

Gas-phase electrophilic addition promoted by $\text{CH}_3\text{S}^+=\text{CH}_2$ ions on aromatic systems

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The gas-phase methylenation reaction between $\text{CH}_3\text{S}^+=\text{CH}_2$ and alkylbenzenes, aniline, phenol and alkyl phenyl ethers, which yields $[\text{M} + \text{CH}]^+$ and CH_3SH , has been studied by Fourier transform ion cyclotron resonance (FT-ICR) techniques and computational chemistry at the DFT level. The methylthiomethyl cation is less reactive than methoxymethyl and, unlike the latter, is unreactive toward benzene. The calculations suggest that reaction with toluene should proceed primarily by addition at the *para* and *ortho* positions resulting in a benzyl-type ion. Reaction with aniline-2,3,4,5,6-*d*₅ reveals that elimination of CH_3SD is kinetically favored by a factor of 5 over elimination of CH_3SH . Experiments with $\text{C}_6\text{H}_6\text{ND}_2$ and theoretical calculations suggest that methylenation at the nitrogen atom is energetically favorable and likely, but the observed results may reflect some H/D scrambling, which occurs after attack at a ring position. By comparison, reaction with phenol-2,3,4,5,6-*d*₅ reveals that methylenation followed by elimination of CH_3SD is kinetically favored by a factor of 3.8 over elimination of CH_3SH . For phenol, the theoretical calculations suggest that attack by $\text{CH}_3\text{S}^+=\text{CH}_2$ at the *para* or *ortho* position is the only low-energy pathway for methylenation. However, a low-energy pathway for hydrogen scrambling is predicted by the calculations originating from the exit complex, $[\text{CH}_3\text{SH} \cdots \text{CH}_2=\text{C}_6\text{H}_4=\text{OH}]^+$, of reaction at a ring position. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: methylthiomethyl cation; aromatic electrophilic reactions; ion/molecule reactions

INTRODUCTION

The methoxymethyl cation, $\text{CH}_3\text{O}^+=\text{CH}_2$, is a ubiquitous species in gas-phase ion chemistry whose reactivity has been explored by several research groups using a variety of experimental techniques.^{1–10} Four types of ion–molecule reactions have been well established for the $\text{CH}_3\text{O}^+=\text{CH}_2$ cation depending on the nature of the neutral organic substrate (M):¹¹ (1) addition followed by elimination of methanol to yield an $[\text{M} + \text{CH}]^+$ ion; (2) methylation leading to an $[\text{M} + \text{CH}_3]^+$ ion; (3) direct addition with the subsequent formation of an adduct ion; and (4) hydride abstraction to yield an $[\text{M} - \text{H}]^+$ ion. This range of reactivity has made the methoxymethyl cation a useful and specific reagent for chemical ionization.^{12–14}

Considerably less is known about the gas-phase ion chemistry of the methylthiomethyl cation, $\text{CH}_3\text{S}^+=\text{CH}_2$, or similar $\text{RS}^+=\text{CH}_2$ cations, even though they are common fragments in the mass spectrum of thioethers.¹⁵ While similarities might be expected between the ion chemistry of $\text{CH}_3\text{O}^+=\text{CH}_2$ and that of $\text{CH}_3\text{S}^+=\text{CH}_2$, it has been shown that significant differences can be observed in the reactivity

of these ions with conjugated dienes under the typical conditions of a pentaquadrupole mass spectrometer.¹⁶

One of the most intriguing reactions of the $\text{CH}_3\text{O}^+=\text{CH}_2$ cation is its ability to promote the electrophilic addition of a methylene unit to benzene followed by elimination of methanol.¹⁷ Preliminary experiments in our laboratories have revealed that $\text{CH}_3\text{S}^+=\text{CH}_2$ is a weaker gas-phase electrophile, which prompted us to undertake an experimental and theoretical characterization of electrophilic reactions promoted by these ions in simple aromatic systems. Such a study is timely in view of the comprehensive study recently published on the gas-phase nitration of benzene,¹⁸ a reaction that is the classical prototype of aromatic electrophilic substitution. The present investigation of the gas-phase reactions of $\text{CH}_3\text{S}^+=\text{CH}_2$ represents an extension of our earlier work on the reactivity of isomeric $[\text{C}_2\text{H}_5\text{S}]^+$ ions.¹⁹ In this case, the study has been extended to substrates such as phenol and aniline that display two possible sites for electrophilic addition and thus provide an interesting assessment between attack at a ring position as opposed to attack at the heteroatom.

EXPERIMENTAL

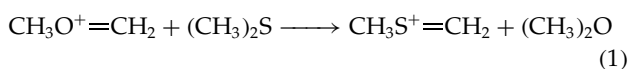
Experiments were carried out in a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer operating at a magnetic field of 1.0 T and provided with a one-region 15.75 cm³ cubic cell. Ionization, ion selection, ion–molecule reactions and detection take place in this cell. The general

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operating conditions of this spectrometer have been previously described in our work related to the identification of triplet state CH_3S^+ and $\text{C}_2\text{H}_5\text{S}^+$ cations.^{19,20}

The $\text{CH}_3\text{S}^+=\text{CH}_2$ ions were directly generated by electron ionization at a nominal energy of 13 eV from $(\text{CH}_3)_2\text{S}$ or $\text{CH}_3\text{SC}_2\text{H}_5$ at nominal pressures of $1.5\text{--}3 \times 10^{-8}$ Torr. Our previous work¹⁹ has shown that electron ionization results, in both cases, in a mixture of isomeric $[\text{C}_2\text{H}_5\text{S}]^+$ ions. The $[\text{C}_2\text{H}_5\text{S}]^+$ (m/z 61) ions were then isolated by a sequence of short, frequency-swept, ejection pulses to remove all unwanted primary and secondary ions (formed before ion isolation). An alternative procedure was also used in some cases to generate the $\text{CH}_3\text{S}^+=\text{CH}_2$ isomer exclusively. This was based on obtaining $\text{CH}_3\text{O}^+=\text{CH}_2$ by electron ionization from dimethoxymethane followed by ion–molecule reaction with $(\text{CH}_3)_2\text{S}$.



Unfortunately, this latter procedure is not always convenient because the $\text{CH}_3\text{O}^+=\text{CH}_2$ ions themselves react with the aromatic substrates.

