
Reactive Collisions in Quadrupole Cells.

3: H/D Exchange Reactions of Protonated Aromatic Amines with ND₃

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The H/D exchange reactions of a variety of protonated aromatic amines with ND₃ in the collision cell of a hybrid BEqQ tandem mass spectrometer have been studied. The MH⁺ ions were prepared by CH₄, *t*-C₄H₁₀, and NH₃ chemical ionization (CI) and, for some amines, by fast-atom bombardment (FAB). Evidence is presented that the kinetic energy of the incident ion as well as its internal energy must be dissipated by nonexchanging collisions before exchange occurs, once deactivated the MH⁺ ions exchange efficiently, which leads, in most cases, to [MH]⁺ *d*_x ions in which all active hydrogens have been exchanged. The MH⁺ ion of 1,3-phenylenediamine formed by gas-phase CI exchanges only very slightly with ND₃ whereas a significant fraction of the MH⁺ ions formed by FAB exchange efficiently. This difference is rationalized in terms of dominant formation of the ring-protonated species in gas-phase CI reactions and significant formation of the N-protonated species by FAB with only the N-protonated species exchanging efficiently. Similar, although less pronounced, differences are observed for the MH⁺ ion of *m*-anisidine. In a number of cases apparent exchange of aromatic hydrogens also is observed. Evidence is presented for the interchange of ring and amine hydrogens in protonated aromatic amines and it is suggested that only the N-protonated species undergoes significant exchange with ND₃. (*J Am Soc Mass Spectrom* 1995, 6, 19–26)

The usefulness of exchanging the hydrogen atoms in an organic sample with deuterium is well established in analytical mass spectrometry. The shift in mass-to-charge ratio after exposure of the sample to a suitable deuterium-containing reagent provides a ready count of the number of hydrogens in a specific environment and has been applied particularly to counting the number of active hydrogens, that is, those bonded to heteroatoms such as N, O, and S. Initially this exchange reaction was carried out prior to introduction of the sample into the mass spectrometer [1] or by introducing the sample and the reagent into the inlet system together [2]. More recently, a number of alternative methods of counting active hydrogens have been developed. Hunt and co-workers [3, 4] have shown that, under chemical ionization (CI) conditions, the use of CH₃OD or ND₃ as reagent gas provides rapid exchange of active hydrogens. This approach has been used by a number of workers [5–12] to establish the number of active hydrogens present in a variety of samples. Even more recently, the use of deuterated matrices, such as glycerol-*O-d*₃, in liquid secondary ion

or fast-atom bombardment (FAB) mass spectrometry [12–15] or of suitable deuterated solvents in electrospray mass spectrometry [16–20] has been shown to provide a count of active hydrogens, although for large peptides conformational effects may limit the number of exchangeable hydrogens [16, 18].

In a classic study, Hunt and Sethi [21] showed that, in addition to active hydrogens, hydrogens in other positions can be selectively exchanged for deuterium under CI conditions. Thus, with D₂O or C₂H₅OD as reagent gases in Brønsted acid CI, the exchange of aromatic hydrogens in alkylbenzenes was observed. This approach was developed by Hawthorne and Miller [22, 23] into a method of counting aromatic hydrogens in alkylbenzenes, alkyltetralins, and alkylindans by using CH₃OD as the CI reagent gas. In Brønsted base CI, Hunt and Sethi [21] showed that the [M – H][–] ions of alkylbenzenes exchanged all benzylic hydrogens with the D₂O reagent whereas the [M – H][–] ions of simple ketones, aldehydes, and esters exchanged enolic hydrogens with the C₂H₅OD reagent.

These various methods encounter difficulties for more complex samples because it can be difficult to deconvolute the H/D exchange pattern from the isotopic pattern that arises from naturally occurring isotopes and, in some cases, H/D exchange may appear

