Gas-phase Methylation of Phenol and Anisole by $CH_3XCH_3^+$ (X = F, Cl, or Br) Ions

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Dimethylhalogenonium ions $CH_3XCH_3^+$ (X = F, Cl, or Br), obtained in the dilute gas state from the γ-radiolysis of the corresponding methyl halide CH_3X, were allowed to react with representative ambident substrates, such as phenol and anisole, either neat or in competition with benzene, in the pressure range 100—760 Torr, and in the presence of a gaseous base (NH_3). The competition between the *n*- and π-type nucleophilic centres of phenol is kinetically biased in favour of *O*-methylation, leading to the predominant ($CH_3FCH_3^+$ 6 : 1; $CH_3ClCH_3^+$ 5 : 1; $CH_3BrCH_3^+$ 4 : 1) formation of anisole with respect to cresols under conditions, *i.e.* high CH_3X pressure and in the presence of NH_3, which favour kinetic control of the products. For ring methylation, both the selected substrates undergo preferential substitution at the *ortho*- and *para*-positions. In general, *ortho*-attack is favoured at low pressure and in the absence of NH_3. The results of competition experiments show that phenol (S) reacts faster than benzene (B) with gaseous $CH_3XCH_3^+$, the substrate selectivity of the electrophile increasing in the order $CH_3FCH_3^+$ (k_S/k_B 2.0) < $CH_3ClCH_3^+$ (k_S/k_B 13.8) < $CH_3BrCH_3^+$ (k_S/k_B 40.9). The same conclusion cannot be reached for anisole because of the occurrence of extensive *O*-methylation with formation of dimethylphenyloxonium ion, which turns out to be very stable under the conditions used. The results are consistent with a model involving kinetically predominant attack on the oxygen atom of the ambident substrate, which, in the case of $CH_3FCH_3^+$ ion, can be preceded by an extensive electrostatic interaction with formation of a ' chelated ' complex. The same interaction helps also explaining the relatively high reactivity of the ring position *ortho* to the *n*-donor substituent, observed at low pressure. The substrate and positional selectivity of the $CH_3XCH_3^+$ ions toward ambident compounds is discussed and compared with related gas-phase results and with conventional Friedel–Crafts methylation data.

THE general features of the electrophilic methylation of pure *n*- and π-type substrates by free dimethylhalogenonium $CH_3XCH_3^+$ (X = F, Cl, or Br) ions in the dilute gas state have recently been investigated.[1] Rather indiscriminate reactivity of the $CH_3FCH_3^+$ ion toward both classes of nucleophiles has been observed, which contrasts with the marked affinity of $CH_3ClCH_3^+$ and $CH_3BrCH_3^+$ ions to *n*-type centres. Such remarkably different behaviour has been linked to the intrinsic electronic and structural features of the electrophile, whose selectivity appears to increase significantly with the sp^3 character of the carbon atom of the methyl groups, in the order $CH_3FCH_3^+ < CH_3ClCH_3^+ < CH_3BrCH_3^+$.

With a view to corroborating the validity of this relationship, this investigation has been extended to the determination of the reactivity pattern of the $CH_3XCH_3^+$ ions toward substrates, such as phenol and anisole, containing both *n*- and π-type nucleophilic sites. It was expected that this study would also contribute to the assessment of the intrinsic reactivity scale of the nucleophilic centres of the representative ambident compounds toward charged methylating reactants, such as $CH_3XCH_3^+$ ions, which are known to be involved in Friedel–Crafts methylation reactions by methyl halides.[2] Despite extensive kinetic [3] and spectroscopic [4] investigations of the topic, the inherent selectivity of the methylating species towards the nucleophilic sites of phenol and anisole is still undetermined. Most of the difficulties encountered in these studies arise from the fact that the intrinsic reactivity of a particular reaction site of an ambident compound toward a given reactant is not only dependent on the electronic state and the structural parameters of the rest of the molecule, but it can be also significantly modified by the specific interactions (solvation, ion pairing, *etc.*) established between the reaction site, or the ionic reactant, and the environment, whose presence precludes any attempt of data generalization concerning a particular process which leaves the specific reaction medium out of consideration.[5]

This paper deals with the intrinsic reactivity order and directive properties of phenol and anisole toward a well defined methylating reactant, the $CH_3XCH_3^+$ ion, generated in the dilute gas state, *i.e.* in the absence of complicating environmental effects, by γ-radiolysis of the parent neutral methyl halide CH_3X (X = F, Cl, or Br).

Previously discussed considerations concerning the nature of gas-phase methylation apply to this study as well, which traces the formation of the neutral methylated products essentially to the reaction of the selected ambident substrates with dimethylhalogenonium ions.

EXPERIMENTAL

Materials.—Methyl halides, oxygen, and ammonia were high purity gases from Matheson, used without further purification. Merck and Fluka provided all the reagent grade chemicals used as starting substrates and as reference compounds in g.l.c. analysis. Phenol, anisole, and benzene were purified by preparative g.l.c. immediately before use. Their purity, with special regard to the absence of methylated derivatives, was checked by g.l.c. on the same columns employed for the analysis of irradiated mixtures.

