JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2002; **15:** 174–186
DOI:10.1002/poc.467

Review Commentary

Modeling intrinsic basicities and acidities

Manuel Alcamí, Otilia Mó and Manuel Yáñez*

Departamento de Química, C-9. Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain

Received 25 July 2001; revised 26 October 2001; accepted 19 November 2001

ABSTRACT: We illustrate the potential of *ab initio* and density functional theory (DFT) methods to model and gain some understanding of the intrinsic reactivity of molecules. We show how the use of high-level *ab initio* or DFT calculations permit to rationalize (a) basicity and acidity trends along a series of homologous compounds, namely thiocarbonyl and selenocarbonyl derivatives, α,β-unsaturated amines, phosphines and arsines, and α,β-unsaturated alkanes, silanes, germanes and stannanes, (b) the role of intramolecular hydrogen bonds in intrinsic acidities and basicities, (c) the incidence of induced proton transfer process effects on the intrinsic basicity of compounds stabilized by intramolecular hydrogen bonds, (d) hybridization effects on intrinsic basicities, (e) the role of non-classical structures in intrinsic basicities and (f) the observation of bond cleavage associated with gas-phase protonation and the influence of these dissociative proton attachment mechanisms on the intrinsic basicity of the system.

KEYWORDS: modeling; basicity; acidity; reactivity

INTRODUCTION

The development of gas-phase ion chemistry has contributed to changing our way of thinking with respect to many conventional process. In fact, many 'well established' concepts, such as the basicity or acidity of a given compound, were traditionally associated with chemical processes in the condensed phase. The absence of solute–solvent interactions reveals a quite different behavior of many systems, and today, for instance, it is well established that basicity or acidity trends in the gas phase may differ completely from those observed in aqueous solution or in other solvents.[1–3] A comparison between gas-phase values and values measured in solution[4] of these or other thermodynamic properties indicates that, in many cases, the solute–solvent interactions are the dominant terms. This means that only in the absence of an interaction with the solvent can we know the real reactivity of the system, usually called *intrinsic reactivity*, to emphasize that it corresponds to the reactivity that the system exhibits due to its own characteristics.

Ab initio quantum chemical calculations[5] are perfectly suited to investigate intrinsic properties because to calculate the properties of a given compound one takes into account exclusively the interaction between the nuclei and the electrons forming the system, i.e. one considers the system truly isolated. On the other hand, the accuracy of so-called high-level *ab initio* calculations[6–8] is high enough to ensure quantitative agreement with the experimental measurements, even when dealing with absolute and not only with relative magnitudes. Actually, the gas-phase basicity scale was anchored in a combined theoretical and experimental study.[9] Further, the calculations also provide reliable geometries of systems which, very often, are elusive compounds or have a short lifetime.[10] At the same time reliable information on the topology of the potential energy surface associated with the isomerization processes or the unimolecular decomposition of the system investigated can be easily obtained. In summary, calculations performed either in the framework of *ab initio* molecular orbital theory or density functional theory (DFT) constitute a very useful, and some times mandatory, tool to gain a deeper understanding of the mechanisms associated with ion–molecule interactions.

In this paper we present a summary of different cases where theory helped to establish basicity or acidity trends in different families of compounds or to understand the behavior of systems which present an unexpected reactivity in the gas phase. We then show the important role that non-classical or non-conventional structures may play in gas-phase ion chemistry. The number of

---

*Correspondence to: M. Yáñez, Departamento de Química, C-9. Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain.
Contract/grant sponsor: DGI; *Contract/grant number:* BQU2000-0245.

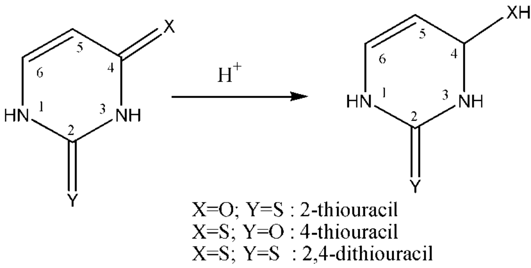
publications devoted to the analysis of these properties is so large that it would be impossible to summarize them in a short review commentary and therefore, for obvious reasons, we shall concentrate our attention mainly on our own experience in this field.

BASICITY TRENDS ALONG SERIES OF HOMOLOGOUS COMPOUNDS

Intrinsic basicity trends of carbonyls, thiocarbonyls and selenocarbonyls

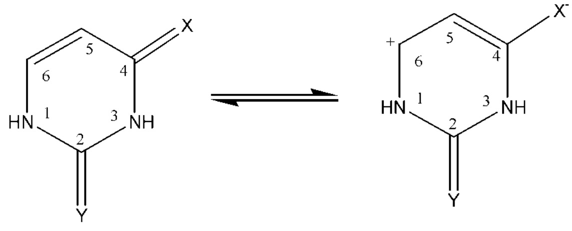
A combined experimental and theoretical study including a large set of thiocarbonyl derivatives showed[11] that they behave as sulfur bases in the gas phase. Even for those compounds which have substituents with very basic alternative centers, such as *N,N*-dimethylthiourea, the protonation on these alternative centers is not competitive with protonation on sulfur. Also, importantly, thiocarbonyl derivatives are more basic than their carbonyl analogs. In this respect it is important to emphasize, however, that thiouracils represent an exception to this general behavior.

Indeed, in a recent study,[12] we found that protonation of thiouracils takes place preferentially at the heteroatom attached to position 4 (see Scheme 1) and hence, although in general thiocarbonyls are stronger bases than carbonyls in the gas phase, 2-thiouracil behaves as an oxygen base. An analysis of the charge distribution of these systems indicated that the zwiterionic structure **Ib** (see Scheme 2) is an important contributor to the stability of these compounds, being the main factor explaining the enhanced basicity of the heteroatom attached to position 4.



X=O; Y=S : 2-thiouracil
X=S; Y=O : 4-thiouracil
X=S; Y=S : 2,4-dithiouracil

Scheme 1



Ia **Ib**

Scheme 2

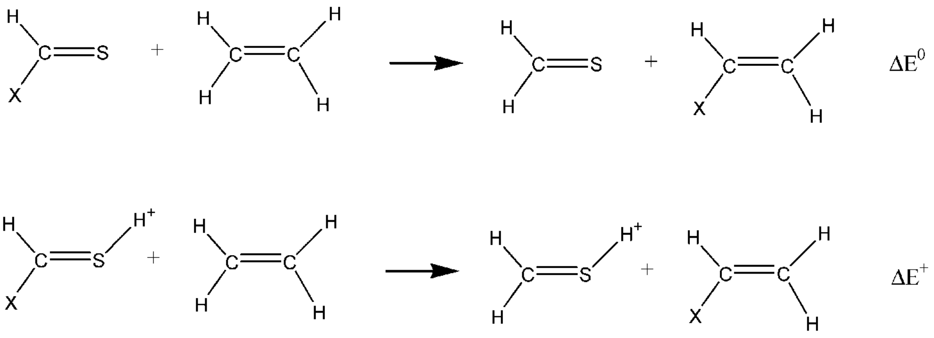
Although, as we have mentioned above, in general, thiocarbonyls are more basic than carbonyls,[11,13] this assertion needs to be qualified, in the sense that the former are much less sensitive to substituent effects than the latter. In other words, if one analyses the basicity change due to substitution, the effect is larger for carbonyl than for thiocarbonyl compounds. In fact, there is a good linear correlation between both sets of intrinsic basicities which fulfills[11] the equation

$$\Delta GB(\text{thiocarbonyl}) = 0.797\Delta GB(\text{carbonyl}) + 6.24$$

$$n = 12, r = 0.9971, \text{SD} = 1.3\ \text{kcal mol}^{-1} \qquad (1)$$

The slope of this correlation indicates that, on average, differential substituent effects on the intrinsic basicities of thiocarbonyl derivatives are about 20% smaller than for carbonyl compounds.

