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Cyclization Effects on the Gas-Phase Basicities of Esters and Ethers. An Experimental and MO Study

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Abstract: Ab initio calculations, at different levels of accuracy, have been performed for different cyclic oxygen bases (2-oxetanone, γ-butyrolactone, oxetane, and tetrahydrofuran), for the corresponding acyclic counterparts (methyl acetate, ethyl acetate, methyl propionate, methyl ethyl ether, dimethyl ether, and methyl propyl ether), and for their protonated species. The gas-phase proton affinities for some of these species were reinvestigated by FT-ICR techniques. Our results show that β-propiolactone, contrary to larger lactones, is less basic (6 kcal/mol) than the corresponding aliphatic ester. This is a consequence of substantial hybridization changes upon cyclization, which for five-membered (or larger) systems are quite small. Cyclization effects on ethers are smaller than those on esters and are in the opposite direction. Accordingly, oxetane is a stronger base than methyl ethyl ether. A topological analysis of the electronic charge density shows that protonation at the carbonyl oxygen atom of lactones produces significant activation of the alkyl C–O bond while the acyl C–O linkage becomes reinforced. Quite on the contrary, protonation at the ether-like oxygen atom activates both C–O bonds, but preferentially the acyl one, which in the particular case of β-propiolactone breaks apart. As a consequence, while γ-butyrolactone protonates at the carbonyl oxygen atom, for β-propiolactone both protonated species (carbonyl-protonated and ether-protonated) are equally stable.

Introduction

In our research on the gas-phase basicity of different organic bases, we have focused our attention on the effects that cyclization has on the intrinsic basicities of different compounds. Quite, recently, we investigated[1] this problem, from both the theoretical and the experimental points of view, in amides, by comparing their gas-phase basicities with those of the respective lactams, and in amines, by comparing the gas-phase basicities of *N*-methylethanamine and *N*,*N*-dimethylethanamine with those of azetidine and *N*-methylazetidine, respectively.

As a natural progression in this investigation, we present in this paper a study of the gas-phase basicities of some esters and their corresponding lactones. Our interest in lactones is threefold. First, they present two active centers for protonation, the carbonyl and the ether-like oxygen atoms, and although it is frequently assumed that the former is the most basic center,[2] it is not well established whether that depends on the size of the lactone. We shall show in this paper that this is indeed the case. Second, little was known about their intrinsic basicities until very recently when Wiberg and Waldron[2] accomplished a quite interesting study on this and other related problems,[3,4] from both the experimental and the theoretical points of view. However, these studies left out the first member of the series (the four-membered ring β-lactone), and in this sense part of the present investigation broadens the scope of the work of Wiberg et al.,[2] mainly if one takes into account that 2-oxetanone is the member of the series which presents more peculiarities when its intrinsic basicity is compared to that of the aliphatic ester due to its ring strain. Third, β-lactone derivatives present a quite important biochemical activity[5-9] (most of them are carcinogenic agents) and it has been frequently assumed that this activity is related to the opening of the ring upon hydrolysis in neutral or slightly acidic media. Furthermore, a unique feature of β-lactones is the occurrence of alkyl C–O bond cleavage rather than the acyl C–O bond fission exhibited by the higher lactones.[10-12]

Accordingly, one of our goals will be also to investigate whether γ-butyrolactone and β-propiolactone may undergo a ring fragmentation upon protonation in the gas phase, either at the carbonyl or at the ether-like oxygens, or whether proton association produces significant activations of the bonds of the ring, even though it does not lead to bond cleavage? In this respect, it can be quite illustrative to compare these effects with those that take place in compounds which present only one type of basic center, i.e., ketones and ethers. Accordingly, we shall also examine the gas-phase basicities of methyl ethyl ether, dimethyl ether, and methyl propyl ether and those of their cyclic counterparts, oxetane (OXT) and tetrahydrofuran (THF). A similar comparison for cyclic ketones and their aliphatic analogs was published by Bouchoux and Houriet.[13]

Experimental Section

Oxetane (OXT) was a commercial product and was purified by preparative GLC. Its gas-phase basicity (GB) was determined from equilibrium proton-transfer reactions conducted in a modified Bruker CMS-47 FT-ICR mass spectrometer.[14] Working conditions were similar to those already described.[15] The average cell temperature was ca. 333 K. These FT-ICR measurements provide the standard free energy change, $\delta\Delta G_{H^+}(g)$, for proton-transfer reaction 1 in the gas phase between a given base B and a reference compound B_{ref}.

The reversibility of reaction 1 was systematically confirmed by means of double-resonance experiments.

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$$\mathrm{BH^+(g) + B_{ref}(g) \rightleftarrows B(g) + B_{ref}H^+(g)} \qquad K_p,\ \delta\Delta G_{\mathrm{H^+}}(\mathrm{g}) \quad (1)$$

The gas-phase proton basicity GB of B is the negative of $\Delta G_{\mathrm{H^+}}(\mathrm{g})$, the standard free energy change for reaction 2. GB values can be obtained by combining $\delta\Delta G_{\mathrm{H^+}}(\mathrm{g})$ data with the GB of the reference bases.

$$\mathrm{B(g) + H^+(g) \rightarrow BH^+(g)} \qquad \Delta G_{\mathrm{H^+}}(\mathrm{g}) \quad (2)$$

The experimental gas-phase basicities for the remaining compounds investigated are mostly published values from Taft's laboratory.[16] Recent work by Meot-Ner (Mautner) and Sieck[17] suggest that Taft's data were determined at 360 K, somewhat above the initially determined value of 320 K. Thus, the original values from Taft's laboratory have been scaled by a factor of 1.125 (360/320), by following Meot-Ner and Sieck's advice.

