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Structural Effects on the Intrinsic Basicities of α,β-Unsaturated Lactones and Ketones

Guy Bouchoux* and Danielle Leblanc

Département de Chimie, Laboratoire des Mécanismes Réactionnels, URA CNRS 1307,
Ecole Polytechnique, 91128 Palaiseau cedex, France

Otilia Mó and Manuel Yáñez

Departamento de Quimica, C-9, Universidad de Madrid, Cantoblanco, 28049-Madrid, Spain

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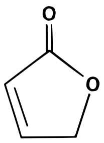
The proton affinities of 2(5*H*)-furanone, **1** (836 kJ/mol), 5,6-dihydro-2*H*-pyran-2-one, **2** (862 kJ/mol), cyclopentenone, **3** (857 kJ/mol), and cyclohexenone, **4** (863 kJ/mol), have been measured by Fourier transform ion cyclotron resonance techniques. A comparison is made with (reexamined) data concerning saturated cyclic and unsaturated aliphatic analogs. Three general observations are made. First, the basicity is found to increase with the size of the ring. Second, unsaturated lactones are more basic than their corresponding aliphatic unsaturated esters. Third, unsaturated and saturated lactones have almost identical gas-phase basicities, while unsaturated and saturated lactones have almost identical gas-phase basicities, while unsaturated cyclic ketones are more basic than their saturated analogs. All these experimental findings have been rationalized by means of *ab initio* calculations up to the G2(MP2,SVP) level. The basicity trends along the series are the result of two main factors: the different hybridization pattern of the carbonyl carbon as the size of the ring changes and, in the case of lactones, the nonbonding interaction between the proton attached to the carbonyl group and the ether-like oxygen which contributes to the enhanced stability of the protonated form. For unsaturated ketones the $C{=}C$ double bond participates fully in the change in charge distribution induced by the protonation, while for unsaturated lactones the existence of an oxygen atom within the ring impedes this shift of the electron density.

Introduction

Lactones have received a great deal of attention because they present important chemical, biochemical, and pharmaceutical properties.[1] Quite recently we have carried out a systematic investigation of the intrinsic basicities of a large series of lactones.[2] In that work it was shown that the gas-phase basicities of saturated lactones increase with the size of the ring and a limit is reached for six- and seven-membered rings whose gas-phase basicities are rather similar. This behavior seems to be consistent with (i) the significant hybridization changes undergone by the carbonyl carbon atom when the size of the ring changes and (ii) an efficient stabilizing interaction between the proton attached to the carbonyl group and the ether-like oxygen. It was also demonstrated[2] that, with the exception of β-propiolactone,[3] the lactones are more basic than the corresponding aliphatic esters which have the same number of carbons. This cyclization effect was rationalized, by means of ab-initio molecular orbital calculations, in terms of the aforementioned hybridization changes and internal stabilization effect.

The aim of the present study is to obtain quantitative information, both experimental and theoretical, on the intrinsic basicities of unsaturated lactones, namely, 2(5*H*)-furanone, **1**, and 5,6-dihydro-2*H*-pyran-2-one, **2**, and the corresponding unsaturated cyclic ketones: cyclopentenone, **3**, and cyclohexenone, **4**. Several problems will be addressed in this work. In the first place, we shall determine which is the most basic site of these compounds, where either protonation at the oxygen atoms or protonation at the unsaturated carbons must be considered. Second, we shall compare the intrinsic basicities of these compounds with those of the corresponding saturated counterparts γ-butyrolactone, **5**, δ-valerolactone, **6**, cyclopentanone, **7**, and cyclohexanone, **8**.



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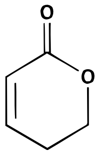

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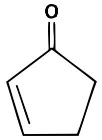

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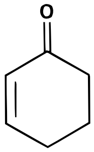

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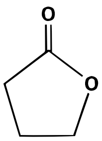

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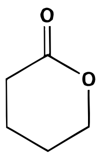

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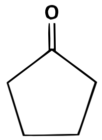

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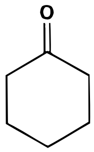

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Finally, we shall also pay attention to the basicities of the corresponding unsaturated aliphatic esters, **9**−**11**, and ketones, **12**−**14**.

Experimental Section

Experimental determination of the intrinsic basicities of the cyclic unsaturated compounds **1**−**4** has been done by the procedure of proton transfer equilibrium measurement. For the other species, **5**−**14**, values were obtained from previously

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[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1997.

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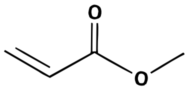
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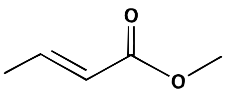
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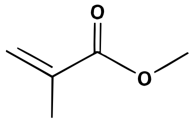
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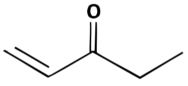
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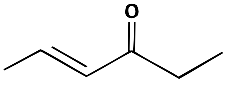
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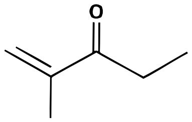
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published studies or adapted from them.[2,7,8] Proton transfer reactions between the species under study (M) and a reference base (B) (reaction 1) were performed on a Bruker Spectrospin CMS 47X FT-ICR mass spectrometer:[4]

$$\mathrm{MH}^{+} + \mathrm{B} \rightleftarrows \mathrm{M} + \mathrm{BH}^{+} \qquad (1)$$

The two substances M and B were introduced via a dual inlet system equipped with two separate Balzers-UDV-035 valves controlling the partial pressure of each component. Experiments were done at a total (indicated) pressure in the range 5×10^{-8} to 2×10^{-7} mbar. A temperature of 320 K has been maintained in the inlet system and in the analyzer cell during all experiments. The ions were produced by "self-chemical ionization" following electron impact inside the ICR cell under the following conditions: filament current = 3.2 A, electron kinetic energy = 50 eV. It has been observed that, after an ionization delay of 4 s, all the ions were relaxed to thermal energies by the presence of the static pressure of neutral reactants. This was checked by measuring the rate constant value for the disappearance of the reactive species MH^+ and assuring that it attains its higher limit. Then, unwanted ions were ejected by a combination of chirp and soft rf pulses, and the remaining ions MH^+ or(and) BH^+ were allowed to react with the neutral molecule(s). In order to check the reversibility of the reaction for each pair of substances, three experiments were done where the selected ions were either, or both, MH^+ or BH^+. Equilibrium was generally achieved after a delay of 5−20 s; no reaction other than the proton transfer process was observed with the couples of bases considerd. The $\mathrm{MH}^+/\mathrm{BH}^+$ ratio together with the ratio of the partial pressures of M and B were then used to calculate the equilibrium constant K_1 and thus to evaluate the standard free energy change of reaction 1:

$$\Delta G°_1 = -RT \ln K_1$$

The temperature of 320 K has been used in the estimation of $\Delta G°_1$. The partial pressure ratio was provided by the indications of an ionization gauge (Balzers-IMR-132). The gauge reading was corrected to account for the different ionization cross-sections of the various compounds by considering the polarizabilities of both M and B.[5] As deduced from several series of experiments, the uncertainty of the determined $\Delta G°_1$ does not exceed ±1−2 kJ/mol.

