

Regular article

Simulation of volume polarization for the influence of solvation on chemical shielding

Daniel M. Chipman

Radiation Laboratory, University of Notre Dame, Notre Dame, IN 46556, USA

Received: 9 January 2003 / Accepted: 18 April 2003 / Published online: 23 January 2004
© Springer-Verlag 2004

Abstract. The effect of bulk dielectric solvation on chemical shielding at nitrogen in CH_3CN is studied with reaction field theory. A previous work has demonstrated the strong influence on this property from volume polarization, which describes that part of the reaction field arising from solute charge density penetrating outside its cavity. The essentially exact treatment of volume polarization used in that work is computationally demanding, and a more facile method for simulation of the volume polarization has recently been proposed. It is found in the present work that this simulation of the volume polarization yields results in excellent agreement with the essentially exact treatment of the strong volume polarization effects on nitrogen shielding in CH_3CN .

Keywords: Chemical shielding – Reaction field theory – Dielectric effects – Volume polarization – Cavity size

1 Introduction

Primarily as a result of the pioneering [1] and considerable ongoing [2, 3] efforts of Prof. Jacopo Tomasi, it is now feasible to routinely include bulk dielectric effects of solvation in quantum mechanical electronic structure calculations. In this approach [4], the solute is placed in a realistic molecular-shaped cavity that has been scooped out of an otherwise continuous dielectric medium. The solvent polarization is determined from reaction field theory, and the responses of the quantum mechanical solute and of the classical solvent to one another are both iterated until mutual self-consistency. The basic mathematical equations describing this scenario are now reasonably well established, and several good computer implementations for their numerical solution are available.

One important direction for developmental research in the field concerns determination of the proper size and shape of the molecular cavity to be used. The strength of a reaction field experienced by a given solute can be easily adjusted by altering the cavity size, and in most instances a cavity size can be empirically found that reproduces almost any given experimental solvation energy. This flexibility is often used to parameterize the cavity to give a good fit to the experimental solvation energy. But fitting just to the energy can potentially lead to a cavity that gives poor results for other solute properties. Ideally, the cavity should be determined to simultaneously give a reasonable account of the solvation energy and of all other solute properties that may be significantly affected by the solvent environment.

Chemical shielding as observed in NMR spectroscopy is often sensitive to bulk dielectric and other solvation effects [5]. Shielding at nitrogen is known [6] to often be especially dependent on solvent, and we [7] have previously used this dependence to study cavity size effects in several small representative nitrogen-containing compounds. We defer to that work [7] for a more comprehensive discussion of the earlier literature on this subject. A recent important contribution from the Tomasi group [8] on chemical shielding at nitrogen should also be noted, in which the influences of both cavity size and of specific interactions with nearby solvent molecules are studied.

It was found in our earlier work [7] that the reaction field volume polarization, which arises from quantum mechanical penetration of solute charge density outside the cavity that nominally encloses it, has an important influence on the shielding. If volume polarization is neglected (denoted surface polarization for electrostatics, SPE, in our nomenclature), the calculated nitrogen shielding is strongly dependent on cavity size, and reproduction of experimental trends requires somewhat larger cavities than are typically used for determination of the solvation energy. On the other hand, when exact volume polarization (denoted surface and volume polarization for electrostatics, SVPE, in our nomenclature) is included, the nitrogen shielding has only a modest dependence on cavity size, and experimental

Contribution to the Jacopo Tomasi Honorary Issue

Correspondence to: D. M. Chipman
e-mail: chipman.1@nd.edu

trends are reproduced with about the same cavity sizes as give reasonable results for solvation energies.

Exact treatment of volume polarization [9, 10, 11, 12, 13] is computationally demanding, but this has recently been ameliorated [11, 12, 14, 15] by a modification [denoted surface and simulation of volume polarization for electrostatics, SS(V)PE, in our nomenclature] that allows volume polarization effects to be very economically simulated. This same simulation is also included in the current manifestation of the integral equation formalising [16, 17] and implicit volume charge [18, 19] methods in the polarization continuum model (PCM) family of approaches. Compared to exact treatment of volume polarization, the simulation usually works very well for solvation energies [20], breaking down [21] only when the cavities are artificially forced to be so small as to produce unrealistically large solvation energies. In the present work we investigate whether or not this simulation of volume polarization also works well in describing the important effects of volume polarization on NMR chemical shielding.

