A Novel Approach to γ-Hydroxy-α,β-unsaturated Compounds

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Abstract: A simple synthesis of (*E*)-alk-1-enyl mesylates from (*E*)-alk-1-enylphosphonates is reported. Construction of γ-hydroxy-α,β-unsaturated compounds was achieved by a two-step process involving dihydroxylation of the enol mesylates followed by HWE reaction of the resulting α-hydroxy aldehydes with activated methylphosphonates. Enantioselective synthesis of the title compounds is also reported.

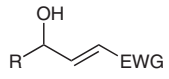
Key words: alk-1-enyl mesylates, dihydroxylation, α-hydroxy aldehydes, Horner–Wadsworth–Emmons reaction, Conant–Swan fragmentation

In recent years, γ-hydroxy-α,β-unsaturated esters **1a** and nitriles **1b** have found wide applicability in organic synthesis. To date numerous examples have been provided, which demonstrate particular utility of these reagents for constructing various biologically active compounds and natural products.[1] In contrast, much less attention has been paid to structurally related γ-hydroxy-α,β-unsaturated phosphonates **1c**[2] (Figure 1).

All these compounds have been preferentially obtained by hydroxylative Knoevenagel condensation of aldehydes with sulfinylacetates, sulfinylacetonitriles and sulfinylmethylphosphonates, respectively (SPAC-reaction).[2,3] Enantioselective approach to esters **1a** and nitriles **1b** using S-chiral sulfinylacetates and sulfinylacetonitriles has been also reported.[1e,4]

A number of different synthetic routes leading to racemic esters **1a** and nitriles **1b** have been described. They are readily available by regioselective oxidation-reduction reactions of α,β,γ,δ-unsaturated alkadienoates and structurally related nitriles with molecular oxygen and triethylsilane in the presence of Co(II) porphyrin.[5] Other equally attractive methods involve oxyselenylation–deselenylation of β,γ-unsaturated esters or nitriles[6] and conjugate addition of Grignard reagents to γ-hydroxybutynenitriles.[7] Optically active nitriles **1b** are accessible by β-elimination of water from nonracemic β,γ-dihydroxyalkanenitriles,[8] cyanation of enantiomerically enriched γ-iodoallylic alcohols with CuCN,[9] and stereoselective S_N2' substitution reaction of enantiomeric O-acylated allylic cyanohydrins.[10]

A simple alternative source of racemic esters **1a** is the addition of Grignard reagents to γ-oxo-α,β-alkanoates.[11]



1a–c

EWG = (**a**) COOR, (**b**) CN, (**c**) P(O)(OR)$_2$

Figure 1 γ-Hydroxy-α,β-unsaturated esters, nitriles, and phosphonates

The optically active O-protected esters **1a** were prepared by irradiation of enantioenriched α,β-epoxydiazomethyl ketones in ethanol as well as by the Wittig olefination of O-protected enantiomeric α-hydroxy aldehydes with stabilized phosphonium ylides.[12]

It has been recently reported that similar Horner–Wadsworth–Emmons (HWE) reaction of enantio-enriched and unprotected α-hydroxy aldehydes with methyl diethylphosphonoacetate affords the esters **1a** displaying high optical purity.[13] Satisfactory result of the latter synthesis was achieved owing to a new and effective approach to the starting aldehydes as well as unconventional protocol of their HWE olefination. The new approach relies on the asymmetric dihydroxylation of α,β-unsaturated sulfones using Sharpless methodology and subsequent elimination of sulfonic acids from the resulting α,β-dihydroxysulfones. Direct HWE reaction of the crude α-hydroxy aldehydes allowed avoiding their easy tautomeric rearrangement into hydroxyl ketones and racemization.[14]

With these observations in hand, it became of interest to develop other methodologically similar synthesis of stereochemically defined γ-hydroxy-α,β-unsaturated compounds bearing different electron-withdrawing groups. We envisaged that alk-1-enyl mesylates (aldehyde enol mesylates) could serve as convenient precursors of α-hydroxy aldehydes.