The proton affinity of M, PA(M), may be deduced from the relationship 2:

$$\mathrm{PA(M)} = \mathrm{PA(B)} + \Delta G°_1 + T[\Delta S°_{1/2}(\mathrm{B}) - \Delta S°_{1/2}(\mathrm{M})] \qquad (2)$$

where $\Delta S°_{1/2}$ is the difference in standard entropy between the protonated and the neutral species. For the reference bases B, PA(B) and $\Delta S°_{1/2}$(B) were taken from the recently published data of Szulejko and McMahon.[6] Several basicity measurements already available in the literature, concerning aliphatic compounds **9**−**14**, have been reconsidered in view of these data. In the case of species M = **1**−**14**, the values of $\Delta S°_{1/2}$ were assumed to be equal to zero, since the molecules are large enough so that the sum of the translational and vibrational entropy contributions is nearly equal for M and for MH^+ and thus cancel in $\Delta S°_{1/2}$. Similarly, as expected for **7** and **8**, no change in the number of rotational degrees of freedom is expected upon protonation if it occurs on the oxygen of the carbonyl group.

All the experimental data and the derived proton affinity of species **1**−**14** are reported in Table 1.

Computational Details

Standard ab-initio calculations have been carried out using the Gaussian 94 series of programs.[9] The geometries of the different systems included in this work were optimized at the HF/6-31G* level. The corresponding harmonic vibrational frequencies were calculated at the same level of theory by means of analytical second-derivative techniques. This permitted us to verify that the stationary points reached in the geometry optimizations correspond to local minima of the potential energy surface and to evaluate the corresponding zero point energies (ZPEs), which were scaled by the empirical factor of 0.893.[10] In this initial step, all possible conformers of either the neutrals or the protonated species were considered. Then, the geometries of the most stable structures were refined at the MP2(Full)/6-31G* level. When several conformers were found to be very close in energy at the HF level, the MP2 optimizations were carried out for all of them. This was particularly important, as we shall discuss in the forthcoming sections, in some specific cases where the inclusion of electron correlation effects led to a change in the predicted relative stabilities.

In order to calculate proton affinity values as reliable as possible, the final energies of the different global minima were obtained in the framework of the G2 theory. Unfortunately, this theory in its most general implementation may not be applicable to molecular systems of this size, for which the MP4 calculations are particularly expensive. A cheaper alternative is the G2(MP2) formalism, where the contributions of either the high angular momentum basis or the diffuse basis are evaluated at the MP2 level, while the high-order correlation corrections are estimated at the QCISD(T)/6-311G(d,p) level. However, even this procedure is prohibitively expensive for five- and six-membered rings, so we have decided to use the G2(MP2,SVP) formalism, where the QCISD(T) calculations are carried out at the 6-31G* level. Radom et al. have shown that this cheaper alternative performs particularly well in reproducing gas-phase proton affinities.[11]

The charge distribution and the bonding properties of neutral and protonated species have been obtained by two different and complementary population analysis techniques, namely, the natural bond orbital (NBO) method of Weinhold et al.[12] and the atoms-in-molecules theory of Bader and coworkers.[13] The first approach will offer information on the hybridization patterns of the different atoms as well as the contribution of the different hybrids to the bonding. The second formalism is based on a topological analysis of the

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Table 1. Experimental Free Energy Change $\Delta G°$ (kJ/mol) for the Reaction $M + [BH]^+ = [MH]^+ + B$ and Related $\Delta S°_{1/2}$ (J/K·mol) and Proton Affinities PA (kJ/mol)

M	B	$\Delta G°_{320}$[a]	$\Delta S°_{1/2}$(B)[b]	PA(B)	$\Delta S°_{1/2}$(M)[b]	PA(M)
2(5*H*)-furanone (**1**)	diethyl ether	+2.0	15	829	(0)	836
	di-*n*-propyl ether	−2.1	(15)	834		
5,6-dihydro-2*H*-pyran-2-one (**2**)	cyclohexenone	+0.4	(0)	863	(0)	862
	acetylcyclopropane	+4.5	8	854		
cyclopentenone (**3**)	acetylcyclopropane	+1.8	8	854	(0)	857
	diisopropyl ether	−4.2	(0)	861		
cyclohexenone (**4**)	acetylcyclopropane	+6.4[d]	8	854	(0)	863
	diisopropyl ether	+3.2[d]	(0)	861		
γ-butyrolactone (**5**)	ethyl acetate	+2.6[d]	15	829	(0)	834
	cyclohexanone	−3.9[d]	(6)	836		
δ-valerolactone (**6**)	acetylcyclopropane	+8.0[d]	8	854	(0)	863
	diisopropyl ether	+3.4[d]	(0)	861		
cyclopentanone (**7**)	acetone	10.9[c]	19	810	(6)	825
cyclohexanone (**8**)	ethyl acetate	6.7[d]	15	829	(6)	837
	acetone	21.3[c]	19	810		
methyl acrylate (**9**)	cyclopentanone	0.3[e]	6	825	(0)	827
methyl crotonate (**10**)	dimethoxyethane	0.6[e]	−10	855	(0)	852
methyl methacrylate (**11**)	ethyl acetate	4.0[e]	15	829	(0)	838
buten-3-one (**12**)	ethyl acetate	−2.1[f]	15	829	(0)	832
2-penten-3-one (**13**)	diisopropyl ether	−4.2[f]	(0)	861	(0)	857
2-methylbuten-3-one (**14**)	di-*n*-propyl ether	−0.4[f]	(0)	839	(0)	838

[a] ±0.5 kJ/mol. [b] $\Delta S°_{1/2}$ is the standard entropy difference between the protonated and the neutral form of the compound considered. When the experimental value is not available, a $\Delta S°_{1/2}$ equal to $R \ln(\sigma_B/\sigma_{BH^+})$ (where σ is the relevant symmetry number) has been assigned; this estimate is indicated into parentheses. [c] $\Delta G°_{320}$ from ref 15 and PA(M) values deduced from the new PA(B) of ref 6. [d] Reference 2. [e] Reference 7. [f] Reference 8.

electronic charge density, ρ, and its Laplacian, $\nabla^2\rho$. Negative values of the Laplacian are associated with regions in space where the electron density is locally concentrated. On the contrary, positive values of the Laplacian are usually found in regions where the charge density was depleted. Hence, changes in Laplacian of ρ are associated with changes in the charge distribution. In general, a less negative value of the Laplacian in a bonding region implies that some amount of charge density has been removed from that area and, accordingly, the corresponding linkage becomes weaker. On the contrary, if the Laplacian becomes more negative, charge density has been accumulated in the bond and it becomes reinforced. This will also be reflected in the value of the charge density at the bond critical points which correspond to points where ρ is minimum along the bond path and maximum in the other two directions. The values of the negative curvatures of ρ at the bond critical point permit us to define the elipticity of the bond as $\epsilon = \lambda_1/\lambda_2 - 1$. Both population analyses were performed on the MP2 electron densities to take into account electron correlation effects. Bader analysis was carried out by using the AIMPAC series of programs.[14]

