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STRUCTURE OF CHEMICAL COMPOUNDS, INCLUDING CONDENSED MEDIA

An Ab Initio Quantum Chemical Investigation of Solvent-Induced Effect on ^{14}N–NQR Parameters of Alanine, Glycine, Valine, and Serine Using a Polarizable Continuum Model[1]

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Abstract—In this paper ab initio quantum mechanical calculations of the ^{14}N–nuclear quadrupole resonance (NQR) parameters of alanine, glycine, valine, and serine obtained from an electric field gradient (EFG) tensor, such as quadrupole frequencies and asymmetry parameters in gas phase and different solvents, have been carried out with the Gaussian 98 software package and the solvent-induced effects on these parameters have been evaluated using density functional theory (DFT). Furthermore, direct and indirect solvent effects on asymmetry parameters have been also calculated. We determined that the NQR parameters of the nitrogen atoms of amino acids are highly sensitive to environmental effects and that the observed solvent-induced shielding variation is strongly related to the values of the dielectric constants of the solvent and whether it is protic or aprotic. For more investigation of the solvent effect, the relative energies of each amino acid in various solvents have been calculated and the graphs of the relative energies versus dielectric constants have been analyzed.

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INTRODUCTION

Increased interest has been shown recently in nuclear quadrupole resonance (NQR) studies of amino acid compounds because of their importance in biochemistry and medicine [1–8]. Amino acid molecules have a zwitterionic structure when they are in liquid or solid phase. A theoretical calculation, using self-consistent field theory combined with an ab initio approach, of the most stable conformation of a single amino acid molecule led to a nonzwitterionic form as a result [9].

The transferability of atomic charges in amino acid compounds has been analyzed in the past. Moreover, the conformational dependence of point charges derived from distributed multipole moments was studied with 3-21 G SCF wave functions in a model dipeptide system [10]. The behavior of distributed multipoles was also analyzed critically for some side chains of naturally occurring amino acids [11]; modeling of side chains with point charges derived from SCF 6-31 G** electrostatic potentials was also explored [12, 13]. Significant changes in the atomic multipoles with torsion angles were found in all cases in side chains [14]. In another study, a comparative theoretical analysis of the structure and vibrations of amino acid compounds was performed using self-consistent reaction field (SCRF) theory [15]. However, in a separate study, Raman spectroscopy and SCRF were used to study the structural and vibrational features of the amino acids in H_2O and D_2O solutions [16].

Ab initio calculation of nuclear quadrupole parameters has become an indispensable aid in the investigation of molecular structures and accurate assignment of the NQR spectra of chemical compounds.

The interaction between the electric field gradient (EFG) at the site of a quadrupolar nucleus ($I \geq 1$) and its quadrupole moment plays a fundamental role in nuclear quadrupole resonance (NQR) spectroscopy. The observed frequency (ν) is related to the quadrupole moment of the nucleus, eq; the component of the EFG tensor along the principal Z-axis, q; and the asymmetry parameter of the EFG. Asymmetry parameter (η) indicates the deviation of the EFG from cylindrical symmetry [10, 11].

We believe that precise knowledge of the coupling constant ($\chi = e^2qQ/h$) and asymmetry parameter (η) may contribute to the understanding of rather complex ^{14}N–NQR spectra in liquid crystal phase and their rela-

[1] The text was submitted by the authors in English.

