Evaluation of the ONIOM(B3PW91:HF) hybrid method for modeling butyltin chlorides

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Abstract: The ONIOM(B3PW91:HF) hybrid method has been evaluated for the purposes of modeling butyltin chlorides, XₙSnCl₄₋ₙ (X = n-butyl, sec-butyl, isobutyl, tert-butyl; n = 1, 2, 3). Three different partitioning schemes of a molecule within ONIOM(B3PW91:HF) were taken into account. For each of these partitioning schemes, conformational analyses of the XₙSnCl₄₋ₙ molecules were performed and then several molecular properties of the resulting rotamers were calculated. The values of molecular properties obtained by ONIOM(B3PW91:HF) were compared in a statistical manner with the reference values calculated by B3PW91. A careful choice of partitioning scheme for XₙSnCl₄₋ₙ allowed ONIOM(B3PW91:HF) to achieve a significant saving in computational cost, together with a relatively small decrease in the accuracy of the XₙSnCl₄₋ₙ molecular properties routinely obtained from conformational analysis (structural parameters, etc.). Unfortunately, the hybrid method turned out to be ineffective in reproducing the ¹H, ¹³C and ¹¹⁹Sn NMR chemical shifts in XₙSnCl₄₋ₙ accurately.

Keywords: Organotin compounds • Butyltin chloride • ONIOM • Chemical shift

1. Introduction

Butyltin chlorides are valuable reagents in laboratory synthesis [1,2]. For instance, they undergo a nucleophilic substitution and thus a wide range of products with other functional groups can be obtained. Butyltin chlorides can also be used in polymerization, catalysis and glass coating [1]. Recent promising applications span polymer-supported butyltin chlorides, acting as reducing catalysts [3], and thin films of SnO₂ formed by the vapour of butyltin trichloride in atmospheric pressure chemical vapour deposition [4]. Butyltin chlorides are generally toxic and their toxicity is dependent on the number of butyl groups attached to the tin atom [2]. Tributyltin chloride has the highest biological activity, in particular toward fungi, and the toxicity diminishes with the successive decrease in the number of butyl groups attached to the tin atom. A possible explanation of the toxic activity of butyltin chlorides toward living organisms seems to be connected with the inhibition of DNA and ATP synthesis [2]. Unfortunately, butyltin chlorides are also hazardous to human health because these compounds can significantly reduce the ability of some human lymphocytes to destroy tumor or viral-infected cells, thereby promoting cancer development and viral infection in humans [2].

Butyltin chlorides have been the subject of several quantum-chemical studies so far [5-8]. The geometry, heat of formation, entropy and Gibbs free energy of formation of butyltin trichloride were obtained from a very accurate fourth-order Møller-Plesset perturbation theory calculation by Allendorf and Melius [5]. The ionization potential of tributyltin chloride was predicted by means of local density functional theory (DFT) in a comparative study (calculations vs. experiment) by Osmekhin et al. [6]. Another DFT method, namely the B3LYP density functional, was used by Akatsuka et al. [7] to determine the geometries of butyltin mono-, di- and trichlorides. The ¹¹⁹Sn NMR chemical shifts of these molecules were calculated and interpreted in terms of group electronegativity, hardness and softness in our previous paper [8].
Since butyltin chlorides exhibit the aforementioned biological activity, theoretical investigations of the interaction between butyltin chlorides and biological macromolecules may be important to elucidate the nature of this interaction at the molecular level. However, the computational cost of standard post-Hartree-Fock (post-HF) methods, that provide results with great accuracy, most often turns out to be too high to perform such investigations. One also encounters the problem of high computational cost in detailed conformational investigations of molecules, even those that are non-biological and moderately large [9], and in calculations of some time-consuming energetic properties [10,11]. In such cases, the application of hybrid methods [12] may be an effective solution. Hybrid methods are capable of achieving significant computational savings by dividing a molecular system into several parts (so-called layers), each of which is treated at a different level of theory. Expensive computational methods are used only for the part of the system where it is necessary, e.g. in the region where the chemical process of interest takes place. ONIOM (our Own N-layer Integrated molecular Orbital molecular Mechanics) [13,14] is a hybrid method that, in principle, can handle any number of layers described by various molecular orbital methods, as well as by molecular mechanics methods. Unfortunately, the division of a molecular system into parts results in some decrease in the accuracy of ONIOM calculations. For the purposes of obtaining reliable results, a careful evaluation of a given ONIOM approach should be carried out prior to using this ONIOM approach in production calculations.

