JOURNAL OF MASS SPECTROMETRY
J. Mass Spectrom. **34**, 670–676 (1999)

Gas-phase Chemistry of Acylium Ions. Seven-to-Five Ring Contraction of 1,3-Dioxepane and 1,3-Dioxep-5-ene

Luiz Alberto B. Moraes,[1] Tapio Kotiaho[1,2] and Marcos N. Eberlin[1]*
[1] Institute of Chemistry, State University of Campinas—UNICAMP, CP 6154, 13083-970 Campinas, SP, Brazil
[2] VTT Chemical Technology, P. O. Box 1401, FIN-02044 VTT, Finland

As shown by pentaquadrupole triple-stage mass spectrometric and ^{18}O-labeling experiments, two seven-membered cyclic acetals, 1,3-dioxepane and 1,3-dioxep-5-ene, fail to react by transacetalization with the gaseous acylium ions $CH_3C^+{=}O$ and $(CH_3)_2NC^+{=}O$. Instead, a novel and less exothermic but more kinetically favored reaction, seven-to-five ring contraction, occurs predominantly, and to great extents with the most reactive acylium ion, $(CH_3)_2NC^+{=}O$. 1,3-Dioxepane yields *O*-acylated tetrahydrofurans; 1,3-dioxep-5-ene yields *O*-acylated 2,5-dihydrofurans. Copyright © 1999 John Wiley & Sons, Ltd.

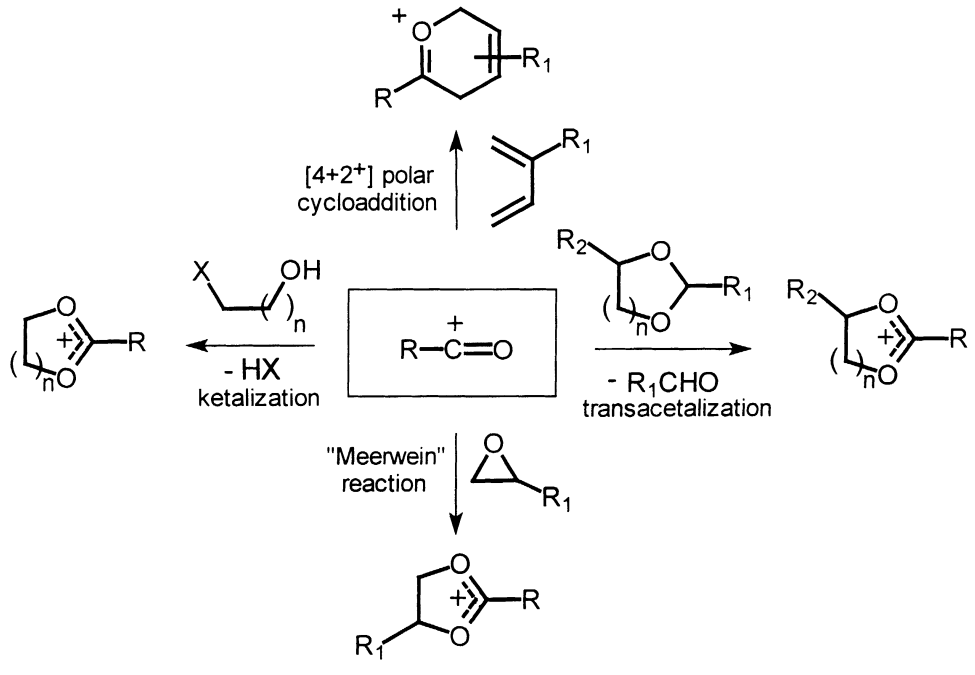
KEYWORDS: acylium ions; seven-membered cyclic acetals; ion–molecule reactions; pentaquadrupole mass spectrometry; transacetalization

INTRODUCTION

In the gas phase, acylium ions ($RC^+{=}O$)[1] and their sulfur analogues, the thioacylium ions ($RC^+{=}S$), and the structurally related sulfinyl cations ($RS^+{=}O$),[2] display a rich, unique and general reactivity.[2–7] With conjugated dienes, acylium and thioacylium ions undergo [4 + 2$^+$] polar cycloaddition;[4] with cyclic acetals and ketals, transacetalization;[2b,5] with diols and analogues, ketalization;[5g,6] and with epoxides, a three-to-five ring expansion reaction,[5g,7] that is, the gas-phase analogue of the condensed-phase Meerwein reaction[8] (Scheme 1). Such unique and general reactivity easily characterizes and distinguishes acylium ions from both isomeric and isobaric species.[4,5]

* *Correspondence to*: M. N. Eberlin, Institute of Chemistry, State University of Campinas—UNICAMP, CP 6154, 13083-970 Campinas, SP, Brazil.
E-mail: eberlin@iqm.unicamp.br

Contract/grant sponsor: Research Support Foundation of the State of São Paulo.
Contract/grant sponsor: Brazilian National Research Council.



