^{14,15}N NMR Shielding Constants from Density Functional Theory

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The prediction of nuclear magnetic resonance (NMR) shielding parameters for the N atom represents a particularly difficult task for most of the Hartree−Fock (HF)-based or density functional theory (DFT)-based methodologies. In fact, for some molecular systems, the effect of the presence of a lone pair and multiple bonds on the N atom makes the use of higher correlated methods absolutely necessary to obtain accurate results. In this article, we present an extensive study covering almost the entire spectrum of nitrogen shielding, from +400 to −50 ppm. The sum-over-states density functional perturbation theory (SOS−DFPT) has been used to calculate the shielding constant of 132 different N atoms. The potential of the various SOS−DFPT local approximations has been assessed through the comparison of N atoms that belong to similar molecular systems to experimental data. This procedure allows us to determine the margin of error to be considered in the SOS−DFPT calculation of the isotropic shieldings for each type of N atom.

I. Introduction

Recent advances in the development of theoretical methods for NMR shieldings have yielded considerable accuracy.[1−8] Nevertheless, the potential of these methodologies has not been fully exploited.

The fact that theoretical calculations give absolute values of the shielding constants has been considered to be a limiting factor, restricting the boundaries of application of the calculations. Actually, the calculated shieldings have been compared to experimental references, either directly in the absolute scale, where the availability of experimental data is limited by the availability of spin rotation constants,[9,10] or in the shift scale, where the experimental chemical shifts are determined in the gas phase. These procedures are a necessary benchmark test for the assessment of the reliability of the method.[11] The majority of NMR experiments are performed in the liquid phase and at room temperature; therefore, it is necessary to evaluate the maximum error that is encountered from a direct comparison of these data to the calculated results. The results will allow NMR shielding calculations to assist in the interpretation of the experimental spectra.

The focus of this work is to determine the maximum error to be considered in the calculation of the nitrogen shieldings for different types of N atoms. This test basically covers the entire N NMR spectrum, and the 132 nitrogen nuclei considered have been analyzed in eight separate groups of similar chemical structure. The first group includes primary, secondary, and tertiary amines, and the second group includes hydrazines. The third group includes amides, ureas, and guanidines, and the fourth group includes cyanides and isocyanides. The fifth group includes azoles, the sixth group includes azines, the seventh group includes azine *N*-oxides, and the eighth group includes nitrates. The ^{14,15}N shielding constants have been determined using sum-over-states density functional perturbation theory (SOS−DFPT).[2] The calculations have been performed using all of the four approximations available in this method: the uncoupled Kohn−Sham (UKS) approximation, local approximation 1 (Loc.1), local approximation 2 (Loc.2), and local approximation 3 (Loc.3). The latter has been recently introduced,[12] and the benchmark tests revealed a very good performance, especially for the nitrogen nucleus, compared to either ab initio calculation from higher correlated methods or experimental references.[11] Through comparison between the results obtained from the four different SOS−DFPT approximations, we were able to determine the influence on the NMR shielding of the exchange-only and exchange-correlation contributions for each type of nitrogen nucleus.

Having assessed the quality of the SOS−DFPT approximations in reproducing the low-density gas-phase NMR shielding constants,[11] to be able to compare calculations to experimental data in the liquid phase realistically, we must be aware of several contributions that add to the deviation from the reference.[13] The most important are (i) the contribution of rovibrational corrections and averaging, which have been determined for only a few systems,[10,14] and (ii) the contribution of intermolecular interactions, or, more generally speaking, solvent effects. The influence of these two factors is fairly constant for similar molecular systems under similar external conditions.[15−17] However, because the ^{14,15}N shielding constants have been determined to be very sensitive to intermolecular interactions,[9,15−17] the largest fraction of the deviation from the experimental data can be considered to be due to solvent effects. Given that no

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attempt has been made to introduce solvent effects, either directly (through a supermolecular approach) or indirectly (with a continuum model), statistical analysis of the results will reveal the systems for which the interaction with the solvent causes significant deviations, and, therefore, it will indicate the range of uncertainty in the calculation for each type of N atom.

II. Computational Method

In this section, we will outline the computational details for the calculation of the N NMR shielding. In addition, a brief introduction to the SOS−DFPT methodology is included, to keep this work reasonably self-contained. A comprehensive description of the theoretical background can be found in the original papers referenced below.

