Comparative ab Initio Treatment (Hartree−Fock, Density Functional Theory, MP2, and Quadratic Configuration Interactions) of the Cycloaddition of Phosphorus Ylides with Formaldehyde in the Gas Phase[1]

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In this study we describe the results of the application of several ab initio methods to the reactions in the gas phase of four unstabilized ylides ($H_3P{=}CH_2$, $H_2MeP{=}CH_2$, $HMe_2P{=}CH_2$, and $Me_3P{=}CH_2$) with formaldehyde to form their respective oxaphosphetanes. At the HF level, $H_3P{=}CH_2$ and $H_2MeP{=}CH_2$ proceeded to the formation of oxaphosphetane. However, at the B3LYP, MP2, and QCISD levels, these ylides react by a nucleophilic attack of the ylidic carbon on the carbonyl group, concomitant with the proton abstraction from the phosphorus atom to form 2-phosphinoethanol. This unusual dependence of the reaction path on the level of theory indicates that $H_3P{=}CH_2$, the most popular ylide for modeling the Wittig reaction, is atypical and raises questions regarding its use as a suitable model for more realistic systems. At all levels of theory (HF, B3LYP, and MP2), the reactions of $HMe_2P{=}CH_2$ and $Me_3P{=}CH_2$ with formaldehyde proceed in a cycloaddition-like fashion to yield oxaphosphetanes. The calculated barriers for these processes varied considerably with the level of correlation and the basis sets employed. The geometries of reactants, intermediates, transition states, and products did not change significantly with the level of theory or basis set employed. The use of B3LYP or MP2 calculations with the 6-31G* basis set is a reasonable compromise between computational expense and level of rigor to describe the Wittig reaction. Our results suggest that for alkyl-substituted ylides, HF geometries along the reaction profile resemble the ones obtained with B3YLP and MP2 methods. Therefore, the Wittig reaction can be properly described at the ab initio level using B3YLP or MP2 single-point energies on the respective HF geometries.

Introduction

Ab initio molecular orbital, MO, methods have been extensively applied to the study of mechanisms of reactions,[2] particularly for reactions where the experimental evidence has led to several interpretations of the possible reaction paths between the reactants and the products.

The reaction of a phosphorus ylide (**1**) with an aldehyde or ketone to form an alkene and a phosphine oxide (**4**) is known as the Wittig olefination reaction (Scheme 1). The Wittig reaction is one of the most important methods for the formation of carbon−carbon bonds in synthetic organic chemistry.[3] Several mechanistic hypotheses that include intermediates such as oxaphosphetanes (**2**) and betaines (**3**) have been considered.[3b,4,5]

Oxaphosphetanes have been observed by NMR spectroscopy for the reactions of unstabilized ylides (R^1 = alkyl). For Wittig reactions involving semistabilized (R^1 = phenyl, vinyl, propargyl) or stabilized ylides ($R^1 = -COOCH_3$, $-CN$) oxaphosphetanes have not been observed spectroscopically[6] presumably because in these cases, oxaphosphetanes are only transient intermediates whose lifetimes are too short compared with the NMR time scale. Betaines have been isolated as stable salts,[3] but they have not been observed spectroscopically. The original mechanism proposed by Wittig[11a,b] and refined by others[11c−g] calls for betaines as mandatory intermediates in order to explain the observed stereochemistry;[11] however, betaine involvement along the reaction path has been questioned.[12]

There are several long-standing controversies[4] regarding the mechanism of the Wittig olefination reaction. Many lines of evidence indicate that the first step in the reaction is a nucleophilic attack of the ylidic carbon on the carbonyl group of the aldehyde or ketone. Whether this attack leads to a stable zwitterionic intermediate such as an “anti” or “syn” betaine has not been completely resolved.[3b,4] The formation of oxaphosphetanes is the next step along the pathway of the olefination. During the course of this paper, we will refer to the step where an ylide reacts with formaldehyde to afford the oxaphosphetane, as the “Wittig half-reaction”. Pseudorotation around the phosphorus atom, placing the oxygen atom in an equatorial position, has been postulated as a necessary step toward the “syn” elimination that leads to the formation of the alkene and the respective phosphine oxide.

Several mechanisms for the Wittig reaction have been postulated throughout the years including stepwise ionic pathways.[4] Vedejs[13] and Schlosser[14] have postulated one-step cycloaddition mechanisms for the direct formation of oxaphosphetanes. Mechanisms involving an electron-transfer reaction have been proposed by Olah[15] and Yamataka.[16] McEwen[17] proposed a mechanism that calls for a spin-paired diradical as an intermediate. All these proposed mechanisms represent attempts to accommodate the experimental evidence. Unfor-

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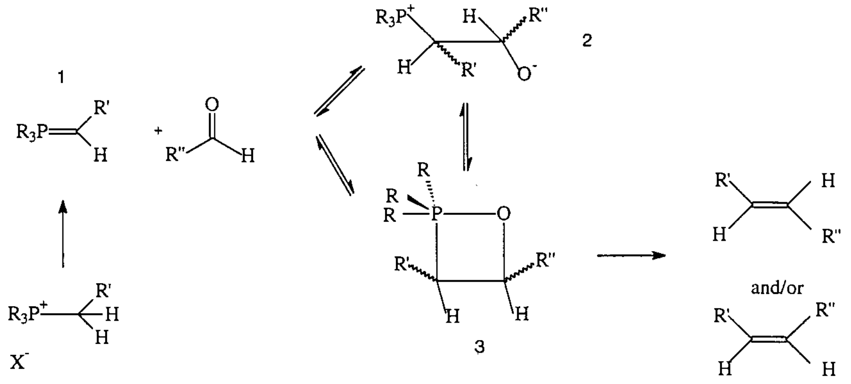
SCHEME 1



tunately, one way or the other, some aspects in all of them remain essentially unsubstantiated.

