

◆ Abstract

Alkyl and aryl phosphites have been modeled using the B3LYP DFT functional and the 6-31++G** basis sets for all atoms. Energies of the reactants are compared to the intermediate and product structures to determine the thermodynamic favorabilities of the different hydrolysis pathways. Hydrolysis mechanisms under acidic, basic, and neutral conditions are explored. Substituent effects on pathway preferences and energies are described. Bronsted base properties of the modeled phosphites have been explored concurrently.

◆ Introduction

Phosphites have been known for their moisture sensitivity for some time. Experimental testing on a few examples have been reported though primarily focus on alkylphosphites.¹ Furthermore, little if any actual mechanistic insight has been gained through these studies and the primary conclusions coming from them is that some are more sensitive than others and some generalized trends have been established.^{2,3} No previously reported computational investigation has been conducted on these types of reactions.

◆ Objectives

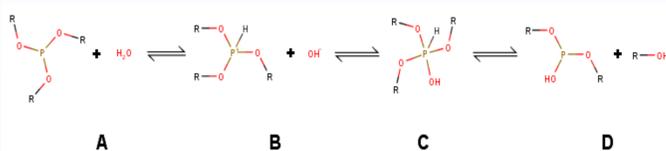
1. Identify possible pathways for the hydrolysis of alkyl and aryl phosphites under acidic, basic, and neutral conditions.
2. Model reactants, intermediates, and products for each pathway identified using the B3LYP DFT functional and 6-311++G** basis sets for all atoms.
3. Determine thermodynamic favorabilities of different hydrolysis pathways while also comparing substituent effects on pathway preference.
4. Determine the viability of gas phase modeling approach for mechanistic determination.

◆ Methods

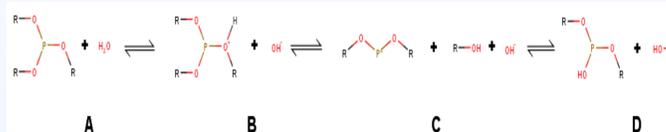
All structures were pre-optimized at the HF/3-21G level of theory and then optimized in the gas phase via DFT methods using the B3LYP method and 6-31++G** basis set.

◆ Mechanisms/Pathways

Neutral Condition Mechanisms:

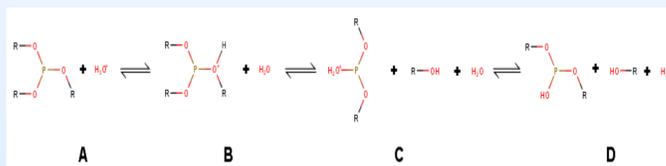


Mechanism 1: Initiated by water, phosphorus protonation.

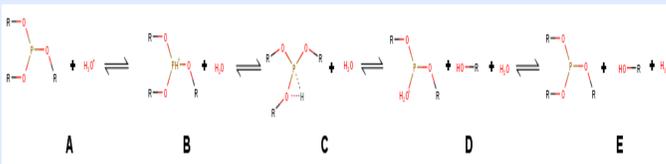


Mechanism 2: Initiated by water, oxygen protonation with phosphonium intermediate.

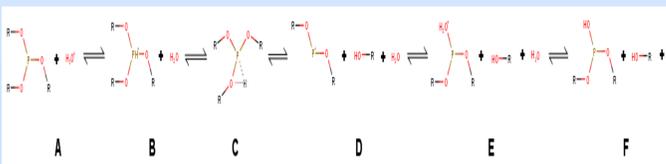
Acidic Condition Mechanisms:



Mechanism 3: Initiated by hydronium, oxygen protonation.

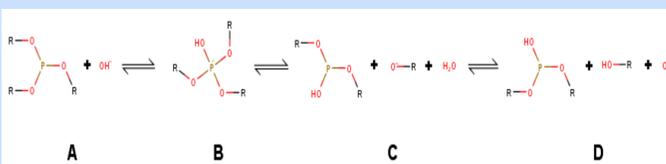


Mechanism 4: Initiated by hydronium, phosphorus protonation with cyclic intermediate.