The N NMR shieldings have been determined through the SOS−DFPT approach as implemented, within the IGLO formalism,[18−20] in Version 1.2 of the deMon-NMR[2,21] program, which is part of the deMon suite.[22−24]

According to SOS−DFPT, the shielding tensor (σ_K) is determined by the standard expression

$$\sigma_K = \left\langle \Psi_0 \left| \frac{\partial^2 H}{\partial \boldsymbol{M_K} \partial \boldsymbol{B}} \right| \Psi_0 \right\rangle - 2 \sum_{I \neq 0} \frac{\left\langle \Psi_0 \left| \frac{\partial H}{\partial \boldsymbol{B}} \right| \Psi_I \right\rangle \left\langle \Psi_I \left| \frac{\partial H}{\partial \boldsymbol{M_K}} \right| \Psi_0 \right\rangle}{\Delta E_{i \rightarrow a}} \tag{II.1}$$

where H represents the Hamiltonian operator in the presence of a magnetic field $\boldsymbol{B}$, whereas Ψ_0 and Ψ_I represent, respectively, the ground and excited states of the system. Moreover, $\boldsymbol{M_K}$ identifies the magnetic moment of the nucleus K and $\Delta E_{i \rightarrow a}$ denotes the energy corresponding to the excitation of an electron from the Kohn−Sham (KS) orbital i to the KS orbital a. The success of SOS−DFPT is strictly bound to the approximation of the excitation energy term $\Delta E_{i \rightarrow a}$. In fact, the straightforward approximation for $\Delta E_{i \rightarrow a}$, which is represented by the simple energy difference between the energies of the KS orbitals, which is also known as the "uncoupled Kohn-Sham" (UKS) approximation, can be refined by the addition of correction terms. In the original SOS−DFPT formalism, two exchange-only correction terms have been developed, namely, "local approximation 1" (Loc.1) and "local approximation 2" (Loc.2). A detailed account of the theoretical background on the SOS−DFPT approach and on its local approximations, Loc.1 and Loc.2, is presented in detail in the original papers.[2,21]

Fairly recently, we introduced a third local approximation, which is called Loc.3, as an elucidation of the physical basis of the SOS−DFPT methodology.[11,12] Loc.3 has its foundations in time-dependent density functional theory (TDDFT)[25] and it has been derived within the Tamm−Dancoff Approximation (TDA)[26] and the two-level model (2LM).[27] Moreover, it has shown very good potential in predicting isotropic and anisotropic NMR shieldings. All the various SOS−DFPT approximations are shown in Table 1 for comparison.

The equilibrium structure of all the molecules has been determined by full geometry optimization through the Broyden−Fletcher−Goldfarb−Shanno (BFGS) algorithm. Because of the absence of solvent effect in the calculation, we make the approximation that the structural changes induced by the presence of the solvent molecules have a negligible effect on the determination of the chemical shielding. This assumption is supported by the results obtained by Manalo and co-workers.[28]

All geometry optimizations and SCF calculations have been performed using Version 3.5 of the deMon−KS[29] program,

TABLE 1: Approximations of the Excitation Energy ($\Delta E_{i \rightarrow a}$) in SOS−DFPT

approximation	$\Delta E_{i \rightarrow a}$
UKS[a]	$\epsilon_a - \epsilon_i$
Loc.1	$\epsilon_a - \epsilon_i - \int \rho_i(r) \frac{\delta \epsilon_{xc}^{LDA}(r)}{\delta \rho_\uparrow(r)} \rho_a(r)\, dr$
Loc.2	$\epsilon_a - \epsilon_i - \int \rho_i(r) \frac{\delta \nu_{xc}^{\uparrow},LDA(r)}{\delta \rho_\uparrow(r)} \rho_a(r)\, dr$
Loc.3	$\epsilon_a - \epsilon_i + 2K_{ia} + \int \rho_i(r) \left(\frac{\delta \nu_{xc}^{\uparrow}LDA(r)}{\delta \rho_\uparrow(r)} + \frac{\delta \nu_{xc}^{\uparrow},LDA(r)}{\delta \rho_i(r)} \right) \rho_a(r)\, dr$

[a] Uncoupled Kohn−Sham approximation: $\epsilon_{a(i)}$ represents the energy of the Kohn−Sham (KS) orbital $a(i)$.

whereas the time-dependent calculations have been performed with Version 3.2 of the deMon−DynaRho program.

