A practical method for synthesis of stable phosphorus ylides in aqueous media

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A convenient one-pot synthesis of stable phosphorus ylides by the condensation of triphenylphosphine with dialkyl acetylenedicarboxylate and CH acids, such as penta-2,4-dione or diethyl propane-1,3-dioate, in the presence of β-cyclodextrin as a catalyst (to increase the solubility of the reactants in water) without using toxic organic solvents was proposed. This methodology is of interest due to the use of water as a solvent, thus minimizing such factors as the cost, operational hazards, and environmental pollution.

Key words: phosphorus ylides, pentane-2,4-dione, diethyl malonate, β-cyclodextrin.

Recently, performing organic reactions in water, which avoids the use of harmful organic solvents, has attracted much attention because water is an environmentally safe and plentiful solvent.[1] Hydrophobic effects strongly enhance[2] the rate of several organic reactions. Previously, the scant solubility of reactants was the main reason preventing the use of water as a solvent.

Various reactions that are traditionally carried out in organic solvents have been equally successful or even more effective in aqueous media.[1—6] In the course of our investigation devoted to the development of synthetic methods for the preparation of organic compounds using phosphorus compounds,[7] we found that the addition of β-cyclodextrin to water provided an efficient system for the synthesis of stable phosphorus ylides in aqueous media.

The preparation of phosphorus ylides generally involves the initial addition of a desired phosphine to an alkyl halide to provide a phosphonium salt. Subsequently, addition of a base to the salt affords the required phosphorus ylide.[8,9] Thus, the preparation of the required phosphorus ylide often needs two steps that involve the formation of phosphonium salts as intermediates and the addition of a base to convert these salts to ylides. Traditionally, these steps often occur in organic solvents, such as diethyl ether, tetrahydrofuran, and toluene.

Phosphorus ylides have earlier[10] been prepared in several steps using a basic aqueous solution. The mechanical generation of phosphonium salts and phosphorus ylides in the solid state followed by the Wittig reaction in the absence of a solvent has been described.[11,12]

This work is devoted to the synthesis of stable phosphorus ylides (**1**) by a remarkably simple and efficient one-pot procedure in water as a solvent without use of a base. However, some catalysts must be added to promote the solubility of reactants in water. These catalysts can be cyclodextrins, *e.g.*, β-cyclodextrin. Several reports in the literature[13,14] are devoted to the study of an increase in the solubility of drugs in water by host—guest complexation. The solubility of polycyclic aromatic hydrocarbons (PAH) in the presence of β-cyclodextrin and carboxymethylcyclodextrin has been studied.[15] The degree of solubilization power of PAH was shown to depend on the "fit" of the size of the PAH structure to the cyclodextrin cavity. Thus, we rationalized that β-cyclodextrin might be suitable for increasing the solubility in water of 1,3-dicarbonyl compounds, acetylenic esters, and triphenylphosphine, whose molecule contains three phenyl rings. We found that in the presence of β-cyclodextrin the reaction of triphenylphosphine with acetylenic esters (**2**) and CH acids, such as 1,3-dicarbonyl compounds (**3**), in water (without additives of organic solvents) afforded the corresponding stable phosphorus ylides **1** in good to excellent yields.

Results and Discussion

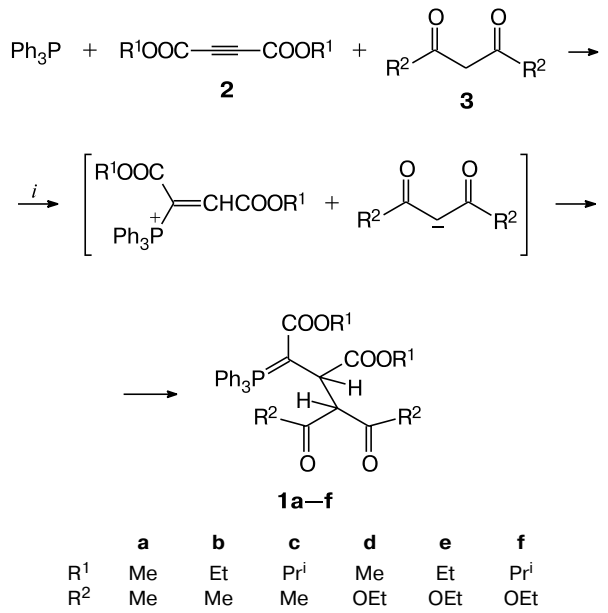
Based on the well studied chemistry of trivalent phosphorus nucleophiles,[16—18] it is reasonable to assume that compound **1** is formed due to the initial addition of triphenylphosphine to acetylenic ester **2** and concomitant protonation of the 1 : 1 adduct by CH acid **3**. Then the enolate anion attacks the positively charged ion to form phosphorane **1** (Scheme 1, Table 1).