Ion–molecule reactions of $\text{CH}_3\text{S}^+=\text{CH}_2$ with different neutral substrates were studied at different partial pressures up to total pressures of 1.5×10^{-7} Torr. No attempts were made to measure the absolute rate constants because of the simultaneous reaction of the reagent ion with its neutral precursor and with the aromatic substrate. Reactions were typically followed up to 10 s of trapping times.

Reagents were obtained from Aldrich and used without further purification. Samples were thoroughly degassed and subjected to several freeze, pump and thaw cycles prior to their introduction in the high vacuum system of the spectrometer. Mass spectra of these samples obtained by running the FT-ICR spectrometer with continuous ionization and short trapping times revealed no detectable impurities. Deuterated toluene- d_3 , aniline- d_5 and phenol- d_5 were obtained from Isotec, St. Louis, MO, USA. N,N -Dideuteroaniline, $\text{C}_6\text{H}_5\text{ND}_2$, was prepared by mixing aniline with excess D_2O , but exchange at the metal walls of the spectrometer prevented full deuteration.

THEORETICAL CALCULATIONS

Theoretical calculations at the DFT level were carried out in order to map out the potential energy surface for the reactions involving $\text{CH}_3\text{S}^+=\text{CH}_2$ and $\text{C}_6\text{H}_5\text{X}$, with $\text{X} = \text{H}$, CH_3 , NH_2 and OH , as well as some similar reactions with $\text{CH}_3\text{O}^+=\text{CH}_2$. Structures for all energy minima and transition state structures were obtained by full geometry optimization using the B3LYP hybrid density functional^{21,22} with the 6-311++G(d,p) basis set. Electronic energies for these stationary points and transition states were computed at the B3LYP/6-311++G(d,p) level. Vibrational frequencies were also calculated to characterize local minima on the potential energy surfaces, first-order saddle points, and to obtain zero-point energies (ZPEs). All calculations reported in this study were performed with the Gaussian03 suite of programs.²³

RESULTS AND DISCUSSION

$[\text{C}_2\text{H}_5\text{S}]^+$ (m/z 61) ions generated by electron ionization from different precursors usually give rise to an isomeric mixture of $\text{CH}_3\text{S}^+=\text{CH}_2$, $\text{CH}_3\text{C}(\text{H})\text{SH}^+$ and triplet $\text{CH}_3\text{CH}_2\text{S}^{+\bullet}$ ions.¹⁹ They can be conveniently distinguished in FT-ICR experiments by the ability of $\text{CH}_3\text{C}(\text{H})\text{SH}^+$ to transfer a proton to substrates of higher proton affinity than thioacetaldehyde, and of triplet $\text{CH}_3\text{CH}_2\text{S}^{+\bullet}$ to undergo fast charge transfer to substrates with ionization energies lower than the recombination energies of the thioethoxy radical cation. Thus, in several of our studies competitive reactions occur from these isomeric ions with the aromatic substrates. High level theoretical calculations suggest that $\text{CH}_3\text{S}^+=\text{CH}_2$ and $\text{CH}_3\text{C}(\text{H})\text{SH}^+$ are unlikely to undergo *unimolecular* isomerization²⁴ on the time scale of FT-ICR experiments, but little is known about the possibility of isomerization induced by bimolecular processes.

Figure 1 illustrates the reactivity of the mixture of isomeric $[\text{C}_2\text{H}_5\text{S}]^+$ ions, obtained by electron ionization from $(\text{CH}_3)_2\text{S}$, with the parent neutral. Figure 2 illustrates the kinetics of the different processes with the $\text{CH}_3\text{C}(\text{H})\text{SH}^+$ leading to formation of $(\text{CH}_3)_2\text{SH}^+$ (m/z 63), triplet $\text{CH}_3\text{CH}_2\text{S}^+$ leading to formation of $(\text{CH}_3)_2\text{S}^{+\bullet}$ (m/z 62), while the unreactive fraction of m/z 61 is attributed to the $\text{CH}_3\text{S}^+=\text{CH}_2$ ion.

Reaction with benzene

Unlike the methoxymethyl cation,¹⁷ $\text{CH}_3\text{S}^+=\text{CH}_2$ is unreactive toward benzene within the time scale of our experiment. This difference in reactivity is well illustrated by the calculated energy surfaces for the reaction of the two ions.

Figure 3 shows the calculated energy surface for the methylene group addition to benzene promoted by $\text{CH}_3\text{O}^+=\text{CH}_2$. This energy profile reveals the typical double well potential that is common to many ion–molecule reactions. The calculations suggest that the reaction proceeds by initial aromatic addition of the electrophile to yield a σ -type arenium ion complex, or *ipso* protonated methoxymethylbenzene (identified as C1) whose energy is predicted to be $12.4 \text{ kcal mol}^{-1}$ lower than the energy of the reactants. The system then proceeds through a transition state (TS) involving proton migration from the aromatic ring to oxygen that is predicted to have the same energy as the reactants. On the

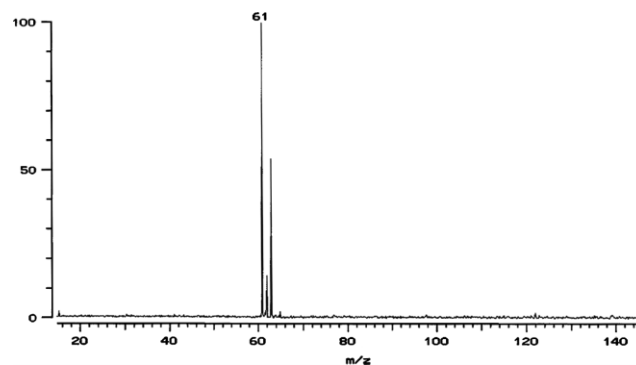


Figure 1. FTMS spectrum obtained after 5 s of reaction time of isolated $[\text{C}_2\text{H}_5\text{S}]^+$ ions, obtained by 20 eV electron ionization from $(\text{CH}_3)_2\text{S}$ at 4×10^{-8} Torr, with their neutral precursor.

