

Regular article

Own N -layered integrated molecular orbital and molecular mechanics study of the reaction of OH^- with polychlorinated hydrocarbons $\text{CH}_{(4-n)}\text{Cl}_n$ ($n = 2-4$)

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Abstract. The reliability of the two-layer own N -layered integrated molecular orbital and molecular mechanics (ONIOM) method was examined for the $\text{S}_{\text{N}}2$ reaction $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$. In the ONIOM calculation, only the methyl chloride and OH^- were treated at a high level and the effect of polychlorination was taken into account only at a low level. The ONIOM results were compared with the “target” CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ results obtained by Borisov et al. [(2001) *J. Phys. Chem. A* 105:7724]. The ONIOM[MP2/aug-cc-pVDZ:B3LYP/6-31+G(d)] was found to reproduce well the target geometry and energy at the MP2/aug-cc-pVDZ level. The single-point improved energetics at the ONIOM[CCSD(T)/aug-cc-pVDZ:MP2/6-31+G(d)] is found to give results nearly as accurate as the target CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ results. The substantially reduced cost, 20% for optimization and 5% for single-point improved energy of the target cost for $n = 4$, as well as small errors suggest that ONIOM is a powerful tool for accurate potential-energy surfaces of the reaction of large polyhalohydrocarbons.

Keywords: Own N -layered integrated molecular orbital and molecular mechanics – Hybrid method – Polychlorinated hydrocarbons – $\text{S}_{\text{N}}2$ reaction

Introduction

Polychlorinated hydrocarbons (PCHCs), such as 1,2-dichloroethane, 1,1,1-trichloroethane, and trichloroethylene, are prevalent contaminants in ground water. Owing to their environmental harmfulness, such as their carcinogenic nature, it is required to estimate the lifetimes of PCHCs in ground water and to characterize

long-lived hazardous species. To do so, the detailed mechanism should be explored for the various degradation processes of PCHCs in ground water. PCHCs are known to be degradable by abiotic processes such as hydrolysis or nucleophilic substitution reaction with various anions dissolved in the ground water. It is known that the most likely transformation to occur is mainly controlled by the number and type of substituted halogens in PCHCs [1]. Although there have already been some studies (both theoretical and [2, 3, 4, 5, 6] experimental [7, 8, 9, 10, 11, 12]) about the hydration process of CHCs and their reaction with OH^- , further exploration would be required for the overall picture for possible reaction pathways as well as the quantitative relation between the reactivity of PCHCs and the degree of chlorination.

Quantum chemical calculation is one of the useful tools to investigate the reaction mechanism in a systematic way. For the reaction of PCHCs in aqueous solution, the detailed mechanism could be systematically clarified by using quantum chemical calculation. The reliability of the potential-energy surface described for the reaction in solution much depends on the level of calculation and the modeling of the solution environment. The solute electronic structure under the effect of solvent can nowadays be calculated inexpensively using a variety of versions of the polarized continuum model [13, 14]. However, for the reaction in aqueous solution where solvent molecules strongly influence the reaction mechanism by intermolecular interactions such as hydrogen bonding, near-range solvent molecules should be explicitly taken into account [15, 16]. Such calculation makes the calculation rather expensive, forcing one to adopt a lower theoretical level of calculation, or, instead, to reduce the number of water molecules included in the calculation. It has been suggested that the quantitative description of the $\text{S}_{\text{N}}2$ reaction requires a high level of correlation treatment with a large basis set [17]. Consequently, a highly accurate calculation on the large system, which is too expensive to perform, is required for

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the quantitative description of a chemical reaction of PCHCs in aqueous solution.

Our own N -layered integrated molecular orbital and molecular mechanics method provides a possibility to overcome the difficulty. We employ for our purpose the two-layer molecular orbital (MO)+MO version of the ONIOM method, sometimes called IMOMO [18, 19], in which the system of interest is divided into a smaller “model” system treated at both “high” and “low” levels of MO calculation and the entire “real” system treated only at the “low” level. The ONIOM total energy is obtained by adding/subtracting the respective energies by an additivity approximation according to the following equation:

$$E(\text{ONIOM, real}) = E(\text{high, model}) + E(\text{low, real}) - E(\text{low, model}).$$

Thus, the “target” calculation, $E(\text{high, real})$, the high-level calculation for the real system, which is too expensive to perform, can be approximated in terms of the three less expensive MO calculations. In the previous study on the S_N2 reaction in a microsolvation cluster, we showed that the ONIOM calculation where all solvent molecules are treated at the low level gives an excellent approximation for a very high level pure ab initio calculation with less than 10% of the target cost [20].

The ultimate goal of the present studies is to explore, at a very high accuracy, the potential-energy surfaces of possible reaction pathways of PCHCs in the ground water environment by using the ONIOM method. The ONIOM method has already been applied to studies of the steric effect for the S_N2 reaction between Cl^- and alkyl chloride and has been found to give a very good approximation for high-level geometry and energetics including the barrier height [18]. (See also Ref. [21] for the halogen substituent effect.) The modest goal of this paper is to examine whether ONIOM can be used to calculate an accurate potential-energy surface of the reaction of polychlorohydrocarbons. Borisov et al. [22] have recently reported a very high level ab initio study on the reaction $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=1-4$) as a benchmark. In the present study, we compare the ONIOM geometries and energetics for the reaction $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=1-4$) with the high-level ab initio results obtained by Borisov et al. in order to assess the reliability of the ONIOM method. One should note that for comparison of the calculated results with experiments, one has to include the effects of the solvent, with an explicit microsolvation model as was done previously for $(\text{H}_2\text{O})_n\text{CH}_3\text{Cl} + \text{OH}^- (\text{H}_2\text{O})_m$ ($n+m=1,2$) [20], or with inclusion of the bulk polarizable continuum model [23], or both.

