Theoretical density functional and *ab initio* computational study of vertical ionization potentials, dipole moments and ^{13}C and ^{14}N-NMR shifts of the 2-mercaptopyridine system. A model for thiated nucleobases†

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Lower valence vertical ionization potentials (VIPs) of pyridine-2(1*H*)-thione (**1**), 1-methylpyridine-2(1*H*)-thione (**3**) and their tautomers (**2** and **4**) from B3LYP/6-311+G(2d,p) calculations were in very good agreement with experimental values when the SCF calculated first VIP was added to the relative energy of the corresponding Kohn–Sham orbitals. Except for the first VIP, the valence VIPs were poorly reproduced by HF or MP2 calculations following Koopmans' theorem. Both MP2 and B3LYP electronic correlation methods using 6-311+G(2d,p) basis sets gave good predictions for the dipole moments of **3** and **4** in benzene solution. Dipole moments from calculations including solvent effects by SCRF methods were very large. Relative ^{14}N and ^{13}C-NMR shifts of **3** and **4** tautomers from the GIAO method applied at the B3LYP/6-311+G(2d,p) level were in good agreement with experimental values using a scaling factor of 0.96.

Introduction

An understanding of the physico-chemical properties of the nucleobases is of fundamental importance in relation to physical organic chemistry. Many papers have tried to model their physico-chemical properties as can be seen in a very recent review.[1] Rotational constants and IR frequencies in the gas phase are correctly reproduced by electronic correlation methods, such as post-HF methods (MP2) or DFT methods (B3LYP), using double-ξ basis sets 6-31G(d,p).[1,2] At the same level of theory, the predicted MP2 and B3LYP dipole moments of NA bases and their model systems without sulfur atoms agree with experimental data, when available, within 0.1–0.3 D; but when sulfur atoms are involved as thiol or thione forms the agreement of B3LYP dipole moments is not so good (*e.g.*, overestimation of 0.3–0.5 D for thiouracil derivatives).[1] Ultraviolet electronic spectra and polarizations have also been studied by INDO/S-CI,[3] CIS/6-31G*[3] and CASPT2[3,4] methods for NA bases and by CNDO/S[5] for their thio analogs. $\pi\rightarrow\pi^*$ transition energies predicted by semiempirical methods from *ab initio* geometries agree well (±0.3 eV) with experimental values generally, but polarizations needed *ab initio* predictions in some cases (*e.g.*, in adenine).

In the present work we use the unequivocal physico-chemical properties of ionization potentials from photoelectron spectra in the gas phase,[6] dipole moments in benzene[7] and ^{13}C and ^{14}N-NMR shifts in acetone[8] of *N*- and *S*-methyl derivatives of pyridine-2(1*H*)-thione to check the electronic treatment of theoretical methods for thiated nucleobases. The pyridine-2(1*H*)-thione (**1**)–pyridine-2-thiol (**2**) system is usually recognized as a model of the thiol–thione rearrangement of thio analogs of NA bases,[1] whereas the well characterized methyl derivatives 1-methylpyridine-2(1*H*)-thione (**3**) and 2-methylthiopyridine (**4**) allowed us to assign the physico-chemical properties unambiguously. The solvent effect was modeled using Onsager[9] and SCIPCM[10] self-consistent reaction fields (SCRF) for nonspecific solute–solvent interactions. The results may provide valuable information on the theoretical study of thiated nucleobases, related heterocyclic systems and DNA.