There is no direct experimental evidence that indicates what is the most likely nature of the transition state involved in the Wittig half-reaction. In addition, the lack of spectroscopic detection of possible transient intermediates such as betaines, spin-paired diradicals, or charge-transfer complexes[15,18] cannot rule out their involvement in the Wittig reaction. Theoretical methods constitute a means to determine and characterize the stationary points involved in chemical processes, including reactants, transition states, and products.

Several theoretical studies have been reported on the Wittig reaction using different levels of theory.[19−24] The first theoretical method to be applied was CNDO by Trindle et al.[19] Since then MNDO,[20] HF/STO-3G,[21] HF/4-31G*,[22] MNDO-PM3,[20,23] HF/3-21G*,[23] HF/6-31G*,[24] HF/DZ+d,[24] and MP2/DZ+d[24] have been applied to the study of the prototype reaction of $H_3P{=}CH_2$ (methylidenephosphorane) with formaldehyde to yield the respective oxaphosphetane (we have named this process the "mythical Wittig half-reaction"). In addition, MNDO-PM3[26] and MNDO[26] calculations have been done on larger systems that bear phenyl substituents on the phosphorus atom. More recently, we have carried out MP2//HF/6-31G* calculations in a series of model reactions of unstabilized ($Me_3P{=}CH{-}CH_3$), semistabilized ($Me_3P{=}CH{-}C{\equiv}CH$), and stabilized ($Me_3P{=}CH{-}C{\equiv}N$) ylides with acetaldehyde in order to compare their reactivity.[27]

Other theoretical studies have been recently carried on the analogous Wittig−Horner reaction[28−30] (also known as the Horner−Wadsworth−Emmons reaction). This reaction involves the cycloaddition of phosphonate reagents with aldehydes. These studies include HF/6-31G*, B3LYP/6-31G*, and MP2//B3LYP/6-31G* calculations in the gas phase[28] and B3LYP/6-311+G**//B3LYP/6-31G* in conjuntion with the PCM/DIR formalism for calculations in solution.[28] Metal ion effects on the Wittig−Horner reaction have also been investigated at ab initio[29,30] and semiempirical[30] levels of theory.

The mythical Wittig half-reaction is an appealing model to describe the formation of the oxaphosphetane; it is the smallest system that can, in principle, undergo the Wittig reaction. Furthermore, it does not exhibit conformational changes that would complicate the analysis of the mechanisms involved in these processes. These features allow the theoretical treatment of the model at reasonably high levels of correlation while keeping the computational expense within reach.

In this work, we use several ab initio molecular orbital calculations to study the mechanism and energetics of the Wittig half-reaction of unstabilized ylides with formaldehyde in the gas phase. Our aim is to analyze the effect of different levels of theory (HF, B3LYP, MP2, and QCISD) and different basis sets (6-31G*, 6-31+G*, and 6-31+G**) on the geometries and energetics of the reaction. We have systematically replaced the H substituents on the phosphorus atom in the mythical reaction by methyl groups in order to develop a more realistic model of the Wittig reaction. The results of this study show that the use of the widely studied mythical Wittig half-reaction in the gas phase, $H_3P{=}CH_2 + CH_2O \rightarrow$ oxaphosphetane, is not adequate to describe the general reaction. Instead, the results from the reaction of methylidenetrimethylphosphorane, $(CH_3)_3P{=}CH_2$, with formaldehyde are a more realistic model of Wittig-like cycloaddition processes.

Methodology

The model reactions selected for the present study are those of the unstabilized ylides methylidenephosphorane ($H_3P{=}CH_2$), methylidenemethylphosphorane ($H_2MeP{=}CH_2$), methylidenedimethylphosphorane ($HMe_2P{=}CH_2$), and methylidenetrimethylphosphorane ($Me_3P{=}CH_2$) with formaldehyde to form their respective oxaphosphetanes (Scheme 2).

We have already justified the importance of such Wittig half-reactions as models for attempting to explain mechanistically the experimental observations for the overall olefination reaction.[22] The model reactions used for this study are based on the assumption that the ylide and the aldehyde are aligned properly for a one-step cycloaddition reaction.