Method of calculation

Details of the ONIOM method have been published elsewhere [18, 19]. The choice of the model system and the low level of method is of importance to archive the accuracy of the ONIOM calculation.

The model system in the present ONIOM calculation, of which the calculation is performed on both the high level and the low level, is the $\text{CH}_3\text{Cl} + \text{OH}^-$ ion. Furthermore spectator Cl atoms are treated only at the low level, and they are replaced by H atoms in the model system as shown in Fig. 1. In the model system, the replaced H atoms are placed onto the respective C–Cl bond axis in the real system. The C–H bond length in the model system is adjusted by a constant scale factor [24]. The target results with which we compare the ONIOM results are very accurate equilibrium and transition-state geometries and their energies [22] obtained at the CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ level of theory, i.e., the single-point calculation at the CCSD(T)/aug-cc-pVDZ (hereafter referred to as CC/b) level at the optimized geometries at the frozen-core MP2/aug-cc-pVDZ (referred to as MP2/b) level. We will choose the target level as the high level of the ONIOM method.

Three types of methods are examined as the low level for the ONIOM geometry optimization: the gradient-corrected density functional theory (DFT) BLYP and the hybrid DFT B3LYP methods [25, 26, 27, 28] as well as the Hartree–Fock (HF) method for comparison. The basis set used for all low levels is 6-31+G(d), the smallest basis set required to describe anionic systems. We also performed single-point energy calculations at the ONIOM optimized geometries in order to improve the accuracy of the energetics. Here, the CC/b method is used as the high level and MP2, B3LYP, BLYP, and HF methods with the 6-31+G(d) basis set are employed as the low level. Hereafter, we use notation like MP2/b:HF that indicates the high level:low level combination in the ONIOM method. All the energies reported in the present paper are without zero-point-energy correction. All calculations were performed by using Gaussian98 [29] and the developmental Gaussian01.

Results and discussion

The potential-energy profiles for the reaction $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=1-4$) calculated by Borisov et al. [22] at the CC/b//MP2/b level are illustrated in Fig. 2. Here RC1–RC4 are the reactant complexes, TS1–TS4 are the tran-

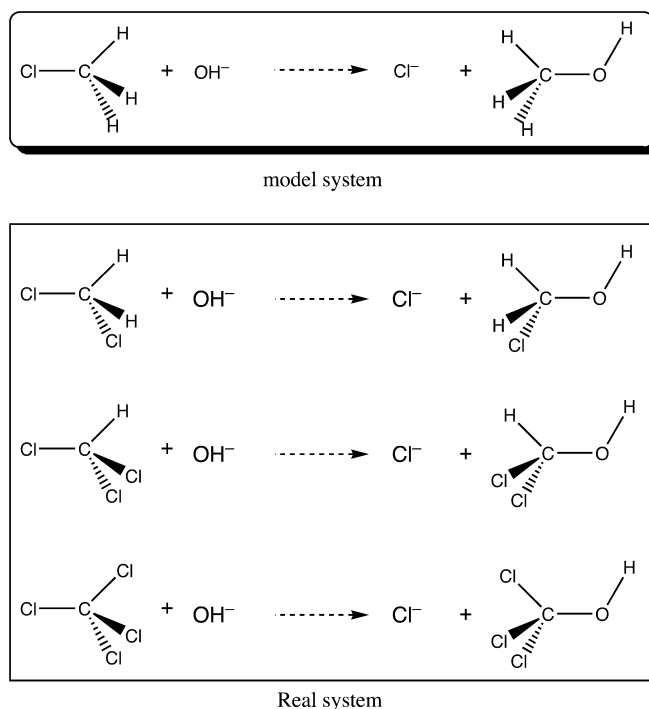


Fig. 1. The own N -layered integrated molecular orbital and molecular mechanics (ONIOM) “model” and “real” systems adopted

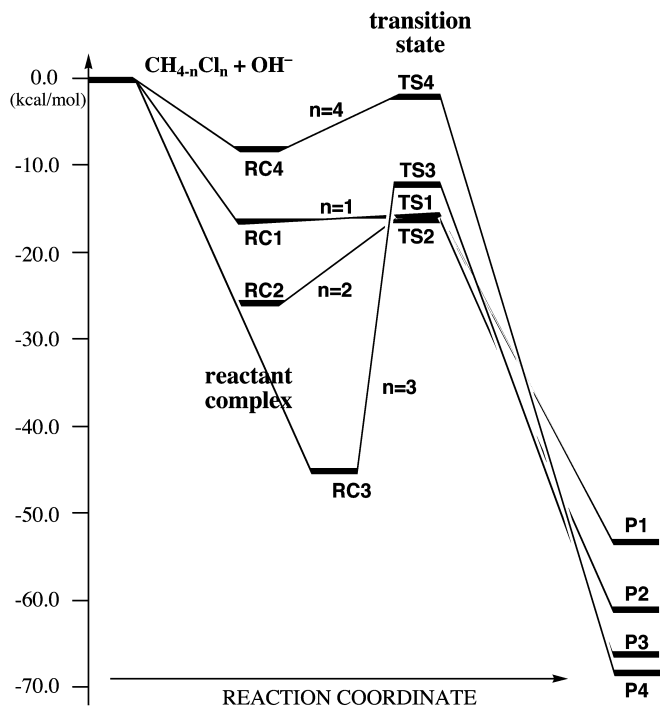


Fig. 2. The target CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ potential-energy profiles for S_N2 reaction, $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=1-4$). Here $RC1-RC4$ are the prereaction complexes, $TS1-TS4$ are the transition states, and $P1-P4$ are the products, respectively [22]

sition states, and $P1-P4$ are the product species. For the reactions of CH_3Cl ($n=1$) and CH_2Cl_2 ($n=2$), the OH^- ion first attacks one of the protons in the chlorinated methane so as to form the reactant complex, $RC1/RC2$, followed by the transition state, $TS1/TS2$. On the other hand, the OH^- ion binds to the central carbon in the reactant complex, $RC4$, for the reaction of CCl_4 owing to the lack of a proton on CCl_4 . For CHCl_3 at the target level, the S_N2 prereactant complex does not exist but a proton-transferred complex was found [22], which we adopt as $RC3$.

