Fundamental Investigations of Mechanistic Pathways of Selected Organic Reactive Intermediates

Carl Whittle
Western Kentucky University

Follow this and additional works at: http://digitalcommons.wku.edu/theses
Part of the Chemistry Commons

Recommended Citation
http://digitalcommons.wku.edu/theses/360
FUNDAMENTAL INVESTIGATIONS OF MECHANISTIC
PATHWAYS OF SELECTED ORGANIC REACTIVE
INTERMEDIATES

A Thesis
Presented to
the Faculty of the Department of Chemistry
Western Kentucky University
Bowling Green, Kentucky

In Partial Fulfillment
of the Requirements for the Degree
Master of Science

by
Carl E. Whittle
December 1997
FUNDAMENTAL INVESTIGATIONS OF MECHANISTIC PATHWAYS OF SELECTED ORGANIC REACTIVE INTERMEDIATES

Date Recommended  5/15/96

Director of Thesis

Date Approved  8/25/97

Director of the Graduate Studies
ACKNOWLEDGEMENTS

To the following people, I wish to express my deepest gratitude and appreciation:

Drs. Les L. Pesterfield and Thomas K. Green for their support and critiquing of the work presented herein.

The entire faculty and staff of the chemistry department for their tolerance of me throughout my undergraduate and graduate career.

My family for their support and guidance in my academic career choices.

Dr. M.L. Gross, University of Nebraska, and Washington University for summer funding and gracious use of the tandem mass spectrometer system so often used throughout this work.

And finally, Dr. Robert W. Holman, without his dedication, inspiration, and faith in me, I would never have made it through.

Carl E. Whittle
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1: ON THE NATURE OF GAS-PHASE ELECTROPHILIC</td>
<td></td>
</tr>
<tr>
<td>AROMATIC SUBSTITUTION OF $\pi$-DEFICIENT AND</td>
<td></td>
</tr>
<tr>
<td>$\pi$-EXCESSIVE AROMATIC COMPOUNDS</td>
<td>1</td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>2</td>
</tr>
<tr>
<td>II. DISCUSSION</td>
<td>5</td>
</tr>
<tr>
<td>A. General Background</td>
<td>5</td>
</tr>
<tr>
<td>1. Nature of Gas-Phase EAS</td>
<td>5</td>
</tr>
<tr>
<td>2. Background of Substituted and Heteroaromatic Species</td>
<td>6</td>
</tr>
<tr>
<td>a. Structural Features of Halobenzenes: $\pi$-Deficient</td>
<td>6</td>
</tr>
<tr>
<td>b. Condensed Phase EAS Reactions of Halobenzenes</td>
<td>7</td>
</tr>
<tr>
<td>c. Structural Features of Heteraromatics: $\pi$-Excessive</td>
<td>7</td>
</tr>
<tr>
<td>d. Condensed Phase EAS Reactions of Heteroaromatics</td>
<td>9</td>
</tr>
<tr>
<td>B. Specific Background</td>
<td>10</td>
</tr>
<tr>
<td>1. Initial Work in Gas-Phase EAS of Benzene</td>
<td>10</td>
</tr>
<tr>
<td>a. Ion Dissociation Characteristics</td>
<td>11</td>
</tr>
<tr>
<td>b. Alkyl Side Chain Isomerizations</td>
<td>11</td>
</tr>
<tr>
<td>III. RESULTS</td>
<td>13</td>
</tr>
<tr>
<td>A. Ion Formation and Characterization</td>
<td>13</td>
</tr>
<tr>
<td>1. Ion Dissociation Characteristics</td>
<td>14</td>
</tr>
<tr>
<td>2. Alkyl Side-Chain Rearrangements</td>
<td>14</td>
</tr>
<tr>
<td>B. The Nature of Substituted Aromatics: $\pi$-Deficient Species</td>
<td>14</td>
</tr>
<tr>
<td>Section</td>
<td>Title</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>I.</td>
<td>INTRODUCTION</td>
</tr>
<tr>
<td>II.</td>
<td>EXPERIMENTAL</td>
</tr>
<tr>
<td>III.</td>
<td>RESULTS AND DISCUSSION</td>
</tr>
<tr>
<td>A.</td>
<td>Structural Characteristics of Acyclic Distonic and Cyclic Radical Cations</td>
</tr>
<tr>
<td>B.</td>
<td>Enthalpies of Cyclization as a Function of Chain Length</td>
</tr>
<tr>
<td>C.</td>
<td>Structural Comparison of the Cyclic Intermediates Generated Upon Cyclization of Distonic Ions With Radical Cations Generated from Neutral Precursors</td>
</tr>
<tr>
<td>D.</td>
<td>Isomerizations of Long-Chain Distonic Radical Cations to Cyclic Radical Cations as a Function of 1° vs. 2° vs. 3° Carbenium/Radical Structure</td>
</tr>
<tr>
<td>E.</td>
<td>Enthalpies of Cyclization in Allylic and Benzylic Systems</td>
</tr>
<tr>
<td>F.</td>
<td>Thermodynamics of Conformationally Restricted Long-Chain Distonic Ions</td>
</tr>
<tr>
<td>IV.</td>
<td>CONCLUSIONS</td>
</tr>
<tr>
<td>V.</td>
<td>BIBLIOGRAPHY</td>
</tr>
<tr>
<td>A.</td>
<td>Part 1</td>
</tr>
<tr>
<td>B.</td>
<td>Part 2</td>
</tr>
<tr>
<td>C.</td>
<td>Part 3</td>
</tr>
</tbody>
</table>
**List of Tables**

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1</td>
<td></td>
</tr>
<tr>
<td>1. Calculational $\Delta \Delta H$ Values for the Various Intermediates on the Potential Energy Surface for the Gas-phase EAS of Halo- and Hetero-aromatic Species...</td>
<td>25</td>
</tr>
<tr>
<td>Part 2</td>
<td></td>
</tr>
<tr>
<td>1. Comparison of the Ethylene Oxide Radical Cation/ethylene Oxide Adduct at Varying Internal Energies...</td>
<td>49</td>
</tr>
<tr>
<td>2. A Comparison of the Predominant Peaks in the Cad Spectra of the Ethylene Oxide Radical Cation/ethylene Oxide Adduct Ion and Selected Model Compounds...</td>
<td>50</td>
</tr>
<tr>
<td>Part 3</td>
<td></td>
</tr>
<tr>
<td>1. Bond Lengths and Bond Angles for the Cyclic Conformations of $+\text{CH}_2(\text{CH}_2)_4\text{CH}_2$, $+\text{CH}_3(\text{CH}_2)_3\text{CH}_2\text{O}$, and $+\text{CH}_2(\text{CH}_2)_3\text{CH}_2\text{NH}$, as Calculated by AM1 Methodology...</td>
<td>70</td>
</tr>
<tr>
<td>2. Enthalpies of Cyclization as a Function of Chain Length. All Enthalpies of Formation are in Kcal/mol were Calculated by Utilizing Am1 Methodology. Absolute Heats of Formation are Reproducible Within +/- 1% Relative...</td>
<td>73</td>
</tr>
<tr>
<td>3. Comparison of Enthalpies of Distonic Ion Precursor, the Cyclic Radical Ion Generated via Rearrangement from the Distonic Ion Precursor, and the Corresponding Radical Ion Generated from a Neutral Precursor. All Calculations by Am1 Methodology. All Enthalpies of Formation are Reported in Kcal/mol, and are Reproducible to Within +/- 1% Relative...</td>
<td>75</td>
</tr>
</tbody>
</table>
4. Comparison of the Enthalpic Driving Force for Cyclization as a Function of 1° vs. 2° vs. 3° Carbenium Ion (Holding the Radical Constant and 1°) for Three Series of Long-Chain Distonic Ions. All Calculations by AM1 Methodology. All Heats of Formation are in Kcal/mol and are Reproducible to Within +/- 1% Relative..........................77
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Heteroaromatic electron densities.</td>
<td>8</td>
</tr>
<tr>
<td>2.</td>
<td>Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of ( R^+ ) versus alkyl chain length for the ions isolated in the reaction of fluoro-, chloro-, and bromo- benzene with the corresponding carbenium ion.</td>
<td>15</td>
</tr>
<tr>
<td>3.</td>
<td>The CAD spectra of deuterated 2-(p-fluorophenyl)-pentane compared to that for 3-(p-fluorophenyl)-pentane.</td>
<td>17</td>
</tr>
<tr>
<td>4.</td>
<td>The CAD spectra of deuterated 2-(p-chlorophenyl)-pentane compared to that for 3-(p-chlorophenyl)-pentane.</td>
<td>18</td>
</tr>
<tr>
<td>5.</td>
<td>The CAD spectra of deuterated 2-(p-bromophenyl)-pentane compared to that for 3-(p-bromophenyl)-pentane.</td>
<td>19</td>
</tr>
<tr>
<td>6.</td>
<td>Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of ( R^+ ) versus alkyl chain length for the ions isolated in the reaction of furan, thiophene, and pyrrole with the corresponding carbenium ion.</td>
<td>20</td>
</tr>
<tr>
<td>7.</td>
<td>Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of ( R^+ ) versus alkyl chain length for the ions isolated in the reaction of all aromatic species studied with the corresponding carbenium ion.</td>
<td>21</td>
</tr>
</tbody>
</table>
8. Histogram representing the metastable dissociations as percent total ion current corresponding to the loss of the alkyl side-chain in the form of R⁺ versus alkyl chain length for the ions isolated in the reaction of all aromatics species with the corresponding carbenium ion.

Part 2

1. CAD mass spectra of C₄H₈O₂ adduct.

2. Geometry and charge distribution of the cyclized long chain distonic a as compared to the radical cation formed by expulsion of one electron from 1,4-dioxane b.

Part 3

1. Differing chain length distonic radical cation.

2. Structures depicting the geometry obtained from geometry optimized calculations of the long-chain distonic ions in question.

3. Structures and energies of allylic and benzylic long-chain distonic ions.
# LIST OF SCHEMES

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Part 1</strong></td>
<td></td>
</tr>
<tr>
<td>1. Textbook electrophilic aromatic substitution mechanism</td>
<td>3</td>
</tr>
<tr>
<td>2. Revised electrophilic aromatic substitution mechanism</td>
<td>3</td>
</tr>
<tr>
<td>3. Alkyl-furan mechanism of interconversion</td>
<td>28</td>
</tr>
<tr>
<td><strong>Part 2</strong></td>
<td></td>
</tr>
<tr>
<td>1. Reaction of ethylene oxide radical cation with neutral ethylene oxide</td>
<td>47</td>
</tr>
<tr>
<td>2. Possible conformations of ethylene oxide radical cation</td>
<td>54</td>
</tr>
<tr>
<td>3. Mechanisms for the reaction of ethylene oxide radical cation with neutral ethylene oxide</td>
<td>55</td>
</tr>
<tr>
<td>4. Origin of excess m/z 44</td>
<td>56</td>
</tr>
<tr>
<td><strong>Part 3</strong></td>
<td></td>
</tr>
<tr>
<td>1. Reaction of ethylene oxide radical cation with neutral ethylene oxide</td>
<td>63</td>
</tr>
<tr>
<td>2. Long-chain distonic cation resonance forms</td>
<td>68</td>
</tr>
</tbody>
</table>
FUNDAMENTAL INVESTIGATIONS OF MECHANISTIC PATHWAYS OF SELECTED ORGANIC REACTIVE INTERMEDIATES

Carl E. Whittle

December 1997

Directed By: Robert W. Holman, Thomas K. Green, and Lester L. Pesterfield

Department of Chemistry

Western Kentucky University

Part 1 of this thesis deals with the role that π-electron density plays in the formation of π-complexes in electrophilic aromatic substitution. Using commercial and synthetic compounds of varying π-electron density, the fact that π-complexes actually exist in these species was determined by a mass spectral investigation that was designed to monitor alkyl side-chain isomerizations. Also, the amount of π-complex was determined for each compound by measuring the amount of alkyl carbenium ion loss in each compound's mass spectrum. Found within the systems was an internal trend showing that the greater the amount of π-electron density in the ring, the less π-complex formed. This trend was further studied utilizing a Spartan 3.0 computational system, and all data found was internally consistent with the experimental data. It was found that the compounds with the greatest π-electron density used the excess π-electron density for greater covalency in the complex.

In Part 2, the gas-phase reaction between the ethylene oxide radical cation and neutral ethylene oxide, when performed in the high-pressure source of a tandem mass spectrometer,
forms a C₄H₈O₂ radical cation adduct. The collisionally activated dissociation (CAD) mass spectrum of the C₄H₈O₂ adduct is nearly identical to that of the 1,4-dioxane radical cation. Computational investigations utilizing semi-empirical AM1, MNDO, and PM3 methodologies were invoked to determine the mechanistic pathways involved in the reaction. The most likely mechanism is a step-wise process involving a long-chain distonic radical cation intermediate that subsequently forms a non-distonic cyclic radical ion. A calculated thermodynamic driving force of ca. 10 Kcal/mol exists for the cyclization of the long-chain distonic radical cation.

