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Predicting the spin state of paramagnetic iron complexes by DFT calculation of proton NMR spectra

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Abstract

Many transition-metal complexes easily change their spin state *S* in response to external perturbations (spin crossover). Determining such states and their dynamics can play a central role in the understanding of useful properties such as molecular magnetism or catalytic behavior, but is often far from straightforward. In this work we demonstrate that, at a moderate computational cost, density functional calculations can predict the correct ground spin state of Fe(II) and Fe(III) complexes and can then be used to determine the ¹H NMR spectra of all spin states. Since the spectral features are remarkably different according to the spin state, calculated ¹H NMR resonances can be used to infer the correct spin state, along with supporting the structure elucidation of numerous paramagnetic complexes.

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Introduction

Many transition-metal complexes can exist in different electronic configurations, leading in turn to states of different spin *S*. The most stable spin state of a given complex can often be empirically predicted on the basis of ligand-field strength arguments (or by comparison with similar ones) but this approach is not always straightforward or feasible. In fact, when the separation between the energy of spin states is small, even subtle changes in the ligands may cause a switch in the relative stability. This phenomenon acquires a major significance whenever the spin transition is triggered by external factors such as temperature (when the energy difference is comparable to kT), pressure (owing to the different bond lengths that are typical of each spin state) or light (LIESST). Such factors may give rise to the so-called spin-crossover (SCO), a phenomenon which is being intensely investigated in molecules, materials,¹ single-molecule magnets² or even ionic liquids³ as a means to store information. Indeed one of the most studied examples of spin crossover is probably that of iron: according to the ligands, Fe(III) complexes (d^6) can exist in the singlet (S = 0), triplet (S = 1) or quintet (S = 2) states; likewise, Fe(III) complexes (d^5) can exist in the S = 1/2, S = 3/2 or S = 5/2 states. In a biochemical context, it is worth recalling that a spin-state change of Fe(III) lies at the root of the catalytic cycle of cytochrome P450.⁴

Clearly, being able to probe and predict the spin state of such kind of complexes represents an attractive perspective, since this would allow to design complexes with desired characteristics for specific tasks. An important advancement in this area is the development of force fields parameterized against the spin-state energies of Fe(II) complexes, which may allow for the exploration of many potential candidates for a given property.⁵

In the case of iron complexes, the spin state is generally assessed by Mössbauer and EPR spectroscopies, or by measuring the molecular magnetic moment via NMR spectroscopy. The former technique, however powerful, is essentially limited to Fe and may require ⁵⁷Fe enrichment, whereas the short relaxation time of Fe(II,III) $(10^{-13} \text{ to } 10^{-11} \text{ s})$ may lead to barely detectable EPR lines. In contrast (and for the same reasons), ¹H NMR spectra of paramagnetic iron complexes are fairly easy to obtain⁶ but are mostly used only to estimate the magnetic moment, despite the wealth of information that could be gathered by a detailed spectral analysis.

On the other hand, the interpretation of such ¹H NMR spectra is complicated by line broadening and major paramagnetic shifts, which lead to "unpredictable" resonance frequencies, to the point that integrated intensities, or the spectra of selectively labeled isotopomers, may be the sole solid ground against which the spectra – if available at all – are interpreted.⁶ Indeed, while

several articles^{1,7,8} have reviewed specific classes of SCO complexes, NMR spectroscopy is not routinely used for their characterization, and such data are hardly assigned or even reported.

Some empirical criteria, which employ DFT calculations, have been proposed to correlate NMR spectra with the electronic configuration and hence on the spin state of iron porphyrins,^{9,10} but their scope may not be general.

Many difficulties can, in principle, be overcome by computing all the needed spectral features by the same quantum-chemistry methods that have been successfully applied to the prediction of the spectra of diamagnetic molecules.¹¹⁻¹³ An analogous approach aimed at open-shell species (including transition-metal complexes) is much more involved, since it also requires the calculation of the *g* tensor and of the hyperfine couplings for any arbitrary spin state.¹¹ Methods for improving the calculation of these quantities are still under development.¹⁴⁻²²

Even with some well-known limitations and caveats of current DFT methods, the NMR spectra of several paramagnetic molecules and complexes have been successfully predicted by DFT at moderate computational cost,^{23,24} but in all cases so far investigated the spin state was unequivocally known.

This evidence leads to the question: is NMR spectroscopy an adequate characterization tool to probe the spin state when it is unknown or when it may change in response to external perturbations? In other words, can NMR spectra distinguish unequivocally among possible spin states? In order to address this issue one needs computational methods that, on top of being sufficiently accurate to provide a meaningful prediction of NMR parameters, should be able to rank the energy of all spin states in the correct order.

The performance of quantum-chemistry methods with regard to spin-state energetics and SCO has been reviewed and density functional theory methods have received special attention.²⁵⁻²⁸ Other pertinent examples include the theoretical analysis of SCO pathways in square-planar grid complexes,²⁹ and the prediction of SCO temperature.³⁰

The B3LYP* functional proposed by Reiher (derived from the widely used B3LYP but with a lower percentage of Hartree-Fock exchange)³¹ was shown to give correct predictions of the spinstate energies of various Fe(II) complexes.^{1,25,31-34} In a different context, Swart indicated a superior performance of Slater basis sets in contrast to gaussian ones with respect to ease of convergence and a good performance of the OPBE functional.^{35,36} A recent systematic investigation by Neese³⁷ concluded that the best results are obtained by the double-hybrid B2PLYP functional,³⁸ where correlation is dealt with in an MP2-like ab initio step. Despite the good results thus obtained, this approach (coupled with a very large basis set as recommended) effectively limits application to smaller systems than those of current interest. This limitation becomes especially severe for the more expensive NMR calculations.