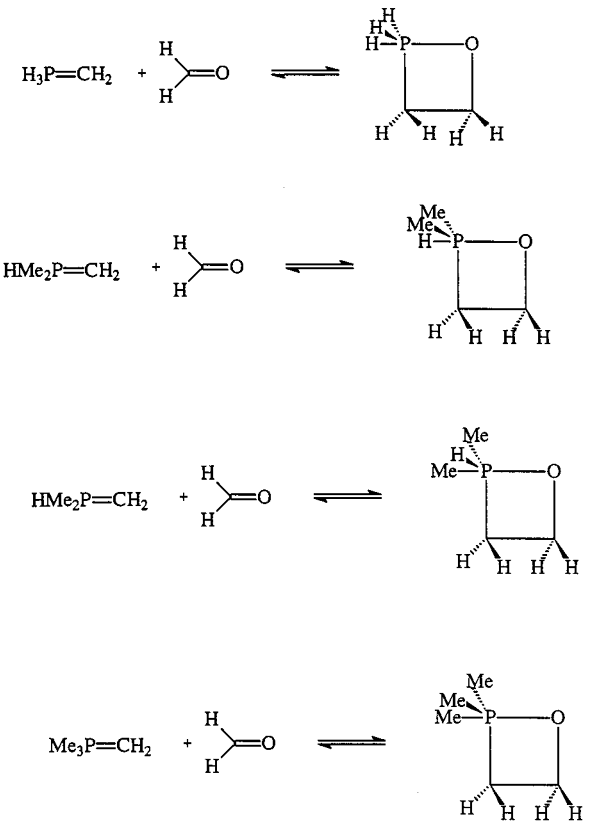
All geometry optimizations and energy calculations were carried out using the Gaussian 94 suite of programs.[31,32] For the reactions of $H_3P{=}CH_2$ and $Me_3P{=}CH_2$ the reactants, intermediates, transition states, and products were fully optimized with the 6-31G*, 6-31+G*, and 6-31+G** basis sets at the Hartree−Fock (HF) and MP2(Full) levels of theory. Calculations using density functional theory methodology were carried out using the three-parameter hybrid functional B3LYP:[33]

$$E_{xc}^{B3LYP} = (1 - a_0)E_x^{LSDA} + a_0E_x^{HF} + a_x\Delta E^{B88} + a_cE_c^{LYP} + (1 - a_c)E_c^{VWN} \quad (1)$$

where $a_0 = 0.20$, $a_x = 0.72$, and $a_c = 0.81$.

In this equation, E_x^{LSDA} is the local Slater exchange energy, E_x^{HF} is the exact exchange energy given by the Hartree−Fock formalism, ΔE^{B88} is Becke's gradient-corrected exchange energy,[34] E_c^{LYP} is the gradient-corrected correlation energy developed by Lee, Yang, and Parr,[35] and E_c^{VWN} is the local correlation energy of Vosko, Wilk, and Nussair.[36] Expression 1 is a variant of Becke's original hybrid functional designed to

SCHEME 2



rectify the failure of conventional DFT in reproducing the exchange-only limit of the adiabatic connection method, ACM.[37]

In the case of the reaction of methylidenephosphorane ($H_3P{=}CH_2$), full optimization was also carried out at the QCISD level of theory with the basis sets described above. For the reactions of $H_2MeP{=}CH_2$ and $HMe_2P{=}CH_2$, calculations were carried out at the MP2/6-31G* level. As a test for the reliability of the structural predictions in this work, geometry optimizations were performed on triisopropylphosphonium isopropylylide (i-$Pr_3P{=}CMe_2$), whose structure has been determined by X-ray crystallography.[38] Further comparison can be drawn from methylidenetrimethylphosphorane, one of the reactants in one of our model reactions, whose structure has been determined by electron diffraction.[39] The calculations were carried out on DEC Alpha AS/600 computers, which are 333 MHz computers[32] at the Multidisciplinary Research Computer Facility at Florida Atlantic University.

The geometrical optimizations for all model reactions were performed using the Berny algorithm.[40] All stationary points were characterized as minima or transition states, TS, by analytical frequency calculations at HF and MP2 levels. Reaction paths were computed using the IRC method developed by Gonzalez and Schlegel.[41] Relative energies were also computed at the QCISD(T)/6-31+G**//MP2/6-31+G** level for the reactions of $H_3P{=}CH_2$ and $Me_3P{=}CH_2$ and at the QCISD(T)/6-31+G**//QCISD/6-31+G** level for the reaction of $H_3P{=}CH_2$. MP2 zero-point energy corrections were also computed and used to obtain the energetics of the reaction.

Results and Discussion

Figure 1shows the geometries of the intermediates, transition states, and products of the model reactions used in this study. The paths for the model reactions (Scheme 2) vary dramatically depending upon the substituents on the phosphorus atom of the ylide and the level of theory employed. For the reaction of $H_3P{=}CH_2$ two substantially different pathways were observed. At the HF level, a classical Wittig-like cycloaddition affording the respective oxaphosphetane is obtained (Figure 1A). However, reaction paths computed with the better correlated formalisms B3LYP, MP2, and QCISD indicate that ylide carbon nucleophilically attacks the carbonyl group while a proton transfers from the phosphorus atom to the carbonylic oxygen to form 2-phosphinoethanol (see Figure 1b). This reaction pathway obtained at the HF level was observed regardless of the basis set employed and indicates that HF might be predicting the wrong mechanism governing these reactions.