Our previous study [7] examined the four solutes CH_3CN , CH_3NO_2 , CH_3NCS , and CH_3ONO_2 , selected for the ready availability of experimental data on the relative shielding at nitrogen in a large variety of solvents. Among these, the nitrogen shielding in CH_3CN is most sensitive to solvent, showing a spread of 23 ppm in different solvents. This is more than twice the spread observed for any of the other three solutes, presumably because the nitrogen atom in CH_3CN is more exposed to solvent than with the other solutes. Since the CH_3NO_2 , CH_3NCS , and CH_3ONO_2 solutes mainly serve just to confirm the behavior seen with CH_3CN , we present detailed results here only for the latter solute. It is found that the simulation provides an excellent account of the strong volume polarization effects on nitrogen shielding in CH_3CN .

2 Theory and methods

All the methods used in this work are well documented in the literature, so we give here only a very brief account. The solute is characterized by an effective quantum mechanical Hamiltonian operator $h_0 + \mathcal{V}$, where h_0 is the internal Hamiltonian as in the gas phase, and \mathcal{V} is a potential-energy function describing the solute-solvent interaction. From this effective Hamiltonian, we approximately solve an effective Schrödinger equation for the ground-state solute to obtain a normalized wave function, Ψ , and approximate Schrödinger energy

$$\mathcal{E} = \langle \Psi | h_0 + \mathcal{V} | \Psi \rangle .$$

The potential-energy function \mathcal{V} actually depends on the solute charge density, and hence on Ψ , so the effective Schrödinger equation for Ψ is nonlinear and must be solved iteratively. The free energy of the system, measured relative to the energy of the unpolarized solvent, is given by

$$G = \mathcal{E} - \frac{1}{2} \langle \Psi | \mathcal{V} | \Psi \rangle ,$$

where the last term on the right-hand side corrects the Schrödinger energy for the reversible work required to polarize the bulk solvent, assuming linear response. Atomic units are assumed throughout this section.

Different models of solvation provide different forms for the classical potential-energy function \mathcal{V} . In dielectric continuum

theory, it is obtained directly from the electrostatic reaction potential $\Phi^{\text{pol}}(\mathbf{r})$ according to

$$\mathcal{V} = \sum_{\nu}^{\text{nuclei}} Z_{\nu} \Phi^{\text{pol}}(\mathbf{R}_{\nu}) - \sum_{i}^{\text{electrons}} \Phi^{\text{pol}}(\mathbf{r}_i) .$$

The total electrostatic potential, $\Phi(\mathbf{r})$, of the solute-solvent system is determined by solving Poisson's equation. The reaction potential is then obtained by subtracting out the potential that the given final solute charge density would produce if it were in a vacuum,

$$\Phi^{\text{pol}}(\mathbf{r}) = \Phi(\mathbf{r}) - \Phi^{\text{vac}}(\mathbf{r}) .$$

The real computational problem is then to solve Poisson's equation for the potential $\Phi(\mathbf{r})$. A dielectric constant of unity is posited inside the cavity, where the polarizability is automatically taken into account by the electronic structure calculation on the solute. The region outside the cavity is assumed to be a linear isotropic homogeneous dielectric continuum characterized by the dielectric constant ϵ observed experimentally for the pure liquid solvent. The consequent discontinuity in dielectric values across the cavity surface leads to an effective surface charge density contribution to the solution of Poisson's equation. In any unconstrained quantum mechanical calculation on the solute, there will inevitably be a tail of the solute charge density that penetrates outside the cavity and into the dielectric continuum region. This leads to an additional effective volume charge density contribution to the solution of Poisson's equation. This volume charge density resides only on and outside the cavity surface, and falls off very rapidly with distance from the surface. The SVPE method produces the exact reaction potential in this situation, although with complicated molecular-shaped cavities the exact treatment of volume polarization can be computationally demanding.

