Mechanistic Study of Hydrogen/Deuterium Exchange Between $[M - 1]^-$ Ions of Chlorinated Benzenes and D_2O or ND_3

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Low-energy collisions between $[M - 1]^-$ ions derived from the three isomers of dichlorobenzene and deuterated water and ammonia are found to produce distinctive hydrogen/deuterium (H/D) exchange reaction product patterns. The predominant products observed for p-, m-, and o-dichlorobenzene are 1, 2, and 3 sequential deuterium exchanges, respectively. The reactivity is substantially higher for D_2O than ND_3 . We postulate a mechanism that involves the formation of a five-membered-ring intermediate. The intermediate is thought to be initiated by the attack of ND_3 or D_2O at the localized negative charge site on the aromatic ring. A successful exchange is followed by the relocation of the charge site to the adjacent carbon. Ion products with higher degrees of deuterium substitution than the expected predominant products of their corresponding isomers are believed to be the results of isomerization of the reactant ions occurring in the ion source. The proposed mechanism fully explains the observed product spectra derived from all the isomers of chlorinated benzenes. The trends for the formation of various H/D exchange products represented by the simulated product-time plots based on the proposed mechanism compare well with the similar trends obtained from the experimental product-pressure plots. The reaction is useful for the mass spectrometric differentiation of chlorobenzene isomers. (*J Am Soc Mass Spectrom* 1994, 5, 282–291)

Mass spectrometric studies on hydrogen-deuterium (H/D) exchange reactions in solution have been used for structure elucidation [1,2]. Kinetic studies on isotopic methane-hydrogen and methane-deuterium systems have demonstrated the feasibility of H/D exchanges in the gas phase [3–5]. Presumably, the reactant ions involved for the exchange reactions include H_3^+ , D_3^+ , CH_3^+ , CD_3^+ , CH_4^+ , CD_4^+ , CH_5^+ , and CD_5^+ . Hunt et al. [6,7] first reported H/D exchanges for organic compounds in the gas phase under chemical ionization (CI) conditions with deuterium oxide reagent. Active hydrogens in organic compounds were determined by H/D exchange reactions between neutral organic molecules and ionic deuterated reagents. Isotopic exchange for amines was observed when either ND_3 [7] or $MeOD$ [8] was used as the CI reagent. Differences in the number of exchanges observed between ND_3^+ or $MeOD_2^+$ and amine molecules allowed the differentiation of primary, secondary, and tertiary amines. Exchange of aromatic hydrogens was first reported by Beauchamp and co-

workers [9] using ion cyclotron resonance spectroscopy for protonated benzene ions. This study suggested that ring protonation was a necessary condition for exchanging aromatic hydrogens of a cation. Further studies by Martinsen and Buttrill [10] on a variety of substituted benzenes confirmed that when protonation occurred on the substituent groups rather than on the aromatic rings, H/D exchange products were not observed.

Deuterium exchanges for the $[M - 1]^+$ ions of a number of organic compounds were first shown by Stewart et al. [11] under flowing afterglow conditions, using D_2O as the reagent. Exchange reactions were also observed for similar types of compounds under both CI and flowing afterglow conditions, using other deuterated reagents such as ND_3 , $MeOD$, $EtOD$, and CF_3CD_2OD [12,13]. Based on the results obtained from a flowing afterglow instrument, Depuy and Bierbaum [14] have concluded that, as a general rule, H/D exchange can usually be observed between an anion and an exchange reagent which is as much as 20 kcal less acidic. The significance of using H/D exchange reactions for differentiating isomers has been demonstrated by several research groups [15–17].

In this work, we postulate a reaction mechanism for the H/D exchange reaction between the hydrogen

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on the $[M - 1]^-$ ions of aromatic compounds and molecules of D_2O and ND_3 . Isomers of chlorinated benzenes were the model compounds chosen for this study. The results demonstrate the potential of using $[M - 1]^-$ ions as reagents for differentiating aromatic isomers.