Reported herein is a stereospecific approach to (*E*)-alk-1-enyl mesylates and their utility in the preparation of racemic γ-hydroxy-α,β-unsaturated esters, nitriles, and phosphonates. Preliminary studies on their enantioselective synthesis are also described. The literature contains only a few examples of simple alk-1-enyl mesylates and there is no general method for their effective and stereoselective preparation.[15]

Our synthesis of these compounds begins with dihydroxylation of (*E*)-α,β-unsaturated phosphonates **2** with a catalytic amount of OsO_4 in the presence of *N*-methylmorpholine *N*-oxide (NMO) as a co-oxidant leading to the corresponding *syn*-1,2-dihydroxyphosphonates **3**[16] (Scheme 1).

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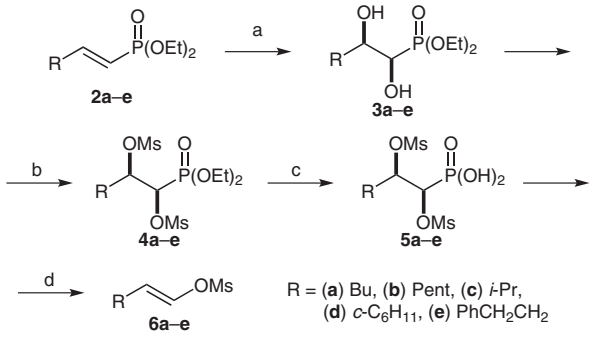
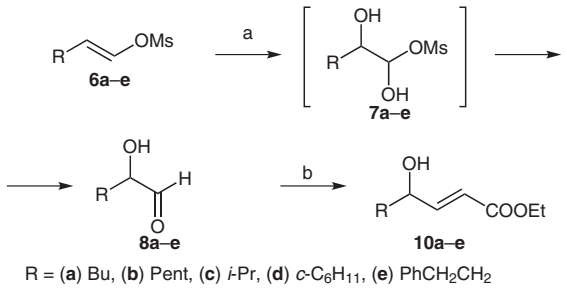


Scheme 1 *Reagents and conditions*: (a) NMO (1.1 equiv), OsO_4 (cat.), *t*-BuOH–acetone (4:1), 25 °C, 3 d; (b) Et_3N (2.5 equiv), $MeSO_2Cl$ (2 equiv), CH_2Cl_2, 25 °C, 20 h; (c) Me_3SiBr (4 equiv), CH_2Cl_2, 25 °C, 5 d, then EtOH; (d) Et_2O, aq sat. $NaHCO_3$, 2 h, 25 °C.

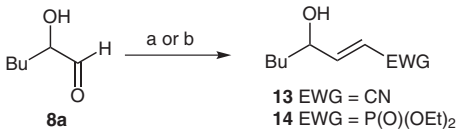


Scheme 2 *Reagents and conditions*: (a) NMO (1.1 equiv), OsO_4 (cat.), *t*-BuOH–acetone (4:1), 25 °C, 3 days; (b) $(EtO)_2P(O)CH_2CO_2Et$ (**9**, 1 equiv), NaH (1 equiv), THF, 20 h, 25 °C.

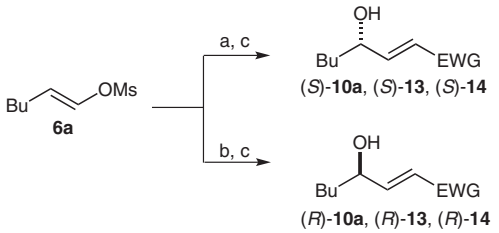
Subsequent mesylation of both hydroxyl groups in **3** afforded *syn*-1,2-dimesyloxyphosphonates **4**.[17] Routine deesterification of phosphonates **4** by sequential treatment with bromotrimethylsilane and ethanol gave the *syn*-1,2-dimesyloxyphosphonic acids **5**.[18] Finally, treatment of the crude acids **5** with aqueous saturated sodium hydrogen carbonate resulted in the Conant–Swan fragmentation[19] to afford (*E*)-alk-1-enyl mesylates **6**, which were purified by column chromatography.

