High resolution NMR of free radicals: ^{13}C magic angle spinning of two solid organic free radicals derived from 4,5-dihydro-1*H*-imidazol-3-oxide-1-oxyl and theoretical calculation of their NMR properties

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Dedicated to our friend Prof. Julio Alvarez-Builla on the occasion of his 65th anniversary

Abstract
The ^{13}C CPMAS NMR spectra of two 4,4,5,5-tetramethyl-2-(1*H*- and 2*H*-pyrazol-3-yl)-2-imidazoline-1-oxyl-3-oxides have been recorded and their signals assigned, through unrestricted density functional theory (UDFT) calculations of their absolute shieldings, with satisfactory results.

Keywords: Nitronylnitroxide radicals, ^{13}C CPMAS NMR, GIAO, 6-311++G(d,p)

Introduction

In recent years, interest in creation of new classes of magnetically active materials has developed enormously. Syntheses of polyfunctional stable organic radicals and studies of their magnetostructural correlations have become an essential part of this research. Polyfunctional nitroxides are highly effective in design of n-dimensional heterospin systems capable of magnetic ordering.[1] The α-nitronyl nitroxides derived from azoles (imidazoles, triazoles) exhibit extremely strong ferro- and antiferro-magnetic interactions, for organic radicals in which the hydrogen bonds have been involved.[2]

The purpose of the present paper is twofold. On one hand to record in the solid state the ^{13}C CPMAS NMR spectra of two nitronylnitroxide radicals **3** and **4**, and on the other, to evaluate the

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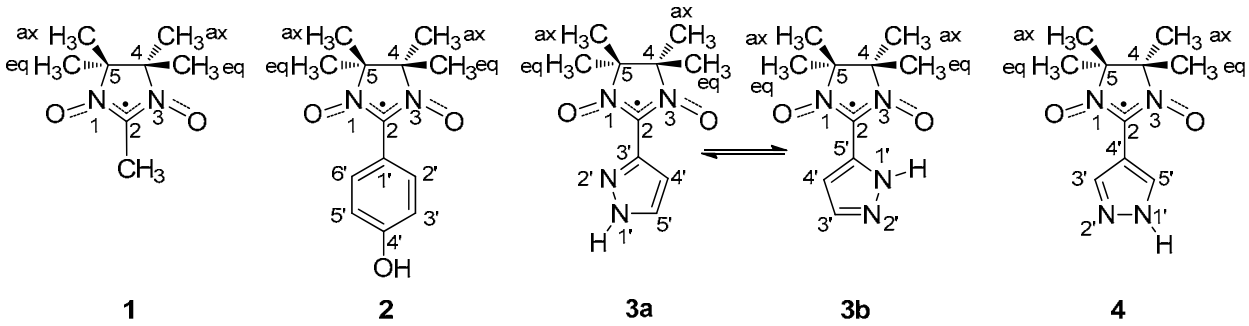
utility of unrestricted DFT calculations to obtain absolute shieldings of these radicals and those of 4,4,5,5-tetramethyl-2-methyl-imidazoline-1-oxyl-3-oxide **1** and of 4,4,5,5-tetramethyl-2-(4'-hydroxyphenyl)-2-imidazoline-1-oxyl-3-oxide **2**.



Scheme 1. The four studied compounds, including both tautomers of **3**.

Nitronylnitroxides have been studied by one of us in considerable detail; in particular pyrazolyl derivatives.[1,3-9] The X-ray structure of tautomer **3b** was described in 2006.[10,11] Another important contribution to pyrazolyl-nitronylnitroxides is that of Catala, Feher, Amabilino, Wurst and Veciana who prepared compound **4**.[2] Note that we published in 1995 a ^{13}C NMR study in solution of paramagnetic Co(II) complexes.[12] The present paper is one of the rare publications where experimental and theoretically calculated NMR chemical shifts of radicals are reported.

