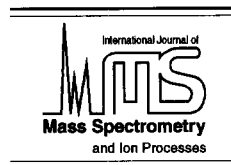




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Gas-phase reactions of chloro- and bromoanisoles with methyl- and dimethylamine via radical cations

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Abstract

Ionic gas-phase reactions of chloro- and bromoanisoles with CH_3NH_2 and $(\text{CH}_3)_2\text{NH}$ via radical cations were investigated by FT-ICR spectrometry using an external ion source. Protonated *N*-methylanisidines are formed quantitatively from bromoanisole radical cations with CH_3NH_2 by *ipso* substitution of the bromo atom. The analogous reaction of chloroanisole radical cations produce a mixture of protonated and radical cationic *N*-methylanisidines, the latter ions arising by loss of HCl from the addition complex and corresponding also to *ipso* substitution products. The branching ratio of product ions and the reaction efficiencies depend on the structure of the haloanisole radical cations, the efficiencies ranging from 1.3% to 24%. The observed dependence of the reactivity on the substitution pattern is in good agreement with earlier results of the reactions of dihalobenzene radical cations with NH_3 and shows that all substitution reactions proceed by the same multistep mechanism in which the addition of the amine to the aromatic radical cation in the collision complex is rate determining. The reactions of $(\text{CH}_3)_2\text{NH}^+$ with neutral bromoanisoles in the ICR cell produce protonated *N,N*-dimethylanisidines besides bromoanisole radical cations by charge exchange. Chloroanisoles produce with $(\text{CH}_3)_2\text{NH}^+$ additionally *N,N*-dimethylanisidine radical cations by loss of HCl. Deuterium labelling experiments reveal that the H atom eliminated with HCl originates from the amino group. The kinetic behaviour of both substitution processes indicates that branching between loss of Cl and HCl occurs after the rate determining addition step in a chemically activated intermediate. Competition of loss of Cl and by elimination of HCl is observed only for reactions of low reaction efficiencies and is apparently controlled by the excess energy of the excited intermediate adduct.

Keywords: FT-ICR; Gas phase substitution; Haloanisoles; Ion/molecule reaction; Radical cations

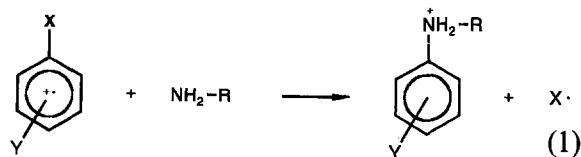
1. Introduction

In previous reports [1,2] the gas phase substitution reactions of halobenzenes with NH_3 , CH_3NH_2 , and $(\text{CH}_3)_2\text{NH}$ via radical cations were discussed. The reaction (1) of halobenzene and dihalobenzene radical cations with

NH_3 or CH_3NH_2 corresponds to a *nucleophilic ipso* substitution of an activated halobenzene [3]. These reactions show a distinct dependence of the individual reaction rates on the differences of the ionization energies (IE) of the amine and the arene as well as on the substitution pattern of the dihalobenzene. These results were explained by an addition–elimination mechanism and interpreted by the

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use of a modified *configuration mixing* model of Shaik and Pross [4].

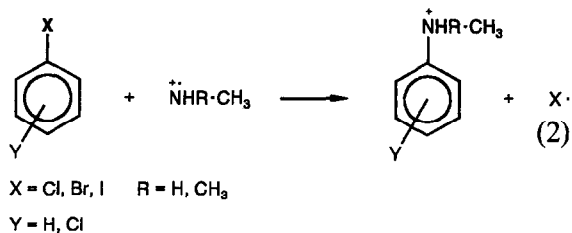


X = Cl, Br, I R = H, CH₃

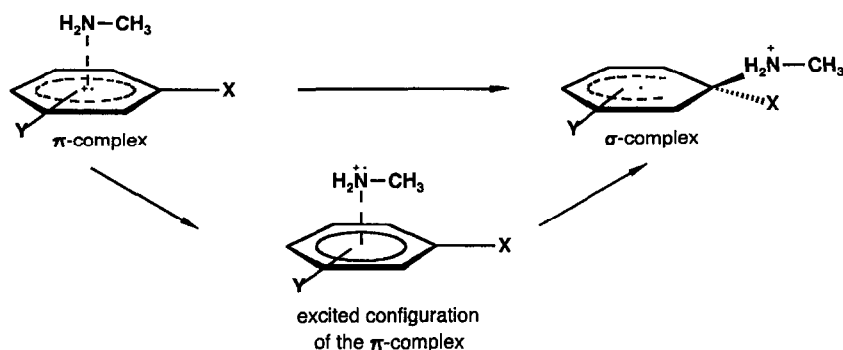
Y = H, F, Cl, Br

For a further investigation of the mechanism(s) of the aromatic substitution via radical cations in the gas phase, the haloanisoles with a substantially lower IE [5] are used in this study. The IE difference (ΔIE) between the haloanisoles and CH₃NH₂ is similar to that of dihalobenzenes and NH₃. Hence, the reactions of chloro- and bromoanisole radical cations with amines are expected to exhibit a close analogy with the corresponding reactions of dihalobenzene radical cations and NH₃ and provide a useful additional test for the mechanistic effects discussed previously.

The *electrophilic ipso* substitution reaction of neutral halobenzenes by amine radical cations in the gas phase was also studied (reaction (2)) [2]. The *configuration mixing model* [4] predicts a small activation barrier for the addition step of this process.



