Three-component one-pot synthesis and multinuclear NMR study of some β-phosphorus ylides

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A one-step synthesis of sterically congested phosphorus ylides in moderate to good yields by the reaction of dialkyl acetylenedicarboxylates, NH-acids, dialkyl acetylene dicarboxylates and triphenylphosphine or tri-*p*-tolylphosphine are reported. The characterisation of these compounds were confirmed by IR, ^{1}H, ^{31}P, and ^{13}C NMR spectroscopy and elemental analysis. NMR spectra showed that some of these compounds (in $CDCl_3$ as solvent) contained two rotamers with unequal populations that equilibrate rapidly at higher temperatures.

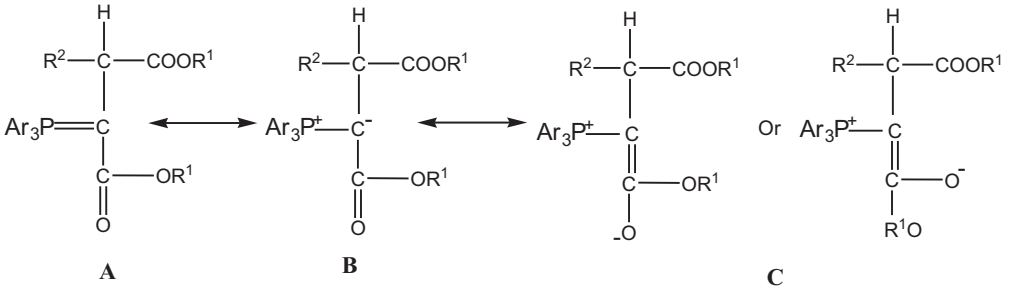
Keywords: ylide, triphenylphosphine, tri-*p*-tolylphosphine, rotamer

Phosphorus ylides are reactive compounds that take part in many reactions of value in the synthesis of organic products.[1-4] These compounds are synthetic targets of interest, because of their value for a variety of industrial, biological and chemical synthetic uses.[5-10] Several methods have been developed for the preparation of phosphorus ylides. These are usually prepared by treatment of a phosphonium salt with a base. Phosphonium salts are usually obtained from the phosphine and alkyl halide. Phosphonium salts are also prepared by Michael addition of phosphorus nucleophiles to activated olefins in other ways.[4] In recent years there have been established a one-pot method for the synthesis of stabilised ylides.[11-14] The phosphonium salts are most often converted to ylides by treatment with a strong base, though weaker bases can be used if the salt is acidic enough. The coordination chemistry of the phosphoranes of the type α-keto stabilised ylides Ph_3P =CHCOR have shown useful applications in organometallic chemistry (due to their ambidentate character as ligands) and also they act as reactants or valuable key intermediates in metal-mediated organic synthesis. This ambidentate character as ligands can be rationalised in terms of the resonance forms A–C (where **C** is represented by the *cis* and *trans* geometrical isomers). The chemical behaviour of carbonyl-stabilised ylide is largely dominated by the **C**(ylide)-coordination while very few examples of *O*-coordinated ylides are known.[15,16]

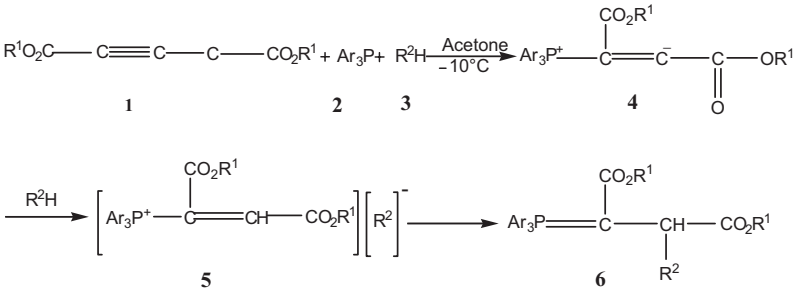
In this paper, we follow the preparation of sterically congested phosphorus ylides from electron-deficient acetylenic esters such as dialkylacetylenedicarboxylates (**1**), triarylphosphine (**2**) and NH acids (imidazol, 1,5-diphenylcarbazone and 2-aminopyridine) (**3**) (Scheme 2).

