Modeling Deoxyribose Radicals by Neutralization-Reionization Mass Spectrometry. Part 1. Preparation, Dissociations, and Energetics of 2-Hydroxyoxolan-2-yl Radical, Neutral Isomers, and Cations

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Collisional neutralization of several isomeric $C_4H_7O_2$ cations is used to generate radicals that share some structural features with transient species that are thought to be produced by radiolysis of 2-deoxyribose. The title 2-hydroxyoxolan-2-yl radical (**1**) undergoes nearly complete dissociation when produced by femtosecond electron transfer from thermal organic electron donors dimethyl disulfide and N,N-dimethylaniline in the gas phase. Product analysis, isotope labeling (2H and ^{18}O), and potential energy surface mapping by ab initio calculations at the G2(MP2) and B3-PMP2 levels of theory and in combination with Rice-Ramsperger-Kassel-Marcus (RRKM) kinetic calculations are used to assign the major and some minor pathways for **1** dissociations. The major (~90%) pathway is initiated by cleavage of the ring C-5-O bond in **1** and proceeds to form ethylene and $\dot{C}H_2COOH$ as main products, whereas loss of a hydrogen atom forms 4-hexenoic acid as a minor product. Loss of the OH hydrogen atom forming butyrolactone (**2**, ~9%) and cleavage of the C-3-C-4 bonds (<1%) in **1** are other minor pathways. The major source of excitation in **1** is by Franck-Condon effects that cause substantial differences between the adiabatic and vertical ionization of **1** (5.40 and 6.89 eV, respectively) and vertical recombination in the precursor ion **1**⁺ (4.46 eV). $^{+}NR^{+}$ mass spectra distinguish radical **1** from isomeric radicals 2-oxo-(1H)oxolanium (**3**), 1,3-dioxan-2-yl (**9**), and 1,3-dioxan-4-yl (**10**) that were generated separately from their corresponding ion precursors. (J Am Soc Mass Spectrom 2004, 15, 1055–1067) © 2004 American Society for Mass Spectrometry

Reactive radicals that are formed in solution or solid state by ionizing radiation or chemical processes are known to attack the nucleobase and sugar moieties in DNA, resulting in chemical damage [1]. While a number of stable products of DNA damage have been isolated and identified, a more difficult task is to characterize transient intermediates resulting from the very first steps in radical attack. With carbohydrates in general and deoxyribose in particular, solution-formed radicals (OH, aryl, etc.) are known to abstract hydrogen atoms from one of the furanose ring

positions [2, 3], forming transient intermediates that undergo a variety of further reactions. Among those, ring cleavages cause strand breaks in DNA and form small oxygenated molecules and radicals that undergo a plethora of mostly unknown secondary reactions [4].

In addition to radiolysis and radical reactions in solution, recent efforts have been focused on carrying out bimolecular reactions between charge-tagged aryl radicals and carbohydrates in the highly rarefied gas phase [5], such as it exists in an ion cyclotron resonance cell [6]. This approach has the advantage of performing the reactions under well-controlled conditions and in the absence of walls, solvents, quenchers, and radical scavengers, and it is facilitated by prompt product analysis by mass spectrometry. However, since mass spectrometry is capable of detecting only charged species, the information on the properties of neutral carbo-

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Scheme 1

hydrate radicals is often lost or it could be inferred only indirectly.

The kinetics of H atom abstraction has been measured in solution [7, 8], and early *ab initio* calculations at the Hartree-Fock level showed that carbohydrate radicals have very similar relative energies [9–12]. From previous studies of hydrogen atom abstraction from carbohydrates and model oxygen heterocycles, it follows that the acetal position C-1 is particularly susceptible to radical attack, as shown for 2-deoxyribose (Scheme 1). However, the intrinsic chemical properties of the pertinent radical intermediates are unknown.

The present work utilizes neutralization-reionization mass spectrometry [13] to generate radicals that contain structure motifs common to carbohydrate radicals. 2-Hydroxyoxolan-2-yl (1) and its isotope-labeled derivatives 1a–1c represent a model system for studying furanose acetal radicals resulting from H atom abstraction at C-1.

In an accompanying communication [14] we investigate the chemistry of 3-hydroxyoxolan-3-yl radical that models radical intermediates initiating strand breaks in DNA. Our experimental approach consists of specific preparation of a stable gas-phase cation that has the same bond connectivity as the target radical. The cation is selected by mass and accelerated to $134,600 \text{ ms}^{-1}$ velocity corresponding to an 8150 eV kinetic energy. The cation is discharged by a glancing collision with CH_3SSCH_3 as an electron donor. Because of the short duration of the collision, which is estimated at 7.5 fs from the collision kinematics, the electron transfer is considered to be a vertical process, so that the nascent radical is formed with the geometry of the precursor cation. Unimolecular dissociations of 1 are observed on the time scale of 4.5 μs , and the products are analyzed by mass spectrometry following non-selective ionization by collisions with O_2 . In addition to product analysis from NR mass spectra, the electronic properties and relative energies of 1 and isomers, as well as dissociation and transition state energies, are obtained by *ab initio* and density functional theory calculations. The reaction and transition state energies are further used for RRKM calculations of unimolecular rate constants to assess the competitive dissociations of the gas-phase radicals.

Experimental

Materials

Chemicals and solvents (γ -butyrolactone, succinic anhydride, dimethyl disulfide, N, N-dimethylaniline, acetonitrile, acetone- d_6) were purchased from Sigma-Aldrich (Milwaukee, WI) and used as received. Pure gases (CH_4 , NH_3 , ND_3) were purchased from Matheson (Montgomeryville, PA).

γ -Butyrolactone-4,4- d_2 (2b) was prepared by LiAlD_4 reduction of succinic anhydride according to [15, 16]. GCMS, m/z (% rel. intensity): 88 (35), 86(4), 56 (29), 55 (6), 44 (100), 43 (48).

