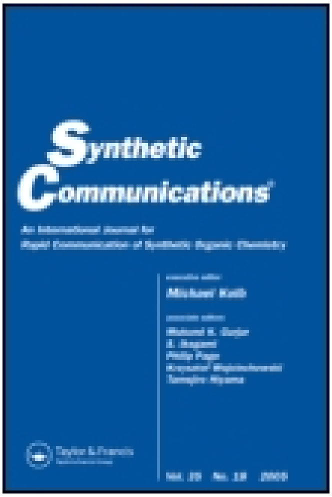

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Three-Component Reaction of Triphenylphosphine, Dimethyl Acetylenedicarboxylate, and Aldehyde Benzoylhydrazones: An Efficient One-Pot Synthesis of Stable Phosphorus Ylides

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Three-Component Reaction of Triphenylphosphine, Dimethyl Acetylenedicarboxylate, and Aldehyde Benzoylhydrazones: An Efficient One-Pot Synthesis of Stable Phosphorus Ylides

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Abstract: Protonation of the reactive 1:1 intermediate produced in the reaction between dimethyl acetylenedicarboxylate and triphenylphosphine by benzoylhydrazones leads to vinylphosphonium salts, which undergo Michael addition with the conjugate base of the NH acid to produce highly fanctionalized, salt-free phosphorus ylides in excellent yields.

Keywords: Benzoylhydrazones, dimethyl acetylenedicarboxylate, NH acids, phosphorus ylides, triphenylphosphine

Phosphorus ylides are reactive systems, which take part in many reactions of value in organic synthesis.[1–7] Several methods have been developed for the preparation of phosphorus ylides. These ylides are usually prepared by treatment of an appropriate phosphonium salt with a base; the corresponding phosphonium salts are usually obtained from the phosphine and an alkyl halide.[1,2] Phosphonium salts are also prepared by Michael addition of phosphorus nucleophiles to activated olefins.[1] Reaction of acetylenic esters with triphenylphosphine in the presence of an organic compound containing an acidic hydrogen has also been reported to produce phosphorus ylides.[8]

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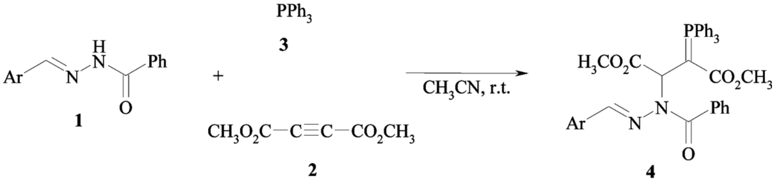
In continuation of our work on the reaction between trivalent phosphorus nucleophiles and electron-deficient acetylenic compounds in the presence of organic N-H, O-H, or C-H acids,[9–19] we herein report an efficient synthetic route to stable phosphorus ylides using triphenylphosphine, dimethyl acetylenedicarboxylate, and benzoylhydrazones. Thus, the reaction of the benzoylhydrazones **1** with dimethyl acetylenedicarboxylate **2** in the presence of triphenylphosphine **3** leads to the corresponding ylides **4** in good yields (Scheme 1).

The ^1H NMR spectrum of compound **4a** displays two sharp lines (δ 2.82, 3.60 ppm) for the methyl groups, a doubled signal for the methine proton at 5.72 ($^3J_{HP} = 16\,H_Z$), a single signal at 8.35 ppm for the $CH{=}N$ proton, and multiplets between 7.06 and 7.32 ppm for aromatic protons. The ^{31}P NMR spectrum of compound **4a** consists of one signal at 23.2. This shift is similar to those observed for other stable phosphorus ylides.[20,21] The structural assignments made on the basis of the NMR spectra of compounds **4a**–**f** are supported by their IR spectra. The carbonyl region of the spectrum exhibits absorption bands at 1650–1747 cm^{-1} for the ester groups.

