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# Facile and stereoselective synthesis of vinylphosphonates

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**Abstract**

Stereoselective syntheses of mono-, di- and trisubstituted diethyl alk-1-enylphosphonates, starting from readily available alk-1-ynylphosphonates, have been developed, using catalytic hydrogenation or cuprate addition on the triple bond.

*Keywords:* Phosphonates; Stereoselective synthesis; Hydrogenation; Cuprate addition; Vinylphosphonates

## 1. Introduction

Among the compounds with C–P bonds, vinylphosphonate derivatives find wide applications as polymer additives [1–7], flame retardants [8–10], intermediates for drugs [11–13], or agrochemical compounds [14], and as useful tools in organic transformations [15,16]. Accordingly, they are of great economical and biological interest. However, few methods are known for the preparation of stereoisomerically pure vinylphosphonates [16]. Our current interest in these compounds, as intermediates for the synthesis of new phosphomycin analogues [17], led us to search for easy methods to obtain them with high stereoselectivity. We previously reported our preliminary results concerning the stereoselective preparation of disubstituted vinylphosphonates **4** by conversion of alk-1-ynylphosphonates **1** into the corresponding alkenyl cuprates **2** using alkyl or aryl iodo cuprates in diethyl ether followed by hydrolysis [18] (path b′, Scheme 1). Further, we have extended our research (i) to the preparation of trisubstituted vinylphosphonates **5** by investigating the behaviour of **2** towards other electrophilic reagents (path b″, Scheme 1); (ii) to the preparation of monosubstituted vinylphosphonates **3** by catalytic hydrogenation of **1** (path a, Scheme 1).

We report here our full results, which constitute simple and facile procedures for the synthesis of stereoisomerically pure mono-, di- and trisubstituted vinylphosphonates starting from the readily available alk-1-ynylphosphonates **1** [19].

## 2. Results and discussion

### 2.1. Synthesis of 2-monosubstituted diethyl alk-1-enylphosphonates 3 (path a, Scheme 1)

Alk-1-ynylphosphonates **1** [19] are reduced by hydrogenation, in the presence of Lindlar catalyst [20], into the corresponding alk-1-enylphosphonates **3** (Scheme 2).

In contrast with some results from the literature [12,21], we observed that the obtained compounds are not stereochemically pure. Indeed, the $^{31}$P NMR spectra of the crude product show the expected *Z* alk-1-enylphosphonates together with 5–10% of the *E* isomer, and 2–4% of the corresponding alkanephosphonates. Pure *Z* isomers can easily be obtained by column chromatography (Table 1).

The stereochemistry of the compounds was established by the $^{31}$P NMR spectra of the crude products: for such vinylic $P^{IV}$ compounds, the major signal of the *Z* isomer appears at higher field than that of the *E* isomer [23]. Further, the stereochemical assignments are substantiated by the vicinal coupling constants $^{3}J_{PH}$ and $^{3}J_{HH_3}$ in the $^{1}$H NMR spectra: the values (ca. 53.0 Hz) of the $^{3}J_{PH}$ coupling constants are clearly in the range normally associated with the *cis* double bonds (45–

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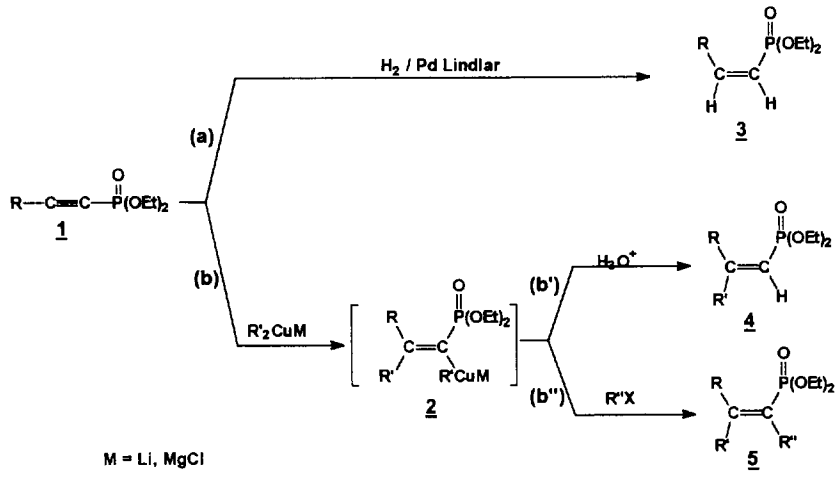
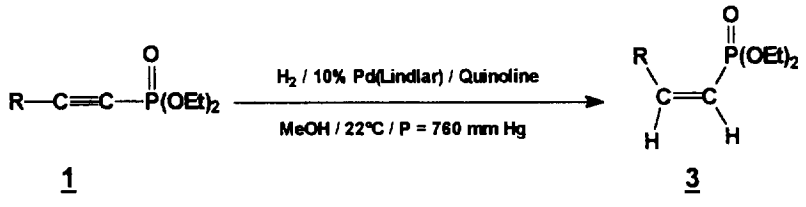



Scheme 1.




Scheme 2.

55 Hz) [24]. In the case of styrylphosphonate **3c**, the non-aromatic proton (PhC*H*=) is concealed under the aromatic signals and its chemical shift cannot be obtained.

### 2.2. Synthesis of diethyl 2,2-disubstituted alk-1-enylphosphonates 4 (path b', Scheme 1)

Alk-1-ynylphosphonates **1** react readily with an excess of alkyl- or aryl-magnesium in the presence of cuprous chloride, at −30 °C in ether, to provide after hydrolysis high yields of the corresponding β-alkylated or arylated α,β-alkenylphosphonates **4** (Scheme 3) (Table 2) [18]. Furthermore, the addition reaction is highly stereoselective, producing almost exclusively the product of *cis* addition to the triple bond.

At higher temperature, a mixture of *cis* and *trans* addition products is obtained: for example, a mixture of isomers *Z*/*E* **4a** (30/70) is formed in refluxing diethylether.

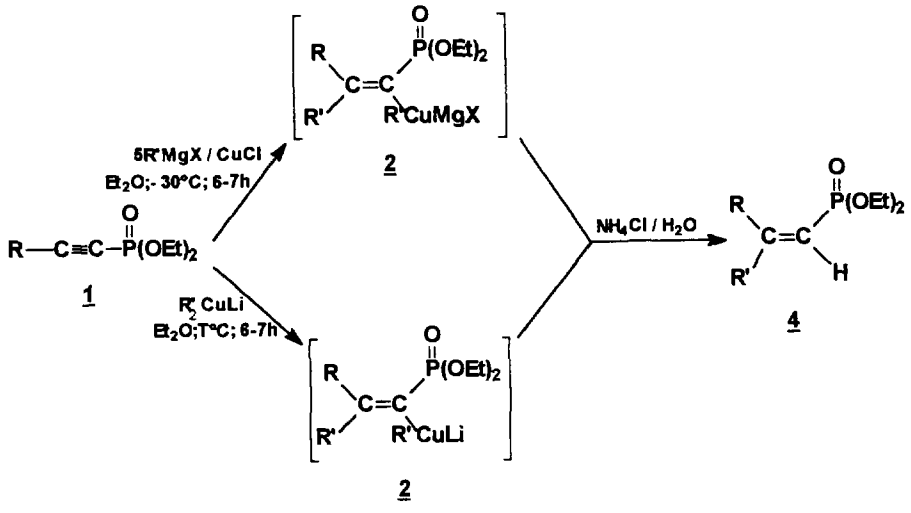
This reaction is also selective (no by-products were detected by $^{31}$P NMR), but requires five equivalents of Grignard reagents: with a smaller quantity, the reaction is slower and loses its chemio- and stereoselectivity. The influence of the excess Grignard reagent upon the result of this reaction seems difficult to explain.

It is interesting to note that lithium dialkyl- or diarylcuprates can also react in ether, at low temperature, with acetylenic phosphonates **1** (in a stoichiometric amount) to provide after hydrolysis compounds **4** in good yields and high regio- and stereoselectivity (Table 2) (Scheme 3). In this case, the crude product generally contains 2

Table 1
Synthesis of monosubstituted *Z*-alk-1-enylphosphonates **3** (Scheme 2)

| Compound | R | Yield [a] (%) | $\delta^{31}$P (ppm) ($CDCl_3$) | $^1$H NMR ($CDCl_3$): $\delta$ (ppm); *J* (Hz) | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | $H_1$ | $^2J_{P-H_1}$ | $H_2$ | $^3J_{P-H_2}$ | $^3J_{H_1-H_2}$ |
| **3a** | $^n$Bu | 80 | 17.92 [b] | 5.5 | *19.92* | 6.4 | *53.00* | *12.99* |
| **3b** | $^n$Pr | 68 | 17.74 | 5.5 | *20.04* | 6.4 | *53.05* | *13.04* |
| **3c** | Ph | 70 | 16.50 | 5.8 | *15.59* | | | *14.23* |

[a] Isolated pure compounds.
[b] $\delta^{31}$P ($CDCl_3$) 17.83 ppm in Ref. [22].




