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Stereoselective synthesis of substituted 2-(diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-dienes

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Summary — The lithiated derivative of diethyl 3-(trimethylsilyl)prop-1-enylphosphonate **1** added easily, but with a poor diastereoselectivity, to various aldehydes leading to alcohols **5**, whose dehydration under neutral conditions gave the title dienes **7** as stereomeric mixtures. Noticeable improvement in the (*E,E*)-stereoselective access to the dienes **7** was achieved by using a one-pot procedure, which combined the above aldolization reaction with a phosphorylation–elimination sequence.

lithiated diethyl 3-(trimethylsilyl)prop-1-enylphosphonate / aldolization / dehydration / phosphorylation elimination / 2-(diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-dienes / (*E,E*)-stereoselectivity

Résumé — **Synthèse stéréosélective de 2-(diéthylphosphono)-4-(triméthylsilyl)buta-1,3-diènes substitués.** L'addition du dérivé lithié du 3-(triméthylsilyl)prop-1-énylphosphonate de diéthyle **1** sur différents aldéhydes s'effectue facilement, mais avec une faible diastéréosélectivité, pour conduire aux alcools **5**, dont la déshydratation en milieu neutre fournit les diènes **7** attendus, sous la forme d'un mélange de stéréoisomères. Une amélioration notable de la stéréosélectivité de la synthèse des diènes **7** de géométrie-(*E,E*) est obtenue en combinant, dans une opération réalisée en un seul réacteur, la réaction d'aldolisation précédente avec une séquence de phosphorylation élimination.

3-(triméthylsilyl)prop-1-énylphosphonate de diéthyle lithié / aldolisation / déshydratation / phosphorylation élimination / 2-(diéthylphosphonyl)-4-(triméthylsilyl)buta-1,3-diènes / (*E,E*)-stéréosélectivité

Introduction

Dialkylphosphonyl-substituted dienes [1], as well as their trialkylsilyl-substituted counterparts [2], are attractive building blocks in organic synthesis. For example, both of them lead to Diels–Alder cycloadducts which can be used for further structural conversions [2, 3]. On the other hand, as electron-deficient alkenes, phosphonodienes undergo Michael nucleophilic addition reactions [4], while dienylsilanes give rise to the specific reactions of vinylsilanes with electrophiles [2]. To the best of our knowledge, no example of a conjugated diene substituted by phosphonyl and silyl groups at once, has been reported. Nevertheless, the presence, on the same conjugated system, of substituents of opposite electronic effects, might be profitably exploited for the regio-control of the reactivity of the diene.

In a previous article, we described a general synthesis of variously substituted 2-(diethylphosphonyl)buta-1,3-dienes from allylic phosphonates, by an aldolisation–dehydration sequence [5]. More recently, we illustrated the synthetic potentialities of in situ generated α-silylated allylic phosphonate carbanions for the synthesis of 2-phosphono-1,3-dienes [6], of 1-alkoxy-2-phosphono-1,3-dienes [7] and of some other functional unsaturated phosphonates [6, 8]. Pursuing this work, we decided to study the synthetic applications of the α-silylated ambident carbanion derived from the diethyl 3-(trimethylsilyl)prop-1-enylphosphonate **1**. A recent paper of Modro *et al.* [9] describing some reactions of this reagent has prompted us to publish our results in this field.

Results and discussion

Developing the methodology used for the synthesis of 2-phosphonobuta-1,3-dienes [5], we realized a first set of experiments in order to prepare precursory alcohols **5** from the lithiated derivative **2** and aldehydes (scheme 1). Phosphonate **1** was obtained by trimethylsilylation of the lithiated derivative of diethyl allylphosphonate as early reported [10], using lithium diisopropylamide (LDA) as a base and stoichiometric amounts of reagents, in order to avoid side processes as bis-silylation [11] or isomerization reactions [9].

When treated with a slight excess of LDA, in THF, at −70 °C, phosphonate **1** was quantitatively transformed into the lithiated derivative **2**, whose formation could be monitored by ^{31}P NMR spectroscopy (δ (THF) = 41) [12]. After addition, at the same temperature, of an aromatic or aliphatic aldehyde, the resulting

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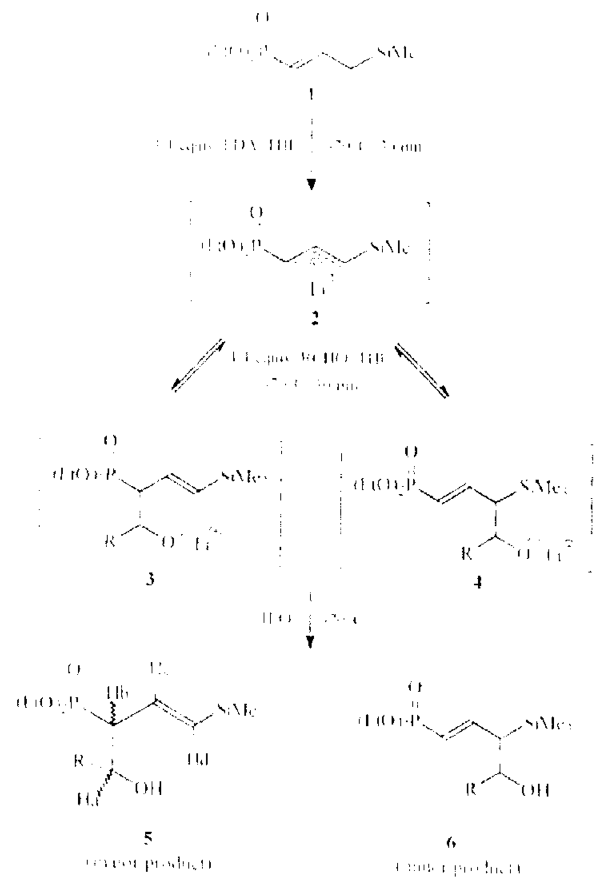