Computational Details

Ab initio calculations were carried out with the GAUSSIAN-90 series of computer codes.[18] The geometries of the neutrals considered, β-propiolactone (**1**), methyl acetate (**2**), oxetane (**3**), methyl ethyl ether (**4**), γ-butyrolactone (**5**), methyl propionate (**6**), ethyl acetate (**7**), tetrahydrofuran (**8**), diethyl ether (**9**), and methyl propyl ether (**10**), and their corresponding protonated species were optimized at the 6-31G* level[19] using gradient techniques. For esters and lactones, protonation at both oxygen atoms was considered. Since, as we shall show later for the particular case of β-lactone, the difference is stability between the two protonated species was found to be quite small and, on the other hand, protonation at the ether-like oxygen atom is accomplished by acyl C–O bond cleavage, which should imply significant changes in electronic correlation effects, we have considered it important to refine the corresponding molecular structures at the correlated level. Accordingly, the geometries of the neutral β-propiolactone and those of its two protonated species were recalculated using the Møller–Plesset perturbation theory at second order (MP2/6-31G*). For similar reasons, the same procedure was adopted for oxetane and methyl ethyl ether and their protonated species.

The harmonic vibrational frequencies were determined by analytical second-derivative techniques at the HF/6-31G* level and used to characterize stationary points of the potential energy surface and to evaluate zero-point energies, which were scaled by the empirical factor of 0.89.[20] For 2-oxetanone, the harmonic vibrational frequencies were obtained at the MP2/6-31G* level and scaled by the empirical factor of 0.93.

Since we have found[1] that electronic correlation effects, although small, are not negligible, when cyclization effects on intrinsic basicities are discussed, the corresponding protonation energies were obtained as the MP2/6-31G*//6-31G* energy difference between protonated and unprotonated species. For the particular cases of β-propiolactone, oxetane, and methyl ethyl ether, the values obtained using the MP2-optimized geometries are also reported.

The corrections due to the BSSE were evaluated via the Boys and Bernardi counterpoise technique[21] at the HF level in all cases.

Bond activations were studied by taking advantage of the topological analysis of the electronic charge density and its Laplacian. As we have shown recently,[22] bond activation in protonation processes can be detected by comparing the Laplacians of the charge densities of the protonated and neutral species. As has been demonstrated by Bader,[23–25] the Laplacian of the electronic charge density ($\nabla^2\rho$) identifies regions of space wherein ρ is locally concentrated ($\nabla^2\rho < 0$) or depleted ($\nabla^2\rho > 0$). Hence, bond activation should be accompanied by a decrease in the absolute value of $\nabla^2\rho$, while bond reinforcement would imply a more negative value of the Laplacian. Furthermore, bonding characteristics can be also quantitatively characterized by locating the bond critical points, i.e., points where the electronic charge density presents one positive curvature (λ_3) along the bond and two negative ones (λ_1, λ_2) in the other directions. The values of the electronic density and its Laplacian, at these critical points, ρ_c and $\nabla^2\rho_c$, respectively, often provide quantitative information on the nature and strength of the linkage.

Changes in the intrinsic basicity upon cyclization will be also discussed in terms of the topological characteristics of $\nabla^2\rho$. Actually, we have shown[1,26] that the nonbonded maxima in the valence-shell charge concentrations of the base (maxima of $|\nabla^2\rho|$ which are associated with the lone pair of electrons bear a direct relationship to the intrinsic basicity of the base, since the greater the charge density associated with the lone pair, the easier is the charge transfer from the base to the incoming bare proton.

Results and Discussion

1. Structures. The optimized structures of the species under investigation have been schematized in Figure 1. All of them correspond to minima of the potential energy surface. It must be mentioned that the structures of neutral γ-butyrolactone and methyl acetate have been already reported by Wiberg and Waldron[2] at the same level of accuracy, but they were included in Figure 1 for the sake of a better comparison with the structures of the corresponding protonated compounds.

The total energies as well as the scaled ZPE corrections are summarized in Table I.

Although a detailed discussion of the geometries of these species is not the aim of this paper, several features should be singled out for comment.

(a) Our optimized structural parameters for β-propiolactone are in fairly good agreement with the experimental values obtained from electron diffraction[27] and microwave spectroscopy.[28,29] However, similar to what has been reported in previous ab initio calculations at lower levels of accuracy,[30,31] our results differentiate both C–O ring bonds, while experimental values are identical. More importantly, this prediction does not change when electron correlation effects are taken into account, since, at the MP2/6-31G* level, the acyl C–O bond is found to be shorter (1.382 Å) than the alkyl C–O bond (1.471 Å). It must be also observed that these bond lengths are not significantly different from those in methyl acetate, in contrast with the experimental results,[28,29] which predict not only identical bond lengths for both C–O bonds of β-lactone but also an abnormally long acyl C–O bond (1.43 Å) with respect to that in methyl acetate (1.36 Å). This structural feature is consistent with the topological characteristics of the electronic charge density (see Table II) which show that the electronic density at the acyl C–O bond is higher than at the alkyl C–O bond, indicating that no delocalization of the ring electrons