Results and Discussion

The experimental gas-phase basicities and proton affinities of the systems under investigation reported in Table 1 reveal some essential trends. First, the basicities of lactones and, to a lower extend, those of cyclic ketones increase as the size of the ring increases. This influence of the size of the ring on the intrinsic basicities of unsaturated lactones **1** and **2** is comparable to the one described for saturated lactones.[2] As we shall discuss later, the origin of this effect is similar in both saturated and unsaturated systems even if some peculiarities of the unsaturated compounds deserve a closer attention. Second, it is also found that unsaturated lactones **1** and **2** are more basic than their unsaturated aliphatic counterparts. A similar behavior has been reported before for the series of saturated lactones with respect to saturated esters.[1] This cyclization effect is however not so clearly evidenced in the ketone series. Finally, it seems clear that the unsaturated cyclic ketones, cyclopentenone, **3**, and cyclohexenone, **4**, are more basic than their saturated counterparts, cyclopentanone, **7**, and cyclohexanone, **8**. In contrast, unsaturated lactones **1** and **2** present almost identical basicities to their saturated analogs **5** and **6**.

Concerning the ab-initio calculations, the MP2/6-31G* optimized structures of the most stable conformations of compounds **1**−**14** and their protonated forms are given in Figure 1. The total G2(MP2,SVP) energies of these species are given in Table 2.

The total energies of the remaining conformers as well as their geometries are available from the authors upon request. However, information concerning the relative energies and structural features of some important species will be given in the following discussion. Table 2 also includes the calculated 298 K proton affinities estimated from the total G2(MP2,SVP) energies of the neutral and protonated forms, while the thermal corrections have been made at the HF/6-31G* level. It can be seen that the difference between these calculated values and the experimental ones presents a standard deviation of ca. 3 kJ/mol, which is below the expected accuracy for G2(MP2,SVP) calculated enthalpies.

Structures and Stabilities of the Neutral and Protonated Species. The neutral forms of both unsaturated lactones **1** and **2** are characterized by a tilt of the C=O group toward the ring oxygen, the values (7.0° and 3.2°, respectively) are quite close to those reported[2] for the corresponding saturated lactones **5** and **6**. This seems to indicate that the presence of a conjugated double bond in the ring has an almost negligible effect on this tilt which is usually related to a two-electron stabilizing interaction between the carbonyl lone pair and the C−O antibonding orbital.[2] Consistent with this mechanism, the tilt decrease significantly upon protonation at the carbonyl oxygen (3.7° and 0.6°, respectively).

Our results indicate that protonation at the carbonyl oxygen is clearly favored for **1** and **2**. Therefore, unsaturated lactones, as their saturated counterparts, are

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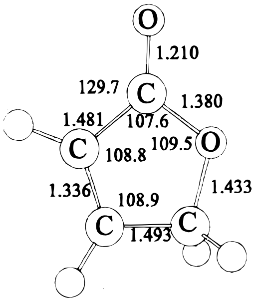

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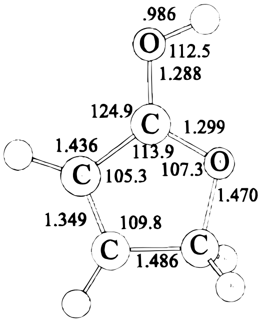
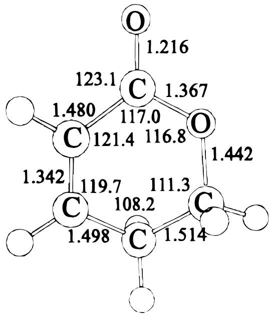


1H+



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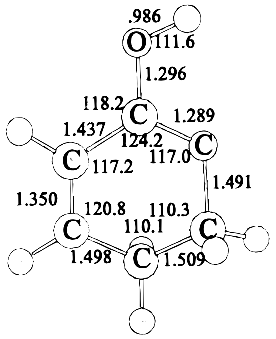

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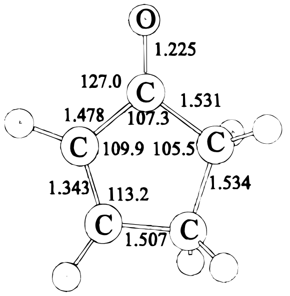

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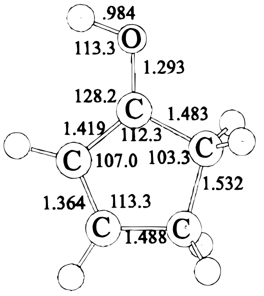

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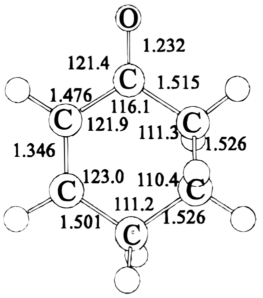

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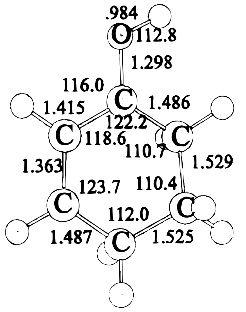
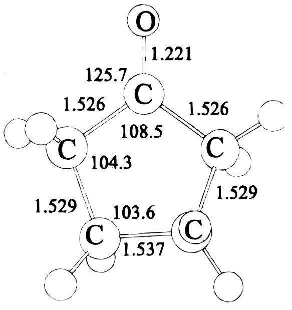


4H+



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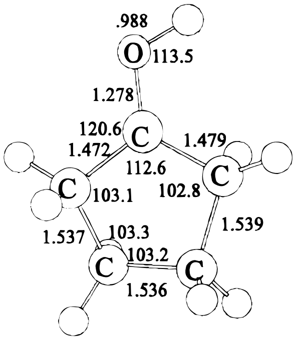
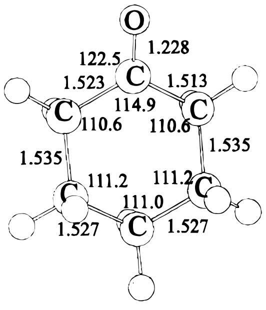


