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Understanding, the regio- and stereoselective in McKenna Reaction using DFT calculation

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ABSTRACT

In this study, we used DFT B3LYP/6-31G(d) to determine certain thermodynamic properties, global indices and chemical potentials of the reaction between phosphine and bromotrimethylsilane (McKenna Reaction). Our results show that phosphine behaves as a nucleophile, while bromotrimethylsilane behaves as an electrophile. The nucleophilic attack takes place preferentially at the oxygen atom of the double bond of phosphine. The reaction is exothermic, regioselective and stereoselective.

Keywords: DFT B3LYP/ 6-31(d), regioselectivity, stereoselectivity, nucleophilicity, Parr functions.

INTRODUCTION

Phosphonic acids having a hetero atom in position α and β have attracted much attention in recent years because they are involved in many biological processes such inhibitors, these compounds have been widely applied in medicine and biochemistry, as antibacterial agents, enzymes renin, thrombin, and anti-HIV agents. [1]

Acid bis-naphthyl β -ketophosphonate, for example, appears as a new non-peptide inhibitor of neutrophil cathepsin G ($K_i = 38\mu\text{M}$) and chymase ($K_i = 2,3\mu\text{M}$). [2] The glutamyl- β -ketophosphonate adenosine (Glu-KPA) is a competitive inhibitor of glutamyl-tRNA synthetase from Escherichia coli (GluRS) with the K_i 18 μm , while the α , α -difluoro- β -cetophosphonates serve as 'effective inhibitors of protein tyrosine phosphatase. [3]

Regarding similar α - α -cétophosphonates of glutarate, they are known to inhibit the activity of the isolated α -cétoglutaratedéshydrogénase complex from the brain and cultured cells. [4]

For these reasons, the development of simple and stereoselective methods to prepare phosphonates has become important in organic synthesis. [5] Even though there are numerous methods for their syntheses, [6] those relying on the formation of silicon-phosphorous bonds by transition metal catalyzed cross coupling or addition reactions are particularly noteworthy due to their overall efficiency and selectivity. [7] Our aim in this work is to present a theoretical study of McKenna Reaction, Which Oxygen Attacks Bromotrimethylsilane? (Figure 1) and compared the results of our calculations with experimental results available in the literature. [8]

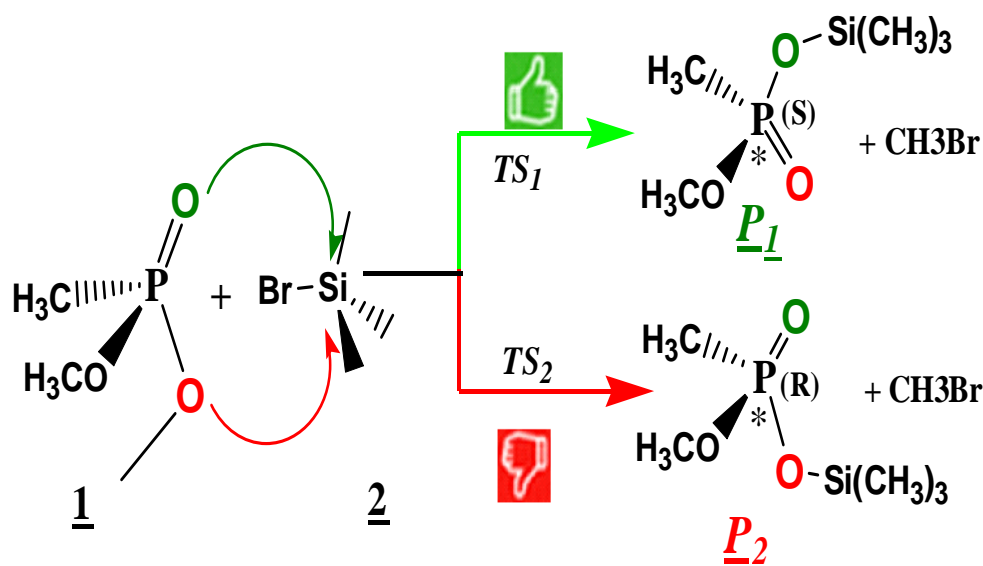


Fig. 1: Reaction between bromotrimethylsilane

MATERIALS AND METHODS

COMPUTATIONAL METHODS

DFT computations were carried out using the B3LYP functional, [9] together with the standard 6-31G/ basis set. [10] The optimizations were carried out using the Berny analytical gradient optimization method. [11] The stationary points were characterized by frequency computations in order to verify that TSs have one and only one imaginary frequency. The IRC paths [12] were traced in order to check the energy profiles connecting each TS to the two associated minima of the proposed mechanism using the second order González–Schlegel integration method. [13]