S-value test

The accuracy of the ONIOM description depends greatly on the correct choice of the low level of calculation. We initially look for the low-level method that most accurately reproduces the high-level calculation on the full system, when used in the ONIOM method. To do this, the S -value test [30] is useful. The error of the ONIOM energy relative to the correct target energy, $E(\text{high, real})$, is given by

$$\begin{aligned} \delta S &= E(\text{ONIOM, real}) - E(\text{high, real}) \\ &= [E(\text{low, real}) - E(\text{low, model})] \\ &\quad - [E(\text{high, real}) - E(\text{high, model})] \\ &= S(\text{low}) - S(\text{high}). \end{aligned}$$

The quantity in the square brackets in the second equation that represents the energy difference between

the real and model systems at a given level is called the S value or the effect of the “substituents” on the model system. If $S(\text{low})$ happens to be equal to $S(\text{high})$, the ONIOM error, δS , is zero, and the ONIOM results are exactly the same as the target high-level results. Although actual S values in any ONIOM calculation are not equal between the high and low levels, one should choose a low level that gives the smallest δS . In practice, if one has, say, ten large systems to which the ONIOM method is to be applied, one may perform the expensive $S(\text{high})$ calculations for a few of them and determine the best choice of the low level via the S -value test, and apply the ONIOM method to the rest of the systems.

For all of the reactant complexes, transition states, and product species of the present system, we compare the δS values of the energy (relative to the reactants, $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$) at B3LYP, BLYP, and HF levels with the MP2/b as the high level. The results are summarized in Table 1. The δS values at the HF level are only shown for the $n=2$ for comparison. In the case of $n=2$, the average absolute error in the δS values is 0.7, 0.7, and 1.5 kcal/mol for the B3LYP, BLYP, and HF methods, respectively. This tells us that the ONIOM method in which the high level is MP2/b and the low is the B3LYP or the BLYP method does work with less than 1 kcal/mol of the error for the energy description. Instead, the usage of the HF method as the low level will lead to twice the error as the previously mentioned combinations when the ONIOM calculation is performed. The δS values for $n=3$ are 0.9 and 1.1 kcal/mol larger than those for $n=2$ for the B3LYP and BLYP methods, respectively. The average absolute error is, however, nearly unchanged for $n=4$. Consequently, both the B3LYP and BLYP methods are good candidates for the low level in the ONIOM calculation, where the high level is MP2/b. Such an ONIOM calculation is expected to give the energy accurate to within 1 kcal/mol as compared with the target pure MP2/b.

As shown here, the comparison of the S values is a very useful tool for the choice of the low-level method. It should be mentioned that the S -value test requires the expensive $E(\text{high, real})$ calculation. In usual applications of the ONIOM method, the $E(\text{high, real})$ calculation is prohibitive, and thus one has to adopt a few smaller real systems for the test.

ONIOM geometries

Reactants and products

In all ONIOM calculations, the model system is methyl chloride and the OH^- ion. The Cl_n ($n=2-4$) atoms are all replaced by link H atoms in the model system, and are treated only at the low level. In other words, the low-level method is responsible for the description of the effect of polychlorination.

The ONIOM optimized geometries of the reactants in Fig. 3 reproduce well the target MP2/b geometries with

Table 1. Calculated relative energies E and δS values [kcal/mol, relative to the reactants $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=2-4$)], evaluated at the MP2/b (high level) and various lower-level molecular orbital methods. All calculations were performed at the geometries determined at the MP2/aug-cc-pVDZ level

Method	E [$\delta S = S(\text{low}) - S(\text{MP2/b})$ in parentheses]			
	MP2/b	B3LYP	BLYP	HF
$n=2$				
$\text{OH}^- + \text{CH}_2\text{Cl}_2$ (R2)	0.0	0.0	0.0	0.0
$[\text{OH} \cdots \text{CH}_2\text{Cl}_2]$ (RC2)	-11.6	-12.1 (-0.5)	-12.0 (-0.4)	-12.5 (-0.9)
$[\text{OH} \cdots \text{CH}_2\text{Cl} \cdots \text{Cl}]^-$ (TS2)	-3.6	-3.2 (0.4)	-3.2 (0.4)	-1.2 (2.4)
$\text{Cl}^- + \text{CH}_2\text{ClOH}$ (P2)	-8.5	-9.6 (-1.1)	-9.8 (-1.4)	-9.8 (-1.3)
Average absolute error of δS		(0.7)	(0.7)	(1.5)
$n=3$				
$\text{OH}^- + \text{CHCl}_3$ (R3)	0.0	0.0	0.0	
$[\text{OH} \cdots \text{CHCl}_3]^-$ (RC3)	-35.6	-37.3 (-1.7)	-38.0 (-2.3)	
$[\text{OH} \cdots \text{CHCl}_2 \cdots \text{Cl}]^-$ (TS3)	-1.2	0.1(1.1)	-0.2 (1.0)	
$\text{Cl}^- + \text{CHCl}_2\text{OH}$ (P3)	-14.3	-16.3 (-2.0)	-16.4 (-2.1)	
Average absolute error of δS		(1.6)	(1.8)	
$n=4$				
$\text{OH}^- + \text{CCl}_4$ (R4)	0.0	0.0	0.0	
$[\text{OH} \cdots \text{CCl}_4]^-$ (RC4)	5.7	6.4 (0.7)	4.7 (-1.0)	
$[\text{OH} \cdots \text{CCl}_3 \cdots \text{Cl}]^-$ (TS4)	11.7	12.6(1.1)	12.2(0.5)	
$\text{Cl}^- + \text{CCl}_3\text{OH}$ (P4)	-16.0	-18.9 (-2.9)	-18.8 (-2.8)	
Average absolute error of δS		(1.6)	(1.4)	

