Transacetalization with Acylium Ions. A Structurally Diagnostic Ion/Molecule Reaction for Cyclic Acetals and Ketals in the Gas Phase

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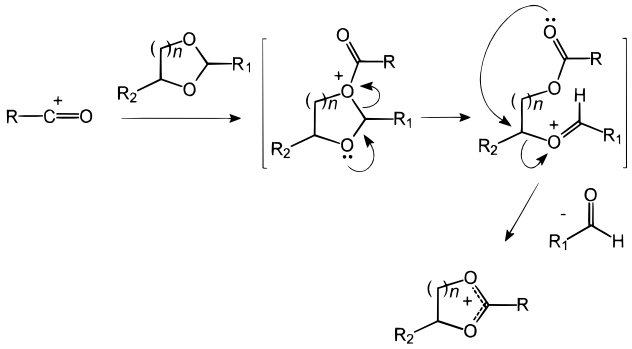
Transacetalization takes place in high yields in gas phase ion/molecule reactions of acylium ions ($RC^+{=}O$) with a variety of cyclic acetals and ketals, that is, five-, six-, and seven-membered 1,3-O,O-heterocycles and their *mono*-sulfur and nitrogen analogues. A general, structurally diagnostic method for the gas phase characterization of cyclic acetals and ketals is therefore available. Transacetalization occurs *via* initial O(or S)-acylation, followed by a ring-opening/ring-re-forming process in which a neutral carbonyl compound is eliminated and cyclic "ionic ketals" (that is, cyclic 1,3-dioxonium ions and analogues) are formed. The nature of the substituents at the 2-position, which are eliminated in the course of the reaction, is found to affect considerably the extent of transacetalization. Substituents not at the 2-position remain in the ionic products; hence positional isomers produce different cyclic "ionic ketals" and are easily differentiated. The triple-stage (MS^3) mass spectra of the cyclic "ionic ketals" show in all cases major dissociation to re-form the reactant acylium ion, a unique dissociation chemistry that is equivalent to the hydrolysis of neutral acetals and ketals and which is then determined to be a very general characteristic of cyclic "ionic ketals". Additionally, the ^{18}O-labeled transacetalization product of 1,3-dioxolane shows dissociation to both $CH_3C^+{=}{}^{18}O$ and $CH_3C^+{=}O$ to the same extent, which confirms its cyclic "ionic ketal" structure and the "oxygen-scrambling" mechanism of transacetalization. *Ab initio* MP2/6-31G(d,p)//6-31G-(d,p) + ZPE energy surface diagrams show that transacetalization is the most exothermic, thermodynamically favorable process in reactions of $CH_3C^+{=}O$ with 1,3-dioxolane and 1,3-oxathiolane, whereas 1,3-dithiolane is unreactive due to the endothermicity of the initial acylation step.

Introduction

Acylium ions ($RC^+{=}O$), due to their ease of preparation and relatively high stability, constitute one of the best characterized classes of stable carbocations in condensed phase.[1] Acylium ions also participate as key ionic reaction intermediates in solution, and the most typical example is the classical Friedel−Crafts acylation reaction.[2] In the gas phase, a variety of stable acylium ions have been generated, isolated, and reacted, and a rich and unique chemistry has been observed.[3] In analogy to solution phase reactions, acylation is also a common reaction for acylium ions in the gas phase.[3d] Other gas phase reactions of acylium ions include oxygen replacement by sulfur,[3e,g] alkylation,[3c] and bromine replacement.[3b]

Scheme 1



Recently[4] it was reported that a variety of acylium ions undergo in the gas phase an unprecedented [4 + 2$^+$] polar cycloaddition with conjugated dienes, a reactivity that allows their characterization and distinction from several isomers. Many acylium[5] and the related sulfinyl cations ($RS^+{=}O$)[6] also were shown recently to undergo a novel gas phase transacetalization reaction with two cyclic acetals (Scheme 1), and a very selective test for the characterization of acylium ions based on this ion/

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(3) (a) Chatfield, D. A.; Bursey, M. M. *J. Am. Chem. Soc.* **1976**, *98*, 6492. (b) Staley, R. H.; Wieting, R. D.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 5964. (c) Kumakura, M.; Sigiura, T. *J. Phys. Chem.* **1978**, *82*, 639. (d) Sparapani, C.; Speranza, M. *J. Am. Chem. Soc.* **1980**, *102*, 3120. (e) Kim, J. K.; Caserio, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4624. (f) Attinà, M.; Cacace, F. *J. Am. Chem. Soc.* **1983**, *105*, 1122. (g) Caserio, M. C.; Kim, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6896. (h) Paradisi, C.; Kenttämaa, H.; Le, Q. T.; Caserio, M. C. *Org. Mass Spectrom.* **1988**, *23*, 521. (i) Rahman, N. A.; Fisher, C. L.; Caserio, M. C. *Org. Mass Spectrom.* **1988**, *23*, 517. (j) Kotiaho, T.; Eberlin, M. N.; Shay, B. J.; Cooks, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 1004. (k) Creaser, C. S.; Williamson, B. L. *J. Chem. Soc., Perkin Trans. 2* **1996**, 427.

(4) (a) Eberlin, M. N.; Majumdar, T. K.; Cooks, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 2884. (b) Eberlin, M. N.; Cooks, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 9226.