Solvent effects of acetonitrile were taken into account through single point energy calculations using the polarisable continuum model (PCM) as developed by Tomasi's group [14] in the framework of the self-consistent reaction field (SCRF). [15] The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method. [16] All computations were carried out with the Gaussian 09 suite of programs. [17] The global electrophilicity index [18] ω , is given by the following expression, $\omega = (\mu^2/2\eta)$, in terms of the electronic chemical potential μ and the chemical hardness η . Both quantities may be approached in terms of the one-electron energies of the frontier molecular orbital HOMO and LUMO, e_H and e_L , as $\mu = (e_H - e_L)/2$ and $\eta = (e_L - e_H)$, respectively. [19] Recently, we introduced an empirical (relative) nucleophilicity index N , [20] based on the HOMO energies obtained within the Kohn–Sham scheme, [21] and defined as $N = E_{\text{HOMO}}(\text{Nu}) - E_{\text{HOMO}}(\text{TCE})$. The nucleophilicity is referred to tetracyanoethylene (TCE), because it presents the lowest HOMO energy in a large series of molecules already investigated in the context of polar cycloadditions. This choice allows us to handle conveniently a nucleophilicity scale of positive values. Electrophilic P_k^+ and nucleophilic P_k^- Parr functions, [22] were obtained through the analysis of the Mulliken atomic spin density (ASD) of the radical anion and radical cation of the reagents. The local electrophilicity indices and local nucleophilicity indices, [22] were evaluated using the following expressions: $\omega_k = \omega \cdot P_k^+$, $N_k = N \cdot P_k^-$. [22]

RESULTS AND DISCUSSION

3.1. Analysis of the reactivity indices of the reactants.

The static global properties, namely electronic chemical potential μ , chemical hardness η , global electrophilicity index ω and global nucleophilicity index N of phosphite and bromotrimethylsilane are the chemical properties which we used to analyse reactivity at the various sites in the reactants (Table1).

Table 1: DFT/B3LYP/6-31G(d) Electronic chemical potential, μ , chemical hardness, η , electrophilicity ω , and nucleophilicity N values, in eV

	η	μ	ω	N
phosphite	6.90	-3.43	0.85	2.64
Bromotri-methylsilane	8.08	-3.52	0.76	1.96

We can deduce from table 1 that:

- The electronic chemical potential of phosphite is greater than that of the bromotrimethylsilane, which implies that electron transfer takes place from phosphite to the bromotrimethylsilane.
- The nucleophilicity index of the phosphite (2.64 eV) is greater than that of the bromotrimethylsilane (1.96 eV), implying that in this reaction phosphite behaves as a nucleophile while the bromotrimethylsilane behave as electrophiles.

3.2. Prediction of the regioselectivity of the reaction using local electrophilicity and local nucleophilicity indices.

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.^{24,25} 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 phosphite and ω_k for bromotrimethylsilane in order to predict the most likely electrophile/nucleophile interaction throughout the reaction pathway and so explain the regioselectivity of the reaction.

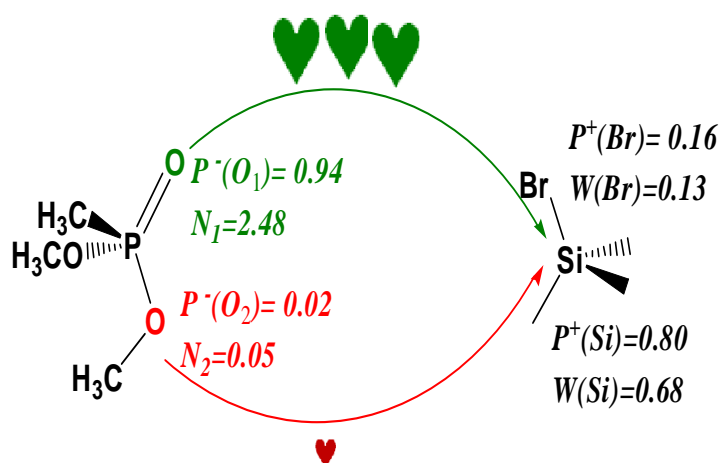


Figure 2: Local nucleophilicity N_k (eV) of phosphine and local electrophilicity ω_k (eV) of bromotrimethylsilane

The silane atom of bromotrimethylsilane is the most electrophilic active site ($\omega_{Si} = 0.68$ eV). The O1 ($N_{O1} = 2.48$ eV) atom of the double bond of phosphine is more nucleophilic and more active than O2 ($N_{O2} = 0.05$ eV) atom. Figure 2 shows the most active sites of phosphine and bromotrimethylsilane. We can therefore deduce that the most favored interaction will take place between the O1 atom of the double bond of phosphine and the Si atom of bromotrimethylsilane.

3.3. Kinetic study of the two modes of attack (Determination of the kinetic parameters).

Calculation of the enthalpies, free energies and entropies of the reactants, the products obtained, TS1 and TS2. Show that the attack is kinetically preferred at oxygen atom O1 (Table 2). Using the data given in Table 1, we can sketch the energy profile of the reaction (Fig. 3).