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to be incomplete because of back exchange with unlabeled components in the atmosphere, particularly when the ions are produced at atmospheric pressure as in electrospray methods. In addition, in each of the foregoing methods, the observation of H/D exchange is intimately linked to the method of ion production, which could limit the applicability of the method. An alternative approach, which has been demonstrated recently [24, 25], is to examine the H/D exchange reactions of mass-selected ions in low energy gas-phase collisions with suitable deuterium-containing reagent gases. In this way the exchange reaction is separated from the ion formation process and the mass selection eliminates the problem of deconvoluting the exchange pattern from the natural isotopic pattern. By using such an approach, Ranasinghe et al. [24] showed that the number of active hydrogens in a variety of aromatic compounds could be determined from the mass shift that occurred when the protonated species, formed by chemical ionization, was allowed to collide with ND₃ in the collision cell of a triple quadrupole mass spectrometer. In a related study, Ni and Harrison [25] showed that the number of enolic hydrogens in simple ketones and esters could be determined by allowing the enolate ions to undergo H/D exchange with CH₃OD or C₂H₅OD in the quadrupole collision cell of a hybrid BEqQ mass spectrometer. Nourse et al. [26] obtained some distinction among methylguanidine isomers from the rate and extent of exchange of the mass-selected MH⁺ ions with D₂O in a Fourier transform mass spectrometer. Cheng and Fenselau [27] reported a study of the H/D exchange reactions of protonated peptides, produced by FAB, with ND₃ at low collision energies in the collision cell of a tandem four sector mass spectrometer: For the more complex peptides, incomplete exchange of the active hydrogens was observed. Very recently, Stone [28] reported a study of the exchange reactions of some protonated alkylbenzenes with D₂O and CD₃OD in the collision cell of a triple quadrupole mass spectrometer: A rather large unreactive component was reported for the MH⁺ ions, and the overall extent of exchange was much less than that reported [29] in the reaction of protonated alkylbenzenes with CH₃OD. We report here our study of the exchange reactions of protonated aromatic amines with ND₃ in the quadrupole collision cell of a hybrid BEqQ mass spectrometer. Although to some extent these results complement the earlier work of Cooks and co-workers [24], we present a more detailed examination of the effect of reactant ion kinetic energy on the extent of H/D exchange as well as a study of the effect of the method of reactant ion preparation on the extent of exchange. In particular, substantial differences are reported for the extent of exchange of protonated *m*-anisidine and protonated 1,3-phenylenediamine depending on whether the MH⁺ ion is prepared by gas-phase CI reactions or by FAB; these differences are discussed in terms of the site of protonation in CI and FAB formation of the MH⁺ ion.

Experimental

All experimental work was carried out using a ZAB-2FQ hybrid BEqQ mass spectrometer (VG Analytical Ltd., Wythenshawe, Manchester, UK), which has been described in detail previously [30]. Briefly, this instrument is a reversed-geometry (BE) double-focusing mass spectrometer that is followed by a deceleration lens system, an rf-only quadrupole collision cell (q), and a quadrupole mass analyzer (Q). The appropriate MH⁺ ions were mass selected by the BE double-focusing mass spectrometer at 6-keV ion energy, decelerated to a kinetic energy of 1-4 eV on the laboratory scale, and introduced into the quadrupole collision cell, which contained ND₃ at an indicated pressure of 4×10^{-6} torr as read by the ionization gauge attached to the pumping line leading from the quadrupole stage. It is estimated that the actual pressure in the quadrupole cell is 100 to 1000 times the indicated pressure. The reaction products were analyzed by the final quadrupole mass analyzer and the resulting mass spectra were accumulated on a multichannel analyzer with typical accumulation of 25-50 2-s scans.

The incident ion kinetic energy is an important parameter in determination of the extent of exchange of the MH⁺ ion and, to obtain reproducible results on one mass spectrometer (let alone from one instrument to another), it is necessary to establish a reproducible incident ion energy. The protocol we have adopted was presented earlier [25], but it is well to repeat it here. The ZAB-2FQ instrument provides no facility for measuring the potential difference between the ion source and the collision cell directly (such a measurement would be difficult with both floating at 6-8 kV with respect to ground); however, there is provision to set the "collision" energy and the absolute potential applied to the collision cell separately. With the collision energy potentiometer set to zero, the potential applied to the collision cell was adjusted to reduce the incident ion beam signal just to zero. The "collision" energy or injection energy of the ions into the cell was then set by the collision energy potentiometer. It is necessary to carry out this adjustment with the ND₃ in the collision cell because the collision gas affects the absolute potential of the collision cell, presumably through the development of surface potentials. The term "collision" energy is used advisedly in the present situation because, as will be discussed subsequently, there is substantial evidence that the incident ion loses both internal energy and kinetic energy in nonexchanging collisions before it undergoes H/D exchange due to collision with ND₃.

