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Gas-phase ion-molecule reaction of alpha-phenylvinyl cation towards substituted benzenes in the environment of an ITMS

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Ion-molecule reactions between the α-phenylvinyl cation (α-PVC) and mono-substituted benzenes have been investigated using a quadrople ion-trap mass spectrometer. The α-PVC, generated by chemical ionization from phenylacetilene, was found to react selectively with mono-substituted benzenes bearing electron withdrawing groups to give the product ions $[M+103]^+$ and the *trans*-vinylating product ions $[M+25]^+$. To characterize the reaction products, a combination of collision-induced dissociation, isotope-labeling experiments and model compounds were used. The results indicate, in addition to direct heteroatom alkylation, high extent of *ortho* attack. We attributed the positional selectivity of the α-PVC to the nature of the substituent on the neutral molecule. In particular, hydroxy and amino groups promoted the alkenylation at *ortho* position. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: α-phenylvinyl cation; ion-molecule reaction; ITMS; substituted benzenes; positional selectivity

INTRODUCTION

α-Phenylvinyl cations (α-PVCs), first postulated in 1964,[1] are by now accepted as reactive intermediates in numerous reactions. In solution, α-PVCs have been generated as transient intermediates in the course of numerous reactions, such as electrophilic addition to alkynes and allenes,[2] photolysis of vinyl halides,[3] solvolysis of vinylic substrates[4] and spontaneous β-decay of tritiated styrene using the nuclear chemical method.[5a-b] Due to their brief lifetime, their investigation, concerning their exact nature and chemical behaviour, was based mainly on indirect techniques like kinetic measurements and product analyses.[6] In fact, α-PVCs, although predicted to be rather stable thermodynamically,[7a-c] are too elusive for direct spectroscopic observation. The only exceptions is the NMR spectroscopic observation and characterization of the 1-(*p*-anisyl)vinyl cations reported by H.U. Siehl and co-workers, who were able to generate the vinyl cations as persistent species in solution, by protonation of alkynes in superacidic media at temperatures below −100 °C.[8]

In contrast to the liquid phase, α-PVC is readily generated in the gas phase by using two techniques. Mass spectrometry and the nuclear decay of tritium have shown to be useful and practical methodologies to generate and investigate α-PVCs in absence of solvent and counterion effects. Nevertheless, the chemical reactivity of α-PVCs has been studied extensively in solution,[6] whereas, to the best of our knowledge, only one paper dealing with nuclear-decay studies has appeared on the reactivity of the α-PVC in the gas phase.[9] However, these studies have not been carried out under conditions ensuring against radiolytic artefacts, and, therefore, their results must be used with considerable caution.[10] Concerning mass spectrometry, it has provided useful information on the structures and chemical properties of carbocations in the gas phase.[11a-g] Despite this, mass spectrometric investigation of α-PVCs has received only little attention with most of the emphasis devoted to the energetics of the formation,[12] the isomerisation[13] and the determination of the gas-phase basicity, i.e. for ring-substituted phenylacetylenes,[14a-b] whereas, to our knowledge, their gas-phase chemistry in a mass spectrometer has not been reported until now. With the aim to increase our understanding of the intrinsic reactivity of the gaseous α-PVC, we decided to investigate the reactions of the α-PVC with neutral analytes in the gas-phase environment of a traditional ion trap mass spectrometer (ITMS). From the early stage of its development, ion trap has proved to be a useful and simple device for the study of gas-phase ion-molecule reactions.[15a-h] In fact, ion trap instruments show capabilities for mass selection of reagent ions, long reaction times (RTs) ensuring collisional stabilization of the reaction product with the bath gas and collision-induced dissociation (CID) of the reaction products to yield fragment ions which provide structural information.

In this work, we report a systematic study which includes substrate selectivity, site of attack and reaction mechanisms. To this aim, α-PVC has been easily generated by protonation of phenylacetilene and subjected to ion-molecule reaction towards a series of mono-substituted aromatic compounds. The structural characterization of the ion-molecule reaction products was achieved by comparing their CID spectra with that generated from CI-CID experiments of labelled compounds and model ions produced by organic synthesis. These data also provided evidence for the reaction mechanisms.

EXPERIMENTAL

Ion-molecule reaction was examined with a Varian Saturn 2000 ITMS, operating under CI conditions, coupled with a Varian 3800

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gas chromatograph (Varian, Walnut Creek, CA). 3 ml of a mixture of phenylacetylene and methanol (molar ratio 1:0.1) was introduced in the CI reservoir bulb and used as reagent gas. Details on the use of the Saturn ion trap for ion-molecule reaction have been reported previously.[15h] The CI parameters for the generation of the CI reagent gas were set as follow: CI ionization storage level *m/z* 20; CI reagent ion eject amplitude 17 V; background mass *m/z* 25; RT 128 ms; CI ionization time (IT) 400 μs; target tic 10 000 counts. The pressure inside the ion source was $\sim 3 \times 10^{-3}$ Torr. Under this condition, the spectrum of the reagent gas was characterized by high yields of α-PVC (*m/z* 103), that was the predominant one, along with lesser amount of protonated methanol (*m/z* 33, relative abundance (*R.A.*) 7%), and protonated dimethyl ether (*m/z* 47, *R.A.* 6%)[16] (Fig. 1a).

The reactivity of α-PVC towards the aromatic compounds **1–9** was studied by mass selecting the reagent ion at *m/z* 103 and storing it in the space of the IT. Isolation of the *m/z* 103 ions was achieved by using the standard MS/MS isolation function available via the Saturn GC/MS Workstation version 5.41 software and keeping the CID energy at 0 V in order to avoid the activation of decomposition processes (Fig. 1b). Each neutral analyte (**1–9**) was introduced in the ion trap via a GC system and allowed to react with the selected *m/z* 103 reagent ion at its characteristic retention time, for a RT of 200 ms (Fig. 1c and Table 1). Each reaction product, obtained from the reaction of the neutral analyte with the reagent gas, was isolated and then collisionally activated prior to mass analysis. CIDs were carried out by using helium as the collision gas (gas purity (He) was 99.9999%). For MS/MS experiments, the collision energy was varied in such a way that the relative abundance of the surviving precursor ions was 10–25%. An excitation time of 20 ms and an isolation width of 2 *m/z* for the precursor ion were used. Each MS/MS spectrum was an average of five scans.

