A Facile Synthesis of Stable Heterocyclic Phosphorus Ylides†

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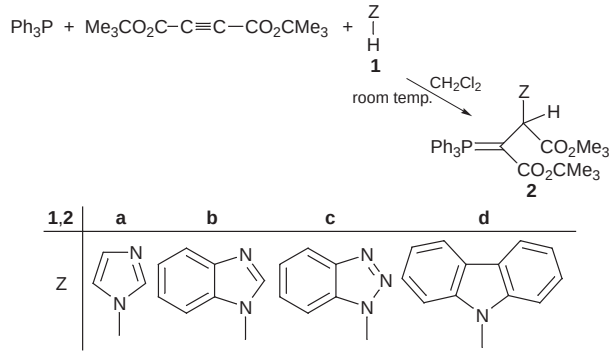
Issa Yavari,*[a] Malek Taher Maghsoodlou,[b] Hoorih Djahaniani[a] and Norollah Hazeri[b]

[a] *Department of Chemistry, University of Tarbiat Modarres, P. O. Box 14155-4838, Tehran, Iran*
[b] *Department of Chemistry, University of Sistan and Baluchestan, Zahedan, Iran*

Stable crystalline phosphorus ylides are obtained in excellent yields from the 1 : 1 : 1 addition reaction between triphenylphosphine, dialkyl acetylenedicarboxylate and strong NH-acids, such as imidazole, benzimidazole, benzotriazole or carbazole.

Phosphorus ylides are reactive systems, which take part in many reactions of value in organic synthesis.[1–7] Several methods have been developed for preparation of phosphorus ylides. These ylides are usually prepared by treatment of a phosphonium salt with a base, and phosphonium salts are usually prepared from the phosphine and an alkyl halide.[1,2] Phosphonium salts are also prepared by Michael addition of phosphorus nucleophiles to activated olefins among other methods.[1] The phosphonium salts are most often converted to the ylide by treatment with a strong base, though weaker bases can be used if the salt is acidic enough. We report here an efficient synthetic route to stable phosphorus ylides using triphenylphosphine, di-*tert*-butyl acetylenedicarboxylate and heterocyclic NH-acids, such as imidazole, benzimidazole, benzotriazole or carbazole. Thus, reaction of NH-acids **1** with di-*tert*-butyl acetylenedicarboxylate in the presence of triphenylphosphine leads to the corresponding stable heterocyclic phosphorus ylides **2** in excellent yields (Scheme 1).



Scheme 1

On the basis of the well established chemistry of trivalent phosphorous nucleophiles[1–7] it is reasonable to assume that phosphorus ylide **2** results from the initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the 1 : 1 adduct by the NH-acid. Then, the positively charged ion is attacked by the anion of the NH-acid to form phosphorane **2**.

The structures of compounds **2a–d** were deduced from their elemental analyses and their ^{1}H and ^{13}C NMR and IR spectral data. The nature of these compounds as 1 : 1 : 1 adducts was apparent from the mass spectra which displayed molecular ion peaks at *m/z* 556, 606, 607, and 655 for **2a**, **2b**, **2c** and **2d**, respectively.

The ^{1}H NMR spectrum of **2a** exhibited two sharp lines (δ 1.1 and 1.6) arising from *tert*-butyl protons along with a signal for methine proton at δ 4.37, which appears as a doublet ($^3J_{HP}$ 16.7 Hz). The aromatic protons appear as a multiplet at δ 7.4–8.1.

The ^{13}C NMR spectrum of **2a** displayed fifteen distinct resonances in agreement with the phosphorane structure. Partial assignments of the ^{13}C resonances in compound **2a** are given in Experimental section. Athough the presence of the ^{31}P nucleus complicates both the ^{1}H and ^{13}C NMR spectra[8] of **2a**, it helps in assignment of the signals by long-range couplings with ^{1}H and ^{13}C nuclei. The ^{1}H and ^{13}C NMR spectra of **2b**, **2c** and **2d** are similar to those of **2a**, except for the heterocyclic moieties, which exhibited characteristic resonances with appropriate chemical shifts.

