A facile synthesis, dynamic ^{1}H NMR, and theoretical study of novel stable heterocyclic phosphorus ylides containing a tetrazole ring

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Abstract

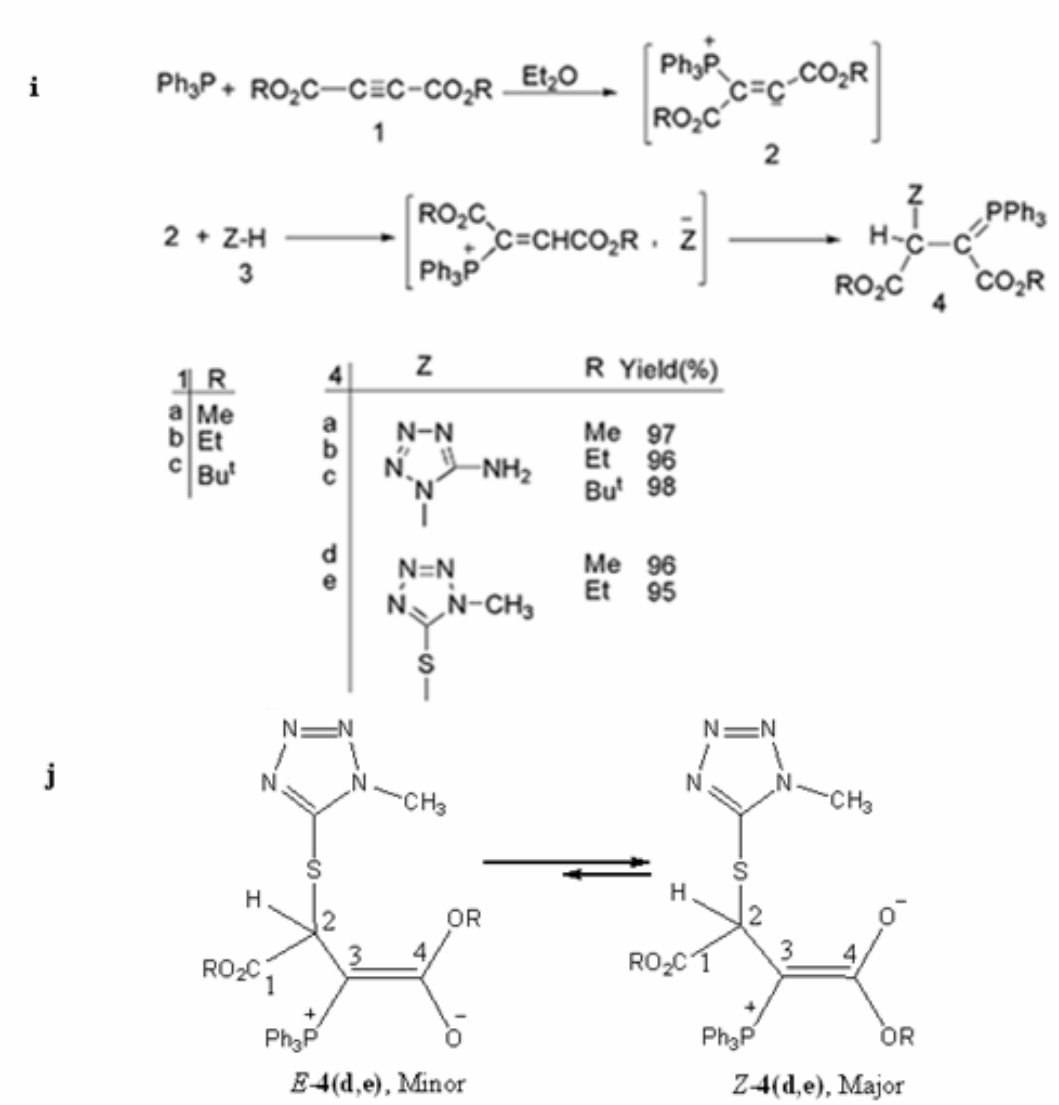
A general and practical route has been considered for the synthesis of stable heterocyclic phosphorus ylides by a one-pot condensation reaction between dialkyl acetylenedicarboxylates and triphenylphosphine in the presence of -SH or -NH heterocyclic compounds such as 5-mercapto-1-methyltetrazole or 5-aminotetrazole. The stable ylides involving **4d-e** exist in solution as a mixture of two isomers, while **4a-c** indicate only one isomer. Dynamic parameters including $\Delta H\neq$, $\Delta S\neq$ and $\Delta G\neq$ were determined on the basis of dynamic ^{1}H NMR data. In addition, the assignments of more stable *Z*- or *E*- isomers were investigated using the theoretical calculations.

