



Special Issue Celebrating the 20th Anniversary of *EJMS—European Journal of Mass Spectrometry*

Gas-phase lithium cation affinity of glycine

Sophie Bourcier,^a Ru Xuan Chia,^{a,b} Rosa Ngo Biboum Bimbong^c and Guy Bouchoux^{a,d*}

^aLaboratoire de Chimie Moléculaire, Ecole Polytechnique, UMR 9168 CNRS, 91128 Palaiseau, France. E-mail: guy.bouchoux@polytechnique.edu

^bNanyang Technological University, 21 Nanyang Link, 637371 Singapore

^cUniversité de Tours, Département de Chimie, Parc Grandmont, 37200 Tours, France

^dUniversité Paris-Sud XI, 91400 Orsay, France

The gas-phase lithium cation binding thermochemistry of glycine has been determined theoretically by quantum chemical calculations at the G4 level and experimentally by the extended kinetic method using electrospray ionization quadrupole time-of-flight tandem mass spectrometry. The lithium cation affinity of glycine, $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$, i.e. the $\Delta_{\text{Li}}H_{298}^{\circ}$ of the reaction $\text{GlyLi}^+ \rightarrow \text{Gly} + \text{Li}^+$, given by the G4 method is equal to $241.4 \text{ kJ mol}^{-1}$ if only the most stable conformer of glycine is considered or to $242.3 \text{ kJ mol}^{-1}$ if the 298 K equilibrium mixture of neutral conformers is included in the calculation. The $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$ deduced from the extended kinetic method is obviously dependent on the choice of the Li^+ affinity scale; thus, $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$ is equal to $228.7 \pm 0.9(2.0) \text{ kJ mol}^{-1}$ if anchored to the recently re-evaluated lithium cation affinity scale, but shifted to $235.4 \pm 1.0 \text{ kJ mol}^{-1}$ if G4 computed lithium cation affinities of the reference molecules are used. This difference of 6.3 kJ mol^{-1} may originate from a compression of the experimental lithium affinity scale in the high $\Delta_{\text{Li}}H_{298}^{\circ}$ region. The entropy change associated with the reaction $\text{GlyLi}^+ \rightarrow \text{Gly} + \text{Li}^+$ reveals a gain of approximately $15 \text{ J mol}^{-1} \text{ K}^{-1}$ with respect to monodentate Li^+ acceptors. The origin of this excess entropy is attributed to the bidentate interaction between the Li^+ cation and both the carbonyl oxygen and the nitrogen atoms of glycine. The computed G4 Gibbs free energy, $\Delta_{\text{Li}}G_{298}^{\circ}(\text{GLY})$, is equal to $205.3 \text{ kJ mol}^{-1}$; a similar result, $201.0 \pm 3.4 \text{ kJ mol}^{-1}$, is obtained from the experiment if the $\Delta_{\text{Li}}G_{298}^{\circ}$ of the reference molecules is anchored on the G4 results.

Keywords: lithium cation affinity scale, extended kinetic method, G4 computation, amino acids

Introduction

Thermochemical parameters associated with the attachment of a cationic species to isolated organic and bio-organic molecules have been the subject of intense research activities since the 1970s. From this point of view, protonation, as the most ubiquitous process in gas-phase chemistry, is by far the most documented.^{1–7} However, quantitative data concerning metal and alkali cations binding to organic and bio-organic molecules have increasingly accumulated during the past decades.^{8,9} In this area, lithium cation binding thermochemical parameters have been a matter of debate during the past 24 years.^{10–18} A recent re-examination of the lithium binding energies of a large set of reference molecules corrects previous estimates by no less than several tenths of kJ mol^{-1} .¹⁸ These results questioned the validity associated with molecules of

biological interest, such as the amino acids. The present work aimed to determine the lithium cation binding energy and entropy of the simplest amino acid, glycine, by reference to a set of monodentate compounds recently re-examined.

Formally, cation binding enthalpies, $\Delta_{\text{cat}}H_T^{\circ}(\text{M})$, entropies, $\Delta_{\text{cat}}S_T^{\circ}(\text{M})$, and Gibbs free energies, $\Delta_{\text{cat}}G_T^{\circ}(\text{M})$, of a molecule M are defined from the gas-phase dissociation reaction:



Concerning the commonly used nomenclature, when $\text{Cat}^+ = \text{H}^+$, the standard enthalpy, $\Delta_{\text{H}}H_T^{\circ}(\text{M})$, and Gibbs free energies, $\Delta_{\text{H}}G_T^{\circ}(\text{M})$, of reaction (1) are also called proton affinity, $\text{PA}(\text{M})$, and gas-phase basicity, $\text{GB}(\text{M})$, respectively. Introducing the entropy of reaction (1), $\Delta_{\text{H}}S_T^{\circ}(\text{M})$, the term

'protonation entropy' has been applied to the difference, $\Delta\Delta_{\text{H}}S_{\text{T}}^{\circ}(\text{M}) = S_{\text{T}}^{\circ}(\text{MH}^+) - S_{\text{T}}^{\circ}(\text{M})$, thus leading to the relationship $\Delta_{\text{H}}S_{\text{T}}^{\circ} = S_{\text{T}}^{\circ}(\text{Cat}^+) - \Delta\Delta_{\text{H}}S_{\text{T}}^{\circ}(\text{M})$. It is perhaps interesting to underline that most of the tabulated PA(M), GB(M) and $\Delta\Delta_{\text{H}}S_{\text{T}}^{\circ}(\text{M})$ values are given at a temperature $T = 298\text{K}^{1-7}$. By analogy with gas-phase protonation thermochemistry, gas-phase lithium cation affinity, $\text{LCA}_{\text{T}}(\text{M})$, and gas-phase lithium cation basicity, $\text{LCB}_{\text{T}}(\text{M})$, have been defined by the enthalpy and Gibbs free energy changes of reaction (1), respectively, with $\text{Cat}^+ = \text{Li}^+$. In the following lines, however, we will make use of the more explicit notations, $\Delta_{\text{L}}H_{\text{T}}^{\circ}(\text{M})$, $\Delta_{\text{L}}G_{\text{T}}^{\circ}(\text{M})$, $\Delta_{\text{L}}S_{\text{T}}^{\circ}(\text{M})$ and $\Delta\Delta_{\text{L}}S_{\text{T}}^{\circ}(\text{M})$ [i.e. $S_{\text{T}}^{\circ}(\text{MLi}^+) - S_{\text{T}}^{\circ}(\text{M})$].

The most common methods for measuring thermochemical quantities in the gas-phase^{4,19} are based either on (i) cation exchange experiments between M and a reference compound B, such as in equilibrium^{4,20} and thermokinetic^{4,21} methods, or (ii) on competitive dissociations of mixed cationized dimers, MCatB^+ , such as in the so-called kinetic methods^{4,22}. These methods, by principle, provide relative binding parameters. However, in principle, absolute determinations are possible by measurement of the energy threshold for reaction (1) after collisional activation of the MCat^+ parent ions and *ad hoc* data handling.^{16,23} Among these various experimental approaches, the most easily tractable is the kinetic method since it does not need a dedicated experimental apparatus (a standard tandem mass spectrometer may be used) and it may be applied to non-volatile samples. Two attempts at determination of the lithium cation affinity of glycine have been done using the kinetic method.^{24,25} It has been, however, established in recent years that the kinetic method, in its simple version as utilized in references 24 and 25, may be erroneous if binding entropies of M and B are different, as expected in the present case. Accordingly, former quantum chemistry calculations established that glycine behaves as a bidentate base with respect to the proton⁶ or metal cation²⁶⁻³⁰ and thus presents constrained cationized forms that may influence the corresponding thermochemistry. From a theoretical point of view, when considering the previous studies devoted to glycine,²⁶⁻³⁰ it is observed that its estimated lithium cation affinity falls in a very wide range of values, situated between 228kJ mol^{-1} and 276kJ mol^{-1} , depending upon the theoretical level used. The goal of the present study was to reexamine the gas-phase lithium cation binding thermochemistry of glycine by using (i) the extended kinetic method applied to tandem mass spectrometry (MS/MS) experiments, and (ii) the most recent quantum chemical composite method of calculation of thermochemical quantities, G4.³¹

Experimental and computational methods

Electrospray ionization quadrupole MS/MS experiments were carried out in a Waters Q-TOF in a positive ion mode working in the MassLynx 4.1 environment. The cone voltage was set to 30V

while the capillary voltage was varied between 2.0 and 3.5 kV to optimize the conditions for obtaining the maximum intensity of the lithiated dimers. Typical values for the other source parameters were: extraction cone 2V, ion guide 2.4V. The pulse velocity in the T-Wave apparatus was 300ms^{-1} and the source temperature was set to 80°C . Collision-induced dissociation (CID)-MS/MS spectra were obtained using argon as the collision gas at a pressure of $1.5 \times 10^{-3}\text{mbar}$. Experimental data were collected at several different collision energies in the laboratory frame, E_{lab} , of lithiated dimers. It was considered that the kinetic energy of the ions entering the gas cell is related to the voltage difference between the ion guide and the gas cell. This voltage difference is simply given by the sum of the static offset value (so-called 'collision energy') and the ion guide value. Practically, the range of explored i_{lab} values extended from 0 eV to 28 eV. The center-of-mass collision energy, E_{cm} , was calculated by the usual conversion expression $E_{\text{cm}} = E_{\text{lab}}m_{\text{target}}/(m_{\text{target}} + m_{\text{ion}})$. A scan rate of 1s scan^{-1} was used for all experiments with a data-acquisition duration of 60s for each energy step. Six reference bases, B_i , were used to produce the relevant lithiated bound heterodimer $[\text{GlyLiB}_i]^+$. Solutions of glycine, reference base and lithium chloride were prepared in water at 10^{-2}M . Solutions were diluted in a 50/50 mixture of methanol and water. The concentration ratio used to form $[\text{GlyB}_i\text{Li}]^+$ was $10^{-3}/10^{-5}/10^{-3}\text{M Gly/B}_i/\text{LiCl}$. All the solutions were infused at a flow rate of $2\mu\text{Lmin}^{-1}$ with a CIL Cluzeau (Courbevoie, France) syringe. All samples and solvents of HPLC grade were purchased from Sigma-Aldrich (St Quentin Fallavier, France) and used as received without any further purification.