Theory allows us to go a little further in this analysis. In fact, a crucial question would be to know if the aforementioned differences arise from energetic changes in the neutral or in the protonated species, or in both. These questions could be properly answered through the use of the following isodesmic reactions:



The first one measures the stabilizing or destabilizing effect of the substituent on the neutral form, while the

Table 1. Energies[a] (kcal mol^{-1}) for the isodesmic reactions used to estimate substituent effects on the intrinsic basicities of carbonyls and thiocarbonyls

	ΔE°		ΔE^+		ΔE_{H^+}	
Substituent	C=S	C=O	C=S	C=O	C=S	C=O
X						
CH_3	+3.5	+6.2	+13.5	+18.8	−10.0	−12.6
NH_2	+18.9	+21.5	+42.0	+50.3	−23.1	−28.8
OH	+16.4	+26.5	+20.6	+32.3	−4.2	−5.8
F	+4.1	+19.6	−5.5	+6.4	+9.6	+13.1
Cl	+0.2	+8.3	−5.1	−0.7	+5.3	+9.0

[a] Obtained at the G2 level of theory.

second one measures the same effect on the protonated species. The first important conclusion of this analysis, which ratifies previous ones for other families of compounds,[14] is that substituent effects are dominant in the protonated species, although in the present case they are not negligible for the corresponding neutrals (see Table 1). The second important conclusion is that these effects are greater for carbonyl than for thiocarbonyl compounds. It should be noted that the basicity change induced by a substituent X, ΔE_{H^+}, will be given by

$$\Delta E_{H^+} = \Delta E^\circ - \Delta E^+ \qquad (2)$$

This indicates that, surprisingly, the greater basicity of thiocarbonyl derivatives reflects essentially the fact that the parent compound of the thiocarbonyl series, thioformaldehyde, is about 15 kcal mol^{-1} (1kcal = 4.184 kJ) more basic than formaldehyde. Therefore, although differential substituent effects are about 20% greater in carbonyl than in thiocarbonyl derivatives, the gap between the two series of compounds becomes smaller but is still sizable. The enhanced basicity of the sulfur-containing systems originates in the higher polarizability and lower electronegativity of sulfur than oxygen. As a consequence, sulfur accommodates better than oxygen the positive charge of the incoming proton and, on the other hand, its electron donor capacity is higher.

From a more quantitative point of view the correlation between the differential substituent effects on the proton affinity, defined as

$$\Delta PA = PA[\mathrm{XC(H){=}S}] - PA[\mathrm{HC(H){=}S}] \qquad (3)$$

and the field (σ_F), resonance (σ_{R^+}, and polarizability (σ_α) effects of the Taft–Topsom model:[15]

$$\Delta PA = -(19.0 \pm 1.6)\sigma_\alpha - (46.8 \pm 2.0)\alpha_F - (46.4 \pm 1.6)\sigma_{R^+}$$

$$n = 9, r = 0.9978, SD = 1.1 \text{ kcal mol}^{-1} \qquad (4)$$

indicates that field and resonance terms dominate. The dominant contributions of field effects are the result of the large dipole moment exhibited by thiocarbonyl derivatives. The large contribution of the resonance term reflects the favorable π-conjugation between the C=S group and the lone pairs of the substituent.[7] The main consequence is that protonated species are strongly stabilized only when the substituents are σ- and/or π-electron donors, while σ-electron-withdrawing groups destabilize them (see Table 1). This explains the enhanced basicity of the methyl and amino derivatives and the low basicity of the halogen derivatives. Qualitatively similar effects were found for the analogous series of selenocarbonyl derivatives.[16] From a quantitative point of view, these effects are close to those found for thiocarbonyl compounds and, as a consequence, selenocarbonyl derivatives exhibit an intrinsic basicity very close to that of their thiocarbonyl analogs, and also higher than the corresponding carbonyl derivatives. In fact, the correlation between both sets of intrinsic basicities has a slope not very different from unity:

$$PA(\text{selenocarbonyl}) = 1.11PA(\text{thiocarbonyl}) - 22.3$$

$$n = 9, r = 0.997, \mathrm{SD} = 1.2 \text{ kcal mol}^{-1} \qquad (5)$$

One of the main conclusions that can be obtained from the comparison of these three families of compounds is that bases containing first-row atoms as active centers behave differently from those where the basic center is a second- or third-row atom. Indeed, thiocarbonyls and selecarbonyls exhibit almost identical behavior, whereas this is not the case for the carbonyls. The similarity between the intrinsic basicities of selenocarbonyl and thiocarbonyl derivatives can be understood if one takes into account that Se and S should exhibit similar electron donor ability as they have identical electronegativity. The fact Se is more polarizable than S explains the slightly enhanced basicity of selenocarbonyl derivatives.

These differences between carbonyls and thiocarbonyls are observed[17] also for reference acids different from H^+, e.g. Li^+ and CH_3^+. In a systematic theoretical study including H^+, Li^+ and CH_3^+ as reference acids, we have shown[17] that the widely used molecular electrostatic potential maps yield only a rough estimation of the preferred site for association. For this purpose, it is advisable to use instead the Laplacian of the charge density, $\nabla^2\rho(r)$. In many cases the local maxima in $-\nabla^2\rho(r)$ can even provide quantitative information on the basicity trends. This is particularly so for closely related compounds, where the changes in the hybridization of the basic center, as we shall discuss later, induce changes in the intrinsic basicity. It must be mentioned, however, that in the case of carbonyl and thiocarbonyl derivatives although the Laplacian predicts correctly the preferred site for H^+ or CH_3^+ attachment, it is not useful to explain the observed trends. This simply indicates that in many systems, the reactivity trends cannot be rationalized in terms of the properties of the isolated base, because the perturbations caused by the attacking ion can be a crucial factor in the stability of the complex. We shall see, for instance, in later sections, how the formation or the destruction of an intramolecular hydrogen bond can deeply affect the intrinsic basicity or acidity of a given compound.

Basicity and acidity trends in α,β-unsaturated amines, phosphines and arsines

Similarly to what has been found for O, S and Se bases, the analysis of the basicity and acidity trends in α,β-unsaturated amines, phosphines and arsines revealed[18] that amines exhibit an exceptional behavior with regard to the analogous bases of Group Va.

The first important difference is that whereas vinyl- and ethynylamine protonate preferentially on C_β, and therefore behave as carbon bases in the gas phase, the corresponding phosphorus and arsenic analogs protonate preferentially on the heteroatom. This different behavior can be easily understood by using a set of appropriate isodesmic reactions such as those shown in Fig. 1, where the relative stability of the different neutral and protonated species of the unsaturated compounds is compared with that of the corresponding saturated ethyl analog. The first difference between phosphines and arsines with respect to amines is that on going from the saturated to the unsaturated system, the stabilization of the neutral is sizably larger for vinylamine than for vinylphosphine, while vinylarsine (not shown) becomes destabilized. In all cases the heteroatom-protonated form becomes slightly destabilized owing to an unfavorable interaction of the XH_3^+ group with the π-system. Nevertheless, the most dramatic difference affects the relative stability of the C_β-protonated form. As illustrated in Fig. 1, whereas for the amine there is a strong stabilization of the cation (by $14.7\ \mathrm{kcal\ mol^{-1}}$), for phosphines and arsines there is a large destabilization (by 11.1 and $11.0\ \mathrm{kcal\ mol^{-1}}$, respectively). This a direct consequence of the different ability of the NH_2 and the PH_2 (or AsH_2) groups to stabilize the $[CH_3\text{—}CH\text{—}XH_2]^+$ carbocation. This has another important consequence which is illustrated by the diagram in Fig. 2. It can be seen that the isomerization of vinylamine ($CH_2{=}CHNH_2$) to ethylidenimine ($CH_3CH{=}NH$) is energetically favorable. The same is true for the corresponding P and As analogs. On the other hand, owing to the aforementioned enhanced stability of the $[CH_3\text{—}CH\text{—}NH_2]^+$ carbocation, ethylidenimine is predicted to be a nitrogen base much stronger than vinylamine, which as mentioned before behaves as a carbon base. Conversely, ethylidenephosphine and ethylidenarsine are weaker bases than their vinylic isomers.