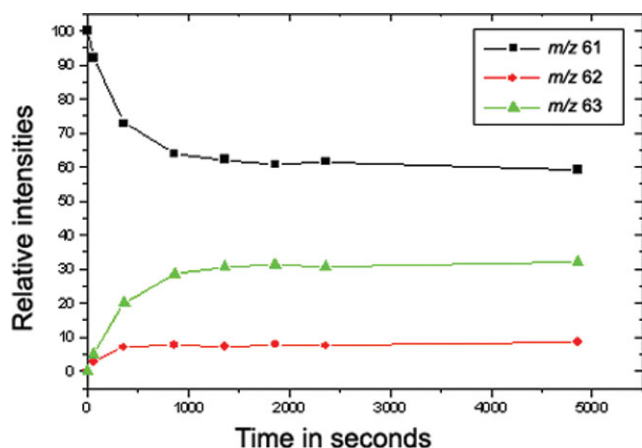
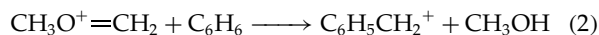


Figure 2. Kinetic plot of the reaction of the m/z 61 ions obtained as indicated in Fig. 1 showing the formation of $(\text{CH}_3)_2\text{S}^+$ (m/z 62) and $(\text{CH}_3)_2\text{SH}^+$ (m/z 63).

exit side of the reaction, the system forms a stable complex between the benzyl ion, $\text{C}_6\text{H}_6\text{CH}_2^+$, and the nascent CH_3OH molecule (identified as C2), prior to dissociation into the final

separated products as shown below.



$$\Delta H^\circ(0 \text{ K, calcd}) = -14.6 \text{ kcal mol}^{-1}$$

The calculated pathway for the reaction leads to the formation of the benzyl cation (P1) and methanol. Figure 3 also displays a qualitative outline of the barrier for isomerization of benzyl ion to the more stable tropylium ion structure (P2) as the final ionic product. This isomerization is unlikely in this case because the barrier for such a process has been estimated to be in the range of 65–69 kcal mol^{-1} .^{25–27}

Figure 4 shows the calculated energy diagram for the reaction of $\text{CH}_3\text{S}^+=\text{CH}_2$ with benzene. The general features of the energy surface are similar, but the initial arenium complex is calculated to be considerably less stable (only 6.4 kcal mol^{-1} below the reagents) than for the case of $\text{CH}_3\text{O}^+=\text{CH}_2$. More important, the TS on this double well potential surface is now predicted to be 4.6 kcal mol^{-1} above the energy of the reagents. Although energy barriers calculated by DFT methods must often be viewed with some caution, our calculations suggest that the rate constant for the

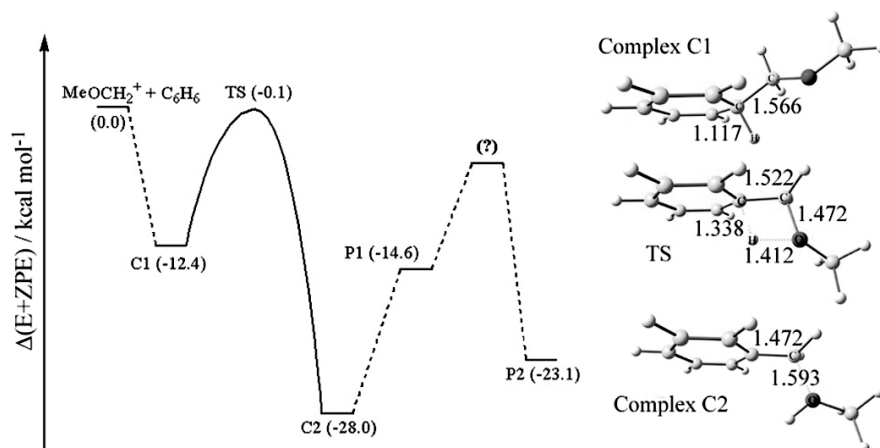


Figure 3. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the methylene-induced addition on benzene by $\text{CH}_3\text{O}^+=\text{CH}_2$. The P1 product refers to the formation of the benzyl cation and methanol, whereas P2 refers to the possibility of isomerization to the tropylium ion.

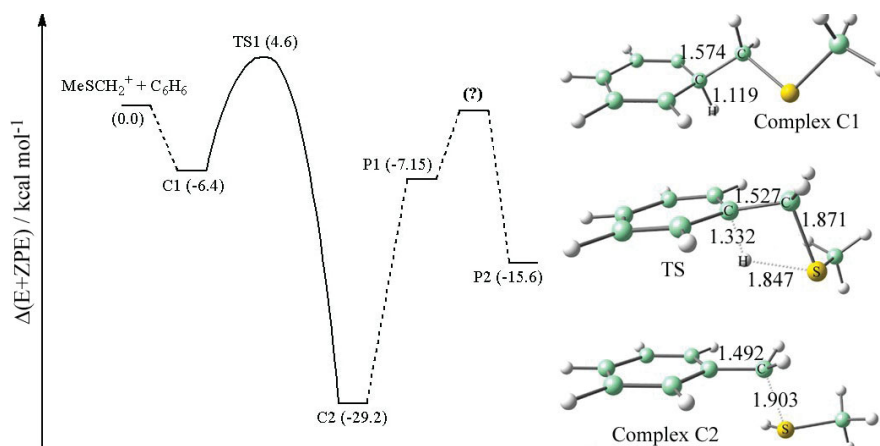


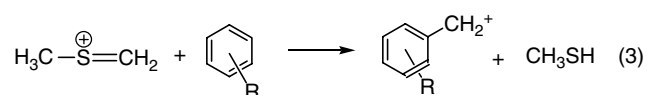
Figure 4. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the methylation of benzene by $\text{CH}_3\text{S}^+=\text{CH}_2$. The P1 product refers to the formation of the benzyl cation and methanethiol, whereas P2 refers to the possibility of isomerization to the tropylium ion.

$\text{CH}_3\text{S}^+=\text{CH}_2$ reaction should be several orders of magnitude less than that for the $\text{CH}_3\text{O}^+=\text{CH}_2$ reaction, in agreement with the experimental observations.