The CIDs of the mass selected $[\text{GlyHB}_i]^+$ ions were examined by the extended kinetic method, i.e. the natural logarithm of the fragment ions abundances $y_i = \ln([\text{GlyLi}]/[\text{B}_i\text{Li}]^+)$ was correlated with the lithium cation affinity of the reference base B_i , $\Delta_{\text{L}}H_{298}^{\circ}(\text{B}_i)$. The $[\text{GlyLi}]^+$ and $[\text{B}_i\text{Li}]^+$ intensities were evaluated by summing the fragment ion abundances of each lithiated species. This procedure is essentially correct if no further excitation energy is given to the produced fragment ions in the T-Wave collision cell, as checked by controlling that an increase in argon pressure does not lead to a noticeable change in the relative ion abundances.³² The results discussed below correspond to y_i determined at several typical E_{cm} values situated between 0.5 eV and 5.0 eV.

Standard *ab initio* molecular orbital theory and density functional theory calculations were carried out with the Gaussian09 computer program.³³ The various possible conformations of neutral and lithiated glycine and reference compounds were first examined at the B3LYP/6-31 + G(d,p) level. A high-level G4 composite procedure³¹ was then used to determine accurate lithium binding thermochemical parameters at 298K and 373K. In the G4 approach, geometry optimization is conducted at the B3LYP/6-31G(2df,p) level. The corresponding equilibrium structure is used to calculate harmonic frequencies, which are scaled by a factor of 0.9854 to calculate the zero-point energy (ZPE). This latter point is a change from the previous G2^{34,35} and G3³⁶ theories in which HF/6-31G(d) was used to evaluate

ZPE. Another novelty of the G4 theory includes an extrapolation procedure to obtain the Hartree–Fock energy using Dunning's basis set, up to aug-cc-pV5Z. In addition, the total G4 energy is obtained from a series of single-point correlation energy limit calculations involving coupled cluster theory [CCSD(T)/6-31G(d) level] and MP2 and MP4 calculations using larger basis sets that include diffuse and polarization functions (up to 3d on the first row atoms). Finally, spin-orbit and high level corrections parameters are included to take into account remaining deficiencies.

It may be emphasized that recently the G4 method was demonstrated as currently being the most accurate way to calculate Li^+ , Na^+ and K^+ affinities and basicities¹⁸.

Results and discussion

As indicated in the experimental part, and will be developed in the section Essential basis of the extended kinetic method, the kinetic method involves several reference compounds B_i for which the $\Delta_{\text{Li}}H_{298}$ is well defined. In the present study, the set of B_i allowing the determination of $\Delta_{\text{Li}}H_{298}(\text{GLY})$ includes: **DMF** [*N,N*-dimethylformamide, $\text{HCON}(\text{CH}_3)_2$], **DMSO** [dimethyl sulfoxide, $(\text{CH}_3)_2\text{SO}$], **DMA** [*N,N*-dimethylacetamide, $\text{CH}_3\text{CON}(\text{CH}_3)_2$], **NMA** [*N*-methylacetamide, $\text{CH}_3\text{CONH}(\text{CH}_3)$], **TMP** [trimethyl phosphine, $\text{OP}(\text{OCH}_3)_3$] and **PENT** [2,4-pentanedione, $\text{CH}_3\text{COCH}_2\text{COCH}_3$]. Two additional species, namely water, **H₂O**, and pyridine, **PYR**, are also considered here since their $\Delta_{\text{Li}}H_{298}$ values have been used as anchoring points in a number of previous studies. All these compounds, together with glycine, were studied by quantum chemistry methods up to the G4 level of theory. This section is organized in four parts. In the first one, theoretical results related to neutral and lithiated glycine and reference molecules are presented. The present status of the lithium affinity scale is summarized in the second part, while parts 3 and 4 present the extended kinetic method and the results obtained for glycine during our investigation.

Computed lithium binding thermochemistry of glycine and of reference compounds

Optimized structures of neutral and lithiated glycine, **GLY** and **GLYLi⁺**, at the B3LYP/6-31G(2df,p) level (as used in the G4 procedure) are reported in Figure 1. Similar data concerning the structures of neutral reference compounds **NMA**, **DMF**, **DMSO**, **DMA**, **PENT**, **PYR**, **H₂O** and their lithiated counterparts are collected in Figure 2.

Previous theoretical works demonstrated the existence of four stable conformations for neutral glycine in an enthalpy range of $\sim 7 \text{ kJ mol}^{-1}$.⁶ This is confirmed at the G4 level of theory as illustrated in Figure 1. The most stable conformer, **GlyI**, presents a $\text{NH}_2 \cdots \text{OCOH}$ favorable bisected interaction and a OCOH *syn* arrangement allowing an internal extra stabilization. A slight rotation of the NH_2 group leads to conformer **GlyI'** in which a single $\text{NH} \cdots \text{OCOH}$ interaction is operating. Conformer **GlyII** is characterized by a strong $\text{OH} \cdots \text{NH}_2$ hydrogen bonding

which almost overcomes the loss of the stabilizing effect of the HOCO *anti* arrangement. Finally, a 180° rotation of the acidic group in **GlyI** produces conformer **GlyIII**. At 298K and at the G4 level, these four conformations are predicted to represent a population **GlyI/GlyI'/GlyII/GlyIII** of 82/6/6/6%.

In lithiated glycine, the most stable conformer, **GlyLiIa**, may be seen to result from the cationization of conformer **GlyI**. Indeed, in **GlyLiIa** the lithium cation is coordinated to the oxygen carbonyl ($\text{O} \cdots \text{Li}$ distance = 1.844 \AA) and strongly interacts with the nitrogen of the amino group ($\text{Li} \cdots \text{N}$ distance = 2.049 \AA). Changing the HOCO arrangement from *syn* to *anti* produces the new conformer **GlyLiIb** which lies 22 kJ mol^{-1} above **GlyLiIa**. It is noteworthy that the lithiated zwitterionic form

