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Theoretical study of the regioselectivity of the reaction between tetrachloromethane and triethyl phosphite using DFT B3LYP/6-31G (d)

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ABSTRACT

In this study we used DFT B3LYP/6-31G(d) to determine certain thermodynamic properties, transition states, energies of the highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO), the difference between the two energies ($\epsilon_{LUMO} - \epsilon_{HOMO}$), global indices and chemical potentials of the reaction between tetrachloromethane and triethyl phosphite $P(OEt)_3$. Our results show that triethyl phosphite behaves as a nucleophile, while tetrachloromethane behaves as an electrophile. The nucleophilic attack takes place preferentially at the chlorine atom of the tetrachloromethane rather than at the carbon atom. The reaction is exothermic and regioselective, and the reaction mechanism is controlled by charge transfer.

Key words: Charge transfer, exothermic, global indices, regioselectivity, transition state.

INTRODUCTION

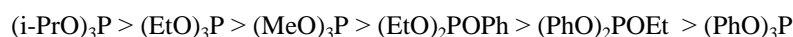
Phosphorus is not widely present in nature, being found essentially in the form of phosphate (PO_4^{3-}) in apatite deposits ($Ca_3F(PO_4)_3$). It is extremely important for life, as adenosine triphosphate (ATP) is the vehicle which transports chemical energy within cells. Together with nitrogen (N) and potassium (K), it is one of the three fundamental elements needed for plant development.

Phosphorus chemistry is a very active sector of the chemical industry, particularly in the production of fertiliser, insecticides and detergents, and in the treatment of metals.

On the academic side, phosphorus has been used to develop numerous molecules with high synthetic potential, such as the Wittig reagents which are the precursors of choice for the preparation of olefins.

In recent decades, phosphorus chemistry has developed considerably, with regard to both synthesis and reactivity. Bibliographic research shows that the reaction of the trivalent phosphorus derivatives $[(RO)_3P, (RO)_2P-R', \dots]$ with certain polyhalogenoalkanes ($CCl_4, BrCCl_3, \dots$) leads to the formation of a number of products [1, 2] some of which have numerous applications in industry [3, 4, 5] and biology [6].

The reactivity of trivalent phosphorus with regard to polyhalogenomethanes in general and tetrachloromethane in particular has already been the subject of several studies [7, 8]. This reactivity varies according to the nature of the substituents carried by the phosphorus atom and increases as its electropositivity increases.



A variety of reaction mechanisms have been proposed to describe these reactions [7, 9, 10, 11]. In addition, a number of theories have been put forward to explain chemical reactivity. The most widely used are transition state theory [12] and frontier molecular orbital theory (FMO) [13]. Recently new chemical concepts and reactivity indices derived from density functional theory (DFT) have emerged as powerful tools for the prediction of reactive sites in molecular systems [14, 15]. Some of these concepts are already familiar to chemists, e.g. electronic chemical potential μ and electronegativity χ . New concepts such as electrophilicity ω and chemical hardness η have been derived from the fundamental equations of DFT.

Our aim in this work was to carry out a theoretical study, using DFT B3LYP/6-31G(d), of the reactivity of CCl_4 with triethyl phosphite in order to determine whether the phosphorus attacks the carbon or the chlorine of the tetrachloromethane (Figure 1).

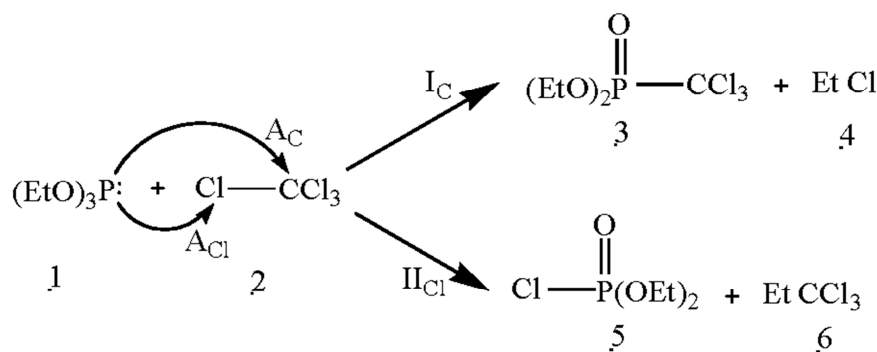


Figure 1. Reaction between tetrachloromethane (CCl_4) and triethyl phosphite (EtO_3P)

