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DFT calculation of isotropic hyperfine coupling constants of spin adducts of 5,5-dimethyl-1-pyrroline-*N*-oxide in benzene and water

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ABSTRACT

Isotropic hyperfine coupling constants (HFCCs) of spin adducts of 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) are calculated by DFT method with solvation effect. Geometries of ring conformers and rotational conformers of trapped radicals are optimized and their HFCCs are calculated. Boltzmann weighted average of HFCCs of low energy conformations shows very good agreement with the experimental value in benzene. Two or four water molecules hydrogen bonded to the spin adduct have to be explicitly incorporated in the case of water. The results show time-independent averaging of relevant conformers is a very practical method for calculation of HFCCs of DMPO spin adducts.

1. Introduction

5,5-Dimethyl-1-pyrroline-*N*-oxide which is known as DMPO is one of the most widely used spin-trapping reagent to detect unstable radicals like hydroxyl or superoxide anion as relatively stable nitroxide spin-adducts by electron spin resonance (ESR) spectroscopy [1–3]. Their spectra are quite simple as only nitrogen atom and β hydrogen of DMPO give hyperfine splitting and their isotropic hyperfine coupling constants (HFCCs) are easily determined. While nitrogen HFCCs of the spin-adducts show small variation with the trapped radical species, β hydrogen HFCCs show large changes and their values can be utilized for identification of the trapped radical species. For example, DMPO spin adducts of hydroxyl radical (DMPO-OH) and superoxide (DMPO-OOH) in aqueous solution show very distinct ESR spectra of four and six lines with β hydrogen HFCCs of 14.7 and 11.9 Gauss, respectively [2,3].

When the number of possible radical species is limited, assignment of the species detected by ESR spectra is rather straightforward and determination of HFCCs may be unnecessary. However, if several radical species may exist in the system whose HFCCs are not known, absence of hyperfine splitting arising from the nuclei in the trapped radicals hamper their identification. In such a case it would be very helpful if HFCCs of the spin adducts can be theoretically predicted. In relation to the subject of the author, DMPO spin trapping has been employed for studies on chemical degradation of proton exchange membranes in the fuel cells and identification of the so-called carbon-centered radicals (CCRs) whose HFCCs shift slightly with molecular structure of the trapped radicals is crucial for speculation of the reaction mechanism [4,5].

While various effects on HFCCs of nitroxides have already been theoretically studied extensively [6], and large number of experimental values of HFCCs of DMPO spin adducts have been accumulated [3], there are relatively few studies on quantum chemical calculations of HFCCs of DMPO spin-adducts, not only for CCRs but even for DMPO-OH and DMPO-OOH adducts. Villamena and his colleagues have performed quantum chemical calculations of HFCCs of those radicals>, Their calculated values do not necessarily show quantitative agreement with the experimental values but also seem to have failed to reproduce their trends such as relative magnitude of HFCCs of β hydrogen of DMPO-OH and DMPO-OOH [7–9]. Houriez et al. have pointed out that although Villamena et al. identified presence of rotational isomers of DMPO-OOH, they did not take into account DMPO ring conformers which have largely different HFCC values [9,10]. They have applied a new method to average HFCCs of different conformers of DMPO spin-adducts in aqueous solutions by sampling their geometries from nanosecond MD trajectories and calculated HFCCs by DFT calculation [10,11]. There are two ring conformers whose carbon atoms at 3 position is either upper or lower side of the ring plane determined by the atoms at 1, 2 and 5 positions, which are denoted as $^3T_4$ and $^4T_3$, respectively. They obtained MD trajectories with different

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population ratio of two ring conformers and found that HFCCs are almost linearly dependent on their population ratio: In the case of DMPO-OH calculated HFCC with $^3T_4$ population of around 70% gave the best agreement with the experimental value. Hermosilla et al. calculated HFCCs of DMPO-H by sampling configurations of MD trajectories with refined force field parameters [12]. They also investigated solvent effect by using polarizable continuum model (PCM) calculation in benzene and water and for latter case explicit consideration of hydrogen bonding water molecules.

Although we admit that time-dependent averaging is a proper approach for statistical averaging of physical parameters of the spin adducts in solution, a large number of DFT calculations with molecular geometries sampled from the MD trajectories would be time consuming. Furthermore, setting up and execution of MD simulation are still less familiar than DFT calculation for experimental chemists and it would not be practical unless some automated procedure is prepared. However, if the trajectories are relatively restricted around some local minima on the potential energy surface during the MD simulation, globally averaged molecular parameters are expected to be properly calculated by assuming their relative population as Boltzmann distribution. Such a time-independent approach seems to be more practical as it can be performed by using only popular quantum chemical calculation codes.

In this paper such a method is applied for calculation of HFCCs of DMPO spin adducts: Geometries of $^3T_4$ and $^4T_3$ ring conformers as well as rotational conformers of DMPO spin adducts are optimized and their HFCCs are calculated. Although HFCCs of β-hydrogen show large variations with conformations and do not agree with the experimental values by themselves, their Boltzmann weighted averages give fairly good agreement with the experimental values in benzene solution. HFCCs of DMPO spin adducts in water are also calculated by explicitly including two or four water molecules hydrogen bonded to the spin adducts. The efficiency of the present method compared to the time-dependent approach is briefly discussed.