Thus, there remains the need for a computational method that is sufficiently accurate and inexpensive to satisfy the two-fold requirement of energetics and NMR, along with a general scope of application. With this aim in mind, we have focused on a series of Fe(II,III) complexes in all their allowed spin states, following a preliminary benchmark investigation of various combinations of density functionals and basis sets.

Computational and Experimental section

Computational details. We have proceeded along two parallel paths, i.e. adopting either gaussian or Slater basis sets in order to check for the robustness of a given combination of density functional and basis set. The calculations were carried out with Gaussian 09³⁹ and ADF⁴⁰ software, respectively.

In calculations with gaussian basis sets, the geometries of complexes in groups (a) and (b) (see below) were optimized with several functionals (hybrid: B3LYP, B3LYP*, X3LYP, PBE0; meta-hybrid: M06, M06-2X; meta-GGA: M06-L) and the 6-31G(d,p) basis set, followed by vibrational analysis to yield zero-point energies. Final energies were computed with each respective functional; NMR parameters only with B3LYP*. The cc-pVTZ basis set was employed in both cases. The B3LYP* functional in Gaussian 09 is invoked through the following route: B3LYP IOp(3/76=1000001500) IOp(3/77=0720008000) IOp(3/78=0810010000).

The contact contribution ($\sigma_{FC} = -\delta_{FC}$) to the total shielding σ was determined according to eq. (2), so that $\sigma = \sigma_{orb} + \sigma_{FC}$ and $\delta = \sigma_{ref} - \sigma$, with $\sigma_{ref} = 31.08$ ppm (for TMS at the same theoretical level). The temperature was set to the value indicated in the reference works.

In calculations with Slater basis sets, geometries were optimized at the OPBE/TZP level (i.e. with a GGA functional), followed by single-point energy calculations with various functionals (B3LYP, B3LYP*, PBE0, M06, M06-L) and the TZ2P basis set. The choice of OPBE was motivated by the good results it afforded, as previously noted,^{36,37} no vibrational analysis was carried out. Complexes (b) were investigated only with the B3LYP* functional along the same lines.

Experimental section. $[Fe^{II}(phen)_2(NCS)_2]$ (11) was synthesized according to literature methods.⁴¹ ¹H NMR spectra were recorded in DMSO-*d*₆ at 298 K on a Bruker Avance III spectrometer operating at a proton resonance frequency of 500.13 MHz. Chemical shifts are referenced to residual DMSO. 128 scans with a spectral width of 200 ppm were acquired

(acquisition time 0.4 s). IR spectra (solid state: KBr pellet; liquid state: DMSO) were recorded on a Perkin Elmer 1720X instrument.

Results

Details of the iron complexes investigated in this work are given in Scheme 1, along with their full structures; in order to facilitate a comparison with the literature, the labeling scheme adopted in the original works was retained wherever possible. The known ground-state multiplicity is given; however, the energy gap to the next spin state is not always experimentally known.

(a) Fe(II) and Fe(III) complexes differing in the ground state multiplicities. The $[Fe^{II}(N_HS_4)(L)]$ series: L = NO⁺ (1), CO (2), PMe₃ (3), PH₃ (4), N₂H₄ (5), NH₃ (6). 1-4 (S = 0); 5-6 (S = 2).^{26,37} [Fe^{III}(por)Cl] (7, S = 5/2); [Fe^{III}(pyPepS)₂]⁻ (8, S = 1/2); [Fe^{III}(tsalen)Cl] (9, S = 3/2); [Fe^{III}(N(CH₂-o-C₆H₄S)₃(1-MeIm)] (10, S = 5/2).^{35,37} These complexes were considered for comparison purposes with regard to their spin-state energies, because their NMR spectra are not available; details are reported only in the Electronic Supplementary Information (ESI).

(b) Fe(III) complexes with assigned experimental NMR spectra: $[Fe^{III}(L)Cl]$ (11, S = 3/2);⁴² $[Fe^{III}(oetpp)(HIm)]^+$ (12, S = 3/2).⁴³

(c) Fe(II) complexes known to exhibit thermal spin crossover: *cis*- and *trans*-[Fe^{II}(phen)₂(NCS)₂] (**13a-b**, S = 2);^{31,37} [Fe^{II}(L1R₁R₂)(py)₂] (**14**: R₁ = OEt, R₂ = CH₃; **15**: R₁ = CH₃, R₂ = CH₃; **16**: R₁ = OEt, R₂ = OEt; S = 2).⁴⁴ Calculations with Slater basis sets were performed only for **1-13a**.

Ligands are abbreviated as follows. $N_HS_4 = 2,2'$ -bis(2-mercaptophenylthio)diethylamine dianion; por = porphyrinate; pyPepS = N-(2-mercaptophenyl)-2-pyridinecarboxamide); tsalen = N,N'-ethylenebis(thiosalicylideneiminato); $N(CH_2-o-C_6H_4S)_3 = 2,2',2''-(nitrilotris(methylene))tribenzenethiolato; MeIM = methylimidazole; L = diethyl 5,14-dimethyl-1,4,8,11-tetraazacyclotetradeca-4,7,11,14-tetraene-6,13-dicarboxylato; oetpp = 2,3,7,8,12,13,17,18-octa-ethyl-5,10,15,20-tetraphenyl-21H,23H-porphinato; HIm = imidazole; phen = 1,10-phenanthroline; L1 = <math>N,N'$ -o-phenylenebis(R,R'-vinylamido).



