Synthesis and variable temperature ^{1}H and ^{31}P NMR study of phosphorus ylides derived from reaction of NH-acids, triarylphosphine and acetylenic esters

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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 and triarylphosphines are reported. Characterisation of the obtained compounds was performed by IR, ^{1}H, ^{31}P, ^{13}C NMR, elemental analysis and mass spectroscopy. 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, triparatolylphosphine, rotamer, NH-acid

Phosphorus ylides are reactive compounds, which 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.[5-9] Several methods have been developed for the preparation of phosphorus ylides. These ylides are usually prepared by treatment of a phosphonium salt with a base, and 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]

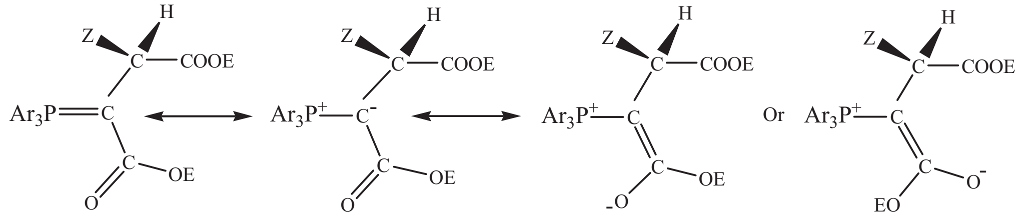
In recent years a one-pot method for the synthesis of stabilised ylides has been established.[10-13] The phosphonium salts are most often converted to ylides by treatment with a strong base, though weaker bases can be used if the salt is acidic enough. The coordination chemistry of the phosphoranes of 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** (Scheme 1) (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.[14]

In this paper we are followed the preparation of sterically congested phosphorus ylides from electron-deficient acetylenic esters such as dialkyl acetylenedicarboxylates (**1**), triarylphosphine (**2**) and NH acids (phthalimide and *N,N'*-diacetylhydrazine) (**3**) (Scheme 2).

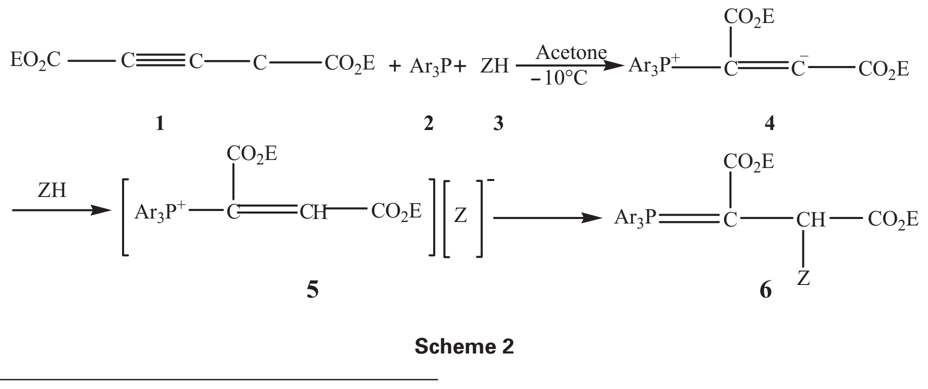
Results and discussion

The three-component one-pot synthesis leads to **6a–h** ylides in Table 1. The ylide **6** 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 (**5**) to form the stabilised phosphoranes **6**.

The structures **6a–h** were deduced from their IR, ^{1}H, ^{31}P, ^{13}C NMR spectra, elemental analysis and Mass spectroscopy. The nature of these compounds as 1:1:1 adducts was apparent from their mass spectra which displayed fairly weak molecular ion peaks. Initial fragmentations involve loss of the complete side chain or partially loss of the side chains and scission of the heterocyclic ring system.



Scheme 1



Scheme 2

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Table 1 Ylide components **6a–h**

6	E	ZH	Ar	Yield/%	Ref.
a	Me	Phthalimide	Ph	79	15
b	Me	*N,N'*-diacetylhydrazine	Ph	77	This work
c	Me	Phthalimide	*p*-tolyl	74	This work
d	Me	*N,N'*-diacetylhydrazine	*p*-tolyl	80	This work
e	t-Bu	Phthalimide	Ph	69	This work
f	t-Bu	*N,N'*-diacetylhydrazine	Ph	67	This work
g	t-Bu	Phthalimide	*p*-tolyl	84	This work
h	t-Bu	*N,N'*-diacetylhydrazine	*p*-tolyl	83	This work

The NMR spectra of some of these compounds exhibited two peaks at different chemical shifts for one absorbent.[14] For example in ^{31}P NMR, δ_1 = 20.122 and 20.213 ppm for **6a** and 21.652 and 23.369 ppm for **6b** in $CDCl_3$ are related to major and minor rotamers (**7** and **8**) in unequal populations (Scheme 3).