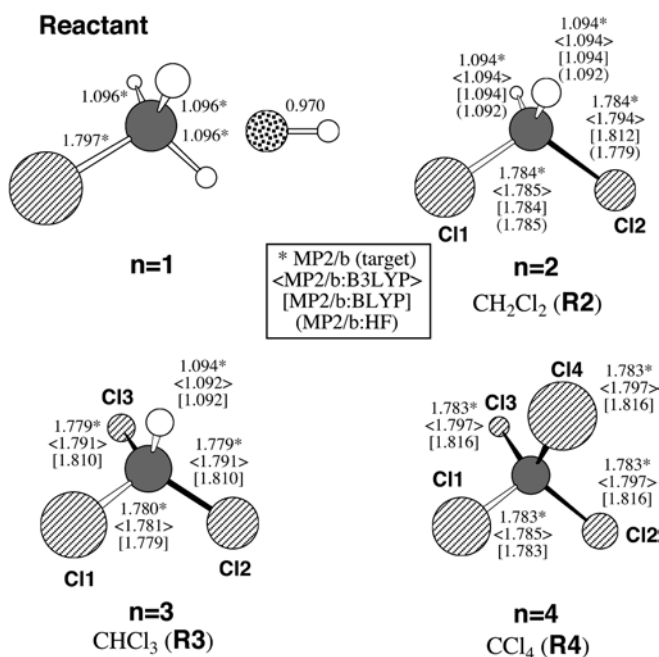


Fig. 3. ONIOM optimized geometries (Å) of the reactant species. The target pure MP2/b values (indicated with an asterisk) in Figs. 3, 4, 5, and 6 are taken from Ref. [22]

errors of less than 0.03 Å. In all geometries, C-H and C-Cl¹ distances are quite similar to those at the target MP2/b level. On the other hand, the deviations from the target MP2/b values are relatively large for C-Cl_n ($n=2-4$) bond distances (dark solid bonds), since these distances in the ONIOM calculation are determined using the low-level B3LYP or BLYP method. The averaged absolute errors compared with MP2/b are $\langle 0.01 \text{ Å} \rangle$ and $[0.03 \text{ Å}]$ for the $\langle \text{MP2/b:B3LYP} \rangle$ and $[\text{MP2/b:BLYP}]$ methods (note that $\langle \rangle$, $[\]$ and $()$ are used to match with the figure), respectively. Note that the (MP2/b:HF) method gives a slightly shorter C-Cl²

bond distance for R2 in comparison with the corresponding value at the target MP2/b. This propensity is consistent with that seen in the low level of the pure MO calculation. The C-Cl bond distance in CH_3Cl is calculated to be 1.785, 1.830, and 1.805 Å at the HF/6-31+G(d), BLYP/6-31+G(d), and B3LYP/6-31+G(d) levels of pure MO methods. In comparison with the target MP2/b value, 1.797 Å, the C-Cl bond is longer at the B3LYP and BLYP levels, and shorter at the HF level of calculation.

Similar results are obtained for the optimized geometries for the product species as shown in Fig. 4. As expected, the C-Cl bonds are all longer in the ONIOM results than those at the MP2/b level. In comparison with the target calculation, the errors in the geometrical parameters are less than 0.02 Å for $\langle \text{MP2/b:B3LYP} \rangle$, which is smaller than 0.04 Å for $[\text{MP2/b:BLYP}]$.

Reaction complexes and transition states

The ONIOM optimized geometries of the reactant complexes for $n=1-4$ are illustrated in Fig. 5. The target MP2/b geometries are reasonably well reproduced at all the ONIOM levels we examined, except for the (MP2/b:HF) geometry ($n=2$ only), in which the hydrogen-bond distance, $\text{CH} \cdots \text{O}$, is much shorter than for MP2/b.

For the reactions of $n=1-3$, the OH^- ion first binds to one of the hydrogens in the chlorinated methane to form the reactant complex. The chlorinated methane becomes more acidic with increasing numbers of chlorine atoms, resulting in the formation of a stronger intermolecular hydrogen bond between the CH group and O. In going from $n=1$ to $n=2$ (from RC1 to RC2), the elongation of the C-H bond and the shortening of the hydrogen-bonding distance, $\text{CH} \cdots \text{O}$, are 0.07 and -0.26 Å, respectively, at the target MP2/b level. These values are nearly completely reproduced in the ONIOM calculation. In the ONIOM method, the high-level

