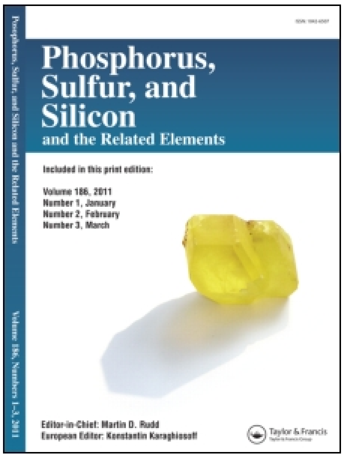

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Stereoselective Synthesis of 1,5-Diionic Organophosphorus Compounds

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STEREOSELECTIVE SYNTHESIS OF 1,5-DIIONIC ORGANOPHOSPHORUS COMPOUNDS

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The reactive 1:1 intermediate produced in the reaction between triphenylphosphine and alkyl propiolates or ethynyl phenyl ketone was trapped by isopropylidene Meldrum's acid (5-isopropylidene-2,2-dimethyl-1,3-dioxane-4,6-dione) to produce alkyl 3-(isopropylidenemalonate-5-yl-5-ylid)-3-methyl-2-triphenylphosphoniomethylidene-butanoates or 3-(isopropylidenemalonate-5-yl-5-ylid)-3-methyl-2-triphenylphosphoniomethylidene-butanone in 75–86% yield. These 1,5-diionic phosphorus betaines exist as (Z) geometrical isomer in $CDCl_3$ solution.

Keywords: 1,5-Phosphorus betaines; acetylenic esters; acetylenic ketones; triphenylphosphine

INTRODUCTION

The development of new stereoselective reactions has been a major topic in synthetic organic chemistry, resulting now in a wide variety of such reactions.[1–3] Controlling the stereochemical aspects of reaction, selectivity always has been a prime challenge to synthetic organic chemists. These concerns are especially pressing when the preparations of multifunctional substances of specific biological action are involved.

Organophosphorus compounds, that is, those bearing a carbon atom directly bound to a phosphorus atom, are synthetic targets of interest, not in the least because of their value for a variety of industrial, biological, and chemical synthetic uses.[4–6] The attack by nucleophilic

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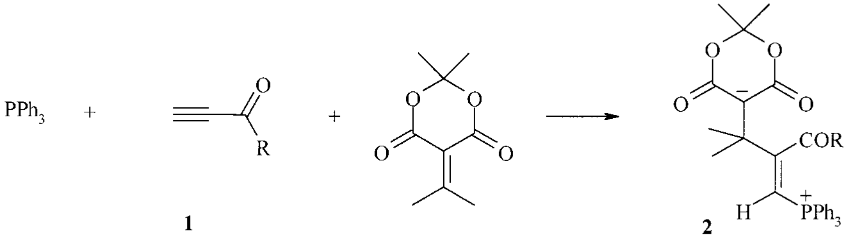
trivalent phosphorus on a carbon atom is facilitated when the latter is part of, or conjugated with, a carbonyl group, or when it is part of an unsaturated bond otherwise activated.[4–12] There are many studies on the reaction between trivalent phosphorus nucleophiles and α,β-unsaturated carbonyl compounds in the presence of a proton source such as alcohol or phenol.[4,12,13] We report a simple one-pot stereoselective reaction between triphenylphosphine and alkyl propiolates or ethynyl phenyl ketone in the presence of a polarized olefin, such as isopropylidene Meldrum's acid, leading to 1,5-diionic phosphorus betaines **2** (see Scheme 1).

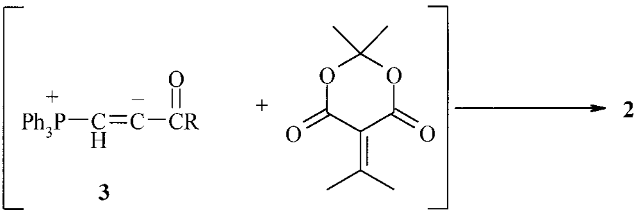


1,2	R	%Yield
a	OMe	75
b	OEt	77
c	Ph	86

SCHEME 1

RESULTS AND DISCUSSION

Compound **2** apparently results from the initial addition of triphenylphosphine to the acetylenic system and subsequent attack of the reactive zwiterionic intermediate **3** to isopropylidene Meldrum's acid leading to 1,5-diionic compound **2** (see Scheme 2).



