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ARTICLE *in* JOURNAL OF MASS SPECTROMETRY · JUNE 2004

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J. Mass Spectrom. 2004; **39**: 647–654
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jms.632

Site of alkylation of *N*-methyl- and *N*-ethylaniline in the gas phase: a tandem mass spectrometric study

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Received 18 November 2003; Accepted 9 February 2004

***N*-Methylaniline (NMA) was ethylated and *N*-ethylaniline (NEA) was methylated under chemical ionization conditions using C_2H_5I and CH_3I, respectively, as reagent gases. The structures of the resulting *m/z* 136 adduct ions have been probed using metastable ion and collision-induced dissociation (CID) methods. From the similarity of the spectra obtained and from the presence of structure-diagnostic ions at *m/z* 59 ($CH_3NHC_2H_5^{+\bullet}$) and *m/z* 44 ($CH_3NHCH_2^+$), it is concluded that predominantly *N*-alkylation occurs in both systems. This interpretation was aided by the use of C_2D_5I and CD_3I as reagents. Adduct ions of *m/z* 136 were also formed by ethylation of the isomeric toluidines and by methylation of the ring-ethylanilines. The resulting CID mass spectra were distinctly different from those obtained for the *m/z* 136 ions obtained by alkylation of NMA and NEA. Protonation of *N*-ethyl-*N*-methylaniline using $CH_3C(=O)CH_3$ as Brønsted acid reagent produced an *m/z* 136 species whose CID mass spectrum also featured intense ion signals at *m/z* 59 and 44. This observation led to the conclusion that protonation with acetone as reagent results, in this case, in dominant *N*-protonation. However, the CID mass spectrum of the *m/z* 136 ion formed when CH_3OH was the protonating agent featured a weak signal at *m/z* 44 and no signal at *m/z* 59. Hence it was concluded that the latter *m/z* 136 ion contains a larger contribution from the ring-protonated adduct. Copyright © 2004 John Wiley & Sons, Ltd.**

KEYWORDS: aniline; chemical ionization; collision-induced dissociation; alkylation; protonation

INTRODUCTION

The site of protonation and alkylation of functionalized aromatic and heterocyclic molecules in solution and in the gas phase is a topic of considerable interest which has received a great deal of attention.[1–19] Protonation and alkylation of such molecules in the gas phase can conveniently be performed in the chemical ionization (CI) source of a mass spectrometer. The structure of the reaction products, and hence the site of electrophile attachment, can then be probed by examining their metastable ion (MI)[20] and collision-induced dissociation (CID)[21,22] mass spectra.

Aniline is a prime example of an aromatic molecule whose gas-phase proton and alkyl ion attachment reactions have been studied considerably.[1–19] Aniline is a well-known nitrogen base in solution. In the gas phase, calculations at various levels of theory including G2(MP2) invariably predict *N*-protonation as being slightly more favourable, by 1–3 kcal mol^{-1} (1 kcal = 4.184 kJ)[19] than protonation at the *para* position of the ring. In line with this, there have been several experimental studies of the gas-phase protonation of different anilines in which both ring- and *N*-protonation have been reported.[3,4,7,11,13] Furthermore, experimental studies of the alkylation of aniline in the gas phase also have yielded conflicting results concerning the site of attachment.[5,7,11,12] In this context, it should be mentioned that chemical ionization-type protonation experiments are not necessarily thermodynamically controlled.[23]

Maquestiau *et al*.[5] used MI and CID spectra to study the protonation and ethylation of a series of aromatic amines. For the anilines they observed that the MI and CID spectra of protonated 2-, 3- and 4-ethylaniline were similar to those of ethylated aniline but differed considerably from those of protonated *N*-ethylaniline. Therefore, it was concluded that the ring-alkylanilines underwent ring protonation whereas aniline underwent ring ethylation. There was, however, predominant *N*-protonation of *N*-ethylaniline. In the same study, Maquestiau *et al*. found that, under CI conditions using CH_4, pyridine was ethylated at the nitrogen site. This followed from the observation that the MI and CID mass spectra of the product of the ethylation of pyridine were characteristically different from those of the protonated ring-substituted ethylpyridines. Additionally, the MI and CID mass spectra of the product of ethylation of pyridine-d_5 showed loss of $C_2H_4D^\bullet$, whereas in the corresponding experiment with unlabelled pyridine there was loss of $C_2H_5^\bullet$. Therefore, nominal loss of $C_2H_5^\bullet$ occurred by consecutive losses of $H^\bullet + C_2H_4$.

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Contract/grant sponsor: Natural Sciences and Engineering Research Council (Canada).

Cooks and co-workers[7] used both low- and high-energy CID experiments to investigate the site of H^+, CH_3^+ and $C_2H_5^+$ attachment to aniline and other aromatic molecules. The reagents were isobutene for protonation, methane and ethyl bromide for ethylation and methyl fluoride and methyl chloride for methylation. They noted that varying the methylating or ethylating agent yielded similar high-energy CID mass spectra. They compared the CID mass spectra of the CH_3^+ and $C_2H_5^+$ attachment ions of aniline with the isomeric ion formed by proton attachment to the ring-methyl-or ethylanilines and concluded that the alkyl cations attached to the nitrogen site whereas proton attachment occurred on the ring. In a later study, Cooks and co-workers[11] employed CID to investigate the relationship between charge stripping and ring versus nitrogen attachment to the same compounds as in the previous study. They observed that when the aromatic compounds underwent cation attachment to the ring, there was a direct correlation with the extent of charge stripping under high-energy collisional activation, i.e. ring-adduct ions underwent a higher incidence of charge stripping than substituent-adduct ions. Using this criterion, they concluded that aniline underwent ring protonation and substituent alkylation.