Scheme 1

CCC 1076–5174/99/060670–07 $17.50

Received 4 January 1999
Accepted 10 March 1999

The novel ketalization and transacetalization reactions of acylium ions occur in the gas phase by pathways that are very similar to the respective condensed-phase acetalization and transacetalization. Both gas-phase reactions form cyclic 'ionic ketals' (Scheme 1), that is, resonance-stabilized cyclic 1,3-dioxonium ions,[5,6] and as for the carbonyl compounds in the 'neutral' reactions, the acylium ions become protected against their most characteristic reactions.[5] When collisionally activated, the cyclic ionic ketals re-form the acylium ions in high yields, a step that is therefore equivalent to the re-forming hydrolysis of neutral acetals and ketals in the condensed phase. Just as condensed-phase hydrolysis of acetals and ketals frees the protected aldehydes or ketones, so gas-phase collision-induced dissociation (CID) of the ionic ketals frees the protected acylium ions.

Recently, gaseous acylium ions were shown to react extensively via transacetalization with many cyclic acetals and ketals and their sulfur and nitrogen analogues.[5b] Transacetalization with gaseous acylium ions was then proposed as a general and structurally diagnostic reaction to characterize cyclic acetals and ketals. Transacetalization occurs *via* initial *O*-acylation, followed by ring opening/ring re-forming pathways in which a neutral carbonyl compound is eliminated and cyclic 'ionic ketals' are formed (Scheme 1).

That the product ions of transacetalization display cyclic ionic ketal structures was proved by dissociating the ^{18}O-labeled ionic ketals formed by reacting $CH_3C^+{=}{}^{18}O$ with 2-pentamethylene-1,3-dioxolane, a five-membered cyclic acetal,[5b] and with 1,3-dioxane, a six-membered cyclic acetal.[2b] As a result of the 'oxygen-scrambling' mechanism of transacetalization, both product ions dissociate, to the same extent, to both the labeled ($CH_3C^+{=}{}^{18}O$) and unlabeled acylium ion ($CH_3C^+{=}O$). Reactions of acylium ions with several five-, six- and a seven-membered cyclic ketal (1,3-dioxep-5-ene) also yielded abundant products that were all assumed to be formed by transacetalization, and hence to display the cyclic ionic ketal structures.

We now show, however, via triple-stage mass spectrometric and ^{18}O-labeling experiments, that seven-membered cyclic acetals fail to react with acylium ions predominantly by transacetalization. Instead, a novel, less exothermic but more kinetically favored reaction, seven-to-five ring contraction, occurs predominantly or exclusively, yielding *O*-acylated hydrofurans.

METHODS

The gaseous ions were produced, reacted and their products analyzed *via* double-stage (MS^2) and triple-stage (MS^3) mass spectrometric experiments performed with an Extrel (Pittsburgh, PA, USA) pentaquadrupole mass spectrometer.[9,10] The instrument, denoted $Q_1q_2Q_3q_4Q_5$, is composed of a sequential arrangement of three mass-analyzing (Q_1, Q_3, Q_5) and two 'r.f.-only' ion-focusing reaction quadrupoles (q_2, q_4). By 70 eV electron ionization, appropriate precursors form the reactant acylium ions: tetramethylurea forms $(CH_3)_2NCO^+$, acetone CH_3CO^+ and [^{18}O]acetone (ISOTEC), $CH_3C^{18}O^+$. When performing MS^2 ion–molecule reactions, Q_1 was used to mass select the ion of interest for further reactions in q_2 with a selected neutral reagent. Ion translational energies were set to near 1 eV as calibrated by the *m/z* 39 : 41 ratio in neutral ethylene–ionized ethylene reactions.[11] Product ion spectra were acquired by scanning Q_5, while operating Q_3 in the broad-band r.f.-only mode. The target gas pressures in q_2 caused typical beam attenuations of 50–70%, i.e. multiple collision conditions were used, which increases reaction yields and promotes collisional quenching of both the reactant and product ions.[10]

For the MS^3 experiments,[12] Q_3 is used to mass select a q_2 product ion of interest for further 15 eV collision dissociation with argon in q_4, while scanning Q_5 for spectral acquisition. 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 2×10^{-6} (ion source), 8×10^{-6} (q_2) and 8×10^{-5} (q_4) Torr, respectively (1 Torr = 133.3 Pa).

Energies and optimized geometries were obtained by molecular orbital calculations using Gaussian 94 (Gaussian, Inc., Pittsburgh, PA, USA). Density functional theory (DFT) at the Becke3LYP/6–31G(d) level of theory was applied.[13]

RESULTS AND DISCUSSION

Figure 1 compares product spectra for reactions of the acylium ion $(CH_3)_2NCO^+$ with the two seven-membered cyclic acetals 1,3-dioxepane and its unsaturated analogue 1,3-dioxep-5-ene. With $(CH_3)_2NCO^+$, the reactivity of both acetals is notable, and just a single product ion (of *m/z* 144 and 142, respectively) is formed in both reactions. These products correspond to neutral loss of formaldehyde from the adducts; hence they were initially (but incorrectly) assumed to be formed exclusively by transacetalization (Scheme 2) and to display seven-membered cyclic ionic ketal structures.

