Aromatic Acylation in Homogeneous Solution and in the Gas-phase: The Mechanistic Relevance of the Mesitylene/Durene Reactivity Ratio
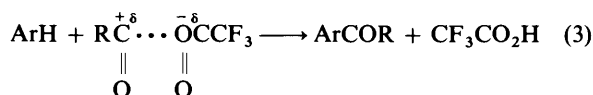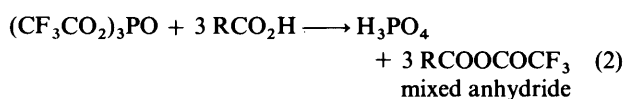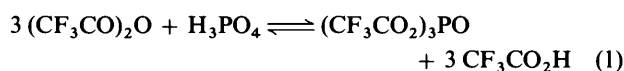
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By means of a mixed acetic–trifluoroacetic anhydride a scale of relative substrate reactivity for aromatic acetylation is obtained, which spans over eight powers of ten from benzene to 2-methylthiophene. Correlation of these reactivity data with relevant substrate parameters is attempted, to gain an understanding of the possible nature of the electrophilic substitution mechanism at work, i.e. either an ionic (two-electron) or a single-electron route. The study includes gas-phase reactivity data on the reaction of free acetylium ion, which has been generated by a radiolytic method. From this comparative approach a 'conventional' ionic mechanism for the aromatic acetylation reaction is substantiated.

Friedel–Crafts electrophilic acylation is a powerful synthetic tool for the functionalization of aromatic compounds.[1] Acyl halides in combination with Lewis acids are the most common reagents used. Unfavourable interference between the Lewis acid and other functional groups already present in the aromatic substrate may impose some limitations on this approach; heterogeneity is another drawback, when one is interested in a meaningful kinetic investigation.
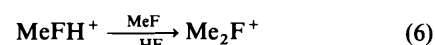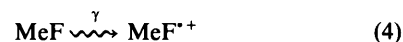
A few years ago a novel Friedel–Crafts acylation reaction was described, which occurs efficiently under very mild homogeneous conditions.[2] Alkanoic acids are used directly without preliminary conversion into the acyl halide: a mixed anhydride is formed in situ from the carboxylic acid and excess trifluoroacetic anhydride under catalysis by phosphoric acid. A possible pathway to the formation of the mixed anhydride has been suggested[3] [eqns. (1)–(3)].

$$3 (CF_3CO)_2O + H_3PO_4 \rightleftharpoons (CF_3CO_2)_3PO$$
$$+ 3 CF_3CO_2H \quad (1)$$

$$(CF_3CO_2)_3PO + 3 RCO_2H \longrightarrow H_3PO_4$$
$$+ 3 RCOOCOCF_3 \quad (2)$$
$$\text{mixed anhydride}$$

$$ArH + R\overset{+\delta}{C} \cdots \overset{-\delta}{O}CCF_3 \longrightarrow ArCOR + CF_3CO_2H \quad (3)$$
$$\qquad\quad \underset{O}{\|} \quad \underset{O}{\|}$$

The mixed anhydride acts as a powerful acylating agent. The simplicity of the procedure, its mild conditions and good yields make this acylation reaction a convenient synthetic choice.[2,4] In addition, the homogeneity of the medium has allowed kinetic studies to be performed.[5]

Recently, electrophilic aromatic substitutions have witnessed a surge of mechanistic interest, with regard to the problem of fixing the boundaries of the conventional ionic mechanism versus an alternative electron-transfer one.[6-9] It seemed of interest to exploit the above acylation reaction for a reactivity study covering a variety of substrates of widely different structure. The goal was to find a property of the substrate (e.g. σ- or π-basicity, ionization potential, or the like) to which more confidently to ascribe the reactivity trend, and possibly be able to single out the nature of the mechanism at work (either ionic or electron transfer).