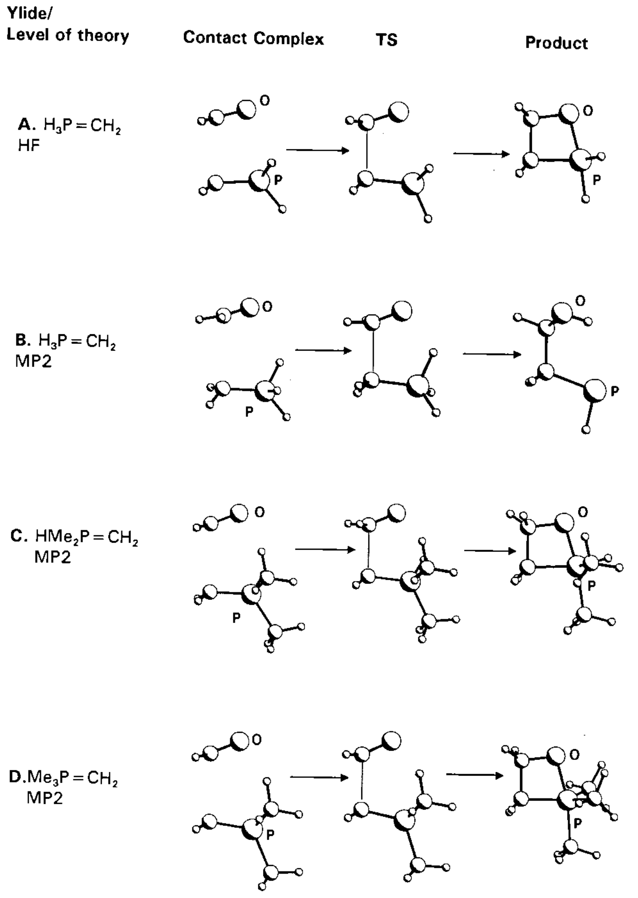


Figure 1. Calculated geometries of the reactants (contact complex), transition states, and products (oxaphosphetanes and 2-phosphinoethanol) for the reactions of $H_3P{=}CH_2$ (A and B), $HMe_2P{=}CH_2$ (C), and $Me_3P{=}CH_2$ (D) at different levels of theory using the 6-31G* basis set.

Proton abstraction is also observed for the reaction of $H_2CH_3P{=}CH_2$ (methylidenemethylphosphorane) with formaldehyde using the MP2/6-31G* level of theory (not shown in Figure 1), whereas a Wittig-like cycloaddition is predicted for the reaction of $HMe_2P{=}CH_2$ (methylidenedimethylphosphorane) with formaldehyde at the same level of theory (Figure 1c). Since proton abstractions are not possible for the reaction of $(CH_3)_3P{=}CH_2$ with formaldehyde, Wittig-like cylcloadditions were obtained instead at all levels of theory (HF, B3LYP, and MP2) with all basis sets (Figure 1d).

All these model reactions proceed through a stepwise process where the first step involves the formation of a contact complex. This contact complex undergoes cycloaddition or proton abstraction depending upon the level of theory employed and the specific reacting ylide as discussed above.

The contact complex is likely to be formed by electrostatic interactions between the ylide and the dipole of the aldehyde.

TABLE 1: Relevant Geometrical Parameters for the Transition States and Relative Energies[a] to the Reactants of the Half-Reaction $H_3P{=}CH_2 + H_2C{=}O \rightarrow$ Product

level	contact complex[b]	TS[b]	oxaphosphetane	2-phosphinoethanol	barrier[c]	C−C[d]	O−P[d]	PCCO[d]	O−H [b,c]
HF/6-31G*	−12.51	37.70	−108.99	−253.01	50.21	2.06	2.69	−0.71	
HF/6-31+G*	−11.13	36.15	−98.83	−242.17	47.28	2.08	2.72	−0.07	
HF/6-31+G**	−11.17	37.28	−94.93	−249.78	48.45	2.08	2.71	0.04	
MP2/6-31G*	−17.32	−1.63	−151.38	−262.71	15.69	2.13	2.86	25.60	1.91
MP2/6-31+G*	−18.62	−8.16	−146.44	−254.18	10.46	2.18	2.92	27.19	2.04
MP2/6-31+G**	−18.79	−12.38	−144.64	−260.54	6.40	2.17	2.9	24.47	2.00
B3LYP/6-31+G**	−13.97	−6.95	−116.48	−241.92	7.03	2.19	2.91	−22.49	1.98
QCISD/6-31G*[e]	−13.39	12.80	−133.43	−264.89	26.19	2.08	2.86	22.57	1.93
QCISD/6-31+G*[e]	−14.94	4.64	−129.20	−259.03	19.58	2.13	2.91	25.10	2.06
QCISD/6-31+G**[e]	−14.77	1.42	−129.66	−263.34	16.19	2.12	2.89	24.76	2.03
QCISD(T)//MP2/6-31G*	−14.52	6.86	−134.64	−260.66	21.34				
QCISD(T)//MP2/6-31+G*	−16.65	−1.76	−132.26	−255.10	14.89				
QCISD(T)//MP2/6-31+G**	−16.61	−5.44	−130.83	−260.70	11.17				
QCISD(T)//B3LYP/6-31G	−15.02	−1.38	−131.71	−260.91	13.68				
QCISD(T)//QCISD/6-31G*	−14.52	7.07	−134.52	−260.62	21.59				
QCISD(T)//QCISD/6-31+G*	−16.65	−1.59	−130.41	−255.10	15.06				
QCISD(T)//QCISD/6-31+G**	−16.65	−5.27	−130.88	−260.83	11.34				

[a] Energies in kJ/mol. [b] Species correspond to the mythical Wittig reaction at the HF level and to the proton abstraction reaction at the B3LYP, MP2, and QCISD levels. [c] Barriers computed from adduct to transition states (intrinsic barriers). [d] Bond distances in angstroms and dihedral angle in degrees. [e] All QCISD and QCISD(T) profiles using MP2 zero-point corrections with the corresponding basis set.

