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NMR study and quantum mechanical calculations for determination of more stable isomer of the *E* and *Z* isomers as a major or minor form in stable phosphorus ylide involving a 2-mercapto pyrimidine

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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 SH-heterocyclic compound, such as 2-mercapto pyrimidine. These stable ylides exist in solution as a mixture of the 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, NMR study and the stability of the *Z*- and the *E*- isomers were undertaken for the two rotamers of phosphorus ylides involving a 2-mercapto pyrimidine [namely dimethyl 2-(pyrimidine-2-sulfanyl)-3-(triphenyl phosphanylidene) butanedioate] by natural population analysis (NPA) and atoms in molecules (AIM) methods.

KEYWORDS

Stable phosphorus ylides;
Dialkyl
acetylenedicarboxylates;
Z and *E* rotamers;
AIM method.

INTRODUCTION

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[1-17]. Several methods have been developed for preparation of phosphorus ylides[10,11]. These ylides are usually prepared by treatment of a phosphonium salt with a base, and phosphonium salts are usually prepared from the phosphine and alkyl halide[2,3]. Phosphonium salts are also prepared by Michael addition of phosphorus to activated olefines[1]. The phosphonium salts are most often converted to the ylides by treatment with a strong base, though weaker bases can be used if the salt is acidic enough. Michael addition of phosphorus (III) compounds such as triphenylphosphine to acetylenic esters leads to reactive 1, 3-dipolar intermediate betaines which are not detected even at low temperature. These unstable species can be trapped by a protic reagent, ZH, such as methanol, amide, imide, etc. to produce various compounds e.g. ylides[4-17].

These ylides usually exist as a mixture of the two geometrical isomers, although some ylides exhibit one geometrical isomer. Assignment of the stability of the two *Z*- and *E*- isomers is impossible in phosphorus ylides by experimental methods such as ^{1}H and ^{13}C NMR and IR spectroscopy, mass spectrometry and elemental analysis data. For this reason quantum mechanical calculation has been performed in order to gain a better understanding of the most important geometrical parameters and also relative energies of both the geometrical isomers.

RESULTS AND DISCUSSION

Calculations

A facile synthesis of the reaction between triphenylphosphine 1, dialkyl acetylendicarboxylates 2 and 2-mercapto pyrimidine 3 (as a SH- heterocyclic compound) for generation of phosphorus ylides 4a-b involving the two geometrical isomers such as *Z* and *E* isomers have been earlier reported[18]. The reaction is shown in Figure 1. For assignment of the two *Z* and *E* isomers as a minor or major form in phosphorus ylides 4a-b containing a 2-mercapto pyrimidine, first the *Z*- and the *E*- isomers were optimized for all ylide structures at HF/6-31G(d,p) level of theory[19] by Gaussian98 package program[20]. The relative stabilization energies in both the geometrical isomers have been calculated at HF/6-31G(d,p) and B3LYP/6-311++G** levels. Atoms in molecules (AIM)[21], natural population analysis (NPA) methods and CHelpG keyword at HF/6-31G(d,p) level of theory have been employed in order to gain a better understanding of most geometrical parameters of both the *E*-4(a, b) and the *Z*-4(a, b) 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. The relative stabilization energies for the two [*Z*-4(a, b) and *E*-4(a, b)] isomers (See Figures 2 and 3) are reported in TABLE 1, as can be seen, *E*-4a and *E*-4b isomers are more stable than *Z*-4a and *Z*-4b forms (0.95 and 0.45 kcal/mol, respectively) at B3LYP level. In addition, J_{x-y}, the values of proton and carbon coupling constants and also chemical shifts (δ^{H}_{iso}, δ^{C}_{iso}) have been calculated at mentioned level using SPINSPIN keyword.

