# The Gas-Phase Meerwein Reaction

**Luiz Alberto B. Moraes and Marcos N. Eberlin***[a]

**Abstract:** A systematic investigation of a novel epoxide and thioepoxide ring expansion reaction promoted by gaseous acylium and thioacylium ions is reported. As ab initio calculations predict, and $^{18}$O-labeling and MS$^3$ pentaquadrupole experiments demonstrate, the reaction proceeds by initial O(S)-acylation of the (thio)epoxides followed by rapid intramolecular nucleophilic attack that results in three-to-five-membered ring expansion, and forms cyclic 1,3-dioxolanylium, 1,3-oxathiolanylium, or 1,3-dithiolanylium ions. This gas-phase reaction is analogous to a condensed-phase reaction long since described by H. Meerwein (*Chem. Ber.* **1955**, *67*, 374), and is termed as "the gas-phase Meerwein reaction"; it occurs often to great extents or even exclusively, but in some cases, particularly for the most basic (thio)epoxides and the most acidic (thio)acylium ions, proton transfer (eventually hydride abstraction) competes efficiently, or even dominates. When (thio)epoxides react with (thio)acylium ions, the reaction promotes O(S)-scrambling; when epoxides react with thioacylium ions and the adducts are dissociated, it promotes S/O replacement. An analogous four-to-six-membered ring expansion also occurs predominantly in reactions of trimethylene oxide with acylium and thioacylium ions.

**Keywords:** epoxides · thioepoxides · acylium ions · thioacylium ions · ion – molecule reactions · mass spectrometry

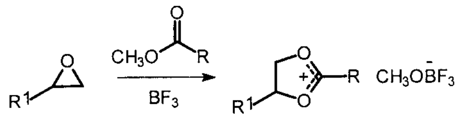
## Introduction

Epoxides are common reagents, and key intermediates in a variety of synthetically important reactions.[1] The high strain of their three-membered rings makes epoxides very reactive, particularly by ring-opening, a process often accelerated by acid catalysis that increases, through O-coordination, the electrophilicity of the ring carbon atoms and the lability of C–O ring bonds.

Ring-opening of epoxides is generally assisted by the attack of an external nucleophile, but nucleophilic sites suitably positioned on the epoxide molecule may also participate, as exemplified by the isomerization of epoxides to aldehydes or ketones through intramolecular hydride ion attack,[1] the rearrangement of acetoxy epoxydes to $\alpha$-acetoxy ketones,[2] and the ring expansion of epoxyesters to six-membered lactones.[3]

Nucleophilic sites of intermediates formed by electrophilic attack at the ring oxygen may also assist ring-opening, and promote the expansion of the epoxide ring. For instance, as first reported by Bogert and Roblin,[4a] aldehydes and ketones react efficiently with epoxides to form 1,3-dioxolanes by three-to-five-membered ring expansion.[4] The reaction is promoted by Lewis acids that coordinate with the carbonyl compound thus facilitating binding to the epoxide; 1,3-dioxolanes are formed by fast intramolecular nucleophilic attack.

In 1955 H. Meerwein[5] reported an interesting variant of the three-to-five-membered ring expansion reaction of epoxides, namely, the reaction of epoxides with esters in the presence of $BF_3$ that form 1,3-dioxolanylium ion salts (Scheme 1).



Scheme 1.

The resonance-stabilized 1,3-dioxolanylium ion may be formed by initial nucleophilic addition of the epoxide to the $BF_3$/ester complex, followed by ring expansion promoted by intramolecular nucleophilic attack, and elimination of $CH_3OBF_3^-$ (Scheme 2).

Alternatively, acylium ion intermediates (Scheme 3 reaction (1)) may O-acylate the epoxide, and promote ring expansion by intramolecular nucleophilic attack (Scheme 3 reaction (2)).

In these alternative mechanisms, the key intermediate is either an acylium ion or ions (the two isomeric $BF_3$ O-coordinated carbonyl compounds) that are adequately mimicked by an acylium ion ($\mathrm{R{-}\overset{+}{C}{=}O}$).

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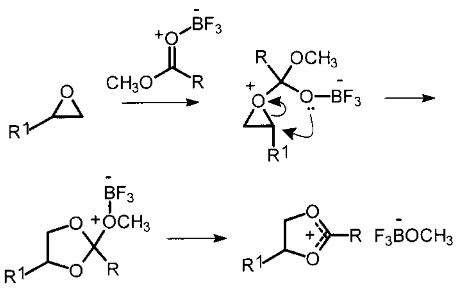
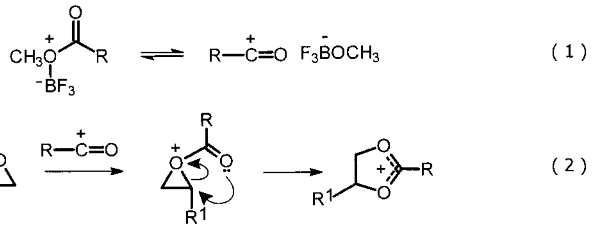
[a] M. N. Eberlin, L. A. B. Moraes
State University of Campinas - UNICAMP
Institute of Chemistry
CP6154 13083 – 970 Campinas, SP (Brazil)
Fax: (+55) 19-788-3073
E-mail: eberlin@iqm.unicamp.br



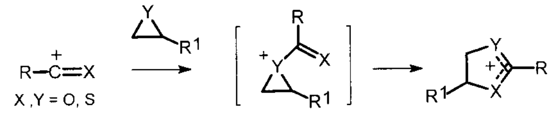
Scheme 2.



Scheme 3.

In the condensed phase, acylium ions[6] are important and highly reactive reaction intermediates, but their detection or trapping is often not a simple task. In the gas phase, however, acylium ions and their sulfur analogues, the thioacylium ions $(R\overset{+}{C}C{=}S)$, are easily formed, easily isolated, and very stable.[6] Acylium and thioacylium ions also display a rich reactivity in the gas phase:[7–10] for instance, with conjugated dienes, gaseous acylium and thioacylium ions undergo $[4+2^+]$ polar cycloaddition;[8] with cyclic acetals and ketals, transacetalization;[9] and with diols and analogues, ketalization.[10] This unique reactivity characterize gaseous acylium ions, and distinguish them from both isomeric and isobaric species.[8–10]

We recently reported for distonic acylium ions[9e] that the gas-phase reactivity of acylium ions also includes three-to-five-membered ring expansion of epoxides by O-acylation (Scheme 4), and termed the reaction as "the gas-phase Meerwein reaction"[11] for it is analogous to that reported by H. Meerwein[5] and forms the same 1,3-dioxolanylium ions. We now report on a systematic experimental and theoretical study of this novel reaction, in which several gaseous acylium and thiacylium ions were allowed to react with epoxides, thioepoxides, and larger O-heterocycles; the structures of the resulting products were investigated by $^{18}$O-labeling, MS$^3$ experiments, and ab initio calculations.