Results and Discussion

^{13}C CPMAS NMR of compounds (3) and (4)

We have represented in Figure 1 the ^{13}C CPMAS NMR spectra of compounds **3** (it corresponds to tautomer **3b**)[10,11] and **4**. The spectra have been recorded in two halves and we checked there were no signals in the central missing part; they cover approximately a range of +1010 to –750 ppm.

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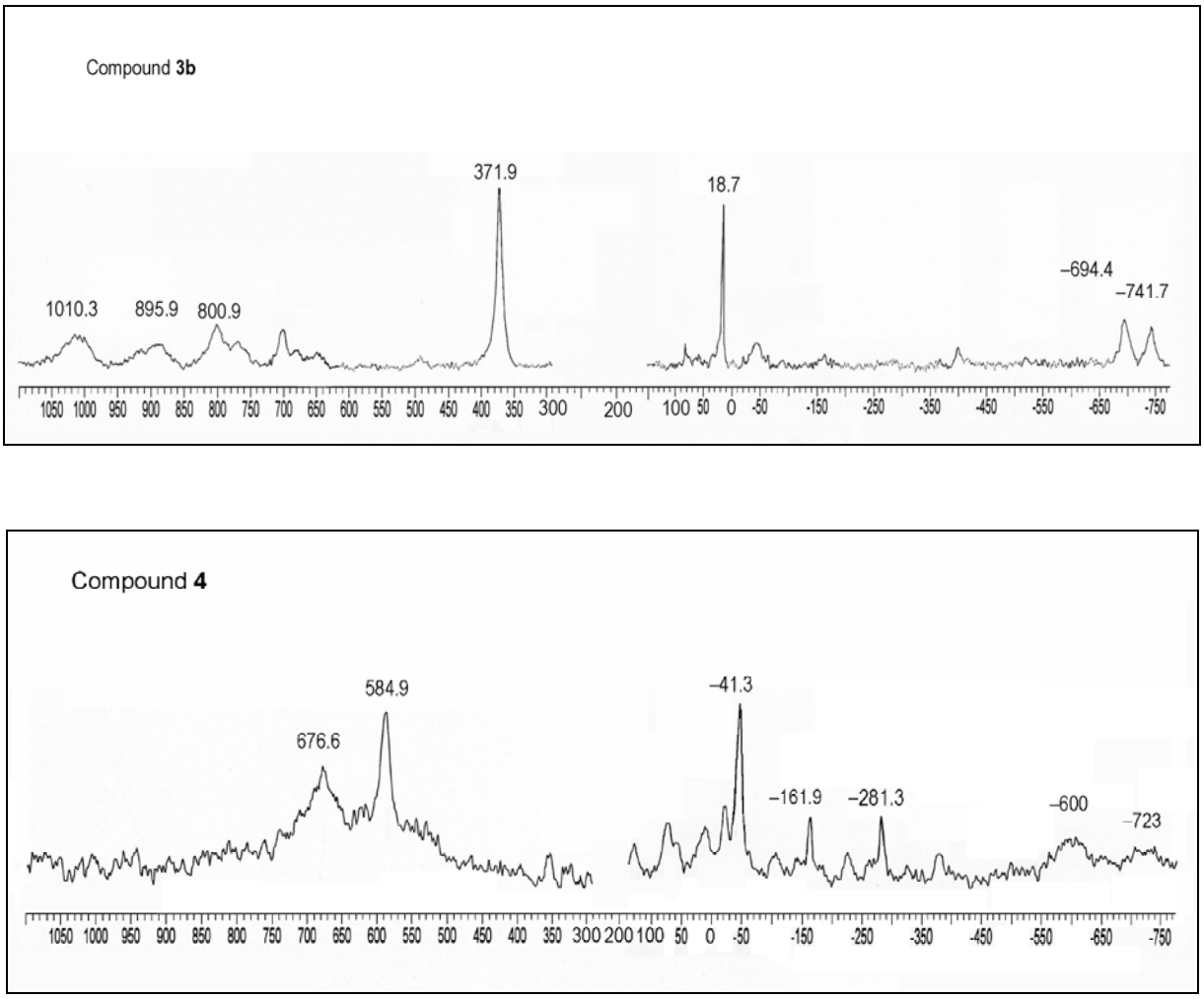

Figure 1. ^{13}C CPMAS NMR spectra of nitronylnitroxide radicals **3** and **4**.