Keywords: Triphenylphosphine, stable phosphorus ylides, *Z*- or *E*- isomers, intramolecular hydrogen bond, theoretical calculations

Introduction

The synthesis of phosphorus ylides is important in organic chemistry because of their application in the synthesis of organic products,[1-19] and especially the synthesis of naturally occurring products with biological and pharmacological activity.[20-24] Phosphorus ylides are usually prepared by deprotonation of phosphonium salts, which can be prepared most often by the reaction of triphenylphosphine and an alkyl halide.[1-3] In recent years a three- component method has been developed [25-28] for the synthesis of organophosphorus compounds using a novel approach employing vinylphosphonium salts. This method is successful for the preparation of 1,4-di-ionic organophosphorus compounds.[29-33] The tetrazole moiety and its derivatives are important in medicinal chemical research.[33] Herein we describe an efficient synthetic route to stable phosphorus ylides in excellent yields from 5-mercapto-1-methyltetrazole or 5-aminotetrazole. An "atoms in molecules" (AIM) analysis [35] at the HF/6-31G level of theory has

been performed in order to gain a better understanding of most geometrical parameters of both the *E*-**4(a, d)** and *Z*-**4 (a, d)** phosphorus ylides (Scheme 1).

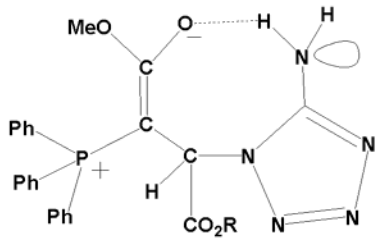


Scheme 1. (i) Reaction between triphenylphosphine**,** dialkyl acetylenedicarboxylate **1** (**1a**, **1b** or **1c**) and 5-aminotetrazole or 5-mercapto-1-methyltetrazole **3** for generating stable phosphorus ylides **4a-e. (j)** *Z*- and *E*- isomers (major and minor) of stable phosphorus ylides **4d-e** are shown for 5-mercapto-1-methyltetrazole.

Results and Discussion

The reaction between triphenylphosphine and dialkyl acetylenedicarboxylates **1** led to the zwitterion **2**, which was followed by attack by the nitrogen anion of the 5-aminotetrazole, or sulfur anion of the 5-mercapto-1-methyltetrazole, to generate the phosphorus ylides *E*-**4** and *Z*-**4**.

These reactions were carried out in diethyl ether at ambient temperature and were complete after 5 hours. The ^{1}H, ^{13}C and ^{31}P NMR spectra of the crude products clearly indicated the formation of the phosphorus ylides **4**. No product other than **4** could be detected by NMR spectroscopy. The structures of compounds **4a-e** were deduced from the elemental analyses, mass, IR, ^{1}H, ^{13}C, and ^{31}P NMR spectra. The ^{1}H NMR spectrum of **4a** showed two singlets at δ=3.16 and 3.77 ppm for methoxy protons, a doublet at δ=5.40 ppm (*J*=16.0) arising from methine proton (C*H*-C-P group), and a significant signal at δ=6.01 for the NH_2 group. The aromatic protons appeared as a multiplet at δ=7.48-7.73 ppm. As can be seen in the Experimental Section, the ^{13}C NMR spectrum of **4a** displayed eleven distinct resonances which is in accord with only one isomer. This observation is attributed to the plausible intramolecular hydrogen bond in stable ylides **4a-c** containing 5-aminotetrazole (Scheme **2**).



Scheme 2. Plausible intramolecular hydrogen bond in stable ylides **4a-c** containing 5-aminotetrazole.