Low resolution mass spectrometric experiments on the model compounds **10–23** were carried out under CI conditions using methanol as reagent gas.

Compounds **1–23** (1 μl aliquots of 1.0×10^{-5} M solutions in chloroform) were introduced into the trap through the gas chromatograph inlet system. A FactorFour Lowbleed/MS capillary column (30 m, 0.25 mm i.d., 0.25 μm film thickness) was used. The oven temperature was programmed from 50 °C (held for 5 min) to 250 °C at 20 °C/min (held for 2 min). The transfer line was maintained at 250 °C and the injector port (30/1 split) at 280 °C.

Phenylacetylene, methanol, benzene **1**, toluene **2**, phenol **3**, phenol-2,3,4,5,6-d_5 **3′**, anisole **4**, aniline **5**, N,N-diethylaniline **6**, bromobenzene **7**, nitrobenzene **8**, benzaldehyde **9** and 2,2-diphenylpropane **12** were purchased from Aldrich and used without further purification.

Anisole-OCD_3 **4′** and anisole-2,3,4,5,6-d_5 **4″** were prepared according to method reported elsewhere starting from phenol and ICD_3 for compound **4′** and starting from phenol-d_5 (**3′**) and ICH_3 for compound **4″**.[17]

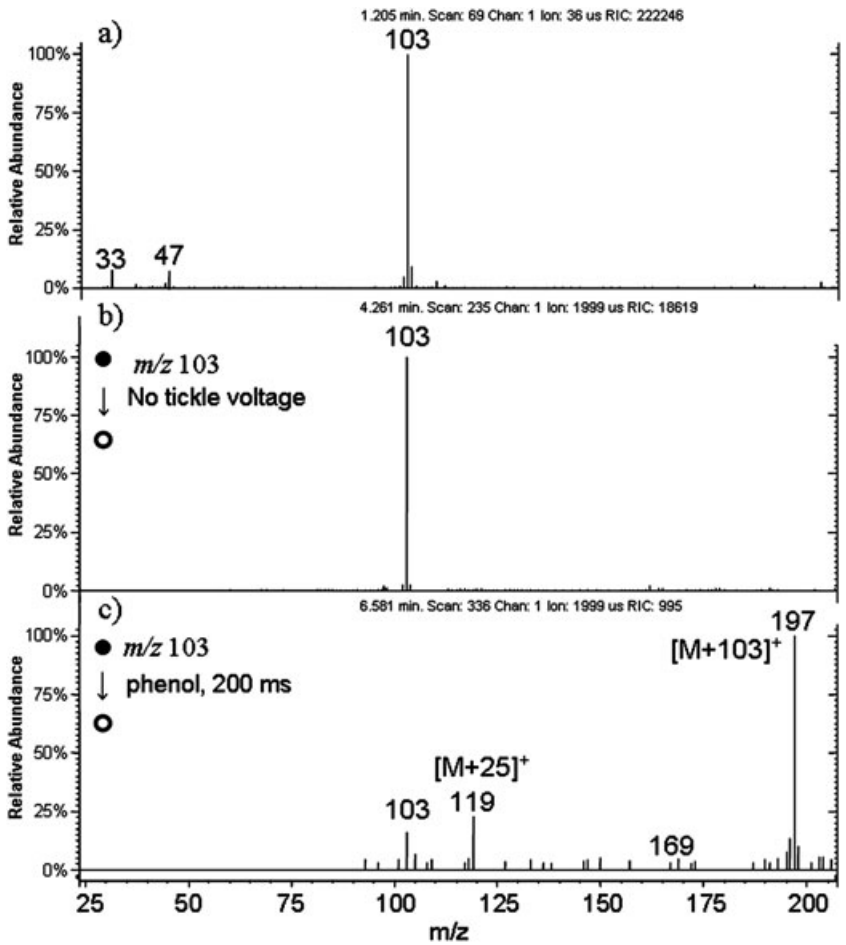


Figure 1. a) Full scan mass spectrum of the reagent gas. b) Isolation of the α-PVC (*m/z* 103) in the IT. c) Experimental evidence of the ion molecule reaction of α-PVC with neutral phenol.

Journal of MASS SPECTROMETRY

Table 1. Product ions formed in the reaction of the α-PVC (*m/z* 103) with mono-substituted benzenes **1–9** (M). * Kcal/mol

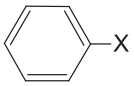
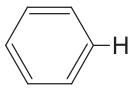
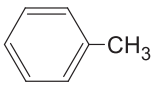
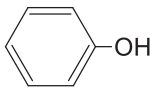
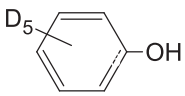
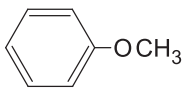
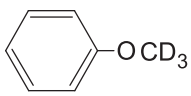
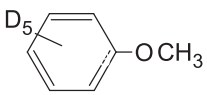
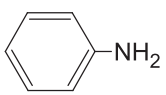
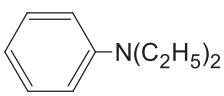
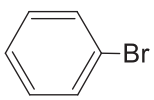
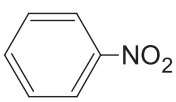
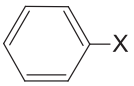
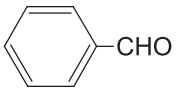
	Neutral reagents (M)			Reaction products		
		Mass	Proton affinity (PA)*	Proton transfer $[M+H]^+$	Alkenylation $[M+103]^+$	*Trans*-vinylation $[M+25]^+$
1		78	179.4	None	*m/z* 181 (15) (**1a**)	*m/z* 103 (100) (**1b**)
2		92	187.4	None	*m/z* 195 (15) (**2a**)	*m/z* 117 (100) (**2b**)
3		94	195.3	None	*m/z* 197 (100) (**3a**)	*m/z* 119 (25) (**3b**)
3′		99	-	None	*m/z* 202 (100) (**3′a**)	*m/z* 123 (23) (**3′b**)
4		108	200.7	109 (12)	*m/z* 211 (100) (**4a**)	*m/z* 133 (20) (**4b**)
4′		111	-	112 (9)	*m/z* 214 (100) (**4′a**)	*m/z* 136 (15) (**4′b**)
4″		113	-	114 (10)	*m/z* 216 (100) (**4″a**)	*m/z* 137 (16) (**4″b**)
5		93	210.9	94 (100)	*m/z* 196 (45) (**5a**)	*m/z* 118 (4) (**5b**)
6		149	229.4	150 (100)	*m/z* 252 (76) (**6a**)	*m/z* 174 (2) (**6b**)
7		156	180.2	None	None	None
8		123	191.3	None	None	None

