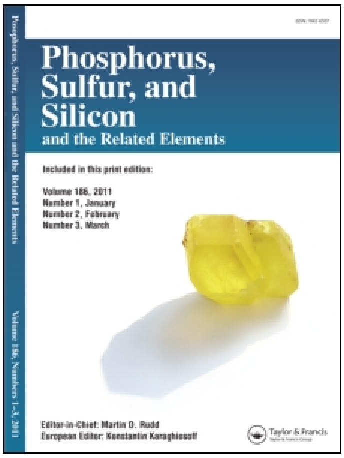

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SYNTHESIS OF DIASTEREOMERIC ETHYL 1-BENZOYL-6-(BROMOMETHYL)-2,2,2,4-TETRAPHENYL-3,7-DIOXA-2λ^5-PHOSPHABICYCLO- [3.2.0]HEPT-4-ENE-6-CARBOXYLATE

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SYNTHESIS OF DIASTEREOMERIC ETHYL 1-BENZOYL-6-(BROMOMETHYL)-2,2,2,4-TETRAPHENYL-3,7-DIOXA-2λ^5-PHOSPHABICYCLO-[3.2.0]HEPT-4-ENE-6-CARBOXYLATE

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Stable diastereomeric ethyl 1-benzoyl-6-(bromomethyl)-2,2,2,4-tetraphenyl-3,7-dioxa-2λ^5-phosphabicyclo[3.2.0]hept-4-ene-6-carboxylate was obtained in 98% yield from the reaction between dibenzoylacetylene as electron-deficient acetylenic compound, and ethyl 3-bromopyruvate in the presence of triphenylphosphine in dry ether.

Keywords: Dibenzoylacetylene; ethyl 3-bromo pyruvate; three-component reaction; triphenylphosphine

In recent years there has been increasing interest in the synthesis of organophosphorus compounds, that is, those bearing a carbon atom bond directly to a phosphorus atom. This interest has resulted from the recognition of the value of such compounds in a variety of biological, industrial, and chemical synthetic uses. A large number of methods have appeared describing novel syntheses of organophosphorus compounds.[1–3] The successful attack by nucleophilic trivalent phosphines on a carbon atom is facilitated when the latter is conjugated with a carbonyl group, or when it is part of an unsaturated bond otherwise activated.[1–9] There have been many studies on reactions between trivalent phosphorus nucleophiles and α, β-unsaturated carbonyl compounds in the presence of a proton source such as an alcohol or a CH-acid.[1,9,10]

Here we report a simple, one-pot, three-component synthesis of diastereomeric ethyl 1-benzoyl-6-(bromomethyl)-2,2,2,4-tetraphenyl-3,7-dioxa-2λ^5-phosphabicyclo[3.2.0]hept-4-ene-6-carboxylate. Thus, the reaction of triphenylphosphine and dibenzoylacetylene[11,12] in the presence of ethyl 3-bromopyruvate leads to phosphabicyclo[3.2.0]hept-4-ene-6-carboxylate **1** (Scheme 1).

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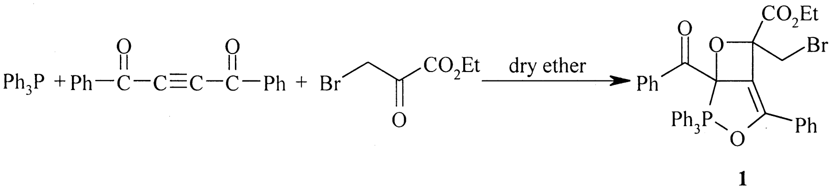


1

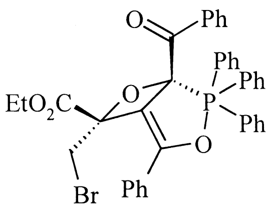
Major: 65% **minor**: 35%

SCHEME 1

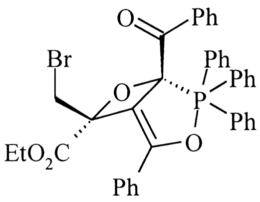
RESULTS AND DISCUSSION

The reaction of dibenzoylacetylene with triphenylphosphine in the presence of ethyl 3-bromopyrurvate proceeded spontaneously at room temperature in dry ether and was completed within 30 min. The ^{1}H, ^{13}C, and ^{31}P NMR spectra of the crude product clearly indicated the formation of ethyl 1-benzoyl-6-(bromomethyl)-2,2,2,4-tetraphenyl-3,7-dioxa-2λ^5-phosphabicyclo[3.2.0]hept-4-ene-6-carboxylate **1**. Any product other than **1** could not be detected by NMR spectroscopy. The structure of **1** was deduced from elemental analyses and IR, ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectra. The IR spectrum of **1** exhibited carbonyl group absorptions at 1741 and 1702 cm^{-1} together with the absorption bands of the triphenylphosphine moiety around 1430, 1100, and 996 cm^{-1} (see Experimental section). The mass spectrum of **1** displayed molecular ion peak at $m/z = 691$.

