



# Chemoselective synthesis of stable phosphorus ylides containing a $\beta$ -amino group

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**Abstract**—A facile and chemoselective one-pot synthesis of stable phosphorus ylides containing a  $\beta$ -amino group has been developed via reaction of triphenylphosphine, dialkyl acetylenedicarboxylate and 1,2-phenylenediamine in the presence of phenol or 2-aminophenol on its own at ambient temperature. © 2003 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Phosphorus ylides are reactive intermediates, which have been used in many reactions and are involved a lot in the synthesis of organic compounds.<sup>1–8</sup> In recent years a method for the synthesis of organophosphorus compounds using a novel approach employing vinyl phosphonium salts has been developed.<sup>9–14</sup> Although this method is successful for the preparation of phosphorus ylides and 1,4-diiionic organophosphorus compounds<sup>15</sup> from one CH-acid,<sup>9,10</sup> OH or NH<sub>2</sub><sup>16,17</sup> functional group, the chemoselectivity in the presence of several functional groups has not been studied thus far.

In our investigation we found that 1,2-phenylenediamine reacts with triphenylphosphine and acetylenic esters in the presence of phenol, to produce stable  $\beta$ -amino substituted phosphorus ylides **3** in a chemoselective manner and at the end of the reaction, phenol was recovered. It is pertinent to note that this reaction is an intermolecular chemoselective reaction. In this reaction,  $\beta$ -phenoxy substituted stable phosphorus ylides **4** were not observed.

In order to investigate chemoselectivity of an intramolecular reaction for the preparation of phosphorus ylides, the reaction of 2-aminophenol with dialkyl acetylenedicarboxylate carried out in the presence of triphenylphosphine and in the absence of phenol. It was found out that not only 1,2-phenylenediamine in the presence of phenol produces compound **3** but compound **6** was also formed in the reaction of 2-aminophenol with acetylenic esters.

**Keywords:** stable phosphorus ylides; 1,2-phenylenediamine; phosphoranes.

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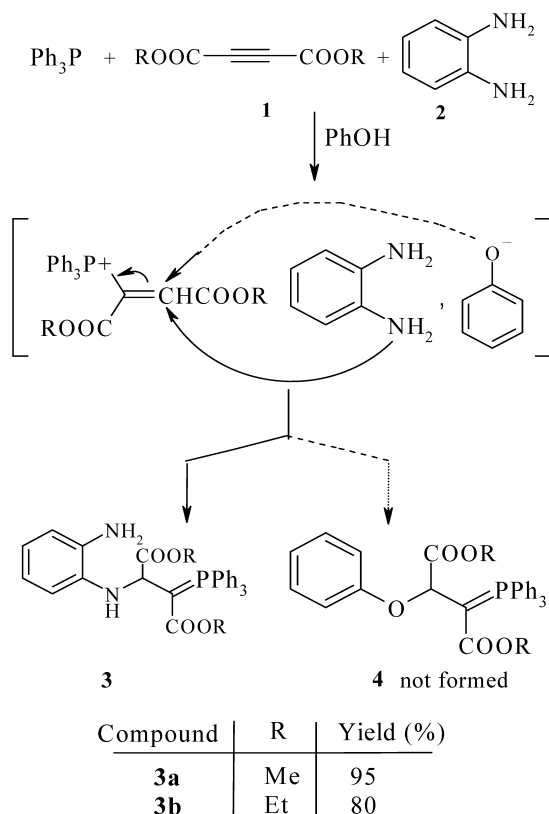
## 2. Results and discussion

On the basis of the well established chemistry of trivalent phosphorus nucleophiles,<sup>18–21</sup> it is reasonable to assume that phosphorus ylide **3** results from the initial addition of triphenylphosphine to the acetylenic ester and a concomitant protonation of the 1:1 adduct by phenol OH. Then the positively charged ion is attacked by the NH<sub>2</sub> group to form phosphorane **3**. This process shows that in the final step the amino group acts as a stronger nucleophile than the phenoxy anion (Scheme 1).