Results and discussion

The molecules were first studied by conformational analysis to find the most stable structures in the gas phase at B3LYP, HF and MP2(full)/6-311+G(2d,p) levels of theory. As Table 1 shows, we found two minima for thioimidate forms, one when the N^1–C^2–S^7–X dihedral angle equals zero (conformers **2a** and **4a**) and another when it is 180° (conformers **2b** and **4b**). In methyl derivatives **3** and **4**, the methyl group adopts a C^2–N^1–C–H dihedral angle of 180° in the tautomer **3** and a C^2–S^7–C–H dihedral angle of 180° in conformers **4a** and **4b**. When these dihedral angles of the methyl group in **3** and **4a** were zero, the resulting rotamers were saddle points 6.3 and 3.7 kJ mol^{-1} higher, respectively. These B3LYP/6-311+G(2d,p) calculations agree with estimations for analogous rotational barriers of the methyl group in 1-methylpyridin-2(1*H*)-one (6.3 kJ mol^{-1})[11] and 2-methoxypyridine (5.0 kJ mol^{-1}),[11] and they were slightly better than from B3LYP/6-31G(d) calculations (7.0 and 2.6 kJ mol^{-1}, respectively). Relative stabilities between conformers (**2a**/**2b** and **4a**/**4b**) calculated by *ab initio* methods without electronic correlation (HF) were essentially the same as by the MP2 or DFT method (B3LYP) within 0.9 kJ mol^{-1} (Table 1). Vibrational zero point energies (ΔZPE) favoured thioimidate (**2a** and **4a**) *vs.* thioamide (**1** and **3**) forms by −10.7 and −6.2 kJ mol^{-1} respectively. When those ΔZPE were added to electronic energies (ΔE_{elec} in Table 1), *ab initio* [HF or MP2(full)] and B3LYP methods predicted thioimidate forms as the more stable tautomers in the gas phase in agreement with experimental data.[12,13]

In contrast to hydrogen tautomers, electronic correlation methods [B3LYP and MP2(full)] differed very much from the HF method in the relative stabilization of the thioamide form of methyl derivatives (**3** *vs.* **4a**). Hyperconjugation between the methyl group and the π system seems to be responsible in part for that disagreement. As reported recently, MP2 overestimates the effects of hyperconjugation,[14] and the B3LYP method does it slightly.[15] The highest OMO of π type for methyl thioamide

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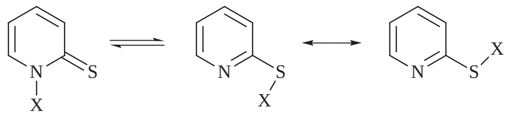
† Supplementary data (SUPPL. NO. 57453, pp. 13) is available from the British Library. For details of the Supplementary Publications Scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 2*, available *via* the RSC web page (http://www.rsc.org/authors). For direct electronic access see http://www.rsc.org/suppdata/perkin2/1999/33/.

Table 1 Gas-phase electronic energies (E_{elec}) and dipole moments (μ) using the 6-311+G(2d,p) basis set at B3LYP, HF and MP2(full) levels of theory for geometries and wavefunctions



1, X = H
3, X = CH_3

2a, X = H
4a, X = CH_3

2b, X = H
4b, X = CH_3

	B3LYP			HF			MP2		
Compound	E_{elec}[a]	ΔE_{elec}[b]	μ[c]	E_{elec}[a]	ΔE_{elec}[b]	μ[c]	E_{elec}[a]	ΔE_{elec}[b]	μ[c]
1	−646.5831157	*0.0*	5.61	−644.3012904	*0.0*	6.47	−645.5998796	*0.0*	5.52
2a	−646.5802752	*7.5*	2.00	−644.3024091	*−2.9*	2.21	−645.6009017	*−2.7*	2.10
2b	−646.5785763	*11.9*	3.11	−644.3009121	*1.0*	3.36	−645.5989723	*2.4*	3.24
3	−685.9011909	*0.0*	5.38	−683.3366624	*0.0*	6.20	−684.8209185	*0.0*	5.31
4a	−685.9057534	*−12.0*	1.14	−683.3455242	*−23.3*	1.44	−684.8243627	*−9.0*	1.35
4a	−685.9025129	*−3.5*	3.24	−683.3419624	*−13.9*	3.49	−684.8210467	*−0.3*	3.34

[a] In atomic units (1 a.u. = 2625.5 kJ mol^{-1}). [b] In kJ mol^{-1}. [c] In Debyes (1 D = 3.33564 10^{-30} C m). Dipole moments of *N*-methyl derivative **3** and *S*-methyl derivative **4** in benzene were 5.22 and 1.68 D respectively (ref. 7).