γ -Butyrolactone-($\text{C}=\text{O}^{18}\text{O}$) (2c). γ -Butyrolactone (2, 1 g, 11.6 mmol) was mixed with 1 mL of H_2^{18}O (Cambridge Isotope Laboratories, 99% ^{18}O) containing 5% sulfuric acid and allowed to stand overnight. The solution was saturated with sodium chloride, 2c was extracted in dichloromethane, the solution was dried over anhydrous magnesium sulfate, and the solvent was distilled off. The product (0.84 g) was degassed in vacuo and gave essentially single peak (>96%) by GCMS; m/z (% relative intensity): 88 (21), 87 (5), 86 (5), 42 (100). IR(neat, cm^{-1}): 1745 ($\text{C}=\text{O}^{18}\text{O}$, 76%), 1772 ($\text{C}=\text{O}^{16}\text{O}$, 24%). The content (81%) and distribution of ^{18}O indicated 94% selective incorporation in the carbonyl group.

Measurements

Neutralization-reionization mass spectra were measured on a tandem quadrupole acceleration-deceleration mass spectrometer equipped with electron impact (EI) and chemical ionization (CI) ion sources [17]. Liquid samples were degassed by several freeze-pump-thaw cycles and introduced into the ion source from a glass liquid introduction system at room temperature and $2\text{--}3 \times 10^{-6}$ torr partial pressure. The ion source conditions were as follows. EI: emission current 500 μA , temperature 150–200 $^\circ\text{C}$. CI: emission current 1 mA, temperature 230–250 $^\circ\text{C}$, CI gas pressure $2\text{--}3 \times 10^{-4}$ torr (as measured on an ionization gauge located at the source diffusion pump intake). The ions were extracted from the ion source, passed through the MS-1 r.f.-only quadrupole filter that was tuned to maximize transmission of the ion of interest, and accelerated to 8250 eV. The ions were focused on the neutralization collision cell that was floated at the acceleration potential (negative for cations, positive for anions), where dimethyl-disulfide vapor was admitted to achieve 70% transmission of the ion beam. Residual ions were reflected by an electrostatic lens maintained at $\pm 250 \text{ V}$, and the neutral beam was allowed to drift to the reionization cell. Cations were produced by collisions with oxygen at pressures allowing 70% beam transmittance, decelerated to 75–80 eV, energy filtered, and mass analyzed by scanning the MS-2 quadrupole mass filter that was operated to achieve unit mass resolution. The instrument was tuned daily to match the reference $^{+}\text{NR}^{+}$

mass spectrum of CS_2 . Variable-time NR mass spectra were measured as described previously [18, 19]. Collisionally activated dissociation (CAD) mass spectra were measured on a JEOL HX-110 mass spectrometer at 10 keV ion kinetic energy. Air was used as the collision gas that was admitted in the first field-free region at pressures allowing 70% transmittance of the ion beam. CAD spectra were obtained by scanning the electrostatic and magnet sector while maintaining a constant B/E ratio. The mass resolution in the B/E scans was >500 . Accurate mass measurements in CAD spectra were performed by closing the slits on the JEOL HX-110 instrument to achieve a mass resolution ≥ 3000 , which was sufficient to resolve the COOH and $\text{C}_2\text{H}_5\text{O}$ doublets that require $m/\Delta m = 1237$. GCMS spectra were measured on an HP-5971A instrument. FT-IR spectra were measured in thin film on a Perkin-Elmer spectrometer.

Calculations

Standard ab initio calculations were performed using the Gaussian 98 suite of programs [20]. Optimized geometries were obtained by density functional theory calculations using Becke's hybrid functional (B3LYP) [21, 22] and the 6-31 + G(d,p) basis set. Spin unrestricted calculations were performed for all open-shell systems. Contamination by higher spin states was low in the UHF and UMP2 calculations, and was corrected by spin projection [23, 24] that lowered the total energies by ≤ 2 millihartree for local minima and ≤ 5 millihartree for transition states. Stationary points were characterized by harmonic frequency calculations with B3LYP/6-31 + G(d,p) as local minima (all real frequencies) and first-order saddle points (one imaginary frequency). The optimized geometries and harmonic frequencies are available from the corresponding author upon request. The calculated frequencies were scaled with 0.963 [25] and used to obtain zero-point energy corrections, enthalpies, entropies, and RRKM rate constants. Improved energies were obtained by single-point calculations at four levels of theory. Composite G2(MP2) [26] energies were obtained from quadratic configuration interaction calculations with single, double and perturbational triple excitations, QCISD(T) [27] with the 6-311G(d,p) basis set, and basis set expansions from 6-311G(d,p) through 6-311 + G(3df,2p) via perturbational Møller-Plesset calculations [28], MP2 (frozen core). Since we mostly dealt with isogyric reactions in which the number of valence electrons is conserved, empirical corrections for the number of valence electrons [26] were not used. Energies from these high-level calculations are compared with composite B3-MP2 energies that were performed with the 6-311 + G(3df,2p) basis set, as described previously [29–32].

RRKM calculations were performed using Hase's program [33] that was recompiled and run under Windows NT [34]. Direct count of quantum states was used in 2 kJ mol $^{-1}$ steps from the transition state energy up to 420 kJ mol $^{-1}$ above it. Rotational states were treated

Scheme 2

adiabatically. The calculated microscopic rate constants, $k(E, J, K)$, were Boltzmann averaged over the rotational states at 473 K, corresponding to the ion source temperature that defines the precursor ion rotational temperature, to give microcanonical rate constants $k(E)$.

Results and Discussion

Precursor Ion Formation

The generation of transient radicals by $^{\pm}\text{NR}^{\pm}$ mass spectrometry [35] relies on the knowledge of precursor ion structures that are prepared by reliable methods of gas-phase ion chemistry. Since radical 1 corresponds to a hydrogen atom adduct, a logical strategy consists of site-selective protonation followed by collisional reduction of the stable cation (Scheme 2). Selective protonation of 1 relies on the different topical proton affinities of the carbonyl and ring oxygen atoms in oxolan-2-one (γ -butyrolactone, 2) that have been calculated as 838 and 764 kJ mol $^{-1}$, respectively [36]. An ion-molecule reaction of 2 with $(\text{CH}_3)_2\text{COH}^+$, generated by chemical ionization of acetone ($\text{PA}(\text{acetone}) = 821 \text{ kJ mol}^{-1}$ [37]), can thus occur by exothermic proton transfer to the carbonyl group forming cation 1^+ , but not competitively to the ring oxygen to form an isomeric cation (3^+). The latter ion can be co-formed by highly exothermic protonation with CH_5^+ ($\text{PA}(\text{CH}_4) = 543 \text{ kJ mol}^{-1}$ [37]) as discussed later. Selective deuteration with $(\text{CD}_3)_2\text{COD}^+$ was used to prepare cation $1a^+$, while protonation of labeled γ -butyrolactones $2b$ and $2c$ formed ions $1b^+$ and $1c^+$, respectively.