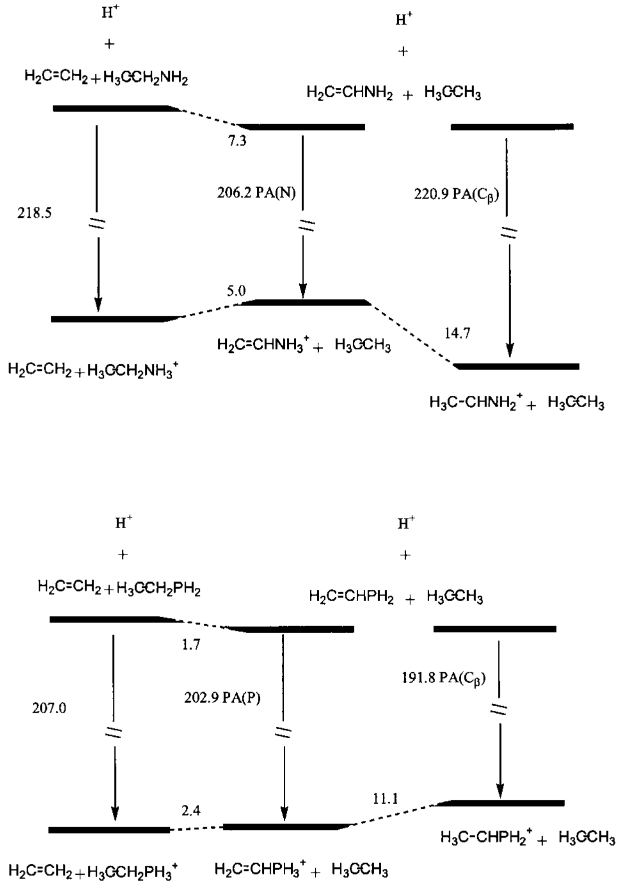


Figure 1. Relative energies of vinylamine and vinylphosphine and their protonated species compared with the corresponding saturated ethyl analogs. All values in $\mathrm{kcal\ mol^{-1}}$. PA = proton affinity. The basic center is indicated in parentheses. Values obtained at the G2 level of theory

Similar differences are found for the corresponding ethynyl ($HC{\equiv}CXH_2$, X = N, P, As) derivatives.[18]

As far as the their intrinsic acidities are concerned, all these compounds were found to be more acidic than the saturated analogs. This is clearly due to the stabilization of the anions because of a favorable interaction of the XH^- group with the C—C double or triple bond. We have also found that this stabilizing effect is maximum for amines and minimum for arsines and, as a consequence, the acidity decreases down the group.

Acidity trends in α,β-unsaturated alkanes, silanes, germanes and stannanes

The $H_2C{=}CHXH_3$ and $HC{\equiv}CXH_3$ (X = C, Si, Ge, Sn) series of compounds constitute another example of the singularity of first-row compounds with respect to their analogs of the second, third and fourth rows. In this case, in contrast with what was found for amines, phosphines and arsines, the acidity strength increases down the group,[14] mainly owing to the lower electronegativity of C, Si, Ge and Sn compared with N, P and As.

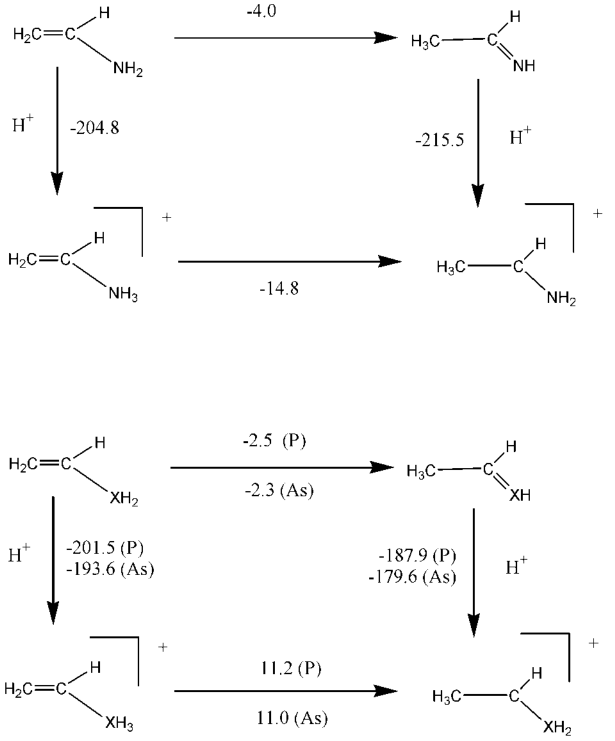
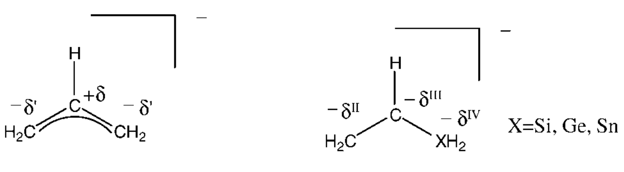


Figure 2. Energetics of the isomerization from vinylamine, -phosphine and -arsine into ethylidenimine, -phosphine and -arsine and for the corresponding protonated species. Values obtained at the G2 level of theory

Furthermore, the acidifying effect due to the unsaturation is much larger for C than for Si, Ge or Sn derivatives.[19] This is due to the enhanced stability of the allyl anion, due to favorable resonant effects. In fact, in the $[CH_2—CH—CH_2]^-$ anion most of the negative charge is located at the terminal CH_2 groups, the central atom being positively charged (see Scheme 3), contributing to a reinforcement of both C—C bonds. Conversely, for the Si, Ge and Sn derivatives the negative charge is more delocalized, and now the central atom bears a negative charge, destabilizing the bonds of the anion.

ROLE OF INTRAMOLECULAR HYDROGEN BONDS IN INTRINSIC ACIDITIES AND BASICITIES

The intramolecular hydrogen bonds (IHB) are almost exclusive to the gas phase, and their relevance to the reactivity in condensed media is much smaller. This is so because, in general, the hydrogen bond donor of an IHB prefers to form intermolecular hydrogen bonds with the solvent molecules, mainly when they are good hydrogen bond acceptors, such as water or ammonia, rather than being involved in the IHB itself.[20] However, their role in the intrinsic properties of a given system is not negligible. This role may be due to the perturbation undergone by these kinds of bonds[21] when they exist already in the neutral system, or to their formation during the protonation process.[22] Tropolone is a paradigmatic example of the first situation.[21] The characterization of the O—H···O IHB deserves a great deal of attention, but we shall concentrate here on the changes undergone upon protonation. As expected, protonation at the carbonyl oxygen is strongly favored, but the effects on the strength of the IHB are not easily predicted. In principle, protonation should lead to a decrease in the hydrogen bond acceptor capacity of the carbonyl group, which should result in a weakening of the IHB. However, simultaneously, the acidic character of the O—H group should increase and therefore its hydrogen bond (HB) donor capacity should also increase leading to a reinforcement of the IHB. A detailed analysis of the topology of the charge density of the IHB in both the neutral and the protonated species (see Fig. 3) clearly



Scheme 3

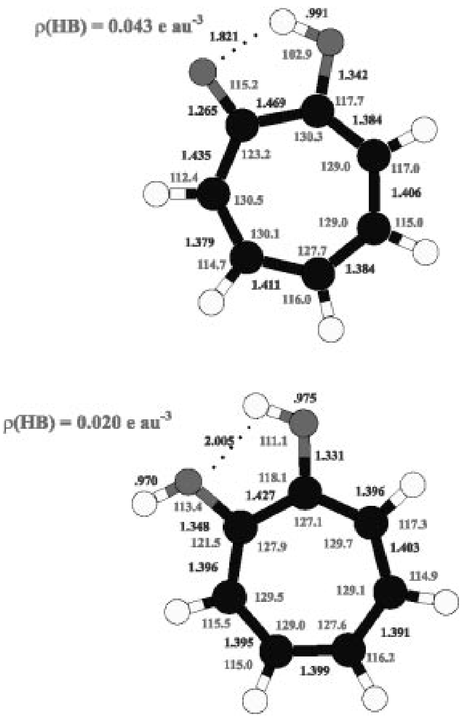


Figure 3. Geometries of neutral and protonated tropolone obtained through MP2/6–31*G(d,p) optimizations. Bond lengths in Å and bond angles in degrees. The value of the charge density at the intramolecular hydrogen bond critical point is also given to show that protonation implies a significant weakening of this linkage

showed[21] that the first effect dominates, and the IHB is significantly weaker in the protonated species than in the neutral species. This weakening tends to counterbalance the stabilization by resonance of the cation, and the result is that tropolone is found to be slightly less basic than tropone.[15] The fact that tropolone is less basic than tropone is a direct consequence of the chelation in the former, which decreases the intrinsic proton acceptor capacity of the carbonyl oxygen atom.[21]

The effect of the IHB is also very important regarding its acidity, because the stabilizing effect of the IHB in the neutral species not only disappears in the anion, but is replaced by a repulsive interaction between the lone pairs of both oxygen atoms. However, this effect is also counterbalanced by a significant resonance stabilization mechanism and tropolone is found to be more acidic than benzoic acid.[21]

Another interesting case is represented by thiomalonaldehyde, where its IHB can be considered a good example of an ‘asymmetric’ IHB, since the donor and the acceptor are atoms of different nature. The important point regarding this system is that gas-phase protonation is followed by what we have termed an induced proton transfer.[23] In thiomalonaldehyde, the enol and the enethiol tautomers are predicted to be equally stable,[24] because the IHB is much stronger in the enolic than in the enethienolic form, and therefore one must conclude that both forms should co-exist in the gas phase. On the other hand, surprisingly, both tautomers are predicted to be oxygen bases, because the protonation at the OH group of the enolic form leads to a spontaneous shift of the proton involved in the IHB (see Fig. 4), in such a way that both tautomers lead upon protonation to a common **T1H**$^+$ cation.[23] If one takes into account that the other two alternative protonation processes are less favorable by more than 4 kcal mol^{-1} (see Fig. 4), it is reasonable to expect that only the **T1H**$^+$ cation is formed in the gas phase. This induced proton transfer is also predicted for the sulfur protonation of the enethiol tautomer, but this process is more than 4 kcal mol^{-1} less favorable than the oxygen protonation.