For Part 3, an array of acyclic long-chain distonic radical cations was generated and analyzed by semi-empirical AM1 computational methods. In general, an enthalpic driving force for the isomerization of the distonic ions to cyclic non-distonic ions was observed. The enthalpies of the isomerizations were evaluated as a function of chain length, identity of the atom (C, O, N) bearing the radical site, and substitution of the radical and carbenium ion sites. The structures, electron distribution, free spin distribution, and thermodynamic stabilities of the cyclic ions generated upon isomerization of the distonic ions were nearly identical to those formed by direct removal of an electron from the corresponding cyclic neutral precursor.
Part 1:

ON THE NATURE OF THE GAS-PHASE ELECTROPHILIC AROMATIC SUBSTITUTION OF $\pi$-DEFICIENT AND $\pi$-EXCESSIVE AROMATIC COMPOUNDS
I. INTRODUCTION

Arenium ions or σ-complexes are known to be produced as intermediates in the electrophilic aromatic alkylation (EAS) of benzenoid species.\textsuperscript{1,2} The long-accepted mechanism, known generally as the arenium ion mechanism, involves electrophilic attack to give an arenium ion (σ-complex), 1 (Scheme 1), followed by the departure of an appropriate leaving group in a final step.

As early as 1946, Dewar\textsuperscript{3} proposed that π-complexes also play an important role in EAS. In later research, the pioneering work of Olah and coworkers\textsuperscript{4-11} provided convincing arguments that the arenium ion mechanism indeed does involve π-complex intermediacy. Recently, we have presented evidence indicating that σ- and π-complexes coexist as interconvertible species when arenes are protonated in the gas phase.\textsuperscript{12} This finding, coupled with insight gained from the earlier work of Olah, has led to a modified arenium ion mechanism that invokes an early π-complex that can then collapse to a σ-complex (Scheme 2).

While evidence for π-complex intermediacy is convincing, debate still exists as to whether the formation of the π-complex is rate determining. Many research findings conclude that π-complex formation is not rate determining and that the formation of the σ-complex is the rate determining step,\textsuperscript{13-18} while others conclude that the formation of the π-complex is
Scheme 1  Textbook electrophilic aromatic substitution mechanism.

1) \[
\begin{align*}
&X \\
&\xrightarrow{Y^+ \text{ slow}} \\
&\xrightarrow{\text{slow}} \\
&X
\end{align*}
\]

2) \[
\begin{align*}
&X \\
&\xrightarrow{\text{fast}} \\
&Y
\end{align*}
\]

Scheme 2  Revised electrophilic aromatic substitution mechanism.
rate determining.\textsuperscript{4,6-10} One supposition emerging from this debate is that $\pi$-complex intermediates do exist on the potential energy surface of benzenoid electrophilic aromatic substitution and are apparently energetically accessible in some specific reactions and not in others (depending on factors such as the strength of the electrophile, extent of free-cation character in the attacking electrophile, nature of catalyst interaction with electrophile, etc.).

The question of the nature of the reactive intermediates involved in the gas-phase EAS of benzene has received much literature attention. However, less attention has been paid to the EAS of substituted aromatic and heteroaromatic compounds. Whether $\pi$-complexes form between electrophiles with either substituted or heteroaromatic species is uncertain. Further, if $\pi$-complexes are involved, the nature of the interplay between the $\sigma$- and $\pi$-complexes would be intriguing, especially in light of what is known about the benzenoid systems. The specific motivation for this work described herein is to discuss the role that aromatic $\pi$-electron density plays on the interplay between $\pi$- and $\sigma$-complex formation in gas-phase EAS.
II. DISCUSSION

A. GENERAL BACKGROUND

1. Nature of Gas-Phase EAS

The limiting factor in the study of the intermediates formed in electrophilic aromatic substitutions in the condensed phase is the inability to isolate readily such transient species. However, the investigation of the intermediate(s) generated when an aromatic reacts with an electrophile in the gas phase is not subject to such limitations. The ionic intermediate(s) can be readily formed within the source of a tandem mass spectrometer and directly analyzed within the same instrument. Further, catalysts are not necessary for the promotion of the reaction, hence simplifying the chemistry.

The goal of the present work is to establish the structure(s) of the ionic intermediates formed when substituted aromatic and heteroaromatic species react with alkyl carbenium ions in the gas phase. The substituted aromatics chosen include fluorobenzene, chlorobenzene, and bromobenzene. The heteroaromatic species chosen include pyrrole, furan, thiophene, and pyridine. Specific interest lies in (a) assessing the role, if any, \(\pi\)-complexes play in this chemistry, (b) comparing and contrasting the chemistry of the aromatics in light of their differing degrees of aromaticity, differing extent of \(\pi\)-excessiveness, and relative basicities, and (c) comparing and contrasting these results with those obtained for benzene.

It is likely that the properties of the ionic intermediates in the gas phase will not differ
markedly from those in the condensed phase because the physical characteristics, relative reactivities, and relative stabilities of aliphatic carbenium ions in the condensed phase are subject to very little dependence on media change.\textsuperscript{19} In addition, a comparison of recent mass spectrometric and calorimetric measurements shows no essential change in enthalpy trends for isomeric gas-phase secondary and tertiary carbenium ions over those in the condensed phase. And finally, the pioneering work of Cacace,\textsuperscript{20-28} Speranza,\textsuperscript{41} and coworkers has shown that gas-phase arenium ion chemistry has common features with condensed-phase investigations, thus forging an important link in this work.

2. Background of Substituted and Heteroaromatic Species

a. Structural Features of Halobenzenes: $\pi$-Deficient Aromatics

Halogens are unique in that they are deactivating yet direct to the ortho- and para-positions. They are deactivating because they are strongly electron-withdrawing from an inductive standpoint. However, halogens deactivate the ortho- and para- positions less than the meta position, primarily attributable to an electron donating resonance effect.

The halo substituents act as electron donors by the resonance mechanism, but the dipole associated with these substituents operate in the opposite direction. The $\sigma_i$ ($\sigma$ value for induction based upon the dual-substituent-parameter equation) for F, Cl, and Br are, respectively, 0.50, 0.46, and 0.44. Therefore, fluorine is the most electron withdrawing by induction and bromine the least. The $\sigma_R$ ($\sigma$ value for resonance donation) for F, Cl, and Br is -0.31, -0.18, and -0.16, respectively. Thus, the most electron donating by resonance is fluorine and the least electron donating is bromine. These $\sigma$ values are calculated from equilibrium reaction in solution. Our reactions are conducted in the absence of solvent, and with respect to $\pi$-complex formation, steric considerations must also be considered. The $\sigma$
values from the literature do not incorporate any steric considerations. Hence, strict correlations between extent of $\pi$-complex formation in our gas-phase reactions with $\sigma_r$ and $\sigma$ values are unlikely. Nevertheless, each of these halo species is less $\pi$-deficient than benzene.

b. Condensed Phase EAS Reactions of Halobenzenes

The major condensed-phase electrophilic aromatic alkylations for halo-substituted benzenes generally come in three mechanistic classes: (1) reactions with alkenes/Lewis acid catalysts, (2) reactions with alkyl halides/Lewis acid catalysts, typically referred to as Friedel-Crafts alkylations, and (3) reactions with alcohols/Lewis acid catalysts. In all three mechanistic classes of electrophilic reaction, the species thought to react with the aromatic substrate is some form of carbenium ion: either a free carbenium ion, a carbenium ion/catalyst ion pair, or a polarized carbenium ion/catalyst complex. Because of the vast array of different reaction conditions and catalysts involved, it is not possible to generalize the extent to which all condensed-phase electrophilic alkylations follow an identical mechanism. The below treatment is a summary of the known electrophilic alkylation chemistry of the various heteroaromatics central to the current investigation.

c. Structural Features of Heteroaromatics: $\pi$-Excessive Aromatics

The $\pi$-excessive heteroaromatic species pyrrole, furan and thiophene all possess common features with respect to electron distribution. In each species the carbons possess high $\pi$-electron density while the heteroatom possesses, relatively speaking, low electron density.$^{30}$ (Figure 1).

The implications with respect to the current study are twofold. First, all three species are more reactive towards EAS than benzene. Electron density calculations indicate that the
Figure 1. Heteroaromatic electron densities.
carbons in pyrrole, the most reactive of these heteroaromatic species, are more electron rich than are those in phenol or even aniline.\textsuperscript{30} Furan, next most reactive, also possesses carbons more electron rich than the most activated substituted benzene. Thiophene, while being the least reactive of these heteroaromatics towards EAS, is still more reactive than benzene. Second, since the heteroatom possesses low electron density, it is unlikely that these species will either alkylate or protonate at the heteroatom. No evidence of any N-alkylation of pyrrole has been reported. The gas-phase proton affinity of pyrrole is 207.6 Kcal/mol,\textsuperscript{31} which means it can be readily protonated; however it is known not to N-protonate but instead undergoes protonation at carbon. Neither furan or thiophene have been shown to alkylate at the heteroatom, while both have lower proton affinities (192.2 Kcal/mol and 196.5 Kcal/mol, respectively) protonating on carbons rather than the heteroatom.

d. Condensed Phase EAS Reactions of Heteroaromatics

Pyrrole. Pyrrole readily undergoes electrophilic sulfonation and halogenation, though is not readily amenable to Friedel-Crafts alkylations. This difference is due to the plethora of side reactions that the highly reactive pyrrole substrate undergoes in the condensed-phase media needed for electrophilic alkylation (reactions with catalysts, catalyst-promoted reactions with itself, etc.). Several electrophilic alkylations, however, have been reported. The introduction of a t-butyl group into the pyrrole ring has been accomplished using t-butyl acetate in the presence of sulfuric acid\textsuperscript{44} and also with t-butyl chloride in the presence of a Lewis acid.\textsuperscript{45}

Furan. Furan typically reacts rapidly with the Lewis acid catalysts utilized in electrophilic alkylation chemistry. Thus very few electrophilic alkylations have been reported. Furan has been successfully alkylated with 2-methyl-2-butene/BF\textsubscript{3} in diethyl ether
at a yield of 17% of t-pentyl furan, and with isobutylene/\( \text{BF}_3 \) in diethyl ether at a yield of 10% of t-butylfuran.\(^{43} \) A true Friedel-Crafts alkyl halide-type alkylation of furan has not been reported. Finally, because of polymerization problems, it is not possible to alkylate furan under alcohol alkylation conditions.

**Thiophene.** The electrophilic alkylation of thiophene tends to be a low yield reaction, and consequently is rarely performed. The low yields are typically attributed to thiophene polymerizations and/or reaction with the Lewis acid catalysts necessary for the promotion of the reaction. Nevertheless, alkylations have been reported. Thiophene has been alkylated utilizing propene/\( \text{H}_2\text{SO}_4 \) at a yield of 75%.\(^{32} \) Alkylation utilizing alkenes and catalysts such as \( \text{BF}_3 \), silica-alumina-zinc chloride, \( \text{SnCl}_4/\text{CH}_3\text{NO}_2 \), \( \text{TiCl}_4 \) and \( \text{AlCl}_3 \) have also been successful.\(^{33-40} \) Thiophene is very resistant to alkylation when an alkyl halide/\( \text{AlCl}_3 \) (Friedel-Crafts conditions) is used.\(^{41} \) Typically, an alpha-substituent needs to be present on the thiophene before it can be alkylated under Friedel-Crafts conditions, and then only when large excesses of \( \text{AlCl}_3 \) are used. Only one reference of thiophene being alkylated under alcohol alkylation conditions has been reported\(^{42} \) because of thiophenes propensity to polymerize under these conditions.

**B. SPECIFIC BACKGROUND**

1. **Initial Work in Gas-Phase EAS of Benzene**

It was previously determined that when benzene undergoes electrophilic alkylation in the gas-phase, both \( \pi \)-complexes and arenium ions (\( \sigma \)-complexes) are generated.\(^{12} \) These ions interconvert with one another on a common potential energy surface. The experimental evidence interpreted in order to arrive at these conclusions were generated via mass spectrometric investigation. The gas-phase alkylations were conducted and the product ions
analyzed in a tandem mass spectrometer. Specifically, the evidence consistent with the participation of a π-complex can be segmented into two categories: (A) ion dissociation characteristics, and (B) alkyl side chain isomerizations.

**a. Ion Dissociation Characteristics**

The dissociation properties of the ion(s) formed when benzene is reacted with short chain (CH3+, C2H5+) alkyl carbenium ions, both collisionally activated and metastable, were found to possess the characteristics of a σ-complex (i.e., fragmentation of the portion of the alkyl group). When benzene is reacted with a larger alkyl carbenium ion (C3H7+ or larger), the resulting ion(s) possesses properties consistent with a π-complex. The dissociation process attributed to the π-complex is the loss of the entire alkyl chain as a carbenium ion. As the size of the alkyl carbenium ion is increased, the extent of R+ loss from the adduct ion increases while the amount of side-chain fragmentation decreases.