The reactions of CH₃NH₂⁺ ions with the halobenzenes proceed with nearly unit efficiency; the corresponding reactions of (CH₃)₂NH⁺ radical cations are distinctly less efficient, however [2]. The slow reactions of (CH₃)₂NH⁺ radical cation were attributed to an additional rearrangement step besides addition and elimination steps. The initial addition of the amine radical cation to the aromatic ring is energetically favored at the *ortho*- or *para*-position relative to the leaving substituent. Hence, migration of the amino moiety by consecutive 1,2-shifts around the aromatic ring has to take place to arrive eventually at the reactive *ipso*-adduct. The rearrangement of the amino group by this “ring walk” is very likely associated with an activation energy and should depend on the presence of other substituents at the aromatic ring. Eventually this rearrangement may become the rate determining step for less exothermic reactions. To corroborate these explanations and to test the influence of other parameters, the reactions of (CH₃)₂NH⁺ radical cations with neutral



Scheme 1.

chloro- and bromoanisoles are investigated in the second part of this work.

2. Experimental section

The bromoanisoles are commercially available and were used without further purification; chloroanisoles were prepared from the corresponding chlorophenoles by *O*-methylation with methyl *p*-toluenesulfonate [6]. *N*-methyl anisidines were prepared by reaction of the corresponding anisidines with trimethyl orthoformate and subsequent acidic amide cleavage of the *N*-methyl-*N*-formyl anisidines [7]. The purity of the haloanisoles and the anisidines was better than 99% (by gas chromatography) with the exception of 3-bromoanisole which contained 1–2% of 4-bromoanisole. Methylamine (97%) and dimethylamine (99%) were obtained from Merck. Deuterated chloroanisoles were prepared by stirring the chloroanisoles with 74% to 95% D₂SO₄ in D₂O at 100°C.

FT-ICR measurements were performed with a Spectrospin CMS 47X FT-ICR spectrometer [8] equipped with a 4.7 T superconducting magnet, a 24 bit/128 k-word ASPECT 3000 computer, a cylindrical cell of 6 cm diameter and 6 cm length, and an external ion source [9]. The radical ions were generated in the external ion source by electron impact (16–20 eV) from the haloanisoles or amines, and were transferred into the ICR cell. The trapping voltages at the front and back trapping plates were ca. 1 V, the other plates were kept at 0 ± 0.1 V. Selection of the reacting radical cations was achieved by broad band (frequency sweep) ejection of fragment ions of $m/z > 50$. The excitation voltage was attenuated by an attenuator of 6, corresponding to 88 V_{p-p} . Ions of masses below m/z 50 and the isotopomers of the aromatic radical cations containing ¹³C, ³⁷Cl, and ⁸¹Br isotopes were ejected by fixed frequency rf pulses (“single shots”) of 14 V_{p-p} and of 1.5 ms

duration. Special care was taken to remove any kinetic energy from the selected radical cations. The collisional “cooling” of the isolated ions was achieved by a short pulse of argon admitted to the ICR cell by a pulsed valve (opening time 15 ms) prior to the reaction. After a delay time of 500 ms to remove the argon from the cell, any fragment ions formed were ejected by “single shots” (14 V_{p-p} , 1.5 ms). This ejection method diminishes the probability of re-excitation of the reacting ions by the ejection procedure.

The neutral reactant gas was continuously introduced from a reservoir into the ICR cell by a leak valve at a constant pressure of 2×10^{-8} to 7×10^{-7} mbar. The purity of the neutral reactant gas phase in the ICR cell was controlled by a mass spectrum obtained with the internal ionization mode of the spectrometer. The pressure readings of the ionization gauge attached to the vacuum envelope near the diffusion pump of the ICR cell were calibrated by measuring the rates of the reactions $\text{CH}_4^+ + \text{CH}_4$ ($k = 1.5 \times 10^{-9} \text{ cm}^3 \text{ s}^{-1}$ [10]), $\text{NH}_3^+ + \text{NH}_3$ ($k = 2.2 \times 10^{-9} \text{ cm}^3 \text{ s}^{-1}$ [11]), and $\text{CH}_3\text{NH}_2^+ + \text{CH}_3\text{NH}_2$ ($k = 1.8 \times 10^{-9} \text{ cm}^3 \text{ s}^{-1}$ [12]). The relative experimental calibration factors of CH₄, NH₃, and CH₃NH₂ correspond to the known relative sensitivities of the ionization gauge toward these gases [13]. Therefore, the calibration factors of dimethylamine and the aromatic compounds were calculated from the corresponding ion gauge sensitivities by a standard literature procedure [13].

FT-ICR spectra were obtained with 32 K or 64 K data for about 20 different reaction times, covering up to 95% conversion of the reacting ions. After exponential multiplication and Fourier transformation, the ion intensities of the magnitude spectra were normalized with respect to the sum of ions formed after the corresponding reaction time. Pseudo-first order reaction kinetics were obtained from the exponential decay of the signal of the reacting ions.

To ensure correct measurements of the true ion abundances the variation of the sum of the absolute ion intensities with reaction time was examined and compared with the variation of the intensity of trapped unreactive ions at the corresponding delay times (“trapping characteristics”). This method allows a correction of erroneous ion abundance measurements as described in detail elsewhere [8]. If more than one product ion is formed in considerable amounts, this method is not very exact, and the determination of the branching ratio in competitive substitutions of two substituents may be less accurate. In these cases special care was taken to avoid “picket-fence” errors [14] by a suitable gaussian multiplication and use of 64 K data.

Collision activation (CA) spectra of ions formed by ion/molecule reactions in the ICR cell were obtained by rf excitation of the relevant ions and collision with argon. To avoid reactions of the fragment ions with the reactant gas CH_3NH_2 , the amine was introduced by a pulsed valve and pumped off for 10 to 15 s after a reaction delay. In spite of this long pumping time some CH_3NH_2 remains in the ICR cell, giving rise to the formation of CH_3NH_3^+ ions by the reaction with fragment ions formed during the CA experiment. The center-of-mass energy E_{cm} of the collision was adjusted to 17 eV by applying the proper excitation pulse for the molecular ions to the FT-ICR cell. The kinetic energy of the ions after rf excitation was obtained by the following equation [15]:

$$E_{\text{kin}} = \beta^2 \frac{V_{\text{p-p}}^2 q^2 t^2}{8md^2} \quad (3)$$

The parameter β is a factor depending on the geometry of the ICR cell. For a cylindrical cell of length 6 cm and diameter $d = 6$ cm, $\beta = 0.809$ is obtained [15]. $V_{\text{p-p}}$ is the peak-to-peak voltage of the rf-pulse and t the corresponding time. Mass and charge of the ion are given by m and q .