To check whether the above conclusions regarding the nature of compound **2** are reasonable, we measured the phosphorus-31 NMR spectra of **2a–d**. A single ^{31}P signal was observed at δ *ca.* 24 (downfield from 85% H_3PO_4) for these compounds. These shifts are similar to those observed for stable phosphorus ylides ($Ph_3P=C$).[8,9]

The structural assignments made on the basis of the ^{1}H and ^{13}C NMR spectra of compounds **2a–d** were supported by measurement of their IR spectra. The carbonyl region of the spectrum exhibited two distinct absorption bands at 1723–1735 cm^{-1} for each compound (see Experimental Section).

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were measured on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.4 MHz, respectively. ^{31}P NMR spectra were measured with a Bruker DRX-500 AVANCE spectrometer at 202.46 MHz. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Triphenylphosphine, di-*tert*-butyl acetylenedicarboxylate, imidazole, benzimidazole, benzotriazole and carbazole were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

The process for the preparation of *di*-tert-*butyl* 2-*(imidazol-1-yl)*-3-*(triphenylphosphoranylidene)butanedioate* **(2a)** is described as an example. To a magnetically stirred solution of imidazole (0.067 g, 1 mmol) and triphenylphosphine (0.262, 1 mmol) in CH_2Cl_2 (6 ml) was added, dropwise, a mixture of di-*tert*-butyl acetylenedicarboxylate (0.226 g, 1 mmol) in CH_2Cl_2 (2 ml) at −10 °C for 10 min. The reaction mixture was then allowed to warm up to room temperature and stand for 24 h. The solvent was removed under reduced pressure and the solid residue was washed by cold diethyl ether (2 × 3 ml) and the product **2a** was obtained as colorless crystals, mp 173–174 °C, yield 0.50 g (90%). IR (KBr) (ν_{max}/cm^{-1}); 1728 (C=O), 1627 (C=C). ^{1}H NMR: δ 1.05 and 1.60 (18 H, 2 s, 2 C*Me*$_3$); 4.36 (1 H, d, $^3J_{HP}$ 16.7 Hz, C*H*CO$_2$CMe$_3$); 6.80 (1 H, br s, CH); 7.17 (1 H, br s, CH); 7.28 (1 H, br s, CH); 7.4–8.1 (15 H, m, 6 C_6H_5). ^{13}C NMR: δ 27.81 and 27.97 (2 C*Me*$_3$); 43 .3 (d, $^1J_{CP}$ 128.6 Hz, P–C); 60.35 (d, $^2J_{CP}$ 16.4 Hz, P–C–*CH*); 77.20 and 80.83 (2 *C*Me$_3$); 118.9 and 127.7 (2 *CH*–N); 136.7 (CH), 126.54 (d, $^1J_{CP}$ 94.8 Hz, C_{ipso}), 128.39 (d, $^3J_{CP}$ 12.8 Hz, C_m); 133.25 (d, $^2J_{CP}$ 10.0 Hz, C_o);

* To receive any correspondence.
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131.97 (d, $^4J_{CP}$ 2 Hz, C_p); 168.32 (d, J_{CP} 11.9 Hz, C=O ester), 169.86 (d, J_{CP} 11.8 Hz, C=O ester). ^{31}P NMR: δ 23.87 ($Ph_3P=C$). MS (m/z, %): 556 (M^+, 2); 455 (5); 262 (12); 183 (32); 68 (54); 57 (100) (Found: C, 71.2; H, 6.7; N, 5.0. $C_{33}H_3N_2O_4P$ requires C, 71.22; H, 6.69; N, 5.03%).

2b: colorless crystals, mp 170–171 °C, yield 0.56 g, (94%). IR (KBr) (ν_{max}/cm^{-1}): 1731, (C=O); 1632 (C=C). ^{1}H NMR: δ 1.02 and 1.50 (18 H, 2 s, 2 C*Me*$_3$); 4.64 (1 H, d, $^2J_{HP}$ 16.7 Hz, C*H*CO$_2$CMe$_3$); 6.2–7.8 (19 H, m, 3 C_6H_5, C_6H_4), 8.64 (1H, CH–N). ^{13}C NMR: δ 27.68 and 27.89 (2 C*Me*$_3$); 42.84 (d, $^1J_{CP}$ 127.7 Hz, P–C); 57.94 (d, $^2J_{CP}$ 16.4 Hz, P–C–*CH*); 77.32 and 80.82 (2 *C*Me$_3$); 126.18 (d, $^1J_{CP}$ 91.3 Hz, C_{ipso}); 128.33 (d, $^3J_{CP}$ 11.9 Hz, C_m); 133.03 (d, $^2J_{CP}$ 10.0 Hz, C_o); 131.81 (d, $^4J_{CP}$ 2 Hz, C_p); 108.47, 119.06, 120.57, 121.26, 128.23, 142.72 and 143.98 (7C, C_6H_4, *CH*–N); 168.64 (d, J_{CP} 13.7 Hz, C=O ester), 169.21 (d, J_{CP} 11.9 Hz, C=O ester). ^{31}P NMR: δ 24.27 ($Ph_3P=C$). MS (m/z, %): 606 (M^+, 2); 449 (5); 262 (13); 183 (42); 118 (58); 57 (100) (Found: C, 72.4; H, 6.5; N, 4.3. $C_3H_{39}N_2O_4P$ requires C, 73.26; H, 6.43; N, 4.62%).