Sample Preparation and Irradiation.—The experimental techniques used for the preparation of the samples and their irradiation have been described previously.[1] The radiation dose, as measured with a Fricke dosimeter, was 4.8 Mrad, delivered at rate of 0.35 Mrad h^{-1} at 37.5 °C, in a ^{60}Co Gammacell (Atomic Energy Canada Ltd.). Control experiments at higher doses showed that the *relative* yields of products and their isomeric composition are largely independent of the dose, at least up to *ca.* 14 Mrad.

Product Analysis.—Analysis of the products was performed by injecting measured portions of the reaction mixture into a Hewlett–Packard model 5700 A gas chromatograph, equipped with a flame-ionization detection unit. The products were identified by comparison of their retention volumes, on at least two different columns, with those of authentic samples. Individual calibration curves for the detector response were determined to measure the yields of each product. The identity of the products were further confirmed by g.l.c.–m.s., using a Micromass VG 7070 mass spectrometer.

Some irradiations were carried out on mixtures containing methoxy[^{14}C]benzene, as the substrate. Methoxy[^{14}C]benzene was prepared in good yield by methylating phenol with $^{14}CH_3I$ (0.5 mCi, 0.35 mCi mmol^{-1}; Amersham Radiochemical Centre) in the presence of silver oxide. The recovered radioactive product was purified by preparative g.l.c. and the specific activity of the anisole obtained (0.2 mCi mmol^{-1}) measured by liquid scintillation counting (Mark II; Nuclear Chicago Division). The actual position of the ^{14}C label in either the radioactive anisole, before irradiation, and its methylated derivatives, recovered in the irradiated mixtures, was checked by acid cleavage (56% HI) of the CH_3–O bond of the methoxy-benzene (or -toluene) with formation of the corresponding hydroxyaromatic compound. Comparison of the specific activity of the phenol obtained with that of its ether precursor gives an accurate estimate of the percentage ^{14}C contained in the methyl group of the corresponding anisole.

RESULTS

The irradiation of the gaseous CH_3X in the presence of the selected substrates and O_2, used as a thermal radical scavenger, yields the corresponding methylated products, namely anisole and cresols from phenol, and methylanisoles from anisole. Their overall absolute yields (G_M value) and isomeric composition have been measured under various experimental conditions and are reported in Tables 1 and 2, along with the composition of the system. The results of the competitive experiments, carried out using benzene (B) as the reference substrate, are shown in Table 3, which gives the apparent substrate (k_S/k_B values) and positional selectivity of each of the $CH_3XCH_3^+$ ions considered. The data represent the mean of at least three runs and are affected by a standard deviation of *ca.* 10%. Comparison of the G_M values of Tables 1 and 2 with those concerning previous investigation in related systems [1] indicates that methylation of the selected substrates represents the major reaction channel available to the ionic species from the radiolysis of methyl halides. This view is further confirmed by the relative distribution of the irradiation products, of which >70% is accounted for by the methylated substrate(s). A sharp decrease in the G_M values is observed when ammonia, an efficient ion trapper, is added to the system (with a 4 Torr NH_3 partial pressure, the overall absolute yield of the methylated products is depressed by a factor >4), confirming the ionic nature of the methylating reactant.[6]

The major features of the gas-phase methylation of the selected substrates can be summarized as follows. As indicated by the apparent k_S/k_B ratios of Table 3, phenol is more reactive than benzene toward each individual $CH_3XCH_3^+$ ion. The substrate selectivity of $CH_3XCH_3^+$ species toward this pair of compounds measured under kinetically controlled conditions, *i.e.* at high pressure and in the presence of NH_3, increases in the order $CH_3FCH_3^+$ (k_S/k_B 2.01) < $CH_3ClCH_3^+$ (k_S/k_B 13.8) < $CH_3BrCH_3^+$ (k_S/k_B 40.9). Much less straightforward are the data concerning the anisole–benzene systems, since the intermolecular selectivity of $CH_3XCH_3^+$ toward this pair seems to increase in the order $CH_3BrCH_3^+ < CH_3ClCH_3^+ \simeq CH_3FCH_3^+$. In addition, while the reactivity order of the anisole–benzene pair toward $CH_3BrCH_3^+$ (k_S/k_B 2.02) and $CH_3ClCH_3^+$ (k_S/k_B 5.63) is consistent with the typical pattern of the classical electrophilic substitutions, an apparently ***reverse*** substrate selectivity is observed for the $CH_3FCH_3^+$ ion in these systems (k_S/k_B 0.25). In general, the apparent reactivity ratios measured from the competition experiments significantly increase in the absence of NH_3 the minor variations being observed in the CH_3F systems.

O-Methylation of phenol predominates under all experimental conditions, exceeding ring substitution by a factor >2 (Table 1). The *O- versus* ring-methylation ratios appear to be appreciably dependent on the experimental conditions. In the $CH_3FCH_3^+$ case, *O*-methylation increases at high

TABLE 1

Product yields from the gas-phase attack of $CH_3XCH_3^+$ (X = F, Cl, or Br) ions on phenol