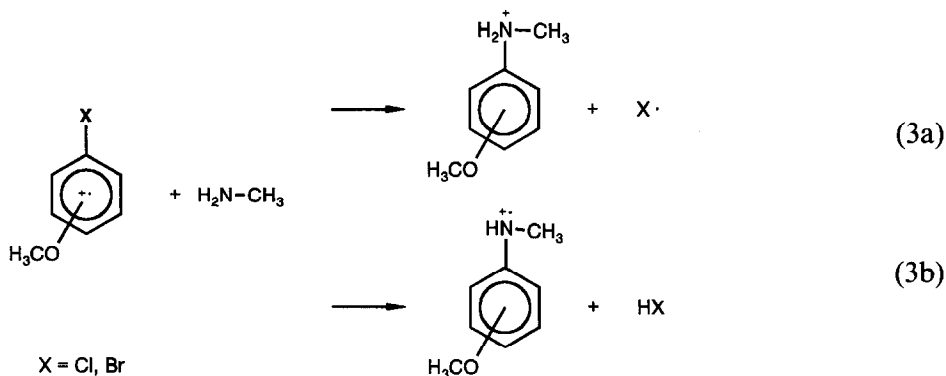
3. Results

Bromoanisole radical cations react with CH_3NH_2 by substitution of the Br atom and formation of protonated *N*-methyl anisidines (reaction 3a), but chloroanisole radical cations yield additionally *N*-methyl anisidine radical cations by elimination of HCl (reaction 3b). The total reaction efficiencies depend on the substitution pattern of the haloanisole radical cation (Table 1). The reactivity is by far highest for the *ortho* isomers and lowest for the *para* isomers. Qualitatively, this reactivity order corresponds to that found for reactions (1) of the dihalobenzene radical cations with ammonia. However, the reactions of *meta* haloanisoles radical ions are comparatively slow. For example, the substitution efficiencies of *ortho*-, *meta*-, and *para*-chloroanisole by CH_3NH_2 are 19%, 3.1%, and 1.3%, while for the analogous reactions of *ortho*-, *meta*-, and *para*-chlorofluoro-benzene radical cations with NH_3 [1] these efficiencies are 12%, 8.4%, and 2.3%, respectively. Similarly, the reactions of isomeric bromoanisole radical cations with CH_3NH_2 exhibit efficiencies of 24%, 4.9%, and 4.3% compared with efficiencies of 14%, 7.5%, 2.8% for the reactions of the bromofluoro-benzene radical cations with NH_3 [1]. A substitution by loss of HCl from haloarene radical

Table 1
Rates constants (k) and efficiencies (eff.) for the reactions (3) of chloro- and bromoanisole radical cations with CH_3NH_2

Radical cation of	k^a	Eff. ^b (%)	$k_{\text{Cl}}/k_{\text{HCl}}^c$	Eff. ^{b,d} (%)	Eff. ^{b,e} (%)
<i>o</i> -Chloroanisole	31	19	10	17	1.7
<i>m</i> -Chloroanisole	5.0	3.1	0.15	0.4	2.7
<i>p</i> -Chloroanisole	2.1	1.3	0.09	0.1	1.2
<i>o</i> -Bromoanisole	37	24			
<i>m</i> -Bromoanisole	7.7	4.9			
<i>p</i> -Bromoanisole	6.8	4.3			

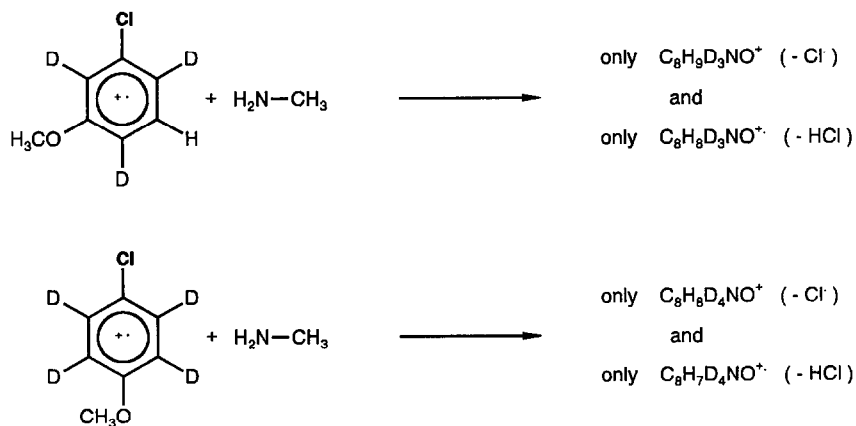
^a $\times 10^{-11} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$. ^b Efficiency = k/k_{cap} ; capture rate, k_{cap} , according to parametrized trajectory calculations [20]. ^c $k_{\text{Cl}}/k_{\text{HCl}}$ = branching ratio of reactions (3a) and (3b). ^d Reaction (3a). ^e Reaction (3b).



cations has previously been observed only for chloriodobenzene radical cations [1], which are not very reactive towards NH_3 because of their low IE. A low IE is also typical of haloanisoles, and the branching ratios for the loss of Cl and HCl (reactions (3a) and (3b)) from these ions are shown in Table 1. The efficiency of reaction (3b) is small for all three isomers and not very different, so the variation of the total reaction efficiencies is mainly due to different rates of reaction (3a).