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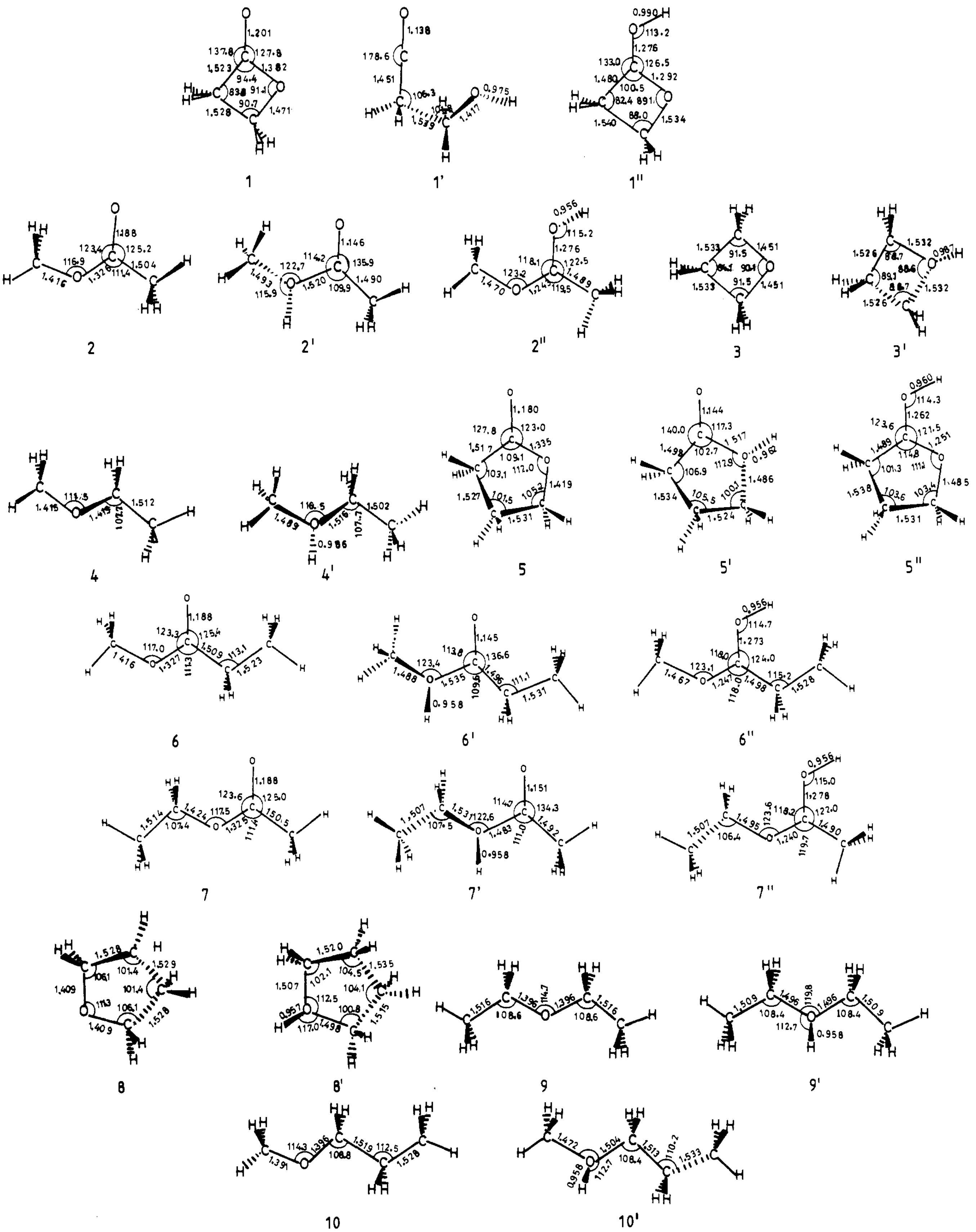

Figure 1. Optimized structures (bond angles in degrees, bond lengths in Å). For species **1**, **1'**, **1''** and **3**, **3'** optimized values were obtained at the MP2/6-31G* level. For the remaining species they were calculated at the HF/6-31G* level.

takes place, which was suggested[29] as a possible explanation of the uniformity of the experimentally determined ring distances.

(b) The harmonic vibrational frequencies, evaluated at the MP2/6-31G* level, for β-propiolactone are in remarkably good agreement with the two set of experimental values reported in the literature[32,33] (see Table III). It should be noticed, however, that this agreement is slightly better when comparison is made with the recent work of Jalkanen and Stephens[33] than with the older

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Table I. Total Energies (au) and Scaled Zero-Point Energies (kcal/mol) for the Systems Included in This Study

	6-31G*//6-31G*			
compd	SCF	ZPE	MP2[a]	MP2[b]
1	–265.641 24	41.7	–266.369 74	–266.393 90
1′	–265.955 13	47.7	–266.672 74	–266.699 40
1″	–265.961 44	49.1	–266.677 28	–266.701 24
2	–266.836 83	54.2	–267.569 64	
2′	–267.123 94	60.1	–267.856 19	
2″	–267.164 74	61.5	–267.887 05	
3	–191.909 38	52.5	–192.469 61	–192.488 57
3′	–192.238 68	60.2	–192.790 59	–192.809 75
4	–193.104 87	65.1	–193.673 03	–193.691 48
4′	–193.428 57	72.6	–193.990 16	–194.008 91
5	–304.705 18	59.5	–305.561 92	
5′	–305.002 99	65.8	–305.858 06	
5″	–305.043 43	67.0	–305.887 61	
6	–305.872 60	71.4	–306.735 95	
6′	–306.163 28	77.3	–307.026 13	
6″	–306.203 38	78.8	–307.056 43	
7	–305.876 63	71.1	–306.740 19	
7′	–306.169 79	77.1	–307.031 44	
7″	–306.208 87	78.4	–307.061 99	
8	–230.976 45	70.3	–231.668 57	
8′	–231.307 99	77.9	–231.992 17	
9	–232.144 88	82.0	–232.844 02	
9′	–232.474 09	89.5	–233.166 63	
10	–232.139 57	82.1	–232.838 25	
10′	–232.465 38	89.7	–233.157 41	

[a] Values obtained at the 6-31G* HF geometries. [b] Values obtained after geometry optimization at the MP2/6-31G* level.

values of Durig.[32] Furthermore, the assignment of the different bands is coincident with that proposed by the former authors.[33] It may be also observed that our calculated value for the ring puckering vibration is 56 cm^{-1} higher than that reported by Durig[32] (which was obtained indirectly on the basis of the assignment of a difference band) and 44 cm^{-1} lower than that reported by Jalkanen and Stephens[33] but is in very good agreement with the assignment of Boone et al.[28] based on the microwave spectrum of the molecule. Our calculated dipole moment is also in fairly good accord with that reported in the latter reference.

