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Synthesis of novel 5-hydroxyalkenylphosphonates by addition of aromatic aldehydes to zirconacyclopentenylphosphonates

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Abstract—Novel 5-hydroxyvinylphosphonates were obtained in a regio- and stereoselective manner, by addition of aromatic aldehydes to zirconacyclopentenylphosphonates in the presence of $AlMe_3$, in 68–82% isolated yields. The reaction is specific for aromatic aldehydes.

1. Introduction

Vinylphosphonates are valuable compounds because of their widespread applications. They are used as intermediates to prepare biologically and pharmacologically active compounds,[1–5] are present in polymers,[6] in agriculture,[7] in flame retardants,[8] and are employed in further organic transformations.[9] In the last few years, we reported the synthesis of several classes of vinylphosphonates utilizing zirconacyclopropenylphosphonates, titanacyclopropenylphosphonates, and zirconacyclopentenylphosphonates.[10] Owing to their importance, vinylphosphonates are also attainable by numerous other methods.[11]

2. Results and discussion

It has been established that when an alkyne is added to the Negishi reagent (Cp_2ZrCl_2/2 *n*-BuLi), ligand exchange occurs to produce the active zirconacyclopropenyl intermediates.[12] On the other hand, alkynes insert into the reagent (Cp_2ZrCl_2/2-EtMgBr) to form zirconacyclopentenes.[13] Utilizing zirconacyclopentenes, we reported the synthesis of 5-hydroxyalkenylboranates through addition of aldehydes to zirconacyclopentenylboronates.[14] Surprisingly, unlike zirconacyclopentenylboronates and other simple alkynes, all efforts to date to implement these conditions to obtain 5-hydroxyalkenylphosphonates from zirconacyclopentenylphosphonates **2** were unsuccessful. Various promoters including, Pd, Ni, Co, Rh, Pt, Zn etc. did not improve the reaction. However, we found that the presence of 2 equiv of AlR_3 (R=Me, Et) or $CeCl_3$ and 1.2 equiv of an aromatic aldehyde are essential to obtain the desired 5-hydroxyvinylphosphonates **5** (Scheme 1). Using less than 2 equiv of the reagent significantly reduced the yield of **5**. The reagents $AlMe_3$, $AlEt_3$, and $CeCl_3$ were all similar with respect to the yields and selectivity of the reaction. In addition, the reaction time was crucial. Stirring the reaction for longer than 1 h at room temperature resulted in the formation of unknown side products.

In a typical experiment, the reaction mixture was extracted into ether and separated on silica gel-chromatography to afford pure **5**. All products were analyzed by NMR spectroscopy, GC–MS, and elemental analysis. Unexpectedly, all efforts to produce compound **5** from aliphatic aldehydes were unsuccessful; the ethylated product, alkenylphosphonate **4**, was obtained together with the alkylated alcohol product of the corresponding aldehydes (Scheme 1). Yields for **5** were obtained in the range of 68–82%, which proceeded in a regio- and stereoselective manner. The insertion of the aldehyde occurrs on C4 relative to phosphorous (Table 1). No other regio- and stereo-isomers were detected. The regio- and stereoselectivity of the products were determined by the ^1H NMR chemical shifts and spin–spin coupling constants. Deuterium labeling of the zirconacycloheptenylphosphonates **3a** showed the incorporation of one deuterium atom in the product **6** (65% yield). Presumably, the two zirconium bonds in **3** were replaced by deuterium atoms, but during the isolation process, the oxygen deuterium bond was hydrolyzed to give a OH bond (Eq. 1).