The difference in behavior between $\text{CH}_3\text{O}^+=\text{CH}_2$ and $\text{CH}_3\text{S}^+=\text{CH}_2$ can be attributed to a higher dispersal of the positive charge by the more polarizable sulfur atom. This would make $\text{CH}_3\text{S}^+=\text{CH}_2$ considerably less electrophilic in its attack at the carbon atom. Table 1 shows the calculated Mulliken charges for both cations that support this intuitive chemical point of view.

Reaction with alkylbenzenes

A dramatic difference occurs upon reacting $\text{CH}_3\text{S}^+=\text{CH}_2$ ions with alkylbenzenes. For simple alkyl groups, the prototype reaction (3) ($\text{R} = \text{alkyl}$) proceeds to completion rapidly (in less than 5 s) under our experimental conditions.



Methylenation at a ring position was established by using toluene- α,α,α - d_3 as the aromatic substrate. The spectrum shown in Fig. 5 clearly reveals that all the deuterium atoms are retained in the ionic product, $\text{C}_8\text{H}_6\text{D}_3^+$ (m/z 108).

Table 1. Calculated Mulliken atomic charges (in atomic units) for the $\text{CH}_3\text{O}^+=\text{CH}_2$ and $\text{CH}_3\text{S}^+=\text{CH}_2$ cations. Δ is the difference between the atomic charges in both ions

	$\text{CH}_3\text{O}^+=\text{CH}_2$	$\text{CH}_3\text{S}^+=\text{CH}_2$	Δ
C	0.058	-0.346	0.404
H	0.253	0.271	-0.018
H	0.229	0.247	-0.018
O/S	0.084	0.723	-0.639
C	-0.298	-0.563	0.265
H	0.182	0.195	-0.013
H	0.246	0.237	0.009
H	0.246	0.237	0.009

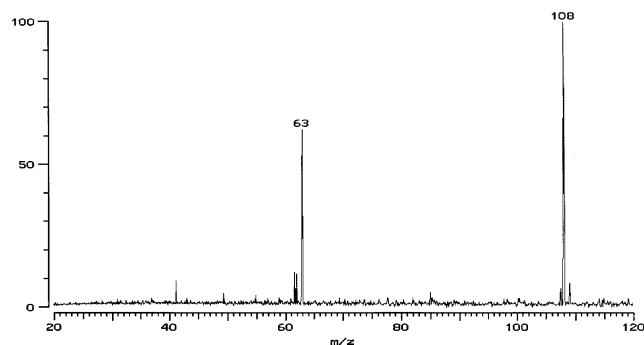


Figure 5. FTMS spectrum obtained after 3 s of reaction between $\text{CH}_3\text{S}^+=\text{CH}_2$ ions and toluene- α,α,α - d_3 at 8×10^{-8} Torr. The product ions at m/z 62 and m/z 63 are due to the reaction of the other isomeric m/z 61 ions with their neutral precursor as illustrated in Fig. 1.

Our theoretical calculations are again useful for understanding the energy surface for this reaction and for visualizing the preferred ring positions of attack. The energy surface is similar to those shown in Figs 3 and 4 and it is outlined in Fig. 6 for pathways originating from attack at either the *para* or *ortho* position of toluene. The *para* and *ortho* positions are the most favorable pathways, although attack at the *meta* position is also estimated to yield a stable arenium ion complex as shown in Table 2. Thus, it is possible that addition of a CH_2 group promoted by $\text{CH}_3\text{S}^+=\text{CH}_2$ ions at thermal energies can actually proceed at all three ring positions but preferentially at the *para* position.

A comparison between Figs 4 and 6 reveals that the methyl group of toluene has a pronounced effect on the stability of the initial arenium ions (C1) and in lowering the barrier for proton migration to the sulfur atom.

Reaction with aniline

The reactions of $\text{CH}_3\text{S}^+=\text{CH}_2$ with aniline, $\text{C}_6\text{H}_5\text{NH}_2$, is of potential interest because the reagent ion can in principle attack the ring positions, the heteroatom, or

Table 2. Relative energy (in kcal mol^{-1} with ZPE included) of the initial intermediate arenium ion complex resulting from addition of $\text{CH}_3\text{S}^+=\text{CH}_2$ to different ring positions and at the heteroatom. Calculations were performed at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) level considering the energy of the reagents, $\text{CH}_3\text{S}^+=\text{CH}_2$ and the aromatic substrate, as zero energy

Energy	<i>Para</i>	<i>Meta</i>	<i>Ortho</i>	Heteroatom
Toluene	-14.48	-9.60	-10.67	
Aniline	-33.75	-11.67	-32.86	-36.04
Phenol	-19.43	-5.22	-23.24	-10.86

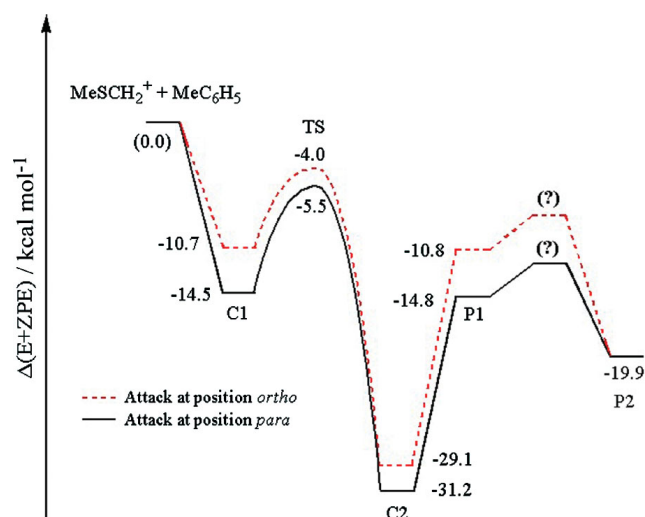


Figure 6. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the $\text{CH}_3\text{S}^+=\text{CH}_2$ induced methylenation at the *para* and *ortho* position of toluene. The P1 products refer to the formation of benzyl-type cations and methanethiol, whereas P2 refers to the possibility of isomerization to the tropylium ion.