Also in a similar process to that exhibited in Scheme 1 the phosphoranes **6a–b** are formed and the phosphorus ylides **7** are not formed (Scheme 2).

The structures of compounds **3a–b** and **6a–b** were deduced from their elemental analyses and their IR, high-field <sup>1</sup>H and <sup>13</sup>C NMR spectra. The <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of phosphoranes **3a–b** and **6a–b** exhibited a mixture of two rotational isomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group and the rotation about the partial double bond in **3-(E)**, **3-(Z)** and **6-(E)**, **6-(Z)** geometrical isomer pairs is low on the NMR timescale at ambient temperature (Scheme 3). Rotamer forms in phosphoranes have been previously established and reported in the literature.<sup>22–24</sup>

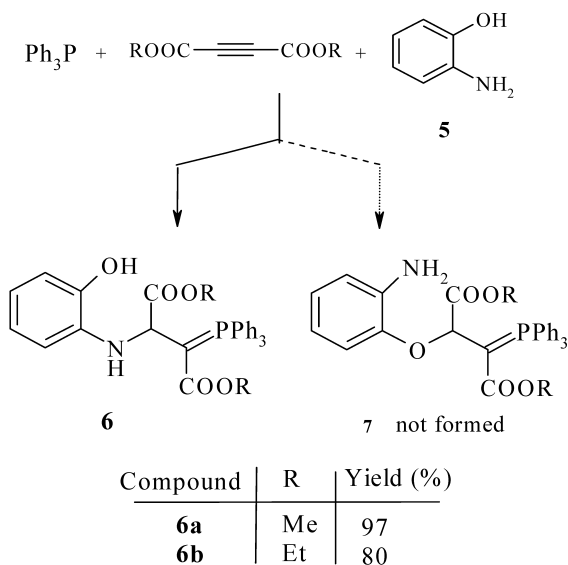
The <sup>1</sup>H NMR spectrum of **3a** showed four sharp lines ( $\delta$ =3.08, 3.62, 3.69 and 3.70 ppm) due to methoxy protons along with signals for methine protons at  $\delta$ =4.10 and 3.98 ppm, which appear as two doublets (<sup>3</sup>J<sub>PH</sub>=14.6 Hz) and (<sup>3</sup>J<sub>PH</sub>=16.4 Hz), respectively, for the major and minor geometrical isomers and two fairly broad signals at  $\delta$ =3.53 and 4.50 ppm, for protons of NH and NH<sub>2</sub> groups,



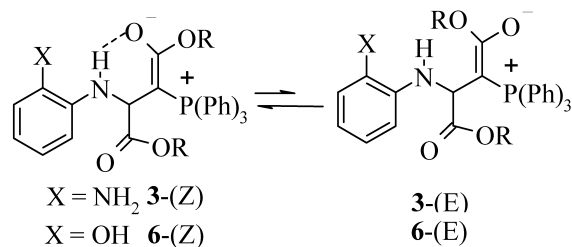
Scheme 1.

respectively. The  $^{13}\text{C}$  NMR spectrum of **3a** displayed 29 distinct resonances in agreement with the mixture of two rotamers. Although the presence of the  $^{31}\text{P}$  nucleus complicates both the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **3a**, it helps in assignment of signals by long-range spin–spin couplings with  $^1\text{H}$  and  $^{13}\text{C}$  nuclei.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of phosphorus ylide **3b** are



Scheme 2.



