

Theoretical study of the chemical reactivity of the reaction between trichloromethylphosphine oxide and triethyl phosphite using the DFT B3LYP/6-311G(d,p) method

Ali Barhoumi¹, Salem Bakkas¹ and Abdeslam El Hajbi^{2}*

¹ Laboratory of Organic, Bio-organic and Environmental Chemistry, Department of Chemistry, Faculty of Science, Chouaïb Doukkali University, BP 20, 24000 El Jadida, Morocco

² Laboratory of Physical Chemistry, Department of Chemistry, Faculty of Science, Chouaïb Doukkali University, BP 20, 24000 El Jadida, Morocco

Abstract

In this study we used the DFT B3LYP/6-311G(d,p) quantum mechanical method to propose a theoretical explanation of the regioselectivity observed experimentally in the reaction between trichloromethylphosphine oxide and triethyl phosphite using a variety of approaches, notably frontier molecular orbital theory and calculation of activity energies and reactivity indices. Our results show that triethyl phosphite functions as a nucleophile while trichloromethylphosphine oxide behaves as an electrophile. The nucleophilic attack takes place preferentially at the chlorine atom of trichloromethylphosphine oxide rather than at the carbon, and the reaction is polar and regioselective. These results are comparable with those obtained experimentally.

* Corresponding author:
a_elhajbi@yahoo.fr

Received 06 Nov 2017,
Revised 29 April 2018,
Accepted 03 July 2018

Keywords: triethyl phosphite; trichloromethylphosphine oxide; DFT B3LYP/6-311G(d,p); reactivity indices; FMO; activation energy; free enthalpy; reaction enthalpy; local indices.

1.Introduction

Organophosphates are increasingly used in modern organic chemistry because of their potential in such varied domains as biology [1-2], medicine [3-4], agriculture (as plant growth regulators) and biochemistry [5]. They are also of great interest as precursors in organic synthesis [6-7]. This versatility arises from the variable valency of phosphorus [8-9]. Several attempts have been made to demonstrate simple and effective ways of forming the C---P bond and synthesizing new organophosphate compounds. An excellent review of the formation of carbon-phosphorus bonds has been published by Engel and Cohen [5]. Of particular interest are the organophosphonates A and organophosphinates B (figure 1). The presence of a phosphonyl group in a molecule often results in specific applications arising either from activation of the carbon linked to the phosphorus [10], or from the biological properties of the phosphoric group itself [11]. A large number of natural compounds containing C---P bonds have been identified [12-15].

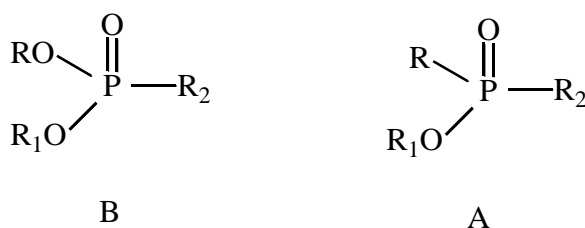


Figure 1: Organophosphonates (A) and organophosphinates (B)

Surprisingly, the reactivity of the polyhalogenoalkanes is not very well understood, even though these products are involved in a large number of reactions [16-17], particularly with trivalent phosphoric derivatives such as triethyl phosphite. In the present work, we used DFT B3LYP/6-311G(d,p) to study the regioselectivity of the reaction between trichloromethylphosphine oxide $(\text{CCl}_3)\text{PO}(\text{Ph})_2$ and triethyl phosphite $(\text{EtO})_3\text{P}$. We made use of a variety of theoretical approaches in order to describe the reaction mechanism and we compared our results with those obtained experimentally [18]. Does the phosphorus atom, which is presumed to be a nucleophilic centre, attack the carbon (A_C) or the chlorine (A_Cl) of trichloromethylphosphine oxide, both of which are presumed to be electrophilic centres (figure 2)?

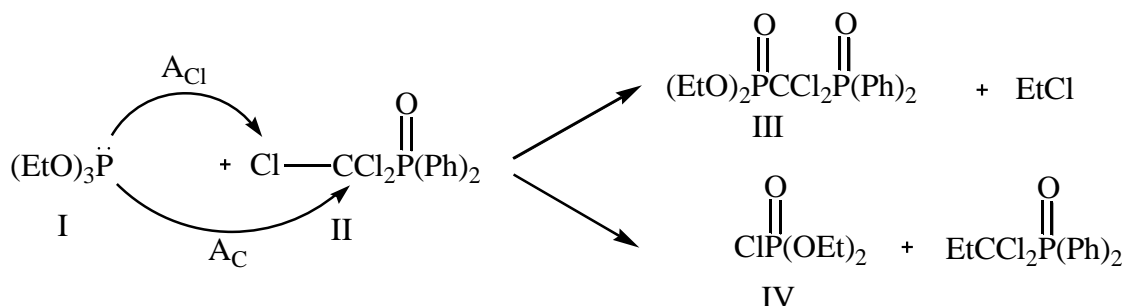


Figure 2: The reaction between trichloromethylphosphine oxide $(\text{CCl}_3)\text{PO}(\text{Ph})_2$ and triethyl phosphite $(\text{EtO})_3\text{P}$