This dissociation behavior is consistent with participation of both σ- and a π-complexes. The ability of the alkyl moiety of the alkylated benzene to accommodate carbenium ion character increases with increasing alkyl chain length in accord with polarizability arguments. It is for this reason that the probability of forming a π-complex increases with increasing stability of the incipient carbenium ion.

**b. Alkyl Side Chain Isomerizations**

In order to evaluate the nature of the alkyl portion of these ions, it is necessary that the structural integrity of the alkyl moiety be maintained in the formation of the ion, which is not possible if the ion is formed via direct gas-phase EAS because the free carbenium ion can rearrange prior to the formation of the complex. However, an alternative means exists for the formation of these gas-phase ions: the protonation of the alkyl aromatics. When the
ion is generated in this manner, the initial structure of the alkyl chain is known; therefore, any rearrangement of the alkyl chain must take place within the protonated ion itself. When isomeric alkyl benzenes are protonated in the gas-phase and the resulting ion’s structure is probed via CAD mass spectrometry, the alkyl side chains were found to rearrange. Protonated sec-pentyl and 3-pentyl benzene gave identical CAD spectra. A deuterium labeled investigation of protonated sec-butyl benzene made clear that the near thermo-neutral side chain isomerizations were taking place. The more exothermic isomerizations (e.g. 1° alkyl to 2° alkyl to 3° alkyl) were only inferred because the energy released causes the \( \pi \)-complex to decompose to benzene and a carbenium ion. These isomerizations were concluded to be possible only if a \( \pi \)-complex of sufficient lifetime is involved in the chemistry.
III. RESULTS

The nature of the ions formed in the gas-phase alkylation of substituted benzenoid and the heteroaromatic species pyrrole, furan, thiophene, and pyridine will be assessed in this investigation via similar methodology to that employed in the previously addressed benzenoid system. Specific emphasis will lie in determining the ion(s) structure and comparing it to benzenoid analogs.

A. ION FORMATION AND CHARACTERIZATION

Mass spectrometric techniques were chosen to investigate the properties of gas-phase heteroarenium ions. The gas-phase heteroarenium ions were produced via electrophilic aromatic substitution (EAS). The reactions of the appropriate alkyl carbenium ions with neutral heteroaromatic species were performed within the high pressure chemical ionization (CI) source of a tandem mass spectrometer. Tandem mass spectrometry (MS/MS) was then employed to determine the structures of the ionic species. These mass spectrometric techniques allow for the facile formation, isolation, and detection of such transient species.

1. Ion Dissociation Characteristics

From earlier work centering upon the dissociations of the ions generated from the reaction of benzene and alkyl carbenium ions, it was established that the ions being analyzed were an interconverting mixture of σ-complexes and π-complexes (Scheme 2). The extent of π-complex within the ion mixture was quantitatively linked to the extent of R+ formation observed in the CAD spectra. The governing assumption is that the diagnostic dissociation
for a \( \pi \)-complex is the loss of the entire alkyl moiety as a carbenium ion (R+). The same assumption is made in the evaluation of the CAD spectra of the ions generated from the reaction of the aromatic species with alkyl carbenium ions in this current investigation.

2. Alkyl Side-Chain Rearrangements

In order to probe for alkyl side-chain rearrangements in the haloaromatic/carbenium ion complexes, it is necessary to control the initial structure of the alkyl moiety. Because the reacting carbenium ion in gas-phase EAS is free to rearrange prior to reacting with the aromatic/heteroaromatic species, it is not possible to evaluate rearrangements within the haloaromatic/carbenium ion complex(es). However, the nature of the alkyl moiety within these complexes can be probed when the complex is generated via protonation of an alkyl substituted haloaromatic of known structure.

B. THE NATURE OF SUBSTITUTED AROMATICS: \( \pi \)-DEFICIENT SPECIES

A histogram comparing the extent of R+ formation in the CAD mass spectra of the ions generated in the reaction of haloaromatic species with alkyl carbenium ions as a function of alkyl chain length is presented in Figure 2.

As evident from the histogram, the amount of R+ formation, and thus the concentration of \( \pi \)-complex, is greatest when the halogen is fluorine. The extent of R+ formation is the least when the halogen is bromine, inferring that the ion mixture possesses a lesser percent of \( \pi \)-complex than the ion mixtures for the other species. Thus, R+ formation in the CAD spectra of halobenzene/carbenium ion product mixtures steadily decrease in the order of fluorine > chlorine > bromine.

When benzene is systematically reacted with increasingly larger carbenium ions, the resulting product ion mixtures dissociate to R+ to a greater extent. The ability of the alkyl
Figure 2.

Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of R+ versus alkyl chain length for the ions isolated in the reaction of fluoro-, chloro, and bromobenzene with the corresponding carbenium ions.

**CAD: HALOAROMATIC SPECIES**

**CARBENIUM ION LOSS VS CHAINLENGTH**

![Bar chart showing percent abundance of carbonium ion loss for propyl, butyl, and pentyl chains in fluoro-, chloro-, and bromo-species. Each bar is divided into three sections representing fluoro, chloro, and bromo, respectively.]
moiety to accommodate carbenium ion character increases with increasing alkyl chain length in accord with polarizability arguments. For this reason, the probability of forming a π-complex becomes much greater as the stability of the incipient carbenium ion increases. From Figure 2, it is clear that the same trends are exhibited for each of the haloaromatic/carbonium ion mixtures. In each case, the percent of π-complex formation (magnitude of R+ formation) increases with increasing size of the alkyl carbenium ion. This result correlates well with that observed in the gas-phase EAS of benzene and is consistent with π-complex formation in haloaromatic EAS.

A comparison of the CAD spectra of protonated 2-(p-fluorophenyl)-pentane versus that for 3-(p-fluorophenyl)-pentane (Figure 3) illustrates that the two ions are identical—suggesting there must have been some isomerization taking place in the alkyl side chain. In order for such an isomerization to occur, a significant extent of carbenium ion character must exist on the side chain. A π-complex meets this criteria. Evidence for similar isomerizations between 2-(p-chlorophenyl)-pentane and 3-(p-chlorophenyl)-pentane and between 2-(p-bromophenyl)-pentane and 3-(p-bromophenyl)-pentane is presented in Figures 4 and 5.

C. THE NATURE OF HETERAROMATIC: π-EXCESSIVE SPECIES

A histogram comparing the extent of R+ formation in the CAD mass spectra of the ions generated in the reaction of heteroaromatic species with alkyl carbenium ions as a function of alkyl chain length is presented in Figure 6.

Alkyl carbenium ion (R+) formation in the CAD spectra of the heteroarene/carbonium ion product mixtures steadily decrease in the order of furan > thiophene > pyrrole (Figure 7). These results indicate that the ion mixture generated in the
Figure 3.
The CAD spectra of deuterated 2-(p-fluorophenyl)-pentane compared to that for 3-(p-fluorophenyl)-pentane.
The CAD spectra of deuterated 2-(p-chlorophenyl)-pentane compared to that for 3-(p-chlorophenyl)-pentane.
Figure 5.

The CAD spectra of deuterated 2-(p-bromophenyl)-pentane compared to that for 3-(p-bromophenyl)-pentane.
Figure 6.

Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of R+ versus alkyl chain length for the ions isolated in the reaction of furan, thiophene, and pyrrole with the corresponding carbenium ion.
Histogram representing the CAD as percent total ion current corresponding to the loss of the alkyl side-chain in the form of $R^+$ versus alkyl chain length for the ions isolated in the reaction of all aromatic species studied with the corresponding carbenium ion.
EAS of the most π-excessive species, pyrrole, possesses a lesser percent of π-complex than the ion mixtures for the other less π-excessive species. From the histogram, it is clear that the trends are consistent with the notion that R+ formation, and hence extent of π-complex formation, increases with increasing ability of the alkyl moiety to accommodate carbenium ion character. This result correlates well with that observed in the gas-phase EAS of benzenoid species and is consistent with π-complex formation in haloaromatic EAS.

D. OVERALL EFFECT OF π-ELECTRON DENSITY ON π-COMPLEX FORMATION

When the extent of R+ formation in the CAD spectra of all the aromatic/carbenium ion complexes are plotted as a function of alkyl chain length (Figure 7), several trends are evident. The same trends are observed when these ions are allowed to dissociate in the absence of collision gas, i.e., metastable ion dissociation (Figure 8). First, for each aromatic the extent of π-complex formation increases with the alkyl moiety’s ability to accommodate carbenium ion character. Second, the extent of π-complex formation is greatest for those aromatics that are π-deficient and least for those that are π-excessive. Since π-deficient aromatics generate a greater amount of π-complex, ions with significant cation character on the alkyl moiety, then π-excessive aromatics must generate ions with a greater amount of cation character in the ring (i.e., σ-complex and ArH+). Therefore, excess π-electron density in the aromatic is apparently used in increased covalency between the ring and the alkyl moiety. Thus, the ion mixtures generated in the reaction of π-excessive aromatics with carbenium ions are enriched in adducts that are σ-complex-like, which possess greater cation character within the ring. The π-deficient aromatic/carbenium ion mixtures are more enriched in π-complexes that possess significant carbenium ion character on the alkyl chain.
Figure 2.

Histogram representing the metastable dissociations as percent total ion current corresponding to the loss of the alkyl side-chain in the form of $R^+$ versus alkyl chain length for the ions isolated in the reaction of all aromatic species with the corresponding carbenium ion.

METAStABLE: ALL AROMATIC SPECIE CARBENIUM ION LOSS VS CHAINLENG
E. COMPUTATIONAL INSIGHT INTO AROMATIC/CARBENIUM ION COMPLEXES

Semi-empirical computations were utilized to gain insight into the ions in question. Specifically, enthalpies of formation were calculated for isolated starting materials (aromatic and free carbenium ion), σ-complexes, and π-complexes. In addition, computations were performed to gain insight into a significant fragmentation outlet observed in the CAD spectra of these ions (ArH+ plus neutral alkene). From this data, enthalpy differences (ΔΔH) between starting materials and σ-complex, starting materials and π-complex, and starting materials and ArH+/alkene can be determined (Table 1).

Enthalpic calculations indicate that the ionic mixture formed upon gas-phase EAS of heteroaromatics should be mostly composed of ions in which the charge resides in the ring—that is, the enthalpic driving force for σ-complex formation and ArH+ formation is great. Hence, π-complex formation is comparatively less competitive. In the substituted aromatics, the enthalpic driving force for σ complex formation is much less than is the case in the heteroaromatics. Further, ArH+ formation is dramatically less competitive than in heteroaromatics. In fact, in the haloaromatics, the enthalpic driving force for π-complex formation exceeds that for ArH+ formation.

These computational results indicate that the π-deficient haloaromatics should, upon gas-phase EAS, produce an ion mixture enriched in π-complex with respect to the ion mixture generated upon gas-phase EAS of the π-excessive heteroaromatics. The more π-excessive the system, the less π-complex is formed. Thus, the excess π electron density is utilized more in the formation of covalent bonding, i.e., the formation of σ-complex, than it is for π-complexation. When a π-excessive aromatic reacts with a carbenium ion, it donates more of its electron density to the carbenium ion than would a π-deficient aromatic.
Table 1.

Calculational $\Delta \Delta H$ Values for the Various Intermediates on the Potential Energy Surface for the Gas-phase EAS of Halo- and Hetero-aromatic Species.

<table>
<thead>
<tr>
<th>aromatic</th>
<th>alkyl</th>
<th>$\Delta H_{SM \rightarrow \sigma}$</th>
<th>$\Delta H_{SM \rightarrow \pi}$</th>
<th>$\Delta H_{SM \rightarrow \text{ArH}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluorobenzene</td>
<td>propyl</td>
<td>22.8</td>
<td>2.9</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>20.8</td>
<td>2.8</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>18.5</td>
<td>3.2</td>
<td>2.0</td>
</tr>
<tr>
<td>chlorobenzene</td>
<td>propyl</td>
<td>22.0</td>
<td>4.6</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>20.0</td>
<td>3.9</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>17.6</td>
<td>3.4</td>
<td>1.4</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>propyl</td>
<td>19.2</td>
<td>5.2</td>
<td>-2.4</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>17.0</td>
<td>3.8</td>
<td>-0.4</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>14.9</td>
<td>3.4</td>
<td>-1.4</td>
</tr>
<tr>
<td>furan</td>
<td>propyl</td>
<td>40.0</td>
<td>6.8</td>
<td>14.1</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>37.9</td>
<td>5.3</td>
<td>15.1</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>30.3</td>
<td>4.0</td>
<td>15.0</td>
</tr>
<tr>
<td>thiophene</td>
<td>propyl</td>
<td>37.2</td>
<td>5.7</td>
<td>15.0</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>35.5</td>
<td>4.3</td>
<td>15.3</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>32.7</td>
<td>4.9</td>
<td>14.1</td>
</tr>
<tr>
<td>pyrrole</td>
<td>propyl</td>
<td>50.2</td>
<td>14.1</td>
<td>25.7</td>
</tr>
<tr>
<td></td>
<td>butyl</td>
<td>48.4</td>
<td>11.1</td>
<td>27.4</td>
</tr>
<tr>
<td></td>
<td>pentyl</td>
<td>47.5</td>
<td>8.8</td>
<td>26.2</td>
</tr>
</tbody>
</table>

*All reported values are in kcal/mol.
Hence, there exists a more covalent interaction between the \( \pi \)-excessive aromatic and the carbenium ion. The resulting ion mixture then should be enriched in ions that possess delocalized positive charge within the ring, i.e., \( \sigma \)-complex and \( \text{ArH}^+ \) formation, consistent with both the CAD spectra of these species and with the computational enthalpies in Table 1.