Mechanism 5: Initiated by hydronium, phosphorus protonation with cyclic and phosphonium intermediate.

Basic Condition Mechanism:



Mechanism 6: Initiated by hydroxide, negative intermediate.

◆ Pathway Energies

Neutral Condition Energies (kcal):

Mechanism 1 Energies

Species	A	B	C	D
P(OMe) ₃	0	173.76	3.93	816.06
P(OPh) ₃	0	176.05	4.34	-4.72

Mechanism 2 Energies

Species	A	B	C	D
P(OMe) ₃	0	188.82	1026.10	816.06
P(OPh) ₃	0	186.18	203.43	-4.72

Under neutral conditions, the mechanism appears to be unfavorable beginning at the protonation step. The mechanism with the phosphonium being attacked is especially unfavorable.

Acidic Condition Energies (kcal):

Mechanism 3 Energies

Species	A	B	C	D
P(OMe) ₃	0	-540.14	-47,679.05	-47,139.55
P(OPh) ₃	0	-542.78	-48,498.18	-47,960.33

Mechanism 4 Energies

Species	A	B	C	D	E
P(OMe) ₃	0	-555.20	-540.14	-47,679.05	-47,139.55
P(OPh) ₃	0	-552.91	-542.78	-48,498.18	-47,960.33

Mechanism 5 Energies

Species	A	B	C	D	E	F
P(OMe) ₃	0	-555.20	47,415.48	297.15	-47,679.05	-47,139.55
P(OPh) ₃	0	-552.91	47,412.84	-525.52	-48,498.18	-47,960.33

Under acidic conditions, mechanisms 3 and 4 appear to be extremely favorable. Mechanism 5 is unfavorable when the ROH leaves making it an unlikely mechanism due to the hill it would have to overcome. Compared to the neutral conditions, the acidic conditions ends with a hydronium ion which is what makes the products so favorable. In the neutral conditions, the water at the beginning is used up in the mechanism.

Basic Condition Energies (kcal):

Mechanism 6 Energies:

Species	A	B	C	D
P(OMe) ₃	0	138.70	-47,964.67	-47,139.55
P(OPh) ₃	0	116.79	-48,002.04	-47,960.33

Under basic conditions the mechanism is very favorable when looking at the products. The biggest hill for this mechanism is leaving of the RO- group. This is similar to the protonation steps of mechanisms 1 and 2 which are under neutral conditions. Otherwise, this mechanism has the same energy favorability as mechanism 3 and 4 which are under acidic conditions.

◆ Discussion

When looking at the relative energies of the pathways, it appears that acidic and basic conditions are more favorable for the hydrolysis of phosphites versus neutral conditions. The neutral conditions seem to be less favorable because the water that hydrolyzes the phosphite is consumed in the process; whereas, the hydronium and hydroxide ions are part of the products at the end of the acidic and basic condition pathways. We also show that triphenylphosphite is more susceptible to hydrolysis (independent of pathway) when compared to trimethylphosphite. This is especially surprising for O-protonation steps given the presumed partial delocalization of electron density from the oxygen into the phenyl ring. These geometries were modeled in the gas phase (i.e. not accounting for solvent effects). After looking at the numbers, it appears that an alternative method might be yield better results. The energy values are of a high enough magnitude to cause us to view them with skepticism.

◆ Future Work

After scouting the beginnings of this project, there are several directions that it could take.

1. Exploring other DFT functionals to compare their effects.
2. Modeling with solvent effects accounted for via implicit and/or explicit approaches.
3. Replacing alkoxy group(s) with other substituents to compare the effects it has on the hydrolysis of the remaining alkoxy group(s).
4. Begin experimental determinations of hydrolysis kinetics via ³¹P NMR.

◆ References

1. Westheimer, F. H.; Huang, S.; Covitz, F. J. *Am. Chem. Soc.* **1988**, *110*, 181-185.
2. Oberhauser, W.; Manca, G. *Inorg. Chem.* **2018**, *57*, 4824-4827.
3. Aksnes, G.; Froyen, P. *Phosphorus, Silicon, Sulfur, and Relat. Elem.* **1991**, *63*, 45-50.

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