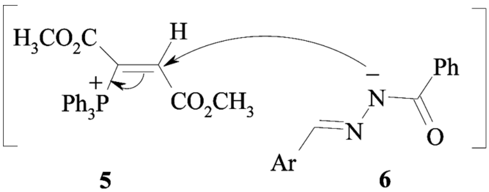
It is reasonable to assume that ylide **4** results from the initial addition of triphenylphosphine to dimethyl acetylene dicarboxylate (DMAD) and subsequent protonation of the 1:1 adduct by the NH-acidic benzoylhydrazone. The positively charged **5** is then attacked by the benzoylhydrazone anion **6** to form the phosphorane **4** (Scheme 2).

In summary, we report hearin that three-component reaction of triphenylphosphine, dimethyl acetylenedicarboxylate, and benzoylhydrazones



4	Ar	%Yield
a	phenyl	90
b	o-CH_3O-phenyl	93
c	p-CH_3O-phenyl	89
d	o-Cl-phenyl	90
e	p-Cl-phenyl	91
f	p-NO_2-phenyl	87

Scheme 1. Three-component reaction of triphenylphosphine, dimethyl acetylenedicarboxylate, and benzoylhydrazones.



5 **6**

Scheme 2. Mechanism of formation of ylide **4**.

produces functionalized phosphoranes in good yields. The reaction is carried out under neutral conditions, and starting materials are used without any need for purification or modification.

EXPERIMENTAL

All melting points are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on Bruker DRX-500 Avance spectrometer at 500, 128.5, and 202.5 MHz, respectively. ^{1}H, ^{13}C, and ^{31}P NMR spectra were obtained on solution in dimethyl sulfoxide (DMSO) using tetramethylsilane (TMS) as internal standard or 85% H_3PO_4 as external standard. The chemicals used in this work purchased from Fluka (Buchs, Switzerland) and were used without further purification.

General Procedure

A mixture of dimethyl acetylenedicarboxylate (0.28 g, 2 mmol) in acetonitrile (3 ml) was added dropwise to a magnetically stirred solution of triphenylphosphine (0.52 g, 2 mmol) and benzaldehyde benzoylhydrazone (0.45 g, 2 mmol) in acetonitrile (15 ml) at room temperature over 2 min. The reaction mixture was then stirred for 2 h. The solvent was evaporated at reduced pressure. The residue was precipitated in a mixture of diethyl ether–hexane. The solid was filtered and washed with diethyl ether to give the pure product.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-(N-benzoyl-N-benzylidene-hydrazino) Succinat (4a)

Yellow powder; mp 192–194°C. IR (KBr) (ν_{max}, cm^{-1}): 1747, 1695, 1650 (C = O). Calcd. for $C_{38}H_{33}N_2O_5P$: C, 72.60; H, 5.29; N, 4.46%. Found: C, 72.8; H, 5.4; N, 4.7%. MS (m/z, %): 628 (M^+, 7). ^{1}H NMR (500 MHz, d_6-DMSO): δ 2.82 (3 H, s, OCH_3), 3.60 (3 H, s, OCH_3), 5.72 (1 H, d, $^3J_{PH} = 16$ Hz), 7.06–7.32 (25 H, m, aromatic), 8.35 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 49.4 (d, $^1J_{PC} = 122$ Hz, C = P), 52.8, 53.2 (2 OCH_3), 59.7 (d, $^2J_{PC} = 15$ Hz, CH), 126.2 (d, $^1J_{PC} = 91$ Hz), 128.9 ($^2J_{PC} = 12$ Hz), 132.4 (d, $^4J_{PC} = 2$ Hz), 133.7 (d, $^3J_{PC} = 10$ Hz), 127.2, 127.7, 128.8, 129.8, 129.9, 130.1, 135.8, 136.2 (2 ph), 152.6 (C = N), 161.3 (C = O), 168.6 (d, $^2J_{PC} = 12$ H_Z C = O), 172.2 (d, $^3J_{PC} = 17$ 17 H_Z C = O). ^{31}P NMR (202.5 MHz, d_6-DMSO): δ 23.19.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-[N-benzoyl-N-(2-methoxybenzylidene)-hydrazino] Succinat (4b)