Product

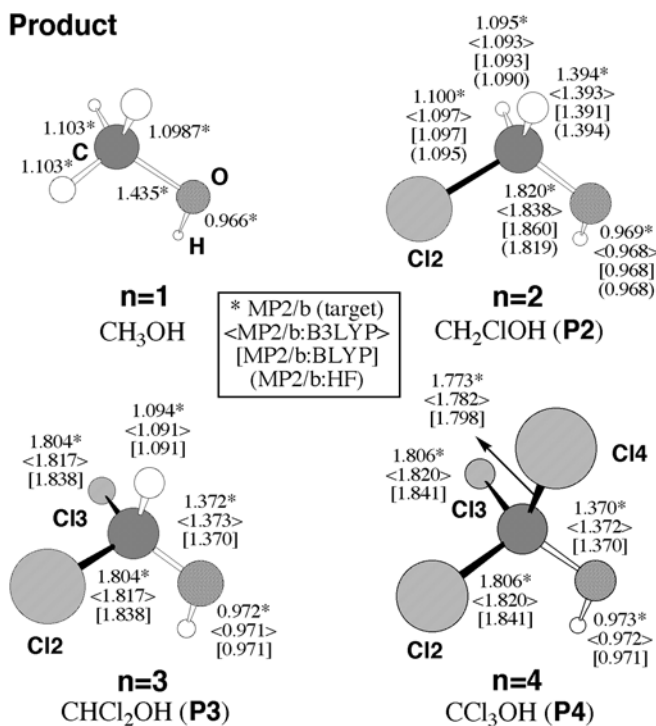


Fig. 4. ONIOM optimized geometries (Å) of the product species

calculation is done only on CH₃Cl and the OH⁻ moiety, and the change in the acidity of the chlorinated species is described only at the low level. Nevertheless, excellent agreement is obtainable as described above, showing the successful integration of levels in the ONIOM method for the present system. Note that C-Cl_n (*n*=2-4) distances are, as expected, <0.02-0.03 Å and [0.05-0.06 Å] longer in the <MP2/b:B3LYP> and [MP2/b:BLYP] methods compared with the target values.

In the case of *n*=3, the reactant complex for the S_N2 reaction could not be located at the MP2/b level of theory; instead, the proton-transferred complex, denoted as RC3, is located [22]. This is due to the strong acidity of chloroform compared with CH₃Cl and CH₂Cl₂. The ONIOM methods provide the same results as the target, although the C⁻...HOH distance is 0.07-0.08 Å longer in the MP2/b:DFT than the target. The OH⁻ ion binds to the central carbon atom of CCl₄ shown in RC4, where there is no hydrogen atom. Such a geometry is also well reproduced in the ONIOM calculations. Note that the [MP2/b:BLYP] method did not locate RC4 as a minimum. This is also the case when the pure BLYP calculation is performed.

The ONIOM geometries for the transition states are depicted in Fig. 6. In all geometries, the OH⁻ ion coordinates to the central carbon atom of the chlorinated methane. General features of the target transition-state geometries are well reproduced by the ONIOM calculation, although the C-Cl¹ bond length is slightly longer in the ONIOM calculations. It was reported in the study of Borisov et al. [22] that C-O and C-Cl distances in the transition states are shorter and longer, respectively, than the corresponding values in the reactant complexes. For *n*=1-4, the elongations of C-Cl bonds are 0.23, 0.27, 0.26, and 0.23 Å, while the shortenings of C-O bonds are -0.61, -0.51, -0.68, and -0.81 Å, respectively, at the MP2/b level. Such features in the transition states are correctly reproduced at the ONIOM levels we examined. For instance, in the <MP2/b:B3LYP> geometries for *n*=2-4, the elongations of C-Cl bonds are 0.29, 0.30, and 0.26 Å, while the shortenings of C-O bonds are -0.52, -0.72, and -0.89 Å, respectively. Another feature of the transition states is that the C-Cl bond becomes longer while the C-O bond becomes

Reactant Complex

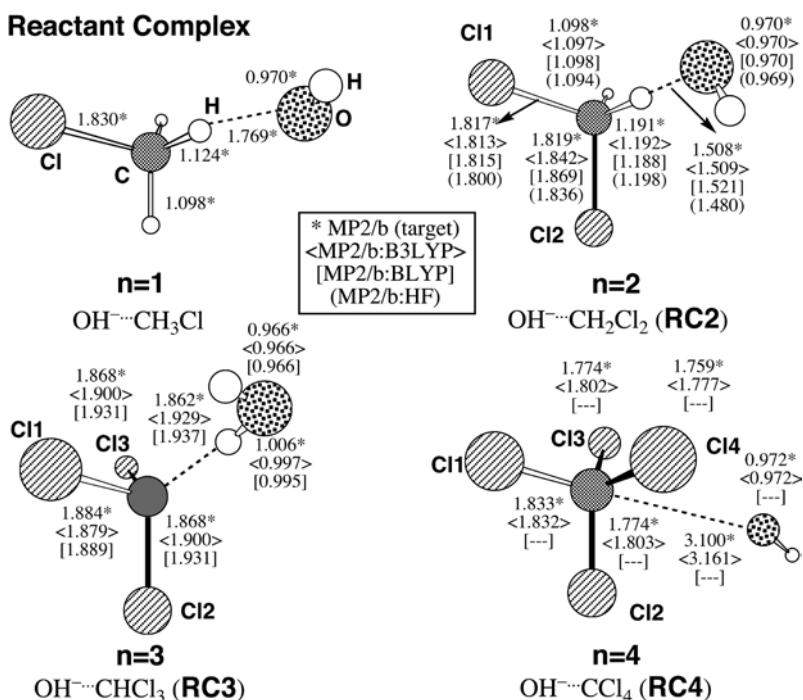


Fig. 5. ONIOM optimized geometries (Å) of the reactant complexes. Note for *n*=4, [MP2/b:BLYP], we could not locate RC4