Last but not least, acylation reactions of aromatic compounds have been studied in the gas-phase by a radiolytic approach, characterized by the use of γ-radiation to generate the ionic species of interest [eqns. (4)–(7)] in a relatively high pressure (ca. 1 atm) medium.[10,11]

$$MeF \overset{\gamma}{\rightsquigarrow} MeF^{\cdot +} \quad (4)$$

$$MeF^{\cdot +} \xrightarrow[-CH_2F]{MeF} MeFH^+ \quad (5)$$

$$MeFH^+ \xrightarrow[-HF]{MeF} Me_2F^+ \quad (6)$$

$$Me_2F^+ + CO \longrightarrow MeCO^+ + MeF \quad (7)$$

$$MeCO^+ + ArH \longrightarrow ArCOMe + H^+ \quad (8)$$

The present study on the reactivity of selected substrates, as determined in solution by means of the mixed anhydride approach, has thus been complemented by the comparison with the gas-phase relative reactivity of a diagnostic pair of aromatics, to gain an understanding on the influence of the environment on the pattern of the acylation process, with specific reference to a possible shift of its mechanism.

Results
The acylation of a number of aromatic substrates has been studied in CH_3CN solutions of acetic acid [eqn. (3), R = CH_3] containing a large excess of $(CF_3CO)_2O$ and a small amount of H_3PO_4 at 50.0 °C.

Kinetic Measurements.—The progress of the reaction was monitored by UV spectroscopy, measuring the increase of the absorption in the 290–295 nm region,[3,5] where the ketone products exhibit useful absorption bands. Pseudo-first-order conditions were adopted, typical concentrations being: [ArH] 6×10^{-4}, [CH_3CO_2H] 4×10^{-5}, [H_3PO_4] 1×10^{-4} and [$(CF_3CO)_2O$] 0.1 mol dm^{-3}. As already observed,[5] the A vs. time profiles showed a short induction period (ca. 10–20%), possibly due to the above mentioned pre-equilibration [eqns. (1) and (2)] required to produce the acetylating species. Such steps are however fast if compared to the subsequent acylation step, as suggested by the fact that, after the inflection point, the

Table 1 Acetylation rate constants in CH_3CN at 50.0 °C

Compound[a]	k/dm^3 mol^{-1} s^{-1}[b]	$\log(k_X/k_H)$[c]	σ^{+}[d]
2MeOT	4.35	1.37	−0.78
2MeT	3.27	1.24	−0.31
3MeT	0.659	0.55	−0.07
2BrT	4.66×10^{-2}	−0.60	0.15
T	0.187	0.00	0.0
Furan	1.68	not included	—
Anisole	6.56×10^{-2}	not included	—

[a] 2MeOT = 2-methoxythiophene; 2MeT and 3MeT = 2-methyl-and 3-methylthiophene, respectively; 2BrT = 2-bromothiophene. [b] From spectrophotometric kinetic determinations; runs in triplicate, average errors 3–6%. [c] Reported in Fig. 1. [d] Of the substituent (see text).

Table 2 Relative reactivity of substrate from competition experiments in CH_3CN at 50 °C[a]

Relative reactivity[b]		Reaction time/min	Conversion[c] (%)
2MeT/T	16.7 + 0.4	10	61 and 4.3
Furan/T	9.10 ± 0.21	10	28 and 3.5
3MeT/T	3.43 ± 0.22	10	31 and 10
T/AN	2.88 ± 0.09	20	13 and 5
T/BT	12.5 ± 0.5	45	18 and 1.7
AN/PMB	18.8 ± 1.3	120	23 and 1.4
PMB/MES	4.45 ± 0.17	180	15 and 3.8
MES/m-XYL	5.40 ± 0.30	180	0.57 and 0.11
MES/DUR	9.90 ± 0.60	180	3.1 and 0.33
DUR/TOL	27.8 ± 2.1	300	0.82 and 0.027
TOL/BEN	102 ± 8	900	0.023 and 0.0003

[a] From GLC analysis. See Table 1 for short-hand notation of compounds; in addition: BT = benzothiophene, PMB = pentamethylbenzene, MES = mesitylene, m-XYL = m-xylene, DUR = durene, TOL = toluene, BEN = benzene. [b] Corrected for the statistical factor of the substrate (see text). [c] With respect to each of the parent substrates.

reaction progressed according to a clean pseudo-first-order behaviour up to ca. 85% conversion. The reported second-order rate constants (Table 1) are the average of at least three measurements and are corrected for the statistical factor of the substrates. Extension of the kinetic study to other substrates was unfortunately prevented by the fact that the absorption bands of their carbonyl groups fall under the absorption band of $(CF_3CO)_2O$. However, the investigation could be expanded by determining relative reactivities in competition experiments.