MATERIALS AND METHODS

The mechanism and the equilibrium geometries of the reaction between tetrachloromethane and triethyl phosphite, as well as the transition states corresponding to the two approaches at A_c and A_{cl} , were studied using density functional theory (DFT) with base B3LYP/6-31G (d) [16, 17]. Transition states were localised and their existence confirmed by the presence of a single imaginary frequency in the Hessian matrix. The Intrinsic Reaction Coordinate (IRC) was calculated [18] and plotted in order to show that the transition state is indeed linked to the two minima (reactants and products). Values of enthalpy, entropy and free energy were calculated using standard statistical thermodynamics. All calculations were carried out with Gaussian 09 software [19] using DFT B3LYP/6-31G (d).

In order to demonstrate the electrophilic/nucleophilic character of the reactants, we calculated electronic chemical potential μ and global hardness η . These two values can be calculated from the energies of the HOMO and LUMO frontier molecular orbitals as $\mu = (\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}})/2$ and $\eta = (\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}})$ respectively [20]. The global electrophilicity index $\omega = (\mu^2/2\eta)$ is also defined as the energy stabilisation due to charge transfer [21].

The index of nucleophilicity N is expressed with reference to the HOMO energy of tetracyanoethylene (TCE) as $N = \epsilon_{\text{HOMO}(\text{NU})} - \epsilon_{\text{HOMO}(\text{TCE})}$ [22].

The reactivity indices were calculated from the HOMO and LUMO energies in the base state of the molecules using DFT B3LYP/6-31G (d). The static local electrophilicity index ω_K and local nucleophilicity index N_K can reliably predict the most favoured electrophile/nucleophile interaction for the formation of a chemical bond between two atoms [23, 24]. The expressions $\omega_K = \omega \cdot P_K^+$ and $N_K = N \cdot P_K^-$ correspond respectively to the local electrophilicity index ω_K and the local nucleophilicity index N_K . P_K^+ and P_K^- are obtained by analysing the Mulliken atomic spin density of the anion and the cation [25].

RESULTS AND DISCUSSION

1.1. Thermodynamic study

We studied the reaction of tetrachloromethane CCl_4 with triethyl phosphite $\text{P}(\text{OEt})_3$ (Figure 1) and used DFT B3LYP/6-31G(d) to determine the variation in energy ΔE_r , enthalpy ΔH_r and free enthalpy ΔG_r in reactions I_c and II_{cl} (Table 1).

Table 1. Values calculated for the variation in energy ΔE_r , enthalpy ΔH_r and free enthalpy ΔG_r (Kcal/mol)

Products	Reaction	ΔH_r	ΔE_r	ΔG_r
3+4	I _C	-25.307	-25.915	-26.385
5+6	II _{Cl}	-46.571	-47.712	-46.113

As Table 1 shows, the variations in free enthalpy ΔG_r of reactions I_C et II_{Cl} are all negative. This means that these reactions are possible and are thermodynamically favoured. Furthermore, we noted that the variation in free enthalpy ΔG_r corresponding to the reaction of formation of compounds 5 and 6 is greater in absolute value than that which corresponds to the reaction of formation of compounds 3 and 4. We can therefore conclude that compounds 5 and 6 are more thermodynamically stable than compounds 3 and 4, showing that the attack on the chlorine atom is the most favoured.

We found that the values of variation in enthalpy ΔH_r and in free enthalpy ΔG_r of the reactions of formation of compounds 3 and 4, as well as of compounds 5 and 6, are negative, meaning that these reactions are exothermic.

We also found that the value of the variation in energy ΔE_r which corresponds to the reaction of formation of compounds 5 and 6 is more important in absolute terms than that which corresponds to the reaction of formation of compounds 3 and 4. This further confirms that the most favoured site for the attack is the chlorine atom.