Yellow powder; mp 140–142°C. IR (KBr) (ν_{max}, cm^{-1}): 1747, 1699, 1639 (C = O). Calcd. for $C_{39}H_{35}N_2O_6P$: C, 71.11; H, 5.36; N, 4.25%. Found: C, 71.4; H, 5.2; N, 4.4%. MS (m/z, %): 658 (M^+, 9). ^{1}H NMR (500 MHz, d_6-DMSO): δ 3.14 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 5.98 (1 H, d, $^3J_{PH} = 16$ H_Z), 6.91–8.14 (24 H, m, aromatic), 8.72 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 49.2 (d, $^1J_{PC} = 122$ Hz, C = P), 52.5, 55.7, 55.8 (3 OCH_3), 59.9 (d, $^2J_{PC} = 15$ Hz, CH), 126.9 (d, $^1J_{PC} = 91$ Hz), 129.7 ($^2J_{PC} = 12$ Hz), 132.2 (d, $^4J_{PC} = 2$ 2 Hz), 133.7 (d, $^3J_{PC} = 10$ Hz), 120.8, 122.8, 128.0, 128.4, 128.7, 128.8, 128.9, 131.6, 131.7, 144.5 (2 ph), 158.2 (C = N), 164.2 (C = O), 168.6 (d, $^2J_{PC} = 12$ H_Z C = O), 170.3 (d, $^3J_{PC} = 17$ H_Z C = O). ^{31}P NMR (202.5 MHz, d_6-DMSO): δ 23.37.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-[N-benzoyl-n-(4-methoxybenzylidene)-hydrazino] Succinat (4c)

Yellow powder; mp 198–200°C. IR (KBr) (ν_{max}, cm^{-1}): 1743, 1684, 1638 (C = O). Calcd. for $C_{39}H_{35}N_2O_6P$: C, 71.11; H, 5.36; N, 4.25%. Found: C, 71.4; H, 5.2; N, 4.4%. MS (m/z, %): 658 (M^+, 7). ^{1}H NMR (500 MHz, d_6-DMSO): δ 3.09 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 5.03 (1 H, d, $^3J_{PH} = 16$ Hz), 6.95–7.64 (24 H, m, aromatic), 8.62 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 49.6 (d, $^1J_{PC} = 122$ Hz, C = P), 52.8, 53.1, 55.8 (3 OCH_3), 60.0 (d, $^2J_{PC} = 15$ Hz, CH), 126.6 (d, $^1J_{PC} = 91$ Hz), 129.7 ($^2J_{PC} = 12$ Hz), 132.5 (d, $^4J_{PC} = 2$ Hz), 133.9 (d, $^3J_{PC} = 10$ Hz), 114.4, 126.9, 127.3, 129.1, 129.2, 130.4, 134.1, 136.6 (2 ph) 153.7 (C = N), 161.3 (C = O), 169.6 (d, $^2J_{PC} = 12$ Hz C = O), 172.6 (d, $^3J_{PC} = 17$ Hz C = O). ^{31}P NMR (202.5 MHz, d_6-DMSO): δ 23.34.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-[N-benzoyl-n-(2-chloro-benzylidene)-hydrazino] Succinat (4d)

Yellow powder; mp 195–197°C. IR (KBr) (ν_{max}, cm^{-1}): 1749, 1693, 1649 (C = O). Calcd. for $C_{38}H_{32}ClN_2O_5P$: C, 68.83; H, 4.86; N, 4.22%. Found: C, 68.7; H, 5.1; N, 4.5%. MS (m/z, %): 662 (M$^+$, 4). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 2.87 (3 H, s, OCH$_3$), 3.60 (3 H, s, OCH$_3$), 5.72 (1 H, d, $^3J_{PH}$ = 16 Hz), 6.91–7.51 (24 H, m, aromatic), 8.52 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 49.5 (d, $^1J_{PC}$ = 122 Hz, C = P), 51.1, 52.6 (2 OCH$_3$), 59.7 (d, $^2J_{PC}$ = 15 Hz, CH), 126.9 (d, $^1J_{PC}$ = 91 Hz), 129.7 ($^2J_{PC}$ = 12 Hz), 132.2 (d, $^4J_{PC}$ = 2 Hz), 133.7 (d, $^3J_{PC}$ = 10 Hz), 120.8, 122.8, 128.0, 128.4, 128.7, 128.8, 128.9, 131.6, 131.7, 144.5 (2 ph), 152.6 (C = N), 161.9 (C = O), 169.6 (d, $^2J_{PC}$ = 12 Hz C = O), 171.7 (d, $^3J_{PC}$ = 17 Hz C = O). ^{31}P NMR (202.5 MHz, d$_6$-DMSO): δ 23.11.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-[N-benzoyl-n-(4-chloro-benzylidene)-hydrazino] Succinat (4e)