System composition [a]				Product distribution (%)				Total absolute yield (G_M) [b]
					Cresol			
Substrate (Torr)	X	CH_3X (Torr)	NH_3 (Torr)	Anisole	*ortho*	*meta*	*para*	
0.6	F	760	4	85.7	3.2	3.7	7.3	0.21
0.3	F	760		83.4	6.7	1.7	8.2	0.87
0.4	F	300		78.0	14.7	2.4	4.9	0.71
0.4	F	100		73.6	22.6	1.4	2.4	0.88
0.5	Cl	760	4	82.4	2.0	1.4	13.3	0.05
0.5	Cl	760		84.5	6.0	n.d. [c]	9.5	0.49
0.3	Cl	300		84.3	15.7	n.d.	n.d.	0.52
0.3	Cl	100		83.3	16.6	n.d.	n.d.	0.12
0.5	Br	760	4	79.1	5.6	4.7	10.6	0.01
0.5	Br	760		89.2	3.2	2.6	4.9	0.78
0.4	Br	300		92.2	5.2	1.1	1.5	0.61
0.5	Br	100		98.8	1.2	n.d.	n.d.	0.34

[a] O_2 4 Torr. Radiation dose 4.8 Mrad (dose rate 0.35 Mrad h^{-1}). [b] G_M as the number of molecules produced per 100 eV of absorbed energy. Standard deviation of data *ca.* 10%. [c] n.d. = not detectable ($G_M < 1 \times 10^{-4}$).

TABLE 2

Product yields from the gas-phase attack of $CH_3XCH_3^+$ (X = F, Cl, or Br) ions on anisole

System composition [a]				Product distribution (%)			Total absolute yield
Substrate (Torr)	X	CH_3X (Torr)	NH_3 (Torr)	Methylanisole *ortho*	*meta*	*para*	(G_M) [b]
0.7	F	760	4	66.0	12.0	22.0	0.13
0.6	F	760	2	59.1	9.6	31.2	0.34
0.7	F	760		59.5	8.1	32.4	0.74
0.4	F	300		60.0	10.0	30.0	0.50
0.2	F	100		60.6	6.6	32.8	0.54
0.4	Cl	760	4	58.3	7.9	33.8	0.002
0.5	Cl	760	2	57.0	8.5	34.5	0.04
0.7	Cl	760		76.9	n.d.[c]	23.1	0.16
0.4	Cl	300		77.2	3.8	19.0	0.21
0.7	Cl	100		79.3	8.8	11.9	0.08
0.4	Br	760	4	50.0	18.8	31.2	0.003
0.7	Br	760	2	52.3	17.0	30.7	0.04
0.9	Br	760		61.8	12.9	25.3	0.08
0.5	Br	300		64.3	19.0	16.7	0.14
0.8	Br	100		63.8	20.5	15.7	0.10

[a-c] See Table 1.

pressure and in the presence of NH_3. The reverse is true for the $CH_3BrCH_3^+$ ion, whereas in the CH_3Cl systems variations of the *O- versus* ring-methylation ratio with the irradiation conditions fall within the experimental uncertainty. Concerning ring methylation, both phenol and anisole undergo preferential substitution at the *ortho-* and *para-*positions (Tables 1 and 2). In general, *ortho-*attack is favoured at lower pressures and in the absence of NH_3.

TABLE 3

Competitive experiments

System composition [a]					Product distribution (%)	Ring methylated substrate			
Substrate S (Torr)	Benzene (Torr)	X	CH_3X (Torr)	NH_3 (Torr)	Anisole	*ortho*	*meta*	*para*	$k_S/k_{B_{app}}$ [b]
Phenol, 0.4	0.4	F	760	4	71.5	7.6	3.3	17.6	2.01
Phenol, 0.4	0.4	F	760		71.3	2.6	2.3	23.8	2.42
Phenol, 0.4	0.4	Cl	760	4	68.3	12.6	2.6	16.5	13.8
Phenol, 0.5	0.5	Cl	760		63.9	15.2	4.3	16.5	42.3
Phenol, 0.4	0.4	Br	760	4	69.6	7.4	3.6	19.4	40.9
Phenol, 0.4	0.4	Br	760		65.6	8.2	6.4	19.8	321.3
Anisole, 0.4	0.4	F	760	4		57.9	10.5	31.6	0.25
Anisole, 0.6	0.6	F	760			27.4	19.6	53.0	0.60
Anisole, 0.4	0.4	Cl	760	4		56.4	7.2	36.4	5.63
Anisole, 0.5	0.5	Cl	760			46.2	7.5	46.3	21.4
Anisole, 0.4	0.5	Br	760	4		56.0	8.0	36.0	2.02
Anisole, 0.6	0.6	Br	760			39.8	10.2	50.0	5.28

[a] See footnote *a* of Table 1. [b] $k_S/k_{B_{app}}$ = [MeS][B]/[MeB][S]. Standard deviations of the $k_S/k_{B_{app}}$ ratios, *ca.* 20%.

When submitted to methylation by each individual $CH_3XCH_3^+$ species under different conditions (100—760 Torr CH_3X partial pressure), methoxy[^{14}C]benzene gives the isomeric ring methylated derivatives. By degradation with HI, each [^{14}C]methylanisole formed gives the corresponding cresol. The most significant result of these experiments was the conspicuous absence of ^{14}C in the cresol examined, which is therefore thought to arise from a [^{14}C]-methylanisole, wherein the ^{14}C label is maintained at the position originally occupied (the methoxy-group) in the parent anisole.