TABLE 2: Relevant Geometrical Parameters for the Transition States and Relative Energies[a] to the Reactants of the Half-Reaction $Me_3P{=}CH_2 + H_2C{=}O \rightarrow$ Oxaphosphetane

level	contact complex	TS[b]	oxaphosphetane	barrier	C−C[b]	O−P[b]	PCCO[b]
HF/6-31G*	−30.58	6.94	−88.66	37.53	2.07	3.07	0.00
HF/6-31+G*	−14.06	24.39	−62.76	38.45	2.09	3.11	−9.35
HF/6-31+G**	−14.10	25.69	−58.24	39.79	2.09	3.10	−8.51
MP2/6-31G*	−31.46	−24.85	−134.39	6.61	2.15	3.13	−0.04
MP2/6-31+G*	−27.11	−21.25	−124.64	5.81	2.24	3.20	−15.83
MP2/6-31+G**	−28.45	−21.84	−124.60	6.61	2.21	3.18	−17.74
B3LYP/6-31+G**	−20.96	−16.15	−88.24	4.81	2.16	3.17	0.00
QCISD(T)//MP2/6-31G*[c]	−27.28	−16.78	−119.87	10.54			
QCISD(T)//MP2/6-31+G*[c]	−24.89	−15.78	−112.42	9.12			
QCISD(T)//MP2/6-31+G**[c]	−26.02	−15.73	−112.09	10.29			

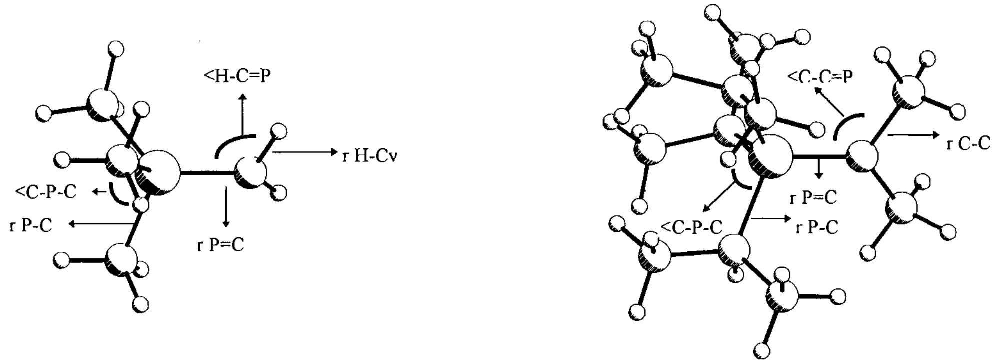
[a] Energies in kJ/mol. [b] Bond distances in angstroms and bond dihedral angles in degrees. [c] All QCISD(T) profiles using MP2 zero-point corrections with the corresponding basis set.

There is no evidence of covalent bonding between the reacting fragments at this stage. The complexes then proceed to form a transition state, which, depending upon the level of theory, will acquire a cycloaddition-like (oxaphosphetane-like) conformation or an abstraction-like (phosphinoethanol-like) conformation. For either mechanism we found only one transition state. By use of eigen-following techniques and the IRC method,[41] it was confirmed that all transition states were connected to their corresponding reactants (complexes) and products (oxaphosphetane or 2-phosphinoethanol, depending on the level of theory).

For the cycloaddition processes (parts A, C, and D of Figure 1), as the C−C formation proceeds, subsequent P−O bond formation requires a rehybridization of the phosphorus atom where the substituents occupy either an axial or an equatorial position on the trigonal-bipyramidal geometry. The TS is a four-centered moiety, where the phosphorus atom, the ylidic carbon, the carbonylic carbon, and the oxygen atom are involved in the concerted bond-forming/bond-breaking process. For the proton abstraction path (Figure 1B), we started with the geometries of the cycloaddition-like path predicted by the HF calculations, where the phosphorus atom, the ylidic carbon, and the carbonyl group lie on the same plane. However, as the proton abstraction proceeds, a rotation around the P−C and the C−C axis (to a lesser extent) brings one of the equatorial protons nearly planar with the phosphorus atom, ylidic carbon, and carbonyl group. Thus, a transition state is formed in which five centers are involved in the bond-forming/bond-breaking process.

Geometries. Tables 1 and 2 show the relevant geometrical parameters at the TS and the relative energies of the different species involved in the Wittig half-reaction of the mythical unstabilized ylide $H_3P{=}CH_2$ and $(CH_3)_3P{=}CH_2$, respectively. For the Wittig type reactions (involving $H_3P{=}CH_2$ at HF and $(CH_3)_3P{=}CH_2$ at all levels) these tables show that adding diffuse functions on the heavy atoms increases the C−C and the O−P distances at the TS by ca. 0.06−0.08 Å. Similar trends are observed in the case of the hydrogen abstraction involving $H_3P{=}CH_2$, as predicted by MP2, B3LYP, and QCISD, where addition of diffuse functions on the heavy atoms lengthens the C−C, O−P, and O−H bonds by at most 0.05, 0.06, and 0.13 Å respectively. In addition, inclusion of a set of polarization functions on the hydrogens decreases the O−H bond lengths by ca. 0.03−0.04 Å. In general, the results obtained from B3LYP computations are in very good agreement with those from the more computationally demanding MP2 and QCISD levels of theory.