(c) For both γ-butyrolactone and β-propiolactone, there is a sizable tilt of the C=O group toward the ring oxygen. This is a well-known experimental fact which was explained in terms of negative hyperconjugative effect by Norskov-Lauritsen et al.[34] and Sudhakar et al.[35] Quite significantly, these effects are much smaller in the corresponding aliphatic esters and they are also greater for β-propiolactone than for γ-butyrolactone as was already predicted by the MNDO calculations of Sudhakar et al.[35] It must be noticed however that the tilts predicted by our ab initio calculations are in quite good agreement with the experimental values obtained in the crystal,[36] but they are less than half those obtained by using the MNDO method.[35]

(d) Our optimized structures for oxetane and THF are in good agreement with the most recently reported experimental ones obtained from their microwave spectra.[37,38]

(e) Protonation of β-propiolactone at the ring oxygen atom is accompanied by an acyl bond fission, yielding the noncyclic structure (**1′**). Quite on the contrary, for γ-butyrolactone (**5**) protonation at the ring oxygen yields a stable cyclic minimum (**5′**).

(f) Protonation of both lactones at the carbonyl oxygen atom yields two local minima, depending on the relative position of the attaching proton with respect to the cyclic oxygen. In both cases the most stable one corresponds to the *cis* isomer (that shown in Figure 1), being the alternative *trans* confomer, which is about 2.7 kcal/mol less stable at the MP2/6-31G*//6-31G* level. This result seems to point to the existence in the *cis*-protonated species of an intramolecular hydrogen bond. Actually, the distance between the attaching proton and the cyclic oxygen atom (~2.4 Å) is smaller than the sum of the respective van der Waals radii. Nevertheless, a topological analysis of their electronic charge distribution shows no bond critical points between these two atoms. Accordingly, we must conclude that the *cis* isomer is stabilized by a more favorable electrostatic interaction between the negatively charged cyclic oxygen and the incoming proton, but a true hydrogen bond is not formed. It is interesting to indicate that Olah and Ku[11] have shown that in 1:1 FSO_3H–SbF_5 mixtures at –80 °C β-propiolactone clearly protonates at the carbonyl group, the protonated species being stable up to room temperature. Interestingly enough, β-butyrolactone also protonates at the carbonyl group,[11] but on warming, cleavage occurs and NMR analysis of the product shows that alkyl–oxygen bond fission takes place.

2. Gas-Phase Basicities. For the discussion which follows we shall adopt the following conventions: the number of the neutral with a prime will designate the protonated form obtained upon protonation at the ether-like oxygen atom, while the number of the neutral with a double prime will correspond to the protonated species obtained upon protonation at the carbonyl oxygen atom. The calculated protonation energies are compared with the experimental ones in Table IV. Since experimental values are usually given as standard free energy changes, the corresponding entropy terms, to transform them to proton affinities, were obtained in our SCF/6-31G* calculations.

The first conspicuous fact of Table IV is that our theoretical results predict that lactones and esters protonate preferentially at the carbonyl oxygen atom. However, while for aliphatic esters and γ-butyrolactone the difference between the intrinsic basicities of both oxygen atoms amounts to about 18 kcal/mol (at the MP2/6-31G*//6-31G* level), for β-propiolactone this difference is reduced to 3 kcal/mol, as a consequence of the fact that protonation at the ether-like oxygen is accompanied by the acyl C–O bond cleavage. The second significant result is that while cyclization in the four-membered systems is accompanied by a decrease of the gas-phase basicity of about 6 kcal/mol (at the MP2/6-31G*//6-631G*) quantitatively similar to that reported previously for β-lactams, for five-membered systems cyclization implies an increase of about 4.0 kcal/mol. Hence, we must conclude that the basicity enhancement on going from the aliphatic esters to lactones, which was already discussed and analyzed by Wiberg and Waldron,[2] is only observed in five-membered or larger systems, where cyclization does not imply dramatic hybridization changes (see below). It must be also observed that our calculations indicate that methyl propionate is slightly more basic than ethyl acetate, in very good agreement with the experimental values (see Table IV).

It must be also observed that cyclization implies also a slight increase of the intrinsic basicity of the four-membered ether since our results predict a gas-phase basicity for oxetane which is 2.2 kcal/mol (a the MP2/6-31G*//6-31G* level) greater than that for methyl ethyl ether. Similarly, the intrinsic basicities at the ether-like oxygen atoms of the three aliphatic esters considered also increase upon cyclization. This effect is particularly dramatic in the case of methyl acetate, since, as we have mentioned above, the ether-like protonation of the corresponding lactone yields an extrastabilized open structure. The aforementioned difference between the gas-phase basicities of oxetane and methyl ethyl ether does not conform with previously reported experimental values[16] (see Table IV). In view of this discrepancy, we have reoptimized the structures of both neutrals and their respective protonated species at the MP2 correlated level, to check whether this difference arise from the limitations inherent in the use of

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Table II. 6-31G* Values of ρ (e/au^3) and $\nabla^2\rho$ (e/au^5) for the Critical Points of the Relevant Bonds of Compounds Included in This Study

	C=O(C$_1$—X)		C$_1$—O		C$_3$—O		C$_1$—C$_2$	
compd	ρ	$\nabla^2\rho$	ρ	$\nabla^2\rho$	ρ	$\nabla^2\rho$	ρ	$\nabla^2\rho$
1	0.452	0.611	0.310	–0.206	0.246	–0.182	0.270	–0.758
1′	0.525	1.825			0.275	–0.258	0.237	–0.248
1″	0.375	0.089	0.381	0.087	0.196	0.001	0.277	–0.847
2	0.438	0.484	0.314	–0.074	0.242	0.080	0.275	–0.814
2′	0.478	0.935	0.198	–0.447	0.176	0.443	0.312	–1.268
2″	0.355	0.021	0.384	0.136	0.192	0.389	0.273	–0.871
3			0.262	–0.273	0.262	–0.273	0.256	–0.679
3′			0.181	0.094	0.181	0.094	0.261	–0.717
4			0.265	–0.101	0.268	–0.109	0.265	–0.739
4′			0.176	0.342	0.192	0.392	0.265	–0.755
5	0.446	0.497	0.308	–0.125	0.247	–0.024	0.271	–0.778
5′	0.480	0.928	0.189	–0.233	0.183	0.359	0.267	–0.822
5″	0.368	0.029	0.380	0.131	0.193	0.201	0.276	–0.874
6	0.437	0.487	0.313	–0.068	0.242	0.077	0.274	–0.806
6′	0.479	0.948	0.178	–0.206	0.179	0.437	0.264	–0.826
6″	0.357	0.060	0.381	0.110	0.194	0.379	0.269	–0.844
7	0.438	0.473	0.314	–0.071	0.237	0.080	0.275	–0.813
7′	0.474	0.863	0.200	–0.195	0.159	0.354	0.269	–0.837
7″	0.354	0.012	0.387	0.142	0.180	0.337	0.274	–0.867
8			0.260	–0.181	0.260	–0.181	0.261	–0.705
8′			0.177	0.254	0.181	0.269	0.263	–0.735
9			0.265	–0.010	0.265	–0.010	0.265	–0.737
9′			0.181	0.339	0.181	0.339	0.265	–0.752
10			0.265	–0.095	0.268	–0.107	0.266	–0.740
10′			0.175	0.350	0.193	0.389	0.264	–0.753