Table 1. *(Continued)*

	Neutral reagents (M)			Reaction products		
		Mass	Proton affinity (PA)*	Proton transfer $[M+H]^+$	Alkenylation $[M+103]^+$	*Trans*-vinylation $[M+25]^+$
9		106	199.4	107 (68)	None	None

1-Vinyl-4-phenoxybenzene **10** was prepared by hydrogenation of 1-ethynyl-4-phenoxybenzene using Lindlar catalyst.[18]

1,1-Diphenylethene **11**, 1-(toluyl)-1-phenylethene **13** and 1-(2-hydroxyphenyl)-1-phenylethylene **15** were prepared by the reaction of phenylacetylene with benzene, toluene and phenol, respectively, in dry *ortho*-dichlorobenzene in the presence of KSF-montmorillonite (Fluka).[19]

α-Phenoxystyrene **14** was synthesized by the reaction of phenylbenzoate with Tebbe's reagent, prepared following the typical procedure from titanocene dichloride and a toluene solution of trimethylaluminium.[20]

1-(4-Hydroxyphenyl)-1-phenylethylene **16** was prepared from the reaction of 4-hydroxyacetophenone with phenylmagnesium bromide.[21]

1-(2-Methoxyphenyl)-1-phenylethene **17** and 1-(4-methoxyphenyl)-1-phenylethene **18** were prepared according to the general procedure starting from phenylacetylene and anisole.[19]

N-(1-phenylethylidene)aniline **19** was prepared from aniline and acetophenone according to the general procedure.[22]

1-Phenyl-1-(2-aminophenyl)ethylene **20** and 1-phenyl-1-(4-aminophenyl)ethylene **21** were prepared by the reaction of phenylacetylene with aniline in the presence of KSF-montmorillonite (Fluka).[23]

1-Phenyl-1-(2-N,N-diethylaminophenyl)ethylene **22** and 1-phenyl-1-(4-N,N-diethylaminophenyl)ethylene **23** were prepared starting from 1-(2-(diethylamino)phenyl)-1-phenylethanol and from 1-(4-(diethylamino)phenyl)-1-phenylethanol according to the methods reported elsewhere.[24a-b]

RESULTS AND DISCUSSION

The gas phase reaction of α-PVC with neutral benzene **1** and its ring-substituted derivatives **2–6** (Table 1) produces the product ions $[M+103]^+$ (**1–6a**) and the $[M+25]^+$ ions (**1–6b**). The data reported in Table 1 indicate that when the substituent is an electron withdrawing group, such in the case of bromobenzene **7**, nitrobenzene **8** and benzaldehyde **9**, the product ions $[M+103]^+$ and $[M+25]^+$ were not observed at all, suggesting that the substrate selectivity of the reaction with the α-PVC is likely due, or in part, to the activating and deactivating properties of the substituent. Proton transfer reactions have been observed only for benzaldehyde and nitrogen-containing compounds accordingly to their high proton affinities (PAs) relative to that of phenylacetylene. Phenylacetylene has a PA of 198.6 ± 0.5 kcal/mol, whereas benzaldehyde has a PA of 199.4 kcal/mol, aniline and *N,N*-diethylaniline have a PAs between 210.8 and 229.4 kcal/mol.[25] However, it should be noted that the high amount of protonated aniline (*m/z* 94) and *N,N*-diethylaniline (*m/z* 150) could also be due in some extent to the fragmentation process of the reaction products **5a** and **6a**, respectively (*vide infra*).

The $[M+25]^+$ ions **1-6b** originate from the dissociation of the $[M+103]^+$ reaction products **1-6a**, as demonstrated by the CID experiments reported in Figs. 2-6. In fact, the common fragmentation behaviour characteristic of the $[M+103]^+$ reaction products are mainly two, i.e. the re-formation of the starting reactant α-PVC (*m/z* 103) and the nominal loss of 78 Da, ascribed to the elimination of neutral benzene, yielding the $[M+25]^+$ ions **1–6b** (Scheme 1 and Table 1). The structural characterization of the latter ions was readily achieved upon closer inspection of the CID spectra of reaction products **1–6a** and their deuterated analogs **3'a**, **4'a** and **4''a**. In particular, when neutral phenol (**3**) was replaced by phenol-d_5 (**3'**), the reaction product **3'a** with the α-PVC generates, upon CID, a $[M+25]^+$ **3'b** ion that is shifted of four mass units, that is, from *m/z* 119 to 123 (Table 1 and Fig. 3a and b). An analogous behaviour was found when neutral anisole (**4**) was replaced by anisole-d_5 (**4''**) generating the mass shifts from *m/z* 133 to 137 (loss of C_6H_5D) and to *m/z* 138 (loss of C_6H_6), reasonably due to an isotope effect (Table 1 and Fig. 4a and c). These shifts indicate that the loss of neutral benzene from the $[M+103]^+$ reaction products involves the aromatic portion of the starting α-PVC rather than that of the neutral molecule that is still incorporated into the $[M+25]^+$ ion. Furthermore, the shift by 14, 16, 30, 15, 71 and 33 *m/z* units in the masses of the $[M+25]^+$ ions observed when neutral substituted benzenes **2–6** and **4'** (X = CH_3, OH, OCH_3, NH_2, $N(C_2H_5)_2$, OCD_3) were used, with respect to the $[M+25]^+$ ion from **1** (X = H; *m/z* 103), shows that these ions must retain the different X moieties in their structures (Table 1). These data suggest that the $[M+25]^+$ ion would most likely have the structure of the vinylated ions depicted in Scheme 1, and it is thus proposed that the interaction between the neutral reagents **1–6** and the α-PVC also results formally in a vinyl cation transfer. Hence, this process can be considered a *trans*-vinylation reaction. These findings unequivocally identify the site of the attack on the α-PVC. In fact, even if the α-PVC could be considered a multicenter electrophyle with most of the charge on the aryl portion located on the *para* position (Scheme 2),[26] however, the benzene loss involved in the *trans*-vinylation reaction is inconsistent with the structure of the *para*-substituted phenylvinyl cation **3c**. It seems logical to assume that, under our conditions, the electrophylic attack occurs at the carbenium site of the α-PVC to generate the structure **3a** (the attack on the substituent of the phenol depicted in Scheme 2 is for illustrative purposes only). Further confirmation of this hypothesis was obtained by comparing the CID spectrum of the reaction product