Scheme 3.

to 5% unidentified by-products (detected by $^{31}P$ NMR), which are easily eliminated by chromatography. The temperature also plays an important role in the chemio- and stereoselectivity of this reaction: for example, in the case of compounds **4f** when the temperature increases (from −70 to −40°C) the *Z*/*E* ratio of compounds decreases (from 99/1 to 13/67) and the by-products increase (from 4 to 25%).

The formation of alk-1-enylphosphonates **4** in these reactions can be explained by assuming the intermediate formation of alkyl(1-phosphono-alk-1-enyl)cuprates **2** (Scheme 3).

The *syn*-stereoselective addition to alk-1-ynylphosphonates **1** has been established unambiguously by $^{13}C$ NMR spectroscopy of compounds **4a–4g**: as in the case of vinylphosphine oxides [23], the $^{3}J_{P-C}$ *trans* values (20.9–24.7 Hz) are much larger than the $^{3}J_{P-C}$ *cis* values (6.5–7.8 Hz) (Table 3). For the compounds with a phenyl substituent, it is interesting to note that in $^{1}H$ NMR spectra the shape and the chemical shift of the methylenic phosphonate protons depend on the *cis* or *trans* orientation of the phenyl group towards the phosphonate function. In the *cis* orientation they appear as a multiplet upfield (3.5–3.9 ppm), shielded by the induced diamagnetic field of the aromatic ring. In the *trans* orientation they are essentially unaffected by the diamagnetic anisotropy, and appear as a quintuplet at 4.1 ppm. This difference could allow us to assign stereochemistry quite confidently when only a single isomer is available.

### 2.3. Synthesis of diethyl trisubstituted alk-1-enylphosphonates 5 (path b'', Scheme 1)

Phosphono-dialkenylcuprates **2** react with a range of electrophiles to provide trisubstituted alkenylphosphonates **5** in good yields and high retention of configuration (Scheme 4).

The results quoted in Table 4 indicate the following.

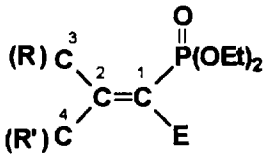
(i) The iodination reaction seems to be one of the easiest reactions to perform with **2**. Addition of two equivalents of solid iodine to a solution of 1-phos-

Table 2
Synthesis of diethyl 2,2-disubstituted alk-1-enylphosphonates **4** (Scheme 3)

| Compound | R | R | Organometallic reagents | Temperature (°C) | Reaction time (h) | Yield [a] (%) | $\delta^{31}P$ (ppm) ($CDCl_3$) |
|---|---|---|---|---|---|---|---|
| **4a** | Ph | $^{n}$Oct | R'MgX | −30 | 6 | 77 | 17.1 |
| **4b** | $^{n}$Pr | $^{n}$Oct | R'MgX | −30 | 7 | 85 | 19.2 |
| **4c** | $^{n}$Pr | Ph | R'MgX | −30 | 6 | 88 | 18.5 |
| **4d** | Ph | 4-Tol | R'MgX | −30 | 7 | 75 | 17.6 |
| **4e** | $^{n}$Pr | Me | R'MgX | −30 | 6 | 95 | 18.3 |
| | | | R'Li | −50 | 6 | 80 | 18.3 |
| **4f** | Ph | $^{n}$Bu | R'MgX | −30 | 6 | 81 | 17.3 |
| | | | R'Li | −70 | 6 | 84 | 17.3 |
| **4g** | $^{n}$Bu | Ph | R'Li | −50 | 6 | 77 | 18.5 |

[a] Isolated pure compounds.

Table 3
$^{13}C$ NMR data of the vinylphosphonates **3**, **4**, **5**

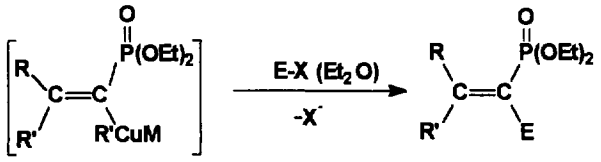



| Compound | R | R' | E | $^{13}C$ ($CDCl_3$) (ppm) $J_{P-C}$ (Hz) | | | |
|---|---|---|---|---|---|---|---|
| | | | | $C_1$ | $C_2$ | $C_3$ *cis* | $C_4$ *trans* |
| **3a** | $^n$Bu | H | H | 116.19 | 153.81 | 30.47 | — |
| | | | | *182.95* | *4.70* | | |
| **3b** | $^n$Pr | H | H | 116.34 | 153.75 | 32.36 | — |
| | | | | *182.90* | *4.65* | | |
| **3c** | Ph | H | H | 116.38 | 146.74 | 135.13 | — |
| | | | | *184.20* | *1.90* | | |
| **4a** | Ph | $^n$Oct | H | 113.40 | 162.90 | 139.76 | 41.26 |
| | | | | *191.30* | *3.90* | *7.80* | *21.10* |
| **4b** | $^n$Pr | $^n$Oct | H | 110.80 | 167.10 | 35.30 | 37.83 |
| | | | | *188* | *6.87* | *7.00* | *22.40* |
| **4c** | $^n$Pr | Ph | H | 113.80 | 163.50 | 34.1 | 140.8 |
| | | | | *188.90* | *8.7* | *6.50* | *23.70* |
| **4d** | Ph | 4-Tol | H | 113.40 | 159.80 | 138.4 | 138.4 |
| | | | | *191.30* | *6.14* | *7.50* | *22.30* |
| **4e** | $^n$Pr | Me | H | 112.30 | 163.30 | 36.66 | 25.33 |
| | | | | *189.30* | *7.41* | *6.80* | *24.70* |
| **4f** | Ph | $^n$Bu | H | 113.80 | 163.20 | 139.86 | 41.02 |
| | | | | *191.30* | *3.90* | *7.80* | *20.90* |
| **4g** | $^n$Bu | Ph | H | 113.5 | 163.80 | 32.29 | 140.92 |
| | | | | *192.30* | *8.67* | *6.59* | *23.70* |
| **5a** | Ph | $^n$Bu | Me | 121.2 | 156.10 | 142.50 | 36.55 |
| | | | | *182* | *8.61* | *8.50* | *17.7* |
| **5b** | $^n$Pr | Me | Me | 117.66 | 155.34 | 38.62 | 20.35 |
| | | | | *180.30* | *13.18* | *7.26* | *19.19* |
| **5c** | $^n$Bu | Ph | Me | 120.42 | 158.61 | 36.33 | 141.9 |
| | | | | *176.50* | *13.9* | *6.9* | *22.64* |
| **5d** | Ph | $^n$Bu | I | 88.60 | 165.40 | 140.40 | 47.64 |
| | | | | *197.50* | *9.17* | *5.93* | *14.22* |
| **5d'** [a] | $^n$Bu | Ph | I | 86.79 | 169.75 | 37.45 | 147.10 |
| | | | | *188.4* | *14.33* | *4.16* | *18.82* |
| **5e** | $^n$Pr | Me | I | 85.46 | 116.17 | 38.69 | 32.8 |
| | | | | *194* | *13.80* | *5.00* | *16.20* |
| **5f** | Ph | $^n$Bu | $PhCH_2$ | 125.77 | 160.12 | 142.91 | 37.16 |
| | | | | *175.90* | *9.02* | *8.46* | *17.62* |
| **5g** | Ph | $^n$Bu | $CH_2=CHCH_2$ | 123.74 | 158.36 | 141.93 | 36.22 |
| | | | | *181.20* | *8.92* | *8.50* | *17.67* |
| **5h** | $^n$Pr | Me | PhCO | 128.68 | 159.49 | 38.44 | 21.16 |
| | | | | *177.40* | *6.50* | *7.98* | *18.40* |

[a] By-products isolated from the reaction **5c**.

phono-alk-1-enylcuprates **2** affords, after 3 h at 22 °C, good yields (63–66%) of the corresponding 1-iodo alk-1-enyl phosphonates (**5d**, **5e**) (Table 4), with total retention of stereochemistry. The alkenyl iodides obtained are very interesting synthons, since they could lead to the corresponding lithium reagent via halogen–metal exchange with $^n$BuLi [25]. These lithium reagents would react with ketones, aldehydes and esters: all reactions which cannot be performed with cuprates.

(ii) Alkylation with methyl iodide (two equivalents) provides after seven days at room temperature the expected trisubstituted vinylphosphonates in good yield (60–70%) and total stereochemical purity. Likewise, benzyl bromide, allyl bromide and benzoyl chloride afford after four days the corresponding trisubstituted vinylphosphonates (**5f**, **5g**, **5h**) in good yield (56–69%) and stereochemical purity higher than 99%. The coupling of 1-phosphono-alk-1-enylcuprates **2** with other electrophilic reagents (iodoethane, iodobutane, methyl chloroformiate, N-bromomethylphtalimide, diethyl chlorophosphate, etc.) does not occur under a variety of conditions.