The elemental composition of the product ions of reactions (3a) and (3b) was confirmed by high resolution ($m/\Delta m > 10^5$) FT-ICR mass spectrometry. Reaction (3a) has previously been shown to correspond to an *ipso*-substitution for dihalobenzenes [1,2,16], and this is also assumed for the haloanisoles. The structures of the substitution products of reaction (3b) were investigated by collision induced decomposition (CID) in the FT-ICR cell by comparison with reference CA spectra of the molecular ions $\text{C}_8\text{H}_{11}\text{NO}^+$, m/z 137, of authentic *N*-methyl anisidines prepared by 20 eV EI ionization and analysed by CID under the same conditions. Several experimental factors may influence the excitation efficiency in FT-ICR spectrometry [17], but under the conditions used the actual center-of-mass energies are nearly identical for all CA spectra. However, the CA spectra of the substitution products were measured with a background of CH_3NH_2 , which could not be removed completely from

the ICR cell prior to the CID, and which gave rise to some CH_3NH_3^+ ions. The uncontrolled formation of CH_3NH_3^+ ions gives rise to changes in the relative fragment ion intensities, thus variations may not be as indicative for structural differences as for undisturbed CA spectra. The CA spectra of the product ions $\text{C}_8\text{H}_{11}\text{NO}^+$ and reference ions are listed in Table 2 with the exception of the CA spectrum of the product ions of *ortho*-chloroanisole radical cations because of their low relative intensity. A comparison of the reference CA spectra of the isomeric *N*-methyl anisidine radical cations shows that the *meta* isomer is clearly distinguished by the characteristic fragment ions at m/z 108, m/z 106, and m/z 93, as well as by the missing ions at m/z 122 and m/z 95. The CA spectra of the *ortho* and *para* isomers contain ions of identical masses, but with different intensities. Characteristic fragment ions are observed at m/z 122, m/z 94, and m/z 77. Neglecting the CH_3NH_3^+ ions, m/z 32, the CA spectra of the substitution product ions from *meta* and *para* chloroanisole radical cations are almost identical to the respective reference CA spectra. It is evident from the abundant ions at m/z 93, m/z 106, and m/z 108, that *N*-methyl *meta*-anisidine radical cations are formed exclusively by the substitution reaction of *meta*-chloroanisole radical cations with CH_3NH_2 . The interpretation of the CA spectrum of the $\text{C}_8\text{H}_{11}\text{NO}^+$ product ions of *para*-chloroanisole is not as straightforward.



Scheme 2.

However, the structure of *N*-methyl *para*-anisidine can be assigned reliably by the high relative abundance (28.9%) of the $[\text{M}-\text{CH}_3]^+$ fragment ions, m/z 122, and the low intensity of the ions m/z 77 (below the detection limit). Therefore, the aromatic substitution by loss of HCl corresponds also to an *ipso*-substitution.

In order to settle the origin of the H atom eliminated with HCl the substitution reactions

of deuterated *meta*- and *para*-chloroanisoles with CH_3NH_2 were studied. During the reaction of the deuterated chloroanisoles shown in Scheme 2, HCl is eliminated exclusively. Neither the methyl group of the methoxy group nor that of the methylamine is obviously involved in the reaction, because these are intact in the product ions (see CA spectra). In the case of the 2,4,6-trideutero-3-chloroanisole loss of HCl by participation of H atoms at the aromatic ring would correspond to the exclusive elimination of the remaining H atom. This would be a very unlikely regiospecificity with respect to participation of the other D atoms at the aromatic ring and, hence, can be excluded. Therefore, the H atom eliminated with HCl originates from the NH_2 group of the invading CH_3NH_2 molecule.

$(\text{CH}_3)_2\text{NH}^+$ ions react with chloro- and bromoanisoles by the loss of Cl^- or Br^- (reaction (4a)) and of HCl (reactions (4b)). However, additionally, charge exchange (4c), proton transfer (4d), and H atom transfer (4e) are observed. The elemental compositions of the ionic reaction products were confirmed by high resolution, but their structures were not investigated by separate experiments.

The total reaction rates are large (Table 3), with the *meta*-isomers being least reactive.