DISCUSSION

The electrophile used in the present study is the gaseous $CH_3XCH_3^+$ ion, formed in high yields from the γ-radiolysis of the corresponding methyl halide and thermolysed by a large number of unreactive collisions with the parent molecules, as discussed in detail in the previous paper.[1,7] Methyl transfer from $CH_3XCH_3^+$ to the selected substrates is an energetically allowed process (Table 4) and represents the only significant reaction channel available to the $CH_3XCH_3^+$ species.[6] Hence, the reactivity ratios established by the competition experiments of Table 3 provide a good measure of the apparent overall nucleophilicity of the substrates considered.

Any reaction scheme for gas-phase attack of the CH_3X-CH_3^+ ion on the selected ambident substrates should account for the relatively high extent of *O*-methylation, observed for phenol under all experimental conditions, and the isomeric composition of the ring methylated products, which follows the typical *ortho–para-*distribution of classical electrophilic substitutions.

It is, therefore, suggested that the methylation mechanism occurring in the irradiated systems involves competitive attack of the dimethylhalogenonium ion on the *n-* and π-type centres of the ambident substrate, giving respectively the corresponding methylphenyloxonium ion [I] and the isomeric arenium ions [II], excited by the exothermicity of the reaction [equation (1)]. Collisional stabilization of the methylated intermediates

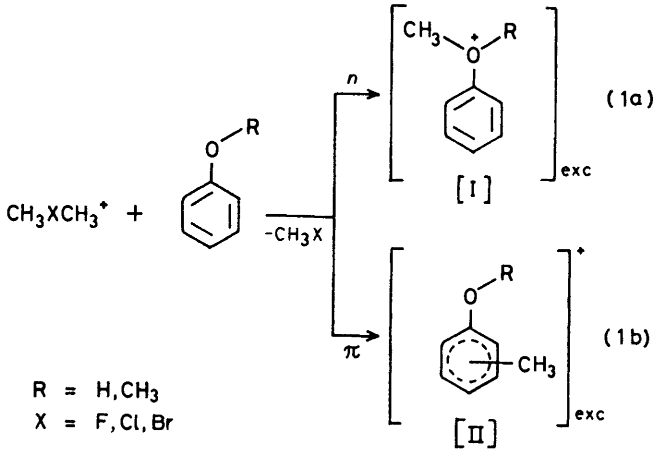
TABLE 4

Methyl cation affinities of various species [a]

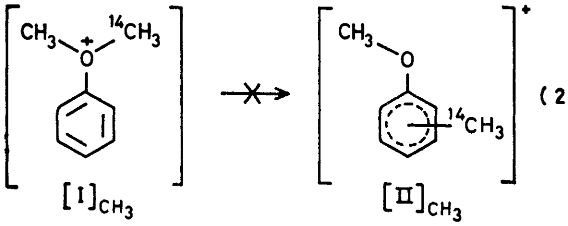
Species	Methyl cation affinities (kcal mol^{-1})	Reference
CH_3F	44 ± 8	8
CH_3Cl	⩾51	8
CH_3Br	⩾56	8
CH_3OH	82	1
C_6H_6	88	1
C_6H_5OH (ring)	~99	*b*
C_6H_5OH (oxygen)	~82	*c*
$C_6H_5OCH_3$ (ring)	~107	*b*
NH_3	102	1

[a] As defined in ref. 8. [b] Calculated using ΔH_f^0 139 kcal mol^{-1}, for the 4-protonated *p*-cresol, and 142 kcal mol^{-1}, for the 4-protonated *p*-methylanisole (J. L. Devlin, III, J. F. Wolf, R. W. Taft, and W. J. Hehre, *J. Am. Chem. Soc.*, 1976, **98**, 1990; Y. K. Lau and P. Kebarle, *ibid.*, p. 7452). [c] Calculated using ΔH_f^0 156 kcal mol^{-1} for the oxygen-protonated anisole (J. Catalan and M. Yanez, *J. Am. Chem. Soc.*, 1979, **101**, 3490).

[I] and [II], followed, when possible, by proton transfer to a gaseous base (*e.g.* the substrate itself, ammonia, *etc.*) provides a direct route to the methylated substrate.*



In contrast to the oxonium ion [I] from $CH_3XCH_3^+$ ion attack on the oxygen of phenol, dimethylphenyloxonium ion from methylation of anisole cannot collapse into isolable alkylated products without preliminary isomerization to an arenium ion. In this case, however, owing to its symmetry, the dimethylphenyloxonium ion would transfer either of its methyl groups at the same rate, irrespective of their origin. This possibility has been checked by using methoxy[^{14}C]benzene, as the substrate. The fact that no $^{14}CH_3$ group migration to the aromatic ring of the substrate was observed under very different experimental conditions indicates that the intra- or inter-molecular isomerization reaction (2), even though thermodynamically favoured,[9] does not occur to any appreciable extent, and that, therefore, the oxonium ion $[I]_{CH_3}$ is a stable species under the experimental conditions used.



Exclusive ring methylation [equation (1b)] in the case of anisole could represent an alternative explanation for the [^{14}C]anisole behaviour, which however contrasts with the predominant *O*-substitution typical of phenol, and with the comparable affinity of the oxygen atom of anisole and phenol toward positive ions.[9,10]

An estimate of the significance of these two mechanistic hypotheses, as a function of the nature of the $CH_3XCH_3^+$ ions, can be inferred from a comparison of the overall G_M values of the methylated derivatives of phenol (Table 1) and anisole (Table 2) from the same CH_3X system.

