

Gas phase protonation of α , β and γ -dicarbonyls: Thermochemistry and structures

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A paper dedicated to the memory of Sharon Lias

Abstract

An experimental and theoretical study of the protonation of representative dicarbonyl compounds $M=2,3$ -butanedione (biacetyl), **1**, 2,4-pentanedione (acetylacetone), **2**, 2,5-hexanedione (acetylacetonone), **3**, and methyl-acetoacetate, **4** has been carried out. The experimental proton affinities and protonation entropies have been obtained by the extended kinetic method using the orthogonal distance regression (ODR) treatment. Theoretical proton affinities are calculated at the G2MP2 level of theory while protonation entropies were estimated after a detailed treatment of the internal rotations. The data show that protonation of **1** and **2** is associated with negligible protonation entropies while significant negative values are obtained for molecules **3** and **4**. Protonation of 2,3-butanedione, **1a**, is associated with a tautomerisation inside the proton transfer complex thus leading to protonated 2-hydroxy-butenone, **1bH⁺**. Protonation thermochemistry of 2,4-pentanedione **2** may be simply rationalized by the protonation of its most stable tautomer, the 4-hydroxy-3-pentene-2-one, **2b**, to give its most stable protonated form **2bH⁺** stabilized by a strong intramolecular hydrogen bond. Protonation of 2,5-hexanedione **3a** most probably produces a cyclic structure stabilized by a covalent bonding, **3aHc⁺**. The structure of neutral methyl acetoacetate **4** sampled during protonation in mass spectrometry experiments appears to be its diketonic form **4a**; its protonation leading to an internally hydrogen bonded stabilized structure **4aH⁺**.
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Keywords: Proton affinity; Protonation entropy; Gas phase basicity; Dicarbonyl; Diketones

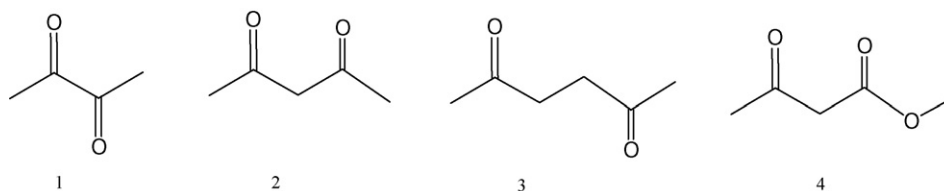
1. Introduction

In the last decades, it has long been recognized that, by its ability to handle isolated ions, mass spectrometry is an essential tool for the study of gas phase ion kinetics and thermochemistry. In this context, determination of intrinsic basicities of individual molecules has been, and is still, a field of stimulating research in the mass spectrometry community. The current NIST tabulation established by Hunter and Lias [1] is probably the most evident and useful illustration of this fundamental activity.

Proton is the simplest monocharged cation, it is unique in having no electron around its nucleus and thus has the smallest

radius as compared to all other ions (10^{-15} m against $\sim 10^{-10}$ m). One consequence of this characteristic is a considerable electrostatic and polarizing power on neighbour atoms or molecular entities. This phenomenon is, in particular, at the origin of the strength of the hydrogen bond in protonated molecules. Accordingly, since a hydrogen bond energy between two molecules is typically equal to ca. 10–20 kJ/mol, this quantity attains values in the range 100 to 150 kJ/mol if one partner is a protonated specie [2]. This large stabilization energy has consequences on the structure of hydrogen bonded ion-molecule adducts and allows chemistry to occur inside the ion-molecule complex. From this latter point of view, the most frequently encountered chemical process is proton transfer reactions. However, more extensive changes in covalent structure, leading for example to isomerization or dissociation, may also take place. Similarly, in polyfunctional molecules, the formation of intramolecular

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Scheme 1.

hydrogen bond may be also at the origin of structural changes which have consequences on the intrinsic basicity or acidity of the considered species [1–3] but may also favour isomerisation or dissociation processes.

Polycarbonyls constitute an important class of molecules prone to tautomerism, to internal hydrogen bonding and to inter-functional interactions eventually leading to structural changes upon protonation. In the present study we (re)examine the protonation thermochemistry of a series of representative dicarbonyl molecules: 2,3-butanedione (biacetyl), **1**, 2,4-pentanedione (acetylacetone), **2**, 2,5-hexanedione (acetylacetonone), **3**, and methyl-acetoacetate, **4** (Scheme 1).

For this purpose, the gas phase basicity, GB(M), and the proton affinity, PA(M), of molecules $M = \mathbf{1-4}$, defined by the Gibbs free energy change $\Delta_1 G^\circ$ and the enthalpy $\Delta_1 H^\circ$ of reaction (1) at 298 K [1]:



together with the protonation (or “half-reaction”) entropy $\Delta_p S^\circ(M) = S^\circ(\text{MH}^+) - S^\circ(M)$ were determined both experimentally and theoretically [1]. The experimental proton affinity and protonation entropy of molecules $M = \mathbf{1-4}$ were determined by the extended kinetic method [4,5] and compared with previous determinations obtained by the equilibrium method [22,23]. Molecular orbital calculations conducted up to the G2MP2 level have been used to perform conformational analysis of M and MH^+ and to obtain reliable theoretical proton affinities. Theoretical protonation entropies were estimated using statistical thermodynamic calculations using an improved treatment of the internal hindered rotations.

2. Experimental and computational section

2.1. MIKE and CID-MIKE experiments

The experimental data presented below were obtained on a B-E tandem mass spectrometer of the type VG ZAB 2F operating in the mass analyzed ion kinetic energy (MIKE) mode or in the collision induced dissociation (CID) mode. The ion source was operating under chemical ionization conditions (electron energy: 250 V; emission current: 500 μA ; source temperature: 480 K; accelerating voltage 7800 V). For each molecule $M = \mathbf{1-4}$, a series of reference bases B_i has been used to produce the relevant proton bound dimer MHB_i^+ . Equal amounts (ca 10 μl) of both samples were introduced in the heated inlet system. In these conditions, the ion source pressure is sufficient to allow thermalization and self-chemical ionization of the samples. In MIKE experiments, MHB_i^+ ions were selected by

the magnetic sector B and allowed to spontaneously dissociate before analysis of the fragments ions by the electric sector E. In CID experiments, MHB_i^+ ions are also selected by the magnet B but further activated by collisions with argon in the collision cell located between the sectors B and E before analysis of the fragment ions by the electric sector. Product ions MH^+ and $B_i\text{H}^+$ abundances were measured from peak intensities (peak height) of the corresponding ions, and, when necessary, with addition of their subsequent dissociation products. For each adduct MHB_i^+ a mean of four experiments has been done by different experimentalists at several months interval. The mean values have been used for the kinetic method treatment described in Section 3.1.

2.2. Computational methods

Molecules **1-4** and their protonated forms were examined at the MP2/6-31G(d) level in order to locate the most favourable conformations and to determine the rotational barriers used in the entropy calculations (see below). Zero point vibrational energies, ZPVE, and thermal contributions to the enthalpy at 298 K, $H_{298}(M) - H_0(M)$, were estimated from the scaled (by a factor 0.893) harmonic frequencies calculated at the HF/6-31G(d) level of theory.

Proton affinities are computed, according to reaction (1), from the standard enthalpy change given by:

$$\text{PA}_{\text{calc}}(M) = E_{\text{tot}}(M) - E_{\text{tot}}(\text{MH}^+) + \Delta_1 \text{ZPVE} + \Delta_1 H_{0 \rightarrow 298}$$

with E_{tot} being the calculated total energy of the considered species, $\Delta_1 \text{ZPVE}$ the zero point vibrational energy difference $\text{ZPVE}(M) - \text{ZPVE}(\text{MH}^+)$ and $\Delta_1 H_{0 \rightarrow 298}$ the thermal correction to enthalpy including the 298 K enthalpy contribution of the proton (i.e., $\Delta_1 H_{0 \rightarrow 298} = [H_{298}(M) - H_0(M)] - [H_{298}(\text{MH}^+) - H_0(\text{MH}^+)] + 6.2 \text{ kJ mol}^{-1}$). It has been demonstrated that in order to obtain accurate ($\pm 5 \text{ kJ mol}^{-1}$) proton affinities by this procedure, very high levels of correlation and very large basis sets must be used [6]. Various protocols are available, ranging from W1, W2 [7], G2, G3 [8] to CBS-Q [9] procedures. In the present study, we have adopted the method of highest accuracy practicable owing to the size of the investigated systems i.e., the G2MP2 method. All calculations have been undertaken using the Gaussian98 and Gaussian03 suites of programmes [10].

To compare experimental and computed gas-phase basicities, GB(M), it is necessary to know the entropy change associated with reaction (1) since, at a temperature T , $\text{GB}(M) = \text{PA}(M) - T \Delta_1 S^\circ$. As noted in the beginning of this section, the entropy difference $\Delta_1 S^\circ$ may be expressed by $[S^\circ(\text{H}^+) - \Delta_p S^\circ(M)]$ where

$\Delta_p S^\circ(M) = S^\circ(\text{MH}^+) - S^\circ(M)$. At 298 K the entropy of the proton $S^\circ(\text{H}^+)$ is equal to $108.8 \text{ J K}^{-1} \text{ mol}^{-1}$ and the protonation entropy $\Delta_p S^\circ(M)$ can be estimated by calculating the absolute third law entropy of both M and MH^+ . The calculation of entropies in the Gaussian suites of programmes uses standard statistical thermodynamic formulae in order to obtain the electronic, translational, rotational and vibrational contributions to entropy. The latter terms are estimated using the harmonic oscillator approximation. However, it is well known that the lowest frequencies are generally highly anharmonic and thus poorly described by the harmonic oscillator approximation. This is particularly true for internal rotations. It should also be noted that the lowest frequencies are those, which give the largest contributions to the vibrational entropy. In the systems considered, the possibility of intramolecular hydrogen bonds will considerably change the barrier for internal rotation between M and MH^+ and consequently strongly affect the corresponding vibrational frequencies. In order to correctly estimate the protonation entropy $\Delta_p S^\circ(M)$ it is thus essential to circumvent this problem. We consequently treat separately each internal rotation as hindered rotor by using a model developed by Pitzer and Gwinn [11] and applied to monofunctional molecules containing one, two or three internal rotations by East and Radom [12] and to the protonation of bifunctional bases by us [13]. Briefly, this procedure involves calculation of the rotational energy barrier, V_0 , appearing in the variation of the potential energy with the dihedral angle ϕ , $V_0(\phi) = V_0/2 (1 - \cos n\phi)$. The reduced moment of inertia, I_{red} , of the two rotating groups around the axis containing the bond is also required. In the present study, the rotational potential energy barriers, V_0 , were obtained at the MP2/6-31G(d) level using a relaxed rotation approach without symmetry constraint (i.e., all geometrical parameters were optimised except the dihedral angle considered). A complete scan of the dihedral angle, between 0 and 360° by steps of 20° , was explored for each torsional mode. The V_0 values used in the entropy calculations were equated with the difference between maxima and minima of the smoothed potential energy curves.