The protonated amines were prepared by Brønsted acid CI by using NH₃ (PA(NH₃) = 204 kcal mol⁻¹ [31]), *i*-C₄H₁₀ (PA(*i*-C₄H₈) = 196 kcal mol⁻¹ [31]) or CH₄ (PA(CH₄) = 132 kcal mol⁻¹, PA(C₂H₄) = 163 kcal mol⁻¹ [31]) as reagent gases to explore the effect of protonation exothermicity on the H/D exchange efficiency. The source temperature was 170 °C and the

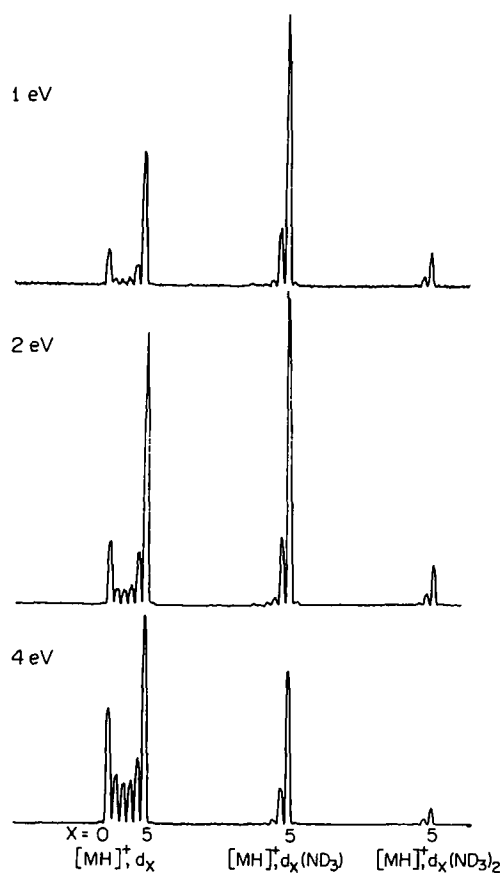


Figure 1. Mass spectra obtained from reaction of MH^+ ions of 1,2-phenylenediamine with ND_3 at three incident ion energies (MH^+ produced by FAB).

amine samples were introduced through a heated inlet system for liquid samples and by a direct insertion probe for solid samples. Because the ionization energies of the aromatic amines are low, molecular ions (M^+), frequently were observed in the CI experiments [32]. These lead to ^{13}C isotopic peaks that are isobaric with the MH^+ ion signals. In addition, if the M^+ (and ^{13}C variant) ion exchanges with ND_3 , ion signals that are isobaric with the exchanged MH^+ ion signals may be observed. The data in the following discussion have been corrected for this interference by recording the spectra obtained when the M^+ ion was mass selected under identical conditions and the intensity of M^+ was measured relative to that for MH^+ . Figure 1 is an exception in that it presents raw data output. In general the corrections were 10–50% of the observed residual MH^+ ion signal. The contributions to the $[\text{MH}]^+ d_x$ ion signals were significant only for the aminophenols and aminobenzoic acids.

In several cases the MH^+ ions also were produced by fast-atom bombardment (FAB) ionization by using a 1:1 thioglycerol–2,2-dithiodiethanol matrix saturated with oxalic acid and an argon atom beam of 7–8-keV energy. Separate experiments showed that the matrix did not produce ions at the same mass-to-charge ratio as the MH^+ ion of interest.

All the aromatic amines were obtained from the Aldrich Chemical Co. (Milwaukee, WI) and were used as received. The CI reagent gases were obtained from Matheson and Co. (Whitby, Ontario, Canada) whereas the ND_3 (99 atom % D) was obtained from CDN Isotopes (Vaudreuil, Québec, Canada).

Results and Discussion

The extent of H/D exchange depends strongly on the pressure of ND_3 in the collision cell and on the incident ion kinetic energy. A brief study showed that an indicated ND_3 pressure of 4×10^{-6} torr in the collision cell was optimum for observing H/D exchange, that is, a reasonable compromise was reached between the extent of exchange and the extent of signal loss in the MH^+ region due to clustering and to scattering. All subsequent experiments were carried out at this pressure. A more detailed study of the effect of the incident ion kinetic energy was carried out. Figure 1 shows typical results obtained for the MH^+ ion of 1,2-phenylenediamine (produced by FAB ionization) at incident ion kinetic energies of 1, 2, and 4 eV. $[\text{MH}]^+ d_x$ ($x = 0-5$)¹ and cluster ions that contain one and two molecules of ND_3 are observed. As pointed out previously [24], the more highly exchanged $[\text{MH}]^+$ ions show a greater tendency to cluster than do the unexchanged $[\text{MH}]^+$ ions or those that have exchanged only a few hydrogens. This is most clearly indicated by the scan at 4-eV incident ion energy, where significant ion signals are observed for all the species $[\text{MH}]^+ d_0$ to $[\text{MH}]^+ d_5$, but the cluster ions that contain one ND_3 are of significant intensity only for $[\text{MH}]^+ d_4$ and $[\text{MH}]^+ d_5$. Ranasinghe et al. [24] interpreted this observation as indicative that the cluster ions undergo exchange more readily than the unclustered $[\text{MH}]^+$ ions. An alternative explanation is that the ions that have undergone multiple exchanges have been extensively cooled, that is, their internal energy and kinetic energy have been collisionally dissipated, with the result that the collision complex $[\text{MH}]^+ d_x(\text{ND}_3)^*$ has a longer lifetime and is more effectively stabilized. This stabilization occurs by collision of the complex with a neutral ND_3 molecule, which either carries away the excess energy or reduces the energy of the complex by displacing the ND_3 molecule in the complex [33].