Scheme 1

product exhibited two signals in ^{31}P NMR spectroscopy of unequal intensity at δ (THF) ≈ 32 for the signal of higher intensity, attributed to alkoxide **3** and at δ (THF) ≈ 21 for the signal of lower intensity, attributed to alkoxide **4** [13]. As expected, subsequent acidic hydrolysis of the reaction medium at −70 °C led to a crude mixture composed of carbinol **5** as a pair of diastereomers, as the major constituents (two signals at δ ^{31}P ($CDCl_3$) ≈ 25 ppm), resulting from the α-addition reaction and of minor constituents (two signals at δ ^{31}P ($CDCl_3$) ≈ 18 ppm, in a ratio of ≈ 80:20), attributed to the diastereomeric alcohols **6**, resulting from the γ-reactivity of the ambident anion **2**. In most cases, the percentage in alcohol **6** (determined in the crude mixture by ^{31}P NMR integration measurements, in comparison to carbinol **5**) was lower than 10%; it reached 15% for the reaction with propanal (table I, entry **e**) [14].

In each case, the crude mixture was purified by column chromatography over SiO_2 (eluent: hexane/ether, in gradient) without any decomposition [15]. However, we were not able to entirely discard the γ-adduct by this process. Finally, we assigned the *threo*- and *erythro*-diastereomers of the main products **5** according to the $^3J_{HaHb}$ coupling constant measurement in their ^1H NMR spectra, as previously reported [5]; from the same spectra, we established unequivocally the (*E*)-configuration of the double bond in **5**, by measurement of the $^3J_{HcHd}$ coupling constant (see experimental part). As observed in the non-silylated series [5], we generally noted here too the predominant formation of the *threo* adduct *th*-**5**. In one case (**5d**), no stereoselectivity was observed [16].

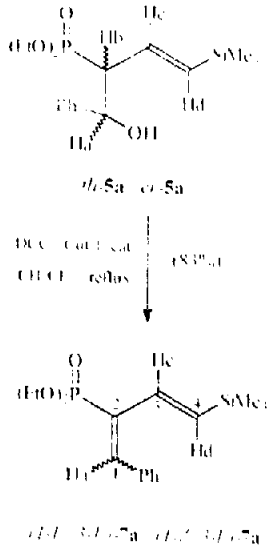
This relatively poor diastereoselectivity of the reaction of carbanion **2** with aldehydes was a strong handicap for the preparation of stereohomogeneous phosphonodienes from alcohols **5**. For example, when a mixture of diastereomeric alcohols **5a** was submitted to the previously selected dehydration reaction conditions [5], namely dicyclohexylcarbodiimide (DCC) catalyzed by anhydrous copper(II) chloride (scheme 2), a mixture of (1*E*)/(1*Z*)-buta-1,3-diene **7a** in a ratio 71:29, very close to that (74:26) of the starting *th*-**5a**/*er*-**5a** mixture [17], was obtained, as expected for such a stereospecific dehydration process.

In a second set of experiments, we decided to examine a more stereoselective way to prepare phosphonodienes **7**. Recently, we used an effective hydroxyalkylation-elimination sequence for a one-pot (*E*)-stereoselective synthesis of alkenylphosphonates [18]. The key step of this process lies in the β-elimination reaction of an intermediate phosphate, using potassium *tert*-butoxide as base [19]. Therefore, we anticipated that this method could be suitable for the selective preparation of (1*E*, 3*E*)-phosphonodienes **7** from phosphonate **1**. Thus, when the mixture of alkoxides **3** and **4**, resulting from the addition of an aldehyde to the solution of carbanion **2** (as depicted in scheme 1), was treated at −70 °C with 1.1 equiv of diethyl chlorophosphate, the phosphorylation reaction took place at −70 °C,

Table I. Reaction of the lithiated derivative of diethyl 3-(trimethylsilyl)prop-1-enylphosphonate **1** with aldehydes.

Entry	R	Ratio **5**/**6** in crude (purified product)[a]	Ratio *th*-**5**/*er*-**5**[b]	^{31}P NMR ($CDCl_3$) δ *th*-**5**, *er*-**5**, **6**	Yield (%) in purified product
a	C_6H_5	93:7 (98:2)	74:26	25.5, 25.2, 18.5	66
b	4-Cl-C_6H_4	93:7 (95:5)	59:41	25.0, 24.9, 18.4	80
c	4-Me-C_6H_4	98:2 (98:2)	64:36	25.6, 25.4, 18.5	84
d	Me	93:7 (94:6)	50:50	25.8, 25.9, 19.4	91
e	Et	85:15 (90:10)	68:32	26.1, 26.2, 19.3	95
f	*n*-C_5H_{11}	93:7 (100:0)	64:36	26.0, 26.2, 19.1	77

[a] Determined by ^{31}P NMR integration measurements. [b] Determined on the purified product [17] by ^{31}P NMR, ^1H NMR and GC integration measurements. [c] δ ^{31}P of the major diastereomer.

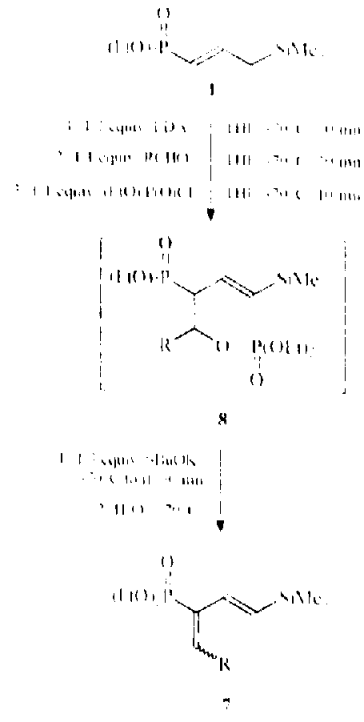


Scheme 2

leading to the diastereomeric phosphates **8** (scheme 3), as proved by ^{31}P NMR spectroscopy [20]. Stabilization of the oxyanion by the neighboring trimethylsilyl group in **4** might explain the low nucleophilicity of this anion toward chlorophosphate, in comparison to that of anion **3**, and might justify the formation of phosphate **8** only, as a result of shift equilibrium [13].