Table 1. Collisionally activated dissociation mass spectra of ions 1^+ , $1a^+$, $1b^+$. Relative intensity^a

<i>m/z</i>	1a				1a⁺	1b⁺		1c⁺	
	Acetone-Cl	CH ₃ CN-Cl	CH ₃ OH-Cl	CH ₄ -Cl	Acetone-d ₆ -C1	Acetone-Cl	CH ₄ -Cl	CH ₃ CN-CN	CH ₄ Cl
88	-	-	-	-	-	8.5	1.4	11	0.6
87	-	-	-	-	14.3	6	1.7	2.5	0.4
86	11.8	11.6	5.2	2.0	2.3	0.5	-	1.3	-
85	2.9	2.1	2.1	1.6	1	1.5	-	-	-
84	2.0	1.0	-	-	-	-	-	-	-
71	-	-	-	-	-	1.5	3.0	1.3	3.4 ^b
70	-	-	-	-	0.8	2.5	2.0	-	-
69	2.4 ^b	1.7 ^b	3.7 ^b	4.7 ^b	1.3	-	0.2	1.3	4.1 ^b
68	0.7	0.7	0.4	-	0.7	-	-	-	-
61	-	-	-	-	-	-	0.3	-	-
60	-	-	-	-	0.5	3	1.4	2.2	0.3
59	-	-	-	-	2.8	2.5	0.2	1.3	0.4
58	3.5	2.7	2.3	1	1.3	3.5	0.2	2.2	0.2
57	2.4	2.1	2.1	1.1	1	3	0.2	2.8	1.1
56	3.0	2.1	2.1	1.2	2.5	-	1.6	1.3	-
55	4.2	3.4	2.9	2.6	2.7	-	1.4	-	-
53	-	1.0	-	-	-	-	-	-	-
47	-	-	-	-	-	15 ^b	22.7 ^b	10.0 ^b	11.2 ^b
46	-	1.7	-	-	15.5 ^b	1	1.3	0.9	-
45	13.3 ^b	13.3 ^b	16.3 ^b	18.0 ^b	1.7	7	3.0	16.1 ^b	32.5 ^b
44	2.3	2.1	0.6	1	7.8	10 ^b	23.0 ^b	2.8	2.6
43	17.9 ^b	18.1 ^b	32.6 ^b	36.1 ^b	12.5 ^b	25.0 ^b	11.7 ^b	26.1 ^b	-
42	4.1	4.4	4.6	6.1	4	3	1.6	3.8	5.4
41	4.9	5.1	5.2	4.0	3.5	2.5	1.4	4.1	3.2
40	2.2	1.7	0.4	0.5	2	3	1.9	1.3	-
39	5.7	6.5	5.0	4.3	5.8	2	1.1	5.7	3.7
38	2.2	1.7	-	1.5	1.5	-	-1.3	-	-
37	-	1.4	-	-	0.6	-	-	1.3	-
33	-	-	-	-	-	-	-	1.6	0.4
32	-	-	-	-	2	1	-	-	-
31	2.6	2.4	2.7	2.3	-	1	0.8	2.2	0.9
30	0.6	3.4	-	-	1	1.5	1.1	-	0.3
29	3.1	3.4	3.3	2.7	3.7	1.5	0.6	2.2	0.4
28	2.9	4.8	2.9	2.6	2.7	3	1.7	2.5	0.9
27	3.5	2.1	3.7	3.7	2.7	2.5	1.4	3.5	1.3
26	2.0	0.5	2.1	2.1	1.2	1	0.2	1.9	0.3

^a% Relative to sum of CAD fragment intensities.^bMajor fragments also in metastable-ion spectra.

Precursor Ion Dissociations

Although elucidating ion dissociations was not the goal of this study, ion dissociations contribute to fragment formation in the $^+NR^+$ mass spectra [38] and need to be distinguished from dissociations of neutral species. For example, collisional neutralization by electron transfer is accompanied by collisionally activated dissociation (CAD) of precursor ions forming neutral fragments that are not separated from the reduced species of interest. Using polarizable neutralization targets (CH₃SSCH₃ or N,N-dimethylaniline) [39] substantially reduces CAD in favor of collisional electron transfer, but does not completely prevent CAD. Secondly, collisional reionization of intermediate neutral species results in ion excitation that drives post-reionization dissociations whose products can overlap with those from non-dissociative ionization of fragments formed by neutral dissociations [38]. With **1** and its cation, isotope labeling provides a reliable means of distinguishing the ion and neutral

dissociations. Therefore, ion dissociations, as inferred from the CAD and electron ionization (EI) mass spectra of isotopically labeled derivatives (Table 1) are briefly summarized first.

The CAD spectrum of 1^+ shows abundant fragment ions formed by loss of H (m/z 86), H₂O (m/z 69), C₂H₅O⁺ (m/z 45, loss of ketene) and C₂H₃O⁺ (m/z 43, loss of C₂H₄O) (Table 1). The m/z 69, 45, and 43 ions also appear in the metastable-ion spectrum of 1^+ which corresponds to spontaneous ion dissociations occurring in the time window of 1–2 μ s. The m/z 45 ion consists of variable proportions of C₂H₅O⁺ and COOH⁺, as confirmed by accurate mass measurements in high resolution spectra. For example, in metastable-ion spectra the m/z 45 ion consists mainly (>95%) of C₂H₅O⁺, whereas in the CAD spectrum the composition is 82% C₂H₅O⁺ and 18% COOH⁺. Mass shifts in the CAD spectra due to ²H and ¹⁸O labeling (Table 1) indicate the following. Loss of H involves 32% of hydrogens from the C-5

Scheme 3

methylene group, which is only slightly higher than the 29% fraction for a purely statistical loss of H ($100 \times 2/7 = 28.6\%$). Likewise, 1a^+ eliminates 14% D from the OD group, which is equal to the $100 \times 1/7 = 14.3\%$ statistical fraction. Thus, loss of H from 1^+ appears to proceed by non-specific mechanisms that include hydrogen scrambling involving the ring positions and OH group, multiple dissociation pathways, or both. Loss of water involves both the hydroxyl and ring oxygen atoms in 1^+ in a 1.1:1 ratio as inferred from the CAD spectrum of 1c^+ . The $[\text{MH} - \text{H}_2\text{O}]^+ / [\text{MH} - \text{HDO}]^+$ ion intensity ratios in the CAD spectra of 1a^+ (34:66) and 1b^+ (40:60) are not very different from the statistical ratios (29:71 and 50:50, respectively). We conclude that the loss of water is a non-specific dissociation of 1^+ .