Competition Experiments.—For experimental convenience these were run under slightly different conditions, namely: [ArH] 0.1, [ArH'] 0.2, [CH_3CO_2H] 0.06, [H_3PO_4] 0.1 and [$(CF_3CO)_2O$] 0.4 mol dm^{-3}, where ArH' represents the less reactive of the two substrates in competition. Both substrates were in excess with respect to the acetylating species. The reactions were run in CH_3CN at 50 ± 1 °C, and the amount of the two ketone products was determined by gas chromatography. The experimental data were treated according to the standard equation[12] for competitive reactions. The relative reactivities obtained (Table 2) derive from at least duplicate experiments and are corrected for the statistical factor of the substrates. Anisole gave only the *para*-acetylated isomer. Only the *para* partial rate factor is given for toluene, since the corresponding product, *i.e.* *para*-methylacetophenone, overwhelmed the *ortho*-isomer at least by a factor of 20:1. In the case of *meta*-xylene, only attack at the 4-position is reported, the 5-position being at least thirty times less reactive. The five-

membered-ring heteroaromatic compounds gave only α-acetylated isomers; benzothiophene (BT), instead, gave only the β-isomer.[5] The reported reactivity of 3-methylthiophene (3MeT) accounts for the overall attack at the α-positions, the two isomeric α-ketones (the 2,3- and the 2,4-isomers) being formed in a 3:1 ratio, respectively. It is reassuring to find that the relative reactivities of: 2MeT vs. T, furan vs. T, 3MeT vs. T and T vs. anisole, as obtained from these competition experiments, are in excellent agreement with the ratios of their absolute rate constants from the direct kinetic experiments (Table 1: relative reactivities of 17.5, 9.0, 3.5 and 2.9, respectively).

From the kinetic competition data, a ladder of relative acetylation rates was derived (Table 3), spanning over eight powers of ten from benzene to the heteroaromatic compounds.

Gas-phase Investigation.—A gas-phase radiolytic study on the reactivity of acetylium ions with several aromatic compounds has already been reported.[13] For the scope of the present work, it was of interest to obtain relative reactivity data from the MES/DUR couple (see Discussion section). The composition of the gaseous reaction mixtures was as follows: MeF (100 Torr)/CO (600 Torr)/O_2 (10 Torr)/MES (1.8 Torr)/DUR (0.40 Torr). The irradiations were carried out in a gamma cell at a total dose of 1×10^4 Gy; under these conditions the aromatic substrates undergo less than 1% conversion into the products, which means that their concentration is effectively constant. The yields of acetylation products gave MES/DUR reactivity ratios of 1.6 (corrected by statistical factors).

The ionic reaction sequences [eqns. (4)–(7)][11] triggered by ionization of the MeF/CO gaseous mixture lead to Me_2F^+, which transfers a methyl cation to CO in a 24 kcal mol^{-1} exothermic process.[14],* The excess internal energy laid on CH_3CO^+ by its formation process is rapidly removed by unreactive collisions with the MeF/CO bulk mixture prior to reaction with the aromatic substrate [ca. 3×10^{-3} mol% in the gaseous mixture; eqn. (8)]. The reliability of the observed substrate reactivity ratio is corroborated by the presence of O_2 (which suppresses possible radical routes to acetylated products) and by its invariance with respect to the addition of a powerful base (Et_3N, 1.8 Torr), which intercepts the acetylated arenium ions by fast deprotonation prior to any conceivable further reactions.

Discussion

Solution Study.—The present acetylation data comprise one of the widest substrate series ever investigated under comparable conditions in an electrophilic aromatic substitution. Previous studies of similar scope were limited to classes of structurally related compounds; for example, the series of polyalkylbenzenes,[15–17] or the set of the five-membered aromatic heterocycles.[18,19] The reactivity interval between thiophene and benzene we obtain (namely, 6.8×10^6) is paralleled only by the data[20,21] for chlorination and bromination reactions, *i.e.* 1.3×10^7 and 1.9×10^9, respectively.

Such an extended set of kinetic data spurs the quest for a correlation in the framework of structure–reactivity analyses. The kinetic data pertaining to the acetylation of substituted thiophenes (Table 1) responds to a Hammett-type[22] treatment. Four of the substrates gave a straight line ($r = 0.987$) with $\rho = -4.0$ (Fig. 1). The highly reactive 2-methoxythiophene deviates strongly from the correlation: it is possible that the formation of the mixed anhydride [eqns. (1) and (2)] becomes

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* 1 cal = 4.184 J.