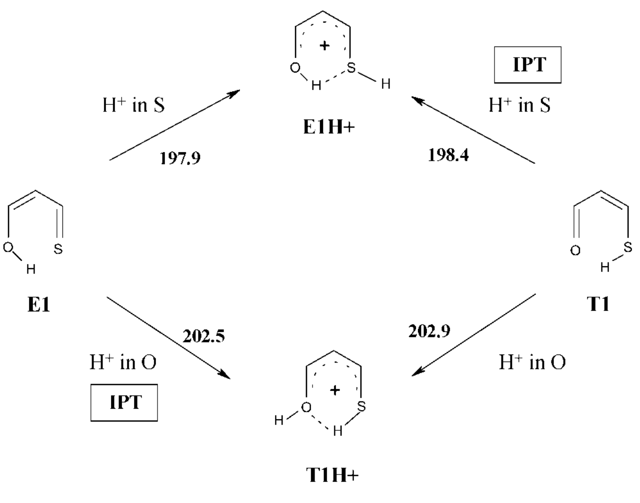


Figure 4. Protonation of the enol and enethiol forms of thiomalonaldehyde. All values in kcal mol^{-1}. IPT = induced proton transfer. All values obtained at the B3LYP/6–311 + G(3df,2p) level of theory

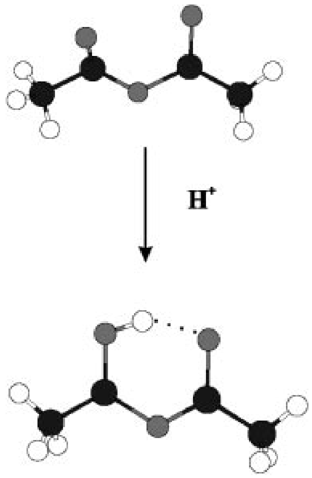


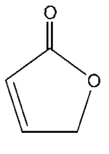
Figure 5. Structure of acetic anhydride and its most stable protonated form

The enhanced basicity of acetic anhydride is a paradigmatic example of the second situation,[22] in which the intrinsic reactivity is affected by the formation of an intramolecular hydrogen bond (see Fig. 5). In fact, the most stable conformation of the protonated form of acetic anhydride has a fairly stable O—H···O IHB, as reflected by the charge density at the corresponding bond critical point (0.04 e au^{-3}), which clearly contributes to stabilizing the protonated form. In this respect, it should be noted that the IHB not only implies the existence of a new weak linkage, but at the same time alleviates the repulsion between the oxygen lone pairs. This repulsion is responsible for the fact that in the neutral species the two C=O groups do not lie in the same plane, whereas in the protonated species the C—O—H···O=C moiety is coplanar. The sizable entropy loss upon protonation is a second important factor which contributes to increase the value of the measured proton affinity of this compound.[22] This is an important contributor always to be considered when dealing with systems that can exhibit an IHB.

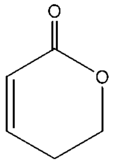
HYBRIDIZATION EFFECTS ON INTRINSIC BASICITIES

The intrinsic basicity of a given compound is a measure of its capacity to transfer a considerable amount of electronic charge (typically around 0.5 e$^-$) to the incoming proton. This capacity changes, of course, with the environment of the basic center and more particularly with changes in the hybridization it presents. Only in this way is it possible to explain the basicity differences between open-chain esters and lactones or between open-chain amides and lactams. Let us discuss here, in more detail, as a suitable example, the former.

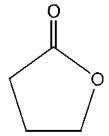
Lactones, namely 2-(5*H*)-furanone, 5,6-dihydro-2*H*-pyran-2-one, γ-butyrolactone and δ-valerolactone, are more basic than the corresponding aliphatic esters having the same number of carbons in their structures.[25] Only the β-propiolactones are an exception to this general rule.[25,26] On the other hand, the intrinsic basicity of lactones increases with increasing size of the ring. Both effects are closely related with the hybridization changes undergone by the carbonyl carbon on going from the aliphatic to the cyclic species.



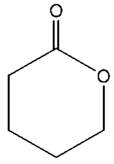
2(5H)-furanone



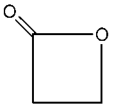
5,6-dihydro-2H-pyran-2-one



γ-butyrolactone



δ-valerolactone



β-propiolactone

In lactones the C—C(O)—O bond angle, the central atom being the carbonyl carbon, is constrained by the size of the ring, and this affects the intrinsic basicity of the carbonyl oxygen. Indeed, by means of *ab initio* calculations, it is possible to demonstrate[25] that the intrinsic basicity of the carbonyl group increases linearly with increase in the C—C(O)—O bond angle. This is shown in Fig. 6, where the protonation energy of $H_2C{=}CH{-}C(O){-}O{-}CH_3$ is plotted as a function of the C—C(O)—O angle.[24] This would immediately explain the low basicity of β-lactones, which exhibit a small angle (around 90°) and therefore a reduced intrinsic basicity.

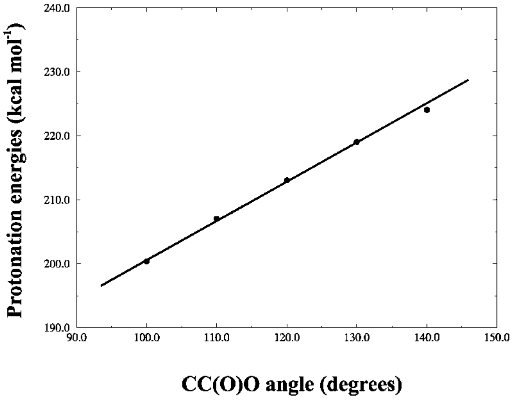
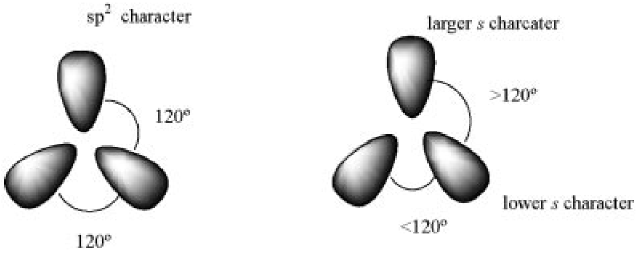


Figure 6. Linear correlation between the protonation energies of $H_2C{=}CH{-}C(O){-}O{-}CH_3$ and the C—C(O)—O angle. Values obtained at the MP2/6–31 G* level of theory



Scheme 4

This can be rationalized in terms of the hybridization changes undergone by the carbonyl carbon when the C—C(O)—O bond angle changes. If the three orbitals centered at the carbonyl carbon were strictly equivalent (pure sp^2 hybrids), the three angles around this carbon would be identical and equal to 120°. However, in β-propiolactone the endocyclic angle is forced to be close to 90°. That means that the two hybrids involved must have a small s character (see Scheme 4). By orthogonality, the hybrid involved in the C=O linkage must substantially increase its s character, which results in an enhancement of the electronegativity of the carbonyl carbon with respect to oxygen.