The structures of phosphoranes **1a—f** were deduced from their ^{1}H and ^{13}C NMR and IR spectra. The nature

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2084—2087, December, 2002.

1066-5285/02/5112-2244 $27.00

Scheme 1



i. H_2O, β-cyclodextrin.

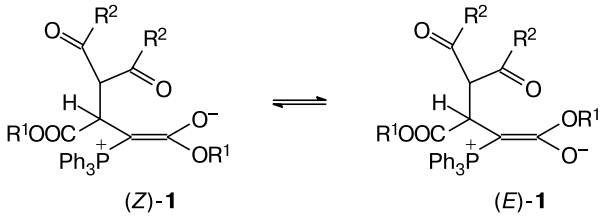
of these compounds as 1 : 1 : 1 adducts was apparent from the corresponding mass spectra, which displayed fairly weak molecular ion peaks at *m/z* 504, 532, 560, 564, 592, and 620 for phosphoranes **1a—f**, respectively. The initial fragmentation involves the loss of the [Ph_3P, R^1OH, $COOR^1$, $R^2COCHCOR^2$, R^1CO] chain. The ^1H and ^{13}C NMR spectroscopic data for phosphoranes **1a—f** exhibit a mixture of two rotational isomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group, and the rotation about the partial double bond in the (*E*)-**1** and (*Z*)-**1** geometrical isomers at room temperature is slow on the NMR time scale (Scheme 2).

For example, the ^1H NMR spectrum of compound **1a** exhibits eight sharp lines (δ 2.10, 2.17, 2.20, 2.28, 3.57, 3.59, 3.63, and 3.88) arising from the methyl and methoxy protons along with signals from the vicinal methine protons at δ 3.88, 5.50, and 5.25, which appear as a doublet of

Table 1. Melting points and yields of compounds **1a—f** in an organic solvent (AcOEt) (I) and in an aqueous medium (II)

Compound	M.p. /°C	Yield (%)	
		I	II
1a	175—176	82	90
1b	164—166	79	87
1c	142—143	64	72
1d	191—192	61	70
1e	163—165	49	61
1f	140—141	43	55

Scheme 2



doublets ($^3J_{P,H}$ = 17.9 and $^3J_{H,H}$ = 10.5 Hz) and two doublets ($^3J_{H,H}$ = 10.5 and $^3J_{H,H}$ = 10.5 Hz) for the major and minor geometrical isomers, respectively. The ^{13}C NMR spectrum of compound **1a** exhibits thirty distinct resonance lines, which are in agreement with the mixture of two rotational isomers. Although the presence of the ^{31}P nucleus complicates both the ^1H and ^{13}C NMR spectra of phosphorane **1a**, it helps to assign the signals by long-range spin-spin couplings with the ^1H and ^{13}C nuclei.

The ^1H and ^{13}C NMR spectra of phosphorus ylides **1b** and **1c** are similar to those of compound **1a**, except for the signals from the ester groups, which appear as characteristic resonance lines with the corresponding chemical shifts. The ^1H and ^{13}C NMR spectroscopic data for compounds **1d—f** are also consistent with the presence of two geometrical isomers. The structural assignments made for phosphoranes **1a—f** on the basis of the ^1H and ^{13}C NMR spectra were supported by their IR spectra. The carbonyl region of the spectra exhibits four distinct IR absorption bands for each compound. Of special interest is the absorption of the ester groups of such compounds at 1765—1630 cm^{-1}. The conjugation of one ester group with the negative charge is a plausible factor in the decrease in the wave number of the corresponding carbonyl absorption bands.

To estimate the effect of an aqueous medium on the reaction, we synthesized the same phosphorus ylides in organic solvents. The results were identical with those obtained in an aqueous medium. The yields of phosphorus ylides **1** obtained using water as a solvent are higher than those for any other organic solvent (see Table 1). An additional advantage of the use of water was the easy isolation of the products.