Taking into account the low concentration of the ambident substrate in each system, and the high efficiency of the ionic processes leading to $CH_3XCH_3^+$ from the primary ions generated by radiolysis of CH_3X,[8,11] the $G_{CH_3XCH_3^+}$ values for each individual system are expected to be approximately the same in both phenol and anisole experiments.

In spite of this, the overall product yields from methylation of anisole (G^{A}_{M}; Table 2) turn out to be substantially lower than those of the corresponding methylation of phenol (G^{P}_{M}; Table 1) in either the $CH_3BrCH_3^+$ ($G^{P}_{M}/G^{A}_{M} = 3$—10) and $CH_3ClCH_3^+$ ($G^{P}_{M}/G^{A}_{M} = 1.5$—$25$) systems. This argument rules out the hypothesis of an anisole methylation mechanism involving exclusive attack of the $CH_3XCH_3^+$ ions on the substrate ring, in favour of the alternative path thought as proceeding predominantly *via* *O*-methylation [equation (1a)] with formation of the very stable intermediate $[I]_{CH_3}$ [equation (2)]. Then predominance of the non-productive step (1a) in the methylation of anisole is further supported by the fact that, under conditions favouring kinetic control of products (high pressure, presence of NH_3), the G^{A}_{M} values (Table 2) are quite comparable with the ring methylation product yields from phenol ($G^{P}_{\mathrm{ring}} = G^{P}_{M} \times \%_{\mathrm{ring}}/100$; from Table 1) in both $CH_3BrCH_3^+$ ($G^{P}_{\mathrm{ring}}/G^{A}_{M} = 0.7$—$1.0$) and $CH_3ClCH_3^+$ ($G^{P}_{\mathrm{ring}}/G^{A}_{M} = 0.5$—$4.4$) systems. It can therefore be concluded that the total product yields from $CH_3XCH_3^+$ (X = Cl or Br) methylation of anisole (G^{A}_{M}) involve exclusively process (1b), while the competing path (1a) leads to a very stable intermediate $[I]_{CH_3}$ [equation (2)], which, under the irradiation conditions, does not further isomerize to any isolable methylated derivative (*e.g.* $[II]_{CH_3}$), as demonstrated by the [^{14}C] methyl anisole experiments.

As to the $CH_3FCH_3^+$ methylation pattern, the product yields from anisole are only slightly lower than those from phenol measured under the same conditions ($G^{P}_{M}/G^{A}_{M} = 1.2$—$1.6$). Furthermore, in this case, the G^{A}_{M} values (Table 2) do not match with the corresponding G^{P}_{ring} figures calculated from Table 1, at high pressure and in the presence of NH_3 ($G^{P}_{\mathrm{ring}}/G^{A}_{M} = 0.03$—$0.6$). This evidence confirms the peculiar behaviour of $CH_3FCH_3^+$ among the dimethylhalogenonium ions and is suggestive of an additional step in the general methylation mechanism which becomes apparent only in the case of this reactant ion.

In many gas-phase electrophilic aromatic alkylations, direct evidence does exist in favour of a mechanism involving preliminary electrostatic ' chelation ' of the gaseous ionic electrophile between the *n*- and π-type nucleophilic sites of an ambident substrate, when the positive ion is characterized by a high degree of charge delocalization on its hydrogen atoms.[9,10f,12] In some cases, the ' chelated ' complex is stable enough to sur-

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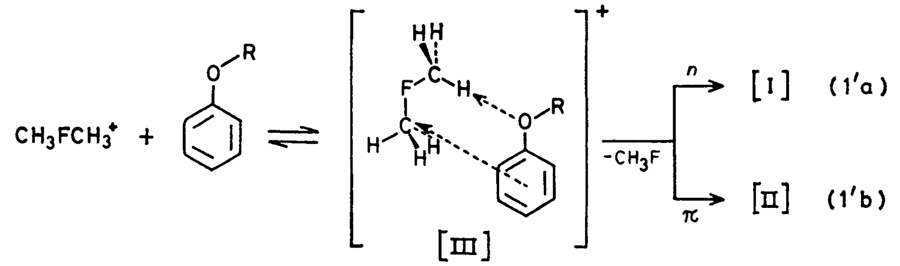
* Other gaseous bases available to the intermediates [I] and [II], could be formed from the γ-radiolysis of the batch gas. The basic centres of the glass walls of the bulb can behave as good proton acceptors as well.

vive many unreactive collisions at atmospheric pressure.[12b]

In the dimethylhalogenium ion series, the $CH_3FCH_3^+$ ion possesses the maximum degree of charge delocalization on its methyl groups and, therefore, it best fulfils all the requirements for a ' chelating ' species.