Scheme 4.

## Methods

The gaseous ions were produced and allowed to react, and their products analyzed, by double- or triple-stage (MS$^3$) mass spectrometric experiments performed with an Extrel (Pittsburgh, PA) pentaquadrupole mass spectrometer.[12] The instrument, denoted $Q_1q_2Q_3q_4Q_5$, is composed of a sequential arrangement of three mass analyzing (Q1, Q3, Q5) and two "rf-only" ion-focusing reaction quadrupoles (q2, q4). By 70 eV electron ionization (EI), appropriate precursors form the reactant acylium ions: acetone forms $CH_3{-}\overset{+}{C}{=}O$; $^{18}$O-acetone (ISOTEC, 99 % $^{18}$O), $CH_3{-}\overset{+}{C}{=}{}^{18}O$; cyclopentanone, $CH_2{=}CH{-}\overset{+}{C}{=}O$; acetophenone, $Ph{-}\overset{+}{C}{=}O$; tetramethylurea, $(CH_3)_2N{-}\overset{+}{C}{=}O$; tetramethylthiourea, $(CH_3)_2N{-}\overset{+}{C}{=}S$, and thioacetamide, $CH_3{-}\overset{+}{C}{=}S$. When performing ion–molecule reactions, the ion of interest was mass-selected by Q1 for further reactions in q2 with a neutral reagent. Ion translational energies were set to near 1 eV as calibrated by the $m/z$ 39 to $m/z$ 41 abundance ratio in neutral ethylene/ionized ethylene reactions.[13]

Product ion mass spectra were acquired by scanning Q5, while operating Q3 and q4 in the broad band rf-only mode. The target gas pressures in q2 caused typical beam attenuations of 50–70 %, namely, multiple collision conditions were used, which increases reaction yields and promotes collisional quenching of both the reactant and product ions.[14]

For the MS$^3$ experiments,[14, 15] Q3 was used to mass-select a q2 product ion of interest for further 15 eV collision dissociation with argon in q4, while scanning Q5 to acquire the spectra. The 15 eV collision energies were taken as the voltage difference between the ion source and the collision quadrupoles. The indicated pressures in each differentially pumped region were typically $2 \times 10^{-6}$ (ion-source), $8 \times 10^{-6}$ (q2) and $8 \times 10^{-5}$ Torr (q4), respectively.

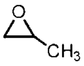
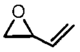
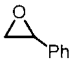
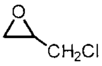
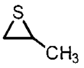
Energies and optimized geometries of the species were obtained by molecular orbital calculations run on Gaussian98 (Gaussian, Inc., Pittsburgh, PA).

## Results and Discussion

**Epoxides and thioepoxides**: Table 1 summarizes the major products (and relative abundances) arising from reactions of mass-selected acylium or thioacylium ions ($A^+$) with neutral epoxides or thioepoxides ($M$). The reactions most often yield the ion–molecule adduct $(MA)^+$, or the protonated neutral molecule $(M{+}H)^+$,[16] or both; and eventually $(M-H)^+$, formally, the hydride abstraction product. As calculations predict, and MS$^3$ experiments and $^{18}$O-labeling demonstrate (see the following sections), the adducts $(MA)^+$ are the products of the gas-phase Meerwein reaction (Scheme 4), that is, the respective cyclic 1,3-dioxolanylium ions or their mono- or disulfur analogues.

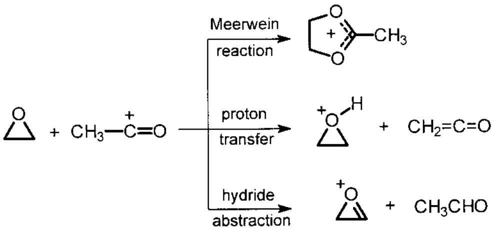
From the results summarized in Table 1, some general reactivity trends are noted. For the gas-phase Meerwein reaction, $Ph{-}\overset{+}{C}{=}O$ and $(CH_3)_2N{-}\overset{+}{C}{=}O$ are the most reactive ions; they form mainly $(M{+}A)^+$ with all epoxides and thioepoxides tested (Table 1). For epoxides reacting with acylium ions, ethylene oxide and epichlorohydrin are the most reactive; however, their reactivity with thioacylium ions is limited. Propylene oxide, butadiene oxide, and styrene oxide also react promptly by the gas-phase Meerwein reaction, particularly with $Ph{-}\overset{+}{C}{=}O$, $(CH_3)_2N{-}\overset{+}{C}{=}O$, and $(CH_3)_2N{-}\overset{+}{C}{=}S$; with the proton-donor ions $CH_3{-}\overset{+}{C}{=}O$, $CH_2{=}CH{-}\overset{+}{C}{=}O$, and $CH_3{-}\overset{+}{C}{=}S$,[17] however, these epoxides act mostly as bases favoring proton transfer, whereas propylene oxide also readily transfer a hydride. For the thioepoxides, ethylene sulfide undergoes the gas-phase Meerwein reaction efficiently only with $Ph{-}\overset{+}{C}{=}O$ and $(CH_3)_2N{-}\overset{+}{C}{=}O$; propylene sulfide, in contrast, reacts to great a extent with all acylium and thioacylium ions except $CH_3{-}\overset{+}{C}{=}O$. These different reactivities likely result from the competition between the three

Table 1. Major ionic products [$m/z$ (relative abundance)] formed in reactions of mass-selected acylium or thioacylium ions with epoxides or thioepoxides. Products are identified as follow: the ion–molecule adduct $(M{+}A)^+$, that is, the cyclic 1,3-dioxolanylium ions or their sulfur or disulfur analogues formed by the gas-phase Meerwein reaction; the protonated molecule $[(M{+}H)^+]$[a]; and the hydride abstraction product $[(M-H)^+]$.