Concerning the choice of exchange-correlation potentials, the geometry optimization has been performed using the PLAP3 functional.[30,31] The latter represents one of the most sophisticated and reliable functionals for the determination of molecular structure.[32,33] On the other hand, for all self-consistent field (SCF) and time-dependent calculations, we used only the local density approximation (LDA) exchange-correlation functional, with Vosko, Wilk, Nusair (VWN) parametrization.[34] The LDA functional does not always show the best performance for the NMR shielding calculation, although, for ^{14,15}N shielding, its performance is significantly better than that of HF.[35] Nonetheless, the choice of the LDA functional is required for consistency.[36] In fact, because all the local correction terms in SOS−DFPT—Loc.1, Loc.2, and Loc.3—are defined in terms of the LDA functional, the KS orbitals and their energies then should also be defined in terms of the LDA functional.

deMon−KS uses numerical grids and auxiliary basis functions to evaluate exchange-correlation integrals and to eliminate four-center integrals. For all calculations, we used a Fine grid, which is defined by 26 angular points per radial shell, where each atom has been surrounded by 64 radial shells; as an auxiliary basis function, we used the (5,2;5,2) set for heavy atoms and the (5,1;5,1) set for H atoms. In regard to orbital basis sets, for geometry optimizations, we used the triple-ζ basis sets: [4s3p1d] for heavy atoms and [2s1p] for H atoms, with contraction schemes (7111/411/1) and (41/1), respectively. For the SCF and time-dependent calculations, we used the IGLO-III basis set, which entails the [11s7p2d] basis for heavy atoms and the [4s2p] basis for H atoms, with contraction schemes (5111111/211111/11) and (4111/11), respectively. All auxiliary and orbital basis sets have been taken from the deMon basis-set library.

III. Results and Discussion

In this section, we present the analysis and discussion of the results obtained in the calculation of the ^{14,15}N NMR shieldings. An overview of the SOS−DFPT performance across the entire ^{14,15}N spectrum is shown in Figure 1. Data regarding the ^{14,15}N NMR shieldings for each group are presented in the Supporting Information. However, as previously mentioned in Section I, to be able to consider the environmental effects as approximately constant, we limit the comparison of the results within similar molecular systems.

The calculated absolute shieldings are referenced to neat liquid nitromethane, for which the absolute shielding value has

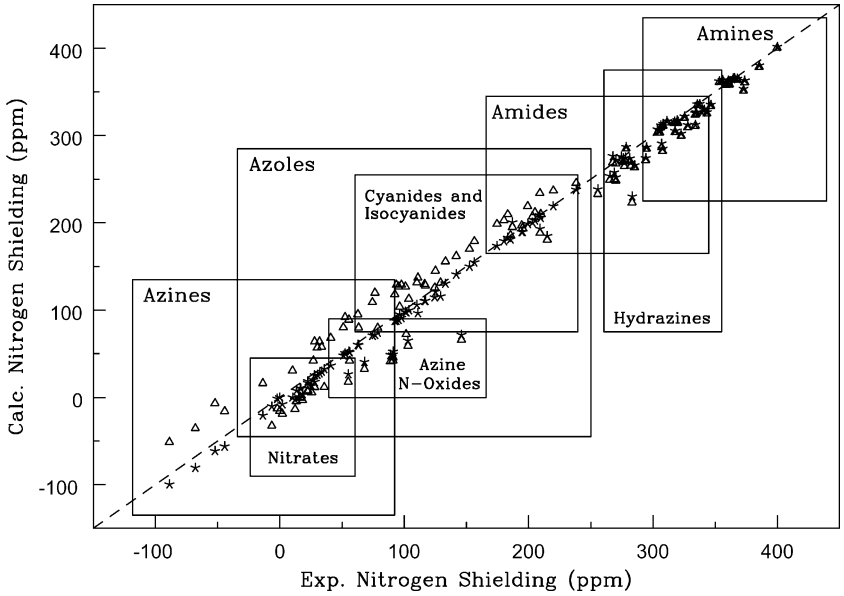

Figure 1. Distribution of SOS−DFPT calculated ^{14,15}N NMR shieldings against the experimental references. For clarity, only the Loc.3 (star-shaped symbols) and the UKS results (open triangles) are shown. Regions pertaining to each type of nitrogen nucleus are highlighted.