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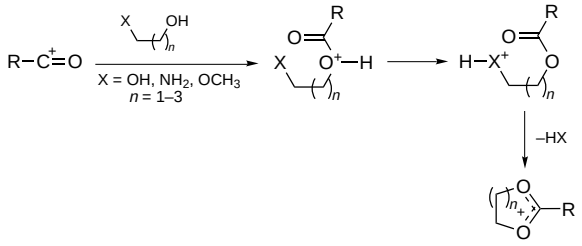
Scheme 2



molecule reaction and a neutral gain/neutral loss MS^3 scan has been proposed.[7]

Gas phase direct ketalization with acylium ions of a variety of diols, their nitrogen and sulfur analogues, and monoalkyl derivatives also has been reported recently (Scheme 2).[8] These two novel gas phase reactions therefore occur by ways that are very similar to the condensed phase acetalization (or ketalization) and transacetalization reactions, respectively. Cyclic "ionic ketals" (Scheme 1), that is, resonance-stabilized cyclic 1,3-dioxonium ions, are formed,[5,8] and as for the carbonyl compounds in the "neutral" reactions, "protection" of the acylium ions against their most characteristic reactions is accomplished.[8] Interesting also is the fact that collision-induced dissociation of the cyclic "ionic ketals" reforms the acylium ions in high yields, a step that is equivalent to the re-forming hydrolysis of neutral acetals and ketals in condensed phase. Transacetalization has also been performed under acetone and 3-pentanone chemical ionization conditions,[9] and distinction of 1,3-dioxolanes and their monosulfur analogues has been achieved.

In the present study,[10] the results of a detailed investigation via multiple stage pentaquadrupole mass spectrometry[11] and ^{18}O-labeling of the novel transacetalization[12] reaction are presented. The generality of transacetalization and the effects of ring size, ring substitution, and oxygen replacement by sulfur or nitrogen were evaluated by employing a variety of mainly 1,3-O,O- as well as 1,3-O,S-, 1-S,3-NH-, and 1,3-S,S-cyclic neutral acetals and ketals. The preferable reaction sites of the 1,3-O,S- and 1-S,3-NH-acetals, which could in principle form two different transacetalization products, were also determined. *Ab initio* potential energy surface diagrams have been elaborated for three representative cases, and the most likely reaction mechanisms and products have been established.

Methods

The MS^2 and MS^3 experiments were performed using a fast and high-transmission Extrel [Pittsburgh, PA] pentaquadrupole mass spectrometer, which has been described in detail elsewhere.[7] This mass spectrometer is a versatile "laboratory" for gas phase ion/molecule reaction studies[11] and consists basically of three mass analyzing (Q1, Q3, Q5) and two "*rf*-only" reaction quadrupoles (q2, q4). Ion/molecule reactions were performed by MS^2 experiments in which Q1 was used to mass select the ion of interest. Ion/molecule reactions were performed further in q2 with a selected neutral reagent in conditions such as collision energy (typically near 0 eV) and pressure of the neutral reagent that were only slightly adjusted in each experiment to maximize the yields of the products. The product spectrum was recorded by scanning Q5, while operating Q3 in the "full-transmission" *rf*-only mode.

For the MS^3 experiments,[13] each ion/molecule reaction product of interest was mass-selected by Q3 and dissociated further in q4 by 15 eV collisions with argon. The total pressures inside each differentially pumped region were typically 2×10^{-6} (ion-source), 8×10^{-5} (q2), and 8×10^{-5} (q4) Torr, respectively. The collision energies were calculated as the voltage difference between the ion source and the collision quadrupoles.

Ab initio molecular orbital calculations were carried out by using Gaussian94.[14] The closed-shell ions were optimized at the restricted (RHF) Hartree−Fock level of theory by employing the polarization 6-31G(d,p) basis set.[15] Improved energies were obtained by using single-point calculations at the 6-31G(d,p) level and incorporating valence electron correlation calculated by second-order Møller−Plesset (MP2) perturbation theory,[16] a procedure denoted as MP2/6-31G(d,p)//6-31G(d,p). Harmonic vibrational frequencies were calculated at the RHF/6-31G(d,p) level to characterize the stationary points and to obtain the zero-point vibrational energies (ZPE).

Results and Discussion

1,3-O,O-Cyclic Acetals and Ketals. (1) Generality of Transacetalization. The ion/molecule product spectra for reactions of the mass-selected acylium ion $CH_2{=}CHC^+{=}O$[17] with a series of neutral cyclic acetals and ketals of diols (that is, 1,3-O,O-heterocycles) are displayed in Table 1 and Figures 1−4. Transacetalization is found to be very general and to occur for all 1,3-O,O-cyclic acetals and ketals studied (except only for 1,3-benzodioxole, see the following text) regardless of the size of the ring or the nature and position of the substituents. It is interesting to note that, as expected from the proposed reaction mechanism (Scheme 1), 1,4-dioxane,

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(11) For details and recent examples of the application of pentaquadrupole mass spectrometry to the study of gas phase ion/molecule reactions, see: (a) Eberlin, M. N.; Kotiaho, T.; Shay, B. J.; Yang, S. S.; Cooks, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 2457. (b) Gozzo, F. C.; Eberlin, M. N. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 554. (c) Gozzo, F. C.; Eberlin, M. N. *J. Mass Spectrom.* **1995**, *30*, 1553. (d) Gozzo, F. C.; Eberlin, M. N. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 554. (e) Sorrilha, A. E. P. M.; Pimpim, R. S.; Gozzo, F. C.; Eberlin, M. N. *J. Am. Soc. Mass Spectrom.* **1996**, *7*, 1126. (f) Eberlin, M. N.; Sorrilha, A. E. P. M.; Gozzo, F. C.; Pimpim, R. S. *J. Am. Chem. Soc.* **1997**, *119*, 3550. (g) Eberlin, M. N. *Mass Spectrom. Rev.* In press.

(12) The reaction was originally[5] termed as "oxirane addition" for analogy with a solution reaction that invoked oxirane addition to carbonyl compounds, see: Bogert, M. T.; Roblin, R. L. *J. Am. Chem. Soc.* **1933**, *55*, 3741. Transacetalization is, however, a more general term for the reaction, which is shown in the present study to occur not only by net "oxirane (C_2H_4O) addition" addition but also by "ethylene sulfide (C_2H_4S)", "oxetane (C_3H_6O)", "thietane (C_3H_6S)", and "2,5-dihydrofuran (C_4H_6O)" net additions. Moreover, transacetalization also describes the reaction more precisely by indicating the type of mechanism that operates and the class of product (cyclic "ionic ketals") that are formed, whereas pointing out the interesting correlation with the analogous condensed phase transacetalization reactions.

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(14) Gaussian 94, Revision B.3. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Lahem, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1995.

