Proposal of Calculation Protocols for Implicit Solvation Methods in Conformational Analysis Involving the Gauche Effect

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INTRODUCTION

Conformational analyzes in solution media still present many challenges in computational chemistry and one of the main reasons is the little magnitude of interaction energies involved[1]. In order to diminish the arising relative errors very often costly computations are required, with sophisticated methods. One example of such methods is to take into account explicitly the solvent molecular structure, by modeling the solute or the solute supermolecule via quantum methods and the bulk structure via classical approaches. One low cost alternative method is the implicit solvent model, where the solvent bulk is represented by a continuum dielectric medium and the solute is immersed in an arbitrary cavity in the dielectric. This is the case of the PCM[1] (Polarizable Continuum Model), based on Onsager theory of Self-consistent Reaction Field (SCRF). Today, modern versions of this theory are implemented in many computational chemistry programs like Gaussian, Orca, ADF, among others, like the PCM model of Tomasi[1] and more recently the Truhlar SMD model[2]. Given the empirical fashion of the PCM model and its large number of parameters, mainly related to the cavity definition, there are a lot of protocols available in different programs, especially Gaussian[3], and a proper and conscious choice usually is a difficult task. Our group is interested in conformational analysis of systems where a suitable prediction of the rotamers distribution is of importance. Directly related to this problem is the well known gauche effect (GE) or generalized anomeric effect. In order to investigate the performance of PCM protocols in this subject, we choose the 1,2-haloethanes (CH$_2$X-CH$_2$X, where X=F, Cl, Br and I) as model compounds for a GE analysis in polar and non-polar solvents (CHCl$_3$, C$_6$H$_{12}$, CCl$_4$, DMSO). The experimental results for t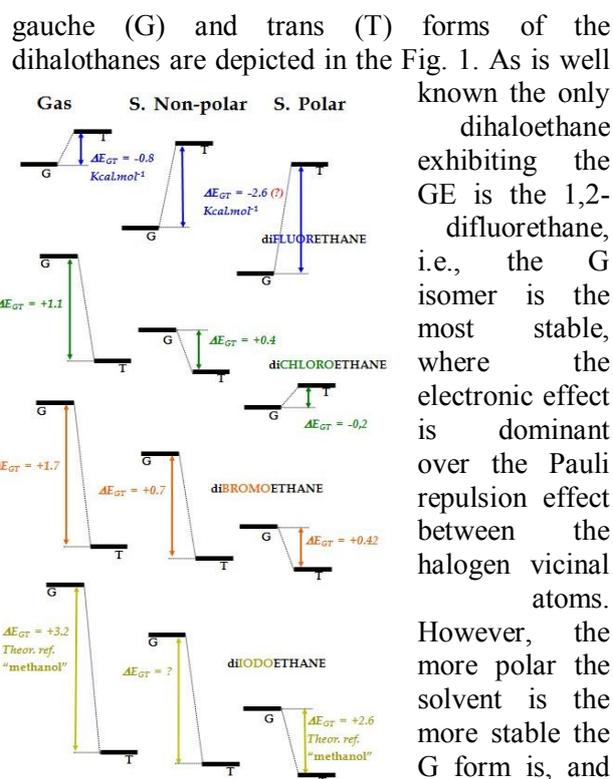he energy difference (ΔG^{GT}) between the gauche (G) and trans (T) forms of the dihalothanes are depicted in the Fig. 1. As is well known the only dihaloethane exhibiting the GE is the 1,2-difluorethane, i.e., the G isomer is the most stable, where the electronic effect is dominant over the Pauli repulsion effect between the halogen vicinal atoms. However, the more polar the solvent is the more stable the G form is, and in the case of dichloroethane, very polar media favor the G isomer (see Fig. 1). In Fig. 1, question marks are written where there is experimental uncertainty[4,5].

Fig.1.Experimental ΔG^{GT} for dihaloethanes CH$_2$X-CH$_2$X.

METHODS

The used PCM models, based on the apparent surface of charges concept (ASC) and the resolution of the nonhomogeneous Poisson equation, split in two classes concerning the building method of the cavity, namely: (i) by superposition of atomic spheres (IEFPCM-"integral equation formalism-PCM", CPCM-"conductor like model-PCM", SMD-"Density-based solvation model") and (ii) from the solute electronic density (IPCM e SCIPCM). For the IEFPCM and CPCM there are different radii

models for the atomic spheres: UFF (Universal force field-based model), UA0, UAHF, UAKS (the last three are "United-Atom"-based models), Pauling e Bondi. After geometry optimizations with frequency determinations for minimum states characterization, single point calculations were done in the G and T forms. The quantum methods were DFT with the functionals B3LYP and M05-2X, with the following basis sets: 6-31G*, 6-31+G*, 6-311G*, 6-311+G*, CCPVTZ, CCPVTZ-PP for bromine, Def2TZVP). For iodine atom, the following effective core potentials were adopted: CRENBL, LanL2DZ, Stuttgart (StuttRLC) for the same above basis sets for light atoms, for SMD model (For PCM models, only the 6-31+g* basis was used for light atoms in diiodoethane). Two versions of Gaussian Program were employed, G03 and G09, but only the results for the latter will be shown here, and a comparison with several experimental works was made[4,5].