Although the presence of the ^{31}P nucleus has complicated both the ^{1}H and ^{13}C NMR spectra of **4a**, it helps in assignment of signals by long- range spin-spin couplings with ^{1}H and ^{13}C nuclei. The ^{1}H and ^{13}C NMR spectra of compounds **4b** and **4c** are similar to those of **4a**, except for the signals from the ester group, which appear as characteristic resonance lines with the corresponding chemical shifts. The ^{1}H, ^{13}C, and ^{31}P NMR spectra of compounds **4d-e** showed the mixture of two isomers [Scheme 1, **(j)**]. The assignments of *E*-**4** (**d**, **e**) and *Z*-**4** (**d**, **e**) isomers as the major or minor form in phosphorus ylides have been reported previously.[34-38]The ^{1}H NMR spectrum of **4d** exhibited two singlets (δ 3.17 and 3.73 ppm) arising from the methoxy group in the *Z*- isomer, and two singlets at 3.59 and 3.70 ppm for that in the *E*- isomer. The methyl group at 3.17 in the *Z*- isomer is shielded due to the anisotropic effect of a phenyl group of triphenylphosphine. This effect confirms why the *Z*-**4d** and *E*-**4d** isomers could appear as the major and minor forms, respectively, with the percentage of both isomers as reported in the Experimental Section. The signals for methine protons appeared as two doublets at δ=5.37 (*J*=16.7) and δ=5.40 (*J*=16.2), respectively for the *Z*- and *E*- isomers. The ^{13}C NMR spectrum of **4d** displayed 24 distinct resonances in agreement with the presence of two isomers. The ^{1}H and ^{13}C NMR spectra of compound **4e** are similar to that of **4d** except for the signals from the ester group. In addition, products **4d** and **4e** displayed ^{13}C NMR resonances at δ 163.77 ppm and δ 163.99 ppm, respectively for the N=C-S unit.[16,34] For the ^{13}C NMR spectroscopy the anisotropic effect could not be reported for the methoxy group in the *Z*- isomer because of the small different

of their chemical shifts. The carbonyl region of these compounds **4a–e** exhibited absorption bands for each compound. The ester absorption is at 1747-1616cm^{-1}, the conjugation of negative charge of the ylide moiety with the adjacent carbonyl group accounting for the reduction in frequency of the carbonyl bands, and allows determination of the ratio between the *E*- and *Z*-isomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group, and rotation around the partial double bond in *E*-**4** (**d**, **e**) and *Z*-**4** (**d**, **e**) isomers is slow on the NMR time scale at ambient temperature [Scheme **1 (j)**].

Dynamic ^{1}H NMR [39,40] were also observed for compound **4d.** The C-2 methine of the ^{1}H NMR spectrum of **4d** in $CDCl_3$ at ambient temperature exhibits two sharp doublets at δ= 5.41, 5.38 ppm for the H ($^3J_{PH}$) group of the (*E*-) and (*Z*-) isomers and two singlets at δ= 3.77, 3.16 for the OCH_3 groups, in $CDCl_3$ at ambient temperature. Increasing the temperature results in coalescence of the H ($^3J_{PH}$) and the OCH_3 resonances at approximately 63 ^oC and 65 ^oC, respectively. The variable coalescence temperature in the ^{1}H NMR spectrum and calculation of kinetic constant by $k_C = \pi\Delta\upsilon/\sqrt{2}$ allowed us to calculate $\Delta G^{\neq}$, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ for the interconversion of *E*- and *Z*- isomers (Table 1).

Table 1. Selected proton chemical shifts (at 500.1 MHz, in ppm, Me_4Si) and thermodynamic parameters (kJ/mol) for **4d** in $CDCl_3$ solvent**.**

Group	Tc (^oC)	$\Delta G^{\neq}$ [2] (kJ/mol)	Δυ (Hz)	k_C [1] (S^{-1})	$\Delta H^{\neq}$ [3] (kJ/mol)	$\Delta S^{\neq}$ [3] (kJ/mol)
H ($^3J_{PH}$)	63	72.73	15.00	33.316	401.609	0.979
OCH_3	65	70.79	35.00	77.738		

1: $k_c = \frac{\pi \Delta \nu}{\sqrt{2}}$ 2: $\Delta G^{\#} = 4.57 T_c \left(9.97 + \log \frac{T_c}{\Delta \nu} \right)$ 3: $\Delta H^{\#} = -R \times 2.303 \times \frac{\Delta \log k_c / Tc}{\Delta 1 / T_c}$

4: $\Delta S^{\#} = \frac{\Delta H^{\#} - \Delta G^{\#}}{T}$

Experimental Section

General Procedures. Dialkyl acetylenedicarboxylates, triphenylphosphine, 5-mercapto-1-methyl tetrazole and 5-aminotetrazole were obtained from Fluka (Buchs, Switzerland) and used without further purification. Melting points and IR spectra were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. The mass spectra were recorded on a Shimadzu QP 1100 EX mass spectrometer operating at an ionization potential of 70ev. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid

analyzer. The ^{1}H, ^{13}C and ^{31}P NMR spectra were obtained from a Bruker DRX-500 AVANCE instrument with $CDCl_3$ as solvent, at 500.1, 125.8 and 202.5 MHz, respectively.