TABLE 2: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Amines, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	9.4	10.5	11.3	13.2
slope	0.9619	0.9624	0.9613	0.9551
correlation	0.9476	0.9488	0.9498	0.9493
average deviation[b]	5.9	5.4	5.3	5.4
maximum deviation[c]	21.2	19.9	19.5	19.4

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

been taken to be $\sigma_{abs}^{CH_3NO_2}$ (298−300 K) = −135.8 ppm.[9] We can realistically disregard the influence of temperature on the nitrogen shielding of nitromethane, because it has been determined to be small, with a temperature coefficient of 0.0045 ppm/K.[17]

The sign convention adopted is logically the same as that used for the experimental reference. Therefore, we determined the relative nitrogen shielding as follows:

$$\sigma = \sigma_{abs}^{calc} - \sigma_{abs}^{CH_3NO_2}$$

In regard to the shielding scale, a plus sign indicates an increase of magnetic shielding and a minus sign indicates a decrease in magnetic shielding. Note that the experimental references, to which the calculations have been compared, have been chosen based on the nature of the solvent. In fact, the experimental data determined in an aprotic solvent with a low dielectric constant represent the most desirable choice. However, unfortunately, the selection must be limited also by the accessibility to reliable experimental data.

A. Amines. The results of a statistical analysis of the data obtained in the calculation of the ^{14,15}N shielding in amines are shown in Table 2. The four SOS−DFPT approximations yield very similar results, indicating an extremely small contribution of exchange and exchange-correlation corrections. The minor effect of the local approximations indicates that the NMR shielding paramagnetic component is prevalently determined by higher excitations for which exchange and exchange-correlation corrections are, in fact, negligible.

For primary amines (NH_2R), the calculated shieldings are very similar to the experimental results, independent of the solvent used. Specifically, the average absolute deviation obtained with Loc.3 for NH_2R is only 2.9 ppm. The only exceptions are given by $PrNH_2$ and $BuNH_2$, which exhibit a slightly larger error. The results obtained for $BuNH_2$, *i*-$BuNH_2$, *s*-$BuNH_2$, and *t*-$BuNH_2$ show the ability of the calculation to reproduce very accurately the effect of the alkyl substitution on the ^{14,15}N shielding. In particular, for $BuNH_2$ and *i*-$BuNH_2$, in which only one of the H atoms of the carbon in the β-position is substituted by an alkyl group, we obtained ^{14,15}N shieldings within the uncertainty range designated by the average deviation. However, noticeable and progressive deshielding is calculated for *s*-$BuNH_2$ and *t*-$BuNH_2$ which have, respectively, two and three H atoms of the β-carbon substituted by alkyl groups.

The average deviation is almost doubled for secondary amines (NHR_2) and tertiary (NR_3) amines. The maximum deviation for all four approximations is represented by the ^{14,15}N shielding of Me_3N, for which the experimental reference has been determined in the gas phase.

B. Hydrazines. The nitrogen in hydrazines is still an sp^3 hybrid and, as in the previous case, the ^{14,15}N shielding is reproduced quite accurately by the SOS−DFPT calculations. The calculation results follow the same pattern illustrated for the amines. For instance, the highest accuracy of the calculations is obtained for the N atoms bonded to the smallest number of alkyl groups and the contribution of the local (Loc.) corrections does not drastically change the UKS performance.

The solvent effect is expected to be of the same order as that for the amine ^{14,15}N shielding; therefore, the larger average absolute deviation obtained for the hydrazines (see the statistical analysis in Table 3) can be attributed to the presence of a second N atom in the α-position.

C. Amides, Ureas, and Guanidines. Amido moieties represent a more difficult case. Their higher polarity, compared to that of amines and hydrazines, causes the solvent effect to be crucial. Therefore, the identification of trends in the variation of the ^{14,15}N shielding is rather difficult. The statistical analysis is presented in Table 4.