We are inclined to include a preliminary adduct formation step (1′) in the methylation process of the ambident substrate, whose occurrence could accommodate the discrepancies observed in the $CH_3FCH_3^+$ case. In fact, according to this view, the reactivity of phenol and anisole toward $CH_3FCH_3^+$ is mainly determined by the rate of formation of the ' chelated ' adduct [III] and, therefore, it is expected to be essentially the same for both substrates, on account of their comparable ability in establishing electrostatic interactions with positively charged species.[9,10]



On the other hand, the regioselectivity of electrophilic substitution involving complex [III] is controlled by the subsequent conversion of the ' chelated ' adduct into the oxonium ion [I] or the arenium ion [II]. Since this does not necessarily involve breaking of the electrostatic interaction in [III], formation of both the oxonium [I] and the *ortho*-methylated arenium [II] is favoured over the other conceivable reaction paths. Thus, at high pressures, when adduct [III] is readily deactivated by collisional quenching with the batch molecules, the low-energy *O*-methylation path predominates over the competitive high-energy *ortho*-methylation by the other CH_3 group of $CH_3FCH_3^+$, which instead becomes possible at lower pressures.*

In the case of phenol, *O*-methylation from [III] can be promoted by rapid proton transfer from the oxygen to the ring of a substrate molecule or to some other acceptor, as demonstrated by the increased relative yield of anisole measured in the presence of NH_3. A similar process cannot occur in the anisole systems, on account of the comparatively low mobility of the methyl group of the substrate, which therefore favours the occurrence of the competitive ring-methylation path (1′b).

The overall $CH_3FCH_3^+$ methylation yield, however, should be mostly related to the efficiency of adduct [III] formation, which is expected and found to be approximately the same for both substrates.

An effective electrostatic interaction similar to that of the adduct [III] seems less probable for the $CH_3ClCH_3^+$ and $CH_3BrCH_3^+$ ions, since most of their charge is located on the halogen atom and, therefore, their ' chelating ' properties are much less pronounced. Rather, a direct attack on the nucleophilic sites of the substrate takes place [equations (1a and b)]. In this case, methylation of the *n*-centre of anisole gives $[I]_{CH_3}$, which is so stable that it acts as a non-productive $CH_3ClCH_3^+$ or $CH_3BrCH_3^+$ ion sink. Finally, the increased relative yields of *O*- and *ortho*-methylated derivatives of phenol and anisole observed at low CH_3Cl and CH_3Br partial pressures, *i.e.* under conditions which should favour formation of the thermodynamically more stable *meta*-isomer, suggests that the (1b) step might be reversible.

From the above considerations, it appears that the phenol : benzene reactivity ratios (Table 3), measured under kinetically controlled conditions, *i.e.* in the presence of NH_3, can be regarded as a measure of the *intrinsic* overall nucleophilicity of phenol toward gaseous $CH_3XCH_3^+$ ions. The rather unselective behaviour of $CH_3FCH_3^+$ toward different classes of nucleophilic substrates is confirmed by the relatively small values of the k_S/k_B ratios (*ca.* 2). Besides, if the isomeric distribution of the methylated derivatives of phenol is taken into account, the competitive results indicate no appreciable selectivity of $CH_3FCH_3^+$ between the aromatic ring of benzene and that of phenol, although activated by an OH group. The sharp discriminating power between *n*- and π-type nucleophilic centres, previously observed for $CH_3ClCH_3^+$ and $CH_3BrCH_3^+$,[1] is supported by the present competitive experiments as well. Thus the oxygen of phenol is *ca.* 9 times more reactive than the π-system of benzene toward $CH_3ClCH_3^+$, while this ratio is *ca.* 28 for $CH_3BrCH_3^+$.

An appreciable selectivity is displayed by these ions toward the π-systems of phenol and benzene as well, as demonstrated by the corresponding k_S/k_B values, if the percentage of ring methylation ($\%_{\text{ring}}$) of phenol is taken into account: $k_S/k_B\ \%_{\text{ring alkylation}}/100 = 4(CH_3ClCH_3^+)$ and $12(CH_3BrCH_3^+)$.

In conclusion, the substrate and positional selectivity of the dimethylhalogenium ions considered can be expressed by the following ratios: *O*-phenol : ring-phenol : benzene = 2 : 1 : 1 ($CH_3FCH_3^+$); 9 : 4 : 1 ($CH_3ClCH_3^+$); 28 : 12 : 1 ($CH_3BrCH_3^+$). The above conclusions substantiate the hypothesis previously advanced,[1] that methylation of arenes by $CH_3XCH_3^+$ is largely dominated by an activation barrier, required for the inversion of the configuration of the CH_3 moiety on moving from the electrophile

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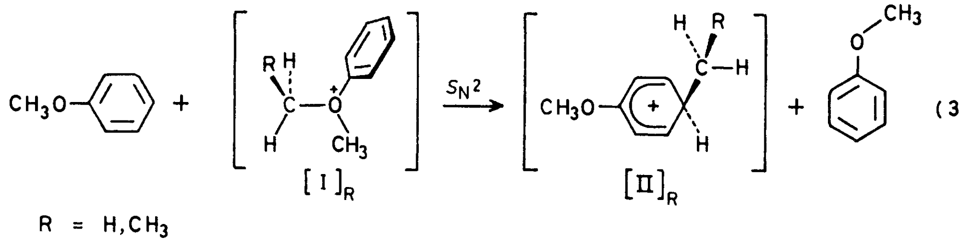
* A small, but appreciable kinetic preference toward *n*-bases is observed even for the relatively highly reactive $CH_3FCH_3^+$ ion.[1]

to the substrate. The height of the energy barrier is related to the degree of sp^3 hybridization associated with the carbon atoms of the electrophile, and increases in the order $CH_3FCH_3 < CH_3ClCH_3^+ < CH_3BrCH_3^+$.

