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Structurally diagnostic ion–molecule reactions: acylium ions with α-, β- and γ-hydroxy ketones

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Gas-phase reactions of four acylium ions and a thioacylium ion with three isomeric α-, β- and γ-hydroxy ketones are performed by pentaquadrupole mass spectrometric experiments. Novel structurally diagnostic reactions are observed, and found to correlate directly with interfunctional group separation. All five ions tested (CH_3CO^+, $CH_2{=}CHCO^+$, $PhCO^+$, $(CH_3)_2NCO^+$ and $(CH_3)_2NCS^+$) react with the γ-hydroxy ketone (5-hydroxy-2-pentanone) to form nearly exclusively a cyclic oxonium ion of *m/z* 85 that formally arises from hydroxy anion abstraction. With the β-hydroxy ketone (4-hydroxy-2-pentanone), $CH_2{=}CHCO^+$, $PhCO^+$ and $(CH_3)_2NCO^+$ form adducts that undergo fast cyclization via intramolecular water displacement, yielding resonance-stabilized cyclic dioxinylium ions. With the α-hydroxy ketone (3-hydroxy-3-methyl-2-butanone), $PhCO^+$, $(CH_3)_2NCO^+$ and $(CH_3)_2NCS^+$ form stable adducts. Evidence that these adducts display cyclic structures is provided by the triple-stage mass spectra of the $(CH_3)_2NCS^+$ adduct; it dissociates to $(CH_3)_2NCO^+$ via a characteristic reaction–dissociation pathway that promotes sulfur-by-oxygen replacement. If cyclizations are assumed to occur with intramolecular anchimeric assistance, relationships between structure and reactivity are easily recognized. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: Gas-phase ion–molecule reactions; acylium ions; pentaquadrupole mass spectrometry; hydroxy ketones

INTRODUCTION

Class-selective reactions have been extensively used in solution for chemical recognition.[1] Functional groups confer on molecules specific reactivity that reveals their presence and other structural details such as molecular geometry and relative positions of substituents. In the gas phase, the easy access and manipulation of ions of many classes, particularly when multiple-stage mass spectrometric techniques[2] are applied, has motivated the development of a variety of class-selective, structurally diagnostic ion–molecule reactions.[3] Ideal ion–molecule reactions for structural elucidation are selective for, and general to, molecules or ions bearing specific functional groups. It is desirable that such reactions also provide fine structural information such as relative positions of substituents. Reactions with these characteristics demand ions of high reactivity which interact with the neutral molecule in a way sensitive to structural modifications.

Acylium ions ($R{-}C^+{=}O$) are common and easily accessible stable carbocations and, in the family of condensed[4] and gas-phase ions,[5] they are as important and diversely reactive as the neutral related carbonyl compounds. Gaseous acylium ions have been used, therefore, in several structurally diagnostic ion–molecule reactions.[5] This paper reports reactions of some gaseous acylium ions and a thioacylium ion with three isomeric α-, β- and γ-hydroxy ketones. According to the specific interfunctional group separation of the isomeric hydroxy ketones, the ions react distinctively via mechanisms readily rationalized if cyclizations with intramolecular anchimeric assistance are assumed. In these reactions, direct relationships between structure and reactivity are easily recognized.

EXPERIMENTAL

The gaseous acylium ions were produced, reacted and their products analyzed via double- (MS^2) or triple-stage (MS^3) mass spectrometric experiments performed with an Extrel (Pittsburgh, PA, USA) pentaquadrupole ($Q_1q_2Q_3q_4Q_5$) mass spectrometer.[6] The reactant ions were formed by 70 eV electron ionization (EI) of acetylacetone (**1**, co-generated with nearly 7% of $CH_2{=}C{=}OH^+$),[7] methyl vinyl ketone (**2**), methyl phenyl ketone (**3**),[7] tetramethylurea (**4**)[12] and tetramethylthiourea (**5**).[8] For the MS^2 ion–molecule reactions, Q1 was used to mass-select the ion of interest for further reactions in q2 with a selected hydroxy ketone. Ion translational energies were set to near 0 eV as calibrated by the *m/z* 39 : 41 ratio in neutral ethylene–ionized ethylene reactions.[9] Product ion mass spectra were acquired by scanning Q5, while Q3 and q4 were operated in the broadband r.f.-only mode.