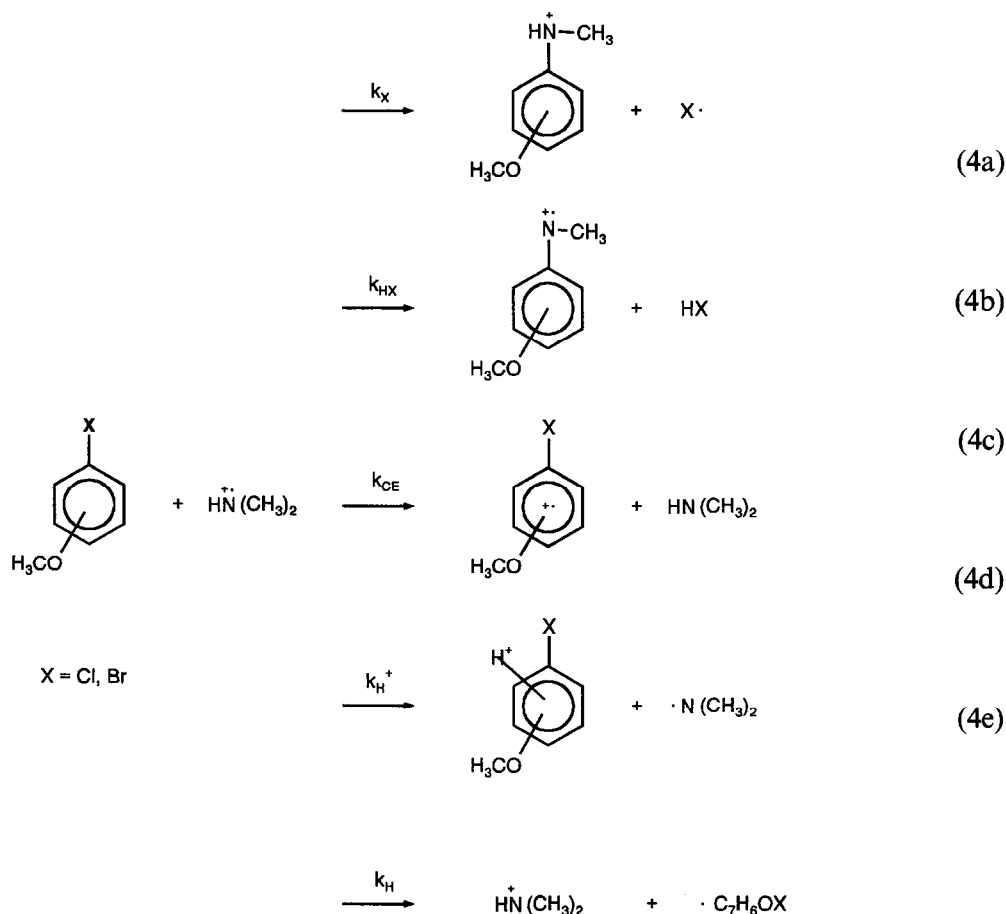
Table 2

CA spectra of $\text{C}_8\text{H}_{11}\text{NO}^+$ ions, m/z 137, formed by reaction of chloroanisole radical cations with CH_3NH_2 and of reference ions from IE (20 eV) of *N*-methyl anisidines

m/z	reaction products m/z 137 ^a		molecular ions of <i>N</i> -methyl anisidines ^b		
	<i>meta</i>	<i>para</i>	<i>ortho</i>	<i>meta</i>	<i>para</i>
137 (M^+)	4.5	3.5	1.5	4.7	2.5
136 $[\text{M}-\text{H}]^+$	1.8	—	—	6.3	—
122 $[\text{M}-\text{CH}_3]^+$	—	28.9	17.9	—	56.5
108 $[\text{M}-\text{CHO}]^+$	13.1	—	—	25.0	—
106 $[\text{M}-\text{CH}_3\text{O}]^+$	8.7	—	—	19.1	—
95	—	—	12.7	—	2.0
94 ($\text{C}_6\text{H}_8\text{N}$)	—	21.3	41.5	1.8	28.2
93 ($\text{C}_6\text{H}_7\text{N}$)	25.6	2.5	—	30.1	—
77	3.7	—	10.1	5.4	2.3
67	—	4.3	4.9	—	3.8
65	3.3	12.6	6.4	1.3	4.7
32 (CH_3NH_3^+)	25.1	17.8	—	—	—
28	—	—	5.0	—	—

^a Rf excitation 9.8 $V_{\text{p-p}}$, 140 μs , ion kinetic energy 120 eV (Eq. (1)).

^b Rf excitation 9.8 $V_{\text{p-p}}$, 110 μs , ion kinetic energy 74 eV (Eq. (1)).



The efficiency of the substitution reaction, eff_{sub} , is obtained by calculating the branching ratio of all processes involved, as shown in Table 4 for the chloroanisoles. Eff_{sub} of *para*-chloroanisole appears to be lower than that of *meta*-chloroanisole, but this is very likely an artefact due to the especially extensive competition of the charge exchange reaction (4c) in this case. The reason is a considerably lower ionization energy (IE) (*para*-chloroanisole) of 7.8 eV [5] compared to $IE((\text{CH}_3)_2\text{NH})$ of 8.23 eV [5]. The substitution of Br of the bromoanisoles by $(\text{CH}_3)_2\text{NH}^+$ is much more straightforward. No loss of HBr is observed and side reactions are limited to a moderate charge exchange, occurring dominantly again only for *para*-bromoanisole. It is evident from

Table 3
Rate constants (k) and efficiencies ($eff.$) for the reactions of chloro- and bromoanisoles with $(\text{CH}_3)_2\text{NH}^+$ ions

Compound	$IE(\text{eV})^a$	k^b	$Eff.^c$ (%)	k_{sub}/k^d	$Eff.^e_{\text{sub}}$ (%)
<i>o</i> -Chloroanisole	8.4	12	46	0.71 ± 0.1	33
<i>m</i> -Chloroanisole		2.9	12	0.40 ± 0.1	4.8
<i>p</i> -Chloroanisole	7.8	9.6	39	0.07 ± 0.01	2.7
<i>o</i> -Bromoanisole		20	79	0.62 ± 0.1	49
<i>m</i> -Bromoanisole		9.1	37	0.76 ± 0.1	28
<i>p</i> -Bromoanisole	8.1	26	109	0.32 ± 0.1	35

^a From Ref. [5]. ^b $\times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$. ^c Efficiency = k/k_{cap} ; capture rate, k_{cap} , according to parametrized trajectory calculations [20]. ^d k_{sub} = rate of the combined substitution reactions (4a) and (4b).

Table 4
Branching ratios of the reactions^a of chloroanisoles with $(\text{CH}_3)_2\text{NH}^+$ ions

Compound	$k_{\text{sub,Cl}}$ (%)	$k_{\text{sub,HCl}}$ (%)	k_{CE} (%)	k_{H^+} (%)	k_{H} (%)
<i>o</i> -Chloroanisole	71	—	21	8.3	—
<i>m</i> -Chloroanisole	24	16	8.7	4.3	47
<i>p</i> -Chloroanisole	5.5	1.5	83	10	—

^a See reaction (4).

eff_{sub} in Table 3, that the substitution reaction of *neutral meta*-bromoanisole by $(\text{CH}_3)_2\text{NH}^+$ ions is slow compared to the *ortho*- and *para*-isomers. This reactivity pattern is different from the *ortho* > *meta* > *para* reactivity order which is valid for the reactions of haloanisole and dihalobenzene *radical cations* with neutral amines, but matches the pattern found for reactions of $(\text{CH}_3)_2\text{NH}^+$ radical ions with *neutral* dichlorobenzenes and chloriodobenzenes [2].