The ^{1}H NMR spectra of these ylides showed one doublet attributed to the methinic proton ($CHCO_2E$) between 4.63 to 5.16 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).

Variable temperature ^{1}H and ^{31}P NMR study for **6a** showed that the two rotamers equilibrate rapidly at higher temperatures (Fig. 1).

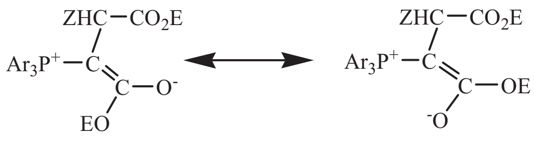
Experimental

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 are reported relative to TMS and 85% phosphoric aãd. Mass spectra were performed using a Shimadzu GC-MS QP1100 Ex/UP 1100 spectrometer (EI at 70 eV). The reagents and solvents used in this work were obtained from Merck and used without further purification.

Synthesis:dimethyl2-(Phthalimide-N-yl)-3-(triphenylphosphanylidene) butanedioate (**6a**) *Typical procedure*

To a magnetically stirred solution of triphenylphosphine (0.262 g, 1 mmol) and phthalimide (0.147 g, 1 mmol) in acetone (15 ml) was added drop wise 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 petroleum benzine and then crystallised from ethyl acetate light petroleum ether (1:3). Crystals were collected by filtration. Yield: (79%); white crystals; m.p. 187–189°C (lit.[15] 125–127°C). IR (KBr) ν (cm^{-1}): 1748, 1708 and 1652 (CO), 903 (P=C). ^{1}H NMR δ: 3.17 and 3.63 (R_1 and R_2) (3H, 2 s, CO_2CH_3), 3.73 (3H, s, CO_2CH_3), 4.81 and 4.82 (1H, 2d, $^3J_{PH}$ = 15.77 Hz (R_1), $^3J_{PH}$ = 17.74 Hz (R_2), $CHCO_2Me$), 7.52–7.72 (19H, m, arom.). ^{31}P NMR δ_P: 20.12 and 20.21 (R_1 and R_2). ^{13}C NMR δ_C: (P=C, was not observed), 48.75 and 50 (R_1 and R_2) (CO_2CH_3), 52.23 (CO_2CH_3), 54.83 (d, $^2J_{PC}$ = 13.7 Hz, *C*H), 122.56–133.52 (arom.), 167.19 (2*C*=*O* (phthalimide)), 170.77 and 171.34 (2*C*=*O*, (ester)). MS (EI 70 eV): *m/z* (%) = 277 (72), 222 (52), 179 (61), 147 (100), 76 (65). Anal. Calcd For $C_{32}H_{26}NO_6P$: C, 69.69; H, 4.75; N, 2.54. Found: C, 69.31; H, 4.65; N, 2.48.

Dimethyl 2-(N,N'-diacetylhydrazine-N-yl)-3-(triphenylphosphanylidene)butanedioate (**6b**): Yield: (77%); white crystals, m.p. 191–192°C. IR (KBr) ν (cm^{-1}). 1735, 1707, 1672 and 1610 (CO), 898 (P=C). ^{1} H NMR δ_H: 1.95 and 2.00 (R_1 and R_2) (3H, 2 s, $COCH_3$), 2.05 (3H, s, $COCH_3$), 3.18 and 3.56 (R_1 and R_2) (3H, 2 s, CO_2CH_3), 3.75 (3H, s, CO_2CH_3), 5.09 and 5.13 (1H, 2d, $^3J_{PH}$ = 18 Hz (R_1), $^3J_{PH}$ = 19.44 Hz (R_2), $CHCO_2CH_3$), 7.53–7.82 (15H, m, arom.), 8.15 (1H, s, N*H*). ^{31}P NMR δ_P: 21.65 and 23.37 (R_1 and R_2). ^{13}C NMR δ_C: 20.67 ($2COCH_3$), 40.20 (d, $^1J_{PC}$ = 127.49 Hz, P=C), 48.97 and 49.73 (R_1 and R_2) (CO_2CH_3); 52.06 (CO_2CH_3), 58.72 (d, $^2J_{PC}$ = 18.86 Hz, *C*H), 123.65-133.61 (arom.), 169.58, 170.35, 170.69, 171.29, 171.93 and 172.40 (NH*C*=*O*, N*C*=*O* and 2*C*O (ester), including R_1 and R_2). MS (EI 70 eV): *m/z* (%) = 520 (M$^+$, 0.5), 461 (29), 405 (100), 262 (74), 43 (26). Anal. Calcd for $C_{28}H_{29}N_2O_6P$: C, 64.61; H, 5.62; N, 5.38. Found: C, 64.87; H, 5.74; N, 5.62.



