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# Lactone Enols Are Stable in the Gas Phase but Highly Unstable in Solution

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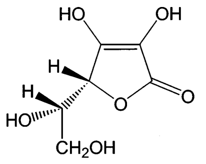
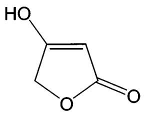
***Abstract:*** 2-Hydroxyoxol-2-ene (**C$_5$-1**), the enol tautomer of $\gamma$-butyrolactone, was generated in the gas phase as the first representative of the hitherto elusive class of lactone enols and shown by neutralization−reionization mass spectrometry to be remarkably stable as an isolated species. Ab initio calculations by QCISD(T)/6-311+G(3df,2p) provided the enthalpies of formation, proton affinities, and gas-phase basicities for gaseous lactone enols with four- (**C$_4$-1**), five- (**C$_5$-1**), and six-membered rings (**C$_6$-1**). The acid−base properties of **C$_4$**−**C$_6$** lactones and enols and reference carboxylic acid enols $CH_2{=}C(OH)_2$ (**3**) and $CH_2{=}C(OH)OCH_3$ (**4**) were also calculated in aqueous solution. The **C$_4$**−**C$_6$** lactone enols show gas-phase proton affinities in the range of 933−944 kJ mol$^{-1}$ and acidities in the range of 1401−1458 kJ mol$^{-1}$. In aqueous solution, the lactone enols are 15−20 orders of magnitude more acidic than the corresponding lactones, with enol p$K_a$ values increasing from 5.6 (**C$_4$-1**) to 14.5 (**C$_6$-1**). Lactone enols are moderately weak bases in water with p$K_{BH}$ in the range of 3.9−8.1, whereas the lactones are extremely weak bases of p$K_{BH}$ in the range of −10.5 to −17.4. The acid−base properties of lactone enols point to their high reactivity in protic solvents and explain why no lactone enols have been detected thus far in solution studies.

## Introduction

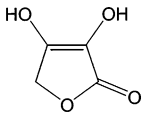
The combination of the enol group, C═C−OH, and a lactone ring appears in several stable compounds, as typified by ascorbic acid (***I***),[1] tetronic acid (***II***),[2] tetrone diol (***III***), and other so-called reductones.[3]



L-Ascorbic acid (***I***)



Tetronic acid (***II***)



Tetrone diol (***III***)

In contrast, stable compounds incorporating enolized lactone groups, C═C(OH)−O, are virtually unknown.[4,5] Even in the presence of stabilizing aromatic rings[6] or $\beta$-carbonyl groups, the lactone functionality avoids enolization, as exemplified by ***II*** and ***III*** which retain the lactone carbonyl group.[3] In contrast, the formation of enolates[7] or enols as reactive intermediates is an important step in the alkylation,[8] silylation,[9] and oxidation[10] of lactones and is used to introduce functional groups[7] or modify the lactone ring.[11] Considering the importance and ubiquity of lactone rings in terpenes, alkaloids, antibiotics, and other natural products, investigations of the properties of lactone enols are of interest.

Unstable enols have been studied extensively in solution and gas phase, as reviewed.[12,13] The gas phase, in particular, is a convenient medium for the generation of elusive and highly reactive molecules, which can be investigated in the absence of solvents and walls that can otherwise catalyze undesirable

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reactions.[14] For reactive enols, the rarefied gas phase, such as it exists in the vacuum system of a mass spectrometer, provides a suitable inert environment that has been utilized for the generation and study of a number of simple enols,[13] dienols,[15] and ene diols.[16] In contrast to the low stability of neutral simple enols, gas-phase enol cation radicals are very stable species that often represent the most stable isomers in a given group of ions.[17] Consequently, enol cation radicals have been studied extensively as stable species as well as intermediates of gas-phase ion dissociations.[18] Enol cation radicals also provide stable precursors for the generation of transient neutral enols that are studied by neutralization−reionization mass spectrometry (NRMS).[19] This is achieved by collisional electron transfer from a polarizable electron donor to a stable enol cation radical that has been accelerated to 100 000−200 000 m $s^{-1}$. At these ion velocities, collisional electron transfer takes place within 5−10 fs, so that the enol molecule is formed with the bond connectivity of the precursor cation radical. The transient fast enol molecules and their dissociation products are ionized by a second collision, separated by a mass spectrometer, and detected as ions. Additional information on the transient neutral intermediates can be obtained by collisional activation,[19c] or variable-time measurements of neutral and ion lifetimes.[20]

Enols derived from cyclic ketones and carboxylic acid derivatives have been studied in solution.[21] The enols have been generated by hydrolysis of enolates, Norrish type II photoelimination, photohydration, and other methods.[22] Despite these ingenious approaches to transient enol generation, lactone enols remain an elusive class of compounds whose chemical properties are unknown. Enols of simple carboxylic acids have also been studied computationally at high levels of ab initio theory and found to be substantially destabilized against their oxo forms.[23]

In this work, we report the first generation of a lactone enol in the gas phase. Because of our ongoing interest in radicals derived from deoxyribose and its deoxygenated analogues that incorporate the oxolane ring, we focused on 2-hydroxy-2-oxolene (**$C_5$-1**), which is the enol of butane-4-lactone (**$C_5$-2**). G2(MP2) calculations were used to assess the thermochemical properties of **$C_5$-1**, its homologues **$C_4$-1** and **$C_6$-1**, and the corresponding lactones **$C_4$-2** through **$C_6$-2**. The **$C_4$−$C_6$** symbols denote the ring size in the species in question. The gas-phase acidities and basicities are compared to the p$K_a$ values calculated in aqueous solution for the enols and lactones under study. This provides a connection between the acid−base properties of lactones and enols in solution[21,24] and the gas phase, as recently studied by Brauman and co-workers[25] using ion cyclotron resonance mass spectrometry.

## Experimental Section

**Materials.** Butane-4-lactone, 2-acetylbutane-4-lactone (**IV**), ethyl acetoacetate, ethyl acetoacetate-1,3-$^{13}C_2$, oxirane, and oxirane-$d_4$ were purchased from Aldrich. 2-Acetyl-2-*d*-butane-4-lactone (**IVa**) was prepared from **IV** by H/D exchange ($K_2CO_3$, $D_2O$, 3h at 20 °C) and characterized by mass spectrometry. Mass spectrum, *m*/*z* (rel intensity): 129 ($M^{+\bullet}$, 3), 87 (53), 86(50), 43(100). 2-Acetyl-3,3,4,4-$d_4$-butane-4-lactone (**IVb**) and 2-(1′-$^{13}C$-acetyl)-1-$^{13}C$-butane-4-lactone (**Ic**) were prepared by a modified literature procedure[26] as described here for **IVb**.

Ethyl acetoacetate (2.6 g, 20 mmol) was dissolved in methanol (30 mL) and treated with NaOH (0.8 g, 20 mmol) at 0 °C under argon for 30 min. The solution was cooled to −10 °C, and 2.4 g (50 mmol) of gaseous oxirane-$d_4$ was slowly introduced through a glass capillary reaching under the surface of the solution. After 1 h at −10 °C, the solution was allowed to warm to 20 °C and stirred for 15 h. Methanol was evaporated in vacuo, the solution was acidified with 5% HCl, the product was extracted in ether, worked up, and distilled at 118 °C/15 Torr. Yield: 1.7 g (64% based on ethyl acetoacetate), ∼95% pure by GCMS. Mass spectrum: 132 ($M^{+\bullet}$, 6), 90 (95), 43 (100). **IVc** was prepared analogously from ethyl acetoacetate-1,3-$^{13}C_2$ and oxirane. Yield: 57%, ∼95% pure by GCMS. Mass spectrum: 130 ($M^{+\bullet}$, 4), 87 (77), 44 (100).