Journal of MASS SPECTROMETRY

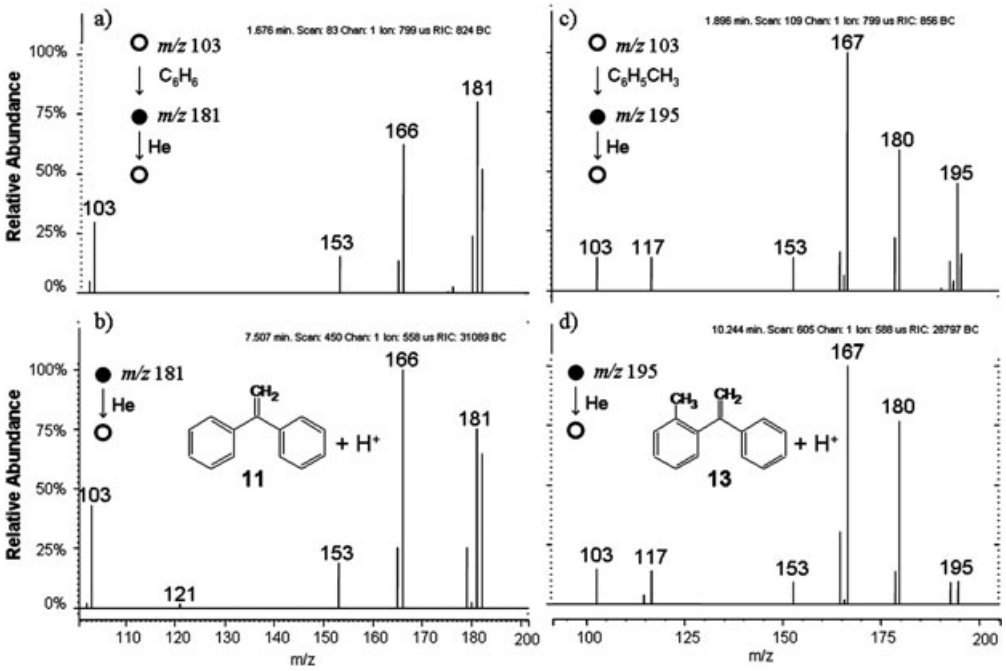


Figure 2. CID spectra of the ion molecule reaction products **1a** (*m/z* 181) and **2a** (*m/z* 195) obtained from the ion molecule reaction of α-PVC (*m/z 103*) with (a) benzene and (c) toluene, respectively. CI-CID spectra of (b) 1,1-diphenylethene **11**, and d) 1-(toluyl)-1-phenylethene **13**, respectively.

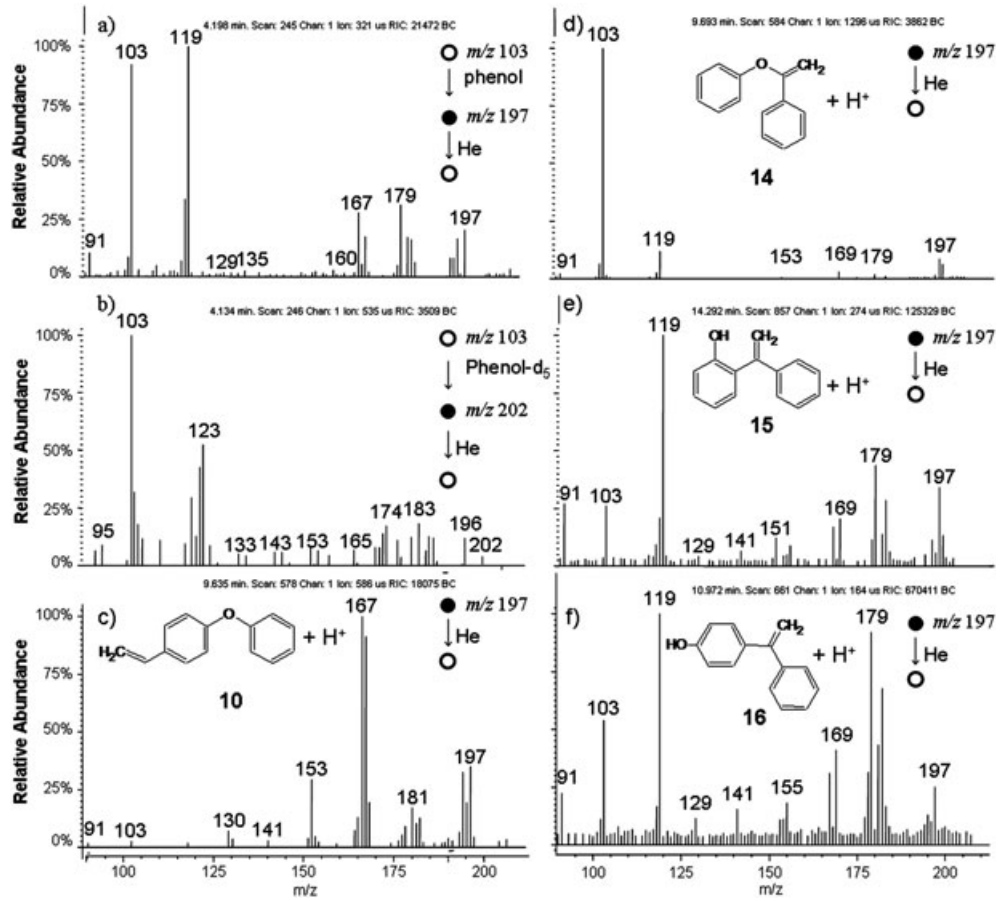


Figure 3. CID spectra of the reaction products **3a** (*m/z* 197), and **3'a** (*m/z* 202) obtained from the ion molecule reactions of α-PVC (*m/z* 103) with (a) phenol and (b) phenol-D_5, respectively. CI-CID spectra of protonated c) 1-vinyl-4-phenoxybenzene **10**, d) α-phenoxystyrene **14**, e) 1-(2-ydroxyphenyl)-1-phenylethylene **15** and f) 1-(4-hydroxyphenyl)-1-phenylethylene **16**.