Then, treating the mixture at −70 °C with potassium *tert*-butoxide and rising the temperature to 20 °C for about 30 min, achieved the complete elimination of diethyl phosphate from the *O*-phosphorylated intermediate **8**, leading to phosphonodiene **7** as a mixture of two geometrical (*1-E*, *3-E*)/(*1-Z*, *3-E*)-isomers in a ratio higher than 85:15, determined by ^{31}P NMR integration measurement on the crude product (scheme 3, table II). Chromatographic separation of the crude mixture over silica gel (eluent: hexane/ether, in gradient) allowed us to isolate a purified product containing at least 94% of the (*1-E*, *3-E*)-phosphonodiene **7**.

The significant improvement in the ratio between the diene isomers (*1-E*, *3-E*)-**7** and (*1-Z*, *3-E*)-**7** resulting from the one-pot addition elimination sequence (scheme 3), in comparison to the one resulting from the two-step process (isolation of diastereomeric alcohol **5**, then dehydration by DCC), seems to be consistent with



Scheme 3

an E1cB mechanism for the elimination of phosphate in the transient phosphonate phosphate **8**, leading to the formation of the less sterically strained (*1-E*, *3-E*)-diene [21].

Conclusion

In this work, we describe an efficient and stereoselective one-pot synthesis of substituted 2-(diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-dienes **7** from the readily available diethyl 3-(trimethylsilyl)prop-1-enylphosphonate **1**. Despite the poor diastereoselectivity of the reaction of the lithiated derivative of **1** with aldehydes, we have obtained a very good degree of (*E*)-stereoselectivity in the formation of the 1,2-double bond of the diene, by using a transient phosphate moiety as leaving group. Finally, a subsequent standard chromatographic separation furnishes the expected dienes **7** in an (*E*,*E*)-stereoisomeric purity higher than 94%, usable for further syntheses [22].

Table II. Synthesis of 2-(diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-dienes **7**.

Product	*R*	*Ratio* (1-*E*)/(1-*Z*) *in crude (purified) product*[a]	^{31}P *NMR* (*CDCl*$_3$) (1-*E*)-**7**, (1-*Z*)-**7**	*Yield* (%) *in purified product*
7a	C_6H_5	93:7 (100:0)	17.3, 13.9	67
7b	4-Cl-C_6H_4	86:14 (98:2)	16.8; 13.7	50
7c	4-Me-C_6H_4	90:10 (96:4)	17.7, 14.1	72
7d	4-F$_3$C-C_6H_4	87:13 (94:6)	16.3; 13.4	77
7e	4-MeO-C_6H_4	97:3 (100:0)	17.8; 14.5	61
7f	2-furyl	92:8 (100:0)	18.0; 14.0	63
7g	Me	93:7 (100:0)	17.0, 15.0	58

[a] Determined by ^{31}P NMR integration measurements.

Experimental section

All syntheses were performed under an atmosphere of dry argon. THF was dried over CaH_2 and distilled from sodium/benzophenone ketyl before use. TLC was performed on Merck 60 F-254 silica gel plates and column chromatography over silica gel (230–400 mesh). Mass spectra were obtained with a GC-MS Hewlett Packard 5970 mass selective detector. NMR spectra were recorded on a Bruker AC 200 spectrometer operating at 200 MHz for proton, 50.3 MHz for carbon and 81.01 MHz for phosphorus; chemical shifts (δ) are expressed in ppm relative to TMS for ^1H and ^{13}C nuclei and to H_3PO_4 for ^{31}P nucleus; coupling constants (J) are given in hertz; coupling multiplicities are reported using conventional abbreviations.

Diethyl 3-trimethylsilylprop-1-enylphosphonate **1**

This compound was prepared according to [10].

2-Diethylphosphonyl-4-trimethylsilylbut-3-enols **5**: *general procedure*

To a stirred solution of BuLi in hexanes (7.5 mL; 8.8 mmol) kept at −70 °C was added dropwise diisopropylamine (0.9 g, 8.8 mmol) in THF (10 mL). After 30 min, the phosphonate **1** (2 g, 8 mmol) in THF (10 mL) was slowly added. Stirring was continued at −70 °C for about 30 min until complete metallation was achieved, as shown by ^{31}P NMR spectroscopy. Then, the aldehyde (8.8 mmol) in THF (10 mL) was slowly added to the mixture and stirring continued at −70 °C for 30 min until the complete consumption of the lithiated derivative **2**, as proved by ^{31}P NMR spectroscopy. Then acidic hydrolysis was rapidly performed at −70 °C with 2 M HCl until the pH reached 2–3 and the mixture was allowed to warm to room temperature. The aqueous phase was extracted with Et_2O (4 × 15 mL) and the combined organic layers dried ($MgSO_4$). The solvent was removed under reduced pressure to give the crude mixture which was analyzed by GC, ^{31}P and ^1H NMR spectroscopy and then purified by column chromatography over silica gel (eluent: ethyl acetate/Et_2O mixture) affording the pure product **5** contaminated mainly with traces of the two diastereoisomeric alcohols **6** and **6'**. Physical data of alcohol **5** prepared are given below. Moreover, in two cases, the presence of a few percent of alcohol **6** was clearly detected in the corresponding ^{13}C NMR spectra of the product (**6d**–**6e**).