Scheme 1. Structures of complexes 11-16. In 12, the porphyrin system is strongly non-planar; therefore the ethyl groups may be "up" or "down" with respect to the imidazole ligand. The labeling scheme adopted in the original works was retained as much as possible. For 14-16, two axial pyridine ligands are not drawn.

Spin-state energies

The triplet state (S = 1) was also considered for Fe(II) complexes, but was never found to be more stable than the singlet or the quintet; therefore it will not be further discussed, except for a single illustrative example (see below).

Various density functionals were tested with gaussian and Slater basis set on complexes (a), as noted above. It is difficult to draw general conclusions, because most energy gaps between the spin states are known at best in a semi-quantitative way (if SCO is observed, ΔE should be of the order of kT; see below). In general, hybrid and meta-hybrid functionals tended to stabilize high-spin states, as known, whereas the OPBE (GGA) and M06-L (meta-GGA) functionals provide correct energies in most cases (the former may be recommended for larger systems, owing to its faster evaluation). However, the best overall performance was observed with B3LYP*.

The results for complexes **1-16** are presented graphically in Scheme 2 at the B3LYP*/ccpVTZ level; complete results (including those with Slater basis sets, which yielded the same results) are provided in the ESI (Table S1: compact form; Tables S2-S3: detailed).



Scheme 2. Summary of relative energies of spin states of iron complexes at the B3LYP*/cc-pVTZ level. See the ESI for results with other density functionals (Tables S1-S3) and Scheme 1 for structures. (a) Fe(II), (b) Fe(III). Energies (in kJ mol⁻¹) are ranked with respect to the most stable spin state and the known ground-state multiplicity is highlighted in a box. Hence, a highlighted value of zero indicates a correct prediction.

The predicted ground state is correct for 1-6. Fe(III) complexes are predicted correctly except for the porphyrinate 7; however, the difference between the two states is less than 8 kJ mol⁻¹, which is within the expected error of DFT methods. Remarkably, SCO complexes give energy differences of ca. 4 kJ mol⁻¹ between the S = 0 and S = 2 states for 14-16, indicating that this method is capable of correctly highlighting complexes with such a feature. When the calculated energies are close to each other (less than 20 kJ mol⁻¹), inclusion of zero-point energies may reverse the relative stability, as in the case of 16, where the prediction is incorrect without ZPE; otherwise the balance is essentially unaffected.

In summary, the B3LYP* functional, which was designed to remedy the known tendency of B3LYP to overstabilize high-spin states,³¹ seems to be a good choice to predict spin-state energetics at the same computational cost as the all-purpose B3LYP. This conclusion holds for both gaussian and Slater basis sets, thereby allowing for a wide choice of methods.

NMR spectra

The acquisition and assignment of NMR spectra for paramagnetic compounds is not trivial, because the signals appear at unusual resonance frequencies (generally unrelated to typical structural effects) and are often broadened, sometimes beyond detectability. The reason is that the resonance frequencies of paramagnetic molecules are dominated by interactions between nuclear and electron magnetic moments (i.e. the Fermi contact and dipolar interactions) which add to the usual diamagnetic (orbital) contribution. In general, the observed shift for a paramagnetic molecule can be written as eq. $(1)^6$

$$\delta = \delta_{\rm orb} + \delta_{\rm FC} + \delta_{\rm PC} \tag{1}$$

The orbital term (δ_{orb}) is equivalent to shielding for diamagnetic molecules and generally it lies close to that of an analogue diamagnetic system. The Fermi contact term (δ_{FC}) originates from the scalar interaction between the magnetic moment of the resonant nucleus and the effective local field arising from the unpaired electron density at the same nucleus, as given by eq. (2)

$$\delta_{FC} = \frac{2\pi}{\gamma_{\rm I}} g_{\rm iso} \mu_{\rm B} A \frac{S(S+1)}{3kT}$$
(2)

where γ_1 is the magnetogyric ratio of the nucleus *I*, g_{iso} the isotropic electron *g*-factor, μ_B the Bohr magneton, *A* the isotropic hyperfine coupling constant in frequency units, and *kT* the thermal energy.⁶ Contact shifts have therefore been estimated through eq. (2) taking advantage of calculated values of g_e and *A* for each assumed *S* value of complexes **11-16**.

The pseudocontact term (δ_{PC}) couples the nuclear magnetic moments with the static induced magnetic moment of the molecule: this term depends on the anisotropy of the magnetic susceptibility tensor (or, in an alternate view, on the anisotropy of the *g* tensor). Its evaluation requires an accurate prediction of the components of the *g* tensor; even then, this would not guarantee to obtain accurate pseudocontact shifts, since the current approach⁶ adopts a metal-centered, point-dipole approximation which is probably inadequate for systems with highly delocalized spin densities as those dealt with herein. However, in most transition-metal complexes (except lanthanides) δ_{PC} is negligible with respect to δ_{FC} ;⁶ therefore, this contribution will be neglected.