| |  | | |  | | |  | | |  | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ |
| $CH_3{-}\overset{+}{C}{=}O$ | 87(100) | 45(4) | 43(6) | none | 59(54) | 57(100) | none | 71(100) | none | none | 121(100) | none |
| $H_2C{=}CH\overset{+}{C}{=}O$ | 99(100) | 45(28) | 43(3) | none | 59(21) | 57(100) | none | 71(100) | none | none | 121(100) | none |
| $Ph{-}\overset{+}{C}{=}O$ | 149(100) | 45(1) | none | 163(100) | none | none | 175(100) | 71(13) | none | 225(100) | 121(5) | none |
| $(CH_3)_2N{-}\overset{+}{C}{=}O$ | 116(100) | 45(6) | 43(7) | 130(100) | 59(1) | 57(4) | 142(100) | 71(9) | none | 192(100) | 121(2) | none |
| $CH_3{-}\overset{+}{C}{=}S$ | none | 45(100) | 43(5) | 117(4) | 59(62) | 57(100) | none | 71(100) | none | none | 121(100) | 119(3) |
| $(CH_3)_2N{-}\overset{+}{C}{=}S$ | 132(4) | 45(100) | 43(1) | 146(100) | none | none | 158(100) | none | none | 208(100) | 121(7) | 119(4) |
| |  | | |  | | |  | | | | | |
| | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^{+[a]}$ | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ | $(M{+}A)^+$ | $(M{+}H)^+$ | $(M-H)^+$ | | | |
| $CH_3{-}\overset{+}{C}{=}O$ | 135(100) | 57(72) | none | none | 61(100) | 59(1) | none | 75(100) | 73(1) | | | |
| $H_2C{=}CH\overset{+}{C}{=}O$ | 147(100) | 57(83) | none | 115(15) | 61(100) | 59(2) | 129(100) | 75(28) | 73(1) | | | |
| $Ph{-}\overset{+}{C}{=}O$ | 197(100) | none | none | 165(100) | 61(37) | none | 179(100) | 75(21) | 73(1) | | | |
| $(CH_3)_2N{-}\overset{+}{C}{=}O$ | 164(100) | none | none | 132(100) | none | none | 146(100) | 75(1) | none | | | |
| $CH_3{-}\overset{+}{C}{=}S$ | 151(28) | 57(100) | none | none | 61(100) | nd[c] | 133(100) | 75(45) | none | | | |
| $(CH_3)_2N{-}\overset{+}{C}{=}S$ | none | 57(100) | none | none | 61(100) | 59(3) | 162(100) | 75(21) | none | | | |

[a] The relative abundance of the proton bound dimer $(M\cdots H^+\cdots M)$, observed sparsely, was also summed into that of $(M{+}H)^+$. [b] Protonated epichlorohydrin loses HCl to form an ion of $m/z$ 57, and this ion, perhaps the acylium ion $C_2H_5\overset{+}{C}O^+$,[9] reacts further with epichlorohydrin to form an adduct of $m/z$ 149/151. [c] For ethylene sulfide, the $(M-H)^+$ product is isobaric ($m/z$ 59) with $CH_3{-}\overset{+}{C}{=}S$.

major reactions (as exemplified in Scheme 5), that is, from changes in the acidity, hydride affinity, and electrophilicity of the ions as well as in the nucleophilicity and basicity of the neutral (thio)epoxides.



Scheme 5.

Figure 1 exemplifies the product spectra for reactions of: a) $Ph{-}\overset{+}{C}{=}O$ with epichlorohydrin; b) $(CH_3)_2N{-}\overset{+}{C}{=}O$ with propylene sulfide; c) $(CH_3)_2N{-}\overset{+}{C}{=}S$ with propylene epoxide; and d) $CH_2{=}CH{-}\overset{+}{C}{=}O$ with ethylene oxide. For the three first pairs of reactants, the gas-phase Meerwein reaction is highly favored (Figures 1a–c); the adducts (the respective 1,3-dioxolanylium or 1,3-oxathiolanylium ions) are formed in high yields (high ion conversion to products), and nearly exclusively. The acylium ion $CH_2{=}CH{-}\overset{+}{C}{=}O$ (Figure 1c) also undergoes the gas-phase Meerwein reaction to a great extent forming the cyclic 1,3-dioxolanylium ion of $m/z$ 99, but this more acidic[17] ion also reacts to a minor extent with ethylene oxide by proton transfer ($m/z$ 45) and hydride abstraction ($m/z$ 43).

**Structural characterization**: (Thio)acylium ions may form adducts with neutral (thio)epoxides more likely by: a) simple O(S)-acylation, or b) O(S)-acylation followed by rapid three-to-five-membered ring expansion (the gas-phase Meerwein reaction; Scheme 4). To verify which process dominates, and which product ion is formed, triple-stage (MS$^3$) mass spectra and $^{18}O$-labeling were applied.

**MS$^3$**: Figure 2 compares sequential product ion mass spectra collected after collision-induced dissociation (CID) of some representative adduct ions. The $(CH_3)_2N{-}\overset{+}{C}{=}O$/propylene sulfide adduct dissociates to regenerate exclusively the $(CH_3)_2N{-}\overset{+}{C}{=}O$ reactant ion (Figure 2a). This dissociation is typical of the cyclic 1,3-dioxolanylium ions[9] expected for the gas-phase Meerwein reaction, but not distinctive since the primary simple O-acylation products are expected to dissociate similarly.

However, the $(CH_3)_2N{-}\overset{+}{C}{=}S$/propylene oxide adduct (Figure 2b) dissociates, differently, and by a structurally revealing pathway; it does not regenerate the reactant ion $(CH_3)_2N{-}\overset{+}{C}{=}S$, but dissociates to form predominantly the O-analogue acylium ion $(CH_3)_2N{-}\overset{+}{C}{=}O$. Reaction of $(CH_3)_2N{-}\overset{+}{C}{=}S$ with propylene oxide followed by CID of the adduct results, therefore, in the conversion of $(CH_3)_2N{-}\overset{+}{C}{=}S$ to $(CH_3)_2N{-}\overset{+}{C}{=}O$, that is, in the replacement of sulfur by oxygen (S/O). This reaction/dissociation sequence is structurally revealing since it can only be rationalized assuming the three-to-five-membered ring expansion, S/O scrambling mechanism of the gas-phase Meerwein reaction, and that common (most likely positional isomers, see below) 1,3-oxathiolanylium ions are formed for both analogous acylium ion/thioepoxide and thioacylium ion/epoxide reactions (Scheme 6). Note that, if the loss of a neutral thioepoxide