The solvent effect for systems such as HCONHR (with R = Me or H) has been determined to be ∼8 ppm.[17] Consequently,

TABLE 3: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Hydrazines, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−36.7	−36.4	−36.8	−31.0
slope	1.0693	1.0737	1.0769	1.0585
correlation	0.9182	0.9186	0.9184	0.9215
average deviation[b]	15.3	13.6	13.2	12.9
maximum deviation[c]	25.6	24.0	23.5	22.7

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

TABLE 4: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Amides, Ureas and Guanidines, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−14.1	−9.0	−7.3	−3.2
slope	1.0045	0.9938	0.9902	0.9793
correlation	0.9203	0.9198	0.9196	0.9210
average deviation[b]	14.9	13.9	13.6	13.0
maximum deviation[c]	60.2	56.4	55.1	53.1

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

differences in ^{14,15}N shieldings as the shift introduced by the progressive substitution of the amide H atoms with methyl groups (as in the following series: $HCONH_2$, HCONHMe, $HCONMe_2$) are entirely covered by the solvent effect and not decipherable from the calculation. The substitution of the H atom attached to the carbonyl group in formamide ($HCONH_2$) by a methyl group to obtain acetamide ($MeCONH_2$) does not seem to have any effect on the calculated ^{14,15}N shielding, although the two systems have fairly different experimental values.

Larger deviations can be observed following the substitution of $HCONH_2$ with a phenyl group (Ph−), an ethoxy group (EtO−), or an amino group to form urea. All these effects exceed the solvent-induced shift and are reproduced quite well by the calculations.

The most significant deviations are found for the cyclic amides (pyridones, piperidones, and pyrrolidones), which could be due to the solvent effect as well as the tautomeric equilibrium. The maximum absolute deviation for all approximations is associated with the ^{14,15}N shielding in the C═NH moiety of $Me_2C(NH)OMe$, and this is most probably caused by the strong association with the solvent, which is due to the very high basicity of the system.

D. Cyanides and Isocyanides. A significant discrepancy in the performance between the calculations for cyanides (R−CN) and isocyanides (R−NC) can be observed from the results of the statistical analysis shown, respectively, in Tables 5 and 6. One of the causes could be related to the different type of interactions that R−CN and R−NC can engage with the solvent. In fact, the ^{14,15}N shielding of cyanides is known to be highly dependent on the solvent effect. It has been determined that solvent interactions cause the ^{14,15}N shielding constant in alkyl cyanides to experience considerable shielding in the range of 22−26 ppm,[15,17,37] indicating direct interaction of the nitrogen lone pair with solvent molecules. On the other hand, in isocyanides, the more difficult access to the N atom, which is known as "the site effect",[38] reduces the strength of the direct solvent−solute dipolar interaction, with the result being considerably smaller solvent-induced shifts.[39]

TABLE 5: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Cyanides, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−92.3	−95.7	−96.5	−157.1
slope	1.3973	1.4882	1.5148	2.0503
correlation	0.4890	0.4753	0.4712	0.5638
average deviation[b]	41.4	33.2	30.5	22.5
maximum deviation[c]	55.8	50.1	48.2	43.5

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

TABLE 6: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Isocyanides, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−15.5	6.4	12.7	33.3
slope	1.0113	0.9290	0.9058	0.8231
correlation	0.9822	0.9839	0.9822	0.9633
average deviation[b]	13.2	7.9	6.3	2.6
maximum deviation[c]	16.1	10.2	9.3	6.9

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

However, here, the influence of the solvent in the cyanides ^{14,15}N shielding has been minimized. This is especially true for nitriles (i.e., alkyl cyanides), where the majority of the chosen experimental references have been determined in cyclohexane. In fact, the solvent effect induced by cyclohexane has been calculated to be only ∼2 ppm.[40] Furthermore, the accuracy level attained in the calculation of ^{14,15}N shieldings in nitriles is rather good, especially with the Loc.3 correction.

The divergence in the performance seems to be related mainly to the significant difficulty that is encountered by the SOS−DFPT approach with aryl cyanides. For these systems, all the different SOS−DFPT approximations predict ^{14,15}N shieldings that are significantly too deshielded. *p*-$(CN)_2$-Ph corresponds to the maximum deviation for all approximations. The effect of the strong ring current induced by the extended electron delocalization in these systems can be hardly described by the SOS−DFPT defined within the LDA functional. Because of the lack of a current dependent functional, the use of a more sophisticated nonlocal approach is definitely needed to improve the results.