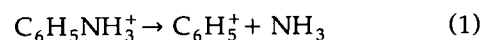
The pattern of intensities in the $[\text{MH}]^+ d_0$ to $[\text{MH}]^+ d_5$ region and the change in this pattern with increasing incident ion kinetic energy is unexpected in that the $[\text{MH}]^+ d_0$ ion is the second most intense at all ion energies and becomes particularly pronounced at 4-eV incident ion energy. The extent of exchange is expected to decrease with increasing ion energy because the number of collisions decreases, but this should not lead to the pattern observed where the two most

¹The symbolism $[\text{MH}]^+ d_x$ represents an MH^+ ion which has exchanged x hydrogens for deuterium

intense ion signals correspond to the completely exchanged and the completely nonexchanged MH^+ ion. The results are most readily interpreted as indicative that the incident ion must be cooled kinetically before significant exchange occurs and that once this cooling has occurred, H/D exchange occurs readily and leads to exchange of all active hydrogens. We estimate that at 2-eV incident ion energy, the MH^+ ion undergoes 10-30 collisions with ND_3 in the quadrupole cell. It also should be noted that up to three H/D exchanges could occur in a single MH^+/ND_3 encounter.

It also appears that the internal energy of the incident ion must be collisionally dissipated before effective exchange occurs. Figure 2 presents, in bar graph form, results obtained at 2-eV incident ion kinetic energy for the $[MH]^+$ ion of o-anisidine, where the $[MH]^+$ ion was prepared by CH_4 , $i-C_4H_{10}$, and NH_3 CI and by FAB. Protonation of o-anisidine ($PA = 215$ kcal mol⁻¹ [31]) in CH_4 CI should be much more exothermic than protonation in either $i-C_4H_{10}$ or NH_3 CI, and one might expect that the $[MH]^+$ ions would have a higher internal energy when formed by CH_4 CI. We observe (Figure 2) a considerably higher ion signal for the unexchanged ion $[MH]^+ d_0$ in the CH_4 case than in the other spectra. This was a general observation in all the systems studied as indicated by the results presented in Table 1. The internal energy that the MH^+ ion can accommodate is limited by the critical energy for the lowest energy fragmentation pathway. For protonated aniline (second entry, Table 1) the available thermochemical data [31] indicate that

$\Delta H^\circ = 81$ kcal mol⁻¹ for the lowest energy fragmentation reaction



Thus, because $PA(C_6H_5NH_2) = 210$ kcal mol⁻¹ [31], protonation by NH_4^+ ($PA(NH_3) = 204$ kcal mol⁻¹ [31]) will be 6 kcal mol⁻¹ exothermic and protonation by $C_4H_9^+$ ($PA(i-C_4H_8) = 198$ kcal mol⁻¹ [31]) will be 12 kcal mol⁻¹ exothermic, whereas protonation by CH_5^+ ($PA(CH_4) = 132$ kcal mol⁻¹ [31]) will be 78 kcal mol⁻¹ exothermic. Protonation by $C_2H_5^+$ ($PA(C_2H_4) = 163$ kcal mol⁻¹ [31]), also present in the methane plasma, will be 47 kcal mol⁻¹ exothermic. There is substantial evidence [32, 34-36] that most of the exothermicity of the protonation reaction in Brønsted acid CI resides as internal energy of the MH^+ ion. The thermochemistry of reaction (1) and the exothermicity of protonation by CH_5^+ strongly suggests that the MH^+ ions will have a much higher internal energy when formed by CH_4 CI. Thermochemical data are not available with respect to fragmentation of the other MH^+ ions studied, but the critical energy for fragmentation is likely to be high because substituted phenyl cations are the most likely fragmentation products in each case. Thus all MH^+ ions are likely to have a much higher internal energy when formed by CH_4 CI than when formed by other methods. It is interesting to note that the results of Figure 2 and Table 1 indicate that the MH^+ ions formed by FAB have low internal energies, comparable to the MH^+ ions formed by $i-C_4H_{10}$ or NH_3 CI.