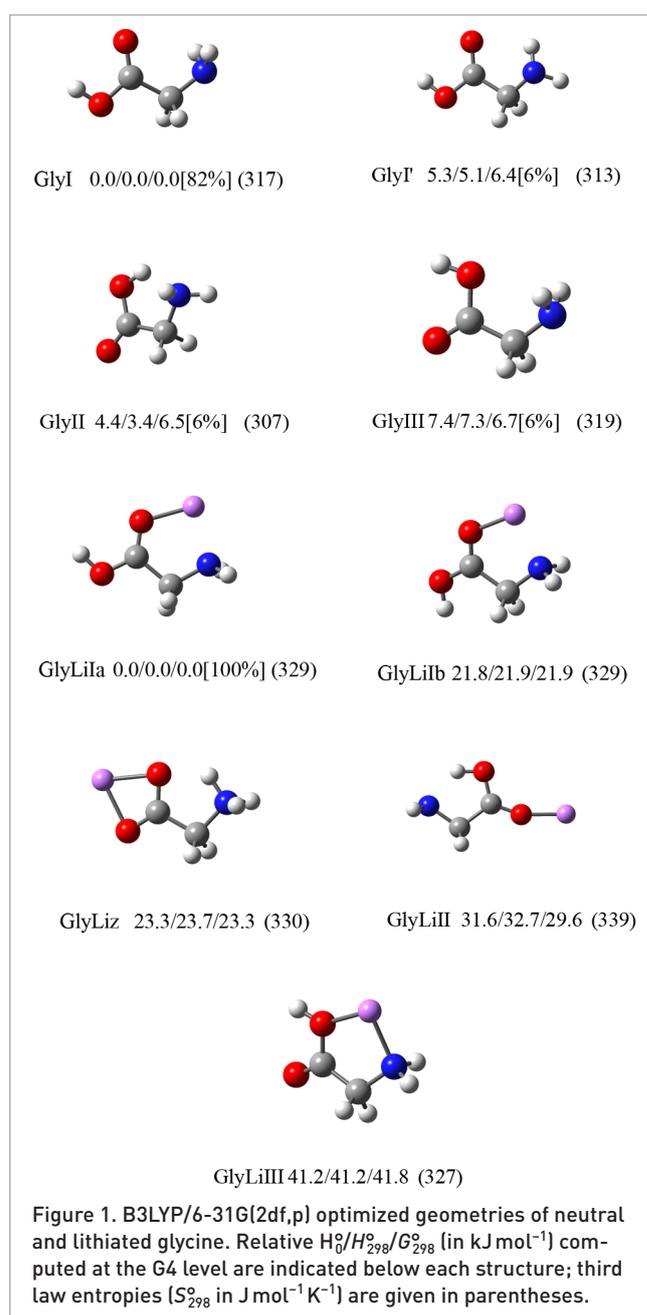
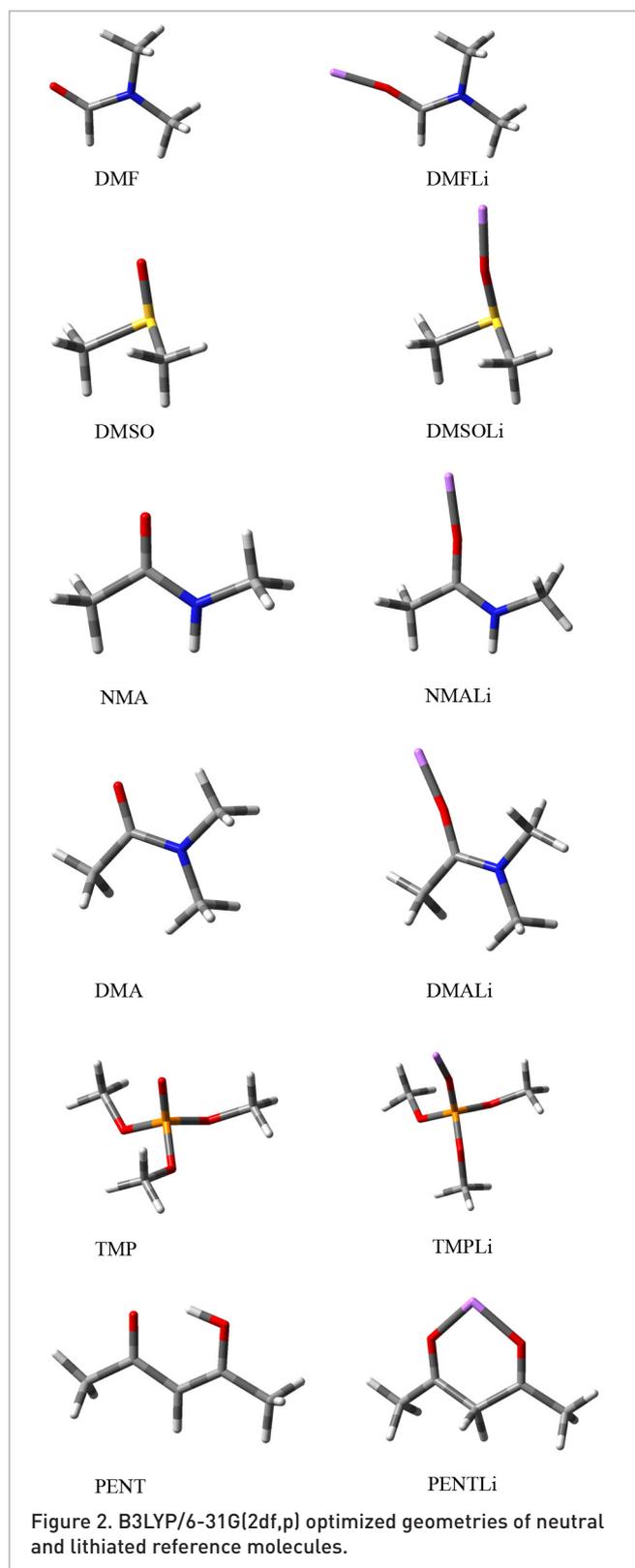


Figure 1. B3LYP/6-31G(2df,p) optimized geometries of neutral and lithiated glycine. Relative $H_0^{\circ}/H_{298}^{\circ}/G_{298}^{\circ}$ (in kJ mol^{-1}) computed at the G4 level are indicated below each structure; third law entropies [S_{298}° in $\text{J mol}^{-1} \text{K}^{-1}$] are given in parentheses.



of glycine, **GlyLiz**, is close in energy to **GlyLiIb**, while it is known that glycine zwitterion is not a stable species in the gas phase. Lithiation of the neutral conformer **GlyII** leads to the high-energy species **GlyLiII** situated ca. 30 kJ mol^{-1} above

GlyLiIa. The last conformer of lithiated glycine presented in Figure 1, namely **GlyLiIII**, is situated more than 40 kJ mol^{-1} above **GlyLiIa**. In summary, at 298K, the most stable conformer **GlyLiIa** is predicted to be lying more than 20 kJ mol^{-1} below the other conformers and consequently represents the exclusive form of lithiated glycine in the gas phase.

Most of the reference molecules are oxygen bases and are expected to react with Li^+ to form a monodentate complex. Figure 2 shows that this is, indeed, the case, except for 2,4-pentanedione, **PENT**. This neutral molecule is more stable in its tautomeric form in which an internal hydrogen bond ($\text{C}=\text{O}\cdots\text{HO} = 1.59 \text{ \AA}$) imposes a rigid conformation of the heavy atom skeleton. The most stable lithiated species, **PENTLi⁺**, is characterized by the formation of a chelate between Li^+ and 2,4-pentanedione in its diketonic form. The two $\text{O}\cdots\text{Li}$ distances are identical and equal to 1.845 \AA , thus slightly elongated with respect to the $\text{O}\cdots\text{Li}$ distances of $\sim 1.7 \text{ \AA}$ that occur in the other reference molecules.

A summary of the computed G4 thermochemistry of glycine and of the above-mentioned reference species is presented in Table 1. Comparison with other high-level calculations is also documented in Table 1.

A first comment arising from a global examination of Table 1 is that the G4 and G3 methods lead to similar $\Delta_{\text{Li}}H_{298}^{\circ}$ values. This observation confirms those of Mayeux *et al.*¹⁷ and of Rogers and Armentrout,¹⁶ who claimed that the best performances for lithium cation calculations are obtained with these high-level methods. By contrast, a systematic underestimate of $\Delta_{\text{Li}}H_{298}^{\circ}$ values seems to be associated with G2 and G2MP2 results. In fact, considering the nine species M quoted in Table 1, the average difference [$\Delta_{\text{Li}}H_{298}^{\circ}(\text{G4}) - \Delta_{\text{Li}}H_{298}^{\circ}(\text{G2MP2})$] is equal to $5.8 \pm 1.2 \text{ kJ mol}^{-1}$. These non-negligible differences should be attributed to deficiencies of the G2 and G2MP2 recipes, which are largely corrected in the latest versions of the Gn composite procedures G3 and G4. An illustrative remark concerns the ionization energy of gaseous lithium, $\text{IE}(\text{Li})$. The experimental value (5.392 eV) is correctly reproduced by G3 and G4 methods while G2MP2 and G2 underestimate this quantity by 0.05 eV . The difference $\text{IE}(\text{Li}, \text{G4}) - \text{IE}(\text{Li}, \text{G2MP2})$ represents no less than 6.7 kJ mol^{-1} and, undoubtedly, this has repercussions on the corresponding $\Delta_{\text{Li}}H_{298}^{\circ}$ differences.

The lithium cation affinity of glycine, $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$, given by the G4 method is equal to $241.4 \text{ kJ mol}^{-1}$ if only conformer **GlyI** is considered, or to $242.3 \text{ kJ mol}^{-1}$ if the 298K equilibrium mixture of neutral conformers is included in the calculation. Another way to consider the theoretical results presented in Table 1 is to say that $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$ is higher than $\Delta_{\text{Li}}H_{298}^{\circ}(\text{H}_2\text{O})$ and $\Delta_{\text{Li}}H_{298}^{\circ}(\text{PYR})$ by 100 kJ mol^{-1} and 55 kJ mol^{-1} , respectively. As indicated in Table 1, the G4 calculated entropy difference $\Delta\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) = S_{298}^{\circ}(\text{GLYLi}^+) - S_{298}^{\circ}(\text{GLY}) = 12 \text{ J mol}^{-1} \text{ K}^{-1}$. This value is not significantly changed if the mixture of neutral glycine conformers in thermal equilibrium at 298K is taken into account. By contrast, the reference compounds **DMF**, **DMSO**, **NMA**, **DMA**, **TMP** and **PENT** possess an average $\langle\Delta\Delta_{\text{Li}}S_{298}^{\circ}\rangle$ value equal to $33.1 \pm 5.1 \text{ J mol}^{-1} \text{ K}^{-1}$. It is interesting to examine the reasons of these differences. Let us take **DMF**

Table 1. Theoretical Li⁺ binding enthalpies, $\Delta_{\text{Li}}H_0^\circ$ (kJ mol⁻¹), Gibbs free energies, $\Delta_{\text{Li}}G_0^\circ$ (kJ mol⁻¹) and entropy differences, $\Delta\Delta_{\text{Li}}S_{298}^\circ = S^\circ(\text{MLi}^+) - S^\circ(\text{M})$ (J mol⁻¹ K⁻¹), computed at various levels of theory.^a