Compound **1** has two stereogenic centers, and therefore two diastereomers are expected (Scheme 2). The ^{1}H-, ^{13}C-, and ^{31}P NMR spectra of compound **1** are consistent with the presence of two isomers in nearly 2:1 ratio. Selected ^{1}H-, ^{13}C-, and ^{31}P NMR chemical shifts and coupling constants in the major (M) and minor (m) stereoisomers of compound **1** are shown in Table I.



(1S,6S)-1 or (1R,6R)-1



(1S,6R)-1 or (1R,6S)-1

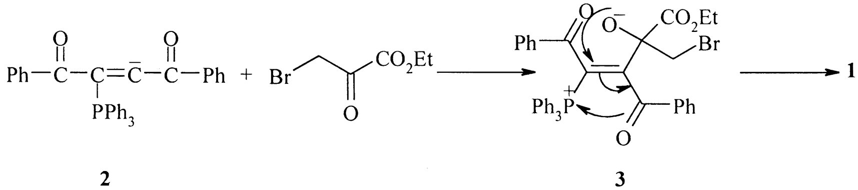
SCHEME 2

TABLE I Selected ^{1}H-, ^{13}C-, and ^{31}P NMR Chemical Shifts (δ in ppm) and Coupling Constants (J in Hz) for CO_2Et, CH_2Br, C_1, C_4, C_5, and C_6 in the Major (M) and Minor (m) Stereoisomers of **1**

Isomer	^{1}H NMR			^{13}C NMR				
(%)	CH_3 ($^{3}J_{HH}$)	CH_2Br ($^{3}J_{AB}$)	CH_2 ($^{3}J_{AB}$, $^{3}J_{HH}$)	C_1 ($^{1}J_{CP}$)	C_4 ($^{2}J_{CP}$)	C_5	C_6	^{31}P NMR
M (65)	1.37 (7.0)	2.74 (10.3)	4.38–4.44 (m)	56.86 (114.7)	140.79 (10.7)	124.01	103.89	18.88
m (35)	1.42 (7.1)	3.48 (10.4)	4.20–4.30 (m)	56.86 (114.7)	141.70 (10.9)	124.08	104.21	18.63

Partial assignments of the ^{1}H and ^{13}C resonances are given in the Experimental section. The proton-decoupled ^{31}P spectrum of the major and minor isomers of **1** exhibited two sharp signals at about $\delta = 18.88$ and 18.63 respectively. The phosphorus shifts are similar to those observed for stable hydroxyphosphoranes.[13]

A plausible mechanism for the formation of **1** is indicated in Scheme 3. On the basis of the well-established chemistry of trivalent phosphorus nucleophiles,[1–5] it is reasonable to assume that compound **1** results from initial addition of triphenylphosphine to the acetylenic compound and subsequent attack of the resulting anion **2** to the carbonyl carbon (ketone) of ethyl 3-bromopyruvate to yield betaine **3** which apparently cyclizes, under the reaction conditions employed, to produce compound **1** (Scheme 3).



SCHEME 3

The presented method carries the advantage that, not only is the reaction performed under neutral conditions, but the substances can be mixed without any activation or modification. The simplicity of the present one-step procedure makes it an interesting alternative to complex multistep approaches.

EXPERIMENTAL

Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H, ^{13}C, and ^{31}P, spectra were recorded at 500.1, 125.7, and 202.5, MHz, respectively, on a BRUKER DRX 500-AVANCE FT-NMR instrument with $CDCl_3$ as solvent. The reagents and solvents used in this work were obtained from Fluka (Buchs, Switzerland) and used without further purification. Dibenzoylacetylene was prepared according to a published procedure.[11,12]

Preparation of Diastereomeric Ethyl 1-Benzoyl-6-(bromomethyl)-2,2,2,4-tetraphenyl-3,7-dioxa-2λ^5-phosphabicyclo[3.2.0]hept-4-ene-6-carboxylate (1)