- *Threo-2-diethylphosphonyl-1-phenyl-4-trimethylsilylbut-3-en-1-ol: th-***5a** (*a*)

^1H NMR ($CDCl_3$): δ −0.2 and 0.0 (2s, 9H), 1.1–1.3 (m, 6H), 2.8 (ddd, J_{H1P} = 18, J_{H2H3} = J_{H2P} = 9, 1H), 3.9–4.1 (m, 4H), 4.75 (br s, 1H), 5.1 (dd, J_{H1H2} = 11.8, J_{H1OH} = 3 Hz), 5.4 (dd, J_{H3H4} = 15.3, J_{H3P} = 18.3, 1H), 5.8 (ddd, J_{H4H3} = 15.2, J_{H4H2} = 9.2, J_{H4P} = 18.1, 1H), 7.2 (s, 5H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 (2s, $Si(CH_3)_3$), 16.0 (2d, J = 5.6, CH_3CH_2O), 53.9 (d, J = 131, C_2), 61.6 and 62.8 (2d, J = 7.1, J = 6.9, CH_3CH_2O), 71.6 (d, J = 1.6, C_1), 125.0–129.6 (m, *m*, *o*, *p* C_{arom}), 135.0 (d, J = 7.5, *i* C_{arom}), 138.6 (d, J = 11.2, C_3), 141.6 (d, J = 11.9, C_4).

- *(Threo)-1-(4-chlorophenyl)-2-(diethylphosphonyl)-4-(trimethylsilyl)but-3-en-1-ol: th-***5b** (*59%*)

^1H NMR ($CDCl_3$): δ −0.2 and 0.0 (2s, 9H), 1.1–1.3 (m, 6H), 2.8 (ddd, J_{H2P} = 17.4, J_{H2H1} = J_{H2H3} = 8.7, 1H), 3.9–4.1 (m, 4H), 4.1 (br s, 1H), 5.0 (dd, J_{H1H2} = 11.8, J_{H1H3} = 8.7, 1H), 5.4 (dd, J_{H3H4} = 3.0, J_{H3H2} = 18.7, 1H), 5.8 (ddd, J_{H4H3} = 1.9, J_{H4H2} = 8.7, J_{H4H3} = 18.7, 1H), 7.1 (s, 4H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 (2s, $Si(CH_3)_3$), 16.0 (2d, J = 5.6, CH_3CH_2O), 54.1 (d, J = 131.3, C_2), 62.3 and 62.4 (2d, J = 6.9, J = 7.2, CH_3CH_2O), 72.1 (d, J = 1.1, C_1), 126.9–128.2 (m, *m*, *o*, C_{arom}), 132.9 (s, *p* C_{arom}), 138.4 (d, J = 9.5, *i* C_{arom}), 137.6 (d, J = 10.7, C_3), 140.4 (d, J = 14.2, C_4).

MS *m*/*z* (for the *O*-trimethylsilyl derivative): 147 (M-15), 322, 249, 213, 179, 153, 121, 73, 45.

- *Erythro-1-(4-chlorophenyl)-2-(diethylphosphonyl)-4-(trimethylsilyl)but-3-en-1-ol: er-***5b** (*41%*)

^1H NMR ($CDCl_3$): δ −0.2 and 0.0 (2s, 9H), 1.1–1.3 (m, 6H), 2.8 (ddd, J_{H2P} = 20.9, J_{H2H1} = 9.3, J_{H2H3} = 2.3, 1H), 3.9–4.1 (m, 4H), 4.1 (br s, 1H), 5.0 (dd, J_{H1H2} = 8.8, J_{H1OH} = 2.3, 1H), 5.3–5.5 (m, 1H), 5.8 (ddd, J_{H4H3} = 5.5, J_{H4H2} = 9.3, J_{H4H3} = 18.7, 1H), 7.1 (s, 4H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 (2s, $Si(CH_3)_3$), 16.0 (2d, J = 5.6, CH_3CH_2O), 54.7 (d, J = 132.4, C_2), 61.7 and 62.9 (2d, J = 7.5, J = 6.8, CH_3CH_2O), 71.1 (d, J = 1.5, C_1), 126.9–128.2 (m, *m*, *o*, C_{arom}), 132.5 (s, *p* C_{arom}), 138.6 (d, J = 7.4, *i* C_{arom}), 139.2 (d, J = 11.2, C_3), 140.3 (d, J = 15.2, C_4).

- *Threo-2-diethylphosphonyl-1-(2-methylphenyl)-4-trimethylsilylbut-3-en-1-ol: th-***5c** (*a*)

^1H NMR ($CDCl_3$): δ −0.2 and 0.0 (2s, 9H), 1.2–1.4 (m, 6H), 2.25 (s, 3H), 2.9 (ddd, J_{H2P} = 17.0, J_{H2H1} = J_{H2H3} = 8.5, 1H), 3.9–4.2 (m, 5H), 5.1 (dd, J_{H1H2} = 11.5, J_{H1OH} = 8.5, 1H), 5.5 (dd, J_{H3H4} = 15.2, J_{H3H2} = 18.1, 1H), 5.9 (ddd, J_{H4H3} = 15.2, J_{H4H2} = 8.5, J_{H4H3} = 18.1, 1H), 7.0–7.2 (m, 4H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 (2s, $Si(CH_3)_3$), 16.0 (2d, J = 5.6, CH_3CH_2O), 20.8 (s, CH_3), 53.1 (d, J = 130.8, C_2), 62.1 and 62.3 (2d, J = 6.8, J = 7.2, CH_3CH_2O), 72.9 (d, J = 1.6, C_1), 125.9–128.3 (m, *m*, *o*, C_{arom}), 135.1 (d, J = 2.5, *i* C_{arom}), 136.8 (s, *p* C_{arom}), 139.8 (d, J = 10.7, C_3), 138.5 (d, J = 14.1, C_4).

MS *m*/*z*: 325 (M-15), 250, 235, 207, 182, 153, 121, 75, 45.