GIAO calculations of compounds (1, 2, 3a, 3b and 4)

We have carried out GIAO/B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p) calculations as implemented in the Gaussian 03 program (see computational details). This level is comparable to that used by Rastelli and Bagno [GIAO/cc-pVTZ//B3LYP/6-31G(d,p)] in their recent study on the use of DFT calculations to predict the NMR spectra of paramagnetic molecules, including free radicals.[13] These theoretical calculations correspond to isolated molecules, so consequently the optimized geometries could not agree with the structures found in the corresponding crystals. However, as the studied compounds have rather rigid geometries, we are confident that the calculated geometries are close to the experimental ones. This has been tested with compound **3b** whose geometry has been determined by X-ray crystallography:[10,11] the calculated and the experimental geometries are nearly identical, the most important difference concerns the torsion angle between both rings that amount to 8.6º (crystal) and to 0.8º (calculation). Besides, we have

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published several papers where absolute shieldings (σ) calculated for isolated molecules are successfully compared with chemical shifts (δ) determined in the solid state by CPMAS NMR.[14-16]

Relative stability of tautomers (3a) and (3b)

We have reported in Table 1 the energetic results of the calculations. Tautomer **3b** is 31.3 kJ mol^{-1} more stable than tautomer **3a**, therefore, in the discussion of the CPMAS NMR chemical shifts only tautomer **3b** will be considered. Remember that only the latter was found in the crystal structure.[10,11] Usually, in N*H*-pyrazoles, 3-substituted tautomers are more stable than 5-substituted ones,[17] but in this case an intramolecular hydrogen bond stabilizes **3b**.

Table 1. B3LYP/6-311++G(d,p) energies (hartree) and relative energies (kJ mol^{-1}) of compounds depicted in Scheme 1 (not including the zero point energy correction)

Compound	Symmetry	E_{total}	Dipole (D)	E_{rel}
1	C_1	–573.89046	2.77	-----
2	C_1	–840.91874	2.52	-----
3a	C_1	–759.62182	0.80	31.3*
3b	C_1	–759.63372	5.32	0.0
4	C_1	–759.63214	3.63	-----

* At the B3LYP/6-31G(d) level including the zero point energy correction E_{rel} amounts to 30.7 kJ mol^{-1}.

These systems should present in solution a pseudorotation mechanism of the imidazoline ring with very low barriers that we have calculated at the B3LYP/6-31G(d) level to be in the range between 3 and 5 kJ mol^{-1}.

AIM analysis

An AIM analysis (see computational details) was carried out on all the radicals. The topological analysis of the electron density (Figure 2) shows the presence of bond critical points between the oxo groups of the imidazole moiety with the groups in *ortho* of the additional ring. In all cases they correspond to O···H interactions with the exception of an O···N contact in the **3a** structure. Interactions between electronegative atoms have been described in the literature,[18-20] and in some cases were considered to explain the extra stability of those systems in which they are present.[21,22] However, in this case, tautomer **3b** shows an O···H interaction that appears to be more stabilizing than the O···N one.