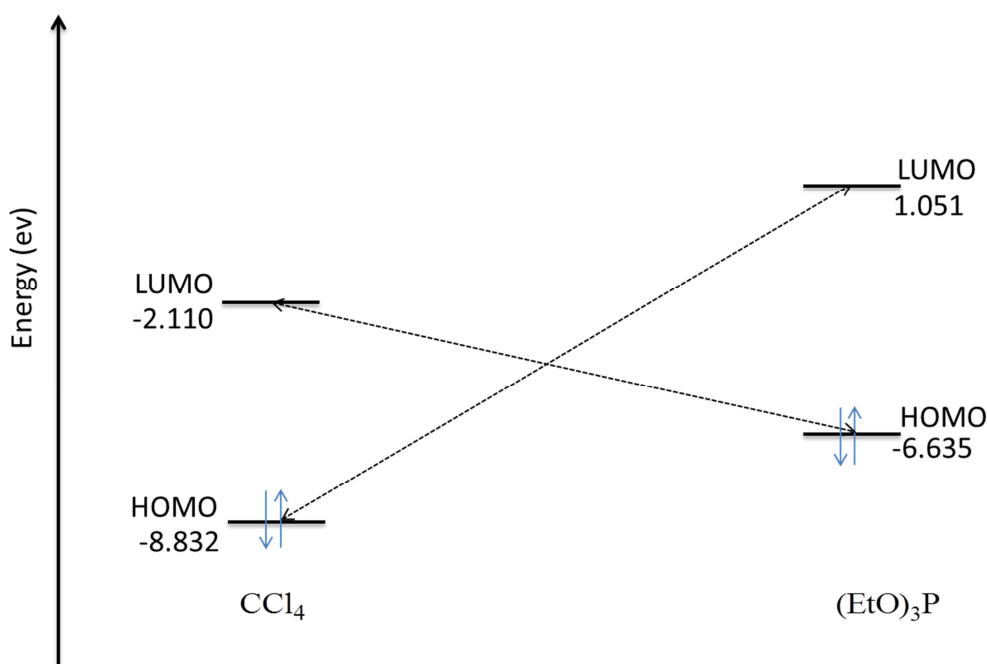
1.2. Study of frontier orbitals

We used DFT B3LYP/6-31G(d) to calculate the LUMO and HOMO energies of tetrachloromethane and triethyl phosphite (Table 2).

According to frontier orbital theory, the orbitals to consider in the interaction between two molecules are the HOMO of one and the LUMO of the other, chosen in such a way that the energy difference between them ($\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$) is as low as possible [26]. As Figure 2 shows, the orbital diagram gives a good qualitative indication of the reactivity of the system. We note that the main interaction takes place between the energy of the LUMO of tetrachloromethane and that of the HOMO of triethyl phosphite. Table 2 shows that the LUMO-HOMO energy difference is smaller than the HOMO-LUMO energy difference, which explains why the reaction between tetrachloromethane and triethyl phosphite is favoured.

Table 2. LUMO and HOMO energies of tetrachloromethane and triethyl phosphite (eV)

Reactant	ϵ_{LUMO}	ϵ_{HOMO}	$\epsilon_{\text{LUMO2}} - \epsilon_{\text{HOMO1}}$	$\epsilon_{\text{LUMO1}} - \epsilon_{\text{HOMO2}}$
1	1.051	-6.635	4.525	9.883
2	-2.110	-8.832		

**Figure 2.** Orbital diagram of tetrachloromethane and triethyl phosphite

1.3. Predicting the nature of the reaction mechanism and the electrophile/nucleophile character of the reaction

In order to determine the nucleophile (electron donator) or electrophile (electron acceptor) character of the two reactants, we calculated the HOMO/LUMO energy gaps between the two (Table 3).

Table 3. Difference between the two possible HOMO/LUMO combinations for triethyl phosphite and tetrachloromethane (eV)

Reactant	ϵ_{LUMO}	ϵ_{HOMO}	$\epsilon_{\text{HOMO}}-\epsilon_{\text{LUMO}}(\text{CCl}_4)$	$\epsilon_{\text{HOMO}}(\text{CCl}_4)-\epsilon_{\text{LUMO}}$
CCl_4	-2.110	-8.832	-	-
$(\text{EtO})_3\text{P}$	1.051	-6.635	4.525	9.883

Our results show that the $\epsilon_{\text{HOMO}}-\epsilon_{\text{LUMO}}(\text{CCl}_4)$ gap is less than the $\epsilon_{\text{HOMO}}(\text{CCl}_4)-\epsilon_{\text{LUMO}}$ gap, and that therefore triethyl phosphite behaves as a nucleophile while tetrachloromethane behaves as an electrophile.