Transition State

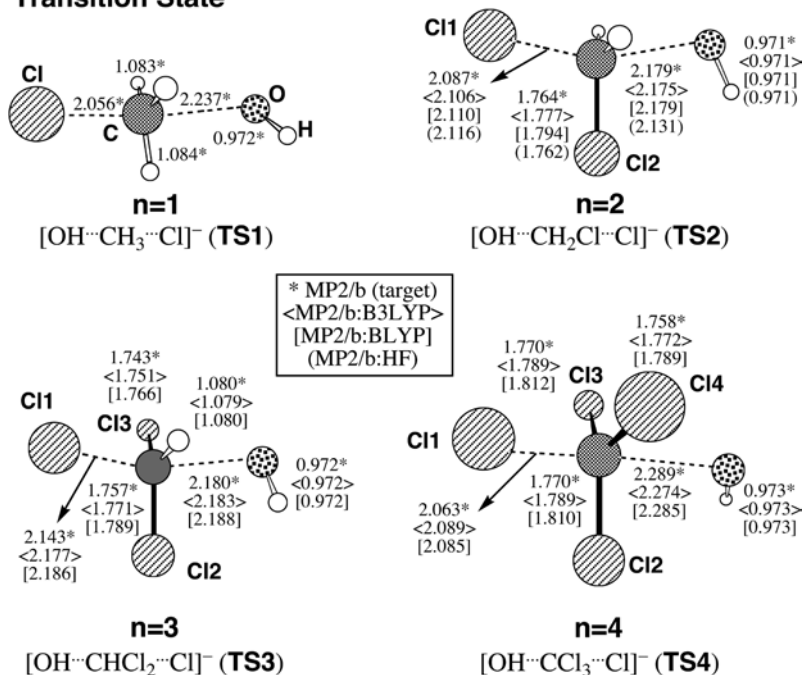


Fig. 6. ONIOM optimized geometries (Å) of the transition states

shorter with increasing number of chlorine atoms from $n=1$ to $n=3$. This trend is also reproduced by both MP2/b:DFT methods.

Summarizing the results in the present section, the ONIOM method with the hybrid and pure DFT methods as the low level provides a good approximation of the target MP2/b geometries for the S_N2 reaction $\text{CH}_{(4-n)}\text{Cl}_n + \text{OH}^-$ ($n=1-4$). The best ONIOM geometry, compared with the target MP2/b geometry, is obtained at the <MP2/b:B3LYP> level, although the C-Cl $_n$ ($n=2-4$) distances are always longer than those at the target level.

ONIOM energies

Energy of reaction

The energetics of the MP2/b and ONIOM(MP2/b:low) methods (low=B3LYP, BLYP, and HF) for the S_N2 reaction between $\text{CH}_{(4-n)}\text{Cl}_n$ ($n=2-4$) and the OH^- ion obtained at the respective ONIOM and MP2/b optimized geometries are summarized in Table 2. In order to assess the reliability of the ONIOM(MP2/b:low) approximations, we compare the energetics between the ONIOM method and the results of Borisov et al. [22] at the pure MP2/b level. The energies of reaction (without zero-point-energy correction) for $n=1-4$ are -51.7 , -59.2 , -64.5 , and -65.9 kcal/mol, respectively, at the target MP2/b level.

For $n=2$, the three ONIOM methods tend to overestimate the reaction energy compared to those at the target MP2/b level. The absolute error is, however, only 1.5 kcal/mol. The errors become large, from 2 to 3 kcal/mol, with increasing number of chlorine atoms from 3 to 4.

Although the absolute error values are increased, their amounts are still 3–5% of the total energies of reaction, and the ONIOM energies could be a good approximation for the target reaction energies. It is worth mentioning that the ONIOM energies at both the ONIOM geometries and the pure MP2/b geometries are in close agreement with each other. This supports the reliability of the ONIOM geometries.

Reaction barrier heights

The energy barriers from the reactant complex (RC n) to transition states (TS n) are, at the target MP2/b level, 3.0, 10.5, 32.2, and 7.2 kcal/mol, respectively, for $n=1-4$. Note that the energy barrier for $n=3$ is not actually the barrier from the S_N2 reactant complex that does not exist but is that from the proton-transferred complex denoted as RC3.

In the case of $n=2$, the stabilization energy of the reactant complex is overestimated by 0.5–1.0 kcal/mol with the ONIOM methods in comparison with MP2/b. In contrast, the energy of the transition states relative to the reactant is slightly higher with the ONIOM method than with MP2/b. Consequently, the barrier heights become large at the ONIOM level compared with those at the target MP2/b. The calculated energy barriers are 11.4, 11.5, and 14.0 kcal/mol for the (MP2/b:B3LYP), (MP2/b:BLYP), and (MP2/b:HF) methods. A similar propensity is found for $n=3$. On the other hand, the errors in the ONIOM calculations, compared with the MP2/b values, are essentially the same for the reactant complexes and the transition states at $n=4$. The ONIOM methods thus give nearly correct values for the barrier heights, where the absolute errors are less than 0.5 kcal/mol.

Table 2. Calculated relative energies (kcal/mol) of the S_N2 reaction $CH_{(4-n)}Cl_n + OH^-$ ($n=2-4$) obtained at various own N -layered integrated molecular orbital and molecular mechanics (ONIOM) levels with MP2/b as the target level at different optimized geom-

etries. The numbers in parentheses are the differences from the target MP2/b calculation. MP2/b = MP2/aug-cc-pVDZ; B3LYP = B3LYP/6-31 + G(d); BLYP = BLYP/6-31 + G(d); HF = HF/6-31 + G(d)