The formation of $\text{C}_2\text{H}_3\text{O}^+$ by loss of $\text{C}_2\text{H}_4\text{O}$ shows 46% retention of the OH oxygen, a 62:38 ratio of $\text{C}_2\text{H}_3\text{O}^+$ and $\text{C}_2\text{H}_2\text{DO}^+$ species from 1a^+ , and a 43:34:23 ratio of $\text{C}_2\text{H}_3\text{O}^+$, $\text{C}_2\text{H}_2\text{DO}^+$, and $\text{C}_2\text{HD}_2\text{O}^+$ species from 1b^+ . These label distributions are not far from a statistical distribution of hydrogen and deuterium atoms in the $\text{C}_2\text{H}_3\text{O}^+$ ions, e.g., $[\text{C}_2\text{H}_3\text{O}^+]:[\text{C}_2\text{H}_2\text{DO}^+] = 57:43$ from 1a^+ and $[\text{C}_2\text{H}_3\text{O}^+]:[\text{C}_2\text{H}_2\text{DO}^+]:[\text{C}_2\text{HD}_2\text{O}^+] = 40:40:20$ from 1b^+ . Thus, both the ^{18}O and D labeling indicate extensive atom scrambling preceding the dissociation to $\text{C}_2\text{H}_3\text{O}^+$ and $\text{C}_2\text{H}_4\text{O}$.

In contrast to these largely non-specific dissociations, the elimination of ketene shows mainly retention of the C-5 methylene ($>95\%$) and OD ($>93\%$) in the product ion and practically no hydrogen scrambling accompanying the dissociation. Likewise, ^{18}O labeling shows that the oxygen atom in the neutral ketene fragment

originates 80% from the ring position and 20% from the hydroxyl group. These data can be interpreted by the ion dissociation mechanism shown in Scheme 3 in which the oxolane ring in 1^+ rearranges through an oxirane intermediate (4^+) to protonated 2-methylene-1,3-dioxolane (5^+). Ring cleavage in the latter should result in elimination of a ketene molecule containing no ^{18}O or D_2 label. The fraction of ketene containing ^{18}O is explained by a migration of the original hydroxyl proton in a fraction of 5^+ that scrambles the oxygen atoms but does not result in H/D scrambling between the OH groups and ring positions. It should be noted that the formation of $[\text{COOH},\text{D}]^+$ is more prominent from 1a^+ than from 1^+ and it accounts for 37% of the peak intensity in the CAD spectrum of 1a^+ . The label distribution is 88% COOD^+ and 12% COOH^+ , indicating minor proton migration preceding the dissociation.

The energetics of ion dissociations (Table 2) indicate that elimination of water producing protonated furan has the lowest thermochemical threshold at 298 K, $\Delta H_{\text{rxn},298} = 125 \text{ kJ mol}^{-1}$. The eliminations of $\text{C}_2\text{H}_2\text{O}$, C_3H_6 , and $\text{C}_2\text{H}_4\text{O}$ are $>220 \text{ kJ mol}^{-1}$ endothermic, and their threshold energies depend on the product ion and neutral structures (Table 2). Intermediates 4^+ and 5^+ for the dissociation by elimination of ketene are 277 and 229 kJ mol^{-1} above 1^+ , respectively, which both are above the threshold for the formation of $\text{CH}_3\text{CH}=\text{OH}^+$ (221 kJ mol^{-1}). Loss of an H atom is a highly endothermic dissociation that has the lowest threshold energy for the formation of the 2-hydroxyoxol-2-ene cation-radical (6^+), $\Delta H_{\text{rxn},298} = 383 \text{ kJ mol}^{-1}$, which is the global energy minimum among the known $\text{C}_4\text{H}_6\text{O}_2^+$

Table 2. Ion relative and dissociation energies

Reaction	Relative energy ^{a,b}
$1^+ \rightarrow 3^+$	71
$1^+ \rightarrow 4^+$	277
$1^+ \rightarrow 5^+$	229
$1^+ \rightarrow 12^+$	121
$1^+ \rightarrow [\text{Furan} + \text{H}]^+ + \text{H}_2\text{O}$	125 ^c
$1^+ \rightarrow \text{CH}_3\text{CO}^+ + \text{Oxirane}$	278 ^c
$1^+ \rightarrow [\text{Oxirane} + \text{H}]^+ + \text{CH}_2=\text{C}=\text{O}$	328 ^{c,d}
$1^+ \rightarrow \text{CH}_3\text{CH}=\text{OH}^+ + \text{CH}_2=\text{C}=\text{O}$	221 ^{c,c}
$1^+ \rightarrow \text{CH}_3\text{OCH}_2^+ + \text{CH}_2=\text{C}=\text{O}$	282
$1^+ \rightarrow \text{COOH}^+ + \text{CH}_2=\text{CHCH}_3$	292
$1^+ \rightarrow \text{COOH}^+ + \text{cyclopropane}$	325
$1^+ \rightarrow 2^{++} + \text{H}^+$	489
$1^+ \rightarrow 6^{++} + \text{H}^+$	383
$1^+ \rightarrow 7^{++} + \text{H}^+$	396
$1^+ \rightarrow 8^{++} + \text{H}^+$	524

^aIn units of kJ mol⁻¹.^b298 K relative enthalpies.

^cThe relevant standard enthalpies of formation in kJ mol⁻¹ were used as follows: 1^+ (325) [35], 5 (556) [44, 45], [oxirane + H]⁺ (703) [36], oxirane (-52.6) [36], $\text{CH}_3\text{CH}=\text{OH}^+$ (596) [46], $\text{CH}_2=\text{C}=\text{O}$ (-49.6) [47], $\text{CH}_3\text{OCH}_2^+$ (657) [36], propene (20.4), cyclopropane (53) COOH^+ (597), 2-hydroxyoxol-2-ene cation-radical (6^{++} , 488), (Furan + H)⁺ (692), H_2O (-242), H⁺ (218), *all-anti-(E,E)-1,4*-dihydroxybuta-1,3-diene cation radical (7^{++} , 501), (2-hydroxyeth-1-yl)ketene cation-radical (8^{++} , 629).