**Methods.** Neutralization−reionization ($^+NR^+$) mass spectra were measured on a tandem quadrupole acceleration−deceleration mass spectrometer, as described previously.[27] Precursor $C_4H_6O_2$ cation radicals were generated by electron ionization, accelerated to 8250 eV kinetic energy, and neutralized by collisions with $CH_3SSCH_3$ at pressures to achieve 70% precursor beam transmittance. Following ion deflection, neutral intermediates were reionized by collisions with $O_2$ at 70% beam transmittance, filtered by kinetic energy, and mass-analyzed. Typically, 40−50 scans were accumulated and averaged per spectrum. Neutral collisional activation (spectra denoted as $^+NCR^+$) was performed with He at 50% beam transmittance. Variable-time measurements were performed as described previously.[20] The variable flight times of neutral intermediates were 0.43, 1.25, 2.10, 2.90, and 4.41 $\mu$s.

**Calculations.** Standard ab initio calculations were performed using the Gaussian 98 suite of programs.[28] Geometries were optimized by density functional theory calculations using Becke's hybrid functional

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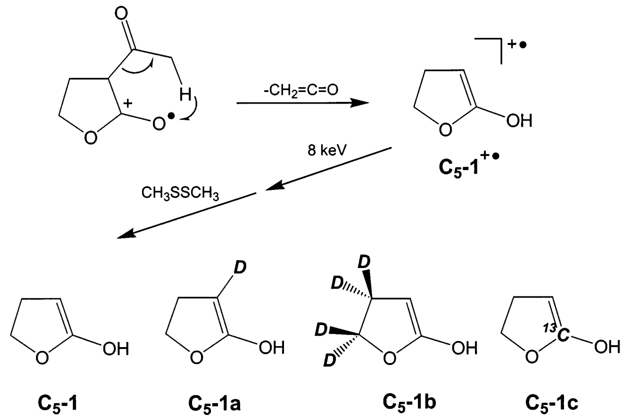
*Scheme 1*



(B3LYP)[29] and the 6-31+G(d,p) basis set. The optimized geometries were characterized by B3LYP/6-31+G(d,p) frequency calculations as local minima or first-order saddle points. The optimized geometries and harmonic frequencies are available from the corresponding author upon request. The frequencies were also used for zero-point energy, enthalpy, and entropy calculations using the rigid-rotor harmonic oscillator approximation, except for low-frequency modes of $\nu \leq 200$ cm$^{-1}$, corresponding to ring or OH group torsional motions, which were treated as free rotors. Mulliken populations were obtained from B3LYP/6-311+G(2d,p) calculations. Single-point energies were obtained by G2(MP2)[30] and B3-MP2/6-311+G(3df,2p)[31] calculations. The B3-MP2 scheme relies on cancellation of errors inherent to B3LYP and MP2 calculations, such that simple averaging of the calculated B3LYP and PMP2 energies results in substantially more accurate proton affinities, bond dissociation energies, and activation energies for a number of closed-shell and open-shell systems.[31] The theoretical background for the B3-MP2 scheme can be found in the recent study of correlation energy effects by Pople and co-workers.[32] For selected systems, G2-(MP2) energies were obtained with both QCISD(T)[33] and CCSD(T)[34] single-point calculations which gave practically identical (within 1 kJ mol$^{-1}$) relative and dissociation energies. Solvation free energies were calculated by B3LYP/6-31+G(d,p) using the polarization continuum model (PCM).[35] Enol and lactone structures were reoptimized by PCM-B3LYP/6-31+G(d,p) using standard parameters (water dielectric constant, atomic, and van der Waals radii) included in Gaussian 98.[28,35]

## Results and Discussion

**Enol Generation.** Enol cation radicals are conveniently generated by the McLafferty rearrangement of a suitable precursor ion.[13,36] To generate **C$_5$-1**$^{+\bullet}$ we used 2-acetylbutane-4-lactone which upon ionization eliminates a molecule of ketene from the side chain to form an abundant $C_4H_6O_2^{+\bullet}$ ion at *m*/*z* 86 (Scheme 1). This reaction is analogous to the photochemical Norrish type II elimination that is used to generate transient enols in solution.[22] The integrity of ion **C$_5$-1**$^{+\bullet}$ was supported by accurate mass measurements (measured 86.0368, $C_4H_6O_2$ requires 86.0368). Mass shifts due to the presence of deuterium and $^{13}$C isotopes, which showed retention of one deuterium atom in **C$_5$-1a**$^{+\bullet}$ (*m*/*z* 87), four deuterium atoms in **C$_5$-1b**$^{+\bullet}$ (*m*/*z* 90), and one $^{13}$C atom in **C$_5$-1c**$^{+\bullet}$ (*m*/*z* 87), confirmed that the ketene molecule originated from the acetyl side chain, in keeping with structure **C$_5$-1**$^{+\bullet}$. Ion **C$_5$-1**$^{+\bullet}$ was further characterized by the collisionally activated dissociation (CAD) spectrum that showed major peaks due to eliminations of a hydrogen atom (*m*/*z* 85), water (*m*/*z* 68), CO (*m*/*z* 58), $CO_2$ (*m*/*z* 42) and ring cleavage dissociations (*m*/*z* 55, 41, 39, 29, and 28). The CAD spectrum of **C$_5$-1**$^{+\bullet}$ (Figure 1) was distinctly different from those of several other $C_4H_6O_2^{+\bullet}$ isomers, namely, butane-4-lactone, oxolan-3-one (**5**), 3-butenoic acid, and *trans*-2-butenoic acid, that were obtained for reference. The mechanisms of gas-phase dissociations of **C$_5$-1**$^{+\bullet}$ and **C$_5$-2**$^{+\bullet}$ were elucidated by a combination of isotope labeling and detailed mapping of the potential energy surface by ab initio calculations. The intriguing ion chemistry of **C$_5$-1**$^{+\bullet}$ is the subject of a separate detailed study.[37]

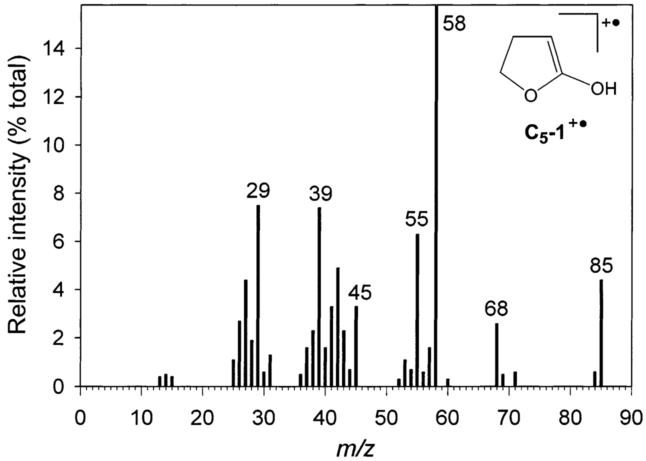


***Figure 1.*** Collisionally activated dissociation spectrum of **C$_5$-1**$^{+\bullet}$ obtained at 10 keV with air as collision gas at 70% precursor ion transmittance.