Keywords: Vinylphosphonates; 5-Hydroxyalkenylphosphonates; Zirconacyclopentene.
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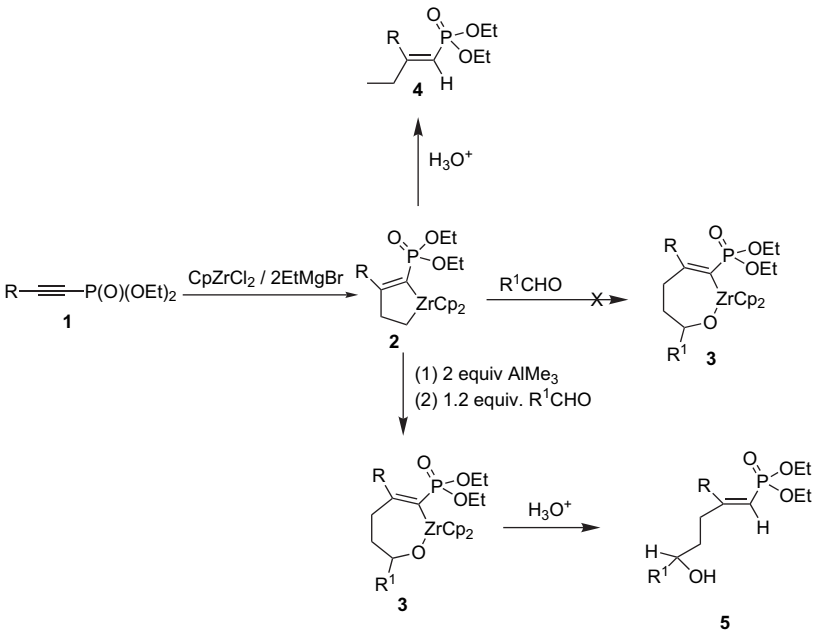
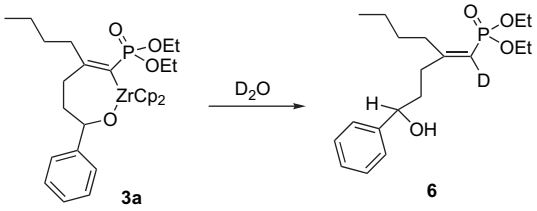


Scheme 1. Addition of aromatic aldehydes to zirconacyclopentenylphosphonates in the presence of $AlMe_3$ to form 5-hydroxyalkenylphosphonates.

Table 1. Synthesis of 5-hydroxyvinylphosphonates **5**, by addition of aromatic aldehydes to zirconacyclopentenylphosphonates in the presence of $AlMe_3$

Entry	Aldehyde	R	R^1	Conversion[a]/yield[b]
3a	Benzaldehyde	*n*-Bu	Phenyl	95/75
3b	*p*-Fluorobenzaldehyde	*n*-Bu	*p*-Fluoro-phenyl	95/72
3c	*o*,*p*-Dichlorobenzaldehyde	*n*-Bu	*o*,*p*-Dichloro-phenyl	95/81
3d	*p*-Nitrobenzaldehyde	*n*-Bu	*p*-Nitro-phenyl	95/82
3e	*o*-Tolualdehyde	*n*-Bu	*o*-Tolyl	95/76
3f	*p*-Tolualdehyde	*n*-Bu	*p*-Tolyl	95/80
3g	*trans*-Cinnamaldehyde	*n*-Bu	*trans*-Cinnamyl	95/80
3h	*p*-Anisaldehyde	*n*-Bu	*p*-Anisyl	95/80
3i	Benzaldehyde	Ph	Phenyl	92/73
3j	*o*,*p*-Dichlorobenzaldehyde	Ph	*o*,*p*-Dichloro-phenyl	90/68

[a] Determined by ^{31}P NMR.
[b] Isolated yield after chromatography.



(1)

In conclusion, hydroxyvinylphosphonates are interesting intermediates for the synthesis of phosphorus containing amino acids, which are known to be active against epilepsy and Parkinson's disease,[15,16] and in organic transformations.[17] In the last few years, we reported the syntheses of 2- and 3-hydroxyvinylphosphontes based on the addition of aldehydes and ketones to zirconacyclopropenylphosphonates, and titanacyclopropenphosphonates, respectively.[18] Also, other protocols have been emerged.[19] However, to the best of our knowledge, the synthesis of 5-hydroxyalkenylphosphonate, has not been previously described. The reaction is general for aromatic aldehydes, and proceeded smoothly for several substituted aromatic aldehydes on various positions of the aromatic ring to give novel 5-hydroxyalkenylphosphonate **5** in high yield and in a regio- and stereoselective manner.