In contrast, \( \pi \)-deficient aromatics possess less electron density to donate towards \( \sigma \)-bond formation, and hence, the resulting ion mixture should be enriched with ions possessing significant positive ion character on the alkyl side chain. More \( \pi \)-complex formation should be observed in the gas-phase EAS of these species, which is consistent with both the mass spectral and computational results.

The extent of \( \pi \)-electron density in the aromatic may manifest itself not only in the amount of \( \pi \)-complex formed but also in the nature of the \( \pi \)-complex itself. In the construction of the \( \pi \)-complexes whose energies are reported in Table 1, an optimal distance between the carbenium ion and the aromatic was determined by systematically varying the distance between the ring and the carbenium ion and evaluating the corresponding energies in search of a minimum value. Upon finding the optimal distance, it was noted that the \( \pi \)-complex formed in the heteroaromatics was a full angstrom closer on average than those observed in the haloaromatics. Further, the calculated charge on the central carbon of a propyl group in a \( \pi \)-complex with fluorobenzene, chlorobenzene, and bromobenzene is +0.61, +0.54, and +0.57, respectively, whereas the same carbon in \( \pi \)-complexes with furan, thiophene and pyrrole is +0.52, +0.48, and +0.50, respectively. Thus, computations suggest that the alkyl group in the \( \pi \)-complexes formed between carbenium ions and \( \pi \)-excessive
aromatics is closer to the aromatic and possesses less carbenium ion character than the alkyl group in the corresponding complexes with \( \pi \)-deficient aromatics.

**F. ALKYL SIDE-CHAIN REARRANGEMENTS**

When the CAD spectra of protonated 2-pentyl furan is compared to that for 3-pentyl furan, the spectra are similar, but clearly not identical (Figure 9), which is in contrast with the CAD spectra of isomeric pentyl-benzenes and pentyl-halobenzenes. The similarities between the spectra suggests that partial interconversion between the structures takes place. This conclusion is supported by the evaluation of the ratio of \( \text{C}_2\text{H}_5/\text{C}_3\text{H}_7 \) losses in the protonated species versus that for the corresponding molecular ions. As expected, the ratio of \( \text{C}_3\text{H}_7/\text{C}_3\text{H}_7 \) loss from the molecular ion of 2-pentyl furan is ca. 1:7, and that for the molecular ion of 3-pentyl furan is ca. 9:1. If the \( \pi \)-complexes generated upon protonation were not to undergo any isomerization, then the ratio of \( \text{C}_2\text{H}_5/\text{C}_3\text{H}_7 \) loss in each of the isomeric complexes would not change appreciably. However, the ratio for protonated 2-pentyl furan is ca. 1:3, and that for protonated 3-pentyl furan is ca. 1:1. Thus, some of the \( \pi \)-complex generated from protonated 2-pentyl furan isomerizes to 3-pentyl furan, but this isomerization is not complete and the predominant outlet is to fall back to a 2-pentyl furan \( \sigma \)-complex (Scheme 3).

Further explanation for the lack of total interconversion can be taken from the arguments proposed in previous sections. It has been shown that \( \pi \)-excessive aromatics do not yield very much \( \pi \)-complex. Since a \( \pi \)-complex is required to interconvert the isomers, and there is little \( \pi \)-complex at all, chances are poor that isomerization will take place. Also, from the data presented, the \( \pi \)-complex which forms is different in nature to the \( \pi \)-
Scheme 3. Alkyl-furan mechanism of interconversion.
complexes formed in benzene and halobenzenes—that is, the \( \pi \)-complex that does forms is \( \pi \)-complex-like enough to lose \( R^+ \), but has less charge on the alkyl chain and hence isomerization is not facile.

**G. ALTERNATIVE POSSIBILITIES**

Whereas the general properties of aromatic/carbenium ion complexes dissociations are evidence for the existence of \( \pi \)-complex intermediates, these results do not preclude the existence of other loosely bound species such as H-bonded complexes.

The predominant dissociations expected of H-bonded complexes are those that are observed for the aromatic/carbenium ion complexes—that is, both protonated aromatic and a carbenium ion (a protonated alkene) should form. The preferred ion species involves the constituent (aromatic or alkene) having the greater proton affinity. The proton affinities of ethylene and propylene are less than that of the aromatics studied, whereas the \( \text{C}_4\text{H}_8 \) and \( \text{C}_5\text{H}_{10} \) olefins possess higher proton affinities. As a result, the ethyl and propylaromatic ion mixtures should predominantly dissociate to \( \text{ArH}^+ \) and neutral alkene, whereas the larger ion mixtures would predominantly give \( R^+ \) and neutral aromatic, and this is indeed observed.

Previous results\(^{12}\) have shown that the CAD spectra of protonated n-alkyl aromatics are not identical to those for protonated secondary alkyl aromatics. The rearrangement none the less does take place, but, owing to the process being exothermic and the chemistry being performed in the dilute gas phase, the energy is utilized to expell \( R^+ \) as a carbenium ion. Thus, the rearranged \( \pi \)-complex never relaxes to the rearranged sigma complex, and the CAD spectra are different. If a H-bonded complex is invoked, there is no carbenium ion character on the side chain; therefore interconversion cannot occur through a carbenium ion rearrangement. If isomerization were to occur without a carbenium ion going from \( 1^\circ \) ---
2°, then there is little exothermicity in the process. Therefore, it would be expected that the H-bonded complex would collapse to both $\sigma_{\text{ison}}$-complex and the original $\sigma$-complex. If this were the case, then $n$-alkyl aromatics would give the same spectra as $2^o$-alkyl aromatics, which is clearly not observed.
IV. CONCLUSIONS

The extent of π-electron density within the aromatic plays a significant role on the amount and nature of π-complex formed in gas-phase EAS. The ion mixture formed in the gas-phase EAS of π-deficient aromatics are enriched in π-complex with respect to π-excessive aromatics. The excess π-electron density within π-excessive aromatics is utilized in the development of greater covalency between the aromatic and the alkyl group; thus these species are enriched in sigma complex and ArH+ formation. The relative order for π-complex formation, as measured by extent of R+ formation in the CAD mass spectra of the adducts, is fluorobenzene > chlorobenzene > bromobenzene > furan > thiophene > pyrrole.
V. EXPERIMENTAL

A. METHODS

All CAD experiments were performed on a Kratos MS50 triple analyzer mass spectrometer\textsuperscript{16} which consists of a Nier-Johnson geometry high resolution mass spectrometer followed by an electrostatic analyzer (ESA). The ions formed in the source were mass selected at a mass resolution of 2500-3500 (10% valley definition) by using MS-1 (ESA-1 and the magnetic sector). The ion-molecule adduct was then activated by collisions with helium gas in the second collision cell. The second ESA is scanned to give the CAD spectrum of the resulting fragment loss. In a typical CAD experiment 20-40 scans are acquired and signal averaged using software written in-house. The precision for all peak heights reported was approximately 5% relative as determined by replicate experiments. The CI source was operated at 280 eV with total emission current of 500 $\mu$A. The ion accelerating voltage was 8000 V.

The gas-phase EAS experiments were carried out by simultaneously admitting the aromatic species and an alkyl bromide via control leak valves into to CI source. The alkyl bromide serves as the precursor to alkyl carbenium ion. All ionic species were accelerated to 8 KeV into the MS-1 portion of the tandem mass spectrometer. MS-1 was set to allow the passage of only the ions of interest, those with a mass corresponding to the aromatic plus the carbenium ion, at a mass resolution of ca. 2500 (10% valley definition). The ions were then activated in field-free region III by collision with He in a chamber pressurized with
sufficient He to suppress the beam by 50%. The fragment ion mass spectrum was then obtained by scanning ESA-II from zero to the main beam voltage. A minimum of 20 scans were averaged for each spectra.

For producing the protonated aromatics, an alkylaromatic was admitted into the high pressure chemical ionization (CI) source through a controllable leak valve. The chemical ionization reagent gas (CH₄, CD₄) was also admitted into the CI source chamber through a second leak valve system. Protonation by CH₅⁺ or deuteration by CD₅⁺ of the alkylaromatic to give the arenium ion was conducted in the CI source. All ionic species were accelerated to 8 KeV into the MS-I portion of the tandem mass spectrometer. MS-I was set to allow the passage of only one mass ion, the arenium ion of interest, at a resolution of 2500 (10% valley definition). The arenium ion was activated in field free region III (between the magnet and ESA-II) by collision in a chamber pressurized with sufficient He such that 50% of the main beam intensity was supressed. The fragment ion mass spectrum (CAD spectrum) was then obtained by scanning ESA-II from zero volts to the the main beam voltage. All reported CAD spectra are the average of a minimum of 20 scans.

1. Synthesis

a. 3-(p-Chlorophenyl)-pentane

The procedure for the synthesis of the 3-(p-chloro phenyl)-pentane was carried out in three steps. A three-neck round bottom flask was fitted with an addition funnel, a water condensor, and a thermometer. Twenty mL of carbon disulfide along with 17.69 g of aluminum chloride were added to the flask. The mixture was placed in a sodium chloride ice bath to bring the temperature to -5°C. Next, 0.1327 moles of chlorobenzene were mixed with 0.1376 moles of acetyl or propionyl chloride and then added dropwise to the reaction
vessel via the addition funnel to avoid raising the temperature above 0°C. Once the addition was complete, the solution was allowed to stir overnight. A color change from yellow to green to brown was observed in this time period. Then 20.39 mL of concentrated HCl were added to 101.9 g of ice. The contents of the reaction vessel was then added to the HCl/ice mixture. After the separation of the layers the aqueous phase was washed multiple times with ether. Finally, the organic phase was dried and its volume reduced in vacuo. The resulting product was p-chloropropiophenone with roughly a 90% yield.

All the steps were followed by one or more of the following analytical techniques: IR, GC/MS, 1H NMR, 13C NMR, 13C DEPT NMR. The results of this step were confirmed using GC/MS with a peak coming off the column at 0.559 minutes with a molecular ion with a m/z of 168/170 in a 3:1 ratio with a base peak at 139 amu corresponding to the loss of 29 amu (ethyl group).

Next, a three-necked round bottom flask was set up with a calcium chloride packed column, a water condensor, and a septum. To the flask were added 25 ml of diethylether followed by 10 ml of the p-chloropropiophenone. Next, 28 mL of 0.3 M ethylmagnesium bromide in ether were added to the reaction mixture via syringe through the septum. Solid formed upon addition of the Grignard reagent. To aid in the breaking up of this solid, 15 mL of ether were added. The solution was then cooled on an ice bath and 3.0 M HCl was added dropwise until the solution was slightly acidic. Once the solution was acidic, 10 ml of additional water was added and the aqueous layer was separated and washed several times with ether. All the washes were combined with the original organic layer and the solvent was removed in vacuo and finally dried over magnesium sulfate--the resulting product being 3-p-chlorophenyl-3-pentanol with an 80% yield.
The results were confirmed via IR, GC/MS, and $^{13}$C DEPT NMR. The infrared spectrum showed a definite O-H stretch at 3390 cm$^{-1}$ and aromatic overtones between 1600 cm$^{-1}$ and 1660 cm$^{-1}$. The GC/MS results showed a peak coming off the column at 0.658 minutes which was determined to show no molecular ion, but did have a m/z 169/171 in a 3:1 ratio due to the loss of 29 amu (ethyl group) from the tertiary alcohol. From the $^{13}$C DEPT NMR: CH$_3$ carbons (8.1 ppm), CH$_2$ carbons (35.2 ppm), CH carbons (125.3, 126.8 ppm), C carbons (82.5, 129.2, 135.1 ppm).