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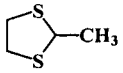
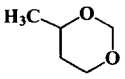
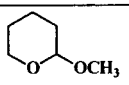
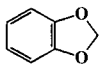
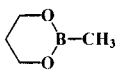
(16) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(17) The vinyl α,β-unsaturated acylium ion $CH_2{=}CHC^+{=}O$ was chosen because it was found to react extensively via transacetalization with 2-methyl-1,3-dioxolane[5] and it can be easily generated at high yields from several precursors such as ethyl vinyl ketone.

Table 1. Products of Ion/Molecule Reactions with the Acylium Ion CH_2=CHCO$^+$

Entries	Compound	M.W.	Products m/z (Relative Abundance)			
			Transacetalization	Proton Transfer	H (or alkyl) abstraction	Other Products
1		102	99(100)	103 (19)	87(4)	87(4)
2		116	99 (100)	117 (6)	87 (2)	--
3		90	99(28), 115(100)	91 (30)	89 (46)	59 (15)
4		106	--	107 (78)	105 (100)	106 (18)
5		120	--	121(100)	119(94)	120(21),105(61)
6		102	127(100)	103(7)	101 (3)	--
7		88	--	89(90)	87(100)	--
8		104	--	105(100)	103 (23)	75 (6), 104 (32)
9		116	--	117 (7)	--	71 (14), 85 (100), 99 (6), 169 (10)
10		89	98 (25), 115 (90)	90 (100)	--	118 (35)
11		122	--	123 (43)	--	177 (100)[a]
12		100	--	101 (8)	99 (2)	155 (100)[a]

[a] The intact adduct.

its monosulfur analogue, and 2-methyl-1,3,2-dioxaborinane (Table 1, entries 7, 8, and 12), which are not acetals, as well as tetrahydrofuran and tetrahydrothiophene (spectra not shown), a monooxygenated and a monosulfurated heterocyclic, respectively, are completely unreactive toward transacetalization. They react with CH_2=CHC$^+$=O mainly by proton transfer, hydride abstraction, and/or adduct formation.

Considering the mechanism proposed in Scheme 1, substituents at the 2-position of cyclic acetals and ketals are expected to affect considerably the extent of transacetalization by either favoring or inhibiting the ring-opening process. As seen in Table 1 (entries 1 and 2) and in Figure 2, the results for a series of 2-substituted 1,3-dioxolanes show that 2-alkyl and 2-phenyl groups notably favor transacetalization over the competitive proton transfer and hydride (or alkyl) abstraction.[11e] A remarkable result is obtained for 2-phenyl-1,3-dioxolane (Figure 2b), for which practically only the transacetalization product of *m/z* 99 is formed. Note that such remarkably high-yield "clean" ion/molecule reactions are rare. Charge-stabilizing 2-substituents such as alkyl groups should facilitate the ring-opening process (Scheme 1), and this effect is expected to be much more pronounced for the phenyl group owing to its great ability to stabilize the positive charge (Scheme 3).

The 2-methoxy substituent (Figure 3b), on the other hand, is observed to decrease greatly the extent of transacetalization (*m/z* 99) with CH_2=CHCO$^+$ (*m/z* 55). Although the 2-OCH_3 group would be expected to facilitate ring-opening, other competitive processes could also be favored, that is, proton transfer and "exocylic" O-acylation. The protonated molecule (*m/z* 105) is not observed at all, but most likely dissociates rapidly by methanol (*m/z* 73) and formaldehyde loss (*m/z* 75). Note also that transacetalization cannot take place if initial

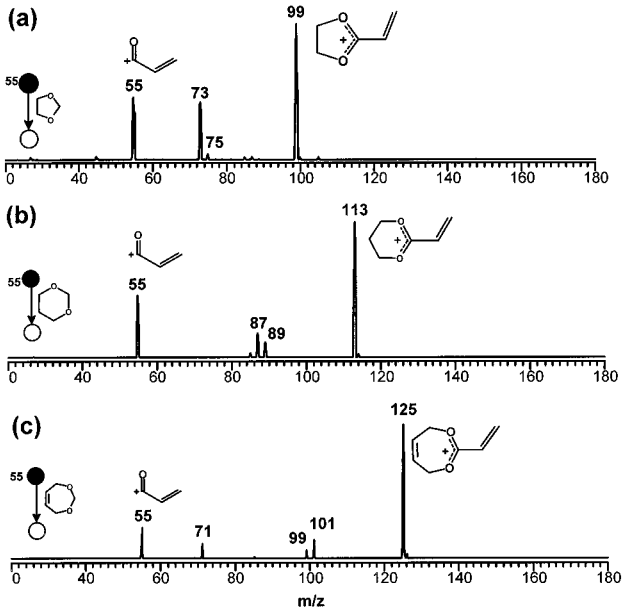


Figure 1. Double-stage (MS^2) product spectrum for ion/molecule reactions of the acylium ion $CH_2{=}CHCO^+$ with (a) 1,3-dioxolane, (b) 1,3-dioxane, and (c) 1,3-dioxep-5-ene. Note in all cases the abundant transacetalization products of *m/z* 99, 113, and 125, respectively. In the terminology used to describe the type of experiment and scan mode employed, a filled circle represents a fixed (or selected) mass and an open circle a variable (or scanned) mass, while the neutral reagent or collision gas that causes the mass transitions is shown between the circles. For more details on this terminology, see ref 13a.

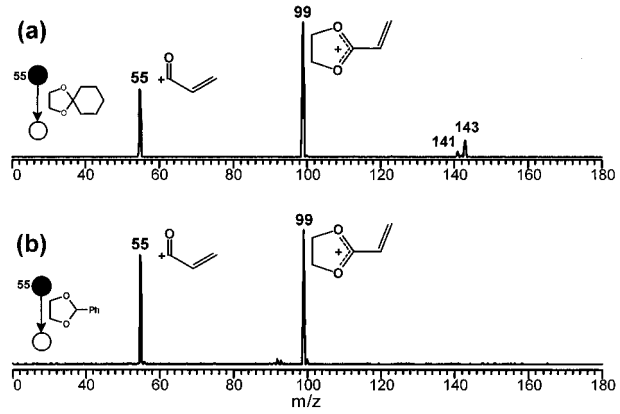


Figure 2. Double-stage (MS^2) product spectrum for ion/molecule reactions of the acylium ion $CH_2{=}CHCO^+$ with (a) 2,2-pentamethylene-1,3-dioxolane and (b) 2-phenyl-1,3-dioxane. Note in both cases the same transacetalization product of *m/z* 99, and its high relative abundance particularly in spectrum b.

acylation occurs at the exocyclic oxygen, the corresponding acylated product being expected to undergo dissociation by methyl acrylate loss (Scheme 4) to yield also the product ion of *m/z* 73.