both sites. Ion–molecule reactions of $\text{CH}_3\text{O}^+=\text{CH}_2$ with NH_3 and CH_3NH_2 are known to proceed by methylene insertion to yield the corresponding protonated imines, $\text{CH}_2=\text{NH}_2^+$ and $\text{CH}_3\text{NH}^+=\text{CH}_2$, respectively, with rate constants comparable to the collision rate constants.¹⁰ The mechanism for the NH_3 reaction has been previously explored by computational chemistry^{9,28} and the calculated energy surface is similar to those presented in Figs 3, 4 and 6. Similar reactions have also been observed in our laboratories with $\text{CH}_3\text{S}^+=\text{CH}_2$ as the reagent ion.²⁹

The mixture of $[\text{C}_2\text{H}_5\text{S}]^+$ isomeric ions reacts rapidly with aniline to yield $\text{C}_6\text{H}_5\text{NH}_2^+\bullet$ by charge transfer (presumably from triplet $\text{C}_2\text{H}_5\text{S}^+$), $(\text{C}_6\text{H}_5\text{NH}_2)\text{H}^+$ by proton transfer (presumably from $\text{CH}_3\text{C}(\text{H})\text{SH}^+$) and $\text{C}_7\text{H}_8\text{N}^+$ by addition–elimination from $\text{CH}_3\text{S}^+=\text{CH}_2$. It is this reaction that needs to be better understood. For example, reaction of $\text{CH}_3\text{S}^+=\text{CH}_2$ with aniline-2,3,4,5,6-*d*₅ (99+% D) provides in principle the possibility of comparing the relative ease of electrophilic attack at ring positions as opposed to attack at the heteroatom. The resulting spectrum, shown in Fig. 7, reveals the formation of $\text{C}_7\text{H}_4\text{D}_4\text{N}^+$ (*m/z* 110) with elimination of CH_3SD and $\text{C}_7\text{H}_3\text{D}_5\text{N}^+$ (*m/z* 111) with elimination of CH_3SH in a 5.1 ± 0.3 ratio (uncorrected for ¹³C contribution). By comparison, reaction of $\text{CH}_3\text{S}^+=\text{CH}_2$ with $\text{C}_6\text{H}_5\text{ND}_2$ (~80% D) yields $\text{C}_7\text{H}_6\text{D}_2\text{N}^+$ (*m/z* 108), $\text{C}_7\text{H}_7\text{DN}^+$ (*m/z* 107) and $\text{C}_7\text{H}_8\text{N}^+$ (*m/z* 106). The product distribution suggests that CH_3SH is essentially the only neutral eliminated in the formation of the three product ions because the relative abundance of the observed products closely reflects the isotopic deuterium atom purity of the aniline sample measured by mass spectrometry. The significance of these results can be explored further with the help of theoretical calculations.

Theoretical calculations are helpful for visualizing the energy surface involving possible attack at ring positions and at the nitrogen center, as well as possible mechanisms for hydrogen–deuterium scrambling. The relative stability of the initial complexes C1 resulting from addition of $\text{CH}_3\text{S}^+=\text{CH}_2$ to the different ring positions and to nitrogen are given in

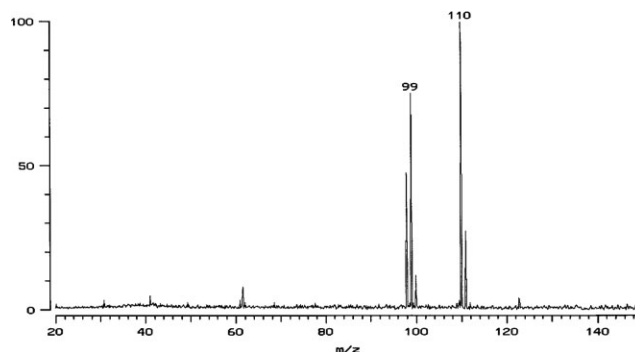
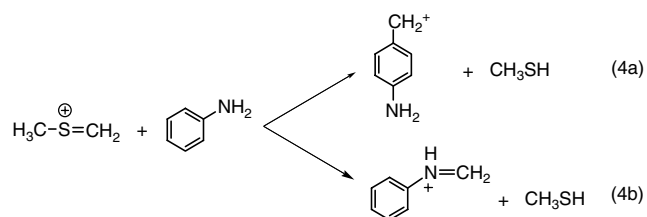


Figure 7. Spectrum obtained after 3 s of reaction between $\text{CH}_3\text{S}^+=\text{CH}_2$ ions and aniline-2,3,4,5,6-*d*₅ at 8×10^{-8} Torr. The product ions at *m/z* 98 ($\text{C}_6\text{D}_5\text{NH}_2^+\bullet$) and *m/z* 99 ($\text{C}_6\text{D}_5\text{NH}_3^+$) are due to the reaction of the other isomeric *m/z* 61 ions with aniline-2,3,4,5,6-*d*₅.

Table 2. It is clear from our calculated values that initial addition to the *para* and *ortho* position, or to the nitrogen atom, is greatly preferred over attack at the *meta* position. Figure 8 shows the full reaction energy diagram for the $\text{CH}_3\text{S}^+=\text{CH}_2$ /aniline reaction considering attack at the *para* position of the ring (reaction 4a), whereas Fig. 9 shows the energy diagram for attack on nitrogen (reaction 4b).



Although the calculations reveal that addition of the reagent ion to nitrogen is slightly more stable than addition at the *para* ring position, the calculated energy barriers for elimination of CH_3SH clearly favor reaction at the ring.

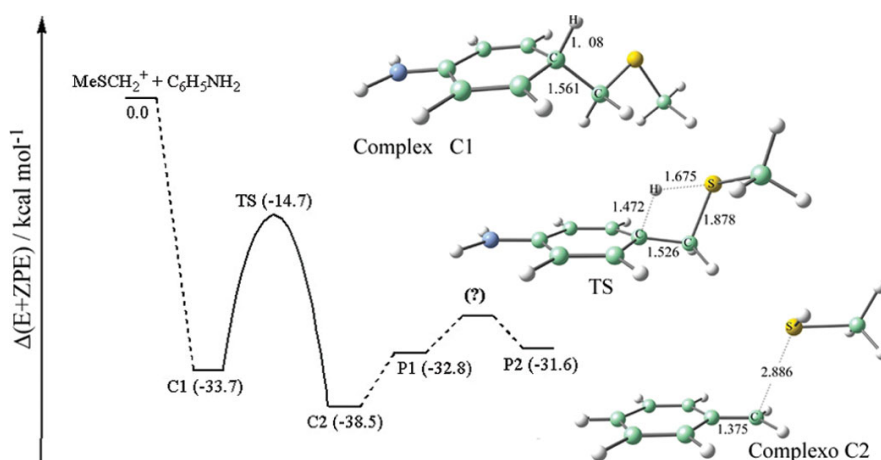


Figure 8. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the $\text{CH}_3\text{S}^+=\text{CH}_2$ induced methylenation at the *para* position of aniline. The P1 products refer to the formation of benzyl-type cations and methanethiol, whereas P2 refers to the possibility of isomerization to a tropylium ion structure. Attack at the *ortho* position yields a similar energy profile but the local transition state is calculated to be $10.9 \text{ kcal mol}^{-1}$ below the reagents.