Table III. Experimental and Calculated (MP2/6-31G*) Vibrational Frequencies (cm^{-1}) for β-Propiolactone

calcd[a]	exptl		normal mode
3008	3028[b]	3017[c]	α-,β-CH$_2$ antisym str[d]
2995	3001	2983	α-,β-CH$_2$ antisym str[d]
2940	3000	2965	α-,β-CH$_2$ sym str[d]
2934	2935	2916	α-,β-CH$_2$ sym str[d]
1797	1882	1851	C=O str
1474		1480	β-CH$_2$ def
1412	1427	1411	α-CH$_2$ def
1285	1319	1314	β-CH$_2$ wag
1179	1199	1196	α-CH$_2$ wag
1151		1184	α-CH$_2$ twis
1102	1139	1135	β-CH$_2$ twist
1058	1093	1097	ring str (C—O)
1013	1046	1045	α-CH$_2$ rock
978		1013	ring str (C=C)
905	924	910	ring str (C—O) ring def
856	891	879	ring def
772	790	789	β-CH$_2$ rock
700	746	753	ring def
484	513	511	C=O in-plane bend
463	490	494	C=O out-of-plane bend
160	113	204	puckering

[a] Values scaled by an empirical factor of 0.93. [b] Taken from ref 32. [c] Taken from ref 33. [d] Our theoretical calculations predict very nearly equal participation of α-CH$_2$ and β-CH$_2$ coordinates in each C—H stretching mode.

Table IV. Protonation Energies (kcal/mol) of the Compounds Included in this Study

compd	HF/6-31G*[a]	MP2/631G*//6-31G*[a]	$\Delta(\Delta G)_{\text{exp}}$[b]	PA$^{\text{exp}}$[c]
1	189.6(O′) 193.0(O″)	184.1(O′) (182.4)[d] 185.6(O″) (183.5)[d]		
2	173.9(O′) 198.1(O″)	173.9(O′) 191.9(O″)	+7.3	200.3
3	198.4	193.7 (191.9)[d]	+8.4 +7.6[e]	199.1 201.1[e]
4	195.1	191.5 (189.7)[d]	+9.0	198.5
5	180.2(O′) 204.2(O″)	179.4(O′) 197.3(O″)	+2.5	205.6
6	176.2(O′) 199.8(O″)	175.9(O′) 194.2(O″)	+4.7	203.2
7	177.6(O′) 200.8(O″)	176.6(O′) 195.1(O″)	+3.9	203.7
8	200.0	195.5	+5.8	202.2
9	198.5	195.0	+4.8	202.7
10	196.2	192.7	+8.0	199.5

[a] HF and MP2 values include BSSE and scaled ZPE corrections by the empirical factor 0.89. [b] Experimental ΔG values with respect to NH$_3$, taken from ref 16. [c] Experimental PA values in kcal/mol taking PA(NH$_3$) = 208.3 kcal/mol, using the $\Delta(\Delta G)$ values of the previous column and theoretically calculated entropy terms (see text). [d] Values obtained after geometry optimization at the MP2/6-31G* level. O′ corresponds to the ether-like oxygen atom, and O″, to the carbonyl oxygen atom. [e] Value obtained in the present work.

Table V. Experimental Data Pertaining to the Determination of GB(OXT)[a,b]

standard base	$\Delta\Delta G_{\text{H}^+}$(std)[c]	$\delta\Delta(G_{\text{H}^+}$(g)	$\Delta\Delta G_{\text{H}^+}$(g)	$\Delta\Delta G_{\text{H}^+}$(g)(av)
tert-butyl mercaptan	8.21	–0.52	7.69	7.6 ± 0.2
methyl acetate	7.31	+0.12	7.43	

[a] Defined in the text. [b] All values in kcal/mol. [c] Taken from ref 16. See text.

SCF-optimized structures. The new values obtained for their basicities, although slightly smaller than those obtained using the HF geometries (see Table IV), still maintain the same difference between them (2.2 kcal/mol).

This disagreement prompted us to revise the experimental gas-phase basicity of oxetane. Table V presents the results of proton-transfer equilibria 1 between oxetane and standard reference bases. The values of $\delta\Delta G_{\text{H}^+}$(g) given in Table V are defined as

$$\delta\Delta G_{\text{H}^+}(\text{g}) = -\text{R}T \ln K_{\text{p}} \qquad (3)$$

All GBs are referred to ammonia. Thus, with respect to this reference, GB(OXT) = $-\Delta\Delta G_{\text{H}^+}$(g) for the reaction

$$\text{OXT(g)} + \text{NH}_4^+\text{(g)} \rightarrow \text{OXTH}^+\text{(g)} + \text{NH}_3\text{(g)} \qquad \Delta\Delta G_{\text{H}^+}(\text{g}) \quad (4)$$

$\Delta\Delta G_{\text{H}^+}$(g) is the average of the ΔG values obtained from the expression

$$\Delta\Delta G = \delta\Delta G_{\text{H}^+}(\text{g}) + \Delta\Delta G_{\text{H}^+}(\text{std}) \qquad (5)$$

where $\Delta\Delta G_{\text{H}^+}$(std) pertains to the reaction

$$\text{B}_{\text{ref}}\text{(g)} + \text{NH}_4^+\text{(g)} \rightleftarrows \text{B}_{\text{ref}}\text{H}^+\text{(g)} + \text{NH}_3\text{(g)} \qquad (6)$$