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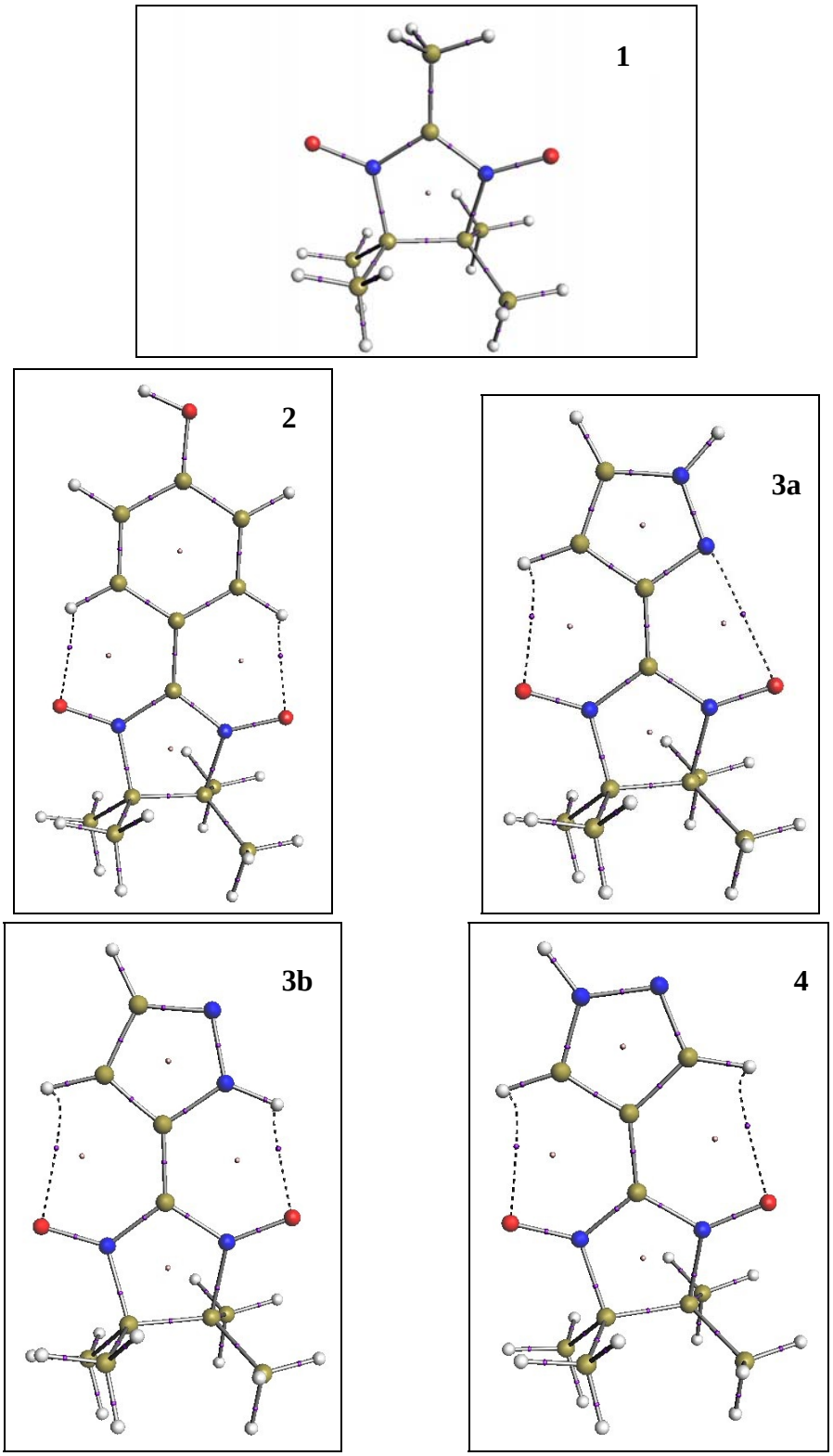

Figure 2. Molecular graphs of **1**, **2**, **3a**, **3b** and **4**. Bond critical points (bcp) and ring critical points (rcp) are shown as well as the bond paths. Note the N–H···O˙ bond path that stabilizes the 5'-substituted tautomer **3b**.

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The *ortho-ortho'* interactions observed in these molecules show small values of the electron density and positive values of the Laplacian, similar to those found in hydrogen bond interactions.[23] The seven O···H interactions found range between 2.1 and 2.6 Å, showing exponential relationships between the interatomic distances and the values of the electron density and Laplacian at the bond critical point.[23,24]

The analysis of the spin density shows that it is concentrated over the atoms 1, 2, 3 and the two oxygen atoms attached to 1 and 3. We have reported these calculations for compound **3b** (Figure 3).