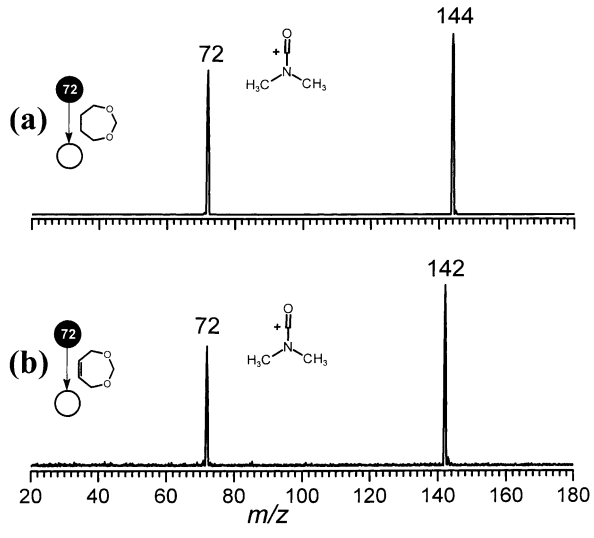
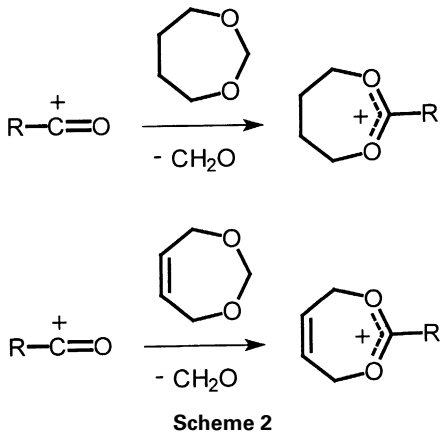


Figure 1. Double-stage (MS^2) product ion spectrum for reactions of the acylium ion $(CH_3)_2NCO^+$ with (a) 1,3-dioxepane and (b) 1,3-dioxep-5-ene.



Scheme 2

Figure 2 compares the triple-stage collision-induced dissociation (CID) mass spectra of the two reaction products. That of *m/z* 144 from 1,3-dioxep-5-ene (Fig. 2(b)) dissociates exclusively and to a great extent to re-form the reactant acylium ion of *m/z* 72; this dissociation behavior is typical of cyclic ionic ketals.[5] However, the product ion of *m/z* 142 from 1,5-dioxepane (Fig. 2(a)) fails to show such typical dissociation behavior. It does dissociate to re-form the reactant ion of *m/z* 72, but two other major dissociation pathways also operate, yielding the fragment ions of *m/z* 90 and 55.

^{18}O labeling

To verify whether the oxygen-scrambling mechanism of transacetalization (Scheme 1) operates for the two seven-membered cyclic acetals, they were reacted with both CH_3CO^+ and its ^{18}O-isotopomer $CH_3C^{18}O^+$. Figure 3 exemplifies product ion spectra for 1,3-dioxep-5-ene. Reactions with the more acidic CH_3CO^+ (CH_3CO^+ can be viewed as protonated ketene) forms the expected product ion of *m/z* 113 (Figure 1(a)), but proton transfer (*m/z* 101) competes to a large extent; the protonated molecule also loses formaldehyde to some extent yielding *m/z* 71 (Fig. 2(b)). In reactions with $CH_3C^{18}O^+$ (Fig. 3(b)), the product thought to be the cyclic ionic ketal is shifted, as

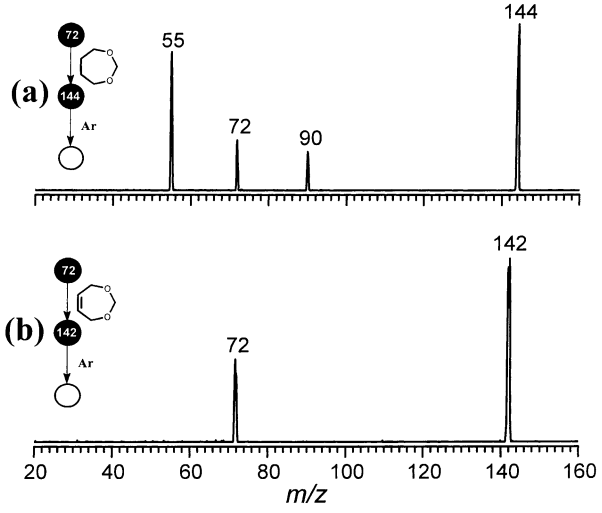


Figure 2. Triple-stage (MS^3) sequential product ion spectrum of products from reactions of $(CH_3)_2NCO^+$ with (a) 1,3-dioxepane and (b) 1,3-dioxep-5-ene.