SCHEME 2

The structure of compounds **2a–c** were deduced from their elemental anslyses and their ^1H, ^{13}C, and ^{31}P NMR spectra. The mass spectra of these compounds are fairly similar and display molecular ion peaks, any initial fragmentation involve the loss of Ph_3P and separation of the heterocyclic ring system. The ^1H NMR spectrum of each isolated compound exhibited two sharp lines ($\delta = 1.6$ and 1.7) arising from methyl protons along with a signal for methine proton at about $\delta = 6.5$–7.2 ppm, which appears as a doublet ($^2J_{HP} = 21$–25 Hz). The ^{13}C NMR spectrum of each compound displayed resonances in agreement with the betaine structure. Although the presence of ^{31}P nucleus complicates both the ^1H and ^{13}C NMR spectra[14] of **2a–c**, it helps in assignment of the signals by long-range coupling with ^1H and ^{13}C nuclei (see Experimental). Of particular interest are the three-bond carbon-phosphorus coupling constants, $^3J_{CP}$, which provide information about the P—CH=C—C torsion. The $^3J_{CP}$ depends on geometry, as expected, transoid coupling being larger than cisoid ones. The Karplus relation can be derived from the data for organophosphorus compounds with tetra- and penta-coordinate phosphorus.[15] The observation of $^3J_{CP}$ of 12.5–14.2 Hz for the *C*(Me)$_2$ carbon atom is in agreement with the trans arrangment of P—CH=C—C(Me)$_2$ moiety. The $^3J_{CP}$ for the carbon atom of *C*OR group is 0.5–4.1 Hz, which corresponds to a cis arrangement.

In summary, functionalized phosphorus betaines **2a–c** may be considered as potentially useful synthetic intermediates. The procedure described here may be an acceptable method for the preparation of 1,5-phosphorus betaines with variable functionalities.

EXPERIMENTAL

Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for the C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were measured on a Shimadzu IR-460 spectrometer. ^1H, ^{13}C, and ^{31}P NMR spectra were measured with a BRUKER DRX-500 AVANCE spectrometer at 500.1, 125.8, and 202.4 MHz respectively. ^1H, ^{13}C, and ^{31}P spectra were obtained on solutions in $CDCl_3$ using TMS as internal standard or 85% H_3PO_4 as external standard. Ethynyl phenyl ketone was prepared by addition of ethynylmagnesium bromide to benzaldehyde[16] and subsequent oxidation[17] of the propargylic alcohol derivative. Other chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and are used without further purification.

Preparation of Methyl 3-(Isopropylidenemalonate-5-yl-5-ylid)-3-methyl-2-triphenylphosphoniomethylidene-butanoate 2a

General Procedure

To a magnetically stirred solution of methyl propiolate (0.166 g, 2 mmol) and isopropylidene Meldrum's acid (0.36 g, 2 mmol) in dichloromethane (20 mL) was added dropwise a mixture of triphenylphosphine (0.52 g, 2 mmol) in dichloromethane (10 mL) at −5°C over 2 min. The reaction mixture was then allowed to warm to room temperature and to stand for 2 h. The solvent was removed under reduced pressure and the solid residue was washed with diethyl either (3 × 20 mL), 0.80 g of **2a** (75%) were obtained as a white powder, m.p. 154–157°C. Analysis: Calc for $C_{31}H_{31}O_6P$ (530): C, 70.19; H, 5.85%. Found: C, 70.3; H, 5.9. IR (KBr) (ν_{max}, cm^{-1}): 1711 (C=O, ester), 1590 (C=O, carbonyl group of ring), 1573 (Ph), 1430 (P—Ph), 1105 (P—Ph), 990 (P—Ph); δ_H ($CDCl_3$): 1.64 and 1.68 (12 H, 2 s, 2 CMe_2), 3.09 (3 H, s, OCH_3), 6.47 (1 H, d $^2J_{HP}$ 22.3 Hz, CH), 7.62–7.80 (15 H, m, C_6H_5); δ_C ($CDCl_3$): 25.20 (2 CH_3), 27.56 (2 CH_3), 43.31 [d $^3J_{CP}$ 12.6 Hz, *C*(Me)$_2$], 51.53 (OMe), 78.22 [*C*(CO)$_2$], 99.37 [*C*(Me)$_2$], 104.31 (d $^1J_{CP}$ 93.4 Hz, CH), 120.81 (d $^1J_{CP}$ 92.5 Hz, C_{ipso} of PPh_3), 129.42 (d, $^3J_{CP}$ 13.1 Hz, C_{meta} of Ph_3P), 133.10 (d $^2J_{CP}$ 10.4 Hz, C_{ortho} of Ph_3P), 133.64 (d, $^4J_{CP}$ 2.8 Hz, C_{para} of Ph_3P), 165.22 (CO of ring), 165.71 (d $^2J_{CP}$ 5.0 Hz, Ph_3PC=*C*), 176.33 (d, $^3J_{CP}$ 2 Hz CO2Me). δ_P ($CDCl_3$): 17.67 (Ph_3P^+-C). MS (*m/z*, *%*): 530 (M^+, 3), 262 (42), 183 (55), 83 (54), 43 (100).