Another prominent feature of paramagnetic NMR spectra are the broad lines, which can be understood in terms of two main electron-nuclear interaction mechanisms (dipolar and hyperfine) leading to fast nuclear relaxation. The longitudinal and transverse relaxation times can be expressed by the Solomon-Bloembergen equations which include structural parameters, such as the electronnuclear distance (*r*) and the electron-nuclear hyperfine coupling constant (*A*), along with moleculardynamics parameters like the rotational correlation time (τ_r) and the correlation times for the electronic and exchange interactions (τ_S , τ_M). In this work, line widths $W = 1/\pi T_2$ (where T_2 is the transverse relaxation time) have been estimated from Solomon-Bloembergen equations (eq. S1-S2), using calculated values of *r*, g_{iso} and *A* for each assumed *S* value. The electron relaxation time τ_e was assumed to be 5×10^{-13} s for Fe(II) and 10^{-10} s for Fe(III).⁶ Rotational correlation times were estimated from calculated molecular volumes: note that uncertainties in correlation times will systematically affect all line widths (See ESI for details).

NMR results are presented graphically, as a comparison of experimental and calculated spectra; all numerical data are collected in Table S4. A more detailed analysis (correlation plots of δ_{calc} vs. δ_{exp}) is collected in the ESI (Figure S2). Isosurfaces (isovalue 4 × 10⁻⁴ au) of the spin densities for some complexes are displayed in Figure 1; they give a qualitative picture of the degree of spin delocalization and associated shifts.

We remark that NMR parameters have been computed only with the B3LYP* functional. Hybrid functionals with a larger percentage of Hartree-Fock exchange have been recommended for computing the shielding of paramagnetics (e.g. modifying BPW91 with 30% exchange).²³ Our choice is motivated by the need of retaining the same method that provided correct spin-state energies (and therefore a correct electronic structure), which is justified *a posteriori* by the good agreement with experiment thus attained.





11, S = 3/2









13b, S = 2



Figure 1. Isosurfaces (isovalue 4×10^{-4} au) of the spin densities for representative iron complexes.

[Fe^{III}(L)Cl] (11). This complex is known to adopt the S = 3/2 state in the 278-348 K temperature range, showing an ideal Curie behavior which indicates the presence of a single spin state.⁴² Calculated relative energies clearly indicate an S = 3/2 ground state, with the low- and high-spin states well above in energy (35-40 kJ mol⁻¹; Scheme 2).

Calculated shifts are plotted against experiment in Figure S2a, while NMR spectra are collected in Figure 2; the correlation for S = 3/2 is excellent across ca. 300 ppm. Note that the CH₂ ligand bridge protons (H-5,5' and H-6,6') are not equivalent and give rise to four distinct resonances. Also, the spin density is delocalized across the whole framework; most protons (except H-4 at -188 ppm) experience only moderate shifts. The spectral patterns that arise from each *S* value are strikingly different in the shift range, relative ordering of signals and their widths.



Figure 2. Experimental and calculated ¹H spectra of **11**. (a) Experimental spectrum at 318 K. (b)-(d) Calculated spectra with S = 1/2 (b), 3/2 (c) and 5/2 (d). Experimental spectra reprinted with permission from B. Weber, F. A. Walker, K. Karaghiosoff, *Z. Anorg. Allg. Chem.* **2013**, 1498-1503. Copyright 2013 Wiley-VCH.

 $[Fe^{III}(oetpp)(HIm)]^+$ (12). This complex was reported by Nakamura and coworkers⁴³ as a cytochrome *c'* model; it is known to be in the quartet state (*S* = 3/2) at room temperature and to undergo spin crossover to a mixed (*S* = 5/2, *S* = 1/2) phase below 60 K. Well-resolved ¹H spectra, spread over a 100-ppm range, are available and were analyzed and assigned also by correlation experiments. Only three signals are experimentally found for the imidazole ligand, probably owing to ligand and proton exchange. Most differences between calculated and experimental spectra are

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due to the mobile ethyl group attached to the rigid porphyrin core; this is somewhat expected because we did not investigate the possible alkyl-chain conformers in any detail, nor the effects of conformational processes involving the whole porphyrin core.¹⁰

Calculated energies definitely favor the S = 3/2 state, whereas the S = 5/2 state is ca. 45 kJ mol⁻¹ higher in energy; the S = 1/2 state could not be calculated, owing to lack of SCF convergence. Calculated shifts for S = 3/2 and 5/2 are plotted against experiment in Figure S2b and NMR spectra are collected in Figure 3. The calculated spectrum for S = 3/2 matches experiment better than the one for S = 5/2 as expected,⁴³ even though the calculated shifts span a similar range.



Figure 3. Experimental and calculated ¹H spectra of **12**. (a) Experimental spectrum at 298 K, and detail of the crowded region between 30 and -5 ppm. (b)-(c) Calculated spectra with S = 3/2 (b) and S = 5/2 (c). Experimental spectra reprinted with permission from A. Ikezaki, M. Takahashi, M. Nakamura, *Angew. Chem. Int. Ed.* **2009**, *48*, 6300-6303. Copyright 2009 Wiley-VCH.

 $[Fe^{II}(phen)_2(NCS)_2]$ (13). This compound is the prototype of spin-crossover complexes and has been the subject of numerous experimental⁴⁵ and computational^{26,31,37,46,47} investigations. It is

generally assumed to have a diamagnetic ground state (S = 0) and to undergo a spin transition to S = 2 at 175 K in the solid state⁴⁸ The experimentally determined thermodynamic parameters for the interconversion are: $\Delta H = 8.6$ kJ mol⁻¹, $\Delta S = 49$ J mol⁻¹ K⁻¹,^{45(a)} which correspond to $\Delta G = ca. 0$ kJ mol⁻¹.

It can exist in a *cis* (13a) or *trans* (13b) configuration; the two are easily distinguished by IR spectroscopy, because the CN stretching band occurs as a single or double peak for the *trans* and *cis*, respectively. The IR spectrum in the solid state is consistent with the *cis* isomer, whereas in DMSO solution (adopted for NMR) the complex is present in the *trans* configuration, as shown by the single peak at 2055 cm⁻¹ (Figure S3).