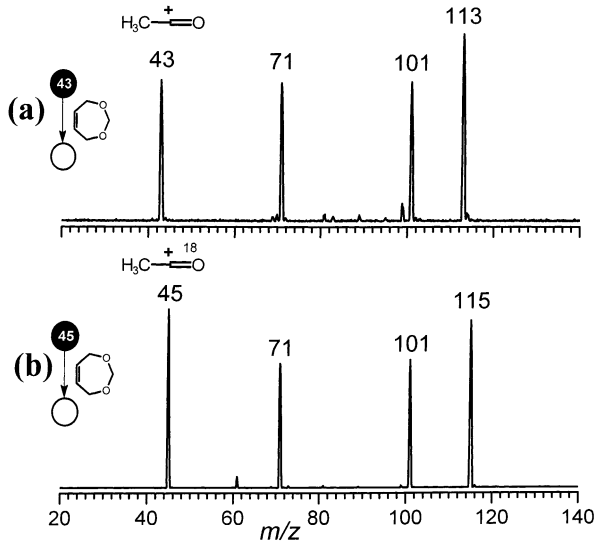


Figure 3. Double-stage (MS^2) product spectrum for reactions of the acylium ions (a) CH_3CO^+ and (c) $CH_3C^{18}O^+$ with 1,3-dioxep-5-ene.

expected, to *m/z* 115. Analogous spectra (not shown) were obtained for 1,3-dioxepane.

Figure 4 compares triple-stage CID mass spectra of the products thought to be formed by transacetalization of $CH_3C^{18}O^+$ with 1,3-dioxolane, 1,3-dioxane, 1,3-dioxepane and 1,3-dioxep-5-ene. For the five-membered (Fig. 4(a)) and the six-membered cyclic acetals (Fig. 4(b)), the product ions re-form, to the same extent, both the labeled and unlabeled ion. As

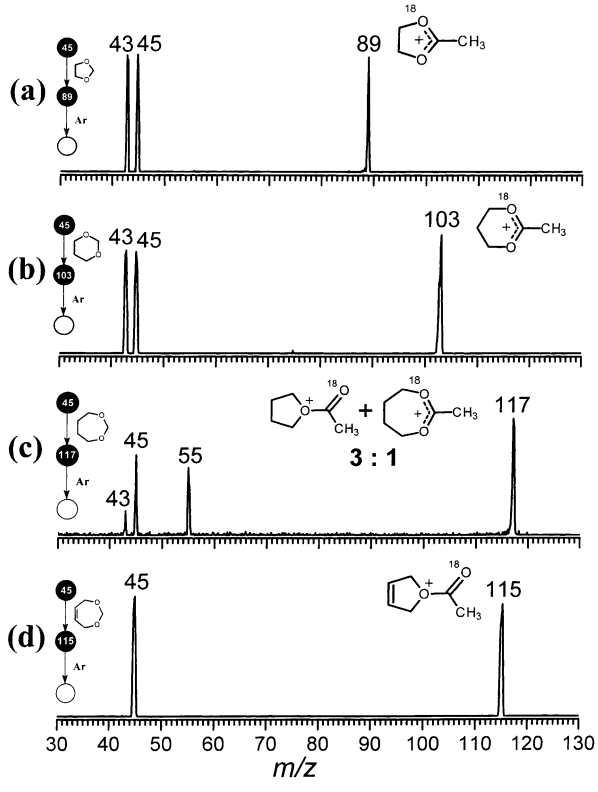


Figure 4. Triple-stage (MS^3) sequential product ion spectra of products from reactions of $CH_3C^{18}O^+$ with (a) 1,3-dioxolane, (b) 1,3-dioxane, (c) 1,3-dioxepane and (d) 1,3-dioxep-5-ene.

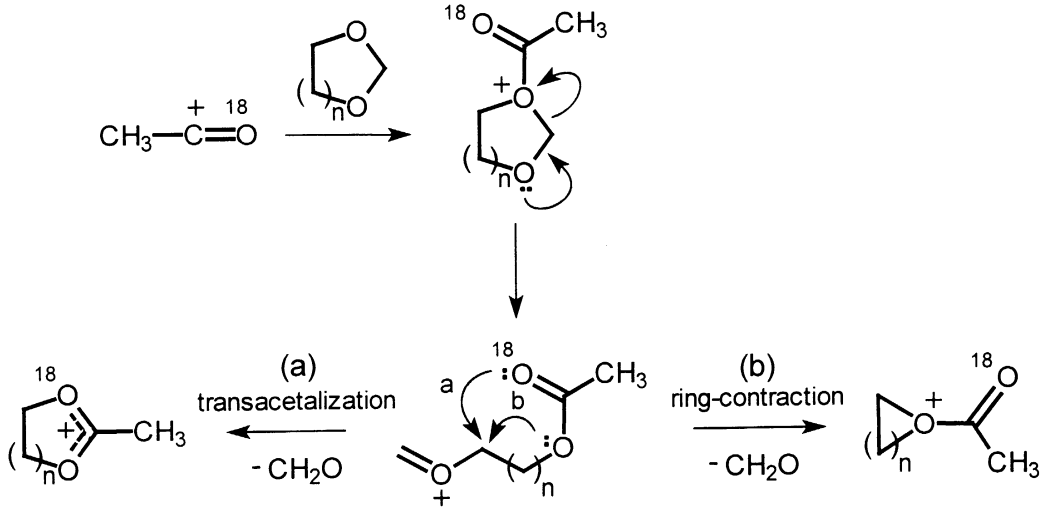
already discussed, this characteristic dissociation behavior proves the operation of the oxygen-scrambling ring opening/recyclization mechanism of transacetalization, and that cyclic ionic ketals are formed exclusively.[2b,5]

However, the product ions from the seven-membered cyclic acetals dissociate differently. That from 1,3-dioxep-5-ene (Fig. 4(d)) re-forms exclusively the ^{18}O-labeled reactant acylium ion of *m/z* 45, and that from 1,3-dioxepane (Fig. 4(c)) mainly the labeled ion of *m/z* 45 but also, to a small extent, the unlabeled ion of *m/z* 43; loss of C_4H_6 that yields *m/z* 55 also operates (Fig. 4(c)). These dissociation behaviors eliminate major contribution of the cyclic ionic ketal structure to the product ion from 1,3-dioxep-5-ene; from 1,3-dioxepane, a mixture of structures is formed with a minor contribution of the seven-membered cyclic ionic ketal.