For compounds with more than one accessible conformation a correction for the entropy of mixing was included. Rigorously, the total entropy of one mole of a mixture of N components with molar fractions x_i is given by:

$$(S_T^\circ)_{\text{total}} = \sum_1^N x_i i (S_T^\circ)_i - R \sum_1^N x_i \ln x_i \quad (2)$$

where the second term is the entropy of mixing. If we assume that we are dealing with N equally populated conformations, $x_i = 1/N$ and thus the entropy of mixing reduces to $-R \ln(1/N)$. It will be also assumed that the entropy S°_i is the same for all conformations. Thus, calling S°_{low} the entropy of the conformer of lowest energy, the molar entropy may be approximated by:

$$S^\circ(\text{total}) = S^\circ_{\text{low}} + R \ln N \quad (3)$$

The number of distinguishable conformers, N , has been determined after a MP2/6-31G(d) conformational analysis. Considering that the temperature of the mass spectrometric experiments are less than 500 K, conformers more than

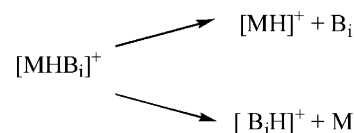
10 kJ/mol higher than the most stable have not been included in the counting since they will not contribute significantly to an equilibrium mixture. Finally, because only distinguishable conformers should participate to the entropy of mixing, the symmetrical CH_3 terminal groups of **1–4** do not contribute (while internal rotations do contribute) to the estimate of N .

3. Results and discussion

3.1. Basicity measurements

Only few mass spectrometry techniques allow the determination of the proton affinity, $\text{AP}(M)$, and the protonation entropy $\Delta_p S^\circ(M)$ of a molecule, namely, the variable temperature equilibrium method [2,14,15] and the extended kinetic method [4,5]. Gas phase basicities of the diketones **1–3** have been previously determined by the equilibrium method at variable temperature [20]. These experiments have brought the first proton affinity and protonation entropy values for these molecules. A few years after, equilibrium constant measurements performed at 300 K on an ion cyclotron resonance mass spectrometer confirmed the gas phase basicity values for $M = 1–3$ [23]. In view of recent controversy concerning the validity of the data derived from the extended kinetic method, the efficiency of this method to estimate the protonation thermochemistry of diketones **1–3** was of interest. On the other hand, no thermochemical data concerning the protonation of methyl acetoacetate **4** was available. We thus examine experimentally the four molecules **1–4** by the extended kinetic method using the most recent statistical treatment of the data.

The extended kinetic method has been extensively described in the recent years [16–21], only the main features will be recalled here. The kinetic method considers the competitive dissociations of a series of proton bound dimers $[\text{MHB}_i]^+$, involving the molecule of interest M and a reference base B_i :



Then, considering the canonical transition state theory and several simplifying assumptions, the natural logarithm of the ratio of measured peak intensities $[\text{MH}]^+ / [\text{B}_i\text{H}]^+$ may be expressed by:

$$\begin{aligned} y_i &= \ln \left(\frac{[\text{MH}]^+}{[\text{B}_i\text{H}]^+} \right) \\ &= \frac{[G_T^\circ(M) + G_T^\circ(\text{B}_i\text{H}^+) - G_T^\circ(\text{MH}^+) - G_T^\circ(\text{B}_i)]}{RT} \quad (4) \end{aligned}$$

where T is an “effective temperature” [16,17]. It may be easily shown that eq. (4) can also be written:

$$y_i = \frac{[\text{PA}_{298}(M) - \text{PA}_{298}(\text{B}_i) + T\Delta S^\circ_i + \Delta H^\circ_{298 \rightarrow T} + T\Delta S^\circ_{298 \rightarrow T}]}{RT} \quad (5)$$

where PA_{298} is the proton affinity at 298 K of the species of interest and $\Delta S_i^\circ = \Delta_p S_{298}^\circ(M) - \Delta_p S_{298}^\circ(B_i)$. The terms $\Delta H^\circ_{298 \rightarrow T}$ and $\Delta S^\circ_{298 \rightarrow T}$ are thermal corrections for enthalpy and entropy, respectively, which, because of the structural similarities of $MH^+ + B_i$ in one hand and $M + B_iH^+$ in the other, is generally assumed to cancel to zero. In this hypothesis, eq. (5) reduces to:

$$y_i = \frac{[PA_{298}(M) - PA_{298}(B_i) + T\Delta S_i^\circ]}{RT} \quad (6)$$

and thus, for a series of experiments using several bases B_i at a temperature T , y_i versus $PA_{298}(B_i)$ follows a linear relationship characterized by a slope equal to $1/RT$ and an intercept with the PA_{298} scale given by $PA_{inter} = PA_{298}(M) + T \langle \Delta S_i^\circ \rangle$ (where $\langle \Delta S_i^\circ \rangle$ is the mean value of the ΔS_i° terms). To obtain both $PA_{298}(M)$ and $\langle \Delta S_i^\circ \rangle$ it is necessary to use several sets of experiments realized under different conditions of activation of the adduct ion and thus corresponding to different effective temperatures T_j . This forms the basis of the “extended” kinetic method [5]. A straightforward method for extracting thermochemical information from the extended kinetic method consists to use directly the totality of the experimental observables y_{ij} obtained from n_j experiments differing in the adduct ion activation conditions and, for each j , from the n_i points corresponding to the number of reference bases B_i [18,19]:

$$y_{ij} = \ln \left(\frac{k_{MH}}{k_{BH}} \right)_j = \frac{\Delta S_i^\circ}{R} + \frac{[PA_{298}(M) - PA_{298}(B_i)]}{RT_j} \quad (7)$$

Accordingly, the y_{ij} versus $PA_{298}(B_i)$ points may be fitted by a set of regression lines $(y_{ij})_{calc} = y_0 + b_j(x_0 - x_i)$ intersecting in a common point of coordinate $y_0 = PA_{iso}(M)$ and $x_0 = \Delta S^\circ_{iso}/R$,

called the “isothermal” [18,19] or “isoequilibrium” [20] point. A statistical treatment of eq. (7), leading to $PA_{iso}(M)$, $\Delta S^\circ_{iso}/R$ and the values of the n_j effective temperatures T_j , has been proposed recently by Ervin and Armentrout [20]. The method is based on the orthogonal distance regression (ODR) method [20b], a least-square regression analysis which takes into account simultaneously all the $[n_i, n_j]$ data points. Using model systems, the authors reported results predicting that the proton affinities and protonation entropies determined by the extended kinetic method would present noticeable systematic errors on both proton affinities and protonation entropies. Moreover, the systematic error on proton affinities seems to be larger for systems with large protonation entropies. The extend of these systematic deviations has been delineated in a recent study considering the experimental data obtained for a set of bi- or tri-dentate bases [21].

The experimental y_i values obtained for molecules $M = 1-4$ with various reference bases B_i are reported in the Table 1. Results obtained after the ODR treatments T_j are indicated in bold in Table 2 and illustrated by the graphs presented in Fig. 1. In constructing these graphs, the $GB(B_i)$ and $PA(B_i)$ values were taken from the Hunter and Lias compilation [1]. Uncertainties of ± 0.2 and ± 4 kJ/mol have been uniformly assumed in the ODR calculations for y_i and $PA(B_i)$ respectively. It may be noted that in [1], the protonation entropy of a number of bases were assigned by comparison with homologue molecules. This is for example the case for all the asymmetric ketones for which a $\Delta_p S^\circ$ value of $2 \text{ J K}^{-1} \text{ mol}^{-1}$ is assumed by using $\Delta_p S^\circ(\text{CH}_3\text{CHO}) = 1.5 \text{ J K}^{-1} \text{ mol}^{-1}$. This latter value is however derived from theory [27] and compares hardly with experiment. Accordingly, Mautner proposes a value

Table 1
Auxiliary data used in the extended kinetic method

M	B_i	PA (B_i) ^a kJ mol ⁻¹	$\Delta_p S^\circ(B_i)$ ^a J K ⁻¹ mol ⁻¹	ln(MH)/(BH)	
				MIKE	CID/MIKE
2,3-Butanedione, 1	1-Butanol	789.2	7	2.95	0.61
	2-Propanol	793.0	7	1.32	0.41
	Butyronitrile	798.4	6	0.69	0.33
	Acetone	812.0	9	-2.59	-0.82
	Cyclohexyl cyanide	815.0	6	-2.38	-0.54
2,4-Pentanedione, 2	Acetophenone	861.1	5	1.53	0.95
	3-Methyl acetophenone	868.2	5	-1.03	-0.43
	Ethyl-vinyl ether	870.1	9	-1.27	-0.81
	Mesityl oxide	878.7	5	-3.22	-1.14
	Di cyclopropyl ketone	880.4	9	-2.90	-1.51
2,5-Hexanedione, 3	Mesityl oxide	878.7	5	2.70	0.64
	Di cyclopropyl ketone	880.4	9	3.00	0.70
	2-F-pyridine	884.6	2	0.04	-0.40
	Dimethyl formamide	887.5	5	-0.11	-0.69
	Methoxy-2-propene	894.9	6	-2.10	-3.00
3-Methyl aniline	895.8	2	-3.20	-2.80	
Methyl acetoacetate, 4	Acetophenone	861.1	5	2.35	1.39
	2,4-Pentanedione	865.1	7	0.51	-0.77
	3-Methyl acetophenone	868.2	5	-0.79	-1.26
	Ethyl-vinyl ether	870.1	9	-1.84	-1.89

^a From [1] except the $\Delta_p S^\circ$ of asymmetrical ketone which was assigned the value of $5 \text{ J K}^{-1} \text{ mol}^{-1}$ (see text).

Table 2
Experimental protonation thermochemistry of molecules **1–4**

M	Methods	GB (M) ^a	PA (M) ^a	$\Delta_p S^\circ$ (M) ^b
2,3-Butanedione, 1	Equilibrium at variable <i>T</i>	770.1 ^c	802.8 ^c	-1 ± 9^c
	Equilibrium at 300 K	770.0 ± 0.8^d		
	Extended kinetic	769.1 ± 2.0^e	$801.5 \pm .9(4.6)^f$	$7 \pm 1(3)^f$
2,4-Pentanedione, 2	Equilibrium at variable <i>T</i>	838.7 ± 0.8^c	873.8 ± 1.7^c	-9 ± 5^c
	Equilibrium at 300 K	836.8 ± 1.1^g	870.7 ± 1.6^g	-5 ± 4^g
	Extended kinetic	$835.0^h, 836.5 \pm 1.4^e$	$865.1 \pm 3.6(8.9)^f$	$8 \pm 5(12)^f$
2,5-Hexanedione, 3	Equilibrium at variable <i>T</i>	852.7 ± 2.0^c	893.2 ± 2.7^c	-27 ± 7^c
	Equilibrium at 300 K	$850.7 \pm 1.4^d, 851.7 \pm 1.4^e$		
	Extended kinetic	855.6 ± 3.6^f	$894.9 \pm 3.3(7.7)^f$	$-18 \pm 5(12)^f$
Methyl acetoacetate, 4	Extended kinetic	832.8 ± 5.5^f	$873.3 \pm 3.9(10.9)^f$	$-20 \pm 13(37)^f$

^a kJ mol⁻¹.

^b J K⁻¹ mol⁻¹.

^c Variable temperature high pressure experiments [22].

^d ICR experiments [23].

^e FT-ICR unpublished results, G.Bouchoux, W. Bertrand, D. Leblanc.

^f This work, $\Delta_p S^\circ(M) = \Delta S^\circ_{\text{iso}} + \langle \Delta_p S^\circ(B_i) \rangle$ indicated errors are standard deviations and, into parentheses, the 95% confidence interval.

^g Variable temperature high pressure experiments. McMahon T. unpublished results.