The exact volume polarization potential can be simulated by replacing the exact volume polarization charge density with a certain additional surface polarization charge density. This simulation can be arranged to produce the exact electrostatic potential everywhere inside the cavity, differing from it only by the potential produced in the less important region outside the cavity. In the SS(V)PE method a single equation is solved that gives the combined surface charge densities arising from both the dielectric constant discontinuity and the simulation of volume polarization. The SS(V)PE method provides a very efficient computational approach.

Finally, the solute charge penetration can be ignored while solving Poisson's equation by simply neglecting all volume polarization contributions. This corresponds to the simple SPE method.

The exact polarization charge densities are continuous distributions. In practice, these are approximated by a collection of finite point charges located on a specified grid. The solution of Poisson's equation for the potential is thereby transformed into a matrix equation for the values of point charges that produce the potential. Such matrix equations are readily solved with modern digital computers.

We prefer to define the molecular shape that determines the cavity surface by means of a solute electronic isodensity contour, although this is not an essential feature. This surface is usually very similar to the surface determined by the union of atomic spheres such as used in PCM approaches. One significant difference is that the isodensity surface is automatically smooth even in the regions where two or more atoms intersect one another. Another difference is that the various atomic radii need not be specified. The isodensity prescription uniquely defines the cavity shape, leaving only a single parameter, ρ_0 , specifying the value of the solute electronic isodensity contour to determine the overall cavity size.

The nuclear magnetic shielding constant at the solute nucleus, N , in the presence of solvent is given as

$$\sigma_N = 1 + \left. \frac{\partial^2 G(\mathbf{B}, \mathbf{m}_N)}{\partial \mathbf{B} \partial \mathbf{m}_N} \right|_{\mathbf{B}=\mathbf{m}_N=0} .$$

This involves mixed derivatives of the free energy with respect to perturbations due to an external magnetic field, \mathbf{B} , and to the nuclear magnetic moment, \mathbf{m}_N . The gauge problem is handled by

utilizing an efficient implementation [22] involving gauge-including atomic orbitals (GIAO). Only isotropic chemical shielding at nitrogen is considered in this work.

A practical difficulty arises because straightforward evaluation of σ_N from the solute wave function, as perturbed by solvent, would correspond to taking derivatives of the effective Schrödinger energy, \mathcal{E} , instead of the free energy, G . In most cases this would lead to a solvent dependence of the shielding that is too large by approximately a factor of 2. We have previously described [7] a simple and effective means to work around this problem through replacing the solute-solvent potential-energy function, \mathcal{V} , with a scaled function, $\lambda\mathcal{V}$. Straightforwardly evaluating the shielding by equilibrating the wave function to a set of fixed scaled reaction field point charges then leads to a shielding function, $\sigma_N[\lambda]$. Thus, calculation of the gas-phase shielding produces the value of $\sigma_N[0]$, while calculation of the shielding in the presence of the full reaction field produces the value of $\sigma_N[1]$. One further calculation must then be carried out with a set of manually halved reaction field point charges, producing the value of $\sigma_N[\frac{1}{2}]$. An effective approximation to the correct σ_N that would be obtained by taking derivatives of the free energy is then obtained by using the second-order formula

$$-\frac{1}{2}\sigma_N[0] + 2\sigma_N\left[\frac{1}{2}\right] - \frac{1}{2}\sigma_N[1] .$$

A derivation and full justification of this procedure is given in the appendix of the previous work [7].

To maintain consistency with the previous study [7], calculations were carried out using the Hartree-Fock method with the 6-311G(3d,3p) basis set [23, 24, 25, 26]. Although electron correlation effects and basis set limitations that are neglected here may be significant for determining the absolute shielding, this level of theory should be adequate to describe the influence of solvation on the relative shielding.