3. Experimental

3.1. General

All reactions were carried out under a nitrogen atmosphere, using vacuum line, a glove-box and schlenk techniques. Solvents were purified by distillation from appropriate drying agents (sodium/benzophenone) under a nitrogen atmosphere. ^1H NMR (300 MHz), ^{13}C NMR (75 MHz), and ^{31}P NMR (121.4 MHz) were recorded in $CDCl_3$. GC–MS analyses were performed on HP GC–MS instrument (Model GCD PLUS), equipped with an EI detector and 30 m methyl silicone column.

3.2. Procedure for the synthesis of 5

To (0.306 g, 1.05 mmol) of zirconocene dichloride dissolved in THF (6 ml) at −78 °C was added 2 M EtMgBr in THF (1.05 ml, 2.1 mmol) dropwise in a 25 ml round-bottom flask.

After stirring for 5 min at −78 °C, 1 mmol of alkynylphosphonate was added and the reaction was gradually warmed to 25 °C and stirred for 3 h. Then the reaction was cooled to 0 °C and $AlMe_3$ (2 mmol) was added under a dry atmosphere, followed by the addition of aldehyde (1.2 mmol). The reaction was then warmed to 25 °C. After stirring for 1 h, the reaction was quenched with dilute HCl solution. The oily product was extracted by Et_2O (2×10 ml) separated by silica gel column chromatography (50% petroleum ether/50% ethyl acetate), and was analyzed by GC–MS, elemental analysis, and NMR spectroscopy.

3.2.1. (*E*)-Diethyl 2-(3-hydroxy-3-phenylpropyl)hex-1-enylphosphonate (5a). ^{1}H NMR (300 MHz): δ 0.86 (t, 3H, J_{HH}=6.9 Hz), 1.28 (dt, 6H, J_{HH}=6.9 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.55 (overlap, 4H), 1.80–1.95 (overlap, 2H), 2.21 (m, 1H), 2.35 (m, 1H), 2.45 (br t, 2H, J_{HH}=6.6 Hz), 2.51 (br s, 1H), 3.95–4.15 (m, 4H), 4.62 (br t, 1H, J_{HH}=6.5 Hz), 5.35 (d, 1H, $^2J_{PH}$=18.5 Hz), 7.20–7.50 (overlap, 5H); ^{31}P NMR (121.4 MHz): δ 19.65; ^{13}C NMR (75.5 MHz): δ 13.8, 16.0 (d, $^3J_{PC}$=6.9 Hz), 22.7, 30.5 (d, $^4J_{PC}$=2.0 Hz), 33.6 (d, $^3J_{PC}$=7.2 Hz), 34.3 (d, $^3J_{PC}$=22.7 Hz), 36.9, 61.1 (d, $^2J_{PC}$=5.7 Hz), 73.5, 110.9 (d, $^1J_{PC}$=190.0 Hz), 125.7, 127.4, 128.3, 144.6, 167.2 (d, $^2J_{PC}$=7.2 Hz); MS(EI): *m*/*z* (%) 354 (0.9), 336 (3.9), 297 (15.7), 248 (35.29), 235 (100), 206 (26.5), 169 (32.35), 107 (24.5), 91 (47.1), 79 (51.0), 77 (34.3), 29 (14.7); Anal. Calcd for $C_{19}H_{31}O_4P$: C, 64.39; H, 8.82; P, 8.74. Found: C, 64.22; H, 8.97; P, 8.71.