Energy Geometry	MP2b ^a MP2b	(MP2/b:B3LYP) (MP2/b:B3LYP)	(MP2/b:B3LYP) MP2b	(MP2/b:BLYP) (MP2/b:BLYP)	(MP2/b:BLYP) MP2b	(MP2b:HF) (MP2b:HF)	(MP2b:HF) MP2b
$n=1$							
$OH^- + CH_3Cl$	0.0						
$OH^- \cdots CH_3Cl$	-16.4						
$[OH^- \cdots CH_3 \cdots Cl]^-$	-13.4						
$Cl^- + CH_3OH$	-51.7						
$n=2$							
$OH^- + CH_2Cl_2$ (R2)	0.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
$OH^- \cdots CH_2Cl_2$ (RC2)	-25.2	-25.7 (-0.5)	-25.7 (-0.5)	-25.8 (-0.6)	-25.6 (-0.4)	-26.2 (-1.0)	-26.1 (-0.9)
$[OH^- \cdots CH_2Cl \cdots Cl]^-$ (TS2)	-14.7	-14.3 (0.4)	-14.3 (0.4)	-14.3 (0.4)	-14.3 (0.4)	-12.2 (2.5)	-12.3 (2.4)
$Cl^- + CH_2ClOH$ (P2)	-59.2	-60.3 (-1.1)	-60.3 (-1.1)	-60.6 (-1.4)	-60.6 (-1.4)	-60.5 (-1.3)	-60.5 (-1.3)
Average absolute error		(0.7)	(0.7)	(0.8)	(0.7)	(1.6)	(1.5)
$n=3$							
$OH^- + CHCl_3$ (R3)	0.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
$OH^- \cdots CHCl_3$ (RC3)	-43.3	-45.5 (-2.0)	-44.7 (-1.7)	-46.6 (-3.0)	-45.3 (-2.3)		
$[OH^- \cdots CHCl_2 \cdots Cl]^-$ (TS3)	-11.1	-10.0 (1.1)	-9.9 (1.2)	-10.3 (0.8)	-10.8 (0.3)		
$Cl^- + CHCl_2OH$ (P3)	-64.5	-66.4 (-1.9)	-66.4 (-1.9)	-66.6 (-2.1)	-66.6 (-2.1)		
Average absolute error		(1.7)	(1.6)	(2.0)	(1.6)		
$n=4$							
$OH^- + CCl_4$ (R4)	0.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)		
$OH^- \cdots CCl_4$ (RC4)	-8.2	-7.9 (0.3)	-7.5 (0.7)		-9.2 (-1.0)		
$[OH^- \cdots CCl_3 \cdots Cl]^-$ (TS4)	-1.0	-0.1 (0.9)	-0.1 (0.9)	-0.7 (0.3)	-1.6 (-0.6)		
$Cl^- + CCl_3OH$ (P4)	-65.9	-68.7 (-2.8)	-68.7 (-2.8)	-68.6 (-2.7)	-68.7 (-2.8)		
Average absolute error		(1.3)	(1.5)	(1.5)	(1.5)		

^a Target calculation

For the overall energetics of the S_N2 reaction $CH_{(4-n)}Cl_n + OH^-$, the (MP2/b:DFT) methods are found to be a good approximation to the pure MP2/b, where the average absolute errors of the ONIOM methods are less than 2 kcal/mol compared with the target calculation. Both the (MP2/b:B3LYP) and (MP2/b:BLYP) methods have comparable accuracy. On the other hand, the (MP2/b:HF) method does a poor job, suggesting the importance of the electron-correlation treatment for the weak complex and the transition state in the correct description for the energetics of the present system.

Improvement of energies

Borisov et al. [22] reported that CC/b//MP2/b energetics, i.e., geometry optimization at the MP2/aug-cc-pVDZ level and refined single-point-energy calculation at the CCSD(T)/aug-cc-pVDZ level, gives a nearly quantitatively correct description of the potential-energy profiles, although even higher-level energetics are also reported. In Table 3, we summarize the energetics of the reaction refined at various levels of single-point-energy calculations at the (MP2/b:DFT) geometries and compare them with the target CC/b//MP2/b results. In the case of $n=2$, the CC/b calculation at the (MP2/b:DFT) geometries quantitatively reproduces the target CC/b//MP2/b values with an average absolute error of 0.1–0.2 kcal/mol. The reliability of the ONIOM geometries is again supported. At the same time, it has been shown that the (MP2/b:B3LYP) method does slightly better than the (MP2/b:BLYP) method in describing the geometries in the

present system. In both geometries, the comparison of the refined energies at the (CC/b:MP2) and (CC/b:DFT) levels shows that MP2 is slightly more favorable than B3LYP as the low level when the CC/b method is used as the high level in the ONIOM calculation. The propensity is more apparent for $n=3$ and $n=4$.

Table 3 also lists the energy barriers from the reactant complex to the transition state for $n=2-4$ evaluated with the ONIOM methods together with the target CC/b//MP2/b method. For $n=2$, each ONIOM method reproduces the target value to within 0.6 kcal/mol of the error. The errors become larger with increasing number of chlorine atoms up to $n=4$. The (CC/b:MP2) method gives a consistently increasing error with large n , while the (CC/b:B3LYP) method gives random errors. We justify this finding that while MP2 errors are systematic by the nature of the perturbation theory, B3LYP errors are random because the parameters in the hybrid density functional have been determined to minimize the least-squares errors for the test set.

With all these analyses, one can conclude that the ONIOM(CC/b:MP2) energetics at the (MP2/b:B3LYP) optimized geometries could be the best candidate for further investigation of the system. This would provide an excellent approximation for the geometry and energetics with less than 2 kcal/mol of the error even for large n .

Computational time requirements

Finally, brief documentation is given for the computational cost in the ONIOM calculation. The ONIOM

Table 3. Calculated relative energies (kcal/mol) of the S_N2 reaction $CH_{(4-n)}Cl_n + OH^-$ ($n=2-4$) obtained at various ONIOM levels with CCSD(T)/b as the target level at various optimized geometries. The numbers in parentheses are the differences from the

target CC/b//MP2/b calculation. CC/b = CCSD(T)/aug-cc-pVDZ; B3LYP = B3LYP/6-31 + G(d); BLYP = BLYP/6-31 + G(d); HF = HF/6-31 + G(d)