Finally, 9.993 g of sodium iodide were added to a three neck round bottom flask fitted with a water condensor, a stopper and a septum, followed by the addition of 3.48 mL of acetonitrile and 8.46 ml of chlorotrimethylsilane. To the mixture 2.3 mL of the alcohol from the above reaction mixed with 11.11 mL of hexane was added. There was an observable color change from yellow to red-orange upon the addition. The reaction was allowed to proceed over night--during which time, a dark precipitate formed. Next, 12 mL of water was added to the solution which was then agitated and the organic layer was separated from the aqueous layer proceeded by several washings with ether. The washings were followed by drying and removal of the solvent resulting in a final product of p-chloro-(1-ethylpropyl)benzene (p-chloro-pentylbenzene). Results from the final step were confirmed by means of GC/MS and $^{13}$C DEPT NMR. The GC/MS gave a peak with a retention time of 0.532 minutes with a molecular ion at m/z 182/184 in a 3:1 ratio with a major loss of 29 amu (ethyl cleavage) and a base peak at m/z 125 corresponding to the loss of both ethyl groups of the side chain. From the $^{13}$C DEPT NMR: CH$_3$ carbons (16.5 ppm), CH$_2$ carbons (23.3 ppm), CH carbons (49.2, 129.0, and 130.3 ppm), C carbons (129 and 132 ppm).
b. 2-(p-Chlorophenyl)-pentane

The procedure was much the same as that described above. The main differences being that acetylchloride was used in place of propionylchloride in step one, and in step two, propylmagnesiumchloride was substituted for ethylmagnesiumbromide. All steps were followed in a similar fashion with one or more of the techniques listed above. Step 1 results were confirmed via GC/MS in which there was a peak in the GC trace that had a retention time of 0.496 minutes with a molecular ion at m/z 154/156 in a 3:1 ratio. The spectrum also had a base peak at m/z 139 suggesting a loss of 15 amu (methyl group of the acetyl unit). These peaks confirmed our product as p-chloroacetophenone.

Step 2 results were confirmed via GC/MS as well. The product had a retention time of 0.711 minutes was determined to have no molecular ion due to the loss of water from the tertiary alcohol, giving a parent ion of m/z 180 (loss of 18, water), with prominent peaks at m/z 155/157 in a three to one ratio which is resulting from the loss of 43 amu (propyl group). This data confirmed our product as p-chloro-(1-methyl-1-butanol)-benzene.

Step 3 results were confirmed via GC/MS and 13C DEPT NMR. From the GC/MS data, the product had a retention time of 0.438 minutes with a molecular ion at m/z 182/184 in a 3:1 ratio with a base peak at m/z 139/141 corresponding to the loss of 43 amu due to the loss of a propyl group. The 13C DEPT NMR gave the following peaks: CH₃ carbons (14.8, 22.9 ppm), CH₂ carbons (21.2, 41.0 ppm), CH carbons (39.0, 128, and 131 ppm), C carbons (129 and 133 ppm), confirming the product as p-chloro-(1-methylbutyl)benzene.

The procedure for the synthesis of the isomeric p-fluoro-pentylbenzenes involved the same three steps as those outlined above for the chloro-compounds with the singular exception that fluorobenzene was substituted for chlorobenzene. The 13C DEPT NMR for
2-(p-fluorophenyl)-pentane gave CH3 carbons (15.3 and 24.1 ppm), CH2 carbons (20.6 and 39.8 ppm), CH carbons (38.4, 129.1, and 132 ppm), and C carbons (128.5 and 133.3 ppm). The 13C DEPT NMR for 3-(p-fluorophenyl)-pentane gave a CH3 carbon (18.4 ppm), CH2 carbon (20.3 ppm), CH carbons (48.2, 127.9, and 131.3 ppm), and C carbons (128.3 and 133.8).

For the synthesis of 2-(p-bromophenyl)-pentane, the same three steps were employed as those described for the chloro- and fluoro- compounds with the exception that bromobenzene was used in the place of the chlorobenzene. However, the synthesis of 3-(p-bromophenyl)-pentane was performed using a thallium(III) acetate catalyst to brominate sec-pentylbenzene.

c. General Procedure for Alkylthiophene Synthesis

A 50 mL round bottom flask was set up with a septum. The system was then flushed with nitrogen and 10 mL of tetrahydrofuran were added. To the flask, 7.7 mL of 2.6M n-butyllithium in heptane was added followed by the addition of 1.6 mL of thiophene diluted with an equal amount of THF. The solution was allowed to stir at room temperature for 30 min. After this time, 1.8 mL of the respective (n-, 2-, or 3-) iodopentane were added to the solution. Again, the solution was allowed to stir at room temperature overnight. During this time the solution became dark brown. After this time had expired the contents of the flask were poured over 25 g of ice. The layers were separated and the aqueous layer washed with three portions of diethylether. Each of the washes was added to the original organic phase. The solvent is then removed in vacuo leaving a mixture of the respective pentyli thiophene and unreacted iodopentane and thiophene. Identification of all the compounds synthesized
was based on $^{13}$C DEPT utilizing a JEOL CPF 270 MHz NMR and Hewlett Packard 5890 GC/MS. A list of peaks is as follows:

n-pentylthiophene: CH$_3$ carbons (14.2 ppm), CH$_2$ carbons (22.5, 29.8, 31.2, 31.3 ppm), CH carbons (122.8, 123.8, 126.5 ppm), C carbons (146.0 ppm).

2-pentylthiophene: CH$_3$ carbons (14.0, 21.1 ppm), CH$_2$ carbons (26.1, 29.4 ppm), CH carbons (35.5, 122.5, 126.9, and 127.1 ppm), C carbons (147.8 ppm).

3-pentylthiophene: CH$_3$ carbons (11.5 ppm), CH$_2$ carbons (27.6 ppm), CH carbons (44.6, 122.1, 124.1, 127.1 ppm), C carbons (136.8 ppm).

d. General Procedure for Alkyl Furan Synthesis

A 25 mL round bottom flask was sealed with a rubber septum and then flushed with nitrogen. To the flask was added 5.75 mL of THF followed by 5.2 mL n-butyllithium and 0.7875 mL of furan. This reaction mixture was allowed to stir for twenty minutes at room temperature. The temperature of the solution was then raised to 40°C, and 1 mL of the appropriate (n-, 2-, or 3-) iodopentane was then added to the reaction mixture. After this addition, the temperature of the mixture was then raised to 55°C and allowed to stir at constant temperature for 5 hrs. After this time the solution was then poured over 15 g of ice, followed by a separation of the layers and three washings of the aqueous layer with diethylether, adding the wash to the organinc layer. The solvent was then removed in vacuo leaving the pentylfuran and unreacted iodopentane and furan. The furans were identified via $^{13}$C DEPT NMR with the results as follows:

n-pentylfuran: CH$_3$ carbons (14.1 ppm), CH$_2$ carbons (22.3, 27.9, 28.1, 31.5 ppm), CH carbons (104.7, 110.1, 140.5 ppm), C carbons (156.7 ppm).
2-pentylfuran: CH₃ carbons (16.2 and 22.6 ppm), CH₂ carbons (27.1 and 28.5 ppm), CH carbons (36.5, 123.6, 127.1, and 127.3 ppm), C carbons (146.8 ppm).

3-pentylfuran: CH₃ carbons (12.6 ppm), CH₂ carbons (25.6 ppm), CH carbons (45.8, 122.4, 125.1, and 127.5 ppm), C carbons (138.6 ppm).

e. Procedure for the Synthesis of 2- and 3-Iodopentane

The 2- and 3-iodopentane reagents used in the aforementioned syntheses were obtained from the simple Sₙ₂ reaction. The corresponding 2- and 3- bromopentane were reacted with a 15% by weight solution of sodium iodide in acetone. After letting the mixture stir at room temperature for 3 hrs, the solution was poured over water and then multiply extracted with ether. The solvent was then removed leaving the corresponding 2- or 3-iodopentane. Identification of 2- and 3-iodopentane was determined as before.

2-iodopentane: CH₃ carbons (13.2, 30.5 ppm), CH₂ carbons (23.0, 29.2 ppm), CH carbons (45.0 ppm).

3-iodopentane: The identity of 3-iodopentane was determined by GC/MS alone. It gave a molecular ion at m/z 198 with a base peak at m/z 71 corresponding to the loss of iodine. Another major peak was from the loss of 29 amu which comes from the fragmentation of an ethyl group.
PART 2:

ON THE REACTION OF THE ETHYLENE OXIDE RADICAL CATION WITH
NEUTRAL ETHYLENE OXIDE
I. INTRODUCTION

The structure and bimolecular reactivity of the gas-phase ethylene oxide radical cation has been extensively studied utilizing mass spectrometric, electron spin resonance, and ion cyclotron resonance (ICR) methodologies.\textsuperscript{1-18} For an excellent review of distonic ion molecule reactions in general and of ethylene oxide radical cation reactions, see Kenttamaa et al.\textsuperscript{19} The specific reaction between the ethylene oxide radical cation and neutral ethylene oxide was first addressed in detail by Blair and Harrison\textsuperscript{20} and then by Beauchamp.\textsuperscript{21} The conclusions from these early investigations are two-fold. First, the ethylene oxide radical cation reacts with its own neutral to yield protonated ethylene oxide via proton and/or H-atom transfer:

\[
\text{C}_2\text{H}_4\text{O}^* + \text{C}_2\text{H}_4\text{O} \rightarrow \text{C}_2\text{H}_5\text{O}^* + \text{C}_2\text{H}_3\text{O} \quad (1)
\]

The product ion from this reaction, protonated ethylene oxide, has itself been the focus of many investigations.\textsuperscript{22-27} The second process observed when the ethylene oxide radical cation reacts with its own neutral is CH\textsubscript{2}\textsuperscript{+} transfer to yield C\textsubscript{3}H\textsubscript{5}O\textsuperscript{+}, which subsequently loses H by unimolecular decomposition giving the product ion C\textsubscript{3}H\textsubscript{5}O\textsuperscript{+}:

\[
\text{C}_2\text{H}_4\text{O}^* + \text{C}_2\text{H}_4\text{O} \rightarrow (\text{C}_3\text{H}_6\text{O}^*)^* \rightarrow \text{C}_3\text{H}_5\text{O}^* + \text{H} \quad (2)
\]

These early investigations involved reactions conducted under conditions where stable adduct ion formation was either not possible or not the focus of the study.

In this article, we report an investigation of the bimolecular reaction of ethylene oxide radical cation with its own neutral precursor. This reaction is conducted in the high-pressure
source of a tandem mass spectrometer, where stabilizing conditions allow for the production of adduct ions determined by MS/MS methodologies. The central focus of this study is to elucidate the structure of the adduct $\text{C}_4\text{H}_8\text{O}_2$ radical cation that is found in the ethylene oxide ion-molecule reaction.
II. EXPERIMENTAL

All CAD experiments were performed on a Kratos MS50 triple analyzer mass spectrometer which consisted of a Nier-Johnson geometry high resolution mass spectrometer followed by an electrostatic analyzer (ESA). The ions formed in the chemical ionization source were mass selected at a mass resolving power of 2500-3500 (10% valley definition) by using MS-1 (ESA-1 and the magnetic sector). The ion-molecule adduct was then activated by collisions with helium gas in the second collision cell. The second ESA was scanned to give the collisionally activated dissociation (CAD) spectrum of the resulting fragment loss. In a typical CAD experiment, 20-40 scans were acquired and signal averaged by using the Kratos Mach 3 software package. The precision for all peak heights reported is approximately +/- 5% relative as determined by replicate experiments.

The electron beam was operated at 280 eV with total emission current of 500 µA. The ion accelerating voltage was 8000 V. Typical source pressures for bimolecular reaction were ca. 0.1 torr. The efficiency of adduct formation was measured with the Kratos MS-50 triple analyzer. The elemental composition of the adduct was established by peak matching, using as a reference ion the ethylene oxide radical cation.

All theoretical calculations were performed on a Hewlett-Packard series 715 Unix-based system employing the Spartan 3.0 molecular modeling program produced by Wavefunction, Inc. The predominant semi-empirical computational level utilized was the AM1 basis set. PM3 and MNDO semi-empirical computations were also extensively
employed. Although only AM1 values are reported in this article, all computational trends were consistent with those found by using MNDO and PM3.

The AM1, PM3, and MNDO basis sets, as configured within the Wavefunction Program, automatically minimize to the lowest energy state, and hence do not allow specific placement of an ion or radical site in the radical cation. To compute the energies/conformations, etc., of distonic ions with specified initial placement of charge and radical site, molecules were built in fragments and then each fragment was minimized. To build the whole molecule, the fragments were positioned together utilizing distance constraints. These constraints approximated normal bond distances between the atoms, i.e., 1.54 Å for carbon-carbon single bonds and 1.45 Å for oxygen-carbon single bonds. Once these constraints were in place, the whole molecule was again minimized to yield a conformation from which electron density, spin distributions, heats of formation, etc., could be calculated. All calculations were run multiple times and were found to be highly reproducible. The validity of this technique for generating input structures was rigorously tested by generating numerous structures of known properties and comparing the calculated heats of formation, electron densities, etc., with those that are known. The calculated heats of formations agreed in each instance to within several Kcal/mol, and all other properties were nearly identical to known values.
III. RESULTS AND DISCUSSION

The gas-phase reaction between the radical cation of ethylene oxide and neutral ethylene oxide yields under high-pressure conditions (>0.5 torr) an adduct, \( C_4H_8O_2 \), at \( m/z=88 \). The high-energy collisionally activated dissociation (CAD) mass spectrum of the adduct reveals that the radical ion is largely covalent because the adduct dissociates to give ions that are higher than \( m/z \) 44 (see Figure 1).