It is interesting to note, however, that the extent of transacetalization to the 2-methoxy derivative varies significantly with the nature of the acylium ion employed (Figure 3). For the less reactive[5] $C_2H_5CO^+$ ion, a very minor transacetalization product is formed (*m/z* 101, Figure 3a). A product of medium abundance is observed for $CH_2{=}CHCO^+$ (*m/z* 99, Figure 3b), whereas the cyclic "ionic ketal" of *m/z* 116 is the main ionic product (Figure 3c) for the most reactive[5,8] $(CH_3)_2NCO^+$ acylium ion. These results show that the extent of transacetalization can be controlled by selecting the appropriate reactant acylium ion and that the reaction can be dominant even for the less reactive cyclic acetals and ketals.

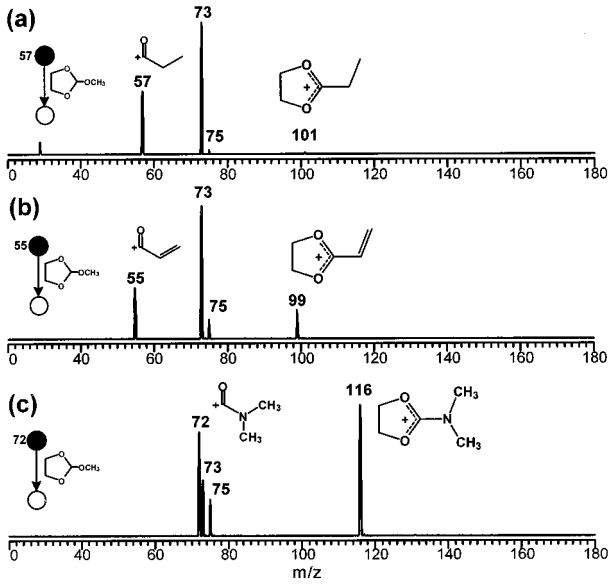


Figure 3. Double-stage (MS^2) product spectrum for ion/molecule reactions of 2-methoxy-1,3-dioxolane and the acylium ions (a) $C_2H_5CO^+$ (b) $CH_2{=}CHCO^+$, and (c) $(CH_3)_2NCO^+$. Note that the extent of transacetalization varies significantly, and that this reaction is dominant (*m/z* 116) for the most reactive, less acidic acylium ion $(CH_3)_2NCO^+$.

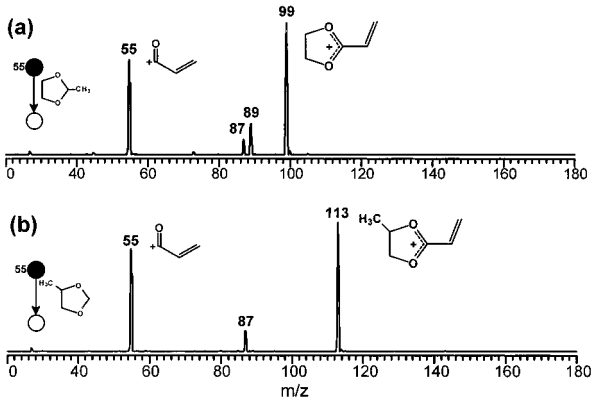
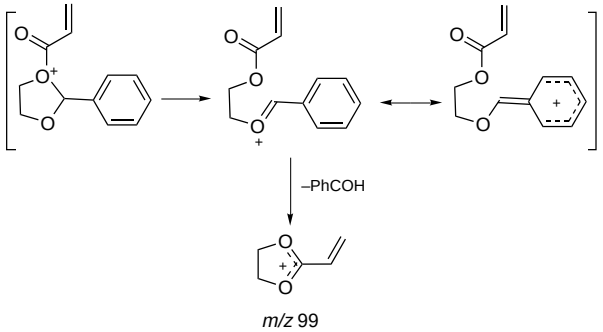
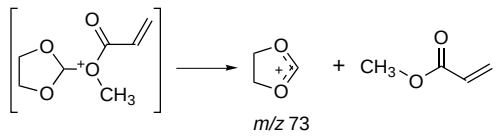


Figure 4. Double-stage (MS^2) product spectrum for ion/molecule reactions between the acylium ion $CH_2{=}CHCO^+$ and two positional isomers: (a) 2-methyl-1,3-dioxolane and (b) 4-methyl-1,3-dioxolane. The 2-methyl group is eliminated (*m/z* 99) whereas the 4-methyl group remains in the cyclic "ionic ketal" product of *m/z* 113.

Scheme 3



Scheme 4



(2) 1,3-Benzodioxole. A unique and interesting behavior was observed for 1,3-benzodioxole, the cathechol acetal of formaldehyde. In reactions with $CH_2{=}CHCO^+$ (Table 1, entry 11) and $(CH_3)_2NCO^+$ (spectrum not shown) only the intact adduct, which was not observed in the other cases, is formed. Two effects could then be conceived as suppressing transacetalization in this very particular case. For instance, acylation may take place at the phenyl ring which is activated toward electrophilic attack by the two alkoxy substituents or formaldehyde loss (Scheme 1) may be hampered since intramolecular displacement would occur on an aromatic sp^2 carbon. It is interesting to note that the intact adduct of 1,3-benzodioxole does not lose formaldehyde even when activated upon collision (spectrum not shown), but instead they dissociate exclusively to re-form the original reactant ion.