Table 3 Relative reactivity of acetylation in CH_3CN vs. relevant experimental parameters of the substrates

Compound[a]	Reactivity[b] (k_{rel})	log k_{rel}	log K_B[c]	$E°/V$[d]	GB[e]/ kcal mol^{-1}	vE_i/eV[h]	χ/eV[i]
BEN (1)	1.00	0.0	−9.2	2.9	174.6	9.23	4.1
TOL (2)	$1.0_2 \times 10^2$	2.01	−6.3	2.64	182.0	8.82	3.9
DUR (3)	$2.8_4 \times 10^3$	3.45	−2.2	2.07		8.05	
m-XYL (4)	$5.2_0 \times 10^3$	3.72	−3.2	2.38	188.1	8.56	3.7[j]
MES (5)	$2.8_1 \times 10^4$	4.45	−0.4	2.35	193.6	8.42	3.7
PMB (6)	$1.2_5 \times 10^5$	5.10	0.8	1.99 (1.84)[f]		7.92	
BT (7)	$5.4_1 \times 10^5$	5.73				8.13	
Anisole (8)	2.35×10^6	6.37		(1.96)[f]	192.5	8.39	3.55
T (9)	6.76×10^6	6.83		(1.91)[g]	188.4	8.87	3.8
3MeT (10)	2.32×10^7	7.37					
Furan (11)	6.16×10^7	7.79		(1.70)[g]	185.0	8.89	3.5
2MeT (12)	1.13×10^8	8.05			197.9	8.43	

[a] See Tables 1 and 2 for short-hand notation of the compounds. [b] From competitive experiments (Table 2) and referred to benzene. [c] Sigma basicity as log K_B for protonation in HF; data from ref. 23. [d] In CF_3CO_2H vs. NHE; data from ref. 26. [e] Gas-phase basicity data from ref. 30 [f] Irreversible $E_{\frac{1}{2}}$ value in CH_3CN vs. SCE; data from ref. 25(b). [g] Irreversible $E_{\frac{1}{2}}$ value in AcOH vs. SCE; data from ref. 26(b). [h] Vertical ionization potential from photoelectron spectroscopy; data from ref. 31. [i] Absolute electronegativity; data from ref. 29. [j] From para-isomer.
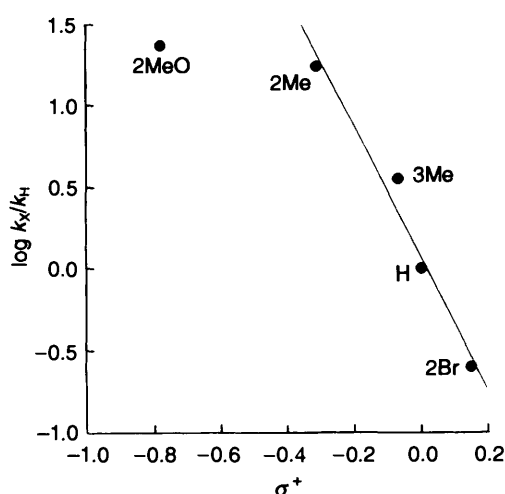

Fig. 1 Correlation of the kinetic data of the acetylation reaction of substituted thiophene derivatives by means of the mixed anhydride (from Table 1) vs. the σ^+ parameter ($\rho = -4.0$; $r = 0.987$)
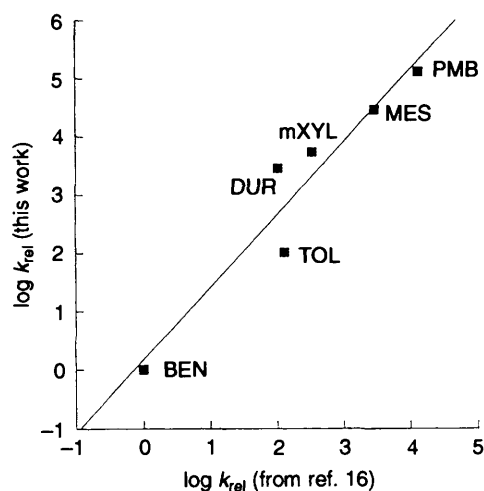