^h ICR experiments [45].

of $\Delta_p S^\circ(\text{CH}_3\text{CHO}) = 5.0 \text{ J K}^{-1} \text{ mol}^{-1}$ based of variable temperature equilibrium measurement [2b]. In the same vein, Szulejko and McMahon [24] determined experimentally $\Delta_p S^\circ$ values of 5, 4 and 8 J K⁻¹ mol⁻¹ for acetophenone, cyclopropylmethyl ketone and methylvinyl ketone. We consequently systematically assumes a value of 5 J K⁻¹ mol⁻¹ for the protonation entropy of asymmetric ketones.

3.2. 2,3-Butanedione, **1**

The structure of the 2,3-butanedione (biacetyl) molecule, **1**, has been explored experimentally and theoretically since a long time [25–32]. Its crystal structure has been determined by X-ray crystallography [25] while its gas phase structure has been established by electrons diffraction [26]. Vibrational spectroscopy (IR and Raman) of **1** in various physical states were also reported and interpreted [27–29]. All these studies lead to the conclusion that 2,3-butanedione, **1**, exists in only one conformation characterized by a *trans* arrangement of the carbonyl groups. Molecular orbital calculations confirm this expectation since the potential energy profile for internal rotation around the central CC bond exhibits a single minimum for the *trans* conformation while the *cis* conformation is a transition structure situated ca. 25–30 kJ/mol above [23,29–32].

No such abundant structural information is available for the protonated form of **1** except an earlier molecular orbital calculation [23]. Recently, the detailed unimolecular dissociations of gaseous **1H**⁺ ions have been reported [33]. These mass spectrometry experiments show that **1H**⁺ ions evolves via three reaction routes leading to *m/z* 59, 45 and 43 fragment ions. The critical energies for these three processes are estimated, from experiment, to be in the range 210–320 kJ/mol [33].

The results of the present theoretical investigation are reported in Tables 2 and 3 and illustrated by Schemes 2–4 and by Fig. 2.

As observed at various levels of theory [23,29–32], only the *trans* conformation (**1a**, Scheme 2 and Fig. 2) is found to correspond to a minimum of potential energy at the MP2/6-31G(d) level. The critical energy calculated for the rotation around the central CC bond is equal to 29 kJ/mol (Table 4), structure **1a'** (Scheme 2) being the transition structure for this rotation. The keto-enol tautomeric form of **1** presents several stable conformations corresponding to OCCO and HOCC dihedral angles of 0 or 180° (Scheme 2), the most stable of which being the conformer **1b** (Fig. 2). This structure is clearly stabilized by an intramolecular hydrogen bond. Rotation around the central CC bond passes through a maximum at 54 kJ/mol before obtaining the **1b'** structure situated 33 kJ/mol above **1b**. Similarly, the rotation of the OH moiety in structure **1b** needs 47 kJ/mol of critical energy and leads to structure **1b''**, which is less stable than **1b** by 30 kJ/mol.

At all the levels of theory considered, structure **1a** is found to be more stable than structure **1b**. The energy difference is however significantly affected by the type of calculation. At the simple MP2/6-31G(d) level, **1b** is situated ~50 kJ/mol above **1a**, this energy difference reduces to 37 kJ/mol with the density functional (fully correlated) B3LYP method. The energy difference between **1a** and **1b** decreases further when using a composite method (G2MP2 and G3MP2: 23 and 18 kJ/mol enthalpy difference at 298 K, respectively) or a complete basis set approach (CBS-Q: 19 kJ/mol enthalpy difference at 298 K). Since these latter methods are expected to provide the better energy estimates, we adopt the consensual value of ca. 20 kJ/mol for the enthalpy difference $H^\circ_{298}(\mathbf{1b}) - H^\circ_{298}(\mathbf{1a})$. The 298 K entropy calculated for these two tautomers are $S^\circ(\mathbf{1a}) = 354 \text{ J}/(\text{mol K})$

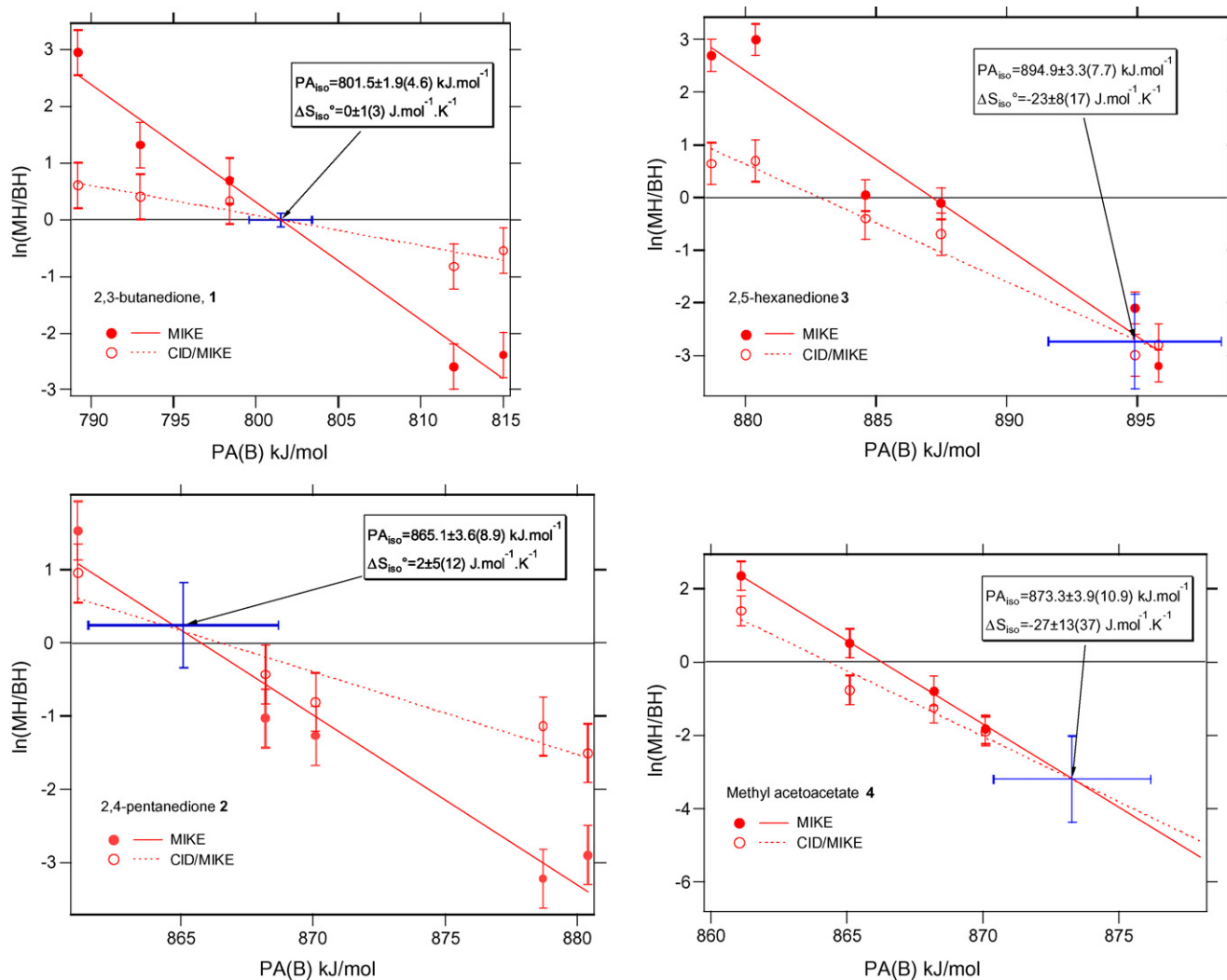
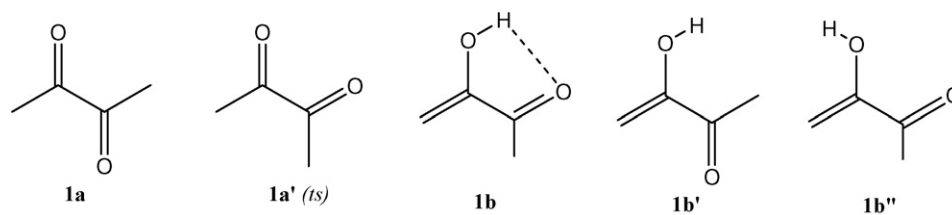


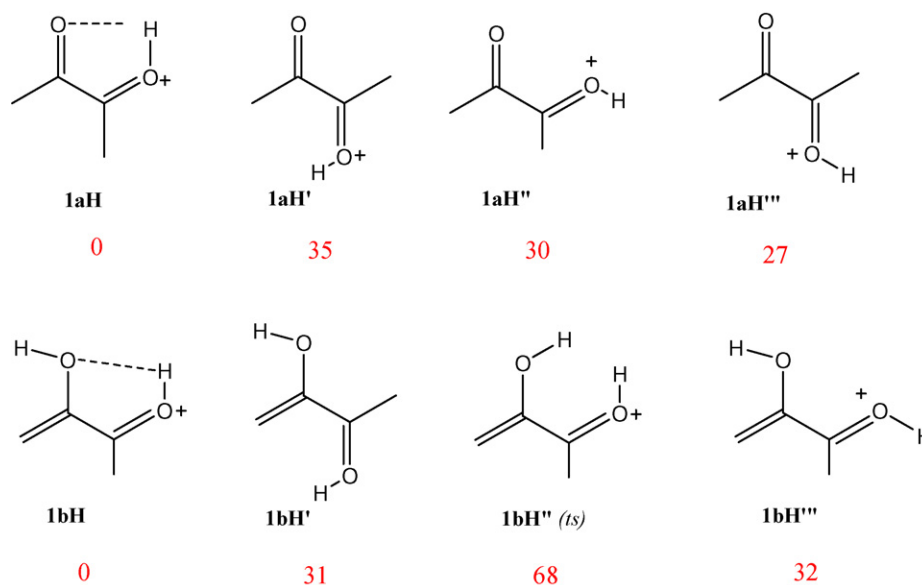
Fig. 1. Kinetic method plots obtained for 2,3-butanedione, **1**; 2,4-pentanedione, **2**; 2,5-hexanedione, **3** and methyl acetoacetate, **4**. Isothermal points were located using the ODR method.

Table 3
Calculated total (relative) energies in Hartree (kJ/mol) at different theoretical levels for molecules **1–5** and their protonated forms

Molécule	B3LYP/6-31G(d)	MP2/6-31G(d)	G2MP2 (H°_0)	G2MP2 (H°_{298})
1a	-306.474949 (0)	-305.548658 (0)	-305.980954 (0)	-305.972769 (0)
1b	-306.460878 (36.9)	-305.528823 (52.1)	-305.971729 (24.2)	-305.964106 (22.7)
1aH⁺	-306.788973 (3.1)	-305.852484 (0)	-306.278674 (11.6)	-306.270270 (12.1)
1bH⁺	-306.790144 (0)	-305.848488 (10.5)	-306.283092 (0)	-306.274871 (0)
2a	-345.794724 (13.5)	-344.719426 (0)	-345.212027 (7.2)	-345.202541 (8.6)
2b	-345.799879 (0)	-344.717719 (4.5)	-345.214759 (0)	-345.205732 (0)
2aH⁺	-346.138312 (18.5)	-345.051498 (6.6)	-345.536821 (14.5)	-345.527217 (14.9)
2bH⁺	-346.145370 (0)	-345.053995 (0)	-345.542335 (0)	-345.532879 (0)
3a	-385.112625 (0)	-383.890958 (0)	-384.442048	-384.431213
3b	-385.092842 (52)	-383.867493 (61.6)		
3c	-385.071473 (108)	-383.841599 (129.6)		
3aH⁺	-385.467042 (0)	-384.231749 (11.2)	-384.775531 (7.9)	-384.764882 (9.8)
3aHc⁺	-385.464147 (7.6)	-384.236013 (0)	-384.778544 (0)	-384.768617 (0)
4a	-421.025418 (2.4)	-419.765942 (0)	-420.359357 (5.0)	-420.348878 (6.7)
4b	-421.026347 (0)	-419.762957 (7.8)	-420.361258 (0)	-420.351439 (0)
4aH⁺	-421.373125 (0)	-420.1027495 (0)	-420.688595 (0)	-420.678013 (0)
4bH⁺	-421.371122 (5.3)	-420.096817 (15.6)	-420.687087 (4.0)	-420.676801 (3.2)



Scheme 2.