In the case of Wittig-like cycloadditions (HF entry in Table 1 and all entries in Table 2), a relatively small P−C−C−O dihedral angle is obtained for the transition state. The degree of puckering seems to be affected by the flexibility of the basis sets used. Thus, although completely planar transition states were found at HF/6-31G* and MP2/6-31G*, some degree of



Parameter	Exp.	Level	Basis Set 6-31G*	 6-31+G*	 6-31+G**
< C-P-C	116.5	HF	115.0	114.7	114.6
		MP2	115.2	114.9	114.9
< H-C=P	120.0	HF	118.4	118.8	118.8
		MP2	116.9	117.7	117.4
r P=C	1.81	HF	1.87	1.68	1.68
		MP2	1.67	1.68	1.68
r P-C	1.64	HF	1.83	1.83	1.83
		MP2	1.83	1.83	1.83
r H-Cy	1.06	HF	1.08	1.08	1.08
		MP2	1.09	1.09	1.08

Parameter	Exp.	HF/6-31G*
< C-P-C	122.1	111.2
< C-C=P	111.2	121.6
r P-C	1.83	1.88
r P=C	1.73	1.69
r C-C	1.50	1.52

Figure 2. Calculated geometries for methylidenetrimethylphosphosphorane ($Me_3P{=}CH_2$) and triisopropylphosphonium isopropylylide (*i*-$Pr_3P{=}CMe_2$) at the HF/6-31G* level. The calculated geometrical parameters at the various basis sets are compared with the known experimental (Exp.) values.[26,27]

puckering was found when larger basis sets were employed. The most puckering was found with MP2/6-31+G** calculations ($\angle PCCO = -17.74°$). A planar transition state is predicted by B3LYP/6-31+G** (Table 2). The relatively long P−O distances observed in the case of the reaction of $(CH_3)_3P{=}CH_2$ clearly suggest that these model Wittig half-reactions become more asynchronous when methyl groups are attached to the phosphorus atom.

As in the case of $Me_3P{=}CH_2$, Wittig-like cycloadditions are obtained for the reaction of $HMe_2P{=}CH_2$. It is noticeable that for these reactions HF calculations provide the same geometries that are obtained at higher levels. In addition, HF geometries are comparable to the ones obtained experimentally for methylidenedimethylphosphorane ($Me_3P{=}CH_2$) by electron diffraction[39] and for triisopropylphosphonium isopropylylide (*i*-$Pr_3P{=}CMe_2$) by X-ray crystallography.[38] Figure 2 shows the calculated geometries of $Me_3P{=}CH_2$ and *i*-$Pr_3P{=}CMe_2$ at the HF/6-31G* level. A comparison of the relevant geometrical parameters calculated at several levels of theory with the experimental ones is also included.

As previously reported by Bachrach for other ylides,[42] the use of basis sets larger than 6-31G* or higher levels of theory resulted in little geometric change. However, unlike Bachrach's ylides, which bear only hydrogen atoms as substituents on the phosphorus atom, our calculations are on ylides that bear alkyl substituents on the phosphorus atom. The calculated structures are in agreement with the experimental geometries of these ylides. Bond distance deviations of less than 0.03 Å for $Me_3P{=}CH_2$ and less than 0.04 Å for *i*-$Pr_3P{=}CMe_2$ are obtained. *p*-Alkyl-substituted unstabilized ylides have nonplanar ylidic carbon geometries, which indicates that the ylide form (ionic species) is predominant.[43] The excellent agreement between the experimental and calculated geometries of these ylides should not be extended to the rest of the Wittig reaction. Profound effects on the reaction path and energetics (see below) are noticed when larger basis sets and higher levels of theory are used.

Energetics. Relative energies associated with the reactions of $H_3P{=}CH_2$ and $(CH_3)_3P{=}CH_2$ are given in Tables 1 and 2, respectively. The results obtained at the various levels of theory used in this study show that the initial contact complexes are predicted to lie 12.5−18.8 kJ/mol below the isolated reactants for the reaction involving $H_3P{=}CH_2$ and to be 14.0−31.5 kJ/mol for the reaction of $(CH_3)_3P{=}CH_2$. The relative energies of these complexes seem to be dependent upon the level of theory but are unaffected by the basis set. The greatest deviation with respect to the QCISD and QCISD(T) results is observed in the case of HF, which underestimates the stabilization energy of the contact complexes by a almost a factor of 2 (Table 2). MP2 and B3LYP predict relative energies for the complexes in significantly better agreement with the QCISD data.

More pronounced energetic differences are observed in the case of the transition states and products (oxaphosphetanes and 2-phosphino-ethanol); although HF predicts transition states lying above the reactants (ca. 37.3 kJ/mol for $H_3P{=}CH_2$ and 25.7 kJ/mol for $(CH_3)_3P{=}CH_2$), B3LYP, MP2, and QCISD results show the opposite, indicating the importance of electron correlation in these processes.