In this work, we present the evaluation of the ONIOM combination of two molecular orbital methods, namely B3PW91 and HF. Various molecular properties of butyltin chlorides were calculated by this ONIOM combination. Additionally, three ONIOM partitioning schemes of the molecules were probed. The butyl groups attached to the tin atom were in the form of n-butyl (‘nBu) or in the branched-chain isomeric forms, that is, sec-butyl (‘sBu), isobutyl (‘iBu) or tert-butyl (‘tBu). For the resulting series of $X_nSnCl_{4-n}$ molecules ($X = 'sBu, 'iBu, 'Bu, N = 1, 2, 3$), structural parameters, relative conformational energies, electric dipole moments, Sn-Cl vibrational frequencies and $^1H$, $^{13}C$ and $^{119}Sn$ NMR chemical shifts were calculated. Among these properties, the $^{119}Sn$ NMR chemical shifts seem to be particularly important and interesting. $^{119}Sn$ NMR spectroscopy plays a central role in determining the structure and reactivity of organotin compounds [1,2] and, from this perspective, theoretical predictions of $^{119}Sn$ chemical shifts may complement experimental data and aid in establishing structure-spectrum relationships. To the best of our knowledge, no evaluation of the ONIOM hybrid method applied to calculating $^{119}Sn$ NMR chemical shifts has been reported so far.

2. Theoretical procedure

A two-layer ONIOM approach was used for the $X_nSnCl_{4-n}$ molecules. The ONIOM core layer consisted of the Sn and Cl atoms and the fragments of the X groups bonded to Sn. This layer was treated with the B3PW91 density functional [15,16]. The IGLO-II basis set [17] was ascribed to the Sn atom whereas the IGLO-III basis sets [17] were adopted for the H, C and Cl atoms. The choice of B3PW91/IGLO was motivated mainly by the methodology applied successfully in previous studies [8,18-21] to calculate $^{119}Sn$ NMR chemical shifts. The IGLO-II basis set is one of very few basis sets that cover the Sn nucleus in tetramethyltin calculated using IGLO-II is closer to experimental data than that obtained using the TZV basis set, despite the fact that TZV has a greater number of s, p and d primitives compared to IGLO-II. On the other hand, the IGLO basis sets are based on Huzinaga’s basis sets [24] and the quality of their valence part should be sufficient to describe reasonably other molecular properties. The ONIOM surrounding layer consisted of the remaining fragments of the X groups. This layer was described at the HF/3-21G* level of theory. The HF method in conjunction with a small basis set is the lowest acceptable level of ab initio theory that is capable of predicting NMR properties [25].

Three partitioning schemes, I to III, assigning different parts of the X groups to the core layer and to the surrounding layer were considered. In partitioning scheme I, the C atoms at the α positions and the H atoms bonded to these C atoms belonged to the core layer. In partitioning scheme II, the core layer covered the C atoms at the α and β positions (for ‘sBu, one of the two C atoms at the β position) along with their H atoms. Partitioning scheme III had the smallest surrounding layer containing the most distant terminal methyl groups. It should be noted that it was possible to adopt all three partitioning schemes only for $X = 'sBu and ‘Bu. The fragments of the $X_nSnCl_{4-n}$ molecules that belonged to the core and surrounding layers are presented in Fig. 1, using various visual representations.
Conformational analysis was performed for the $X_nSnCl_{4-n}$ molecules by changing the dihedral angles in the $X$ groups and the dihedral angles governing the arrangement of the $X$ groups with respect to each other. For each molecule, at least two rotamers were taken into account (see Supplementary Table 1 for the numbers of rotamers found for the $X_nSnCl_{4-n}$ molecules). The optimized geometries of rotamers were subjected to frequency calculations and the rotamers were then ordered with respect to their ONIOM energies, the values of which included the zero-point energy correction. A separate set of optimization and frequency calculations was carried out for each partitioning scheme.