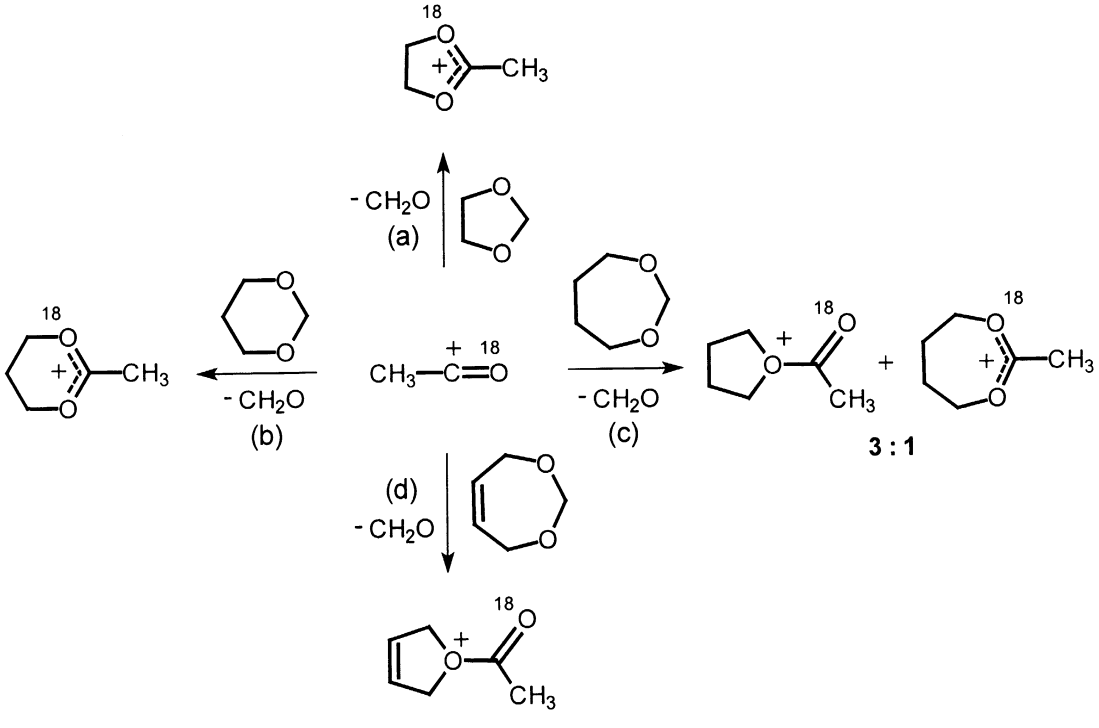
Transacetalization versus seven-to-five ring contraction

Scheme 3 exemplifies, for $CH_3C^{18}O^+$ and cyclic acetals of different ring sizes, the products of two of their most likely reactions: (a) transacetalization that yields cyclic ionic ketals and (b) ring contraction that forms *O*-acylated cyclic eters.

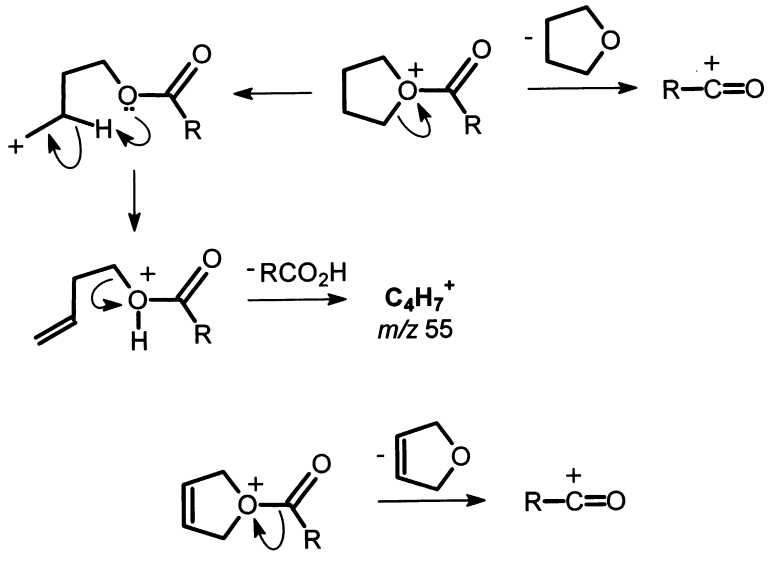
Considering the reaction mechanisms decipted in Scheme 3, the kinetic preference of either ring contraction or transacetalization can be rationalized. For the five-membered cyclic acetals, transacetalization requires a five-membered transition state (TS) and ring contraction a three-membered cyclic TS. The complete oxygen scrambling shown by the ionic product (Fig. 3(a)) proves that the five-membered cyclic ionic ketal is formed exclusively