As for the apparent substrate selectivity displayed by $CH_3XCH_3^+$ in the anisole–benzene competitive experiments, it should be noted that the existence of a non-productive methylation channel in anisole leading to formation of $[I]_{CH_3}$ gives to the measured k_S/k_B ratios the value of a lower limit of the overall nucleophilicity of anisole toward the gaseous $CH_3XCH_3^+$ ions, accounting therefore for the apparently lower reactivity of the anisole ring toward $CH_3FCH_3^+$, when compared with that of benzene.

Comparison with Related Gas- and Condensed-phase Studies.—The results outlined in the previous sections provide a definite answer to the question concerning the competition between the *n*- and π-type nucleophilic centres of phenol and anisole toward a specific methylating reactant, the $CH_3XCH_3^+$ (X = F, Cl, or Br) ion, in the dilute gas state, where the intrinsic reactivity scale of the nucleophile is not affected by extraneous and variable environmental factors. The conclusions reached for the nucleophilic reactivity of pure *n*- and π-type compounds toward each individual $CH_3XCH_3^+$ ion [1] are confirmed by the present study.



The contrast between low substrate discrimination and high positional selectivity, which has been shown to be a typical feature of gas-phase aromatic substitutions by alkyl cations,[12] corroborates the hypothesis of a ' carbenium-like ' nature for $CH_3FCH_3^+$, which is responsible for its ' chelating ' properties toward the *n*-electrons of the ambident substrate (' linear or bent co-ordination ').[12,13] The same interaction is less effective for $CH_3ClCH_3^+$ and $CH_3BrCH_3^+$ ions, wherein the positive charge is mostly localized on the halogen atom.[3b,11c] Their methylating ability is therefore almost exclusively restricted to *n*-type nucleophilic centres, whose interaction with the CH_3 of the $CH_3XCH_3^+$ ion provides enough energy to overcome the activation barrier required for the inversion of the configuration of the methyl group of the electrophile.

The gas-phase results, characterized by a remarkable extent of *O*-methylation, closely parallel those of solution-chemistry studies on related methylation processes, especially if comparison is restricted to recent kinetic investigations carried out under carefully controlled conditions in aprotic media. Thus, Olah and Melby,[4a] using dimethylhalogenonium hexafluoroantimonate, reported exclusive *O*-methylation of anisole at −120 °C. Methylation of anisole by methyl chloroformate and $AgSbF_6$ was reported to involve predominant attack on the oxygen of anisole,[14] yielding a dimethylphenyloxonium ion as the major reaction intermediate. Under conditions favouring thermodynamic control of products, *e.g.* at higher temperatures,[4a] the dimethylphenyloxonium ion was found to isomerize intermolecularly to the *C*-methylated isomer, by attacking preferentially the *para*-position of an unreacted anisole, if available.

Similar isomerizations are frequently met in the gas phase.[9,12b] The tendency of a given alkylmethylphenyloxonium intermediate to rearrange and the nature of the isomerization process were found to be strictly related to the ' free-ion ' character of the moving alkyl group, which in turn is correlated to the thermodynamic stability of the corresponding alkyl cations. Thus, a t-butylmethylphenyloxonium ion was found to be particularly prone to intermolecular isomerization giving the isomeric *para*-t-butylarenium ion.[9b-d] Evidence has been provided, indicating that isomerization may occur *via* an S_N1-like mechanism. On the other hand, isomerization of the oxonium ion $[I]_R$ mainly occurs through the S_N2-like intermolecular displacement (3), owing to the low tendency of primary alkyl groups to move as ' free-ions '.[4a,14] The fact that, in the present experiments, isomerization (3) does not take place, in spite of the presence of unreacted anisole in the irradiated mixtures, suggests that the reactivity of the oxonium ion $[I]_R$ towards a π-type nucleophilic centre (the unreacted anisole ring) can be regulated by the same electronic and structural factors governing $CH_3ClCH_3^+$ and $CH_3BrCH_3^+$ ions. This similarity arises from the comparable, if not greater, overall donor ability of oxygen *versus* chlorine (or bromine), when adjacent to a C^+ centre,[15] which confers to the alkyl groups of $[I]_R$ and $CH_3XCH_3^+$ (X = Cl or Br) a relatively high degree of sp^3 hybridization and, therefore, a weak tendency to be attacked by delocalized nucleophilic centres, such as the π-system of anisole.

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REFERENCES

[1] M. Speranza, N. Pepe, and R. Cipollini, *J. Chem. Soc., Perkin Trans. 2,* 1979, 1179.

[2] (*a*) G. A. Olah, 'Halonium Ions', ed. G. A. Olah, Wiley, New York, 1975; (*b*) G. A. Olah and J. R. De Member, *J. Am. Chem. Soc.*, 1970, **92**, 718; (*c*) G. A. Olah and E. G. Melby, *ibid.*, 1972, **94**, 6220; (*d*) G. A. Olah, Y. Yamada, and R. J. Spear, *ibid.*, 1975, **97**, 680; (*e*) P. E. Peterson, R. Brockington, and D. W. Vidrine, *ibid.*, 1976, **98**, 2660; (*f*) G. A. Olah, D. J. Donovan, and H. C. Lin, *ibid.*, p. 2661.