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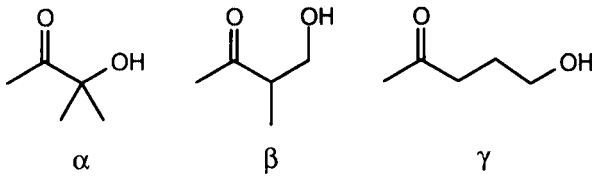
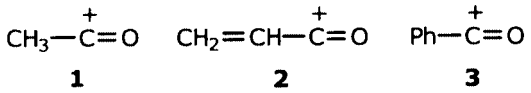
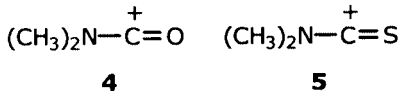
Multiple collision conditions were used in q2, as indicated by typical beam attenuations of 50–70%.







For the MS^3 experiments,[10] a product ion of interest formed in q2 was mass-selected by Q3 for further 15 eV collision-induced dissociation (CID) with argon in q4, while Q5 was scanned to record the mass spectrum. The 15 eV collision energies were taken as the voltage differences 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} (q2) and 8×10^{-5} (q4) torr, respectively (1 torr = 133.3 Pa).

RESULTS AND DISCUSSION

Reactivity of 4

The product ion mass spectra for the reactions of the five ions investigated (Ac^+) with the three isomeric hydroxy ketones (M) are summarized in Table 1. As representative examples, we will first discuss the reactions of **4** and show its product ion mass spectra in Fig. 1. As can be seen, the three spectra are clearly distinctive, revealing direct relationships between structure and reactivity.

γ-Hydroxy ketone

Ion **4** reacts with the γ-hydroxy ketone [Fig. 1(a)] to form, nearly exclusively, a product ion of *m/z* 85. This ion arises from net hydroxy anion abstraction, $[M - OH]^+$, as rationalized in Scheme 1. Acylation at the hydroxy group is followed by intramolecular cyclization through a favored five-membered ring transition state with anchimeric assistance of the γ-carbonyl group (anchimeric assistance is commonly observed in the gas phase; see. e.g., Ref. 11). A good leaving group is displaced (for **4**, a neutral molecule of dimethylcarbamic acid) and a relatively stable cyclic oxonium ion of *m/z* 85 is formed (instead of a rather unstable primary carbocation). Proton transfer followed by water loss from MH^+ is, however, an alternative and undistinguishable route to *m/z* 85, but it should compete favorably only for the more acidic ions, particularly for **1**.

β-Hydroxy ketone

Reaction of **4** with the β-hydroxy ketone proceeds mainly through a single but distinct pathway as it yields

Table 1. Major product ions (*m/z* with relative abundances (%) in parentheses) for reactions of the acylium ions **1**–**4** and the thioacylium ion **5** with the three isomeric hydroxy ketones (102 u)

	α-Hydroxy ketone		β-Hydroxy ketone		γ-Hydroxy ketone	
Reactant ion Ac^+	MAc^+	Proton transfer[a]	$[MAc - H_2O]^+$	Proton transfer[a]	$[M - OH]^+$ *m/z* 85	Proton transfer[a]
1 *m/z* 43	None	103 (42), 187 (11), 205 (100)	None	85 (100), 103 (19), 169 (22), 187 (1)	100	None
2 *m/z* 55	None	85 (1), 103 (52), 187 (98), 205 (100)	139 (100)	85 (49), 103 (41), 169 (32), 187 (3)	100	None
3 *m/z* 105	207 (53)	103 (11), 187 (31), 205 (100)	189 (28)	85 (16), 169 (100), 187 (58), 205 (9)	100	None
4[b] *m/z* 72	174 (32)	103 (2), 187 (42), 205 (14)	156 (100)	85 (7), 103 (2), 169 (1)	100	187 (2)
5 *m/z* 88	190 (100)	205 (16), 187 (22)	None[c]	169 (100)	100	None

[a] Products arising from primary and/or secondary proton transfer reactions: MH^+ (*m/z* 103), $[MH - H_2O]^+$ (*m/z* 85), M_2H^+ (*m/z* 205), $[M_2H - H_2O]^+$ (*m/z* 187) and $[M_2H - 2H_2O]^+$ (*m/z* 169). Note that $[MH - H_2O]^+$ and $[M - OH]^+$ are alternative and indistinguishable routes to *m/z* 85.