M	G4 calculations				Other theoretical $\Delta_{\text{Li}}H_{298}$ estimates		
	$\Delta_{\text{Li}}H_0$	$\Delta_{\text{Li}}H_{298}$	$\Delta_{\text{Li}}G_{298}$	$\Delta\Delta_{\text{Li}}S_{298}^\circ$ ^b	G3	G2	G2MP2
GLY (glycine)	236.9	241.4 242.3	205.3 <i>206.5</i>	12.0 <i>12.8 (7.3)</i>	242.9 ^c [248.2 ^{d,e}]	235.0 ^c [240.4 ^{d,e}]	234.5 ^c –
DMF (N,N-dimethylformamide)	225.8	228.1	198.4	33.4	227.9 ^c 228.0 ^d	222.1 ^c 222.2 ^d	222.1 ^c 222.1 ^f
DMSO (dimethyl sulfoxide)	228.8	231.0	201.3	33.5	229.2 ^c	224.8 ^c	225.0 ^c 226.6 ^f
NMA (anti-N-methylacetamide)	228.1	231.1	197.4	26.9	231.4 ^c	225.2 ^c	225.1 ^c
DMA (N,N-dimethylacetamide)	235.7	237.8	210.4	41.4	238.1 ^c	231.5 ^c	231.6 ^c 229.8 ^f
TMP (trimethyl phosphate)	240.7	242.3 242.7	213.0 <i>213.6</i>	34.7	241.7 ^c	235.6 ^c	235.0 ^c 235.8 ^f
PENT (2,4-pentanedione)	244.6	246.9	215.8	28.8	247.4 ^c	244.3 ^c	243.9 ^c
H₂O (water)	137.3	141.5	114.9	43.8	141.2 ^c 141.0 ^d	136.7 ^c 136.5 ^d	135.8 ^c 135.3 ^f
PYR (pyridine)	184.8	187.0	156.7	31.6	186.9 ^c 187.1 ^d	182.3 ^c 182.0 ^d	181.9 ^c 182.2 ^f

^aItalic font: averaged over the conformers population at 298 K (see text).

^b $\Delta\Delta_{\text{Li}}S_{298}^\circ = S_{298}^\circ(\text{MLi}^+) - S_{298}^\circ(\text{M})$; note that, according to the Seckur–Tetrode equation, $S_{298}^\circ(\text{Li}^+) = 133.1 \text{ J mol}^{-1} \text{ K}^{-1}$ [and $S_{373}^\circ(\text{Li}^+) = 137.7 \text{ J mol}^{-1} \text{ K}^{-1}$].

^cPresent work.

^dFrom Rodgers and Armentrout,¹⁶ corrected to 298K using G4-calculated enthalpy differences between 0K and 298K.

^eProbably obtained by using a neutral glycine conformer different to Glyl.

^fFrom $\Delta_{\text{Li}}G_{298}$ computed at the G2MP2 level in Mayeux et al.,¹⁷ corrected to $\Delta_{\text{Li}}H_{298}$ by using a G4 entropy calculated at 298K.

as a representative case, its entropy difference $\Delta\Delta_{\text{Li}}S_{298}^\circ(\text{DMF}) = S_{298}^\circ(\text{DMFLi}^+) - S_{298}^\circ(\text{DMF})$ is equal to 33.4 J mol⁻¹ K⁻¹ (Table 1). This difference essentially originates from the occurrence of three new vibrational modes in **DMFLi**⁺, with respect to **DMF**, which may be attributed to Li–O = C deformations (114 cm⁻¹ and 128 cm⁻¹) and Li–O stretching (558 cm⁻¹). This contributes 30 J mol⁻¹ K⁻¹, i.e. the major part of $\Delta\Delta_{\text{Li}}S_{298}^\circ(\text{DMF})$. In the case of glycine, the frequencies associated with Li–O = C deformations and Li–O stretching appear at 135 cm⁻¹, 426 cm⁻¹ and 535 cm⁻¹. The corresponding contribution to entropy is ~18 J mol⁻¹ K⁻¹, and thus drastically reduced compared to the case of **DMF**. This contrasting behavior is obviously related to the different structures of **GLYLi**⁺ and **DMFLi**⁺ (see Figure 1). The former acts as a bidentate base, while **DMF** presents a monodentate character with respect to the lithium cation. As a consequence, the most spectacular frequency change corresponds to the *in plane* Li–O = C deformation, which is equal to 128 cm⁻¹ for **DMF** and 426 cm⁻¹ for **GLY**. Finally, to explain the fact that $\Delta\Delta_{\text{Li}}S_{298}^\circ(\text{GLY})$ is equal to 12 J mol⁻¹ K⁻¹ and not 18 J mol⁻¹ K⁻¹, it may be added that several fundamental frequencies that exist in the glycine moiety are modified by the chelation of the Li⁺ cation. This mainly affects the bending modes associated with the CCN skeleton and is responsible for 6 J mol⁻¹ K⁻¹ of the additional decrease of $S_{298}^\circ(\text{GLYLi}^+)$ with respect to $S_{298}^\circ(\text{GLY})$.

The Li⁺ affinity scale

Experimentally, a wide range of $\Delta_{\text{Li}}G_0^\circ$ values have been measured, essentially from ligand exchange equilibria performed in ion cyclotron resonance (ICR) mass spectrometers. The most comprehensive study involves equilibrium constant determinations at temperature $T = 373 \text{ K}$ from which the relative $\Delta_{\text{Li}}G_{373}^\circ$ were deduced^{10–14} and recently re-anchored.¹⁷ A second source of information comes from the measurement of the energy threshold for reaction (1) determined by controlled CID. This method is expected to provide absolute lithium cation binding enthalpies at 0K, $\Delta_{\text{Li}}H_0^\circ$ ¹⁶. To allow comparison between theory and experiment, complementary calculations have been performed at the temperature of 373K in order to obtain homogeneous $\Delta_{\text{Li}}H_{298}^\circ$ experimental values for the reference compounds. The results are summarized in Table 2.

For water and pyridine, the agreement between $\Delta_{\text{Li}}H_{298}^\circ$ obtained from ICR and GIBMS (Guided Ion Beam Mass Spectrometry) experiments is found to be excellent. This is not surprising since both series of experiments were anchored to these reference values. Comparison between experimental [$\Delta_{\text{Li}}H_{298}^\circ(\text{exp})$, Table 2] and G4 calculated [$\Delta_{\text{Li}}H_{298}^\circ(\text{G4})$, Table 1] lithium cation affinities of the eight reference molecules shows a systematic shift situated between 2.2 kJ mol⁻¹ (**PYR**) and 13.6 kJ mol⁻¹ (**PENT**). Roughly, it seems that, in this $\Delta_{\text{Li}}H_{298}^\circ$ region, the difference [$\Delta_{\text{Li}}H_{298}^\circ(\text{G4}) - \Delta_{\text{Li}}H_{298}^\circ(\text{exp})$] increases

Table 2. Experimental Li⁺ binding enthalpies, $\Delta_{\text{Li}}H_0^\circ$, and free energies, $\Delta_{\text{Li}}G_0^\circ$, corrective terms and final 'experimental' $\Delta_{\text{Li}}H_{298}^\circ$ (kJ mol⁻¹).

M	Crude experimental values		Computationally corrected			
	$\Delta_{\text{Li}}H_0^\circ$	$\Delta_{\text{Li}}G_{373}^\circ$	$373\Delta_{\text{Li}}S_{373}^\circ$ ^a	$[\Delta_{\text{Li}}H_T - \Delta_{\text{Li}}H_0]^\circ$ ^a	$\Delta_{\text{Li}}H_{298}^\circ$ [exp] ^b	$\Delta_{\text{Li}}H_{298}^\circ$ [exp/G4] ^g
DMF (<i>N,N</i> -dimethylformamide)		187.4 ^c 173.6 ^d	37.3	2.3 [2.3]	224.7	231.2
DMSO (dimethyl sulfoxide)		189.8 ^c 174.9 ^d	37.4	2.2 [2.2]	227.2	233.8
NMA (<i>anti-N</i> -methylacetamide)		187.4 ^e 173.6 ^d	38.0	3.0 [3.2]	225.2	231.7
DMA (<i>N,N</i> -dimethylacetamide)		195.7 ^c 179.1 ^d	34.3	2.1 [2.2]	229.9	236.8
TMP (trimethyl phosphate)	280.8 ± 14.5 ^f	198.8 ^c 182.8 ^d	36.7	1.6 [1.5]	235.6 [282.4]	242.7
PENT (2,4-pentanedione)		196.3 ^e 180.3 ^d	36.8	2.3 [2.1]	233.3	240.1
H2O (water)	133.1 ± 13.5 ^f	103.6 ^c 103.4 ^d	33.7	4.2 [4.4]	137.1 [137.3]	139.7
PYR (pyridine)	181.0 ± 14.5 ^f	146.7 ^c 146.4 ^d	38.0	2.2 [2.2]	184.7 [183.2]	189.3

^aG4 calculations at 298K and, in parentheses at 373K.