Comparing the results in Table V and those reported in Table IV, one can see that the new value obtained by us for the gas-

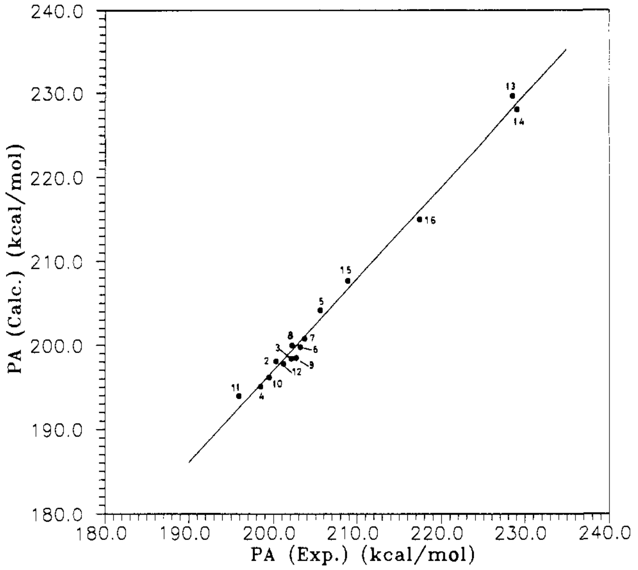

Figure 2. Linear correlation between experimental and calculated proton affinities. For the sake of completeness, this figure includes also the values corresponding to the following ketones, lactams, amines, and amides taken from ref 1: cyclobutanone (**11**), 2-butanone (**12**), azetidine (**13**), *N*-methylethanamine (**14**), 2-azetidinone (**15**), *N*-methylacetamide (**16**). For the sake of consistency, theoretical values are those calculated at the HF/6-31G*//6-31G* level.

phase basicity of oxetane is in fairly good agreement with our theoretical predictions. Now, the $\Delta\Delta G_{H^+}(g)$ for oxetane is 1.4 kcal/mol lower than that for methyl ethyl ether, which results, after including the entropy term correction, in a difference of 2.6 kcal/mol between their proton affinities, favoring the former.

This difference decreases considerably for the next member of the series. Actually our results indicate that THF and diethyl ether present similar basicities, although the former is still 2.8 kcal/mol more basic than methyl propyl ether, in reasonably good agreement with the experimental evidence (see Table IV). In this respect, it should be mentioned that although the experimental results indicate that THF is slightly less basic than diethyl ether, the deviation from our theoretical estimates is only slightly greater than those found for the other compounds of the series and is within the standard deviation of the linear relationship which exists between our theoretical estimations and the experimental outcomes (see Figure 2), once the new value for the experimental proton affinity of oxetane is used.

The question which needs to be addressed now is why cyclization produces opposite effects on the intrinsic basicities of esters depending on their size. Following a procedure similar to that used to investigate an analogous problem in lactams,[1] we shall study first whether this effect can be considered a specific characteristic of the carbonyl oxygen atom. To answer this question we have evaluated the electronic charge density at the oxygen lone pairs by locating the maxima of $|\nabla^2\rho|$ in the neighborhood of these atoms (see Table VI). From Table VI can be seen that the value of $\nabla^2\rho$ for the carbonyl oxygen lone pair of methyl acetate and its electronic charge density are greater (in absolute value) than those for β-propiolactone. Hence, cyclization implies, in this case, a significant decrease of the electronic charge density at the oxygen lone pairs and therefore a decrease in the corresponding intrinsic basicity. The explanation is similar to that offered in ref 1 for the particular caes of β-lactams and cyclobutanone and can be summarized as follows: The C–C–O angle centered at the carbonyl carbon atom amounts to 112° in methyl acetate and is reduced to 94° in the case of β-propiolactone. This dramatic structural change requires also a drastic change of the hybridization pattern at the carbonyl carbon atom. In β-propiolactone the two hybrids which participate in the C—C and C—O bonds must considerably increase their p-character while that involved in the C═O bond must, by orthogonality, increase its s-character. Hence, this carbon atom in β-propiolactone behaves with respect to the carbonyl oxygen atom as a carbon with enhanced electronegativity. This results in a decrease of the charge density at the oxygen lone pairs with respect to the aliphatic ester. As indicated in ref 1, these hybridization changes are consistent with several experimental findings: these kinds of cyclic systems have abnormal chemical shifts of atoms α to the carbonyl group;[39] they present a shortening of the C═O bond with respect to the aliphatic counterparts[40] and an increase of its stretching frequency as well as quite different values of the $^1J_{CC}$ coupling constants.[41]

Table VI. 6-31G* Values of ρ (e/au^3) and $\nabla^2\rho$ (e/au^5) for the Nonbonded Charge Concentrations (i.e., Points Where $|\nabla^2\rho|$ Is Maximum) of Compounds Included in This Study[a]

	carbonyl oxygen lone pairs		ether-like oxygen lone pairs	
compd	ρ	$\nabla^2\rho$	ρ	$\nabla^2\rho$
1	0.955	–6.073	0.954	–5.925
2	0.973	–6.345	0.967	–6.067
3			1.001	–6.756
4			1.002	–6.762
5	0.968	–6.285	0.964	–6.090
6	0.970	–6.300	0.966	–6.064
7	0.973	–6.345	0.963	–6.014
8			1.000	–6.748
9			0.999	–6.719
10			1.001	–6.765

[a] See Figure 1.