Ion **C$_5$-1**$^{+\bullet}$ and its labeled analogues were further used to generate neutral lactone enols by collisional neutralization with $CH_3SSCH_3$. The NR mass spectrum of **C$_5$-1**$^{+\bullet}$ clearly distinguishes the lactone enol from other $C_4H_6O_2$ isomers, as shown for the cyclic isomers butan-4-lactone (**C$_5$-2**) and oxolan-3-one (**5**) (Figure 2). NR of **C$_5$-1**$^{+\bullet}$ gives a dominant peak of survivor **C$_5$-1**$^{+\bullet}$ at *m*/*z* 86 that corresponds to reionization of undissociated **C$_5$-1**, indicating that the lactone enol is a stable species in an isolated state. In contrast, NR of butane-4-lactone (**C$_5$-2**) shows only a very weak survivor ion in addition to ionized $C_3H_6$, $CO_2$, and $C_2H_4$ which are the major dissociation products. Collisional activation of neutral **C$_5$-1** slightly decreased the relative intensity of the survivor ion (Figure 3) but did not change appreciably the relative intensities of the reionized fragments. In particular, dissociation products typical of butane-4-lactone (*m*/*z* 42), 2-butenoic and 3-butenoic acid (*m*/*z* 39) were not enhanced relative to the products typical of **C$_5$-1** (*m*/*z* 68, 58, and 55, Figure 2). This indicated that, upon excitation, lactone enol **C$_5$-1** did not isomerize unimolecularly to the more stable lactone or butenoic acid structures. NR dissociations of **C$_5$-1** were further investigated by variable-time measurements

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***Table 1.*** Syn−Anti Conformer Equilibria of Lactone Enols

| species | gas phase[a] | | | aqueous solution[a,b] | |
|---|---|---|---|---|---|
| | $\Delta H(g)_{298}$ | $\Delta G(g)_{298}$ | $K_{eq}(g)$ | $\Delta G(w)_{298}$ | $K_{eq}(w)$ |
| **$C_4$-1** | 4.2 (3.8)[c] | 5.0 (4.7)[c] | 0.13 (0.15)[c] | -4.4 (−4.7)[c] | 5.9 (6.7)[c] |
| **$C_5$-1** | 5.7 (5.3) | 5.9 (5.6) | 0.09 (0.11) | -3.1 (−3.4) | 3.5 (4.0) |
| **$C_6$-1** | 6.4 (6.1) | 6.9 (6.6) | 0.06 (0.07) | -1.2 (−1.5) | 1.6 (1.9) |
| $CH_2{=}C(OH)_2$ (**3**) | 5.1 (4.8) | 7.0 (6.7) | 0.06 (0.07) | 2.2 (1.9) | 0.41 (0.46) |
| $CH_2{=}C(OH)(OCH_3)$ (**4**) | 6.0 (5.7) | 7.0 (6.6) | 0.06 (0.07) | -0.2 (−0.5) | 0.92 (0.80) |

[a] Energy differences in kJ mol$^{-1}$ and equilibrium constants calculated by QCISD(T)/6-311+G(3df,2p) for the reaction syn → anti. [b] Including B3LYP/6-31+G(d,p) PCM solvation free energies. [c] From B3-MP2/6-311+G(3df,2p) energies.

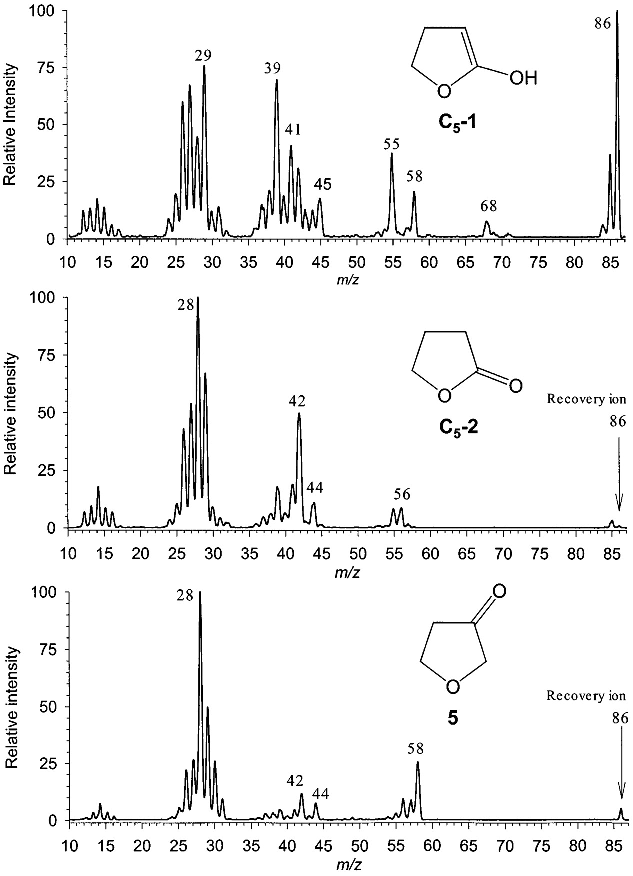

***Figure 2.*** Neutralization ($CH_3SSCH_3$, 70%T)/reionization ($O_2$, 70%T) mass spectra of (top) **$C_5$-1**, (middle) **$C_5$-2**, and (bottom) **5**.

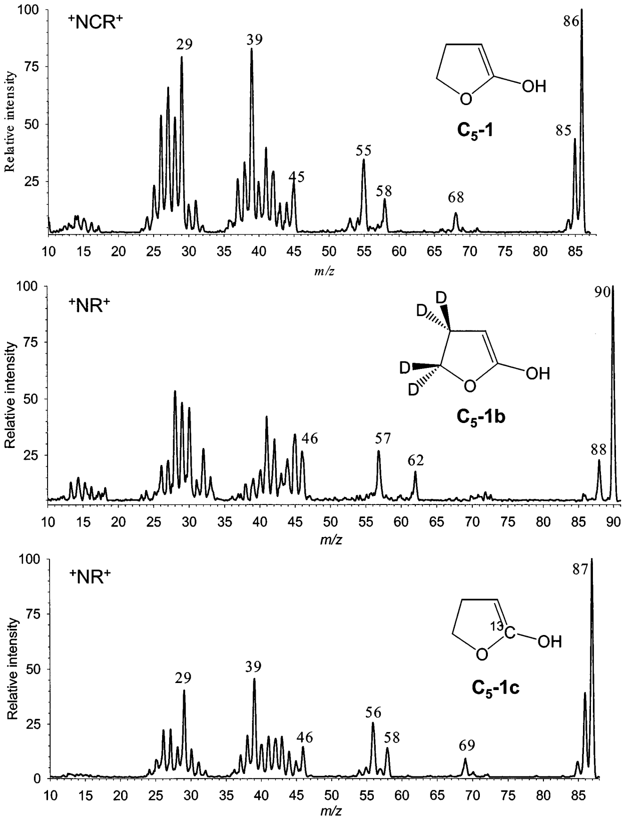

***Figure 3.*** (Top) Neutralization ($CH_3SSCH_3$, 70%T)/collisional activation (He, 50%T)/reionization ($O_2$, 70%T) mass spectrum of **$C_5$-1**$^{+\bullet}$ and $^{+}NR^{+}$ mass spectra of (middle) **$C_5$-1b**$^{+\bullet}$ and (bottom) **$C_5$-1c**$^{+\bullet}$.

that revealed mainly losses of H, CO, and ring fragmentations in reionized **$C_5$-1**$^{+\bullet}$ that were similar to those observed in the CAD spectrum of **$C_5$-1**$^{+\bullet}$ (Figure 1). Changes in the time-resolved NR spectra were observed for the weak peak due to loss of water (*m*/*z* 68), which increased at longer neutral dissociation times, indicating a substantial contribution from neutral dissociation. NR spectra of the labeled derivatives (Figure 3) revealed dissociations that were analogous to those in the CAD spectra of the respective ions.[37] In particular, the loss of H involved exclusively hydrogen atoms from C-4 or C-5 or both, and the elimination of CO involved exclusively C-2. In summary, the NR data point to the fact that enol **$C_5$-1** is a stable species in an isolated state in the gas phase.