Experimental

Two types of tandem quadrupole instruments were used for all experiments. A Finnigan TSQ-70B triple quadrupole mass spectrometer (Finnigan MAT, San Jose, CA) was initially used for both D_2O and ND_3 experiments. The D_2O experiments were then later repeated on a Finnigan TSQ-700 tandem quadrupole instrument. The configuration and the components used for both the instruments are essentially identical, with the exception that the second quadrupole in the Finnigan TSQ-70B instrument is an octopole device in the Finnigan model TSQ-700.

For the experiments performed on the Finnigan TSQ-70B instrument, samples were introduced into the ion source by either a direct insertion probe or from an external glass reservoir connected to the ion source. For the samples in the external glass reservoir, the sample flow rates were controlled by two adjustable leak valves installed between the reservoir and the ion source. As far as possible, a steady-state sample flow rate was maintained during each individual experiment. For the experiments performed on the Finnigan TSQ-700 instrument, samples were introduced into the ion source through the Varian 3400 gas chromatograph (GC) (Varian Associates, Walnut Creek, CA). A capillary column was used (30 m, 0.25 mm i.d., SE-54 phase with 0.25 μ m film thickness) for component separation. The injection port of the GC was set at 250 °C under a splitless injection mode. A transfer line set at 275 °C directed the column effluent into the ion source. Helium was used as the carrier gas at a pressure of 15 psi. The temperature of the GC was programmed from 80 °C to 200 °C at 10 °C/min. The GC temperature program was set such that all the selected compounds emerging from the GC column were at least base-line separated. The isomers of dichlorobenzene were injected into the GC as mixtures. All the samples were dissolved in hexane to a concentration of about 10 ppm for each isomer. The results derived from both instruments are virtually identical. The purpose of repeating the D_2O experiments using GC introduction is to demonstrate the flexibility of carrying out the reaction under different means of sample introduction. GC introduction is especially important for those who are interested in using the technique to analyze samples containing mixtures of isomers.

The $[M - 1]^-$ ions of the test compounds were generated by CI in the ion source at 150 °C using NH_3 as a reagent. In general, the reactant ions extracted from the source were mass-selected by the first quadrupole of one of the tandem quadrupole instruments

for reaction in the second quadrupole (Q2) or the octopole device (O2) where the deuterated reagents were introduced. The last quadrupole was set to scan for the spectra of the ion products of the reactions in Q2 or O2. The collision offset voltage was set at 2.8 V throughout all the experiments. The actual collision energy is estimated to be in the range of 0 to 0.5 eV. The pressure of the reagent gas in the ion source was maintained at 1.5 torr. The collision pressures for ND_3 and D_2O were maintained at approximately 7 and 4 mtorr, respectively, except when indicated otherwise.

All chlorinated isomers (99% grade or better) used in the experiments were purchased from Ultra Scientific (North Kingston, RI). All other halogenated compounds were purchased from Aldrich Chemical Co. (Milwaukee, WI). Deuterated ammonia (99.5 atom %D) was obtained from MSD Isotopes (Montreal, Canada). Deuterated water (99 + % grade) was purchased from Cambridge Isotopes Laboratory (Woburn, MA). All the chemicals were used without further purification.

Results and Discussion

Mechanistic Analysis

Low-energy collision between $[M - 1]^-$ ions of all the isomers of dichlorobenzene and deuterated water or deuterated ammonia produce H/D exchange products. For each isomer, the same exchange products are observed for either D_2O or ND_3 reagent, though not in the same relative abundance. The product mass spectra of the three isomers of dichlorobenzene are shown in Figure 1 for both D_2O and ND_3 . The selected reactant ions at m/z 145 contain only the ^{35}Cl isotope. Each substitution of a deuterium from an exchange reaction with the deuterated reagent is indicated by the gain of 1 mass unit from the mass of the reactant ions. Sequential H/D exchanges of the same ions are indicated by peaks at more than one mass-to-charge ratio unit above the reactant ion mass, thus product ions with all three hydrogens substituted with deuteriums are represented by peaks at m/z 148. Although these isomers are known to produce nearly indistinguishable electron ionization mass spectra, the pattern of H/D exchange products of the $[M - 1]^-$ ion of each isomer is quite distinctive. For the anions of these isomers, only o-dichlorobenzene gives a predominant peak at m/z 148 which corresponds to ion products with all three hydrogens exchanged with deuteriums; the predominant products for m-dichlorobenzene and p-dichlorobenzene are ions substituted with two and one deuteriums, respectively. The dramatic differences in the product patterns observed indicate that the relative positions of the chlorine atoms on the aromatic ring affects the ability of certain ring hydrogens to undergo the H/D exchange reaction.