- *Erythro-2-diethylphosphonyl-1-(2-methylphenyl)-4-trimethylsilylbut-3-en-1-ol: er-***5c** (*36%*)

^1H NMR ($CDCl_3$): δ −0.2 and 0.0 (2s, 9H), 1.2–1.4 (m, 6H), 2.25 (s, 3H), 2.9 (ddd, J_{H2P} = 21.2, J_{H2H1} = 9.1, J_{H2H3} = 2.3, 1H), 3.9–4.2 (m, 5H), 5.0 (dd, J_{H1H2} = 9.1, J_{H1OH} = 2.3, 1H), 5.3–5.5 (m, 1H), 5.9 (ddd, J_{H4H3} = 5.8, J_{H4H2} = 9.1, J_{H4H3} = 18.1, 1H), 7.0–7.2 (m, 4H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 (2s, $Si(CH_3)_3$), 16.0 (2d, J = 5.6, CH_3CH_2O), 20.8 (s, CH_3), 53.9 (d, J = 131.6, C_2), 62.7 and 62.9 (2d, J = 7.1, J = 6.9, CH_3CH_2O), 71.6 (d, J = 1.5, C_1), 125.9–128.3 (m, *m*, *o*, C_{arom}), 136.1 (d, J = 2.5, *i* C_{arom}), 136.9 (s, *p* C_{arom}), 139.9 (d, J = 11.1, C_3), 138.6 (d, J = 13.2, C_4).

• *(Threo)-3-(diethylphosphonyl)-5-(trimethylsilyl)-pent-4-en-2-ol: th-***5d** *(50%)*

^{1}H NMR ($CDCl_3$): δ −0.1 and 0.1 (2s, 9H), 1.0–1.1 (d, 3H), 1.1–1.3 (m, 6H), 2.4–2.8 (m, 1H), 3.5 (br s, 1H), 3.9–4.3 (m, 5H), 6.0 (ddd, J_{HCP} = 4.9, J_{HCH_5} = 9.0, J_{HCHA} = 18.6, 1H), 5.8 (dd, J_{HAP} = 3.0, J_{HAH_4} = 18.6, 1H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 [2s, $Si(CH_3)_3$], 16.0 (1d, J = 6.0, CH_3CH_2O), 21.2 (d, J = 13.3, CH_3), 54.2 (d, J = 131.2, C_3), 61.8 and 62.1 (2d, J = 6.7, J = 7.2, CH_3CH_2O), 65.7 (d, J = 4.7, C_2), 136.6 (d, J = 11.1, C_5), 137.2 (d, J = 10.3, C_4).

MS m/z: 279 (M-15), 250, 235, 182, 153, 121, 75, 45.

• *(Erythro)-3-(diethylphosphonyl)-5-(trimethylsilyl)pent-4-en-2-ol: er-***5d** *(50%)*

^{1}H NMR ($CDCl_3$): δ −0.1 and 0.1 (2s, 9H), 1.0–1.1 (d, 3H), 1.1–1.3 (m, 6H), 2.4–2.8 (m, 1H), 3.5 (br s, 1H), 3.9–4.3 (m, 5H), 6.0 (ddd, J_{HCP} = 1.1, J_{HCH_5} = 8.4, J_{HCHA} = 18.6, 1H), 5.8 (dd, J_{HAP} = 3.8 J_{HAH_4} = 18.6, 1H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.1 [2s, $Si(CH_3)_3$], 16.0 (1d, J = 6.0, CH_3CH_2O), 20.7 (d, J = 11.5, CH_3), 52.7 (d, J = 132.9, C_3), 61.1 and 62.5 (2d, J = 7.3, J = 7.0, CH_3CH_2O), 65.2 (d, J = 5.1, C_2), 135.5 (d, J = 8.0, C_5), 138.5 (d, J = 11.6, C_4).

• *5-(Diethylphosphonyl)-3-(trimethylsilyl)pent-4-en-2-ol* **6d** *(major diastereomer)*

^{13}C NMR ($CDCl_3$): δ −0.2 [s, $Si(CH_3)_3$], 16.0 (m, CH_3CH_2O), 21.3 (d, J = 17.9, C_1), 23.2 (s, CH_3), 61.4–62.5 (m, CH_3CH_2O), 66.1 (d, J = 5.1, C_2), 129.5 (d, J = 173.3, C_5), 143.7 (d, J = 9.0, C_4).

• *(Threo)-4-(diethylphosphonyl)-6-(trimethylsilyl)hex-5-en-3-ol: th-***5e** *(68%)*

^{1}H NMR ($CDCl_3$): δ −0.1 and 0.1 (2s, 9H), 0.7–0.9 (t, 7.2, 3H), 1.0–1.7 (m, 8H), 2.6 (ddd, J_{HCP} = 21.0, J_{HCH_5} = J_{HCH_3} = 8.6, 1H), 3.6–4.0 (m, 6H), 5.7 (dd, J_{HAP} = 4.8, J_{HAH_B} = 18.7, 1H), 6.2 (ddd, J_{HBP} = 4.8, J_{HBH_5} = 8.6, J_{HBHA} = 18.7, 1H).

^{13}C NMR ($CDCl_3$): δ −2.0 and −0.2 [2s, $Si(CH_3)_3$], 8.8 and 10.3 (2s, CH_3), 16.0 (d, J = 5.8, CH_3CH_2O), 27.6 (d, J = 12.7, C-C_3), 52.5 (d, J = 131.2, C_4), 61.7 and 62.1 (2d, J = 6.8, J = 7.2, CH_3CH_2O), 70.1 (d, J = 5.1, C_3), 136.2 (d, J = 11.2, C_6), 137.1 (d, J = 10.5, C_5).

MS m/z (for the O-trimethylsilyl derivative): 365 (M-15), 351, 291, 250, 182, 153, 121, 73, 45.

• *(Erythro)-4-(diethylphosphonyl)-6-(trimethylsilyl)hex-5-en-3-ol: er-***5e** *(32%)*

^{1}H NMR ($CDCl_3$): δ −0.2 and 0.1 (2s, 9H), 0.7–0.9 (t, 7.2, 3H), 1.0–1.7 (m, 8H), 2.1–2.8 (m, 1H), 3.6–4.0 (m, 6H), 5.7 (dd, J_{HAP} = 4.8, J_{HAH_B} = 18.7, 1H), 5.9–6.5 (m, 1H).