**Enol Structure and Energetics.** Because of the high stability of neutral **$C_5$-1** under NR conditions, most information on the dissociation energetics was obtained from ab initio calculations. Lactone enol **$C_5$-1** was calculated to exist as two conformers of which *syn*-**$C_5$-1** is 6 kJ mol$^{-1}$ more stable than *anti*-**$C_5$-1** in the gas phase. The conformers are separated by a 16 kJ mol$^{-1}$ barrier to OH rotation, relative to *syn*-**$C_5$-1**, and interconvert rapidly ($k > 10^{10}$ s$^{-1}$) at excitations of $E \geq 20$ kJ mol$^{-1}$. The greater stability of gaseous *syn*-**$C_5$-1** is probably due to the more favorable orientation of the O−H and C−O$_{ring}$ bond dipoles than in *anti*-**$C_5$-1**, as illustrated by the calculated atomic charge densities (Figure 4). Similar relative stabilities were found for the syn and anti rotamers of **$C_4$-1** and **$C_6$-1** and the acyclic enols **3** and **4** (Table 1). The preference for the syn rotamer in the lactone enols slightly increases with the ring size, which correlates with the increasing dipole moment of the syn rotamers in the gas phase (Figure 4).

The enthalpies of formation of *syn*-**$C_5$-1** and *syn*-**$C_6$-1** were calculated by G2(MP2) from enthalpies of atomization, isomerization, and isodesmic reactions for OH exchange between the enols and ethane, ethylene, and acetaldehyde (Table 2, Scheme 2).[38] The G2(MP2) and B3-MP2 values are practically identical

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(38) Standard enthalpies of formation of ethylene, ethane, ethanol, acetaldehyde, and acetic acid were taken from: *NIST Standard Reference Database No. 69*, February 2000 release. http//:webbook.nist.gov. The enthalpy of formation of vinyl alcohol was from ref 39.

*Table 2.* Thermochemical Properties of Enols, Lactones, and Related Species

| | enthalpy[a] | | | |
|---|---|---|---|---|
| | G2(MP2) | | B3-MP2[b] | |
| species/reaction | $\Delta H_{rxn,298}$ | $\Delta H°_{f,298}$ | $\Delta H_{rxn,298}$ | $\Delta H°_{f,298}$ |
| *syn*-**C$_4$-1** → 3($^3$P)C + 4($^2$S)H + 2($^3$P)O | 3666[c] | −146 | | |
| **C$_4$-2** → 3($^3$P)C + 4($^2$S)H + 2($^3$P)O | 3806[c] | −286 | | |
| *syn*-**C$_5$-1** → 4($^3$P)C + 6($^2$S)H + 2($^3$P)O | 4931[c] | −258 | | |
| *syn*-**C$_5$-1**→ *anti*-**C$_5$-1** | 5.6 | | 5.3 | |
| *syn*-**C$_5$-1** → **C$_5$-2** | −107 | −258 | −106 | −259 |
| *syn*-**C$_5$-1** → **6** | −9 | *d* | −4 | *d* |
| *syn*-**C$_5$-1** → **7** | −79 | *d* | −80 | *d* |
| *syn*-**C$_5$-1** → **8** | −96 | *d* | −98 | *d* |
| *syn*-**C$_5$-1** → **9** | 6 | *d* | 10 | *d* |
| *syn*-**C$_5$-1** → furan + $H_2O$ | −4 | −272 | −16 | −260 |
| *syn*-**C$_5$-1** + $CH_3CH_3$ → **10** + $CH_3CH_2OH$ | 39 | −263 | 43 | −266 |
| *syn*-**C$_5$-1** + $CH_2{=}CH_2$ → **10** + $CH_2{=}CHOH$ | 14 | −262 | 12 | −260 |
| *syn*-**C$_5$-1** + $CH_3CHO$ → **10** + $CH_3COOH$ | −74 | −260 | −74 | −259 |
| *syn*-**C$_5$-1** + $CH_2{=}C(CH_3)CHO$ → **10** + $CH_2{=}C(CH_3)COOH$ | −63 | −272[d] | −61 | −272[d] |
| mean $\Delta H_{f,298}$(*syn*-**C$_5$-1**) | | −262 | | −261 |
| **C$_5$-2** → 4($^3$P)C + 6($^2$S)H + 2($^3$P)O | 5038[c] | −365[e] | | |
| *syn*-**C$_6$-1** → 5($^3$P)C + 8($^2$S)H + 2($^3$P)O | 6122[c] | −297 | | |
| *syn*-**C$_6$-1** + $CH_3CH_3$ → **11** + $CH_3CH_2OH$ | 43 | −307 | 46 | −310 |
| *syn*-**C$_6$-1** + $CH_2{=}CH_2$ → **11** + $CH_2{=}CHOH$ | 16 | −304 | 14 | −302 |
| *syn*-**C$_6$-1**+ $CH_3CHO$ → **11** + $CH_3COOH$ | −70 | −304 | −72 | −303 |
| *syn*-**C$_6$-1** → **C$_6$-2** | −76 | −302 | −75 | −303 |
| mean $\Delta H_{f,298}$(*syn*-**C$_6$-1**) | | −303 | | −304 |
| **C$_6$-2** → 5($^3$P)C + 8($^2$S)H + 2($^3$P)O | 6198[c] | −374[e] | | |
| $CH_3COOH$ → 2($^3$P)C + 4($^2$S)H + 2($^3$P)O | 3237[c] | −433[e] | | |
| $CH_2{=}C(OH)_2$ → 2($^3$P)C + 4($^2$S)H + 2($^3$P)O | 3122[c,f] | −318[f] | | |
| $CH_2{=}C(OH)_2$ → $CH_3COOH$ | −116 | −316[f] | −115[f] | −317[f] |
| $CH_3COOCH_3$ → 3($^3$P)C + 6($^2$S)H + 2($^3$P)O | 4366[c] | −410[e] | | |
| $CH_2{=}C(OH)OCH_3$ → 3($^3$P)C + 6($^2$S)H + 2($^3$P)O | 4254[c,f] | −298[f] | | |
| $CH_2{=}C(OH)OCH_3$ → $CH_3COOCH_3$ | −113[f] | −297[f] | −112[f] | −298[f] |

[a] In units of kJ mol$^{-1}$. [b] From combined single-point energies calculated with the 6-311+G(3df,2p) basis set. [c] 298 K atomization energies. [d] Unknown or uncertain product enthalpies of formation. [e] The experimental $\Delta H°_{f,298}$ (kJ mol$^{-1}$, ref 38) are as follows: **C$_5$-2**: −365 ± 3; **C$_6$-2**: −378; **10**: −72.2; **11**; −112.8; $CH_3COOH$: −432; $CH_3COOCH_3$: −410. [f] Energies for the most stable enol conformers, see refs 23 and 45. For other estimates of enol relative energies and heats of formation, see refs 23 and 46.

for *syn*-**C$_5$-1**, $\Delta H°_{f,298} = -262$ and −261 kJ mol$^{-1}$, respectively (*Table 2*). Note that G2(MP2) gives accurate enthalpies of formation (± 1 kJ mol$^{-1}$ of experimental data) for **C$_5$-2**, acetic acid, methyl acetate, and other molecules that were used as auxiliaries in thermochemical calculations (Table 2).