The calculations indicate that the spin-state energetics are different for the *cis* and *trans* isomers. For **13a** (*cis*) the S = 1 state is ca. 45 kJ mol⁻¹ higher in energy, whereas the energy gap between the S = 0 and S = 2 states does not exceed 8 kJ mol⁻¹, which agrees with experimental results. For **13b** (*trans*), both the S = 0 and 1 states are much higher in energy (by 35-40 kJ mol⁻¹) than S = 2, which can be considered the only populated state at room temperature. Thus, spin crossover is borne out only for the *cis* isomer.

Low-spin Fe(II) complexes are diamagnetic and therefore provide easily assigned spectra. The ¹H NMR spectrum of **13** at room temperature (Figure 4a) features the expected four signals with 1:1:1:1 integrated intensities, paramagnetically shifted, the most prominent feature being a broad signal at 163 ppm. These could not be assigned with correlation experiments, owing to fast relaxation.

Given the spin-state energetics outlined above, the distinction between the two isomers concerns only the S = 2 state. The calculated NMR spectra of **13a** and **13b** are qualitatively similar, except that the *ortho* proton in **13a** and **13b** is predicted respectively at 235 and 181 ppm; the good agreement with the latter confirms that **13b** is present in solution, and allows to assign the signal at 163 ppm as H-o. If the other signals are assigned by arranging them in increasing order (see Figure S2c), a good correlation with a slope close to unity is obtained. In doing so, it is worth to point out that the signal line widths also qualitatively agree with the calculated ones: for example, the signal at 52 ppm is rather broad, as is the calculated one for H-m (77 ppm).

The spin densities of **13a-b** are reported in Figure 1. In the *cis* isomer the spin density is more delocalized onto the aromatic ligand, in agreement with the higher deshielding of all the protons in **13a** with respect to **13b**.

Therefore, the results are consistent with the *trans* isomer (13b) in the quintet state (S = 2) at room temperature. For completeness, the calculated spectrum of the unstable S = 1 state is also

compared with experiment in Figure 4. Even though the correlation is of similar statistical quality (except for the small slope, see Figure S2c), the *ortho* proton (89 ppm) turns out to be much more shielded than experiment (163 ppm) and the experimental and calculated line widths do not match.



Figure 4. Experimental and calculated ¹H spectra of **13b**. (a) Experimental spectrum at 298 K in DMSO. (b)-(c) Calculated spectra with S = 1 (b) and 2 (c).

[Fe^{II}(L1R₁R₂)(py)₂] (14-16). These complexes are known to have a quintet ground-state multiplicity (S = 2) at room temperature, undergoing SCO to the singlet state (S = 0) around 200 K.⁴⁴ The experimentally determined thermodynamic parameters for the interconversion are: $\Delta H = 18.2 \text{ kJ mol}^{-1}$, $\Delta S = 88 \text{ J mol}^{-1} \text{ K}^{-1}$ at 207 K (14) and $\Delta H = 25.5 \text{ kJ mol}^{-1}$, $\Delta S = 121 \text{ J mol}^{-1} \text{ K}^{-1}$ at 211 K (15);⁴⁴ both correspond to $\Delta G = \text{ca. 0 kJ mol}^{-1}$. However, the experimental magnetic susceptibility never reaches the expected values for S = 2 measured for some analogues,⁴⁹ which

suggests that even at room temperature the quintet state is not fully populated. ¹H NMR spectra⁴⁴ are consistent with a paramagnetic state and were empirically assigned; a major feature is an extremely deshielded signal at ca. 500 ppm along with other moderately shifted peaks. Signals from the pyridine ligand were not reported.

The calculated energy gap between S = 0 and 2 is 14 kJ mol⁻¹ at most; upon inclusion of ZPVE, the quintet state becomes less stable than the singlet by < 3.5 kJ mol⁻¹ (Scheme 2), i.e. the two states can be considered isoenergetic within the accuracy expected for this level of theory. The order of magnitude of the computed gap is consistent with experiment.

The calculated spectral parameters for **14-16** in the S = 2 state are plotted against the experimental ones in Figure S2d, and the spectra compared in Figure 5. All parameters fit experiment fairly well, especially **14** and **15**. For **16** the agreement is worse; this complex is characterized by flexible ethyl chains, whose accessible conformational space greatly complicates the analysis. Since even slight conformational changes may cause noticeable changes in *A* (and hence in δ_{FC})^{23,24} the discrepancy is not surprising. A noteworthy feature is the very deshielded H-i peak, which is correctly modeled as the one experiencing the highest spin density (Figure 1). The slopes of the correlation lines are 1.6-1.7, *i.e.* the calculated shifts are much larger than experiment; *e.g.* the H-i peak at ca. 550 ppm is calculated at ca. 900 ppm. This is consistent with the complexes not being completely in the quintet state. The overestimated value can be reconciled with experiment by recalling that at room temperature the two spin states exchange at a much higher rate than the NMR time scale.⁴⁴ Recalling that the high- and low-spin states are essentially isoenergetic, exchange with the singlet state would lead to a substantially smaller shift for H-i. Overall, the spectral features and magnetic susceptibility experiments are consistent with the predictions for the S = 2 state with coexistence of the low-spin diamagnetic state in fast exchange.