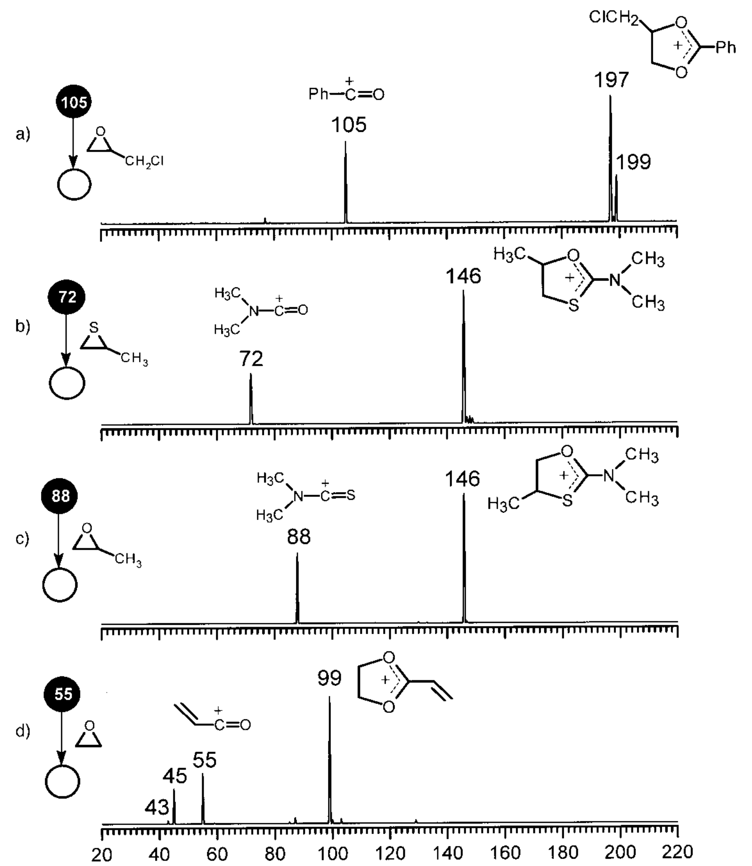


Figure 1. Double-stage (MS$^2$) product ion mass spectra for reactions of: a) Ph–$\overset{+}{C}$=O of *m/z* 105 with epichlorohydrin; b) $(CH_3)_2N$–$\overset{+}{C}$=O of *m/z* 72 with propylene sulfide; c) $(CH_3)_2N$–$\overset{+}{C}$=S of *m/z* 88 with propylene oxide; and d) $CH_2$ = CH–$\overset{+}{C}$=O of *m/z* 55 with ethylene oxide.

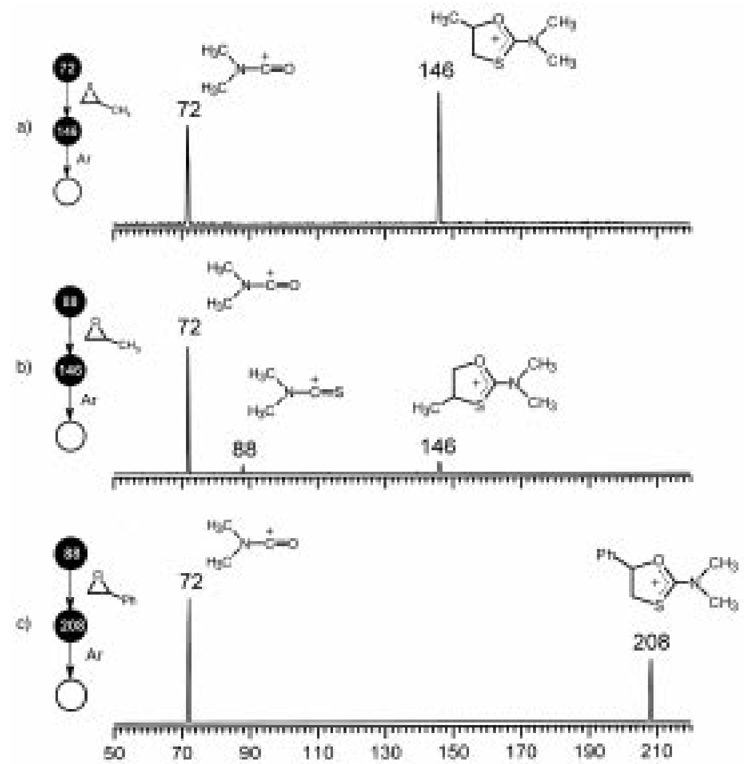
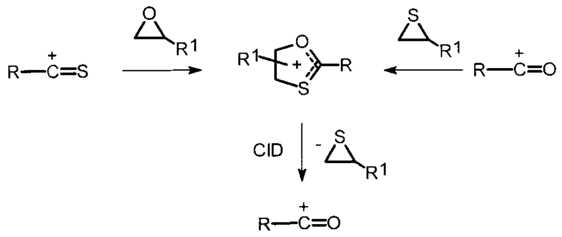


Figure 2. Triple-stage (MS$^3$) sequential product ion mass spectra for the adducts formed in reactions of: a) $(CH_3)_2N$–$\overset{+}{C}$=O with propylene sulfide; b) $(CH_3)_2N$–$\overset{+}{C}$=S with propylene oxide; and c) $(CH_3)_2N$–$\overset{+}{C}$=S with styrene oxide.

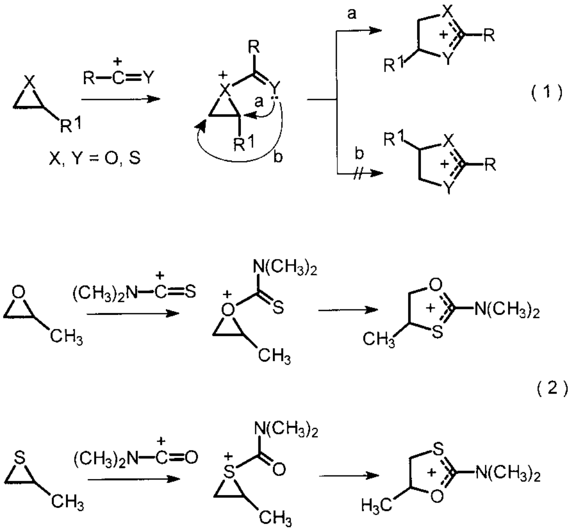


Scheme 6.

molecule is assumed, S/O replacement occurs for both the reactant thioacylium ion and the neutral epoxide.[18]

Additional evidence for the gas-phase Meerwein reaction is gained by dissociating the $(CH_3)_2N$–$\overset{+}{C}$=S/styrene oxide adduct. S/O replacement[19] occurs to completion, and the O-analogue ion $(CH_3)_2N$–$\overset{+}{C}$=O is formed exclusively (Figure 2c).

In reactions of (thio)acylium ions with monosubstituted (thio)epoxides, two isomeric cyclic ions could be formed since intramolecular nucleophilic attack may occur at both the substituted and unsubstituted ring carbons (X$\neq$Y in Scheme 7, reaction (1)). Often, however, the nucleophile attacks the more substituted carbon in acid-catalyzed cleavages of epoxides;[1] hence, pathway (a) is expected to dominate. Therefore, two major positional isomers are expected to form when reacting analogous pairs of acylium ion/thioepoxide and thioacylium ion/epoxide, as exemplified for $(CH_3)_2N$–$\overset{+}{C}$=O/propylene sulfide and $(CH_3)_2N$–$\overset{+}{C}$=S/propylene oxide in Scheme 7, reactions (2).



Scheme 7.

Preferential attack at the more substituted carbon and formation of positional isomers (Scheme 7, reaction (2)) may explain, therefore, the similar, but not identical, CID behavior of the $(CH_3)_2N$–$\overset{+}{C}$=O/propylene sulfide (Figure 2a) and

$(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$/propylene oxide adducts (Figure 2b). For the $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$/propylene oxide adduct, the 4-methyl substituent may facilitate cleavage of the vicinal C–S bond resulting in minor dissociation to $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$ (Figure 2b).