Scheme 3.

similar to those of **3a**, except for the signals from the ester groups, which appear as characteristic resonance lines with the corresponding chemical shifts.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopic data for compounds **6a–b** are also consistent with the presence of two geometrical isomers. The structural assignments made for phosphoranes **3a–b** and **6a–b** on the basis of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were supported by their IR spectra. In the IR spectra of **3a–b** three absorption bands at 3245–3334 and 3404–3418  $\text{cm}^{-1}$  were detected, due to the  $\text{NH}_2$  and  $\text{NH}$  groups, respectively. The IR spectra of phosphorus ylides **6a** and **6b** are similar to those of compounds **3a–b**, except for the absorption band from the  $\text{OH}$  group, which appears at 3200–3280  $\text{cm}^{-1}$  and no  $\text{NH}_2$  group was detected. The carbonyl region of the spectra exhibited two distinct absorption bands for each compound. Of special interest is the ester absorption at 1769–1647  $\text{cm}^{-1}$  for these compounds. Conjugation with negative charge accounts for the reduction of the wavenumbers of the carbonyl absorption bands.

### 3. Experimental

#### 3.1. General

Dialkyl acetylenedicarboxylates, 1,2-phenylenediamine and 2-amino-3-hydroxyaniline were obtained from Merck Chemical Co. and were used without further purification. Melting points were obtained on a Gallenkamp melting point apparatus and are uncorrected. Elemental analyses for C, H and N were performed by National Iranian Oil Company Laboratory (Tehran) using a Heracus CHN-O-Rapid analyzer. IR spectra were measured on a Mattson 1000 FT-IR spectrometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a BRUKER DRX-500 AVANCE spectrometer at 500 and 125.77 MHz, respectively.

**3.1.1. Dimethyl 2-(2-aminoanilino)-3-(triphenylphosphoranylidene)-butanedioate 3a.** At ambient temperature dimethyl acetylenedicarboxylate (0.24 mL, 2 mmol) was added dropwise to a stirred solution of triphenylphosphine (0.53 g, 2 mmol), 1,2-phenylenediamine (0.22 g, 2 mmol) and phenol (0.19 g, 2 mmol) in a mixture of hexane–ethyl acetate (6 mL, 1:2). After the addition was complete (approximately 5 min) the mixture was stirred for an additional 1 h and was subsequently filtered. The solid collected in the filter was washed thoroughly with ethyl acetate to give a pale yellow powder. (0.98 g, mp 140–142°C, yield 95%); IR (KBr) ( $\nu_{\text{max}}$ ,

$\text{cm}^{-1}$ ): 3418 (NH), 3334 and 3245 ( $\text{NH}_2$ ), 1765 and 1666 ( $\text{C}=\text{O}$ ). Anal. calcd for  $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_4\text{P}$  (512.54): C, 70.30; H, 5.70; N, 5.46%. Found: C, 70.20; H, 5.71; N, 5.30%.

Major isomer, **3a-(Z)** (70%),  $^1\text{H}$  NMR:  $\delta$  3.08 and 3.70 (6H, 2s, 2OCH<sub>3</sub>), 3.53 (2H, br. s, 2NH)\*, 4.10 (1H, d,  $^3J_{\text{PH}}=14.6$  Hz, P=C–CH), 4.50 (4H, br. s, 2NH<sub>2</sub>)\*, 6.12–7.51 (38H, m, arom)\*.  $^{13}\text{C}$  NMR:  $\delta$  43.16 (d,  $^1J_{\text{PC}}=122.7$  Hz, P=C), 48.82 and 51.87 (2OCH<sub>3</sub>), 57.97 (d,  $^2J_{\text{PC}}=14.2$  Hz, P=C–CH), 116.14, 119.11, 119.95 and 120.67 (4CH), 126.74 (d,  $^1J_{\text{PC}}=91.8$  Hz,  $\text{C}^{\text{ipso}}$ ), 128.58 (d,  $^3J_{\text{PC}}=12.95$  Hz,  $\text{C}^{\text{meta}}$ )\*, 131.77 (d,  $^4J_{\text{PC}}=1.8$  Hz  $\text{C}^{\text{para}}$ )\*, 133.75 (d,  $^2J_{\text{PC}}=9.8$  Hz,  $\text{C}^{\text{ortho}}$ )\*, 135.54 and 138.28 (2C), 169.82 (d,  $^2J_{\text{PC}}=12.9$  Hz, C=O), 174.67 (d,  $^3J_{\text{PC}}=6.9$  Hz, C=O). \*For two rotamers.