2 5

R = nBu , Aryl , nPr ; R' = Alkyl , Aryl ; M = Li

E = Me , $PhCH_2$ , $CH_2$=$CHCH_2$ , PhCHO , I

Scheme 4.

We also observed that, in contrast to the non-functionalised dialkenylcuprates which possess a much enhanced reactivity and generally decompose at temperatures higher than −15 °C [26], the phosphono-alkenyl cuprates **2** possess a very weak reactivity and are stable at room temperature; this is probably due to the coordination between the phosphonate function and copper [27]. This phenomenon could also partially explain why only activated electrophilic reagents react with **2**.

It is noteworthy that the results mentioned above have been obtained with lithium derivatives of **2**. Studies with the corresponding Grignard derivatives have been undertaken, and it appears as first that alkylation, with iodomethane at 22 and −15 °C, occurs with isomerization of the double bond and a large amount of by-products. Isomerization disappears at −30 °C but the amount of by-products remains important. The use of akyltosylates as electrophilic reagents seems to provide selectively the expected compounds with good yield. For example, by using methyltosylate the compound **5b** is obtained in 86% yield and with complete retention of configuration after five days at −30 °C, but attempts with *n*-butyltosylate failed under the same conditions.

The stereochemical purity of isolated compounds **5a–5b** was unequivocally established by $^{13}C$ NMR spectroscopy (Table 3). The $^3J_{P-C}$ *trans* values (14.22–22.64 Hz) were much larger than the $^3J_{P-C}$ *cis* values (5.0–8.5 Hz).

### 2.4. Conclusion

Suitable methods to obtain stereoisomerically pure mono-, di- and trisubstituted vinylphosphonates have been developed starting from readily available alk-1-ynylphosphonates.

The hydrogenation of alk-1-ynylphosphonates using the Lindlar catalyst provides, after purification, the *Z* isomer of the corresponding alk-1-enylphosphonates in good yields.

The reaction of alk-1-enylphosphonates with magnesium or lithium organocopper reagents provides an easy method for the preparation of stereoisomerically pure 2,2-disubstituted alk-1-enylphosphonates in high yields. The reaction is a useful extension of hitherto known methods.

Further, substituted alkenyl cuprates bearing the phosphonate function may be used as convenient reagents to obtain stereochemically pure trisubstituted vinylphosphonates by reaction with various electrophiles.

## 3. Experimental

### 3.1. General

Unless otherwise specified, the starting materials were commercially available. Solvents and substrates were purified by conventional methods immediately before use. IR spectra were recorded using a Perkin–Elmer 377 spectrometer. The NMR spectra were obtained on Bruker AC-200, AC-250 and WP instruments ($^1H$ NMR at 200.13 and 250.13 MHz, $^{13}C$ NMR at 50.32 MHz and $^{31}P$ NMR at 81.0 MHz).

The crude products were purified by column liquid chromatography at normal pressure on Merck 60-G silica gel. The TLC analyses were conducted on 0.2 mm Merck silica gel plates (60F-254) using UV (254 nm), iodine or 4-(*p*-nitrobenzyl)-pyridine (NBP) [28] as de-

Table 4
Synthesis of diethyl trisubstituted alk-1-enylphosphonates **5** (Scheme 4)

| Compound | R | R' | E–X (2 equiv.) | *T* (°C) | Reaction time | Yield [a] (%) | By-products (%) | $^{31}P$ NMR ($CDCl_3$) |
|---|---|---|---|---|---|---|---|---|
| **5a** | Ph | $^n$Bu | MeI | 22 | 7 days | 60 | 27 [b] | 20.48 |
| **5b** | $^n$Pr | Me | MeI | 22 | 7 days | 69 | 21 [b] | 21.28 |
| | $^n$Pr | Me | MeOTs | −30 | 5 days | 86 | — | 21.28 |
| **5c** | $^n$Bu | Ph | MeI | 22 | 7 days | 70 | 12 [b] | 21.71 |
| **5d** | Ph | $^n$Bu | $I_2$ | 22 | 3 h | 66 | — | 9.68 |
| **5e** | $^n$Pr | Me | $I_2$ | 22 | 3 h | 63 | — | 10.56 |
| **5f** | Ph | $^n$Bu | $PhCH_2Br$ | 22 | 4 days | 65 | — | 19.69 |
| **5g** | Ph | $^n$Bu | $CH_2$=$CHCH_2Br$ | 22 | 4 days | 69 | — | 19.96 |
| **5h** | $^n$Pr | Me | PhCOCl | 22 | 4 days | 56 | — | 12.60 |

[a] Isolated pure compounds.
[b] Essentially the corresponding trisubstituted iodo phosphonates.

veloping agents. The products were collected as homogeneous (according to TLC) fractions.

### 3.2. Synthesis of monosubstituted vinylphosphonates (procedure of hydrogenation) [20]

#### 3.2.1. Preparation of diethyl hex-1(Z)-enylphosphonate 3a

In a flask fitted with inlet gas and magnetic stirrer, 70 ml of methanol, 4 g (18.3 mmol) of diethyl hex-1-ynylphosphonate [19], 400 mg of Lindlar catalyst and 0.5 ml of quinoline were charged. The flask was connected to a low pressure hydrogenation apparatus, where it was evacuated, and hydrogen admitted to a pressure slightly above 1 atm. Stirring was started and the hydrogen absorption recorded. The reaction was stopped as soon as the required amount of hydrogen had been absorbed (18.3 mmol of hydrogen in about 2 h). Then the reaction mixture was filtered through Celite and the solvent removed in vacuo. 50 ml of a 10% aqueous solution of HCl was added to the remaining liquid and stirred. After 15 min, 50 ml of ether was added and the layers were separated. The aqueous layer was washed three times with ether, and the combined organic layers dried over $MgSO_4$ and concentrated on a rotary evaporator to give 3.70 g of a dried pale yellow oil. The analysis of this crude product by $^{31}P$ NMR showed three signals: 17.90 ppm (90%), 19.52 ppm (6%) and 33.25 ppm (4%) respectively corresponding to isomer *Z*, isomer *E* and diethyl hexylphosphonate. A purification by column chromatography gave **3a** as a pale yellow oil [21].

$R_F = 0.45$ ($Et_2O$, $SiO_2$, NBP); 80% yield (3.22 g, 14.6 mmol). $^1H$ NMR ($CDCl_3$): (irradiation at 2.5 ppm) $\delta = 0.84$ (t, 3H, $^3J_{H-H} = 7$, $CH_3CH_2CH_2$), 1.25 (t, 3H, $^3J_{H-H} = 7$, $CH_3CH_2O$), 1.3–1.5 m, 4H, $CH_3CH_2CH_2CH_2$), 2.3–2.5 (m, 2H, $CH_2CH{=}CH$), 4.0 (quint, 4H, $^3J_{H-H} = 7.06$, $^3J_{P-H} = 7.06$, $CH_3CH_2O$), 5.5 (ddt, 1H, $^4J_{HH} = 1.5$, $^2J_{P-H} = 19.92$, $^3J_{H-H} = 12.98$, $CH_d{=}CHP$), 6.4 (ddt, 1H, $^3J_{PH} = 52.98$, $^3J_{HH} = 12.99$, $^3J_{HH} = 7.67$, $CH{=}CHP$). $^{31}P$ NMR ($CDCl_3$): $\delta = 17.9$ (s). $^{13}C$ NMR ($CDCl_3$): $\delta = 153.81$ (d, $^2J_{P-C} = 4.7$, $CH{=}CHP$), 116.19 (d, $^1J_{P-C} = 182.95$, $CH{=}CP$), 60.95 (d, $^2J_{P-C} = 5.5$, $CH_3CH_2O$), 30.95 (d, $^4J_{P-C} = 2.15$, $CH_3CH_2CH_2$), 30.47 (d, $^3J_{P-C} = 8.1$ $CH_2CH{=}CH$), 21.9 (s, $CH_3CH_2CH_2$), 16.19 (d, $^3J_{P-C} = 6.5$, $CH_3CH_2O$), 13.33 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 2950 ($CH_3$), 2880 ($CH_2$), 1630 ($C{=}C$), 1250 ($PO$), 1025 ($POC$).