4. Discussion

The reactions of the bromoanisole radical cations with CH_3NH_2 (Table 5) show an almost perfect analogy with the reactions of dibromobenzene or bromofluorobenzene radi-

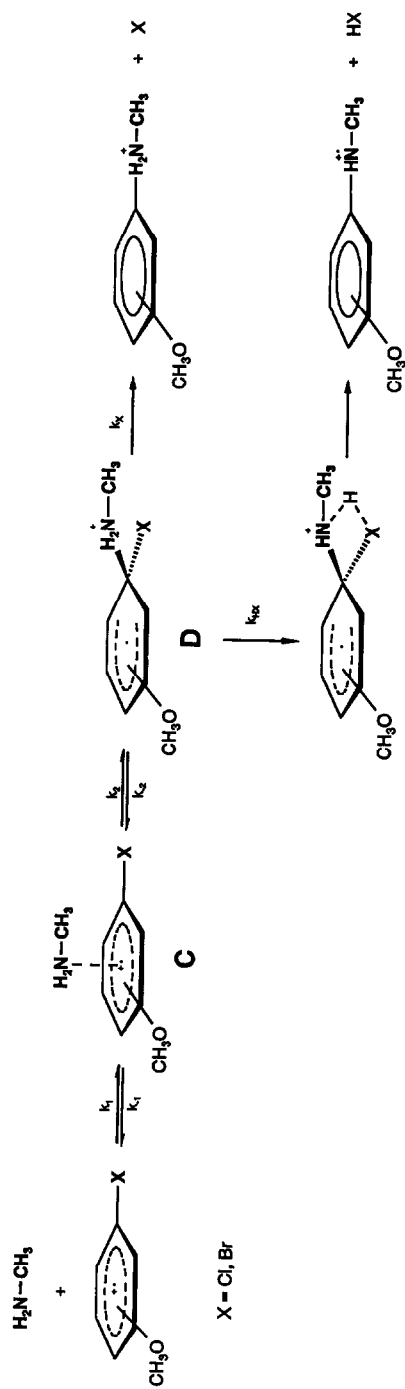
cal cations with NH_3 [1]. The efficiencies of these reactions are fast for small ΔIE of the reactants while a $\Delta IE \approx 2 \text{ eV}$ suppresses any reaction. The reactions of the bromoanisole radical cations ($IE \approx 8.1\text{--}8.4 \text{ eV}$ [5]) with CH_3NH_2 ($IE = 8.97 \text{ eV}$ [5]) have a ΔIE of 0.8–0.9 eV and are in general slightly faster than the reactions of the bromo-fluorobenzene radical cations with NH_3 and a ΔIE of ca. 1.1 eV.

As mentioned before the effect of the aromatic substitution pattern on the reaction efficiencies agrees qualitatively in both series of substitution reactions. It should be emphasized that the variation of the rate of the direct substitution reaction of the haloanisole radical cation and methylamine with the structure of the reactants can be explained convincingly by assuming a mechanism (Scheme 3) with a rate determining formation of the σ -complex **D** from the encounter ion/molecule complex **C**. However, while in the case of the dihalobenzenes radical cations the reactivity order is *ortho* > *meta* \gg *para*, the *ortho*-bromo- and chloroanisole radical cations exhibit an outstanding reactivity (Table 1). This can not be an effect of the dipole moments of the aromatic compounds as discussed before [1]. The

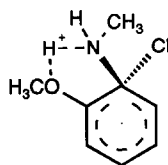
Table 5
Comparison of the reactions of bromoanisole and related bromobenzene radical cations with CH_3NH_2 and NH_3 , respectively

Reaction	ΔIE (eV) ^a	μ_{D} (Ar) ^b	Eff. ^c (%)
<i>o</i> -Bromoanisole ⁺	+ CH_3NH_2	(0.6) ^d	24
<i>m</i> -Bromoanisole ⁺	+ CH_3NH_2	2.35 ^e	4.9
<i>p</i> -Bromoanisole ⁺	+ CH_3NH_2	0.9	4.3
<i>o</i> -Dibromobenzene ⁺	+ NH_3	1.4	14
<i>m</i> -Dibromobenzene ⁺	+ NH_3	1.3	4.1
<i>p</i> -Dibromobenzene ⁺	+ NH_3	1.5	0.91
<i>o</i> -Bromofluorobenzene ⁺	+ NH_3	(1.0) ^d	14
<i>m</i> -Bromofluorobenzene ⁺	+ NH_3	(1.0) ^d	7.5
<i>p</i> -Bromofluorobenzene ⁺	+ NH_3	(1.2) ^d	2.8
<i>p</i> -Bromoanisole ⁺	+ NH_3	2.1	n.r. ^f
Bromobenzene ⁺	+ CH_3NH_2	0.0	58

^a Ref. [5]. ^b Ref. [21]. ^c efficiency = k/k_{cap} ; capture rate, k_{cap} , according to parametrized trajectory calculations [20]. ^d The IE of the bromoarenes are unknown, values given correspond to IE of the chloro derivatives [5]. ^e Estimated from experimental μ_{D} of the *ortho* and *para* isomers, and from MNDO calculations. ^f No reaction. ^g Ref. [2].



Scheme 3.



Scheme 4.

isomers of the haloanisoles have very similar dipole moments (Table 5), and only small reactivity differences between these isomers are expected due to an extra stabilization of the excited reactive configuration of the π -complex (Scheme 1).

The high reactivity of the *ortho* haloanisoles must arise from a special effect of the methoxy substituent. An attractive explanation for the high reactivity of the *ortho* radical cations toward CH_3NH_2 is a stabilization of the reactive *ipso* adduct by a hydrogen bond between the ammonium group and the neighbouring methoxy substituent as indicated in Scheme 4. The special stability of this *ipso* adduct favors its formation either directly during the addition step or by the “ring walk” rearrangement of the amine in the isomeric addition complexes. In contrast, a stabilization of the adduct at the *ortho* position of the methoxy substituent hinders the formation of the *ipso* complexes **D** in the case of the *meta* and *para* haloanisole radical cations. Since formation of **D** is obligatory for the loss of the halogen atom the rates of substitution decrease.