The determination of the NMR chemical shifts of $^1H$, $^{13}C$ and $^{119}Sn$ nuclei in the $X_nSnCl_{4-n}$ molecules required the isotropic shielding constants of these nuclei. The isotropic shielding constants were calculated using ONIOM and the gauge-independent atomic orbitals (GIAO) [26,27]. The chemical shift of a nucleus in a given $X_nSnCl_{4-n}$ molecule was obtained by subtracting the isotropic shielding constant of this nucleus in the $X_nSnCl_{4-n}$ molecule from the isotropic shielding constant of the corresponding nucleus in a reference molecule. In the case of $^{119}Sn$ chemical shifts, tetramethyltin was the reference molecule, whereas $^1H$ and $^{13}C$ chemical shifts were referred to tetramethylsilane. The isotropic shielding constants of nuclei in both reference molecules were calculated using GIAO at the B3PW91/IGLO level of theory.

In order to evaluate the ONIOM(B3PW91:HF) hybrid method combined with each partitioning scheme, the ONIOM results of the molecular properties investigated.
Evaluation of the ONIOM(B3PW91:HF) hybrid method for modeling butyltin chlorides were compared with the corresponding reference results obtained at the B3PW91/IGLO level of theory (see Supplementary Tables 2-59). The comparison was made for the molecular properties of all rotamers revealed by the conformational analysis of the X_SnCl_{4-n} molecules (see Supplementary Table 1). The average absolute error (AAE) and the maximum absolute error (MAE) were determined for each molecular property. The sizes of the populations of the molecular properties used in the statistical treatment are listed in Table 1. The populations of ^1H and ^13C chemical shifts covered the shifts determined for the atomic nuclei in the central region of the X_SnCl_{4-n} molecules, that is, for the C atoms at the α position and, if present, the H atoms bonded to these C atoms.

It should be emphasized that the ONIOM(B3PW91:HF) results were compared statistically with the results obtained by B3PW91, but none of the calculated results were quantitatively compared to any experimental data. It was due to the fact that several computational simplifications were applied to the B3PW91 part of the calculations and transferred to the ONIOM(B3PW91:HF) calculations. First, relativistic effects were neglected in our calculations, although it is known that the inclusion of such effects is important to reproduce experimental ^119Sn chemical shifts accurately [28]. Second, our calculations were performed in the absence of any solvent or crystal surroundings, which is in marked contrast to experimental measurements that are usually taken in solution or in the solid state. Experimental chemical shifts measured in the gas phase are available only for a few butyltin chlorides [29]. Third, the B3PW91 hybrid functional was not augmented with any correction for dispersion forces. The inclusion of such a correction in our calculations might affect the structures and energetics of the investigated rotamers because dispersion forces may be important for the interactions occurring between butyl groups. In order to reduce any errors in the quantitative evaluation of ONIOM(B3PW91:HF) introduced by the above-mentioned simplifications, we compared the ONIOM(B3PW91:HF) results with the corresponding B3PW91 results.

All the results reported in this work were computed using the Gaussian 03 suite of programs [30]. The initial geometries of possible rotamers of X_SnCl_{4-n} were generated with the aid of Molden [31].

### 3. Results and discussion

Table 2 shows the results of the statistical comparison of the molecular properties obtained by ONIOM(B3PW91:HF), in conjunction with each partitioning scheme, with the corresponding properties calculated using the reference B3PW91 method. There is a general trend in the values of AAE and MAE for all molecular properties: the AAE and MAE values decrease when the partitioning scheme is changed from I to II and then to III. It is obvious that the decrease in the AAE and MAE values is associated with the growing size of the ONIOM core layer and the largest core layer in partitioning scheme III results in the smallest values of AAE and MAE. Although the AAE values for partitioning scheme III are generally quite small, this is not always true for MAE, as seen for dihedral angles and ^119Sn chemical shifts. This means that even for the largest core layer, the effect of the HF method, that is, the low level of theory within the framework of our ONIOM approach, is evident. Reducing the size of the ONIOM core layer from partitioning scheme II to partitioning scheme I has a considerable influence on the error values: they increase by at least 50%. A different effect occurs only for dipole moment whose AAE and MAE values seem