Further investigation was undertaken in order to determine more effective factors on stability of the two *Z*- and *E*- isomers, on the basis of AIM calculations at HF/6-31G(d,p) level of theory by the AIM2000 program package[22]. In recent years, AIM theory has often applied in the analysis of H-bonds. In this theory, the topological properties of the electron density distribution are derived from the gradient vector field of the electron density $\nabla\rho(r)$ and on the Laplacian of the elec-

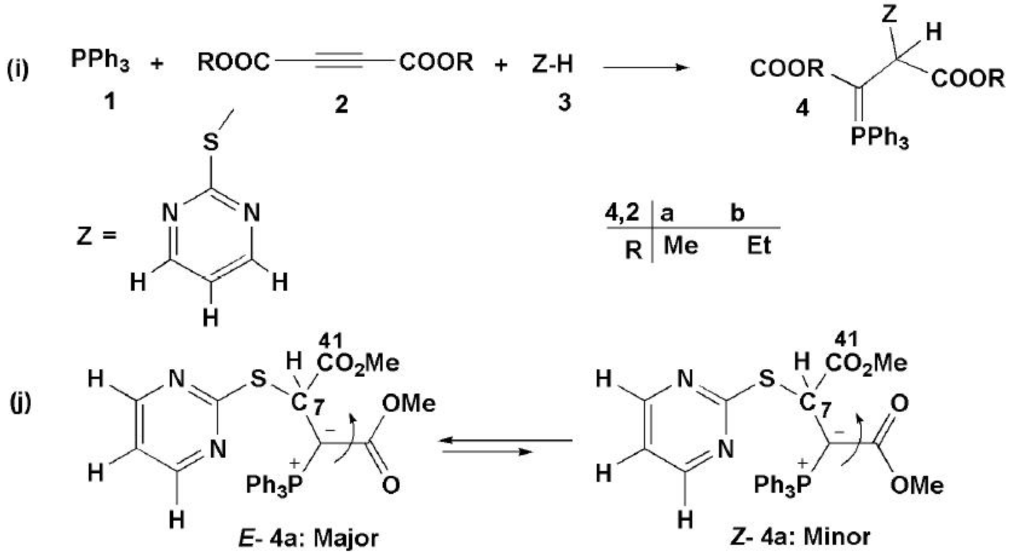

Figure 1 : (i) The reaction between triphenylphosphine 1, dialkyl acetylenedicarboxylate 2 (2a or 2b) and 2-mercapto pyrimidine 3 for generation of stable phosphorus ylides 4 (4a or 4b). (j) The two isomers *Z*-4a and *E*-4a (minor and major, respectively) of ylide 4a.

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

Conformer	HF	B3LYP
Z-4a	1.41	0.95
E-4a	0.00	0.00
Z-4b	1.14	0.45
E-4b	0.00	0.00

tron density $\nabla^2\rho(r)$. The Laplacian of the electron density, $\nabla^2\rho(r)$, identifies regions of space wherein the electronic charge is locally depleted [$\nabla^2\rho(r) > 0$] or built up [$\nabla^2\rho(r) < 0$][21]. Two interacting atoms in a molecule form a critical point in the electron density, where $\nabla\rho(r) = 0$, called the bond critical point (BCP). The values of the charge density and its Laplacian at these critical points give useful information regarding the strength of the H-bonds[22]. The ranges of $\rho(r)$ and $\nabla^2\rho(r)$ are 0.002 – 0.035 e/a_0^3 and 0.024 – 0.139 e/a_0^5, respectively, if H-bonds exist[23]. The AIM calculation indicates intramolecular hydrogen bond critical points (H-BCP) for the two *Z*-4(a, b) and *E*-4(a, b) isomers. Intramolecular H-BCPs along with a part of molecular graphs for the two rotational isomers are shown in Figures 2 and 3 (dotted line). Most important geometrical parameters involving some H-bonds (bond length and their relevant bond angle) are reported in TABLE 2. The electron densities $(\rho)\times10^3$, Laplacian of electron density $\nabla^2\rho(r)\times10^3$, and energy density $-H(r)\times10^4$ are also reported in (TABLES 3 and 4). A negative total energy density at the BCP reflects a dominance of potential energy density, which is the consequence of accumulated stabilizing electronic charge[24]. Herein, the number of hydrogen bonds in both categories (*E*-4a and *Z*-4a) and (*E*-4b and *Z*-4b) are (6 and 5) and also (6 and 5), respectively. The values of ρ and $\nabla^2\rho(r)\times10^3$ for those are in the ranges (0.002 – 0.011 and 0.006 – 0.010 e/a_0^3) and (0.002 – 0.011 and 0.006 – 0.010 e/a_0^3) and also (12.48 – 44.24 and 27.12 – 38.44 e/a_0^5) and (12.56 – 42.00 and 27.24 – 38.24 e/a_0^5), respectively. In addition, the Hamiltonian [$-H(r)\times10^4$] are in the ranges (6.70 – 17.60 and 5.50 – 17.10 au) and (6.50 – 17.30 and 5.50 – 17.20 au), respectively (See