(3) Distinction of Positional Isomers. To some extent transacetalization with acylium ions is also able to differentiate isomeric cyclic acetals and ketals by revealing whether the substituent is localized at the 2-position (R_1) or at other ring positions (R_2, Scheme 1). The case shown in Figure 4 exemplifies this clearly. For 2-methyl-1,3-dioxolane (Figure 4a), transacetalization occurs *via* "loss" of the 2-methyl group (R_1) that is incorporated into the released neutral aldehyde (Scheme 1), and the product of *m*/*z* 99 is formed. On the other hand, the 4-methyl substituent (R_2) of 4-methyl-1,3-dioxolane remains in the cyclic "ionic ketal" product, which consequently display a 14 u higher *m*/*z* 113 ratio (Figure 4b).

As for the five-membered 1,3-dioxolanes, the result for 4-methyl-1,3-dioxane (Table 1, entry 6) indicates that transacetalization is also able to reveal the location of substituents for six-membered cyclic ketals. Distinction between isomeric 2-substituted five-membered and six-membered cyclic acetals and ketals based on formation of different transacetalization products is also possible and straightforward, as seen when comparing Figures 1b and 4a. Although the isomeric 4-methyl-1,3-dioxolane (Figure 4b) and 1,3-dioxane (Figure 1b) display isobaric transacetalization products of *m*/*z* 113, their distinction is still possible because 1,3-dioxane reacts much more readily by proton transfer (*m*/*z* 89). In addition, the triple-stage mass spectrum of the cyclic "ionic ketal" product of 4-methyl-1,3-dioxolane (see Figure 6b) displays a minor but unique fragment of *m*/*z* 41.

1,3-O,S-, 1,3-NH,S-, and 1,3-S,S-Cyclic Acetals. (1) 1,3-O,S- and 1,3-NH,S-Acetals. Transacetalization (Scheme 5) also occurs extensively for the monosulfur cyclic acetals 1,3-oxathiolane (Table 1, entry 3), 2-methyl-1,3-oxathiolane (Figure 5a), and 1,3-oxathiane (Figure 5b). Thiazolidine, a sulfur−nitrogen cyclic acetal, reacts moderately via transacetalization with $CH_2{=}CHCO^+$ (Table 1, entry 10), but the reaction becomes dominant when employing the more reactive acylium ion $(CH_3)_2NCO^+$ (Figure 5c). The relative yields of the cyclic "ionic ketals" and cyclic "ionic *thio*ketals" show that the initial acylation occurs almost exclusively (Figure 5a) or predominantly (Figures 5b and 5c) at the sulfur atom

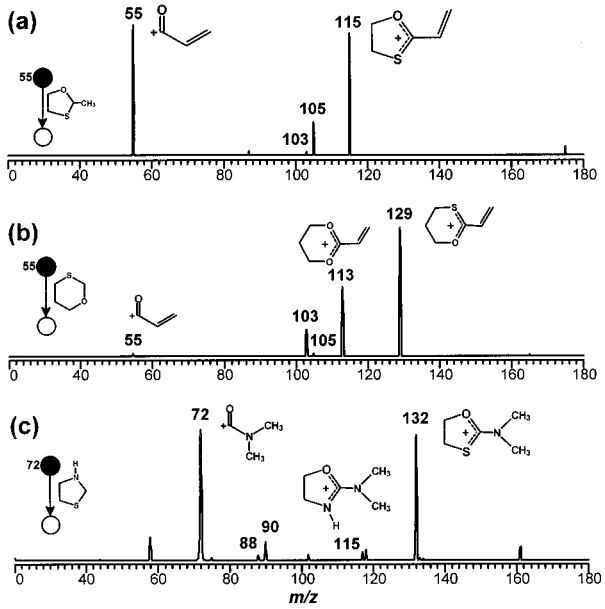
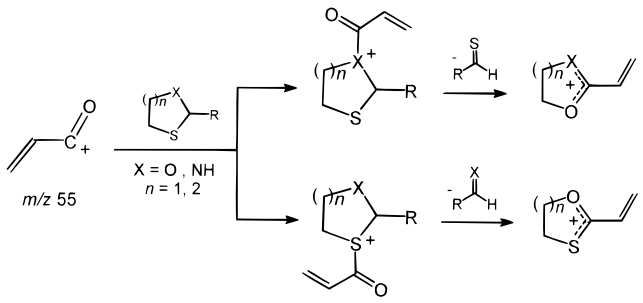


Figure 5. Double-stage (MS^2) product spectrum for ion/molecule reactions of the three sulfur acetals; (a) 2-methyl-1,3-oxathiolane, (b) 1,3-oxathiane, and (c) thiazolidine with the acylium ions $CH_2{=}CHCO^+$ (a and b) and $(CH_3)_2NCO^+$ (c). Note that, as the result of initial acylation mainly at the sulfur atom, cyclic "ionic *thio*ketals" dominate the product spectra.

Scheme 5



(Scheme 5). Note also the very distinct spectra of the two isomeric sulfur acetals (Figures 5a and 5b).

(2) Disulfur analogues. A drastic change in reactivity occurs, however, for the disulfur analogues 1,3-dithiolanes (Table 1, entries 4 and 5). Transacetalization does not occur to any observable extent, and the hydride abstraction and proton transfer reactions dominate. This unique behavior of the 1,3-S,S analogues is most likely a consequence of the instability of the S-acylated 1,3-dithiolanes; see the *ab initio* section that follows. The 1,3-dithiolanes were also found to be unreactive toward transacetalization with several other acylium ions, such as CH_3CO^+, $(CH_3)_2NCO^+$, $C_2H_5CO^+$, and the thioacylium ion CH_3CS^+ (spectra not shown).

Structure[18] of the Cyclic "Ionic Ketals". The MS^3 capabilities of the pentaquadrupole mass spectrometer[7] allow one to interrogate the structure of the cyclic "ionic (*thio*)ketal" products *via* their mass selection and further collision-induced dissociation and the recording of the data in triple-stage mass spectra (Figure 6). With no exceptions, all the cyclic "ionic ketals" and "ionic *thio*ketals", regardless of the ring size (five-, six-, or seven-membered) and the position or nature of the substituents, dissociate exclusively to re-form[19] the reactant acylium

(18) The term "structure" is used in a restricted sense, to denote connectivity rather than detailed structure.