7H+



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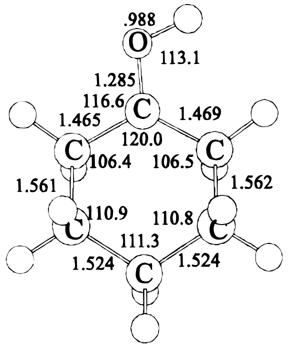
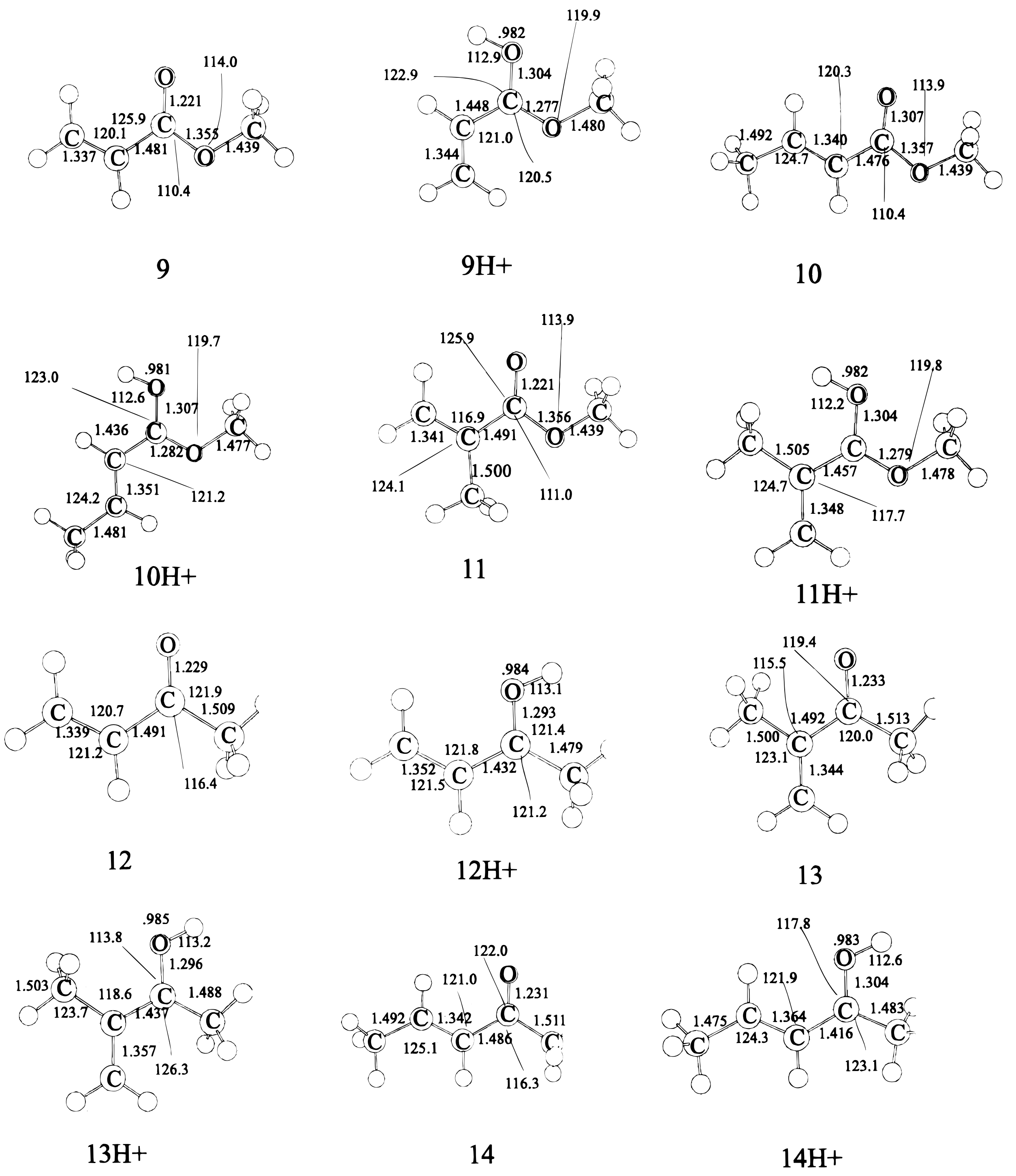


8H+



9 9H+ 10

10H+ 11 11H+

12 12H+ 13

13H+ 14 14H+

Figure 1. MP2(full)/6-31G* optimized geometries of the compounds included in this study. Bond lengths in angstroms and bond angles in degrees.

carbonyl bases. Moreover, the *syn*-protonated species (defined by the relative position of the proton and the carbon in position α with respect to the carbonyl group, Schemes 1 and 2) were found to be less stable than the *anti* conformers by 14 (**1**) and 17 (**2**) kJ/mol. The protonation of both **1** and **2** at the ring oxygen leads to an acyl bond elongation. In the corresponding protonated forms (**1**H-O, **2**H-O; Schemes 1 and 2) the acyl bond is equal to 1.68 Å for **2**H-O and becomes significantly long for **1**H-O (2.143 Å). In these structures, the cyclic arrangement is maintained due to an electrostatic interaction between the positively charged carbon atom of the CO moiety and the oxygen atom of the OH group. The difference in acyl bond length in **1**H-O and **2**H-O is probably related to the difference in strain energy in the five- or six-membered ring species. These structures are lying ca. 80 kJ/mol above the corresponding carbonyl protonated forms **1**H-*anti* and **2**H-*anti*, respectively.

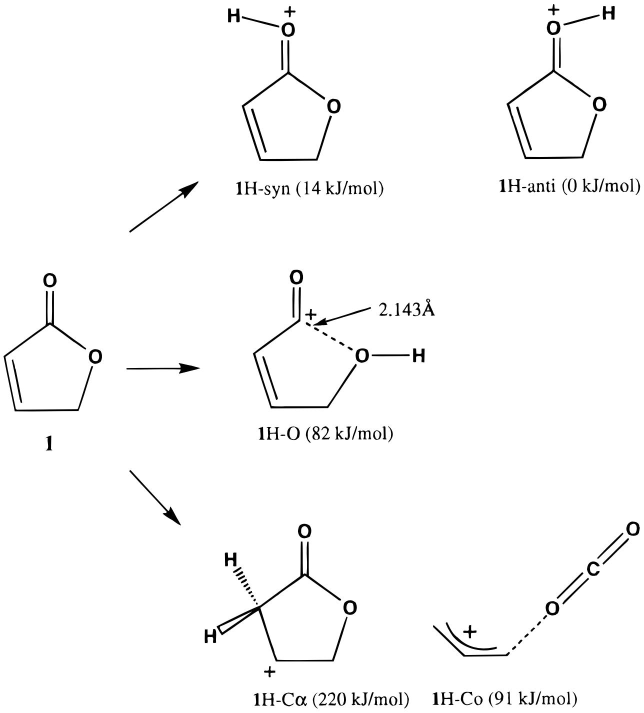
For both lactones **1** and **2**, the protonation at the C=C double bond is the less favorable process. More importantly, protonation at the carbon atom in position α with respect to the carbonyl group leads to the breaking of the C_α−CO bond since this process would yield a stable acylium ion (**1**H-Co, **2**H-Co, Schemes 1 and 2). As long as a bond fission usually implies a substantial change in electron correlation effects, we have found that these

Table 2. G2(MP2,SVP) Total Energies, *E* (hartrees), for the Different Compounds Included in This Study and Their Protonated Species. Calculated Proton Affinities (PA) Are in kJ/mol. Experimental Values Are Given in Parentheses