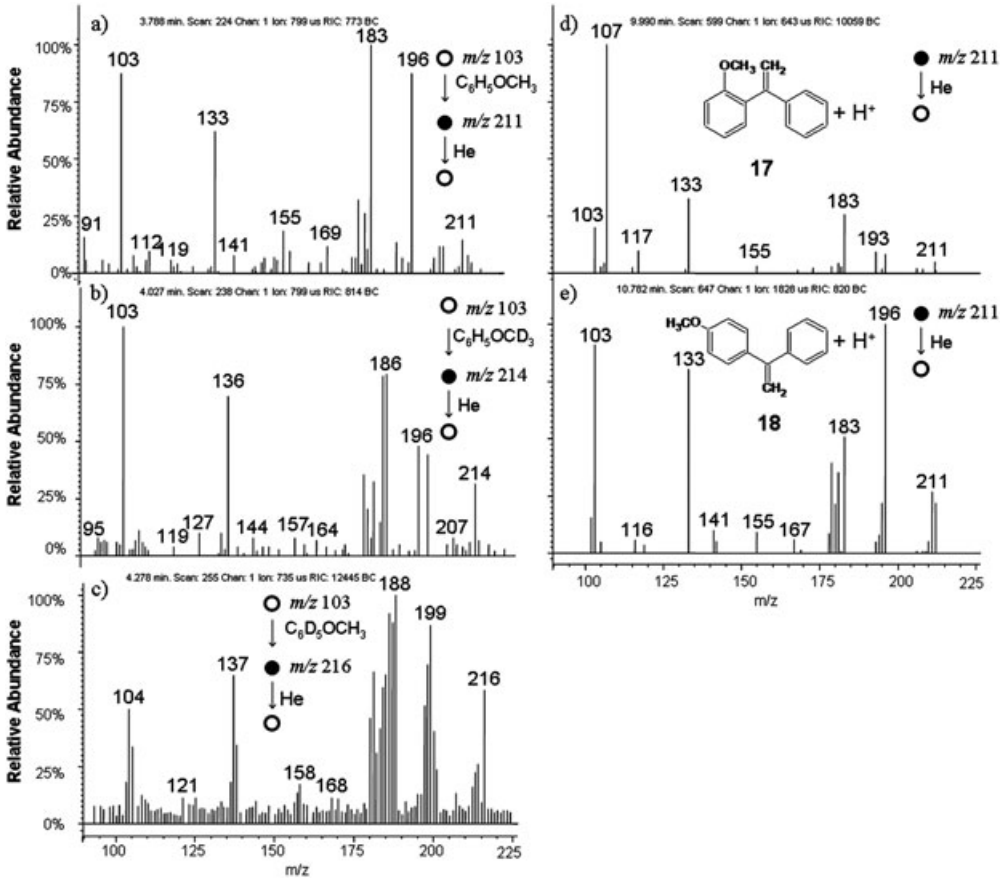


Figure 4. CID spectra of the reaction products **4a** (*m/z* 211), **4'a** (*m/z* 214) and **4''a** (*m/z* 216), obtained from the ion molecule reactions of α-PVC (*m/z* 103) with (a) anisole, (b) anisole-OCD_3 and c) anisole-D_5, respectively. CI-CID spectra of protonated d) 1-(2-methoxyphenyl)-1-phenylethene **17** and e) 1-(4-methoxyphenyl)-1-phenylethene **18**.

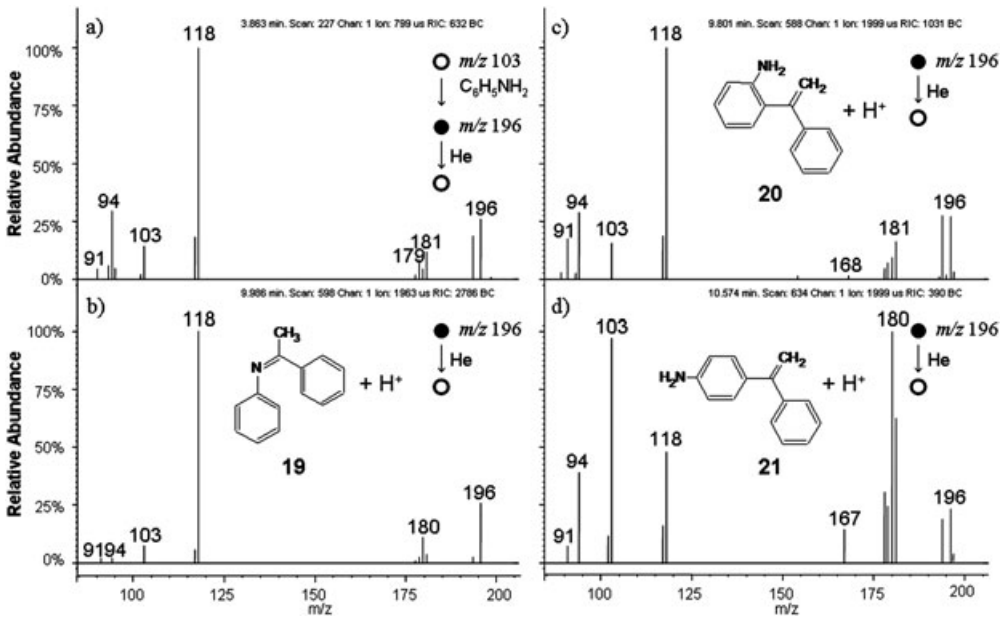


Figure 5. (a) CID spectrum of the reaction product **5a** (*m/z* 196) obtained from the ion molecule reactions of α-PVC (*m/z* 103) with aniline. CI-CID spectra of protonated b) N-(1-phenylethylidene)aniline **19**, c) 1-phenyl-1-(2-aminophenyl)ethylene **20** and d) 1-phenyl-1-(4-aminophenyl)ethylene **21**.