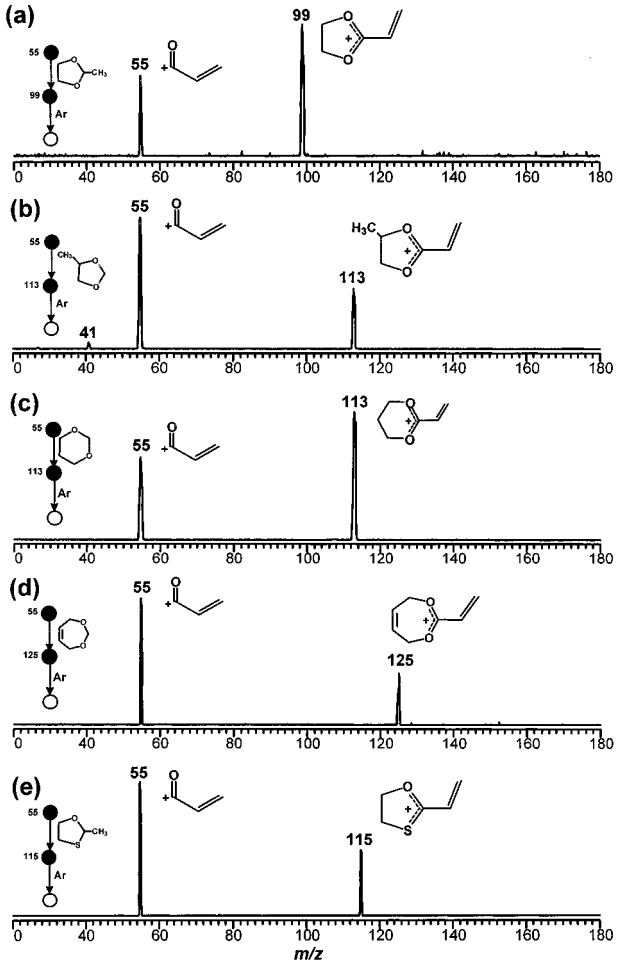
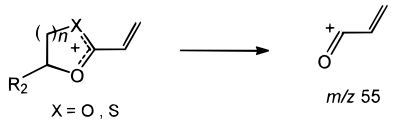


Figure 6. Triple-stage (MS^3) sequential product spectrum of several transacetalization products. Note extensive dissociation in all cases that re-forms the reactant acylium ion $CH_2{=}CHCO^+$ of *m*/*z* 55, a dissociation chemistry that characterizes the cyclic "ionic (*thio*)ketals".

Scheme 6



ion ($CH_2{=}CHC^+{=}O$ of *m*/*z* 55 in Figure 6). This simple and unique dissociation chemistry[5,8] is therefore amply demonstrated to be a characteristic of cyclic "ionic ketals" (Scheme 6). As already mentioned, this interesting re-forming step is equivalent to the hydrolysis of neutral cyclic acetals and ketals that also re-form easily the original carbonyl compound.[20] It was also interesting to note that the alternative dissociation to $CH_2{=}CHC^+{=}S$ (*m*/*z* 69) is not observed to any measurable extent for the cyclic "ionic *thio*ketals" (Figure 6e). Because of the relatively poor 2p−3p π overlap in multiple bonds between carbon and sulfur, thioacylium ions are anticipated to be less stable than the oxygen analogue acylium ions;[21] hence dissociation of cyclic "ionic mono*thio*ketals" should yield predominantly the more stable acylium ion.

Scheme 7

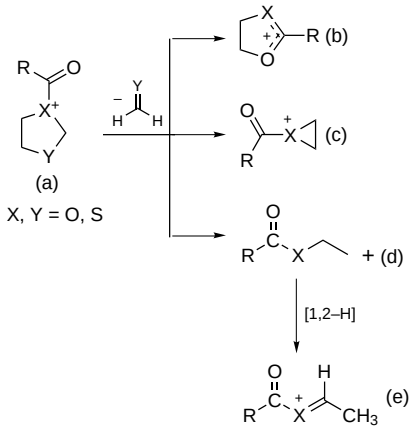


Table 2. Total, ZPE, and Relative Energies from *ab Initio* Full Structure Optimization Calculations

species[a]	MP2/6-31(G(d,p)// 6-31G(d,p) (hartrees)	ZPE (hartrees)[b]	total energy (hartrees)
1,3-dioxolane	−267.57236	0.089414	267.48295
1,3-oxathiolane	−590.18391	0.086333	−590.09758
1,3-dithiolane	−912.79873	0.08272	−912.71601
CH_3CO^+	−152.49495	0.042626	−152.45232
a (X, Y = O)	−420.11132	0.136000	−419.97532
a (X, Y = S)	unstable		
b (X = O)	−305.93493	0.10517	−305.82977
b (X = S)	−628.53471	0.10152	−628.43320
e (X = O)	−305.90415	0.09967	−305.80447
e (X = S)	−628.49564	0.09619	−628.39944
f (X, Y = O)	−267.88847	0.10129	−267.78718
f (X = O, Y = S)	−590.48183	0.09652	−590.38531
f (X = S, Y = O)	−590.50538	0.09605	−590.40932
f (X, Y = S)	−913.11788	0.09242	−913.02546
g (X, Y = O)	−266.72561	0.07949	−266.64612
g (X = O, Y = S)	−589.32789	0.07561	−589.25228
g (X, Y = S)	−911.94037	0.07203	−911.86834
$CH_2{=}O$	−114.18127	0.02579	−114.15548
$CH_2{=}S$	−436.77060	0.02373	−436.74686
$CH_2{=}C{=}O$	−152.16048	0.03034	−152.13014
CH_3COH	−153.37475	0.05276	−153.32199
oxirane	−153.33376	0.05511	−153.27865
ethylene sulfide	−475.96090	0.05257	−475.90833

[a] For structures **a**−**g** see Schemes 7 and 8. [b] Scaled by 0.89. [c] Structures **c** and **d** were found by the calculations to be unstable, see text.