Because the reaction products observed with both D_2O and ND_3 reagents are essentially the same (though

Figure 1. Product spectra obtained from the H/D exchange reactions between the $[M - 1]^-$ ions of the individual isomers of dichlorobenzene and deuterated water and deuterated ammonia. The reactant ions are at m/z 145. Peaks at higher mass units are due to one or more H/D exchange reactions.

in differing relative abundances), we believe that the basic reaction mechanisms for the two species are essentially the same. We postulate the reaction mechanism shown in Scheme I for ortho dichlorobenzene $[M - 1]^-$ ion and D_2O . In this mechanism, a five-membered-ring reaction intermediate is formed between the $[M - 1]^-$ ion and the reagent molecule (either D_2O or ND_3). The formation of this intermediate is initiated by the attack of the deuterated molecule on the charge site (localized at the carbon atom with the missing hydrogen). An electron pair on the neutral reagent molecule reacts with a hydrogen atom adjacent to the charge site to form the intermediate complex. A successful H/D exchange occurs only if the decomplexation of the intermediate complex leaves a D atom at the initial charge site and removes the adjacent H atom. The charge site in the product ion is shifted one carbon atom around the ring from its position in the reactant ion. Further H/D exchange reactions can continue by the same mechanism until no more adjacent aromatic hydrogens remain. Products substituted with three deuteriums are the result of three successful H/D exchanges which, according to the proposed mechanism, requires that the initial reactant ion contain three aromatic hydrogens adjacent or

sequentially adjacent to the initial charge site. In the case of H/D exchange involving D_2O , both the deuterium atoms on a D_2O molecule can be exchanged. The exchange of the second deuterium atom can take place only after an HDO molecule is formed. Subsequent interaction between the partially deuterated carbanion and the HDO molecule is considered as another collision, though they may not be separated from each other completely before the interaction.

The number of adjacent (or sequentially adjacent) hydrogens in the initial reactant ion depends on the location of the charge and the relative positions of the chlorine atoms on the aromatic ring. All the possible charge sites for the three dichlorobenzene isomers are listed in Figure 2. The chlorine positions and the charge locations of the ortho-substituted anions allow sequential deuterium substitution, via the five-membered-ring intermediate, of all three hydrogens. For the meta-substituted anions, three different charge sites are possible. Both structures III and IV contain aromatic hydrogens adjacent to the charge site. These sites allow exchange of two aromatic hydrogens which are adjacent or sequentially adjacent to the charge sites. The third hydrogen located between the two chlorine atoms is separated from the charge sites and cannot be exchanged through the five-membered-ring intermediate. Reactant ions substituted with two deuteriums are shown in the product spectra of m-dichlorobenzene as the predominant products. Structure V shows a meta-substituted anion formed with a charge site sandwiched between two chlorine atoms. Because the location of this charge site is remote from the three

Scheme I

Ortho-substituted anions

- Both structure I & II allow all three hydrogens to be substituted

Meta-substituted anions

* Non-exchangeable hydrogens

- Structure III and IV will substitute up to 2 H's
- Structure V will not react with D₂O but may be isomerized to become II inside the ion source.

Para-substituted anion

- Structure VI allows only one hydrogen to be substituted

Figure 2. The possible charge sites for the $[M - 1]^-$ ions of dichlorobenzene isomers and the consequent location and number of exchangeable hydrogens according to the proposed reaction mechanism.

aromatic hydrogens, deuterium substitution through the five-membered-ring intermediate is not possible for this reactant ion. The relatively larger reactant peak in the product spectrum of m-dichlorobenzene compared to those of the other dichlorobenzene isomers suggests that some of the reactant ions have the structure V configuration. For the para-substituted anions, there is only one possible charge site because all four aromatic hydrogens in the original molecule are equivalent. Structure VI shows that the charge site is adjacent to only one hydrogen and separated from the other two hydrogens by a chlorine atom. By the proposed mechanism such an ionic configuration allows only one hydrogen of the anion to be exchanged. The predominant ions in the product spectrum of p-dichlorobenzene are substituted with only one deuterium. For aromatic anions substituted with non-halogenated functionalities, different H/D patterns were observed by others [13]. Those patterns cannot be explained by our mechanism. It is likely that the H/D exchange mechanisms of the other aromatic systems are very much different from ours.