Obviously, these hybridization changes are practically negligible for five-membered systems. As shown in Figure 1, on going from methyl propionate or ethyl acetate to γ-butyrolactone, the C–C–O bond angle centered at the carbonyl carbon closes only 2°. According to the previous arguments, one should expect the electronic charge density at the carbonyl oxygen lone pairs to be slightly smaller in the cyclic system, in agreement with our results (see Table VI). However, a similar slight decrease of the intrinsic basicity is not observed. The explanation we offer is related to the fact that the conformations of protonated γ-butyrolactone and the corresponding aliphatic esters are different in the sense that, in the former, protonation occurs anti with respect to the acetyl group while in the latter the preferential direction is syn. The origin of these conformational preferences has been nicely explained by Wiberg and Waldron[3] in terms of attractive alignment of the dipoles at the oxygen in these two configurations, which in alternative configurations would be repulsive. The consequence is that while, in the protonated form of γ-butyrolactone (**5″**), there is a stabilizing electrostatic interaction between the ether-like oxygen atom (with negative net charge) and the attaching proton, which is reflected in an O–H distance 0.4 Å smaller than the sum of their respective van der Waals radii, such an interaction is not possible in the protonated esters (**6″** and **7″**). Similar arguments would explain why the intrinsic basicity of the ether-like oxygen of the lactone is also slightly greater than those of the esters.

A second problem which deserves a closer analysis is the behavior of methyl ethyl ether with respect to oxetane. According to the topological characteristics of the oxygen lone pairs, both species should present almost equal gas-phase basicities, in contrast with our theoretical and experimental findings. This seems to indicate that the model of the isolated molecule is not appropriate to describe the gas-phase basicity of oxetane, because some other effects, such as structural changes, appear upon protonation. It may be observed that, in some way, protonation partially alleviates the ring strain in oxetane. As shown in Figure 1, while the neutral

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has a planar ring, this is not the case for the protonated species. Furthermore, the latter presents almost equal bond lengths and bond angles. This alleviation of ring strain would be responsible for the enhanced stability of protonated oxetane, which results in a gas-phase basicity slightly larger than that of the aliphatic ether. This would also explain the quite small difference between the basicities of THF and diethyl ether, since the ring strain in the former is almost negligible.

Bond Activations of Protonated Species

As indicated in previous sections, one of the most interesting problems regarding the chemistry of lactones is their ability to undergo bond cleavage. Since all pertinent information gathered so far has been obtained in solution, the information provided by our ab initio calculations may throw some light on this problem.

The first important point, already mentioned, is that protonation at the ether-like oxygen of β-propiolactone is accompanied by an acyl C–O bond cleavage, which is not observed in γ-butyrolactone. However, as illustrated in Figure 3a,b, in the latter case also a sizable activation of both alkyl and acyl C–O bonds takes place, with the result that, although in the neutral form the latter is stronger than the former, in the protonated species both linkages appear to be similar, but much weaker. This activation is a consequence of the strong charge transfer which takes place from the oxygen atom to the incoming proton in order to form a new O–H covalent bond. Since oxygen is very electronegative, it recovers part of this charge by depopulating the bonds in which its participates. Our topological analysis clearly indicates that although both C–O bonds become depopulated, the effect is stronger for the acyl C–O linkage, which in the particular case of β-propiolactone breaks apart. These results may help to rationalize the ability of β-propiolactone to alkylate nitrogen[42] and phosphorus[43] nucleophiles, the known carcinogenic character[44] of this compound being a likely consequence thereof.[45]

It is interesting to notice that, for oxetane, the observed bond activation effects are quantitatively similar to those found in γ-butyrolactone, and contrary to the case of β-propiolactone, no bond cleavage takes place. This seems to indicate that acyl C—O bond fission is favored in β-propiolactone because it yields a quite stable oxonium ion, while alkyl C—O bond cleavage yields an unstable carbonium ion. Actually, when one tries to optimize the open form corresponding to the alyl C—O bond cleavage, starting with a significantly large C—O bond distance, the structure collapses to the aforementioned minimum. If the terminal CH_2 group is allowed to rotate to be *cis* to the C=O group, then the open structure collapses to the stable protonated cyclic form (**1″**).

Furthermore, the great stability of the oxonium ion **1′** is reflected in a considerable reinforcement of both the C=O and the C—O bonds with respect to the neutral (see Table II).

A comparison of parts a and b of Figure 3 shows that protonation at the carbonyl oxygen implies also a significant charge redistribution within the molecule. The first conspicuous fact is that in this case the alkyl C—O bond is the one which becomes preferentially activated, while the acyl one becomes reinforced. This is corroborated by the values in Table II, which show that ρ_c for both the C=O and the alkyl C—O bonds decreases. These electronic effects are mirrored in the shiftings of the corresponding stretching vibrational frequencies. Our calculated values for γ-butyrolactone indicate that the stretching frequencies of the C=O and alkyl C—O bonds are shifted 314 and 222 cm^{-1}, respectively, to lower frequency values upon carbonyl protonation