Figure 5. Experimental and calculated ¹H spectra of (left to right) **14-16**. Top panel: experimental spectra at 298 K; bottom panel: calculated spectra for S = 2. For clarity, the signal at ca. 500 ppm is not shown. S denotes a solvent peak. Experimental spectra reprinted with permission from B. Weber, F. A. Walker, *Inorg. Chem.* **2007**, *46*, 6794-6803. Copyright 2007 American Chemical Society.

Discussion

The results presented herein further showcase the predictive power of relatively inexpensive DFT calculations at predicting both the relative spin-state energies and the associated paramagnetic NMR spectra. Thus, the B3LYP* functional ranks the energies of all the investigated Fe(II,III) complexes in a qualitatively correct order; the OPBE functional exhibits a similar performance. A large energy gap between the ground spin state and the others is reflected in the presence of a single non-crossover species, whereas for known spin-crossover species the spin-state energy differences lie below 8.5 kJ mol⁻¹. Therefore (at least within the current scope), this approach allows to make reliable predictions of the spin-state energetics and can be put to advantage in designing complexes endowed with the desired characteristics.

Concerning NMR spectroscopic properties, it is firstly confirmed that the major features of paramagnetically shifted NMR spectra are predicted with sufficient accuracy to assign most peaks without recourse to empirical arguments. Noteworthy, these conclusions hold even within a simplified framework like that embodied in eq. (2), and within the accuracy of common DFT methods. Problems may arise in the case of conformationally flexible species, since each conformer

may appreciably differ in its hyperfine coupling constants and therefore provide results that depend heavily on the specific conformer obtained by geometry optimization (similar problems are encountered with diamagnetic molecules too, except that the differences are then much smaller). This shortcoming can probably be addressed by employing the same tools developed and tested for conformationally flexible diamagnetic molecules,^{12,50,51} but does not introduce further conceptual complexity.

A straightforward application of these notions concerns the capability of understanding the spectra of paramagnetic reactive intermediates like those encountered in catalytic cycles mediated by transition-metal complexes; their NMR spectra are generally difficult to obtain, which adds to the difficulties in assignment.⁵² Application to the investigation of such reaction mechanisms can then be envisioned.

The final and most important issue concerns whether NMR spectra provide a reliable tool to establish the spin state unambiguously. As we have seen, the protocol presented here ranks the spin states in a correct energy ladder. Therefore, the same calculations can be used to obtain virtual NMR spectra for each state, including those that are energetically distant or experimentally inaccessible. The question is, then, whether such spectra differ in ways that can be exploited in practice.

In the case of Fe(II) the answer may be "trivial", in the sense that if the only viable states are S = 0 and S = 2 the low-spin state is diamagnetic and is easily told apart. However, even in this relatively simple instance a calculation will allow one to assign the spectrum of the high-spin state (see e.g. 13) and, even more importantly, indicate the presence of a mixed state, as shown in the case of 14-16. Moreover, Fe(II) complexes may in principle also be in the S = 1 state, in which case (see 13) the NMR spectrum will not indicate either state without computational support.

Fe(III) complexes, on the other hand, are always paramagnetic. As clearly shown by complex **11** in Figure 2, the three spin states give rise to deeply different spectral features which, while not predictable in any intuitive way, can nevertheless be calculated and assigned. In this striking case, even the shift ranges are so different that the only spin state observed (S = 3/2) is borne out. In the case of **12** the differences are less marked (Figure 3) but still easily detected, also by a correlation plot (Figure S2b).

Prediction of line widths relies to a great extent on the electronic relaxation time, which is not always available; for this work we have adopted recommended values, which may not be fully adequate for all complexes but would affect all line widths systematically. Nonetheless, these choices do yield relative line widths that match experimental ones (see e.g. the sharp lines of H-a,

H-m and H-p vs. the broad H-o peak in the spectrum of **13b**), thus adding a further constraint for spectral assignment.

As a final comment we recall that, with few exceptions,⁵³ spin-crossover phenomena are observed at such low temperatures that a comparison with experiment is possible only by solid-state NMR which, in the case of paramagnetics, is fraught with several technical difficulties. Along with the unpredictably large paramagnetic shifts, shift anisotropies may reach 1000 ppm,⁵⁴ and anisotropic bulk magnetic susceptibility effects further complicate the picture. In fact, solid-state NMR experiments performed with standard magic-angle spinning (< 10 KHz) will generally yield very broad spectra populated by spinning sidebands with low S/N. Nevertheless, dramatic improvement in the sensitivity and resolution of NMR spectra have been achieved by means of ultrafast magic-angle spinning (above 60 KHz) and short recycle delays.⁵⁵ Furthermore, the problem of overlapping spinning sidebands can be overcome by use of pulse sequences that incorporate adiabatic pulses.⁵⁶

Thus, although the context is challenging, new avenues of investigation can easily be envisioned where the capability to predict the NMR spectral features can be exploited to characterize the structure and spin dynamics of a wide array of paramagnetic materials.

Conclusions

The B3LYP* functional is capable of ranking the energy of the spin states of Fe(II,III) complexes with good accuracy at a moderate computational cost. This method also yields calculated paramagnetic NMR spectra for each spin state, which are sufficiently different to allow for a reliable identification. Most importantly, this evidence suggests that the different features of the NMR spectra of paramagnetic species (based on iron or otherwise) can be exploited both to characterize their structure and to identify their spin states.