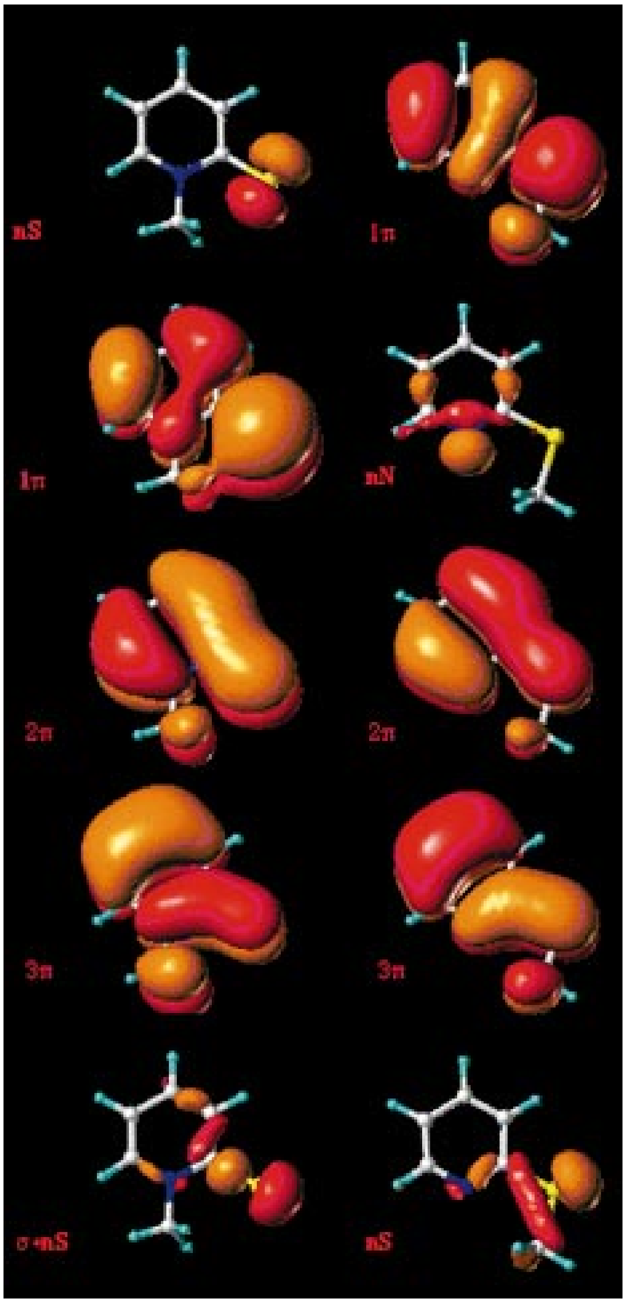


Fig. 1 Five last valence OMO of the methylated tautomers **3** (left) and **4a** (right) calculated by means of the B3LYP/6-311+G(2d,p) method.

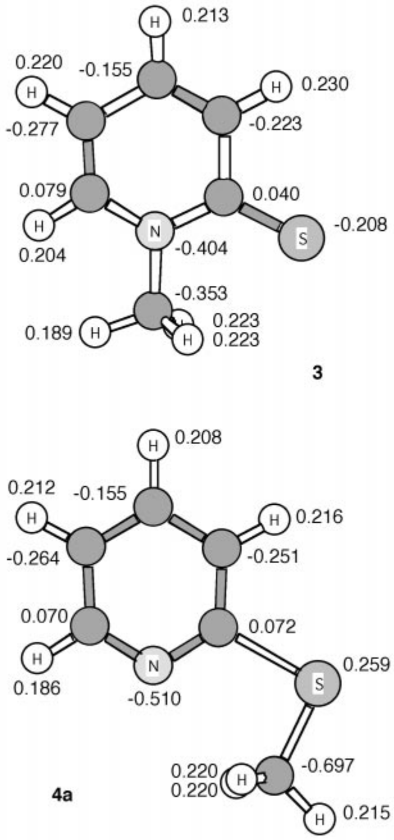


Fig. 2 Charge distribution in **3** and **4a** from Natural Population Analysis at the B3LYP/6-311+G(2d,p) level of theory.