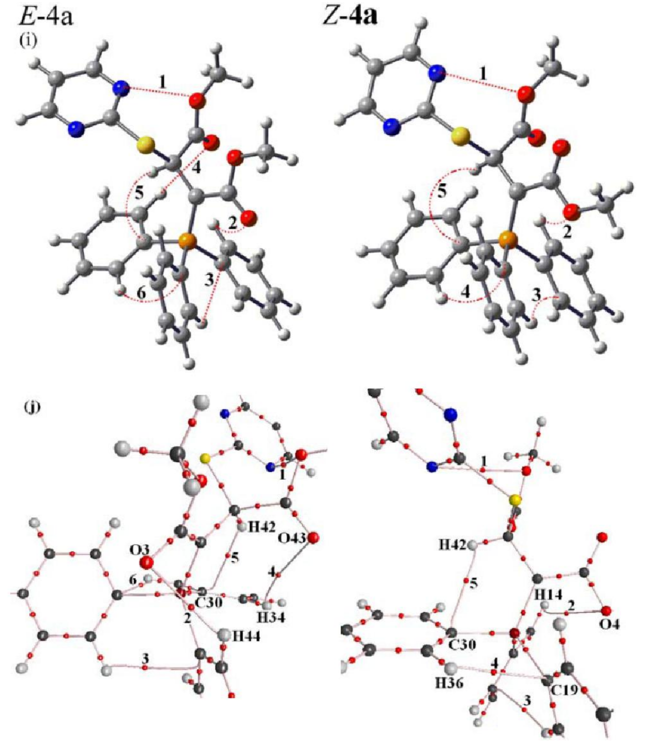

Figure 2 : (i) Intramolecular hydrogen bonds (dotted lines) in the two *E*-4a and *Z*-4a geometrical isomers of stable ylide 4a, (j) Part of molecular graphs, including intramolecular hydrogen bond critical points (BCPS) for the two rotational isomers such as *E*-4a and *Z*-4a. Small red spheres, and lines corresponding to BCPS bond paths, respectively.