7 (R_1 or R_2) **8** (R_1 or R_2)

Scheme 3 R_1 = minor rotamer and R_2 = major rotamer

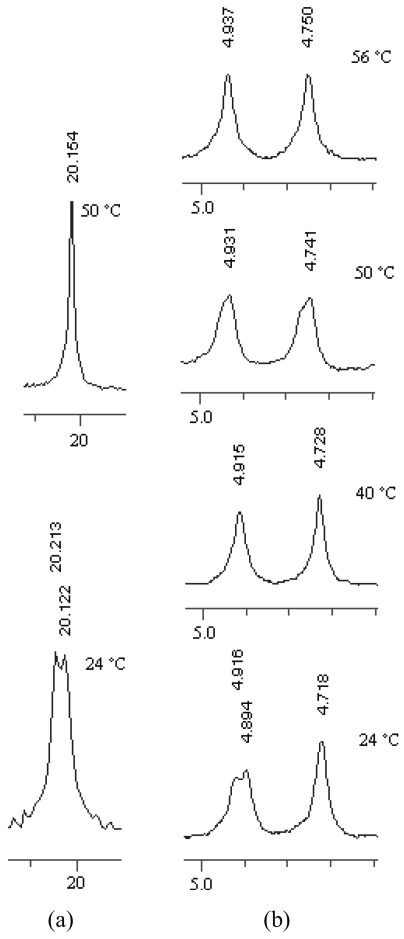


Fig. 1 Variable temperature NMR study on **6a** in $CDCl_3$: a) ^{31}P NMR, b) ^{1}H NMR (doublet of CH).

Dimethyl 2-(Phthalimide-N-yl)-3-(tri-p-tolylphosphanylidene)butanedioate (**6c**): Yield: (74%); m.p. 188–190°C. IR (KBr) ν (cm^{-1}): 1742, 1715 and 1634 (CO), 889 (P=C). ^{1}H NMR δ_H: 2.39 (9H, s, $3CH_3$), 3.18 and 3.61 (R_1 and R_2) (3H, 2 s, CO_2CH_3), 3.72, (3H, s, CO_2CH_3), 4.82 and 4.85 (1H, 2d, $^3J_{PH}$ = 15.68 Hz (R_1), $^3J_{PH}$ = 17.11 Hz (R_2), $CHCO_2CH_3$); 7.267–7.78 (16H, m, arom.). ^{31}P NMR δ_P: 19.29 and 19.35 (R_1 and R_2). ^{13}C NMR δ_C: 21.23 ($3CH_3$); 37.30 and 38.98 (2d, $^1J_{PH}$ = 131.38 Hz (R_1), $^1J_{PH}$ = 139.63 Hz (R_2), P=C), 48.71 and 49.96 (R_1 and R_2) (CO_2CH_3), 52.19 (CO_2CH_3), 54.45 and 54.98 (2d, $^2J_{PC}$ = 16.69 Hz, (R_1), $^2J_{PC}$ = 16.94, (R_2), P=C-*C*H); 121.06

– 142.21 (arom.), 167.21 (2*C*=*O* (phthalimide)), 170.99 and 171.55 ($2C{=}O_{\mathrm{ester}}$). MS (EI 70 eV): m/z (%) = 593 (M^+, 0.5), 319 (76), 304 (100), 211 (93), 122 (60), 78 (32). Anal. Calcd for $C_{35}H_{32}NO_6P$: C, 70.82; H, 5.43; N, 2.36. Found: C, 71.16; H, 5.60; N, 2.15.