General synthetic procedure, exemplified by dimethyl 2-(5-aminotetrazol-1-yl)-3-(triphenylphosphanylidene)succinate (4a)

To a magnetically stirred solution of triphenylphosphine (0.262g, 1mmol) in 4.0 mL of diethyl ether was added, dropwise, a mixture of dimethyl acetylenedicarboxylate (0.12 mL, 1 mmol) and 5-aminotetrazole (0.10g, 1 mmol) in 10 mL of diethyl ether at -5°C over 10 min. The reaction mixture was allowed to warm up to room temperature and stirred for 30 min. The solvent was removed under reduced pressure, the solid residue washed with cold diethyl ether (2×3 mL), and the product was obtained as a white powder, m.p. 79-81°C, yield 0.45g, 93%. IR (KBr) (ν_{max}, cm^{-1}) 1639 and 1746 (C=O), 3380 (NH_2).; ^{1}H NMR (500.12 MHz, $CDCl_3$), δ_H 3.16 and 3.77 (6H, 2s, 2xOC*H*$_3$), 5.40 (1H, d, $^{3}J_{PH}$=16.0 Hz, P-C-C*H*), 6.01 (2H, bs, NH_2), 7.48-7.73 (15H, m, 3xC_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 42.42 (d, $^{1}J_{PC}$= 126.3 Hz, P=C), 51.01 and 52.38 (2x OCH_3), 61.30 (d, $^{2}J_{PC}$=16.2 Hz, P-C-*C*H), 125.11 (d, $^{1}J_{PC}$= 92.5 Hz, C_{ipso}), 129.22 (d, $^{3}J_{PC}$=12.6 Hz, C_{meta}), 132.81 (C_{para}), 133.54 (d, $^{2}J_{PC}$=9.4 Hz, C_{ortho}), 154.62 (N=C), 169.53 (d, $^{3}J_{PC}$= 12.6 Hz, C=O), 171.53 (d, $^{2}J_{PC}$=12.3 Hz, P-C=C). ^{31}P NMR (202.5 MHz, $CDCl_3$); δ_P 24.03. MS, *m/z,* (%): 108 (PPh, 23), 183 (PPh_2, 80), 262 (PPh_3, 25), 275 (M-OCH_3 and PPh_2, 40), 444 (M-OCH_3 and NH_2, 77). Anal. Calcd. for $C_{25}H_{24}N_5O_4P$ (489.19): C, 61.33; H, 4.94; N, 14.31%. Found: C, 61.45; H, 4.86; N, 14.27%.

Diethyl 2-(5-aminotetrazol-1-yl)-3-(triphenylphosphoranylidene)succinate (4b). m.p. 83-85°C; yield 0.50g, 96%. IR (KBr) (ν_{max}, cm^{-1}): 1635 and 1745 (C=O), 3380 (NH_2). ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 0.46 and 1.32 (6H, 2xt, $^{3}J_{HH}$=7.0 Hz, 2x OCH_2CH_3), 3.72 and 4.26 (4H, 2m, 2x ABX_3 system, $^{3}J_{HH}$=7.0 Hz, 2x OCH_2CH_3), 5.39 (1H, d, $^{3}J_{PH}$=16.3 Hz, P-C-C*H*), 6.09 (2H, bs, NH_2), 7.45-7.69 (15H, m, 3x C_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 14.02 and 14.11 (2x O-CH_2CH_3), 41.79 (d, $^{1}J_{PC}$= 127.0 Hz, P-C), 58.81 and 61.22 (2x OCH_2CH_3), 61.27 (d, $^{2}J_{PC}$ = 12.0 Hz, P-C-*C*H), 128.55(d, $^{3}J_{PC}$ = 12.1 Hz, C_{meta}), 129.46 (d, $^{1}J_{PC}$ = 90.0 Hz, C_{ipso}), 132.05 (C_{para}), 133.62 (d, $^{2}J_{PC}$ = 9.9 Hz, C_{ortho}), 154.65 (N=C), 168.94 (d, $^{3}J_{PC}$ = 13.2 Hz, C=O), 171.16 (d, $^{2}J_{PC}$ = 11.6 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P 24.03. MS, *m/z* (%): 77(Ph, 20), 84 (CH_2N_5, 16), 108 (PPh, 29), 183 (PPh_2, 74), 262 (PPh_3, 31), 371 (M-2CO_2Et, 12), 444 (M-CO_2Et, 26). Anal. Calcd. for $C_{27}H_{28}N_5O_4P$ (517.23): C, 62.64; H, 5.46; N, 13.53%. Found: C, 62.81; H, 5.41; N, 13.60%.