3.2.2. (*E*)-Diethyl 2-(3-(4-fluorophenyl)-3-hydroxypropyl)hex-1-enylphosphonate (5b). ^{1}H NMR (300 MHz): δ 0.88 (t, 3H, J_{HH}=6.9 Hz), 1.28 (dt, 6H, J_{HH}=6.9 Hz, $^4J_{PH}$=0.2 Hz), 1.22–1.45 (overlap, 4H), 1.75–1.95 (overlap, 2H), 2.18 (m, 1H), 2.28 (m, 1H), 2.45 (br t, 2H, J_{HH}=6.6 Hz), 2.69 (br s, 1H), 3.95–4.15 (m, 4H), 4.17 (s, 1H), 4.63 (br t, 1H, J_{HH}=6.3 Hz), 5.30 (d, 1H, $^2J_{PH}$=18.3 Hz), 7.00 (t, 2H, J_{HH}=8.7 Hz), 7.28 (dd, 2H, J_{HH}=7.8 Hz); ^{31}P NMR (121.4 MHz): δ 19.42; ^{13}C NMR (75.5 MHz): δ 13.9, 16.3 (d, $^3J_{PC}$=7.3 Hz), 22.8, 30.6 (d, $^4J_{PC}$=2.0 Hz), 33.7 (d, $^3J_{PC}$=6.8 Hz), 34.2 (d, $^3J_{PC}$=22.7 Hz), 36.9, 61.2 (d, $^2J_{PC}$=5.4 Hz), 73.0, 111.2 (d, $^1J_{PC}$=190.0 Hz), 115.1, 127.4, 127.5, 140.3, 166.8 (d, $^2J_{PC}$=6.9 Hz); MS (EI): *m*/*z* (%) 373 (0.1), 372 (0.4), 354 (4.9), 315 (16.7), 248 (36.3), 235 (100), 187 (31.4), 109 (52.0), 97 (42.2), 77 (17.6), 57 (8.7), 41 (8.7); Anal. Calcd for $C_{19}H_{30}FO_4P$: C, 61.28; H, 8.12; F, 5.10; P, 8.32. Found: C, 61.19; H, 8.30; F, 5.03; P, 8.24.

3.2.3. (*E*)-Diethyl 2-(3-(2,4-dichlorophenyl)-3-hydroxypropyl)hex-1-enylphosphonate (5c). ^{1}H NMR (300 MHz): δ 0.87 (t, 3H, J_{HH}=7.2 Hz), 1.27 (dt, 6H, J_{HH}=7.2 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.43 (overlap, 4H), 1.79 (m, 1H), 1.90 (m, 1H), 2.33 (m, 1H), 2.41 (br s, 1H), 2.42 (m, 1H), 2.47 (br t, 2H, J_{HH}=6.7 Hz), 3.90–4.01 (m, 4H), 4.63 (br t, 1H, J_{HH}=6.1 Hz), 5.30 (d, 1H, $^2J_{PH}$=18.6 Hz), 7.30–7.89 (overlap, 3H); ^{31}P NMR (121.4 MHz): δ 19.5; ^{13}C NMR (75.5 MHz): δ 13.8, 16.2 (d, $^3J_{PC}$=6.6 Hz), 22.6, 30.5, 33.7 (d, $^3J_{PC}$=7.2 Hz), 34.8 (d, $^3J_{PC}$=22.7 Hz), 34.9, 36.5, 61.2 (d, $^2J_{PC}$=5.7 Hz), 68.3, 110.9 (d, $^1J_{PC}$=190.0 Hz), 124.1, 127.8, 128.1, 133.4, 140.9, 167.2 (d, $^2J_{PC}$=6.9 Hz); MS (EI): *m*/*z* (%) 426 (0.1), 425 (0.1), 425 (0.1), 424 (0.7), 423 (0.2), 400 (1.0), 364 (7.8), 342 (25.5), 290 (16.7), 249 (40.2), 226 (91.1), 208 (56.9), 191 (59.8), 146 (100), 120 (85.7), 105 (54.9), 92 (53.9), 79 (78.4), 77 (78.4), 67 (53.9), 65 (53.9), 55 (37.3), 41 (30.1); Anal. Calcd for $C_{19}H_{29}Cl_2O_4P$: C, 53.91; H, 6.91; Cl, 16.75; P, 7.32. Found: C, 54.04; H, 7.02; Cl, 16.57; P, 7.20.