^{13}C NMR ($CDCl_3$): δ −2.0 and −0.2 [2s, $Si(CH_3)_3$], 8.8 and 10.3 (2s, CH_3), 15.9 (d, J = 5.9, CH_3CH_2O), 27.1 (d, J = 11.8, C-C_3), 50.8 (d, J = 133.1, C_4), 61.3 and 62.6 (2d, J = 7.2, J = 7.0, CH_3CH_2O), 70.5 (d, J = 6.5, C_3), 135.5 (d, J = 8.1, $C_{[illegible]}$), 138.0 (d, J = 11.7, C_5).

• *6-(Diethylphosphonyl)-4-(trimethylsilyl)hex-5-en-3-ol* **6e** *(major diastereomer)*

^{13}C NMR ($CDCl_3$): δ −0.2 [s, $Si(CH_3)_3$], 10.3 (s, CH_3), 15.9–16.0 (m, CH_3CH_2O), 21.3 (d, J = 17.5, C_4), 30.1 (s, C-C_3), 61.4–62.6 (m, CH_3CH_2O), 70.9 (d, J = 6.0, C_3), 128.6 (d, J = 172.8, C_6), 144.1 (d, J = 8.9, C_5).

MS m/z (for the O-trimethylsilyl derivative): 380, 351, 295, 217, 211, 121, 73, 45.

• *(Threo)-3-(diethylphosphonyl)-1-(trimethylsilyl)-non-1-en-4-ol: th-***5f** *(64%)*

^{1}H NMR ($CDCl_3$): δ −0.2 and 0.1 (2s, 9H), 0.6–0.8 (t, 5.3, 3H), 1.0–1.5 (m, 14H), 2.6 (ddd, J_{HAP} = 23.5, J_{HAH_1} = J_{HAH_5} = 8.5, 1H), 3.6 (br s, 1H), 3.7–4.1 (m, 5H), 5.7 (dd, J_{HAP} = 4.2, J_{HAH_C} = 18.3, 1H), 6.2 (ddd, J_{HCP} = 4.9, J_{HCH_5} = 8.5, J_{HCHA} = 18.3, 1H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.3 [2s, $Si(CH_3)_3$], 13.6 (s, CH_3), 16.0 (d, J = 5.8, CH_3CH_2O), 22.1 (s), 24.0 (s), 31.3 (s), 34.7 (d, J = 11.9, C-C_4), 52.8 (d, J = 131.3, C_3), 61.6 and 62.0 (2d, J = 6.8, J = 7.2, CH_3CH_2O), 69.3 (d, J = 5.1, C_4), 136.2 (d, J = 11.2, C_2), 137.5 (d, J = 10.1, C_1).

MS m/z: 335 (M-15), 279, 250, 235, 207, 182, 153, 121, 73.

• *(Erythro)-3-(diethylphosphonyl)-1-(trimethylsilyl)-non-1-en-4-ol: er-***5f** *(36%)*

^{1}H NMR ($CDCl_3$): δ −0.2 and 0.1 (2s, 9H), 0.6–0.8 (t, 5.3, 3H), 1.0–1.5 (m, 14H), 2.4–2.7 (m, 1H), 3.6 (br s, 1H), 3.7–4.1 (m, 5H), 5.7 (dd, J_{HAP} = 4.2, J_{HAH_C} = 18.3, 1H), 6.2 (ddd, J_{HCP} = 4.9, J_{HCH_5} = 11.3, J_{HCHA} = 18.3, 1H).

^{13}C NMR ($CDCl_3$): δ −1.9 and −0.3 [2s, $Si(CH_3)_3$], 13.6 (s, CH_3), 15.9 (d, J = 6.1, CH_3CH_2O), 22.2 (s), 24.8 (s), 31.2 (s), 34.5 (d, J = 12.8, C-C_4), 51.2 (d, J = 131.3, C_3), 61.3 and 62.5 (2d, J = 7.3, J = 7.0, CH_3CH_2O), 68.9 (d, J = 7.0, C_4), 135.7 (d, J = 8.1, C_2), 138.0 (d, J = 11.7, C_1).

• *2-(Diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-dienes* **7***: general procedure*

To a stirred solution of BuLi in hexanes (7.5 mL, 12 mmol) kept at −70 °C was added dropwise diisopropylamine (1.2 g, 12 mmol) in THF (10 mL). After 30 min, the phosphonate **1** (2.5 g, 10 mmol) in THF (10 mL) was slowly added. Stirring was continued at −70 °C for about 30 min until complete metallation was achieved, as shown by ^{31}P NMR spectroscopy. Then the aldehyde (11 mmol) in THF (10 mL) was slowly added to the mixture and stirring continued at −70 °C for 30 min until the complete consumption of the lithiated derivative **2**, as proved by ^{31}P NMR spectroscopy. Then diethyl chlorophosphate (1.9 g, 11 mmol) in THF (10 mL) was slowly added and stirring continued at −70 °C for 10 min until the complete phosphorylation was achieved as shown by ^{31}P NMR spectroscopy. Then, treating the mixture at −70 °C with potassium *tert*-butoxide (1.5 g, 13 mmol) in THF (15 mL) and rising the temperature to 20 °C for about 30 min achieved the complete elimination of diethyl phosphate from the O-phosphorylated intermediate **8**. Then the mixture was cooled to −70 °C and acidic hydrolysis was rapidly performed with 2 M HCl until the pH reached 2–3 and the mixture was allowed to warm to room temperature. The aqueous phase was extracted with Et_2O (3 × 15 mL) and the combined organic layers dried ($MgSO_4$). The solvent was removed under reduced pressure to give the crude mixture, which was analyzed by GC, ^{31}P and ^{1}H NMR spectroscopy and then purified by column chromatography over silica gel (eluent: hexane/Et_2O, in gradient), giving the pure product **7** as a mixture of the two geometrical (1*E*, 3*E*) + (1*Z*, 3*E*) isomers in a ratio [illegible] (Table II). Physical data of major (1*E*, 3*E*) **7** isomers are given below.