The results of Figure 1 indicate that a 2-eV incident ion energy provided a reasonable compromise between a good extent of exchange and a loss of sensitivity in the $[MH]^+ d_x$ region due to clustering. In general, the extent of clustering was similar to that observed in Figures 1 and 2 except for m-anisidine and 1, 3-phenylenediamine, where no cluster ions were observed, and for the aminobenzoic acids, where more intense cluster ions were observed. Table 1 presents the results obtained at 2-eV incident ion energy for 17 aromatic amines: only the relative ion intensities observed in the $[MH]^+ d_x$ region are presented; complete tables of data including cluster ion intensities and data at 1- and 4-eV incident ion energy may be obtained from the authors.

Several points are evident from the data in Table 1. In most cases there is a much larger unreactive component to the incident ion $[MH]^+ d_0$ when the ion is formed by CH_4 CI than when it is formed by other ionization modes. This is consistent with the arguments presented previously that the internal energy of the incident ion must be collisionally dissipated before effective exchange occurs. On the other hand, in most cases the results for ions formed by $i-C_4H_{10}$ CI, by NH_3 CI, and by FAB are quite similar. In many cases exchange is very extensive and the ion that corresponds to exchange of all active hydrogens (the added hydrogen and those bonded to heteroatoms) is the most abundant. There are three no-

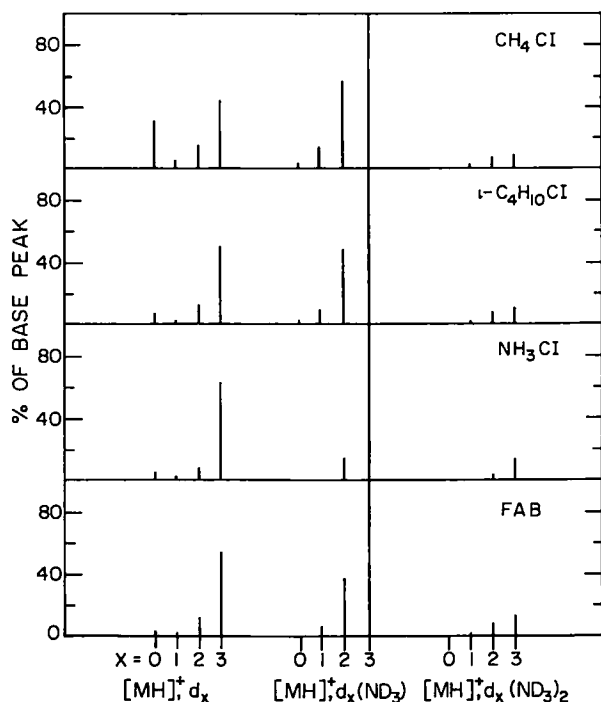


Figure 2. Mass spectra obtained from reaction of MH^+ ions of o-anisidine with ND_3 as a function of the mode of formation of MH^+ (2-eV incident ion energy).

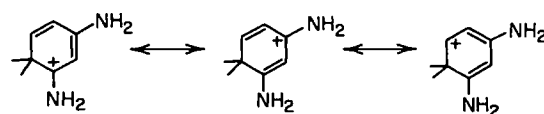
Table I. H/D exchange of protonated amines with ND₃ at 2-eV incident ion energy