3 (1π in Fig. 1), very close to its HOMO, exhibited a strong polarization of the methyl group as one would expect from hyperconjugation. Thus, the calculation of charge distribution in **3** and **4a**, carried out by means of Natural Population Analysis,[16] showed a transfer of 0.28 electrons from the methyl group to the π system (at the sulfur atom mainly) in **3** but not in **4a** (−0.04 electrons) (Fig. 2).

Vertical ionization potentials (VIPs)

Katritzky and co-workers[6] used photoelectron spectroscopy to study protomeric equilibria of mercaptopyridines. With this technique, they determined the first valence VIPs for compounds **1**–**4** in the gas phase, and they also made the corresponding orbital assignments. Table 2 contains the experimental

Table 2 First VIP (in eV[a]) of compounds **1** to **4**

Method[b]	**1**	**2a**	**3**	**4a**
Exper.[c]	7.80	8.79	7.69	8.24
HF	7.90	8.75	7.78	8.39
MP2(full)	7.84	8.71	7.72	8.37
B3LYP[d]	7.74	8.52	7.61	8.20
	(7.65)	(8.42)		

[a] 1 eV = 96.5 kJ mol^{-1}. [b] Calculations using 6-311+G(2d,p) basis set for geometry and energy. [c] From photoelectron spectra, ref. 6. [d] Adiabatic IPs in parentheses.

Table 3 Relative energies (ΔE, in eV) of valence orbitals to HOMO and assignments for methylated **3/4a** tautomers

Compound	Method[a]	ΔE [Assignment][b]				
3	Exper.[c]	0.00	−0.17	−2.81	−2.97	−4.42
	Estimated[c]	[π]	[n_S]	[π]	[π]	*n.j.*[d]
	B3LYP	0.00	−0.07	−2.88	−2.98	−4.09
		[n_S]	[1π]	[2π]	[3π]	[$\sigma + n_S$]
	HF	0.00	−0.71	−3.39	−3.76	−5.51
		[1π]	[n_S]	[2π]	[3π]	[$\sigma + n_S$]
	MP2(full)	0.00	−0.82	−3.45	−3.68	5.68
		[1π]	[n_S]	[2π]	[3π]	[$\sigma + n_S$]
4a	Exper.[c]	0.00	−1.32	−2.01	−2.38	−3.23
	Estimated[c]	[π]	[n_N]	[π]	[π]	[n_S]
	B3LYP	0.00	−1.28	−1.91	−2.23	−2.96
		[1π]	[n_N]	[2π]	[3π]	[n_S]
	HF	0.00	−2.13	−2.70	−2.96	−3.99
		[1π]	[2π]	[3π]	[n_N]	[n_S]
	MP2(full)	0.00	−2.08	−2.67	−3.10	−4.05
		[1π]	[2π]	[3π]	[n_N]	[n_S]

[a] Calculation using 6-311 + G(2d,p) basis set for geometry and energy. [b] Calculated assignments following Fig. 1. [c] From ref. 6. [d] Not justified in ref. 6.

(±0.03 eV) and calculated first VIPs of the compounds. From *ab initio* (HF and MP2) methods, these are simply sign-reversed orbital energies according to Koopmans' theorem[17] (which does not apply to the density functional formalism[18]). For DFT methodology, the first VIP was calculated by subtracting the total energy of the neutral molecule from the total energy of the cationic doublet state, spin-unrestricted B3LYP calculations being performed for both the neutral and cationic states. The HF or MP2(full)/6-311+G(2d,p) methods afforded values of first VIP (negative HOMO energy) close to experimental ones (error ≤0.15 eV). Except for **2a**, *ab initio* first VIPs were slightly greater than experimental values, and electronic correlation diminished the errors. The MP2 VIPs for thioamide derivatives **1** and **3** were in very good agreement with photoelectron spectra (error ≤0.04 eV), but for thioimidates **2a** and **4a**, the errors were 0.08–0.13 eV. The ΔSCF B3LYP/6-311+G(2d,p) methodology yielded good VIPs for **1**, **3** and **4a** (error ≤0.07 eV) giving values slightly less than experimental values, but for **2a** the VIP was abnormally low (error of 0.27 eV). Less stable conformers **2b** and **4b** afforded VIPs of 0.03 and 0.08 eV higher than for the corresponding **2a** and **4a** using *ab initio* calculations. Adiabatic ionization potentials of hydrogen derivatives **1** and **2a**, calculated at the B3LYP level, were 0.10 eV smaller than VIPs, as expected.