• *2-(Diethylphosphonyl)-1-phenyl-4-(trimethylsilyl)buta-1,3-diene* **7a**

^{1}H NMR ($CDCl_3$): δ 0.1 (s, 9H), 1.2–1.5 (m, 6H), 4.0–4.3 (m, 4H), 6.6 (d, J_{HAH_B} = 18.4, 1H), 7.0 (dd, J_{HBP} = 27.7, J_{HBHA} = 18.4, 1H), 7.2–7.5 (m, 5H), 7.6 (d, J_{HCP} = 24.6, 1H).

^{13}C NMR (CDCl$_3$): δ −1.8 (s, Si(CH$_3$)$_3$), 16.0 (d, J = 6.5, CH$_3$CH$_2$O), [illegible] (d, J = 5.3, CH$_3$CH$_2$O), 128.8 (d, [illegible]), 128.0 (s, m C$_{arom}$), 128.7 (s, p C$_{arom}$), [illegible], 135.0 (d, J = 22.6, i C$_{arom}$), 136.4 (d, J = 9.5, C$_3$), 136.9 (d, J = 4.6, C$_1$), 144.4 (d, J = 10.2, C$_4$).

MS m/z: 338, 323, 265, 129, 73, 45.

- *1-(4-Chlorophenyl)-2-(diethylphosphonyl)-4-(trimethylsilyl)buta-1,3-diene* **7b**

^{1}H NMR (CDCl$_3$): δ 0.1 (s, 9H), 1.2–1.4 (m, 6H), 4.0–4.2 (m, 4H), 6.5 (d, J_{HaHc} = 19.4, 1H), 6.8 (dd, J_{HcP} = 26.9, J_{HcHa} = 19.4, 1H), 7.3 (m, 4H), 7.4 (d, J_{HdP} = 23.1, 1H).

^{13}C NMR (CDCl$_3$): δ −1.9 (s, Si(CH$_3$)$_3$), 15.9 (d, J = 6.5, CH$_3$CH$_2$O), 61.7 (d, J = 5.4, CH$_3$CH$_2$O), 129.4 (d, J = 174.1, C$_2$), 128.4 (s, m C$_{arom}$), 131.0 (d, J = 1.9, o C$_{arom}$), 133.3 (d, J = 22.1, i C$_{arom}$), 134.4 (s, p C$_{arom}$), 135.8 (d, J = 9.2, C$_3$), 137.6 (d, J = 4.6, C$_1$), 142.4 (d, J = 10.5, C$_4$).

MS m/z: 372, 371, 299, 284, 243, 163, 121, 73, 45

- *2-(Diethylphosphonyl)-1-(4-methylphenyl)-4-(trimethylsilyl)buta-1,3-diene* **7c**

^{1}H NMR (CDCl$_3$): δ 0.1 (s, 9H), 1.2–1.3 (t, 7.0, 6H), 2.2–2.3 (2s, 3H), 3.9–4.1 (m, 4H), 6.5 (d, J_{HaHc} = 19.6, 1H), 6.8 (dd, J_{HcP} = 28.3, J_{HcHa} = 19.6, 1H), 7.1–7.3 (m, 4H), 7.5 (d, J_{HdP} = 23.6, 1H).

^{13}C NMR (CDCl$_3$): δ −1.7 (s, Si(CH$_3$)$_3$), 16.0 (d, J = 6.6, CH$_3$CH$_2$O), 21.4 (s, CH$_3$), 61.6 (d, J = 5.2, CH$_3$CH$_2$O), 127.9 (d, J = 173.6, C$_2$), 128.8 (s, m C$_{arom}$), 130.0 (d, J = 1.1, o C$_{arom}$), 132.2 (d, J = 21.8, i C$_{arom}$), 136.4 (d, J = 4.6, C$_1$), 136.7 (d, J = 9.4, C$_3$), 139.0 (s, p C$_{arom}$), 144.2 (d, J = 10.4, C$_4$).

MS m/z: 352, 337, 279, 264, 143, 73, 45

- *2-(Diethylphosphonyl)-1-(4-(trifluoromethyl)phenyl)-4-(trimethylsilyl)buta-1,3-diene* **7d**

^{1}H NMR (CDCl$_3$): δ 0.2 (s, 9H), 1.2–1.4 (m, 6H), 3.9–4.2 (m, 4H), 6.4 (d, J_{HaHc} = 18.8, 1H), 6.7 (dd, J_{HcP} = [illegible], J_{HcHa} = 18.8, 1H), 7.4–7.6 (m, 5H).

^{13}C NMR (CDCl$_3$): δ −1.9 (s, Si(CH$_3$)$_3$), 15.9 (d, J = 4.6, [illegible] J = 6.5, CH$_3$CH$_2$O), 62.0 (d, J = 5.4, CH$_3$CH$_2$O), 123.7 (d, J = 272.2, CF$_3$), 124.9 (d, J = 3.7, m C$_{arom}$), 131.1 (d, J = 171.1, C$_2$), 130.0 (d, J = 1.2, o C$_{arom}$), 130.2 (d, J = 33.1, p C$_{arom}$), 135.5 (d, J = 9.1, C$_3$), 138.5 (dd, J_{CP} = 22.0, J_{CF} = 10.0, i C$_{arom}$), 138.9 (d, J = 4.7, C$_1$), 142.0 (d, J = 10.2, C$_4$).