Results and discussion

The three-component one-pot synthesis leads to **5a–g** ylides in Table 1. The ylide **5** may result from initial addition of (triarylphosphine) **2** to the (acetylenic ester) **1** and concomitant protonation of the 1:1 adduct, followed by attack of the (NH-acid anion) **3** on the vinyltriarylphosphonium cation (**4**) to form the stabilised phosphoranes **5**. The structures **5a–g** were deduced from their IR, ^{1}H, ^{31}P, ^{13}C NMR spectra and elemental analysis. The NMR spectra of some compounds exhibited two picks at different chemical shifts for one absorbent.[15-16] For example in ^{31}P NMR, $\delta_1 = 20.55$ and $\delta_2 = 21.496$ ppm for **5a** and $\delta_1 = 19.218$ and $\delta_2 = 21.10$ ppm for **5d** is related to major and minor rotamers (**6** and **7**) in unequal populations (Scheme 3). Thus variable temperature of ^{31}PNMR study for



Scheme 1



Scheme 2

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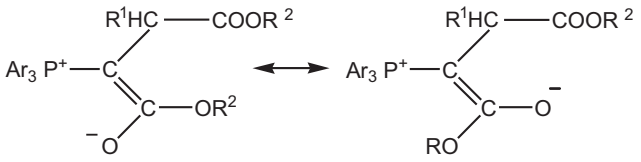

6 (R_1or R_2) **7** (R_1 or R_2)

Scheme 3

Table 1 Ylide components **5a–g**

5	R^1	R^2H	Ar
a	Me	Imidazol	Ph
b	*t*-Bu	Imidazol	Ph
c	Me	Imidazol	*p*-Tolyl
d	*t*-Bu	Imidazol	*p*-Tolyl
e	*t*-Bu	1,5 diphenylcabazone	Ph
f	Me	1,5 diphenylcabazone	Ph
g	Me	2-aminopyridine	Ph

5a showed that the two rotamers equilibrate rapidly at higher temperatures. (Figure 1).

The ^{1}H NMR spectra of these ylides show one doublet resonance attributed to the methine proton $CHCO_2R^2$ between 4.184 ppm to 4.697 ppm. In some cases there are two doublets or broad resonance due to rotamers. This probably arises from very close chemical shifts of the methinic proton of the four diastereoisomers (Scheme 1).

Experimental

Physical measurements: Melting points were measured on a SMPI apparatus. Elemental analysis for C, H and N were performed using a PE 2400 series II analyser. IR and NMR spectra were recorded on a Shimadzu 435-U-04 FT spectrophotometer (KBr pellets) and a 200 MHz Bruker FT-NMR spectrometer with $CDCl_3$ as solvent respectively. Chemical shifts reported are relative to TMS and 85% phosphoric acid. The imidazol, 1,5-diphenylcarbazone, 2-(2-pyridylamino) and solvents used in this work were obtained from Merck and used without further purification.

Synthesis: dimethyl 2-(imidazol-1-yl)-3-(triphenylphosphoranylidene) succinate (**5a**): *Typical procedure:* To a magnetically stirred solution of triphenylphosphine (0.262 g, 1 mmol) and imidazol (0.068 g, 1 mmol) in acetone (15 ml) was added drop wise to a solution of dimethyl acetylenedicarboxylate (0.12 ml 1 mmol) in acetone (3 ml) at –10°C over 15 min. The mixture was allowed to warm up to room temperature. The solvent was removed under reduced pressure and the residue was washed with light petroleum and then crystallised from ethyl acetate-light petroleum ether (1:3). Products were collected by filtration. Yield: 0.396 g, 84%, m.p. 157.0–159.0°C (CH_3Cl). IR ν_{max}/cm^{-1} 1750(s), 1721(s), (2CO). ^{1}H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.97–7.85 (m, $3C_6H_5$, imidazol-1-yl), 4.54 (R_1) (d, ^3J (PCCH) = 16.12 Hz), 4.59 (R_2) (d, ^3J (PCCH) = 17.02 Hz), 3.75 (s, $COCH_3$), 3.18 (R_1) (s, $COCH_3$), 3.61 (R_2) (s, $COCH_3$). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 20.55(R_1) 21.46(R_2). ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 43.47 (d, ^1J (PC)=125.03 Hz), 60.05 (d, ^2J (PCC) = 13.96 Hz), 52.39 ($CO_2{}^{13}CH_3$), 49.12 (R_1) 49.97 (R_2) ($CO_2{}^{13}CH_3$), 119.05–136.77(m, C_6H_5, imidazol-1-yl), 171.30, 169.28 (R_1) 171.87, 169.79 (R_2) ($2CO_{ester}$); Anal. Calcd. for $C_{27}H_{25}N_2O_4P$: C, 68.63; H, 5.33; N, 5.92. Found: C, 69.08; H, 5.64; N, 5.98%.