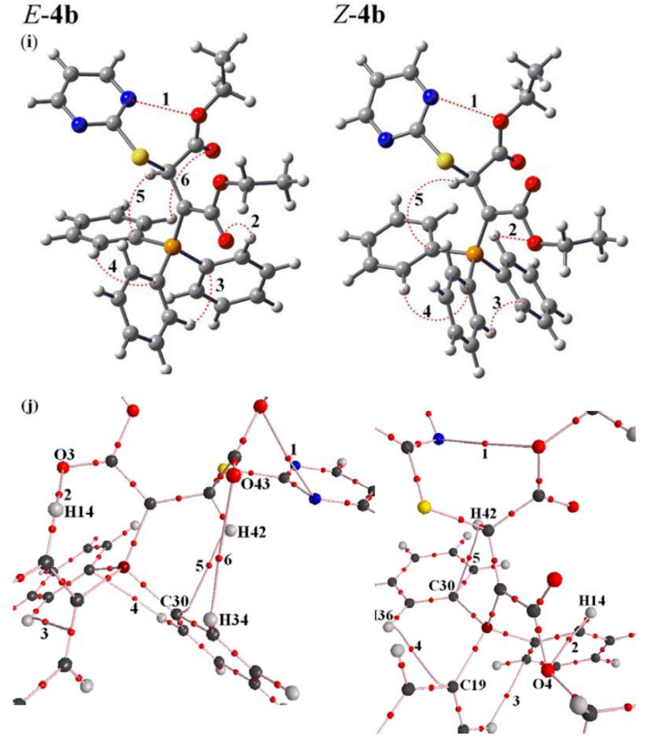

Figure 3 : (i) Intramolecular hydrogen bonds (dotted lines) in the two *E*-4b and *Z*-4b geometrical isomers of stable ylide 4b, (j) Part of molecular graphs, including intramolecular hydrogen bond critical points (BCPS) for the two rotational isomers such as *E*-4b and *Z*-4b. Small red spheres, and lines corresponding to BCPS bond paths, respectively.

TABLES 3 and 4). These HBs show $\nabla^2\rho(r) > 0$ and $H(r) < 0$, which according to classification of Rozas et al.[25] are medium-strength hydrogen bonds. In both ylides the dipole moment for the two *E*-4a and *E*-4b isomers (5.28 and 5.24 D, respectively) are smaller than the two *Z*-4a and *Z*-4b isomers (6.99 and 6.85 D, respectively) and the value of $-H_{tot}$ ($=\sum -H(r) \times 10^4$) for the two *E*-4a and *E*-4b isomers (73.92 and 74.90 au, respectively) are larger than the two *Z*-4a and *Z*-4b isomers (65.30 and 65.00 au, respectively). These differences, involving a small difference in dipole moment and a considerable difference in $-H_{tot}$ and more number of hydrogen bonds (TABLE 5), altogether, make only the slightest stability on these isomers in comparison with the *Z*-4(a, b) forms. Also, the charge on different atoms which are calculated by AIM and NPA methods and also CHelpG keyword at HF/6-31G(d,p) level are reported in TABLE 6 for the two *Z*- and *E*-isomers of ylides 4a and 4b. There is good agreement between the results in three methods.

TABLE 2 : Most important geometrical parameters corresponding to H-bonds (bond lengths and their relevant angles) for the two *Z* and *E* isomers in both ylides 4a and 4b. Bond lengths in Angstroms and bond angles in degrees, respectively

	E-4a	Z-4a	E-4b	Z-4b
$C_{10}H_{14}....O_{3(4)}$*	2.41[a](124.00)[b]	2.75(109.37)	2.45(121.77)	2.78(108.61)
$C_7H_{42}.....C_{30}$	2.55(117.66)	2.61(113.93)	2.55(117.67)	2.62(113.59)
$C_{31}H_{34}....O_{43}$	3.07(129.08)		3.45(114.79)	
$C_{32}H_{36}....C_{19}$		2.73(106.29)		2.74(106.16)

[a] bond length; [b] bond angle; * Is relevant to the *Z* isomer

TABLE 3 : The values of $a=\rho(r)\times10^3$, $b=\nabla^2\rho\times10^3$ and $c=-H(r)\times10^4$ for the two *Z*-4a and *E*-4a isomers of ylide 4a calculated at the hydrogen bond critical points. All quantities are in atomic units.

E	a	b	c	*Z*	a	b	-c
1	7.26	28.04	6.70	1	7.24	27.12	5.50
2	11.67	44.24	10.20	2	6.61	28.48	12.50
3	9.25	32.16	15.10	3	9.71	34.12	14.80
4	2.76	12.48	7.70	4	9.00	32.08	15.40
5	11.68	41.20	16.80	5	10.47	38.44	17.10
6	9.57	36.48	17.60				

TABLE 4 : The values of $a=\rho(r)\times10^3$, $b=\nabla^2\rho\times10^3$ and $c=-H(r)\times10^4$ for the two *Z*-4b and *E*-4b isomers of ylide 4b calculated at the hydrogen bond critical points. All quantities are in atomic units.