*syn*-**C$_5$-1** is less stable than butane-4-lactone (**C$_5$-2**), 2-hydroxy-2,3-dihydrofuran (**6**), 3-butenoic (**7**), and 2-methyl-2-propenoic acids (**8**), but slightly more stable than 2-hydroxy-2,5-dihydrofuran (**9**) (Table 2). *syn*-**C$_5$-1** is calculated to be metastable with respect to dissociation to furan and water, which requires $\Delta H_{rxn,298} = -4$ kJ mol$^{-1}$ at the 298 K thermochemical threshold (Table 2). However, unimolecular elimination of water from *syn*- or *anti*-**C$_5$-1** must involve extensive hydrogen migrations, which provide kinetic stabilization for the enol, as observed in the gas phase.

Enthalpies of atomization and isodesmic reactions were also used to assess the standard enthalpies of formation of the **C$_6$** tautomers. The mean $\Delta H_{f,298}$(*syn*-**C$_6$-1**) = −303 kJ mol$^{-1}$ by G2(MP2) compares well with the B3-MP2 value of −304 kJ mol$^{-1}$ (Table 2). Note that the $\Delta H_{f,298}$(**C$_6$-2**) = −374 kJ mol$^{-1}$ is in good agreement with the experimental value (−378 kJ mol$^{-1}$).[38] The enthalpies of formation in the **C$_4$** system were calculated from the corresponding atomization energies as $\Delta H_{f,298}$(*syn*-**C$_4$-1**) = −146 kJ mol$^{-1}$, $\Delta H_{f,298}$(**C$_4$-2**) = −286 kJ mol$^{-1}$. Lack of reference data for oxacyclobut-2-ene prevented the use of Scheme 2 isodesmic reactions for **C$_4$-1**.

*Table 3.* Enol Lactone Equilibria

| | gas phase[a] | | | aqueous solution[a] | |
|---|---|---|---|---|---|
| species | $\Delta H(g)_{298}$ | $\Delta G(g)_{298}$ | $K_{eq}(g)$ | $\Delta G(w)_{298}$ | $K_{eq}(w)$ |
| *syn*-**C$_4$-1** | 140 | 138 | $5.8 \times 10^{-25}$ | 144 | $5.9 \times 10^{-26}$ |
| *anti*-**C$_4$-1** | 144 | 143 | $5.8 \times 10^{-26}$ | 140 | $3.5 \times 10^{-25}$ |
| *syn*-**C$_5$-1** | 107 | 106 | $2.8 \times 10^{-19}$ | 113 | $1.6 \times 10^{-20}$ |
| *anti*-**C$_5$-1** | 113 | 112 | $2.6 \times 10^{-20}$ | 110 | $5.7 \times 10^{-20}$ |
| *syn*-**C$_6$-1** | 76 | 76 | $4.7 \times 10^{-14}$ | 83 | $2.5 \times 10^{-15}$ |
| *anti*-**C$_6$-1** | 82 | 83 | $2.9 \times 10^{-15}$ | 82 | $4.1 \times 10^{-15}$ |
| *syn*-$CH_2{=}C(OH)_2$ | 116 | 116 | $5.4 \times 10^{-21}$ | 106 | $2.7 \times 10^{-19}$ |
| *anti*-$CH_2{=}C(OH)_2$ | 121 | 123 | $3.2 \times 10^{-22}$ | 109 | $9.4 \times 10^{-20}$ |
| *syn*-$CH_2{=}C(OH)(OCH_3)$ | 113 | 117 | $3.9 \times 10^{-21}$ | 109 | $8.8 \times 10^{-20}$ |
| *anti*-$CH_2{=}C(OH)(OCH_3)$ | 126 | 129 | $2.6 \times 10^{-23}$ | 120 | $9.5 \times 10^{-22}$ |

[a] Energy differences (kJ mol$^{-1}$) and equilibrium constants for the reaction lactone → enol at 298 K.

The enol lactone relative stabilities for gaseous **C$_4$-1**−**C$_6$-1** are summarized in Table 3. Both the $\Delta H$(g) and $\Delta G$(g) decrease with the increasing ring size, indicating less destabilization of the enol system in the larger rings. This can be due in part to the decreasing ring strain analogous to that in the series cyclobutene → cyclopentene → cyclohexene.[40] However, the enol-lactone destabilization for **C$_5$-1** and **C$_6$-1** is less than in the acyclic systems **3** and **4**, indicating that the $\beta$-alkyl substituents exert a weak stabilizing effect on the enol system.[39] A similar effect has been observed for enols of cyclic ketones, where, for example, the enthalpy difference for cyclopentanone → 1-hydroxycyclopent-1-ene is less than for acetone → prop-1-en-1-ol.[41] The calculated $\Delta G$(g) and equilibrium constants

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(39) Tureček, F.; Cramer, C. J. *J. Am. Chem. Soc.* **1995**, *117*, 12243−12253.
(40) Eliel, E. L.; Willen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*, Wiley: New York, 1994; pp 676−677.
(41) Keefe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1988**, *110*, 1993−1995.

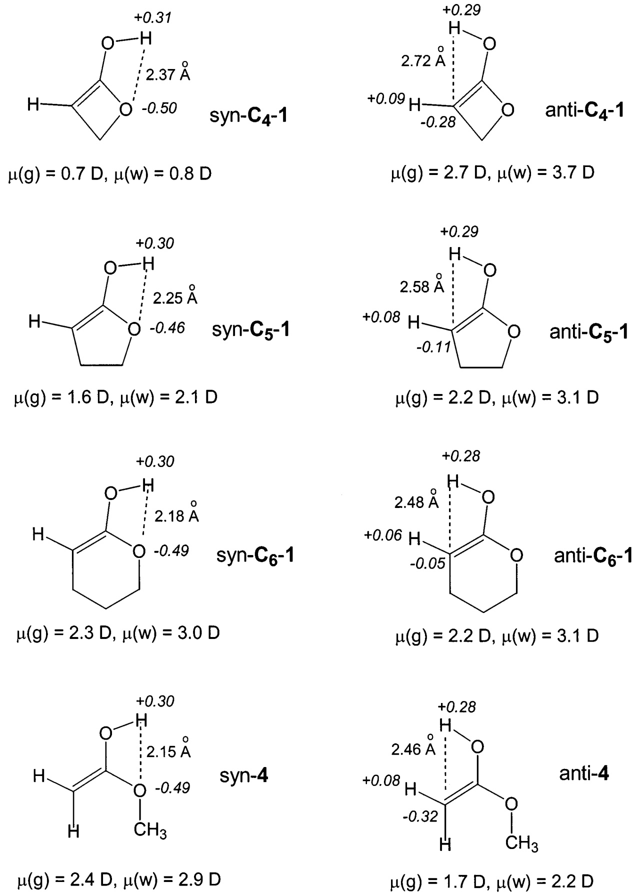
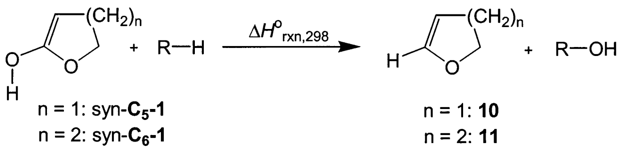


***Figure 4.*** B3LYP/6-311+G(2d,p) atomic charges (italics) and dipole moments for *syn*- and *anti*-**C$_4$-1**−**C$_6$-1** and **4**. $\mu$(g) and $\mu$(w) refer to the dipole moments in units of Debye calculated in the gas phase and aqueous solution, respectively.