Di-tert-butyl 2-(imidazol-1-yl)-3-(triphenylphosphoraniliden)-succinate (**5b**)*:* Yield: 0.372 g, 67%, m.p. 177.0–179.0°C (CH_3Cl). IR ν_{max}/cm^{-1} 1743(s), 1638(s), (2CO). ^{1}H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.96–7.88 (m, $3C_6H_5$, imidazol-1-yl), 4.33 (d, ^3J (PCCH) = 16.12 Hz), 0.96 (s, $COC(CH_3)_3$), 1.53 (s, $COC(CH_3)_3$). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 20.13 ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 43.57 (d, ^1J (PC) = 129.15 Hz), 60.70 (d, ^2J (PCC) = 15.18 Hz), 28.12, 28.25 ($2OC(^{13}CH_3)_3$), 77.58, 81.14 ($2O^{13}C(CH_3)_3$), 119.23–137.0 (m, C_6H_5, imidazol-1-yl), 169.84, 168.33 (R_1) 170.36, 168.87 (R_2) ($4CO_{ester}$). Anal. Calc. for $C_{33}H_{37}N_2O_4P$: C, 71.21; H, 6,69; N, 5.03. Found: C, 71.82; H, 6.77; N, 5.16%.

Dimethyl 2-(imidazol-1-yl)-3-(tri-p-tolylphosphoraniliden)succinate (**5c**): Yield: 0.424 g, 82.5%, m.p. 171.0–173.0°C (CH_3Cl). IR ν_{max}/cm^{-1} 1753(s), 1733(s), (2CO). ^{1}H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.92–7.51 (m, $3C_6H_4$, imidazol-1-yl), 4.52 (R_1) (d, ^3J (PCCH) = 16.03 Hz), 4.58 (R_2) (d, ^3J (PCCH) = 16.03 Hz), 2.40 (s, $3CH_3$), 3.69 (s, $COCH_3$), 3.18 (R_1) (s, $COCH_3$), 3.56 (R_2) (s, $COCH_3$). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 19.56 (R_1), 20.72 (R_2). ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 45.21 (d, ^1J (PC) = 174.5 Hz), 60.28 (d, ^2J (PCC) = 12.88 Hz), 21.27 (s, $(CH_3)_3$), 52.39 ($CO_2{}^{13}CH_3$), 49.09 (R_1) 49.88 (R_2) ($CO_2{}^{13}CH_3$), 119.10–142.84 (m, C_6H_4, imidazol-1-yl), 171.97, 169.31 (R_1) 171.97, 169.87 (R_2) ($4CO_{ester}$). Anal. Calc. for $C_{30}H_{31}N_2O_4P$: C, 70.02; H, 6,07; N, 5.44. Found: C, 70.18; H, 6.23; N, 5.46%.

Di-tert-butyl 2-(imidazol-1-yl)-3-(tri-p-tolylphosphoranilidene)-succinate (**5d**): Yield: 0.487 g, 81.5%, m.p. 162–164°C. (CH_3Cl). IR ν_{max}/cm^{-1} 1744(s), 1636(s), (2CO). ^{1}H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.62–7.53 (m, $3C_6H_4$, imidazol-1-yl), 4.27 (d, ^3J (PCCH) = -16.48 Hz), 2.36 (s, $3CH_3$), 1.47 (s, $COC(CH_3)_3$), 0.91 (s, $COC(CH_3)_3$). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 19.21. ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 132.59 (d, ^1J (PC) = 123.99 Hz), 133,52 (d, ^2J (PCC) = 15.76 Hz), 22.27 (s, $(CH_3)_3$), 28.75 ($2OC(^{13}CH_3)_3$), 80.35, 81.44 (2 s, $2O^{13}C(CH_3)_3$), 121.49–143.36 (m, C_6H_4, imidazol-1-yl), 164.49 (2CO). Anal. Calc. for $C_{36}H_{43}N_2O_4P$: C, 72.22; H, 7.23; N, 4.67. Found: C, 72.83; H, 7.37; N, 4.86%.

Di-tert-butyl 2-(1,5-diphenycarbazono)-3-(triphenylphosphoranilide)succinate (**5e**): Yield: 0.579 g, 79.5%, m.p. 196–198°C. (CH_3Cl). IR ν_{max}/cm^{-1}1732(s), 1704(s), 1690(s) (3CO). ^{1} H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.75–7.66 (m, $5C_6H_5$), 4.85 (d, ^3J (PCCH) = 19.17 Hz), 0.873 (s, $COC(CH_3)_3$), 1.53 (s, $COC(CH_3)_3$, 7.90 (s, NH). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 20.99. ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 39.78 (d, ^1J (PC) = 126.33 Hz), 61.35 (d, ^2J (PCC) = 16.13 Hz), 28.27 (s, $2OC(^{13}CH_3)_3$), 77.37, 80.93 (2 s, $2O^{13}C(CH_3)_3$), 113.48–133.77 (m, C_6H_5), 160.57 ($CO_{carbazone}$), 149.66 (d, ^2J (CO_{ester}) = 17.05 Hz), 171.81 (R_1) (d, ^3J (CO_{ester}) = 12.05 Hz), 170.41 (R2) (d, ^3J (CO_{ester}) = 12.57 Hz). Anal. Calc. for $C_{43}H_{45}N_4O_5P$: C, 70.86; H, 6.22; N, 7.68. Found: C, 70.97; H, 6.31; N, 7.72%.