Thus, we showed that the condensation of triphenylphosphine with dialkyl acetylenedicarboxylates and CH acids in the presence of β-cyclodextrin efficiently occurred in water to provide a convenient and rapid synthesis of organophosphorus compounds **1**. Water was chosen as a solvent due to some advantages, including its low cost, no inflammability, and most important, low toxicity.

Experimental

Dialkyl acetylenedicarboxylates, acetylacetone, diethyl malonate, and β-cyclodextrin (Merck) were used without additional

purification. Melting points were measured on a Gallenkamp melting point apparatus and were not corrected. IR spectra were recorded on a Mattson 1000 FT-IR spectrometer (pellets with KBr). ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DRX-500 AVANCE spectrometer with working frequencies of 500 and 125.77 MHz, respectively. Mass spectra (EI, 70 eV) were measured on a Shimadzu MS-QP2000A mass spectrometer.

Dimethyl [2-(2,4-dioxopent-3-yl)-3-(triphenylphosphoranylidene)]butane-1,4-dioate (1a). Dimethyl acetylenedicarboxylate (0.27 g, 2 mmol) was added dropwise for ~5 min at ~20 °C to a stirred solution of Ph_3P (0.53 g, 2 mmol), acetylacetone (0.2 g, 2 mmol), and β-cyclodextrin (0.1 g, 0.09 mmol) in water (8 mL). The mixture was stirred for 30 min and filtered. The precipitate was thoroughly washed with AcOEt to obtain compound **1a** as a white powder in 90% yield (0.90 g), m.p. 175—176 °C. IR, ν/cm^{-1}: 1741, 1730, 1641, 1635 (C=O). MS, *m/z* (I_{rel} (%)): 504 [M]$^+$ (2), 486 (46), 277 (32), 252 (100), 183 (27), 85 (55).

Major isomer (*Z*)-**1a** (66%).^{1}H NMR, δ: 2.17, 2.28 (both s, 6 H, 2 Me); 3.07, 3.57 (both s, 6 H, 2 OMe); 3.88 (dd, 2 H, P=C—CH, $^3J_{H,H}$ = 10.5 Hz, $^3J_{P,H}$ = 17.9 Hz)*; 5.50 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.5 Hz); 7.47—7.65 (m, 30 H, H arom.)*. ^{13}C NMR, δ: 30.43, 30.45 (2 Me); 39.31 (d, P=C, $^1J_{P,C}$ = 124.3 Hz); 44.27 (d, P=C—CH, $^2J_{P,C}$ = 13.3 Hz); 48.74, 51.68 (2 OMe); 66.74 (d, <u>C</u>H(COMe)$_2$, $^3J_{P,C}$ = 8.1 Hz); 126.73 (d, C_{ipso}, $^1J_{P,C}$ = 85.3 Hz); 128.40 (d, C_m, $^3J_{P,C}$ = 12.1 Hz); 131.96 (C_p); 133.85 (d, C_o, $^2J_{P,C}$ = 8.9 Hz); 169.59 (d, C=O, $^2J_{P,C}$ = 13.2 Hz); 174.99 (d, C=O, $^3J_{P,C}$ = 8.9 Hz); 201.93, 203.71 (2 C=O).

Minor isomer (*E*)-**1a** (34%). ^{1}H NMR, δ: 2.10, 2.20 (both s, 6 H, 2 Me); 3.59, 3.63 (both s, 6 H, 2 OMe); 5.25 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.5 Hz). ^{13}C NMR, δ: 29.78, 32.23 (2 Me); 39.72 (d, P=C, $^1J_{P,C}$ = 128.2 Hz); 43.16 (d, P=C—CH, $^2J_{P,C}$ = 13.2 Hz); 50.07, 51.66 (2 OMe); 68.06 (d, <u>C</u>H(COMe)$_2$, $^3J_{P,C}$ = 7.9 Hz); 126.36 (d, C_{ipso}, $^1J_{P,C}$ = 91.7 Hz); 128.49 (d, C_m, $^3J_{P,C}$ = 11.5 Hz); 131.94 (C_p); 133.87 (d, C_o, $^2J_{P,C}$ = 8.9 Hz); 176.68 (d, C=O, $^2J_{P,C}$ = 19.6 Hz); 175.35 (d, C=O, $^3J_{P,C}$ = 8.7 Hz); 201.89, 203.87 (2 C=O).

Compounds **1b—f** were obtained similarly.