Scheme 3



Scheme 4



Scheme 5

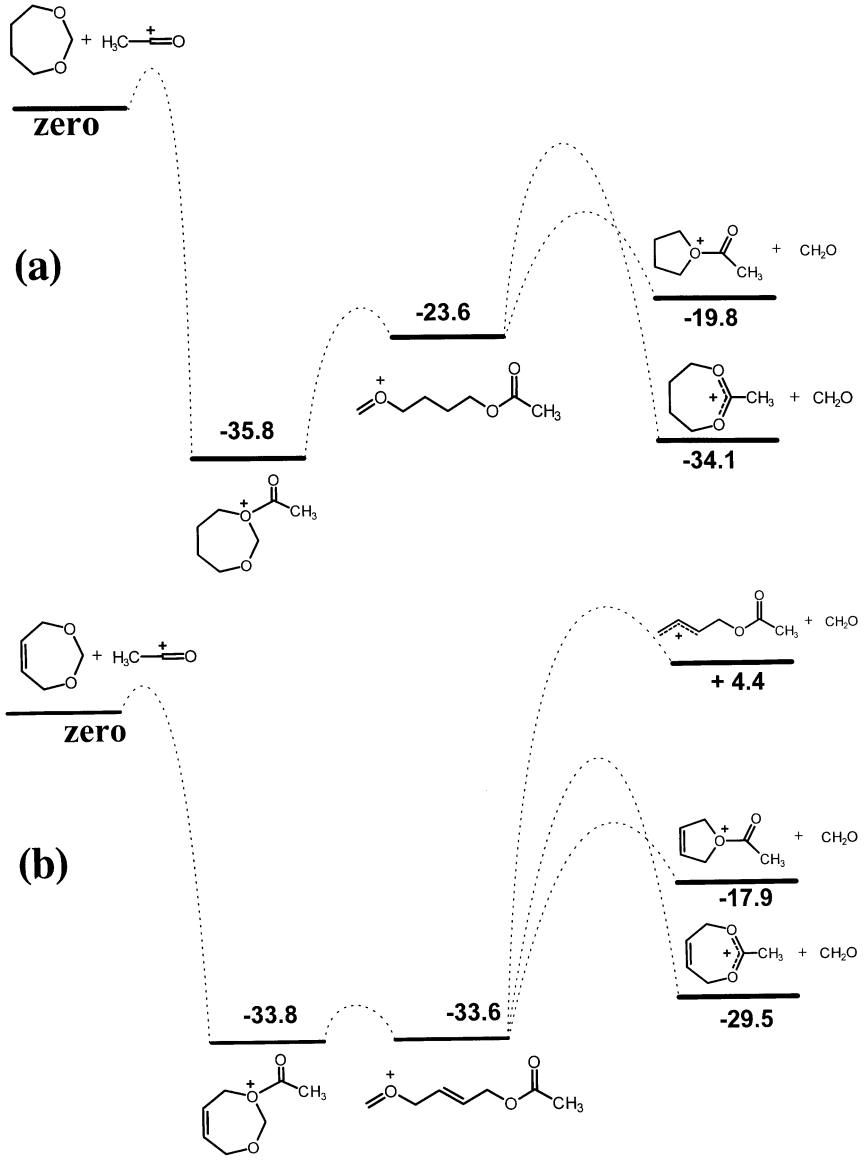
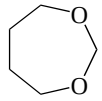
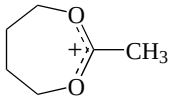
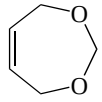
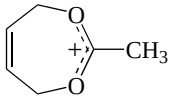
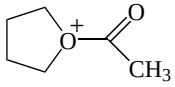
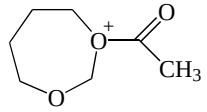
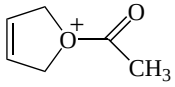
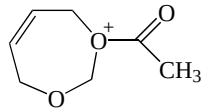
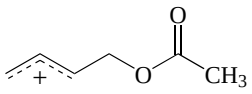
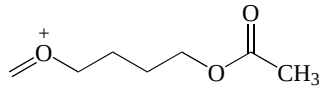
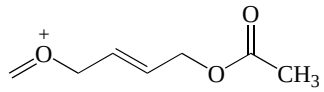


Figure 5. Becke3LYP/6–31G(d) DFT potential energy surface diagram for the reaction of CH_3CO^+ with (a) 1,3-dioxepane and (b) 1,3-dioxep-5-ene. Reaction barriers were not estimated.