General Procedure

To a magnetically stirred solution of 0.47 g of dibenzoylacetylene (2 mmol) and 0.39 g of ethyl 3-bromopyruvate (2 mmol) in 5 mL of dry diethyl ether was added dropwise a solution of 0.52 g of triphenylphosphine (2 mmol) in 3 mL of dry diethyl ether at room temperature over 10 min. The reaction mixture was stirred for 30 min. The resulting solid was filtered off, washed with dry diethyl ether, and dried in the vacuum. White powder, m.p. 103–107°C, yield 1.35 g, 98%. IR (KBr) (ν_{max}, cm^{-1}): 1741 (CO_2Et), 1702 (C=O), 1671 (C=C), 1570 (Ph), 1508 (Ph), 1478 (Ph), 1430 (P—Ph), 1308 (C—O), 1231 (C—O) 1182 (C—O), 1100 (P—Ph), 996 (P—Ph). MS, (*m/z* %): 691 (M^+, 1), 420 (3), 279 (13), 278 (27), 277 (100), 262 (22), 47 (4). Anal. Calcd for $C_{39}H_{32}BrO_5P$ (691.6): C, 67.74; H, 4.66. Found: C, 67.0; H, 4.8.

Major isomer (65%): ^1H NMR (500 MHz, $CDCl_3$): δ_H = 1.37 (3H, t, $^3J_{HH}$ = 7.0 Hz, CH_3), 2.74 (2H, AB system, J_{AB} = 10.3 Hz, CH_2Br), 4.38–4.44 (2H, m, CH_2O), 7.27–7.77 (23H, m, 23CH of $5C_6H_5$), 8.6 (2H, d, $^3J_{HH}$ = 6.1 Hz, $2CH_{ortho}$ of C_6H_5). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 13.76 (CH_3), 30.55 (CH_2Br), 56.86 (d, $^1J_{CP}$ = 114.7 Hz, C_1) 61.04 (CH_2O), 103.93 (C_6 of oxetane), 124.01 (C_5), 125.46 (d, $^1J_{CP}$ = 90.2 Hz, C_{ipso} of C_6H_5), 126.89 (2CH of C_6H_5), 127.42 (2CH of C_6H_5), 127.47 (2CH of C_6H_5), 127.60 (CH of C_6H_5), 128.03 (2CH of C_6H_5), 128.52 (d, $^3J_{CP}$ = 12.3 Hz, $6CH_{meta}$ of $3C_6H_5$), 129.25 (CH of C_6H_5), 131.92 (d, $^4J_{CP}$ = 2.2 Hz, CH_{para} of C_6H_5), 132.76 (d, $^3J_{CP}$ = 8.3 Hz, C_{ipso} of C_6H_5), 133.17 (d, $^2J_{CP}$ = 9.5 Hz, CH_{ortho} of C_6H_5), 136.51 (d, $^3J_{CP}$ = 12.3 Hz, C_{ipso} of C_6H_5CO), 140.79 (d, $^2J_{CP}$ = 10.7 Hz, C_4), 165.40 (CO_2Et), 187.23 (d, $^2J_{CP}$ = 6.5 Hz, C=O). ^{31}P NMR (202.4 MHz, $CDCl_3$): δ_P = 18.88 ($-PO(Ph)_3$).

Minor isomer (35%): ^1H NMR (500 MHz, $CDCl_3$): δ_H = 1.42 (3H, t, $^3J_{HH}$ = 7.1 Hz, CH_3), 3.48 (2H, AB system, J_{AB} = 10.4 Hz, $-CH_2Br$), 4.20–4.30 (2H, m, $-CH_2O$), 7.27–7.77 (23H, m, 23CH of $5C_6H_5$), 7.90 (2H, d, $^3J_{HH}$ = 5.9 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 13.63 (CH_3), 31.98 (CH_2Br), 56.86 (d, $^1J_{CP}$ = 114.7 Hz, C_1), 61.65 (CH_2O), 104.21 (C_6 of oxetane), 124.08 (C_5), 125.14 (d, $^1J_{CP}$ = 90.5 Hz, C_{ipso} of C_6H_5), 126.57 (2CH of C_6H_5), 127.56 (2CH of C_6H_5), 127.65 (2CH of C_6H_5), 127.76 (CH of C_6H_5), 127.91 (2CH of C_6H_5) 128.47 (d, $^3J_{CP}$ = 12.3 Hz, CH_{meta} of C_6H_5), 129.20 (CH of C_6H_5), 131.35 (d, $^3J_{CP}$ = 8.3 Hz, C_{ipso} of C_6H_5), 132.14 (d, $^4J_{CP}$ = 2.6 Hz, CH_{para} of C_6H_5), 132.95 (d, $^2J_{CP}$ = 9.8 Hz, CH_{ortho} of C_6H_5), 141.71 (d, $^2J_{CP}$ = 10.9 Hz, C_4), 164.90 (CO_2Et), 188.21 (d, $^2J_{CP}$ = 7.1 Hz, C=O). ^{31}P NMR (202.4 MHz, $CDCl_3$): δ_P = 18.63 ($-PO(Ph)_3$).

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