Dimethyl2-(1,5-diphenycarbazono)-3-(triphenylphosphoranylidene)-succinate (**5f**): Yield: 0.486 g, 75.4%, m.p. 201–203°C. (CH_3Cl). IR ν_{max}/cm^{-1} 1744(s), 1702(s), 1611(s) (3CO). ^{1} H NMR (200 MHz, 25°C, $CDCl_3$): δ 6.86–7.90 (m, $5C_6H_5$), 5.04 (d, ^3J (PCCH) = 19.71 Hz), 3.05 (s, $COCH_3$), 3.79 (s, $COCH_3$), 8.62 (s, NH). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 21.18. ^{3}C NMR (200 MHz, 25°C, $CDCl_3$): δ 44.22 (d, ^1J (PC) = 133.81 Hz), 59.12 (d, ^2J (PCC) = 14.23 Hz), 50.65, 50.74 (2 s, $2CO_2{}^{13}CH_3$), 111.66–133.63 (m, C_6H_5), 159.52 ($CO_{carbazone}$), 148.35 (d, $^2J_{pc}$ (CO_{ester}) = 16.41 Hz), 170.76 (d, $^3J_{pc}$ (CO_{ester}) = 12.08 Hz). Anal. Calc. for $C_{37}H_{33}N_4O_5P$: C, 68.93; H, 5.15; N, 8.69. Found: C, 69.12; H, 5.18; N, 8.72%.

Dimethyl 2-(2-pyridylamino)-3-(triphenylphosphoranylidene)-succinate (**5g**): Yield: 0.361 g, 72.61%, m.p. 175–177°C. (CH_3Cl). IR ν_{max}/cm^{-1} 1741(s), 1618(s) (2CO). ^{1} H NMR (200 MHz, 25°C, $CDCl_3$): δ 7.21–7.83 (m, $5C_6H_5$), 6.08–6.75 (m, 2-pyridylamino)

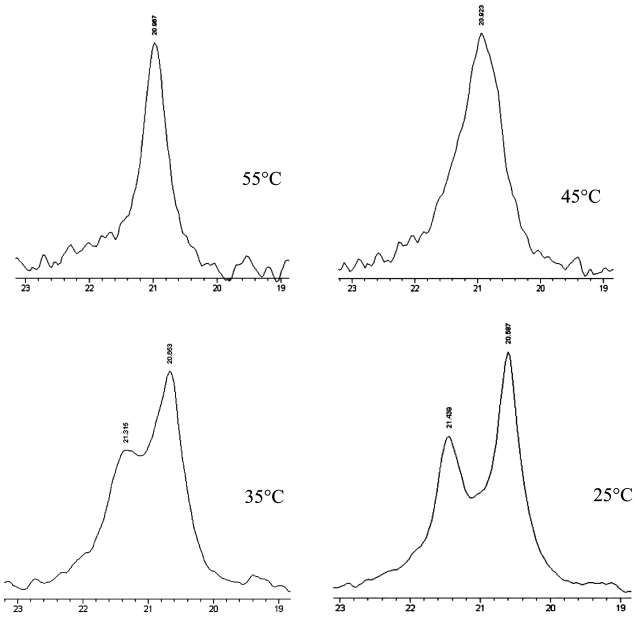

Fig. 1 Variable temperature ^{31}PNMR study in **5a**.

5.58 (s, ^3J (NH) = 7.07 Hz), 4.76 (R_1) (d, ^3J (PCCH) = 7.16 Hz), 4.95 (R_2) (d, ^3J (PCCH) = 7.16 Hz), 3.67 (s, $COCH_3$), 3.10 (R_1) (s, $COCH_3$), 3.53 (R_2) (s, $COCH_3$). ^{31}P NMR (90 MHz, 25°C, $CDCl_3$): δ 19.74 (R_1) 20.58 (R_2). ^{13}C NMR (200 MHz, 25°C, $CDCl_3$): δ 51.01 (d, ^1J (PC) = 116.66 Hz), 53.66 (d, ^2J (PCC) = 15.43 Hz), 52.17, 51.88 (2 s, CO_2CH_3), 109.03–147.26 (m, C_6H_5, 2-pyridylamino), 174.72 (d, ^2J (CO_{ester}) = 8.94 Hz), 157.83 (s, (CO_{ester}). Anal. Calc. for $C_{29}H_{27}N_2O_4P$: C, 69.87; H, 5.45; N, 5.61. Found: C, 70.09; H, 5.52; N, 5.72%.

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