Electrophile attachment of aniline in radiolytic and mass spectrometric experiments was investigated by Attina and Cacace.[8] It was found that *N*-attachment relative to ring-attachment decreases in the order $CH_3CO^+ > t-C_4H_9^+ > (CH_3)_2F^+ > i-C_3H_7^+ \approx C_2H_5^+$ with the CH_3CO^+ ion attaching most readily to the NH_2 moiety. It was further noted that, in the case of ring substitution, the *ortho* products predominated. The authors rationalized the observed order by invoking the hard and soft acid and base (HSAB) concept, which states that hard acids, such as CH_3CO^+, bind preferentially to hard bases, such as NH_2. Ranking the electrophiles according to their hardness would result in the same order as shown above.

Burinsky and Campana[12] used CID to investigate the site of attachment of chlorinated alkyl ions to aniline, phenol, benzaldehyde, benzonitrile and nitrobenzene. It was observed that aniline, benzonitrile and nitrobenzene underwent substituent attack whereas phenol and benzaldehyde underwent both substituent and ring attachment.

Using CD_4 chemical ionization, Harrison[9] recorded the MI mass spectra of the products of $C_2D_5^+$ attachment to ethylbenzene, *p*-ethyltoluene and *N*-ethylaniline. As expected, the spectra of the adducts of $C_2D_5^+$ to ethylbenzene and *p*-ethyltoluene showed equal loss of C_2H_4 and C_2D_4, indicating that the two ethyl groups had become equivalent. By contrast, the MI spectrum of the product of $C_2D_5^+$ addition to *N*-ethylaniline showed unequal loss of C_2H_4 and C_2D_4, indicating that the ethyl groups had not become equivalent. The results were rationalized by proposing that the ethyl cation attacked the ring rather than the nitrogen for *N*-ethylaniline.

Nold and Wesdemiotis[14] used neutralization–reionization mass spectrometry (NRMS)[24] to study the site of protonation of aniline. If aniline undergoes *N*-protonation then an anilinium cation is formed whereas with ring protonation a benzenium ion is formed. On neutralization, the anilinium ion forms a hypervalent ammonium radical, which can dissociate either by rupture of an N—H bond or by rupture of the phenyl—N bond. By contrast, neutralization of the ring-protonated species forms an aminobenzenium radical that may remain intact. On reionization, Nold and Wesdemiotis observed $NH_3^{+\bullet}$, which they assumed arose by fragmentation of the ammonium ion neutral and was thus a measure of *N*-protonation. They also observed $C_6H_8N^+$, the recovered ion signal, which they took as an indicator of ring protonation. For protonated aniline formed by fast atom bombardment (FAB), where *N*-protonation is expected, they observed $[C_6H_8N^+]/[NH_3^{+\bullet}]$ to be 0.7. By contrast, protonation of aniline by Brønsted acid CI using CH_4, CH_3OH, $n-C_3H_7OH$, $i-C_4H_{10}$ and NH_3 gave, upon NRMS, $[C_6H_8N^+]/[NH_3^{+\bullet}]$ ratios in the range 8.5–12.4. They concluded that Brønsted acid CI of aniline resulted in predominantly ring protonation.

Harrison and Tu[18] performed both MI and low-energy CID experiments to determine the site of protonation of *N*-alkylanilines under Brønsted acid CI and FAB ionization conditions. They concluded that, under CI conditions using CH_4, CH_3OH and $CH_3C(=O)CH_3$ as reagents, predominantly ring protonation occurred. In contrast, with $i-C_4H_9NH_2$ as CI reagent and with FAB ionization predominantly *N*-protonation occurred.

To pursue further the study of the site of electrophile attachment to substituted aromatic molecules, we carried out a CI study of the site of $C_2H_5^+$ and CH_3^+ attachment to *N*-methylaniline and *N*-ethylaniline, respectively. The structures of the reaction products (*m/z* 136) were investigated by MI and CID studies. The CID mass spectra obtained were compared with those for the isomeric ions formed by $C_2H_5^+$ attachment to the isomeric toluidines and CH_3^+ attachment to the isomeric *o*-, *m*- and *p*-ethylaniline and 6-ethyl- and *N*-ethyl-*o*-toluidine. The alkylation and protonation reactions were also carried out using the deuterated isotopologues of the alkylating and protonating reagents.