2. Calculation method

All calculations were made using Gaussian 09W software [19]. The molecules were all fully optimised using the DFT B3LYP method [20] with the basis set 6-311G(d,p) [21]. The geometry of the cationic and anionic systems used in calculating local indices was the same as for neutral systems. Electronic populations were calculated using MPA (Mulliken Population Analysis) [22] and NPA (Natural Population Analysis) [23]. Localisation of the transition states was confirmed by the presence of a single imaginary frequency in the Hessian matrix. We calculated the Intrinsic Reaction Coordinate (IRC) [24] in order to show that the transition state is indeed linked to the two minimas (reactants and products). Enthalpy, entropy and free energy were calculated using standard statistical thermodynamics [20].

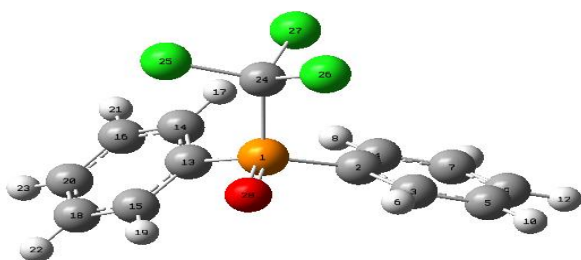
3. Results and discussion

3.1 Structural optimisation of the reactants

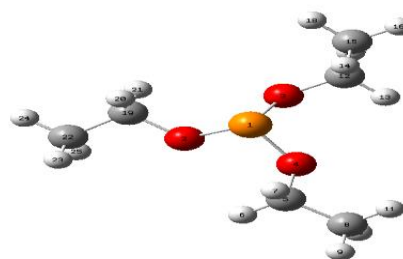
Table 1 shows atomic distances and bond energies of the reactant atoms of trichloromethylphosphine oxide in its most stable form, showing that all the chlorine atoms have the same reactivity with regard to the most nucleophilic site of triethyl phosphite. These parameters were optimised using Gaussian 09 software. Energy analysis shows that the fundamental state of triethyl phosphite stabilises at -804.892 a.u. and that of trichloromethylphosphine oxide at -298.818 a.u., in other words that triethyl phosphite is more reactive.

Table 1: Bond energy and interatomic distance of the reactant atoms in trichloromethylphosphine oxide

X---Y	D(X---Y)°A	E(X---Y) Kcal / mol
C ₂₄ ---Cl ₂₅	1.794	473.117
C ₂₄ ---Cl ₂₆	1.793	472.326
C ₂₄ ---Cl ₂₇	1.809	470.456



Trichloromethylphosphine oxide



Triethyl phosphite

Figure 3: The most stable structure of the two reactants

3.2 Study of the frontier orbitals

We calculated the HOMO/LUMO energy gap for the two possible combinations of the two reactants.

Frontier molecular orbital theory (FMO) makes it possible to analyse the reactivity of molecules in terms of the interactions between the molecular orbitals of the reactants by taking account of only the most important interactions [25]. The orbitals considered in studying the interaction between two reactants are the HOMO (highest occupied molecular orbital) of the one and the LUMO (lowest unoccupied molecular orbital) of the other, chosen in such a way that the $E_{\text{LUMO}} - E_{\text{HOMO}}$ energy gap is as small as possible [26]. As a general rule, the smaller the difference between the orbitals of the two reactants, the stronger the interaction between these orbitals, and the greater the stabilising effect.

As figure 4 shows, the orbital diagramme gives a good idea of the reactivity of the system. We can see that the main interaction takes place between the LUMO of trichloromethylphosphine oxide and the HOMO of triethyl phosphite. Localisation of the molecular orbitals of triethyl phosphite and trichloromethylphosphine oxide shows that the HOMO is very concentrated around the phosphorus atom, while the LUMO is concentrated around the chlorine atom (figure 4). This indicates that the nucleophilic attack by the phosphorus atom takes place essentially at the chlorine atom. This analysis of the reaction for the two modes of attack (A_C and A_{Cl}) correctly explains the regioselectivity observed experimentally [18].