Fig. 2 Comparison of relative reactivity of acetylation from this work vs. the literature data (ref. 16) pertaining to the $AlCl_3$-catalysed reaction of CH_3COCl with the same substrates
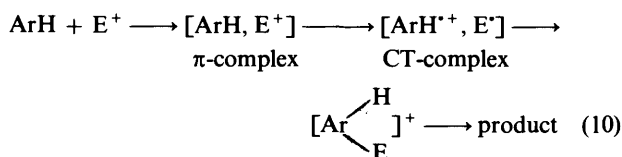
rate determining in this case. The present ρ value can be compared with the reported $\rho = -5.6$ for the $SnCl_4$-catalysed acetylation of the same thiophene derivatives by

Ac_2O in 1,2-dichloroethane at 25 °C.[18] Taking into account the different experimental conditions, the two ρ values can be considered very close. This is indicative of a similar reactive species, more or less 'acetylium-ion-like'. A good agreement is also found with the competitive acetylation data of the polyalkylbenzenes[16] from the $AlCl_3$-catalysed reaction of CH_3COCl in 1,2-dichloroethane at 25 °C. Our acetylation procedure is slightly more selective (Fig. 2, slope = 1.24), but again the consistency in the relative reactivity between the two investigations is likely to be due to the operation of a similar 'acetylium-ion-like' intermediate.

The problem of the 'true' nature of electrophilic aromatic substitution reactions has been the object of much debate[6–9] in recent years, particularly since the proposal of an electron transfer mechanism of substitution in lieu of the 'conventional' ionic mechanism. This subtle controversy may be solved, in principle. In fact, the 'conventional' pathway[1d] [eqn. (9)]

$$ArH + E^+ \longrightarrow [Ar\underset{E}{\overset{H}{\diagdown}}]^+ \longrightarrow ArE + H^+ \quad (9)$$
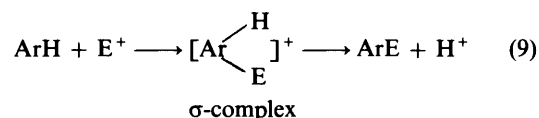
σ-complex

implies a direct relationship between the reactivity of the substrate and the thermodynamic stability of the σ-complex intermediate, which can be approximated by the σ-basicity of the substrate:[23] the more stable the σ-complex, the faster the reaction.[1d,24] The alternative pathway of electrophilic substitution is instead characterized by an electron-transfer step within the π-complex, giving rise to a charge-transfer (CT) complex, which later collapses to the σ-complex.[6,25]

$$ArH + E^+ \longrightarrow [ArH, E^+] \longrightarrow [ArH^{\cdot+}, E^{\cdot}] \longrightarrow$$

π-complex　　　　CT-complex

$$[Ar\underset{E}{\overset{H}{\diagdown}}]^+ \longrightarrow product \quad (10)$$

The TS of the rate-determining step resembles the radical cation of the substrate; consequently, a fit of the reactivity data to a substrate parameter such as the $E°$ value should be expected.

A correlation of the present reactivity data has been attempted with available σ-basicity values[23] (log K_B in Fig. 3, $r = 0.985$) and also with the oxidation potential values[26] ($E°$ in Fig. 4, $r = 0.943$, or 0.891 if the same number of substrates of Fig. 3 is plotted) of the polyalkylbenzenes. It appears that,
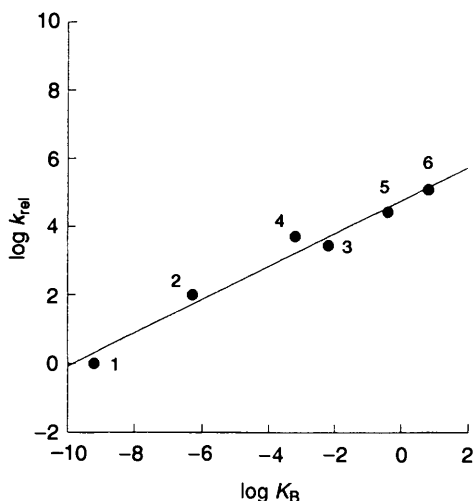
Fig. 3 Relative reactivity of acetylation by means of the mixed anhydride vs. available σ-basicity values of the substrate (log K_B in Table 3; r = 0.985). The aromatic compounds are identified by numbers as indicated in Table 3.
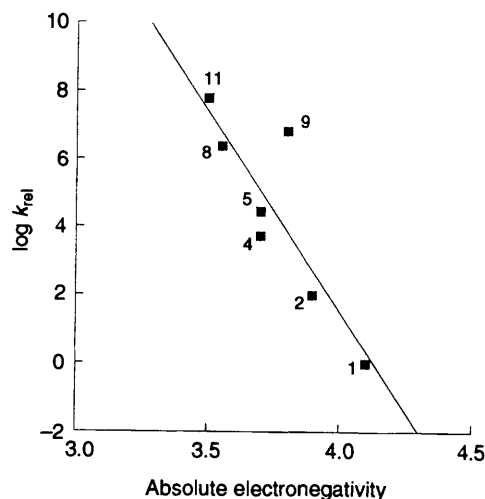