[b] In reactions with the α-hydroxy ketone, **4** also forms $(CH_3)_2NCO_2H_2^+$ of *m/z* 90 (3%), $(CH_3)_2NH_2^+$ of *m/z* 46 (6%), $[M(CH_3)_2NH_2]^+$ of *m/z* 148 (32%) and $[M(CH_3)_2NCO_2H_2]^+$ of *m/z* 192 (100%); see text and Fig. 1(c).

[c] The adduct is formed instead: *m/z* 190 (42%).

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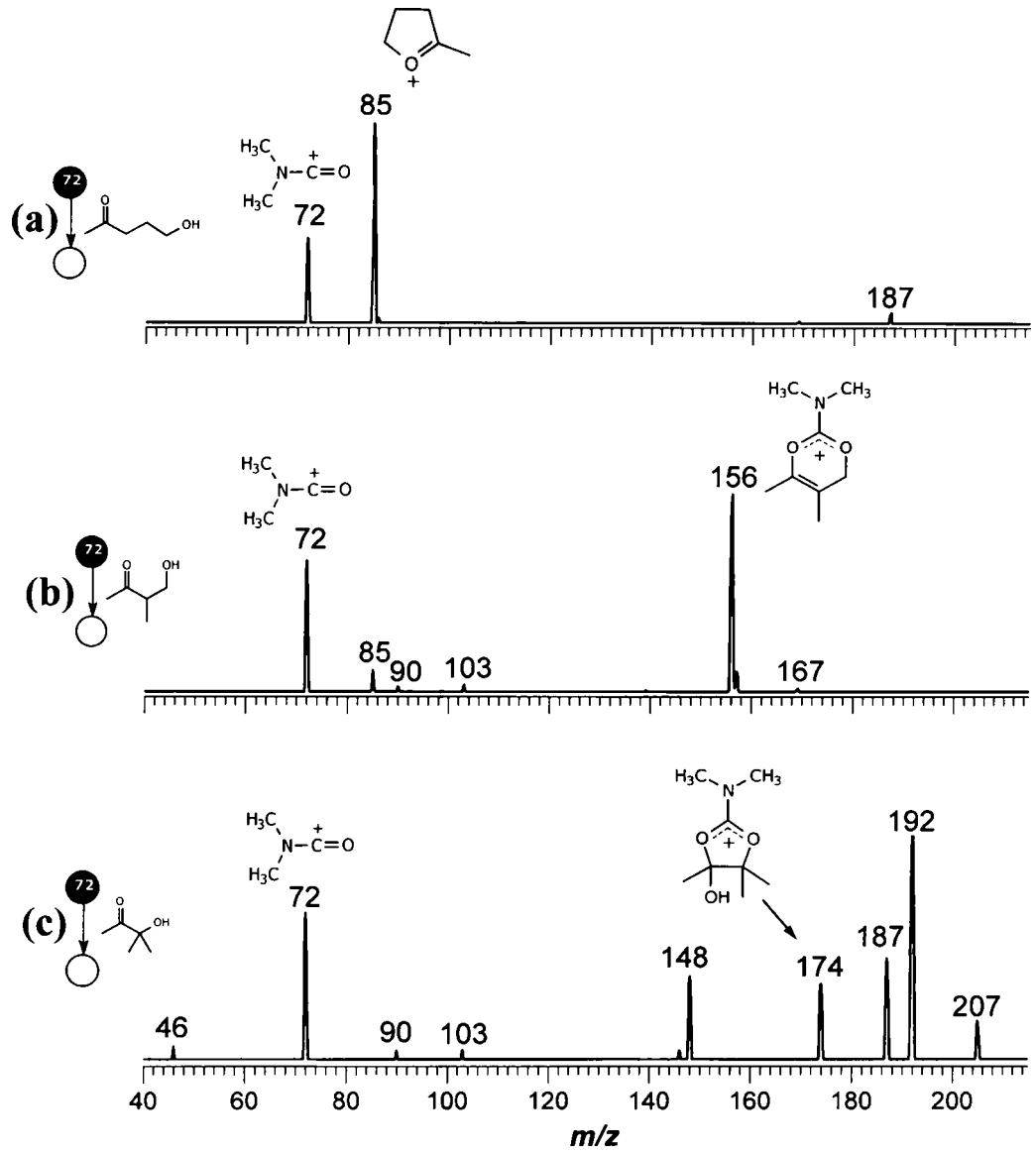
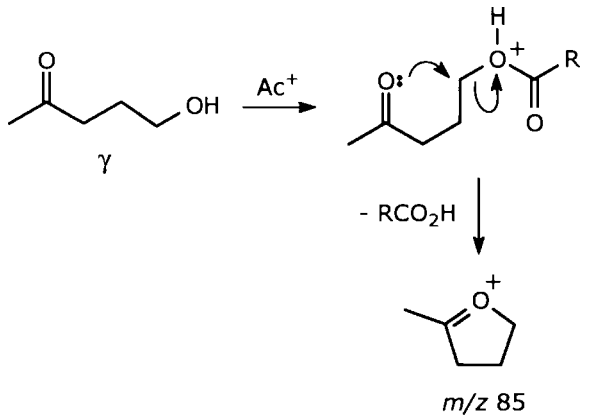