Surface integrations were carried out over a set of 590 Lebedev points on the isodensity cavity surface, using a recently developed module [27] implemented in the Hondo computer package [28]. The same Hondo program was also used for the GIAO nuclear shielding calculations. All SPE results reported previously [7] using other computer programs were recomputed, and agreement with the previous results was verified to within a precision of 0.1 ppm in all cases.

Shielding calculations were carried out for dielectric constants of 1.0(gas), 2.2288, 4.806, 8.93, and 35.94. It was found empirically that the dielectric dependence of the calculated results, for a given computational method and cavity size, could be very closely fitted in all cases by the three-parameter equation

$$\sigma_N = B + A\left(\frac{\epsilon - 1}{\epsilon + C}\right) .$$

After determining the parameters A , B , and C by least-squares fitting to the shieldings calculated at the selected values of ϵ , this functional form was used to smoothly interpolate the results to other values of ϵ that were not explicitly used in the calculations. Full details on this fitting procedure were given in the previous study [7].

3 Results and discussion

Measurements of relative shieldings at nitrogen in CH_3CN have been reported [29] for 13 solvents having known dielectric constants. The experimental shieldings appear to have some rough correlation with solvent dielectric constant. Deviations from any smooth dependence on dielectric constant are to be expected, since other solvation effects besides bulk dielectric polarization also contribute to the observed shieldings. These include [5] short-range solute-solvent interactions due to anisotropy of the solvent magnetizability

and to van der Waals interactions. By fitting to results in a large number of different solvents having widely varying dielectric constants, it is expected that the apparent “scatter” arising from these other influences will average out to some extent, so that a smooth fit as a function of dielectric constant will describe reasonably well the underlying dependence on bulk dielectric polarization. The present work addresses only this long-range interaction with bulk dielectric, and not the additional short-range specific interactions that may also make significant contributions to the shielding in particular solvents.

The present SS(V)PE results that simulate volume polarization in CH_3CN are compared to the previously obtained SVPE results in Table 1, which also includes SPE results for documentation purposes. The differences between SS(V)PE and SVPE are seen there to be 0.3 ppm or less in all cases¹. It can be concluded that SS(V)PE gives an excellent approximation to the exact SVPE method in this example.

For a given dielectric constant, the largest discrepancies between SS(V)PE and SVPE occur for the highest isodensity contour values. This corresponds to simple intuition, since higher contour values produce smaller cavities and therefore stronger reaction fields. By the same reasoning, for a given contour value the stronger reaction fields associated with higher dielectric constants might also be expected to produce larger discrepancies between SS(V)PE and SVPE, but our results do not support that. The calculations indicate instead that higher dielectric constants produce about the same or slightly smaller discrepancies between SS(V)PE and SVPE as do lower dielectric constants.

For the sake of completeness, we also reiterate the comparisons to experiment such as were made in the previous work [7]. The experimental report [29] lists CH_3CN nitrogen shieldings relative to the shielding at nitrogen in neat nitromethane. Since the absolute experimental shieldings are not known, the absolute calculated nitrogen shieldings will be uniformly shifted into the same range as the relative experimental values in order to facilitate comparisons. Full details and justification of this shifting procedure were given in the previous study [7]. In short, the absolute shieldings calculated within a series of different dielectric constants (but with a given computational method and cavity size) are all shifted by a constant amount. The magnitude of the shift is chosen to minimize the least-squares difference between the set of calculations and experiment. Note that such a shift will account not only for the unknown value of the relative shielding scale used experimentally, but may also adjust to some extent for the unknown computational error due to electron correlation and basis set effects. Because of these shifts, meaningful comparisons can be made only with the

¹The results discussed here correspond to final shielding values obtained from the second-order fitting procedure described in the Theory and methods section. The raw shielding calculations with $\lambda=1$ show differences between SS(V)PE and SVPE of up to 0.6 ppm., which still corresponds to only a small fraction of the net magnitude of the full calculated solvent dependence.