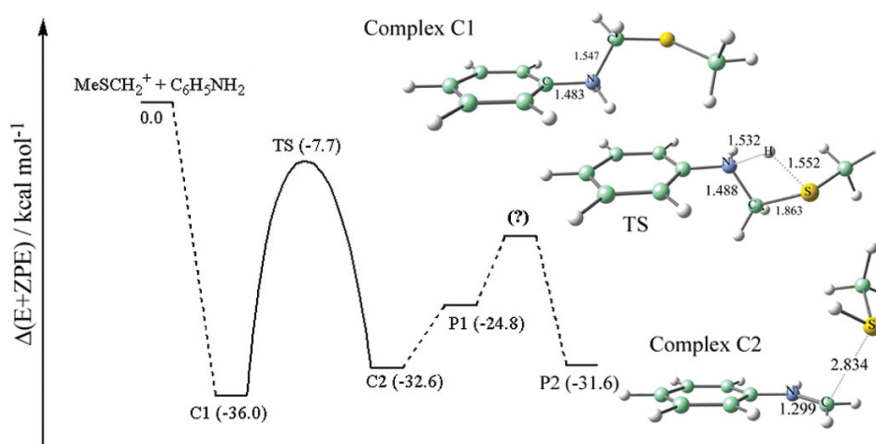


Figure 9. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the $\text{CH}_3\text{S}^+=\text{CH}_2$ induced methylation at the nitrogen atom of aniline. The P1 products refer to the formation of benzyl-type cations and methanethiol, whereas P2 refers to the possibility of isomerization to a tropylium ion structure.

The calculated energy diagrams presented in Figs 8 and 9 and in Table 2 suggest that reactions are energetically possible at all the ring positions and at the nitrogen atom. Unfortunately, the experiments with deuterated anilines are inconclusive for determining the relative extent of reaction at ring positions and at the heteroatom center. Two different mechanisms can be envisioned to contribute to the results obtained with $\text{C}_6\text{D}_5\text{NH}_2$ and $\text{C}_6\text{H}_5\text{ND}_2$:

1. The first possibility is that attack does occur directly at one or more ring positions and at the nitrogen center but a likely isotope effect accounts for a decrease in CH_3SD elimination;
2. A second possibility arises from a scrambling mechanism involving the ring deuterium atoms with the nitrogen protons, or vice versa in the case of $\text{C}_6\text{H}_5\text{ND}_2$. Proton migration from an initial complex resulting from attack at a ring position such as complex C1 in Fig. 8, or *para*-(thiomethoxymethyl)aniline protonated at the *para* ring carbon, seems unlikely. While our calculations reveal that the proton can undergo ring-walk to the *meta*, *ortho* and *ipso* carbon position (relative to the NH_2 group) through energy barriers calculated to be just below the energy of the reactants, migration of the proton from the *ipso* ring position to the NH_2 group involves a barrier of over 14 kcal mol^{-1} . This contention is consistent with the view that ring-protonated and nitrogen-protonated anilines are distinct species in the gas phase.^{30–35} A second mechanism for scrambling can result from the loose ion–molecule complex C2 (Fig. 8). The nascent $\text{CH}_3\text{SH(D)}$ is expected to be relatively free (calculated C–S distance is 2.89 \AA) and able to explore the energy surface prior to final separation into products. In this respect, we find that CH_3SH can exchange protons with the nitrogen protons of the ionic species $[\text{CH}_2=\text{C}_6\text{H}_4-\text{NH}_2]^+$ of the complex through the transition state shown in Fig. 10, located $1.2 \text{ kcal mol}^{-1}$ below the energy of the original reactants.

In summary, the combination of experimental and theoretical results for aniline suggests that attack by $\text{CH}_3-\text{S}^+=\text{CH}_2$ at the ring is preferred over attack at nitrogen. The data also suggest that attack at nitrogen is likely

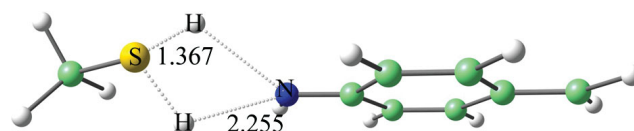


Figure 10. Transition state calculated to be $1.2 \text{ kcal mol}^{-1}$ below the energy of the reactants, $\text{CH}_3\text{S}^+=\text{CH}_2$ and aniline, that could allow for hydrogen–deuterium scrambling in the ion–molecule complex $[\text{CH}_2=\text{C}_6\text{H}_4-\text{NH}_2^+\text{HSC}_2\text{H}_5]^+$. The $[-\text{SH}_2^+]$ moiety has local C_{2v} symmetry.

but a significant isotope effect that would favor CH_3SH over CH_3SD elimination makes it difficult to estimate the extent of attack at nitrogen. Furthermore, the extent of attack at nitrogen, if any, is further complicated by the possibility of hydrogen–deuterium scrambling promoted in the exit complex of the reaction that originally takes place by attack of the electrophile at a ring position.

Reaction with phenol and alkyl phenyl ethers

Methylation promoted by $\text{CH}_3\text{S}^+=\text{CH}_2$, with subsequent CH_3SH elimination, is also observed to be a facile reaction with substrates such as $\text{C}_6\text{H}_5\text{OC}_2\text{H}_5$ and $\text{C}_6\text{H}_5\text{OH}$, as illustrated in Fig. 11.