Diethyl [2-(2,4-dioxopent-3-yl)-3-(triphenylphosphoranylidene)]butane-1,4-dioate (1b). The yield was 0.92 g (87%), m.p. 164—166 °C. IR, ν/cm^{-1}: 1741, 1735, 1642, 1630 (C=O). MS, *m/z* (I_{rel} (%)): 532 [M]$^+$ (5), 459 (35), 433 (36), 277 (87), 262 (100), 183 (97), 84 (46).

Major isomer (*Z*)-**1b** (68%). ^{1}H NMR, δ: 0.44 (t, 3 H, Me, $^3J_{H,H}$ = 7.0 Hz); 1.17 (t, 3 H, Me, $^3J_{H,H}$ = 7.7 Hz); 2.17, 2.29 (both s, 6 H, 2 Me); 3.36 (dd, 2 H, P=C—CH, $^3J_{H,H}$ = 10.2 Hz, $^3J_{P,H}$ = 18.1 Hz)*, 4.05—4.10 (m, 4 H, 2 OCH$_2$); 5.53 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.2 Hz); 7.47—7.69 (m, 30 H, H arom.)*. ^{13}C NMR, δ): 13.88, 14.04, 30.47, 30.49 (4 Me); 39.01 (d, P=C, $^1J_{P,C}$ = 124.7 Hz); 44.39 (d, P=C—CH, $^2J_{P,C}$ = 13.5 Hz); 57.39, 60.69 (2 OCH$_2$); 66.58 (d, <u>C</u>H(COMe)$_2$, $^3J_{P,C}$ = 8.0 Hz); 126.56 (d, P=C, $^1J_{P,C}$ = 92.5 Hz); 128.30 (d, C_m, $^3J_{P,C}$ = 12.3 Hz); 131.90 (C_p); 133.96 (d, C_o, $^2J_{P,C}$ = 9.3 Hz); 169.25 (d, C=O, $^2J_{P,C}$ = 13.5 Hz); 174.56 (d, C=O, $^3J_{P,C}$ = 4.0 Hz); 203.91 (2 C=O).

Minor isomer (*E*)-**1b** (32%). ^{1}H NMR, δ: 1.22 (t, 3 H, Me, $^3J_{H,H}$ = 7.3 Hz); 1.24 (t, 3 H, Me, $^3J_{H,H}$ = 7.1 Hz); 2.10, 2.21 (both s, 6 H, 2 Me); 3.56—3.74 (m, 4 H, 2 OCH$_2$); 5.14 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.2 Hz). ^{13}C NMR, δ: 14.15, 15.21, 29.81, 32.82 (4 Me); 40.06 (d, P=C, $^1J_{P,C}$ = 124.5 Hz); 43.61 (d, P=C—CH, $^2J_{P,C}$ = 13.3 Hz); 58.08, 60.67 (2 OCH$_2$); 68.24 (d, <u>C</u>H(COMe)$_2$, $^3J_{P,C}$ = 7.8 Hz); 126.70 (d, P=C, $^1J_{P,C}$ = 95.0 Hz); 128.60 (d, C_m, $^3J_{P,C}$ = 13.5 Hz); 131.71 (C_p); 133.95 (d, C_o, $^2J_{P,C}$ = 9.4 Hz); 170.35 (d, C=O, $^2J_{P,C}$ = 18.2 Hz); 174.78 (d, C=O, $^3J_{P,C}$ = 4.0 Hz); 201.95 (2 C=O).

Diisopropyl [2-(2,4-dioxopent-3-yl)-3-(triphenylphosphoranylidene)butane-1,4-dioate (1c). The yield was 0.81 g (72%), m.p. 142—143 °C. IR, ν/cm^{-1}: 1750, 1741, 1642, 1630 (C=O). MS, *m/z* (I_{rel} (%)): 560 [M]$^+$ (5), 518 (4), 502 (84), 437 (75), 413 (36), 277 (37), 262 (100), 183 (87), 85 (36).