Table 3 shows the relative energies of the five last valence orbitals from HOMO and corresponding orbital assignments for methylated derivatives **3** and **4a**. Hydrogen derivatives had a similar energy distribution (data not shown). Fig. 1 displays the five highest valence OMOs for **3** and **4a** which correspond to Kohn–Sham orbitals using the B3LYP method as in Table 3. Hartree–Fock orbital types were similar with small differences. There is some controversy about whether the Kohn–Sham orbitals have a physical meaning although it is generally accepted that they are good approximations to the Hartree–Fock orbitals. However, recently it has been established[19] that the Kohn–Sham orbitals are physically sound and are expected to be more suitable for use in qualitative molecular orbital theory than either Hartree–Fock or semiempirical orbitals. Our work on OMOs, and another recent work on LUMOs,[20] present positive arguments for this assertion. As Table 3 shows, the relative energies of valence OMO between B3LYP/6-311+G(2d,p) and experimental values were in good agreement. Deviations increased with descending energy of the OMO, but it was ≤0.3 eV for the last five OMOs. The B3LYP assignments of the orbital types also agreed with estimations from ref. 6 (Table 3). Only the order of the two highest OMOs of **3** differed from the previous estimation. It is known that, for the majority of cyclic unsaturated thiocarbonyl compounds, the π ionization is generally at lower energy or at least equal to that for the lone pair on the sulfur atom.[21] The B3LYP method gave a VIP from the n_S OMO 0.07 eV smaller than for the π type OMO of **3**. The proximity of the nitrogen and sulfur atoms could stabilize the non-bonding n_S OMO,[6] but it seems that an overestimation of hyperconjugation by B3LYP decreased n_S energy below that of π OMO. Basis sets in DFT methodology did not affect the orbital assignments and only slightly affected the energies. The absolute energies of the last five OMOs from B3LYP/6-31G(d) were 0.2–0.3 eV less than those from B3LYP/6-311+G(2d,p), whereas differences in energies relative to HOMO were within ±0.08 eV. As shown from the above data, B3LYP/6-311+G(2d,p) may be a useful tool to obtain precise energies of valence OMO by adding Kohn–Sham relative energies from HOMO (Table 3 data) to the sign-reversed first VIP calculated by the ΔSCF procedure (Table 2 data).

The Koopmans' energies of the last five valence OMO from *ab initio* methods agreed poorly with the experimental VIPs of compounds (Table 3). *Ab initio* methods agreed with the estimation of orbital assignment in the case of thioamide **3**. However, HF or MP2/6-311+G(2d,p) methods assigned the n_N orbital of thioimidates **2a** or **4a** as HOMO-3 instead of HOMO-1 like estimations or B3LYP; with a less large basis set like 6-31G(d), it was assigned as HOMO-2.