Our attempts to use the enol mesylates **6** as substrates for the preparation of γ-hydroxy-α,β-unsaturated esters **10** met with full success (Scheme 2). Dihydroxylation of the enol mesylates **6** by the standard procedure with a catalytic amount of OsO_4 in the presence of NMO was completed within 3 days at 25 °C.

In all cases, the obtained dihydroxyalkyl mesylates **7** spontaneously eliminated methanesulfonic acid fragments to produce α-hydroxy aldehydes **8**. Subsequent HWE olefination of the crude aldehydes **8** with sodium triethylphosphonoacetate, generated from the phosphonate **9** and NaH, resulted in a rapid and effective conversion into the corresponding γ-hydroxy-α,β-unsaturated esters **10** with complete *E*-stereoselectivity. Similarly, the HWE reaction of α-hydroxyhexanal **8a** with activated methylphosphonates, such as diethyl cyanomethylphosphonate (**11**) and tetraethyl methylenediphosphonate (**12**) provided (*E*)-4-hydroxyoct-2-enenitrile (**13**) and diethyl



Scheme 3 *Reagents and conditions*: (a) $(EtO)_2P(O)CH_2CN$ (**11**), (1 equiv), NaH (1 equiv), THF, 20 h, 25 °C; (b) $(EtO)_2P(O)CH_2$-$P(O)(OEt)_2$ (**12**, 1 equiv), NaH (1 equiv), THF, 20 h, 25 °C.



Scheme 4 *Reagents and conditions*: (a) AD-mix-α, $K_2SO_4·H_2O$ (0.8 mol%), *t*-BuOK/H_2O (1:1), $MeSO_2NH_2$ (2 equiv), 72 h, 25 °C; (b) AD-mix-β, $K_2SO_4·H_2O$ (0.8 mol%), *t*-BuOK/H_2O (1:1), $MeSO_2NH_2$ (2 equiv), 72 h, 25 °C; (c) $(EtO)_2P(O)CH_2CO_2Et$ (**9**, 1 equiv) or $(EtO)_2P(O)CH_2CN$ (**11**, 1 equiv) or $(EtO)_2P(O)CH_2P(O)(OEt)_2$ (**12**, 1 equiv), NaH (1 equiv), THF, 20 h, 25 °C.

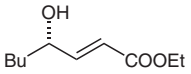
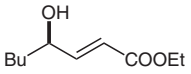
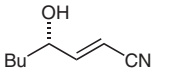
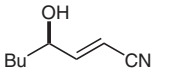
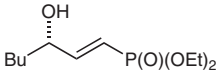
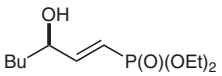
(*E*)-3-hydroxyhept-1-enylphosphonate (**14**), respectively (Scheme 3).

We anticipated that asymmetric Sharpless dihydroxylation of the enol mesylates would allow enantioselective synthesis of α-hydroxy aldehydes with predicable absolute configuration. Thus, the reactions of enol mesylate **6a** with AD-mix-α and AD-mix-β in the presence of additional $K_2OsO_4·H_2O$ in *t*-BuOH–H_2O solvent system (1:1) were carried out for 72 hours at room temperature and provided (*S*)-**8a** and (*R*)-**8a** α-hydroxyhexanals, respectively. The crude aldehydes were subjected to HWE olefination with the previously used activated methylphosphonates to give the corresponding γ-hydroxy-α,β-unsaturated octenoates (*S*)-**10a**, (*R*)-**10a**, octenenitriles (*S*)-**13**, (*R*)-**13**, and heptenylphosphonates (*S*)-**14**, (*R*)-**14** (Scheme 4).