Major isomer (*Z*)-**1c** (66%). ^{1}H NMR, δ: 0.41 (d, 3 H, Me, $^3J_{H,H}$ = 6.0 Hz); 0.73 (d, 3 H, Me, $^3J_{H,H}$ = 5.6 Hz); 1.16 (d, 3 H, Me, $^3J_{H,H}$ = 6.7 Hz); 1.24 (d, 3 H, Me, $^3J_{H,H}$ = 6.0 Hz); 2.16, 2.30 (both s, 6 H, 2 Me); 3.30 (dd, 2 H, P=C—CH, $^3J_{H,H}$ = 10.6 Hz, $^3J_{P,H}$ = 18.0 Hz)*; 4.87—4.97 (m, 2 H, CH(Me)$_2$); 5.55 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.6 Hz); 7.47—7.69 (m, 30 H, H arom.)*. ^{13}C NMR, δ: 21.27, 21.87, 21.89, 21.96, 30.39, 30.41 (6 Me); 38.75 (d, P=C, $^1J_{P,C}$ = 125.3 Hz); 44.83 (d, P=C—CH, $^2J_{P,C}$ = 13.5 Hz); 64.25, 68.05 (2 OCH); 66.56 (d, <u>C</u>H(COMe)$_2$, $^3J_{P,C}$ = 7.8 Hz); 127.78 (d, P=C, $^1J_{P,C}$ = 93.5 Hz); 128.20 (d, C_m, $^3J_{P,C}$ = 12.2 Hz); 131.84 (C_p); 134.11 (d, C_o, $^2J_{P,C}$ = 9.4 Hz); 168.58 (d, C=O, $^2J_{P,C}$ = 13.6 Hz); 174.21 (d, C=O, $^3J_{P,C}$ = 4.0 Hz); 201.87, 204.24 (2 C=O).

Minor isomer (*E*)-**1c** (34%). ^{1}H NMR, δ: 1.13 (d, 3 H, Me, $^3J_{H,H}$ = 6.2 Hz); 1.19 (d, 3 H, Me, $^3J_{H,H}$ = 8.7 Hz); 1.29 (d, 3 H, Me, $^3J_{H,H}$ = 6.0 Hz); 1.33 (d, 3 H, Me, $^3J_{H,H}$ = 6.0 Hz); 2.11, 2.20 (both s, 6 H, 2 Me); 4.70—4.75 (m, 2 H, CH(Me)$_2$); 5.15 (d, 1 H, C<u>H</u>(COMe)$_2$, $^3J_{H,H}$ = 10.6 Hz). ^{13}C NMR, δ: 21.85, 21.98, 22.42, 22.81, 29.83, 32.98 (6 Me); 40.00 (d, P=C, $^1J_{P,C}$ = 133.9 Hz); 44.04 (d, P=C—CH, $^2J_{P,C}$ = 13.3 Hz); 64.83, 68.18 (2 OCH); 68.42 (d, $^3J_{P,C}$ = 7.5 Hz); 127.76 (d, P=C, $^1J_{P,C}$ = 94.5 Hz); 128.35 (d, C_m, $^3J_{P,C}$ = 12.5 Hz); 131.82 (C_p); 134.09 (d, C_o, $^2J_{P,C}$ = 9.3 Hz); 170.00 (d, C=O, $^2J_{P,C}$ = 18.5 Hz); 174.19 (d, C=O, $^3J_{P,C}$ = 4.5 Hz); 201.89, 203.81 (2 C=O).

Dimethyl {2-[di(ethoxycarbonyl)methyl]-3-(triphenylphosphoranylidene)}butane-1,4-dioate (1d). The yield was 0.8 g (70%), m.p. 191—192 °C. IR, ν/cm^{-1}: 1760, 1750, 1741, 1635 (C=O). MS, *m/z* (I_{rel} (%)): 564 [M]$^+$ (1), 505 (2), 277 (100), 262 (11), 183 (43).

Major isomer (*Z*)-**1d** (56%). ^{1}H NMR, δ: 1.18 (t, 6 H, 2 Me, $^3J_{H,H}$ = 7.0 Hz); 3.58, 3.63 (both s, 6 H, 2 OMe); 3.41 (dd, 1 H, P=C—CH, $^3J_{H,H}$ = 10.4 Hz, $^3J_{P,H}$ = 18.0 Hz); 3.97—4.13 (m, 4 H, 2 OCH$_2$); 4.63 (d, 1 H, C<u>H</u>(COOEt)$_2$, $^3J_{H,H}$ = 10.4 Hz); 7.47—7.70 (m, 30 H, H arom.)*. ^{13}C NMR, δ: 13.99, 14.01 (2 Me); 39.89 (d, P=C, $^1J_{P,C}$ = 135.2 Hz); 42.57 (d, P=C—CH, $^2J_{P,C}$ = 13.7 Hz); 51.62, 51.67 (2 OMe); 54.41 (d, <u>C</u>H(CO$_2$Et)$_2$, $^3J_{P,C}$ = 5.0 Hz); 60.86, 60.98 (2 OCH$_2$); 126.79 (d, C_{ipso}, $^1J_{P,C}$ = 92.3 Hz); 128.43 (d, C_m, $^3J_{P,C}$ = 11.8 Hz); 131.87 (C_p); 133.99 (d, C_o, $^2J_{P,C}$ = 9.0 Hz); 168.67, 168.98 (2 C=O); 170.88 (d, C=O, $^2J_{P,C}$ = 18.7 Hz); 174.8 (d, C=O, $^3J_{P,C}$ = 4.2 Hz).