| Property                      | Partitioning scheme |
|-------------------------------|---------------------|
|                               | I       | II       | III      |
| Bond length                   | 1456    | 1288     | 808      |
| Bond angle                    | 2820    | 2496     | 1566     |
| Dihedral angle                | 3816    | 3384     | 2124     |
| Relative conformational energy| 34      | 31       | 19       |
| Dipole moment                 | 46      | 40       | 25       |
| Sn-Cl vibrational frequency   | 78      | 66       | 41       |
| ^119Sn chemical shift         | 46      | 40       | 25       |
| ^13C chemical shift           | 102     | 94       | 59       |
| ^1H chemical shift            | 159     | 157      | 87       |
not to be affected by the change in partitioning scheme from \textbf{III} to \textbf{II}. Further reduction of the size of the ONIOM core layer is accompanied by a subsequent increase in the error values for all molecular properties except for dipole moments and dihedral angles.

The comparison of the AAE and MAE values for various molecular properties reveals that partitioning scheme has a greater effect on the NMR chemical shifts than on the structural and energetic properties. The greater AAE and MAE values of the NMR chemical shifts are, at least to some extent, a consequence of the differences in geometries between the rotamers obtained by ONIOM(B3PW91:HF) and the corresponding rotamers optimized using the reference B3PW91 method. It can also be deduced that in principle NMR chemical shifts seem to be very sensitive to the ONIOM approach and partitioning scheme applied.

ONIOM(B3PW91:HF), in conjunction with partitioning scheme \textbf{I}, yields AAE and MAE values so large that such a methodology definitely cannot be recommended for reliable predictions of NMR chemical shifts in butyltin chlorides. The large values of AAE and MAE arise from the presence of the boundary between the ONIOM layers. This boundary is in the immediate neighborhood of the atoms for which the NMR chemical shifts are determined and included in the statistical evaluation. In the ONIOM core layer there are no other H and C atoms included in the high-level surroundings (that is, treated with B3PW91) for the nuclei whose chemical shifts constitute the population used in the calculation of AAE and MAE.

Apart from the quantitative statistical evaluation of the ONIOM(B3PW91:HF) hybrid method for the predictions of NMR chemical shifts, some qualitative assessments have also been performed. For the $^{119}$Sn NMR chemical shifts of $X_nSnCl_{4-n}$ ($X = \text{Bu}$ and $\text{sBu}$) calculated using partitioning scheme \textbf{III}, their dependence on the number of the $X$ groups is depicted in Fig. 2. This dependence exhibits a U-letter shape for both series of the $X_nSnCl_{4-n}$ molecules. The same was reported by Nakatsuji \textit{et al}. \cite{33} for Me$_nSnCl_{4-n}$. Such a U-shaped dependence suggests a non-additive inductive effect of the Cl atom on the electronic density of tin. For $X = \text{Bu}$ in Fig. 2, another dependence was plotted using the experimental values of $^{119}$Sn chemical shifts. The ONIOM(B3PW91:HF) chemical shifts qualitatively resemble the pattern of the experimental data, although there is a discrepancy in the minimal points of these two relations: ONIOM(B3PW91:HF) reaches its minimum at $n = 2$, whereas the experimental relation has its minimum at $n = 3$.

Trends in the $^{13}$C NMR chemical shifts of the C atoms at the $\alpha$, $\beta$ and $\gamma$ positions for the $\text{Bu}_nSnCl_{4-n}$ series of molecules can also be established for the purposes of the qualitative evaluation of the ONIOM(B3PW91:HF) method and partitioning scheme \textbf{III}. Table 3 presents the calculated and experimental values of these chemical shifts. It is evident that when the number of the $\text{Bu}$ groups grows, the trends in the calculated $^{13}$C chemical shifts for all three carbon positions reproduce the corresponding experimental trends.