Table 2: B3LYP/6-31(d) Gibbs free energies (ΔG in kcal mol⁻¹, enthalpies (ΔH in kcal mol⁻¹), entropies (ΔS in cal mol⁻¹ K⁻¹), and), computed at gaz and in acetonitrile for the reactions S and R

	Reaction S		Reaction R	
	Gaz	acetonitrile	Gaz	acetonitrile
ΔG^\ddagger	11.92	10.66	30.74	22.59
ΔG	-56.47	-48.94	-52.08	-48.31
ΔH^\ddagger	89.10	87.22	108.55	101.02
ΔH	-91.61	+40.78	-35.76	+40.78
ΔS^\ddagger	-30.30	-31.87	-27.169	-27.34
ΔS	9.21	11.33	10.68	9.33

This shows that: The activation Gibbs free energies corresponding to the attack at the two oxygen atoms O1 and O2 of the phosphine are 11.92 kcal mol⁻¹ at O1 and 30.74 kcal mol⁻¹ at O2. The difference between the activation Gibbs free energies of P1 and P2 is around 20.82 kcal mol⁻¹, showing that the formation of S isomers is kinetically preferred to the formation of R isomers. This result is in agreement with experimental results. The formation of P1 and P2 is exothermic, by -56.47 and -48.31 kcal mol⁻¹, respectively. The formation of P1 and P2 is thermodynamically favorable.

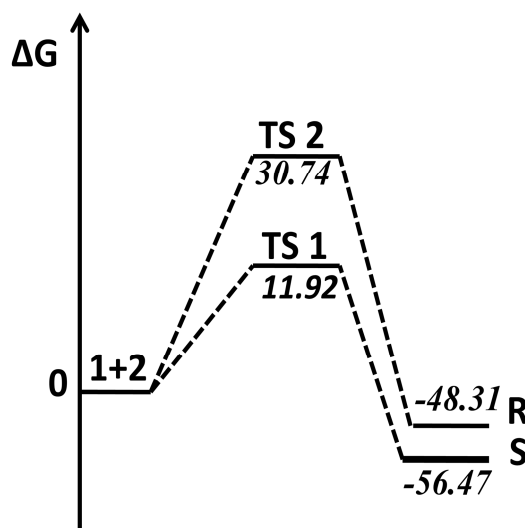


Fig.3: B3LYP/6-31G(d) Gibbs free energy profile (ΔG , in kcal/mol) of the reaction between phosphine and bromotrimethylsilane. Relative Gibbs free energies, in kcal/mol, are in italics

The geometries of the TSs involved in the regioisomeric pathways of these reactions between phosphine and bromotrimethylsilane are given in Fig. 4. The lengths of the O1–Si and C–Br forming bonds at the configuration R are 3.026 and 2.001 Å, while the lengths of the O2–Si and C–Br forming bonds at the configuration S are 3.312 and 2.643 Å. Some appealing conclusions can be drawn from these geometrical parameters: (i) the most favourable configuration R is more asynchronous than the configuration S; (ii) the TSs involved in the configuration R reaction are more asynchronous than those involved in the configuration S.

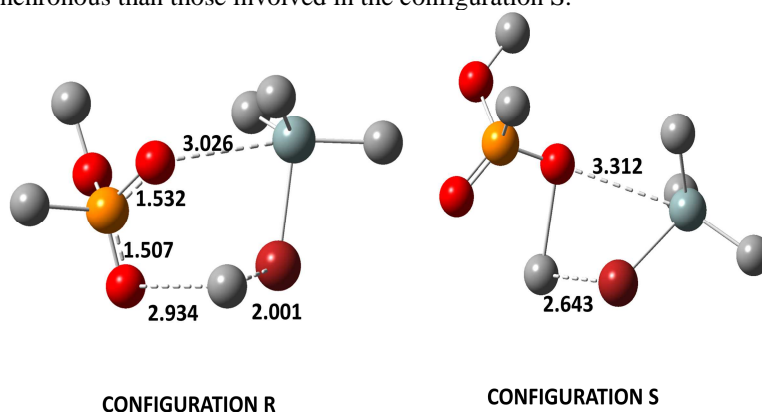


Fig. 4: Geometries of the TSs involved in the regioisomeric pathways associated between phosphine and bromotrimethylsilane. Distances are given in Angstroms

CONCLUSION

The regio- and stereoselectivity of the reaction between phosphine and bromotrimethylsilane was studied using DFT/B3LYP/6-31G(d). Analysis of the global electrophilicity and nucleophilicity indices showed that phosphine behaves as a nucleophile, while bromotrimethylsilane behaves as an electrophile. The regioselectivity found experimentally was confirmed by local indices of electrophilicity and nucleophilicity ω_k and N_k . Calculation of the transition states shows that the formation of the product S is most favored than product R.

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