The structure of the gas-phase radical ion adduct may depend on internal energy, especially if isomerization processes have low energy requirements.\(^\text{28}\) To test for isomerization, the bimolecular reaction of the ethylene oxide radical cation with its neutral precursor was carried out under conditions of different ion-source pressures, which allowed for the preparation of the adduct in different energy states. At the highest pressure extreme (ca. 0.5 torr), the stabilization afforded by collision with excess ethylene oxide molecules yields the lowest internal energy ions that we can achieve in these experiments. At the low pressure extreme, corresponding to a source pressure of ca. 0.025 torr, the extent of collisional stabilization is at a minimum, and a highest internal-energy radical cation will be generated. This experimental approach was successfully utilized in a number of investigations.\(^\text{29-32}\) As the amount of internal energy is increased, activation barriers for isomerizations may be surmounted and rearrangements may occur.

The CAD spectra of the adduct change as a function of internal energy. The percent total ion current for the salient ions produced by collisional activation of the ethylene oxide
Figure 1.

The CAD spectrum of the C₄H₈O₂ adduct.
Scheme 1. Reaction of ethylene oxide radical cation with neutral ethylene oxide.

\[
\text{O}^\cdot + \text{O} \rightarrow \text{C}_4\text{H}_8\text{O}_2^\cdot
\]
radical cation/ethylene oxide adduct as a function of increasing internal energy are tabulated in Table 1.

A. COMPARISON OF C₄H₈O₂ CAD MASS SPECTRA

To elucidate the structure of the C₄H₈O₂ adduct ion, the approach of comparison with the CAD spectra of representative model compounds was employed. The potential acyclic ions that could be generated in this reaction cannot be modeled accurately because the acyclic adduct would be, by definition, a distonic ion. Distonic ions are difficult to generate from a neutral precursor. However, the CAD spectra of an array of radical cations generated from cyclic C₄H₈O₂ model compounds can be compared to those of the adduct. The percent of total ion current for the predominant ions in the CAD spectra of the low-energy adduct ion (generated at ca. 0.5 torr), the high-energy adduct ion (generated at 0.025 Torr), and the radical cations generated from isomeric 1,4-dioxane, 2-methyl-1,3-dioxolane, and 1,3-dioxane are found in Table 2.

The CAD spectra of the radical cation of 1,4-dioxane matches most closely that of the high energy adduct ion. The only incongruities in the two spectra are the abundance of the M/Z 43 and 44 ions, which are inflated with respect to those of the model compound. Because the CAD spectra of the adduct match that of ionized 1,4-dioxane except in the m/z 43-44 region where the adduct produces a greater abundance of m/z 44 ions, the adduct ion may exist as a mixture of completely covalent species and a loosely bound structure that would readily convert to the m/z 44 ion. An alternative to the loosely bound adduct would be an acyclic distonic ion that readily dissociates to starting materials at low energy, and undergoes isomerization to 1,4-dioxane at high energy. The nature of this ion will be addressed in the next section. When assessing the trends in the CAD spectra of the adduct
Table 1. Comparison of the Ethylene Oxide Radical Cation/ethylene Oxide Adduct at Varying Internal Energies.

<table>
<thead>
<tr>
<th>M/Z RATIO</th>
<th>87</th>
<th>73</th>
<th>60</th>
<th>58</th>
<th>57</th>
<th>45</th>
<th>44</th>
<th>43</th>
<th>31</th>
<th>30</th>
<th>29</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOWEST ENERGY ADDUCT</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>14</td>
<td>32</td>
<td>19</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>11</td>
<td>3</td>
<td>18</td>
<td>27</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>22</td>
<td>7</td>
<td>11</td>
<td>16</td>
<td>9</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>HIGHEST ENERGY ADDUCT</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>25</td>
<td>5</td>
<td>8</td>
<td>18</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

*All entries are expressed as percent total ion current.*
Table 2. A Comparison of the Predominant Peaks in the Cad Spectra of the Ethylene Oxide Radical Cation/ethylene Oxide Adduct Ion and Selected Model Compounds

<table>
<thead>
<tr>
<th>M/Z RATIO</th>
<th>87</th>
<th>73</th>
<th>60</th>
<th>58</th>
<th>57</th>
<th>45</th>
<th>44</th>
<th>43</th>
<th>31</th>
<th>30</th>
<th>29</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW ENERGY ADDUCT</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>14</td>
<td>32</td>
<td>19</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>HIGH ENERGY ADDUCT</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>25</td>
<td>5</td>
<td>8</td>
<td>18</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>1,4-DIOXANE</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>26</td>
<td>6</td>
<td>11</td>
<td>13</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>2-METHYL-1,3-DIOXOLANE</td>
<td>16</td>
<td>8</td>
<td>0</td>
<td>&lt;1</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>31</td>
<td>&lt;1</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>1,3-DIOXANE</td>
<td>30</td>
<td>&lt;1</td>
<td>14</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>10</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

**NOTE** 1,3-Dioxane also fragments to give ions of M/Z 70 (2%), 59 (7%), 42 (5%), 41 (3%).

** All entries are expressed as percent of total ion current.
ion as a function of internal energy, it is clear that as adduct ion energy increases, the m/z 88 ion population becomes increasingly dominated by the 1,4-dioxane radical cation while the population of the ion that reverts to starting materials is reduced.

B. MECHANISMS FOR THE REACTION OF THE ETHYLENE OXIDE RADICAL CATION AND ETHYLENE OXIDE

For the ethylene oxide radical cation to react with its own neutral in the generation of a covalently-bound adduct, the initial radical ion must be in ring-opened form. In a landmark computational investigation utilizing elegant ab initio methods, Radom et al. showed that several possible structures for the ring-opened ethylene oxide radical cation can exist.

From Radom’s work, the cyclic form of the ethylene oxide radical cation, 1, is 13 Kcal/mol more stable than the ring-opened distonic ion, 2, which generated from the cyclic species via C-O bond cleavage. Our semi-empirical calculations place ion 1 16 Kcal/mol more stable than ion 2. The formation of 2 is favorable because the C-O bond is labile; however, the results from the computations suggest that 2 would rapidly ring close to the more stable cyclic ion 1. If the ethylene oxide ring opens via breaking the C-C bond, distonic ion 3 would form. This ion can be depicted as of two resonance forms, 3a and 3b. Radom reports that distonic ion 3 is more stable than cyclic ion 1 by 14 Kcal/mol (we calculate a difference of 40 Kcal/mol). These computational observations coupled with the experimental fact that the reactions of ethylene oxide ion with neutral compounds in ion cyclotron resonance (ICR) and Fourier transform mass spectrometry (FTMS) are most consistent with a ring-opened distonic structure 3 make it reasonable to assume that the reactive intermediate involved in adduct formation is ion 3.
At least two potential step-wise mechanistic schemes exist for adduct formation, and are illustrated in Scheme 3. Mechanism A initially involves a free radical coupling between the ring-opened ethylene oxide radical cation and neutral ethylene oxide. The resulting species is a long-chain distonic ion, 4. To calculate the heat of formation of ion 4, in a conformation similar to that presented in Figure 2, geometric constraints need to be invoked to keep the radical and cation sites distant. As such, ion 4 has a heat of formation of 142 Kcal/mol. When the geometric constraints are removed, a local minimum, ion 5, occurs, where the carbenium ion is in close proximity to the lone pairs on the distant oxygen. Structure 5 has a heat of formation of 135 Kcal/mol.

Ion 4 can directly cyclize to ion 6, which has the 1,4-dioxane radical cation structure and a heat of formation of 125 kcal/mol. In addition, it is reasonable that ion 5 can also cyclize to ion 6. Ion 6 is the global minimum in which the radical and ion sites are mechanically brought into proximity of one another. Hence, a greater than 10 Kcal/mol enthalpic driving force exists for the long-chain distonic ion 4 to cyclize to radical cation 6. This energy gain presumably arises from the formation of a partial (one-electron) bond between the radical and cationic sites.

Mechanism B involves an initial interaction of the carbenium ion end of distonic ion 3a, which yields the long-chain distonic ion 4. Distonic ion 4, which is identical to that generated in Mechanism A, then undergoes subsequent cyclization to ion 6, either directly or through ion 5.

A mechanism involving long-chain distonic ion 4 undergoing cyclization to 5 presupposes that a stabilizing interaction exists when the radical site and the carbenium ion site are brought within close proximity of one another. When comparing the fractional
charges on each of the atoms in the structures 4 and 5 to the fractional charges on the corresponding atoms in a cyclic structure, 6, several insights can be gained. The atom in the acyclic structure that initially bore the unpaired electron loses electron density when going to the cyclic ion. Ultimately, a complete redistribution of electron density occurs such that all carbons share the electron deficiency within the radical ion. Therefore, the bonding in cyclic ion 6 not only involves the formation of a partial bond between the initial radical and cation sites but also involves partial bonding with neighboring atoms.

Interestingly, the predicted CAD mass spectrum of ion 5 should be dominated by the formation of m/z 44 (scheme 4). As such, it is reasonable that ion 5 is the source of the additional abundance for the m/z 44 ion that is seen when comparing the CAD spectra of ethylene oxide/ethylene oxide radical cation adduct with that of 1,4-dioxane. Specifically, the ethylene oxide/ethylene oxide product ion mixture analyzed via CAD mass spectrometry consists of ions 5 and 6.

In comparing computational results, the structure and energetics of cyclic radical ion 6 are very nearly identical to those for the radical ion generated via the removal of one electron from neutral 1,4-dioxane. The bond lengths, bond angles, atom-to-atom electron densities, and heat of formation for the two ions are identical to within +/- 0.5% relative.

It should be noted that, although both mechanism A and mechanism B involve the formation of the identical distonic intermediate (4), which then ultimately cyclizes to ion 6, the enthalpies of activation for the two processes are not identical. Mechanism A, a free radical coupling, has an activation barrier that is ca. 20 Kcal/mol lower than that for mechanism B, which involves carbenium ion chemistry. Thus, mechanism A is more likely than is mechanism B.
Scheme 2. Possible conformations of ethylene oxide radical cation.

\[
\begin{align*}
1 & \quad 2 \\
\text{[Diagram]} & \quad 3a \quad 3b
\end{align*}
\]
Scheme 3. Mechanisms for the reaction of ethylene oxide radical cation with neutral ethylene oxide.

MECHANISM A

\[ \begin{array}{c}
\text{3a} \\
\text{\textbullet} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]


MECHANISM B

\[ \begin{array}{c}
\text{3a} \\
\text{\textbullet} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]

\[ \xrightarrow{+} \]

\[ \begin{array}{c}
\text{\textbullet} \\
\text{\textcircled{O}} \\
\text{\textcircled{O}} \\
\end{array} \]
Scheme 4. Origin of excess m/z 44.
Figure 2. Geometry and charge distribution of the cyclized long chain distonic \( a \) as compared to the radical cation formed by expulsion of one electron from 1,4-dioxane \( b \).

\[
\begin{array}{ccc}
\text{angle} & a & b \\
\angle 123 & 115.8 & 115.8 \\
\angle 234 & 105.6 & 105.5 \\
\angle 345 & 105.6 & 105.5 \\
\angle 456 & 115.8 & 115.8 \\
\angle 561 & 105.5 & 105.5 \\
\angle 612 & 105.5 & 105.5 \\
\end{array}
\]

\[
\begin{array}{ccc}
\text{distance} & a & b \\
12 & 1.40 & 1.40 \\
23 & 1.40 & 1.40 \\
34 & 1.59 & 1.59 \\
45 & 1.40 & 1.40 \\
56 & 1.40 & 1.40 \\
61 & 1.59 & 1.59 \\
\end{array}
\]

\[
\begin{array}{ccc}
\text{charge} & a & b \\
1 & .05 & .06 \\
2 & -.15 & -.16 \\
3 & .05 & .06 \\
4 & .01 & .06 \\
5 & -.13 & -.16 \\
6 & .01 & .06 \\
\end{array}
\]
The computational implications then are that the initial ethylene oxide/ethylene oxide adduct ion is a long-chain distonic ion (4) that is formed via a free-radical process. This species subsequently cyclizes to cyclic product (6), that is not a distonic ion, either via direct interconversion or through ion 5. This is reasonable in view of the mass spectral result that the CAD spectra of the adduct ion matches that for the radical cation generated directly from 1,4-dioxane (an ion that likely is not a distonic species).
IV. CONCLUSIONS

Mass spectral results indicate that the adduct ion formed in the reaction between the ethylene oxide radical cation and neutral ethylene oxide undergoes structural change as a function of internal energy. The predominant high-energy adduct ion formed in the reaction is a cyclic non-distonic ion that has the structure of ionized 1,4-dioxane. Computational results show that initial adduct formation occurs via a free radical process generating an acyclic distonic radical cation that subsequently cyclizes to a non-distonic ion similar in structure to 1,4-dioxane. The cyclization is driven by a 5 - 17 Kcal/mol exothermicity for cyclization. These results raise several questions regarding the nature of long-chain distonic ions: (a) Does cyclization always occur in other long-chain distonic ions? What is the effect of chain length on the energetics of cyclization? (b) If cyclization is general, which chain length is optimal for cyclization? (c) What is the effect of the nature of the atoms bearing the cation and radical on cyclization? and (d) Does changing the radical and cation sites to secondary and tertiary change the exothermicity of cyclization? These subjects will be addressed in future studies.
PART 3:

ON THE CYCLIZATION OF LONG-CHAIN DISTONIC RADICAL CATIONS
I. INTRODUCTION

Distonic ions are radical ions with charge and radical sites neither adjacent nor in conjugation with one another. An accepted nomenclature scheme for these intermediates utilizes greek prefixes (i.e., α-distonic, β-distonic, γ-distonic, etc.), (see Figure 1).