Figure 11 shows the kinetics of the mixture of isomeric m/z 61 ions with phenetole, $\text{C}_6\text{H}_5\text{OC}_2\text{H}_5$. The main reaction product, $\text{C}_9\text{H}_{11}\text{O}^+$ (m/z 135), is the result of methylene addition presumably at a ring position because the eventual elimination of CH_3SH from possible addition at the oxygen atom requires a double hydrogen migration. The other products can be identified, as in the case of aniline, to protonation of phenetole, $(\text{C}_6\text{H}_5\text{OC}_2\text{H}_5)\text{H}^+$ (m/z 123), and charge exchange to yield $\text{C}_6\text{H}_5\text{OC}_2\text{H}_5^{+\bullet}$ (m/z 122). These two ionic products are formed by $\text{CH}_3\text{C(H)SH}^+$ and triplet $\text{CH}_3\text{CH}_2\text{S}^+$, respectively.

Figure 12 shows a spectrum obtained after 1 s of reaction time between isolated $[\text{C}_2\text{H}_5\text{S}^+]$ ions (obtained by electron ionization from $\text{CH}_3\text{SC}_2\text{H}_5$) and phenol. In this case, $\text{CH}_3\text{S}^+=\text{CH}_2$ reacts with the parent neutral by hydride abstraction (m/z 75) and with phenol by methylene group addition to yield $\text{C}_7\text{H}_7\text{O}^+$ (m/z 107). Further studies with

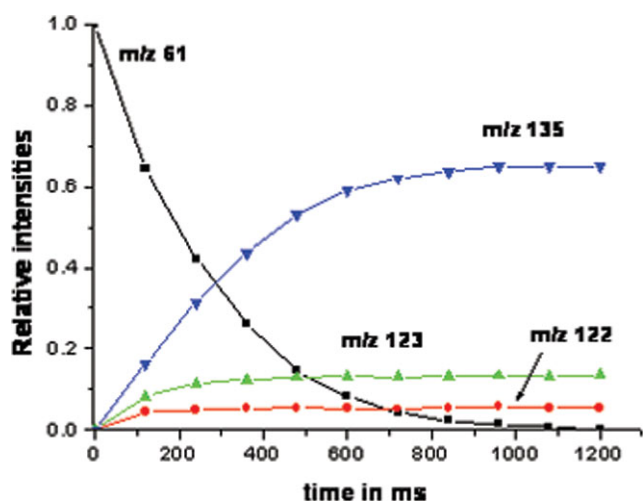


Figure 11. Kinetic plot of the reaction products of isomeric $[C_2H_5S]^+$ ions (m/z 61) with $C_6H_5OC_2H_5$ at a total pressure of 1.5×10^{-7} Torr. Methylation by $CH_3S^+=CH_2$ yields m/z 135, whereas $C_6H_5OC_2H_5^{+\bullet}$ (m/z 122) is attributed to the reaction of triplet $CH_3CH_2S^+$ ions and $(C_6H_5OC_2H_5)H^+$ (m/z 123) to reaction of $CH_3C(H)=SH^+$ or protonated thioacetaldehyde ions.

phenol-2,3,4,5,6- d_5 revealed that reaction with $CH_3S^+=CH_2$ yields both $C_7H_3D_4O^+$ (m/z 111) with loss of CH_3SD , and $C_7H_2D_5O^+$ (m/z 112) with loss of CH_3SH . The ratio $(C_7H_3D_4O^+)/ (C_7H_2D_5O^+)$ has been measured to be 3.8 ± 0.3 .

The results with phenol prompted us to examine the potential energy surface for the methylene addition reaction and to explore two possible reaction pathways.

The structure of the final product ions of reactions (5a) and (5b) is of considerable interest in view of the recent characterization of $C_7H_7O^+$ ions by IR spectroscopy showing that hydroxytropylium ions do not interconvert readily to hydroxybenzyl cations under ICR conditions.³⁶ Table 2 shows that $CH_3S^+=CH_2$ can yield stable complexes by addition to any of the ring positions of phenol as well as

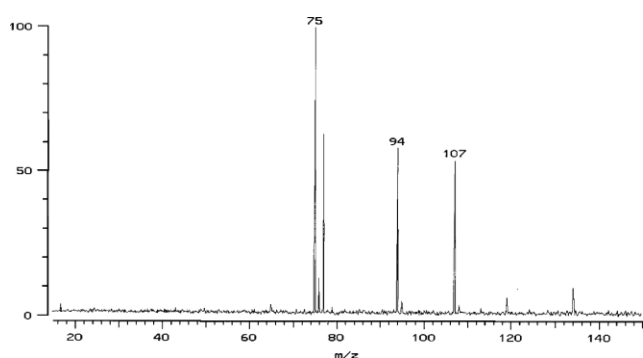
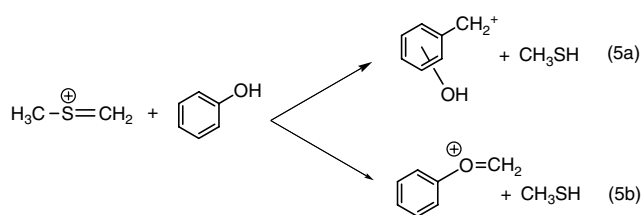


Figure 12. Spectrum obtained after completion of the reaction of isomeric $[C_2H_5S]^+$ ions (m/z 61), obtained by electron ionization of $CH_3SC_2H_5$, with phenol. Methylation of phenol gives rise to $C_7H_7O^+$ (m/z 107), whereas charge transfer by triplet $CH_3CH_2S^+$ yields $C_6H_5OH^{+\bullet}$ (m/z 94). The m/z 75 and m/z 77 ions are respectively the result of reactions with the parent $CH_3SC_2H_5$ neutral: hydride abstraction by $CH_3S^+=CH_2$ and proton transfer from $CH_3C(H)=SH^+$.



by direct addition to the oxygen atom. Nevertheless, there is a pronounced favoring for attachment at the *para* or *ortho* position and the lowest energy barrier pathway is elimination of CH_3SH after attack at the *para* position (Fig. 13).