#### 3.2.2. Preparation of diethyl pent-1(Z)-enylphosphonate 3b

A procedure as above with 3.75 g (18.4 mmol) of pent-1-ynylphosphonate, 375 mg of Lindlar catalyst and 0.5 ml of quinoline gave 2.57 g, 68% yield. $R_F = 0.40$ ($Et_2O$, $SiO_2$, NBP). $^1H$ NMR ($CDCl_3$): (irradiation at 2.43 ppm) $\delta = 0.84$ (t, 3H, $^3J_{H-H} = 7.5$, $CH_3CH_2CH_2$), 1.23 (t, 3H, $^3J_{H-H} = 7$, $CH_3CH_2O$), 1.4 (sext, 2H, $^3J_{H-H} = 7.5$, $CH_3CH_2CH_2$), 2.43–2.5 (m, 2H, $CH_2CH{=}CH$), 4.0 (quint, 4H, $^3J_{H-H} = 7.0$, $^3J_{P-H} = 7.0$, $CH_3CH_2O$), 5.5 (ddt, 1H, $^2J_{P-H} = 20.04$, $^3J_{H-H} = 13.04$, $^4J_{PH} = 1.6$, $CH{=}CHP$), 6.4 (ddt, 1H, $CH{=}CHP$, $^3J_{P-H} = 53.05$, $^3J_{H-H} = 13.04$, $^3J_{H-H} = 7.67$). $^{31}P$ NMR ($CDCl_3$): $\delta = 17.74$ (s). $^{13}C$ NMR ($CDCl_3$): $\delta = 153.75$ (d, $^2J_{P-C} = 4.65$, $CH{=}CHP$), 116.34 (d, $^1J_{P-C} = 182.95$, $CH{=}CHP$), 61.09 (d, $^2J_{P-C} = 5.5$, $CH_3CH_2O$), 32.36 (d, $^3J_{P-C} = 8.0$, $CH_2CH{=}CH$), 21.88 (d, $^4J_{P-C} = 2.17$, $CH_3CH_2CH_2$), 16.07 (d, $^3J_{P-C} = 6.45$, $CH_3CH_2O$), 13.32 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 2950 ($CH_3$), 2880 ($CH_2$), 1630 ($C{=}C$), 1240 ($PO$), 1025 ($POC$).

#### 3.2.3. Preparation of diethyl (Z)-styrylphosphonate 3c [29].

A procedure as above with 4 g (18.5 mol) of 2-phenyl-ethynylphosphonate, 400 mg of Lindlar catalyst and 0.5 ml of quinoline gave 2.77 g, 70% yield. $R_F = 0.22$ ($Et_2O$, $SiO_2$, UV). $^1H$ NMR ($CDCl_3$): $\delta = 1.16$ (t, 3H, $^3J_{HH} = 7.0$, $CH_3CH_2O$), 3.98 (quint, 4H, $^3J_{HH} = {}^3J_{PH} = 7.4$ $CH_3CH_2O$), 5.80 (dd, 1H, $^2J_{PH} = 15.59$, $^3J_{HH} = 14.23$, $CH{=}CHP$), 7.15–8.0 (m, 6H, $CH{=}CHP$ and 5H aromatic). $^{31}P$ NMR ($CDCl_3$): $\delta = 16.51$ (s). $^{13}C$ NMR ($CDCl_3$): $\delta = 135.15$ (d, $^3J_{P-C} = 8.75$, $C_{ipso}$), 129.40 (d, $^4J_{P-C} = 1.6$, $C_{ortho}$), 129.16 ($C_{meta}$), 127.95 ($C_{para}$), 146.74 (d, $^2J_{P-C} = 1.9$, $CH{=}CHP$), 116.38 (d, $^1J_{P-C} = 184.2$, $CH{=}CHP$), 61.56 (d, $^2J_{P-C} = 5.85$, $CH_3CH_2O$), 15.93 (d, $^3J_{P-C} = 6.55$, $CH_3CH_2O$). IR ($CCl_4$): 2970 ($CH_3$), 2800 ($CH_2$), 1600 ($C{=}C$), 1230 ($PO$), 1025 ($POC$), 680 (aromatic).

### 3.3. Synthesis of 2,2-disubstituted vinylphosphonates

#### 3.3.1. General procedures

All reactions were performed under dry nitrogen in a flask fitted with a low temperature thermometer, a magnetic stirrer and a pressure equalizing addition funnel.

#### 3.3.2. Mode A: addition of magnesium organocuprates to alk-1-ynylphosphonates 1

1.47 g (14.7 mmol) of CuCl was introduced into a stirred solution of Grignard reagent (73.5 mmol) in 125 ml of anhydrous ether at room temperature. After 15 min stirring the temperature was lowered to −30 °C, 14.7 mmol of alk-1-ynylphosphonate slowly added and stirring continued for 6 to 7 h at this temperature. The reaction mixture was then poured, at 0 °C, into 150 ml of a saturated aqueous solution of $NH_4Cl$. The aqueous layer was extracted with ether (3 × 50 ml) and the combined organic layers dried over $MgSO_4$ or $Na_2SO_4$. The solvent was removed on a rotary evaporator and the resulting crude oil purified by column chromatography

on silica gel, with ether as eluent, to give the isolated pure product.

*3.3.3. Mode B: addition of lithium organocuprates to alk-1-ynylphosphonates 1*

To a stirred suspension of 2.60 g (13.70 mmol) CuI in 60 ml of dry ether at −40 °C under nitrogen was added 27.52 mmol of alkyl or aryllithium. When the addition was finished the temperature was allowed to reach −25 °C for 30 min. Then the green reaction mixture was cooled to −70 °C (−50 °C for MeLi or PhLi) and 13.73 mmol diethyl alk-1-ynylphosphonate added. Stirring was continued for 6 or 7 h at this temperature. The reaction mixture was poured into 100 ml of a saturated aqueous solution of $NH_4Cl$. The aqueous layer was extracted with ether (3 × 50 ml) and the combined organic layers dried over $MgSO_4$ or $Na_2SO_4$. The solvent was removed on a rotary evaporator and the resulting crude oil purified by column chromatography on silica gel, with ether as eluent, to give the isolated pure product.

*3.3.4. Diethyl 2-methyl-pent-1(Z)-enylphosphonate 4e*

$R_F$ = 0.42 ($Et_2O$, $SiO_2$, NBP); 95% yield (3.07 g, 13.65 mmol) by mode A, 84% yield (2.54 g, 11.55 mmol) by mode B. $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 0.88 (t, 3H, $^3J_{H-H}$ = 7.3, C$H_3$CH$_2$CH$_2$), 1.25 (t, 3H, $^3J_{H-H}$ = 7.1, C$H_3$CH$_2$O), 1.45 (sext, 2H, $^3J_{H-H}$ = 7.3, CH$_3$CH$_2$CH$_2$), 1.83 (dd, 3H, $^4J_{H-H}$ = 1.16, $^4J_{P-H}$ = 1.05, CH$_3$C=C), 2.43 (dt, 2H, $^3J_{H-H}$ = 7.3, $^4J_{P-H}$ = 2.31, CH$_2$C=CH), 4.01 (dq, 4H, $^3J_{H-H}$ = 7.1, $^3J_{P-H}$ = 7.7, CH$_3$CH$_2$O), 5.5 (dd, 1H, $^2J_{P-H}$ = 19.16, $^4J_{H-H}$ = 1.16, C=CHP). $^{31}P$ NMR ($CDCl_3$): $\delta$ = 18.32 (s). $^{13}C$ NMR ($CDCl_3$): $\delta$ = 163 (d, $^2J_{P-C}$ = 7.4, *C*=CHP), 112.23 (d, $^1J_{P-C}$ = 189, C=*C*HP), 60.8 (d, $^2J_{P-C}$ = 5.5, CH$_3$*C*H$_2$O), 36.6 (d, $^3J_{P-C}$ = 6.8 *cis*, CH$_3$CH$_2$*C*H$_2$), 25.8 (d, $^3J_{P-C}$ = 24.7 *trans*, *C*H$_2$C=CH), 21.1 (d, $^4J_{P-C}$ = 2.0, CH$_3$*C*H$_2$CH), 16.19 (d, $^3J_{P-C}$ = 6.6, *C*H$_3$CH$_2$O), 13.7 (s, *C*H$_3$CH$_2$CH). IR (film): 2950 (*CH*$_3$), 2870 (*CH*$_2$), 1630 (*C*=*C*), 1245 (*PO*), 1030 (*POC*). MS (EI): $M^+$ = 220.