Di-*tert*-butyl 2-(5-aminotetrazol-1-yl)-3-(triphenylphosphoranylidene)succinate (4c). White powder; m.p. 126-127 °C, yield 0.56g, 98%. IR (KBr) (ν_{max}, cm^{-1}): 1616 and 1745 (C=O), 3375cm^{-1} (NH_2). ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 0.94 and 1.52 (18H, 2s, 2xC*Me*$_3$), 5.25 (1H, d, $^{3}J_{PH}$=16.8 Hz, P-C-C*H*), 6.22 (2H, bs, NH_2), 7.51-7.66 (15H, m, 3xC_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 28.03 and 28.22 (2xC*Me*$_3$), 42.04 (d, $^{1}J_{PC}$= 126.6 Hz, P=C), 61.83 (d, $^{2}J_{PC}$=16.5 Hz, P-C-*C*H), 78.62 and 82.15 (2x O*C*Me$_3$), 125.77 (d, $^{1}J_{PC}$= 92.3 HZ, C_{ipso}), 128.96 (d, $^{3}J_{PC}$=12.5 Hz, C_{meta}), 132.59 (C_{para}), 133.52 (d, $^{2}J_{PC}$=9.8 Hz, C_{ortho}), 154.71 (N=C), 167.75 (d, $^{3}J_{PC}$ = 12.5 Hz, C=O), 170.78 (d, $^{2}J_{PC}$ = 11.7 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P

23.67. MS, *m/z* (%): 57 (C*Me*$_3$, 80), 68 (20.0), 108 (PPh, 34), 183 (PPh$_2$, 66), 262 (PPh$_3$, 80), 276 (M-PPh$_2$ and 2xCMe$_3$, 57), 371 (M-PPh$_3$, 34); Anal. Calcd. for $C_{31}H_{36}N_5O_4P$ (573.28): C, 64.89; H, 6.33; N, 12.21. Found: C, 65.01; H, 6.29; N, 12.28%.

Dimethyl 2-(5-mercapto-1-methyltetrazol-S-yl)-3-(triphenylphosphoranylidene)succinate (4d). White powder; (m.p. 120-121 yield 0.49g, 95%); IR (KBr) (ν_{max}, cm^{-1}): 1640 and 1745 (C=O); MS, *m/z* (%):108 (PPh, 34), 183 (PPh$_2$, 77), 262 (PPh$_3$,71), 278 (M-PPh$_2$ and CO_2CH_3, 27), 294 (M-PPh and 2xCO_2CH_3, 23), 337 (M-PPh$_2$,14), 458 (M-2xOCH_3, 79). Anal. Calcd. for $C_{26}H_{25}N_4O_4SP$ (520.20): C, 59.98; H, 4.84; N, 10.77%. Found: C, 60.11; H, 4.91; N, 10.82%.

Major (*Z*)- 4d isomer (65%): ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 3.17 and 3.73 (6H, 2s, 2xOC*H*$_3$), 3.81 (3H, s, CH_3), 5.37 (1H, d, $^3J_{PH}$=16.7 Hz, P-C-C*H*), 7.48-7.69 (15H, m, 3xC_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 34.19 (1xC, N-CH_3), 39.80 (d, $^1J_{PC}$= 131.3 Hz, P=C), 49.39 and 52.98 (2x OCH_3), 63.02 (d, $^2J_{PC}$=17.2 Hz, P-C-*C*H), 125.96 (d, $^1J_{PC}$= 92.3 Hz, C_{ipso}), 129.04 (d, $^3J_{PC}$=12.2 Hz, C_{meta}), 132.43 (C_{para}), 133.49 (d, $^2J_{PC}$=9.9 Hz, C_{ortho}),163.77 (N=C-S), 169.20 (d, $^3J_{PC}$= 11.9 Hz, C=O), 169.65 (d, $^2J_{PC}$=13.0 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P 23.04.