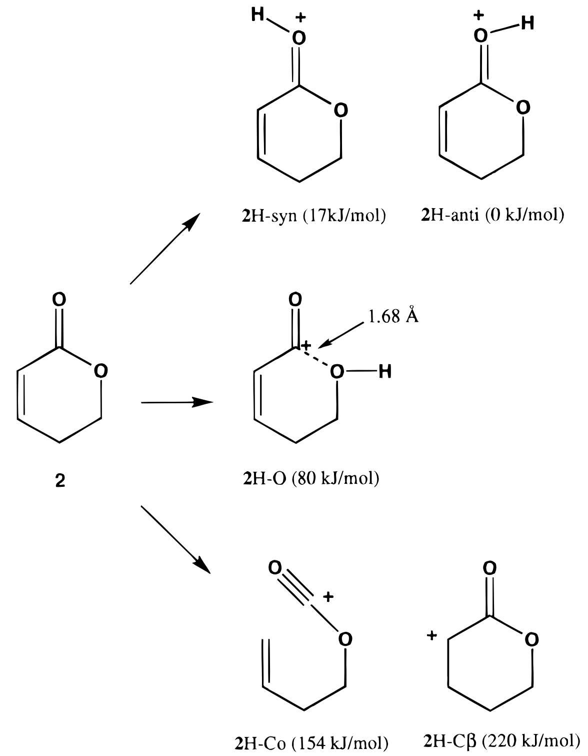
compd	*E*	PA
1	−304.799 35	841.0 (836)[a]
1H$^+$	−305.117 16	
2	−344.005 20	864.8 (862)[a]
2H$^+$	−344.332 10	
3	−268.860 82	850.0 (857)[a]
3H$^+$	−269.182 10	
4	−308.087 19	860.5 (863)[a]
4H$^+$	−308.412 46	
7	−270.060 64	824.6 (824)[b]
7H$^+$	−270.372 38	
8	−309.289 15	840.5 (837)[b]
8H$^+$	−309.606 86	
9	−305.959 29	829.4 (827)[c]
9H$^+$	−306.272 59	
10	−345.192 26	852.8 (852)[c]
10H$^+$	−345.514 54	
11	−345.192 25	840.9 (838)[c]
11H$^+$	−345.510 19	
12	−230.815 79	831.2 (832)[d]
12H$^+$	−231.129 75	
13	−270.044 55	857.9 (857)[d]
13H$^+$	−270.368 74	
14	−270.045 81	837.9 (838)[d]
14H$^+$	−270.362 46	

[a] This work. [b] Taken from ref 2. [c] Taken from ref 7. [d] Taken from ref 8.

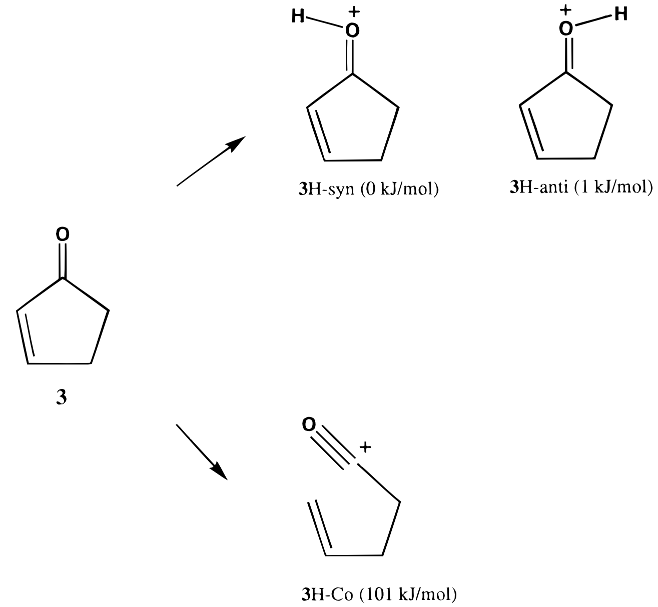
Scheme 1



Scheme 2



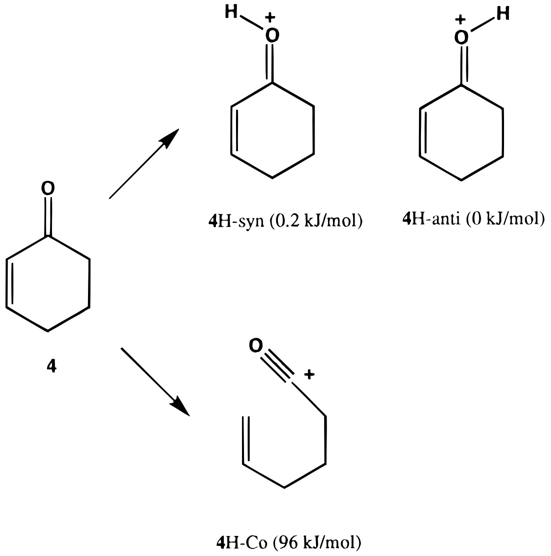
Scheme 3



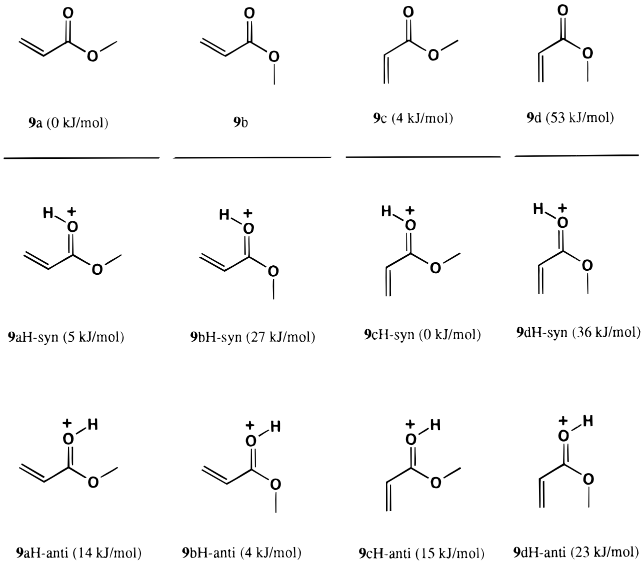
bond-breaking processes are only predicted at the MP2 level. In the case of lactone **1**, the C_α-protonated species which still exhibits a five-membered ring cyclic structure (**1**H-C_α, Scheme 1) corresponds also to a minimum on the potential energy surface. The optimization of the corresponding open structure **1**H-Co leads to a weakly bound complex between the allyl cation $[CH_2CHCH_2]^+$ and a CO_2 molecule. This complex was found to be about 129 kJ/mol lower in energy than the **1**H-C_α cyclic species, at the MP2/6-31G* level. Thus, undoubtedly, protonation of **1** at the C_α carbon atom would lead to the dissociation of the C_α−CO bond. Protonation at the C_β carbon atom is expected to be strongly disfavored, since it would yield a very unstable carbocation. In fact, our results show that this form evolves without activation barrier to the **1**H-C_α protonated species in the case of **1**. For the six-membered ring lactone **2**, the cyclic structure **2**H-C_β (Scheme 2) is a minimum in the potential energy surface, but its energy relative to **2**H-*anti* is as high as 220 kJ/mol.