Fig. 5 Relative reactivity of acetylation by means of the mixed anhydride vs. available Pearson's absolute electronegativity values (χ in Table 3; r = 0.865)
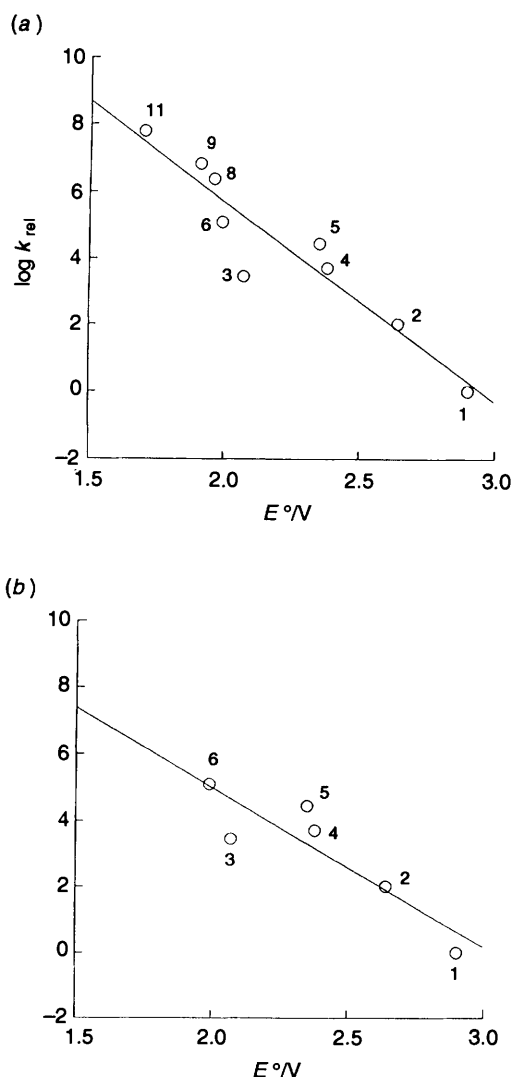

Fig. 4 Relative reactivity of acetylation by means of the mixed anhydride vs. oxidation potential values of the substrate (E° in Table 3). Plot (a), r = 0.943, includes all the substrates whose E° values are available. Plot (b), r = 0.891, is restricted to the substrates which are plotted in Fig. 3.

within this limited number of points, a more satisfactory fit is given by the σ-basicity parameter. No consistent σ-basicity data are available for the heteroaromatic compounds; therefore, it is not possible to ascertain if, on further increasing the nucleophilicity of the substrate (as is the case for the five-membered heteroaromatics), such extended reactivity data would yield a better fit when plotted against E° values or σ-basicities. Unfortunately, the structural factors which increase the stability of the positively charged σ-complex, also increase the ease of oxidation of the molecule to the $ArH^{•+}$ species. Therefore, a linear relationship of the reactivity data to the σ-basicity parameter is not enough, per se, to assess unambiguously the nature of the reaction and the structure of the TS. However, such an ambiguity can be sorted out in the very series of the polyalkylbenzenes,[8] where there are some pairs of substrates for which specific effects lead to significant differences in the prediction of their relative reactivity by the above two parameters. Mesitylene and durene are one such pair. MES is endowed with a higher activation toward electrophilic attack, as predicted by its higher σ-basicity. Conversely, DUR is more easily oxidized to its radical cation. As a consequence, a MES/DUR reactivity ratio larger than 1 becomes evidence of a TS with a σ-complex character, while a TS with a radical-cation character would be associated with a MES/DUR ratio < 1.[8]