E	a	b	c	*Z*	a	b	-c
1	7.28	27.96	6.50	1	7.23	28.92	5.50
2	10.80	42.00	11.50	2	6.28	27.24	12.20
3	9.27	32.12	15.00	3	9.73	34.28	14.90
4	9.55	36.00	17.30	4	8.98	31.72	15.20
5	11.61	40.92	16.80	5	10.36	38.24	17.20
6	2.78	12.56	7.80				

On the basis of theoretical calculations (TABLE 1), the difference between the relative stability of the *E*-4a and *Z*-4a and also *E*-4b and *Z*-4b are small (0.95 and 0.45 kcal/mol, respectively) in gas phase. This result (a slightly difference on stability) is completely consistent with the obtained results on the basis of AIM calculation for determination of the most geometrical parameters. For this reason it is possible to observe the two isomers of 4a and 4b (both the *Z*- and the *E*- isomers). In the synthesis of ylide 4a and 4b[18], the ^1H, ^{13}C, ^{31}P NMR data showed the two isomers for the ylide 4a and 4b with more experimental abundance percentage for the two *E*-4a (65%) and *E*-4b (59%) as the major isomers, those are compatible with the obtained result from the theoretical investigations.

The individual chemical shifts have been characterized by NMR calculations at mentioned level. The total spin-spin coupling constant is the sum of four components: the paramagnetic spin-orbit (PSO), diamagnetic spin-orbit (DSO), Fermi-contact (FC) and spin-dipole (SD) terms. The value of chemical shifts (δ) and coupling constants (J_{X-Y}) are reported in

TABLE 5 : The most important geometrical parameters involving the value of $-H_{tot}$/au, dipole moment/D and the number of hydrogen bonds for the two *Z*- and *E*- isomers of ylides 4a and 4b.

Geometrical isomer	$-H_{tot}$/au	Dipole moment/D	number of hydrogen bond
E-4a	73.92	5.28	6
Z-4a	65.30	6.99	5
E-4b	74.90	5.24	6
Z-4b	65.00	6.85	5

(TABLES 7, 8, 9 and 10) for the two major *E*-4(a, b) and minor *Z*-4(a, b) geometrical isomers. As can be seen, there is good agreement between both the experimental[18] and theoretical chemical shifts (δ) and coupling constants (J_{X-Y}). In the present work, molecular structures of ylides 4a-b involving three large atoms such as sulfur, phosphorus and nitrogen along with the large numbers of other atoms have very huge structures, for this reason, employment of basis set higher than HF/6-31G(d, p) is impossible in a higher performance for more accurate calculations. This limitation causes a small difference between both the experimental and theoretical coupling constants in some functional groups.

TABLE 6 : The charges on different atoms for the two *Z* and *E* isomers in both ylides 4a and 4b, calculated at HF/6-31G(d,p) theoretical level.

Number of atom	*Z*-4a	*E*-4a	*Z*-4b	*E*-4b
C1	-0.80[a](-0.37)[b] (-0.90)[c]	-0.78 (-0.49) (-0.88)	-0.77 (-0.28) (-0.89)	-0.77 (-0.46) (-0.87)
C2	1.86 (0.91) (0.96)	1.85 (0.91) (0.95)	1.85 (0.86) (0.96)	1.84 (0.89) (0.95)
C7	0.24 (0.03) (-0.44)	0.23 (0.05) (-0.45)	0.24 (0.12) (-0.44)	0.26 (0.09) (-0.45)
O3	-1.38 (-0.65) (-0.76)	-1.42 (-0.72) (-0.80)	-1.37 (-0.62) (-0.77)	-1.41 (-0.71) (-0.80)
O4	-1.29 (-0.48) (-0.66)	-1.26 (-0.34) (-0.64)	-1.30 (-0.57) (-0.67)	-1.26 (-0.47) (-0.65)
P6	3.24 (0.07) (1.87)	3.24 (0.15) (1.88)	3.25 (0.13) (1.87)	3.24 (0.14) (1.88)

[a] Calculated by AIM method.; [b] Calculated by CHelpG Keyword.; [c] Calculated by NPA method.