3.2.4. (*E*)-Diethyl 2-(3-hydroxy-3-(4-nitrophenyl)propyl)hex-1-enylphosphonate (5d). ^{1}H NMR (300 MHz): δ 0.87 (t, 3H, J_{HH}=6.9 Hz), 1.25 (dt, 6H, J_{HH}=7.2 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.45 (overlap, 4H), 1.80 (m, 1H), 1.90 (m, 1H), 2.25–2.43 (overlap m, 2H), 2.45 (br t, 2H, J_{HH}=6.7 Hz), 3.80 (br s, 1H), 3.90–4.05 (m, 4H), 5.20 (br t, 1H, J_{HH}=6.4 Hz), 5.31 (d, 1H, $^2J_{PH}$=18.6 Hz), 7.37–7.95 (overlap, 4H); ^{31}P NMR (121.4 MHz): δ 19.55; ^{13}C NMR (75.5 MHz): δ 13.9, 16.2 (d, $^3J_{PC}$=6.6 Hz), 22.8, 30.5, 33.6 (d, $^3J_{PC}$=7.1 Hz), 34.7 (d, $^3J_{PC}$=22.7 Hz), 36, 61.2 (d, $^2J_{PC}$=5.7 Hz), 68.3, 111.0 (d, $^1J_{PC}$=189.7 Hz), 124.2, 127.9, 128.0, 133.4, 141.1, 147.4, 167.1 (d, $^2J_{PC}$=7.2 Hz); MS (EI): *m*/*z* (%) 399 (0.5), 364 (5.0), 342 (11.1), 290 (7.5), 249 (22.2), 226 (61.1), 208 (38.9), 191 (50.0), 146 (83.3), 120 (83.3), 104 (61.1), 77 (100), 66 (77.8), 41 (61.1); Anal. Calcd for $C_{19}H_{30}NO_6P$: C, 57.13; H, 7.57; N, 3.51; P, 7.75. Found: C, 56.99; H, 7.71; N, 3.45; P, 7.67.

3.2.5. (*E*)-Diethyl 2-(3-hydroxy-3-*o*-tolylpropyl)hex-1-enylphosphonate (5e). ^{1}H NMR (300 MHz): δ 0.86 (t, 3H, J_{HH}=6.9 Hz), 1.26 (dt, 6H, J_{HH}=7.2 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.50 (overlap, 4H), 1.77–1.91 (overlap, 2H), 2.29 (br s, 3H), 2.15–2.40 (overlap, 2H), 2.47 (br t, 2H, J_{HH}=6.6 Hz), 2.69 (br s, 1H), 3.93–4.11 (m, 4H), 4.89 (br t, 1H, J_{HH}=6.5 Hz), 5.31 (d, 1H, $^2J_{PH}$=18.3 Hz), 7.08–7.26 (overlap, 4H); ^{31}P NMR (121.4 MHz): δ 19.50; ^{13}C NMR (75.5 MHz): δ 13.8, 16.1 (d, $^3J_{PC}$=6.9 Hz), 18.9, 22.8, 30.6, 33.8 (d, $^3J_{PC}$=7.2 Hz), 34.4 (d, $^3J_{PC}$=22.6 Hz), 35.8, 61.1 (d, $^2J_{PC}$=5.4 Hz), 69.7, 111.0 (d, $^1J_{PC}$=190.0 Hz), 125.1, 126.2, 127.1, 130.3, 134.1, 142.7, 167.1 (d, $^2J_{PC}$=7.2 Hz); MS (EI): *m*/*z* (%) 368 (0.3), 350 (16.7), 311 (18.8), 248 (44.1), 235 (67.6), 206 (44.1), 183 (31.4), 170 (29.4), 105 (72.5), 91 (100), 77 (65.7), 55 (29.4), 41 (30.4), 29 (41.2); Anal. Calcd for $C_{20}H_{33}O_4P$: C, 65.20; H, 9.03; P, 8.41. Found: C, 65.34; H, 8.96; P, 8.34.