The energy profile for the reaction initiated by attack at the OH group reveals a positive energy barrier, and within the accuracy of our calculations this pathway would not be easily observed under thermal ICR experiments. Thus, it was necessary to explore again the possibility that formation of both $C_7H_3D_4O^+$ (m/z 111) and $C_7H_2D_5O^+$ (m/z 112) in the case of ring-deuterated phenol could originate from a hydrogen–deuterium scrambling mechanism. Recent work on the gas-phase infrared spectrum of protonated phenol, $C_6H_7O^+$, clearly identified oxonium-type ions (oxygen protonation) and carbenium-type ions (ring protonation at either the *ortho* or *para* position) as distinct species.³⁷ Theoretical calculations at the B3LYP/6-311G(2df,2pd) level revealed that the barrier for proton scrambling from the ring to the oxygen atom is about 27 kcal mol^{-1} .

As in the case of aniline, a ring-walk mechanism for proton mobility from the *para* position to the *meta*, *ortho* and *ipso* (relative to the OH group) positions is calculated to have energy barriers that are accessible at typical ion thermal energies for 298 K for *para*-(thiomethoxymethyl)phenol protonated at the *para* ring carbon (resulting from initial addition of the methylthiomethyl cation at the *para* position of phenol). However, the transition state that would allow

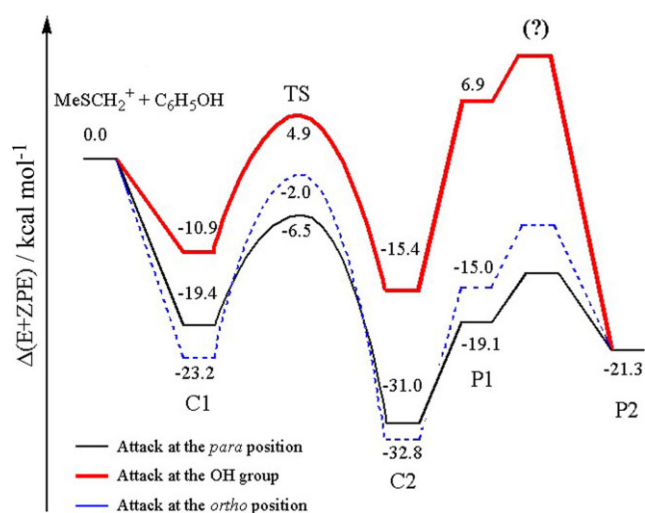


Figure 13. Calculated energy surface and relevant structures calculated at the B3LYP/6-311++G(d,p)/B3LYP/6-311++G(d,p) for the $CH_3S^+=CH_2$ induced methylation at different positions of phenol. The P1 products refer to the formation of benzyl-type cations and methanethiol, whereas P2 refers the tropylium ion structure.

for hydrogen scrambling between the *ipso* carbon and the OH group is calculated to be 31 kcal mol^{-1} above the energy of the reactants. This barrier, even allowing for generous estimates of errors by DFT methods, essentially eliminates the possibility that hydrogen–deuterium scrambling could be important under the conditions of our experiment with phenol- d_5 .

Hydrogen–deuterium scrambling can also occur from the exit ion–molecule complex C2 shown in Fig. 13 resulting from attack of $\text{CH}_3\text{S}^+=\text{CH}_2$ at either the *para* or *ortho* position, namely $[\text{CH}_3\text{SH} \cdots \text{CH}_2=\text{C}_6\text{H}_4=\text{OH}^+]$, as previously discussed for aniline. The loose CH_3SH is found to be able to exchange protons with the OH group through the transition state shown in Fig. 14 that is located 14 kcal mol^{-1} below the energy of the reactants.

Thus, we can conclude from our experimental results with $\text{C}_6\text{D}_5\text{OH}$ and from our theoretical calculations that methylenation takes place exclusively at the *para* and *ortho* ring positions of phenol. Furthermore, the observed elimination of both CH_3SH and CH_3SD in the case of $\text{C}_6\text{D}_5\text{OH}$ can be attributed to an H/D scrambling mechanism that occurs after attack of the $\text{CH}_3\text{S}^+=\text{CH}_2$ electrophile at a ring position and proceeds through the transition state illustrated in Fig. 14.

CONCLUSIONS

Our results indicate that the methylthiomethyl cation can readily promote gas-phase addition of a methylene group to the aromatic ring of alkylbenzenes, aniline, phenol and ethers with elimination of CH_3SH resulting in the formation of an $[\text{M} + \text{CH}]^+$ ion. These reactions bear strong resemblance to the well-known reactions in condensed phases that are used to methylthiomethylate these same substrates.^{38,39} In the case of aniline and phenol, insertion of a methylene group occurs preferentially at the *para* position of the aromatic ring according to theoretical calculations. For aniline, the experimental data and the results of theoretical calculations suggest that addition at the nitrogen atom with subsequent formation of an iminium type ion is very likely.

Our results also indicate that the thiomethoxymethyl cation is less electrophilic than the corresponding methoxymethyl cation. Further evidence of the decrease in reactivity is observed by deactivating toluene with an electron-withdrawing substituent. For example, experiments with *para*-fluorotoluene reveal that $\text{CH}_3\text{O}^+=\text{CH}_2$ is capable of

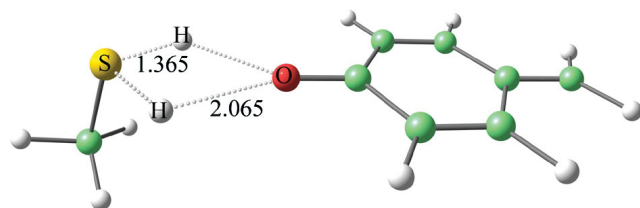


Figure 14. Transition state calculated to be $1.2 \text{ kcal mol}^{-1}$ below the energy of the reactants, $\text{CH}_3\text{S}^+=\text{CH}_2$ and phenol, that could allow for hydrogen–deuterium scrambling in the ion–molecule complex $[\text{CH}_2=\text{C}_6\text{H}_4-\text{OH} \cdots \text{HSCH}_3]^+$. The $[-\text{SH}_2 \cdots]$ moiety has local C_{2v} symmetry.

methylene addition whereas no reaction is observed with $\text{CH}_3\text{S}^+=\text{CH}_2$ within our experimental conditions.

Finally, the actual isomeric composition of the final products of the different reactions studied in this work is an interesting problem that opens the possibility for some challenging studies in the newly developed area of IR spectroscopy of ions.

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