Scheme 3.

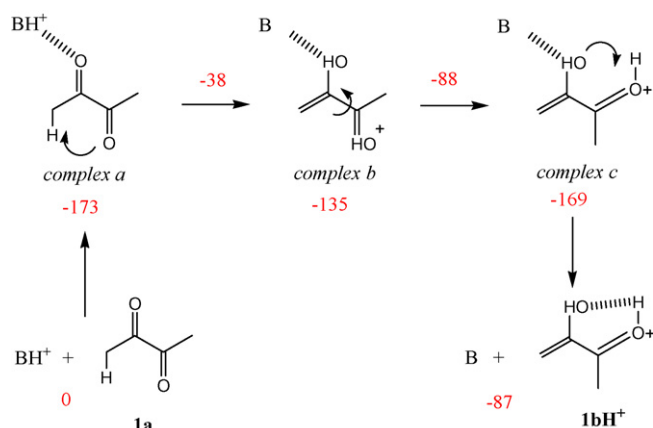
Table 4
Entropy calculation for the neutral and protonated 2,3-butanedione, **1**

Species	(a) $S^\circ_{\text{transl}}, S^\circ_{\text{rot}}, S^\circ_{\text{vib}}$	(b) Hindered rotations			(c) S°_{total}
		Bond	V_0	S°_{hind} (Pitzer)	
1a	164.3	C1C2	3.6	14.0	354.1
	111.1	C2C3	28.8	22.5	
	28.2	C3C4	3.6	14.0	
1aH+	164.5	C1C2	2.9	14.4	358.0
	111.4	C2C3	39.9	20.9	
	28.6	C3C4	2.9	14.4	
		C3O6	116.9	3.8	
1b	164.3	C2C3	54.0	19.3	342.6
	110.9	C3C4	4.8	13.2	
	27.9	C2O5	46.9	6.9	
	164.5	C2C3	61.3	18.8	
1bH+	111.0	C3C4	1.5	14.8	345.7
	27.9	C2O5	68.2	5.0	
		C3O6	109.8	3.7	

(a) Translational, rotational and vibrational contributions to entropies. Hindered rotations are not included in the S°_{vib} term.

(b) Potential energy barrier V_0 of the internal rotation around the “bond”; value in kJ/mol, calculated at the MP2/6-31G(d) level. Contribution to the entropy of the torsional modes are calculated using the Pitzer’s procedure (see text).

(c) Total calculated entropy ($\text{J mol}^{-1} \text{K}^{-1}$) of the species considered.



Scheme 4.

and $S^\circ(\mathbf{1b}) = 343 \text{ J}/(\text{mol K})$ (Table 4). Combining these data, a Gibbs free energy difference $G^\circ_{480}(\mathbf{1b}) - G^\circ_{480}(\mathbf{1a})$ of $\sim 25 \text{ kJ}/\text{mol}$ is calculated, thus excluding any participation of structure **1b** in a possible equilibrium mixture of conformers before the protonation at 480 K (see experimental part).

Protonation of **1a** and **1b** may lead to a number of conformers (Scheme 3, relative energies calculated at the MP2/6-31G(d) level are indicated in red below each structures), the geometries of the two most stable, **1aH⁺** and **1bH⁺**, are detailed in Fig. 2. Both structures present a *cis* OCCO arrangement thus allowing an intramolecular hydrogen bond, obviously at the origin of their high stability. By comparison, their *trans* homologues **1aH'** and **1bH'** are situated 35 and 31 kJ/mol above **1aH⁺** and **1bH⁺**, respectively. Similarly, structures **1aH''** and **1bH''** where the

internal hydrogen bond is also broken, but the *cis* arrangement preserved, are ca 30 kJ/mol above **1aH⁺** and **1bH⁺**. Rotational barriers separating each conformers are given in Table 4, note that, in this context, **1bH''** is the transition structure for the C2O5 rotation.

Tautomeric ions **1aH⁺** and **1bH⁺**, are separated by an enthalpy gap of $\sim 15 \text{ kJ}/\text{mol}$ (G2MP2, G3MP2 and CBS-Q methods give 12, 17 and 16 kJ/mol of enthalpy difference, respectively, at 298 K) in favour of the latter structure. Finally, by using the enthalpy difference $H^\circ_{298}(\mathbf{1aH}^+) - H^\circ_{298}(\mathbf{1bH}^+) = 15 \text{ kJ}/\text{mol}$ and the entropies $S^\circ(\mathbf{1aH}^+) = 358 \text{ J}/(\text{mol K})$ and $S^\circ(\mathbf{1bH}^+) = 346 \text{ J}/(\text{mol K})$ (Table 4), a Gibbs free energy difference $G^\circ_{480}(\mathbf{1aH}^+) - G^\circ_{480}(\mathbf{1bH}^+)$ of $\sim 9 \text{ kJ}/\text{mol}$ is calculated. If a Boltzmann distribution of isomers is considered at the temperature of 480 K, the Gibbs energy difference would lead to a negligible amount of **1aH⁺**.

Theoretical proton affinities, protonation entropies and resulting gas phase basicities of **1a** and **1b** are presented in Table 8. The experimental data reported in Table 2 converge remarkably toward a PA(**1**) value of $802 (\pm 2) \text{ kJ}/\text{mol}$ and point to a negligible protonation entropy $\Delta_p S^\circ(\mathbf{1}) = -1 \pm 9$ to $7 \pm 2 \text{ J}/(\text{mol K})$. If one considers that protonation of the most stable 2,3-butanedione, **1a**, leads to structure **1aH⁺**, or that deprotonation of the most stable protonated form, **1bH⁺**, give structure **1b**, the expected proton affinity value differs considerably (by 20 to 15 kJ/mol) from the experimental result. Even if, in both cases, the protonation entropy terms are in correct agreement with experiment, it seems difficult to consider one or the other possibility. The best way to account for the experimental proton affinity value is to consider that the experiments

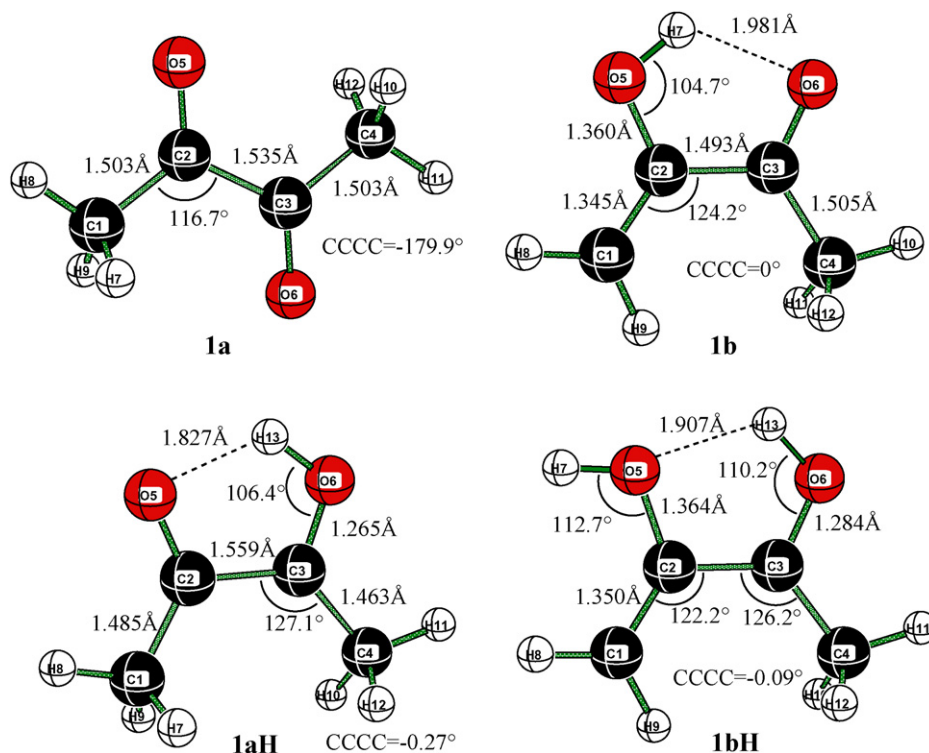


Fig. 2. MP2/6-31G(d) optimized geometries of the most stable conformations of 2,3-butanedione, **1a** and 3-hydroxy-butanone, **1b** and their protonated forms **1aH⁺** and **1bH⁺**.

sampled the most stable neutral and protonated structures **1a** and **1bH⁺**. Under these circumstances, the calculated proton affinity becomes equal to 799 kJ/mol in excellent agreement with experiment. Moreover, the calculated protonation entropy of $-8 \text{ J mol}^{-1} \text{ K}^{-1}$ is within the experimental uncertainty range given by Mautner [22].

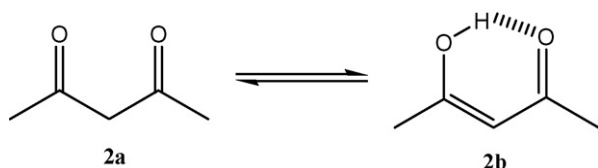
This conclusion implies that an isomerization takes place inside the MHB⁺ adduct during the proton transfer process between the reference base and the molecule of interest. A possible mechanism is depicted in Scheme 4. A first complex, involving BH⁺ and the most stable neutral **1a** is initially produced (*complex a*). Inside this complex, a 1,4-hydrogen migration leads to a new complex (*complex b* Scheme 4) where the conformer **1bH'** interact with the base B. Then, a rotation around the central CC bond leads to the *complex c* which consists in the most stable protonated form **1bH⁺** in interaction with B. Taking B = CH₂O as a model system, we perform quantum chemical calculations at the B3LYP/6-31G(d) level. Relative energies of the various critical points are indicated in Scheme 4. We found that the 1,4-hydrogen migration *complex a* → *complex b* is the energy determining step but is associated with a critical energy of 135 kJ/mol, smaller than the energy difference between *complex a* and its components which is calculated to be 173 kJ/mol. The rotation around the CC bond in *complex b* lead to *complex c* via a barrier of 47 kJ/mol i.e., a value slightly lower than the rotation around the C2C3 bond in nude **1bH⁺** ion (~60 kJ/mol Table 4).