^dThe enthalpy of formation of ketene has been reported as $\Delta H_{f,298} = -49.6$ kJ mol⁻¹ from photodissociation threshold measurements [47], whereas the proton affinity of ketene (817–820 kJ mol⁻¹) [48] combined with the $\Delta H_{f,298}$ (CH_3CO^+) = 656 kJ mol⁻¹ gives -57 to -54 kJ mol⁻¹.

ions [31]. Formation of other logical ion isomers, e.g., γ -butyrolactone (2^{++}), the various distonic isomers of enol 6^{++} [31], and open-chain isomers *all-anti-(E,E)-1,4*-dihydroxy-1,3-butadiene (7^{++}), and (2-hydroxy-1-ethyl) ketene (8^{++}), are still more endothermic (Table 2).

CAD of 1^+ that was prepared by more exothermic protonation with CH_5^+ showed enhanced relative intensities of the $\text{C}_4\text{H}_5\text{O}^+$ (m/z 69), $\text{C}_2\text{H}_5\text{O}^+ + \text{COOH}^+$ (m/z 45) and $\text{C}_2\text{H}_3\text{O}^+$ (m/z 43) fragments, whereas loss of H was suppressed (Table 1). This is consistent with the formation of these ions by metastable ion dissociations, where the fraction of metastable 1^+ is enhanced by the highly exothermic protonation with CH_5^+ . The CAD spectrum of 1b^+ produced by CH_5^+ -CI showed >90% loss of light $\text{C}_2\text{H}_2\text{O}$, consistent with the mechanism in Scheme 3. In the same spectrum, the $[\text{D}_0]$, $[\text{D}_1]$, and $[\text{D}_2]$ isotopomers of $\text{C}_2\text{H}_3\text{O}^+$ were formed in a 49:45:6 ratio.

Dissociations of Radicals 1–1c

Collisional neutralization of 1^+-1c^+ results in substantial dissociation of the intermediate radicals $1-1\text{c}$, so that their $^+\text{NR}^+$ mass spectra show extremely weak or no survivor ions (Figure 1). The main products that are detected after reionization can be sorted out into three groups. The first group involves the m/z 86, 85, 56, and 55 fragments that can be unambiguously assigned to γ -butyrolactone (**2**), as deduced from the reference $^+\text{NR}^+$ mass spectrum of 2^{++} (Figure 2). These fragments also show analogous mass shifts in the $^+\text{NR}^+$ mass spectra of 1b^+ and 2b^+ , and 1c^+ and 2c^+ . Likewise,

Figure 1. Neutralization (CH_3SSCH_3 , 70% transmittance)/reionization (O_2 , 70% transmittance) mass spectra of ions prepared by acetone-Cl. (a) 1^+ , (b) 1a^+ , (c) 1b^+ , and (d) 1c^+ .

these fragments show no mass shifts in the spectrum of 1a^+ , indicating that the hydroxyl hydrogen atom has been specifically lost to form **2**.

The second group involves the abundant fragments at m/z 26–31 which can be in part assigned to dissociations of **2**. The m/z 28 and 29 fragments consist of $\text{CO} + \text{C}_2\text{H}_4$ and $\text{CHO} + \text{C}_2\text{H}_5$, respectively. That these are produced in part as secondary fragments of **2** follows from the mass shifts in the $^+\text{NR}^+$ mass spectra of 1b^+ and 2b^+ , and 1c^+ and 2c^+ which are similar although not identical. The $^+\text{NR}^+$ mass spectrum of 1a^+ shows a partial m/z 29 $\rightarrow$ m/z 30 mass shift that indicates retention of the hydroxyl deuterium in the fragment.

The third group consists of fragments at m/z 39–45. The most abundant fragment in this group at m/z 42 corresponds to ionization of neutral ketene. The isotope pattern for this ketene fragment (Figure 2) is consistent with that for the loss of neutral ketene molecules in the CAD spectra of $1\text{a}^+-1\text{c}^+$, but not with the pattern in the $^+\text{NR}^+$ mass spectra of 2^{++} and its isotopomers. For example, the $^+\text{NR}^+$ mass spectrum of 2b^+ shows a major shift of m/z 42 to m/z 44 (Figure 2b), indicating

Figure 2. $^+\text{NR}^+$ ($\text{CH}_3\text{SSCH}_3/\text{O}_2$, 70% T) mass spectra of (a) 2^{++} , (b) 2b^+ , and (c) 2c^+ . (d) $^-\text{NR}^+$ (O_2/O_2 , 70% T) mass spectrum of $^-\text{CH}_2\text{COOH}$.

Figure 3. $^+NR^+$ mass spectra of 1^+ generated by (a) CH_3CH-NH^+/CH_3CN-Cl , neutralization with CH_3SSCH_3 (b) $CH_3OH_2^+/CH_3OH-Cl$, and (c) CH_5^+/CH_4-Cl .

that the m/z 42 fragment is mostly $C_3H_6^+$. In contrast, the NR mass spectrum of $1b^+$ shows mainly retention of m/z 42 (Figure 1b). The assignment of m/z 42 as being due to ketene that was formed by ion dissociations concurrent with collisional neutralization is further supported by the NR mass spectra of 1^+ and $1c^+$ where the precursor ions were prepared by more exothermic protonations with $CH_3C=NH^+$, $CH_3OH_2^+$, and CH_5^+ (Figure 3). These spectra show enhanced formations of C_2H_2O and C_2H_4O in keeping with the corresponding CAD spectra of the ions. Note that ketene gives a prominent survivor ion in its $^+NR^+$ mass spectrum [40]. Note also that neutralization with *N,N*-dimethylaniline of the CH_3CN-Cl prepared ion 1^+ results in an $^+NR^+$ mass spectrum that showed somewhat enhanced relative intensities of the survivor ion at m/z 87, m/z 86, and 85 fragments assignable to **2**, and an m/z 68 fragment that does not originate from **2**. Because of its low ionization energy (7.12 eV) [37], *N,N*-dimethylaniline can be considered a soft neutralization target, which may explain the increased survivor ion in the $^+NR^+$ mass spectrum.