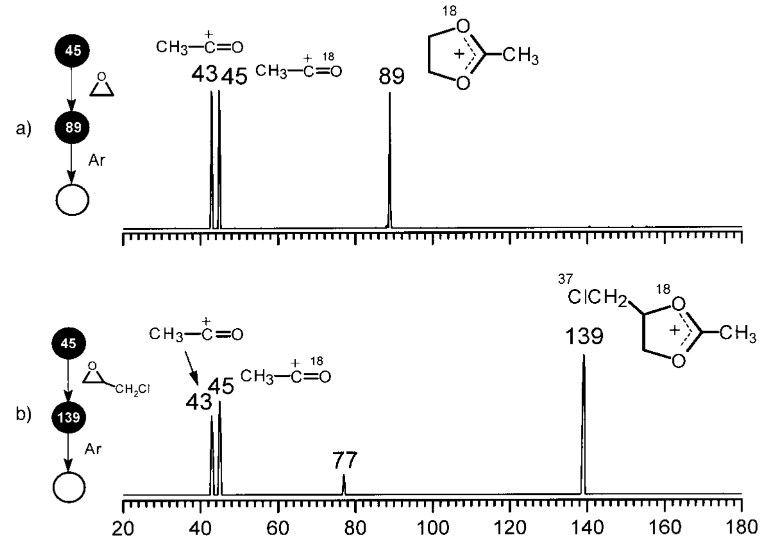
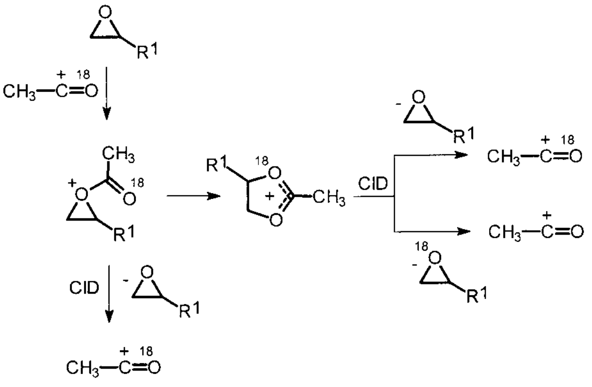


Figure 3. Triple-stage (MS$^3$) sequential product mass ion spectra for the adducts formed in reactions of $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ with: a) ethylene oxide, and b) $^{37}$Cl-epichlorohydrin.

**$^{18}$O-labeling**: To test the complete scrambling of the oxygens, from both the acylium ion and the epoxide, that the gas-phase Meerwein reaction should promote, an $^{18}$O-labeled acylium ion, $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$, was used (Scheme 8). Upon CID, the primary O-acylated $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$/epoxide adduct should dissociate to regenerate exclusively the labeled reactant ion $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$; in contrast, the cyclic 1,3-dioxolanylium ion with scrambled oxygen atoms formed by the gas-phase Meerwein reaction should dissociate to nearly the same extents (if substituent effects for R$^1$ other than H and $^{16}O/^{18}O$ isotope effects are neglected) to form both the labeled $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ and the unlabeled $CH_3\text{–}\overset{+}{C}\text{=}O$ ions.



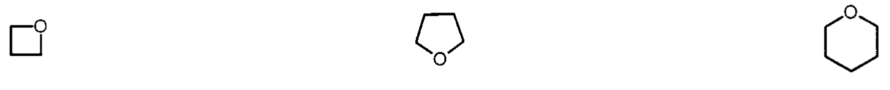
Scheme 8.

Figure 3 shows the sequential product ion mass spectra of the $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ adducts of ethylene oxide and $^{37}$Cl-epichlorohydrin. When the two $^{18}$O-labeled adducts dissociate, both $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ and $CH_3\text{–}\overset{+}{C}\text{=}O$ are formed, and to quite similar extents; this dissociation confirms complete oxygen-scrambling, and that the ring expansion gas-phase Meerwein reaction dominates.

**Larger O-heterocycles**: The ability of acylium ions to promote analogous ring-expansions of larger O-heterocycles was also investigated. Table 2 lists the major products formed when $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$, $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$, and $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ react with trimethylene oxide, tetrahydrofuran, or tetrahydropyran, whereas Figure 4 exemplifies the product ion mass spectra for reactions of trimethylene oxide with $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$ and $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$.

Trimethylene oxide forms adducts to great extents with $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$ and $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$, and to a medium extent with $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$. Tetrahydrofuran forms an adduct to a great extent with $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$, but fails to form adducts with both $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$ and $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$. Tetrahydropyran forms an adduct to a great extent with $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$, and to minor extents with both $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$ and $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$.

Table 2. Major ionic products [*m/z* (relative abundance)] formed in reactions of mass-selected acylium or thioacylium ions with some O-heterocycles. Products are identified as follow: the ion–molecule adduct $(M+A)^+$, that is, the cyclic 1,3-dioxolanylium ions or their sulfur or disulfur analogues formed by the gas-phase Meerwein reaction; the protonated molecule $[(M+H)^+]$,[a] and the hydride abstraction product $[(M-H)^+]$.



| | $(M+A)^+$ | $(M+H)^+$ | $(M-H)^+$ | $(M+A)^+$ | $(M+H)^+$ | $(M-H)^+$ | $(M+A)^+$ | $(M+H)^+$ | $(M-H)^+$ |
|---|---|---|---|---|---|---|---|---|---|
| $(CH_3)_2N\text{–}\overset{+}{C}\text{=}O$ | 130(100) | none | none | 144(100) | 73(13) | 71(2) | 158(100) | 87(8) | 85(2) |
| $(CH_3)_2N\text{–}\overset{+}{C}\text{=}S$ | 146(100) | none | none | none[b] | 73(100) | 71(28) | 174(6) | 87(100) | 85(18) |
| $CH_3\text{–}\overset{+}{C}\text{=}{}^{18}O$ | 103(21) | 59(100) | 57(1) | none | 73(100) | 71(23) | 131(2) | 87(100) | 85(5) |

[a] The abundance of the proton bound dimer $(M\cdots H^+\cdots M)$, observed sparsely, was also summed into that of $(M+H)^+$. [b] Also with $CH_3\text{–}\overset{+}{C}\text{=}S$, tetrahydrofuran forms no stable adduct.