[3] (*a*) G. A. Olah and J. R. De Member, *J. Am. Chem. Soc.*, 1970, **92**, 2562; (*b*) G. A. Olah, J. R. De Member, R. H. Schlosberg, and Y. Halpern, *ibid.*, 1972, **94**, 156.

[4] (*a*) G. A. Olah, and E. G. Melby, *J. Am. Chem. Soc.*, 1973, **95**, 4971; (*b*) G. A. Olah, J. R. De Member, Y. K. Mo, J. J. Svoboda, P. Schilling, and J. A. Olah, *ibid.*, 1974, **96**, 884.

[5] (*a*) D. Bethell and V. Gold, 'Carbonium Ions', Academic Press, London, 1967; (*b*) G. A. Olah, 'Friedel–Crafts Chemistry', ed. G. A. Olah, Wiley, New York, 1973; (*c*) G. A. Olah and J. A. Olah, 'Carbonium Ions', eds. G. A. Olah and P. v. R. Schleyer, Wiley, New York, 1973, vol. II.

[6] (*a*) Z. Luczynski and J. A. Herman, *J. Phys. Chem.*, 1978, **82**, 179; (*b*) M. Colosimo and R. Bucci, *ibid.*, 1979, **83**, 1952; (*c*) unpublished results.

[7] (*a*) P. Giacomello and M. Speranza, *J. Am. Chem. Soc.*, 1977, **99**, 7918; (*b*) M. Speranza and G. Angelini, *ibid.*, 1980, **102**, 3115; (*c*) M. Speranza and C. Sparapani, *ibid.*, p. 3120.

[8] J. L. Beauchamp, D. Holtz, S. D. Woodgate, and S. L. Patt, *J. Am. Chem. Soc.*, 1972, **94**, 2798.

[9] (*a*) M. Attinà, F. Cacace, G. Ciranni, and P. Giacomello, *J. Chem. Soc., Perkin Trans. 2*, 1979, 891; M. Attinà, F. Cacace, G. Ciranni, and P. Giacomello, (*b*) *J. Am. Chem. Soc.*, 1977, **99**, (*b*) 5022; (*c*) 4101; (*d*) M. Attinà, F. Cacace, G. Ciranni, and G. Giacomello, *J. Chem. Soc., Chem. Commun.*, 1974, 466.

[10] (*a*) J. Catalan and M. Yanez, *J. Am. Chem. Soc.*, 1979, **101**, 3490; (*b*) D. P. Martinsen and S. E. Buttrill, jun., *Org. Mass Spectrom.*, 1979, **11**, 762; (*c*) F. M. Benoit and A. G. Harrison, *J. Am. Chem. Soc.*, 1977, **99**, 3980; S. A. Benezra and M. M. Bursey, (*d*) *ibid.*, 1972, **94**, 1024; (*e*) 1975, **97**, 3600; (*f*) D. A. Chatfield and M. Bursey, *ibid.*, 1976, **98**, 6492.

[11] (*a*) D. Holtz, J. L. Beauchamp, and S. D. Woodgate, *J. Am. Chem. Soc.*, 1970, **92**, 7484; (*b*) A. A. Herod, A. G. Harrison, and N. A. McAskill, *Can. J. Chem.*, 1971, **49**, 2217; (*c*) Z. Luczynski, W. Malicki, and H. Wincel, *Int. J. Mass Spectrom. Ion Phys.*, 1974, **15**, 321; (*d*) M. J. K. Pabst, H. S. Tan, and J. L. Franklin, *ibid.*, 1976, **20**, 191; (*e*) S. A. Benezra, M. K. Hoffman, and M. M. Bursey, *J. Am. Chem. Soc.*, 1970, **92**, 7501.

[12] (*a*) D. K. Sen Sharma, and P. Kebarle, *J. Am. Chem. Soc.*, 1978, **100**, 5826; (*b*) M. Attinà and P. Giacomello, *ibid.*, 1979. **101**, 6040; (*c*) E. C. Taylor and A. McKillop, *Acc. Chem. Res.*, 1970. **3**, 345, and references cited therein; (*d*) H. J. S. Dewar, 'Molecular Rearrangements', ed. P. De Mayo, Wiley, New York, 1963; (*e*) R. O. C. Norman and R. Taylor, 'Electrophilic Substitution of Benzenoid Compounds', Elsevier, New York, 1965; (*f*) H. I. Shine, 'Aromatic Rearrangements', Elsevier, New York, 1967.

[13] P. Kovacic and J. J. Hiller, jun., *J. Org. Chem.*, 1965, **30**, 1581.

[14] D. A. Simpson, S. G. Smith, and P. Beak, *J. Am. Chem. Soc.*, 1970, **92**, 1071.

[15] (*a*) R. W. Taft, R. H. Martin, and F. W. Lampe, *J. Am. Chem. Soc.*, 1965, **87**, 2490; (*b*) F. Bernardi, I. G. Csizmadia, and N. D. Epiotis, *Tetrahedron*, 1975, **31**, 3085; (*c*) F. Bernardi, A. Mangini, N. D. Epiotis, J. R. Larson, and S. Shaik, *J. Am. Chem. Soc.*, 1977, **99**, 7465; (*d*) T. Clark and P. v. R. Schleyer, *Tetrahedron Lett.*, 1979, 4641.