The fragments at m/z 43 and 45 are absent in the $^+NR^+$ mass spectrum of 2^+ and thus they must originate from other neutral intermediates formed from **1**. The mass shifts in the spectra of $1a^+-1c^+$ clearly show that the m/z 45 fragment is $COOH$, which must be formed by a ring cleavage in the radical. Note that the m/z 45 ion in the CAD spectrum of 1^+ is mainly $C_2H_5O^+$, not $COOH^+$, so that the products from neutral and post-reionization dissociations are clearly distinguished. Isotope mass shifts are less indicative of allowing an unambiguous assignment of the m/z 43 fragment because of overlaps with neighboring peaks in the spectra.

Finally, the $^+NR^+$ mass spectra of 1^+-1c^+ show OH fragments that retain the hydroxyl hydrogen atom (e.g., m/z 18 in the spectrum of $1a^+$), but scramble the oxygen atoms (e.g., m/z 17 and 19 in the spectrum of $1c^+$).

To aid the identification of the ring-cleavage prod-

Figure 4. $^+NR^+$ (CH_3SSCH_3/O_2 , 70% T) mass spectra of (a) 4-butenic acid and (b) 3-butenic acid.

ucts, we obtained an $^+NR^+$ mass spectrum [35] of $^+CH_2COOH$. The precursor anion was generated by gas-phase desilylation of $(CH_3)_3SiCH_2COOH$ with F^- [41]. The spectrum shows a weak survivor ion for CH_2COOH^+ at m/z 59 and major fragments at m/z 44, 42, and 28 (Figure 2d). These also appear as abundant fragments in the $^+NR^+$ mass spectrum of 1^+ , indicating that $^+CH_2COOH$ is a potential intermediate of dissociations of neutral **1**.

$^+NR^+$ mass spectra were also obtained for 3-hexenoic and 4-hexenoic acid (Figure 4) which are the potential products of ring cleavage in **1** followed by loss of H from a ring position. These $^+NR^+$ mass spectra are dominated by C_3H_3 fragments at m/z 39 which are also prominent in the $^+NR^+$ spectrum of **1**. However, the $^+NR^+$ mass spectrum of 3-hexenoic acid shows fragments at m/z 68, 69, and 71 that are only weak in the spectrum of 1^+ (cf. Figures 1a and 3b). Likewise, the $^+NR^+$ mass spectrum of 4-hexenoic acid shows major peaks at m/z 85 and 58 which are weak or undetectable, respectively, in the spectrum of 1^+ . These results indicate that open chain carboxylic acids are not the major dissociation products of **1**.

Figure 5. Variable-time $^+NR^+$ (CH_3SSCH_3/O_2 , 70% T) mass spectra of 1^+ . The neutral dissociation times were (a) 0.6, (b) 1.4, and (c) 2.1 μs .

Variable-Time NR^+ Mass Spectra of **1**

Additional information about unimolecular dissociations of **1** was obtained from variable-time measurements [18, 19]. In these experiments, the times for dissociations of radicals (t_1) and their reionized counterparts (t_2) were varied stepwise but in an opposite manner, such that the total time $t = t_1 + t_2$ remained constant. The variable-time $^+NR^+$ spectra (Figure 5) showed substantial changes in the relative intensities of the m/z 37–45 and m/z 24–31 groups of fragments, where the fragments of the latter group were increasingly more abundant at longer neutral dissociation times. The relative intensities within each group of fragments also show time dependence, e.g., the decreasing peak at m/z 42 and increasing peak at m/z 28 when the neutral dissociation times were varied from 0.6 μs (Figure 5a) to 2.1 μs (Figure 5c). These measurements indicate that the formation of small m/z 25–29 fragments

Scheme 4

is to a large extent due to consecutive radical dissociations that are enhanced at longer reaction times.

In summarizing the neutral dissociations of radicals **1–1c**, these involve mainly loss of the hydroxyl hydrogen atom and ring cleavages that result in the formation of CH_2COOH , $COOH$, C_3H_3 , and smaller $[C_xH_yO]$ ($x = 0, 1$), C_2H_x ($x = 1–5$), and OH fragments. The convergent dissociation routes forming these small fragments make it difficult to quantify the formation of the primary dissociation products of **1**.

Related $C_4H_7O_2$ Isomers

To investigate the properties of other cyclic $C_4H_7O_2$ radicals we obtained $^+NR^+$ mass spectra of 1,3-dioxolan-2-yl (**9**) and 1,3-dioxolan-4-yl (**10**) that can be viewed as ring-expanded isomers of **1** (Scheme 4). The corresponding precursor cations 9^+ and 10^+ were prepared by loss of methyl upon 70-eV electron ionization of 2-methyl-1,3-dioxane and 4-methyl-1,3-dioxane, respectively. The $^+NR^+$ mass spectra of these isomers (Figure 6) differ from each other as well as from the spectrum of 1^+ (Figure 1). The major distinguishing features are the presence of a survivor ion and the m/z 57 (loss of CH_2O), m/z 32 (CH_3OH), m/z 31 (CH_2OH), and m/z 30 (CH_2O) fragments for **10**, and the low abundance of the m/z 42 fragment for **9**.

Another isomer, 2-oxo-(1*H*)-oxolanium (**3**) was generated by neutralization of ring-protonated **2** (ion 3^+) which was prepared by dissociative ionization of methyl- D_3 4-hydroxybutyrate (**11**). The CD_3 ester was used to distinguish between the loss of the ester methoxy group producing the desired m/z 87 ion and the loss of the terminal CH_2OH group producing an m/z 90 ion from **11**. The acylium ion formed by loss of OCD_3 from **11**, $HOCH_2CH_2CH_2CO^+$ (12^+) was calculated to be 50 $kJ\ mol^{-1}$ less stable than 3^+ (Table 2) and was presumed to spontaneously cyclize to this more stable isomer (Scheme 5). Indeed, DFT calculations showed that only the *all-anti* conformer of 12^+ was a local energy minimum, whereas gauche conformers spontaneously cyclized to 3^+ upon gradient optimization.

Figure 6. $^+NR^+$ (CH_3SSCH_3/O_2 , 70% T) mass spectra of (a) 3^+ , (b) 1,3-dioxan-2-yl (9^+), and (c) 1,3-dioxan-4-yl (10^+).