Another special feature of the reactions of the chloroanisole radical cations with methylamine is the formation of substitution products by elimination of HCl. The loss of HCl during substitution of halogenated benzene radical cations by NH_3 and other nucleophiles was also observed by Baumgärtel and Brutschy [18] during a study of intramolecular reactions in van der Waals’ clusters of halobenzenes and NH_3 subsequent to resonant two-photon ionization. In the present case the structure of the product ions arising from the

Table 6

Reaction efficiencies (eff.) and reaction enthalpies, ΔH_f , of reactions (3a) and (3b)^a

Reactant ion	Elimination of X ^c reaction (3a)		Elimination of HX, reaction (3b)	
	ΔH_f [kJ mol ⁻¹]	Eff. (%)	ΔH_f [kJ mol ⁻¹]	Eff. (%)
<i>o</i> -Chloroanisole	-28	17	-152	1.7
<i>p</i> -Chloroanisole	+39 ^b	0.1	-85 ^b	1.2
<i>o</i> -Bromoanisole	-98 ^c	24	-157 ^c	not
<i>p</i> -Bromoanisole	-71	4.3	-130	observed

^a From experimental enthalpies of formation [5], ΔH_f (*N*-methyl anisidine ion) are unknown and were estimated from ΔH_f of anisidine radical cations and of protonated anisidines [5]. The effects of *N*-methyl groups were approximated by using the ΔH_f difference of the corresponding aniline ions and *N*-methyl aniline ions [5]. ^b The literature value of the *IE* (*para*-chloroanisole) of 7.8 eV [5] is very likely too low, yielding a small ΔH_f of the radical cation and a too positive value of ΔH_f . ^c ΔH_f (*ortho*-bromoanisole radical cation) estimated using ΔH_f (*ortho*-bromoanisole) = 42 kJ mol⁻¹ and *IE* \approx 8.4 eV.

loss of HCl here was determined by CA mass spectrometry which verifies an *ipso* substitution process also for the elimination of HCl from the addition intermediate. The H atom eliminated with HCl certainly originates from the NH_2 group of the methylamine as shown by the reactions of the radical cations of deuterated haloanisoles. The labelling experiments exclude also any exchange of hydrogen atoms of the amine and at the aromatic ring. Thus, an intermediate arising by hydrogen abstraction from the amine by the radical site in the collision complex **C** or in the adduct **D** (Scheme 3) is excluded. More likely, the hydrogen atom migrates directly from the amino group to the leaving chloro substituent.

The values of the respective ΔH_f in Table 6 show that the elimination of HCl is always favored energetically over the loss of the halogen atom. However, although the bromoarene radical cations are substituted with almost identical efficiencies to those of the corresponding chloroderivatives, the loss of HBr is not observed. Furthermore, the elimination of HCl occurs only if the loss of Cl is slow, and

thus has been observed before during the reactions of the unreactive radical cations of chloriodobenzenes [1] with NH_3 and CH_3NH_2 . Clearly, these competing substitution reactions by loss of Cl or HCl lack any correlation with the reaction enthalpy, and obviously in both reactions the rate determining reaction step is *not* bond breaking to the halosubstituent.

The elimination of HCl during the substitution reaction of haloarene radical cations with NH_3 or amines must involve an additional slow reaction step, so that HCl elimination cannot compete with Cl elimination in fast substitution reactions (reaction efficiency > 10%). Furthermore, the occurrence of HCl elimination and the branching between loss of Cl and HCl depend on the particular structure of the haloarene radical cation. For example, in the series of dihalobenzenes the 1-chloro-2-iodobenzene radical cations react about five times faster with NH_3 than the *para* dichlorobenzene radical cations, but only the former ions react by loss of HCl [1]. In addition, the reaction of 1-chloro-2-iodobenzene radical cations with NH_3 is faster by a factor > 300 than that of the 1-chloro-4-iodo isomer, but the ratio for the loss of Cl, HCl, and I is almost identical for both radical cations [1]. Obviously, the rate determining step for both substitution reactions precedes that point on the reaction coordinate where branching between loss of X and HX takes place. The kinetic behavior of the chloroanisole radical cations during the reactions with CH_3NH_2 implies that the rate determining step is the addition step $\text{C} \rightarrow \text{D}$ (Scheme 3). Therefore, the competition between substitution by loss of Cl and HCl takes place in an intermediate chemically activated by the preceding addition step and can be described in analogy to unimolecular decompositions of excited ions by competition between direct bond cleavage and rearrangement processes. Thus, the ions with less internal energy prefer a slow decom-

position by energetically favorable rearrangements, in the case discussed the elimination of HCl, while strongly excited ions decompose rapidly by entropically favored direct bond cleavages, i.e. the loss of Cl. This means that branching between the two substitution routes of the haloarene radical cations is controlled by the activation energy and exothermicity of the dissociation steps for the loss of Cl and HCl *and* by the extent of a chemical activation by preceding reaction steps. This causes a complicated interplay of energetic and entropic effects which is difficult to untangle experimentally.