The obvious consequence is that the carbonyl oxygen must be a poorer electron donor. Conversely, as the size of the ring increases, the endocyclic C—C(O)—O angle also increases, and following the same arguments, the s character of the hybrids involved in the C=O bond decreases, and the carbonyl oxygen becomes a better electron donor. This picture is ratified by a parallel increase in the charge density associated with the oxygen lone pairs. The same kind of hybridization effects explain why β-propiolactam is also significantly less basic than the corresponding aliphatic amide.[27]

These geometric distortions are not exclusive to cyclic compounds but are also important in carbonyl derivatives with bulky substituents. In fact, it has been shown in a combined theoretical and experimental study[28] that sizable strain effects appear in ketones R^1COR^2 where R^1 and R^2 are tertiary carbons. More importantly, these effects where found to be higher in the protonated than in the neutral species, strongly influencing the intrinsic basicity of the system.

Also, the different hybridization pattern exhibited by the basic center along the series CH_3NH_2, $CH_2{=}NH$, $HC{\equiv}N$ explains the observed basicity trends.[29] On going

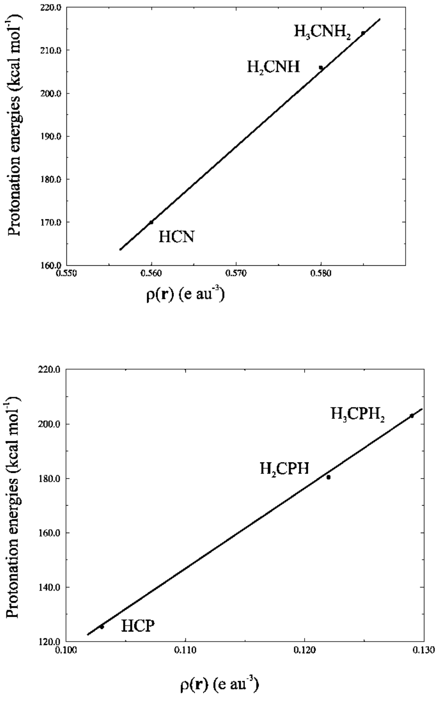


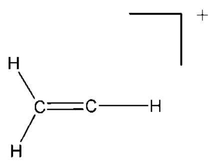
Figure 7. Linear correlations between the proton affinities of sp^3, sp^2 and sp nitrogen and phosphorus bases and the charge density at the heteroatom lone pair. Values obtained at the G2 level of theory

from methylamine to hydrogen cyanide, the hybridization of the nitrogen atoms changes from being sp^3 to sp. This means that the hybrid in which the nitrogen lone pair is located increases its s character as the degree of unsaturation increases, and therefore the lone pair should be more tightly bound[30] in HCN than in $CH_2{=}NH$ or CH_3NH_2. This is consistent with the experimental evidence which indicates that the basicity trends in both nitrogen-and phosphorus-containing bases follow the sequence sp $<sp^2$ $<sp^3$. Consistently, the charge density associated with the corresponding lone pairs follow exactly the same trend and, more importantly, there is a good linear correlation between these charge densities and the intrinsic basicity of the system (see Fig. 7).

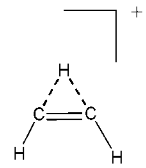
ROLE OF NON-CLASSICAL STRUCTURES IN INTRINSIC BASICITIES

The interaction in the gas phase between an ion and a neutral system often leads to the formation of molecular ions in which the basic center behaves as a hypervalent atom. The consequence is that, in some favorable cases, the structure and connectivity of the protonated species seem to violate the ‘classical’ rules of chemical bonding.

The protonated forms of many hydrocarbons offer a good number of examples, e.g. the vinyl cation, which corresponds to the protonation of acetylene and which can exist as two isomers: the classical carbon-protonated $\mathbf{1}^+$ and the non-classical C—C protonated $\mathbf{2}^+$ structures, the latter being the most stable.[31,32]



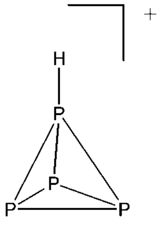
$\mathbf{1}^+$



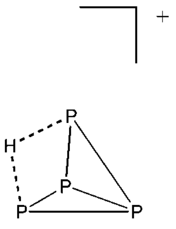
$\mathbf{2}^+$

More recently, it has been shown that these kinds of structures in which the proton bridges between two basic centers of the neutral species can be also observed in systems containing second-row atoms. The enhanced basicity of P_4 is actually due to the formation of these non-classical structures.[33] A systematic survey of the P_4H^+ potential energy surface clearly showed[33] that the classical corner protonated species $\mathbf{3}^+$ is a local minimum which lies about 15 kcal mol^{-1} above in energy of the non-classical side-protonated structure $\mathbf{4}^+$. Furthermore, the excellent agreement between the proton affinity calculated as the enthalpy difference between this non-classical structure and P_4 and the value measured by means of Fourier transform ion cyclotron resonance (FTICR) techniques is indirect evidence of the existence[33] of this non-classical form.

An analysis of the topology of the charge density of this side-protonated species indicates that the original P—P bond of the neutral species has been replaced by a three-center, two-electron P—H—P bond (see the upper part Fig. 8). The formation of these bonds can be easily visualized using a minimum basis model and considering exclusively the three atoms involved in the linkage.



$\mathbf{3}^+$



$\mathbf{4}^+$

Taking into account that we have three atomic orbitals, one s orbital from the hydrogen atom and two p orbitals from the two phosphorus atoms, three linearly independent molecular orbitals can be built up (see the lower part of Fig. 8). The most stable of the three, according to the postulates of quantum mechanics, corresponds to the nodeless combination **a**, while the other two, which present a nodal plane, should lie higher in energy. Since we have only two electrons coming from the P—P bond

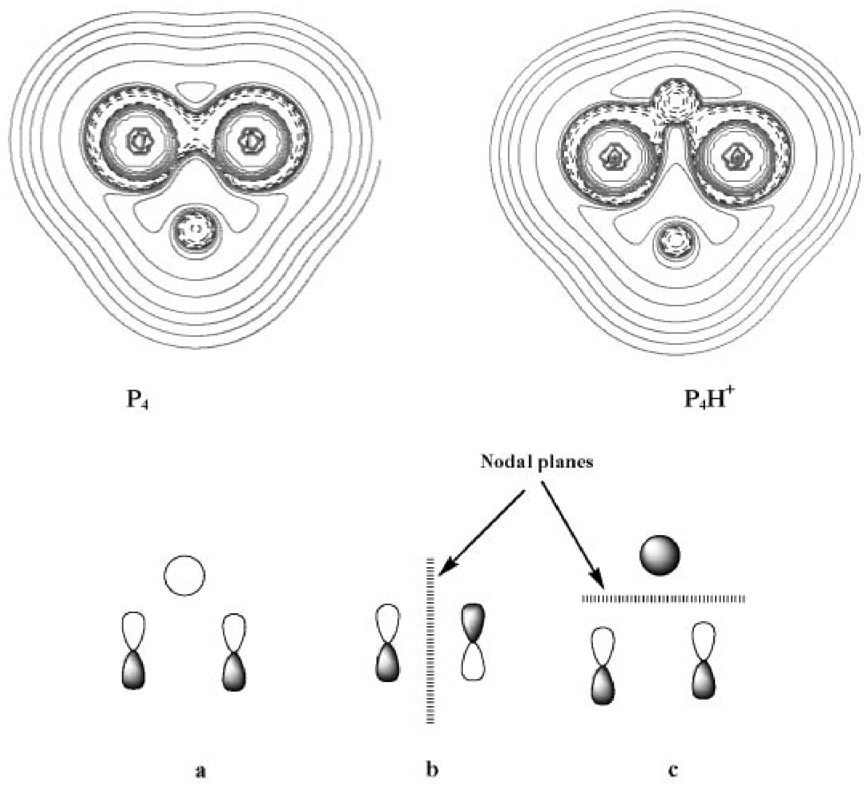
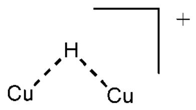


Figure 8. The upper part of the figure shows the contour map of the Laplacian of the charge density of P_4 and P_4H^+ evaluated in a plane which contains the two phosphorus atoms involved in the side-protonation process. It can be seen that the P—P bond of the neutral species has been replaced by a three-center, two-electron bond in the protonated structure. Solid and dashed lines correspond to positive and negative values of the Laplacian, respectively. The lower part of the figure schematizes the three possible interactions between the *s* orbital of H and the two p orbitals of P. Only MO **a** is doubly occupied, while **b** and **c** are empty

of the neutral species, only the MO **a** becomes occupied, yielding a typical three-center, two-electron bond.