Overall, the observed results correlate well with the proposed mechanism. The predominant deuterium exchange observed is one less than the maximum number of hydrogen atoms between the chlorine atoms in each dichlorobenzene isomer. However, a peak representing about 12% of a D₃-substituted product is found in the product spectrum of m-dichlorobenzene, in reactions with the D₂O reagent. For the $[M - 1]^-$ of m-dichlorobenzene, the proposed mechanism would not allow the formation of any D₃-substituted product. Thus, either the proposed mechanism is wrong, or there is an additional process, specific to the m-dichlorobenzene, which is occurring. Two possible additional processes that could result in the D₃-substituted product are: (1) a different substitution mechanism that can breach the intervening Cl atom located between the charge site and the remaining aromatic hydrogen and (2) a possible isomerization of structure V of m-dichlorobenzene to structure II of o-dichlorobenzene. Because the likelihood of the success of a Cl-breaching mechanism is expected to be about the same for both the anions of m- and p-dichlorobenzene, the substantially smaller D₃-substituted product peak observed for the p-dichlorobenzene favors the latter explanation. If the isomerization explanation is true, it appears that the degree of isomerization for the anions of p-dichlorobenzene is substantially lower than that of m-dichlorobenzene.

Collision Pressure Dependence of Products of H/D Exchanges

The number of collisions of an anion with a deuterated reagent while resident in Q2 is affected by the reagent gas pressure in Q2. A higher gas pressure allows a reactant ion to have a higher collision frequency with the deuterated reagent molecules. For ion products derived from a stepwise sequential process, increasing the total number of collisions can enhance the yield of the more highly substituted ion products. For the $[M - 1]^-$ ion of o-dichlorobenzene, the formation of D₃-substituted products requires a minimum of three reactive collisions of the initial reactant ion with deuterated molecules. At low collision pressures, D₃-substituted product ions may not be observed because the reactant ions may leave Q2 before the required number of ion-molecule collisions can occur. For H/D exchanges with D₂O, the collision pressure study shown in Figure 3 supports the sequential process depicted in our proposed mechanism. Products with the highest degree of deuterium substitution are not observed until products with lower degrees of deuterium substitution are formed. The D₁-substituted ions are the predominant products at very low collision pressures. As the collision pressure increases, higher substituted ions replace the less substituted ions as predominant products. At a sufficiently high collision pressure, most of the anions of o-dichlorobenzene are

Figure 3. Plots for product intensity versus collision pressure for H/D exchange reactions between the $[M-1]^-$ ions of dichlorobenzene isomers and D_2O molecules.

fully substituted before they leave Q2. These data support a mechanism that involves the substitution of only one deuterium per reactive collision.

For the reactant ions from m-dichlorobenzene, the pressure-dependence plot shown in Figure 3 indicates that following an increase in collision pressure, the relative intensity of the reactant ions decreases; but the decrease of the reactant ions levels off beginning at about 3.5 mtorr. Thereafter, the contribution of the reactant ions remains at about 25% of the total ion intensity, despite further increases in collision pressure. This result suggests that in the case of m-dichlorobenzene, about 25% of all reactant ions are unreactive with D_2O molecules under any collision pressure conditions. This lack of reactivity can be accounted for within our proposed mechanism, if about 25% of the reactant ions have structure V, in which the charge site is not adjacent to any aromatic hydrogens. Because the contribution of the D_3 -substituted products in the m-dichlorobenzene plot is about 20% at the collision pressure of 5.0 mtorr, we believe that at least

20% of all meta-substituted reactant ions undergo isomerization to reactant anions identical to those from o-dichlorobenzene. This isomerization most likely occurs in the source, possibly as part of the ionization process, though a slow isomerization of the ion, continuing through the ion lifetime in Q2 is also possible.