The reactions of $(\text{CH}_3)_2\text{NH}^+$ radical cations with neutral bromo- and chloroanisoles occur predominantly by substitution of the halogen atom (reaction (4a)) and by charge transfer (reaction (4c)). The loss of bromine or chlorine from the neutral haloanisoles by reaction with $(\text{CH}_3)_2\text{NH}^+$ exhibits the same *ortho* \gg *para* > *meta* reactivity order as the reactions with chloriodobenzenes [2]. This indicates analogous reaction mechanisms; a detailed discussion of the mechanisms of the substitutions of neutral halobenzenes by amine radical cations has been published [2]. However, the reaction of $(\text{CH}_3)_2\text{NH}^+$ with chloroanisoles exhibits some additional features, not observed for dihalobenzenes and for bromoanisoles (Table 3). Substitution by elimination of HCl (reaction (4b)) is observed for *meta*- and *para*-chloroanisole, but not for *ortho*-chloroanisole. In the latter case the loss of Cl is quite efficient, and this is a further example of the rule that elimination of HCl competes only with slow losses of Cl in spite of the much larger reaction exothermicity of HCl loss. The parallel behaviour with respect to the elimination of HCl in *nucleophilic* substitution of chloroanisole radical cations by CH_3NH_2 and *electrophilic* substitution of neutral chloroanisoles by $(\text{CH}_3)_2\text{NH}^+$ radical cation corroborates analogous intermediates in both processes which are responsible for the branching

between loss of Cl and of HCl. This intermediate can only be the σ -complex **D** generated in the addition step. Thus, these results give additional credit to the HCl mechanism discussed above. Note, however, that for *nucleophilic* and *electrophilic* substitutions different amines were used. The internal energy of complex **D** is therefore different for the two processes. The transfer of a proton from the $(\text{CH}_3)_2\text{NH}^+$ to chloroanisoles (reaction (4d)) is certainly induced by the enhanced proton affinity of the chloroanisoles. The proton affinities of the haloanisoles are not known and it remains ambiguous why H^+ transfer is observed for chloroanisoles but not for bromoanisoles. The formation of $(\text{CH}_3)_2\text{NH}_2^+$ (reaction (4e)) corresponds formally to H abstraction from chloroanisole. The reaction $(\text{CH}_3)_2\text{NH}^+ + \text{C}_6\text{H}_5\text{OCH}_3 \rightarrow (\text{CH}_3)_2\text{NH}_2^+ + \text{C}_6\text{H}_5\text{OCH}_2$ is exothermic by -74 kJ mol^{-1} and by analogy a H atom transfer should be exothermic for all bromo- and chloroanisoles. However, the reaction is only observed for the *meta* isomer, and the H transfer very likely occurs by a rather complex and still unknown mechanism.

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References

[1] D. Thölmann and H.Fr. Grützmaier, *J. Am. Chem. Soc.*, 113 (1991) 3281.

- [2] D. Thölmann and H.Fr. Grützmaier, *Int. J. Mass Spectrom. Ion Processes*, 117 (1992) 415,
- [3] J. March, *Advanced Organic Chemistry*, 3rd edn., Wiley, New York, 1985.
- [4] (a) A. Pross and S.S. Shaik, *Acc. Chem. Res.*, 16 (1983) 363. (b) S.S. Shaik, *Prog. Phys. Org. Chem.*, 15 (1985) 197. (c) S.S. Shaik and A. Pross, *J. Am. Chem. Soc.*, 111 (1989) 3537. (d) S.S. Shaik, *Acta Chem. Scand.*, 44 (1990) 205. (e) S.S. Shaik and E. Canadell, *J. Am. Chem. Soc.*, 112 (1990) 1446.
- [5] S.G. Lias, J.F. Liebman, J.L. Holmes, R.D. Levin and W.G. Mallard, *J. Phys. Chem. Ref. Data*, 17 (1988) Suppl. 1.
- [6] F. Drahowzal and D. Klamann, *Monatsh. Chem.*, 82 (1951) 588.
- [7] L.-F. Tietze and T. Eicher, *Reaktionen und Synthesen*, Thieme-Verlag: Stuttgart, 1981.
- [8] M. Allemann, Hp. Kellerhals and K.P. Wanczek, *Int. J. Mass Spectrom. Ion Phys.*, 46 (1983) 139.
- [9] P. Kofel, M. Allemann, Hp. Kellerhals and K.P. Wanczek, *Int. J. Mass Spectrom. Ion Proc.*, 65 (1985) 97.
- [10] D. Smith and N.G. Adams, *Int. J. Mass Spectrom. Ion Phys.*, 23 (1977) 123.
- [11] N.G. Adams, D. Smith and J.F. Paulson, *J. Chem. Phys.*, 72 (1980) 288.
- [12] T.B. McMahon and J.L. Beauchamp, *J. Phys. Chem.*, 81 (1977) 593.
- [13] J.E. Bartmess and R.M. Georgiadis, *Vacuum*, 33 (1983) 149.
- [14] A.J. Noest and C.W.F. Kort, *Comput. Chem.*, 6 (1982) 115.
- [15] P. Kofel, *Dissertation*, Bremen (1987).
- [16] D. Thölmann, R. Wolf and H.-Fr. Grützmaier, *Adv. Mass Spectrom.*, 11A (1989)556.
- [17] (a) C.D. Hanson, E.L. Kerley, M.E. Castro and D.H. Russel, *Anal. Chem.*, 61 (1989) 2040. (b) M. Wang and A.G. Marshall, *Anal. Chem.*, 62 (1990) 515. (c) C.D. Hanson, M.E. Castro, E.L. Kerley and D.H. Russel, *Anal. Chem.*, 62 (1990) 520. (d) A.R. Katrizky, C.H. Watson, Z. Dega-Szafran and J.R. Eyler, *J. Am. Chem. Soc.*, 112 (1990) 2471. (e) P.B. Grosshans and A.G. Marshall, *Int. J. Mass Spectrom Ion Processes*, 115 (1992) 1.
- [18] (a) B. Brutschy, *J. Phys. Chem.*, 94 (1990) 8637. (b) J. Eggert, C. Janes, B. Wassermann, B. Brutschy and H. Baumgärtel, *Ber. Bunsenges. Phys. Chem.*, 94 (1990) 1282. (c) B. Brutschy, J. Eggert, C. Janes and H. Baumgärtel, *J. Phys. Chem.*, 95 (1991) 5041. (d) C. Riehn, J. Avdiew, J. Eggert, B. Wassermann, B. Brutschy and H. Baumgärtel, *J. Mol. Struct.*, 249 (1991) 33. (e) C. Riehn, C. Lahmann and B. Brutschy, *J. Phys. Chem.*, 96 (1992) 3626.