We thus confirm our previous conclusion that an isomerization is accompanying the protonation of 2,3-pentanedione [23]. One may note that other examples of acid catalysed isomerisation of carbonyl molecules in the gas phase have been reported in the literature: they mostly involve pinacolic type rearrangements [34] but also longer range hydrogen migrations involving eventually ion-neutral complex intermediates [34a] comparable to those described in Scheme 4.

3.3. 2,4-Pentanedione, 2

Acetylacetone, is a classical example of a keto-enol system where the two tautomeric forms are present in equilibrium mixture in standard experimental conditions. The equilibrium between the 2,4-pentanedione, **2a**, and (Z)-4-hydroxy-3-pentene-2-one, **2b** (Scheme 5) is markedly influenced by the surrounding medium [35].

However, in the gas phase and at 298 K, the enol structure **2b** is clearly the major component of the equilibrium mixture in cryogenic matrices and in solution in most of the organic solvents [35,36]. The experimentally determined 298 K enthalpy



Scheme 5.

difference value between the two tautomers **2a** and **2b** in the gas phase falls into two groups centred around 9 and 18 kJ/mol, in favour of the enol form [37]. This order of magnitude is correctly reproduced by theory since this enthalpy difference is equal to 8.6 kJ/mol at the G2MP2 level while it attains 13.5 kJ/mol at the B3LYP/6-31G(d) level (Table 3).

Conformational analysis of **2a** reveals that the most stable conformer corresponds to a gauche conformation characterized by a quasi anti-parallel arrangement of the two dipolar carbonyl groups. Barriers for the methyl rotations are equal to 5.8 kJ/mol while that of the internal CC bonds are calculated to be 13.7 kJ/mol (Table 5). Two enantiomeric conformations are expected by rotating around each of the internal CC bonds (**2a/2a*** and **2a'/2a'***, Scheme 6). In fact, the latter diastereoisomers collapse to **2a/2a*** due to the electrostatic repulsion between the oxygen atoms. Consequently, only two conformers have been considered in the entropy of mixing indicated into bracket in the last column of Table 5.

Eight conformers of the enol form of acetylacetone have been identified by theoretical calculations at various levels of theory [38,39]. Each of these conformers is situated at least 45 kJ/mol above conformer **2b** which is internally stabilized by intramolecular hydrogen bond and by the π electrons delocalisation [40]. Our exploration confirms this finding, for example structure **2b'** and **2b''** are less stable than **2b** by 68 and 56 kJ/mol, respectively (Scheme 6). Due to this large energy gap, we can reasonably consider that, at 480 K, only the conformer **2b** should participate to the description of the enol form of acetylacetone. Rotational barriers also reflect the large stability of **2b** with respect to the other conformers since rotation around C3C4 or C2O6 needs around 80 kJ/mol (Table 5).

In summary, in the usual conditions of temperature of mass spectrometric chemical ionization experiments, neutral acetylacetone may essentially exist into the two conformations **2a** and **2b** presented in Fig. 3, the latter being favoured in enthalpy by ca 9 kJ/mol but entropically disfavoured by ca 30 J/mol K. It is noteworthy that using these figures, structures **2b** and **2a** present equivalent Gibbs free energies at 480 K in agreement with a mixture of both tautomers in the gas phase (note that the uncertainties on the calculated enthalpy and entropy differences are too large, probably $\pm 5 \text{ kJ/mol}$ and $\pm 10 \text{ J/mol K}$, to propose a reasonable estimate of the mixture composition).

The two most stable protonated forms of **2a** and **2b**, namely **2aH⁺** and **2bH⁺** (Fig. 3) present also different stabilities, the ketoenol structure **2bH⁺** is more stable than **2aH⁺** by 15 kJ/mol at the G2MP2 level. However, the two ionised structures are both stabilized by an intramolecular hydrogen bond and, as expected, internal rotations are characterized by high energy barriers (Table 5). The most obvious consequence of this internal constraints is that **2aH⁺** and **2bH⁺** have very similar absolute entropies. Concerning **2aH⁺**, no other conformations has been found to possibly participate to a mixture of conformers. It may be, for example, indicated that structure **2aH⁺'** (Scheme 7), which has been found to be a stable species, is situated 45.2 kJ/mol above **2aH⁺**. In addition to the intramolecular H bond, the largest stability of **2bH⁺** may be also attributed

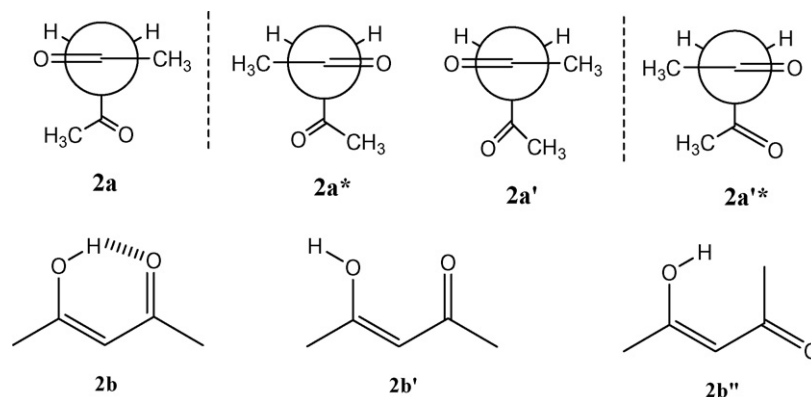
Table 5
Entropy calculation for the neutral and protonated 2,4-pentanedione, **2**

Species	(a)	(b) Hindered rotations			(c)
	$S^\circ_{\text{transl}}, S^\circ_{\text{rot}}, S^\circ_{\text{vib}}$	Bond	V_0	S°_{hind} (Pitzer)	S_{total}°
2a	166.2	C1C2	5.8	12.8	399.8 [405.6]
	115.6	C2C3	13.7	28.2	
	36.0	C3C4	13.7	28.2	
		C4C5	5.8	12.8	
2b	166.2	C1C2	5.9	12.7	373.3
	115.5	C3C4	79.1	19.3	
	40.0	C4C5	1.6	14.8	
		C2O6	84.6	4.8	
2aH⁺	166.3	C1C2	2.0	14.7	388.4
	115.6	C2C3	78.7	19.5	
	37.0	C3C4	65.3	20.3	
		C4C5	1.1	15.0	
2bH⁺	166.3	C1C2	4.7	13.3	381.0
	115.8	C3C4	81.7	19.2	
	45.9	C4C5	0.8	15.0	
		C2O6	59.7	5.5	

(a) Translational, rotational and vibrational contributions to entropies. Hindered rotations are not included in the S°_{vib} term.

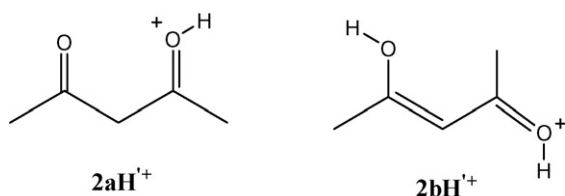
(b) Potential energy barrier V_0 of the internal rotation around the "bond"; value in kJ/mol, calculated at the MP2/6-31G(d) level. Contribution to the entropy of the torsional modes are calculated using the Pitzer's procedure (see text).

(c) Total calculated entropy ($\text{J mol}^{-1} \text{K}^{-1}$) of the species considered. Into brackets, entropy calculation including an entropy of mixing (two conformers assumed, see text).



Scheme 6.

to the existence of a concomitant π -electron conjugation leading to a charge delocalisation. An illustration of this point is the fact that structure **2bH⁺**, which differs from **2bH⁺** by the lack of internal hydrogen bond, is still significantly stabilized since its energy, relative to **2bH⁺**, is only 15 kJ/mol. This energy difference is however too large to consider **2bH⁺** as a possible component of a mixture of tautomeric protonated forms.



Scheme 7.

Experimental gas phase basicity measurements of **2** fall in a narrow range (833–839 kJ/mol, Table 2). Similarly, proton affinity and protonation entropy do not exhibit a too large dispersion ($865 > \text{PA}(\mathbf{2}) > 874$ kJ/mol, $-9 > \Delta_p S^\circ(\mathbf{2}) > +7$ J/mol K). The latter term points to the absence of a significant entropy loss during protonation. When comparing these experimental data with the expectations based on the theoretical proton affinities and protonations entropies (Table 8) it emerges that only the deprotonation processes involving structure **2bH⁺** correspond to a GB value falling in the good range. From examination of Table 8 it appears that both processes **2bH⁺** \rightarrow **2b** + H^+ and **2bH⁺** \rightarrow **2a** + H^+ lead to a GB value close to 835 kJ/mol. Consideration of structure **2aH⁺** would lead to a proton affinity ~ 20 kJ/mol below the observed value. Now, when looking at the entropy, processes **2bH⁺** \rightarrow **2b** + H^+ and **2bH⁺** \rightarrow **2a** + H^+ dispatch a $\Delta_p S^\circ(\mathbf{2})$ of +8 and ca -20 J/mol K, respectively. The

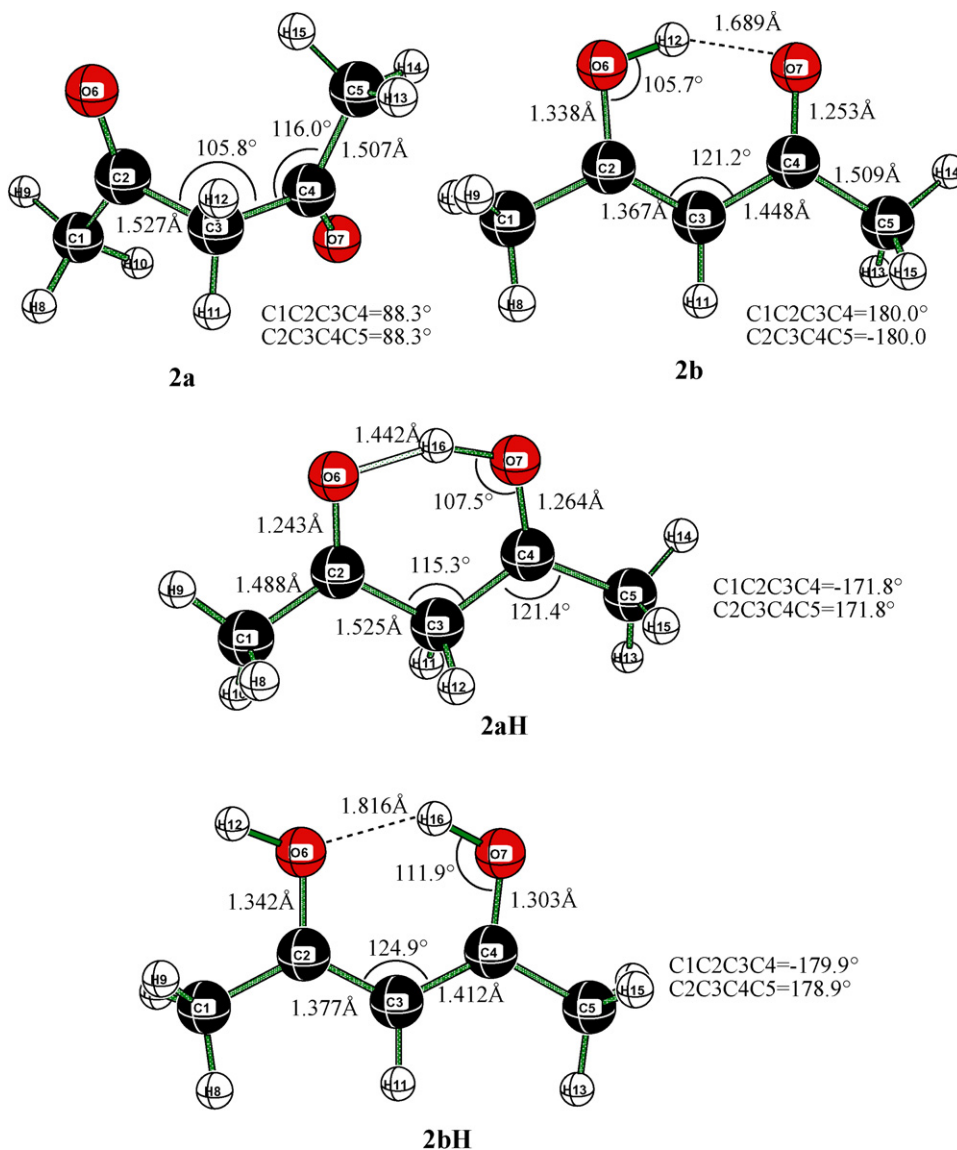


Fig. 3. MP2/6-31G(d) optimised geometries of the most stable conformations of 2,4-pentanedione, **2a** and 3-hydroxy-2-pentenone, **2b** and their protonated forms **2aH**⁺ and **2bH**⁺.