3.2.6. (*E*)-Diethyl 2-(3-hydroxy-3-*p*-tolylpropyl)hex-1-enylphosphonate (5f). ^{1}H NMR (300 MHz): δ 0.89 (t, 3H, J_{HH}=7.5 Hz), 1.29 (dt, 6H, J_{HH}=7.1 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.50 (overlap, 4H), 1.70–1.99 (overlap, 2H), 2.05 (br s, 1H), 2.12–2.40 (overlap, 2H), 2.34 (s, 3H), 2.48 (br t, 2H, J_{HH}=6.9 Hz), 3.95–4.09 (m, 4H), 4.63 (br t, 1H, J_{HH}=6.6 Hz), 5.34 (d, 1H, $^2J_{PH}$=18.0 Hz), 7.10–7.26 (overlap, 4H); ^{31}P NMR (121.4 MHz): δ 19.45; ^{13}C NMR (75.5 MHz): δ 13.8, 16.2 (d, $^3J_{PC}$=6.6 Hz), 21.0, 22.8, 30.5, 33.7 (d, $^3J_{PC}$=7.2 Hz), 34.2 (d, $^3J_{PC}$=23.2 Hz), 61.1 (d, $^2J_{PC}$=5.7 Hz), 73.5, 111.2 (d, $^1J_{PC}$=190.0 Hz), 116.0, 125.7, 129.1, 137.2, 141.4, 167.1 (d, $^2J_{PC}$=7.2 Hz); MS (EI): *m*/*z* (%) 368 (0.9), 350 (31.4), 321 (3.9), 311 (8.8), 248 (29.4), 235 (100), 206 (42.2), 183 (47.1), 170 (37.3), 138 (16.7), 120 (50.0), 105 (61.8), 91 (90.1), 77 (58.9), 65 (40.1), 55 (27.7), 41 (33.9), 28 (95.1); Anal. Calcd for $C_{20}H_{33}O_4P$: C, 65.20; H, 9.03; P, 8.41. Found: C, 65.39; H, 8.93; P, 8.32.

3.2.7. Diethyl (1*E*,6*E*) 2-butyl-5-hydroxy-7-phenylhepta-1,6-dienylphosphonate (5g). ^{1}H NMR (300 MHz): δ 0.89 (t, 3H, J_{HH}=6.9 Hz), 1.25 (dt, 6H, J_{HH}=6.9 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.52 (overlap, 4H), 1.76–1.80 (overlap, 2H),

2.23–2.34 (overlap, 2H), 2.45 (br s, 1H), 2.49 (br t, 2H, J_{HH}=6.3 Hz), 3.97–4.08 (m, 4H), 4.26 (q, 1H, J_{HH}=6.3 Hz), 5.36 (d, 1H, $^2J_{PH}$=18.3 Hz), 6.20 (dd, 1H, J_{HH}=15.9 Hz), 6.47 (d, 1H, J_{HH}=15.9 Hz), 7.20–7.38 (overlap, 5H); ^{31}P NMR (121.4 MHz): δ 19.52; ^{13}C NMR (75.5 MHz): δ 13.9, 16.3 (d, $^3J_{PC}$=6.6 Hz), 22.8, 30.6 (d, $^4J_{PC}$=1.7 Hz), 33.7 (d, $^3J_{PC}$=7.2 Hz), 33.8 (d, $^3J_{PC}$=30.1 Hz), 35.0, 61.2 (d, $^2J_{PC}$=5.7 Hz), 72.1, 111.0 (d, $^1J_{PC}$=190.0 Hz), 126.4, 126.5, 128.5, 130.3, 132.0, 136.5, 167.1 (d, $^2J_{PC}$=6.8 Hz); MS (EI): *m/z* (%) 381 (2.5), 380 (11.8), 362 (4.9), 323 (5.8), 271 (11.1), 247 (43.1), 235 (100), 224 (49.0), 206 (57.8), 133 (39.2), 115 (40.2), 91 (78.4), 79 (40.2), 77 (34.3), 55 (54.9), 41 (19.6), 29 (22.3); Anal. Calcd for $C_{21}H_{33}O_4P$: C, 66.35; H, 8.75; P, 8.19. Found: C, 66.42; H, 8.66; P, 7.95.