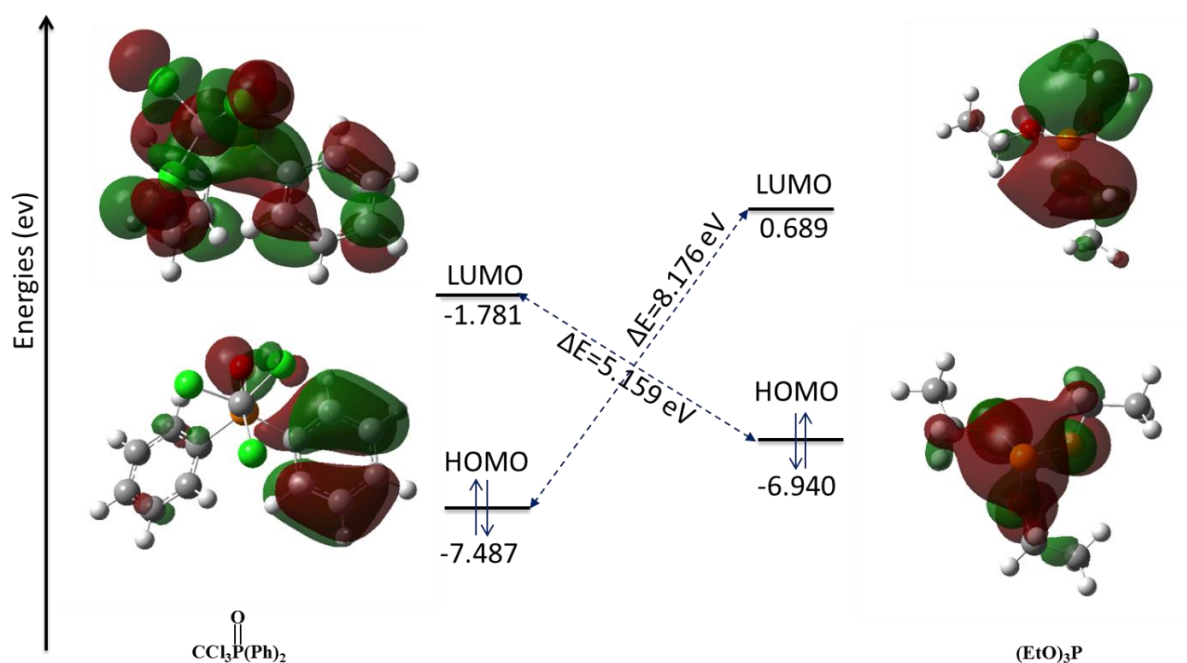


Figure 4: Energy gap between the HOMO of the nucleophile and the LUMO of the electrophile

3.3 Chemical concepts and reactivity indices derived using DFT

3.3.1 Predicting the nature of the reaction mechanism and the electrophilic/nucleophilic character of the two reactants

In order to determine which reactant behaves as a nucleophile (electron donor) and which as an electrophile (electron acceptor), we calculated the HOMO/LUMO energy gaps between them (table 2).

Table 2: Difference between the two possible HOMO/LUMO combinations for trichloromethylphosphine oxide and triethyl phosphite (eV)

Reactant	E_{LUMO}	E_{HOMO}	$ E_{HOMO}((EtO)_3P) - E_{LUMO}((CCl_3)PO(Ph)_2) $	$ E_{HOMO}((CCl_3)PO(Ph)_2) - E_{LUMO}((EtO)_3P) $
$(EtO)_3P$	0.689	-6.940	5.159	8.176
$(CCl_3)PO(Ph)_2$	-1.781	-7.487		

Our results show that the $|E_{\text{HOMO}}((\text{EtO})_3\text{P}) - E_{\text{LUMO}}(\text{CCl}_3\text{PO}(\text{Ph})_2)|$ gap is smaller than the $|E_{\text{HOMO}}(\text{CCl}_3\text{PO}(\text{Ph})_2) - E_{\text{LUMO}}((\text{EtO})_3\text{P})|$ gap, showing that triethyl phosphite behaves as a nucleophile while trichloromethylphosphine oxide behaves as an electrophile. Theoretical study of the HOMO/LUMO gaps of the two reactants allows us to characterise the reaction between the two as NED (Normal Electron Demand) or IED (Inverse Electron Demand). The global indices defined using conceptual DFT/B3LYP [27] are valuable tools for studying the reactivity of polar interactions. The static global properties electronic chemical potential μ , chemical hardness η , global electrophilicity index ω and global nucleophilicity index N are chemical properties which enable us to analyse reactivity. We calculated the electronic chemical potential μ and global hardness η from the energies of the HOMO and LUMO frontier molecular orbitals, as $\mu = (E_{\text{HOMO}} + E_{\text{LUMO}})/2$ and $\eta = (E_{\text{LUMO}} - E_{\text{HOMO}})$ respectively [28]. The global electrophilicity index $\omega = (\mu^2/2\eta)$ [29] is defined as the energy stabilisation due to charge transfer. It has been shown that the nucleophile character of a molecule can be calculated without taking account of its electron density [30]. The nucleophilicity index N is expressed in terms of the HOMO energy of tetracyanoethylene (TCE) as $N = E_{\text{HOMO}}(\text{NU}) - E_{\text{HOMO}}(\text{TCE})$ [31]. These values, together with maximum charge transfer ΔN_{max} [28] and the global electrophilicity gap $\Delta\omega$ are shown in table 3.