Solvent effects on dipole moments

Dipole moments (DM) of **3** and **4** were previously determined in benzene solution,[7] but values in the gas phase remain unknown for methyl (**3** and **4**) and hydrogen (**1** and **2**) derivatives. However, experimental dipole moments for oxo analogs of **1** and **2** have been reported from microwave spectroscopy,[22] and the DM in benzene of oxo analogs of **3** and **4** have been reported.[7] Oxo analogs of **1** and **2** showed gas-phase DM of 0.26–0.31 D greater than the corresponding methylated oxo analogs of **3** and **4** in benzene solution. This agrees with the 0.22–0.27 D increase in dipole moment of **1** *vs.* **3** from either HF, MP2(full) or B3LYP/6-311+G(2d,p) gas-phase calculations (Table 1). It seems that dipole moments in benzene solution are not much different from gas-phase values. The calculated gas-phase DM of **3** is in good agreement with the experimental value in benzene (5.22 D) when electron correlation is taken into account (entries for B3LYP and MP2 in Table 1). On the other hand, the 2-methylthio derivative has two conformers, **4a** and **4b**, separated by 8–9 kJ mol^{-1} in the gas phase and with very different DM. The benzene effect calculated by the Onsager B3LYP/6-31G(d) method for the **4a/4b** rotamers was 1.9 kJ mol^{-1} in favor of the larger DM (**4b**). So the relative concentration of **4a** *vs.* **4b** in benzene should be 14 or 16:1, using gas-phase differences from MP2 or B3LYP (Table 1) and including the above benzene effect. Consequently, and applying the Eliel equation,[23] the calculated DM for **4** in benzene would be about 1.37 or 1.54 D from B3LYP or MP2 methods, respectively, rather close to the experimental value of 1.68 D.

Note that the calculated DM of methylated thioamide **3** was

Table 4 ^{14}N and ^{13}C-NMR chemical shifts relative to nitromethane[a] and TMS[b] respectively

Compound	Method	N1	C2	C3	C4	C5	C6	Me
3	*Experimental*[d]	*189 ± 2*	*181.1*	*134.6*	*135.7*	*113.3*	*142.6*	*45.7*
	HF/6-311+G(2d,p)	259.2	210.0	137.5	141.6	108.8	146.6	43.8
	Scaled[e]	*243.1*	*197.0*	*129.0*	*132.8*	*102.1*	*137.5*	*41.1*
	B3LYP/6-311+G(2d,p)	194.1	193.4	143.1	135.1	113.3	145.2	48.0
	Scaled[e]	*187.1*	*186.4*	*137.9*	*130.2*	*109.2*	*140.0*	*46.3*
4a	*Experimental*[d]	*79 ± 3*	*160.4*	*121.8*	*136.5*	*119.7*	*150.0*	*12.9*
	HF/6-311+G(2d,p)	122.9	171.7	122.0	145.2	118.1	157.5	16.5
	Scaled[e]	*117.9*	*164.7*	*117.0*	*139.2*	*113.3*	*151.0*	*15.8*
	B3LYP/6-311+G(2d,p)	80.2	173.5	125.4	139.1	121.2	155.7	19.5
	Scaled[e]	*76.9*	*166.4*	*120.3*	*133.4*	*116.2*	*149.3*	*18.7*

[a] $\chi_{\mathrm{Compd}} - \chi_{\mathrm{NO_2Me}}$ in ppm. [b] $\chi_{\mathrm{TMS}} - \chi_{\mathrm{Compd}}$ in ppm. [c] Wavefunction and geometry as indicated. [d] Determined in acetone solution from ref. 8. [e] Following ref. 30.

0.2–0.3 D less than that of the hydrogen derivative **1**, whereas the DM of the methyl derivative of the thioimidate **4a** was 0.7–0.9 D less than that of the hydrogen derivative **2a** (Table 1). Furthermore, the methyl rotamer **4b** had a DM 0.1 D bigger than the hydrogen rotamer **2b**. Thus the common practice in DM analysis to attribute similar values for methyl and hydrogen derivatives should be used with care for this type of heterocyclic system.

The SCRF methods overestimated the DM. The Onsager B3LYP/6-31G(d) method assigned 6.24 D to **3** in benzene, 1.02 D bigger than the experimental value. The SCIPCM B3LYP/6-31G(d) method gave 6.59 D for **3**, whereas the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) calculation yielded 6.40 D. Moreover, SCRF methods gave greater differences from the gas phase as well as in the DM of the molecule. Thus Onsager B3LYP/6-31G(d) increased the DM of **4a**, **4b** and **3** in benzene solution by 0.17, 0.29 and 0.66 D respectively from the gas-phase value.