This unique behavior of cyclic "ionic mono*thio*ketals" has been recently applied in a novel gas phase strategy for sulfur replacement by oxygen that leads to the conversion of *thio*acylium ions into acylium ions.[22]

***Ab Initio* Calculations.** As already discussed, the characteristic dissociation revealed by the triple-stage mass spectra provide evidence that cyclic "ionic ketals" and "ionic *thio*ketals" (**b** in Scheme 7) are formed in transacetalization with acylium ions. Formation of **b** would also be expected if one considers that the ring-opening process (Scheme 1) is likely assisted by intramolecular displacement. However, other alternative products (**c**, **d**, and **e**, Scheme 7) could be proposed as the main ionic products of ion/molecule reactions of acylium ions with cyclic acetals and ketals. To determine the most thermodynamically favorable products, *ab inito* potential energy surface diagrams for the reaction of CH_3CO^+ with three representative cyclic acetals (Table 2 and Figure 7) were then elaborated.

(19) Structurally diagnostic ion/molecule reactions and triple-stage mass spectrometry have shown that the cyclic 2-methyl-1,3-dioxolanylium ion forms almost exclusively (99%) the acetyl cation upon collision-induced dissociation, see ref 4b. Therefore, similar behavior is expected for the other homologous and derivatives.

(20) Carey, F. A.; Sunderberg, R. J. In *Advanced Organic Chemistry*, 2nd ed.; Plenum Press: New York, 1984.

(21) Caserio, M. C.; Kim, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6896.

(22) Moraes, L. A.; Eberlin, M. N. *J. Chem. Soc., Perkin Trans. 2.*, in press.

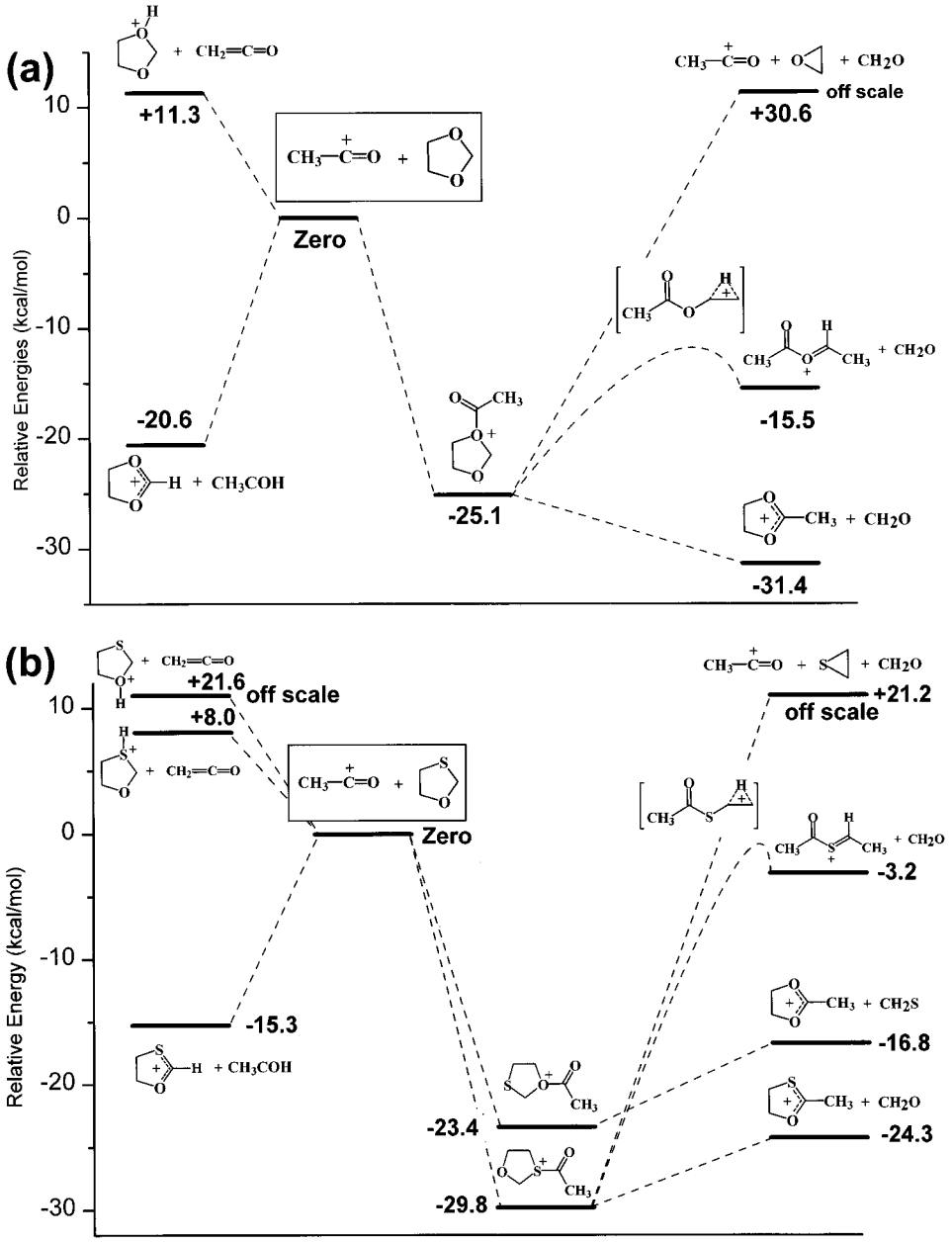
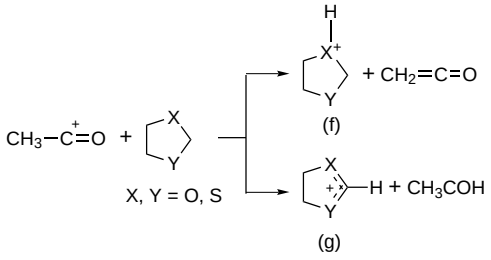


Figure 7. *Ab initio* potential energy surface diagrams for the reaction of the acetyl cation with (a) 1,3-dioxolane and (b) 1,3-oxathiolane. Note in both cases that transacetalization leading to the cyclic "ionic ketals" or "ionic *thio*ketals" products are predicted to be the most exothermic, thermodynamically favorable process.