Journal of MASS SPECTROMETRY

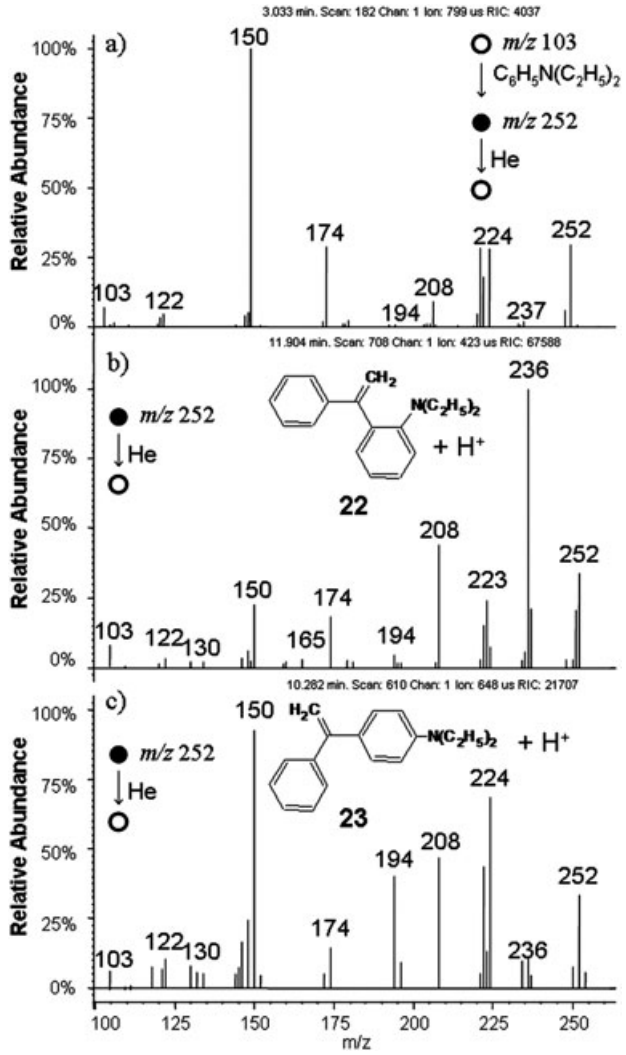
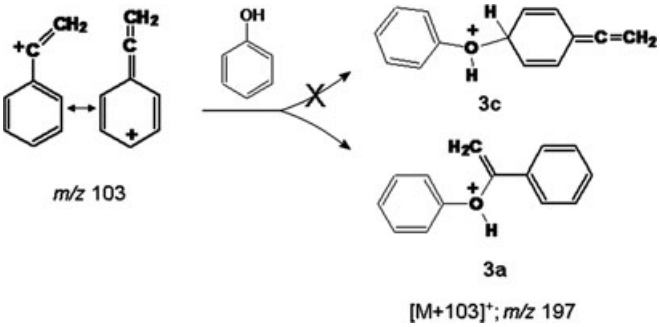


Figure 6. (a) CID spectrum of the reaction product **6a** (*m/z* 252) obtained from the ion molecule reactions of α-PVC (*m/z* 103) with N,N-diethylaniline. CI-CID spectra of protonated b) 1-phenyl-1-(2-N,N-diethylaminophenyl) ethylene **22** and c) 1-phenyl-1-(4-N,N-diethylaminophenyl) ethylene **23**.

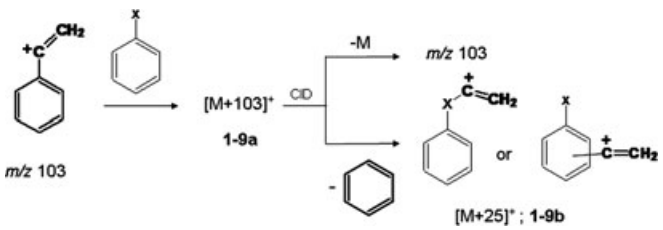
3a, with the CID mass spectrum of the model ion **3c**, generated by chemical ionization of 1-vinyl-4-phenoxybenzene (**10**) (Fig. 3a and c). As expected, upon CID, ion **3c** did not dissociate to the *trans*-vinylation fragment ion (*m/z* 119, base peak in **3a**), but generated the *m/z* 167 ion (bp), and ions at *m/z* 168 and 153, both nearly absent in the CID spectrum of the reaction product **3a**.



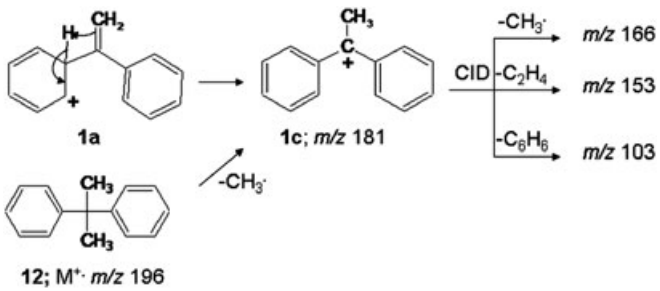
Scheme 2. Structure of the product ions arising from the attack of phenol to the *para* position (**3c**) and to the carbenium site (**3a**) of the α-PVC.