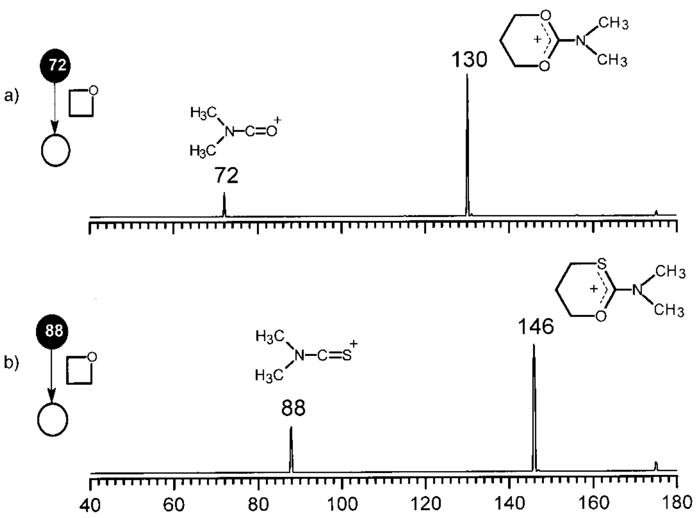
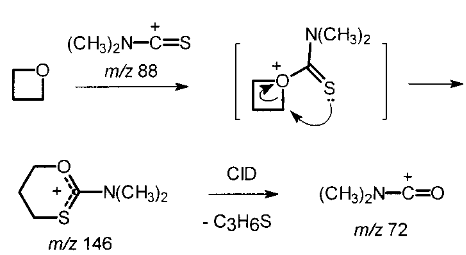


Figure 4. Double-stage ($MS^2$) product ion mass spectra for reactions with trimethylene oxide of: a) $(CH_3)_2N{-}\overset{+}{C}{=}O$ of *m/z* 72 and b) $(CH_3)_2N{-}\overset{+}{C}{=}S$ of *m/z* 88.

**$MS^3$**: Figure 5 collects the CID sequential product ion mass spectra of the $(CH_3)_2N{-}\overset{+}{C}{=}S$/trimethylene oxide and $(CH_3)_2N{-}\overset{+}{C}{=}S$/tetrahydropyran adducts. An analogous four-to-six-membered ring expansion, S/O scrambling reaction (Scheme 9) must then occur predominantly for trimethylene oxide since the O-analogue ion $(CH_3)_2N{-}\overset{+}{C}{=}O$ is nearly the exclusive fragment in the triple-stage mass spectrum of its $(CH_3)_2N{-}\overset{+}{C}{=}S$ adduct (Figure 5a).

Tetrahydropyran fails, however, to undergo analogous six-to-eight-membered ring expansion in reactions with $(CH_3)_2N{-}\overset{+}{C}{=}S$ since its $(CH_3)_2N{-}\overset{+}{C}{=}S$ adduct (most likely the simple O-acylated ion) dissociates to regenerate exclusively the reactant ion $(CH_3)_2N{-}\overset{+}{C}{=}S$ (Figure 5b).



Scheme 9.

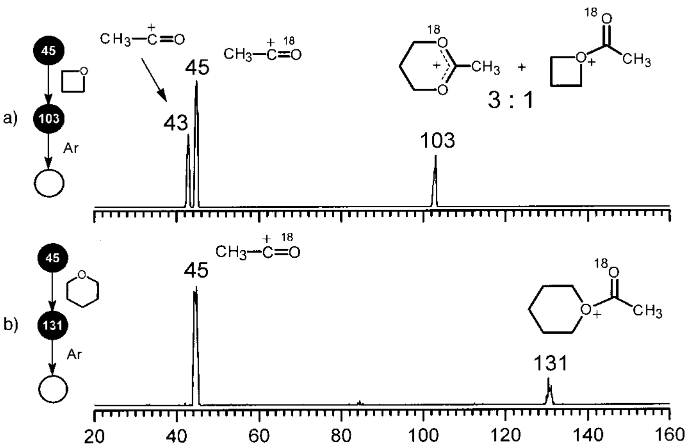


Figure 6. Triple-stage ($MS^3$) sequential product ion spectra for the adducts formed in reactions of $CH_3{-}\overset{+}{C}{=}^{18}O$ with: a) tetramethylene oxide and b) tetrahydropyran.

**$^{18}$O-labeling**: Figure 6 displays the CID sequential product ion mass spectra of the $CH_3{-}\overset{+}{C}{=}^{18}O$/trimethylene oxide and $CH_3{-}\overset{+}{C}{=}^{18}O$/tetrahydropyran adducts. That of trimethylene oxide (*m/z* 103) dissociates to form both $CH_3{-}\overset{+}{C}{=}^{18}O$ and $CH_3{-}\overset{+}{C}{=}O$, but the labeled ion $CH_3{-}\overset{+}{C}{=}^{18}O$ is more abundant (Figure 6a). Hence, trimethylene oxide undergoes ring expansion with $CH_3{-}\overset{+}{C}{=}^{18}O$, but not completely. Under the assumption of similar dissociation rates for the adducts, a 3:1 ratio between the cyclic 1,3-dioxanylium ion and the simple O-acylated product is estimated from the *m/z* 43 to *m/z* 45 abundance ratio.

As the dissociation behavior of its $(CH_3)_2N{-}\overset{+}{C}{=}S$ adduct has already indicated (Figure 5b), tetrahydropyran reacts with $CH_3{-}\overset{+}{C}{=}^{18}O$ to form predominantly the simple O-acylated adduct; six-to-eight-membered ring expansion does not occur since the adduct dissociates exclusively to $CH_3{-}\overset{+}{C}{=}^{18}O$ (Figure 6b).

**Ab initio calculations**: Figure 7 shows a potential energy surface diagram[20] for three-to-five-membered ring expansion of ethylene oxide with $(CH_3)_2N{-}\overset{+}{C}{=}S$, and the dissociation thresholds of the resulting product, the cyclic 1,3-oxathiola-

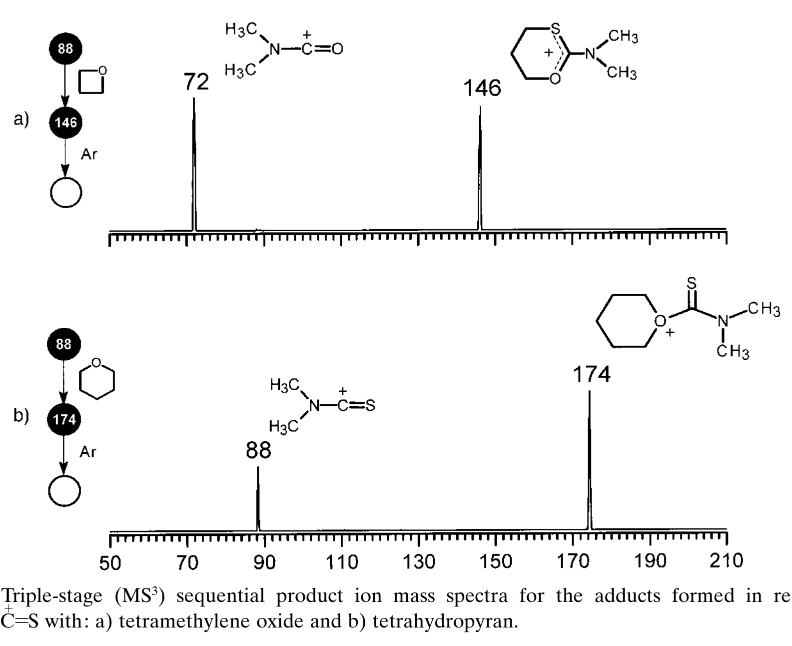


Figure 5. Triple-stage ($MS^3$) sequential product ion mass spectra for the adducts formed in reactions of $(CH_3)_2N{-}\overset{+}{C}{=}S$ with: a) tetramethylene oxide and b) tetrahydropyran.