The pressure-dependence plot for p-dichlorobenzene (Figure 3) indicates that an increase in collision pressure enhances primarily the formation of the D_1 -substituted product. Even at a high collision pressure, the D_1 -substituted product remains predominant. This means that ions substituted with only one deuterium are generally the terminal products for reactions between D_2O and the p-dichlorobenzene $[M-1]^-$ ions. The relatively small contribution of the D_2 - and D_3 -substituted products in the p-dichlorobenzene plot suggests that the p-dichlorobenzene anions are less likely to undergo isomerization than are the anions of m-dichlorobenzene. At the collision pressure of 4.5 mtorr, over 90% of the p-dichlorobenzene anions are converted into the expected predominant D_1 -substituted products.

Collision pressure studies were also performed on reactions with ND_3 reagent. The pressure-dependence plots for H/D exchange reactions involving ND_3 reagent are shown in Figure 4. The trends for the formation of different H/D exchange products for each isomer are the same for both D_2O and ND_3 reagents. The major difference between the two reagents are their relative reactivities toward the anions of the dichlorobenzene isomers for H/D exchange reactions. To achieve a specific H/D exchange product yield, the required collision pressure is higher for ND_3 than for D_2O . A comparison between Figures 3 and 4 suggests that the H/D exchange efficiency of D_2O molecules is about three times better than that of ND_3 molecules. The similarity in the trends of H/D exchange product formation for the two deuterated reagents supports the notion that similar exchange mechanisms are followed by both reagents.

Although H/D exchange products are observed upon collision between dichlorobenzene anions and D_2O or ND_3 reagent, reaction probably does not occur on every single collision. Based on our proposed H/D exchange mechanism, we have generated plots similar to those of Figures 3 and 4 by computer simulation of H/D exchange reactions initiated by reactant ions of all the structures shown in Figure 2 and following our proposed mechanism. In these simulations, the number of collisions times the percent of collisions that are reactive are used instead of the collision pressure as the parameter to calculate the relative intensities for each ion product. A simulated collision-dependence plot for o-dichlorobenzene anions having the structure II configuration is shown in Figure 5. For a specific reactivity (percent of reactive collision), individual plots in terms of relative ion intensity as a function of number of collision can be extracted from the figure.

Figure 4. Plots for product intensity versus collision pressure for H/D exchange reactions between the $[M-1]^-$ ions of dichlorobenzene isomers and ND_3 molecules.

Figure 5. A simulated collision-dependence plot that represents a composite of individual collision-product plots for different percentages of reactive collision. The simulation is based on the proposed H/D exchange reaction mechanism between the structure II anions of *o*-dichlorobenzene and D_2O or ND_3 molecules.

For example, a reactivity based on a 30% reactive collision means that for an average number of collision, 70% of all the reagent ions undergo no reaction. The reaction pathway used for the simulation is shown in Scheme II for the structure II reactant ions. In this study, a reactive collision is defined as either a successful H/D exchange or deuterium/deuterium (D/D) exchange. In our calculations we assume that there is an equal chance for an ion to undergo either an H/D exchange or a D/D exchange where both are possible. For example, for ion 1 shown in Scheme II, the chance of its conversion into either ion 1' or ion 2 is the same. The collision-dependence plot of Figure 5 shows the relative abundance of the reactant and various product ion masses as a function of the number of reactive collisions. In making this plot, it was assumed that no new reactant was added, nor products removed over the time shown. It is also assumed that the percent of collisions that are reactive is the same for all ion structures. A comparison of the collision dependence plot of Figure 5 with the experimental pressure-dependence plot of Figure 3 (top) reveals that the zero input and output flux assumption made in the product-ratio calculations is not valid under our experimental conditions. Continued influx of reactant ions extends their high abundance into the equivalent of higher collision numbers and reduces the relative abundance of the deuterium-exchanged product ions. Departure of ions from the reaction chamber before they have actually undergone the average number of collisions yields finite values for their abundance seen at high average collision numbers.