Dimethyl 2-(N,N'-diacetylhydrazine-N-yl)-3-(tri-p-tolylphosphanylidene)butanedioate (**6d**): Yield: (80%); white crystals, m.p. 193–194°C. IR (KBr) ν (cm^{-1}). 1748, 1703, 1667 and 1618 (CO), 892 (P=C). ^{1}H NMR δ_H: 2.00 and 2.06 (6H, 2 s, $2COCH_3$), 2.40 (9H, s, $3CH_3$), 3.19 and 3.54 (R_1 and R_2) (3H, 2 s, CO_2CH_3,), 3.73 and 3.80 (R_1 and R_2) (3H, 2 s, CO_2CH_3,), 5.11 and 5.16 (1H, 2d, $^3J_{PH}$ = 18.28 Hz (R_1), $^3J_{PH}$ = 19.18 Hz (R_2), $CHCO_2CH_3$), 7.22–7.67 (12H, m, arom.), 8.26 (1H, s, N*H*). ^{31}P NMR δ_P: 20.95 and 22.74 (R_1 and R_2). ^{13}C NMR δ_C: 20.24 and 20.63 (R_1 and R_2) ($COCH_3$), 20.77 ($COCH_3$), 21.14 ($3CH_3$), 40.84, (d, $^1J_{PC}$ = 126.83 Hz, P=C); 48.98 and 51.70 (R_1 and R_2) (CO_2CH_3), 51.88 and 51.98 (R_1 and R_2) (CO_2CH_3), 59.04 (d, $^2J_{PC}$ = 17.30 Hz, P=C-*C*H) 120.45–142.30 (arom.), 168.31, 169.52, 170.36, 170.96, 171.53, 172.03, 172.10 and 172.53 (NH*C*=*O*, N*C*=*O* and 2*C*O (ester), including R_1 and R_2). Anal. Calcd for $C_{31}H_{35}N_2O_6P$: C, 66.18; H, 6.27; N, 4.98. Found; C, 65.81; H, 6.53; N, 5.12.

Di-tert-butyl 2-(Phthalimide-N-yl)-3-(triphenylphosphanylidene) butanedioate (**6e**): Yield: (69%); White crystals; decomposed at 125°C. IR (KBr) ν (cm^{-1}): 1737, 1712 and 1658 (CO), 904 (P=C). ^{1}H NMR δ_H: 0.99 and 1.45 (R_1 and R_2) (9H, s, $C(CH_3)_3$), 1.54 (9H, s, $C(CH_3)_3$), 4.63 (1H, d, $^3J_{PH}$ = 17.47 Hz, $CHCO_2{}^tBu$), 7.49–7.84 (19H, m, arom.). ^{31}P NMR δ_P: 19.65. ^{13}C NMR δ_C: 27.83 and 28.29 (R_1 and R_2) ($C(CH_3)_3$), 28.02 ($C(CH_3)_3$), 36.32 (d, $^1J_{PC}$ = 131.16 Hz, P=C), 55.93 (d, $^2J_{PC}$ = 17.28 Hz, P=C-*C*H); 76.78 and 81.45 (R_1 and R_2) ($2C(Me)_3$), 80.60 ($2C(Me)_3$), 122.56–133.76 (arom.); 167.36 (2*C*=*O* (phthalimide)), 167.97, 169.24 and 169.85 (2*C*=*O* (ester)). MS (EI 70 eV): *m/z* (%) = 277 (100), 222 (26), 147 (100), 104 (100), 76 (100). Anal. Calcd for $C_{38}H_{38}NO_6P$: C, 71.80; H, 6.02; N, 2.20. Found: C, 71.59; H, 6.37; N, 2.19.