Table 1. Energies (Hartree) and relative energies (kcal/mol) in different mediums for different amino acids at the B3LYP/6-311++G(2*d*,2*p*) level of theory

Solvent	ε	Alanine		Glycine		Serine		Valine	
		E	Δ*E*	*E*	Δ*E*	*E*	Δ*E*	*E*	Δ*E*
Water	78.39	−363.123	−13.288	−284.488	−12.242	−399.033	−15.644	−325.818	−15.644
DMSO	46.8	−363.112	−6.187	−284.477	−5.179	−399.019	−6.656	−325.813	−5.674
Nitromethane	38.2	−363.111	−5.748	−284.476	−4.740	−399.018	−6.131	−325.812	−5.358
Methanol	32.63	−363.127	−15.483	−284.490	−13.497	−399.036	−17.327	−325.822	−11.573
Ethanol	24.55	−363.123	−13.220	−284.487	−11.740	−399.032	−15.067	−325.819	−9.488
Aceton	20.7	−363.113	−7.189	−284.477	−5.274	−399.019	−6.855	−325.814	−6.515
Dichloroethane	10.36	−363.111	−5.897	−284.476	−4.605	−399.018	−5.879	−325.813	−5.623
Dichloromethane	8.93	−363.115	−8.176	−284.479	−6.362	−399.021	−8.009	−325.816	−7.817
THF	7.58	−363.110	−5.300	−284.475	−4.081	−399.017	−5.178	−325.812	−5.101
Aniline	6.89	−363.102	0.000	−284.469	0.000	−399.008	0.000	−325.804	0.000
Chlorobenzene	5.62	−363.109	−3.926	−284.473	−2.103	−399.014	−5.441	−325.811	−4.738

tion to the molecular motions and phase transitions associated with the motional degrees of freedom.

It is notable that the ^{14}N-quadrupole coupling constant (χ) and asymmetry parameter (η) of the EFG tensor strongly depend on the molecular structure and the electric charge distribution within the molecule, as well as on the intermolecular interactions and molecular motions [12–21].

Nitrogen-14 ($I = 1$) exhibits, in zero magnetic field, three generally nondegenerate energy levels with the NQR frequencies as bellow [12]:

$$\nu_+ = \frac{3}{4}\frac{e^2qQ}{h}\left(1 + \frac{\eta}{3}\right),$$

$$\nu_- = \frac{3}{4}\frac{e^2qQ}{h}\left(1 - \frac{\eta}{3}\right),$$

$$\nu_0 = \nu_+ - \nu_- = \frac{1}{2}\eta\frac{e^2qQ}{h}.$$

In this paper, the NQR parameters, such as the quadrupole coupling constant, as well as the asymmetry parameters and three NQR frequencies in the gas phase, and different solvents have been calculated at the level of B3LYP/6-311++G (2*d*, 2*p*), and the effects of different solvents on nitrogen NQR parameters have been then evaluated.

Most computational studies carried out in the past treated the molecules in vacuum, totally separated from the effects of the environment [22], and the theoretical study of solvent-induced effects on nitrogen NQR parameters of amino acid compounds have yet to be discussed. The diversity of nitrogen atoms in these molecules makes them good candidates for a preliminary investigation of the influence of solvent polarity on nuclear quadrupole parameters. In the second part of this research, direct and indirect contributions to the total solvation effect have been also examined. Direct effects involve perturbation of the solvent on the electronic wave function of the solute held at fixed geometry; indirect effects are due to the relaxation of the solute geometry under the influence of the solvent [23–25]. For more investigation of the solvent effect, the relative energies of each amino acid in various solvents have been calculated and, finally, the graphs of the relative energies versus dielectric constants have been plotted. The results reported in this work can be considered to provide a good assessment of the ability of Polarizable Continuum Model (PCM) to predict the NQR properties of molecules in solution.

COMPUTATIONAL DETAILS

Gas-phase geometry optimization for all four mentioned amino acids, combined with self-consistent field theory, has been performed. The results of ab initio calculations of NQR parameters of nitrogen atoms have been reported in Table 1. All the calculations have been carried out using the Gaussian 98 program [26]. The model chemistry used for all calculations is B3LYP/6-311++G (2*d*, 2*p*). This corresponds to the approximation that makes use of Becke-style three-parameter density functional theory with the Lee–Yang–Parr correlation functional [27, 28].