Table 1. Calculated nitrogen shielding (ppm) for CH₃CN. The calculated gas phase absolute shielding is -19.0 ppm

Contour ^a	SPE	SS(V)PE	SVPE ^b
$\epsilon = 2.2288$			
0.00025	-14.8		
0.0005	-8.9		
0.001	2.9	-18.3	-18.3
0.002	26.8	-15.5	-15.6
0.003	50.3	-12.5	-12.8
$\epsilon = 4.806$			
0.00025	-12.8		
0.0005	-4.0		
0.001	13.8	-17.1	-17.1
0.002	49.6	-12.2	-12.4
0.003	85.1	-7.2	-7.5
$\epsilon = 8.93$			
0.00025	-11.8		
0.0005	-1.7		
0.001	18.6	-16.3	-16.3
0.002	59.7	-10.3	-10.4
0.003	100.6	-4.1	-4.4
$\epsilon = 35.94$			
0.00025	-10.9		
0.0005	0.4		
0.001	23.2	-15.3	-15.3
0.002	69.4	-8.0	-8.1
0.003	115.5	-0.6	-0.8

^aSolute isodensity contour, ρ_0 , (e/a_0^3) that determines the cavity size

^bPrevious results from the work reported in Ref. [7]

slope and curvature of the experimental data, not their absolute values.

The calculated results, after interpolation and shifting, are compared to experiment in Fig. 1. In order to compress the wide range of dielectric constants, the abscissa is chosen to be the Onsager function $(\epsilon - 1)/(\epsilon + 0.5)$. As expected from the close similarity of the numerical results given in Table 1, values for the fitted interpolation and shift parameters are found to be very nearly the same for SS(V)PE as those obtained previously [7] for SVPE. The SVPE results are not even shown in Fig. 1, because they would be visually indistinguishable from the SS(V)PE lines.

By way of reference, we point out that cavity sizes corresponding to isodensity contours in the range of 0.0005-0.002 e/a_0^3 have been found [13] to give a good

account of the effect of solvation on experimental free-energy differences for conformational changes, with a statistical preference for an optimum value of about 0.001 e/a_0^3 .

SPE results for the nitrogen shielding in CH₃CN are shown in a separate panel of Fig. 1. With SPE, contour values of approximately 0.001 e/a_0^3 or greater give poor fits to experiment owing to significantly too strong dielectric dependence. The best fit to experiment with SPE is given with ρ_0 of about 0.0005 e/a_0^3 , and the fit remains reasonably good for ρ_0 of 0.00025 e/a_0^3 as well. Thus, unusually large cavities are required to reproduce the experimental trends with SPE.

With SS(V)PE each of the contours considered provides a reasonable fit to experiment, and the best fit is obtained for ρ_0 of 0.002 e/a_0^3 . Thus, inclusion of volume polarization allows the experimental dielectric dependence of the nitrogen shielding to be reproduced with about the same cavity sizes as are found most appropriate for fitting to free energies of neutral compounds.

4 Summary and conclusion

If volume polarization is ignored as in SPE, then nitrogen shielding is very sensitive to cavity size and experimental trends can be fit only with cavities that are somewhat larger than those appropriate for solvation free energies. When volume polarization is included, either with SS(V)PE or with SVPE, the nitrogen shielding is much less sensitive to cavity size and experimental trends can be reproduced with cavity sizes about the same as those appropriate for solvation free energies. It has previously been argued [7] that similar behavior should also be found for other second- and higher-order properties such as spin-spin coupling constants, polarizabilities, and magnetizabilities.

The most important new conclusion of this work is that SS(V)PE nitrogen shieldings are found to give excellent approximations to the very important effects of volume polarization, as represented by exact SVPE values, even for the strongest reaction fields examined.