Compound	Mode ^a	[MH] ⁺ d _x (% base peak)							
		d ₀	d ₁	d ₂	d ₃	d ₄	d ₅	d ₆	d ₇
Benzylamine	CH ₄	28	13	30	100	3	1		
	i-C ₄ H ₁₀	6	8	27	100				
Aniline	NH ₃	10	8	18	100				
	CH ₄	100	15	21	96	19	2		
	i-C ₄ H ₁₀	16	5	28	100	29	4		
o-Anisidine	NH ₃	16	4	14	100	26	3		
	CH ₄	59	9	29	100	1			
	i-C ₄ H ₁₀	10	3	25	100				
	NH ₃	5	2	10	100				
m-Anisidine	FAB	11	8	26	100				
	CH ₄	100	14	22	39	21	5		
	i-C ₄ H ₁₀	79	27	61	100	59	15	2	
	NH ₃	100	52	95	96	52	10	1	
p-Anisidine	FAB	20	21	54	100	40	7		
	NH ₃	7	8	25	100				
o-Toluidine	FAB	19	10	24	100				
	CH ₄	48	6	17	100	30	5		
	i-C ₄ H ₁₀	31	8	33	100	13			
	NH ₃	13	6	19	100	11			
m-Toluidine	FAB	29	22	50	100	16			
	CH ₄	69	8	23	100	52	15	2	
	i-C ₄ H ₁₀	26	8	36	100	42	10	2	
	NH ₃	32	6	20	100	50	15	2	
p-Toluidine	FAB	31	21	49	100	45	12	2	
	NH ₃	48	8	15	100	4			
o-Aminophenol	FAB	21	19	46	100	3			
	CH ₄	36	9	12	44	100	1		
	i-C ₄ H ₁₀	9	2	3	23	100			
m-Aminophenol	NH ₃	4	6	9	21	100	1		
	CH ₄	13	54	38	75	100	67	19	3
	i-C ₄ H ₁₀	6	32	25	61	100	66	19	2
p-Aminophenol	NH ₃	13	92	35	70	100	72	23	3
	CH ₄	21	11	33	100	13	6	2	
	i-C ₄ H ₁₀	3	6	18	100	2			
o-Aminobenzoic acid	NH ₃	12	7	15	100	2			
	CH ₄	2	11	29	33	100			
	i-C ₄ H ₁₀	1	2		29	100			
m-Aminobenzoic acid	NH ₃	1	2	5	16	100			
	CH ₄	38	50	29	55	100	8		
	i-C ₄ H ₁₀	11	14	14	41	100	7		
p-Aminobenzoic acid	NH ₃	12	20	29	42	100	9		
	i-C ₄ H ₁₀	2	5	15	45	100			
1,2-Phenylene-diamine	NH ₃	3	8	11	31	100			
	CH ₄	100	9	7	8	15	44		
	i-C ₄ H ₁₀	18	3	2	3	21	100		
	NH ₃	5	1	2	5	26	100		
1,3-Phenylene-diamine	FAB	15	6	5	7	20	100		
	CH ₄	100	10	13	10	9	6		
	i-C ₄ H ₁₀	100	8	13	10	9	8		
	NH ₃	100	8	10	5	3	2		
1,4-Phenylene-diamine	FAB	100	49	63	66	70	68	3	
	CH ₄	100	20	19	26	56	93		
	i-C ₄ H ₁₀	37	3	3	4	19	100		
	NH ₃	5	6	7	10	30	100		
	FAB	47	21	17	16	29	100		

^aCH₄, i-C₄H₁₀, and NH₃ refer to formation of MH⁺ by CI FAB refers to production of MH⁺ by fast-atom bombardment

table exceptions: 1,3-phenylenediamine, *m*-anisidine, and *p*-aminophenol.

As shown in Figure 3, the extent of exchange of the MH^+ ion of 1,3-phenylenediamine is very small when the MH^+ ion is formed by chemical ionization, but is considerably more extensive when MH^+ is formed by FAB. The percentage of deuterium incorporation in each case is calculated to be 18% (CH_4 CI), 19% (*t*- C_4H_{10} CI), 10% (NH_3 CI), and 48% (FAB). Kebarle and co-workers [37] have shown that in the gas phase the thermodynamically favored site of protonation of 1,3-phenylenediamine is on the aromatic ring, which forms the resonance stabilized ion 1. Protonation at the nitrogen was found to be approximately 9 kcal mol⁻¹ less favorable. We conclude that under gas-phase CI conditions protonation occurs predominantly on the ring and that this ring-protonated species undergoes H/D exchange with ND_3 only very slowly, if at all. The proton affinity of the aromatic ring is 222 kcal mol⁻¹ [34] compared to $PA(NH_3) = 204$ kcal mol⁻¹ [31]. Hence, it might be expected that exchange of the ring-protonated species would be slow because it is generally accepted [21] that when the proton affinity difference becomes large, the exchange becomes slow. This exchange would be further hindered by the fact that the ring-protonated species 1 would interact only weakly with ND_3 because of the charge delocalization in the ion. The greater extent of exchange of the MH^+ ion formed by FAB ionization implies, then, that a significant fraction of the MH^+ ions are N-protonated and that these ions exchange relatively readily with ND_3 . The mechanism of ion formation in FAB has not



Structure I

been completely resolved [38-43]: evidence has been presented for preformation of ions in solution [38, 43], formation by ion-molecule reactions in the gas phase [39, 40], and formation by desolvation of charged clusters [41]. In solution, 1,3-phenylenediamine is preferentially protonated on nitrogen [44] because of more effective solvation of the N-protonated species. The observation of a significant fraction of reactive (and, hence, presumably N-protonated) MH^+ ions in the FAB ionization of 1,3-phenylenediamine implies significant formation of MH^+ in solution reactions with either direct transfer of these ions to the gas phase or desolvation of clusters in the gas phase.