Figure 3 shows the profiles for the reaction of $Me_3P{=}CH_2$ calculated at different levels of theory. For HF calculations there is a considerable overestimation of the energies when compared with QCISD(T). On the other hand, the energetics predicted using B3LYP/6-31+G* and MP2/6-31+G* are slightly underestimated when compared to results of QCISD(T) calculations. These profiles show that the energetics predicted by B3LYP/6-31+G** are in good agreement with the more computationally demanding correlated ab initio methods MP2 and QCISD, and this suggests the possibility of adopting this methodology in the treatment of even larger unstabilized ylides undergoing Wittig-like reactions

Table 1 also shows the calculated QCISD(T) energies on the optimized B3LYP, MP2, and QCISD geometries of the reaction of methylidenephosphorane with formaldehyde. For the proton abstraction reaction yielding 2-phosphinoethanol, the relative

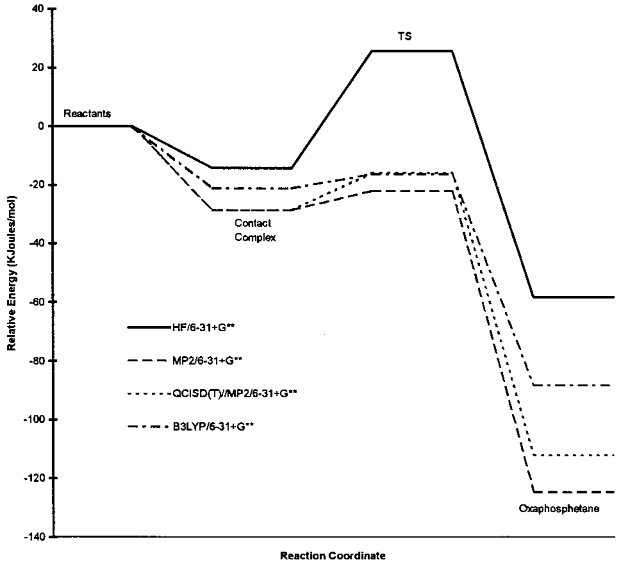


Figure 3. Reaction path profile at different levels of theory for the cycloaddition reaction of $Me_3P{=}CH_2$ with $H_2C{=}O$.

energies calculated at lower levels are in close agreement with those calculated using QCISD(T). However, the energy barriers calculated by QCISD(T) are slightly lower than those predicted by QCISD, which indicates the importance of triple excitations. For the reaction of $Me_3P{=}CH_2$ with formaldehyde giving the corresponding oxaphosphetane, similar trends are observed.

Proton Abstraction vs Cycloaddition. Previous ab initio studies on the Wittig reaction have used the reaction of $H_3P{=}CH_2$ with formaldehyde as a model.[21−24] All these studies have been carried out by using HF calculations, except for a recent study by Naito and co-workers.[24] The use of higher levels of theory (B3LYP, MP2, and QCISD) presents a different scenario for the reaction of $H_3P{=}CH_2$ with formaldehyde; proton abstraction to afford 2-phosphinoethanol is an alternative pathway for the reaction of the mythical ylide.

Our MP2 results are in contrast to those presented by Naito et al.[24] These workers, using the MP2 formalism in conjunction with a mixture of the DZ+d basis for the first-row atoms and effective core potentials for the heavier atoms,[44] predicted that $H_3P{=}CH_2$ undergoes a Wittig-like cycloaddition when it reacts with formaldehyde. In our case, only HF calculations predicted the existence of a transition state for the cycloaddition reactions of $H_3P{=}CH_2$. B3LYP, MP2, and QCISD predicted the proton abstraction process described above. Attempts to obtain a cycloaddition-like transition state for the mythical Wittig half-reaction at the MP2 level always led to the proton abstraction process that produces 2-phosphinoethanol. These attempts included a series of constrained optimizations at the MP2/6-31G*, MP2/6-31+G*, and MP2/6-31+G** levels where the only fixed variable was the interfragment distance and where the geometry reported by Naito et al.[24] was used as a starting point. The same results were obtained using calculations at the B3LYP and QCISD levels.

The surprising difference between our results and the MP2/DZ+d calculations by Naito et al.[24] could be attributed to the use of effective core potentials for the phosphorus atom in their computations. Studies dealing with the applicability of the effective core potential approaches have been well documented in the literature.[45]

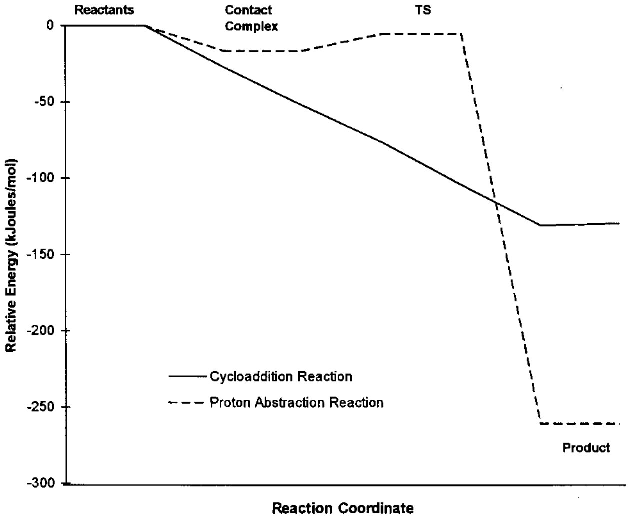


Figure 4. QCISD/6-31G* energy profiles for the possible reactions (cycloaddition and proton abstraction) of $H_3P{=}CH_2$ with formaldehyde.