Theoretical study of the HOMO/LUMO energy gaps between $\text{P}(\text{OEt})_3$ and CCl_4 enabled us to predict the NED (Normal Electron Demand) or IED (Inverse Electron Demand) nature of the interaction between the two reactants. Global and local indices determined using conceptual DFT are effective tools for studying the reactivity of polar interactions [14].

The static global properties, namely electronic chemical potential μ , chemical hardness η , global electrophilicity index ω and global nucleophilicity index N of triethyl phosphite and tetrachloromethane are the chemical properties which we used to analyse reactivity at the various sites in the reactants (Table 4).

Table 4. HOMO and LUMO energies, electronic chemical potential μ , chemical hardness η , global electrophilicity ω and global nucleophilicity N of $(\text{EtO})_3\text{P}$ and CCl_4 (eV)

	ϵ_{LUMO}	ϵ_{HOMO}	μ	η	ω	N	$\Delta\omega$
CCl_4	-2.110	-8.832	-5.471	6.721	2.226	0.287	-
$(\text{EtO})_3\text{P}$	1.051	-6.635	-2.792	7.686	0.507	2.483	1.719

We can see from the data in Table 4 that tetrachloromethane behaves as an electrophile (electron acceptor) while triethyl phosphite behaves as a nucleophile (electron donor). Tetrachloromethane has a higher electrophilicity index ($\omega = 2.226$ eV) and a lower nucleophilicity index ($N = 0.287$ eV). Furthermore, the electronic chemical potential of $\text{P}(\text{OEt})_3$ (-2.792) is higher than that of tetrachloromethane (-5.471 eV). These results confirm that triethyl phosphite is a nucleophile and that tetrachloromethane is an electrophile, implying that electrons are transferred to tetrachloromethane. We can conclude that in this reaction tetrachloromethane behaves as an electrophile.

The difference between the electrophilicity $\Delta\omega$ of tetrachloromethane and triethyl phosphite indicates that the reaction has a highly polar NED character.

Localisation of the HOMO of triethyl phosphite and LUMO of tetrachloromethane represented in Figure 3 shows that the HOMO is extremely condensed around the phosphorus atom whereas the LUMO belongs to both the carbon and the chlorine atoms. This shows that the tetrachloromethane attack takes places mainly at the phosphorus atom.

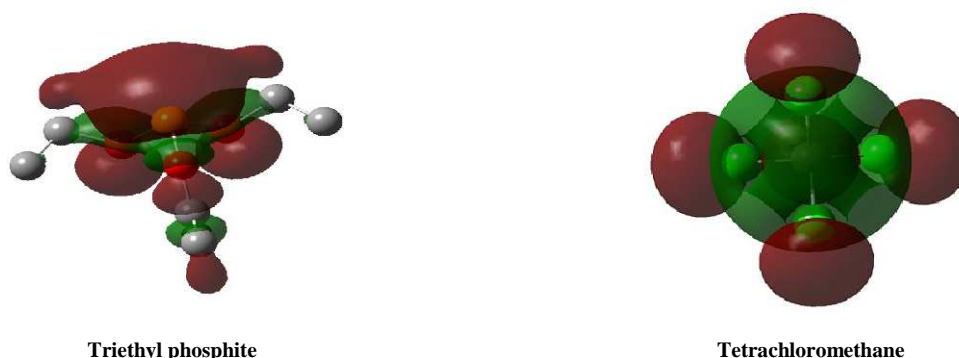


Figure 3. Isodensity map of the HOMO of triethyl phosphite and LUMO of tetrachloromethane

1.4. Predicting the nucleophile attack mode (A_{Cl}/A_C) by determining the indices of electrophilicity and nucleophilicity

According to Chattaraj's polar model, the local philicity indices (ω_k and N_k) can be used to reliably predict the most favoured interaction between two polar centres [27, 28]. The most favourable attack is that which is associated with the highest local electrophilicity index ω_k of the electrophile and the highest local nucleophilicity index N_k of the nucleophile. We calculated the values N_k for triethyl phosphite and ω_k for tetrachloromethane in order to predict the most likely electrophile/nucleophile interaction throughout the reaction pathway and so explain the regioselectivity of the reaction.