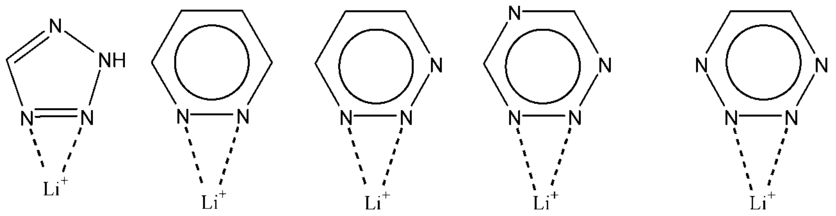
Similar non-classical structures have been predicted to be the most stable protonated species of As_4, Sb_4 and Bi_4 clusters by means of high-level *ab initio* calculations.[34,35] Furthermore, in these cases the energy gap between the non-classical side-protonated form and the classical corner-protonated structure increases as we descend down the group, indicating that the electron donor capacity of the X—X linkages increases on going from P to Bi. Also, the protonation of diphosphatetrahedrane leads to a non-classical structure where the proton bridges between the two phosphorus atoms,[36] although in this case this is not the global minimum which corresponds to a carbon protonated species. We have shown that, generally, strain systems show a certain proclivity to yield non-classical structures when interacting with monocations in the gas phase.[37]

Other typical three-center, two-electron bonds can be found in complexes involving transition metal cations. This is the case with the Cu_2H^+ complex detected[38] in the gas-phase reactions between formamide and Cu^+. This complex can be formally considered as the protonated form of the Cu_2 molecule. The important point is that its structure corresponds, once more, to a non-classical structure **5**$^+$ in which the proton bridges between the two metal nuclei.[38]



5$^+$

It is worth mentioning that when the interaction between the base and the reference acid is essentially electrostatic, as it is typically the case for complexes involving alkali metal monocations, such as Li^+, the role of non-classical structures may be also important. Although in general there is a very good linear correlation between $\Delta G^{\circ}_{\mathrm{Li}^+}$ and $\Delta G^{\circ}_{\mathrm{H}^+}$ in the gas phase,[13] there are noticeable exceptions associated with the formation of structures in which the metal monocation bridges between two basic centers of the neutral. This is the case



Scheme 5

with some triazoles, tetrazoles[39] and azines,[40] whose enhanced basicity with respect to Li^+ is the result of the enhanced stability of these bidentate complexes (see Scheme 5).

Similar structures in which alkali metal monocations bridge between two or more basic centers of the neutral have been reported for guanidine–X^+ (X = Li, Na, K, Rb, Cs) complexes,[41] and also for complexes between Na^+ and disaccharide stereoisomers[42] or between Na^+ and propene, isobutene, butadiene and 1,2-ethanediol.[43]

The complexes P_4Li^+ also have the side-attached complex as the most stable conformation. However, differently to what is observed upon protonation, the face-attached species is predicted to be a local minimum of the potential energy surface.[44] The stability of such a complex reflects the important role of polarization effects in the interactions involving these metal monocations, because in the face-attached species Li^+ polarizes three phosphorus atoms simultaneously. The most important consequence is that both side- and face-attached local minima are very close in energy, and the interconversion barrier between them is very low. This means that at room temperature or above, the Li^+ may evolve freely from one minimum to the other, following trajectories (see Fig. 9) which connect successively a face-attached with a side-attached conformation. Therefore, P_4Li^+ can be considered as a paradigmatic example of what was called a *molecular planetary system*.[44]

Very recently, a similar molecular planetary system corresponding to the ferrocene–lithium cation complex was described.[45] In this case Li^+ has one thermally accessible planar orbit around the central ferrocene moiety.

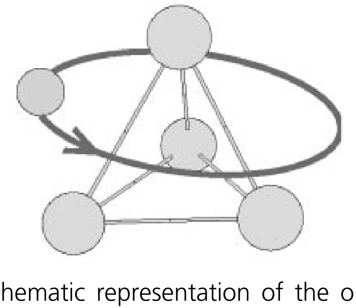


Figure 9. Schematic representation of the orbiting of Li^+ around the P_4 molecule (see text)

INTRINSIC BASICITIES AND BOND CLEAVAGE

One of the most outstanding characteristics of ion chemistry is that the ionization of a system, either by electron detachment or by cation association, is followed by non-negligible charge redistributions. Therefore, one fundamental question is how these charge redistributions affect the bonding of the system which undergoes ionization, and how they affect its intrinsic properties. To answer the first question is necessary to know when ionization induces an increase in the bonding charge density, leading to bond reinforcement, and when the opposite effect is observed, leading to bond weakening. These effects are particularly important in protonation processes, where a very strong charge transfer from the base to the bare proton takes place, and this can be adequately visualized through the use of the AIM theory.[46] Using this theory, we have shown that the nature of the perturbation depends on the center to which the proton is attached.[47] When protonation takes place on the most electronegative atom, the charge density within the bonding region decreases and, as a consequence, the linkage becomes weaker. This is reflected in a greater bond length and in a red shift of the corresponding stretching frequency. Conversely, when the proton attaches to the less electronegative atom, the charge density within the bonding region increases and the linkage becomes reinforced.[47] Consistently, the bond length decreases and the stretching frequency appears blue shifted with respect to the neutral species.

Similarly, Boyd *et al.* found that protonation of CCX (X = C, N, O, F) compounds leads systematically to an increase in the C—X bond lengths.[48] Also in line with the aforementioned bond activation reinforcement (BAR) rule, it was found that the heterolytic bond dissociation energies were much lower in protonated molecules than in the corresponding neutral species. Conversely, when X is a third-row atom, and therefore less electronegative than carbon, the protonation processes lead systematically to a shortening of the C—X bond.[49] The relationship between bond lengthening and lower heterolytic bond dissociation energy was explained in terms of the weight of covalent and ionic resonance contributors to the C—X bond.[50]

An important related question is whether there is a limit to the bond weakening when protonation takes place

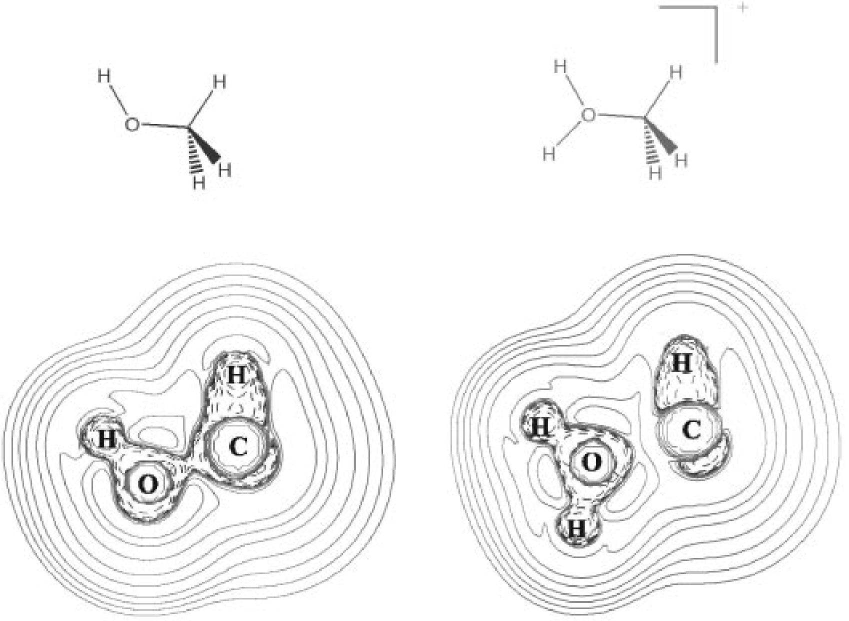


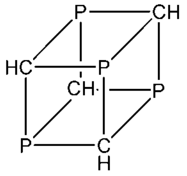
Figure 10. Contour map of the Laplacian of the charge density of neutral and protonated methanol. Conventions as in Fig. 7. It can be seen that in the protonated structure the Laplacian becomes positive within the C—O bonding region, reflecting the large charge depletion in that area

at the most electronegative atom. In other words, can the bond activation be strong enough to produce cleavage of the bond? The answer to this question was given in a previous paper,[36] and it can be visualized by considering, as a suitable example, the protonation of methanol. As illustrated in Fig. 10, in the neutral compound the Laplacian of the charge density is negative within the C—O bonding region, indicating that the electron density is concentrated there as it corresponds to a covalent C—O bond. In contrast, in the protonated species, the Laplacian becomes positive, a clear indication of the strong charge depletion that took place. Consistently, the charge distribution of protonated methanol resembles *grosso modo* that of an ion–dipole complex between CH_3^+ and a water molecule.