Selected data for ethyl 3-(isopropylidenemalonate-5-yl-5-ylid)-3-methyl-2-triphenylphosphoniomethylidene-butanoate ***2b***. White powder, m.p. 134–136°C. Analysis: Calc for $C_{32}H_{33}O_6P$ (544): C, 70.59; H, 6.07%. Found: C, 70.4; H, 6.1. IR (KBr) (ν_{max}, cm^{-1}): 1719 (C=O, ester), 1590 (C=O, carbonyl group of ring), 1573 (Ph), 1430 (P—Ph), 1102 (P—Ph), 992 (P—Ph); δ_H ($CDCl_3$): 0.93 (3 H, t $^3J_{HH}$ 6 Hz, CH_3 of Et), 1.62 and 1.74 (12 H, 2 s, 2 CMe), 3.48 (2 H, quartet $^3J_{HH}$ 6 Hz, CH_2 of Et), 6.44 (1 H, d $^2J_{HP}$ 22.3 Hz, CH), 7.50–7.81 (15 H, m, 3C_6H_5); δ_C ($CDCl_3$): 13.58 (CH_3 of Et), 25.90 (2 CH_3), 28.30 (2 CH_3), 43.85 [d, $^3J_{CP}$ 12.6 Hz, *C*(Me)$_2$], 61.90 (CH_2 of Et), 78.81 [*C*(CO)$_2$], 99.93 [*C*(Me)$_2$], 104.92 (d, $^1J_{CP}$ 78.7 Hz, CH), 121.40 (d, $^1J_{CP}$ 92.5 Hz, C_{ipso} of PPh_3), 129.81 (d, $^3J_{CP}$ 13.1 Hz, C_{meta} of Ph_3P), 133.44 (d, $^2J_{CP}$ 10.4 Hz, C_{ortho} of Ph_3P), 134.09 (d, $^4J_{CP}$ 2.8 Hz, C_{para} of Ph_3P), 165.79 (CO of ring), 166.11 (d, $^2J_{CP}$ 5 Hz, Ph_3PC=*C*), 177.15 (d, $^3J_{CP}$ 4.1 Hz, *C*O_2Et). δ_P ($CDCl_3$): 17.53 (Ph_3P^+—C). MS (*m/z*, *%*): 544 (M^+, 2), 262 (21), 183 (25), 83 (68), 43 (100).

Selected data for 3-(isopropylidenemalonate-5-yl-5-ylid)-3-methyl-2-triphenylphosphoniomethylidene butanone ***2c***. White powder, m.p.

143–145°C. Analysis: Calc for $C_{36}H_{33}O_5P$ (576): C, 75.00; H, 5.73%. Found: C, 75.2; H, 5.7. IR (KBr) (ν_{max}, cm^{-1}): 1654 (C=O ketone), 1595 (C=O carbonyl group of ring), 1586 (Ph), 1435 (P—Ph), 1108 (P—Ph), 995 (P—Ph); δ_H ($CDCl_3$): 1.63 and 1.68 (12 H, 2 s, 2 CMe_2), 7.10 (1 H, d, $^2J_{HP}$ 20.3 Hz, CH), 7.17–8.10 (15 H, m, 3 C_6H_5); δ_C ($CDCl_3$): 25.81 (2 CH_3), 29.61 (2 CH_3), 47.79 [d $^3J_{CP}$ 14.2 Hz, *C*(Me)$_2$], 78.81 [*C*(CO)$_2$], 99.76 [*C*(Me)$_2$], 100.62 (d, $^1J_{CP}$ 75.1 Hz, CH), 119.10 (d, $^1J_{CP}$ 92.5 Hz, C_{ipso} of PPh_3), 128.00 (C_{meta} of C_6H_5), 129.75 (d, $^3J_{CP}$ 13.1 Hz, C_{meta} of Ph_3P), 130.41 (C_{ortho} of C_6H_5), 133.83 (C_{para} of C_6H_5), 134.21 (d, $^2J_{CP}$ 10.4 Hz, C_{ortho} of Ph_3P), 134.66 (C_{para} of Ph_3P), 136.56 (C_{ipso} of C_6H_5), 166.50 (Ph_3PC=*C*), 184.94 (*C*O of ring), 196.91 (d, $^3J_{CP}$ 0.5 Hz, *C*OPh). δ_P ($CDCl_3$): 12.04 (Ph_3P^+—C). MS (*m/z*, %): 576 (M^+, 2), 262 (100), 183 (55), 105 (PhCO, 48).

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