization of it by means of the present limited set of experiments.

Conclusions.—The reactivity picture of the electrophilic substitution reactions, which arises from this work, is rather general. The very fact of working with the same medium composition makes comparison of the results easier, and mechanistically significant differences emerge more clearly. The study of substrate selectivity within diagnostic pairs of compounds proves to be a powerful mechanistic tool, capable of sorting out the kind of mechanism at play. The majority of the electrophilic substitutions examined comply with the 'conventional' ionic mechanism [eqn. (10)], only the nitration reaction may involve a contribution from the competing ET pathway [eqn. (11)].

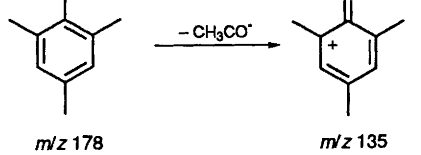
Experimental

^{1}H NMR spectra were taken at 80.13 MHz on a Bruker WP 80 SY spectrometer. GLC analyses were performed on two columns: a 15 m × 0.53 mm methyl silicone gum wide bore capillary column and a 25 m × 0.2 mm HP-1 capillary column. GC–MS analyses were performed on an HP 5890 gas chromatograph equipped with a 12 m × 0.20 mm methyl silicone gum capillary column, coupled with an HP 5970 mass selective detector.

Anodic oxidation was carried out with an Amel 5000 potentiostat in a two-compartment cell using platinum electrodes. A Rayonet RPR-100 photochemical reactor, equipped with 16 lamps emitting in the 350 nm region, was used in the attempted photostimulation of the iodination reaction.

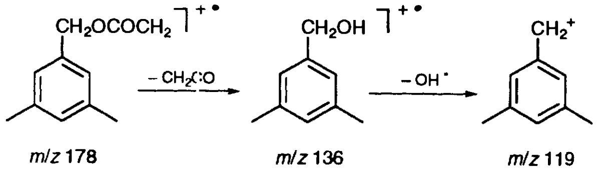
Materials. All the reagents and the solvents were reagent-grade commercial samples. Some products were available from the former study[2] or from previous investigations.[7,24a,25,46]

2-*Acetoxymesitylene.* This compound was obtained from esterification with acetic anhydride of 2,4,6-trimethylphenol (Aldrich). B.p. 118–120 °C at 35 Torr (lit.,[49] 236 °C); $\delta_H(CDCl_3)$ 6.87 (s, 2 H, aromatic protons), 2.33 (s, 3 H, CH_3CO_2), 2.27 (s, 3 H, *p*-Me) and 2.12 (s, 6 H, *o*-Me); *m/z* 178 (M^+, 10), 136 ($M^+ - CH_2CO$, 100), 135 ($M^+ - CH_3CO$, 17), 121 (64) and 119 (2).



(19)

3,5-*Dimethylbenzyl acetate.* This compound was obtained as above from 3,5-dimethylbenzyl alcohol (Aldrich) and $(CH_3CO)_2O$. B.p. 120–122 °C at 37 Torr (lit.,[50] 228–231 °C at 745 Torr); $\delta_H(CDCl_3)$ 6.95 (s, 3 H, aromatic protons), 5.05 (s, 2 H, CH_2OCO), 2.35 (s, 6 H, *m*-Me) and 2.10 (s, 3 H, CH_3CO_2); *m/z* 178 (M^+, 44), 136 ($M^+ - CH_2CO$, 100), 121 (53) and 119 (43).



(20)

1-*Acetoxynaphthalene.* This compound was obtained as above from α-naphthol (C. Erba RPE) and $(CH_3CO)_2O$. B.p. 114–118 °C at 0.5 Torr (lit.,[51] 114–116 °C at 1 Torr). On standing it gave a low melting solid (lit.,[51] m.p. 43–44 °C). $\delta_H(CDCl_3)$ 8.0–7.2 (m, 7 H, aromatic protons) and 2.47 (s, 3 H, CH_3CO_2).

General Procedure.—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) on averaging at least three injections on one or, more frequently, two different columns. The reactivity ratios were calculated from the amounts of products by the use of the standard equation for competitive reactions,[2] taking into account the statistical factors of the substrates. The experiments were at least duplicated.

Experimental details on the iodination methods adopted have been given previously;[2] these were also followed (in particular methods *a* and *d* of ref. 2) in the iodination of the other two pairs of substrates (mesitylene/naphthalene and *m*-/*p*-dimethoxybenzene), however octadecane was used as the internal standard. Typical examples of the other procedures and reactions are given below.