RESULTS AND DISCUSSION

For all the adopted calculation protocols and solvents, the GE ($\Delta E^{GT}=E^G-E^{T+}<0$) was confirmed for difluorethane molecule and, accordingly, the T form was found as the most stable for the haloethanes (X=Cl, Br and I), namely ($\Delta E^{GT}>0$). For the B3LYP functional, the best averaged result was obtained with the 6-31+g* basis set combined with the CPCM/Pauling model, that is, the more balanced choice basis for F, Cl and Br compounds. The IEFPCM as well as the 6-311+g* basis, although a little bit worse, yield similar results as the above ones. As expected, a more pronounced stabilization of the G (polar) form in respect with the T (non polar) form was observed in all the solvents owing to the dipole-induce dipole attractive interactions, but with a much greater extent to polar ones, owing to higher-magnitude dipole-dipole forces. Also, the stabilization of the T form is observed for polar solvents (dipole-induce dipole) and even for non polar solvents, due to the presence of dispersion interaction, as a non electrostatic term of the PCM calculation. For SMD method, using the B3LYP functional, we rather obtain the opposite behavior with the basis 6-31+g*, as it yields poor results, especially for light halogen atoms, F and Cl. In this respect the 6-311+g*, 6-311g* and 6-31+g* yielded better results for the F, Cl and Br in this respective order. As can be seen, the lighter the halogen is the higher the basis set level is needed. In Fig. 2, we can observe the B3LYP-SMD results

for the ΔE^{GT} (electrostatic part of solvation) and ΔG^{GT} (total free energy of solvation) in CHCl$_3$ and DMSO for CH$_2$X-CH$_2$X (X = F, Cl, Br and I). Since the cavitation energy is positive and of high
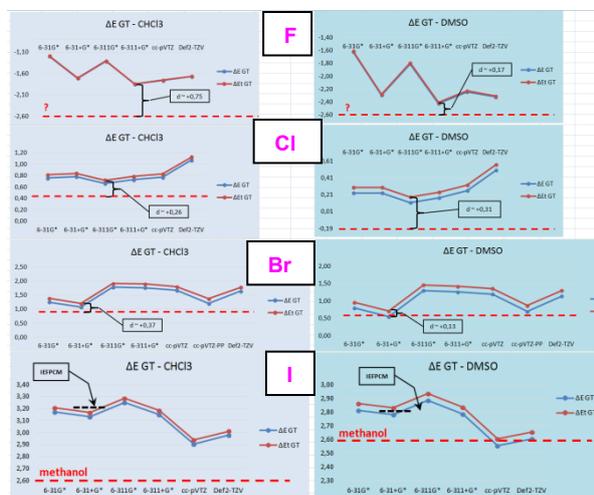
Figure 2. B3LYP/SMD ΔE^{GT} and ΔG^{GT} in CHCl$_3$ and DMSO for CH$_2$X-CH$_2$X (X = F, Cl, Br and I). The red dashed lines shows the experimental value.

magnitude, this term dominates the non electrostatic part of solvation energy and the ΔG^{GT} is invariably above the ΔE^{GT} for all the basis sets. However, we can observe that the difference between the two solvation energies, that is, the non electrostatic contribution is entirely systematic. We can also observe in Fig. 2 that, as expected, the magnitude of solvation energies in the polar (DMSO) solvent is larger than in chloroform. Another interesting aspect is that this term increases as the halogen atomic mass increases, as expected. Furthermore, we can see an alternate pattern in account to the quality of the results among the basis sets, especially for light fluorine. For diiodoethane, the protocol M05-2X/SMD yields the best results, and with the use of LanL2DZ effective core potential, although the experimental result is only qualitative.

CONCLUSIONS

As preliminary results, the B3LYP/6-31+g* furnish the best average results when combined with the CPCM/Pauling model, that is, this is the more balanced choice basis for F, Cl and Br. Also, with this method and also with the SMD, we can conclude that the electrostatic interactions are dominant and are sufficient to explain qualitatively the experimental results. For SMD method, using the B3LYP functional, we rather obtain the opposite behavior with the basis 6-31+g*, since it yields poor results, especially for

lighter halogen atoms, F and Cl. In this respect, the 6-311+g*, 6-311g* and 6-31+g* basis yielded better results for the F, Cl and Br in the respective order. In short, the lighter the halogen is the higher level of the basis set is needed. Finally, for the SMD method, since it was optimized for Truhlar functionals, in general we obtain better results with the M05-2X against the B3LYP. Calculations with this functional for the PCM models used in this work are in progress, for a more complete comparison.

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