Figure 1. Double-stage (MS^2) product ion mass spectra for reactions of **4** of m/z 72 with the (a) γ- (b) β- and (c) α-hydroxy ketones.

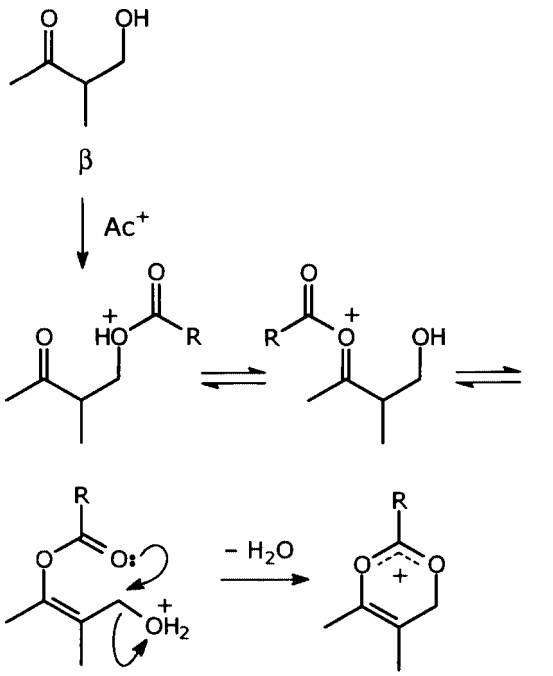
predominantly an ion of m/z 156 [Fig. 1(b)]. This product ion arises from adduct formation followed by water loss, $[MAc - H_2O]^+$. As for the γ-hydroxy ketone, the favorable formation of m/z 156 can be easily rationalized by a pathway (Scheme 2) that, when compared with that depicted in Scheme 1, shows again a direct relationship between structure (functional group separation) and reactivity. Acylation may occur at either the carbonyl or hydroxy group, or at both, and intramolecular acylium ion exchange is likely to operate.[12] Acylation is then followed by fast intramolecular proton transfer and water displacement which proceeds via a favored six-membered ring transition state now with the anchimeric assistance of the carbonyl group from the acylium ion. Again a good leaving group (water) is displaced, and a relatively stable, resonance-stabilized 2-amino-substituted cyclic dioxinylium ion of m/z 156 is formed (Scheme 2, $R = N(CH_3)_2$).