The enantiomeric purities of the products **10a**, **13**, and **14** were established unambiguously by chiral GC analysis and compared with those obtained by ^1H NMR experiments using $Eu(hfc)_3$ as the chiral shift reagent (Table 1). A slight divergence of the found ee values is in line with the accuracy of the latter measurements. Enantiomeric purities of γ-hydroxyphosphonates (*S*)-**14** and (*R*)-**14** could not be determined by GC using available chiral columns.

As illustrated in Table 1, the target products were prepared with high enentioselectivities. It is reasonable to assume that asymmetric dihydroxylation afforded (*R*)- and (*S*)-α-hydroxyhexanals (*R*)- and (*S*)-**8a** with at least the same level of enantiomeric excess. Notably, asymmetric dihydroxylations using AD-mix-α led to the α-hydroxyhexanal (*S*)-**8a** with somewhat lower enantiomeric excess.

Table 1 γ-Hydroxy-α,β-unsaturated Compounds Prepared

Entry	Product		ee[a]	ee[b]
1		(*S*)-**10a**	82	78
2		(*R*)-**10a**	91	89
3		(*S*)-**13**	82	78
4		(*R*)-**13**	91	88
5		(*S*)-**14**	–	76
6		(*R*)-**14**	–	86

[a] Enantiomeric excess was determined by GC.
[b] Enantiomeric excess was determined by ^{1}H NMR spectroscopy.

The absolute configurations of the nitriles (*S*)-(+)-**13** and (*R*)-(–)-**13** obtained were established by comparison of their sign of optical rotation with the literature data.[4d] Therefore, dihydroxylation of the mesylate **6a** with AD-mix-α leads to the (*S*)-α-hydroxyhexanal, while that with AD-mix-β gives the *R*-enantiomer. As a consequence, the absolute configuration of the γ-hydroxy-α,β-unsaturated HWE reaction products **10a**, **13**, and **14** could be assigned as *S* and *R*, respectively. This result is in agreement with the Sharpless model for asymmetric dihydroxylation.[20] According to this model AD-mix-α should favor the formation of (*S*)-α-hydroxy aldehydes from the corresponding (*E*)-alk-1-enyl mesylates.

In summary, the ready access to methanesulfonates of *E*-aldehyde enols coupled with their easy conversion to α-hydroxy aldehydes is described as a profitable method for the preparation of γ-hydroxy-α,β-unsaturated compounds. In addition, asymmetric Sharpless dihydroxylation of the enol mesylates provided α-hydroxy aldehydes with high enantiomeric excess, which opens a new general route to the highly enantioselective synthesis of γ-hydroxy alkanoates and related compounds.

NMR spectra were recorded on a Bruker DPX 250 instrument at 250.13 MHz for ^{1}H, and 62.9 MHz for ^{13}C, and 101.3 MHz for ^{31}P NMR using tetramethylsilane as internal and 85% H_3PO_4 as external standard, respectively. The multiplicities of carbons were determined by DEPT experiments. IR spectra were measured on Specord M80 (Zeiss) instrument. The ee values were determined by GC analysis on Hewlett-Packard 5900 II instrument equipped with γ-Dex-225 column by comparison with the racemates. Elemental analyses were performed on PerkinElmer PE 2400 analyzer. Melting points were determined in open capillaries and were uncorrected. Diethyl alk-1-enylphosphonates **2** were prepared according to the literature procedure.[16]

Diethyl 1,2-Dihydroxyalkylphosphonate 3a–e; General Procedure

To a solution of phosphonate **2** (0.03 mol) in acetone (10 mL) and *t*-BuOH (40 mL) was added NMO (4.5 g, 0.033 mol) and OsO_4 (0.25 mg, 0.1 mmol). The resulting mixture was stirred at 25 °C for 3 d. The mixture was then quenched with aq $Na_2S_2O_3$ (15 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography ($CHCl_3$–acetone, 4:1) affording pure **3**.

Diethyl 1,2-Dihydroxyhexylphosphonate (3a)

Yield: 85%, yellow oil; R_f = 0.20.