Relative solvent effects on the ^{14}N–NQR parameters have been compared with the corresponding value of aniline as a nitrogen-containing reference. Direct ($\Delta\eta_{dir}$) and indirect ($\Delta\eta_{ind}$) solvent effects are obtained with a slight modification of the method used by Cammi [23]. Instead of deriving ($\Delta\eta_{ind}$) from the difference of the PCM-optimized shielding and the PCM shielding of the molecule held at the geometry optimized in vacuum, it is obtained from the shielding cal-

Table 2. Values of $\Delta\eta_{dir}$ and $\Delta\eta_{ind}$ calculated for different amino acids

ε	$\Delta\eta_{dir}$				$\Delta\eta_{ind}$			
	alanine	glycine	serine	valine	alanine	glycine	serine	valine
78.39	0.0736	0.0321	0.0768	0.0427	0.0174	0.0205	0.0314	0.0433
46.8	0.0165	0.0013	0.0084	0.0119	0.0119	0.0043	0.0057	0.0057
38.2	0.0162	0.0007	0.0008	0.0121	0.0111	0.0042	0.0054	0.0054
32.63	0.0699	0.051	0.0723	0.0397	0.0131	0.0193	0.0294	0.0407
24.55	0.0679	0.0496	0.085	0.038	0.0108	0.0187	0.0285	0.0393
20.7	0.0049	0.0058	0.0063	0.013	0.0085	0.0034	0.0043	0.0043
10.36	0.0023	0.0035	0.0028	0.0148	0.0039	0.0399	0.0018	0.0014
8.93	0.0016	0.0014	0.0018	0.0154	0.0027	0.0013	0.0014	0.0014
7.58	0.0006	0.0006	0.0005	0.016	0.0001	0.0004	0.0005	0.0005
5.621	0.0015	0.0013	0.0023	0.015	0.0117	0.0009	0.0013	0.0009

culated in vacuum for a molecule that is geometry-optimized in solution. Thus,

$$\Delta\eta_{dir} = \eta_{Sol}(R_V) - \eta_{Aniline}(R_V),$$

$$\Delta\eta_{ind} = \eta_{Vac}(R_s) - \eta_{Vac}(R_{Aniline}),$$

where $\eta_{Sol}(R_V)$ is the value of the nuclear shielding computed in solution, but with the solute in the geometry optimized in vacuum, and $\eta_{Vac}(R_s)$ is the value of the nuclear shielding in vacuum, but with the solute geometry optimized in solution. $\eta_{Vac}(R_{Aniline})$ are the corresponding parameters for calculations with aniline [23, 24]. The percentage contribution of these effects to the total solvation effect is determined in each case.

RESULTS AND DISCUSSIONS

Solvent Effects on NQR Parameters

The calculated quadrupole coupling constants (QCCs), as well as the NQR frequencies, for all four mentioned amino acids are presented in Table 1. It can be clearly seen that the calculated asymmetry parameter (η) revealed greater values in all different solvents in comparison with the gas phase. It is thought that this variation arises from the fact that η, which was calculated in the gas phase, did not take into account any solvent field contribution. The NQR frequency shifts can be explained by the redistribution of electron density taking place in the system.

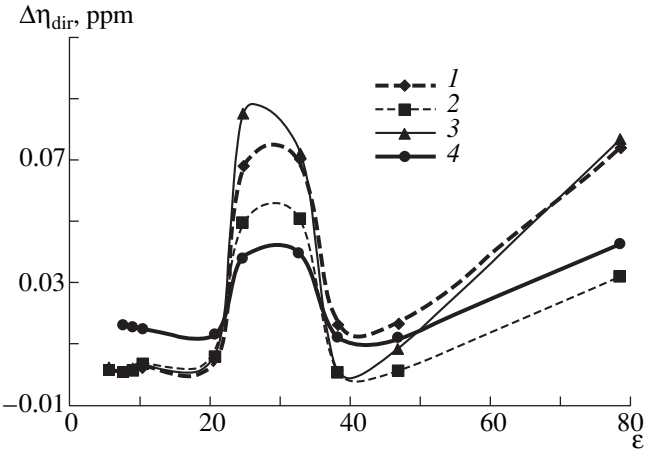

Fig. 1. Calculated solvent effect ($\Delta\eta_{dir}$) for amino acids: *1*—alanine, *2*—glycine, *3*—serine, and *4*—valine.