The higher accuracy obtained for isocyanides is due to the fact that no experimental data on aryl-substituted systems were available; hence, no aryl isocyanides have been examined. The calculated ^{14,15}N shieldings show a good response to the substituent effects. The induced shifts are very well reproduced by the calculations, particularly in the case of the "Loc.3" approximation for which the average absolute deviation is 2.6 ppm. The poor results of the linear regression analysis can be attribued to the shortage of data and the narrowness of the region under study.

In regard to the performance of the four SOS−DFPT corrections, the inclusion of exchange and correlation effects becomes more important than in the case of the sp^3 N atom. The Loc.3 approximation reduces the error, which is estimated as the average absolute deviation, considerably, not only for isocyanides, but also for cyanides. The advantage of the Loc.3 correction is that, contrary to Loc.1 and Loc.2, it also takes

TABLE 7: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Azoles, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
	Pyrrole-Type Azole			
intercept	−28.0	−23.0	−21.5	−16.2
slope	1.0311	1.0195	1.0157	0.9929
correlation	0.9913	0.9923	0.9926	0.9936
average deviation[b]	22.0	19.4	18.5	16.8
maximum deviation[c]	30.2	26.4	25.2	21.4
	Pyridine-Type Azole			
intercept	−16.6	−8.9	−6.4	−0.3
slope	0.8796	0.8657	0.8611	0.8313
correlation	0.8674	0.8712	0.8719	0.8776
average deviation[b]	29.2	25.2	24.5	22.5
maximum deviation[c]	49.0	42.5	41.3	39.6

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

into consideration a correlation contribution (see Table 1 for comparison).

E. Azoles. Azoles present two significantly different N atoms: "pyrrole-type" nitrogen (sp^2 hybrid, with both the lone-pair electrons contributing to the aromaticity of the ring) and "pyridine-type" nitrogen (sp^2 hybrid, with the lone pair directed outward from the ring and only one electron contributing to the aromaticity). The direction of the solvent-induced shifts are opposite for these two types of nitrogen: in the case of the pyridine-type nitrogen, which acts as a hydrogen-bond acceptor, the presence of solvent produces a shielding effect, whereas, for the pyrrole-type nitrogen, a deshielding effect is observed.[41]

The statistical analysis of the ^{14,15}N shieldings for both type of nuclei is shown in Table 7. The calculated shieldings for both pyrrole-type and pyridine-type systems are significantly deshielded, with average absolute deviations, calculated with the Loc.3 approximation, varying from 16.8 ppm for the pyrrole-type nitrogen up to 22.5 ppm for the pyridine-type nitrogen. The only exceptions are given by the N-2 shielding value in 1-Me-1,2,3-triazole and the N-1 and N-3 shielding values of 2-Me-1,2,3-benzotriazole, which are too shielded. In regard to R−CN and R−NC, the lack of accuracy cannot be related entirely to the solvent effect. In fact, based on the choice of the experimental references, the highest solvent-induced shifts we can expect are of the order of 8−12 ppm, for the case of dimethyl sulfoxide (DMSO) as the solvent.[40] The largest part of the error can be attribued to the aforementioned difficulty that the SOS−DFPT approach has in describing aromatic systems. A radical improvement in the accuracy of the calculations is obtained only through the use of multiconfigurational methods.[42]

A fairly good linear regression and correlation analysis are attained for the pyrrole-type nitrogen, indicating that the substituent-induced shifts are reproduced quite well by the calculation. Meanwhile, a much more scattered pattern is observed for the pyridine-type ^{14,15}N shieldings. A quite similar correlation level has been obtained from coupled Hartree−Fock (CHF) calculations.[43] For the pyrrole-type N atom, the SOS−DFPT approach, especially with the local approximations, greatly improves the agreement with the experiments, compared to CHF. On the other hand, the pyridine-type N atom still remains a rather difficult case. The solution to this underperformance, as will be discussed further in the next subsection, lies beyond the introduction of correlation effects at the SOS−DFPT level.