IR (film): 3360, 1216, 1048 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.91 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$), 1.35 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O, 1.36 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, C*H*$_3$CH$_2$O, 1.54–1.80 (m, 6 H, 3 × CH$_2$), 3.40 (br s, 1 H, OH), 3.71 (br s, 1 H, OH), 3.76–3.79 (m, 1 H, PCHC*H*), 3.96–4.07 (m, 1 H, PCH), 4.19 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.15 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH$_3$C*H*$_2$O).

^{13}C NMR ($CDCl_3$): δ = 13.81 (s, *C*H$_3$CH$_2$), 16.23 (d, $^3J_{P,C}$ = 5.60 Hz, *C*H$_3$CH$_2$O), 22.40 (s, CH$_2$), 27.70 (s, CH$_2$), 32.62 (d, $^3J_{P,C}$ = 10.5 Hz, CH$_2$), 62.52 (d, $^2J_{P,C}$ = 7.3 Hz, CH$_3$*C*H$_2$), 62.92 (d, $^2J_{P,C}$ = 7.0 Hz, CH$_3$*C*H$_2$O), 70.34 (d, $^2J_{P,C}$ = 2.1 Hz, PCH*C*H), 70.63 (d, $^1J_{P,C}$ = 159.4 Hz, PCH).

^{31}P NMR ($CDCl_3$): δ = 24.41.

Anal. Calcd for $C_{10}H_{23}O_5P$: C, 47.24; H, 9.12. Found: C, 47.05; H, 9.18.

Diethyl 1,2-Dihydroxyheptylphosphonate (3b)[16]

Yield: 83%; yellow oil; R_f = 0.12.

^{1}H NMR ($CDCl_3$): δ = 0.95 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$), 1.35 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.37 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.54–1.80 (m, 8 H, 4 × CH$_2$), 3.73 (br s, 1 H, OH), 3.96 (br s, 1 H, OH), 4.00–4.11 (m, 1 H, PCHC*H*), 4.14–4.29 (m, 5 H, 2 × CH$_3$C*H*$_2$O, PCH).

^{31}P NMR ($CDCl_3$): δ = 24.24.

Diethyl 1,2-Dihydroxy-3-methylbutylphosphonate (3c)[16]

Yield: 92%; colorless crystals; mp 82–84 °C.

^{1}H NMR ($CDCl_3$): δ = 0.93 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, C*H*$_3$CH), 1.04 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, C*H*$_3$CH), 1.35 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.36 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, C*H*$_3$CH$_2$O), 1.89–2.01 [m, 1 H, (CH$_3$)$_3$C*H*], 3.50 (ddd, $^3J_{H,H}$ = 8.0 Hz, $^2J_{P,H}$ = 6.0 Hz, $^3J_{H,H}$ = 3.5 Hz, 1 H, PCH), 3.72 (br s, 1 H, OH), 4.00–4.10 (m, 2 H, PCHC*H*, OH), 4.15 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.19 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH$_3$C*H*$_2$O).

^{31}P NMR ($CDCl_3$): δ = 25.24.

Diethyl 2-Cyclohexyl-1,2-dihydroxyethylphosphonate (3d)

Yield: 70%; colorless oil; R_f = 0.19.

IR (film): 3352, 1228, 1044 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.00–1.15 (m, 4 H, 2 × CH$_2$), 1.34 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, C*H*$_3$CH$_2$O), 1.35 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, C*H*$_3$CH$_2$O), 1.60–1.94 [m, 7 H, 3 × CH$_2$, C*H*(CH$_2$)$_5$], 3.25 (ddd, $^3J_{H,H}$ = 7.5 Hz, $^3J_{H,H}$ = 6.25 Hz, $^3J_{P,H}$ = 6.0 Hz, 1 H, PCHC*H*), 3.64 (br s, 1 H, OH), 3.92–4.04 (m, 2 H, PCH, OH), 4.18 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH$_3$C*H*$_2$O), 4.20 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.2 Hz, 2 H, CH$_3$C*H*$_2$O).