Reaction with neutral benzene (1)

The reaction of the α-PVC with neutral benzene **1** produced the adduct ion $[M+103]^+$ **1a** at *m/z* 181 (Table 1). Since the only reactive site for the electrophylic attack is the benzene ring, we hypothesized that the structure of the reaction product most likely corresponds to the sigma adduct **1a** depicted in Scheme 3. This structure was confirmed by comparing the CID mass spectrum of the reaction product **1a** at *m/z* 181 with that obtained from the protonated alkenylated benzene **11** (Fig. 2a–b). The similarity of these two spectra indicates that both ions most likely have the same structure. Interestingly, in both spectra the *m/z* 181 ions dissociate under CID experiment to yield predominantly the fragment at *m/z* 166, due to the loss of a methyl radical. This loss suggests that some fraction of the reaction products undergoes a H atom migration from the phenyl ring to the charged carbon atom of the vinyl moiety to form a more stable tertiary carbocation, namely the methyldiphenylmethane ion **1c** (Scheme 3). A reference ion for this structure can be envisioned as the $[M\text{-}CH_3]^+$ ion obtained from 2,2-diphenylpropane **12**. The EI mass spectrum of **12** shows $M^{+\cdot}$ of *m/z* 196 (*R.A.* 22%) and a fragment ion at *m/z* 181 (*R.A.* 100%) formed by the loss of a methyl radical.[27] The CID mass spectrum of the $[M\text{-}CH_3]^+$ fragment from **12** is identical to that of the reaction product **1a** at *m/z* 181, confirming the proposed *intra*-molecular proton transfer. The dissociation of the reaction product also yielded the fragment at *m/z* 153, due to the loss of 28 Da attributed to the elimination of C_2H_4, and a minor fragment at *m/z* 103 which, being the reaction product **1a** symmetrical, could be attributed to the re-formation of the original reagent ion as well as to the $[M+25]^+$ fragment ion **1b** arising from the *trans*-vinylation reaction (*vide supra*).



Scheme 1. Benzene elimination from the reaction product $[M+103]^+$ and possible structures of the *trans*vinylation product $[M+25]^+$.



Scheme 3. Hydrogen transfer and elimination of a methyl radical from the reaction product **1a**.

Reaction with toluene (2)

When the substituent on the neutral analyte is an electron donating group that does not contain heteroatoms, such as in the case of toluene, the benzene ring, activated by the electron-releasing effect, is still the only site of the electrophylic attack. As expected, the CID mass spectra of the reaction products at *m/z* 195 (**2a**) was practically identical with that of the authentic ion generated by protonation of compound **13**. As displayed in Fig. 2c–d, in the CID mass spectra of both **2a** and protonated **13**, the losses of $^{\cdot}CH_3$ and C_2H_4 are still the main fragmentation processes. Analogous to what observed for neutral benzene (**1**), further fragment ions consist in the reformation of the starting phenyl vinyl cation (*m/z* 103), and the formation of the *trans*-vinylation reaction product $[M+25]^+$, i.e. vinyltoluene (*m/z* 117). Unfortunately, since the CID spectra of *ortho* and *para* isomers chosen as model ions were identical, they provide no information as to the exact position of the attack of the α-PVC on the toluene molecule. The CID spectrum of protonated *ortho*-isomer **13** reported in Fig. 2d is for illustrative purpose only.

Reaction with phenol (3)

When the α-PVC reacts with phenol, it produces $[M+103]^+$ reaction product **3a** at *m/z* 197 (Table 1). This reaction has two sites where the attack of the phenylvinyl cation can potentially occur; the oxygen atom and the benzene ring.

In the first case, the unshared electron pair of the oxygen atom of the phenol undergoes electrophilic attack, which leads to the formation of an oxonium ion. In the second case, the reaction consists in the attack of the vinyl cation on the π-electron system of the aromatic ring, resulting in the formation of a σ complex. To get insight into the sites of alkenylation on neutral phenol, we have again explored the dissociation behaviours of the reaction product **3a** using the CID technique (Fig. 3a). As can be seen, the fragmentation pattern of the reaction product at *m/z* 197 shows the elimination of a water molecule (*m/z* 179) that proves that alkylation takes place, or at list in part, on the benzene ring. Unlike water loss, the loss of 28 Dalton (*m/z* 169) from **3a** does not play a diagnostic role for ring alkylation, since it cannot be attributed exclusively to the loss of CO. In fact, the loss of 28 Dalton was also observed in the CID spectra of the products **1a** and **2a** (X = H, CH_3), and it was ascribed to the elimination of C_2H_4 (Fig. 2b and d). Further fragmentation consists again in the formation of *m/z* 103 (*RA*% 80) and the *trans*-vinylation reaction product $[M+25]^+$ at *m/z* 119 (*RA*% 100).

Additional data on the site of alkenylation were achieved by comparing the CID spectra of the reaction product **3a** at *m/z* 197 with those obtained from the CID spectra of $[M+H]^+$ ions from CI of model compounds **14**, **15** and **16** (Fig. 3d–f).

The CID spectrum of protonted *ortho*-alkenylphenol **15** (Fig. 3e) shows similar behaviours to that observed in the CID spectrum of the reaction product **3a**, i.e. the elimination of a water molecule (*m/z* 179 *RA*% 3), of 28 Dalton (*m/z* 169 *RA*% 2) and the elimination of neutral benzene *m/z* 119 (*m/z* 119 *RA*% 100); However, the model compound **15** shows significant differences in the intensity of the peak at *m/z* 103 that is only 25%.

In the CID spectra of protonated α-phenoxystyrene **14** (Fig. 3d), in analogy to the CID spectrum of the reaction product **3a**, the inductive cleavage of the ethereal bond is the most favourite fragmentation process (*m/z* 103, *RA*% 100). This behaviour suggests that oxygen alkylation can also occur. In particular, the *m/z* 103 and *m/z* 119 ratio arising from the CID spectrum of **3a**, indicates that the degree of O-alkylation is very close to that of ring alkylation.

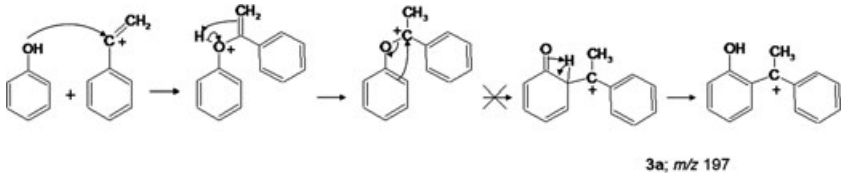
Subsequently, we have investigated the exact site of the electrophylic attack on the phenolic ring by examining the CID mass spectrum the *para* model compound **16** (Fig. 3f). Surprisingly, the CID spectrum of the $[M+H]^+$ ion from the *para*- isomer **16** shows a *R.A.* for ions at *m/z* 179 and *m/z* 169 too high when compared with that of the reaction product **3a** (*m/z* 179 *RA*% 28; *m/z* 169 *RA*% 15) thus suggesting that substitution is disfavoured at *para* position. These data show that, even though the *ortho* and the *para* positions of phenol each receive about the same activation from hydroxyl group, the ring alkylation occurs preferentially on the *ortho* position, yielding very little amount of *para* isomer.