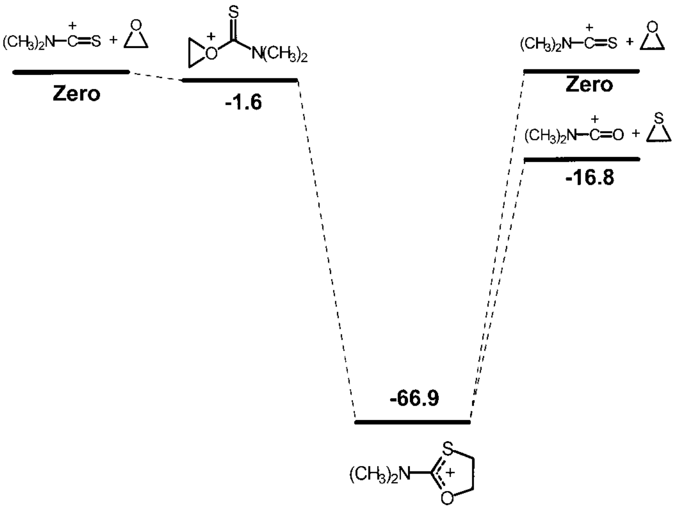


Figure 7. Ab initio MP2/6-311G(d,p)//HF/6-311G(d,p) + ZPE potential energy surface diagram for the gas-phase Meerwein reaction of $(CH_3)_2N{-}\overset{+}{C}{=}S$ with ethylene oxide and the dissociation thresholds of the 1,3-oxathiolanylium ion. Reaction barriers were not estimated, and are not indicated.

nylium ion. Initial O-acylation followed by ring expansion is overall greatly exothermic (−66.9 kcal mol$^{-1}$). Then, when the dissociation thresholds of the 1,3-oxathiolanylium ion are compared, those for dissociations that either regenerate the reactant thioacylium ion $(CH_3)_2N{-}\overset{+}{C}{=}S$ or form, by S/O replacement, the analogous acylium ion $(CH_3)_2N{-}\overset{+}{C}{=}O$, the preference for dissociation to $(CH_3)_2N{-}\overset{+}{C}{=}O$ is evident since the dissociation threshold to $(CH_3)_2N{-}\overset{+}{C}{=}O$ is lower by 16.8 kcal mol$^{-1}$. These theoretical predictions agree perfectly with the exclusive (or nearly exclusive) collision-induced dissociation of the 1,3-(S,O)oxathiolanylium ions, formed by the gas-phase Meerwein reaction, to $(CH_3)_2N{-}\overset{+}{C}{=}O$ (Figure 2).

Figure 8 compares the energetics of the gas-phase Meerwein reactions for either acylium or thioacylium ions with epoxides or thioepoxides. In all cases, three-to-five-membered ring expansion is overall considerably exothermic, and thermodynamically favored. The calculations summarized in Figure 8 also predict that initial acylation is more favored for thioepoxides. Overall, more exothermic and thermodynamically favored three-to-five-membered ring expansions occur for acylium ions with epoxides, and for thioacylium ions with thioepoxides, that is, when 1,3-(O,O)dioxolanylium or 1,3-(S,S)dithiolanylium ions are formed. The O/O and S/S orbitals overlap more favorably (than S/O orbitals), thus stabilizing the O/O and S/S product ions.

Figure 9 compares, for $CH_3{-}\overset{+}{C}{=}O$ and the simplest O-heterocycle, the energetics for analogous three-to-five-, four-to-six-, five-to-seven-, or six-to-eight-membered ring expansions. Ring expansion alleviates the ring strain of ethylene oxide and trimethylene oxide, respectively, and are overall far most exothermic, thermodynamically favored from both the initial reactants and the O-acylated adducts. Although reaction barriers have not been estimated, ring expansions for ethylene oxide and trimethylene oxide should also be the most kinetically favored owing to the labile C–O bond of the three- and four-membered O-heterocycles that are partially (most likely extensively) disrupted at the transition state (TS) (Scheme 10, $n = 1$ and 2).

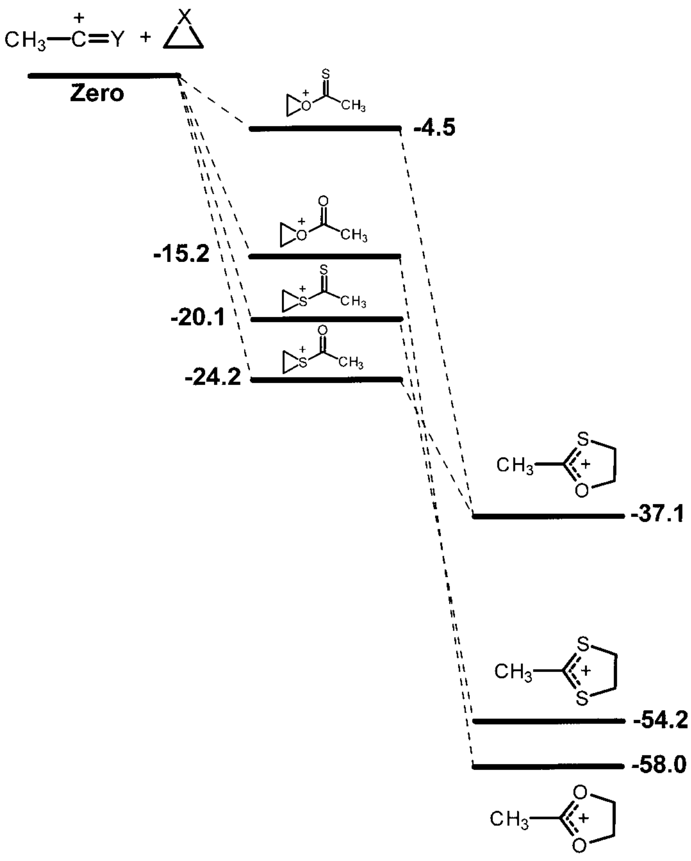


Figure 8. Ab initio MP2/6-311G(d,p)//HF/6-311G(d,p) + ZPE potential energy surface diagram for the three-to-five ring-expansion Meerwein reaction of $CH_3{-}CO^+$ or $CH_3{-}CS^+$ with ethylene oxide (X = O) or ethylene sulfide (X = S). Reaction barriers were not estimated, and are not indicated.

Overall, ring expansions for tetrahydrofuran and tetrahydropyran are also exothermic, but to a lesser extent (Figure 9). From the O-acylated adducts, however, these ring expansions are just slightly exothermic and likely hampered by substantially higher energy barriers since no alleviation of ring strain occurs, and substantially stronger C–O bonds are disrupted at the corresponding TSs (Scheme 10, $n = 3$, 4).