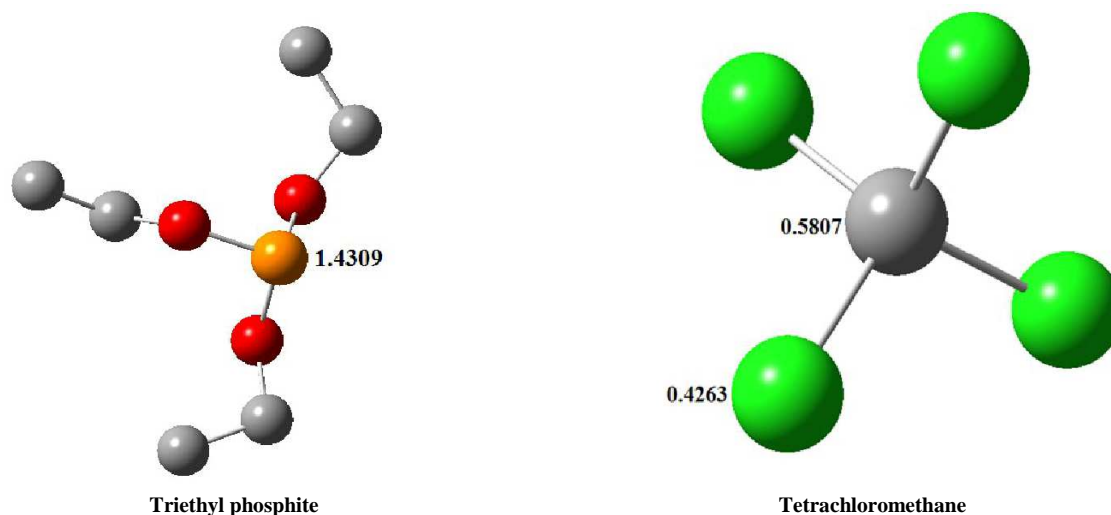


Figure 4. Local nucleophilicity N_k of triethyl phosphite and local electrophilicity ω_k of tetrachloromethane (eV)

Figure 4 shows that the carbon of CCl_4 is the most electrophilic site and the phosphorus atom of $(EtO)_3P$ is the most nucleophilic site. From this we can deduce that the nucleophilic attack takes place preferentially at the carbon atom (A_C) rather than at the chlorine atom (A_{Cl}). This is in agreement with experimental results, since only products 3 and 4 are formed during the reaction between $(EtO)_3P$ and CCl_4 at $80^\circ C$ [11, 12]. However, as the chloride atoms are large, this process is discouraged by the steric hindrance around the carbon atom.

1.5. Kinetic study of the two modes of attack (A_{Cl}/A_C)

1.5.1. Determination of the kinetic parameters

In order to show that the phosphorus preferentially attacks the chlorine atom rather than the carbon, we calculated the energy of the reactants and the products, relative energies, TS_{Cl} and TS_C transition state energy, energy difference between the transition states in the reactions between CCl_4 and $(EtO)_3P$ and the K_{Cl}/K_C ratio (Table 5).

Table 5. Total energy B3LYP/6-31G (d) (E, in a.u.) and relative energy ΔE^\ddagger (kcal/mol) for the stationary points in the reaction between tetrachloromethane and triethyl phosphite

	E (a.u.)	ΔE^\ddagger (Kcal/mol)	$\Delta(TS_C - TS_{Cl})$ Kcal/mol	K_{Cl}/K_C
CCl_4	-1878.854	-	20.08	$3.83 \cdot 10^{14}$
$(EtO)_3P$	-804.735	-		
TS_C	-2683.497	57.730		
TS_{Cl}	-2683.529	37.650		

The potential energy surface (PES) corresponding to the modes of attack at the chlorine and carbon atoms during the reaction between tetrachloromethane and triethyl phosphite (Figure 5) shows that the energy of the transition state corresponding to the attack at the chlorine atom (TS_{Cl}) is 0.032 a.u. (corresponding to 20.080 Kcal/mol) lower than the energy of the transition state corresponding to the attack on the carbon atom (TS_C). The activation energies corresponding to the two modes of attack are 37.650 Kcal/mol for the attack at the Cl atom, and 57.730 Kcal/mol for the attack at the C atom. This indicates that the attack at the chlorine atom is kinetically preferred to that at the carbon atom.