^b $\Delta_{\text{Li}}H_{298}^\circ$ [exp] = $\Delta_{\text{Li}}G_{373}^\circ$ (ICR) + 373. $\Delta_{\text{Li}}S_{373}^\circ - (\Delta_{\text{Li}}H_{373}^\circ - \Delta_{\text{Li}}H_{298}^\circ)$ kJ mol⁻¹ and, in brackets, $\Delta_{\text{Li}}H_{298}^\circ$ [exp] = $\Delta_{\text{Li}}H_0^\circ$ (GIBMS) + $(\Delta_{\text{Li}}H_{298}^\circ - \Delta_{\text{Li}}H_0^\circ)$ kJ mol⁻¹.

^cICR experiments, new $\Delta_{\text{Li}}G_{373}^\circ$ values, from Mayeux *et al.*,¹⁷ anchored to $\Delta_{\text{Li}}G_{373}^\circ$ (PYR) = 146.7 kJ mol⁻¹.

^dICR experiments, old $\Delta_{\text{Li}}G_{373}^\circ$ values from Taft *et al.*¹⁰

^eFrom linear extrapolation using the least-squares relationship: $\Delta_{\text{Li}}G_{373}^\circ$ (from Mayeux *et al.*¹⁷) = -27.47 + 1.241 kJ mol⁻¹ [Burk *et al.*¹⁴].

^fGuided ion beam MS, from Rodgers and Armentrout,¹⁶ anchored to $\Delta_{\text{Li}}H_0^\circ$ (H₂O) = 133.1 kJ mol⁻¹.

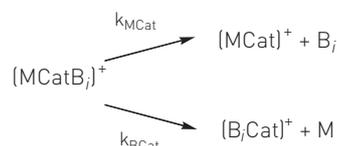
^gUsing $\Delta_{\text{Li}}G_{373}^\circ$ (Mayeux *et al.*¹⁷) adjusted to the temperature of 390K [see text].

with $\Delta_{\text{Li}}H_{298}^\circ$. Comparable remarks have been made earlier by Tsang *et al.*¹⁵ and, more recently, by Mayeux *et al.*¹⁷ The origin of this discrepancy is, however, not clear. The possible correlation between these systematic errors and the $\Delta_{\text{Li}}H_{298}^\circ$ values suggests difficulties during the handling of the experimental data. As pointed out by Mayeux *et al.*,¹⁷ an erroneous estimate of the temperature in the equilibrium constant determination by ICR MS would lead to significant compression (or expansion) of the affinity scale. In the present case, we found that a temperature of 390K, rather than 373K, reconciled the experimental and G4-calculated $\Delta_{\text{Li}}G_{373}^\circ$ scales. Assuming that ICR experiments were conducted at 390K, a new $\Delta_{\text{Li}}H_{298}^\circ$ [exp] can be estimated [denoted $\Delta_{\text{Li}}H_{298}^\circ$ [exp/G4] in Table 2] and is used below as a compromise between $\Delta_{\text{Li}}H_{298}^\circ$ [exp] and $\Delta_{\text{Li}}H_{298}^\circ$ [iG4] scales.

A special mention should be made for $\Delta_{\text{Li}}H_{298}^\circ$ (**TMP**) determined from a GIBMS measurement³⁷ since the value is 40–46 kJ mol⁻¹ higher than that given by the G4 calculation or ICR experiment. This discrepancy has also been underlined by Mayeux *et al.*,¹⁷ who suggested that the results given by GIBMS experiment were erroneous in that case.

Essential basis of the extended kinetic method

The kinetic methods^{4,22} consider the competitive dissociations of a series of mixed cationized dimers [MCatB_i]⁺, involving the molecule of interest, M, and a reference molecule, B_i:



Then, the ratio of measured peak intensities [MCat]⁺/[B_iCat]⁺ is assumed to be equal to the ratio of rate constants $k_{\text{MCat}}/k_{\text{BCat}}$ and, considering the canonical transition state theory and several simplifying assumptions, its natural logarithm may be expressed by:

$$y_i = \ln([\text{MCat}]^+ / [\text{B}_i\text{Cat}]^+) \sim \ln(k_{\text{MCat}} / k_{\text{BCat}}) \quad (2)$$

$$= [G_T^\circ(\text{M}) + G_T^\circ(\text{B}_i\text{Cat}^+) - G_T^\circ(\text{MCat}^+) - G_T^\circ(\text{B}_i)] / RT$$

where T is an 'effective temperature' related to the excitation energy of the dissociating [MCatB_i]⁺ species.^{4,19} Using the thermochemical parameters associated with reaction (1) when Cat⁺ = Li⁺ at 298K, i.e. $\Delta_{\text{Li}}H_T^\circ$, $\Delta_{\text{Li}}G_T^\circ$ and $\Delta_{\text{Li}}S_T^\circ$, it may be easily shown that equation (2) can also be written as:

$$y_i = [\Delta_{\text{Li}}G_T^\circ(\text{M}) - \Delta_{\text{Li}}G_T^\circ(\text{B}_i)] / RT \quad (3)$$

and, anchoring the reference values to the usual temperature of 298 K:

$$\begin{aligned}
 y_i &= \{\Delta_{\text{Li}}H_{298}^\circ(\text{M}) - \Delta_{\text{Li}}H_{298}^\circ(\text{B}_i) - T[\Delta_{\text{Li}}S_{298}^\circ(\text{M}) - \Delta_{\text{Li}}S_{298}^\circ(\text{B}_i)] \\
 &+ \Delta H_{298 \rightarrow T}^\circ + T[\Delta_{\text{Li}}S_{298 \rightarrow T}^\circ(\text{M}) - \Delta_{\text{Li}}S_{298 \rightarrow T}^\circ(\text{B}_i)]\} / RT \quad (4)
 \end{aligned}$$

The terms $\Delta H_{298 \rightarrow T}^{\circ}$ and $\Delta S_{298 \rightarrow T}^{\circ}$ are thermal corrections for enthalpy and entropy, respectively, which, because of the structural similarities of $\text{MCat}^+ + \text{B}_i$ on the one hand and $\text{M} + \text{B}_i\text{Cat}^+$ on the other, are generally assumed to cancel to zero. In this hypothesis, equation (4) reduces to:

$$y_i = \{\Delta_{\text{Li}}H_{298}^{\circ}(\text{M}) - \Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i) - T[\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i)]\}/RT \quad (5)$$

Thus, for a series of experiments using several molecules of reference B_i at a temperature T , y_i vs. $\Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i)$ follows a linear relationship characterized by a slope equal to $1/RT$ and an intercept with the $\Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i)$ scale given by $\Delta_{\text{Li}}H_{298}^{\circ}(\text{M})_{\text{inter}} = \Delta_{\text{Li}}H_{298}^{\circ}(\text{M}) - T[\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle]$ [where $\langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle$ is the mean value of the $\Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i)$ terms]. In the simple kinetic method it is assumed that this latter term is negligible and consequently $\Delta_{\text{Li}}H_{298}^{\circ}(\text{M})$ is assigned the intercept of the regression line with the $\Delta_{\text{Li}}H_{298}^{\circ}(\text{M})$ axis. When $[\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle]$ is different from zero, 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 :

$$y_{ij} = [\Delta_{\text{Li}}H_{298}^{\circ}(\text{M}) - \Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i)]/RT_j - [\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i)]/R \quad (6)$$

Equation (6) forms the basis of the extended kinetic method in which both $\Delta_{\text{Li}}H_{298}^{\circ}(\text{M})$ and $\Delta_{\text{Li}}S_{298}^{\circ}(\text{M})$ may be obtained.⁶ Accordingly, the y_{ij} vs. $\Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i)$ points may be fitted by a set of regression lines ($y_{ij})_{\text{calc}} = y_0 + b_j(x_0 - x_i)$ intersecting in a common 'isothermal' or 'isoequilibrium' point. The coordinates of this intersecting point are: $x_0 = \Delta_{\text{Li}}H_{298}^{\circ}(\text{M})$ and $y_0 = -[\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle]/R$, or $y_0 = [\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) - \langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle]/R$, which introduces the terms $\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) = S_{298}^{\circ}(\text{MLi}^+) - S_{298}^{\circ}(\text{M})$ and $\langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle$, the average of the differences $S_{298}^{\circ}(\text{B}_i\text{Li}^+) - S_{298}^{\circ}(\text{B}_i)$. A least-squares regression analysis which takes into account simultaneously all the $[n_i, n_j]$ data points may provide the essential coordinates x_0 and y_0 . In the present work we used a numerical method based on the orthogonal distance regression (ODR) procedure.^{40,41}

Experimental lithium binding thermochemistry of glycine by the extended kinetic method

The $y_{ij} = \ln\{[\text{GLYLi}]^+ / [\text{B}_i\text{Li}]^+\}$ values determined in the present study, using six reference molecules B_i and three different collision energies ($E_{\text{cm}} = 2 \text{ eV}$, 3 eV and 4 eV), are summarized in Table 3. The corresponding extended kinetic plots y_{ij} vs. $\Delta_{\text{Li}}H_{298}^{\circ}(\text{B}_i)$ are illustrated in Figure 3 using the mixed experimental–G4 lithium affinity scale $\Delta_{\text{Li}}H_{298}^{\circ}(\text{exp}/\text{G4})$ (last column in Table 2). Excellent linear correlations are observed for the three collision energies, as expected from equation (6).