In this respect, it should be mentioned that these dissociations have been known for some time in solution, and actually the scale stability of carbocations in solution was based on the dissociative protonation of alcohols.[51] Similarly, the protonation of RX halogen derivatives was a key process frequently used by Olah and co-workers to generate carbocations.[52–55] Lias and Ausloos also reported experimental evidence of dissociative proton attachment in the gas phase in a study of reactions between alkyl cations and R—X halogen derivatives.[56]

These results are in line with the theoretical predictions reported previously[47] which led to the conclusion that the charge depletion undergone by the bond in which the basic center participates would be stronger the more electronegative is the basic center and the more stable is the cation produced in the heterolytic bond cleavage. This means that when a very electronegative atom such as fluorine or chlorine is attached to a substituent such as adamantyl, which would yield a very stable carbocation, dissociative proton attachment should be observed. This prediction was confirmed, from both the experimental and the theoretical viewpoints,[57] since *ab initio* calculations and FTICR techniques showed that the protonation of fluoro- and chloroadamantanes leads to an ion–dipole complex between the adamantyl cation and a molecule of hydrogen fluoride or hydrogen chloride, respectively, which eventually dissociates.

The gas-phase protonation of alcohols ROH, where R is the precursor of a very stable carbocation, should yield as final products of the gas-phase protonation an ion–dipole complex between the R^+ carbocation and a water molecule. One of the most important consequences of this behavior is that these dissociative proton-attachment processes opened up the possibility of measuring the gas-phase stability of bridgehead carbocations by means of FTICR techniques. Tertiary ions or bridgehead carbocations were normally produced in the gas phase by electron ionization of halogen derivatives which leaves the carbocation with a high internal energy so that not only are rearrangements of the ion likely to occur, but also extensive fragmentation is usually observed. The great advantage of the dissociative proton-attachment process is that it produces weakly bound complexes, which decay to free carbocation and a neutral molecule, leaving the ions with very low internal energy. This



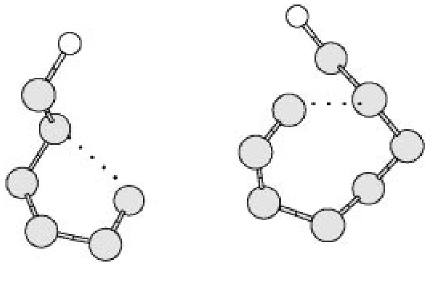
Scheme 6

method has been successfully applied by Abboud and coworkers to establish., for the first time, a gas-phase stability scale for bridgehead carbocations.[4,58]

The bond cleavage that sometimes accompanies the gas-phase protonation of a given compound may also have an important influence on its intrinsic basicity. This is the case, for example, with tetraphosphacubane (see Scheme 6). This compound exhibits an unexpected high basicity,[59] in clear contrast to its low basicity in aqueous solution. The explanation of this unexpected behavior is that tetraphosphacubane behaves as a carbon base in the gas phase, rather than as a phosphorus base as in aqueous solution. Furthermore, carbon protonation is followed by C—P bond cleavages which alleviate significantly the strain of the system,[59] stabilizing considerably the corresponding protonated structure.

A similar case is that of sulfur cycles, where gas-phase protonation is also followed by S—S bond cleavage. We have shown[60] that the S_6H^+ and the S_8H^+ protonated species do not retain a six-or eight-membered ring structure, because in both cases the global minimum of the potential energy corresponds to an SH group attached to a distorted five-or seven-membered ring, respectively[60] (see Scheme 7).

Very recently, we have also shown that it is possible to observe dissociative proton attachments even when the basic center is not a very electronegative atom, provided that the other atoms attached to it are less electronegative. This is the case with α,β-unsaturated silanes, germanes and stannanes.[61] For $H_2C{=}CH{—}XH_3$ and $HC{\equiv}C{—}XH_3$ (X = Si, Ge, Sn) derivatives, C_α is the preferred protonation site in the gas phase. Hence, in these cases, although the basic center is a carbon atom, it is much more electronegative than the atom (Si, Ge, Sn) attached to it. Consequently, gas-phase protonation cleaves the C—X bond and the protonated species is a weakly bound complex between a molecule of ethylene or acetylene and an XH_3^+ cation (see Fig. 11).



Scheme 7

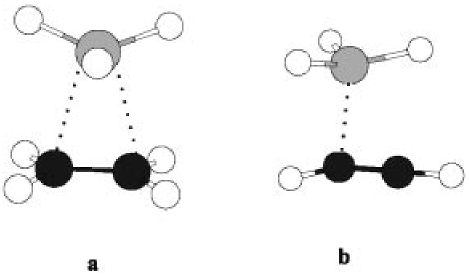


Figure 11. Optimized geometries of the protonated forms of $H_2C{=}C(H)XH_3$ (X = Si, Ge, Sn) and $HC{\equiv}C{—}XH_3$ (X = Si, Ge, Sn). They can be viewed as tightly bound complexes between ethylene and XH_3^+ or acetylene and XH_3^+, respectively. This indicates that the gas-phase protonation of these species is a typical dissociative proton attachment process

Very recently, Esteves *et al.*[62] also concluded, based on MP2/6–31G** *ab initio* calculations, that the most stable structure of protonated adamantane corresponds to a van der Waals complex between adamantyl cation and H_2. This finding is consistent with our previous arguments. On the one hand, protonation takes place at the most electronegative (carbon) atom, which upon protonation enhances its electronegativity, depopulating the C—H linkage. On the other hand, the C—H bond cleavage is also favored by the high stability of the adamantyl cation. Similarly, the mechanism of the unimolecular fragmentation of protonated fluorobenzene, recently reported by Schröder *et al.*,[63] is in line with the bond activation effects which should follow the attachment of the proton to the fluorine atom.

CONCLUSION

We have tried to illustrate in this review commentary the potentiality of *ab initio* or density functional methods to model and gain some understanding of the intrinsic reactivity of molecules. The fact that many of the protonated species generated in the gas phase are elusive to experimental scrutiny renders its theoretical characterization crucial. The theoretical techniques permit us to characterize non-classical or non-conventional structures, which often correspond to the most stable conformation of the protonated species. They also allow us to understand the origin of substituent effects on intrinsic basicities or acidities and to investigate whether these effects are stronger in the neutral or in the protonated or deprotonated species. Also, the analysis of the wavefunction, through the use of different theoretical techniques, makes possible the visualization of the charge redistribution which accompanies systematically the protonation or the deprotonation processes.

Sometimes, these techniques are the only available tool to characterize certain interactions, as intramolecular hydrogen bonding, which may play a crucial role regarding the intrinsic reactivity of many systems, or to detect possible bond activation mechanisms leading eventually to bond dissociation processes.

Acknowledgements

This work was partially supported by the DGI, Project No. BQU2000-0245.