The MES/DUR ratio of 9.9 ± 0.6 obtained in the present study sets the acetylation reaction in CH_3CN at 50 °C (Table 2) within the boundaries of the former mechanistic framework; it becomes 14 ± 1 at 25 °C. This figure is comparable with the ratio of 29 from the acetylation work of Marino and Brown,[16] and with the ratio of 11 for the $AlCl_3$-catalysed benzoylation.[17] Hence, all the available values of the MES/DUR ratio from acylation reactions are consistent with each other and are fully in line with other MES/DUR values larger than 1 which have been reported for various 'conventional' electrophilic aromatic substitutions.[8]

Kochi has recently pointed out a flaw[6c] that might undermine the mechanistic significance of the MES/DUR probe. Although the radical cation of durene may form easily, the collapse of the pair [$durene^{•+}$, $E^•$] to the σ-complex would be retarded by unfavourable spin density at the unsubstituted nuclear positions. This could affect its overall reactivity to such an extent as to make it comparable to mesitylene,[6c] for which the collapse at the three-unsubstituted nuclear positions is unimpeded. In apparent agreement with this point, in the mercuration reaction[27] the reactivity of MES, DUR and PMB levels off. However, Kochi's point seems weak and, anyhow,

the case of the mercuration reaction is not general. In fact, MES/DUR ratios large in value have actually been determined for other reactions,[8] for example, 66 in the bromination[24b] and 50 in the iodination reaction;[28] no sign of a levelling effect appeared in these cases. But, even more fittingly, in the present acetylation study, where the MES/DUR ratio is indeed smaller, pentamethylbenzene is still 4.5 times more reactive than MES, and the reactivity continues to increase further along the substrate series by another three powers of ten before showing any levelling or saturation behaviour. Therefore, it seems that the most economical mechanistic formulation of the acylation reaction is one of a 'conventional' electrophilic process, with a σ-complex-like TS.

The absolute electronegativity parameter χ has been recently proposed by Pearson[29] to characterise the reactivity properties of a substrate series better than the existing ones. It is defined as $\chi = (I + A)/2$, where I is the ionization potential and A is the electron affinity of the substrate, and available χ values yield a fair fit with the present acetylation data (Fig. 5). Furan and, with a larger uncertainty, even thiophene, obey this correlation along with anisole and a few polyalkylbenzenes. As pointed out above, the fact that the χ parameter derives from ionization potential and electron affinity values does not mean that an electron transfer step is involved, since those values reflect the gross availability of the π-electron density, which is responsible for the reactivity of both an ionic (two-electron) and a single-electron process.

Gas-phase Study.—The possibility of an electron-transfer mechanism for the electrophilic aromatic substitution reaction [eqn. (10)] is not excluded, in general, in the reaction of more powerful (and oxidizing) electrophiles, such as NO_2^+ or NO^+,[32] particularly with electron-rich substrates.[7] In addition, there are a few examples in the gas-phase[33] where the interaction of an electrophile (*e.g.* NO_2^+) with an aromatic substrate does not proceed by electrophilic addition, but leads rather to charge- or atom-transfer products[34] [eqns. (11) and (12)].

$$ArH + NO_2^+ \longrightarrow ArH^{\cdot+} + NO_2^{\cdot} \quad (11)$$
or
$$ArH + NO_2^+ \longrightarrow ArHO^{\cdot+} + NO^{\cdot} \quad (12)$$

However, such reactivity patterns, observed in ICR studies run in the 10^{-5} Torr pressure range, should be regarded with extreme caution if one seeks a correspondence with related processes occurring in solution.[10] In the ICR low pressure conditions, the NO_2^+/aromatic molecule interaction takes place under a single collision regime. Thermalisation of the ion-molecule pair (which contains excess internal energy owing to the electrostatic interaction of the partners) being prevented by the low collisional frequency, their reaction(s) may proceed by high energy pathways hardly comparable to the ground state routes followed in solution. In this respect, gas-phase studies become significant when carried out at relatively high pressures, so as to ensure efficient deactivation of 'hot' intermediates.[10] In line with this reasoning, the gas-phase work of Cacace *et al.*,[35] run under chemical ionization conditions with 0.1 Torr CH_4 as the bulk gas, has shown that protonated methyl nitrate, $MeO(H)NO_2^+$, reacting with aromatic substrates, gives nitrated adducts and not just charge-transfer products. Protonated methyl nitrate may be viewed as a NO_2^+ ion internally solvated by a methanol molecule and this fact, together with enhanced collisional deactivation, renders the electrophilic addition by far the prevailing pathway. At the still higher pressure (*ca.* 1 atm) allowed by the radiolytic technique, nitrated substitution products have been obtained, showing selectivity patterns modulated by the 'normal' electronic effects of the substituents on the aromatic ring.[35]