Figure 4 shows the energy profiles for the reaction of $H_3P{=}CH_2$ as predicted by QCISD/6-31+G** calculations. It can be observed that proton abstraction leading to 2-phosphinoethanol is more exothermic, whereas the cycloaddition reaction leading to formation of oxaphosphetane takes place in a barrierless fashion. Both reactions might be competitive; however, it will be difficult to determine which one is favored by examining purely energetic models. The use of methods such as the canonical variational transition-state theory[46] (CVTST) or the RRKM theory[47] might be useful in answering this question. The possibility of proton abstraction as an alternative pathway for the reaction of $H_3P{=}CH_2$ and $H_2MeP{=}CH_2$ is a consequence of using these particular ylides for our model reaction. Dual pathways are not possible in more realistic Wittig reactions, since proton abstraction is not viable for the reaction of alkylidene or phenylidene phosphoranes, the most common case in experimental Wittig chemistry.

The proton abstraction process is not limited to the reaction of methylidenephosphorane ($H_3P{=}CH_2$); the reaction of $H_2MeP{=}CH_2$ proceeds to proton abstraction at MP2/6-31+G**. However, when the same calculations are performed on the reaction of $HMe_2P{=}CH_2$ with formaldehyde, a Wittig cycloaddition is predicted.

Figure 5 shows two perspectives of the geometries of two possible transition states for the reaction of $HMe_2P{=}CH_2$ with formaldehyde. Cycloaddition is favored over the proton abstraction even when the starting geometry is such that the oxygen and the proton are forced to be close to each other. Figure 5A shows the geometry of a transition state where the proton lies in a pseudoequatorial position; this transition state still leads to cycloaddition. Starting geometries that place the hydrogen in a pseudoaxial position (Figure 5B) are likely to favor cycloaddition, since rotation around the P−C axis would be required for proton abstraction. The products of these two possible pathways would yield two different oxaphosphetanes, one with the proton in the equatorial position and the other one with the proton in the axial position of the trigonal-bipiramid geometry around the phosphorus atom. Pseudorotation around the phosphorus atom can interconvert these two isomeric oxaphosphetanes.

These results indicate that proton abstraction depends on the substituents on the phosphorus atom. The substituents are likely to affect the polarization of the electronic density on the phosphorus atom. Thus, in the case of the reaction of $H_3P{=}CH_2$, the positively charged phosphorus atom contains most of the electron density in the moiety, making it reasonably acidic. Under these circumstances, proton abstraction is favored.

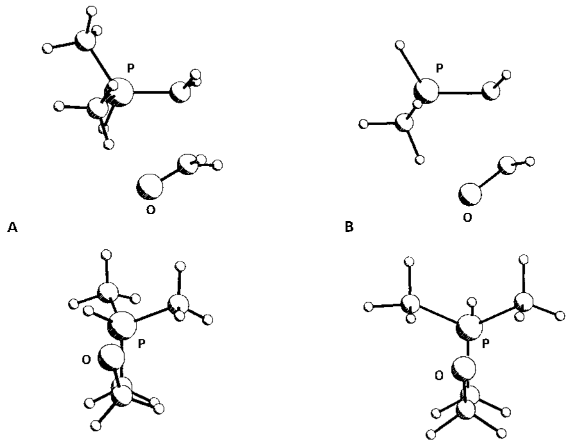


Figure 5. Calculated geometries for the two possible transition states of the reaction of methylidenedimethylphosphorane ($Me_2HP{=}CH_2$) with formaldehyde. In part A the hydrogen substituent on the phosphorus atom is close to the oxygen atom (this proton occupies a pseudoequatorial position in the forming pentavalent geometry around the phosphorus). In part B the hydrogen substituent on the phosphorus atom occupies a pseudoaxial position and is away from the oxygen atom. Two perspectives are shown for sake of clarity.

As the number of methyl substituents increases, the acidic character on the phosphorus atom decreases. This scenario disfavors proton abstraction, as in the case of the reaction of $HMe_2P{=}CH_2$.

Conclusions

We summarize the findings of our current ab initio study as follows. (1) The mythical Wittig reaction ($H_3P{=}CH_2 + HCHO \rightarrow$ oxaphosphetane) in the gas phase is not an adequate model for describing the reaction of most real systems, since a competitive reaction (proton abstraction) is predicted as a likely reaction path. (2) For the reactions of alkylidene phosphoranes, HF calculations yield geometries that are consistent with the results obtained with B3LYP, MP2, and QCISD. However, significant differences in the energies of the reactants, intermediates, and transition states along the reaction paths can be found at this level when compared to the results from B3LYP, MP2, QCISD, and QCISD(T), indicating the importance of correlation corrections in the energetics. (3) Basis sets larger than 6-31G* have little effect on the energetics and geometries of the model reactions studied here. (4) B3LYP calculations using the 6-31G* basis set seem to be a reasonable compromise between computational expense and level of rigor in the treatment of the mechanisms governing the Wittig reaction.

The results presented here are from computations on the simplest unstabilized ylides when they react in the gas phase with formaldehyde. This model very likely requires modifications when applied to the real world of Wittig reactions carried out in moderately polar solvents. Factors such as solvation and the presence of other ionic species in the reaction environment must be considered in order to have a more realistic model of the Wittig cycloaddition process. We are in the process of applying the IPCM formalism to study the reactions of larger unstabilized ylides with aldehydes in solution. The results of these findings will be described elsewhere.

The *Z* matrix of the optimized molecular structures is available from the authors (contact the authors for a suitable media of data transferring).

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