## Conclusion

A novel epoxide and thioepoxide ring expansion reaction promoted by acylium and thioacylium ions—the gas-phase Meerwein reaction—has been demonstrated and systematically investigated. Initial O(S)-acylation of the (thio)epoxide is followed by rapid intramolecular nucleophilic attack that results in three-to-five-membered ring expansion, leading to cyclic 1,3-dioxolanylium, 1,3-oxathiolanylium, or 1,3-dithiolanylium ions as far the more thermodynamically and more kinetically favored products. When (thio)epoxides react with (thio)acylium ions, the reaction promotes O(S)

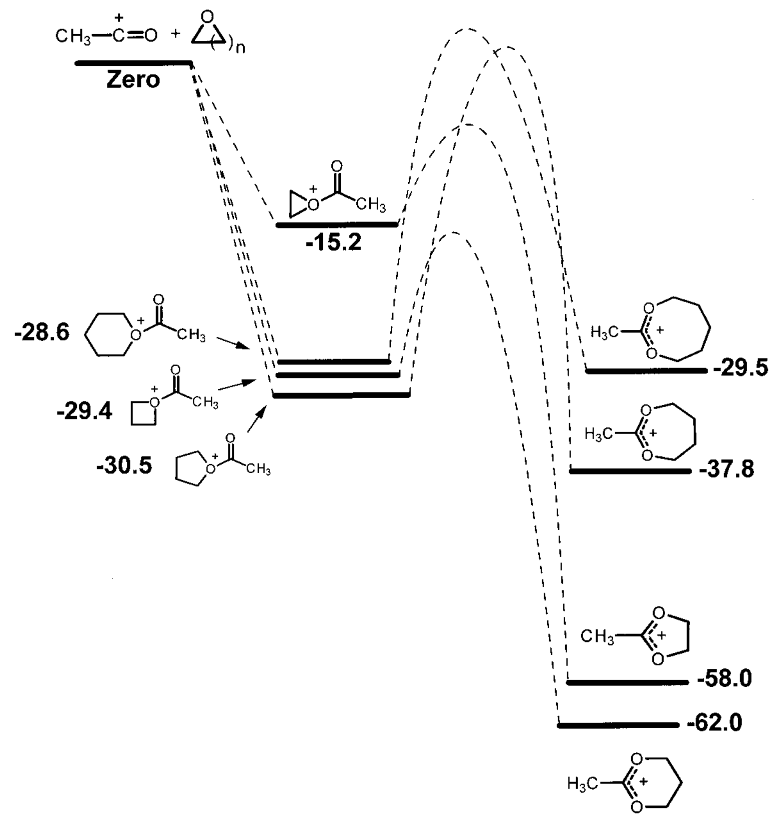
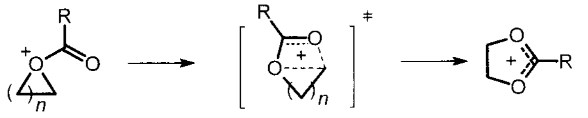


Figure 9. Ab initio MP2/6-311G(d,p)//HF/6-311G(d,p) + ZPE potential energy surface diagram for four-to-six-membered ring-expansion on reactions of $CH_3{-}CO^+$ with ethylene oxide or trimethylene oxide, tetrahydrofuran, and tetrahydropyran. Reaction barriers were not estimated, but expected trends in activation energies are indicated.



Scheme 10.

scrambling; when epoxides react with thioacylium ions and the adducts are dissociated, the reaction promotes S/O replacement.

The gas-phase Meerwein reaction occurs often to great extent or even exclusively; in a few cases, owing to the greater basicity of the (thio)epoxide or to the greater acidity of the (thio)acylium ion, or both, proton transfer (eventually also hydride abstraction) competes efficiently, or even dominates.

No ring expansion occurs for the corresponding six-membered O-heterocycle, tetrahydropyran; it reacts with both $(CH_3)_2N{-}\overset{+}{C}{=}S$ and $CH_3{-}\overset{+}{C}{=}{}^{18}O$ to form exclusively the simple O-acylated product. Tetrahydrofuran forms an abundant adduct with $(CH_3)_2N{-}\overset{+}{C}{=}O$, but whether an analogous five-to-seven-membered ring expansion occurs could not be verified since THF fails to form stable adducts with both $(CH_3)_2N{-}\overset{+}{C}{=}S$ and $CH_3{-}\overset{+}{C}{=}{}^{18}O$. Trimethylene oxide reacts, to a great extent with (thio)acylium ions by an analogous four-to-six-membered ring expansion; it forms the ring-expanded product ion predominantly with $CH_3{-}\overset{+}{C}{=}O$, and exclusively with $(CH_3)_2N{-}\overset{+}{C}{=}S$.

## Acknowledgements

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Verley–Oppenauer (MPVO) reduction (see: H. Meerwein, R. Schmidt, *Liebigs Ann. Chem.* **1925**, *444*, 221), a classical reaction that has also been studied and extended in the gas phase (see: D. Schröder, H. Schwarz, *Angew. Chem.* **1990**, *102*, 925; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 910).

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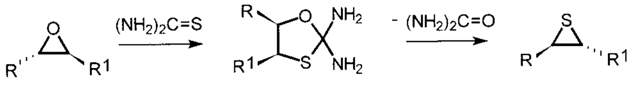
[16] Owing to the multiple collision conditions used for the ion–molecule reactions, proton transfer may occur from either the reactant ion, or from its products ions, or from both.

[17] The ions $CH_3{-}\overset{+}{C}{=}O$, $CH_3{-}\overset{+}{C}{=}S$, and $CH_2{=}CH{-}\overset{+}{C}{=}O$ are protonated forms of $CH_2{=}C{=}O$, $CH_2{=}C{=}S$ and $CH_2{=}C{=}C{=}O$, respectively, and display higher Brønsted acidity than, for instance, with $(CH_3)_2N{-}\overset{+}{C}{=}O$, see refs. [8–10].

[18] It is also noteworthy the similarities between the S/O replacement accomplished by the gas-phase Meerwein reaction/CID sequence (Scheme 6) with the classic reaction of thiourea with epoxides (Scheme 11) that forms thioepoxides and the O-analogue urea: a) J. F. Olin, F. B. Danis, *J. Am. Chem. Soc.* **1930**, *52*, 3322; b) M. Sander, *Chem. Rev.* **1966**, *66*, 297.



Scheme 11.

[19] S/O replacement in thioacylium ions is also performed efficiently by a $MS^3$ transacetalization/CID sequence, see: L. A. B. Moraes, M. N. Eberlin, *J. Chem. Soc. Perkin Trans. 2* **1997**, 2105.

[20] The electronic and ZPE energies of the species are available from the authors upon request.

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