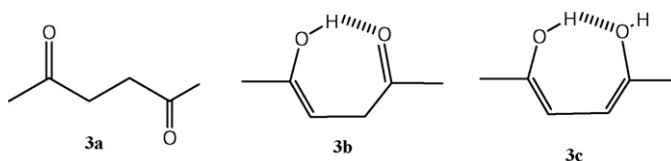
large negative value of the latter is not in agreement with experiment and confirms that the diketone neutral form **2a** is not present in our experimental conditions. In conclusion all the data, either experimental or theoretical, converge on the description of the protonation of acetylacetone as being, as a major process, protonation of (Z)-4-hydroxy-3-pentene-2-one, **2b** to produce its carbonyl protonated counterpart **2bH**⁺.

3.4. 2,5-Hexanedione, **3**

2,5-Hexanedione, **3** (acetylacetone) is not known to show special tautomerism tendency in its neutral form. The present quantum chemistry calculations show that indeed the diketonic form **3a** is by far the most stable structure as compared to its mono- and di-enol tautomers **3b** and **3c** (Scheme 8). At the MP2/6-31G(d) level (Table 3), **3b** and **3c** are situated 60 et 130 kJ/mol above **3a**, respectively, although they present an

intramolecular hydrogen bond. Note that, in the case of **3c**, the π -electron conjugation, expected to bring a stabilizing effect to this structure, is limited by the fact that the planarity of the heavy atoms system cannot be totally achieved. Only structure **3a** will be considered in the following discussion.

Conformational analysis of 2,5-hexanedione **3a** reveals a limited number of minima on the potential energy surface [41,42]. The rotation around the central CC bond points to the gauche conformation **3a** presented in Fig. 4 to be the most stable, its



Scheme 8.

Table 6
Entropy calculation for the neutral and protonated 2,5 hexanedione **3**

Species	(a)	(b) Hindered rotations			(c)
	$S^{\circ}_{\text{transl}}, S^{\circ}_{\text{rot}}, S^{\circ}_{\text{vib}}$	Bond	V_0	S°_{hind} (Pitzer)	S_{total}°
3a	167.8	C1C2	2.7	14.5	443.3 [452.4]
	118.8	C2C3	15.0	28.2	
	39.9	C3C4	11.8	31.9	
		C4C5	15.0	28.2	
		C5C6	2.8	14.0	
3aH⁺	168.0	C1C2	4.4	13.6	427.2
	119.0	C2C3	69.0	21.0	
	48.0	C3C4	74.6	23.1	
		C4C5	67.6	21.0	
		C5C6	4.6	13.5	
3aHc⁺	168.0	C1C2	2.6	14.5	419.7
	117.7	C2C3	116.3	18.4	
	36.6	C3C4	87.3	22.8	
		C4C5	76.7	20.6	
		C5C6	6.9	12.1	
		C5O8	25.0	9.2	

(a) Translational, rotational and vibrational contributions to entropies. Hindered rotations are not included in the S°_{vib} term.

(b) Potential energy barrier V_0 of the internal rotation around the “bond”; value in kJ/mol, calculated at the MP2/6-31G(d) level. Contribution to the entropy of the torsional modes are calculated using the Pitzer’s procedure (see text).

(c) Total calculated entropy ($\text{J mol}^{-1} \text{K}^{-1}$) of the species considered. Into brackets, entropy calculation including an entropy of mixing (three conformers assumed, see text).

trans conformer **3a'** being 8 kJ/mol above. The rotational barrier separating **3a** and **3a'** is equal to 12 kJ/mol (Table 6). Note that **3a** possesses an enantiomeric form (**3a***, Scheme 9) and consequently a contribution of three tautomers has been considered in the calculation of the entropy of mixing (Table 6). Rotation around the lateral CC bonds C2C3 or C4C5 between 0 and 360° generates a minimum in a very flat valley for a CCCC dihedral angle of ca. 30° (**3a**, Scheme 9). A second minimum corresponding to a CCCC dihedral angle of ca. 150° (**3a''**, Scheme 9) was also detected, its energy relative to **3a** is very close to the rotational barrier of 14.8 kJ/mol. It was consequently not considered in the conformer count.

Protonation of **3a** may lead to two different structures stabilized either by an intramolecular hydrogen bond, **3aH⁺**, or by a C–O covalent bond leading to the cyclized structure **3aHc⁺** (Fig. 4). The latter structure is predicted to be more stable than the former by ca. 10 kJ/mol at the G2MP2 level (Table 3). Structure **3aH⁺** has been previously proposed as the potential protonation product of 2,5-hexanedione [41,42] but the cyclic structure **3aHc⁺** has not been considered. Conformational analysis of **3aH⁺**, reveals only one single minima when rotating around each of the three internal CC bond from 0 to 360°. This is obviously due to the existence of a strong internal hydrogen bond in the stable conformation **3aH⁺** (Fig. 4). Breaking this bonding needs ca. 70–100 kJ/mol depending upon the rotating bond, the resulting entropy is consequently lower than that of the starting molecule **3a** (Table 6). Concerning the most stable cyclic structure **3aHc⁺**, internal rotations around several CC or CO bonds are replaced by ring deformations. These vibrational modes, as well as the internal hindered rotations, are not purely harmonic and cannot be treated by simply using the harmonic oscillator model. However, no simple mean is presently available

to calculate entropy contribution associated with ring deformation even if efforts are presently made in this field [44]. It should be noted however that the C5O7 linkage in structure **3aHc⁺** is not a full covalent bond. Its length is equal to 1.64 Å (Fig. 4) and rotations around the CC and CO bonds of the ring are associated with energies in the range 80–120 kJ/mol i.e., values comparable to that obtained for internal rotations in structure **3aH⁺**. We thus corrected the entropy calculation given by Gaussian for **3aHc⁺** by considering ring deformations, as well as the methyl and the hydroxyl groups, as hindered rotor (Table 6).

Experimental gas phase basicity of 2,5-hexanedione is close to 853 kJ/mol (± 3) (Table 2). Variable temperature high pressure experiments provide a PA(**3**) value of $893 \pm 3 \text{ kJ/mol}$ and a significantly negative protonation entropy of $-27 \pm 7 \text{ J mol}^{-1} \text{K}^{-1}$. The extended kinetic treatment presented here leads to a very close PA(**3**) value of $895 \pm 3 \text{ kJ/mol}$ and also to a negative protonation entropy. It may be recalled that the method is known to underestimate the absolute value of this entropic term [17,20,21], consequently the derived value of $-18 \pm 5 \text{ J mol}^{-1} \text{K}^{-1}$ must be considered as an upper limit to $\Delta_p S^{\circ}(\mathbf{3})$, in complete agreement with the Mautner result of $-27 \text{ J mol}^{-1} \text{K}^{-1}$ [22]. Theoretical expectations of these thermochemical quantities based on the two possible deprotonation processes **3aH⁺** \rightarrow **3a** and **3aHc⁺** \rightarrow **3a** are reported in Table 8. Whatever the structure of the protonated form, **3aH⁺** or **3aHc⁺**, it is clear that its tightness is to be opposed to the loose character of **3a**. Consequently, both situations give rise to a negative protonation entropy. Indeed, calculations indicate for $\Delta_p S^{\circ}(\mathbf{3})$ figures between ca. -20 and $-30 \text{ J mol}^{-1} \text{K}^{-1}$ for both **3aH⁺** \rightarrow **3a** and **3aHc⁺** \rightarrow **3a**. The comparison with the experimental value obtained by the equilibrium method at variable temperature i.e., $-27 \text{ J mol}^{-1} \text{K}^{-1}$ is excellent but, obviously, it does not allow

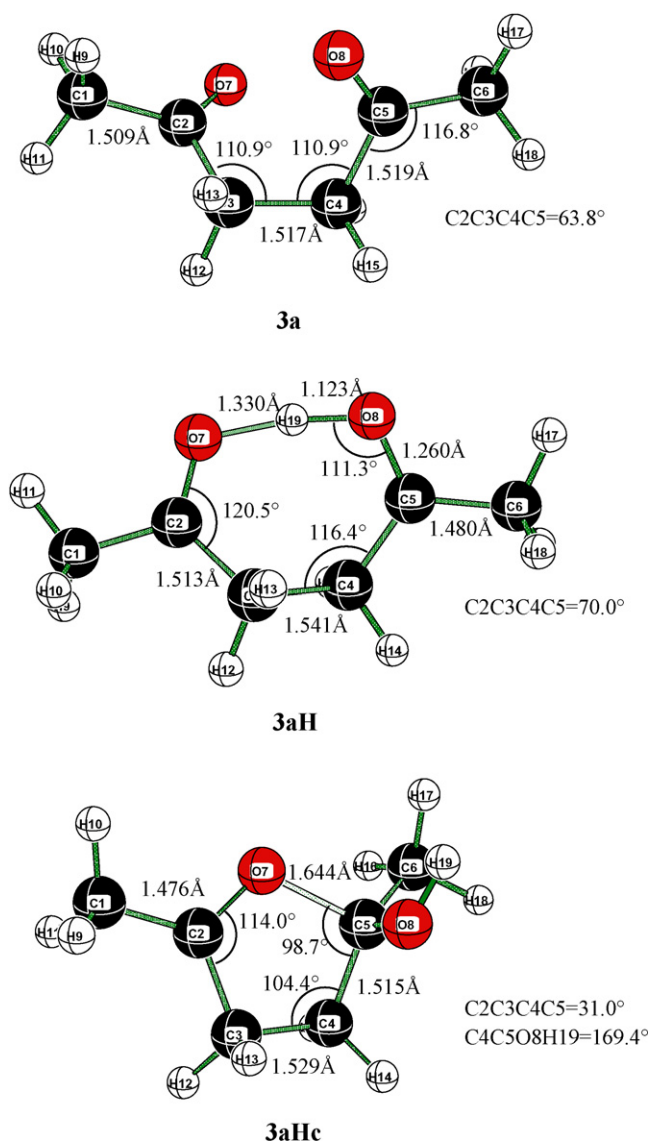
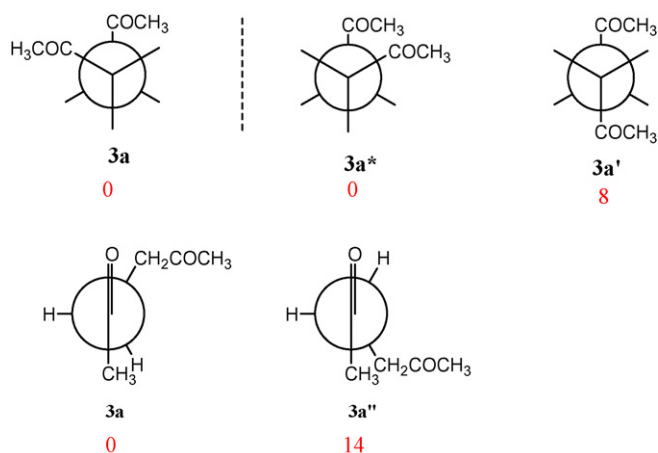


Fig. 4. MP2/6-31G(d) optimized geometries of the most stable conformations of 2,5-hexanedione, **3a** and its protonated forms **3aH⁺** and **3aHc⁺**.