Figure 6 shows a simulated collision-dependence plot for structure I anions of *o*-dichlorobenzene. These reactant ions require at least four reactive collisions to form the D_3 -substituted products. The reaction pathway used for calculating the relative product intensity of the structure I anions is shown in Scheme III. Comparisons between plots obtained from structure I reactant ions and those with structure II show marked differences in the relative abundances of product ions at many points along the collision number axis. Ideally, one could choose between structures I and II based on the comparison of the collision-dependence plots with the pressure-dependence plot. Unfortunately, the dif-

Scheme II

Figure 6. A simulated collision-dependence plot that represents a composite of individual collision-product plots for different percentages of reactive collision. The simulation is based on the proposed H/D exchange reaction mechanism between the structure I anions of o-dichlorobenzene and D_2O or ND_3 molecules.

ferences in conditions between the experimental and simulated data are greater than the differences between the structure I and II simulations thus precluding a clear preference for either one.

For the anions of m-dichlorobenzene, our simulations assume that of the three meta-substituted ionic structures shown in Figure 2, the contribution of structure IV is insignificant compared to structures III and V. To match the experimental results, we further assume that the number of ions with structures IV and V are initially formed in the ion source in a 50:50 ratio. Before the anions enter the collision chamber for H/D exchange reactions, 50% of the initially formed structure V anions are also assumed to isomerize to become structure II anions. As such, the collisional simulations of the anions of m-dichlorobenzene are based on collisions initiated by a mixture of anions with three different structures (50% structure IV, 25% structure V, and 25% structure II). The results are shown in Figure 7 as a collision-dependent plot. The product formation trends represented in this plot compare well with the similar trends shown in the experimental pressure-dependence plot of Figure 3 (middle). This further supports the isomerization explanation and the existence of the unreactive structure for the m-dichlorobenzene anions.

The collision simulations of the anions of p-dichlorobenzene are relatively simple because of the simplicity of the reaction pathway for the formation of the expected predominant products. Figure 8 shows the collision-dependence plot for the anions of p-dichlorobenzene, based on reactant ions with structure VI configuration. In this case, the trends for the formation of the predicted product shown in the simulated plot are comparable to those represented in the experimental pressure-dependence plot of Figure 3 (bottom). Overall, although the relative product abundances rep-

Scheme III

resented in all the simulated collision-dependence plots are different from those shown in the experimental pressure-dependence plots, the general trends for the formation of various H/D exchange products obtained from the simulated results are consistent with the experimental data.

Reactions with Other Aromatic Isomers

We have also used isomers of other chlorinated benzenes to test the proposed mechanism. According to the mechanism, for an $[M-1]^-$ anion to undergo an H/D exchange, there must be at least one aromatic hydrogen adjacent to the charge site on the anion. For the $[M-1]^-$ ions derived from 1,3,5-trichlorobenzene, 1,2,4,5-tetrachlorobenzene, and

Figure 7. A simulated collision-dependence plot that represents a composite of individual collision-product plots for different percentages of reactive collision. The simulation is based on the proposed H/D exchange reaction mechanism between a mixture of different m-dichlorobenzene anions and D_2O or ND_3 molecules. The mixture of anions is assumed to contain 50% structure IV, 25% structure V, and 25% structure II.

Figure 8. A simulated collision-dependence plot that represents a composite of individual collision-product plots for different percentages of reactive collision. The simulation is based on the proposed H/D exchange reaction mechanism between p-dichlorobenzene anions (structure VI) and D_2O or ND_3 molecules.

1,2,3,5-tetrachlorobenzene, none of the possible charge sites have any adjacent aromatic hydrogens and no products resulting from the H/D exchange reactions are observed. The product spectra derived from the reaction of 1,2,3-trichlorobenzene, 1,2,4-trichlorobenzene, and 1,2,3,4-tetrachlorobenzene anions with D_2O , shown in Figure 9, exhibit predominant exchanges of 2, 1, and 1 deuteriums, respectively. According to the proposed mechanism, reactant ions substituted with two deuteriums should be the predominant products for 1,2,3-trichlorobenzene because its neutral configuration contains three sequential hydrogens between the chlorine atoms. The original molecules of both 1,2,4-trichlorobenzene and 1,2,3,4-tetrachlorobenzene contain only two sequential hydrogens between the chlorine atoms; the predominant products should be ions substituted with only one deuterium. All the results are consistent with the proposed mechanism. The small D_2 -substituted peak in the product spectrum of 1,2,4-trichlorobenzene could be due to isomerization of the reactant ions, as described earlier. Similar results are also observed for the same reactions with ND_3 reagent. The dramatic differences in the product patterns for most of the isomers studied suggest that these reactions are useful for differentiating isomers of chlorinated benzenes. The results of the reactions are summarized in Table 1. Because the number of chlorines can be determined from the masses of different $[M - 1]^-$ ions, our studies clearly demonstrate that tandem mass spectrometry along with H/D exchange reactions using ND_3 or D_2O as a reagent can positively identify all the chlorinated benzenes except two of the tetrachlorinated isomers. Product spectra similar to those of the dichlorobenzene isomers are also obtained for the isomers of difluorobenzene and bromochlorobenzene. This strongly