Table 1. Energies from Becke3LYP/6−31G(d) DFT calculations

Species	Energy (hartree)	Species	Energy (hartree)
	−346.97948		−385.45682
	−345.74288		−384.21302
$CH_3-C^+=O$	−152.92353		−385.43413
	−499.96011		−384.19450
	−498.72012		−384.15888
	−499.94062	$CH_2=O$	−114.50047
	−498.71835		

(Scheme 4(a)); hence, overall, transacetalization dominates.

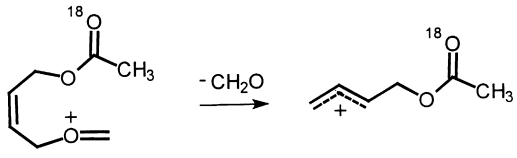
For the six-membered cyclic acetals, transacetalization requires a six-membered TS. Ring contraction requires, however, a much more constrained and hence more energetic four-membered TS. Therefore, transacetalization dominates, as it is the kinetically (and thermodynamically)[2b] favored reaction. Hence, the six-membered cyclic ionic ketal with 'scrambled' oxygens is formed exclusively (Scheme 4(b)); it then dissociates upon collision activation to both the labeled and unlabeled ion (Fig. 4(b)).

For the seven-membered cyclic acetals, transacetalization requires a *seven*-membered TS and ring contraction a *five*-membered TS. Therefore, ring contraction is now the reaction that proceeds via a TS associated with a more favorable activation entropy, that is, ring contraction (Scheme 4(c) and (d)) dominates as the more favorable kinetic reaction, yielding mainly *O*-acylated hydrofuranes. Ring contraction promotes no oxygen scrambling; hence the *O*-acylated hydrofuran re-forms only $CH_3C^{18}O^+$ upon collision activation (Fig. 4(c) and 4(d)). In Fig. 4(c), by taking double the abundance of the fragment of *m*/*z* 43 as an estimate of the contribution of the cyclic ionic ketal, and those of both the fragments of *m*/*z* 45 (excluding that of the superimposed *m*/*z* 45 ion from the cyclic ionic ketal) and *m*/*z* 55 for the acetylated tetrahydrofuran, an approximate ratio of 3 : 1 is calculated.

Considering now that seven-to-five ring contraction occurs predominantly for the seven-membered cyclic acetals, the dissociation behavior of the respective product ions can be adequately rationalized (Scheme 5). For the product ion from 1,3-dioxepane, the saturated five-membered ring favors a dissociation pathway that is preceded by ring opening and H-shift and forms $C_4H_7^+$ of *m*/*z* 55 by loss of RCO_2H. However, the $C_3{=}C_4$ double bond of the 1,3-dioxep-5-ene product which precludes the H-shift step, and eliminates the corresponding dissociation pathway of RCO_2H loss; hence, the reactant acylium ion is reformed exclusively.

Reaction enthalpies: *ab initio* calculations

Figure 5 shows DFT (Table 1) potential energy surface diagrams for the transacetalization and ring contraction reactions (Scheme 4) of CH_3CO^+ with 1,3-dioxepane and 1,3-dioxep-5-ene. For 1,3-dioxep-5-ene, a third alternative reaction was considered, i.e., that by which an acyclic allyl cation is formed (Scheme 6).



Scheme 6

Both diagrams show similar trends (Fig. 5). For 1,3-dioxepane, initial *O*-acylation is exothermic by −35.8 kcal mol^{-1} (1 kcal = 4.184 kJ), thus providing the driving force for the overall reaction. Ring opening of the adduct is +12.2 kcal mol^{-1} endothermic, whereas transacetalization with the concomitant formaldehyde loss that yields the seven-membered cyclic ionic ketal is exothermic from the acyclic adduct by

-10.5 kcal mol^{-1}; overall, transacetalization constitutes the most exothermic process (by -34.1 kcal mol^{-1}). Seven-to-five ring contraction is also overall exothermic by -19.8 kcal mol^{-1}.

For 1,3-dioxep-5-ene, initial *O*-acylation is exothermic by -33.8 kcal mol^{-1} and ring opening is near isothermic. Transacetalization that yields the seven-membered cyclic ionic ketal is endothermic from the acyclic adduct by $+4.1$ kcal mol^{-1}; overall, it constitutes the most exothermic reaction (by -29.5 kcal mol^{-1}), whereas seven-to-five ring contraction is the second most exothermic reaction (by -17.9 kcal mol^{-1}). The acyclic allyl cation is formed from 1,3-dioxep-5-ene in an overall endothermic ($+4.4$ kcal mol^{-1}), thermodynamically unfavorable reaction.

Therefore, for the seven-membered cyclic acetals, that ring contraction dominates over the more exothermic transacetalization must result from a strong kinetic preference for the ring-contracting pathway. As already discussed, transacetalization proceeds via a seven-membered TS and ring contraction, via a five-membered TS (Scheme 3). Hence, ring contraction is the kinetically favored reaction. Although TS energies were not estimated, expected trends in activation energies have been included in Fig. 5.