^{13}C NMR ($CDCl_3$): δ = 16.24 (d, $^3J_{P,C}$ = 5.6 Hz, *C*H$_3$CH$_2$O), 16.27 (d, $^3J_{P,C}$ = 5.5 Hz, *C*H$_3$CH$_2$OP), 25.60 (s, CH$_2$), 26.11 [d, $^3J_{P,C}$ = 15.5 Hz, *C*H(CH$_2$)$_5$], 30.0 (s, 2 × CH$_2$), 31.14 (s, 2 × CH$_2$), 62.46 (d, $^2J_{P,C}$ = 6.5 Hz, CH$_3$*C*H$_2$O), 62.49 (d, $^2J_{P,C}$ = 7.1 Hz,

CH_3CH_2O), 70.42 (d, $^1J_{P,C}$ = 160.2 Hz, PCH), 75.14 (d, $^2J_{P,C}$ = 10.2 Hz, PCH*C*H).

^{31}P NMR ($CDCl_3$): δ = 23.14.

Anal. Calcd for $C_{12}H_{25}O_5P$: C, 51.42; H, 8.99. Found: C, 51.31; H, 9.05.

Diethyl 1,2-Dihydroxy-4-phenylbutylphosphonate (3e)
Yield: 82%; light yellow oil.

IR (film): 3352, 1264, 1024 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.30 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, 2 × C*H*$_3$CH$_2$O), 1.74 (br s, 1 H, OH), 1.84–2.09 (m, 2 H, CH_2), 2.63–2.78 (m, 2 H, PhC*H*$_2$), 3.46 (br s, 1 H, OH), 3.72–3.79 (m, 1 H, PCHC*H*), 3.92–4.06 (m, 1 H, PCH), 4.14 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2O), 4.22 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2O), 7.15–7.31 (m, 5 H, CH_{Ar}).

^{13}C NMR ($CDCl_3$): δ = 16.28 (d, $^3J_{P,C}$ = 5.5 Hz, *C*H$_3$CH$_2$O), 16.32 (d, $^3J_{P,C}$ = 5.8 Hz, *C*H$_3$CH$_2$O), 30.11 (s, PhC*H*$_2$), 36.11 (d, $^3J_{P,C}$ = 10.5 Hz, *C*H$_2$), 62.24 (d, $^2J_{P,C}$ = 6.5 Hz, CH$_3$*C*H$_2$O), 62.27 (d, $^2J_{P,C}$ = 7.0 Hz, CH$_3$*C*H$_2$O), 70.23 (d, $^1J_{P,C}$ = 160.0 Hz, PCH), 75.78 (d, $^2J_{P,C}$ = 10.1 Hz, PCH*C*H), 126.11 (s, 2 × CH_{Ar}), 128.27 (s, CH_{Ar}), 128.40 (s, 2 × CH_{Ar}), 139.86 (s, C_{Ar}).

^{31}P NMR ($CDCl_3$): δ = 19.84.

Anal. Calcd for $C_{14}H_{23}O_5P$: C, 55.64; H, 7.67. Found: C, 55.75; H, 7.71.

Diethyl 1,2-Di(methylsulfonyloxy)alkylphosphonates 4a–e; General Procedure
To a solution of phosphonate **3** in CH_2Cl_2 (30 mL) were added Et_3N (3.45 mL, 0.025 mol) and $MeSO_2Cl$ (1.55 mL, 0.02 mol) at 0 °C and the resulting mixture was stirred for 20 h at 25 °C. The mixture was washed with aq NH_4Cl (20 mL) and dried. Evaporation of the solvent under reduced pressure afforded the crude product, which was purified by column chromatography ($CHCl_3$–acetone, 9:1) to give pure **4**.

Diethyl 1,2-Di(methylsulfonyloxy)hexylphosphonate (4a)
Yield: 94%; yellow oil; R_f = 0.50.