MS m/z: 391 (M-15), 349, 317, 277, 177, 121, 73, 29

- *2-(Diethylphosphonyl)-1-(4-methoxyphenyl)-4-(trimethylsilyl)buta-1,3-diene* **7e**

^{1}H NMR (CDCl$_3$): δ 0.1 (s, 9H), 1.1–1.2 (t, 7.2, 6H), 3.5 (s, 3H), 3.8–4.1 (m, 4H), 6.4 (d, J_{HaHc} = 19.2, 1H), 6.7 (dd, J_{HcP} = 28.2, J_{HcHa} = 19.2, 1H), 6.7–7.2 (m, 4H), 7.4 (d, J_{HdP} = 22.8, 1H).

^{13}C NMR (CDCl$_3$): δ −1.8 (s, Si(CH$_3$)$_3$), 15.9 (d, J = 6.6, CH$_3$CH$_2$O), 54.9 (s, CH$_3$O), 61.5 (d, J = 5.2, CH$_3$CH$_2$O), [illegible], 126.2 (d, J = 174.6, C$_2$), 127.5 (d, J = 22.2, [illegible]), 131.6 (s, o C$_{arom}$), 135.9 (d, J = 4.6, C$_1$), 136.7 (d, J = 9.5, C$_3$), 143.9 (d, J = 10.6, C$_4$), 160.0 (s, p C$_{arom}$).

MS m/z: 368, 353, 295, 279, 159, 121, 73, 45

- *3-(Diethylphosphonyl)-1-(3-pyridyl)-4-(trimethylsilyl)buta-1,3-diene* **7f**

^{1}H NMR (CDCl$_3$): δ 0.1 (s, 9H), 1.0–1.3 (m, 6H), 3.8–4.1 (m, 4H), 6.3–6.4 (m, 1H), 6.4 (d, J_{HaHc} = 19.6, 1H), 6.5 (d, 3.7, 1H), 7.1 (d, J_{HdP} = 23.2, 1H), 7.3 (ddd, J_{HcP} = 31.2, J_{HcHa} = 19.6, 1H), 7.4 (m, 1H).

^{13}C NMR (CDCl$_3$): δ −1.7 (s, Si(CH$_3$)$_3$), 16.0 (d, J = 6.7, CH$_3$CH$_2$O), 61.8 (d, J = 5.0, CH$_3$CH$_2$O), 112 (s, C$_{furyl}$), 116.6 (s, C$_{furyl}$), 123.7 (d, J = 175.4, C$_2$), 129.7 (d, J = 12.7, C$_1$), 136.5 (d, J = 8.2, C$_3$), 137.3 (d, J = 4.6, C$_4$), 141.8 (s, C$_{furyl}$), 151.7 (d, J = 26.5, i C$_{furyl}$).

MS m/z: 328, 313, 285, 255, 223, 121, 73, 45.

- *3-(Diethylphosphonyl)-5-(trimethylsilyl)penta-2,4-diene* **7g**

^{1}H NMR (CDCl$_3$): δ 0.0 (s, 9H), 1.0–1.2 (t, 7.1, 6H), 1.8 (dd, J_{HP} = 3.5, J_{HHx} = 7.3, 3H), 3.8–4.0 (m, 4H), 6.2 (d, J_{HaHc} = 19.3, 1H), 6.5 (dd, J_{HcP} = 26.7, J_{HcHa} = 19.3, 1H), 6.7 (dd, J_{HdP} = 21.9, J_{HdH} = 7.3, 1H).

^{13}C NMR (CDCl$_3$): δ −1.8 (s, Si(CH$_3$)$_3$), 14.3 (d, J = 18.2, CH$_3$), 15.9 (d, J = 6.6, CH$_3$CH$_2$O), 61.2 (d, J = 5.3, CH$_3$CH$_2$O), 129.5 (d, J = 175.3, C$_2$), 134.3 (d, J = 11.5, C$_3$), 135.9 (d, J = 4.8, C$_1$), 143.7 (d, J = 9.6, C$_4$).

MS m/z: 276, 261, 233, 205, 139, 121, 73, 45.

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13 Although the signal of the lithiated derivative **2** (δ (THF) ≈ 14) was not observed in ^{31}P NMR spectroscopy at the end of the reaction, the mixture of alkoxides **3** and **4** was very likely in equilibrium with the reagents, as this was unambiguously proved for the reaction of the lithiated derivative of diethyl propenylphosphonate with aldehydes:
Muller EL, Modro TA, *Bull Soc Chim Fr* (1993) 130, 668

14 Compounds **6** were not isolated, but in some cases (**6f**, **6g**) their structure was clearly identified from the ^{13}C NMR spectra of the reaction products and was confirmed by mass spectrometry (see experimental part).

15 As noticed by Modro et al [9] in the case of the benzaldehyde adduct, all these mixtures underwent extensive decomposition during distillation.

16 We verified that the crude *threo*/*erythro* ratio was not significantly altered during the purification process.

17 The same process proved to be effective for dehydrating some other alcohols **5** (unpublished results).

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20 The ^{31}P NMR spectra of transient diastereomeric phosphates **8** exhibited two sets of pairs of signals, at δ (THF) ≈ 23 to 25 for the phosphonate part and at δ (THF) ≈ −3 to −5 for the phosphate one.

21 a) The generation, in the first step of the E1cB elimination process, of a transitory stabilized carbanion capable of undergoing lone-pair inversion, might explain the (*E*)-stereoselective formation of the 1,2-double bond of **7** from a diastereomeric mixture of phosphates **8**.
b) For general references on the E1cB mechanism, see for example: March EJ, in: *Advanced Organic Chemistry*, 4th Ed, Wiley, New York (1992) 991
c) The E1cB mechanism has been postulated for the formation of 1,3-alkadien-2-ylphosphonic esters from 1-chloroalkenylphosphonates, by dehydrochlorination reaction, under the action of sodium *t*-butoxide: Gurevich IE, Dogadina AV, Ligai SS, Ionin BI, Petrov AA, *Zh Obshch Khim* (1993) 63, 311

22 A preliminary communication of this work was presented at the IRCOF-INTRAMUROS scientific meeting, Rouen, july 1997.