Minor isomer, **3a-(E)** (30%),  $^1\text{H}$  NMR:  $\delta$  3.62 and 3.69 (6H, 2s, 2OCH<sub>3</sub>), 3.98 (1H, d,  $^3J_{\text{PH}}=16.4$  Hz, P=C–CH).  $^{13}\text{C}$  NMR:  $\delta$  44.57 (d,  $^1J_{\text{PC}}=131.4$  Hz, P=C), 50.04 and 51.63 (2OCH<sub>3</sub>), 56.98 (d,  $^2J_{\text{PC}}=13.8$  Hz, P=C–CH), 116.24, 116.54, 118.67 and 119.18 (4CH), 126.17 (d,  $^1J_{\text{PC}}=91.6$  Hz,  $\text{C}^{\text{ipso}}$ ), 135.65 and 137.53 (2C), 170.32 (d,  $^2J_{\text{PC}}=16.8$  Hz, C=O), 174.92 (d,  $^3J_{\text{PC}}=8.1$  Hz, C=O).

**3.1.2. Diethyl 2-(2-aminoanilino)-3-(triphenylphosphoranylidene)-butanedioate 3b.** (0.86 g, pale yellow powder, mp 145–147°C, yield 80%); IR (KBr) ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3404 (NH), 3320 and 3280 ( $\text{NH}_2$ ), 1741 and 1641 ( $\text{C}=\text{O}$ ). Anal. calcd for  $\text{C}_{32}\text{H}_{33}\text{N}_2\text{O}_4\text{P}$  (540.60): C, 71.10; H, 6.15; N, 5.18%. Found: C, 71.00; H, 6.20; N, 5.01%.

Major isomer, **3b-(Z)** (75%),  $^1\text{H}$  NMR:  $\delta$  0.38 (3H, t,  $^3J_{\text{HH}}=7.0$  Hz, CH<sub>3</sub>), 1.18 (3H, t,  $^3J_{\text{HH}}=7.1$  Hz, CH<sub>3</sub>), 3.59 (2H, br. s, 2NH)\*, 3.67 (2H, m, CH<sub>2</sub>), 4.07 (1H, d,  $^3J_{\text{PH}}=15.5$  Hz, P=C–CH), 4.10–4.22 (6H, m, 3CH<sub>2</sub>)\*, 4.54 (4H, br. s, 2NH<sub>2</sub>)\*, 6.12–7.54 (38H, m, arom)\*.  $^{13}\text{C}$  NMR:  $\delta$  13.85 and 14.22 (2CH<sub>3</sub>), 42.77 (d,  $^1J_{\text{PC}}=122.5$  Hz, P=C), 58.05 (d,  $^2J_{\text{PC}}=14.3$  Hz, P=C–CH), 57.25 and 60.55 (2OCH<sub>2</sub>), 116.10, 119.03, 119.63 and 120.67 (4CH), 126.95 (d,  $^1J_{\text{PC}}=91.9$  Hz,  $\text{C}^{\text{ipso}}$ ), 128.26 (d,  $^3J_{\text{PC}}=12.2$  Hz,  $\text{C}^{\text{meta}}$ )\*, 131.71 (d,  $^4J_{\text{PC}}=2.0$  Hz  $\text{C}^{\text{para}}$ )\*, 133.86 (d,  $^2J_{\text{PC}}=9.4$  Hz,  $\text{C}^{\text{ortho}}$ )\*, 135.71 and 138.63 (2C), 169.35 (d,  $^2J_{\text{PC}}=12.4$  Hz, C=O), 173.96 (d,  $^3J_{\text{PC}}=6.8$  Hz, C=O). \*For two rotamers.

