

AIM analysis for the ylide rotamers from the reaction between triphenylphosphine and dialkyl acetylenedicarboxylates in the presence of 2-pyrrolecarbaldehyde

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Abstract: Stable crystalline phosphorus ylides were obtained in excellent yields from the 1:1:1 addition reactions between triphenylphosphine and dialkyl acetylenedicarboxylates, in the presence of NH-acid, such as 2-pyrrolecarbaldehyde. These stable ylides exist in solution as a mixture of two geometrical isomers as a result of restricted rotation around the carbon-carbon partial double bond resulting from conjugation of the ylide moiety with the adjacent carbonyl group. In the recent work, the stability of the Z and E isomers was undertaken for the two rotamers of a phosphorus ylide by means of atoms in molecules (AIM) analysis.

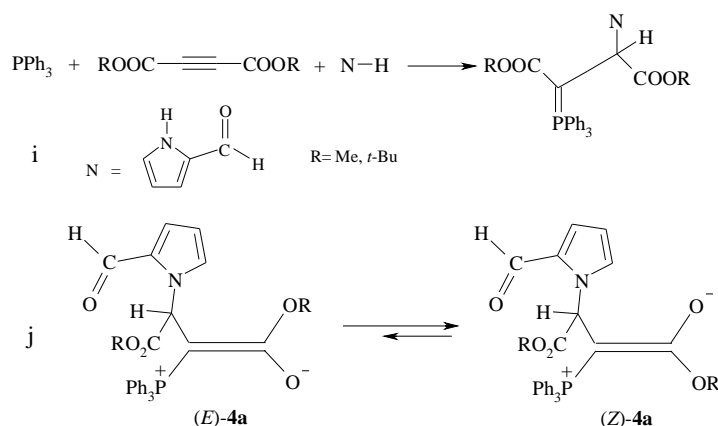
Keywords: Stable phosphorus ylides; Dialkyl acetylenedicarboxylates; Rotamer; AIM

Introduction

Phosphorus ylides are important reagents in synthetic organic chemistry, especially in the synthesis of naturally occurring products, compounds with biological and pharmacological activity [1]. The synthesis of phosphorus ylides is an important reaction in organic chemistry because of the application of these compounds in the synthesis of organic products [2-36]. Phosphorus ylides most often prepare by treatment of a phosphonium salt with a base. Most of the phosphonium salts are usually made from the reaction of phosphine and an alkyl halide [4-8], though they can be obtained by Michael addition of phosphorus nucleophiles to activated olefins [3,4]. A facile synthesis and kinetic investigation of the reaction between triphenylphosphine **1**, dialkyl

acetylenedicarboxylates **2** and 2-pyrrolecarbaldehyde **3** (as a NH-acid) have been earlier reported [37, 38] and depicted in Figure 1. The Z and E isomers were optimized for all ylide structures at HF/6-31G level of theory by Gaussian 98 package program. The energy of both conformers have been calculated at B3LYP/6-311++G** level. Atoms in molecules (AIM) analysis at HF/6-31G level of theory have been performed in order to gain a better understanding of most geometrical parameters of both E-**4(a, c)** and Z-**4(a, c)** of phosphorus ylides. The numbers of critical points and intramolecular hydrogen bonds as well as the charge of atoms that constructed on the Z and E isomers have been recognized. The results altogether reveal the effective factors on stability of Z and E ylide isomers.

Figure 1. (i) The reaction between triphenylphosphine **1**, dialkyl acetylenedicarboxylate **2** (**2a** or **2-c**) and 2-pyrrolecarbaldehyde **3** for generation of stable phosphorus ylides **4** (**4a** or **4c**), (j) Two isomers (Z)-**4a** and (E)-**4a** (Major and Minor) of ylide **4a**.



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Results and Discussion

Theoretical study

Recently, different reports have been published on the synthesis of stable phosphorus ylides from the reaction between triphenylphosphine and reactive acetylenic esters in the presence of N-H, C-H or S-H heterocyclic compounds. These ylides usually exist as a mixture of two geometrical isomers, although some ylides exhibit one geometrical isomer. It is important to remember that in medicinal chemistry sometimes only one of the two geometrical isomers shows biological and pharmacological activity. For this reason quantum mechanical calculations have been performed in order to gain a better understanding of most important geometrical parameters and also relative energies of both geometrical isomers in the case of ylides which have one or two geometrical isomers.

Calculations

Structure and stabilities

In order to determine which is the more stable form of both Z-4(a, c) or E-4(a, c) isomers of ylides 4a and 4c, their structures were first optimized at HF/6-31G level of theory [40] by using the Gaussian 98 program package [41]. Also, relative energies of the two rotamers have been calculated at HF/6-31G and B3LYP/6-311++G(d,p) levels (See Figures 2 and 3). The relative stabilization energies for both Z-4(a, c) or E-4(a, c) isomers are reported in Table 1. As can be seen, Z-4a and Z-4c isomers are more stable than E-4a and E-4c forms (0.10 and 4.03 kcal/mol respectively) at the B3LYP level.

Table 1: The relative energy (kcal/mol) for both Z and E isomers of ylides 4a and 4c, obtained at HF/6-31G and B3LYP/6-311++G(d,p) levels.