The $^+NR^+$ mass spectrum of 3^+ (Figure 6) is distinctly different from that of 1^+ . The major differences are in the relative intensities of the m/z 57, 44, 43, 30, and 16 fragments which are substantially more abundant for 3 . Note that 3 represents a hypervalent oxonium radical which is not likely to be a bound structure [42]. Accordingly, the $^+NR^+$ mass spectrum of 3^+ displays only a negligibly weak survivor ion.

Scheme 5

In spite of the fact that the $^+NR^+$ spectra of the four $C_4H_7O_2$ isomers (1 , 9 , 10 , and 3) are quite distinct, the absence of a characteristic fragment in the spectrum of 10 does not allow one to exclude a partial isomerization of 1 to 10 on the basis of the experimental data alone.

Dissociation Energies and Mechanisms for Radical 1

In order to interpret the dissociations of radicals that were deduced from $^+NR^+$ mass spectrometric product analysis, we have used the dissociation, isomerization, and transition state (TS) energies obtained by high-level G2(MP2) or B3-PMP2 calculations. The potential energy surface (PES) for 1 is shown schematically in Figure 7. The adiabatic ionization energy of 1 is calculated by G2(MP2) as $IE_a(1) = 5.38$ eV, the B3-PMP2 value is 5.40 eV. However, vertical neutralization of 1^+ to the ground doublet electronic state of 1 results in vibrational excitation in the radical, which receives 84 kJ mol $^{-1}$ internal energy. The vertical recombination energy of 1^+ is calculated as $RE_v(1^+) = 4.46$ eV by B3-PMP2 and does not include zero-point corrections. The excitation in vertically-formed 1 is caused by differences in the equilibrium geometries between it and ion 1^+ (Figure 8). The latter has short C-2–O-1 (1.279 Å) and C-2–O-2 (1.284 Å) bonds that have a partial double-bond character, and the hemiacetal group is essentially planar about C-2. In contrast, in relaxed radical 1 these bonds are 7–9% longer and the bonds about C-2 are pyramidal (Figure 8). Hence, vertical neutralization of 1^+ forms radical 1 with compressed C–O bonds and a flattened ring which both contribute to the Franck-Condon energy. Franck-Condon effects are also apparent in vertical ionization of relaxed 1 , where the vertical ionization energy is $IE_v(1) = 6.89$ eV by B3-PMP2. The E_{FC} in 1 is combined with the internal energy of the precursor ion 1^+ which has a lower bound at 35 kJ mol $^{-1}$ for an ion thermalized at the ion source temperature (523 K). This combined internal energy, $84 + 35 = 119$ kJ mol $^{-1}$ is sufficient to drive dissociations of 1 by loss of the hydroxyl hydrogen atom through **TS1**, ($E_{TS} = 100$ kJ mol $^{-1}$) and ring opening by cleavage of the O-1–C-5 bond through **TS2** ($E_{TS} = 59$ kJ mol $^{-1}$). In contrast, loss of a hydrogen atom from C-3 forming the less stable 2-hydroxyoxol-2-ene (6) has an energy threshold at 146 kJ mol $^{-1}$ and should not compete with the loss of the OH hydrogen atom. Likewise, dissociation of the C-3–C-4 bond in 1 is calculated to require 136 kJ mol $^{-1}$ in **TS3** to form the open-ring intermediate 13 which is 76 kJ mol $^{-1}$ less stable than 1 . Although 13 is a logical intermediate for further exothermic dissociation to C_2H_4 and CH_2COOH , the high **TS3** energy for its formation appears to be prohibitive for this dissociation pathway to occur.

The exothermic ring opening by O-1–C-5 bond cleavage in 1 does not result in immediate fragmentation, but forms the gauche isomer of 4-carboxyprop-1-yl radical

Figure 7. Schematic potential energy surface for isomerizations and dissociations of **1**. Energies are given in kJ mol^{-1} and refer to 0 K. Roman numerals: B3-PMP2/6-311 + G(3df,2p) relative energies. Bold italics: G2(MP2) relative energies.

(**14a**) which can dissociate to cyclopropane and $\cdot\text{COOH}$. However, an energetically more favorable pathway involves a series of internal rotations in **14a** to form the most stable anti-rotamer (**14b**), which dissociates by C–C bond cleavage to C_2H_4 and $\cdot\text{CH}_2\text{COOH}$. This dissociation has a very low thermochemical threshold which is only 15 kJ mol^{-1} above **1**. The activation energy for ethylene loss from **14b** (TS6, 42 kJ mol^{-1} relative to **1**) is 17 kJ mol^{-1} below TS2 for the ring opening in **1**. This implies that the ring opening in **1** is the rate determining step in the overall dissociation leading to C_2H_4 and $\cdot\text{CH}_2\text{COOH}$, assuming that the chain rotation in $\text{14a} \rightarrow \text{14b}$ through the low-lying TS5 is fast in the vibrationally excited intermediates. Radical **14b** can also undergo loss of H to form 4-butenic acid of 67 kJ mol^{-1} threshold energy and $E_{\text{TS}} = 82 \text{ kJ mol}^{-1}$ in TS7 (all energies relative to **1**). However, product

analysis in the $^+\text{NR}^+$ spectrum of **1a**⁺ indicates that this dissociation does not compete effectively with the loss of C_2H_4 , in line with the 40 kJ mol^{-1} difference in the E_{TS} for these dissociations.

Interestingly, OH group migration in **14a** to form the stable 3-hydroxyethylcarbonyl radical (**12**) requires a substantial energy in TS4, which should disfavor this isomerization against the loss of C_2H_4 . Note that radical **12** would be a logical intermediate for the formation of ketene and CO (Figure 7).

Vertical neutralization of **3**⁺ produces an unstable, high-energy, radical (**3**) that can spontaneously eliminate the oxonium hydrogen atom, or undergo O–1–C–2 or O–1–C–5 ring cleavage forming **12** or **14**, respectively. Because of the substantial potential energy deposited in vertically formed **3** (190 kJ mol^{-1}) the ring-open intermediates must be formed in high vibrational states and can be expected to undergo fast and perhaps non-specific dissociations.

Figure 8. B3LYP/6-31 + G(d,p) optimized structures of **1**⁺ and **1**. Bond lengths in angstroms.