Minor isomer (*E*)-**1d** (44%). ^{1}H NMR, δ: 1.20 (t, 6 H, 2 Me, $^3J_{H,H}$ = 6.9 Hz); 3.08, 3.66 (both s, 6 H, 2 OMe); 3.30 (dd, 1 H, $^3J_{H,H}$ = 10.8 Hz, $^3J_{P,H}$ = 18.1 Hz); 3.85—3.87 (m, 4 H, 2 OCH$_2$); 4.87 (d, 1 H, C<u>H</u>(COOEt)$_2$, $^3J_{H,H}$ = 10.8 Hz). ^{13}C NMR, δ: 13.89, 13.97 (2 Me); 38.86 (d, P=C, $^1J_{P,C}$ = 125.2 Hz); 43.53 (d, P=C—CH, $^2J_{P,C}$ = 13.8 Hz); 48.69, 50.08 (2 OMe); 53.13 (d, <u>C</u>H(CO$_2$Et)$_2$, $^3J_{P,C}$ = 4.5 Hz); 61.00, 61.02 (2 OCH$_2$); 126.69 (d, C_{ipso}, $^1J_{P,C}$ = 89.1 Hz); 128.34 (d, C_m, $^3J_{P,C}$ = 11.1 Hz); 131.84 (C_p); 133.99 (d, C_o, $^2J_{P,C}$ = 8.9 Hz); 168.81, 169.12

* For two rotamers.

(2 C=O); 169.31 (d, C=O, $^2J_{P,C}$ = 13.3 Hz); 174.54 (d, C=O, $^3J_{P,C}$ = 4.3 Hz).

Diethyl {2-[di(ethoxycarbonyl)methyl]-3-(triphenylphosphoranylidene)}butane-1,4-dioate (1e). The yield was 0.72 g (61%), m.p. 163—165 °C. IR, ν/cm^{-1}: 1765, 1741, 1740, 1630 (C=O). MS, *m/z* (I_{rel} (%)): 592 $[M]^+$ (8), 520 (100), 474 (37), 433 (40), 277 (41), 262 (43), 183 (49).

Major isomer (*Z*)-**1e** (56%). ^{1}H NMR, δ: 1.20 (t, 12 H, 4 Me, $^3J_{H,H}$ = 7.1 Hz); 3.31 (dd, 1 H, P=C—CH, $^3J_{H,H}$ = 10.6 Hz, $^3J_{P,H}$ = 18.2 Hz); 3.99—4.13 (m, 8 H, 4 OCH_2); 4.64 (d, 1 H, C<u>H</u>$(COOEt)_2$, $^3J_{H,H}$ = 10.6 Hz); 7.47—7.72 (m, 30 H, H arom.)*. ^{13}C NMR, δ: 13.88, 13.96, 14.17, 15.03 (4 Me); 39.96 (d, P=C, $^1J_{P,C}$ = 135.7 Hz); 42.82 (d, P=C—CH, $^2J_{P,C}$ = 13.8 Hz); 54.53 (d, <u>C</u>H$(CO_2Et)_2$, $^3J_{P,C}$ = 4.7 Hz); 57.29, 60.52, 60.81, 60.93 (4 OCH_2); 126.88 (d, C_{ipso}, $^1J_{P,C}$ = 96.0 Hz); 128.35 (d, C_m, $^3J_{P,C}$ = 12.8 Hz); 131.81 (C_p); 134.03 (d, C_o, $^2J_{P,C}$ = 8.0 Hz); 168.78, 169.04 (2 C=O); 168.93 (d, C=O, $^2J_{P,C}$ = 11.8 Hz); 174.36 (d, C=O, $^3J_{P,C}$ = 4.5 Hz).