Table 3: HOMO and LUMO energy, electronic chemical potential μ , hardness η , electrophilicity ω , global nucleophilicity N , maximum charge transfer ΔN_{max} and global electrophilicity gap $\Delta\omega$ between $(\text{EtO})_3\text{P}$ and $(\text{CCl}_3)\text{PO}(\text{Ph})_2$

	E_{LUMO}	E_{HOMO}	μ (eV)	η (eV)	ω (eV)	N (eV)	$\Delta\omega$	ΔN_{max}
$(\text{EtO})_2\text{P}$	0.689	-6.940	-3.125	7.629	0.640	2.428	-	0.409
$(\text{CCl}_3)\text{PO}(\text{Ph})_2$	-1.781	-7.487	-4.634	5.706	1.881	1.881	1.241	0.812

$E_{\text{HOMO}}(\text{TCE}) = -9.368$ eV and $\Delta N_{\text{max}} = -\mu/\eta$

Our results show that trichloromethylphosphine oxide behaves as an electrophile while triethyl phosphite behaves as a nucleophile. Trichloromethylphosphine oxide has the highest electrophilicity index ($\omega=1.881$ eV) and the lowest nucleophilicity index ($N=1.881$ eV). Additionally, the electronic chemical potential of $(\text{OEt})_3\text{P}$ (-3.125 eV) is situated at a higher energy level than that of trichloromethylphosphine oxide (-4.634 eV), $[\mu((\text{EtO})_3\text{P}) > \mu((\text{CCl}_3)\text{PO}(\text{OPh})_2)]$, in other words a stream of electrons circulating from $(\text{EtO})_3\text{P}$ to $(\text{CCl}_3)\text{PO}(\text{Ph})_2$ stabilises the system. These results confirm that triethyl phosphite behaves as a nucleophile and trichloromethylphosphine oxide as an electrophile in this reaction.

The maximum charge transfer of trichloromethylphosphine oxide ($\Delta N_{\text{max}}=0.812$ eV) is greater than that of triethyl phosphite ($\Delta N_{\text{max}}=0.409$ eV) and the electrophilicity gap ($\Delta\omega$) between trichloromethylphosphine oxide and triethyl phosphite is high, showing that the reaction is polar.

3.3.2 Predicting the direction of electron flow using the dual indices γ_1 and γ_2

The direction of electron flow in the reaction can be determined using the dual indices γ_1 and γ_2 [32] defined as:

$$\gamma_1 = \omega((\text{EtO})_3\text{P}) + N((\text{CCl}_3)\text{PO}(\text{Ph})_2) = 2.521 \text{ eV} \quad (1)$$

$$\gamma_2 = N((\text{EtO})_3\text{P}) + \omega((\text{CCl}_3)\text{PO}(\text{ph})_2) = 4.309 \text{ eV} \quad (2)$$

Using the electrophilicity and nucleophilicity indices, respectively ω and N , we find that $\gamma_2 > \gamma_1$, confirming that the reaction is polar, and that the electron flow takes place from triethyl phosphite to trichloromethylphosphine oxide.

3.3.3 Predicting the local reactivity of the reactants

3.3.3.1 Application of the Gazquez-Mendez rule using local condensed softnesses (S_k^+ and S_k^-)

In order to explain the regioselectivity of the reactions, Gazquez and Mendez proposed that "two chemical species interact through atoms of equal or similar softness" [33-34]. We used natural population analysis (NPA) to calculate the local softness S_k^+ and S_k^- of the reactant atoms of trichloromethylphosphine oxide and triethyl phosphite respectively (table 4).

Table 4: Fukui indices f_k^- and f_k^+ and local softness S_k^- and S_k^+ of the reactant atoms of triethyl phosphite and trichloromethylphosphine oxide calculated using NPA

	(EtO) ₃ P				(CCl ₃)PO(Ph) ₂			
	P ₁	O ₂	O ₃	O ₄	C ₂₄	Cl ₂₅	Cl ₂₆	Cl ₂₇
f_k^+					0.044	-0.140	-0.132	-0.104
f_k^-	-0.29	-0.103	-0.103	-0.102				
S_k^+					0.003	-0.012	-0.011	-0.009
S_k^-	-0.018	-0.006	-0.006	-0.006				

where:

$$S_k^+ = S f_k^+ \quad (S = \frac{1}{2\eta} = 0.0876 \text{ eV}^{-1}) \quad \text{and} \quad S_k^- = S f_k^- \quad (S = \frac{1}{2\eta} = 0.0655 \text{ eV}^{-1})$$

$f_k^+ = [q_k(N+1) - q_k(N)]$ in the case of a nucleophilic attack and $f_k^- = [q_k(N) - q_k(N-1)]$ in the case of an electrophilic attack [35]

$q_k(N)$: electronic population of the k atom in the neutral molecule

$q_k(N+1)$: electronic population of the k atom in the anionic molecule

$q_k(N-1)$: electronic population of the k atom in the cationic molecule

These results show that the most favoured interaction takes place between the phosphorus atom of triethyl phosphite and one of the chlorine atoms of trichloromethylphosphine oxide (similar local softness). This is in good agreement with the experimental results [18].