The statistical treatment of the data by the ODR procedure^{40,41} leads to $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY}) = 235.4 \pm 1.0(2.1) \text{ kJ mol}^{-1}$ (indicated errors are standard deviation and, in parentheses, a 95% confidence limit), using mixed experimental/theory $\Delta_{\text{Li}}H_{298}^{\circ}(\text{exp}/\text{G4})$ values. The entropy difference $\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) - \langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle$ is equal to $-14.7 \pm 1.8(3.9) \text{ J mol}^{-1} \text{ K}^{-1}$. The average $\langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle$ value being equal to $33.1 \pm 5.1 \text{ J mol}^{-1} \text{ K}^{-1}$ results in $\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) = 18.4 \pm 5.4(6.4) \text{ J mol}^{-1} \text{ K}^{-1}$. Owing to the error limits, this value

Table 3. Experimental $y_i = \ln\{[\text{GLYLi}]^+ / [\text{B}_i\text{Cat}]^+\}$ values obtained at center of mass collision energies $E_{\text{cm}} = 2 \text{ eV}$, 3 eV and 4 eV .

B_i	y_{i2}	y_{i3}	y_{i4}
DMF (<i>N,N</i> -dimethylformamide)	-0.55	-0.9	-1.2
DMSO (dimethyl sulfoxide)	-0.8	-1.2	-1.5
NMA (<i>anti-N</i> -methylacetamide)	-0.4	-0.8	-1.2
DMA (<i>N,N</i> -dimethylacetamide)	-2.2	-2.3	-2.5
TMP (trimethyl phosphate)	-4.5	-3.6	-2.8
PENT (2,4-pentanedione)	-3.7	-2.85	-2.07

is close to the result of $12 \text{ J mol}^{-1} \text{ K}^{-1}$ given by G4 calculations. It, however, differs from the average $\langle \Delta_{\text{Li}}S_{298}^{\circ}(\text{B}_i) \rangle$ value of $33.1 \text{ J mol}^{-1} \text{ K}^{-1}$ observed for the monodentate reference molecules **DMF**, **DMSO**, **NMA**, **DMA** and **TMP** (and also **PENT**, which behaves as a monodentate molecule since both the neutral and the lithiated forms are similarly constrained). This confirms that lithiated glycine is more constrained than its neutral counterpart, as expected from its bidentate behavior with respect to the lithium cation. Table 4 summarizes these various results together with previous estimates of lithium cation thermochemical parameters.

As recalled in the introduction, two tentative determinations of the lithium cation thermochemistry of glycine have been reported so far.^{24,25} Both used the kinetic method in its simple version, i.e. at only one effective temperature. Bojesen

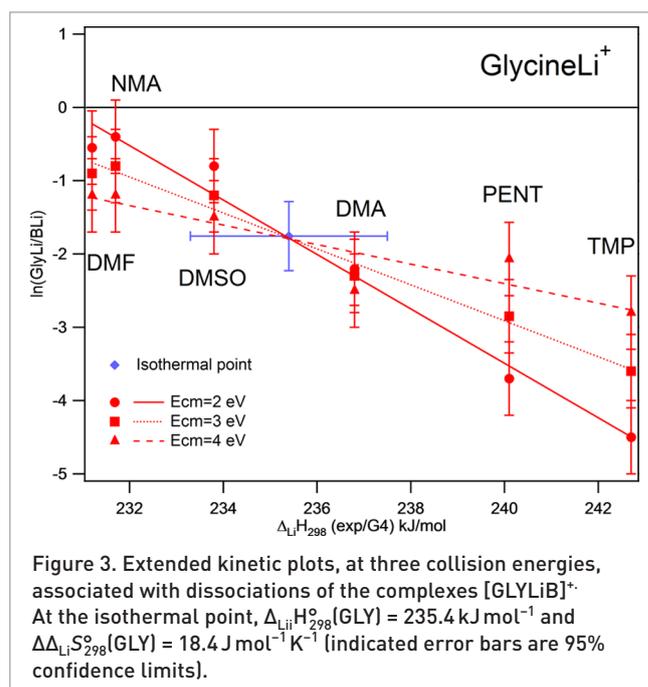


Figure 3. Extended kinetic plots, at three collision energies, associated with dissociations of the complexes $[\text{GLYLiB}]^+$. At the isothermal point, $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY}) = 235.4 \text{ kJ mol}^{-1}$ and $\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) = 18.4 \text{ J mol}^{-1} \text{ K}^{-1}$ (indicated error bars are 95% confidence limits).

Table 4. Summary of the experimental and computed lithium binding thermochemistry of glycine.

	$\Delta_{\text{Li}}H_{298}(\text{GLY})$ (kJ mol ⁻¹)	$\Delta\Delta_{\text{Li}}S_{298}(\text{GLY})$ (J mol ⁻¹ K ⁻¹)	$\Delta_{\text{Li}}G_{298}(\text{GLY})$ (kJ mol ⁻¹)
Experiment			
Extended kinetic	228.7 ± 1.0 ^a	18.4 ± 5.4 ^a	194.5 ± 1.9 ^a
	235.1 ± 3.1 ^b	18.3 ± 6.5 ^b	200.9 ± 4.0 ^b
	235.4 ± 1.0^c	18.4 ± 5.4^c	201.2 ± 1.9^c
Simple kinetic	(233.3) ^{d,e}	(12.0) ^e	197.2 ± 3.2 ^d
GIBMS	224.5 ± 8.0 ^f	(12.0) ^e	(188.4) ^f
Theory			
G2MP2	234.5	12.0	198.4
G4	241.4(242.3)	12.0(12.8)	205.3(206.5)

^aThis work, using, for the reference molecules, $\Delta_{\text{Li}}H_{298}(\text{exp})$, penultimate column in Table 2.

^bThis work, using, for the reference molecules, $\Delta_{\text{Li}}H_{298}(\text{G4})$, third column in Table 1.

^cThis work, using, for the reference molecules, the proposed mixed $\Delta_{\text{Li}}H_{298}(\text{exp}/\text{G4})$ scale, last column in Table 2.

^dFrom experimental data of Feng *et al.*²⁵, assumed to be performed at an effective temperature of 298 K.

^eG4-computed $\Delta\Delta_{\text{Li}}S_{298}(\text{GLY})$ value.

^fFrom Rodgers and Armentrout¹⁶ and using $373\Delta_{\text{Li}}S_{373}(\text{GLY}) = 45.6$ kJ mol⁻¹ and $(\Delta_{\text{Li}}H_{298} - \Delta_{\text{Li}}H_0) = 4.5$ kJ mol⁻¹.

*et al.*²⁴ produced cluster ions by fast atom bombardment and examined the spontaneous dissociations that occurred in the first field-free region of an electric-magnetic (E-B) sector mass spectrometer by the B/E scan method. They indirectly determined that $\Delta_{\text{Li}}G_7^{\circ}(\text{GLY})$ should be larger than $\Delta_{\text{Li}}G_7^{\circ}(\text{DMF})$ by 4.2 kJ mol⁻¹. Unfortunately, the effective temperature T was not determined during these experiments. Feng *et al.*²⁵ studied lithium cation binding energies of several amino acids by a simple kinetic method using a quadrupole ion-trap mass spectrometer. Cationized mixed dimers were formed in an external electrospray ion source and isolated in the ion trap where they were subjected to collisional activation. Three reference compounds B_i , namely **DMF**, **NMA** and **DMA**, were used to anchor the lithium cation binding energy of glycine. The authors deduced that $\Delta_{\text{Li}}G_7^{\circ}(\text{GLY})$ is higher than the $\Delta_{\text{Li}}G_7^{\circ}(\text{DMF})$ and $\Delta_{\text{Li}}G_7^{\circ}(\text{NMA})$ by 3.3 kJ mol⁻¹ and 2.1 kJ mol⁻¹ and lower than $\Delta_{\text{Li}}G_7^{\circ}(\text{DMA})$ by 2.9 kJ mol⁻¹. The published data²⁵ allow the effective temperature of 295 K to be calculated. We can thus safely write $\Delta_{\text{Li}}G_{295}^{\circ}(\text{GLY}) \sim \Delta_{\text{Li}}G_{298}^{\circ}(\text{GLY})$ and deduce an average $\Delta_{\text{Li}}G_{298}^{\circ}(\text{GLY})$ of 197.2 ± 3.2 kJ mol⁻¹ using the $\Delta_{\text{Li}}G_{298}^{\circ}(B_i)$ deduced from ICR experiments.²⁵ This estimate compares favorably with the present results (to within a few kJ mol⁻¹). A GIBMS determination of $\Delta_{\text{Li}}H_0^{\circ}(\text{GLY})$ is given in Rodgers and Armentrout.¹⁶ After including the 0 → 298 K thermal correction to the enthalpy, we obtained a value of $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY}) = 224.5 \pm 8.0$ kJ mol⁻¹, i.e. more than 10 kJ mol⁻¹ below the value of 235.4 ± 1.0 kJ mol⁻¹ obtained here.