3.2.8. (*E*)-Diethyl 2-(3-hydroxy-3-(4-methoxyphenyl)propyl)hex-1-enylphosphonate (5h). ^{1}H NMR (300 MHz): δ 0.88 (t, 3H, J_{HH}=7.2 Hz), 1.28 (dt, 6H, J_{HH}=7.2 Hz, $^4J_{PH}$=0.2 Hz), 1.20–1.45 (overlap, 4H), 1.80 (m, 1H), 1.95 (m, 1H), 2.14 (m, 1H), 2.29 (m, 1H), 2.43 (br s, 1H), 2.46 (br t, 2H, J_{HH}=6.6 Hz), 3.96–4.09 (m, 4H), 4.60 (br t, 1H, J_{HH}=6.0 Hz), 5.31 (d, 1H, $^2J_{PH}$=18.0 Hz), 6.86 (d, 2H, J_{HH}=8.7 Hz), 7.23 (d, 2H, J_{HH}=9.0 Hz); ^{31}P NMR (121.4 MHz): δ 19.52; ^{13}C NMR (75.5 MHz): δ 13.9, 16.3 (d, $^3J_{PC}$=6.9 Hz), 22.8, 30.6, 33.7 (d, $^3J_{PC}$=6.9 Hz), 34.3 (d, $^3J_{PC}$=22.7 Hz), 36.8, 55.2, 61.1 (d, $^2J_{PC}$=5.7 Hz), 73.3, 111.0 (d, $^1J_{PC}$=190.0 Hz), 113.8, 127.0, 136.60, 159.0, 167.1 (d, $^2J_{PC}$=7.2 Hz); MS (EI): *m/z* (%) 384 (3.1), 366 (3.5), 327 (3.9), 271 (10.3), 248 (28.7), 235 (100), 206 (51.7), 163 (18.4), 150 (51.7), 137 (78.2), 121 (57.5), 109 (47.1), 94 (42.5), 91 (27.8), 77 (57.5), 55 (27.6), 41 (31.0); Anal. Calcd for $C_{20}H_{33}O_5P$: C, 62.48; H, 8.65; P, 8.06. Found: C, 62.42; H, 8.80; P, 7.97.

3.2.9. (*Z*)-Diethyl 5-hydroxy-2,5-diphenylpent-1-enylphosphonate (5i). ^{1}H NMR (300 MHz): δ 1.02 (dt, 6H, J_{HH}=6.9 Hz, $^4J_{PH}$=0.2 Hz), 1.75–1.95 (overlap, 2H), 2.02 (br s, 1H), 2.66 (m, 1H), 2.82 (m, 1H), 3.60–3.80 (m, 4H), 4.62 (br t, 1H, J_{HH}=6.5 Hz), 5.72 (d, 1H, $^2J_{PH}$=17.4 Hz), 7.10–7.40 (overlap, 10H); ^{31}P NMR (121.4 MHz): δ 17.63; ^{13}C NMR (75.5 MHz): δ 16.0 (d, $^3J_{PC}$=6.9 Hz), 36.2, 38.0 (d, $^3J_{PC}$=21.2 Hz), 61.3 (d, $^2J_{PC}$=5.7 Hz), 68.4, 114.2 (d, $^1J_{PC}$=180.14 Hz), 124.3, 127.6, 128.0, 128.1, 128.3, 133.5, 140.3, 147.6, 162.4 (d, $^2J_{PC}$=7.2 Hz); MS(EI): *m/z* (%) 374 (0.9), 359 (3.1), 329 (100), 301 (14.5), 281 (29.7), 273 (59.5), 255 (48.6), 238 (24.3), 207 (75.7), 193 (35.1), 181 (18.4), 165 (32.4), 149 (70.3), 136 (10.8), 105 (24.3), 77 (27.1), 41 (47.9); Anal. Calcd for $C_{21}H_{27}O_4P$: C, 67.37; H, 7.27; P, 8.27. Found: C, 67.22; H, 7.44; P, 8.23.