Protonation of unsaturated cyclic ketones **3** and **4** shows similar trends (Schemes 3 and 4). The favored protonation site is still the oxygen of the carbonyl group but the two possible conformers *syn* and *anti* have almost identical energies. This result is in contrast with that obtained for the lactones for which the conformers anti

Scheme 4



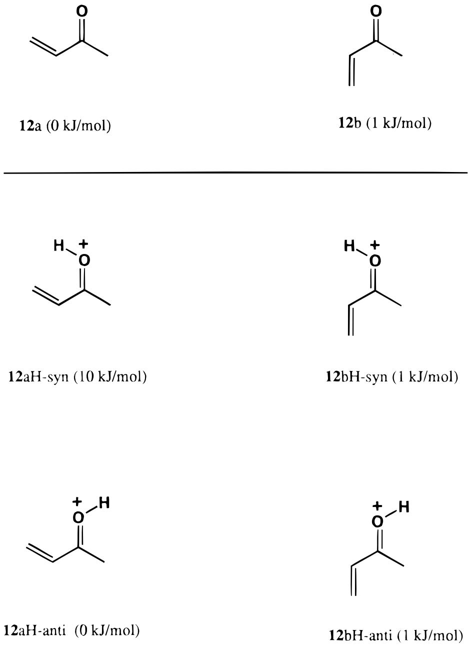
Scheme 5



were favored. This is in agreement with the fact that protonated lactones take part of their stability from the favorable interaction between the incoming proton and the ether-like oxygen.[2]

For both ketones **3** and **4**, protonation at the C=C bond leads to a ring opening along the C_α–CO bond. This may occur either by protonation at C_α followed by the C_α–CO bond elongation, or by protonation at C_β followed by a 1,2-hydride shift and C_α–CO bond elongation. Each elementary step of these reaction routes involves essentially no activation barrier. The resulting open structures **3**H-Co and **4**H-Co are ca. 100 kJ/mol less stable than the carbonyl-protonated species.

Scheme 6



The potential energy surfaces associated with the unsaturated aliphatic esters and ketones are more complicated since there are many possible conformers for both the neutral and the protonated species. As illustrative examples we have schematized the various conformers of **9** and **12** in Schemes 5 and 6, respectively, disregarding the different possible orientations of the methyl groups. For the protonated species, we have restricted our investigation to protonation at the carbonyl group. As a general rule, the most stable conformation of the neutral unsaturated esters **9**–**11** corresponds to the linear configuration of the CCCOC frame (e.g. **9a** in Scheme 5; see also Figure 1). We note however that conformers such as **9c**, in which the C=C double bond and the carbonyl group are in position s-trans, are lying only few kJ/mol above the most stable s-cis conformers. Finally, structures **9b** and **9d** (Scheme 5) do not seem to correspond to stable species, all attempts of geometry optimization lead to the corresponding rotamers **9a** and **9c**, respectively (the relative energy of 53 kJ/mol given for **9d** was obtained by imposing a C_s symetry constrain during geometry optimization).

Quite interestingly, protonation of unsaturated aliphatic esters, in contrast with what was found for lactones, yields a *syn* conformer as the most stable one. It is apparent that the orientation of the C=C moiety has only a limited influence on the relative stabilities of the various conformers of the *syn*-protonated species (Scheme 5). It is also observed that conformations in which a stabilizing interaction exists between the methyl group and the oxygen of the carbonyl group are favored. However, in order to minimize the repulsion between the incoming proton and the hydrogen(s) attached to C_β, the C=C moiety rotates to be s-trans with respect to the carbonyl group (**9**cH-*syn*, Scheme 5). The *anti*-protonated conformers are, in contrast, more stable when the methyl group is opposed to the oxygen of the carbonyl in order to favor the stabilizing interaction between the incoming proton and the ether-like oxygen. As a consequence, **9**bH-*anti* and **9**cH-*syn* have similar total energies.

For unsaturated ketones, the s-cis and the s-trans conformers of the neutrals are of comparable stability, the former being slightly favored (**12a**, Scheme 6, see also Figure 1). The only exception is **14** where the global minimum corresponds to the s-trans conformer (see Figure 1). This is likely a consequence of the repulsive interactions between both methyl groups which in the s-cis conformer are much closer than in the s-trans conformation. A similar situation arises for the protonated forms. In the most stable structure, the proton attached to the carbonyl is preferentially *anti* with

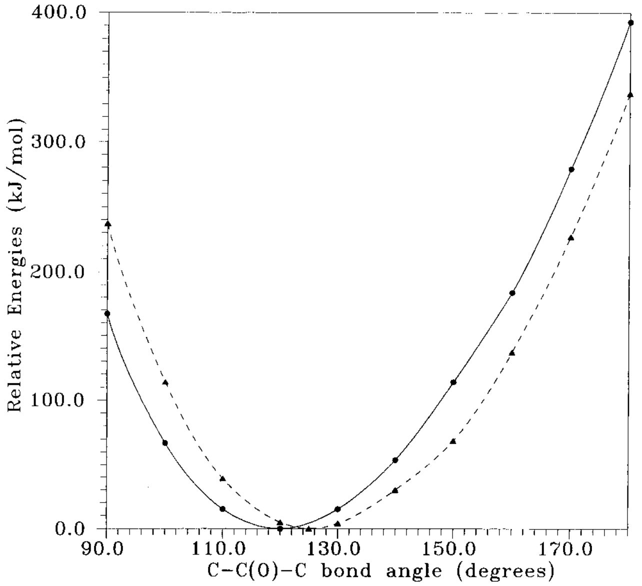


Figure 2. Variation of the total energies of compound **12** (solid line) and its protonated form (dashed line) as a function of the C−CO−C bond angle. The C=C bond was kept always *trans* with respect to the carbonyl group.

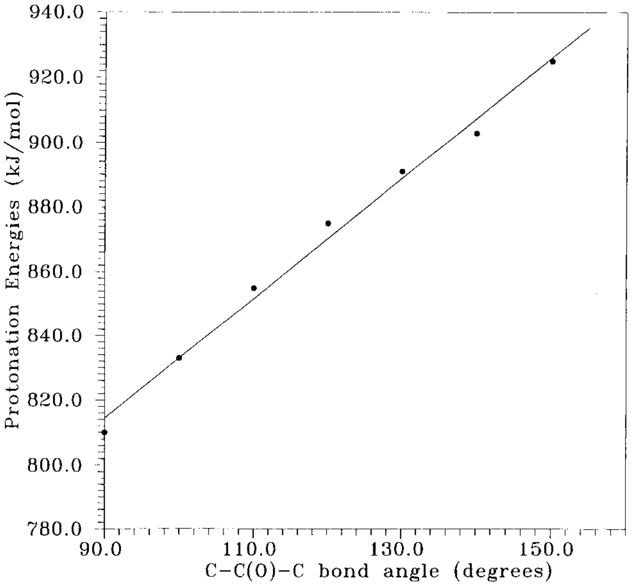


Figure 3. Variation of the calculated protonation energy of compound **12** as a function of the C−CO−C bond angle. These protonation energies were obtained keeping the C=C bond always *trans* to the carbonyl group.

respect to the C=C double bond which lies preferentially in the s-cis conformation (**12**aH-*anti*, Scheme 6).

Ring Size Effect. As mentioned above, for both unsaturated lactones and cyclic ketones, there is a noticeable influence of the ring size on the intrinsic basicities. This effect is partly a consequence of the significant hybridization change supported by the carbonyl carbon when changing the size of the ring. In fact, the ring constrain imposes the value of the C(CO)O or C(CO)C bond angle centered at the carbonyl carbon and dictates its hybridization. In the case of lactones, a second phenomenon, related to the existence of an internal hydrogen bonding in the protonated form, enhances the ring size effect.