| Property | Partitioning scheme |
|----------|---------------------|
|          | I      | II      | III     |
| Bond length (Å) | 0.0102 | 0.0076 | 0.0041 |
|           | (0.0418) | (0.0319) | (0.0263) |
| Bond angle (°) | 0.55   | 0.47   | 0.28   |
|           | (3.57) | (3.02) | (1.49) |
| Dihedral angle (°) | 1.5    | 1.6    | 0.8    |
|           | (14.3) | (13.2) | (8.9)  |
| Relative conformational energy (kcal/mol) | 0.31   | 0.16   | 0.05   |
|           | (1.60) | (0.40) | (0.15) |
| Dipole moment (D) | 0.06   | 0.06   | 0.06   |
|           | (0.25) | (0.15) | (0.15) |
| Sn-Cl vibrational frequency (cm$^{-1}$) | 2.6    | 1.2    | 0.3    |
|           | (6.5)  | (3.2)  | (1.2)  |
| $^{119}$Sn chemical shift (ppm) | 45.5   | 17.5   | 3.4    |
|           | (102.1) | (49.4) | (21.9) |
| $^{13}$C chemical shift (ppm) | 14.0   | 4.2    | 0.8    |
|           | (23.5) | (10.8) | (2.6)  |
| $^1$H chemical shift (ppm) | 0.581  | 0.127  | 0.024  |
|           | (1.007) | (0.429) | (0.071) |
Conclusions

In this work the ONIOM(B3PW91:HF) hybrid method was systematically evaluated for the purposes of modeling various molecular properties of butyltin chlorides, \( X_nSnCl_{4-n} \) (\( X = \text{nBu, sBu; } n = 0 - 4 \)) series of molecules. For such properties as structural parameters, relative conformational energies, dipole moments and Sn-Cl vibrational frequencies, this hybrid method, combined with the core layer consisting of the Sn atom, the Cl atoms, the C atoms at the \( \alpha \) and \( \beta \) positions and the H atoms bonded to these C atoms, seems to provide a reasonable compromise between the computational cost and the accuracy of the calculated results. ONIOM(B3PW91:HF) reproduces the reference DFT chemical shifts of \( ^1H \), \( ^{13}C \) and \( ^{119}Sn \) nuclei with reasonable accuracy only when the largest possible core layer is used. In this case the savings in computational effort are very small and seem not to compensate for the decrease in the accuracy of the obtained chemical shifts. To summarize, the ONIOM(B3PW91:HF) hybrid method performs well in the conformational analysis of butyltin chlorides but fails in the predictions of their NMR chemical shifts. This conclusion may be important for future ONIOM(B3PW91:HF) studies of alkyltin chlorides with the alkyl groups being higher homologs than butyl, as well as of systems containing butyltin chlorides and some model molecules mimicking biological macromolecules. In order to draw more general conclusions on the performance of ONIOM(DFT:HF) for modeling organotin molecules, it is necessary to carry out further investigations in which other density functionals describing the ONIOM core layer and other basis sets assigned to atoms in the core and surrounding layers will be taken into consideration.

Table 3. Calculated and experimental \( ^{13}C \) NMR chemical shifts in a series of \( X_nSnCl_{4-n} \) (\( X = \text{nBu; } n = 1, 2, 3 \)) molecules. The experimental values are taken from [29] and are indicated in parentheses. The calculated chemical shifts were obtained using ONIOM(B3PW91:HF) and partitioning scheme III for the lowest-energy rotamers.

| Molecule | \( ^{13}C_\alpha \) ppm | \( ^{13}C_\beta \) ppm | \( ^{13}C_\gamma \) ppm |
|----------|----------------|----------------|----------------|
| \text{nBuSnCl}_3 | 28.2 (33.7) | 28.2 (26.4) | 26.6 (25.2) |
| \text{nBu}_2SnCl_2 | 22.7 (26.7) | 27.8 (26.3) | 27.1 (25.4) |
| \text{nBu}_3SnCl | 16.2 (17.5) | 29.3 (27.8) | 27.8 (26.7) |
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Supplementary data

The results of the conformational analysis of the X₅SnCl₄ₙ molecules and the properties of all rotamers calculated by means of the reference B3PW91 method.

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