TABLE 7 : Selected ^{1}H NMR chemical shift (δ in ppm) and coupling constants (J in Hz) for some functional groups in the *E*-4a isomer as a major form.

Groups	δ^H/ppm	J_{PH}/Hz
1H, t, Ar-H	6.71[a] (6.52)[b]	
6H, 2s, 2 CO_2Me	3.59 (3.50) and 3.69 (3.53)	
15H, m, $3C_6H_5$	7.40 - 7.74 (7.40 - 7.83)	
2H, d, Ar-H	8.17 (8.47)	
1H, d, P=C-CH	4.86 (3.91)	19.20[a] (19.32)[b]

[a] Experimental data in accord with the results reported in the literature[18]; [b] Theoretical data.

TABLE 8 : Selected ^{1}H NMR chemical shift (δ in ppm) and coupling constants (J in Hz) for some functional groups in the *Z*-4a isomer as a minor form.

Groups	δ^H/ppm	J_{PH}/Hz
2H, d, Ar-H	8.18[a] (8.31)[b]	
1H, t, Ar-H	6.73 (6.50)	
6H, 2s, 2 CO_2Me	3.69 (3.80) and 3.41 (3.63)	
15H, m, $3C_6H_5$	7.40 - 7.74 (7.59 - 7.73)	
1H, d, P=C-CH	4.86 (3.86)	18.10[a] (17.67)[b]

[a] Experimental data in accord with the results reported in the literature[18]; [b] Theoretical data.

TABLE 9 : Selected ^{13}C NMR chemical shift (δ in ppm) and coupling constants (J in Hz) for some functional groups in the *E*-4a isomer as a major form.

Groups	δ^C/ppm	J_{PC}/Hz
d, C^{41}=O	169.38[a] (168.89)[b]	
d, C_{ortho}	132.63 (134.11)	9.70[a] (10.34)[b]
d, C_{ipso}	124.87 (127.64)	92.30 (90.80)
d, C_{meta}	127.59 (126.27)	
2s, 2OMe	48.94 (46.12) and 49.21 (47.00)	
s, $2NCH_{arom}$	155.45 (157.70)	
d, C_{para}	130.84 (132.22)	
d, P=C-C^7H	49.02 (44.82)	
NCN	172.23 (178.04)	

[a] Experimental data in accord with the results reported in the literature[18]; [b] Theoretical data.

TABLE 10 : Selected ^{13}C NMR chemical shift (δ in ppm) and coupling constants (J in Hz) for some functional groups in the *Z*-4a isomer as a minor form.

Groups	δ^C/ppm	J_{PC}/Hz
d, C_{ortho}	132.45[a] (132.79)[b]	9.50[a] (10.66)[b]
d, C_{ipso}	125.53 (126.87)	92.10 (92.89)
d, C_{meta}	127.48 (126.75)	
d, C^{41}=O	168.96 (169.04)	
s, $2NCH_{arom}$	156.28 (157.57)	
d, C_{para}	130.86(132.17)	
d, P=C-C^7H	49.65(46.00)	
2s, 2OMe	45.33 (51.22) and 47.12 (51.58)	
NCN	172.00 (178.38)	

[a] Experimental data in accord with the results reported in the literature[18]; [b] Theoretical data.

CONCLUSION

The assignment of the *Z*- and *E*- isomers as a minor or major form in both the ylides 4a and 4b were undertaken by AIM and NPA methods and also CHelpG keyword. Quantum mechanical calculation was clarified how the ylides 4a and 4b exist in solution as a mixture of the two geometrical isomers. This result was in good agreement with the experimental data. In addition the NMR study on the basis of theoretical calculations were employed for determination of chemical shifts and coupling constants of the two major *E*-4(a, b) and minor *Z*-4(a, b) geometrical isomers.

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