EXPERIMENTAL

The experiments were performed on the McMaster University VG Analytical (Manchester, UK) ZAB-R instrument of BE_1E_2 geometry (B = magnet, E = electric sector).[25] The alkylation reactions were performed in a CI source at a total pressure in the (1–5) $\times 10^{-5}$ Torr (1 Torr = 133.3 Pa) range as read by the ionization gauge attached to the source housing and using the alkylating agent in excess. A typical CI mass spectrum of CH_3I and *N*-ethylaniline (NEA) showed ions at *m/z* 142 (100%, $CH_3I^{+\bullet}$), *m/z* 157 (70%, $(CH_3)_2I^+$), *m/z* 284 (100%, $(CH_3I)_2^{+\bullet}$), *m/z* 121 (35%, $NEA^{+\bullet}$) and *m/z* 136 (5%, $(NEA + CH_3)^+$). Very little protonation of the *N*-ethylaniline or dissociation of the molecular ion occurred. The reaction forming the CH_3^+ adduct is not confidently known but may involve CH_3^+ transfer from the $(CH_3)_2I^+$ ion. The NEA molecular ion may originate by charge transfer from the CH_3I^+ ion ($IE(CH_3I) = 9.5$ eV, $IE(NEA) = 7.7$ eV).[27] A typical CI mass spectrum of C_2H_5I and *N*-methylaniline (NMA) displayed the $NMA^{+\bullet}$ ion (*m/z* 107) as the base peak with the ions derived from C_2H_5I, *m/z* 156 ($C_2H_5I^{+\bullet}$), *m/z*

185 ($(C_2H_5)_2I^+$) and *m/z* 312 ($(C_2H_5I)_2^{+\bullet}$) having relative abundances of 15, 35 and 30%, respectively. Significant protonation of both NMA and C_2H_5I also occurred. The ethyl ion adduct ($(NMA + C_2H_5)^+$) typically had an intensity of ~15% of the base peak.

Although the respective adduct ions at *m/z* 136 were not the major ions in the spectra, their MI and CID mass spectra were easily recorded. The MI mass spectra were recorded for fragmentation reactions occurring in the second field-free region whereas the CID mass spectra were recorded for fragmentation reactions occurring in the second field-free region using O_2 as the collision gas (70% transmittance) at 8 keV translational energy. Ions of *m/z* 136 were also prepared by ethylation of the isomeric toluidines and methylation of the isomeric ring ethylanilines and their CID mass spectra recorded. In addition, ions of *m/z* 136 were prepared by Brønsted acid chemical ionization of *N*-methyl-*N*-ethylaniline and 6-ethyl- and *N*-ethyl-*o*-toluidine using CH_3OH or $CH_3C(=O)CH_3$ as reagent gas. Metastable ion and CID experiments also were carried out for the adducts $(NEA + CD_3)^+$ and $(NMA + C_2D_5)^+$ generated from alkylation reactions of CD_3I with NEA and C_2D_5I with NMA.

The anilines studied and the various (labelled) reactants were obtained from Aldrich Chemical.

RESULTS AND DISCUSSION

Alkylation of *N*-methylaniline (NMA) and *N*-ethylaniline (NEA)

To probe the structures of the *m/z* 136 ions generated via the ethylation of NMA and the methylation of NEA we obtained their MI and CID mass spectra. MI mass spectra represent the spontaneous dissociation of mass-selected ions in one of the field-free regions of the instrument. These ions have a higher internal energy content than those sampled by CID experiments.[22] For precursor ions prepared by electron ionization, the fraction of metastable ions in the ion beam is often fairly high, with the result that reliable MI spectra are usually easily obtained. However, in CI experiments the fraction of metastable ions in the ion beam frequently is much smaller, creating the possibility that the MI spectra may become contaminated with CID peaks resulting from residual background gas or by artefact signals. With this caveat in mind, we interpreted the weak metastable ion signals of the *m/z* 136 ions generated by the alkylation reactions and also the *m/z* 139 ions obtained by methylation of NEA with CD_3I and the *m/z* 141 ions obtained by the ethylation of NMA with C_2D_5I.

Table 1 records the MI mass spectra obtained. Three fragmentation reactions are observed, loss of $CH_3^\bullet$, elimination of C_2H_4 and loss of $C_2H_5^\bullet$. Deuterium labelling shows that the methyl group lost does not originate from the ethyl groups but rather is the original methyl group present (NMA) or added (NEA). Harrison[17] observed these three fragmentation reactions at low collision energies in the fragmentation of protonated *N*-methyl-*N*-ethylaniline prepared by electrospray ionization where protonation most likely occurs at nitrogen. The similar fragmentation modes in the present systems strongly suggest that alkylation has occurred at nitrogen rather than on the aromatic ring. Thermochemically, elimination of C_2H_4 from the adducts is favoured as the following data[26] show:

Table 1. Metastable ion fragmentation of adducts

Neutral species lost	Adduct studied: $C_2H_5^+$–NMA	$C_2D_5^+$–NMA	CH_3^+–NEA	CD_3^+–NEA
$CH_3^\bullet$	10	13	—[a]	
$CD_3^\bullet$				30
C_2H_4	100		67	50
C_2D_4		100		
$C_2H_5^\bullet$	45		100	100
$C_2D_5^\bullet$		50		

[a] 100% in the MI spectrum but there is contribution from $NEA^{+\bullet}$, *m/z* 121, as can be determined from the normal mass spectrum. The percentage contribution was not determined.

$$C_6H_5NH(CH_3)(C_2H_5)^+ \longrightarrow C_6H_5NHC_2H_5^{+\bullet} + {}^\bullet CH_3 \quad \Sigma\Delta H_f \text{ (Prod)} \leq 225 \text{ kcal mol}^{-1} \tag{1}$$

$$\longrightarrow C_6H_5NHCH_4^+ + C_2H_4 \quad \Sigma\Delta H_f \text{ (Prod)} = 181 \text{ kcal mol}^{-1} \tag{2}$$

$$\longrightarrow C_6H_5NHCH_3^{+\bullet} + {}^\bullet C_2H_5 \quad \Sigma\Delta H_f \text{ (Prod)} = 217 \text{ kcal mol}^{-1} \tag{3}$$