Minor isomer (*E*)-**1e** (44%). ^{1}H NMR, δ: 0.45 (t, 3 H, Me, $^3J_{H,H}$ = 6.7 Hz); 1.25 (t, 9 H, 3 Me, $^3J_{H,H}$ = 6.6 Hz); 3.28 (dd, 1 H, P=C—CH, $^3J_{H,H}$ = 10.1 Hz, $^3J_{P,H}$ = 15.0 Hz); 3.52—3.87 (m, 8 H, 4 OCH_2); 4.90 (d, 1 H, C<u>H</u>$(COOEt)_2$, $^3J_{H,H}$ = 10.1 Hz). ^{13}C NMR, δ: 13.87, 13.98, 14.00, 14.07 (4 Me); 38.57 (d, P=C, $^1J_{P,C}$ = 127.8 Hz); 43.55 (d, P=C—CH, $^2J_{P,C}$ = 13.9 Hz); 53.13 (d, <u>C</u>H$(CO_2Et)_2$, $^3J_{P,C}$ = 4.5 Hz); 58.17, 60.54, 60.78, 60.97 (4 OCH_2); 126.86 (d, C_{ipso}, $^1J_{P,C}$ = 95.9 Hz); 128.24 (d, C_m, $^3J_{P,C}$ = 13.3 Hz); 131.79 (C_p); 134.00 (d, C_o, $^2J_{P,C}$ = 7.9 Hz); 168.95, 169.20 (2 C=O); 170.48 (d, C=O, $^2J_{P,C}$ = 18.7 Hz); 174.06 (d, C=O, $^3J_{P,C}$ = 4.2 Hz).

Diisopropyl {2-[di(ethoxycarbonyl)methyl]-3-(triphenylphosphoranylidene)}butane-1,4-dioate (1f). The yield was 0.68 g (55%), m.p. 140—141 °C. IR, ν/cm^{-1}: 1760, 1750, 1741, 1635 (C=O). MS, *m/z* (I_{rel} (%)): 620 $[M]^+$ (1), 534 (6), 399 (4), 262 (100), 183 (97).

Major isomer (*Z*)-**1f** (54%). ^{1}H NMR, δ: 0.32 (d, 3 H, Me, $^3J_{H,H}$ = 6.15 Hz); 0.86 (d, 3 H, Me, $^3J_{H,H}$ = 6.0 Hz); 1.20 (t, 6 H, 2 Me, $^3J_{H,H}$ = 10.0 Hz)*, 1.31 (d, 3 H, Me, $^3J_{H,H}$ = 6.3 Hz); 1.33 (d, 3 H, Me, $^3J_{H,H}$ = 6.2 Hz); 3.25 (dd, 1 H, P=C—CH, $^3J_{H,H}$ = 10.9 Hz, $^3J_{P,H}$ = 19.0 Hz); 4.03—4.13 (m, 4 H, 2 OCH_2); 4.64 (d, 1 H, C<u>H</u>$(COOEt)_2$, $^3J_{H,H}$ = 10.9 Hz); 4.76, 5.03 (m, 2 H, 2 OCH); 7.29—7.75 (m, 30 H, H arom.)*. ^{13}C NMR, δ: 13.98, 14.02, 21.90, 21.91, 22.21, 22.71 (6 Me); 39.91 (d, P=C, $^1J_{P,C}$ = 135.6 Hz); 42.99 (d, P=C—CH, $^2J_{P,C}$ = 13.8 Hz); 54.57 (d, <u>C</u>H$(CO_2Et)_2$, $^3J_{P,C}$ = 4.9 Hz); 60.75, 60.90 (2 OCH_2); 64.93, 67.90 (2 OCH); 126.79 (d, C_{ipso}, $^1J_{P,C}$ = 92.3 Hz); 128.44 (d, C_m, $^3J_{P,C}$ = 11.8 Hz); 131.87 (C_p); 133.99 (d, C_o, $^2J_{P,C}$ = 9.0 Hz); 168.90, 169.09 (2 C=O); 170.15 (d, C=O, $^2J_{P,C}$ = 18.5 Hz); 173.72 (d, C=O, $^3J_{P,C}$ = 5.0 Hz).