Yellow powder; mp 188–190°C. IR (KBr) (ν_{max}, cm^{-1}): 1742, 1659, 1633 (C = O). Calcd. for $C_{38}H_{32}ClN_2O_5P$: C, 68.83; H, 4.86; N, 4.22%. Found: C, 68.7; H, 5.1; N, 4.5%. MS (m/z, %): 662 (M$^+$, 6). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 3.07 (3 H, s, OCH$_3$), 3.86 (3 H, s, OCH$_3$), 6.06 (1 H, d, $^3J_{PH}$ = 16 Hz), 7.35–7.67 (24 H, m, aromatic), 8.61 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 49.3 (d, $^1J_{PC}$ = 122 Hz, C = P), 52.3, 52.8 (2 OCH$_3$), 59.3 (d, $^2J_{PC}$ = 15 Hz, CH), 126.9 (d, $^1J_{PC}$ = 91 Hz), 129.6 ($^2J_{PC}$ = 12 Hz), 132.2 (d, $^4J_{PC}$ = 2 Hz), 133.6 (d, $^3J_{PC}$ = 10 Hz), 125.4, 128.4, 128.6, 128.9, 129.9, 132.0, 133.4, 135.9 (2 ph), 151.1 (C = N), 163.8 (C = O), 169.3 (d, $^2J_{PC}$ = 12 Hz C = O), 171.8 (d, $^3J_{PC}$ = 17 Hz C = O) .^{31}P NMR (202.5 MHz, d$_6$-DMSO): δ 23.14.

Dimethyl 3-(Triphenyl-λ^5-phosphanylidene)-2-[N-benzoyl-n-(4-nitro-benzylidene)-hydrazino] Succinat (4f)

Yellow powder; mp 182–184°C. IR (KBr) (ν_{max}, cm^{-1}): 1742, 1672, 1629 (C = O). Calcd. for $C_{38}H_{32}N_3O_7P$: C, 67.75; H, 4.79; N, 6.24%. Found: C, 67.9; H, 4.6; N, 6.5%. MS (m/z, %): 673 (M$^+$, 6). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 2.99 (3 H, s, OCH$_3$), 3.76 (3 H, s, OCH$_3$), 5.87 (1 H, d, $^3J_{PH}$ = 16 Hz), 7.34–7.68 (24 H, m, aromatic), 8.59 (1H, s, CH = N). ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 50.0 (d, $^1J_{PC}$ = 122 Hz, C = P), 52.8, 53.4 (2 OCH$_3$), 59.7 (d, $^2J_{PC}$ = 15 Hz, CH), 125.9 (d, $^1J_{PC}$ = 91 Hz), 130.0 ($^2J_{PC}$ = 12 Hz), 132.3 (d, $^4J_{PC}$ = 2 Hz), 133.9

(d, $^3J_{PC} = 10$ Hz), 125.3, 128.2, 128.3, 128.9, 130.2, 133.5, 135.9, 142.1 (2 ph), 148.7 (C = N), 162.9 (C = O), 169.5 (d, $^2J_{PC} = 12$ Hz C = O), 171.9 (d, $^3J_{PC} = 17$ Hz C = O). ^{31}P NMR (202.5 MHz, d_6-DMSO): δ 23.11.

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