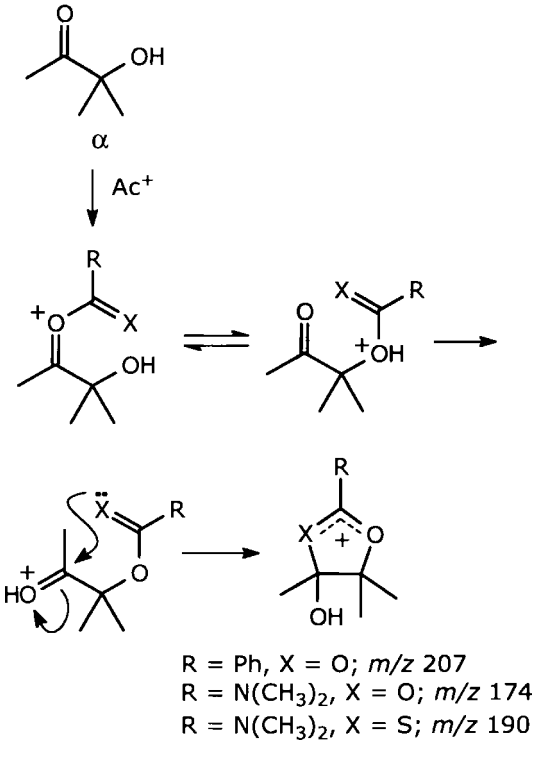
Scheme 1

α-Hydroxy ketone

Ion **4** also reacts distinctly with the α-hydroxy ketone [Fig. 1(c)] forming a variety of products, mainly those of m/z 46, 90, 148, 174, 187, 192 and 205. That of m/z 205 is the α-hydroxy ketone proton-bond dimer, M_2H^+, formed by proton transfer to M followed by M addition to MH^+. Another secondary proton transfer product is that of m/z 187, $[M_2H - H_2O]^+$. Owing to the low acidity of **4**,[12] it is



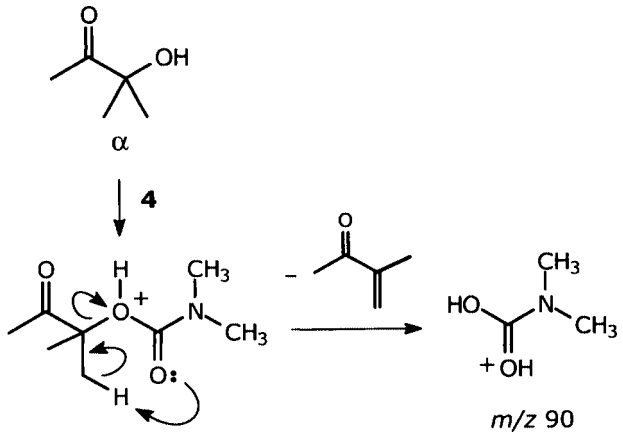
Scheme 2



Scheme 3

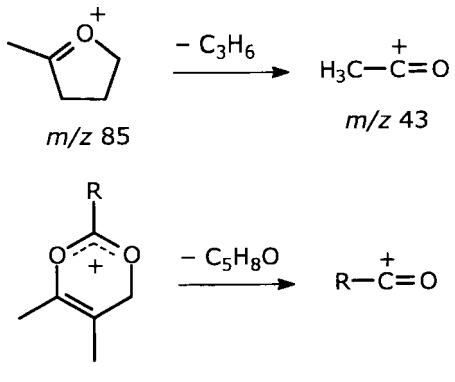
likely that proton transfer occurs mainly from its reaction products.

The adduct of m/z 174, MAc^+, is also a major product, and it is noteworthy that the adduct is formed only with the α-hydroxy ketone. Favorable intramolecular cyclization[13] could be assumed for m/z 174 (Scheme 3) so as to form a relatively stable, resonance-stabilized 4-hydroxy 1,3-dioxolanylium ion. But, contrary to the analogous β-hydroxy ketone adduct (Scheme 2), no favorable pathway for water loss is available for the cyclic m/z 174 ion. Evidence for cyclic adducts is provided by MS^3 data (see below).



Scheme 4

The remaining product ions arise from a reaction sequence which is unique for **4** and is likely initiated by water abstraction that yields a protonated dimethyl carbamic acid of m/z 90, $[(CH_3)_2NCO_2H + H]^+$. This ion dissociates by CO_2 loss to form $(CH_3)_2NH_2^+$ of m/z 46 and reacts further with the neutral ketone to form $[M(CH_3)_2NCO_2H_2]^+$ of m/z 192. A subsequent reaction of m/z 46 with M forms $[M(CH_3)_2NH_2]^+$ of m/z 148. These assignments are supported by MS^3 data (not shown), and by the reactivity of **4** with diols.[14] A mechanism for water abstraction by **4** from the α-hydroxy ketone that initiates this reaction sequence is rationalized in Scheme 4.



Scheme 5

General reactivity

With the γ-hydroxy ketone, the four acylium ions **1**–**4** and the thioacylium ion **5** react likewise (Table 1), and the hydroxy abstraction product ion of m/z 85, $[M - OH]^+$, is formed exclusively, or nearly exclusively. As already noted, proton transfer followed by water loss is an alternative and undistinguishable route to m/z 85, but it should compete favorably only for the more acidic ions, particularly for **1**.