Distonic ions are difficult to form by direct ionization; they usually arise from unimolecular rearrangement-fragmentation, bimolecular reaction, or isomerization. Experimental and computational evidence has shown that certain distonic ions are quite stable. Early investigations of simple gas-phase distonic radical cations were conducted by Schwarz, and Holmes and Terlouw. Computational investigations have predominantly centered upon α-distonic ions, the results of which suggest that α-distonics are often lower in energy than their corresponding conventional molecular ions. Additional molecular orbital calculations have shown that there are a number of β-distonic ions that are stable and exist in local minima on their potential energy surfaces. Gas-phase distonic ions have been generated via bimolecular reaction in a wide variety of investigations.

In the preceding article, it was shown that reaction of the ethylene oxide radical cation with neutral ethylene oxide within the high-pressure chemical ionization source of a tandem mass spectrometer produces a \( \text{C}_4\text{H}_8\text{O}_2 \) distonic radical cation adduct (Scheme 1). The initial distonic radical cation, a zeta-distonic ion, undergoes rapid cyclization to a cyclic non-distonic ion whose structure is depicted as that of the 1,4-dioxane radical cation.
Figure 1. Differing chain length distonic radical cations.
Scheme 1. Reaction of ethylene oxide radical cation with neutral ethylene oxide.
Our goal then is to investigate cyclization of long-chain (delta, epsilon, zeta, and eta) distonic radical cations to pseudo-cyclic non-distonic ions. Specifically, the questions posed are: (a) Is there an enthalpic driving force for cyclization?, (b) Will cyclization take place in distonic radical cations in which the radical site is a heteroatom?, and (c) What roles do ring size and the extent of substitution at the cation and radical sites play in the cyclization? Computational methodologies have been chosen to gain insight into these questions because this approach allows for the estimation of relative thermodynamic values not readily measured experimentally. Moreover, this computational approach can serve as the foundation for the future experimental formation of long-chain distonic ions in the gas phase.
II. EXPERIMENTAL

All calculations were performed on a Hewlett-Packard series 715 Unix-based system employing the Spartan 3.0 molecular modeling program produced by Wavefunction, Inc. Semi-empirical methodologies were chosen over ab Initio methodologies due to time considerations. Most of the structures dealt with possess over six heavy atoms, and as such, ab initio computations are time-preclusive. The semi-empirical computational level utilized was the AM1 basis set. This basis set, as configured within Spartan 3.0, automatically minimizes to the lowest energy level, and hence does not allow specific placement of an ion or radical site. As a result, to compute energies/conformations, etc., of distonic ions with specified initial placement of charge and radical site, the molecules were built in fragments and each fragment minimized. To build the whole molecule, the fragments were coupled utilizing normal bond distances between the atoms involved (1.54 Å for carbon-carbon bonds, 1.45 Å for oxygen-carbon bonds, and 1.47 Å for nitrogen-carbon bonds). The energy of the whole molecule was again minimized to obtain the conformational minimum, electron density and spin distributions, heat of formation, etc. All calculations were run multiple times and were found to be highly reproducible. The validity of this technique for generating input structures was rigorously tested by generating numerous structures of known properties and comparing the calculated heats of formation, electron densities, etc., with known values. The calculated enthalpies of formations agreed in each instance within several Kcal/mol, and all other properties were nearly identical to known values.
III. RESULTS AND DISCUSSION

When the acyclic $\text{C}_5\text{H}_{10}\text{O}$ zeta distonic radical cation, A, is used as an input structure and is then allowed to undergo conformational change, the structure adopted is one that approximates the cyclic structure, B (Scheme 2).

Interestingly, structure B is not formally a distonic ion because the charge and radical sites are delocalized over common atoms (a feature to be more fully discussed later). Therefore, structures A and B are not merely different conformations of the same intermediate because the electronic distribution of charge and spin density changes in going from the acyclic structure to the cyclic form. Further, because structures A and B represent different reactive intermediates, they are not resonance forms of one another. Long-chain distonic ions, such as A, and cyclic non-distonic ions, such as B, are perhaps best described as isomers.

The cyclization of A to B arises from an initial stabilizing interaction between the radical and cationic sites. To determine the energetic driving force for the conversion or "isomerization" of A to B, it is necessary to "freeze out" structure A, the acyclic $\text{C}_5\text{H}_{10}\text{O}$ zeta distonic radical cation, in order to prevent it from cyclizing. Structure A was generated by placing dihedral constraints upon four central atoms of the input structure such that cyclization was precluded. Energies reported are with a dihedral constraint of 180°, however, upon changing this dihedral constraint to various points between 180° and 100° the energy only changes within 5% relative. At the 180° constraints, the distonic ion was allowed to
minimize (to a local minimum), and its heat of formation (and other properties) calculated.

When compared to the heat of formation of structure $\mathcal{B}$, (formed from structure $\mathcal{A}$, free of constraints and hence allowed to cyclize), a 45 kcal/mol difference was observed. Similar significant enthalpic driving forces for cyclization were observed in every long-chain distonic ion investigated.

A. STRUCTURAL CHARACTERISTICS OF ACYCLIC DISTONIC AND CYCLIC RADICAL CATIONS

To establish the structural characteristics of representative long-chain distonic radical cations and their corresponding cycles, three different types of ions were considered; $\text{+CH}_2\text{(CH}_2\text{)}_4\text{CH}_2$, $\text{+CH}_2\text{(CH}_2\text{)}_4\text{O}$, $\text{+CH}_2\text{(CH}_2\text{)}_4\text{NH}$. Utilizing appropriate constraints, it is possible to generate, in separate computations, the acyclic intermediate (which is a local minimum), and the cyclic intermediate (which in all cases is the global minimum). The structures of the cyclic intermediates of $\text{+CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$, $\text{+CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$, $\text{+CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}$ are shown in Figure 2, illustrating their twisted-chair conformations.

The corresponding bond lengths and bond angles for each of the structures in Figure 2 are shown in Table 1. When comparing the fractional charges on each of the atoms in the acyclic structure to the fractional charges on the corresponding atoms in a cyclic structure (see Figure 2), several insights can be gained. In each system, the atom in the acyclic structure that initially bore the radical loses electron density when going to the cyclic radical cation. Simultaneously, that atom that initially bore the cation gains electron density in going to the cyclic radical cation. As such, the free radical site donates electron density to the carbon that initially bore the cation. Further, both the carbon alpha to the original cation site (labeled carbon 2 in each structure from Figure 2) and the carbon alpha to the original
Scheme 2. Long-chain distonic cation resonance forms.
Figure 2. Structures depicting the geometry obtained from geometry optimized calculations of the long-chain distonic ions in question.

structure 1  structure 2  structure 3
Table 1. Bond Lengths and Bond Angles for the Cyclic Conformations of +CH₂(CH₂)₄CH₂, +CH₂(CH₂)₃CH₂O, and +CH₂(CH₂)₃CH₂NH, as Calculated by AmI Methodology.

<table>
<thead>
<tr>
<th>ATOMS</th>
<th>+CH₂(CH₂)₄CH₂</th>
<th>+CH₂(CH₂)₃CH₂O</th>
<th>+CH₂(CH₂)₃CH₂NH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>1.46 Å</td>
<td>1.50 Å</td>
<td>1.52 Å</td>
</tr>
<tr>
<td>2-3</td>
<td>1.51 Å</td>
<td>1.54 Å</td>
<td>1.54 Å</td>
</tr>
<tr>
<td>3-4</td>
<td>1.51 Å</td>
<td>1.51 Å</td>
<td>1.51 Å</td>
</tr>
<tr>
<td>4-5</td>
<td>1.54 Å</td>
<td>1.51 Å</td>
<td>1.53 Å</td>
</tr>
<tr>
<td>5-6</td>
<td>1.46 Å</td>
<td>1.40 Å</td>
<td>1.43 Å</td>
</tr>
<tr>
<td>6-1</td>
<td>2.01 Å</td>
<td>1.40 Å</td>
<td>1.43 Å</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1-2-3</th>
<th>2-3-4</th>
<th>3-4-5</th>
<th>4-5-6</th>
<th>5-6-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2-3</td>
<td>114°</td>
<td>111°</td>
<td>111°</td>
<td>114°</td>
<td>102°</td>
</tr>
<tr>
<td>2-3-4</td>
<td>111°</td>
<td>109°</td>
<td>112°</td>
<td>118°</td>
<td>124°</td>
</tr>
<tr>
<td>3-4-5</td>
<td>111°</td>
<td>112°</td>
<td>112°</td>
<td>115°</td>
<td>124°</td>
</tr>
<tr>
<td>4-5-6</td>
<td>114°</td>
<td>118°</td>
<td>115°</td>
<td>118°</td>
<td>124°</td>
</tr>
<tr>
<td>5-6-1</td>
<td>102°</td>
<td>124°</td>
<td>124°</td>
<td>124°</td>
<td>124°</td>
</tr>
</tbody>
</table>

**Atom numbers correspond to those from Figure 2.**
radical site (labeled carbon 5) display a change in electron density in going from the acyclic structure to the cyclic structure.

In the cyclic heteroatomic systems (structures 2 and 3), the two carbons adjacent to the heteroatom (carbon 1, which was initially the carbenium ion, and carbon 5) bear identical fractional charge. As such, the bonding in the cyclic radical cation does not merely involve the formation of a partial bond between the initial radical and cation sites but also involves partial bonding with neighboring carbons—as evidenced by the fact that in structure 2 the two C--O interatomic distances are equal at 1.40 Å (see Table 2). Both the C--N interatomic distances in Structure 3 are also equal to one another at 1.43 Å, again indicating partial bonding involving more than two atoms.

In structure 1, the carbon atoms that initially bore the isolated radical and the isolated cation possess nearly identical charge. The process again involves electron donation from the carbon that initially bore the radical to that which initially bore the carbenium ion. In this structure, the C6--C1 internuclear distance is 2.01 Å whereas all other C--C interatomic distances are near the conventional 1.54 Å. Thus, the predominant partial bonding is localized between the initial reactive sites, which likely then delocalizes throughout the ring in a similar fashion to the related system shown in Scheme 2. Internal symmetry dictates the observed electron density distribution.

B. ENTHALPIES OF CYCLIZATION AS A FUNCTION OF CHAIN-LENGTH

Three different types of ions are considered here; \( +\text{CH}_2(\text{CH}_2)_n\text{CH}_3, +\text{CH}_2(\text{CH}_2)_n\text{O}, +\text{CH}_2(\text{CH}_2)_n\text{NH} \). The input structures utilized were the delta, epsilon, zeta, and eta distonic ions for each of the three above systems. Table 2 displays the enthalpies of formation for four, five, six and seven membered chains (terminated with the radical site on a carbon,
nitrogen or oxygen) for acyclic and cyclic systems, as well as the gain in energy obtained by cyclization.

For the carbon-based distonic ions, the enthalpic driving force for forming a cyclic intermediate is least when a four membered ring is generated and greatest when a six-membered ring is made. This is reasonable in terms of ring-strain/torsional strain arguments. In assessing the driving-force for the formation of cyclic intermediates from oxygen and nitrogen containing distonic ions, similar internal trends are observed, again in accord with ring strain/torsional strain arguments.

Within the six-membered system, the enthalpic driving force for the cyclization of the nitrogen-containing distonic ion is greater than that for the oxygen by ca. 26 Kcal/mole. Correspondingly, the oxygen-containing distonic ion cyclizes more readily than the all-carbon distonic by ca. 27 Kcal/mole. This trend, that the nitrogen distonic ions have the greatest driving force for cyclization and the all-carbon distonics have the least, is consistent within all systems independent of ring-size. A partial explanation for the observed enthalpies of cyclization is that the lone pairs on the oxygen and nitrogen atoms engage in a stabilizing interaction with the remote carbenium ion, an interaction not possible for the carbocycle. Further, the all-carbon distonic ion (see Figure 2) involves an initial partial bond between C1--C6 that is elongated to 2.01 Å, whereas in both structures 2 and 3, the partial bonding is more readily delocalized.