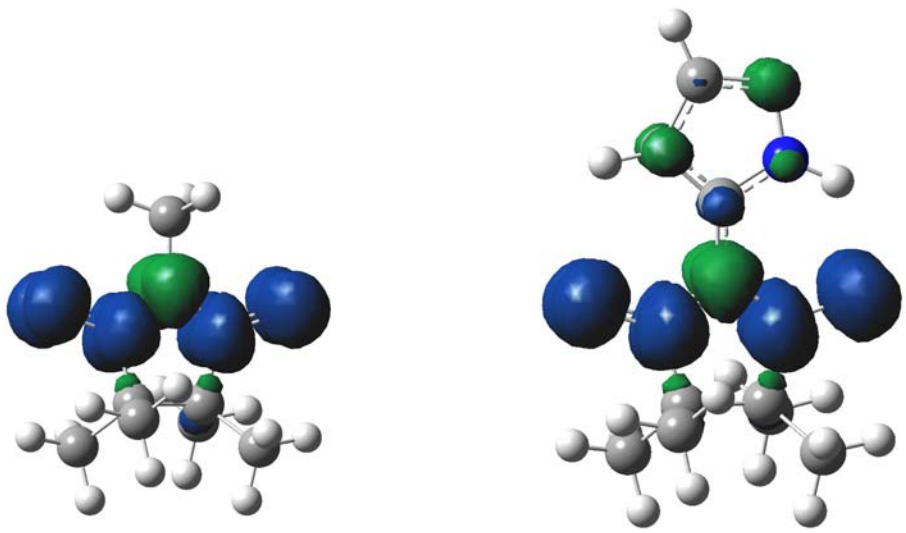

Figure 3. Analysis of the spin density for compound **3b**.

^{13}C NMR absolute shieldings and chemical shifts

Table 2 summarizes all the information available on the five compounds of Scheme 1. A simple regression of these data led to the following equation:

$$\delta^{13}\text{C (ppm)} = (174\pm28) - (0.92\pm0.04)\ \sigma^{13}\text{C (ppm)},\ n = 34,\ R^2 = 0.93 \qquad (1)$$

This equation is very similar to Eq. 2 we obtained using the data of a large set of diamagnetic compounds in solution:[25]

$$\delta^{13}\text{C (ppm)} = (175.7\pm0.2) - (0.963\pm0.003)\ \sigma^{13}\text{C (ppm)},\ n = 461,\ R^2 = 0.996 \qquad (2)$$

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Table 2. Experimental ^{13}C chemical shifts and calculated ^{13}C absolute shieldings (both in ppm)

Compound	carbon atom	chemical shift	absolute shielding	reference
1	C2	not observed	3823.7	14
	C4	–670	849.0	
	C5	–635	848.6	
	2-Me	466	–489.2	
	4-Me ax	573	–288.1	
	4-Me eq	1135	–841.7	
	5-Me ax	650	–303.2	
	5-Me eq	1170	–860.9	
2	C2	not observed	3908.5	14
	C4	–367 [a]	801.5	
	C5	–633	811.9	
	C1'	704	–877.8	
	C2'	25	–133.0	
	C3'	241	–181.7	
	C4'	–120	340.2	
	C5'	241	–255.3	
	C6'	–85	456.5	
	4-Me ax	1080	–877.8	
	4-Me eq	363	–133.0	
	5-Me ax	369	–181.7	
	5-Me eq	1250	–885.2	
3b	C2	not observed	3730.0	This work
	C4	–694.4	793.4	
	C5	–741.7	858.3	
	C3'	371.9	–295.8	
	C4'	18.7	500.3	
	C5'	800.9	–929.5	
	4-Me ax	371.9	–291.5	
	4-Me eq	895.9	–878.3	
	5-Me ax	371.9	–270.1	
	5-Me eq	1010.3	–889.3	
4	C2	not observed	3687.6	This work
	C4	–600	801.5	
	C5	–723	845.5	