With the β-hydroxy ketone, the relative extents by which proton transfer and cyclization occur vary drastically. Both the thioacylium ion **5** (which forms an otherwise

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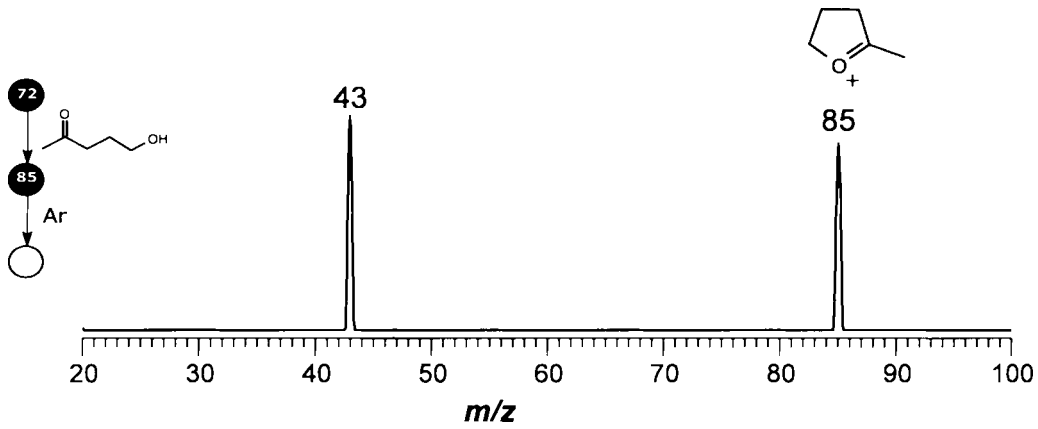


Figure 2. Triple-stage (MS^3) sequential product ion mass spectrum of the m/z 85 product ion formed in reactions of **4** with the γ-hydroxy ketone.

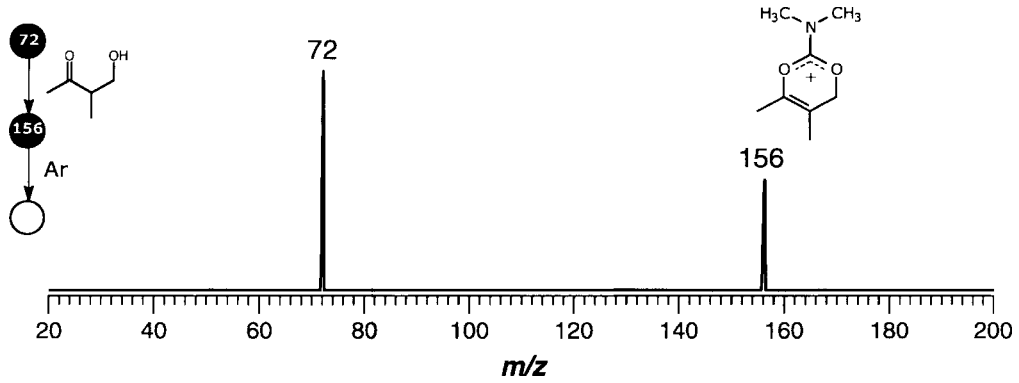


Figure 3. Triple-stage (MS^3) sequential product ion mass spectrum of the m/z 156 product ion formed in reactions of **4** with the β-hydroxy ketone.