C. STRUCTURAL COMPARISON OF THE CYCLIC INTERMEDIATES GENERATED UPON CYCLIZATION OF DISTONIC IONS WITH RADICAL CATIONS GENERATED FROM NEUTRAL PRECURSORS

The initial adduct formed when the ethylene oxide radical cation reacts with neutral ethylene oxide is a zeta-distonic ion. This initially formed distonic ion is known to cyclize
Table 2. Enthalpies of Cyclization as a Function of Chain Length. All Enthalpies of Formation are in Kcal/mol were Calculated by Utilizing Am1 Methodology. Absolute Heats of Formation are Reproducible to Within +/- 1% Relative.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Acyclic Ion</th>
<th>Cyclic Ion</th>
<th>Exothermicity To Cyclize</th>
</tr>
</thead>
<tbody>
<tr>
<td>+CH$_2$(CH$_2$)$_2$CH$_2$</td>
<td>237.17</td>
<td>230.32</td>
<td>- 6.85</td>
</tr>
<tr>
<td>+CH$_2$(CH$_2$)$_3$CH$_2$</td>
<td>230.56</td>
<td>211.89</td>
<td>- 18.67</td>
</tr>
<tr>
<td>+CH$_2$(CH$_2$)$_4$CH$_2$</td>
<td>219.62</td>
<td>199.88</td>
<td>- 19.74</td>
</tr>
<tr>
<td>+CH$_2$(CH$_2$)$_5$CH$_2$</td>
<td>216.35</td>
<td>197.10</td>
<td>- 19.25</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_2$O</td>
<td>217.19</td>
<td>201.10</td>
<td>- 16.09</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_3$O</td>
<td>206.31</td>
<td>159.49</td>
<td>- 46.82</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_4$O</td>
<td>197.47</td>
<td>150.92</td>
<td>- 46.55</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_5$O</td>
<td>193.67</td>
<td>147.06</td>
<td>- 46.61</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_2$NH</td>
<td>253.71</td>
<td>212.66</td>
<td>- 41.05</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_3$NH</td>
<td>244.97</td>
<td>174.62</td>
<td>- 70.35</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_4$NH</td>
<td>236.29</td>
<td>163.43</td>
<td>- 72.86</td>
</tr>
<tr>
<td>+CH$_3$(CH$_2$)$_5$NH</td>
<td>228.45</td>
<td>157.83</td>
<td>- 70.62</td>
</tr>
</tbody>
</table>
to an ion equivalent in structure to the radical cation generated directly from 1,4-dioxane. Therefore, it is reasonable to assess whether the cyclic radical ions that are generated upon rearrangement from long-chain distonic ions in this investigation are similar to the corresponding radical ions generated from cyclic neutral precursors. The enthalpies of formation for each of the four, five, six, and seven-membered cyclic structures that are formed via rearrangement from long-chain distonic ions, and the corresponding radical ions generated upon direct ionization of the appropriate cyclic precursor, are found in Table 3.

The thermodynamic data clearly show that the cyclic radical cations that arise from the long-chain distonic radical cations are very similar to the radical cations generated directly from ionization of the cyclic analog. Further, the conformations of both ions are nearly identical in virtually every case, as are each of the interatomic distances, and the partial charges on each atom.

D. ISOMERIZATIONS OF LONG-CHAIN DISTONIC RADICAL CATIONS TO CYCLIC RADICAL CATIONS AS A FUNCTION OF 1° VS. 2° VS. 3° CARBENIUM/RADICAL STRUCTURE

The relative stability of the cation site within the acyclic distonic radical cation directly affects the enthalpy for cyclization of the distonic radical cation. Within the six-membered all-carbon system, the enthalpic driving force for the cyclization of a 1° carbenium ion with a 1° radical is 25.15 Kcal/mol greater than that of a 2° carbocation with a 1° radical, which is 10.10 Kcal/mol more exothermic than that for a 3° carbocation with a 1° radical (see Table 4). The cyclization of the 3° carbocation with the 1° radical is endothermic.

When the carbenium ion is held constant (as a 1° ion) and the structure of the radical is altered from 1° to 2° to 3°, the enthalpic driving force for cyclization also decreases. The cyclization of the 1° radical is ca. 16 Kcal/mol more exothermic than the 2° radical cyclization, which is ca. 2 Kcal/mol more exothermic than that for the 3° radical.
Table 3. Comparison of Enthalpies of Distonic Ion Precursor, the Cyclic Radical Ion Generated via Rearrangement from the Distonic Ion Precursor, and the Corresponding Radical Ion Generated from a Neutral Precursor. All Calculations by AM1 Methodology. All Enthalpies of Formation are Reported in Kcal/mol, and are Reproducible to Within +/- 1% Relative.

<table>
<thead>
<tr>
<th>Initial Distonic Ion</th>
<th>Enthalpy of Rearranged Cycle</th>
<th>Cyclic Neutral Precursor</th>
<th>Enthalpy of Cyclic Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{CH}_2$</td>
<td>230.32</td>
<td>cyclobutane</td>
<td>234.87</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{CH}_2$</td>
<td>211.89</td>
<td>cyclopentane</td>
<td>210.40</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{CH}_2$</td>
<td>199.88</td>
<td>cyclohexane</td>
<td>199.27</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{CH}_2$</td>
<td>197.10</td>
<td>cycloheptane</td>
<td>196.65</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{O}$</td>
<td>201.10</td>
<td>propylene oxide</td>
<td>201.09</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_3\text{O}$</td>
<td>159.49</td>
<td>tetrahydrofuran</td>
<td>159.06</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_3\text{O}$</td>
<td>150.92</td>
<td>terahydropyran</td>
<td>150.61</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_3\text{O}$</td>
<td>145.86</td>
<td>oxacycloheptane</td>
<td>145.56</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{NH}^-$</td>
<td>212.66</td>
<td>azetidine</td>
<td>212.57</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{NH}^-$</td>
<td>174.62</td>
<td>pyrrolidine</td>
<td>174.59</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_2\text{NH}^-$</td>
<td>163.43</td>
<td>piperidine</td>
<td>163.13</td>
</tr>
<tr>
<td>$\text{+CH}_2(\text{CH}_2)_3\text{NH}$</td>
<td>157.83</td>
<td>azacycloheptane</td>
<td>157.51</td>
</tr>
</tbody>
</table>
That the less stable (primary) carbenium ion has a greater driving force than the more stable (secondary and tertiary) carbenium ions, is in accord with the axiom that reactivity is inversely related to stability. This axiom also governs the observed trends for the $1^\circ$ vs. $2^\circ$ vs. $3^\circ$ radical cyclizations. That the differences in exothermicity for cyclization are larger when going from a $1^\circ \rightarrow 2^\circ \rightarrow 3^\circ$ cation (while holding the radical constant) than they are in going from a $1^\circ \rightarrow 2^\circ \rightarrow 3^\circ$ radical (while holding the cation constant), is reasonable in light of the relative differences in the stabilities of the isolated intermediates themselves.

E. ENTHALPIES OF CYCLIZATION IN ALLYLIC AND BENZYLIC SYSTEMS

Stabilization of the radical and cation in secondary and tertiary systems lowers the cyclization energetics. As an extension then, what effect does the stabilization of the radical and/or cation sites by resonance delocalization in allylic and benzylic systems have on cyclization energetics?

Acyclic distonic ion 4 with an allylic cation cyclizes either to ion 5 or ion 6, with gains of ca. 32 and ca. 17 Kcal/mol, respectively. It should be noted that ions 5 and 6 possess the same heats of formation, spin/electron distributions, and geometries as the ions generated via the loss of an electron from their corresponding models --- cycloheptene and allylcyclopentane. Ion 7 possesses a delocalized benzylic cation with a suitably disposed $1^\circ$ radical set up to cyclize to non-distonic ion 8. The thermodynamic driving force to cyclize is ca. 21 Kcal/mol. Hence, both allyl and benzyl systems will cyclize even though the initial ion is delocalized.

F. THERMODYNAMICS OF CONFORMATIONALLY RESTRICTED LONG-CHAIN DISTONIC IONS

That a thermodynamic driving force for cyclization exists for each of the aforementioned systems raises the question of whether any long-chain distonic ions would
Table 4. Comparison of the Enthalpic Driving Force for Cyclization as a Function of 1° Vs. 2° Vs. 3° Carbenium Ion (Holding the Radical Constant and 1°) for Three Series of Long-chain Distonic Ions. All Calculations by AM1 Methodology. All Heats of Formation are in Kcal/mol and are Reproducible to Within +/- 1% Relative.

<table>
<thead>
<tr>
<th>ACYCLIC DISTONIC ION STRUCTURE</th>
<th>H_f FOR ACYCLIC DISTONIC</th>
<th>H_f FOR PSEUDO-CYCLE</th>
<th>Exothermicity To Cyclize</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="Image1" alt="Distonic ION STRUCTURE" /></td>
<td>221.47</td>
<td>186.04</td>
<td>-35.43</td>
</tr>
<tr>
<td><img src="Image2" alt="Distonic ION STRUCTURE" /></td>
<td>199.26</td>
<td>183.29</td>
<td>-15.97</td>
</tr>
<tr>
<td><img src="Image3" alt="Distonic ION STRUCTURE" /></td>
<td>185.75</td>
<td>185.91</td>
<td>+0.16</td>
</tr>
<tr>
<td><img src="Image4" alt="Distonic ION STRUCTURE" /></td>
<td>211.92</td>
<td>178.33</td>
<td>-33.59</td>
</tr>
<tr>
<td><img src="Image5" alt="Distonic ION STRUCTURE" /></td>
<td>191.80</td>
<td>183.36</td>
<td>-8.44</td>
</tr>
<tr>
<td><img src="Image6" alt="Distonic ION STRUCTURE" /></td>
<td>178.87</td>
<td>180.53</td>
<td>+1.66</td>
</tr>
<tr>
<td><img src="Image7" alt="Distonic ION STRUCTURE" /></td>
<td>207.36</td>
<td>179.93</td>
<td>-27.43</td>
</tr>
<tr>
<td><img src="Image8" alt="Distonic ION STRUCTURE" /></td>
<td>185.17</td>
<td>179.73</td>
<td>-5.44</td>
</tr>
<tr>
<td><img src="Image9" alt="Distonic ION STRUCTURE" /></td>
<td>173.13</td>
<td>175.01</td>
<td>+1.88</td>
</tr>
</tbody>
</table>
Figure 3. Structures and energies of allylic and benzylic long-chain distonic ions.

4 (219.90)  

5 (188.27)  

6 (202.74)  

7 (220.64)  

8 (199.63)  

9 (285.27)
exist as stable entities. Radical ion 9, an eta distonic ion, with an internal alkyne at the three position is conformationally restricted such that carbons one and six are too remote to interact. The global minimum for ion 9 corresponds to a heat of formation of 285 Kcal/mol with a C1-C6 through space distance of ca. 5.5 Å. The entire radical character resides on C6 while the carbenium ion character is localized at C1 such that ion 9 is a true distonic ion. When C1 and C6 are forced into proximity (C1-C6 = 1.5 to 2.0 Å) so that the radical and cation sites can interact (mimicking the cyclization processes discussed above), the heat of formation actually increases to between 296 and 328 Kcal/mol, depending upon C1-C6 distance. Therefore, the stabilization gained by delocalization of the radical and cation is less than the extent of destabilization associated with altering the geometry of the alkyne.
IV. CONCLUSIONS

If a distonic radical cation is generated (via ion/molecule reaction, dissociation, etc.) and possesses sufficient radical/charge separation (i.e., being a delta, epsilon, zeta, or eta distonic), it will be an exceedingly transient species that will rapidly adopt a non-distonic cyclic structure via intramolecular isomerization. The driving force for isomerization stems from an initial stabilizing interaction between radical and cation sites brought into proximity during cyclization. Upon having cyclized, charge and radical sites are delocalized. The structure of the non-distonic cyclic intermediate formed is very similar to the radical cation generated directly from the analogous cyclic neutral molecule. The thermodynamic driving force for cyclization, as calculated via semi-empirical AM1 methodology, is a function of the size of the cyclic ring formed, the identity of the atom bearing the radical (C, O, or N), and the extent of substitution and/or resonance delocalization of the radical and cation sites in the original distonic ion.

Cyclization of long-chain distonic radical cations were found to be endothermic in two cases. The first is when a 3° cation is involved. Lack of cyclization in this case is likely due to the combination of distonic ion stability and steric hindrance to cyclization. The second case is when the long-chain distonic ion is conformationally restricted such that bringing the ion and radical sites within suitable proximity to interact unduly places geometric strain upon the system.
These computational results are in accord with the experimental finding that the initial adduct formed in the reaction of the ethylene oxide radical cation with its own neutral, a zeta-distonic ion, cyclizes to a non-distonic cyclic radical ion. Finally, it is likely that these computations predict well the behavior of gaseous intermediates, where radical and ion sites are not solvated. These predictions, however, do not necessarily relate to distonic ions formed in the presence of solvent.
V. BIBLIOGRAPHY

Part 1


**Part 2**


Part 3


19) Part 2.