At the light of these insights, we have hypothesised that the phenolic hydroxyl group must participate directly in some way to account for the unexpected experimental results, i.e. formation predominantly of ether and *ortho*-alkenylphenol.

Initially, we supposed that an *o*-alkylation *via* the protonated alkyl phenyl ether could occur (Scheme 4). However, we found that the CID mass spectrum of the protonated authentic phenyl vinyl ether **14** (Fig. 3d) is quite different from that of the reaction product **3a**, thus demonstrating that it does not rearrange to give the protonated *o*-alkenylphenol. Subsequently, we found that, when anisole was reacted with the α-PVC, *ortho*-phenylethenylanisole was not formed (*vide infra*), thus suggesting that an interaction between the hydrogen of the hydroxyl group and the vinyl moiety could have a directing effect.

Reaction with anisole (4)

The reaction of the α-PVC with neutral anisole leads to the formation of the reaction product **4a** at *m/z* 211 (Table 1). Upon CID, the product ion dissociated predominantly to the *m/z* 196 (loss of $CH_3^{\cdot}$), *m/z* 183 (loss of 28 Da), *m/z* 133 (loss of benzene) and *m/z* 103 as shown in Fig. 4a. For comparison, protonated *o*- and *p*-alkenylated anisole were generated by methanol chemical ionization of the reference compounds **17** and **18**, respectively (Fig. 4d and 4e). Under CID experiments each reference ion dissociated to give ions at *m/z* 103, 133, 183 and 196. However, only protonated *o*-isomer gave a characteristic peak at *m/z* 107 completely absent in the CID spectrum of the reaction product **4a**. Although the CID spectrum of the reaction products **4a** at *m/z* 211 is not absolutely identical with any of the reference CID spectra, the lack of ion at *m/z* 107 and the high intensity of



Scheme 4. *Ortho* alkenylation of phenol *via* protonated phenyl ether.

Journal of MASS SPECTROMETRY

m/z 196 indicate that the reaction product most likely has the structure of the protonated *p*-alkenylanisole.

Reaction with aniline (5) and N,N-diethylaniline (6)

The reaction of the α-PVC with neutral aniline generates the product ion **5a** at *m/z* 196 (Table 1). Upon CID, in addition to the formation of the ions at *m/z* 181 (loss of $^{\cdot}CH_3$), *m/z* 118 (loss of benzene) and *m/z* 103, the reaction product shows elimination of NH_3 (*m/z* 179) and of neutral phenylacetilene to yield protonated aniline (*m/z* 94) (Fig. 5a). These behaviours provide evidence for the structure of the protonated ring-alkenylated aniline for the reaction products **5a**, or, at least, for part of its population. In particular, the loss of NH_3 is a typical feature of the CI spectrum of primary anilines.

The higher intensity of ions at *m/z* 180 (100%), *m/z* 181 (60%) and *m/z* 103 (98%), in the CID mass spectrum of the protonated *p*-alkylated compound **21** (Fig. 5d), rules out the possibility that the ring alkenylation occurred at the *para* position, supporting therefore an *ortho* attack. The CID spectrum of the reaction product **5a** was then compared with that obtained from the protonated *N*-alkylated compound **19** (Fig. 5b). It must be pointed out that, even if the synthesized compound **19** shows an enamine structure, the only synthetically accessible, however, also its imine counterpart reasonably contributes to the CID spectrum, reflecting the systematically higher stability of ionized imine than the corresponding ionized enamine.[28] Unfortunately, the absence of diagnostic fragment ion in the CID spectrum of the protonated *N*-alkylated compound **19** and the similarity of the latter with the CID mass spectrum of the *ortho*-alkylated compound **20** (Fig. 5c) did not allow us to establish if, together with *ortho*-alkylation, the attack occurred in some extent also on the nitrogen atom.

To gain more insight into the mechanism of formation of the *ortho*-alkylated product ion **5a**, we investigated the effect of the *N*-substitution on the reaction with the phenylvinyl cation: we found that, in analogy to what observed for anisole, *N,N*-diethylaniline **6** gave only *para* alkylation. In fact, although the CID spectrum of the reaction products **6a** (*m/z* 252) reported in Fig. 6a is not completely superimposable with any of the reference CID spectra arising from protonated **22** and **23**, namely *ortho*- and *para*-alkylated *N,N*-diethylanilines, respectively (Fig. 6b–c), however, the lack of ion at *m/z* 236 and the high intensity of *m/z* 150 indicated that the product ion **6a** most likely has the structure of the protonated *p*-alkenyl-*N,N*-diethylaniline **23**.

We therefore supposed that the *ortho*-alkylation of α-PVC on neutral aniline (**6**) proceeds throughout the same interaction observed for phenol.

CONCLUSIONS

The α-PVC reacts selectively in a traditional ITMS with monosubstituted benzenes bearing electron donating groups. The typical reaction product consists in an alkenylated product ion $[M + 103]^+$ which shows a characteristic site of attack depending on the nature of the substituent on the neutral molecule. The reaction of PVC with phenol and aniline has shown, together with direct substituent alkenylation, an unexpectedly large extent of *ortho* alkenylation products. This result has been explained by an interaction which involves the hydrogen of the hydroxyl/amino group and the vinyl moiety of the α-PVC. When the heteroatom of the substituent is bonded to alkyl groups, such as in the case of anisole and N,N-disubstituted aniline, the attack on the phenyl ring of the PVC occurs exclusively at the *para* position. Significant product ions also appearing in the spectrum correspond to the *trans*-vinylation reaction products $[M + 25]^+$ which arise from the $[M + 103]^+$ product ions *via* elimination of the aromatic portion of the α-PVC.

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