Similar, although not quite as clear cut, results are obtained in exchange studies of the MH^+ ion of *m*-anisidine. As shown in Figure 4, there is a significant unreactive component when the MH^+ ion is formed by gas-phase chemical ionization methods, whereas the MH^+ ion formed by FAB is essentially completely reactive. Again, Kebarle and co-workers [37] have shown that the thermodynamically favored site of protonation of *m*-anisidine in the gas phase is the ring, where protonation of the nitrogen is less favorable by approximately 4 kcal mol⁻¹. The results can be rationalized by assuming that the ring-protonated species exchanges more slowly and that this form is produced to a significant extent by gas-phase CI. By contrast,

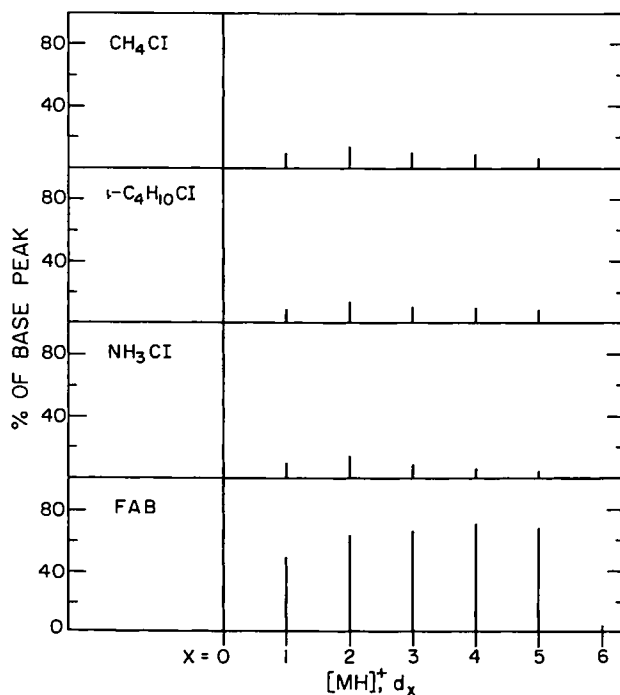


Figure 3. H/D exchange pattern for MH^+ ions of 1,3-phenylenediamine as a function of the mode of preparation of MH^+ (2-eV incident ion energy).

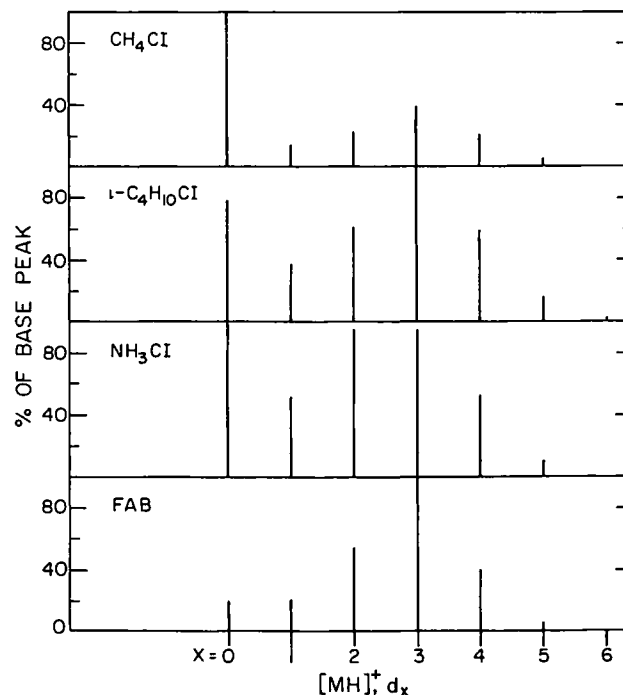
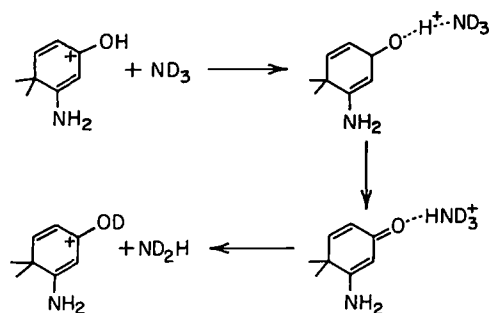


Figure 4. H/D exchange pattern for MH^+ ions of *m*-anisidine as a function of the mode of preparation of MH^+ (2-eV incident ion energy).

FAB ionization appears to produce predominantly the N-protonated species, which indicates in this case, as well, a significant contribution to the total FAB MH^+ ion signal of ions preformed in solution. It should be noted, however, that the ring proton affinity of m-anisidine (218 kcal mol⁻¹ [37]) is lower than that of 1,3-phenylenediamine and exchange of the ring-protonated species with ND_3 is more likely in this case.