^{13}C and ^{14}N-NMR chemical shifts

A comparison of the experimental and theoretical NMR spectra can be very useful in making correct assignments and understanding the basic chemical shift–molecular structure relationship. Semiempirical methods[24] provide a correct qualitative understanding of magnetic shielding tensors (χ), but they are not quantitatively accurate. *Ab initio* methods have been remarkably successful by applying the gauge factors to atomic orbitals (GIAO method[25]) or to localized molecular orbitals (IGLO[26] or LORG[27] methods). A new implementation of the GIAO method was claimed to be better for studying molecules with delocalized electron structure,[28] as in the case of **1** to **4**. The minimum recommended model for predicting NMR properties is GIAO HF/6-31G(d)//B3LYP/6-31G(d), but the triple-ξ basis set at HF level reproduces much better chemical shifts.[29] We have used this method, and we have also analyzed electron correlation by means of DFT (B3LYP) theory. Table 4 shows the relative chemical shifts for both methylated tautomers **3** and **4a**. The GIAO HF/6-311+G(2d,p) method properly reproduced the relative order of ^{13}C-NMR shifts in **4a**, and it explained up to 99% of experimental shift variance. When a scaling factor of 0.959 was introduced,[30] then the error of calculated shifts diminished from 4.8 ± 5.0 ppm to 0.0 ± 4.5 ppm. The GIAO *ab initio* method also predicted nearly 98% of experimental shift variance in thioamide **3**, but the C2 shift was placed further downfield than the experimental value. On the contrary, the GIAO HF method shifted ^{14}N to much higher fields than experimental values for both **3** and **4a**. In spite of that, GIAO HF/6-311+G(2d,p) could be considered an acceptable method to assign correct ^{13}C-NMR shifts.

The GIAO B3LYP/6-311+G(2d,p) method introduced electronic correlation through an impure DFT method, but it was a very efficient tool for the quantitative reproduction of both ^{14}N and ^{13}C-NMR shifts, as Table 4 shows. Scaling factors of 0.959 for **4a** and 0.964 for **3** were statistically deduced as the best to fit GIAO B3LYP shifts to experimental ones.[30] The errors obtained for **4a** and **3** ^{13}C-NMR shifts in acetone using scaled GIAO B3LYP/6-311+G(2d,p) data in the gas phase were 0.5 ± 4.3 ppm and −0.5 ± 4.3 ppm respectively, and they explained more than 99% of experimental variance. Relative ^{14}N-NMR shifts were reproduced exactly by scaled GIAO B3LYP methodology, even within experimental error (Table 4). Scaling factors were essentially the same for HF and B3LYP/6-311+G(2d,p) methods and also for **4a** and **3** tautomers,[31] and could be approximated by 0.96. Geometries of the compounds are an important factor to be considered in the reproduction of NMR shifts. Thus GIAO HF/6-311+G(2d,p)//B3LYP/6-31G(d) gave relative **4a** ^{13}C-NMR shifts 1–2 ppm higher than from B3LYP/6-311+G(2d,p) geometry.

Conclusions

Both **1** and **2** Koopmans' ionization potentials from HF, or MP2(full)/6-311+G(2d,p) were accurate within ±0.10 eV of experimental values. Except for **2**, vertical IPs of **1** through **4** from B3LYP/6-311+G(2d,p) were more exact than Koopmans' IPs from HF and MP2 calculations. However, DFT methodology gave a more accurate description of known relative energies of valence molecular orbitals for compounds **1** through **4** than *ab initio* methodology. Dipole moments in benzene solution of **3** and **4** were better reproduced by calculations in the gas phase than by SCRF methods. Methods which include electronic correlation, like MP2(full) or B3LYP/6-311+G(2d,p), were necessary to approximate dipole moments. However, HF/6-311+G(2d,p) gave poor results. The ^{14}N-NMR shifts of **3** and **4** in acetone were exactly reproduced by B3LYP but poorly by HF calculations using GIAO methodology and a 6-311+G(2d,p) basis set. Except for C2, which was overestimated (>10 ppm), experimental ^{13}C-NMR shifts of **3** and **4** in acetone agreed well with calculated shifts from both HF and B3LYP/6-311+G(2d,p) methods in the gas phase. A scaling factor of 0.96 is recommended to fit calculated relative ^{14}N and ^{13}C-NMR chemical shifts to experimental ones at the above levels of theory.