***Scheme 2***



further indicate that lactone enols exist at negligibly low concentrations in equilibrium mixtures with the corresponding lactones.

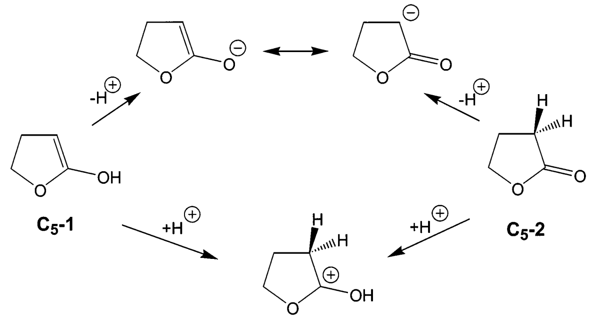
**Ionization Energies.** For *syn*- and *anti*-**C$_5$-1** produced by collisional electron transfer, the corresponding vertical and adiabatic ionization and recombination energies are of interest (Table 4). The adiabatic ionization energies of *syn*- and *anti*-**C$_5$-1**, 7.73 and 7.79 eV, respectively, are substantially lower than those of simple enols which range between 8.1 and 9.18 eV.[13,39] The facile ionization of **C$_5$-1** reflects the destabilization of the neutral lactone enol and the stabilization of the corresponding cation radical. The Franck−Condon energies in vertical ionization of *syn*-**C$_5$-1** ($E_{\mathrm{FC}} = 43$ kJ mol$^{-1}$) and vertical electron capture by *syn*-**C$_5$-1**$^{+\bullet}$ ($E_{\mathrm{FC}} = 37$ kJ mol$^{-1}$) are low, as judged from the differences of the B3-PMP2 adiabatic and vertical ionization energies. Hence, excitation due to Franck−Condon effects is insufficient to drive unimolecular dissociations of *syn*-**C$_5$-1** and *syn*-**C$_5$-1**$^{+\bullet}$, which accounts for both the presence of the dominant survivor ion in the NR mass spectrum and the low efficiency of collisionally activated dissociation of **C$_5$-1**.

***Table 4.*** Ionization Energies of $C_4H_6O_2$ Isomers

| | energy[a] | | |
|---|---|---|---|
| species | $IE_a$[b] | $IE_v$[c] | $RE_v$[d] |
| *syn*-**C$_5$-1** | 7.73 (7.91)[e] | 8.18 | 7.35 |
| *anti*-**C$_5$-1** | 7.79 (7.96)[e] | 8.17 | |
| **C$_5$-2** | 10.08 (10.10)[e] | 10.43 | 9.79 |
| **5** | 8.28 | | |
| **6** | 9.62 | | |

[a] In units of electronvolt, 0 K values from B3-PMP2 single-point energies. [b] Adiabatic ionization energy. [c] Vertical ionization energy. [d] Vertical recombination energy of the ion. [e] From G2(MP2) calculations including the 0.131 eV empirical correction for the different number of valence electrons in the molecule and cation radical (ref 30).

***Scheme 3***



**Gas-Phase Acidities and Basicities.** Deprotonation and protonation of lactone enols produces gas-phase ions that are identical to those formed from the corresponding lactones as shown for **C$_5$-1** and **C$_5$-2** (Scheme 3). The thermochemistries of proton-transfer reactions in lactones and enols are therefore closely linked to the lactone enol relative energies. Table 5 summarizes the calculated $\Delta H$(g) and $\Delta G$(g) for deprotonation, corresponding to gas-phase acidities, and protonation, corresponding to proton affinities of **C$_4$** through **C$_6$** enols and lactones. A comparison with the recent experimental acidities of **C$_4$-2** through **C$_6$-2**,[25] acetic acid, and methyl acetate[38] shows a very satisfactory agreement (4 kJ mol$^{-1}$ rmsd), which is well within the uncertainty of the experimental acidities (± 9 kJ mol$^{-1}$).[25] The proton affinity of **C$_5$-2** is also reproduced very well by the calculations (Table 5). Because of their higher relative enthalpies, lactone enols are substantially more acidic and basic than the corresponding lactones. The gas-phase acidities of **C$_4$-1**−**C$_6$-1** are comparable to those of carboxylic acids (e.g., acetic acid, Table 5) and indicate facile deprotonation by reactions with bases in the gas phase or on surface. Likewise, the proton affinities of **C$_4$-1**−**C$_6$-1** (Table 5) are quite high for oxygen-containing molecules and match those of aliphatic primary amines (e.g., *tert*-butylamine, PA = 934 kJ mol$^{-1}$). These data indicate that enols **C$_4$-1**−**C$_6$-1** should be vulnerable to acid−base-catalyzed isomerization to the more stable lactones, in particular by reactions occurring on acid−base active surfaces such as glass or metal oxides.[42] Hence, generation of lactone enols in the gas phase by methods other than NRMS is predicted to be experimentally very challenging.

**Lactone Enol Properties in Solution.** Solvation by a protic solvent results in changes in enol properties and energetics. Because of the solvent−solute dipole−dipole interactions, enol anti conformers of larger dipole moments are better solvated in

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(42) (a) Tureček, F. Brabec, L.; Korvola, J. *J. Am. Chem. Soc.* **1988**, *124, 110*, 7984−7990. (b) Tureček, F. In *Advances in Mass Spectrometry 1988*; Longevialle, P., Ed.; Wiley: New York, 1989; pp 1079−1097.