CONCLUSION

In contrast to the general and extensive transacetalization reactivity of five- and six-membered cyclic acetals, seven-membered cyclic acetals fail to react predominantly with acylium ions by transacetalization. Instead, a novel reaction, seven-to-five ring contraction, dominates. According to DFT calculations, ring contraction is less exothermic than transacetalization; it dominates, however, owing to strong kinetic favoring. The ring contraction reaction occurs to a great extent with the most reactive ion $(CH_3)_2NC^+=O$; for the more acidic $CH_3C^+=O$, it competes with proton transfer. As shown by MS^3 and O^{18}-labeling experiments, the reaction of $CH_3C^+{=}{=}^{18}O$ with 1,3-dioxepane yields a near 3 : 1 mixture of the *O*-acetylated tetrahydrofuran and the seven-membered ionic ketal; with 1,3-dioxep-3-ene, *O*-acetylated 2,5-dihydrofuran is formed exclusively.

Acknowledgements

This work was supported by the Research Support Foundation of the State of São Paulo (FAPESP) and the Brazilian National Research Council (CNPq).

REFERENCES

1. G. A. Olah, A. Gramain and A. M. White, in *Carbonium Ions*, edited by G. A. Olah and P. von R. Schleyer, Vol. 5, Chapt. 35, 2084. Wiley–Interscience, New York, (1976).
2. (a) F. C. Gozzo, A. E. P. M. Sorrilha and M. N. Eberlin, *J. Chem. Soc., Perkin Trans. 2* 587 (1996); (b) L. A. B. Moraes and M. N. Eberlin, *J. Chem. Soc., Perkin Trans. 2* 2105 (1997).
3. (a) D. A. Chatfield and M. M. Bursey, *J. Am. Chem. Soc.* **98**, 6492 (1976); (b) R. H. Staley, R. D. Wieting and J. L. Beauchamp, *J. Am. Chem. Soc.* **99**, 5964 (1977); (c) M. Kumakura and T. Sigiura, *J. Phys. Chem.* **82**, 639 (1978); (d) C. Sparapani and M. Speranza, *J. Am. Chem. Soc.* **102**, 3120 (1980); (e) J. K. Kim and M. C. Caserio, *J. Am. Chem. Soc.* **104**, 4624 (1982); (f) M. Attinà and F. Cacace, *J. Am. Chem. Soc.* **105**, 1122 (1983); (g) M. C. Caserio and J. K. Kim *J. Am. Chem. Soc.* **105**, 6896 (1983); (h) C. Paradisi, H. I. Kenttämaa, Q. T. Le and M. C. Caserio, *Org. Mass Spectrom.* **23**, 521 (1988); (i) N. A. Rahman, C. L. Fisher and M. C. Caserio, *Org. Mass Spectrom.* **23**, 517 (1988); (j) T. Kotiaho, M. N. Eberlin, B. J. Shay and R. G. Cooks, *J. Am. Chem. Soc.* **115**, 1004 (1993); (k) C. S. Creaser and B. L. Wiliamson, *J. Chem. Soc., Perkin Trans. 2* 427 (1996).
4. (a) M. N. Eberlin, T. K. Majumdar and R. G. Cooks, *J. Am. Chem. Soc.* **114**, 2884 (1992); (b) M. N. Eberlin and R. G. Cooks, *J. Am. Chem. Soc.* **115**, 9226 (1993).
5. (a) M. N. Eberlin and R. G. Cooks, *Org. Mass Spectrom.* **28**, 679 (1993); (b) L. A. B. Moraes, F. C. Gozzo, M. N. Eberlin and P. Vainiotalo, *J. Org. Chem.* **62**, 5096 (1997); (c) M. C. Carvalho, L. A. B. Moraes, C. Kascheres and M. N. Eberlin, *J. Mass Spectrom.* **32**, 1137 (1997); (d) M. C. Carvalho, V. F. Juliano, C. Kascheres and M. N. Eberlin, *J. Chem. Soc., Perkin Trans. 2* 2347 (1997); (e) L. A. B. M. Moraes and M. N. Eberlin, *J. Am. Chem. Soc.* **120**, 11136 (1998); (f) F. Wang, S. Ma, W. Andy Tao and R. G. Cooks, *Angew. Chem. Int. Ed.* **38**, 386 (1999); (g) F. Wang, W. A. Tao, R. G. Cooks, F. C. Gozzo and M. N. Eberlin, *J. Org. Chem.* **64**, 3213 (1999).
6. L. A. B. Moraes, R. S. Pimpim and M. N. Eberlin, *J. Org. Chem.* **61**, 8726 (1996).
7. L. A. B. Moraes and M. N. Eberlin, *J. Am. Chem. Soc.* submitted for publication.
8. H. Meerwein, *Angew. Chem.* **67**, 374 (1955).
9. V. Juliano, C. Kascheres, F. C. Gozzo, M. N. Eberlin and C. L. Lago, *Anal. Chem.* **68**, 1328 (1996).
10. M. N. Eberlin, *Mass Spectrom. Rev.* **16**, 113 (1997).
11. T. O. Tiernan and J. H. Futrell, *J. Phys. Chem.* **72**, 3080 (1968).
12. J. C. Schwartz, A. P. Wade, C. G. Enke and R. G. Cooks, *Anal. Chem.* **62**, 1809 (1990).
13. P. M. W. Gill, B. G. Johnson and J. A. Pople, *Chem. Phys. Lett.* **197**, 499 (1992).