Energy Geometry	CC/b ^a MP2/b	CC/b (MP2/b:B3LYP)	(CC/b:MP2) (MP2/b:B3LYP)	(CC/b:B3LYP) (MP2/b:B3LYP)	CC/b (MP2/b:BLYP)	(CC/b:MP2) (MP2/b:BLYP)	(CC/b:BLYP) (MP2/b:BLYP)
<i>n</i> = 2							
OH ⁻ + CH ₂ Cl ₂ (R2)	0.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
OH ⁻ ⋯CH ₂ Cl ₂ (RC2)	-25.9	-25.8 (0.1)	-26.6 (-0.7)	-26.5 (-0.6)	-25.6 (0.3)	-26.2 (-0.3)	-26.7 (-0.8)
[OH ⁻ ⋯CH ₂ Cl ₂ ⋯Cl] ⁻ (TS2)	-16.3	-16.4 (-0.1)	-17.1 (-0.8)	-16.4 (-0.1)	-16.4 (-0.1)	-17.2 (-0.9)	-16.5 (-0.2)
Cl ⁻ + CH ₂ ClOH(P2)	-61.4	-61.4 (0.0)	-61.6 (-0.2)	-62.4 (-1.0)	-61.3 (0.1)	-61.5 (-0.1)	-62.6 (-1.2)
Average absolute error		(0.1)	(0.6)	(0.6)	(0.2)	(0.4)	(0.7)
Barrier: <i>E</i> (TS2)− <i>E</i> (RC2)	9.6	9.4 (-0.2)	9.6 (0.0)	10.1 (0.5)	9.2 (-0.4)	9.0 (-0.6)	10.2 (0.6)
<i>n</i> = 3							
OH ⁻ + CHCl ₃ (R3)	0.0		0.0 (0.0)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)
OH ⁻ ⋯CHCl ₃ (RC3)	-46.3		-46.7 (-0.4)	-48.3 (-2.0)		-46.4 (-0.1)	-49.5 (-3.2)
[OH ⁻ ⋯CHCl ₂ ⋯Cl] ⁻ (TS3)	-12.8		-14.4 (-1.6)	-12.7 (0.1)		-14.5 (-1.7)	-13.1 (-0.3)
Cl ⁻ + CHCl ₂ OH(P3)	-66.9		-67.2 (-0.3)	-68.4 (-1.5)		-67.2 (-0.3)	-68.7 (-1.8)
Average absolute error			(0.8)	(1.2)		(0.7)	(1.8)
Barrier: <i>E</i> (TS3)− <i>E</i> (RC3)	33.5		32.3 (-1.2)	35.6 (2.1)		31.9 (-1.6)	36.4 (2.9)
<i>n</i> = 4							
OH ⁻ + CH ₂ Cl ₄ (R4)	0.0		0.0 (0.0)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)
OH ⁻ ⋯CCl ₄ (RC4)	-8.6		-8.6 (0.0)	-8.5 (0.1)			
[OH ⁻ ⋯CCl ₃ ⋯Cl] ⁻ (TS4)	-2.4		-4.1 (-1.7)	-2.4 (0.0)		-4.0 (-1.6)	-3.0 (-0.6)
Cl ⁻ + CCl ₃ OH(P4)	-68.6		-69.2 (-0.6)	-70.7 (-2.1)		-69.1 (-0.5)	-70.7 (-2.1)
Average absolute error			(0.8)	(0.7)		(1.1)	(1.4)
Barrier: <i>E</i> (TS4)− <i>E</i> (RC4)	6.2		4.5 (-1.7)	6.1 (-0.1)			

^a Target calculation

method can give results nearly as accurate as the target calculation as shown in the previous sections. Whether the ONIOM method can be employed in the actual application or not depends on the amount of computational time saving in the ONIOM calculation compared with the target calculation. In the ONIOM calculation on the present system, the low-level cost increases with increasing system size from CH₃Cl to CCl₄, while the high-level cost is unchanged. Therefore, the cost increase is determined at the low level and is much less steep than that of the target calculation. The timing data for CCl₄ species obtained with a personal computer with an Intel Xeon central processing unit are as follows:

Geometry optimization (per cycle)

CCl₄ + OH⁻

Pure MP2/b = 770 s

ONIOM(MP2/b : B3LYP) = 150 s

Single-point-energy calculation

CCl₄

Pure CC/b = 3686 s

ONIOM(CC/b : MP2) = 190 s

The cost of ONIOM(MP2/b:B3LYP) geometry optimization is about 20% of pure MP2/b optimization, and the cost of ONIOM(CC/b:MP2) single-point-energy calculation is 5% of the pure CC/b calculation. This

ratio is expected to decrease substantially as the size of the real system becomes larger.

Conclusion

We have examined the reliability of the two-layer version of ONIOM methods for the S_N2 reaction $CH_{(4-n)}Cl_n + OH^-$. In the ONIOM calculation, only a methyl chloride and the OH⁻ ion were treated at a high level, and all substituted Cl_{*n*} ($n=2-4$) atoms were treated at a low level of MO calculation. That is, the effect of polychlorination on the reaction was treated only with a low level. The MP2/b and CC/b methods were used for the high level, while the B3LYP, BLYP, and HF methods were used for the low level in the ONIOM calculation.

For the geometry optimization, we found that the ONIOM(MP2/b:DFT) combinations can reproduce the target MP2/b geometries satisfactorily for the reactants, reactant complexes, transition states, and products of the reaction. The best ONIOM geometries were obtained by using the (MP2/b:B3LYP) method. The energetics were then improved by performing better single-point ONIOM energy calculation at the ONIOM optimized geometries. We found that the target CC/b//MP2/b energetics can be well reproduced with the (CC/b:MP2)/(MP2/b:B3LYP) method with 0.7 kcal/mol for the average absolute error. The computational cost for this calculation for $n=4$ was found to be about 20% for optimization and 5% for single point improved energy of the target calculation. Therefore, the (CC/b:MP2)/(MP2/b:B3LYP) method is a powerful

candidate for further systematic investigation of the reaction mechanism of PCHCs in a ground water environment.

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