Minor (*E*)- 4d isomer (35%): ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 3.59 and 3.70 (6H, 2s, 2xOC*H*$_3$), 3.79 (3H, S, CH_3), 5.40 (1H, d, $^3J_{PH}$=16.2 Hz, P-C-C*H*), 7.48-7.69 (15H, m, 3xC_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 34.30 (1xC, N-CH_3), 40.67 (d, $^1J_{PC}$= 141.4 Hz, P=C), 50.48 and 52.64 (2x OCH_3), 62.37 (d, $^2J_{PC}$=17.1 Hz, P-C-*C*H), 125.34 (d, $^1J_{PC}$= 92.5 Hz, C_{ipso}), 128.95 (d, $^3J_{PC}$=12.3 Hz, C_{meta}), 132.38 (C_{para}), 133.41 (d, $^2J_{PC}$=9.9 Hz, C_{ortho}), 163.84 (N=C-S), 169.26 (d, $^3J_{PC}$= 12.0 Hz, C=O), 170.68 (d, $^2J_{PC}$=17.0 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P 23.32.

Diethyl 2-(5-mercapto-1-methyltetrazole-S-yl)-3-(triphenylphosphoranylidene)succinate (4e). White powder; (m.p. 75-76 yield 0.45g, 82%); IR (KBr) (ν_{max}, cm^{-1}): 1619, 1642 and 1747 (C=O); MS, *m/z* (%):108 (PPh, 42), 116 ($C_2H_3N_4S$, 22), 183 (PPh$_2$, 79), 262(PPh$_3$, 83), 275 (M-PPh$_2$ and 2xOCH_2CH_3, 34). Anal. Calcd. for $C_{28}H_{29}N_4O_4SP$ (548.23): C, 61.29; H, 5.33; N, 10.21%. Found: C, 61.41; H, 5.29; N, 10.31.

Major (*Z*)-4e isomer (72%). ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 0.42 and 1.17 (6H, 2t, $^3J_{HH}$=7.1 Hz, 2x O-CH_2CH_3), 3.78 (3H, S, CH_3), 3.73 and 4.13 (4H, 2m, 2 ABX_3 system, 2x O*CH*$_2$$CH_3$), 5.37 (1H, d, $^3J_{PH}$=17.0 Hz, P-C-C*H*), 7.50-7.71 (15H, m, 3C_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 13.76 and 14.08 (2xOCH_2CH_3), 34.37 (N-CH_3), 39.90 (d, $^1J_{PC}$= 126.5 Hz, P=C), 58.11 and 61.98 (2xO*CH*$_2$$CH_3$), 62.81 (d, $^2J_{PC}$=17.0 Hz, P-C-*C*H), 125.80 (d, $^1J_{PC}$= 92.5 HZ, C_{ipso}), 128.95 (d, $^3J_{PC}$=12.6 Hz, C_{meta}), 132.07(C_{para}), 133.57(d, $^2J_{PC}$=10.8 Hz, C_{ortho}), 163.93 (N=C-S), 168.50 (d, $^3J_{PC}$= 11.8 Hz, C=O), 169.19 (d, $^2J_{PC}$=11.6 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P 23.02.

Minor (*E*)-4e isomer (28%). ^{1}H NMR (500.1 MHz, $CDCl_3$), δ_H 1.16 and 1.33 (6H, 2t, $^3J_{HH}$=7.1 Hz, 2x OCH_2CH_3), 3.82 (3H, s, CH_3), 4.09 and 4.26 (4H, 2m, 2x ABX_3system, 2x O*CH*$_2$$CH_3$), 5.32 (1H, d, $^3J_{PH}$=16.3, P-C-C*H*), 7.50-7.71 (15H, m, 3xC_6H_5); ^{13}C NMR (125.8 MHz, $CDCl_3$), δ_C 14.62 and 15.30 (2xO*CH*$_2$$CH_3$), 33.70 (1C, N-$CH_3$), 40.63 (d, $^1J_{PC}$= 134.2 Hz, P=C), 58.86 and 61.87 (2xO*CH*$_2$$CH_3$), 62.18 (d, $^2J_{PC}$=17.1 Hz, P-C-*C*H), 125.16 (d, $^1J_{PC}$= 92.5 HZ, C_{ipso}),

129.05 (d, $^3J_{PC}$=14.0 Hz, C_{meta}), 132.13 (C_{para}), 133.48 (d, $^2J_{PC}$=10.8 Hz, C_{ortho}), 164.93 (N=C-S), 168.50 (d, $^3J_{PC}$= 11.8 Hz, C=O), 169.19 (d, $^2J_{PC}$=11.6 Hz, P-C=*C*); ^{31}P NMR (202.46 MHz, $CDCl_3$); δ_P 23.50.