*3.3.5. Diethyl 2-phenyl-pent-1(E)-enylphosphonate 4c*

$R_F$ = 0.30 ($SiO_2$, $Et_2O$, UV); 88% yield (3.65 g, 12.9 mmol) by mode A. $^1H$ NMR ($CDCl_3$): $\delta$ = 0.87 (t, 3H, $^3J_{H-H}$ = 7.3, C$H_3$CH$_2$CH$_2$), 1.33 (t, 3H, $^3J_{H-H}$ = 7.1, C$H_3$CH$_2$O), 1.37–1.50 (m, 2H, CH$_3$C$H_2$CH$_2$), 2.95 (dt, 2H, $^3J_{H-H}$ = 7.8, $^4J_{P-H}$ = 2.4, C$H_2$C=CH), 4.10 (dq, 4H, $^3J_{H-H}$ = 7.1, $^3J_{P-H}$ = 7.7, CH$_3$C$H_2$O), 5.75 (d, 1H, $^2J_{P-H}$ = 17.2, C=C*H*P), 7.30–7.45 (m, 5H aromatic). $^{31}P$ NMR ($CDCl_3$): $\delta$ = 18.51 (s). $^{13}C$ NMR ($CDCl_3$): $\delta$ = 163.66 (d, $^2J_{P-C}$ = 8.7, *C*=CHP), 140.6 (d, $^3J_{P-C}$ = 23.7 *trans*, $C_{ipso}$), 128.71 (s, $C_{para}$), 126.25 and 128.3 ($C_{ortho}$, $C_{meta}$), 113.79 (d, $^1J_{P-C}$ = 189, C=*C*HP), 61.2 (d, $^2J_{P-C}$ = 5.7, CH$_3$*C*H$_2$O), 34.2 (d, $^3J_{P-C}$ = 6.6 *cis*, *C*H$_2$C=C), 21.7 (d, $^4J_{P-C}$ = 2.05, CH$_3$*C*H$_2$CH), 16.2 (d, $^3J_{P-C}$ = 6.5, *C*H$_3$CH$_2$O), 13.6 (s, *C*H$_3$CH$_2$CH$_2$). IR (film): 2950 (*CH*$_3$), 2870 (*CH*$_2$), 1610 (*C*=*C*), 1575 (aromatic), 1250 (*P*=*O*), 1020 (*POC*). Anal. Found: C, 63.53; H, 8.29; O, 17.04. $C_{15}H_{23}O_3P$ (282.32) Calc.: C, 63.80; H, 8.15; O, 17.02%.

*3.3.6. Diethyl 2-propyl-dec-1(E)-enylphosphonate 4b*

$R_F$ = 0.30 ($Et_2O$, $SiO_2$, UV); 85% yield (3.98 g, 12.5 mmol) by mode A. $^1H$ NMR ($CDCl_3$): $\delta$ = 0.9 (t, 6H, $^3J_{H-H}$ = 7.01, C$H_3$CH$_2$CH$_2$), 1.1–1.3 (m, 18H, C$H_3$CH$_2$O and CH$_3$(C$H_2$)$_6$CH$_2$). 1.38–1.47 (m, 2H, CH$_3$C$H_2$CH$_2$), 2.1 (t, 2H, $^3J_{H-H}$ = 7.0, CH$_3$(CH$_2$)$_6$C$H_2$C=C), 2.4 (dt, 2H, $^4J_{P-C}$ = 2.2, $^3J_{H-H}$ = 5.7, CH$_3$CH$_2$C$H_2$C=C), 3.9–4.10 (dq, 4H, $^3J_{H-H}$ = 7.0, $^3J_{P-H}$ = 7.1, CH$_3$C$H_2$O), 5.28 (d, 1H, $^2J_{P-H}$ = 18.7, C=C*H*P). $^{31}P$ NMR ($CDCl_3$): $\delta$ = 19.21 (s). $^{13}C$ NMR ($CDCl_3$): $\delta$ = 167.1 (d, $^2J_{P-C}$ = 6.8, *C*=CHP), 110.81 (d, $^1J_{P-C}$ = 189, C=*C*HP), 60.7 (d, $^2J_{P-C}$ = 5.6, CH$_3$*C*H$_2$O), 37.83 (d, $^3J_{P-C}$ = 22.48 *trans*, CH$_3$(CH$_2$)$_6$*C*H$_2$), 35.30 (d, $^3J_{P-C}$ = 7.0 *cis*, *C*H$_2$C=C), 31.53 (s, CH$_3$(CH$_2$)$_4$*C*H$_2$), 29.00 (d, CH$_3$CH$_2$)$_3$CH$_2$), 27.2 (d, $^4J_{P-C}$ = 0.5, CH$_3$(CH$_2$)$_5$*C*H$_2$), 22.34 (s, CH$_3$*C*H$_2$(CH$_2$)$_4$CH$_2$), 21.7 (d, $^4J_{P-C}$ = 2.05, CH$_3$*C*H$_2$CH), 16.0 (d, $^3J_{P-C}$ = 6.5, *C*H$_3$CH$_2$O), 13.6 (s, *C*H$_3$CH$_2$CH$_2$). IR (film): 2950 (*CH*$_3$), 2860 (*CH*$_2$), 1625 (*C*=*C*), 1250 (*PO*), 1030 (*POC*). Anal. Found: C, 63.80; H, 11.02; O, 14.97. $C_{17}H_{35}O_3P$ (318.44) Calc.: C, 64.12; H, 11.08; O, 15.07%.

*3.3.7. Diethyl 2-phenyl-hex-1(E)-enylphosphonate 4g*

$R_F$ = 0.20 ($Et_2O$, $SiO_2$, UV); 77% yield (3.14 g, 105.6 mmol) obtained by mode B. $^1H$ NMR ($CDCl_3$): $\delta$ = 0.87 (t, 3H, $^3J_{H-H}$ = 7.2, C$H_3$CH$_2$CH$_2$), 1.31–1.38 (m, 10H, C$H_3$CH$_2$O and CH$_3$C$H_2$C$H_2$), 2.98 (dt, 2H, $^3J_{H-H}$ = 7.28, $^4J_{P-H}$ = 2.42, C$H_2$C=CH), 4.12 (dq, 4H, $^3J_{H-H}$ = 7.11, $^3J_{P-H}$ = 7.01, CH$_3$C$H_2$O), 5.75 (d, 1H, $^2J_{P-H}$ = 17.2, C=C*H*P), 7.2–7.4 (m, 5H aromatic). $^{31}P$ NMR ($CDCl_3$): $\delta$ = 18.51 (s). $^{13}C$ NMR ($CDCl_3$): $\delta$ = 163.86 (d, $^2J_{P-C}$ = 8.67, *C*=CHP), 140.92 (d, $^3J_{P-C}$ = 23.75 *trans*, $C_{ipso}$), 128.35–129.06 ($C_{ortho}$, $C_{meta}$, $C_{para}$), 113.49 (d, $^1J_{P-C}$ = 192.31, C=*C*HP), 61.33 (d, $^2J_{P-C}$ = 5.67, CH$_3$*C*H$_2$O), 32.29 (d, $^3J_{P-C}$ = 6.59 *cis*, *C*H$_2$C=C), 26.73 (s, $^4J_{P-C}$ = 2.05, CH$_3$CH$_2$*C*H$_2$), 22.54 (s, CH$_3$*C*H$_2$CH), 16.23 (d, $^3J_{P-C}$ = 6.54, *C*H$_3$CH$_2$O), 13.71 (s, *C*H$_3$CH$_2$CH$_2$). IR (film): 2960 (*CH*$_3$), 2860 (*CH*$_2$), 1600 (*C*=*C*), 1575 (aromatic), 1245 (*PO*), 1025 (*POC*). Anal. Found: C, 64.57; H, 8.27; O, 16.37. $C_{16}H_{25}O_3P$ (296.35) Calc.: C, 64.85; H, 8.50; O, 16.20%.

*3.3.8. Diethyl 2-phenyl-hex-1(Z)-enylphosphonate 4f*

$R_F$ = 0.20 ($Et_2O$, $SiO_2$, UV); 81% yield (3.53 g, 11.9 mmol) by mode A, 84% yield (3.42 g, 11.56 mmol) by mode B. $^1H$ NMR ($CDCl_3$): $\delta$ = 0.81 (t, 3H, $^3J_{H-H}$

= 7.3, $CH_3CH_2CH_2$), 1.06 (t, 6H, $^3J_{H-H}$ = 7.1, $CH_3CH_2O$), 1.28–1.36 (m, 4H, $CH_3CH_2CH_2$), 2.42 (t, 2H, $^3J_{H-H}$ = 6.87, $^4J_{P-H}$ = 2.42, $CH_2C$=CH), 3.57–3.84 (m, 4H, $CH_3CH_2O$), 5.63 (d, 1H, $^2J_{P-H}$ = 17.7, C=CHP), 7.29 (s, 5H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 17.32 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 163.2 (d, $^2J_{P-C}$ = 3.9, *C*=CHP), 139.88 (d, $^3J_{P-C}$ = 7.8 *cis*, $C_{ipso}$), 127.37–127.87 ($C_{ortho}$, $C_{meta}$, $C_{para}$), 113.8 (d, $^1J_{P-C}$ = 191.31, C=*C*HP), 61.04 (d, $^2J_{P-C}$ = 6.05, $CH_3CH_2O$), 41.02 (d, $^3J_{P-C}$ = 21.1 *trans*, $CH_2C$=), 29.39 (d, $^4J_{P-C}$ = 1.03, $CH_3CH_2CH_2$), 21.92 (s, $CH_3CH_2CH$), 15.87 (d, $^3J_{P-C}$ = 6.72, $CH_3CH_2O$), 13.59 (s, $CH_3CH_2CH_2$). IR (film): $\nu$ = 2960 ($CH_3$), 2860 ($CH_2$), 1600 (*C*=*C*), 1575 (aromatic), 1245 (*PO*), 1025 (*POC*). Anal. Found: C, 64.47; H, 8.18; O, 16.40. $C_{11}H_{23}O_3P$ (234.28) Calc.: C, 64.85; H, 8.50; O, 16.20%.