A comparison of these experimental results with G4 calculations reveals noticeable differences (Table 4). Indeed, the experimental $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$ seems to be underestimated by 6.0 kJ mol⁻¹ with respect to the G4 calculations and $\Delta\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY})$ overestimated (by 6 J mol⁻¹ K⁻¹) with respect to the G4 calculations. At this stage, it must be recalled that the extended kinetic method tends to provide underestimates of cation affinities and entropies but that, generally, the Gibbs free energies are correctly estimated.^{4,40,42} Combining experimentally determined $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY}) = 235.4 \pm 1.0$ kJ mol

⁻¹ and $\Delta\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) = 18.4 \pm 5.4$ J mol⁻¹ K⁻¹ one may deduce $\Delta_{\text{Li}}G_{298}^{\circ}(\text{GLY}) = 201.2 \pm 1.9$ kJ mol⁻¹. As observed in Table 4, this estimate is in reasonable agreement with the direct G4 calculation, which gives $\Delta_{\text{Li}}G_{298}^{\circ}(\text{GLY}) = 205.3$ kJ mol⁻¹.

Concluding remarks

The aim of the present study was to examine, both theoretically and experimentally, the lithium cation binding thermochemistry of glycine. For this purpose, high-level composite quantum chemistry recipes, Gn, and the extended kinetic method applied to MS/MS experiments were used. The following findings can be emphasized:

- Quantum chemistry calculations demonstrate that lithiated glycine is essentially described by one conformer, **GLYLi⁺**, which exhibits a covalent O–Li bonding and a Li...NH₂ stabilizing interaction, giving a bidentate character to this species.
- Composite G4 and G3 methods provide similar thermochemical parameters values (for example, $\Delta_{\text{Li}}H_{298}$ present a mean absolute deviation of 0.5 kJ mol⁻¹) while G2MP2 (and also G2) give significantly underestimated values (a difference of ~6 kJ mol⁻¹ is observed for $\Delta_{\text{Li}}H_{298}$ between G4 and G2MP2).
- The G4-computed $\Delta_{\text{Li}}H_{298}^{\circ}(\text{GLY})$ value is equal to 242 kJ mol⁻¹, i.e. 100 kJ mol⁻¹ and 55 kJ mol⁻¹ above $\Delta_{\text{Li}}H_{298}^{\circ}(\text{H}_2\text{O})$ and $\Delta_{\text{Li}}H_{298}^{\circ}(\text{PYR})$, respectively.
- An entropy difference $\Delta\Delta_{\text{Li}}S_{298}^{\circ}(\text{M}) = S_{298}^{\circ}(\text{MLi}^+) - S_{298}^{\circ}(\text{M})$ equal to 33 J mol⁻¹ K⁻¹ is calculated for the monodentate molecules **M** = **DMF**, **DMSO**, **NMA**, **DMA**, **TMP** and the peculiar bidentate species **PENT**. This difference mainly originates from the three additional vibrational modes occurring in the lithiated species. In the case of glycine, the difference $\Delta\Delta_{\text{Li}}S_{298}^{\circ}(\text{GLY}) = S_{298}^{\circ}(\text{GLYLi}^+) - S_{298}^{\circ}(\text{GLY})$ amounts to only 12 J mol⁻¹ K⁻¹, demonstrating a strong constraint in the lithiated molecule. Indeed, the in-plane

Li–O = C deformation mode is shown by the calculation to be dramatically hindered in **GLYLi⁺**.

- (v) The lithium affinity scale has been reexamined in the light of the G4 theory. A systematic shift, seemingly a linear function of $\Delta_{\text{Li}}H_{298}$, is observed between the G4 calculation and $\Delta_{\text{Li}}H_{298}$ deduced from recent ICR experiments. It is suggested that a compression of the experimental lithium cation affinity scale was occurring in the high $\Delta_{\text{Li}}H_{298}$ region. A mixed scale of lithium cation affinities, $\Delta_{\text{Li}}H_{298}(\text{exp/G4})$, is proposed.
- (vi) Application of the extended kinetic method to CIDs of **GLYLiB⁺** adducts in a Q-TOF mass spectrometer leads to $\Delta_{\text{Li}}H_{298}(\text{GLY}) = 235 \text{ kJ mol}^{-1}$. From the same experiments, a $\Delta\Delta_{\text{Li}}S^{\circ}_{298}(\text{GLY})$ value equal to $18 \text{ J mol}^{-1} \text{ K}^{-1}$ is deduced. Compared to the direct G4 results [$\Delta_{\text{Li}}H_{298}(\text{GLY}) = 242 \text{ kJ mol}^{-1}$ and $\Delta\Delta_{\text{Li}}S^{\circ}_{298}(\text{GLY}) = 12 \text{ J mol}^{-1} \text{ K}^{-1}$], it is confirmed that the extended kinetic method provides slightly biased enthalpic and entropic quantities. As already observed in protonation thermochemistry, a compensation effect allows us to determine the correct Gibbs free energies. In the present case, $\Delta_{\text{Li}}G_{298}(\text{GLY}) = 201 \text{ kJ mol}^{-1}$ is deduced from the extended kinetic method while a similar value, $\Delta_{\text{Li}}G_{298}(\text{GLY}) = 205 \text{ kJ mol}^{-1}$, is obtained from direct G4 calculations.

References

- S.G. Lias, J.F. Liebman and R.D. Levin, "Evaluated gas phase basicities and proton affinities of molecules; heats of formation of protonated molecules", *J. Phys. Chem. Ref. Data*, **13**, 695 (1984). doi: <http://dx.doi.org/10.1063/1.555719>
- E.P. Hunter and S.G. Lias, "Evaluated gas phase basicities and proton affinities of molecules: an update", *J. Phys. Chem. Ref. Data*, **27**, 4131 (1998). doi: <http://dx.doi.org/10.1063/1.556018>
- E.P. Hunter and S.G. Lias, in *NIST Chemistry WebBook*, Ed by P.J. Linstrom and W.G. Mallard. National Institute of Standards and Technology, Gaithersburg, MD (2013).
- G. Bouchoux, "Gas phase basicities of polyfunctional molecules. Part 1: Theory and methods", *Mass Spectrom. Rev.* **26**, 775 (2007). doi: <http://dx.doi.org/10.1002/mas.20151>
- G. Bouchoux and J-Y. Salpin, "Gas phase basicities of polyfunctional molecules. Part 2: Saturated basic sites", *Mass Spectrom. Rev.* **31**, 353 (2012). doi: <http://dx.doi.org/10.1002/mas.20343>
- G. Bouchoux, "Gas phase basicities of polyfunctional molecules. Part 3: Amino-acids", *Mass Spectrom. Rev.* **31**, 391 (2012). doi: <http://dx.doi.org/10.1002/mas.20349>
- G. Bouchoux, "Gas phase basicities of polyfunctional molecules. Part 4: Carbonyl groups as basic sites", *Mass Spectrom. Rev.* doi: 10.1002/mas.21416. doi: <http://dx.doi.org/10.1002/mas.21416>
- M.T. Rogers and P.B. Armentrout, "A thermodynamic "vocabulary" for metal ion interactions in biological systems", *Acc. Chem. Res.* **37**, 989 (2004). doi: <http://dx.doi.org/10.1021/ar0302843>
- C. Laurence and J-F. Gal, *Lewis Basicity and Affinity Scales: Data and Measurement*. Wiley, Chichester (2010).
- R.W. Taft, F. Anvia, J-F. Gal, S. Walsh, M. Capon, M.C. Holmes, K. Hosn, G. Oloumi, R. Vasanwala and S. Yazdani, "Free energies of cation–molecule complex formation and cation–solvent transfers", *Pure Appl. Chem.* **62**, 17 (1990). doi: <http://dx.doi.org/10.1351/pac199062010017>
- E. Bunzel, M. Decouzon, A. Formento, J-F. Gal, M. Herreros, L. Li, P-C. Maria, I. Koppel and R. Kurg, "Lithium-cation and proton affinities of sulfoxides and sulfones: a Fourier transform ion cyclotron resonance study", *J. Am. Soc. Mass Spectrom.* **8**, 262 (1997). doi: [http://dx.doi.org/10.1016/S1044-0305\(96\)00255-3](http://dx.doi.org/10.1016/S1044-0305(96)00255-3)
- E. Bunzel, A. Chen, M. Decouzon, S. A. Fancy, J-F. Gal, M. Herreros and P-C. Maria, "Fourier transform ion cyclotron resonance determination of lithium cation basicities by the kinetic method: upward extension of the scale to phosphoryl compounds", *J. Mass Spectrom.* **33**, 757 (1998). doi: [http://dx.doi.org/10.1002/\(SICI\)1096-9888\(199808\)33:8<757::AID-JMS676>3.0.CO;2-0](http://dx.doi.org/10.1002/(SICI)1096-9888(199808)33:8<757::AID-JMS676>3.0.CO;2-0)
- M. Herreros, J-F. Gal, P-C. Maria and M. Decouzon, "Gas-phase basicity of simple amides toward proton and lithium cation: an experimental and theoretical study", *Eur. J. Mass Spectrom.* **5**, 259 (1999). doi: <http://dx.doi.org/10.1255/ejms.282>
- P. Burk, I.A. Koppel, I. Koppel, R. Kurg, J-F. Gal, P-C. Maria, M. Herreros, R. Notario, J-L. Abboud, F. Anvia and R.W. Taft, "Revised and expanded scale of gas-phase lithium cation basicities. An experimental and theoretical study", *J. Phys. Chem. A* **104**, 2824 (2000). doi: <http://dx.doi.org/10.1021/jp9931399>
- Y. Tsang, F.M. Siu, N.L. Ma and C.W. Tsang, "Experimental validation of Gaussian-3 lithium cation affinities of amides: implications for the gas-phase lithium cation basicity scale", *Rapid Commun. Mass Spectrom.* **16**, 229 (2002). doi: <http://dx.doi.org/10.1002/rcm.570>
- M.T. Rodgers and P.B. Armentrout, "A critical evaluation of the experimental and theoretical determination of lithium cation affinities", *Int. J. Mass Spectrom.* **267**, 167 (2007). doi: <http://dx.doi.org/10.1016/j.ijms.2007.02.034>
- C. Mayeux, P. Burk, J-F. Gal, I. Kaljurand, I. Koppel, I. Leito and L. Sikk, "Gas-phase lithium cation basicity: revisiting the high basicity range by experiment and theory", *J. Am. Soc. Mass Spectrom.* **25**, 1962 (2014). doi: <http://dx.doi.org/10.1007/s13361-014-0970-4>
- C. Mayeux and P. Burk, "Evaluation of alkali metal cation affinities and basicities using extrapolation to the complete basis set limit", *J. Phys. Chem. A* **118**, 1906 (2014). doi: <http://dx.doi.org/10.1021/jp4090316>