Di-tert-butyl2-(N,N'-diacetylhydrazine-N-yl)-3-(triphenylphosphanilidene)butanedioate (**6f**): Yield: (67%); white crystals, m.p. 187–189°C. IR (KBr) ν (cm^{-1}). 1740, 1701, 1663 and 1617 (CO), 894 (P=C). ^{1}H NMR δ_H: 0.98 and 1.52 (18H, 2 s, 2 $C(CH_3)_3$), 2.03 and 2.09 (6H, 2 s, $2COCH_3$), 4.96 (1H, d, $^3J_{PH}$ = 18.10 Hz, $CHCO_2C^tBu$), 7.36–7.82 (15H, m, arom.), 8.25 (1H, s, N*H*). ^{31}P NMR δ_P: 21.50. ^{13}C NMR δ_C: 21.04 and 21.25 ($2COCH_3$), 28.19 and 28.35 (2 $C(CH_3)_3$), 40.23 (d, $^1J_{PC}$ = 126.88 Hz, P=C), 59.66 (d, $^2J_{PC}$ = 17.82 Hz, P=C-*C*H), 77.57 and 81.11 ($2C(Me)_3$), 124.74–134.07 (arom.), 170.35, 170.44, 170.76, 171.30 and 172.256 (NH*C*=*O*, N*C*=*O* and 2*C*O (ester), including R_1 and R_2). MS (EI 70 eV): *m/z* (%) = 461 (3), 405 (100), 262 (50), 43 (62). Anal. Calcd for $C_{34}H_{41}N_2O_6P$: C, 67.54; H, 6.83; N, 4.63. Found: C, 67.55; H, 7.01; N, 5.00.

Di-tert-butyl 2-(Phthalimide-N-yl)-3-(tri-p-tolylphosphanylidene) butanedioate (**6g**): Yield: (84%); white to green crystals; m.p. 182–184°C. IR (KBr) ν (cm^{-1}): 1725, 1712 and 1655 (CO), 906 (P=C). ^{1}H NMR δ_H: 1.00 and 1.51 (R_1 and R_2) (9H, s, $C(CH_3)_3$), 1.53 (9H, s, $C(CH_3)_3$), 2.39 (9H, s, $3CH_3$), 4.66 (1H, d, $^3J_{PH}$ = 17.38 Hz, $CHCO_2{}^tBu$), 7.19–7.78 (1H, m, arom.). ^{31}P NMR δ_P: 18.71. ^{13}C NMR δ_C: 21.56 (s, $3CH_3$), 28.05 (s, $2C(CH_3)_3$), (P=C, was not observed), (P=C-*C*H, was not seen); 123.37–142.48 (arom.), 164.48 (2*C*=*O* (phthalimide)). Anal. Calcd for $C_{41}H_{44}NO_6P$: C, 72.66; H, 6.54; N, 2.07. Found: C, 72.98; H, 6.32; N, 2.22.

Di-tert-butyl2-(N,N'-diacetylhydrazine-N-yl)-3-(tri-p-tolylphosphanylidene)butanedioate (**6h**): Yield: (83%); white crystals, m.p. 201–202°C. IR (KBr) ν (cm^{-1}). 1737, 1714, 1656 and 1612 (CO), 872 (P=C). ^{1}H NMR δ_H: 0.99 and 1.51 (18H, 2 s, 2 $C(CH_3)_3$), 1.98 and 2.08 (R_1 and R_2) (3H, 2 s, $COCH_3$), 2.05, (3H, s, $COCH_3$), 2.04 (9H, s, $3CH_3$), 4.98 (1H, d, $^3J_{PH}$ = 18.19 Hz, $CHCO_2C^tBu$), 7.27–7.66 (12H, m, arom.), 8.30 (1H, s, N*H*). ^{31}P NMR δ_P: 20.80. ^{13}C NMR δ_C: 19.04 and 19.58 (R_1 and R_2) ($COCH_3$), 19.79 ($COCH_3$), 38.19 (d, $^1J_{PC}$ = 128.004 Hz, P=C), 58.34 (d, $^2J_{PC}$ = 17.32 Hz, P=C-*C*H), 75.38 and 78.74 ($2C(Me)_3$), 120.30–140.54 (arom.), 166.57, 168.33, 168.69, 168.97, 169.21 and 169.94 (2N*C*=*O* and 2*C*O (ester), including R_1 and R_2). MS (EI 70 eV): *m/z* (%) = 419 (96), 319 (30), 304 (100), 211 (17), 122 (22). Anal. Calcd for $C_{37}H_{47}N_2O_6P$: C, 68.71; H, 7.32; N, 4.33. Found: C, 68.79; H, 7.60; N, 4.69.

We are highly grateful to the University of Bu–Ali Sina for a grant and M.H. Zebarjadian for recording the NMR spectra.

Received 14 May 2007; accepted 26 June 2007
Paper 07/4645 doi: 10.3184/030823407X225518

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