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Table 2. Continued

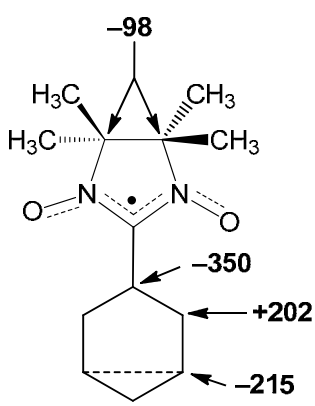
Compound	carbon atom	chemical shift	absolute shielding	reference
	C3' [b]	–161.9	315.5	
	C4'	676.6	–843.9	
	C5' [b]	–281.3	448.7	
	4-Me ax	584.9	–275.6	
	4-Me eq	not observed	–855.7	
	5-Me ax	584.9	–277.7	
	5-Me eq	not observed	–883.8	

[a]The assignment[29] of the signal at –367 ppm to the C4 of **2** could be an error. [b]Note the non-equivalence of carbons C3' and C5' of **4** due to the absence of proton transfer in the solid state.

However, the residuals do not appear to be at random. Thus, we tried a model including four dummy variables (1 if present, 0 if absent): C4,5 of the imidazoline ring (C2 carries too much spin and it is not observed),[29] C*ipso*, C*ortho* and C*meta* of the substituent at position 2 (for pyrazoles, C*ortho* and C*meta* are C4' and C3' in **3b** and C*ortho* is C3' and C5' in **4**).

$$\delta^{13}\text{C (ppm)} = (237\pm33) - (0.97\pm0.05)\ \sigma^{13}\text{C (ppm)} - (98\pm74)\ \text{C4,5} - (350\pm51)\ \text{C}\textit{ipso} + (202\pm74)\ \text{C}\textit{ortho} - (215\pm55)\ \text{C}\textit{meta},\ n = 34,\ R^2 = 0.98 \quad (3)$$

Equation 3 indicates that the calculations underestimate or overestimate some carbons depending on the distance to position 2.



Rastrelli and Bagno[13] have calculated several types of paramagnetic molecules, including the four radicals depicted in Scheme 2. In most cases, they averaged the calculated absolute shieldings since the observed experimental chemical shifts, due to conformational freedom, correspond to average signals.

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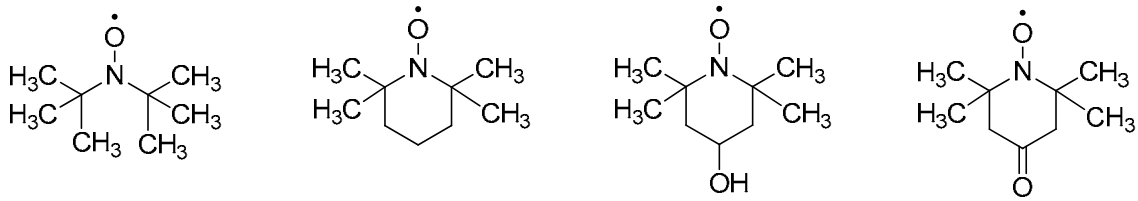
From their data, calculated at the GIAO/BPW91-30HF//cc-pVTZ//B3LYP/6-31G(d,p) level, the following trendline can be calculated (Equation 4) which is similar to that found in Equation 1.

$$\delta^{13}\text{C (ppm)} = (165\pm44) - (1.21\pm0.06)\ \sigma^{13}\text{C (ppm)},\ n = 14,\ R^2 = 0.98 \qquad (4)$$



5 **6** **7** **8**

Scheme 2. The four studied compounds of reference **Error! Bookmark not defined.**.

In summary, for free radicals it becomes possible to measure chemical shifts in the solid state as well as to calculate absolute shieldings in the gas phase, but with some snags. The quality of the spectra is not as good as those of diamagnetic molecules, the computational level should be improved to reproduce all the carbon chemical shifts with the same accuracy and, as crystal field effects must be take into account, all the molecules present in the unit cell should be calculated.[26-28] It is expected that this type of research will considerably develop in the future, both in what experimental measurements and theoretical calculations are concerned.