However, there is substantial evidence[17,27,28] that fragmentation of ammonium ions occurs by way of ion/neutral complexes as outlined in Scheme 1 and that the relative importance of the fragmentation channels is determined by the relative energies of the complexes $[R^+ \cdots NH_{4-n}R_{n-1}]$ (pathway 1 in Scheme 1) and $[R_{n-1}H_{4-n}N^{+\bullet} \cdots R]$ (pathway 2 in Scheme 1). Thus, using standard thermochemical data[26] we derive the following, where *BE* is the binding energy in the complex:

$$C_6H_5NH(CH_3)(C_2H_5)^+ \longrightarrow C_6H_5NHC_2H_5^{+\bullet} \cdots {}^\bullet CH_3 \quad \Sigma\Delta H_f \text{ (Complex)} = 225 - BE \text{ kcal mol}^{-1} \tag{4}$$

$$\longrightarrow C_6H_5NHCH_3 \cdots {}^+C_2H_5 \quad \Sigma\Delta H_f \text{ (Complex)} = 236 - BE \text{ kcal mol}^{-1} \tag{5}$$

$$\longrightarrow C_6H_5NHCH_3^{+\bullet} \cdots {}^\bullet C_2H_5 \quad \Sigma\Delta H_f \text{ (Complex)} = 217 - BE \text{ kcal mol}^{-1} \tag{6}$$

Assuming that intermediate complexes are formed, the three reaction pathways now become more competitive with regard to energy requirements. It should be noted that fragmentation of the $[C_6H_5NHCH_3^{+\bullet} \cdots {}^\bullet C_2H_5]$ complex to give the final products of Eqn (3) is endothermic whereas proton transfer and decomposition of the $[C_6H_5NHCH_3 \cdots {}^+C_2H_5]$ complex to give the final products (Eqn (2)) is an exothermic reaction. Although the metastable ion peak shapes for both

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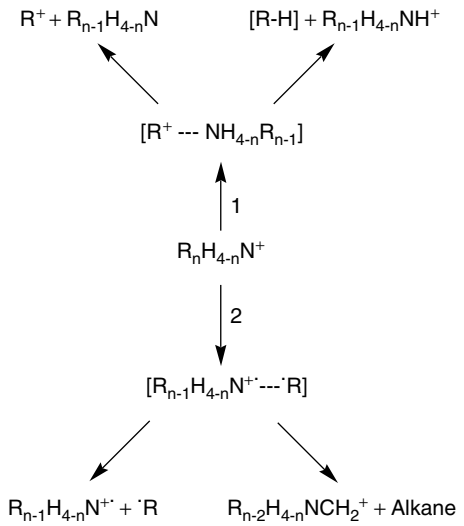


Scheme 1

loss of C_2H_4 and loss of $C_2H_5^{\bullet}$ were Gaussian in shape, that for the former was broader and hence consistent with the conclusion that the final step in C_2H_4 elimination is exothermic. The relative metastable ion signals for loss of C_2H_4 and $C_2H_5^{\bullet}$ are substantially different for the $C_2H_5^+$–NMA adduct and the CH_3^+–NEA adduct (see Table 1). Harrison[17] observed that, under low-energy CID conditions, the relative signals for C_2H_4 and $C_2H_5^{\bullet}$ loss are strongly energy dependent, with loss of $C_2H_5^{\bullet}$ increasing in relative importance with increasing internal energy. The metastable ion experiments can be interpreted in terms of a higher energy content of the CH_3^+–NEA adduct.

The CID mass spectra obtained for the CH_3^+–NEA and $C_2H_5^+$–NMA adducts are presented in Fig. 1. The close similarity of the two spectra suggests that the same structure is involved in each case, presumably the *N*-cationized species. Major peaks are observed at *m/z* 120, 107, 106 and 77. In the low-energy CID of protonated *N*-methyl-*N*-ethylaniline prepared by ESI, Harrison[17] reported major ions at *m/z* 107, 106 and 77 and proposed the reaction sequence shown in Scheme 2. Harrison did not observe a significant ion signal at *m/z* 120, formally corresponding to loss of CH_4 (or consecutive losses of $H^{\bullet}$ and $CH_3^{\bullet}$), in the low-energy CID spectrum. Further support for *N*-alkylation in both systems is the presence of ion signals at *m/z* 59 and 44 in the CID mass spectra in Fig. 1. As the CID spectra in Fig. 2 show, these ion signals shift to *m/z* 62 and 47 for the CD_3^+/NEA adduct and to *m/z* 64 and 46 for the $C_2D_5^+$/NMA adduct. These results indicate collision-induced loss of the phenyl radical from the adduct to form $CH_3NHC_2H_5^{+\bullet}$ (*m/z* 59), which further fragments to form $CH_3NHCH_2^+$ (*m/z* 44), a known fragmentation of ionized methylethylamine. It should be noted that the spectra in Fig. 2 show that the loss of CH_4 or consecutive losses of $H^{\bullet}$ and $CH_3^{\bullet}$ (to form *m/z* 120) in the CID of the adducts involves loss of $CH_3^{\bullet}$ from the ethyl group accompanied, most likely, by loss of $H^{\bullet}$ from the nitrogen whereas loss of $CH_3^{\bullet}$ involves the methyl group present (or added).