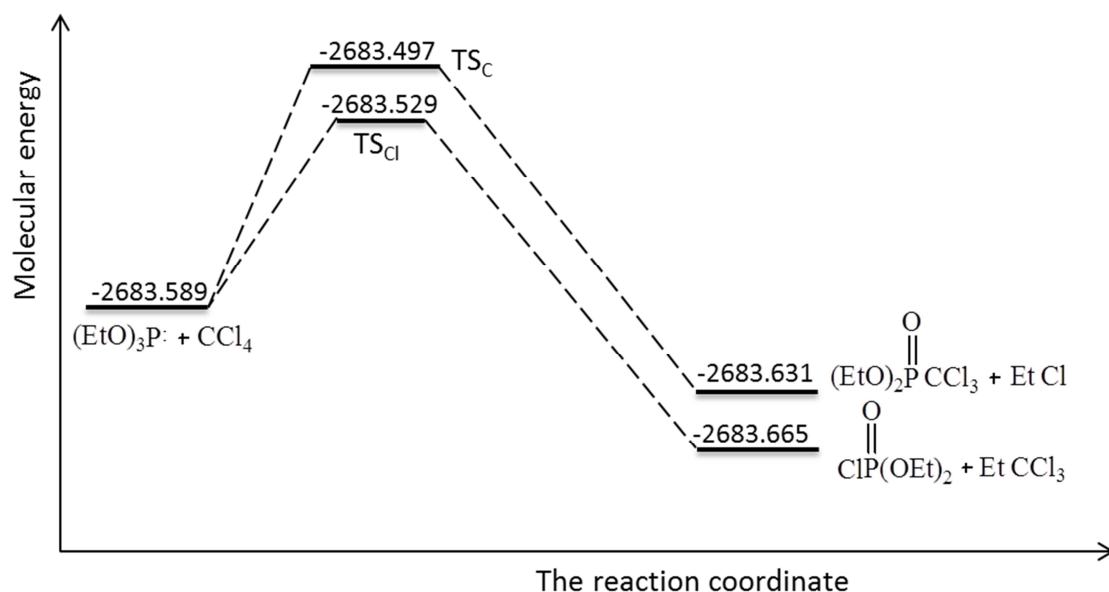


Figure 5. Energy profile for the reaction between CCl_4 and $(\text{EtO})_3\text{P}$ (a.u.)

1.5.2. Determination of the reaction pathway (IRC)

In order to check that the transition states are correct, we determined the IRC (intrinsic reaction coordinate) at each transition state of the two modes of attack ($A_{\text{Cl}}/A_{\text{C}}$), by determining the reaction pathway and connecting the transition state to the minimum (product). The IRC corresponding to the two modes of attack in the "Forward only" direction (towards the product) is shown in Figure 6.