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 isomers. The determination of the more stable isomer is impossible by the ^{31}P, ^{13}C and ^{1}H NMR techniques. For this reason quantum mechanical calculations have been performed in order to gain a better understanding of most important geometrical parameters and also the relative energies of both isomers.

Calculations

Structure and stabilities

In order to determine which is the more stable form of both *Z*-**4(a, d)** and *E*-**4(a, d)** isomers of ylides (**4a** and **4d** are selected as typical ylides from the different categories of **4a-c** and **4d-e**, respectively), their structures were first optimized at the HF/6-31G level of theory[42] by using the Gaussian 98 program package.[43] Also, the relative energies of the two isomers have been calculated at the HF/6-31G and B3LYP/6-311++G (d,p) levels (see Figures **1** and **2**). The relative stabilization energies for both *Z*-**4(a, d)** or *E*-**4(a, d)** isomers are reported in Table **2**. As can be seen, *Z*-**4a** and *E*-**4d** conformers are more stable than the *E*-**4a** and *Z*-**4d** forms (3.50 and 0.26 kcal/mol, respectively) at the B3LYP level.

Further investigation was undertaken in order to determine more effective factors on the stability of both isomers, on the basis of AIM calculations[44] at the HF/6-31G level of theory by the AIM2000 program package.[45] As noted in the literature,[46] the ranges of $\rho(r)$ and $\nabla^2\rho(r)$ are 0.002-0.035e/a_0^3 and 0.024-0.139 e/a_0^5, respectively, if H-bonds exist.

Table 2. The relative energy (kcal/mol) for both *Z*- and *E*- isomers of ylides **4a** and **4d**, calculated at the HF/6-31G and B3LYP/6-311++G(d,p) levels

Conformer	HF	B3LYP
Z*-4a	0.00	0.00
E*-4a	3.69	3.50
Z**-4d	0.00	0.26
E**-4d	0.05	0.00

***** 5-Aminotetrazole phosphorus ylides **(4a)** involving *Z*-**4a** and *E*-**4a** isomers.
****** 5-Mercapto-1-methyltetrazole phosphorus ylides **(4d)** involving *Z*-**4d and** *E*-**4d** isomers.

The number of hydrogen bonds in both categories (*Z*-**4a** and *E*-**4a**) and (*Z*-**4d** and *E*-**4d**) are (9 and 10) and also (8 and 9), respectively. In addition, the ranges of their electron densities are in (0.0022 - 0.0184 and 0.0021 - 0.0210 au) and also (0.0038 - 0.0190 and 0.0390 -0.0190 au), respectively. With respect to the large number of hydrogen bonds in both the *Z*- and *E*- isomers it is difficult to make a precise decision for determination of the more stable isomer.