3.3.3.2 Calculation of local electrophilicity ω_k and local nucleophilicity N_k using Parr functions P_k^+ and P_k^-

Reactivity indices were calculated from HOMO and LUMO energies in the ground state of the molecules. According to Domingo's polar model, static indices of local electrophilicity ω_k and local nucleophilicity N_k are reliable predictors of the most favoured electrophile-nucleophile interaction between two polar centres [30, 36-37]. The most favoured interaction is that associated with the highest index of local electrophilicity ω_k of the electrophile and the highest index of local nucleophilicity N_k of the nucleophile. We used Parr functions to calculate local electrophilicity P_k^+ of trichloromethylphosphine oxide and local nucleophilicity P_k^- of triethyl phosphite. We calculated N_k for triethyl phosphite and ω_k for trichloromethylphosphine oxide in order to predict the most probable electrophile-nucleophile interaction throughout the reaction pathway, in order to explain the regioselectivity of the reaction. The chlorine atom is the most electrophilic site of trichloromethylphosphine oxide ($\omega_{Cl} = 0.180 \text{ eV}$), while the phosphorus atom is the most nucleophilic site of triethyl phosphite ($N_P = 0.905 \text{ eV}$). Table 5 shows the most active sites of the two reactants. We can conclude from these results that the most favoured interaction takes place between the phosphorus atom of triethyl phosphite and the chlorine atom of trichloromethylphosphine oxide.

Table 5: Parr functions P_k^+ and P_k^- , local electrophilicity ω_k and local nucleophilicity N_k of the reactant atoms of trichloromethylphosphine oxide and triethyl phosphite

	(EtO) ₃ P				(CCl ₃)PO(OEt) ₂			
	P ₁	O ₂	O ₃	O ₄	C ₂₄	Cl ₂₅	Cl ₂₆	Cl ₂₇
P_k^+					0.090	0.096	0.082	0.050
P_k^-	0.373	0.195	0.196	0.194				
ω_k					0.169	0.180	0.154	0.094
N_k	0.905	0.473	0.475	0.471				

3.4 Kinetic and thermodynamic study of the nucleophilic modes of attack of (EtO)₃P on (CCl₃)PO(OEt)₂

3.4.1 Thermodynamic study

We studied the feasibility and the regioselectivity of the reaction between trichloromethylphosphine oxide (I) and triethyl phosphite (II) from a thermodynamic point of view. In order to compare the reactivity of the two modes of attack (A_C and A_{Cl}), we calculated the differences in reaction energy ΔE_r , reaction enthalpy ΔH_r and free enthalpy ΔG_r corresponding to the formation of compounds III and IV (table 6).

Table 6: Calculated values (Kcal /mole) of the differences in reaction energy ΔE_r , reaction enthalpy ΔH_r and free enthalpy ΔG_r

Reactants	Product	ΔH_r	ΔE_r	ΔG_r
I + II	III	-25.939	-26.704	-22.225
	IV	-42.204	-45.058	-39.165

As table 6 shows, variations in free enthalpy ΔG_r are negative whatever the mode of attack. It follows that these reactions are possible and are thermodynamically favoured. We also found that the variation in free enthalpy ΔG_r corresponding to the formation of compound IV is greater in absolute terms than that corresponding to the formation of compound III. The formation of compound III resulting from an attack on the carbon atom (A_C) is thermodynamically less favoured than the formation of compound IV. Free enthalpy of formation of the latter is greater in absolute terms than that of compound III. The value of ΔE_r corresponding to the formation of compound IV is greater in absolute terms than that corresponding to the formation of compound III. This shows that the most favourable site for an attack is the halogen Cl rather than the carbon C.

3.4.2 Structure and energy of the transition states

In order to determine the more favoured mode of attack (A_C or A_{Cl}) and thus the most favoured product of the reaction between triethyl phosphite and trichloromethylphosphine oxide, we localised the transition states and calculated the activation barriers for the two possible reaction pathways (table 7).

The transition states TS_C and TS_{Cl} , corresponding to the two modes of attack, were localised. These two transition states were confirmed by the presence of one and only one negative eigenvalue in the force constant matrix: in other words there is a single imaginary frequency in the Hessian matrix, corresponding to the vibration mode of the formation of the bonds P---CCl₂ and P---Cl respectively and the splitting of bonds C---Cl and Cl---CCl₂ respectively. The two transition states TS_C and TS_{Cl} are shown in figure 5.