REFERENCES

1. Kebarle P. *Annu. Rev. Phys. Chem.* 1977; **28**: 445–476.
2. Kebarle P. *Jerusalem Symp. Quantum Chem. Biochem.* 1976; **8**: 81–94.
3. McMahon TB, Kebarle P. *J. Am. Chem. Soc.* 1974; **96**: 5940–5942.
4. Müller P, Rossier J-C, Abboud J-LM. *J. Phys. Org. Chem.* 2000; **13**: 569–573.
5. Hehre WJ, Radom L, Schleyer PvR, Pople JA. *Ab Initio Molecular Orbital Theory*. John Wiley & Sons: New York, 1986.
6. Curtiss LA, Raghavachari K, Trucks GW, Pople JA. *J. Chem. Phys.* 1991; **94**: 7221–7230.
7. Curtiss LA, Raghavachari K, Redfern PC, Rassolov V, Pople JA. *J. Chem. Phys.* 1998; **109**: 7764–7776.
8. Petersson GA, Tensfeldt TG, Montgomery JA Jr. *J. Chem. Phys.* 1991; **94**: 6091–6101.
9. Smith BJ, Radom L. *J. Am. Chem. Soc.* 1993; **115**: 4885–4888.
10. Gerbaux P, Wentrup C, Flammang R. *Mass Spectrom. Rev.* 2000; **19**: 367–389.
11. Abboud JLM, Mó O, de Paz JLG, Yáñez M, Esseffar M, Bouab W, El-Mouhtadi M, Moklisse R, Ballesteros E, Herreros M, Homan H, Lopez-Mardomingo C, Notario R. *J. Am. Chem. Soc.* 1993; **115**: 12468–12476.
12. Lamsabhi M, Alcamí M, Mó O, Bouab W, Esseffar M, Abboud JLM, Yáñez M. *J. Phys. Chem. A* 2000; **104**: 5122–5130.
13. Chuchani G, Mishima M, Notario R, Abboud J-LM. In *Advances in Quantitative Structure–Property Relationships*, vol. 2, JAI Press, Stamford, CT, 1999; 35–116.
14. Catalan J, De Paz JLG, Yáñez M, Claramunt RM, Lopez C, Elguero J, Anvia F, Quian JH, Taagepera M, Taft RW. *J. Am. Chem. Soc.* 1990; **112**: 1303–1312.
15. Taft RW, Topsom RD. *Prog. Phys. Org. Chem.* 1983; **12**: 247–252.
16. González AI, Mó O, Yáñez M. *J. Phys. Chem. A* 1999; **103**: 1662–1668.
17. Alcamí M, Mó O, Yáñez M. In *Molecular Electrostatic Potentials Concepts and Applications*, vol. 3, Murray JS, Sen K. (eds). Elsevier: Amsterdam, 1996; 407–456.
18. Mó O, Yáñez M, Decouzon M, Gal J-F, Maria P-C, Guillemin J-C. *J. Am. Chem. Soc.* 1999; **121**: 4653–4663.
19. Gal J-F, Decouzon M, Maria P-C, González AI, Mó O, Yáñez M, El Chaouch S, Guillemin J-C. *J. Am. Chem. Soc.* 2001; **123**: 6353–6359.
20. Mó O, Yáñez M. *J. Phys. Chem. A* 1998; **102**: 8174–8181.
21. Mó O, Yáñez M, Esseffar M, Herreros M, Notario R, Abboud JLM. *J. Org. Chem.* 1997; **62**: 3200–3207.
22. Bouchoux G, Gal JF, Maria PC, Szulejko JE, McMahon TB, Tortajada J, Luna A, Yáñez M, Mó O. *J. Phys. Chem. A* 1998; **102**: 9183–9192.
23. González L, Mó O, Yáñez M. In *Recent Theoretical and Experimental Advances in Hydrogen Bonded Clusters*, Xantheas SS (ed). Kluwer: Dordrecht, 2000, pp. 393–402.
24. González L, Mó O, Yáñez M. *J. Phys. Chem. A* 1997; **101**: 9710–9719.
25. Bouchoux G, Drancourt D, LeBlanc D, Yáñez M, Mó O. *New J. Chem.* 1995; **19**: 1243–1257.
26. Bordeje MC, Mó O, Yáñez M, Herreros M, Abboud JLM. *J. Am. Chem. Soc.* 1993; **115**: 7389–7396.
27. Abboud JLM, Canada T, Homan H, Notario R, Cativiela C, Diaz de Villegas MD, Bordeje MC, Mó O, Yáñez M. *J. Am. Chem. Soc.* 1992; **114**: 4728–4736.
28. Homan H, Herreros M, Notario R, Abboud JLM, Esseffar M, Mó O, Yáñez M, Foces-Foces C, Ramos-Gallardo A, Martinez-Ripoll M, Vegas A, Molina MT, Casanovas J, Jimenez P, Roux MV, Turrion C. *J. Org. Chem.* 1997; **62**: 8503–8512.
29. NIST Standard Reference Data Base, No. 69, July 2001.
30. Ijjaali F, Mó O, Yáñez M, Abboud JLM. *Theochem* 1995; **338**: 225–233.
31. Klopper W, Kutzelnigg W. *J. Phys. Chem.* 1990; **94**: 5625–5630.
32. Glukhovtsev MN, Bach RD. *Chem. Phys. Lett.* 1998; **286**: 51–55.
33. Abboud JLM, Herreros M, Notario R, Esseffar M, Mó O, Yáñez M. *J. Am. Chem. Soc.* 1996; **118**: 1126–1130.
34. Alcamí M, Mó O, Yáñez M. *J. Chem. Phys.* 1998; **108**: 8957–8963.
35. González AI, Mó O, Yáñez M. *J. Chem. Phys.* 2000; **112**: 2258–2264.
36. Yáñez M. *J. Phys. Org. Chem.* 1998; **11**: 678–683.
37. Alcamí M, Mó O, Yáñez M. *Recent Res. Dev. Phys. Chem.* 1998; **2**: 827–840.
38. Luna A, Amekraz B, Tortajada J, Morizur JP, Alcamí M, Mó O, Yáñez M. *J. Am. Chem. Soc.* 1998; **120**: 5411–5426.
39. Alcamí M, Mó O, Yáñez M, Anvia F, Taft RW. *J. Phys. Chem.* 1990; **94**: 4796–4804.
40. Alcamí M, Mó O, De Paz JJG, Yáñez M. *Theor. Chim. Acta* 1990; **77**: 1–15.
41. Burda JV, Sponer J, Hobza P. *J. Phys. Chem.* 1996; **100**: 7250–7255.
42. Cerda BA, Wesdemiotis C. *Int. J. Mass Spectrom.* 1999; **189**: 189–204.
43. McMahon TB, Ohanessian G. *Chem. Eur. J.* 2000; **6**: 2931–2941.
44. Abboud JLM, Alkorta I, Davalos JZ, Gal JF, Herreros M, Maria PC, Mó O, Molina MT, Notario R, Yáñez M. *J. Am. Chem. Soc.* 2000; **122**: 4451–4454.
45. Irigoras A, Mercero JM, Silanes I, Ugalde JM. *J. Am. Chem. Soc.* 2001; **123**: 5040–5043.
46. Bader RFW. *Atoms in Molecules. A Quantum Theory*. Clarendon Press: Oxford, 1990.
47. Alcamí M, Mó O, Yáñez M, Abboud JLM, Elguero J. *Chem. Phys. Lett.* 1990; **172**: 471–477.
48. Boyd SL, Boyd RJ, Bessonette PW, Kerdraon DI, Aucoin NT. *J. Am. Chem. Soc.* 1995; **117**: 8816–8822.
49. Boyd SL, Boyd RJ. *J. Phys. Chem. A* 1999; **103**: 7087–7093.
50. Mayer PM, Glukhovtsev BMN, Gauld CJW, Radom L. *J. Am. Chem. Soc.* 1997; **119**: 12889–12895.
51. Gold V, Hawes BWV. *J. Chem. Soc.* 1951; 2102–2111.
52. Schleyer PVR, Fort RC Jr, Watts WE, Comisarow MB, Olah GA. *J. Am. Chem. Soc.* 1964; **86**: 4195–4197.
53. Olah GA, Bollinger JM, Brinich J. *J. Am. Chem. Soc.* 1968; **90**: 6988–6992.
54. Olah GA, Kiovsky TE. *J. Am. Chem. Soc.* 1968; **90**: 2583–2586.
55. Olah GA. *Science* 1970; **168**: 1298–1311.
56. Lias SG, Ausloos P. *Int. J. Mass Spectrom. Ion Phys.* 1977; **23**: 273–292.
57. Abboud JLM, Notario R, Ballesteros E, Herreros M, Mó O, Yáñez M, Elguero J, Boyer G, Claramunt R. *J. Am. Chem. Soc.* 1994; **116**: 2486–2492.
58. Abboud JLM, Castano O, Della EW, Herreros M, Müller P, Notario R, Rossier JC. *J. Am. Chem. Soc.* 1997; **119**: 2262–2266.
59. Abboud J-LM, Herreros M, Notario R, Mó O, Yáñez M, Regitz M, Elguero J. *J. Org. Chem.* 1996; **61**: 7813–7818.
60. Abboud JLM, Esseffar M, Herreros M, Mó O, Molina MT, Notario R, Yáñez M. *J. Phys. Chem. A* 1998; **102**: 7996–8003.
61. Mó O, Yáñez M, Gal JF, Maria PC, Guillemin JC. *J. Phys. Org. Chem.* in press.
62. Esteves PM, Alberto GG, Ramírez-Solís A, Mota CJA. *J. Phys. Chem. A* 2001; **105**: 4308–4311.
63. Schröder D, Oref I, Hrusak J, Weiske T, Nikitin EE, Zummack W, Schwarz H. *J. Phys. Chem.* 1999; **103**: 4609–4620.