RRKM Kinetics

The $^+\text{NR}^+$ mass spectrum of **1** (Figure 1) shows several fragments due to radical dissociations. Even though many of these fragments can be assigned to primary dissociation products (**2**, $\cdot\text{CH}_2\text{COOH}$, $\cdot\text{COOH}$, C_2H_4 , etc.), secondary dissociations of the latter, both as neutrals and following reionization, caused overlaps that made quantitative product analysis very difficult.

To gain some insight into the relative importance of the dissociation pathways in **1**, we used the calculated G2(MP2) and B3-PMP2 TS energies to obtain the corresponding unimolecular rate constants. The dissociations of **1** are presumed to follow a simple kinetic scheme for competing O–H, O–C-5 and C-3–C-4 bond cleavages with the corresponding rate constants denoted as $k_{\text{O-H}}$, $k_{\text{O-C-5}}$ and $k_{\text{C-3-C-4}}$. Although the O–C-5 bond cleavage does not result in immediate fragmentation, the consecutive steps, e.g., the **14a** → **14b** rotation and C-2–C-3 bond cleavage, have much lower activation energies (Figure 7) and thus are presumed to occur with rate constants greater than $k_{\text{O-C-5}}$. Moreover, the reverse ring closure in **14a** → **1** was calculated to be 4–6 orders of magnitude slower than the O–C-5 bond dissociation in **1** for a wide range of internal energies, $E = 125\text{--}420\text{ kJ mol}^{-1}$, indicating that when formed, **14a** would proceed to dissociation.

The RRKM rate constants (Figure 9) were convoluted with an internal energy distribution function ($P(E)$), given by eq 1, where the onset (E_0) and width (W) parameters were

$$P(E) = \frac{4(E-E_0)}{W^2} e^{-\frac{2(E-E_0)}{W}} \quad E \geq E_0$$

$$P(E) = 0 \quad E \leq E_0 \quad (1)$$

chosen such as to both reproduce the relative intensity of residual **1** ($\approx 0.1\%$, Figure 1) in the $^+\text{NR}^+$ mass spectrum (eq 2) and fit the most probable internal energy of radical **1**. The latter was given by $E_{\text{max}} = E_0 + W/2 \approx E_{\text{FC}} + E_{\text{ion}} = 119\text{ kJ mol}^{-1}$, where E_{FC} is the excitation due to

$$[\mathbf{1}] = [\mathbf{1}]_0 \int_{E_a}^{420} P(E) e^{-[k_{\text{O-H}}(E) + k_{\text{O-C-5}}(E) + k_{\text{C-3-C-4}}(E)]t} dE \quad (2)$$

Franck-Condon effects acquired upon vertical electron transfer, and E_{ion} is the precursor ion internal energy. We have shown previously that $P(E)$ functions of the type shown in eq 1 provide good estimates for internal energy distribution in several neutral intermediates formed by femtosecond electron transfer [43]. The en-

Figure 9. Internal energy distribution function ($P(E)$) for vertically neutralized **1**, and RRKM unimolecular rate constants ($k(E)$) for dissociations. Filled circles: C-5–O bond cleavage in **1**, empty circles: O–H bond dissociation in **1**, filled upward triangles: C-3–C-4 bond cleavage in **1**.

ergy range for integration was truncated at 420 kJ mol^{-1} which accounts for 97% of energies under the $P(E)$ curve in eq 1, where the best fit parameters are $E_0 = 57\text{ kJ mol}^{-1}$ and $W = 124\text{ kJ mol}^{-1}$. The energy-convoluted rate constants gave the energy-averaged branching ratios for dissociations of **1** (eq 3) as $k_{\text{rel}}(\text{O–H}) = 0.085$, $k_{\text{rel}}(\text{O–C-5}) = 0.91$, and $k_{\text{rel}}(\text{C-3–C-4}) = 0.005$.

$$k_{\text{rel}}(\text{O–H}) = \frac{\int_{E_a(\text{O–H})}^{420} k_{\text{O–H}}(E) P(E) dE}{\int_{E_a(\text{O–H})}^{420} k_{\text{O–H}}(E) P(E) dE + \int_{E_a(\text{O–C-5})}^{420} k_{\text{O–C-5}}(E) P(E) dE + \int_{E_a(\text{C-3–C-4})}^{420} k_{\text{C-3–C-4}}(E) P(E) dE} \quad (3)$$

Similar results were obtained from RRKM calculations that used TS energies from B3-PMP2/6-311 + G(3df,2p) calculations which are 6–13 kJ mol^{-1} lower

than those from G2(MP2) (Figure 7). Best fits were obtained for $E_0 = 53\text{ kJ mol}^{-1}$ and $W = 133\text{ kJ mol}^{-1}$ that yielded the branching ratios $k_{\text{rel}}(\text{O–H}) = 0.14$,

$k_{\text{rel}}(\text{O-C-5}) = 0.85$, and $k_{\text{rel}}(\text{C-3-C-4}) = 0.01$. Both these sets of data indicate that ring cleavage **1** $\rightarrow$ **14a** should be the major dissociation pathway of **1** that accounts for about 85–91% of reactivity and triggers further fragmentation to $\text{CH}_2\text{COOH} + \text{C}_2\text{H}_4$, $\text{C}_3\text{H}_6 + \text{COOH}$, and their dissociation products such as HCO , CO , C_2H_x ($x = 1-3$), OH , and CH_x ($x = 0-2$). This result is consistent with the dominant presence of small fragments in the $^+\text{NR}^+$ mass spectrum of **1** and the low relative abundance of fragments that are assigned to **2**. Hence the RRKM analysis appears to give a realistic description of the competitive dissociations of **1** for potential energy surfaces at what currently are the best levels of theory.

Conclusions

This combined experimental and computational study shows that gaseous radical **1** undergoes preferential ring-cleavage dissociations producing small fragments. Dissociations by loss of hydrogen atoms that preserve the oxolane ring are less abundant and account for 8–14% of overall fragmentation. The gas-phase dissociations are driven by the substantial Franck-Condon energy the radical receives upon collisional electron transfer. The dissociations observed under NR mass spectrometric conditions reflect the chemistry of isolated hyperthermal species. However, the ab initio calculated potential energy surface for competing dissociations indicates that ring-cleavages should also dominate unimolecular dissociations of radical **1** under thermal conditions.

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