Acknowledgements. Helpful discussions with I. Carmichael are acknowledged. The research described herein was supported by the Office of Basic Energy Sciences of the Department of Energy. This

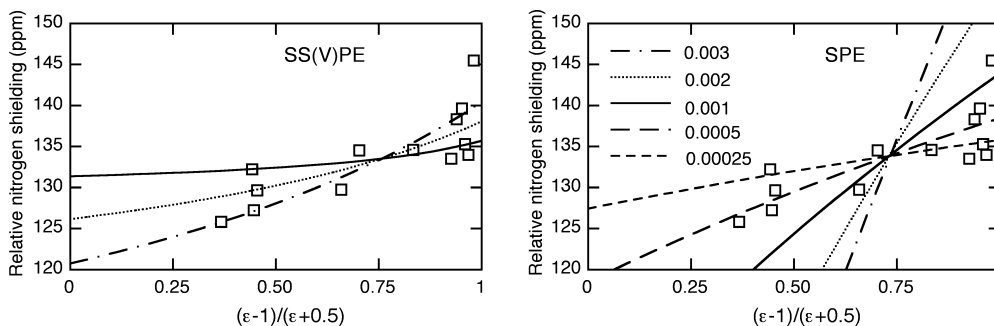


Fig. 1. Nitrogen shielding in CH₃CN as a function of solvent dielectric constant. Boxes show the experimental results relative to neat nitromethane. Lines show the results from shifted and

smoothly interpolated surface and simulation of volume polarization for electrostatics or surface polarization for electrostatics calculations, each line corresponding to a different cavity size

is contribution no. NDRL-4427 from the Notre Dame Radiation Laboratory.

References

1. Miertuš S, Scrocco E, Tomasi J (1981) *Chem Phys* 55: 117
2. Tomasi J, Persico M (1994) *Chem Rev* 94: 2027
3. Tomasi J, Cammi R, Mennucci B, Cappelli C, Corni S (2002) *Phys Chem Chem Phys* 4: 5697
4. Cramer CJ, Truhlar DG (1999) *Chem Rev* 99: 2161
5. Buckingham AD, Schaefer T, Schneider WG (1960) *J Chem Phys* 32: 1227
6. Witkowski M, Stefaniak L, Webb GA (1981) In: Webb GA (Ed) *Annual reports on NMR spectroscopy*, vol 11B. Academic, New York, p 35
7. Zhan C-G, Chipman DM (1999) *J Chem Phys* 110: 1611
8. Mennucci B, Martínez JM, Tomasi J (2001) *J Phys Chem A* 105: 7287
9. Chipman DM (1996) *J Chem Phys* 104: 3276
10. Mennucci B, Tomasi J (1997) *J Chem Phys* 106: 5151
11. Chipman DM (1997) *J Chem Phys* 106: 10194
12. Zhan C-G, Bentley J, Chipman DM (1998) *J Chem Phys* 108: 177
13. Zhan C-G, Chipman DM (1998) *J Chem Phys* 109: 10543
14. Chipman DM (1999) *J Chem Phys* 110: 8012
15. Chipman DM (2000) *J Chem Phys* 112: 5558
16. Mennucci B, Cammi R, Tomasi J (1998) *J Chem Phys* 109: 2798
17. Cancès E, Mennucci B (2001) *J Chem Phys* 114: 4744
18. Cossi M, Rega N, Scalmani G, Barone V (2001) *J Chem Phys* 114: 5691
19. Cossi M, Scalmani G, Rega N, Barone V (2002) *J Chem Phys* 117: 43
20. Chipman DM (2002) *Theor Chem Acc* 107: 80
21. Chipman DM (2002) *J Chem Phys* 116: 10129
22. Wolinski K, Hinton JF, Pulay P (1990) *J Am Chem Soc* 112: 8251
23. Hehre WJ, Ditchfield R, Pople JA (1972) *J Chem Phys* 56: 2257
24. Hariharan PC, Pople JA (1973) *Theor Chim Acta* 28: 213
25. Krishnan R, Binkley JS, Seeger R, Pople JA (1980) *J Chem Phys* 72: 650
26. Frisch MJ, Pople JA, Binkley JS (1984) *J Chem Phys* 80: 3265
27. Chipman DM, Dupuis M (2002) *Theor Chem Acc* 107: 90
28. Dupuis M, Marquez A, Davidson ER (1999) HONDO 99, a computer program based on HONDO 95.3. Quantum Chemistry Program Exchange, Indiana University, Bloomington, IN
29. Witkowski M, Sicinska W, Webb GA (1989) *Magn Reson Chem* 27: 380