### 3.3.9. Diethyl 2-phenyl-2-p-tolyl (E)-vinylphosphonate **4d**

$R_F$ = 0.33 ($Et_2O$, $SiO_2$, UV); 75% yield (3.64 g, 11.02 mmol) by mode A. $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.1 (t, 6H, $^3J_{H-H}$ = 7.3, $CH_3CH_2O$), 2.35 (s, $CH_3C_6H_4$), 3.72–3.93 (m, 4H, $CH_3CH_2O$), 6.1 (d, 1H, $^2J_{P-H}$ = 15.63, C=C*H*P), 7.34 (s, 5H aromatic), 7.05–7.16 (q, $J_{H-H}$ = 8.45, 4H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 17.58 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 159.8 (d, $^2J_{P-C}$ = 6.4, *C*=CHP), 139.34 (s, $C'_{para}$), 138.84 (d, $^3J_{P-C}$ = 7.5 *cis*, $C_{ipso}$), 138.36 (d, $^3J_{P-C}$ = 22.3 *trans*, $C'_{ipso}$), 129.53 (s, $C'_{meta}$), 129.50 (s, $C_{meta}$), 128.4 (s, $C_{para}$), 127.90 (s, $C'_{ortho}$), 127.57 (s, $C_{ortho}$), 113.4 (d, $^1J_{P-C}$ = 193.91, C=*C*HP), 61.2 (d, $^2J_{P-C}$ = 6.04, $CH_3CH_2O$), 20.96 (s, $pCH_3C_6H_4$), 15.4 (d, $^3J_{P-C}$ = 6.70, $CH_3CH_2O$). IR (film): 2990 ($CH_3$), 2920 ($CH_2$), 1590 (*C*=*C*), 1510–1490 (aromatic), 1250 (*PO*), 1025 (*POC*). Anal. Found: C, 69.38; H, 7.03; O, 15.02. $C_{19}H_{23}O_3P$ (330.36) Calc.: C, 69.07; H, 7.01; O, 14.52%.

### 3.3.10. Diethyl 2-phenyl-dec-1(E)-enylphosphonate **4a**

$R_F$ = 0.30 ($Et_2O$, $SiO_2$, UV); 77% yield (3.98 g, 11.32 mmol) by mode A. $^1$H NMR ($CDCl_3$): $\delta$ = 0.83 (t, 3H, $^3J_{H-H}$ = 6.83, $CH_3CH_2CH_2$), 1.05 (t, 6H, $^3J_{H-H}$ = 7.04, $CH_3CH_2O$), 1.15–1.45 (m, 12H, $CH_3(CH_2)_6CH_2$), 2.45 (t, 2H, $^3J_{H-H}$ = 6.94, $CH_2C$=C), 3.6–3.9 (m, 4H, $CH_3CH_2OP$), 5.65 (d, 1H, $^2J_{P-H}$ = 17.8, C=C*H*P), 7.3 (s, 5H, aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 17.13 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 162.94 (d, $^2J_{P-C}$ = 6.8, *C*=CHP), 139.76 (d, $^3J_{P-C}$ = 7.80 *cis*, $C_{ipso}$), 127.28, 127.52 and 127.73 ($C_{ortho}$, $C_{meta}$, $C_{para}$), 113.4 (d, $^1J_{P-C}$ = 191.32, C=*C*HP), 60.85 (d, $^2J_{P-C}$ = 6.03, $CH_3CH_2OP$), 41.21 (d, $^3J_{P-C}$ = 21.11 *trans*, $CH_2C$=C), 31.47 (s, $CH_3(CH_2)_5CH_2$), 28.65, 28.8 and 28.95 ($C_3H_7(CH_2)_3CH$), 27.12 (s, $CH_3CH_2CH_2$), 22.30 (s, $CH_3CH_2(CH_2)_4CH_2$), 15.77 (d, $^3J_{P-C}$ = 6.69, $CH_3CH_2O$), 13.75 (s, $CH_3(CH_2)_6$). IR (film): 2910 ($CH_3$), 2850 ($CH_2$), 1615 (*C*=*C*), 1570 (aromatic), 1240 (*PO*), 1025 (*POC*). Anal. Found: C, 67.87; H, 9.42; O, 13.83. $C_{20}H_{33}O_3P$ (352.45) Calc.: C, 68.00; H, 9.63; O, 13.58%.

## 3.4. Synthesis of trisubstituted vinylphosphonates

### 3.4.1. General procedures

All reactions were performed under dry nitrogen in a flask fitted with a low temperature thermometer, a magnetic stirrer and a pressure equalizing addition funnel.

### 3.4.2. Addition of lithium organocuprates to alk-1-ynylphosphonates **1** followed by substitution with electrophilic reagents

To a stirred suspension of 2.60 g (13.70 mmol) CuI in 60 ml of dry ether under nitrogen, at −40 °C, were added 27.52 mmol of a solution of alkyl or aryllithium in ether. When the addition was finished the temperature was allowed to reach −25 °C for 30 min. Then, the reaction mixture was cooled to −70 °C (−50 °C for MeLi or PhLi), and 13.73 mmol of diethyl alk-1-ynylphosphonate was added. Stirring was continued for 6 or 7 h at this temperature.

*3.4.2.1. Alkylation.* 27.52 mmol of electrophilic reagent (iodomethane, benzoyl chloride, benzyl bromide, allyl bromide, etc.) was added and the mixture allowed to warm to room temperature. After the required time (four to seven days), the reaction mixture was poured into 150 ml of a saturated aqueous solution of $NH_4Cl$, at 0 °C. The aqueous layer was extracted with ether (3 × 50 ml) and the combined organic layers dried over $MgSO_4$ or $Na_2SO_4$. The solvent was removed on a rotary evaporator and the resulting crude oil purified by column chromatography on silica gel, with ether as eluent, to give the isolated pure product.

*3.4.2.2. Iodination.* 27.52 mmol of finely crushed solid iodine was added at once, and the mixture allowed to warm to room temperature. After 3 h, the reaction mixture was hydrolyzed with 100 ml of a saturated aqueous solution of $NH_4Cl$, at 0 °C. The aqueous layer was extracted with ether (3 × 50 ml) and the combined organic phases washed twice with an aqueous solution of sodium thiosulfate and dried over $MgSO_4$ or $Na_2SO_4$. The solvent was removed on a rotary evaporator and the resulting crude oil purified by column chromatography on silica gel, with ether as eluent, to give the isolated pure product.

### 3.4.3. Diethyl 1,2-dimethyl-pent-1(Z)-enylphosphonate **5b**

$R_F$ = 0.42 ($SiO_2$, $Et_2O$, NBP); 69% yield (2.22 g, 9.49 mmol). $^1$H NMR ($CDCl_3$): $\delta$ = 0.89 (t, 3H, $^3J_{H-H}$

= 7.3, $CH_3CH_2CH_2$), 1.27 (t, 3H, $^3J_{H-H}$ = 7.3, $CH_3CH_2O$), 1.45 (sext, 2H, $^3J_{H-H}$ = 7.5, $CH_3CH_2CH_2$), 1.74–1.77 (m, 3H, =C($CH_3$)P), 1.8 (d, 3H, $^4J_{P-H}$ = 0.7, $CH_3C$=C), 2.5 (dt, 2H, $^3J_{H-H}$ = 7.3, $^4J_{P-H}$ = 1.45, $CH_2C$=C), 4.05 (dquint, 4H, $^3J_{H-H}$ = 7.1, $^3J_{P-H}$ = 7.1, $CH_3CH_2O$). $^{31}$P NMR ($CDCl_3$): $\delta$ = 21.28 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 155.34 (d, $^2J_{P-C}$ = 13.18, *C*=CP), 117.66 (d, $^1J_{P-C}$ = 180.3, C=*C*P), 60.82 (d, $^2J_{P-C}$ = 6.26, $CH_3CH_2O$), 38.62 (d, $^3J_{P-C}$ = 7.26 *cis*, $CH_3CH_2CH_2$), 21.66 (d, $^4J_{P-C}$ = 2.45, $CH_3CH_2CH$), 20.35 (d, $^3J_{P-C}$ = 19.91 *trans*, $CH_3C$=C), 16.21 (d, $^2J_{P-C}$ = 12.78, =C($CH_3$)P), 16.15 (d, $^3J_{P-C}$ = 6.57, $CH_3CH_2O$), 13.95 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 2960 ($CH_3$), 2885 ($CH_2$), 1625 (C=C), 1250 (*PO*), 1030 (*POC*), 1430 ($CH_2$). Anal. Found: C, 56.34; H, 10.03; O, 20.33. $C_{11}H_{23}O_3P$ (234.28) Calc.: C, 56.38; H, 9.90; O, 20.49%.