In order to investigate the influence of the hybridization change on the basicity of the carbonyl group, we have carried out calculations on buten-3-one, **12**, and its most stable protonated form, **12**aH-*anti*. In these calculations we have optimized the geometries of both the neutral and the protonated species for different values of the C(CO)C bond angle, ranging from 90° to 180°, by steps of 10°. In these model calculations the C=C double bond was constrained to be always in a s-trans conformation. The results obtained have been plotted in Figure 2.

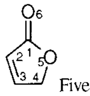
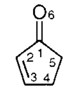
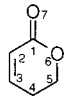
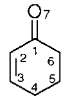
The total energy of the neutral passes through a minimum for a value of the C(CO)C angle close to 120°. As expected the minimum for the protonated species is found for values slightly larger because the repulsion between the methyl group and the C=C moiety must be greater than that in the neutral form. The most important finding however is that variations of the total energies with the C(CO)C angle present similar amplitudes for both neutral and protonated forms. This is so because both potential energy curves described essentially the C(CO)C bending modes which must have similar force constants in both species, where the hybridization at the carbonyl carbon is rather similar. In fact, assuming a harmonic behavior of the C(CO)C bending mode in both species and taking into account that their force constants are similar, the shift of the potential energy curve of the protonated form with respect to that of the neutral must result in a linear dependence of the protonation energies with the C(CO)C bond angle. This expected linear increase of the basicity of carbonyl bases with the bond angle centered at the carbonyl carbon is illustrated in Figure 3.

This linear relationship would explain why cyclohexenone, **4**, is more basic than cyclopentenone, **3**, but also why lactone **2** is more basic than lactone **1**. It is worth noting, however, that the ring size effect is more pronounced in lactones than in ketones. This difference may be ascribed to the fact that a nonbonding stabilizing interaction between the proton attached to the carbonyl group and the ether-like oxygen is also, in part, responsible of the stability of the protonated lactones. This favorable interaction increases as the size of the ring increases simply because the interspecies distance is decreasing. Of course, this interaction is absent in the case of ketones, where only the first factor related to the different hybridization of the carbonyl carbon holds.

It may be noticed that the presence of a conjugated C=C bond slightly reduces the extent of the hybridization effect as revealed by the comparison of the basicity differences between the cyclic unsaturated ketones **3** and **4** (exptl 5 kJ/mol; calcd 10 kJ/mol) and the saturated ketones **7** and **8** (exptl 13 kJ/mol; calcd 16 kJ/mol). Moreover, it appears that the ring size effect observed for unsaturated lactones **1** and **2** is almost identical to that found for the saturated lactones **5** and **6**. This identical increase of proton affinity when passing from the five-membered to the six-membered ring seems to indicate a negligible role of the conjugated C=C bond on the protonation energetic; this point will be discussed after examination of the influence of the cyclic structure upon the basicities of molecules **1**−**8**.

Cyclization Effects. Both the experimental and the theoretical results indicate that unsaturated lactones are more basic than the corresponding aliphatic unsaturated esters. These differences can be rationalized if one takes into account the quite different geometrical arrangements

Table 3. Charge Densities, ρ ($e{\cdot}au^{-3}$), Laplacians of the Charge Densities, $\nabla^2\rho$ ($e{\cdot}au^{-5}$), and Ellipticities, ϵ, at the Bond Critical Points of the Unsaturated Lactones and Unsaturated Cyclic Ketones. Values Obtained at the MP2/6-31G* Level

 Five-membered rings			**1**		**1H⁺**					**3**		**3H⁺**	
Bond	ρ	$\nabla^2\rho$	ε	ρ	$\nabla^2\rho$	ε	Bond	ρ	$\nabla^2\rho$	ε	ρ	$\nabla^2\rho$	ε
C1-O6	0.410	0.168	0.141	0.344	-0.239	0.065	C1-O6	0.393	0.216	0.083	0.331	-0.011	0.083
C1-C2	0.274	-0.713	0.123	0.295	-0.839	0.155	C1-C2	0.275	-0.705	0.106	0.304	-0.846	0.163
C1-O5	0.281	-0.511	0.005	0.338	-0.215	0.059	C1-C5	0.251	-0.594	0.055	0.272	-0.713	0.068
C2-C3	0.343	-0.984	0.343	0.337	-0.962	0.307	C2-C3	0.341	-0.978	0.330	0.332	-0.949	0.246
C3-C4	0.264	-0.657	0.072	0.272	-0.701	0.073	C3-C4	0.255	-0.607	0.040	0.260	-0.665	0.045
C4-O5	0.250	-0.478	0.015	0.217	-0.251	0.043	C4-C5	0.243	-0.553	0.010	0.244	-0.560	0.010
 Six-membered rings			**2**		**2H⁺**					**4**		**4H⁺**	
Bond	ρ	$\nabla^2\rho$	ε	ρ	$\nabla^2\rho$	ε	Bond	ρ	$\nabla^2\rho$	ε	ρ	$\nabla^2\rho$	ε
C1-O7	0.406	0.150	0.148	0.339	-0.250	0.049	C1-O7	0.388	0.192	0.080	0.327	0.000	0.104
C1-C2	0.274	-0.722	0.112	0.293	-0.851	0.148	C1-C2	0.276	-0.723	0.097	0.307	-0.897	0.162
C1-O6	0.288	-0.477	0.019	0.344	-0.224	0.048	C1-C6	0.259	-0.639	0.045	0.269	-0.705	0.046
C2-C3	0.340	-0.973	0.358	0.337	-0.968	0.308	C2-C3	0.337	-0.961	0.345	0.330	-0.949	0.251
C3-C4	0.259	-0.638	0.030	0.261	-0.648	0.030	C3-C4	0.258	-0.632	0.035	0.265	-0.670	0.036
C4-C5	0.257	-0.631	0.033	0.259	-0.643	0.029	C4-C5	0.247	-0.575	0.008	0.247	-0.576	0.016
C5-O6	0.240	-0.427	0.028	0.200	-0.160	0.066	C5-C6	0.246	-0.567	0.012	0.243	-0.559	0.015

in lactones and esters for either their neutral or their protonated forms. Let us take **9** as a suitable model system to illustrate this point. As mentioned above, the most stable conformer of the neutral corresponds to that in which both the O−CH_3 and the C=C groups are linearly arranged (**9a**, Scheme 6) while that in which the CCCOC skeleton defines a cyclic arrangement that lies 53 kJ/mol above the global minimum (**9d**, Scheme 6). The important point is that this energy gap decreases dramatically to only 23 kJ/mol upon protonation.

Accordingly, as mentioned before, protonation of the unsaturated ester **9a** leads to the most stable protonated form **9**cH-*syn* after a 180° rotation of the vinyl group (Scheme 5). If we turn now to the conformation **9d**, its most stable protonated form is **9**dH-*anti*. In this structure, the conformation of the methoxy group favors the stabilizing interaction between the positively charged hydrogen attached to the carbonyl group and the ether-like oxygen. This stabilizing effect counterbalances the unfavorable steric interaction responsible for the unstability of **9**d with respect to **9**a.