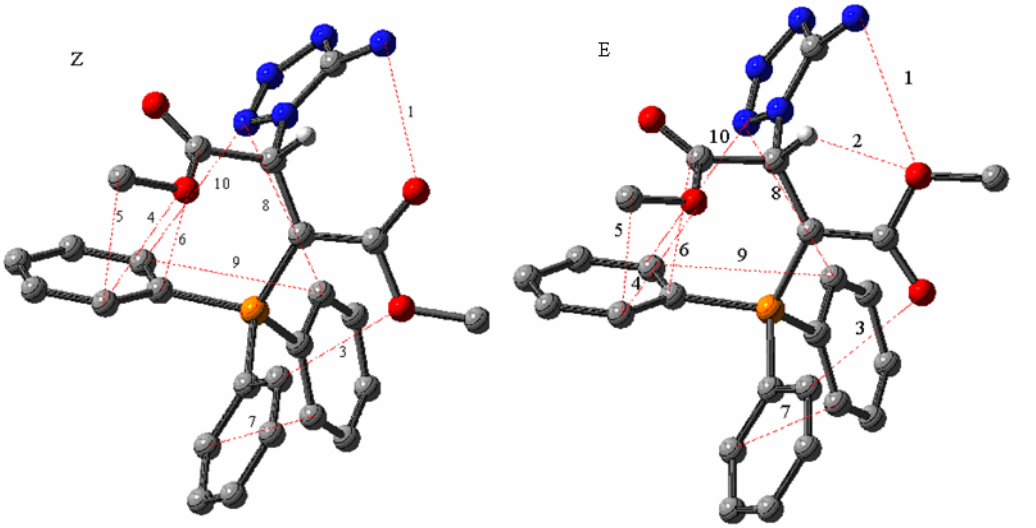


Figure1. Intramolecular hydrogen bonds (dotted lines) in *Z*-**4a** and *E*-**4a** isomers of stable ylides containing 5-aminotetrazole.

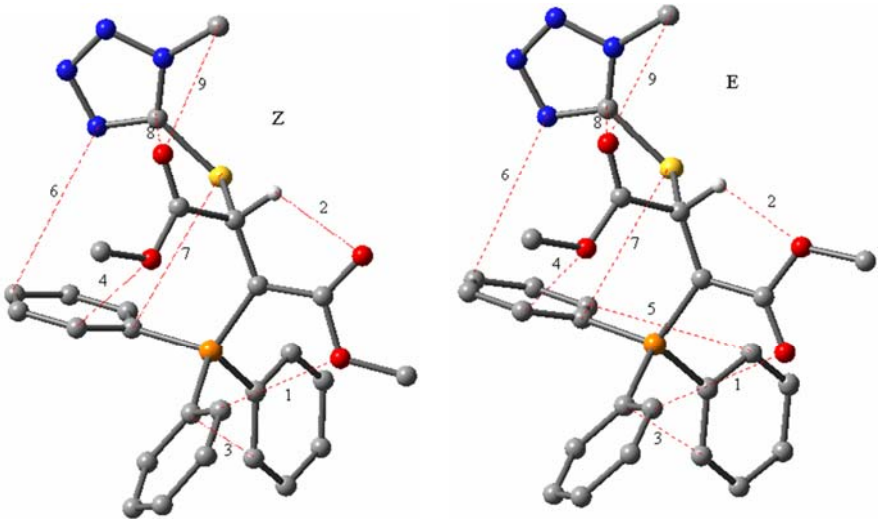


Figure 2. Intramolecular hydrogen bonds (dotted lines) in *Z*-**4d** and *E*-**4d** isomers of stable ylides containing 5-mercapto-1-methyltetrazole.

On the basis of theoretical calculations (Table **2**), the difference between the relative stability of the *E*-**4d** and *Z*-**4d** isomers in the gas phase is small (0.26 kcal/mol), while it is considerably greater in the *E*-**4a** and *Z*-**4a** isomers (3.50 kcal/mol). Perhaps this noticeable difference is taken

more in solution media for **4a,** and for this reason it is possible to observe only one isomer of **4a** (*Z* or *E*). In the Experimental Section both the ^{1}H NMR and ^{13}C NMR spectroscopies indicated only one isomer, in accordance with the category of the ylides **4a-c**. Nevertheless, the result of our calculations is different for ylide **4d** (observed as the two isomers), which may be attributed to the negligible difference in relative stability of *Z*-**4d** and *E*-**4d** isomers. Perhaps this negligible difference is not taken more considerably in solution media for **4d** and for this reason it is possible to see the two isomers of **4d** (both *Z* and *E* isomers). In recent case, the ^{1}H, ^{13}C, ^{31}P NMR data showed the two isomers for the category of ylides **4d-e** which were consistent with the obtained result from the theoretical investigations.

Conclusions

We have prepared the novel tetrazole stable phosphorus ylides using a one-pot reaction between triphenylphosphine and acetylenic compounds in the presence of NH or SH heterocyclic compounds such as 5-mercapto-1-methyltetrazole or 5-aminotetrazole. The present method has the advantage that not only is the reaction performed under neutral conditions, but also the substances can be mixed without any activation or modification. In addition, dynamic ^{1}H NMR of **4d**, and also the assignment of the *Z*- and *E*- isomers as a major or minor form in both of **4a** and **4d** ylides were undertaken in the theoretical study.

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