Table 7: Thermodynamic values (E, H, G) and activation barriers of the reaction between trichloromethylphosphine oxide and triethyl phosphite

System	E (a.u.)	ΔE (Kcal/mol)	H (a.u.)	ΔH (Kcal/mol)	G (a.u.)	ΔG (Kcal/mol)	ν (cm ⁻¹)
(EtO) ₃ P	-804.891		-804.664		-804.723		
(CCl ₃)PO(Ph) ₂	-2298.818		-2298.604		-2298.669		
TS _C	-3103.653	53.140	-3103.210	36.395	-3103.313	49.573	-363.23
TS _{Cl}	-3103.654	34.513	-3103.212	35.140	-3103.320	45.180	-81.07
P _C	-3103.745	-57.730	-3103.302	-57.730	-3103.421	-67.771	
P _{Cl}	-3103.779	-78.438	-3103.335	-77.183	-3103.457	-85.968	

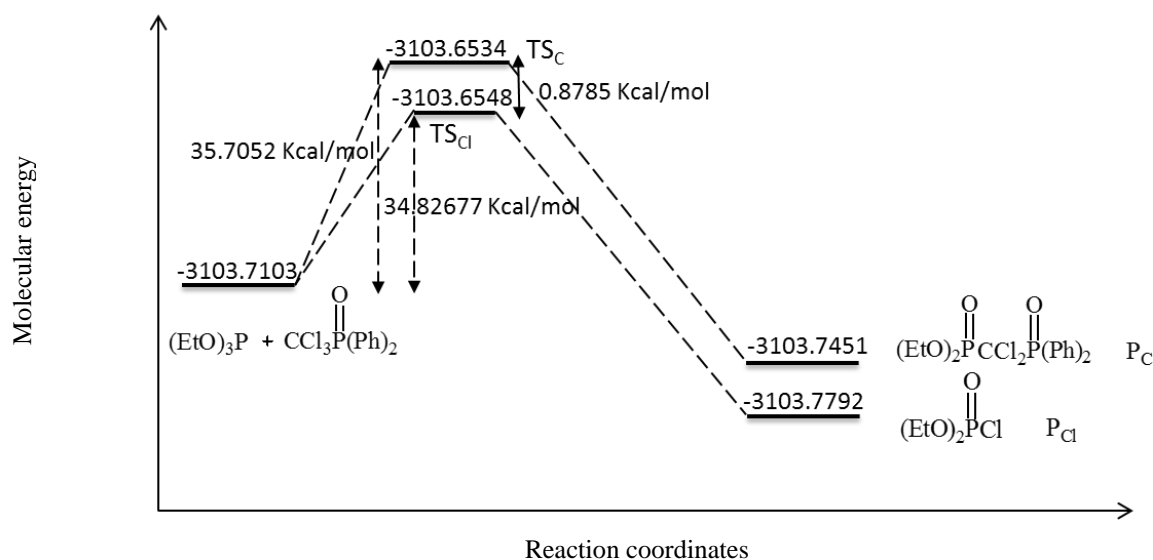


Figure 5: Energy profile in a.u. of the reaction between trichloromethylphosphine oxide and triethyl phosphite

The potential energy surface (PES) corresponding to the two modes of attack shows that the energy of the transition state corresponding to the attack on the chlorine atom TS_{Cl} is 0.8785 Kcal/mol below the energy of the transition state corresponding to the attack on the carbon atom TS_C. The activation energy is 35.7052 Kcal/mol for A_C and 34.8267 Kcal/mol for A_{Cl}. In other words, the attack on the chlorine atom is kinetically preferred to the attack on the carbon atom. We can conclude from this theoretical investigation that, while both modes of attack by triethyl phosphite on trichloromethylphosphine oxide (A_{Cl} and A_C) are thermodynamically possible, the products formed by the attack on the chlorine atom are kinetically and thermodynamically preferred. The structure of the transition state associated with reaction pathway A_{Cl} is more stable than that associated with A_C. The two structures optimised using DFT B3LYP/6-311G(d,p) are shown in figure 6. Phosphite tends to react more with chlorine than with carbon because of the difference in length between bonds P---CCl₂ and P---Cl in the transition state D(P---Cl) < D(P---Cl₂).