Scheme 9.

a choice between the two possible protonated forms. The two protonation routes are however distinguishable from their associated proton affinities and gas phase basicities. The proton affinity of 2,5-hexanedione, PA(**3**), calculated for the process **3aHc⁺** → **3a**, is indeed equal to 892 kJ/mol (Table 8), in very close agreement with experiment while consideration of protonated structure **3aH⁺** corresponds to a PA(**3**) value too low by 10 kJ/mol. A similar observation stands for the gas phase basicities. This may be taken as evidences in favour of the formation of the cyclic **3aHc⁺** structure upon protonation of **3a** but additional studies are clearly needed to ascertain this structural assignment.

3.5. Methyl acetoacetate, **4**

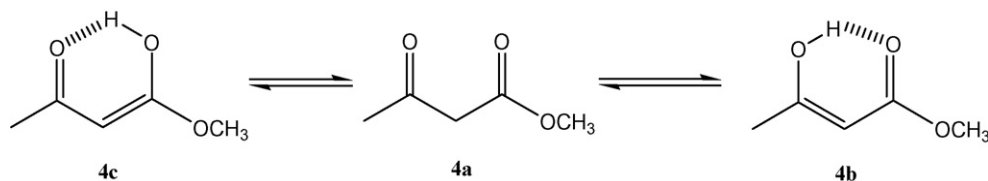
Methyl acetoacetate is another example of dicarbonyl compound for which the keto-enol tautomerism has attracted a large interest. The three possible tautomeric forms of methyl acetoacetate are the ketoester **4a**, the enolester **4b** and the ketoenol **4c** (Scheme 10).

¹H NMR spectra of methyl acetoacetate in the gas phase, at temperature between 380 and 420 K, have been interpreted in terms of a mixture of tautomers, with, probably a higher amount of enol structure(s) [37b]. Recently [43], a gas phase electron diffraction study is also interpreted by assuming a mixture of enolester **4b** (80 ± 7%) and ketoester **4a** (20 ± 7%) at 309 K. Only the enolester form **4b**, not the ketoenol **4c**, is claimed to be present in the mixture, a point also supported by molecular orbital calculations. The present quantum chemical calculations indicate that the 298 K enthalpy of the enolester **4b** is smaller than that of the ketoester **4a** by 6.7 kJ/mol at the G2MP2 level (Table 3). We also confirm that structure **4c** does not correspond to a minimum in the potential energy surface, all the tentative of optimisation converge toward **4b** by a simple shift of the hydroxyl hydrogen.

Concerning the ketoester structure **4a**, it may first be recalled that a Z arrangement of the OCOC atoms of the methoxycarbonyl group is always more stable than the E arrangement. Accordingly, the conformer E-**4a** is situated 37 kJ/mol above Z-**4a** (Scheme 11 and Fig. 5), and it could certainly not be representative of the structure **4a** present in the conditions of the mass spectrometry experiments.

The rotational barrier associated with Z-**4a** → E-**4a** is equal to 60 kJ/mol, a high value illustrating the large degree of conjugation of the lone pair of the oxygen of the methoxy group with the π electrons of the carbonyl. On the contrary, rotations around C2C3 and C3C4 bonds are associated with barriers less than 6 kJ/mol, thus allowing facile conformational change.

A conformational study of structure **4a** has been reported in [43], the authors identified three conformers of comparable energies. Our investigation of the rotational barriers extends these conclusions. Beside the previously identified conformers **4a-4a''** we also find that structure **4a'''** lies in a shallow potential energy well. Newman projections along the C2C3 axis of these four accessible conformations are summarized in Scheme 11. At the MP2/6-31G(d) level, conformers **4a-4a'''** are situated in a 3 kJ/mol energy range. It should be noted that **4a**, **4a''**



Scheme 10.

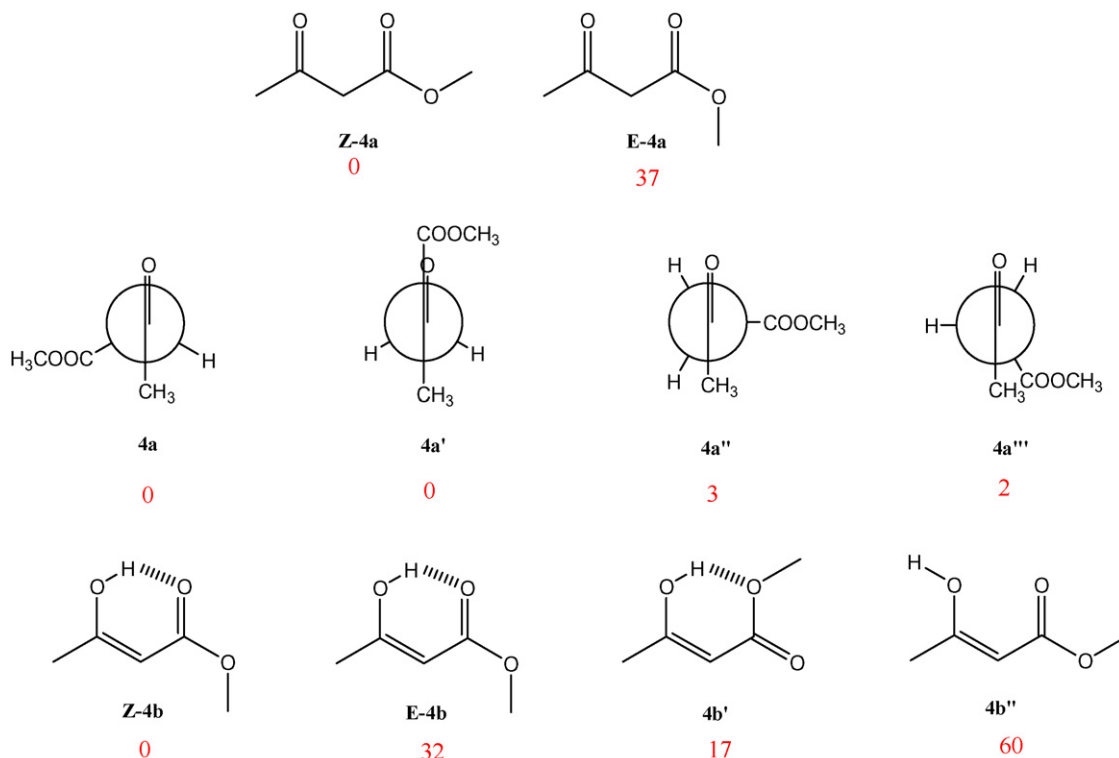
and **4a'''** possess enantiomeric homologues. We consequently approximate the molar entropy of **4a** by considering nine conformations of identical individual entropy and an entropy of mixing of $18 \text{ J mol}^{-1} \text{ K}^{-1}$ ($S^\circ(\mathbf{4a})$, Table 7).

The situation is less complex for the enol-ester form **4b**, since all the conformers other than the (*Z*)-**4b** structure (**4b**, Fig. 5) are so high in energy that, assuming that they possess similar entropies, they are not able to participate to a conformer mixture at room temperature. It is for example the case of structures **E-4b**, **4b'** and **4b''** which are situated 32, 17 and 60 kJ/mol above (*Z*)-**4b**, respectively. The heights of the barriers connecting all these structures with the most stable form **4b** are in the range 55–75 kJ/mol as reported in Table 7.

During our MP2/6-31G(d) conformational investigation, we find that the most stable protonated forms of **4a** and **4b** are the **4aH⁺** and **4bH⁺** structures depicted in Fig. 5. At all levels of theory the two structures are of comparable stability, with a slight preference for the **4aH⁺** structure. The 298 K enthalpy difference calculated at the G2MP2 level is equal to 3.2 kJ/mol, a value probably below the limit of accuracy of the method. Several other minima in the corresponding potential energy surface have been

identified and summarized in Scheme 12. The corresponding rotational barriers are close to 70 kJ/mol as indicated in Table 7. These data clearly show that it is sufficient to consider only the **4aH⁺** and **4bH⁺** structures as possible protonation products in the condition of temperature used in the mass spectrometry experiments.

To the best of our knowledge, no determination of the gas phase basicity of methylacetoacetate has been reported in the literature. The extended kinetic method results indicated in Table 2 are consequently the lone available data. Comparison of these experimental GB(**4**) and PA(**4**) values (833 ± 6 and 873 ± 6 kJ/mol, respectively) with the theoretical predictions given in Table 8 is hardly conclusive. Protonation of both **4a** and **4b** to give **4aH** and **4bH**, respectively, lead to a gas phase basicity close to 830 kJ/mol as experimentally observed. Some differences appear in the theoretical proton affinity values depending upon the structures considered. As evidenced in Table 7, the PA(**4**) values calculated by considering protonation of the neutral structure **4a** (867–870 kJ/mol) appear to be closer to the experimental result. The important point to note from examination of the experimental results of Table 2, is the occurrence



Scheme 11.