TABLE 8: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Azines, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−60.4	−45.9	−41.4	−32.5
slope	1.2239	1.1363	1.1103	1.0427
correlation	0.9921	0.9918	0.9915	0.9900
average deviation[b]	52.8	39.9	36.6	30.6
maximum deviation[c]	74.9	59.4	54.6	45.4

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

F. Azines. The determination of the ^{14,15}N shielding of azines represents one of the most difficult tasks of this work. In addition to the problems related to their aromatic character, we can also recognize the significant influence of both correlation and solvent effects. The impact of these contributions is highly dependent on the number and proximity of other pyridine-type N atoms.[44,45] To be able to gauge the influence of these two different effects, we tried to minimize the solvent-induced shift by evaluating the results against experimental data determined in the lowest-possible dielectric medium (i.e., cyclohexane and CCl_4). Nonetheless, the average deviation, as shown in Table 8, is the largest that has been determined so far.

The most significant deviations are found for azines with more than one nitrogen nucleus. For example, 1,2,4-triazine and 1,2-diazine represent the most difficult cases. The latter shows the widest range of solvent-induced shifts (48 ppm), indicating a very high sensitivity to the polarity of the solvent and, among the other unsubstituted azines, the highest basicity in the gas phase, whereas 1,2,4-triazine has the most basic character among the unsubstituted triazines.[45] However, having considered, for both cases, the experimental references determined in cyclohexane, we can only expect a minor shift induced by the solvent. The major cause of the deviation is related to correlation effects, which are extremely important for double-bonded N atoms.[3,46] SOS−DFPT, including some level of correlation, represents a considerable improvement over CHF.[44] Furthermore, among all the different approximations, Loc.3 exhibits the best performance. Still, the average deviation calculated for Loc.3 is 30.6 ppm.

Even if the influence of correlation effects in the ^{14,15}N shielding of double-bonded N atoms has been determined to be slightly less important for aromatic systems, compared to nonaromatic systems,[46] numerous studies that are based on coupled-cluster (CC) shielding constant calculations of systems such as N_2, N_2O, and CH_3N_2 have proven that experimental accuracy is only attained if the effect of connected triple excitations is included.[3,47] Consequently, we believe that the reason behind the shortfall of SOS−DFPT for azines is related to their aromatic character and the inadequate description of correlation effects in diazines and triazines.

G. Azine N-Oxides. A similarly large average deviation is also calculated for the azine N-oxides (see Table 9). This result is not unexpected, because the ^{14,15}N shielding of azines and of their N-oxide equivalents are rather highly correlated.[15] To check if this linear relationship was reproduced by the calculation, we determined the correlation coefficient between the results obtained for the azines and the azine N-oxides and between the two sets of experimental data that have been chosen as reference. The resulting correlation coefficients are 0.9047 for UKS, 0.9082 for Loc.1, 0.9023 for Loc.2, 0.9016 for Loc.3, and 0.8381 for the experimental data. The latter can be justified by the fact that the two sets of experiments were performed in

TABLE 9: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Azine N-Oxides, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−1.9	3.9	4.1	8.2
slope	0.5052	0.4835	0.4982	0.4714
correlation	0.9295	0.9268	0.9374	0.9311
average deviation[b]	46.5	42.6	41.1	39.4
maximum deviation[c]	80.1	77.2	74.3	74.4

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

TABLE 10: Statistical Analysis of the Calculated ^{14,15}N Shieldings[a] in Nitrates, Relative to Neat Liquid Nitromethane

	Value			
parameter	UKS	Loc.1	Loc.2	Loc.3
intercept	−19.1	−11.6	−9.2	−4.2
slope	1.0544	0.9269	0.8877	0.7716
correlation	0.9392	0.9221	0.9139	0.8977
average deviation[b]	18.3	12.5	10.7	7.3
maximum deviation[c]	26.0	19.7	17.8	14.8

[a] Shieldings given in units of ppm. [b] Average absolute deviation from the experimental references. [c] Maximum deviation from the experimental references.

solvents of quite different polarity. However, the ^{14,15}N shielding of the azine N-oxides is slightly less sensitive to solvent effects than the ^{14,15}N shielding of azines, given that the direct interaction of the solvent molecules with the lone pair is now replaced by the direct interaction with the O atom.[15,48]

The poor results obtained in the linear regression analysis are mainly caused by the large deviation of the calculated ^{14,15}N shielding of 2-OMe-pyridine N-oxide. This system also represents the most difficult case for all the SOS−DFPT approximations.