Alternatively the same product may be prepared as follows: 1.47 g (14.7 mmol) of CuCl is introduced into a stirred solution of Grignard reagent (73.5 mmol) in 125 ml of anhydrous ether. The temperature is then lowered to −30 °C and 14.7 mmol of alk-1-ynylphosphonates **1** slowly added. Stirring is continued for 6 to 7 h at this temperature. Then 29.5 mmol of methyl tosylate is added and, after stirring for five days, the reaction mixture is poured into a (4/1) aqueous mixture solution of saturated $NH_4Cl$ and 17% aqueous ammonia at 0 °C. The aqueous layer is extracted with ether (3 × 50 ml), and the combined organic layers are dried over $MgSO_4$ or $Na_2SO_4$. The solvent is removed on a rotary evaporator and the resulting crude oil purified by column chromatography on silica gel with ether as eluent to yield 86% (2.96 g, 12.64 mmol) of the isolated pure product.

### 3.4.4. Diethyl 1-methyl-2-phenyl-hex-1(E)-enylphosphonate **5c**

$R_F$ = 0.38 ($SiO_2$, $Et_2O$, UV); 70% yield (2.99 g, 9.63 mmol). $^1$H NMR ($CDCl_3$): $\delta$ = 0.78 (t, 3H, $^3J_{H-H}$ = 6.64, $CH_3CH_2CH_2$), 1.10–1.30 (m, $CH_3CH_2CH_2CH_2$), 1.33 (t, 3H, $^3J_{H-H}$ = 7.05, $CH_3CH_2O$), 1.62 (d, 3H, $^3J_{P-H}$ = 13.7, C=C($CH_3$)P), 2.83–2.87 (m, 2H, $CH_2C$=C), 4.07 (dq, $^3J_{H-H}$ = 7.05, $^3J_{P-H}$ = 7.74, $CH_3CH_2O$). $^{31}$P NMR ($CDCl_3$): $\delta$ = 21.71 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 158.61 (d, $^2J_{P-C}$ = 13.9, *C*=CP), 141.94 (d, $^3J_{P-C}$ = 22.64 *trans*, $C_{ipso}$), 128.05 ($C_{para}$), 127.22 ($C_{ortho}$), 126.67 ($C_{meta}$), 120.42 (d, $^1J_{P-C}$ = 176.5, C=*C*P), 61.0 (d, $^2J_{P-C}$ = 5.75, $CH_3CH_2O$), 36.63 (d, $^3J_{P-C}$ = 6.9 *cis*, $CH_3CH_2CH_2CH_2$), 30.33 (d, $^4J_{P-C}$ = 2.23, $CH_3CH_2CH_2$), 22.66 (s, $CH_3CH_2CH_2$), 18.33 (d, $^2J_{P-C}$ = 11.5, =C($CH_3$), 16.33 (d, $^3J_{P-C}$ = 6.4, $CH_3CH_2O$), 13.67 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 2960 ($CH_3$), 2860 ($CH_2$), 1590 (*C*=*C*), 1250 (*PO*), 1020 (*POC*).

### 3.4.5. Diethyl 1-methyl-2-phenyl-hex-1(Z)-enylphosphonate **5a**

$R_F$ = 0.36 ($SiO_2$, $Et_2O$, UV); 60% yield (2.56 g, 8.27 mmol). $^1$H NMR ($CDCl_3$): $\delta$ = 0.80 (t, 3H, $^3J_{H-H}$ = 6.30, $CH_3CH_2CH_2$), 1.04 (t, $^3J_{H-H}$ = 7.08, $CH_3CH_2O$), 1.14–1.40 (m, $CH_3CH_2CH_2CH_2$), 2.0 (d, 3H, $^3J_{P-H}$ = 13.9, C=C($CH_3$)P), 2.40 (t, 2H, $^3J_{H-H}$ = 6.61, $CH_2C$=C), 3.55–3.83 (m, 4H, $CH_3CH_2O$), 7.17–7.31 (m, H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 20.48 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 156.09 (d, $^2J_{P-C}$ = 8.61, *C*=CP), 142.5 (d, $^3J_{P-C}$ = 8.5 *cis*, $C_{ipso}$), 127.84 ($C_{ortho}$), 127.39 ($C_{meta}$), 126.93 ($C_{para}$), 121.2 (d, $^1J_{P-C}$ = 182, C=*C*P), 60.87 (d, $^2J_{P-C}$ = 6.3, $CH_3CH_2O$), 36.55 (d, $^3J_{P-C}$ = 17.7 *trans*, $CH_3CH_2CH_2CH_2$), 29.04 (d, $^4J_{P-C}$ = 2.46, $CH_3CH_2CH_2$), 22.55 (s, $CH_3CH_2CH_2$), 16.22 (d, $^2J_{P-C}$ = 12.1, =C($CH_3$), 15.94 (d, $^3J_{P-C}$ = 6.6, $CH_3CH_2O$), 13.73 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 2960 ($CH_3$), 2860 ($CH_2$), 1600 (*C*=*C*), 1245 (*PO*), 1025 (*POC*), 750 ($C_6H_5$).

### 3.4.6. Diethyl 1-benzoyl-2-methyl-pent-1(Z)-enylphosphonate **5h**

$R_F$ = 0.41 ($SiO_2$, $Et_2O$, UV); 56% yield (2.49 g, 7.70 mmol). $^1$H NMR ($CDCl_3$): $\delta$ = 0.97 (t, 3H, $^3J_{H-H}$ = 7.32, $CH_3CH_2CH_2$), 1.09 (t, $^3J_{H-H}$ = 6.8, $CH_3CH_2O$), 1.55 (sex, $^3J_{H-H}$ = 7.5, $CH_3CH_2CH_2$), 1.64 (d, 3H, $^4J_{P-H}$ = 1.79, ($CH_3$)C=CP), 2.55 (dt, 2H, $^3J_{H-H}$ = 7.5, $^4J_{P-H}$ = 2.2, $CH_2C$=C), 3.88–4.01 (m, 4H, $CH_3CH_2O$), 7.36–7.95 (m, 5H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 20.48 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 195.79 (d, $^2J_{P-C}$ = 12.1, $COC_6H_5$), 159.49 (d, $^2J_{P-C}$ = 6.5, $CH_2C$=C), 136.68 (d, $^3J_{P-C}$ = 1.4, $C_{ipso}$), 134.13 (s, $C_{para}$), 129.42 ($C_{meta}$), 128.68 (d, $^1J_{P-C}$ = 177.4, C=*C*P), 128.55 (s, $C_{ortho}$), 62.02 (d, $^2J_{P-C}$ = 6.05, $CH_3CH_2O$), 38.44 (d, $^3J_{P-C}$ = 7.98 *cis*, $CH_3CH_2CH_2$), 21.33 (d, $^4J_{P-C}$ = 1.85, $CH_3CH_2O$), 21.16 (d, $^3J_{P-C}$ = 18.43 *trans*, ($CH_3$)C=C), 15.97 (d, $^3J_{P-C}$ = 6.6, $CH_3CH_2O$), 14.08 (s, $CH_3CH_2CH_2$). IR (film): 2970 ($CH_3$), 2880 ($CH_2$), 1670 (*C*=*O*), 1615 (*C*=*C*), 1235 (*PO*), 1025 (*POC*), 750 ($C_6H_5$). Anal. Found: C, 62.86; H, 7.97; O, 20.12. $C_{17}H_{25}O_4P$ (324.36) Calc.: C, 62.95; H, 7.77; O, 19.73%.