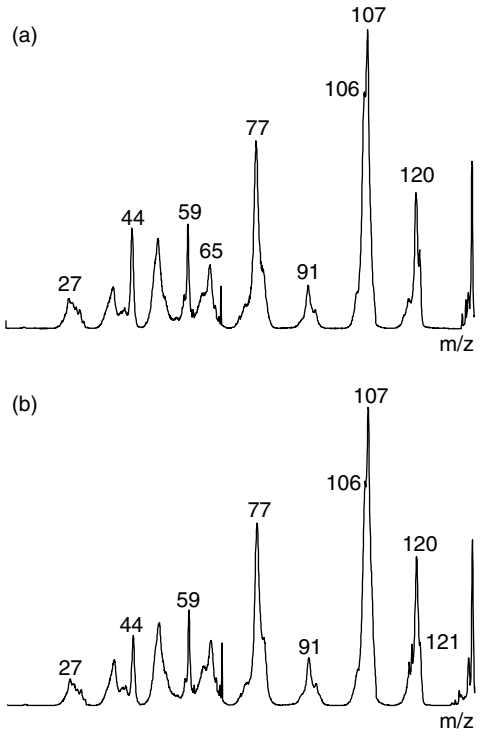
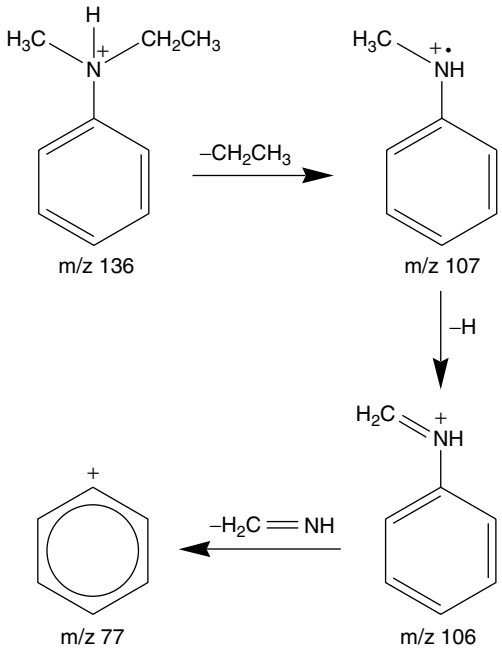


Figure 1. CID mass spectra of the $C_9H_{14}N^+$ (*m/z* 136) ions formed by (a) CH_3^+ addition to NEA and (b) $C_2H_5^+$ addition to NMA.



Scheme 2

Ethylation of toluidines and methylation of ring-ethylanilines

In aromatic electrophilic substitution of aniline in the solution phase, the *ortho* and *para* positions are attacked, with a preference for the *para* position.[29] Assuming *N*-ethylation of the toluidines, the *m/z* 136 adduct formed should yield a CID mass spectrum similar to that for the product of ring

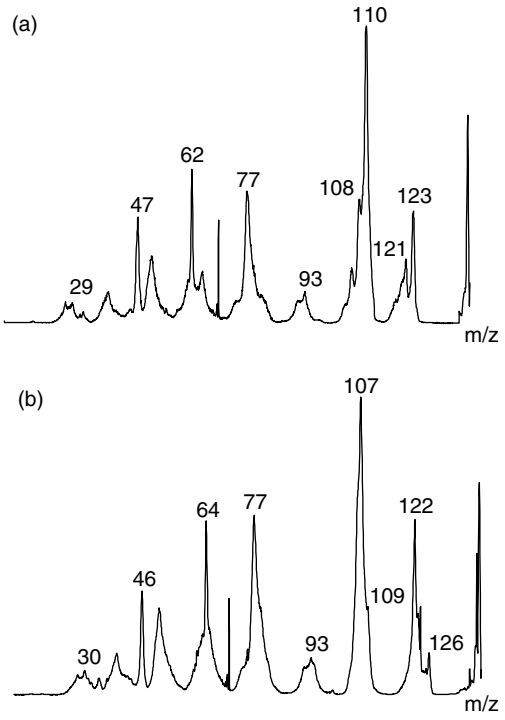


Figure 2. CID mass spectra of the ions generated by (a) CD_3^+ addition to NEA and (b) $C_2D_5^+$ addition to NMA.

methylation of NEA. Similarly, *N*-methylation of the ring-ethylanilines should yield an *m/z* 136 product with a CID mass spectrum similar to that expected for ring ethylation of NMA.

The CID mass spectra obtained for the *m/z* 136 ions formed by ethylation of *o*-, *m*- and *p*-toluidine and by methylation of *o*-, *m*- and *p*-ethylaniline are shown in Figs. 3 and 4, respectively. The spectra do not extend to *m/z* 135 since there was an overwhelmingly intense peak corresponding to loss of $H^\bullet$ from the adducts. There are other distinct differences from the spectra in Fig. 1. The spectra in Fig. 3 showed major peaks at *m/z* 108 and 107, corresponding to loss of C_2H_4 and loss of $C_2H_5^\bullet$, respectively, from the adduct. Harrison[17] observed these losses as the major fragmentation paths for phenylethylammonium and phenyldiethylammonium ions under low-energy CID conditions. This similarity suggests that ethylation of the toluidines has occurred to a greater extent at nitrogen. In such a case, one might have expected to see the formation of *m/z* 45, $CH_3CH_2NH_2^{+\bullet}$, analogous to the formation of *m/z* 59 in the spectra in Fig. 1. An ion signal at *m/z* 45 is not observed, although there are weak signals at *m/z* 44 ($CH_3CH{=}NH_2^+$) and *m/z* 30 ($CH_2{=}NH_2^+$). The latter ions are the expected fragment ions from ionized ethylamine.