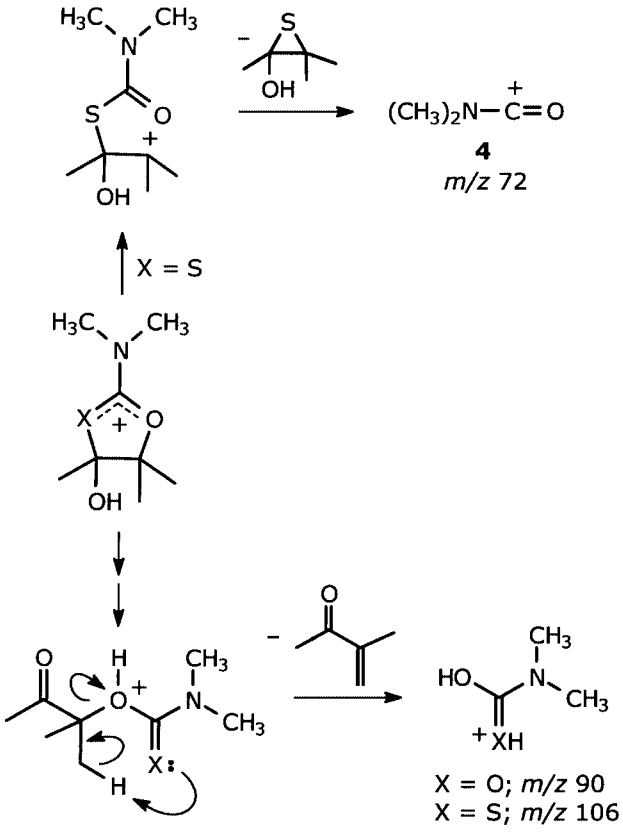
stable adduct) and the relatively acidic acylium ion **1** fail to form the corresponding $[MAc - H_2O]^+$ products (Scheme 2) of m/z 127 and 172, and proton transfer dominates (Table 1). Cyclization with water loss that likely forms cyclic dioxinylium ions, $[MAc - H_2O]^+$, occurs to a medium extent for **2** (m/z 139) and **3** (m/z 189), whereas it largely dominates for **4** (m/z 156).

With the α-hydroxy ketone, **1** and **3** fail to form MAc^+adducts, and proton transfer dominates. Ions **2** and **4** form $MAc^+$to medium extents, whereas **5** forms MAc^+ predominantly.

MS^3 experiments

The structures of major product ions were investigated by collecting their triple-stage 15 eV CID sequential product ion mass spectra. Figure 2 shows the triple-stage mass spectrum of m/z 85, the single product ion formed in reactions of **4** with the γ-hydroxy ketone [Fig. 1(a)]. In accordance with its proposed structure, and the dissociation of the authentic ion formed by 70 eV EI of 2,2-dimethyltetrahydrofuran (spectra not shown), m/z 85 dissociates upon 15 eV CID with argon exclusively to m/z 43 (Scheme 5), as do all the m/z 85 ions formed from the other reactant ions.

Figure 3 shows the triple-stage spectrum of m/z 156, the $[M - H_2O]^+$ ion formed in reactions of **4** with the β-hydroxy ketone. Similarly to the $[M - H_2O]^+$ ions from **2** (m/z 189) and **3** (m/z 139), m/z 156 dissociates exclusively to the precursor