Iodination via *anodic oxidation.* Mesitylene (2.9 mmol) and durene (5.6 mmol) were dissolved in a 3:1 AcOH/CH_3CN mixed solvent (37 cm^3), being 0.1 mol dm^{-3} in Bu_4NBF_4 as the supporting electrolyte, and placed in the anodic compartment of the cell; the Bu_4NBF_4 solution (15 cm^3) was placed in the cathodic compartment. Iodine (1.4 mmol) was then added to the anodic compartment with stirring under argon, and the electrolysis was started at a 100 mA constant current, while the cell was kept at *ca.* 25 °C with an external bath. After 250 Coulomb had been supplied (*ca.* 1 h), the electrolysis was stopped, hexadecane was added and the solution worked up as usual.[2] 2-Iodomesitylene (0.27 mmol) and 3-iododurene (9.6×10^{-3} mmol) were obtained, along with 2,4,5-trimethylbenzyl acetate (0.083 mmol), 2,4,5-trimethylbenzaldehyde (0.02 mmol) and compound **A** (0.19 mmol). The amount of these side-chain derivatives was subtracted from the initial amount of durene for the determination of the relative reactivity.[2]

Iodination by Fenton's reagent. Iodine (0.5 mmol) was dissolved in the '3:1' solvent (13 cm^3) containing durene (4.5 mmol) and mesitylene (2.0 mmol), followed by $FeSO_4$ (139 mg, 0.5 mmol); H_2O_2 (80 mm^3, 1.0 mmol) was then added. After 60 min the reaction mixture was worked up as usual to give 2-iodomesitylene (0.12 mmol), 3-iododurene (3.8×10^{-3} mmol) and 2,4,5-trimethylbenzyl acetate (0.05 mmol).

Iodination via *the mixed anhydride.* Iodine (0.6 mmol) and $(CF_3CO_2)_2Hg$ (0.5 mmol) were dissolved in the 'mixed' solvent (5 cm^3); after 10 min equilibration,[14] they were quickly added to the solution of durene (4.5 mmol) and mesitylene (2.0 mmol) in the same solvent (8 cm^3). The reaction was quenched after 16 min and worked up as usual, to give 2-iodomesitylene (0.47 mmol) and 3-iododurene (1.8×10^{-2} mmol).

Bromination with Br_2. Durene (4.0 mmol) and mesitylene (2.0 mmol) were dissolved in the '3:1' solvent (10 cm^3); a mother solution (3 cm^3) of Br_2 (45 mg, 0.28 mmol) in the same solvent was then added. The reaction was worked up after 4 h, and afforded 2-bromomesitylene (0.25 mmol) and 3-bromodurene (6.3×10^{-3} mmol).

Bromination with CAN. Durene (4.5 mmol) and mesitylene (2.0 mmol) were dissolved in the '3:1' solvent (13 cm^3); CAN (0.51 mmol) and Et_4NBr (0.60 mmol) were then added, and the mixture stirred under argon for 21 h. After work-up, the residue was subjected to exhaustive acetoxylation in boiling AcOK/AcOH and gave 2-bromomesitylene (0.39 mmol), 3-bromodurene (2.3×10^{-2} mmol), 2,4,5-trimethylbenzyl acetate (0.29 mmol) and compound **A** (7.7×10^{-2} mmol).

Bromination with peroxydisulfate. To durene (4.5 mmol) and mesitylene (2.0 mmol) in the 'mixed' solvent (13 cm^3) were added, in order, $Cu(OAc)_2$ (0.58 mmol), Et_4NBr (0.55 mmol) and $(NH_4)_2S_2O_8$ (0.24 mmol). After 23 h, work-up as above gave 2-bromomesitylene (0.44 mmol), 3-bromodurene (3.0×10^{-2} mmol), 2,4,5-trimethylbenzyl acetate (0.14 mmol) and compound **A** (9.1×10^{-3} mmol).