The CID mass spectra of the methylated *o*-, *m*- and *p*-ethylanilines (Fig. 4) are distinctly different from the spectra in Figs. 1 and 3, suggesting that a different structure or structures is/are formed. The site of methylation is not entirely clear. Following the observations of Cooks and co-workers[11] that cationization on the aromatic ring leads to charge stripping, the observation of strong signals for 136^{2+} and 120^{2+} suggests ring methylation. At the same time, the observation of a (weak) signal at *m/z* 30 ($CH_2{=}NH_2^+$) is

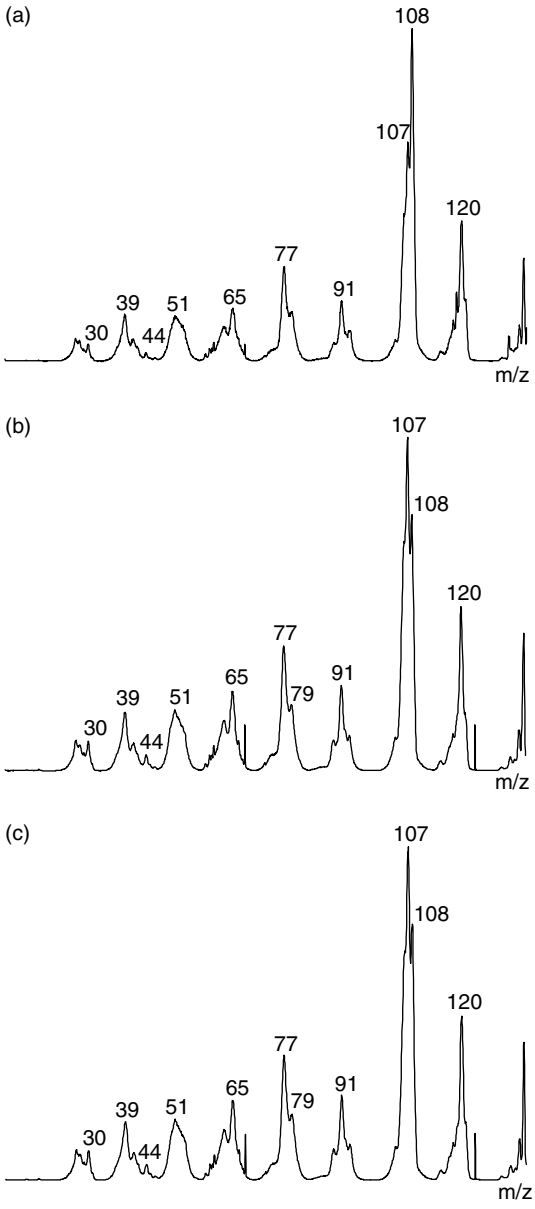


Figure 3. CID mass spectra of the $C_9H_{14}N^+$ (*m/z* 136) ions formed by $C_2H_5^+$ addition to (a) *o*-toluidine, (b) *m*-toluidine and (c) *p*-toluidine.

most readily interpreted in terms of *N*-methylation and it is probable, in this case, that both *N*-methylation and ring methylation have occurred, although it is not possible to determine the relative importance of the two reactions. It is clear from Figs. 3 and 4 that the position of ring alkylation cannot be determined from the CID spectra.

Protonation of *N*-ethyl-*N*-methylaniline, *N*-ethyl-*o*-toluidine and 6-ethyl-*o*-toluidine

Figure 5 shows the CID mass spectra obtained (a) for the *m/z* 136 ion obtained by Brønsted acid CI of *N*-ethyl-*N*-methylaniline using $CH_3C(=O)CH_3$ as reagent, (b) for the *m/z* 137 ion obtained by deuteration of *N*-ethyl-*N*-methylaniline using $CD_3C(=O)CD_3$ as Brønsted acid reagent and (c) for the *m/z* 136 ion obtained by Brønsted acid CI of the ethylmethylaniline using CH_3OH as reagent. Note that the spectra in Fig. 5 have features that are also contained in