Figure 9. Product spectra for the tetrachlorobenzene and trichlorobenzene isomers that produce H/D exchange ion products. The H/D exchange products are due to reactions between the $[M - 1]^-$ ions of isomers indicated and D_2O molecules. No H/D exchange products are observed for the other tetrachlorobenzene and trichlorobenzene isomers.

Table 1. Maximum number of H/D exchanges for the $[M - 1]^-$ ions of isomers of chlorinated benzenes (in cases of no isomerization)

Type of Cl Substitution	Position of Cl on an aromatic ring	Maximum number of D substitutions
Mono	(no isomers)	4
Di	1,2	3
	1,3	2
	1,4	1
Tri	1,2,3	2
	1,2,4	1
	1,3,5	0
Tetra	1,2,3,4	1
	1,2,3,5	0
	1,2,4,5	0
Penta	(no isomers)	0

suggests that the same mechanism is operating on all halogenated benzenes.

We have begun studies on larger chlorinated aromatic compounds. For a molecule made up of fused benzene rings, the initial negative charge site of an $[M - 1]^-$ ion may be on a different ring than the exchanging aromatic hydrogens. For example, sequential H/D exchanges for aromatic hydrogens on different rings of a chlorinated naphthalene molecule require the formation of a six-membered-ring intermediate for relocation of charge site from one ring to another, assuming a similar mechanism is also operating. The product spectrum of 1-chloronaphthalene shown in Figure 10 indicates that reactant ions with all six hydrogens substituted with deuteriums are the predominant products. For the $[M - 1]^-$ anion of 1-chloronaphthalene, substituting more than three hydrogens requires a mechanism of relocating the charge site from one ring to the other. In this case, the mechanism should involve the formation of a six-membered-ring intermediate, as shown in Scheme IV. It is quite possible that the same mechanism may also apply to chlorinated compounds with more than two adjacent rings.

Conclusions

By using ND_3 or D_2O as a reagent, H/D exchange reactions are found to occur between the reagents and the $[M - 1]^-$ ions of halogenated benzenes originating from molecules with two or more sequential aromatic hydrogens. The reactivity of D_2O is about three times that of NH_3 in the exchange reactions. A mechanism involving the formation of a five-membered-ring intermediate is consistent with the results derived from the isomers of all the chlorinated benzenes in this study. The results obtained from the isomers of fluorinated

Scheme IV

and brominated benzenes strongly suggest that the same mechanism is also applicable to all halogenated benzenes. The number of deuterium substitutions for the predominant H/D exchange products is one less than the number of sequential aromatic hydrogens in the original molecules of chlorobenzene. It is possible that a mechanism involving a six-membered-ring intermediate is used for exchanging hydrogens across two or more fused benzene rings.

Computer simulations based on the proposed mechanism are also consistent with the product formation trends derived from the experimental results. The anions of *m*-dichlorobenzene are more susceptible to isomerization than the anions of *o*- and *p*-dichlorobenzene. A comparison among the experimental pressure-dependence plots suggests the existence of an unreactive structure for the anions of *m*-dichlorobenzene which is predicted by our proposed mechanism. For most chlorinated benzenes, we have demonstrated the potential of using H/D exchange reactions for isomeric differentiation.

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Figure 10. A product spectrum for H/D exchange reactions between the $[M - 1]^-$ ions of 1-chloronaphthalene and D_2O molecules. Reactant ions having all their six hydrogens substituted with deuteriums are the predominant products.

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