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Electronic Supplementary Information available. Structures and spin density isosurfaces of complexes 1-10, detailed energies of spin states, details of the calculation of line widths, IR spectra of 13, Cartesian coordinates of all complexes considered. See DOI:

References

1 (a) Spin Crossover in Transition Metal Compounds, Ed. P. Gütlich, H. A. Goodwin, Springer, Berlin, 2010. Other leading references: (b) M. Niheia, T. Shiga, Y. Maeda, H. Oshio, Coord. Chem. Rev., 2007, 251, 2606-2621. (c) I. Krivokapic, M. Zerara, M. L. Daku, A. Vargas, C. Enachescu, C. Ambrus, P. Tregenna-Piggott, N. Amstutz, E. Krausz, A. Hauser, Coord. Chem. Rev., 2007, 251, 364-378. (d) K. S. Murray, Eur. J. Inorg. Chem., 2008, 3101-3121. (e) P. Gütlich, Eur. J. Inorg. Chem., 2013, 581–591.

- 2 A. Dei, D. Gatteschi, Angew. Chem. Int. Ed., 2011, 50, 11852-11858.
- 3 M. Okuhata, Y. Funasako, K. Takahashi, T. Mochida, Chem. Commun., 2013, 49, 7662.

4 S. Shaik, S. P. De Visser, in *Cytochrome P450: Structure, Mechanism, and Biochemistry, 3rd Ed.*; Ortiz de Montellano, P. R., Ed. Plenum: New York, 2005.

- 5 (a) R. J. Deeth, A. E. Anastasi, M. J. Wilcockson, J. Am. Chem. Soc., 2010, 132, 6876-6877. (b)
- C. M. Handley, R. J. Deeth, J. Chem. Theory Comput., 2012, 8, 194-202.
- 6 Solution NMR of Paramagnetic Molecules: Applications to Metallobiomolecules and Models., Ed.
- I. Bertini, C. Luchinat, G. Parigi, Elsevier, Amsterdam, 2001.
- 7 J. A. Kitchen, S. Brooker, Coord. Chem. Rev., 2008, 252, 2072-2092.
- 8 P. J. van Koningsbruggen, Top. Curr. Chem., 2004, 233, 123-149.
- 9 A. Ikezaki, Y. Ohgo, M. Nakamura, Coord. Chem. Rev., 2009, 253, 2056-2069.

10 T. Ikeue, M. Handa, A. Chamberlin, A. Ghosh, O. Ongayi, M. G. H. Vicente, A. Ikezaki, M. Nakamura, *Inorg. Chem.*, 2011, **50**, 3567–3581.

- 11 Calculation of NMR and EPR Parameters: Theory and Applications, Ed. M. Kaupp, M. Bühl, V.
- G. Malkin, Wiley-VCH, Weinheim, 2004.
- 12 A. Bagno, G. Saielli, Theor. Chem. Acc., 2007, 117, 603-619.

13 M. W. Lodewyk, M. R. Siebert, D. J. Tantillo, Chem. Rev., 2012, 112, 1839-1862.

14 G. M. Sandala, K. H. Hopmann, A. Ghosh, L. Noodleman, J. Chem. Theory Comput., 2011, 7, 3232-3247.

15 A. Bencini, Inorg. Chim. Acta, 2008, 361, 3820-3831.

16 (a) J. Autschbach, B. Pritchard, *Theor. Chem. Acc.*, 2011, **129**, 453-466. (b) P. Verma, J. Autschbach, *J. Chem. Theory Comput.*, 2013, **9**, 1052-1067.

17 (a) T. O. Pennanen, J. Vaara, *Phys. Rev. Lett.*, 2008, **100**, 133002. (b) J. Mareš, H. Liimatainen, T. O. Pennanen, J. Vaara, *J. Chem. Theory Comput.*, 2011, **7**, 3248-3260.

18 (a) W. Van den Heuvel, A. Soncini, *Phys. Rev. Lett.*, 2012, **109**, 073001. (b) W. Van den Heuvel, A. Soncini, *J. Chem. Phys.*, 2013, **138**, 054113.

19 (a) J. Autschbach, S. Patchkovskii, B. Pritchard, J. Chem. Theory Comput., 2011, 7, 2175-2188.

(b) F. Aquino, N. Govind, J. Autschbach, J. Chem. Theory Comput., 2011, 7, 3278-3292. (c) B. Pritchard, J. Autschbach, Inorg. Chem., 2012, **51**, 8340-8351.