2c: colorless crystals, mp 158–160 °C, yield 0.57 g, (95%). IR (KBr) (ν_{max}/cm^{-1}); 1728 (C=O); 1626; 1617 (C=C). ^{1}H NMR: δ 1.03 and 1.48 (18 H, 2 s, 2 C*Me*$_3$); 5.65 (1 H, d, $^2J_{HP}$ 16.8 Hz, C*H*CO$_2$CMe$_3$); 7.2–8.5 (19 H, m, 3 C_6H_5 and C_6H_4). ^{13}C NMR: δ 27.85 and 28.05 (2C*Me*$_3$); 41.28 (d, J_{CP} 125.9 Hz, P–C); 65.1 (d, $^2J_{CP}$ 13.7 Hz, P–C–*CH*), 77.36 and 81.07 (2 *C*Me$_3$); 126.23 (d, $^1J_{CP}$ 91.2 Hz, C_{ipso}); 128.36 (d, $^3J_{CP}$ 11.8 Hz, C_m); 133.32 (d, $^2J_{CP}$ 10.1 Hz, C_o); 131.89 (d, $^4J_{CP}$ 2 Hz, C_p); 113.28, 118.57, 122.81, 126.27, 128.22 and 146.06 (6C, C_6H_4); 168.15 (d, J_{CP} 11.9 Hz, C=O ester); 171.18 (d, J_{CP} 13.6 Hz C=O ester). ^{31}P NMR: δ 24.85 ($Ph_3P=C$). MS (m/z, %): 607 (M^+, 3); 450 (5); 262 (16); 183 (40); 119 (42); 57 (100) (Found: C, 71.3; H, 6.4; N, 6.8. $C_{36}H_{38}N_3O_4P$ requires C, 71.5; H, 6.3; N, 6.92%).

2d: white powder, mp 210–211 °C, yield 0.99 g, (98%). IR (KBr) (ν_{max}/cm^{-1}): 1622 and 1724 (C=O). ^{1}H NMR: δ 1.0 and 1.56 (18 H, 2 s, 2 C*Me*$_3$); 5.1 (1H, d, $^3J_{HP}$ 8 Hz, CH); 7–8 (23 H, m, arom.). ^{13}C NMR: δ 28.26 and 28.49 (2 C*Me*$_3$); 40.62 (d, $^1J_{CP}$ 124.3 Hz, P–C); 58.8 (d, $^2J_{CP}$ 15.7 Hz, P–C–*CH*); 77.04 and 80.51 (2 *C*Me$_3$); 110.92 and 140.36 (4 C, carbazole); 118.17, 119.15, 123.10 and 124.89 (8 CH, carbazole); 126.93 (d, $^1J_{CP}$ 92.0 Hz, C_{ipso}); 128.3 (d, $^3J_{CP}$ 11.9 Hz, C_m); 168.48 (d, $^2J_{CP}$ 11.6 Hz, C=O, ester); 170.10 (d, $^3J_{CP}$ 15.7 Hz, C=O, ester). ^{31}P NMR: δ 24.49 ($Ph_3P=C$). MS (m/z, %): 655 (M^+, 2); 405 (45); 309 (30); 262 (100); 183 (70); 167 (60); 108 (22) (Found: C, 76.9; H, 6.4; N, 2.2. $C_{42}H_{42}NO_4P$ requires C, 76.9; H, 6.4; N, 2.13%).

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