A comparison of the energies involved during protonation of **9a** and **9d** is provided by the diagram presented in Figure 4. It is obvious that the latter conformer, in which the atoms arrangement is closely related to the lactone structure, exhibits a much higher protonation energy than the former, explaining the fact that lactones are more basic than the corresponding aliphatic esters.

Unsaturation Effects. The proton affinities of saturated and unsaturated lactones **1** and **5** on one hand, and **2** and **6** on the other (Table 1), are essentially identical, showing the negligible effect of the unsaturation on the intrinsic basicities of this functional group. On the contrary, unsaturation stabilizes significantly the protonated forms of the unsaturated cyclic ketones. The difference in proton affinities between **3** and **7**, or between **4** and **8**, attains 34 and 26 kJ/mol, respectively.

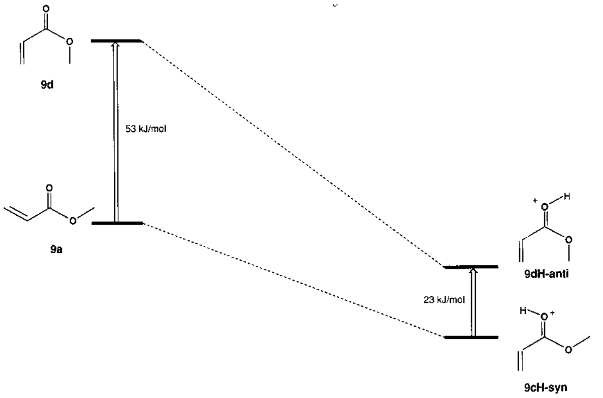


Figure 4. Schematic representation on the stability changes of unsaturated esters upon protonation at the carbonyl group, showing that the *E* conformer is more basic than the *Z* one. Values obtained at the MP2/6-31G* + ZPE level.

In principle one may expect an increase in the basicity of unsaturated systems, since the presence of the C=C double bond which contains a highly polarizable π-system would favor the shift of the electron density from the base to the bare proton. However, the charge redistribution which follows may be affected by the presence of an oxygen atom within the cycle and therefore explains the different behavior of lactones and ketones. For both kinds of systems, the protonation at the carbonyl group induces an electron transfer to the proton by depopulating the C=O bond. This is accompanied by the decrease of the charge density, ρ, at the corresponding bond critical point (see C1−O6 or C1−O7, Table 3). Consistently, the

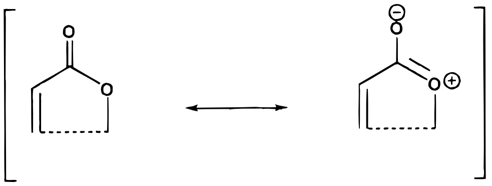
C=O bond becomes weaker and longer (see Figure 1). This effect is transmitted to the substituents of the carbonyl group. Obviously, the mechanism must be different in lactones **1** and **2**, where the carbonyl carbon is attached to an unsaturated carbon and to an oxygen atom, than in ketones **3** and **4** where it is bonded to two carbon atoms.

In the latter case, as can be seen in Table 3, the bonding charge densities and the ellipticities of the C1−C2 and C1−C5 linkages increase upon protonation, while those of the C2−C3 bond decrease. In other words, the double-bond character of the two former bonds increases while that of the C2−C3 linkage decreases. This is consistent with the results obtained at a NBO analysis, which indicate that the π-C2−C3 bond is significantly polarized toward C2. Actually, while in the neutral both carbon atoms contribute about equally to the π-MO (52% C2, 48% C3), in the protonated species the contribution from the C2 atomic orbitals clearly dominates (61% C2, 39% C3). As a consequence, the protonation of ketones implies a delocalization of the π-charge density which enhances the basicity of the system, since favoring the electron donation to the incoming proton.

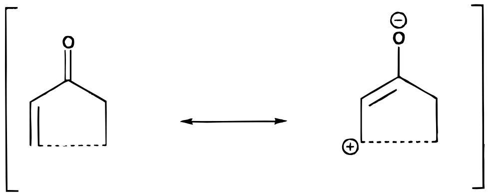
In the case of lactones, the carbonyl carbon tries to withdraw negative charge from C2 and from the ether-like oxygen attached to it. However, in the latter case, the high electronegativity of the oxygen atom limits the charge transfer to the C1−O bond. This is reflected by a significant increase of the charge density and the ellipticity of the C1−O5 (or C1−O6) bond, which accordingly becomes sizeably shorter (see Figure 1). Consistent with this, a NBO analysis indicates that while the C1−O likage of the neutral is a typical single bond, it has a double-bond character in the protonated species where the π-MO presents, as expected, a dominant contribution of the p orbitals of the oxygen atom (82% O, 18% C1). The net result is that the participation of the C=C moiety during the charge transfer induced by the protonation process is essentially absent. This would explain the negligible enhancement effect of the conjugated C=C bond on the intrinsic basicities of unsaturated lactones **1** and **2** with respect to their saturated counterparts **5** and **6**.

In summary, the fact that unsaturated ketones are sizeably more basic than their saturated analogs is a consequence of the stabilization of the protonated form due to the polarizability of the π-system which favors a greater charge transfer to the incoming proton. For unsaturated lactones, the existence of an oxygen atom within the cycle overshadows this possibility, and the protonated species have a stability unsensitive to the presence of a conjugated C=C bond. In a more pictorial view, this would imply that the delocalization which dominates in lactones is rather different from that which dominates in ketones:

1 or **2**



3 or **4**



Conclusion

In both series of compounds, ring size effects similar to those found for the saturated analogs have been observed. In general the basicity increases with the size of the ring, due to the corresponding hybridization change undergone by the carbonyl carbon. Small values of the bond angle centered at the carbonyl carbon result in an enhanced electronegativity of this atom and in a poorer donor capacity of the carbonyl group. The ring size effect observed for lactones is also due to a stabilizing interaction between the incoming proton and the ether-like oxygen, which enhance the basicity of larger rings.

Second, for the unsaturated lactones there is significant cyclization effect, which implies that lactones are more basic than the corresponding aliphatic unsaturated ester. This is essentially the consequence of the differences in structure of the most stable neutral and the protonated forms of both compounds.

Finally, unsaturated lactones are found to have almost identical gas-phase basicities as their saturated counterparts, while unsaturated cyclic ketones are sizeably more basic than their saturated analogs. This is a consequence of a negligible π-C=C electron delocalization in the former molecules; the C=C unsaturation effect is efficient only in the case of unsaturated ketones. An important consequence of this effect is that, while saturated lactones are more basic than the cyclic saturated ketones of the same size, this is not longer true for unsaturated lactones. Lactone **2** exhibits the same intrinsic basicity as cyclohexenone, **4**, but lactone **1** is less basic than cyclopentenone, **3**.

Supporting Information Available: Optimized geometry (MP2(full)/6-31G* level) of the most stable conformations of the neutral structures **1**−**14** and their protonated forms (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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