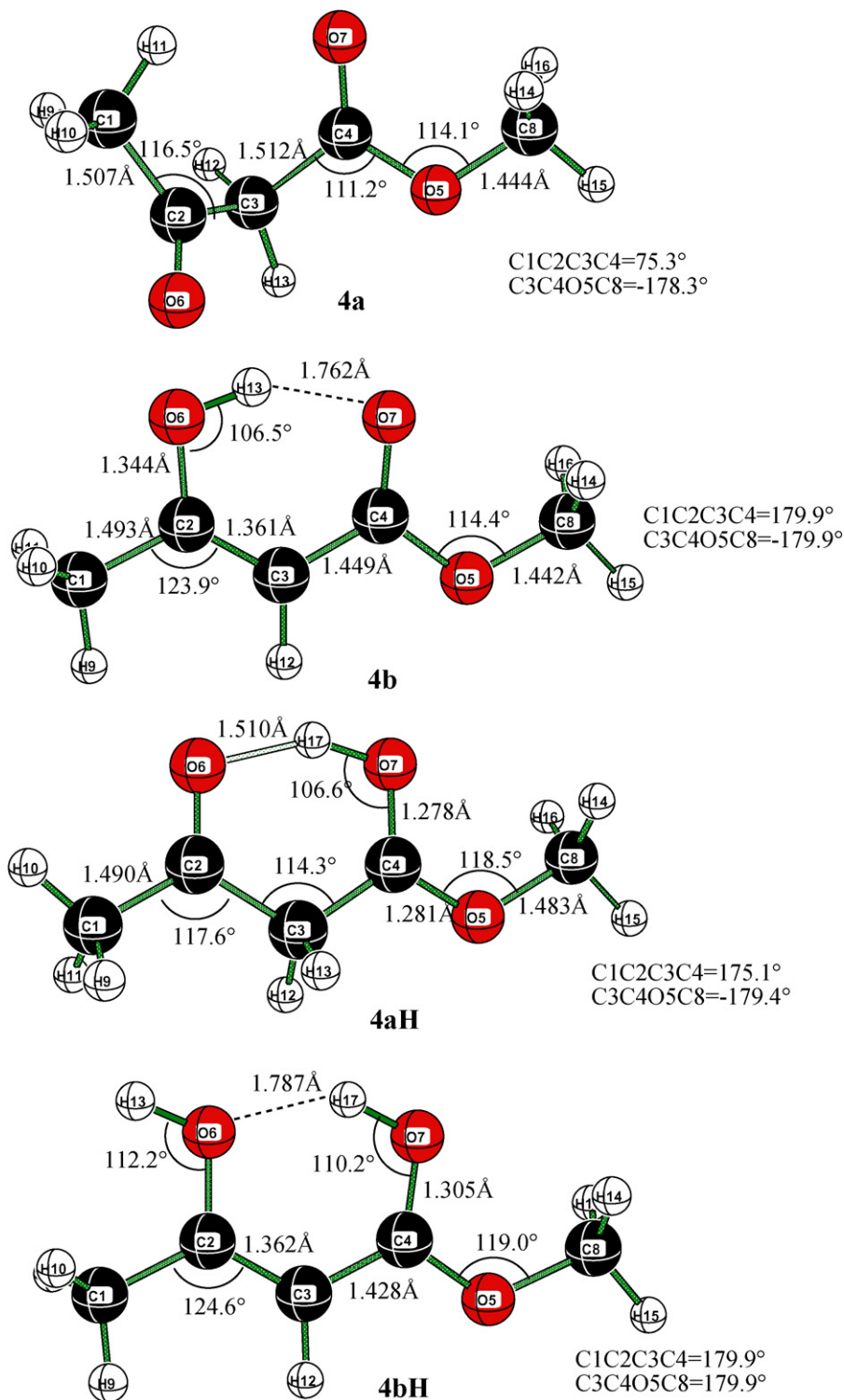


Fig. 5. MP2/6-31G(d) optimised geometries of the most stable conformations of methyl acetoacetate **4a** and methyl 3-hydroxy-2-ene-butanoate, **4b** and their protonated forms **4aH⁺** and **4bH⁺**.

of a large, negative, protonation entropy. Considering the drawback of the extended kinetic method, this observation points to a significant entropy loss during protonation, probably lower than $-20 \text{ J mol}^{-1} \text{ K}^{-1}$. Calculated thermochemistry reported in Table 8 shows that a negative protonation entropy is a charac-

teristic of the protonation of the ketoester structure **4a**. Thus, **4a** is necessarily present in the (possible) mixture of neutrals. Note that this is in contrast with the case of 2,4-pentanedione **2** where a negligible protonation entropy is measured in agreement with the existence of almost exclusively the ketoenol form **2b** as the

Table 7
Entropy calculation for the neutral and protonated methyl acetoacetate 4

Species	(a) $S^\circ_{\text{transl}}, S^\circ_{\text{rot}}, S^\circ_{\text{vib}}$	(b) Hindered rotations			(c) S°_{total}
		Bond	V_0	S°_{hind} (Pitzer)	
4a	168.0	C1C2	3.1	14.3	439.3 [457.5]
	119.3	C2C3	5.4	33.2	
	36.7	C3C4	4.1	34.7	
		C4O5	60.5	19.4	
		O5C8	4.4	13.7	
4b	168.0	C1C2	6.5	12.3	402.0
	118.8	C3C4	64.9	21.2	
	43.5	C4O5	52.7	19.7	
		C2O6	76.0	5.0	
		O5C8	4.6	13.5	
4aH⁺	168.2	C1C2	1.8	14.8	417.9
	118.9	C2C3	76.2	20.1	
	42.7	C3C4	70.2	20.9	
		C4O5	76.7	18.0	
		O5C8	3.5	14.3	
4bH⁺	168.2	C1C2	6.6	12.3	407.9
	119.1	C3C4	68.9	20.8	
	44.0	C4O5	63.3	18.8	
		C4O7	70.4	5.1	
		O5C8	2.9	13.9	
		C2O6	57.1	5.7	

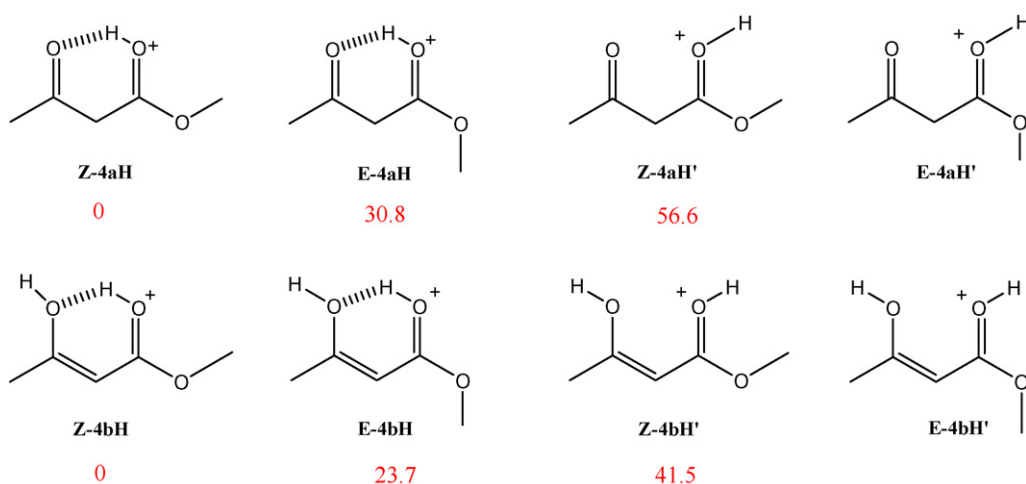
(a) Translational, rotational and vibrational contributions to entropies. Hindered rotations are not included in the S°_{vib} term.

(b) Potential energy barrier V_0 of the internal rotation around the “bond”; value in kJ/mol, calculated at the MP2/6-31G(d) level. Contribution to the entropy of the torsional modes are calculated using the Pitzer’s procedure (see text).

(c) Total calculated entropy ($\text{J mol}^{-1} \text{K}^{-1}$) of the species considered into brackets, entropy calculation including an entropy of mixing (nine conformers assumed, see text).

neutral specie. To return back to methyl acetoacetate, consideration of enolester **4b** would lead to a negligible, though slightly positive, protonation entropy (Table 8). Consequently, its presence in small amount in the neutral mixture cannot be completely excluded from the protonation entropy measurement. The most logical conclusion here, if we suppose that no tautomerization occurs in either the neutral or the protonated forms of methyl acetoacetate, is that the mass spectrometry experimental

results may be interpreted by a major, even exclusive, participation of the $\mathbf{4aH}^+ \rightarrow \mathbf{4a} + \text{H}^+$ process plus a possible minor $\mathbf{4bH}^+ \rightarrow \mathbf{4b} + \text{H}^+$ contribution. Obviously, this conclusion is at variance from that derived from the electron diffraction study of [43]. It should be noted however that different temperatures are used in both experiments. The higher temperature used in mass spectrometry experiment (i.e., $\sim 480 \text{ K}$) samples the higher entropy component **4a**.



Scheme 12.

Table 8
Calculated proton affinities, protonation entropies and gas phase basicities of molecules **1–4**

M	Assumed species	PA(M) ^{a,b}	$\Delta_p S^\circ$ (M) ^c	GB(M) ^{a,d}
2,3-Butanedione, 1	1aH ⁺ → 1a	781.9	4	750.7
	1bH ⁺ → 1a	799.1	–8	764.2
	1aH ⁺ → 1b	810.0	15	782.0
	1bH ⁺ → 1b	817.0	3	785.5
2,4-Pentanedione, 2	2aH ⁺ → 2b	850.2	15	822.2
	2aH ⁺ → 2a	858.6	–11 [–17]	822.9 [821.1]
	2bH ⁺ → 2b	865.0	8	835.0
	2bH ⁺ → 2a	873.4	–19 [–25]	835.3 [833.6]
2,5-Hexanedione, 3	3aH ⁺ → 3a	882.2	–16 [–25]	844.8 [842.1]
	3aHc ⁺ → 3a	892.0	–24 [–33]	852.2 [849.5]
Methyl acetoacetate, 4	4bH ⁺ → 4b	860.4	6	829.8
	4aH ⁺ → 4b	863.6	16	835.9
	4bH ⁺ → 4a	867.1	–31 [–50]	825.4 [819.8]
	4aH ⁺ → 4a	870.3	–21 [–40]	831.6 [826.0]

^a kJ mol^{–1}.

^b G2MP2 results.

^c J K^{–1} mol^{–1}.

^d Calculated using the relationship GB(M) = PA(M) – 298[108.7 – $\Delta_p S^\circ$ (M)]10^{–3} kJ/mol and the data in columns 3 and 4.

4. Conclusions

An experimental and theoretical study of the protonation of representative dicarbonyl compounds M = **1–4** has been carried out. For M = **1–3**, the experimental gas phase basicity values given by the extended kinetic method, using the ODR treatment, are very close to that derived from equilibrium measurements. In the average, the deviations in GB(M) are less than 3 kJ/mol i.e., less than the experimental uncertainties. This comparison also confirms that the extended kinetic method provides only an upper limit to the protonation entropy. This limitation in mind, the data show that protonation of **1** and **2** is associated with negligible protonation entropies while significant negative values are obtained for molecules **3** and **4**.

The comparison between experimental and theoretical thermochemical data reveals the following specific behaviours:

- The protonation of 2,3-butanedione, **1a**, is associated with a tautomerisation inside the proton transfer complex thus leading to protonated 2-hydroxy-butenone, **1bH**⁺; a simple mechanism, involving an intramolecular 1,4-hydrogen migration, may account for this result.
- The protonation thermochemistry of 2,4-pentanedione **2** may be simply rationalized by the protonation of its most stable tautomer, the 4-hydroxy-3-pentene-2-one, **2b**, to give its most stable protonated form **2bH**⁺.
- If the structure of neutral 2,5-hexanedione is without doubt the dicarbonyl form **3a**, the comparison between experimental and theoretical protonation thermochemistry suggests that its protonation, under the experimental mass spectrometric conditions, would produce the cyclic **3aHc**⁺ structure stabilized by a covalent bonding; formation of a structure stabilized by an internal hydrogen bond, **3aH**⁺, can not be however completely excluded in view of the present data alone.

- The structure of neutral methyl acetoacetate **4** sampled during protonation in mass spectrometry experiments is most probably its diketonic form **4a**; its protonation leads to the structure **4aH**⁺.

This study shows again that the protonation of polyfunctional compounds could not only produce species stabilized by internal hydrogen bond but also that more profound structural changes, such as tautomerisation or covalent bond forming, may be also operative. It also illustrates the necessary interplay between experiment and theory to interpret conveniently the data.

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