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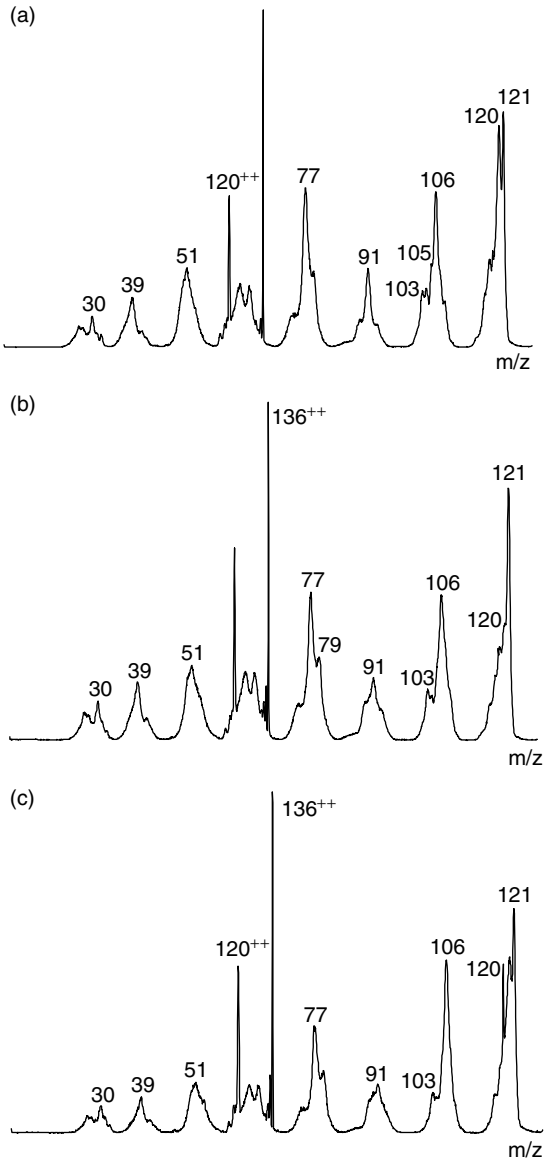

Figure 4. CID mass spectra of the $C_9H_{14}N^+$ (*m/z* 136) ions formed by CH_3^+ addition to (a) *o*-ethylaniline, (b) *m*-ethylaniline and (c) *p*-ethylaniline.

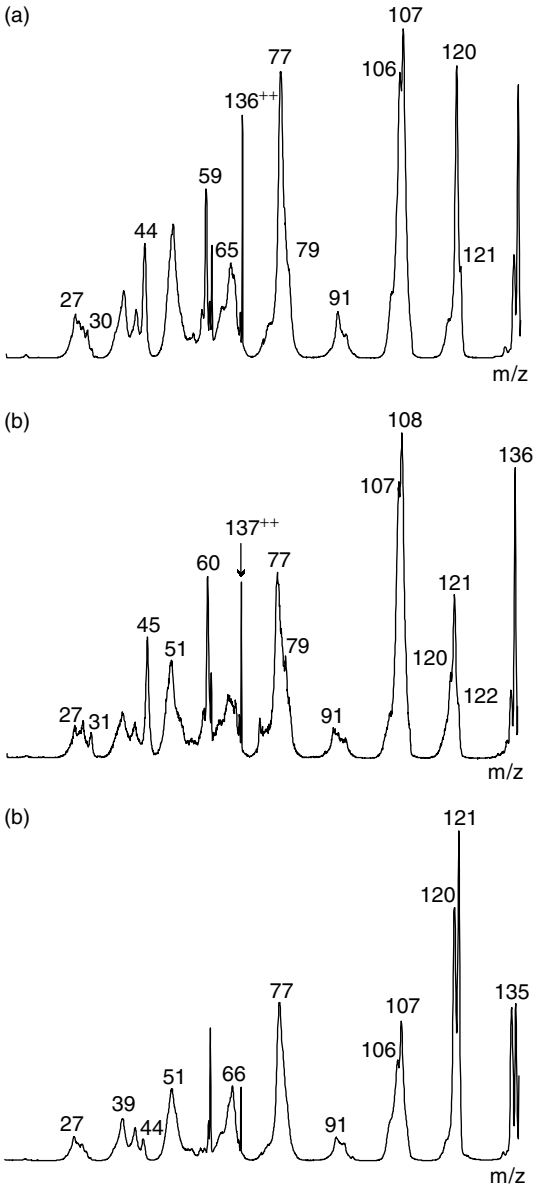

Figure 5. CID mass spectra of (a) the $C_9H_{14}N^+$ (*m/z* 136) ions formed by the $CH_3C(=O)CH_3$ CI of *N*-ethyl-*N*-methylaniline, (b) the $C_9H_{13}DN^+$ (*m/z* 137) ions formed by the $CD_3C(=O)CD_3$ CI of *N*-ethyl-*N*-methylaniline and (c) the $C_9H_{14}N^+$ (*m/z* 136) ions formed by the CH_3OH CI of *N*-ethyl-*N*-methylaniline.

the spectra in Fig. 4. These spectra contain charge stripping signals for 136^{2+} and 120^{2+}.

The spectrum in Fig. 5(a) contains similar fragment ions to those in the spectra in Fig. 1, including ion signals at *m/z* 59 and 44; these ions are indicative of *N*-protonation. As the spectrum in Fig. 5(b) shows, these structure-characteristic ions shift to *m/z* 60 and 45 when a D^+ is added to the aniline, again consistent with *N*-protonation. The CID mass spectrum obtained for the *m/z* 136 ion produced by protonation with CH_3OH as reagent (Fig. 5(c)) is different; compare Fig. 5(a) and 5(c). Presumably, protonation with CH_3OH forms m/z 136 ions having different contributions from the ring-protonated and the N-protonated structures.