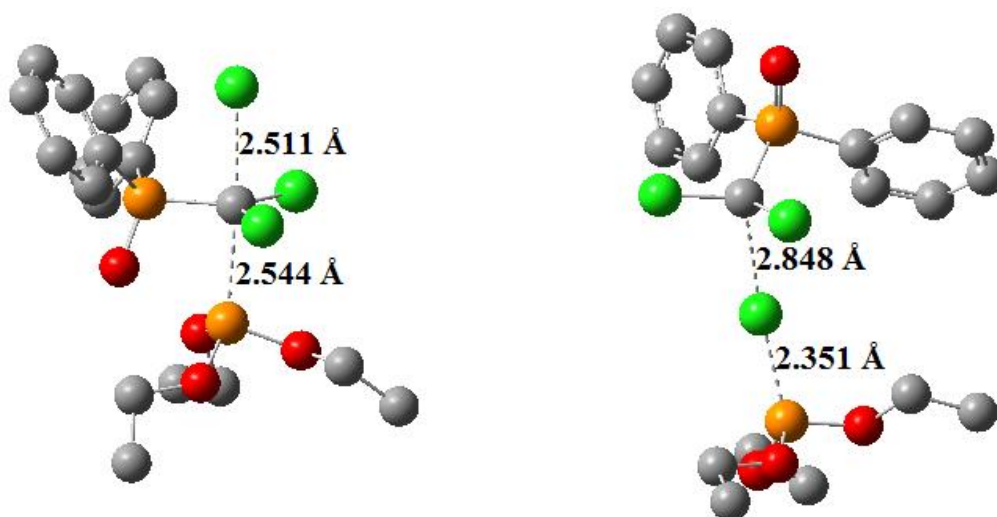


Figure 6: Bond lengths of the transition states in the reaction between triethyl phosphite and trichloromethylphosphine oxide

3.5 Determination of the intrinsic reaction coordinates (IRC)

On the basis of the optimised geometry of the transition state we calculated the IRC (Intrinsic Reaction Coordinate) [24] in order to confirm that the transition state indeed links the reactants and the products. Figure 7 presents the reaction pathway corresponding to the two modes of attack and shows that the transition state is indeed linked to the two minima (reactants and products).

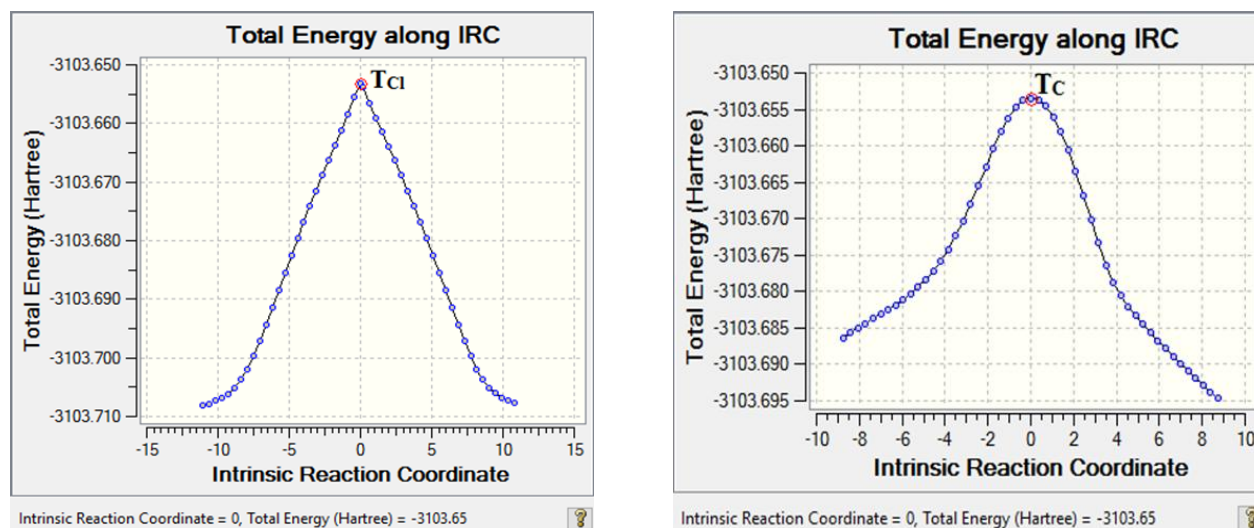


Figure 7: IRC of the reaction between triethyl phosphite and trichloromethylphosphine oxide (A_{Cl}/A_C)

Natural population analysis of the reaction shows that the charge transfer from the nucleophile to the electrophile is 0.492(e) for transition state TS_C and 0.599(e) for transition state TS_{Cl} . This indicates that TS_{Cl} is more stable and favorable, and that the reaction is polar in character. These results confirm the findings obtained from the HOMO/LUMO energy gaps and the global indices ω , N and μ .

4. Conclusion

Theoretical study of the reaction between trichloromethylphosphine oxide and triethyl phosphite using DFT B3LYP/6-311G (d,p) shows that whatever the mode of attack of the phosphorus atom (A_{Cl} and A_C) on trichloromethylphosphine

oxide, the corresponding variations in free enthalpy ΔG_r are negative, indicating that these attacks are thermodynamically possible.

Calculation of the global indices shows that triethyl phosphite behaves as a nucleophile and trichloromethylphosphine oxide as an electrophile. The reaction is characterised by a relatively high charge transfer, implying a polar mechanism.

The variation in reaction enthalpy ΔH_r is highly exothermic for the reaction leading to formation of compound IV. Consequently this reaction is favoured, since the products formed are stable and their formation releases energy.

Localisation of the HOMO of triethyl phosphite and the LUMO of trichloromethylphosphine oxide shows that the phosphorus atom is the nucleophile centre of the former while the chlorine atom is the electrophile centre of the latter. The thermodynamic and kinetic study shows that the stable products of the reaction between trichloromethylphosphine oxide and triethyl phosphite are those resulting from the attack on the chlorine atom.