Furthermore, it is well known that structural vibrations of molecules in the gas state produce an averaging of the field gradient that may disturb quadrupole interactions by modulating both the values and orientations of the EFG tensor components. The resulting fluctuations of the EFG change the quadrupole frequencies and other NQR parameters. Moreover, an interesting conclusion that can be drawn from the results is that the greater values of NQR parameters are related to the protic solvents. This may indicate the specific interaction between four amino acids with protic solvents, especially due to their strong intramolecular hydrogen-bonding interaction.

Therefore, it can be concluded that ab initio quantum mechanical calculation of NQR parameters is a very useful method of gaining information on the dynamics of molecules.

Solvent Effects on $\Delta\eta_{dir}$ and $\Delta\eta_{ind}$

From this point of view, the solvation effect on NQR parameters consists of two parts: $\Delta\eta_{dir}$ and $\Delta\eta_{ind}$, which are reported in Table 2. The results are presented in Figs. 1 and 2. It might be suggested that optimization of solute molecule in solvent followed by calculation of NQR parameters is similar to that of solvent–solute as an isolated system. However, if the molecule is first optimized in gas phase and then NQR shielding calculations is performed in the solvent, the solvent–solute

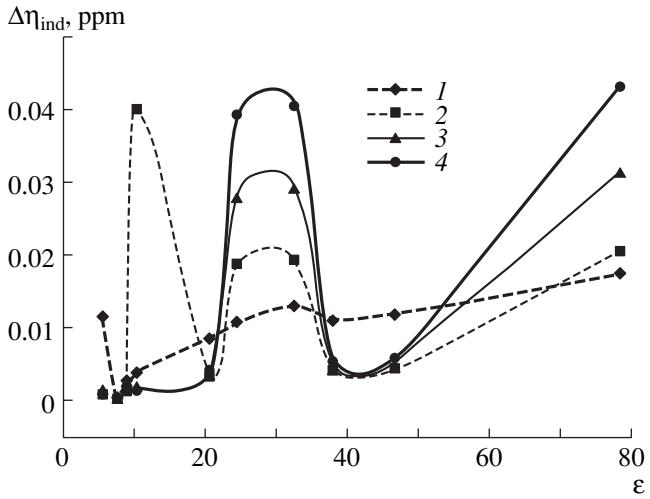

Fig. 2. Calculated solvent effect ($\Delta\eta_{ind}$) for amino acids; *1–4*—see Fig. 1.

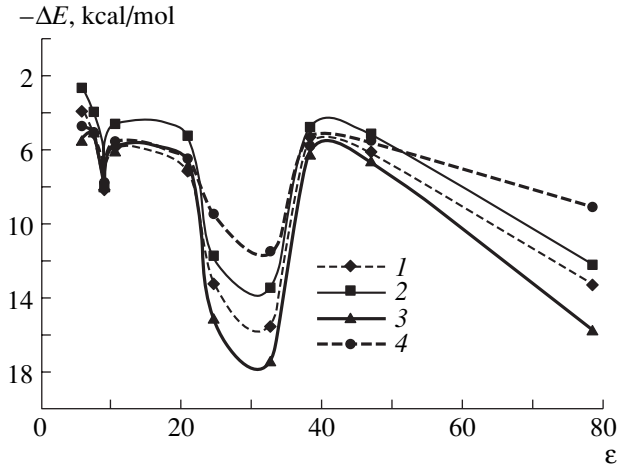

Fig. 3. Relative energies of different amino acids in different mediums; *1–4*—see Fig. 1.

interactions are taken into consideration for calculation of NQR parameters.