In the case of p-aminophenol the dominant ion signal corresponds to exchange of only three hydrogens; exchange of the fourth (presumably hydroxylic) hydrogen occurs to only a slight extent. It is not clear whether this lack of exchange of the hydroxylic hydrogen is due to a conformational effect or an energetics effect. The proton affinity of the oxygen in p-aminophenol is not known; the proton affinity of phenol is 196 kcal mol⁻¹ [31], but this is known to refer to protonation at the aromatic ring [45]; the oxygen proton affinity is lower. DeFrees et al. [46] have estimated that the oxygen proton affinity of phenol is 13–20 kcal mol⁻¹ less than the ring proton affinity. Thus the oxygen proton affinity of p-aminophenol could be as much as 19–26 kcal mol⁻¹ lower than that of ammonia (PA(NH_3) = 204 kcal mol⁻¹ [31]). Thus, it is possible that proton-deuteron transfer from ND_3H^+ to the hydroxyl position in an ion-dipole complex would be energetically unfavorable; it is clear that such a transfer is necessary to exchange the hydroxyl hydrogen with deuterium from the ammonia. It should be noted, however, that in agreement with Ranasinghe et al. [24], we observe that the most prominent cluster ion signal corresponds to $[MH]^+ d_4(ND_3)$; the reasons for this difference are not apparent. The energetics argument should apply equally to the other aminophenols, however, the MH^+ ion of o- and m-aminophenol both readily exchange the fourth hydrogen, which suggests that the lack of exchange for the para isomer may be the result of conformational effects. We note that for the meta isomer the intensity of the $[MH]^+ d_1$ ion is particularly pronounced; this raises the possibility that the hydroxylic hydrogen is exchanged very easily in this case, possibly from a ring-protonated species as outlined in Scheme I. The ortho hydroxylic hydrogen is sufficiently close to the amine function to undergo ready exchange. One might have expected the aminobenzoic acids to exhibit a behavior similar to that of the aminophenols; however, all the benzoic acid derivatives exchange the carboxylic hydrogen readily. The reasons for this difference in behavior are not apparent.

A number of compounds show exchange of more hydrogens than are bonded to heteroatoms, which indicates apparent exchange of aromatic ring hydrogens with ND_3 . These include aniline, the toluidines, m-anisidine (Figure 4), and m-aminophenol. It should be noted that these compounds are all examples where the ring proton affinity and the N-proton affinity are very similar [37, 47, 48]. It is not clear whether this extra exchange indicates that H/D exchange occurs by



Scheme I.

interaction of a ring-protonated species with ND_3 or whether the H/D exchange occurs only between the N-protonated species and ND_3 with concurrent interchange of the aromatic and ring hydrogens. Some evidence for the latter was obtained from the following experiment. Aniline- $N,N-d_2$, prepared by exchange of aniline with D_2O in the inlet system, was ionized by chemical ionization by using CD_4 reagent gas to produce aniline- $N,N-d_2D^+$ (with the site of D^+ attachment unknown). This species was mass selected by the BE double-focusing mass spectrometer and underwent CID on collision with N_2 at 50-eV collision energy in the quadrupole cell. The major fragmentation channel was elimination of ammonia and we observed the following neutral losses from the d_3 species: $-ND_3$: $-ND_2H$: $-NDH_2$: $-NH_3$ = 44:100:38:7. Clearly, there is interchange of the N-bonded and C-bonded hydrogens either before or after collisional activation. This is not particularly surprising given the similarity of the proton affinities of the ring and the amine function in these compounds. Consequently, it is possible that all H/D exchange occurs through interaction of the N-protonated species with ND_3 and the extra exchange observed results from interchange between the ring and nitrogen positions.

Finally, we note that the extent of exchange we have observed for the MH^+ ions produced by $i-C_4H_{10}$ CI is considerably greater than that reported by Ranasinghe et al. [24] for MH^+ ions produced by $i-C_4H_{10}$ CI (R. G. Cooks, private communication) and undergoing exchange with ND_3 in the collision cell of a triple quadrupole cell at pressures and nominal ion kinetic energies similar to those used in the present work. Because the ND_3 pressure, the incident ion kinetic energy, and the ion path length in the collision cell all affect the number of collisions and, thus, the extent of exchange, the exact reasons for this difference are not clear. The present results and the results of Ranasinghe et al. [24] do indicate that it is relatively easy to obtain reproducible results on one instrument but much more difficult to reproduce results quantitatively from one instrument to another.

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