3.2.10. (*Z*)-Diethyl 5-(2,4-dichlorophenyl)-5-hydroxy-2-phenylpent-1-enylphosphonate (5j). ^{1}H NMR (300 MHz): δ 1.10 (dt, 6H, J_{HH}=7.2 Hz, $^4J_{PH}$=0.2 Hz), 1.70–1.90 (overlap, 2H), 2.02 (br s, 1H), 2.45–2.70 (overlap, 2H), 3.68–3.85 (m, 4H), 4.66 (br t, 1H, J_{HH}=6.3 Hz), 5.72 (d, 1H, $^2J_{PH}$=17.4 Hz), 7.20–7.33 (overlap, 8H); ^{31}P NMR (121.4 MHz): δ 16.00; ^{13}C NMR (75.5 MHz): δ 16.0 (d, $^3J_{PC}$=6.6 Hz), 36.6, 37.7 (d, $^3J_{PC}$=22.4 Hz), 61.3 (d, $^2J_{PC}$=5.7 Hz), 73.5, 114.6 (d, $^1J_{PC}$=191.8 Hz), 125.8, 127.7, 127.7, 128.0, 128.2, 128.5, 128.9, 139.0, 139.7, 144.2, 162.4 (d, $^2J_{PC}$=6.9 Hz); MS (EI): *m/z* (%) 445 (0.1), 444 (0.4), 443 (0.2), 442 (1.0), 390 (1.7), 344 (3.5), 298 (2.2), 196 (100), 165 (5.1), 91 (64.7), 77 (3.2), 65 (3.4), 51 (2.3), 41 (2.1), 29 (3.4); Anal. Calcd for $C_{21}H_{25}Cl_2O_4P$: C, 56.90; H, 5.68; Cl, 16.00; P, 6.99. Found: C, 57.02; H, 5.60; Cl, 15.90; P, 7.05.

3.2.11. (*E*)-Diethyl 2-deuterio-2-(3-hydroxy-3-phenylpropyl)hex-1-enylphosphonate (6). ^{1}H NMR (300 MHz): δ 0.88 (t, 3H, J_{HH}=6.9 Hz), 1.28 (dt, 6H, J_{HH}=7.1 Hz, $^4J_{PH}$=0.2 Hz), 1.22–1.45 (overlap, 4H), 1.78–1.94 (m, 2H), 2.26 (m, 1H), 2.30 (m, 1H), 2.43 (br t, 2H, J_{HH}=7.6 Hz), 2.60 (br s, 1H), 3.95–4.05 (m, 4H), 4.64 (br t, 1H, J_{HH}=7.5 Hz), 7.20–7.35 (overlap, 5H); ^{31}P NMR (121.4 MHz): δ 19.54; ^{13}C NMR (75.5 MHz): δ 13.9, 16.3 (d, $^3J_{PC}$=6.6 Hz), 22.8, 30.6, 33.6 (d, $^3J_{PC}$=6.9 Hz), 34.3 (d, $^3J_{PC}$=23.9 Hz), 36.8, 61.1 (d, $^2J_{PC}$=5.7 Hz), 73.7, 109.8 (d, $^1J_{PC}$=189.22 Hz), 125.8, 127.6, 128.4, 144.5, 166.9 (d, $^2J_{PC}$=6.9 Hz); MS (EI): *m/z* (%) 356 (1.0), 337 (4.4), 298 (15.7), 249 (30.7), 236 (100), 207 (21.6), 170 (30.4), 105 (20.6), 91 (47.1), 79 (45.1), 77 (34.3), 55 (5.9), 41 (5.8); Anal. Calcd for $C_{19}H_{30}DO_4P$: C, 64.21; H, 9.07; P, 8.71. Found: C, 64.32; H, 9.02; P, 8.64.

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