***Table 5.*** Gas-Phase Proton-Transfer Energetics of Lactone Enols and Lactones

| | gas-phase acidity[a] | | | |
|---|---|---|---|---|
| species/reaction | $\Delta H(g)_{298}$[b] | $\Delta H_{exp}$ | $\Delta G(g)_{298}$[b] | $\Delta G_{exp}$ |
| *syn*-enol → enolate$^-$ + $H^+$ | | | | |
| **$C_4$-1** | 1410 (1401)[c] | | 1378 (1369)[c] | |
| **$C_5$-1** | 1442 (1433) | | 1411 (1403) | |
| **$C_6$-1** | 1466 (1458) | | 1435 (1427) | |
| $CH_2{=}C(OH)_2$ (**3**) | 1433 (1424) | | 1404 (1395) | |
| $CH_2{=}C(OH)(OCH_3)$ (**4**) | 1462 (1453) | | 1431 (1422) | |
| lactone → enolate$^-$ + $H^+$ | | | | |
| **$C_4$-2** | 1550 (1539)[c] | 1543 ± 9[d] | 1517 (1506)[c] | 1504 ± 9[d] |
| **$C_5$-2** | 1549 (1538) | 1546 ± 9[d] | 1517 (1507) | 1508 ± 9[d] |
| **$C_6$-2** | 1542 (1533) | 1537 ± 9[d] | 1511 (1502) | 1500 ± 9[d] |
| $CH_3COOH \rightarrow CH_3COO^- + H^+$ | 1454 (1448) | 1456−1459 ± 9[e] | 1419 (1413) | 1427−1430 ± 8[e] |
| $CH_3COOH \rightarrow CH_2{=}C(OH)O^- + H^+$ | 1555 (1545)[c] | | 1526 (1516)[c] | |
| $CH_3COOCH_3$ | 1574 (1565) | 1573[e] | 1547 (1538) | |
| (**$C_4$-2** + H)$^+$ → **$C_4$-2** + $H^+$ | 792 (789) | | 761 (757) | |
| (**$C_4$-2** + H)$^+$ → *syn*-**$C_4$-1** + $H^+$ | 933 (927) | | 899 (894) | |
| (**$C_5$-2** + H)$^+$ → **$C_5$-2** + $H^+$ | 838 (836) | 840[e] | 807 (804) | 808[e] |
| (**$C_5$-2** + H)$^+$ → *syn*-**$C_5$-1** + $H^+$ | 945 (942) | | 912 (909) | |
| (**$C_6$-2** + H)$^+$ → **$C_6$-2** + $H^+$ | 868 (866) | | 836 (834) | |
| (**$C_6$-2** + H)$^+$ → *syn*-**$C_6$-1** + $H^+$ | 944 (941) | | 912 (909) | |

[a] In units of kJ mol$^{-1}$ at 298 K. [b] From G2(MP2) energies and B3LYP/6-31+G(d,p) enthalpies and entropies. [c] Values in parentheses are from B3-MP2/6-311+G(3df,2p) energies. [d] From ref 25. [e] From ref 38

aqueous solution. This results in a reversal of *syn*−*anti*-enol equilibria for **$C_4$-1**−**$C_6$-1** where the anti conformers are more stable in water, whereas syn conformers are more stable in the gas phase (Table 1). The anti conformers of enols **3** and **4** also gain 5−7 kJ mol$^{-1}$ stabilization in water. With **3**, the relative stabilization by solvation of the anti conformer does not correlate with the overall dipole moment which is slightly greater in the syn conformer (2.6 D) than in the anti conformer (2.5 D). Rather, the PCM energy terms indicate that the anti conformer stabilization results from electrostatic interactions of atomic charges with the polar continuum.

Solvation effects also affect the enol-lactone equilibria by destabilizing the *syn*−enol tautomers while stabilizing the anti conformers (Table 3). The overall solvent effect is small, resulting in free energy changes on the order of 2−6 kJ mol$^{-1}$ further favoring the lactone tautomers over the most stable enol conformers in aqueous solution. A similar effect of enol destabilization is obtained for **4**, while **3** is stabilized against acetic acid, e.g., $\Delta G(w)_{298} = 106$ kJ mol$^{-1}$ for *syn*-**3**, compared to the gas-phase equilibrium, for which $\Delta G(g)_{298} = 116$ kJ mol$^{-1}$ (Table 3). We note that the relative stabilization by solvent of **3** parallels the previous findings for simple enol−oxo pairs of vinyl alcohol−acetaldehyde and prop-1-en-2-ol-acetone.[39] The enol-lactone equilibrium constants in water are extremely low, $K_{eq}(w) < 10^{-14}$ (Table 3), compared to those for simple enol-oxo systems, where typically $K_{eq}(w) > 10^{-8}$,[12] and further indicate that generation of lactone enols in solution would be a challenging task.

**Solution Acidities and Basicities.** The calculated solvation energies of lactones, enols, their protonated forms, and enolates allowed us to calculate the acid−base equilibria in water and the corresponding p$K_a$ values (Table 6). The previous work of Barone et al. has shown that although PCM calculations do not provide accurate absolute p$K_a$ of carboxylic acids, the calculated and experimental values correlate.[43] The absolute deviations in the p$K_a$ values are mainly due to inaccurate solvation free energies for the ions involved, that is, $H_3O^+$, $OH^-$, and carboxylates.[35,43] In the present calculations, we used eqs 1 and 2 for enolates $(A - H)^-$ to evaluate p$K_a$ values, and eqs 3 and 4 for the protonated forms $(A + H)^+$ to evaluate p$K_{BH}$. Averaging the $\Delta G$(w) for reactions 1 and 2, and similarly for 3 and 4, resulted in error cancellation in the ion solvation energies and provided improved agreement with experiment. For example, the averaged p$K_a$ of acetic acid from eq 1 and (2), p$K_a$ = 4.6 (Table 6), is close to the experimental value of 4.76.[44]

$$A + H_2O \rightarrow (A - H)^- + H_3O^+ \tag{1}$$

$$A + OH^- \rightarrow (A - H)^- + H_2O \tag{2}$$

$$A + H_2O \rightarrow (A + H)^+ + OH^- \tag{3}$$

$$A + H_3O^+ \rightarrow (A + H)^+ + H_2O \tag{4}$$

The $\Delta G$(w) and p$K_a$ values in Table 6 show that lactones **$C_4$-2**−**$C_6$-2** are practically inert toward $OH^-$ and $H_3O^+$ in water. In contrast, enol **$C_4$-1**, p$K_a$ = 5.6, is more acidic than *p*-nitrophenol (p$K_a$ = 7.15) and related organic *O*-acids,[44] and is expected to deprotonate rapidly in water. The enol acidity decreases with the increasing ring size, such that **$C_6$-1** of p$K_a$ = 14.5 is less acidic than phenol (p$K_a$ = 9.89).[44] The p$K_a$ values of **3** and **4** are close to that of **$C_5$-1**.

The enol basicities, expressed as p$K_{BH}$ of the conjugate acids, $(A + H)^+$ (Table 7), show a similar trend as do the enol acidities. **$C_4$-1** is a moderately weak base, p$K_{BH}$ = 8.1, which is comparable to that of cyclic amines, for example, morpholine of p$K_{BH}$ = 8.33.[44] Increasing the ring size in **$C_5$-1** and **$C_6$-1** results in a decreasing basicity, such that the latter enol (p$K_{BH}$ = 3.9) resembles weakly basic aromatic amines, for example, halogenated anilines or benzidine.[44] The ring-size effects on the