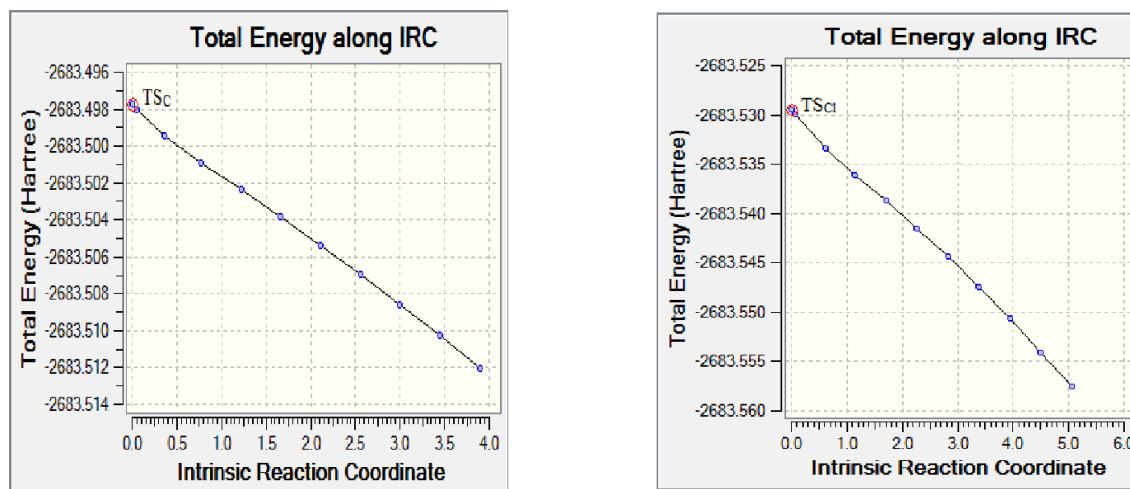
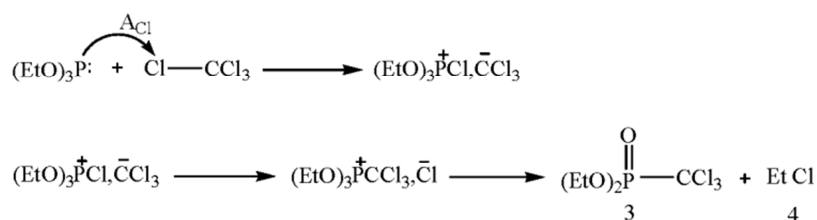


Figure 6. IRC of the reaction between triethyl phosphite and tetrachloromethane calculated using DFT B3LYP/6-31G(d)

We can deduce from this theoretical study that:

- Both modes of attack by $\text{P}(\text{OEt})_3$ on CCl_4 ($A_{\text{Cl}}/A_{\text{C}}$) are thermodynamically possible.
- Even though the local electrophilicity of carbon is greater than that of chlorine, the A_{C} attack is discouraged by the steric hindrance generated by the chlorine atoms.
- The A_{C} attack is kinetically impossible in view of the very high value of the ratio of the speed constants of the two modes of attack ($K_{\text{Cl}}/K_{\text{C}}$).



In order to align these theoretical results with our experimental results, we propose a reaction mechanism in which the first step is a nucleophilic attack on the chlorine in CCl_4 (A_{Cl}) leading to formation of the ion pair $(\text{EtO})_3\text{P}^+\text{Cl}^-\text{CCl}_3$. Since the CCl_3 carbanion is unstable, it exchanges rapidly with chlorine to give the ion pair $(\text{EtO})_3\text{P}^+\text{CCl}_3\text{Cl}^-$ leading to formation of products 3 and 4 in reaction I_{C} [9]. In order to demonstrate unambiguously that the nucleophilic attack takes place at the chlorine (A_{Cl}) rather than at the carbon (A_{C}) atom we would have to select the substituents carried by the phosphorus atom (R_3P) and the type of polyhalogenomethane (XCCl_3).

CONCLUSION

In this work we used DFT (density functional theory) with the standard base 6-31G(d) and B3LYP functional to determine the variation in free enthalpies of reaction ΔG_{r} and show that these reactions are theoretically possible and involve an attack at the chlorine atom.

Calculation of the global indices of electrophilicity and nucleophilicity and chemical potential using the same method shows that the reactant $(\text{EtO})_3\text{P}$ behaves as a nucleophile and that tetrachloromethane behaves as an electrophile.

The variation in enthalpy in the reaction ΔH_{r} is highly exothermic for the formation of products 5 and 6. It follows that the reaction II_{C} is most favoured since the products formed are stable and their formation releases energy.

The energy difference between the LUMO of tetrachloromethane and the HOMO of triethyl phosphite is greater than 2 eV, showing that the reaction is controlled by charge transfer.

Calculation of the transition states shows that the kinetic products of the reaction between tetrachloromethane and triethyl phosphite $(\text{EtO})_3\text{P}$ result from the attack on the chlorine atom.

We have proposed a reaction mechanism to explain the experimental results. This mechanistic proposal will be refined in the future by choosing the substituents carried by the phosphorus (R_3P) and the polyhalogenomethane (XCCl_3).

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