19. K. Ervin, "Experimental techniques in gas-phase ion thermochemistry", *Chem. Rev.* **101**, 391 (2001). doi: <http://dx.doi.org/10.1021/cr990081l>
20. R. Wu and T.B. McMahon "Structures, energetics, and dynamics of gas phase ions studied by FTICR and HPMS", *Mass Spectrom. Rev.* **28**, 546 (2009). doi: <http://dx.doi.org/10.1002/mas.20223>
21. G. Bouchoux, J.-Y. Salpin and D. Leblanc "A relationship between the kinetics and thermochemistry of proton transfer reactions in the gas phase", *Int. J. Mass Spectrom.* **153**, 37 (1996). doi: [http://dx.doi.org/10.1016/0168-1176\(95\)04353-5](http://dx.doi.org/10.1016/0168-1176(95)04353-5)
22. S.A. McLuckey, D. Cameron and R.G. Cooks, "Proton affinity from dissociation of proton bound dimmers", *J. Am. Chem. Soc.* **103**, 1313 (1981). doi: <http://dx.doi.org/10.1021/ja00396a001>
23. M.T. Rogers and P.B. Armentrout, "Noncovalent metal–ligand bond energies as studied by threshold collision-induced dissociation", *Mass Spectrom. Rev.* **19**, 215 (2000). doi: [http://dx.doi.org/10.1002/1098-2787\(200007\)19:4<215::AID-MAS2>3.0.CO;2-X](http://dx.doi.org/10.1002/1098-2787(200007)19:4<215::AID-MAS2>3.0.CO;2-X)
24. G. Bojesen, T. Breindahl and U.N. Andersen "On the sodium and lithium ion affinities of some amino acids", *Org. Mass Spectrom.* **28**, 14482 (1993). doi: <http://dx.doi.org/10.1002/oms.1210281215>
25. W.Y. Feng, S. Gronert and C. Lebrilla, "The lithium cation binding energies of gaseous amino acids", *J. Phys. Chem. A* **107**, 405 (2003). doi: <http://dx.doi.org/10.1021/jp022112d>
26. S. Hoyau and G. Ohanessian, "Interaction of alkali metal cations (Li⁺–Cs⁺) with glycine in the gas-phase: a theoretical study", *Chem. Eur. J.* **4**, 1561 (1998). doi: [http://dx.doi.org/10.1002/\(SICI\)1521-3765\(19980807\)4:8<1561::AID-CHEM1561>3.0.CO;2-Z](http://dx.doi.org/10.1002/(SICI)1521-3765(19980807)4:8<1561::AID-CHEM1561>3.0.CO;2-Z)
27. T. Marino, N. Russo and M. Toscano, "Gas-phase metal ion (Li⁺, Na⁺, Cu⁺) affinities of glycine and alanine", *J. Inorg. Biochem.* **79**, 179 (2000). doi: [http://dx.doi.org/10.1016/S0162-0134\(99\)00242-1](http://dx.doi.org/10.1016/S0162-0134(99)00242-1)
28. M. Remko and B.M. Rode, "Effect of metal ion (Li⁺, Na⁺, K⁺, Mg²⁺, Ni²⁺, Cu²⁺, and Zn²⁺) and water coordination on the structure of glycine and zwitterionic glycine", *J. Phys. Chem. A*, **110**, 1960 (2006). doi: <http://dx.doi.org/10.1021/jp054119b>
29. J. Jover, R. Bosque and J. Sales, "A comparison of the binding affinity of the common amino acids with different metal cations", *Dalton Trans.* 6441 (2008). doi: <http://dx.doi.org/10.1039/b805860a>
30. J. Jover, R. Bosque and J. Sales, "Quantitative structure–property relationship estimation of cation binding affinity of the common amino acids", *J. Phys. Chem. A* **113**, 3703 (2009). doi: <http://dx.doi.org/10.1021/jp810391z>
31. L. A. Curtiss, P. C. Redfern and K. Raghavachari, "Gaussian-4 theory", *J. Chem. Phys.* **126**, 084108 (2007). doi: <http://dx.doi.org/10.1063/1.2436888>
32. G. Bouchoux, S. Desaphy, S. Bourcier, C. Malosse and R. Ngo Biboum Bimbong, "Gas-phase protonation thermochemistry of arginine", *J. Phys. Chem. B* **112**, 3410 (2008). doi: <http://dx.doi.org/10.1021/jp709677c>
33. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery, Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J. E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski and D.J. Fox, *Gaussian 09, Revision D.01*. Gaussian, Inc., Wallingford, CT (2013).
34. L.A. Curtiss, K. Raghavachari, G.W. Trucks and J.A. Pople, "A Gaussian-2 theory for molecular energies of first- and second-row compounds", *J. Chem. Phys.* **94**, 7221 (1991). doi: <http://dx.doi.org/10.1063/1.460205>
35. L.A. Curtiss, K. Raghavachari and J.A. Pople, "Gaussian-2 theory using reduced Moller–Plesset orders", *J. Chem. Phys.* **98**, 1293 (1993). doi: <http://dx.doi.org/10.1063/1.464297>
36. L.A. Curtiss, K. Raghavachari, P.C. Redfern, V. Rassolov and J.A. Pople, "Gaussian-3 (G3) theory for molecules containing first and second-row atoms", *J. Chem. Phys.* **109**, 7764 (1998). doi: <http://dx.doi.org/10.1063/1.477422>
37. C. Ruan, H. Huang and M.T. Rogers, "A simple model for metal cation–phosphate interactions in nucleic acids in the gas-phase: alkali metal cations and trimethyl phosphate", *J. Am. Soc. Mass Spectrom.* **19**, 305 (2008). doi: <http://dx.doi.org/10.1016/j.jasms.2007.10.006>
38. G. Bouchoux, F. Djazi, F. Gaillard and D. Vierezet, "Application of the kinetic method to bifunctional bases. MIKE and CID-MIKE test cases", *Int. J. Mass Spectrom.* **227**, 479 (2003). doi: [http://dx.doi.org/10.1016/S1387-3806\(03\)00092-7](http://dx.doi.org/10.1016/S1387-3806(03)00092-7)
39. G. Bouchoux, D.A. Buisson, S. Bourcier and M. Sablier "Application of the kinetic method to bifunctional bases. ESI tandem quadrupole experiments", *Int. J. Mass Spectrom.* **228**, 1035 (2003). doi: [http://dx.doi.org/10.1016/S1387-3806\(03\)00219-7](http://dx.doi.org/10.1016/S1387-3806(03)00219-7)
40. K. Ervin and P.B. Armentrout "Systematic and random errors in ion affinities and activation entropies from the extended kinetic method", *J. Mass Spectrom.* **39**, 1004 (2004). doi: <http://dx.doi.org/10.1002/jms.682>

- 41.** P.T. Boggs, R.H. Bird, J.E. Rogers and R.B. Schnabelm, *ODRPACK version 2.01*, Report NISTIR 92-4834. National Institute of Standards and Technology; Gaithersburg, MD (1992).
- 42.** G. Bouchoux "Evaluation of the protonation thermochemistry obtained by the extended kinetic method", *J. Mass Spectrom.* **41**, 1006 (2006). doi: <http://dx.doi.org/10.1002/jms.1055>