Therefore, in solvent effect studies, it is more advisable to carry out NQR calculations in solution even with a fixed (gas phase optimized) solute geometry, than to perform NQR computations in vacuum for a solute with the geometry optimized in solution. These changes seem noticeable where the protic solvents, water, ethanol, and methanol, are used. In such a case, the maximum region may be observed in the graphs. It is apparent that, for a more accurate prediction of solvent effects on NQR parameters and relative energies, it is necessary to consider specific solute–solvent interactions by introducing one or several solvent molecules in the calculations.

Solvent Effects on the Relative Energies of Amino Acids

Different structures of amino acid compounds in various solvents have distinct physicochemical properties. One of the most explicit properties of the structure of a molecule is its energy. In this part of the study, the energy values of the four mentioned amino acids in different media and their optimized structures are reported in Table 3. The graphs of the relative energies versus dielectric constants have been plotted Fig. 3. According to the results, the smaller energy values belong to the protic solvents. Thus the minimum value appearing at this point is related to the protic solvents. Therefore, it is well observed that energy values increase nonlinearly with a decrease in dielectric constants.

Table 3. Energies and relative energies in different mediums for different amino acids at the B3LYP/6-311++G (2*d*,2*p*) level of theory

Solvent	ε	$-E$, Hartree	$-\Delta E$, kcal/mol	$-E$, Hartree	$-\Delta E$, kcal/mol	$-E$, Hartree	$-\Delta E$, kcal/mol	$-E$, Hartree	$-\Delta E$, kcal/mol
		Alanine		Glycine		Serine		Valine	
Water	78.39	363.12369	13.2884	284.4886093	12.2425	399.03378	15.6449	325.8188014	9.0627
DMSO	46.8	363.11237	6.1879	284.4773528	5.1790	399.01946	6.6569	325.8134024	5.6747
Nitromethane	38.2	363.11167	5.7488	284.476654	4.7405	399.01862	6.1315	325.8128991	5.3589
Methanol	32.63	363.12719	15.4833	284.4906089	13.4973	399.03646	17.3274	325.8228032	11.5738
Ethanol	24.55	363.12358	13.2202	284.4878095	11.7407	399.03286	15.0677	325.8194793	9.4880
Aceton	20.7	363.11327	7.1890	284.4775051	5.2745	399.01977	6.8559	325.8147425	6.6156
Dichloroethane	10.36	363.11191	5.8973	284.4764392	4.6057	399.01822	5.8790	325.8133202	5.6231
Dichloromethane	8.93	363.11554	8.1763	284.4790809	6.2634	399.02161	8.0099	325.8168166	7.8172
THF	7.58	363.11096	5.3005	284.4756036	4.0814	399.01710	5.1785	325.8124885	5.1012
Aniline	6.89	363.10251	0.0000	284.4690995	0.0000	399.00885	0.0000	325.8043591	0.0000
Chlorobenzene	5.621	363.10904	3.9262	284.4734076	2.7033	399.01452	5.4112	325.8111191	4.7382

CONCLUSIONS

A study was undertaken to investigate if NQR parameters, such as the quadrupole coupling constant, asymmetry factor, and NQR frequencies obtained from electric field gradient tensor, can provide sufficient information to make inferences regarding the solvent effect on these parameters of a compound studied. This work presents a self-consistent reaction field study of the NQR parameters of nitrogen atoms and the relative energies for the four mentioned amino acids. Our calculations determined that the quality of reproduction of NQR parameters seems to be a very good test of various ab initio methods, especially the DFT method. This work also presented the application of PCM for calculation of nitrogen NQR parameters. It can be concluded that the standard approach of the PCM appears to be useful in theoretical investigation of the effect of solvent on nuclear quadrupole parameters. Moreover, it is well observed that the energy values decrease nonlinearly with increase in dielectric constant.

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