Harrison and Tu[18] examined the site of protonation of *N*-methyl-, *N*,*N*-dimethyl- *N*-ethyl-, and *N*,*N*-diethylaniline in Brønsted acid CI and in FAB ionization. In Brønsted acid CI using CH_4, CH_3OH and $CH_3C(=O)CH_3$ as reagents, they observed significant loss of H_2 in fragmentation of MH^+. Such a loss of H_2 was not observed for the MH^+ ion prepared by FAB, where *N*-protonation is expected. Also, loss of a hydrogen molecule was not observed for MH^+ ions prepared by Brønsted acid CI using *i*-$C_4H_9NH_2$ as reagent, where protonation of the ring (with *i*-$C_4H_9NH_3^+$) is endothermic. Harrison and Tu[18] concluded that the loss of H_2 from MH^+ was indicative of ring protonation. From the relative signals for H_2 loss in metastable ion fragmentation, it appeared that the reagents CH_4 and CH_3OH gave approximately the same extent of ring protonation whereas $CH_3C(=O)CH_3$ reagent gave significantly less. This is in qualitative agreement with the present observations that acetone gives appreciably more *N*-protonation than does methanol. However, the charge stripping peaks are more intense in Figs. 5(a) and (b) than in Fig. 5(c). Following earlier proposals,[11] this would suggest a

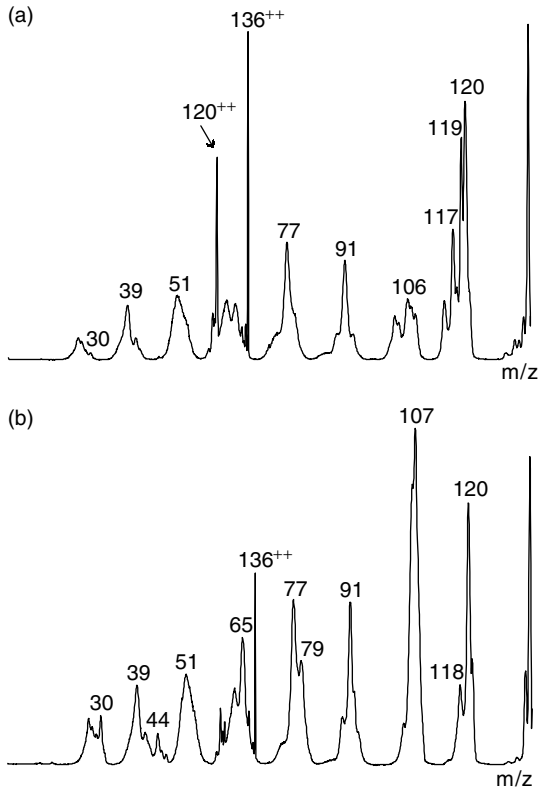

Figure 6. CID mass spectra of the $C_9H_{14}N^+$ (*m/z* 136) ions formed by the $CH_3C(=O)CH_3$ CI of (a) 6-ethyl-*o*-toluidine and (b) *N*-ethyl-*o*-toluidine.

greater extent of ring protonation when acetone is the reagent gas, contrary to the other evidence, that is, the presence of *m/z* 44 and 59 in Fig. 5(a). This puzzling result is not clearly understood and it may be that the extent of charge stripping does not provide sufficient indication of ring-protonation.

Figure 6 presents the CID mass spectra obtained for the *m/z* 136 ions formed by protonation of 6-ethyl-*o*-toluidine and *N*-ethyl-*o*-toluidine using $CH_3C(=O)CH_3$ as the reagent gas. It was expected that, if *N*-protonation occurred, the spectrum for protonated *N*-ethyl-*o*-toluidine would be similar to that of the *m/z* 136 ion derived by ethylation of *o*-toluidine (Fig. 3(a)), where it was concluded that substantial *N*-ethylation occurred. However, the two spectra show substantial differences and hence it is likely that, for *N*-ethyl-*o*-toluidine, a different ratio of ring-protonated and *N*-protonated structures is formed.

Protonated 6-ethyl-*o*-toluidine was studied as a model of the ion that might be formed by ring ethylation of *o*-toluidine. Not surprisingly, the CID spectrum (shown in Fig. 6(b)) is different from that of ethylated *o*-toluidine (Fig. 3(a)). Again, it is likely that predominant *N*-protonation has not occurred.

CONCLUSIONS

This work presents strong evidence for predominant *N*-ethylation of *N*-methylaniline and *N*-methylation of *N*-ethylaniline. This conclusion is derived, in part, from the similarity of the MI and CID mass spectra of the two adduct ions. In addition, structure-diagnostic ions appear at *m/z* 59 and 44, which show the appropriate mass shifts when $C_2D_5^+$ or CD_3^+ is added to the relevant *N*-alkylaniline. The CID mass spectra obtained are distinctly different from those observed for ethylation of the toluidines or methylation of the ring-ethylanilines. Protonation of *N*-ethyl-*N*-methylaniline using $CH_3C(=O)CH_3$ as reagent yields a species whose CID mass spectrum features ion signals that are also present in the CID mass spectra of $C_2H_5^+$–NMA and CH_3^+–NEA. This indicates that predominant *N*-protonation has occurred. However, protonation of *N*-ethyl-*N*-methylaniline using CH_3OH as reagent produces a species which shows a significantly different CID mass spectrum, suggesting that *N*-protonation is not the dominant reaction.

Acknowledgement

We are indebted to the Natural Sciences and Engineering Research Council (Canada) for continuing financial support.

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