Minor isomer, **3b-(E)** (25%),  $^1\text{H}$  NMR:  $\delta$  1.22 (3H, t,  $^3J_{\text{HH}}=7.0$  Hz, CH<sub>3</sub>), 1.26 (3H, t,  $^3J_{\text{HH}}=6.9$  Hz, CH<sub>3</sub>), 3.95 (1H, d,  $^3J_{\text{PH}}=15.3$  Hz, P=C–CH).  $^{13}\text{C}$  NMR:  $\delta$  14.23 and 15.06 (2CH<sub>3</sub>), 44.50 (d,  $^1J_{\text{PC}}=131.2$  Hz, P=C), 57.08 (d,  $^2J_{\text{PC}}=14.2$  Hz, P=C–CH), 58.11 and 60.53 (2OCH<sub>2</sub>), 116.21, 116.46, 119.21 and 119.81 (4CH), 126.39 (d,  $^1J_{\text{PC}}=92.2$  Hz,  $\text{C}^{\text{ipso}}$ ), 135.80 and 137.81 (2C), 170.01 (d,  $^2J_{\text{PC}}=17.6$  Hz, C=O), 174.42 (d,  $^3J_{\text{PC}}=7.5$  Hz, C=O).

**3.1.3. Dimethyl 2-(2-hydroxyphenylamino)-3-(triphenylphosphoranylidene)-butanedioate 6a.** At ambient temperature dimethyl acetylenedicarboxylate (0.24 mL, 2 mmol) was added dropwise to a stirred solution of triphenylphosphine (0.53 g, 2 mmol) and 2-aminophenol (0.22 g, 2 mmol) in a mixture of hexane–ethyl acetate (6 mL, 1:2). After the addition was complete (approximately 5 min) the mixture was stirred for an additional 1 h and was subsequently filtered. The solid collected in the

filter was washed thoroughly with ethyl acetate to give a white powder. (1.0 g, mp 119–121°C, yield 97%); IR (KBr) ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3375 (NH), 3280–3200 (a broad peak for OH), 1749 and 1645 ( $\text{C}=\text{O}$ ). Anal. calcd for  $\text{C}_{30}\text{H}_{28}\text{NO}_5\text{P}$  (513.53): C, 70.17; H, 5.49; N, 2.73%. Found: C, 69.92; H, 5.51; N, 2.68%.

Major isomer, **6a-(Z)** (69%),  $^1\text{H}$  NMR:  $\delta$  3.05 and 3.72 (6H, 2s, 2OCH<sub>3</sub>), 3.60 (2H, br. s, 2NH)\*, 4.01 (1H, d,  $^3J_{\text{PH}}=14.1$  Hz, P=C–CH), 5.32 (2H, br. s, 2OH)\*, 6.12–7.71 (38H, m, arom)\*.  $^{13}\text{C}$  NMR:  $\delta$  43.96 (d,  $^1J_{\text{PC}}=120.89$  Hz, P=C), 49.12 and 51.98 (2OCH<sub>3</sub>), 59.49 (d,  $^2J_{\text{PC}}=13.1$  Hz, P=C–CH), 117.09, 120.59 (4CH), 126.11 (d,  $^1J_{\text{PC}}=91.8$  Hz,  $\text{C}^{\text{ipso}}$ )\*, 128.46 (d,  $^3J_{\text{PC}}=12.3$  Hz,  $\text{C}^{\text{meta}}$ )\*, 132.06 (d,  $^4J_{\text{PC}}=2.1$  Hz  $\text{C}^{\text{para}}$ )\*, 133.72 (d,  $^2J_{\text{PC}}=9.8$  Hz,  $\text{C}^{\text{ortho}}$ )\*, 135.83 and 149.84 (2C), 170.89 (d,  $^2J_{\text{PC}}=12.5$  Hz, 2C=O)\*, 174.12 (d,  $^3J_{\text{PC}}=6.5$  Hz, 2C=O)\*. \*For two rotamers.