(1) 1,3-Dioxolane. The diagram for the reaction of 1,3-dioxolane (Figure 7a) shows that O-acylation (**a**) is exothermic by −25.1 kcal/mol. Further dissociation to **b** is also exothermic, which makes transacetalization greatly exothermic by −31.4 kcal/mol. The acyclic structure **d** was shown to be unstable, and depending on its input conformation, isomerization to **e** or cyclization to **b** occurs in the course of structure optimization. Formation of **e** *via* the unstable **d** is, however, a more energy demanding process (+10.4 kcal/mol from the adduct **a**), which must also be hampered by an activation barrier of higher energy (not estimated) for the [1,2-H] shift (Figure 7a). Structure **c** was also found by the calculations to be unstable, dissociating to oxirane and the acetyl cation in a +30.6 kcal/mol endothermic process. The high exothermicity of the dissociation **a** → **b** + CH_2O indicated by the *ab initio* results can also explain the rapid dissociation of the "hot" adducts, which are not observed in the ion/molecule reaction spectra. The energetics of

Scheme 8



the two competitive processes of proton transfer and hydride abstraction (Scheme 8) were also estimated (Figure 7a). Hydride abstraction is also exothermic (−20.6 kcal/mol) but not as much as transacetalization (−31.4 kcal/mol). This indicates that both processes should occur with the predominance of transacetalization, as indeed it is observed for 1,3-dioxolane (Figure 1a); see also the results of this specific reaction in ref 5. Proton

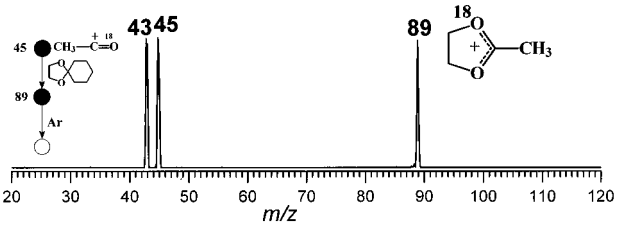


Figure 8. Triple-stage (MS^3) sequential product spectrum of the transacetalization product of 1,3-dioxolane with $CH_3C^+{=}{}^{18}O$. Note dissociations to the same extent to both the labeled ($CH_3C^+{=}{}^{18}O$, *m/z* 45) and unlabeled ($CH_3C^+{=}O$, *m/z* 43) reactant ion.

transfer is, on the other hand, endothermic by +11.3 kcal/mol, and therefore should be disfavored. Note, however, that due to the multiple collision conditions applied, proton transfer may occur also from secondary reaction products.

(2) 1,3-Oxathiolane. Similar results are observed for the 1,3-oxathiolane case (Figure 7b). Again, transacetalization leading to the cyclic "ionic ketal" and "ionic *thio*ketal" products **b** is the most exothermic, thermodynamically favorable process. S-Acylation is −6.5 kcal/mol more exothermic, and therefore it is expected to dominate over O-acylation (Scheme 5), exactly as experimentally observed (Figure 5a,b).

(3) 1,3-Dithiolane. An interesting result was obtained for the disulfur analogue 1,3-dithiolane. Structural optimization of the corresponding adduct **a**, *i.e.*, the S-acetylated 1,3-dithiolane, shows it to be unstable relative to the starting reactants, thus indicating the first step of transacetalization (Scheme 1) to be an endothermic, unfavorable process. On the other hand, hydride abstraction remains quite exothermic (−13.8 kcal/mol, Table 2). This nicely explains the lack of reactivity of 1,3-dithiolane toward transacetalization.

(4) ^{18}O Labeling. A conclusive evidence that cyclic "ionic ketals" are formed via transacetalization with acylium ions was obtained when dissociating the corresponding product of reaction between the ^{18}O-labeled ion $CH_3C^+{=}{}^{18}O$ and 2,2-pentamethylene-1,3-dioxolane. The triple-stage spectrum (Figure 8) shows dissociation to the same extent to both the labeled ($CH_3C^+{=}{}^{18}O$, *m/z* 45) and unlabeled ($CH_3C^+{=}O$, *m/z* 43) reactant ion, a result that can only be explained by assuming the ring-opening/ring-reforming "oxygen-scrambling" mechanism depicted in Scheme 1.

Conclusion

Transacetalization with acylium ions of a large variety of cyclic neutral acetals and ketals, that is, five-, six-, and seven-membered 1,3-O,O-heterocycles and their monosulfur and nitrogen analogues, occurs in high yields in the gas phase, and cyclic "ionic ketals" are formed as the main products. A general, structurally diagnostic ion/molecule reaction for the characterization of cyclic neutral acetals and ketals in the gas phase is therefore available. Positional isomers, more specifically those that bear substituents at the 2-position, are easily identified since these substituents are eliminated in the course of the reaction, whereas substituents at other ring positions remain in the cyclic "ionic ketal" products. MS^3 experiments and ^{18}O-labeling confirm the formation of the cyclic "ionic (*thio*)ketals" via the operation of the "oxygen-scrambling" mechanism of transacetalization. They also reveal that re-forming of the reactant acylium ions in high yields upon collision-induced dissociation is a very general characteristic of cyclic "ionic (*thio*)ketals", a step that is equivalent to the hydrolysis of neutral cyclic acetals and ketals.

A variety of neutral ketals and acetals constitute or are important derivatives of a large variety of biologically and chemically relevant molecules. Therefore, the present results with "model" compounds indicate that transacetalization with acylium ions should be useful as a general structurally diagnostic test for the characterization of many of these compounds in the gas phase. A systematic study on the application of gas phase transacetalization with acylium ions toward this end is underway in our laboratory.

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Supporting Information Available: The XYZ coordinates and energies of optimized structures (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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