Minor isomer (*E*)-**1f** (46%). ^{1}H NMR, δ: 1.27 (d, 3 H, Me, $^3J_{H,H}$ = 6.9 Hz); 1.26 (d, 3 H, Me, $^3J_{H,H}$ = 5.9 Hz); 1.27 (d, 3 H, Me, $^3J_{H,H}$ = 6.9 Hz); 1.35 (d, 3 H, Me, $^3J_{H,H}$ = 5.9 Hz); 3.21 (dd, 1 H, P=C—CH, $^3J_{H,H}$ = 11.2 Hz, $^3J_{P,H}$ = 19.5 Hz); 3.85—4.00 (m, 4 H, 2 OCH_2); 4.87 (d, 1 H, C<u>H</u>$(COOEt)_2$, $^3J_{H,H}$ = 11.2 Hz); 4.89, 4.96 (m, 2 H, 2 OCH). ^{13}C NMR, δ: 13.88, 13.96, 21.17, 21.80, 22.12, 22.22 (6 Me); 38.24 (d, P=C, $^1J_{P,C}$ = 125.8 Hz); 43.91 (d, P=C—CH, $^2J_{P,C}$ = 13.9 Hz); 53.27 (d, <u>C</u>H$(CO_2Et)_2$, $^3J_{P,C}$ = 4.5 Hz); 60.73, 60.94 (2 OCH_2); 64.08, 67.78 (2 OCH); 126.77 (d, C_{ipso}, $^1J_{P,C}$ = 94.5 Hz); 128.33 (d, C_m, $^3J_{P,C}$ = 11.0 Hz); 131.85 (C_p); 133.95 (d, C_o, $^2J_{P,C}$ = 8.9 Hz); 168.22 (d, C=O, $^2J_{P,C}$ = 14.0 Hz); 168.18, 169.26 (2 C=O); 173.68 (d, C=O, $^3J_{P,C}$ = 4.8 Hz).

References

1. C. J. Li and T. H. Chan, *Organic Reactions in Aqueous Media*, J. Wiley and Sons, New York, 1997; A. Lubineau, J. Auge, and Y. Queneau, *Synthesis*, 1994, 741; *Organic Synthesis in Water*, Ed. P. A. Grieco, Blackie Academic and Professional, Glasgow, 1998; C. J. Li, *Chem. Rev.*, 1993, **93**, 2023.
2. R. Breslow and D. C. Rideout, *J. Am. Chem. Soc.*, 1980, **102**, 7816; R. Breslow, *Acc. Chem. Res.*, 1991, **24**, 159.
3. K. Manabe, Y. Mori, and S. Kobayashi, *Tetrahedron*, 2001, **57**, 2537.
4. G. Verspui, G. Elbertse, G. Papadogianakis, and R. A. Sheldon, *J. Organomet. Chem.*, 2001, **621**, 337.
5. S. Venkatraman and C. J. Li, *Tetrahedron Lett.*, 2001, **42**, 781.
6. H. Y. Tian, Y. J. Chen, D. Wang, Y. P. Bu, and C. J. Li, *Tetrahedron Lett.*, 2001, **42**, 1803.
7. I. Yavari and M. R. Islami, *J. Chem. Res. (S)*, 1998, 166.
8. R. Engel, *Synthesis of Carbon—Phosphorus Bond*, CRC Press, Boca Raton, FL, 1988.
9. J. I. G. Cadogan, *Organophosphorus Reagents in Organic Synthesis*, Academic Press, New York, 1979.
10. M. G. Russel and S. Warren, *Tetrahedron Lett.*, 1998, **39**, 7995.
11. V. P. Balema, J. W. Wiench, M. Pruski, and V. K. Pecharsky, *J. Am. Chem. Soc.*, 2002, **124**, 6244.
12. V. P. Balema, J. W. Wiench, M. Pruski, and V. K. Pecharsky, *Chem. Commun.*, 2002, **8**, 724.
13. D. Duchêne, D. Wouessidjewe, and G. Ponchel, *J. Control. Release*, 1999, **62**, 263.
14. B. Pose-Vilarnovo, I. Perdomo-Lopez, M. Echezarreta-Lopez, P. Schroth-Pardo, E. Estrada, and J. J. Torres-Labandeira, *Europ. J. Pharma. Sci.*, 2001, **13**, 325.
15. G. Shixiang, W. Liansheng, H. Qingguo, and H. Sukui, *Chemosphere*, 1998, **37**, 1299.
16. D. E. C. Cobridge, *Phosphorus, An Outline of Chemistry, Biochemistry and Uses*, Elsevier, Amsterdam, 1995.
17. W. A. Johnson and J. C. Tebby, *J. Chem. Soc.*, 1961, 2126.
18. K. B. Beacker, *Tetrahedron*, 1980, **36**, 1717.

Received May 6, 2002;
in revised form June 26, 2002