Acetylation. Durene (4.5 mmol) and mesitylene (1.9 mmol) were weighed in the reaction flask. TFA (7 cm^3) and CH_3CN (3 cm^3) were added and the mixture stirred under argon to cause dissolution; H_3PO_4 85% (1.8 mmol) and AcOH (1.5 mmol) were added using microsyringes; finally, TFAA (1 cm^3) in CH_3CN (2 cm^3) was added. After 20 h, 2-acetylmesitylene (0.36 mmol) and 3-acetyldurene (4.4×10^{-2} mmol) were produced.[25]

Mercuriation. Durene (4.9 mmol) and mesitylene (1.6 mmol) were dissolved in the 'mixed' solvent (13 cm^3); $(CF_3CO_2)_2Hg$ (0.45 mmol) was added and the solution stirred under argon for 10 min. Iodine (0.5 mmol) was then added and the mixture stirred for additional 30 min. 2-Iodomesitylene (0.41 mmol) and 3-iododurene (7.8×10^{-2} mmol) were recovered from this iododemercuriation.

Thallation. Durene (4.5 mmol) and mesitylene (1.8 mmol) were weighed in the reaction flask. TFA (8 cm^3), TFAA (2 cm^3) and CH_3CN (3 cm^3) were added and the mixture stirred under argon to cause dissolution; Tl_2O_3 (0.4 mmol) was then added. After 100 min, an excess of KI in H_2O was added to cause iododethallation of the products.[3] 2-Iodomesitylene (2.4×10^{-2} mmol), 3-iododurene (9.1×10^{-3} mmol) and compound **A** (7.9×10^{-2} mmol) were obtained.

Acetoxylation. These reactions were carried out using *ca.* 3 mmol amount of each substrate (either for mesitylene/durene or for mesitylene/naphthalene) in the appropriate solvent (13 cm^3) (see Table 3); the oxidants were either $(NH_4)_2S_2O_8$ (0.9 mmol) with $Cu(OAc)_2$ (1.8 mmol) or CAN (1.4 mmol). The reactions were run under an argon atmosphere and lasted, respectively, 72 h with peroxydisulfate, 18 h with CAN and mesitylene/durene, and 3 h with CAN and mesitylene/naphthalene. When TFA was present in the medium, trifluoroacetoxylated products were also observed,[35] but on exhaustive acetoxylation they were converted into acetoxylated products for GC quantification. With the mesitylene/durene pair we observed only nuclear acetoxylated mesitylene (*ca.* $2\text{–}4 \times 10^{-4}$ mmol) and the benzylic acetate of durene (*ca.* $3.5\text{–}4.0 \times 10^{-2}$ mmol): the retention times were compared with those of authentic benzylic acetate of mesitylene and of nuclear acetoxylated durene, respectively, to check their identity. This was particularly crucial in the case of the product of mesitylene, due to the very small amount obtained and to the similarity of the retention times of the two isomeric acetates (6.8 min benzylic, 6.1 min nuclear). The GC–MS analysis revealed the presence of a significant ion-fragment (*m*/*z* 135) specific to the nuclear isomer, while the ion-fragment *m*/*z* 119, which is much more abundant in the benzylic isomer, was negligible [compare eqns. (19) and (20)]. As to the mesitylene/naphthalene pair, we obtained 2-acetoxymesitylene (7×10^{-3} mmol) and 1-acetoxynaphthalene (0.21 mmol); they were accompanied by 2-nitromesitylene (1.4×10^{-2} mmol) and nitronaphthalene (4.1×10^{-2}; *vide infra*). In the acetoxylation experiments the reactivity ratios were not corrected for statistical factors.

Nitration. Nitration was effected with Bu_3NNO_3 and the two substrates in competition in the indicated solvent (see Table 3), the reaction time was 45 min for mesitylene/durene and 3 h for mesitylene/naphthalene. In the latter case only nuclear nitro derivatives were obtained (1.09 mmol and 0.14 mmol, respectively). With the former pair, 2-nitromesitylene (2.3×10^{-2} mmol) and 3-nitrodurene (1.3×10^{-2} mmol) were accompanied by side-chain nitrodurene (5.2×10^{-2} mmol), 3-acetoxydurene [0.14 mmol; see eqn. (18) in ref. 2 for its formation *via ipso* attack], 2,4,5-trimethylbenzyl acetate (7.9×10^{-2} mmol), 2,4,5-trimethylbenzyl alcohol (6.3×10^{-2} mmol) and compound **A** (*ca.* 1.5×10^{-2} mmol). We can exclude the formation of side-chain nitroderivative of mesitylene. Our GC column, on the contrary, did not resolve α-NO_2- from β-NO_2-naphthalene.

Acknowledgements

Financial support from *Progetto Finalizzato Chimica Fine del CNR* is gratefully acknowledged.

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Paper 4/00027G
Received 15*th January* 1994
Accepted 15*th February* 1994