Minor isomer, **6a-(E)** (31%),  $^1\text{H}$  NMR:  $\delta$  3.77 and 3.79 (6H, 2s, 2OCH<sub>3</sub>), 3.79 (1H, d,  $^3J_{\text{PH}}=11.8$  Hz, P=C–CH).  $^{13}\text{C}$  NMR:  $\delta$  43.98 (d,  $^1J_{\text{PC}}=124.7$  Hz, P=C), 50.16 and 52.25 (2OCH<sub>3</sub>), 58.30 (d,  $^2J_{\text{PC}}=13.0$  Hz, P=C–CH), 118.69, 120.01, 121.26 and 121.57 (4CH), 132.33 and 150.92 (2C).

**3.1.4. Diethyl 2-(2-hydroxyphenylamino)-3-(triphenylphosphoranylidene)-butanedioate 6b.** (0.87 g, white powder, mp 126–128°C, yield 80%); IR (KBr) ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3375 (NH), 3250–3200 (a broad peak for OH), 1750 and 1661 ( $\text{C}=\text{O}$ ). Anal. calcd for  $\text{C}_{32}\text{H}_{32}\text{NO}_5\text{P}$  (541.58): C, 70.97; H, 5.95; N, 2.58%. Found: C, 70.80; H, 5.90; N, 2.70%.

Major isomer, **6b-(Z)** (81%),  $^1\text{H}$  NMR:  $\delta$  0.33 (3H, t,  $^3J_{\text{HH}}=7.1$  Hz, CH<sub>3</sub>), 1.16 (3H, t,  $^3J_{\text{HH}}=7.1$  Hz, CH<sub>3</sub>), 3.61–3.69 (2H, m, CH<sub>2</sub>), 3.98 (1H, d,  $^3J_{\text{PH}}=13.8$  Hz, P=C–CH), 3.59 (2H, br. s, 2NH)\*, 4.07–4.24 (6H, m, 3CH<sub>2</sub>), 5.23 (2H, br. s, 2OH)\*, 6.11–7.55 (38H, m, arom)\*.  $^{13}\text{C}$  NMR:  $\delta$  13.68 and 14.17 (2CH<sub>3</sub>), 43.64 (d,  $^1J_{\text{PC}}=120.8$  Hz, P=C), 57.83 and 60.79 (2OCH<sub>2</sub>), 59.53 (d,  $^2J_{\text{PC}}=13.5$  Hz, P=C–CH), 117.35, 120.61, 121.64 and 121.73 (4CH), 126.23 (d,  $^1J_{\text{PC}}=91.9$  Hz,  $\text{C}^{\text{ipso}}$ )\*, 128.39 (d,  $^3J_{\text{PC}}=11.3$  Hz,  $\text{C}^{\text{meta}}$ )\*, 131.99 (d,  $^4J_{\text{PC}}=2.3$  Hz  $\text{C}^{\text{para}}$ )\*, 133.86 (d,  $^2J_{\text{PC}}=9.7$  Hz,  $\text{C}^{\text{ortho}}$ )\*, 136.07 and 250.26 (2C), 170.64 (d,  $^2J_{\text{PC}}=12.4$  Hz, 2C=O)\*, 173.48 (d,  $^3J_{\text{PC}}=6.0$  Hz, 2C=O)\*. \*For two rotamers.

Minor isomer, **6b-(E)** (19%),  $^1\text{H}$  NMR:  $\delta$  1.21 (3H, t,  $^3J_{\text{HH}}=7.1$  Hz, CH<sub>3</sub>), 1.23 (3H, t,  $^3J_{\text{HH}}=7.2$  Hz, CH<sub>3</sub>), 3.82 (1H, d,  $^3J_{\text{PH}}=16.6$  Hz, P=C–CH).  $^{13}\text{C}$  NMR:  $\delta$  14.05 and 14.91 (2CH<sub>3</sub>), 43.66 (d,  $^1J_{\text{PC}}=120.7$  Hz, P=C), 58.31 and 61.27 (2OCH<sub>2</sub>), 58.30 (d,  $^2J_{\text{PC}}=12.0$  Hz, P=C–CH), 118.78, 119.84, 120.59 and 121.69 (4CH) 133.57 and 149.87 (2C).

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