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***Table 6.*** Solution Acidities of Lactone Enols and Lactones

| reaction | $\Delta G(g)_{298}{}^{a,b}$ | $\Delta G(w)_{298}{}^{a,b,c}$ | $K_{eq}(w)$ | $pK_a$ |
|---|---|---|---|---|
| $A + OH^- \rightarrow (A - H)^- + H_2O$ | | | | |
| **$C_4$-1** | −228 (−234)$^{d}$ | −63 (−69)$^{d}$ | $1.2 \times 10^{11}$ | 4.7 |
| **$C_5$-1** | −195 (−200) | −32 (−37) | $3.5 \times 10^{5}$ | 10.2 |
| **$C_6$-1** | −172 (−176) | −13 (−18) | $1.9 \times 10^{2}$ | 13.5 |
| $CH_2{=}C(OH)_2$ (**3**) | −196 (−201) | −25 (−30) | $2.2 \times 10^{4}$ | 11.4 |
| $CH_2{=}C(OCH_3)(OH)$ (**4**) | −176 (−180) | −21 (−26) | $5.7 \times 10^{3}$ | 12.0 |
| $A + H_2O \rightarrow (A - H)^- + H_3O^+$ | | | | |
| **$C_4$-1** | 721 (715)$^{d}$ | 48 (41)$^{d}$ | $4.1 \times 10^{-9}$ | 6.6 (5.6)$^{e}$ |
| **$C_5$-1** | 755 (748) | 79 (73) | $1.2 \times 10^{-14}$ | 12.2 (11.2) |
| **$C_6$-1** | 778 (772) | 98 (93) | $6.4 \times 10^{-18}$ | 15.5 (14.5) |
| $CH_2{=}C(OH)_2$ (**3**) | 753 (747) | 86 (80) | $7.5 \times 10^{-16}$ | 13.4 (12.4) |
| $CH_2{=}C(OCH_3)(OH)$ (**4**) | 774 (768) | 90 (84) | $2.0 \times 10^{-16}$ | 14.0 (13.0) |
| $A + OH^- \rightarrow (A - H)^- + H_2O$ | | | | |
| **$C_4$-2** | −90 (−97)$^{d}$ | 81 (73)$^{d}$ | $7.0 \times 10^{-15}$ | 29.9 |
| **$C_5$-2** | −89 (−96) | 81 (75) | $5.7 \times 10^{-15}$ | 30.0 |
| **$C_6$-2** | −96 (−101) | 70 (65) | $4.6 \times 10^{-13}$ | 28.1 |
| $CH_3COOH + OH^- \rightarrow CH_3COO^- + H_2O$ | −187 (−190) | −69 (−72) | $1.4 \times 10^{12}$ | 3.6 |
| $A + H_2O \rightarrow (A - H)^- + H_3O^+$ | | | | |
| **$C_4$-2** | 860 (851)$^{d}$ | 155 (146)$^{d}$ | $8.1 \times 10^{-28}$ | 25.3 (27.6)$^{e}$ |
| **$C_5$-2** | 860 (853) | 192 (185) | $2.0 \times 10^{-34}$ | 32.0 (31.0) |
| **$C_6$-2** | 854 (847) | 182 (175) | $1.6 \times 10^{-32}$ | 30.1 (29.1) |
| $CH_3COOH + H_2O \rightarrow CH_3COO^- + H_3O^+$ | 762 (759) | 42 (38) | $4.7 \times 10^{-8}$ | 5.6 (4.6) |

[a] In units of kJ mol$^{-1}$ at 298 K. [b] From G2(MP2) energies and B3LYP/6-31+G(d,p) enthalpies and entropies. [c] Including PCM solvation free energies calculated by B3LYP/6-31+G(d,p). [d] Values in parentheses are from B3-MP2/6-311+G(3df,2p) energies. [e] Averaged values for reactions with OH$^-$ and H$_2$O, see text.

***Table 7.*** Gas-Phase and Solution Basicities of Lactone Enols and Lactones

| reaction | $\Delta G(g)_{298}{}^{a,b}$ | $\Delta G(w)_{298}{}^{a,b,c}$ | $K_{eq}(w)$ | $pK_{BH}{}^{d}$ |
|---|---|---|---|---|
| | $A + H_2O \rightarrow (A + H)^+ + OH^-$ | | | |
| **$C_4$-1** | 707 (709)$^{e}$ | 49 (51)$^{e}$ | $2.2 \times 10^{-9}$ | 7.1 |
| **$C_5$-1** | 688 (689) | 60 (61) | $2.7 \times 10^{-11}$ | 5.7 |
| **$C_6$-1** | 695 (694) | 74 (73) | $1.2 \times 10^{-13}$ | 2.8 |
| | $A + H_3O^+ \rightarrow (A{+}\ H)^+ + H_2O$ | | | |
| **$C_4$-1** | −242 (−239)$^{e}$ | −62 (−59)$^{e}$ | $6.5 \times 10^{10}$ | 9.1 (8.1)$^{f}$ |
| **$C_5$-1** | −256 (−254) | −54 (−53) | $2.7 \times 10^{9}$ | 7.7 (6.7) |
| **$C_6$-1** | -−255 (−255) | −37 (−37) | $3.4 \times 10^{6}$ | 4.8 (3.9) |
| | $A + H_2O \rightarrow (A + H)^+ + OH^-$ | | | |
| **$C_4$-2** | 848 (848)$^{e}$ | 196 (196)$^{e}$ | $5.2 \times 10^{-35}$ | −18.5 |
| **$C_5$-2** | 800 (799) | 170 (169) | $1.5 \times 10^{-30}$ | −14.0 |
| **$C_6$-2** | 771 (769) | 157 (155) | $2.9 \times 10^{-28}$ | −11.8 |
| | $A + H_3O^+ \rightarrow (A + H)^+ + H_2O$ | | | |
| **$C_4$-2** | −104 (−103)$^{e}$ | 82 (83)$^{e}$ | $3.8 \times 10^{-15}$ | −16.2 (−17.4) |
| **$C_5$-2** | −150 (−150) | 59 (59) | $4.5 \times 10^{-11}$ | −12.1 (−13.0) |
| **$C_6$-2** | −179 (−180) | 46 (45) | $1.5 \times 10^{-10}$ | −9.8 (−10.5) |

[a] In units of kJ mol$^{-1}$ at 298 K. [b] From G2(MP2) energies and B3LYP/6-31+G(d,p) enthalpies and entropies. [c] Including PCM solvation free energies calculated by B3LYP/6-31+G(d,p). [d] p$K_a$ of conjugate acid. [e] Values in parentheses are from B3-MP2/6-311+G(3df,2p) calculations. [f] Averaged values for reactions with H$_2$O and H$_3$O$^+$, see text.

enol basicity in aqueous solution are opposite to those on gas-phase basicities, where the larger enols are more basic. This can be unambiguously ascribed to solvent effects which prefer the more polar (**$C_4$-1** + H)$^+$ cation ($\Delta G_{solv} = -284$ kJ mol$^{-1}$), compared to (**$C_5$-1** + H)$^+$ and (**$C_6$-1** + H)$^+$ of $\Delta G_{solv} = -266$ and $-250$ kJ mol$^{-1}$, respectively.

One consequence of the substantial acidity and basicity of **$C_4$-1**−**$C_6$-1** in water is an enhancement of acid−base-catalyzed isomerization to the more stable lactones. For example, protonation at the basic enol $\beta$-carbon produces an (A + H)$^+$ ion (Scheme 3) in which the OH group is superacidic in water (p$K_{BH} = -17.4$ to $-10.5$). Such a solvated ion should rapidly transfer the hydroxyl proton to the surrounding water molecules forming the lactone tautomer.[22] Considering the large equilibrium constants for the enol reactions with H$_3$O$^+$ (eq 4), protonation can be expected to be rapid even at pH 7 to drive fast enol-lactone isomerization.

## Conclusions

In summary, the acid−base and other thermodynamic properties of lactone enols predict these elusive molecules to be extremely reactive in the gas phase and solution and hence difficult to generate by classical methods of organic chemistry. Despite this pessimistic prediction, lactone enol **1** is found to be perfectly stable as an isolated molecule in the rarefied gas phase, as documented here by its generation and characterization by neutralization−reionization mass spectrometry.

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