2. Computational method

All the calculations were performed by using Gaussian09 program [13]. Long-range corrected hybrid functional (LC-ωPBE) [14–16] and Pople's double-zeta and polarization function (6-31G∗) [17,18] with polarizable continuum model for solvent effect [19,20] were used throughout this study. The functional was selected as it can properly describe dissociation limit of open shell systems. The basis set of double zeta plus polarization type is the same level as those employed in previous studies [10,11] and diffuse functions are not included as they do not affect optimized geometries with PCM model as well as calculated HFCCs. Molecular geometries were illustrated by using MacMolPlt [21].

3. Results and discussion

3.1. HFCCs in benzene

As mentioned above we calculated HFCCs of DMPO adducts in benzene as large number of experimental data already exist [1,3] and specific interaction of solvent molecule is supposed to be unimportant. Fig. 1 shows optimized geometries of two ring conformers of methyl radical adduct of DMPO which does not have rotational isomers of the trapped radical. Total energies and calculated HFCCs are also noted in the figure and $^3T_4$ conformer is more stable and has larger β hydrogen HFCC (a_H) than $^4T_3$ conformer (22.87 vs 13.48 G). In $^3T_4$ conformer β hydrogen is more vertical to the C_5—N_1—C_2 plane, as indicted by the smaller C_5—N_1—C_2—H_β dihedral angle than that of $^4T_3$ conformer (101.2 vs 125.7 degree). Relative population of two conformers was calculated from their total energies and assuming Boltzmann distribution at 298 K they were 0.73 and 0.27, respectively. Finally an averaged a_H was calculated to be 20.32 G, which is in very good agreement with the experimental value of 20.52 G [1].

In the case of DMPO-C_2H_5 adduct three rotational isomers, two in *gauche* and one in *trans* position of the C—C bond of ethyl group against the C_2—N_1 bond of five-membered ring exist for each ring conformer and Boltzmann averaged HFCC was calculated from six conformers. Total energies, a_H and dihedral angles at the optimized geometries of the six conformers are summarized in Table 1. *Trans* conformer is more stable than two gauche conformers in each ring conformer, and $^3T_4$ conformer is more stable than $^4T_3$ conformer as shown in the sum of the relative population of the three rotational isomers. Boltzmann averaged a_H is calculated to be 20.15 G, the value very close to that of DMPO-CH_3 adduct.

If another hydrogen atom on carbon atom of the C-adduct is substituted, six rotational conformers are generated for each ring conformer and in total twelve conformers have to be taken into account to calculate Boltzmann averaged HFCCs of the DMPO-adduct. Actually some conformers give total energies being too high whose contribution can be neglected in Boltzmann averaging. In this study conformation is neglected in averaging whose relative population is estimated to be less than 0.01. In larger radicals such as *n*-butyl radical there are a large number of possible rotational isomers in the alkyl group. However they were neglected in the averaging as those conformational changes hardly affect HFCCs and only all-*trans* conformer was chosen in each rotational conformer of *n*-butyl adduct. This restriction seems to be justified as the averaged a_H of DMPO-*n*-butyl adduct was 20.16 G, which is almost identical to that of DMPO-ethyl adduct and in good agreement with the experimental value of 20.41 G.

Calculated HFCCs of DMPO adducts of C-centered are summarized in Table 2 together with C_5—N_1—C_2—H_β dihedral angles. Calculated data at the optimized geometries of the conformers which are taken into account in Boltzmann averaging are summarized in Table S1 in the supplementary material together with total energies, dihedral angles and relative populations of the conformers. The largest number of the averaged conformers was eight for 1-phenylethyl radical in the case of C-centered radicals.

Most of alkyl radical adducts show a_H around 20 G and calculated values are in excellent agreement with the experimental values. Substitution of hydrogen in 1-position of the alkyl group with phenyl ring little affects a_H (e.g., benzyl, 1-phenylethyl, cyanobenzyl). In these cases both $^3T_4$ and $^4T_3$ ring conformers contribute Boltzmann-averaged a_H to some extent.

Four hydroxyalkyl adducts show slightly larger experimental a_H and they are reproduced in the calculation. In these cases hydrogen bonding of terminal hydroxyl group to oxygen atom in DMPO stabilizes $^3T_4$ conformers and this effect results in larger a_H. For example, only $^3T_4$ conformers are included in Boltzmann averaging in the case of 1-hydroxylbutyl adduct.

DMPO adducts with planar radicals which contain C=O double bond show smaller a_H and trifluoromethyl radical adduct gives the smallest a_H in both of the experimental and calculated values. In these adducts $^4T_3$ conformers are more stable than $^3T_4$ conformers and consequently the averaged a_H become smaller.

The same procedure is applied for DMPO spin adducts of O-, N- and S-centered radicals and their calculated a_H are also summarized in Table 2. These calculated a_H are plotted in Fig. 2 against experimental values. While the calculated a_H of different conformers are largely scattered, Boltzmann averaged values show excellent agreement with the experimental values. Least square fit plotted as dotted line gives $a_H(\text{Calc.}) = 1.071 \times a_H(\text{Exp.}) - 1.73$ with $R^2 = 0.94$.