IR (film): 1216, 1024 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.93 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$), 1.39 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.40 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.41–1.48 (m, 4 H, 2 × CH_2), 1.86–2.00 (m, 2 H, CH_2), 3.14 (s, 3 H, CH_3S), 3.25 (s, 3 H, CH_3S), 4.26 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2O), 4.27 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH_3CH_2O), 4.92–5.00 (m, 2 H,, PCH, PCHC*H*).

^{13}C NMR ($CDCl_3$): δ = 13.51 (s, CH_3 at C-6), 16.14 (d, $^3J_{P,C}$ = 5.6 Hz, *C*H$_3$CH$_2$OP), 22.04 (s, CH_2), 25.98 (s, CH_2), 31.01 (d, $^3J_{P,C}$ = 3.4 Hz, CH_2), 38.78 (s, CH_3S), 39.25 (s, CH_3S), 63.76 (d, $^2J_{P,C}$ = 6.8 Hz, 2 × CH$_3$*C*H$_2$O), 74.92 (d, $^1J_{P,C}$ = 165.9 Hz, PCH), 78.90 (d, $^2J_{P,C}$ = 7.1 Hz, PCH*C*H).

^{31}P NMR ($CDCl_3$): δ = 14.87.

Anal. Calcd for $C_{12}H_{27}O_9PS_2$: C, 35.12; H, 6.63. Found: C, 35.38; H, 6.61.

Diethyl 1,2-Di(methylsulfonyloxy)heptylphosphonate (4b)
Yield: 84%; yellow oil; R_f = 0.50.

IR (film): 1226, 1044 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.90 (t, $^3J_{H,H}$ = 6.7 Hz, 3 H, C*H*$_3$CH$_2$), 1.24–1.35 (m, 2 H, CH_2),1.39 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.40 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.40–1.49 (m, 4 H, 2 × CH_2), 1.90–2.00 (m, 2 H, CH_2), 3.14 (s, 3 H, CH_3S), 3.24 (s, 3 H, CH_3S), 4.15–4.28 (m, 4 H, 2 × CH$_3$C*H*$_2$O), 4.92–5.00 (m, 2 H, PCH, PCHC*H*).

^{13}C NMR ($CDCl_3$): δ = 12.92 (s, CH_3), 15.38 (d, $^3J_{P,C}$ = 5.6 Hz, 2 × *C*H$_3$CH$_2$O), 20.87 (s, CH_2), 22.00 (s, CH_2), 25.91 (s, CH_2), 31.11 (d, $^3J_{P,C}$ = 3.5 Hz, CH_2), 38.75 (s, CH_3S), 39.21 (s, CH_3S), 63.03 (d, $^2J_{P,C}$ = 6.5 Hz, 2 × CH$_3$*C*H$_2$O), 74.19 (d, $^1J_{P,C}$ = 167.5 Hz, PCH), 78.12 (d, $^2J_{P,C}$ = 7.2 Hz, PCH*C*H).

^{31}P NMR ($CDCl_3$): δ = 14.86.

Anal. Calcd for $C_{13}H_{29}O_9PS_2$: C, 36.78; H, 6.89. Found: C, 36.89; H, 6.84.

Diethyl 1,2-Di(methylsulfonyloxy)-3-methylbutylphosphonate (4c)
Yield: 78%; light yellow crystals; R_f = 0.41; mp 112–114 °C.

IR (film): 1216, 1016 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.03 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, C*H*$_3$CH), 1.14 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, C*H*$_3$CH), 1.39 (td, $^3J_{H,H}$ = 7.0 Hz, $^4J_{P,H}$ = 0.5 Hz, 3 H, C*H*$_3$CH$_2$O), 1.40 (td, $^3J_{H,H}$ = 7.0 Hz, $^4J_{P,H}$ = 0.5 Hz, 3 H, C*H*$_3$CH$_2$O), 2.29 [sept d, $^3J_{H,H}$ = 6.7 Hz, $^3J_{H,H}$ = 3.0 Hz, 1 H, (CH$_3$)$_2$C*H*], 3.20 (s, 3 H, CH_3S), 3.27 (s, 3 H, CH_3S), 4.25 (dq, $^3J_{P,H}$ = 8.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.27 (dq, $^3J_{P,H}$ = 8.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.86 (ddd, $^3J_{H,H}$ = 8.2 Hz, $^3J_{P,H}$ = 5.0 Hz, $^3J_{H,H}$ = 3.0 Hz, 1 H, PCHC*H*), 5.00 (dd, $^2J_{P,H}$ = 9.5 Hz, $^3J_{H,H}$ = 8.2 Hz, 1 H, PCH).