### 3.4.7. Diethyl 1-benzyl-2-phenyl-hex-1(Z)-enylphosphonate **5f**

$R_F$ = 0.51 ($SiO_2$, $Et_2O$, UV); 65% yield (3.45 g, 8.9 mmol). $^1$H NMR ($CDCl_3$): $\delta$ = 0.71 (t, 3H, $^3J_{H-H}$ = 6.22, $CH_3CH_2CH_2$), 0.99 (t, $^3J_{H-H}$ = 6.88, $CH_3CH_2O$), 1.12–1.25 (m, $CH_3CH_2CH_2CH_2$), 2.43–2.54 (m, 2H, $CH_2C$=C), 3.46–3.75 (m, 4H, $CH_3CH_2O$), 3.85 (d, $^3J_{P-H}$ = 17.63, =CC$H_2C_6H_5$), 7.17–7.31 (m, H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 19.69 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 160.12 (d, $^2J_{P-C}$ = 9.06, *C*=CP), 142.91 (d, $^2J_{P-C}$ = 8.46 *cis*, $C_{ipso}$),

140.78 (d, $^{3}J_{P-C}$ = 2.26, $C'_{ipso}$), 129.07 (s, $C_{ortho}$), 129.02 ($C'_{ortho}$), 128.9 (s, $C_{meta}$), 128.34 (s, $C'_{meta}$), 127.83 (s, $C_{para}$), 126.80 (s, $C'_{para}$), 125.77 (d, $^{1}J_{P-C}$ = 175.86, C=*C*P), 61.43 (d, $^{2}J_{P-C}$ = 6.43, $CH_3CH_2O$), 37.16 (d, $^{3}J_{P-C}$ = 17.62 *trans* $CH_2CH_2C$=C), 35.89 (d, $^{2}J_{P-C}$ = 11.94, C=C(*C*$H_2$)P), 29.57 (d, $^{4}J_{P-C}$ = 2.07, $CH_3CH_2CH_2$), 22.79 (s, $CH_3CH_2$), 16.058 (d, $^{3}J_{P-C}$ = 6.61, $CH_3CH_2O$), 13.73 (s, $CH_3CH_2CH_2$). IR (film): 2950 ($CH_3$), 2870 ($CH_2$), 1580 (*C*=*C*), 1250 (*PO*), 1020 (*POC*), 750 ($C_6H_5$).

### 3.4.8. Diethyl 1-allyl-2-phenyl-hex-1(Z)-enylphosphonate 5g

$R_F$ = 0.44 ($SiO_2$, $Et_2O$, UV); 69% yield (3.18 g, 9.45 mmol). $^{1}$H NMR ($CDCl_3$): $\delta$ = 0.79 (t, 3H, $^{3}J_{H-H}$ = 6.57, $CH_3CH_2CH_2$), 1.05 (t, $^{3}J_{H-H}$ = 7.08, $CH_3CH_2O$), 1.14–1.25 (m, $CH_3CH_2CH_2CH_2$), 2.40 (t, 2H, $^{3}J_{H-H}$ = 6.36, $CH_2C$=C), 3.19 (q, 2H, $^{3}J_{P-H}$ = 17.53, $^{3}J_{H-H}$ = 7.36, $PCH_2CH$=$CH_2$), 3.57–3.83 (m, 4H, $CH_3CH_2O$), 5.04–5.93 (m, 3H, ABX system $CH$=$CH_2$), 7.16–7.30 (m, 5H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 19.96 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 158.36 (d, $^{2}J_{P-C}$ = 8.92, *C*=CP), 141.93 (d, $^{2}J_{P-C}$ = 8.53, *cis* $C_{ipso}$), 135.82 (d, $^{3}J_{P-C}$ = 2.11, PCCH$_2$*C*H=), 128.04 (d, $^{4}J_{P-C}$ = 1.93, $C_{ortho}$), 127.39 (s, $C_{meta}$), 127.10 (s, $C_{para}$), 123.74 (d, $^{1}J_{P-C}$ = 181.17, C=*C*P), 115.29 (s, CH=$CH_2$), 60.95 (d, $^{2}J_{P-C}$ = 6.3, $CH_3CH_2O$), 36.22 (d, $^{3}J_{P-C}$ = 17.67 *trans*, $CH_2CH_2C$=C), 34.25 (d, $^{2}J_{P-C}$ = 11.94, C=C(*C*$H_2$)P), 29.41 (d, $^{4}J_{P-C}$ = 2.09, $CH_3CH_2CH_2$), 22.63 (s, $CH_3CH_2$), 15.97 (d, $^{3}J_{P-C}$ = 6.69, $CH_3CH_2O$), 13.73 (s, $CH_3CH_2CH_2$). IR ($CCl_4$): 3060 and 3080 (=$CH_2$), 2960 ($CH_3$), 2860 ($CH_2$), 1590 and 1640 (C=C), 1240 (*PO*), 1050 (*POC*), 700 ($C_6H_5$). Anal. Found: C, 66.79; H, 9.05; O, 15.74. $C_{19}H_{29}O_3P$ (336.41) Calc.: C, 67.87; H, 8.69; O, 14.27%.

### 3.4.9. Diethyl 1-iodo-2-phenyl-hex-1(Z)-enephosphonate 5d

$R_F$ = 0.62 ($SiO_2$, $EtO_2$, UV); 66% yield (3.83 g, 9.08 mmol). $^{1}$H NMR ($CDCl_3$): $\delta$ = 0.82 (t, 3H, $^{3}J_{H-H}$ = 7.33, $CH_3CH_2CH_2$), 1.05 (t, 6H, $^{3}J_{H-H}$ = 7.1, $CH_3CH_2O$), 1.26–1.33 (m, $CH_3CH_2CH_2$), 2.7–2.74 (m, 2H, $CH_2C$=CH), 3.68–3.96 (m, 4H, $CH_3CH_2O$), 5.63 (d, 1H, $^{2}J_{P-H}$ = 17.7, CH=C*H*P), 7.12–7.16 (m, 3H aromatic), 7.26–7.22 (m, 2H aromatic). $^{31}$P NMR ($CDCl_3$): $\delta$ = 9.67 (s). $^{13}$C NMR ($CDCl_3$): $\delta$ = 165.4 (d, $^{2}J_{P-C}$ = 9.16, *C*=CHP), 140.4 (d, $^{3}J_{P-C}$ = 5.93 *cis*, $C_{ipso}$), 128.3 (d, $C_{ortho}$, $^{4}J_{P-C}$ = 1.7), 128.5 (s, $C_{meta}$), 128.7 (s, $C_{para}$), 88.6 (d, $^{1}J_{P-C}$ = 197.5, C=*C*HP), 62.52 (d, $^{2}J_{P-C}$ = 6.35, $CH_3CH_2O$), 47.64 (d, $^{3}J_{P-C}$ = 14.22 *trans*, $CH_2C$=), 28.5 (d, $^{4}J_{P-C}$ = 2.05, $CH_3CH_2CH_2$), 22.47 (s, $CH_3CH_2CH$), 15.9 (d, $^{3}J_{P-C}$ = 6.72, $CH_3CH_2O$), 13.83 (s, $CH_3CH_2CH_2$). IR (film): 2960 ($CH_3$), 2860 ($CH_2$), 1580 (*C*=*C*), 1250 (*PO*), 1030 (*POC*), 700 ($C_6H_5$). Anal. Found: C, 46.05; H, 5.87; O, 11.43. $C_{16}H_{24}O_3P$ (422.24) Calc.: C, 45.51; H, 5.73; O, 11.37%.

### 3.4.10. Diethyl 1-iodo-2-methyl-pent-1(Z)-enylphosphonate 5e

$R_F$ = 0.63 ($SiO_2$, $Et_2O$, UV); 63% yield (3 g, 8.67 mmol). $^{1}$H NMR ($CDCl_3$): $\delta$ = 0.90 (t, 3H, $^{3}J_{H-H}$ = 7.31, $CH_3CH_2CH_2$), 1.31 (t, 3H, $^{3}J_{H-H}$ = 7.05, $CH_3CH_2O$), 1.5 (sext, 2H, $^{3}J_{H-H}$ = 7.5, $CH_3CH_2CH_2$), 2.11 (d, 3H, $^{4}J_{H-H}$ = 1.16, $^{4}J_{P-H}$ = 1.70, $CH_3CH$=C), 2.79 (dt, 2H, $^{3}J_{H-H}$ = 7.6, $^{4}J_{P-H}$ = 1.70, $CH_2CH$=CH), 4.05 (dq, 4H, $^{3}J_{H-H}$ = 7.05, $^{3}J_{P-H}$ = 7.3, $CH_3CH_2O$). $^{31}$P NMR ($CDCl_3$): $\delta$ = 10.56. $^{13}$C NMR ($CDCl_3$): $\delta$ = 116.17 (d, $^{2}J_{P-C}$ = 13.8, *C*H=CHP), 85.46 (d, $^{1}J_{P-C}$ = 194, CH=*C*HP), 62.28 (d, $^{2}J_{P-C}$ = 5.4, $CH_3CH_2O$), 38.69 (d, $^{3}J_{P-C}$ = 5 *cis*, $CH_3CH_2CH_2$), 32.8 (d, $^{3}J_{P-C}$ = 16.2 *trans*, $CH_2CH$=CH), 21.8 (d, $^{4}J_{P-C}$ = 1.95, $CH_3CH_2CH$), 16.9 (d, $^{3}J_{P-C}$ = 6.8, $CH_3CH_2O$), 13.71 (s, $CH_3CH_2CH$). IR (film): 2980 ($CH_3$), 2880 ($CH_2$), 1580 (*C*=*C*), 1250 (*PO*), 1025 (*POC*). Anal. Found: C, 34.48; H, 5.98; O, 13.83. $C_{10}H_{20}O_3P$ (346.15) Calc.: C, 34.70; H, 5.82; O, 13.87%.

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