- 20 (a) F. Aquino, B. Pritchard, J. Autschbach, J. Chem. Theory Comput., 2012, **8**, 598-609. (b) P. Verma, J. Autschbach, J. Chem. Theory Comput., 2013, **9**, 1932-1948.
- 21 M. Repiský, S. Komorovský, E. Malkin, O. L. Malkina, V. G. Malkin, *Chem. Phys. Lett.*, 2010, **488**, 94-97.
- 22 E. D. Hedegård, J. Kongsted, S. P. A. Sauer, J. Chem. Theory Comput., 2011, 7, 4077-4087.
- 23 F. Rastrelli, A. Bagno, Chem. Eur. J., 2009, 15, 7990-8007, and references cited therein.
- 24 F. Rastrelli, A. Bagno, Magn. Reson. Chem., 2010, 48, S132-S141, and references cited therein.
- 25 H. Paulsen, V. Schünemann, J. A. Wolny, Eur. J. Inorg. Chem., 2013, 628-641.
- 26 C. J. Cramer, D. G. Truhlar, Phys. Chem. Chem. Phys., 2009, 11, 10757-10816.
- 27 C. R. Jacob, M. Reiher, Int. J. Quantum Chem., 2012, 112, 3661-3684.
- 28 F. Neese, Coord. Chem. Rev., 2009, 253, 526-563.
- 29 (a) E. M. Zueva, E. R. Ryabikh, A. M. Kuznetsov, S. A. Borshch, Inorg. Chem., 2011, 50, 1905-
- 1913. (b) E. M. Zueva, E. R. Ryabikh, S. A. Borshch, Inorg. Chem., 2011, 50, 11143-11151.
- 30 (a) M. Swart, M. Güell, M. Solà, *Phys. Chem. Chem. Phys.*, 2011, **13**, 10449-10456. (b) J. Cirera, F. Paesani, *Inorg. Chem.*, 2012, **51**, 8194-8201.
- 31 M. Reiher, Inorg. Chem., 2002, 41, 6928-6935.
- 32 R. L. Lord, F. A. Schultz, M.-H. Baik, J. Am. Chem. Soc., 2009, 131, 6189-6197.
- 33 L. M. L. Daku, A. Vargas, A. Hauser, A. Fouqueau, M. E. Casida, *ChemPhysChem*, 2005, 6, 1393-1410.
- 34 A. Vargas, I. Krivokapic, A. Hauser, L. M. L. Daku, Phys. Chem. Chem. Phys., 2013, 15, 3752.
- 35 M. Güell, M. J. Luis, M. Solà, M. Swart, J. Phys. Chem. A, 2008, 112, 6384-6391.
- 36 M. Swart, J. Chem. Theory Comput., 2008, 4, 2057-2066.
- 37 S. Ye, F. Neese, Inorg. Chem., 2010, 49, 772-774.
- 38 S. Grimme, J. Chem. Phys., 2006, 124, 034108.

39 Gaussian 09, Revision B.01, 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, 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, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.
40 G. te Velde, F. M. Bickelhaupt, E. J. Baerends, C. Fonseca Guerra, S. J. A. van Gisbergen, J. G.

Snijders, T. Ziegler, J. Comput. Chem., 2001, 22, 931-967.

41 P. Sambasiva Rao, P. Ganguli, B. R. McGarvey, Inorg. Chem., 1981, 20, 3682-3688.

42 B. Weber, F. A. Walker, K. Karaghiosoff, Z. Anorg. Allg. Chem., 2013, 1498-1503.

43 A. Ikezaki, M. Takahashi, M. Nakamura, Angew. Chem. Int. Ed., 2009, 48, 6300-6303.

44 B. Weber, F. A. Walker, Inorg. Chem., 2007, 46, 6794-6803.

45 (a) M. Sorai, S. Seki, J. Phys. Chem. Solids, 1974, 35, 555-570. (b) C. Baldé, C. Desplanches, A. Wattiaux, P. Guionneau, P. Gütlich, J.-F. Létard, Dalton Trans., 2008, 2702-2707. (c) M. Cavallini, I. Bergenti, S. Milita, G. Ruani, I. Salitros, Z. Qu, R. Chandrasekar, M. Ruben, Angew. Chem. Int. Ed., 2008, 47, 8596-8600. (d) S. Shi, G. Schmerber, J. Arabski, J.-B. Beaufrand, D. J. Kim, S. Boukari, M. Bowen, N. T. Kemp, N. Viart, G. Rogez, E. Beaurepaire, H. Aubriet, J. Petersen, C. Becker, D. Ruch, Appl. Phys. Lett., 2009, 043303. (e) A. Tissot, C. Enachescu, M.-L. Boillot, J. Mater. Chem., 2012, 22, 20451. (f) T. Miyamachi, M. Gruber, V. Davesne, M. Bowen, S. Boukari, L. Joly, F. Scheurer, G. Rogez, T. K. Yamada, P. Ohresser, E. Beaurepaire, W. Wulfhekel, Nature Commun., 2012, 3, 1-6.

- 46 T. Bučko, J. Hafner, S. Lebègue, J. G. Angyán, Phys. Chem. Chem. Phys., 2012, 14, 5389-5396.
- 47 A. Domingo, M. A. Carvajal, C. De Graaf, Int. J. Quantum Chem., 2010, 110, 331-337.

48 E. König, K. Madeja, Inorg. Chem., 1967, 6, 48-55.

49 B. Weber, E. S. Kaps, C. Desplanches, J. F. Létard, K. Achterhold, F. G. Parak, *Eur. J. Inorg. Chem.*, 2008, 4891-4898.

50 G. Bifulco, P. Dambruoso, L. Gomez-Paloma, R. Riccio, Chem. Rev., 2007, 107, 3744-3779.

51 A. Bagno, F. Rastrelli, G. Saielli, J. Org. Chem., 2007, 72, 7373-7381.

52 For an example concerning Fe(IV)-oxo chemistry see e.g. O. Y. Lyakin, K. P. Bryliakov, E. P. Talsi, *Inorg. Chem.*, 2011, **50**, 5526-5538.

53 C. Cook, F. Habib, T. Aharen, R. Clérac, A. Hu, M. Murugesu, *Inorg. Chem.*, 2013, **52**, 1825-1831.

- 54 R. J. Clément, A. J. Pell, D. S. Middlemiss, F. C. Strobridge, J. K. Miller, M. S. Whittingham,
- L. Emsley, C. P. Grey, G. Pintacuda, J. Am. Chem. Soc., 2012, 134, 17178-17185.
- 55 A. J. Pell, G. Kervern, L. Emsley, M. Deschamps, D. Massiot, P. J. Grandinetti, G. Pintacuda, J. Chem. Phys., 2011, **134**, 024117.
- 56 G. Kervern, G. Pintacuda, L. Emsley, Chem. Phys. Lett., 2007, 435, 157-162.