Conformer	HF	B3LYP
Z-4a	0.18	0.00
E-4a	0.00	0.10
Z-4c	0.00	0.00
E-4c	2.46	4.03

Further investigation was undertaken in order to determine more effective factors on stability of both isomers, on the basis of AIM calculations [42] at HF/6-31G level of theory by the AIM2000 program package [43]. As noted in the literature [44], the ranges of $\rho(r)$

and $\nabla^2\rho(r)$ are 0.002-0.035e/a₀³ and 0.024-0.139 e/a₀⁵, respectively, if H-bonds exist. The number of hydrogen bonds in both categories (E-4a and Z-4a) and (E-4c and Z-4c) are (6 and 5) and also (6 and 9), respectively (See Tables 2 and 3). In addition, the ranges of their electron densities are in (0.006 - 0.018 and 0.007 - 0.017 au) and also (0.008 - 0.011 and 0.002 - 0.015 au), respectively (See Table 4). With respect to the large number of hydrogen bonds in both Z and E isomers it is difficult to make a precise decision for determination of more stable isomer.

Figure 2: Intramolecular hydrogen bonds (dotted lines) in E-4a and Z-4a geometrical isomers of stable ylide 4a.

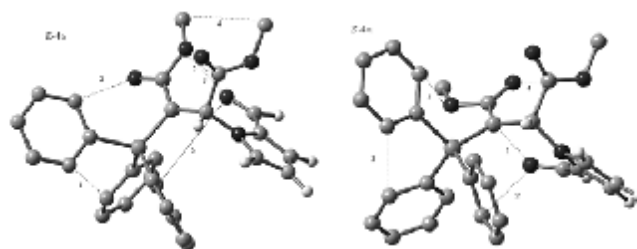


Figure 3: Intramolecular hydrogen bonds (dotted lines) in E-4c and Z-4c geometrical isomers of stable ylide 4c.

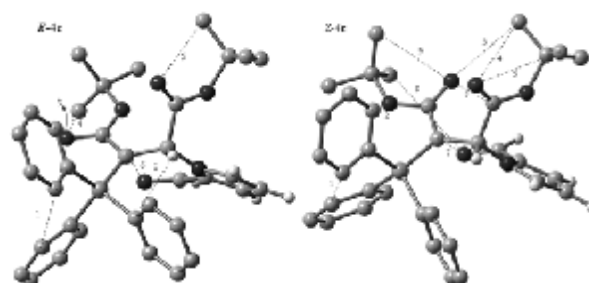


Table 2: The values of $\rho \times 10^{-3}$ and $\nabla^2\rho \times 10^{-3}$ for both Z-4a and E-4a isomers of ylide 4a calculated at the hydrogen bond critical points. All quantities are in atomic units

E	ρ	$\nabla^2\rho$	Z	ρ	$\nabla^2\rho$
1	6.23	-5.50	1	10.75	-9.42
2	17.85	-16.37	2	16.61	-16.34
3	12.18	-11.78	3	8.80	-8.95
4	18.21	-17.82	4	16.66	-16.07
5	17.41	-19.17	5	7.22	-7.84
6	11.35	-11.34			

Table 3: The values of $\rho \times 10^{-3}$ and $\nabla^2\rho \times 10^{-3}$ for both *Z-4c* and *E-4c* isomers of ylide **4c** calculated at the hydrogen bond critical points. All quantities are in atomic units

E	ρ	$\nabla^2\rho$	Z	ρ	$\nabla^2\rho$
1	7.97	-7.51	1	9.16	-9.22
2	11.01	-10.69	2	6.45	-7.10
3	11.29	-11.12	3	5.49	-6.04
4	14.86	-14.50	4	10.76	-10.59
5	12.30	-11.98	5	10.30	-10.06
6	9.64	-7.83	6	15.50	-15.20
			7	10.35	-8.63
			8	2.56	-2.93
			9	12.25	-11.73

On the basis of theoretical calculations (Table 1), the difference between the relative stability of the *E-4a* and *Z-4a* isomers in gas phase is small (0.10 kcal/mol) while it is considerably greater in the *E-4c* and *Z-4c* (4.03 kcal/mol). Perhaps this noticeable difference is taken more in solution media for **4c**, for this reason it is possible to observe only one isomer of **4c** (*Z* or *E*). In recent case (synthesis of ylide **4a**) [37], the ^1H , ^{13}C , ^{31}P NMR data showed the only one isomer for the ylide **4c** which is consistent with the obtained result from the theoretical investigations. Nevertheless, the result of our calculations is different for **4a** ylide (observed as the two isomers) which may be attributed to the negligible difference in relative stability of *E-4a* and *Z-4a* isomers. Perhaps this negligible difference is not taken more considerably in solution media for **4a** and for this reason it is possible to see the two isomers of **4a** (both *Z* and *E* isomers).

Table 4: The charges on different atoms for both *Z* and *E* isomers in both ylides **4a** and **4c** calculated by AIM method

number of atom	<i>Z-4a</i>	<i>E-4a</i>	<i>Z-4c</i>	<i>E-4c</i>
C1	5.60×10^{-1}	5.51×10^{-1}	5.55×10^{-1}	5.59×10^{-1}
C5	1.40×10^{-1}	1.41×10^{-1}	1.43×10^{-1}	1.42×10^{-1}
C10	-7.10×10^{-1}	-6.21×10^{-1}	-6.66×10^{-1}	-6.14×10^{-1}
O6	-1.09	-1.14	-1.13	-1.11
O7	-1.05	-1.03	-1.08	-1.05
P11	2.41	2.37	2.43	2.39

Conclusion

The assignment of the *Z* and *E* isomers as a Major or Minor form in both ylides **4a** and **4c** were undertaken by AIM method. Quantum mechanical calculation was clarified how ylides **4a** and **4b** (its results as same as **4a**) exist in solution as a mixture of two geometrical isomers. These results have also provided useful evidence for the ylide involving **4c**. Noticeable differences between the most important geometrical parameters (for instance, relative energy) provide a suitable chance for ylide **4c** which appears as a single geometrical isomer (*Z-4c*) in solution.

Acknowledgments

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