Scheme 6

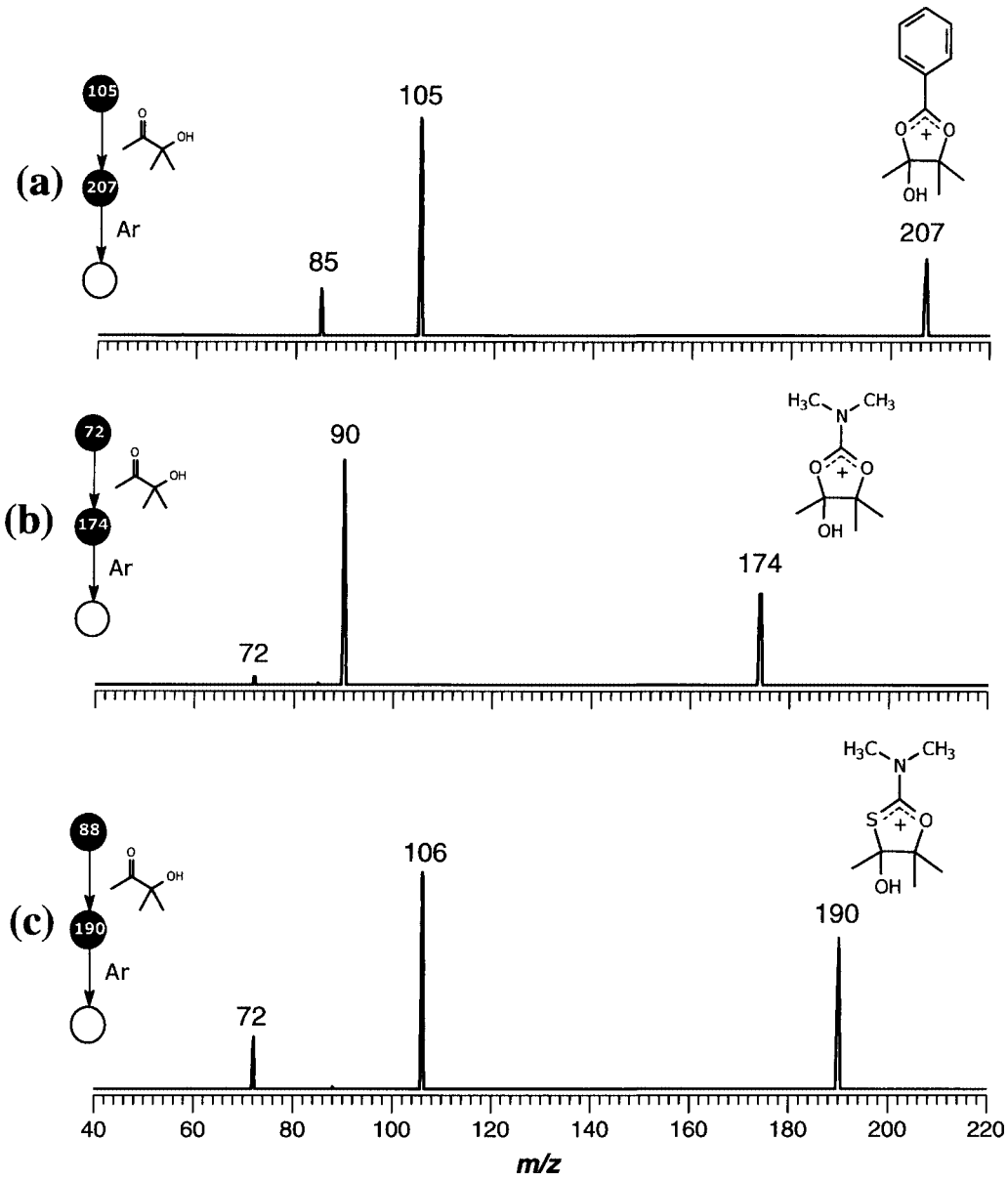


Figure 4. Triple-stage (MS^3) sequential product ion mass spectrum of the adducts formed in reactions of (a) **2**, (b) **4** and (c) **5** with the β-hydroxy ketone.

acylium ion (Scheme 5), in this case **4** of m/z 72, in full accordance with its cyclic dioxinylium ion structure.[14] This dissociation pathway is characteristic of cyclic ionic ketals.[15]

Figure 4 shows the triple-stage mass spectra of the three adducts formed in reactions of **2** (m/z 207), **4** (m/z 174) and **5** (m/z 190) with the α-hydroxy ketone (MAc^+, Table 1). The adduct of **2** [Fig. 4(a)] dissociates mainly by retro-addition to **2** of m/z 105, and to a small extent to m/z 85 by the loss of benzoic acid ($PhCO_2H$). The adduct of **4** [Fig. 4(b)] dissociates mainly to protonated dimethyl carbamic acid, $[(CH_3)_2NCO_2H + H]^+$ of m/z 90 (OH abstraction is therefore accomplished) and very little to **4** of m/z 72. These dissociations can be rationalized both for the cyclic and acyclic adducts (Scheme 3) and therefore provide no conclusive evidence on the structure of MAc^+. Evidence for cyclic structures is provided, however, for the adduct of the thioacylium ion **5**. Similarly to that of **4**, the adduct of **5** dissociates mainly to protonated dimethylthiocarbamic acid, $[(CH_3)_2NCSOH + H]^+$ of m/z 106 (Scheme 6), but a fragment ion of m/z 72 is also formed to a considerable extent. Such an ion corresponds to **4**, the O-analogue of **5**, and is therefore formed by a sulfur-by-oxygen replacement sequence easily rationalized only if the cyclic adduct is considered (Scheme 6). Such unique sulfur-by-oxygen replacement for thioacylium ions with the intermediacy of cyclic 1,3-oxathionium ions has already been observed in transacetalization reactions.[5c,16]

CONCLUSION

Novel structurally diagnostic reactions of gaseous acylium ions with three isomeric α-, β- and γ-hydroxy ketones are reported. These reactions further illustrate the diverse and unique gas-phase reactivity of acylium ions and their application in gas-phase structurally diagnostic ion–molecule reactions. According to α-, β-, or γ-interfunctional group

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separation of the isomeric hydroxy ketones, unique and probably cyclic ionic products are formed. If cyclizations are assumed to occur with intramolecular anchimeric assistance, relationships between structure and reactivity are easily recognized.

Acknowledgements

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