H. Nitrates. Nitrates revealed the most remarkable difference in the performance of the four SOS−DFPT approximations (see Table 10). The local corrections show a considerable improvement over UKS. In fact, the average deviation calculated for UKS (26 ppm) is reduced to less than one-third of that value if we add the Loc.3 approximation (7.3 ppm).

The calculations reproduce the increase of the shielding caused by the electron-withdrawing effect of aromatic rings such as pyrrole and imidazole fairly well.[15] The only exception is given by the calculated ^{14,15}N shielding of $PhNO_2$, which is very similar to the value obtained for $MeNO_2$. The effect of the position of the double bond between two C atoms, with regard to the nitrate group, is also well-reproduced.

The value obtained for the correlation coefficient is dependent on the significant sensitivity of the ^{14,15}N shielding of nitrogroups to the solvent polarity effect.[17] In fact, the experimental references have been obtained in various solvents with considerably different dielectric constants; therefore, we expect a shift in the order of 7−9 ppm, induced by solvents such as DMSO, dimethyl formamide (DMF), and Me_2CO.[15]

IV. Conclusions

The performance of sum-over-states density functional perturbation theory (SOS−DFPT) has been tested on the calculation of the ^{14,15}N NMR shielding of different types of N atoms. The results have been evaluated against experimental data determined in the liquid phase. In view of the significant contribution of the solvent-induced shift in the ^{14,15}N NMR shielding, we considered preferably reference data acquired in aprotic solvents and with the lowest dielectric constant, limited by the availability of experimental studies.

The most accurate results have been obtained for the nitrogen sp^3 hybrids, as in amines and hydrazines. Here, the solvent has a minor effect, compared to the other nitrogen types analyzed in this work, and the calculations reproduce substituent effects, such as the β-effects, quite accurately, of the order of 10−15 ppm. All the SOS−DFPT approximations perform equally well for this nitrogen type; the exchange and exchange-correlation correction contributions are negligible, as it is for the NMR shielding of other nuclei in saturated molecular groups.[11,12]

The higher polarity of amides, ureas, and guanidines makes the solvent effect much more significant. The only substituent effects that can be effortlessly assigned are those that exceed 15 ppm. The delocalization of the lone pair on the nitrogen toward the carbonyl group confers to the amide moiety a partial double-bond character. For nonsaturated systems, the most significant contributions to the paramagnetic shielding is given by the lower excitations, which are improved considerably by the local corrections.[21] Hence, for the amido moiety, all the local (Loc.) approximations reproduce the experimental data equally well and more accurately than the uncoupled Kohn−Sham (UKS) approximation.

One must be more prudent when interpreting the SOS−DFPT results for the nitrogen nuclei involved in highly delocalized systems. The SOS−DFPT, defined within the LDA functional, is unable to describe the strong effect of the ring current in aromatic molecules accurately. Accordingly, significant deviations have been obtained in azoles, azines, azine N-oxides, and aryl cyanides. For azoles, the calculated ^{14,15}N shieldings are too deshielded for both the pyrrole-type and pyridine-type N atoms. The local approximations improve the performance of the UKS approximation considerably, and the highest accuracy is obtained with Loc.3. Nonetheless, the average absolute error remains critical. The correlation of the results obtained for the pyrrole-type N atom is fairly good, whereas, for the pyridine-type N atoms, a rather scattered pattern is observed. The azines and the azine N-oxides represent the most difficult cases analyzed in this work. The extremely high solvent dependence of the ^{14,15}N shieldings and the inadequate description of the correlation contribute to the unsatisfactory performance of the SOS−DFPT. Still, Loc.3 determines yet again the least-inaccurate results among the approximations.

On the other hand, in the determination of the ^{14,15}N shielding of alkyl cyanides, isocyanides, and nitrates, we have examples of the good level of accuracy that can be attained with the SOS−DFPT local approximations, compared to the UKS approximation. Among these approximations, Loc.3 shows the best performance, significantly reducing the average absolute deviations.

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Supporting Information Available: Figures showing the calculated versus experimental ^{14,15}N chemical shifts distribution for each of the groups analyzed. Tables containing all the calculated ^{14,15}N chemical shifts, the relative experimental references, and the solvent in which the experiment has been

conducted. This material is available on the Internet at http://pubs.acs.org.

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