References

1. Akbaş H., Okumuş A., Kılıç Z., Hökelek T., Süzen Y., Koç L.Y., Açık L., Çelik Z. B., *Eur. J. Med. Chem.*, 70 (2013) 294-307.
2. Mudryk Z. J., Perliński P., Antonowicz J., Robak D., *Mar. Pollut. Bull.*, 101 (2015) 566-574.
3. Cupisti A., Zadeh K. K., *Seminars in Nephrology*, 33 (2013) 180-190.
4. Dabrzalska M., Zablocka M., Mignani S., Majoral J. P., Maculewicz B. K., *Int. J. Pharm.*, 492 (2015) 266-274.
5. Engel R., Cohen J. L. I., *Synthesis of Carbon-Phosphorus Bonds*, 2nd ed., CRC Press, Boca Raton, 2003.
6. Kann, N., Rein, T., *Synthesis*, 13 (2003) 579-595.
7. Bricklebank N., *Organophosphorus Chem.*, 33 (2003) 289-320.
8. Ellis B. D., Macdonald C. L. B., *Inorg. Chem.*, 45 (2006) 6864-6874.
9. Gilheany D. G., in Hartley F. R. (ed.), *The Chemistry of Organophosphorus Compounds*, Wiley, Chichester, England, pp. 1-52, 1992.
10. Horner L., Hoffmann H., Wippel H. G., Klahre G., *Eur. J. Inorg. Chem.*, 92 (1959) 2499-2505.
11. Diel P. J., Maier L., *Phosphorus and sulfur*, 20 (1984) 313-321.
12. Hori T., Horiguchi M., Hayashi A., (eds.) *Biochemistry of natural C-P compounds*. Japanese Association for Research on the Biochemistry of C-P Compounds, 1984.
13. Engel R., *Chem. Rev.*, 77 (1977) 349-367.
14. Blackburn G. M., *Chem. Ind.*, 7 (1981) 134-138.
15. Fleisch H., in *Handbook of Experimental Pharmacology*, Baker P. F. (ed.), Springer, Berlin-Heidelberg, 83 (1988) 441-435.
16. Weissmermel K., Arpe H.-J., *Chimie Organique Industrielle*, Masson, Paris, 74, 1981.
17. Rico I., Wakselman C., *Tetrahedron Lett.*, 22 (1981) 323-326.
18. Mouzdahir A., Thèse de Doctorat de 3^{ème} cycle, Chouaib Doukkali University, Faculty of Science, El Jadida, 1995.
19. Frisch M. J. et al., *Gaussian 09*, Gaussian Inc, Wallingford CT (2009).
20. Hehre W. J., Schleyer L. R., Pople J. A., *Ab initio Molecular Orbital Theory*, Wiley, New York, (1986).
21. Castro E. V. R., Jorge F. E., *J. Chem. Phys.*, 108 (1998) 5225-5229.
22. Mulliken R. S., *J. Chem. Phys.*, 23 (1955) 1833-1840.
23. Reed A. E., Weinhold F., *J. Chem. Phys.*, 78 (1988) 4066-4073.
24. Mendez F., Gazquez J. L., *J. Am. Chem. Soc.*, 116 (1944) 9298-9301.

25. Rauk A., Orbital interaction theory of organic chemistry, Wiley, New York (1994).
26. Mebi C. A., *J. Chem. Sci.*, 123 (2011) 727-731.
27. Geerlings P., De proft F., Langenaeker W., *Chem. Rev.*, 103 (2003) 1793-1873.
28. Parr R. G., Yang W., Density-functional Theory of Atoms and Molecules, Oxford University Press, New York/Oxford (1989).
29. Parr R. G., Pearson R. G., *J. Am. Chem. Soc.*, 105 (1983) 7512-7516.
30. Pérez P., Domingo L. R., Duque-Noreña M., Chamorro E., *J. Mol. Struct. (Theochem)*, 895 (2009) 86-91.
31. Domingo L. R., Chamorro E., Pérez P., *J. Org. Chem.*, 73 (2008) 4615-4624.
32. Soto-Delgado J., Domingo L. R., Contreras R., *Org. Biomol. Chem.*, 8 (2010) 3678-3683.
33. Gazquez J. L., Mendez F., *J. Phys. Chem.*, 98 (1994) 4591-4593.
34. Mendez F., Gazquez J. L., *J. Am. Chem. Soc.*, 116 (1994) 9298-9301.
35. Parr R. G., Yang W., *J. Am. Chem. Soc.*, 106, pp. 4049-4050, 1984.
36. Domingo L. R., Aurell M. J., Pérez P., Contreras R., *J. Phys. A*, 106 (2002) 6871-6875.
37. Domingo L. R., Pérez P., Sáez J. A., *RSC Advances*, 3 (2013) 1486-1494.