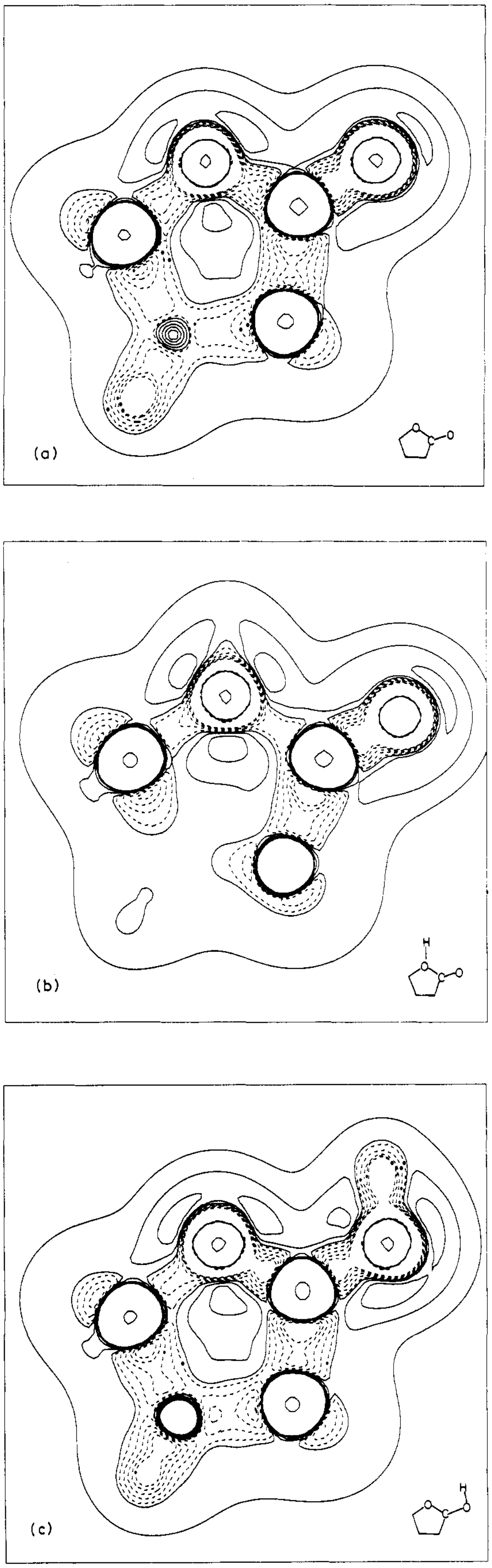

Figure 3. Contour maps of the Laplacians of the charge densities of (a) γ-butyrolactone (**5**), (b) ether-like oxygen protonated γ-butyrolactone (**5′**) (figure shows the Laplacian on the C–O–C plane since **5′** is not planar), and (c) carbonyl oxygen protonated γ-butyrolactone (**5″**). Positive values of $\nabla^2\rho$ are denoted by full lines and negative values by dashed lines. Contour values in au: ±0.05, ±0.25, ±0.50, ±0.75, ±0.95.

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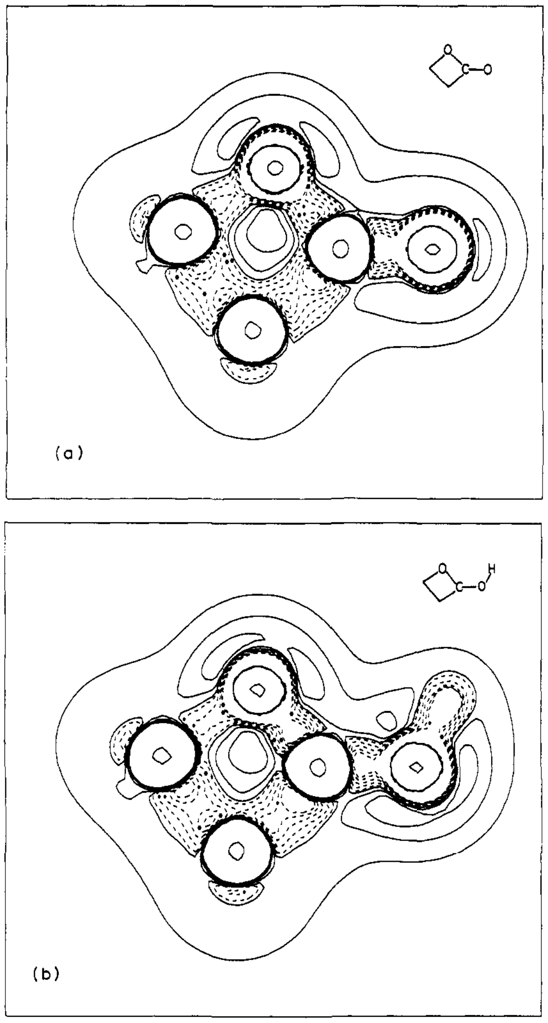

Figure 4. Contour maps of the Laplacians of the charge densities of (a) β-propiolactone (**1**) and (b) carbonyl oxygen protonated β-propiolactone (**1″**). Same conventions as in Figure 2 apply.

whereas the acyl C—O stretching frequency is shifted 428 cm^{-1} to higher values. Figure 4 show that similar effects are observed for β-propiolactone. The aforementioned frequency shiftings are in this case 243, 186, and 524 cm^{-1}, respectively.

Conclusions

Our results show that although, in general, lactones are more basic than the corresponding aliphatic esters, this is not the case for β-propiolactone, which is predicted to have a proton affinity 6 kcal/mol smaller than methyl acetate. This behavior is similar to that found for β-lactams when compared with the corresponding acyclic amides. This smaller basicity of β-lactones with respect to the aliphatic esters is a direct consequence of the hybridization changes undergone by the carbonyl carbon atom and are well described by a topological analysis of the corresponding electronic charge densities. Obviously, these hybridization changes are quite small in larger cycles such as γ-butyrolactone, which accordingly should be only slightly less basic than the corresponding acyclic esters. That γ-butyrolactone presents a gas-phase basicity greater than methyl propionate or acetyl acetate is due to the fact that in lactones the preferrred syn conformation permits a stabilizing interaction between the attaching proton and the ether-like oxygen that in protonated esters is not possible.

Quite on the contrary, cyclization effects on the gas-phase basicity of ethers are quantitatively less pronounced than for esters and occur in the opposite direction. Hence, oxetane is more basic than methyl ethyl ether, and THF, more basic than methyl propyl ether although its basicity differs little from that of diethyl ether.

Protonation of lactones at the carbonyl oxygen atom produces a significant activation of the alkyl C–O bond while the acyl C–O bond becomes reinforced, in both β-propiolactone and γ-butyrolactone. Quite on the contrary, protonation at the ether-like oxygen atom activates both C—O linkages, but preferentially the acyl one. Due to the considerable ring strain in β-propiolactone, this activation leads to a acyl C—O fission, which results in a very stable oxonium ion. This has a very important consequence: while in γ-butyrolactone and larger lactones protonation takes place at the carbonyl oxygen atom, in β-propiolactone both protonated species (carbonyl-protonated and ether-protonated) are almost equally stable. In summary, our ab initio and topological calculations show that, from a qualitative point of view, there are no significant differences between four- and five-membered-ring lactones and that bond activations upon protonation in the gas phase are similar for both species, but while γ-butyrolactone should present alkyl bond cleavage rather than acyl bond cleavage, since it protonates preferentially at the carbonyl oxygen, in β-propiolactone both processes are possible depending on the protonation site.

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