The results from the B3LYP/6-311+G(2d,p) method indicate that it could be a very efficient tool for modeling properties derived from electronic distribution of thiated nucleobases.

Theoretical methods and computational details

All calculations were performed using the GAUSSIAN94 (g94)[32] suite of programs. Geometrical optimizations of neutral molecules in the gas phase were carried out at three different theoretical levels: restricted Hartree–Fock (RHF),[33] second-order Møller–Plesset[34] including all electrons in the correlation calculation (MP2-full), and DFT using the three-parameter hybrid function developed by Becke (B3LYP).[35] The basis sets used were Pople's 6-311+G(2d,p) for H, C, N and S.[33,36] The analytical harmonic vibrational frequency calculations were done to characterize the nature of stationary points on the potential energy surface and to estimate the zero-point vibrational energy (ZPE) at the HF and B3LYP levels. The ZPE values were scaled by 0.89 at the HF level and by 0.98 at the B3LYP level to eliminate known systematic errors.[10,37]

The valence ionization potentials (IPs) were obtained from *ab initio* spin-restricted HF and MP2 calculations following Koopmans' theorem: simple sign-reversed orbital energies. However, DFT IPs were obtained by an ΔSCF procedure using spin-unrestricted calculations. In more detail, the difference between the calculated energies of the neutral and cation at their respective equilibrium geometries, corrected for the ZPE, gave the adiabatic ionization potential (AIP); calculation for the cation at the geometry of the neutral gave the vertical ionization potential (VIP) (no correction for ZPE was made in this case).[38] In all cases, when unrestricted wave functions were used, the spin contamination was small ($\langle S^2 \rangle \leqslant 0.76$).

Magnetic shielding tensors ^{13}C and ^{14}N, calculated at the HF or B3LYP/6-311+G(2d,p) levels from the optimized structures, were obtained following the gauge-independent atomic orbital (GIAO) method.[25,28,39] The differences between magnetic shielding tensors (χ) of nuclei in the reference molecule (tetramethylsilane for ^{13}C-NMR and nitromethane for ^{14}N-NMR) and the studied molecule (**3** and **4**) were considered as relevant chemical shifts.[25]

Nonspecific solvent effects on the geometry and physicochemical properties of the molecules and relative stability at the tautomeric equilibrium were studied using the self-consistent reaction field (SCRF) with the Onsager model[9] and with the self-consistent isodensity polarized continuum model (SCIPCM)[10] developed from a reaction field based on the polarized continuum model proposed by Tomasi and co-workers.[40] In the SCRF calculations, the solute is placed in a uniform electric field of solvent with a dielectric constant ε or a reaction field.

In the SCRF Onsager model, the solute is assumed to occupy a spherical cavity of radius a_0 in the medium. The cavity radius for each conformer, a_0, was determined by performing a single-point calculation with the keyword VOLUME of g94 programs at the optimized geometry of the B3LYP/6-31G(d) level (gas phase). The resulting values of a_0 were 4.45 Å for compound **3**, 4.32 Å for its tautomer **4a** (dihedral angle N1–C2–S–Me = 0°), and 4.19 Å for the conformer **4b** (dihedral angle N1–C2–S–H = 180°).

In the SCIPCM model, the cavity is defined as an isosurface of the molecule, and the coupling of the isosurface and the electron density are taken fully into account. This procedure solves for the electron density that minimizes the energy, including the solvation energy, which itself depends on the cavity which depends on the electron density. In this case, the effects of solvation are folded into the iterative SCF computation rather than comprising an extra step afterwards.

All SCRF geometry optimizations in solution were carried out at the B3LYP/6-31G(d) level of theory. Single-point energy calculations were also performed using SCRF HF or B3LYP/6-311+G(2d,p) wavefunctions and above SCRF B3LYP/6-31G(d) optimized structures.

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