Experimental Section

General. The preparation of the four compounds of this study has been reported in the literature. 4,4,5,5-Tetramethyl-2-methyl-imidazoline-1-oxyl-3-oxide **1** and 4,4,5,5-tetramethyl-2-(4'-hydroxyphenyl)-2-imidazoline-1-oxyl-3-oxide **2** were synthesized by Heise, Kohler, Mota, Novoa and Veciana.[29] The synthesis of 4,4,5,5-tetramethyl-2-(1*H*-pyrazol-3(5)-yl)-2-imidazoline-1-oxyl-3-oxide **3** was described by some of us.[8] Finally, 4,4,5,5-tetramethyl-2-(1*H*-pyrazol-4-yl)-2-imidazoline-1-oxyl-3-oxide **4** was prepared by Catala, Feher, Amabilino, Wurst and Veciana.[2]

Solid state NMR

^{13}C (100.73 MHz) CPMAS NMR spectra were recorded by using a Bruker WB 400 spectrometer at 300 K with a 4 mm DVT probehead. Samples were carefully packed in a 4-mm diameter cylindrical zirconia rotors with Kel-F end-caps. Ramped cross polarization[30,31] from ^{1}H was used to create transverse ^{13}C magnetization with contact time of 0.5 ms. The ^{1}H 90° pulse length was of duration 3.2 μs. TPPM decoupling[32] at a ^{1}H nutation frequency of 78.1 kHz was applied

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during acquisition, using pulse lengths of 5.75 μs. Delay of 17.9 ms was applied for detector recovery, and repetition times of 500 ms. Others acquisition parameters were: spectral width, 100 kHz; acquisition data size, 2394 points, giving an acquisition time of 12 ms; spinning rate, 12 kHz. The FIDS were multiplied by an exponential weighting (lb = 150) before Fourier transformation. ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to the Me_4Si, from the carbonyl atom δ (glycine) at 176.1 ppm. Because of the spectral length (the maximum sw is 993 ppm), the spectra were acquired in two parts.

Computational details

The optimization of the geometries of the structures were first carried out at the B3LYP/6-31G(d) and then reoptimized at the B3LYP/6-311++G(d,p) computational level,[33-38] within the Gaussian-03 package.[39] Frequency calculations at the B3LYP/6-31G(d) level were carried out to confirm that the obtained structures correspond to energy minima.[40] The GIAO approximation[41,42] has been used at the B3LYP/6-311++G(d,p) computational level to calculate the orbital absolute chemical shielding, the hyperfine coupling constant and the electron g tensor. The electron density of the molecules has been analyzed within the atoms in molecules (AIM) methodology[43] with the AIMPAC and MORPHY98 programs.[44-46] The electron density molecular graphs have been represented with the MORPHY3 program.[47]

In the NMR spectroscopy of paramagnetic systems several nonvanishing interactions between the nuclear and electron magnetic moments should be considered. They can be divided in Fermi orbital, contact and dipolar terms, see Equation 5:[13,48]

$$\delta = \delta_o + \delta_{FC} + \delta_{PC} \qquad (5)$$

The orbital term δ_o is similar to the shielding of diamagnetic molecules and thus it can be approximated to that value. The Fermi contact term δ_{FC} is due to the interaction of the magnetic moment of the resonant nucleus and the effective local field generated by the unpaired electron density. In the simpler form, it can be calculated from Equation 6:

$$\delta_{FC} = (2\pi/\gamma_I) g_e \mu_B [S(S+1)/3kT] \qquad (6)$$

where γ_I is the magnetogyric ratio of the nucleus I, g_e the electron g factor, μ_B the Bohr magneton, A the isotropic hyperfine coupling constant, S is the total spin quantum number and kT the thermal energy.

The dipolar term δ_{PC} is in general negligible in organic radical systems and has not been considered in the present calculations.

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