We deemed it interesting to explore the behaviour of the acetylium ion, generated in the gas-phase at *ca.* 1 atm according to eqns. (4)–(7), toward MES and DUR, viewing the possibility of a shift towards an electron-transfer mechanism in the reaction of this free ion. In fact the known ionisation potential (E_i) values, which strictly refer to gaseous isolated species, predict that the acetyl cation $[E_i(CH_3CO^{\cdot}) = 8.05 \pm 0.17$ eV][14a] may undergo approximately thermoneutral electron transfer with DUR $[E_i(\text{durene}) = 8.05 \pm 0.01$ eV],[31a] whereas electron transfer is not feasible in the case of MES $[E_i(\text{mesitylene}) = 8.42 \pm 0.01$ eV].[31a] Therefore, the reactivity of DUR towards the acetylium ion should be enhanced if it were to result from a primary charge-transfer interaction. At variance with this expectation, a MES/DUR reactivity ratio of 1.6 (significantly greater than 1 by gas-phase reactivity standards) was obtained, suggesting that the charge-transfer/radical pair collapse pathway to aromatic substitution reaction is not operative in the present case. The MES/DUR relative reactivity towards free CH_3CO^+ ions fits into the general reactivity ladder of the methylbenzenes, showing toluene as the least reactive (no acetylation products formed), followed by the xylenes, in the order: toluene $\ll$ *p*-xylene (0.01) < *o*-xylene (0.05) < *m*-xylene (0.20) < mesitylene (1.00).[13] Thus, all the available data concur in showing a reactivity pattern conforming to 'normal' electrophilic aromatic substitution reactions *via* σ-complex intermediates, whose formation does not imply a kinetically significant electron transfer step. This same conclusion emerges both from the homogeneous acetylation by mixed anhydrides in CH_3CN solution and from the gas-phase reaction of free acetylium ions.[36]

Experimental

Instrumentation.—Rate measurements were carried out on a Beckman DB GT spectrophotometer fitted with thermostatted cell compartment. GLC analyses were performed on a Varian VISTA 6000 instrument, fitted with a 2 m × 0.4 mm OV-101 packed column. GC–MS analyses were run on a HP 5890 gas chromatograph equipped with a 12 m × 0.2 mm methyl silicone gum capillary column, coupled to a HP 5970 mass selective detector. A 220 Gammacell (Nuclear Canada Ltd.) was employed for the radiolysis experiments.

Materials.—All the substrates were reagent grade commercial samples: purification by distillation was judged necessary in a few cases. Acetonitrile was distilled from P_2O_5. Trifluoroacetic anhydride (Merck, 99%) was used as received. Most of the acetylated products, to be used as gas chromatographic standards, were commercial samples; other samples were available from a previous investigation;[2] 3-acetylbenzothiophene was synthesized from benzothiophene according to the above procedure.[2]

Rate Measurements.—The kinetic technique has been already described.[3,5] Owing to the instability of the A_∞ readings,[3] the experimental data were treated according to the method of Guggenheim.[12]

Competition Experiments.—The reaction mixture of the two substrates, in competition for the acetylating species, was quenched with water after a suitable time, the internal standard (heptadecane) was added and the mixture worked up with diethyl ether. GLC allowed the quantitative determination of the relative amounts of the two reaction products; authentic samples of the products were employed for the determination of the response factors.

Radiolytic Experiments.—Gaseous samples were prepared in sealed Pyrex vessels by standard vacuum techniques.[13] The

irradiations were carried out at 37 °C. The irradiated vessel was then frozen to liquid nitrogen temperature, opened under air-tight conditions and rinsed with a diethyl ether solution of the internal standard. An ethereal solution was recovered, containing the acetylation products and unreacted substrates, which was analysed by GC–MS.

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