^{13}C NMR ($CDCl_3$): δ = 15.84 (s, *C*H$_3$CH), 16.31 (d, $^3J_{P,C}$ = 5.6 Hz, *C*H$_3$CH$_2$O), 20.18 (s, *C*H$_3$CH), 29.07 [s, (CH$_3$)$_2$*C*H], 39.24 (s, CH_3S), 39.63 (s, CH_3S), 63.89 (d, $^2J_{P,C}$ = 7.2 Hz, CH$_3$*C*H$_2$OP), 64.00 (d, $^2J_{P,C}$ = 7.0 Hz, CH$_3$*C*H$_2$O), 74.78 (d, $^1J_{P,C}$ = 164.0 Hz, PCH), 82.82 (d, $^2J_{P,C}$ = 10.7 Hz, PCH*C*H).

^{31}P NMR ($CDCl_3$): δ = 15.40.

Anal. Calcd for $C_{11}H_{25}O_9PS_2$: C, 33.33; H, 6.36. Found: C, 33.21; H, 6.34.

Diethyl 2-Cyclohexyl-1,2-di(methylsulfonyloxy)ethylphosphonate (4d)
Yield: 75%; light yellow oil; R_f = 0.49.

IR (film): 1224, 1020 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22–1.31 (m, 4 H, 2 × CH_2), 1.39 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.40 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.65–1.92 [m, 7 H, 3 × CH_2, C*H*(CH$_2$)$_5$], 3.19 (s, 3 H, CH_3S), 3.27 (s, 3 H, CH_3S), 4.25 (dq, $^3J_{P,H}$ = 8.0 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.26 (dq, $^3J_{P,H}$ = 8.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.82 (ddd, $^3J_{H,H}$ = 8.0 Hz, $^3J_{P,H}$ = 5.5 Hz, $^3J_{H,H}$ = 3.2 Hz, 1 H, PCHC*H*), 5.06 (dd, $^2J_{P,H}$ = 9.7 Hz, $^3J_{H,H}$ = 8.0 Hz, 1 H, PCH).

^{13}C NMR ($CDCl_3$): δ = 16.30 (d, $^3J_{P,C}$ = 5.1 Hz, *C*H$_3$CH$_2$O), 16.34 (d, $^3J_{P,C}$ = 5.0 Hz, *C*H$_3$CH$_2$O), 25.75 (s, CH_2), 26.28 [d, $^3J_{P,C}$ = 18.6 Hz, *C*H(CH$_2$)$_5$], 30.36 (s, 2 × CH_2), 31.49 (s, 2 × CH_2), 39.26 (s, CH_3S), 39.60 (s, CH_3S), 63.89 (d, $^2J_{P,C}$ = 6.9 Hz, CH$_3$*C*H$_2$O), 63.99 (d, $^2J_{P,C}$ = 6.4 Hz, CH$_3$*C*H$_2$O), 74.33 (d, $^1J_{P,C}$ = 164.5 Hz, PCH), 82.52 (d, $^2J_{P,C}$ = 10.1 Hz, PCH*C*H).

^{31}P NMR ($CDCl_3$): δ = 15.55.

Anal. Calcd for $C_{14}H_{29}O_9PS_2$: C 38.53, H 6.70. Found: C 38.68, H 6.67.

Diethyl 1,2-Di(methylsulfonyloxy)-4-phenylbutylphosphonate (4e)
Yield: 79%; yellow oil; R_f = 0.30.

IR (film): 1264, 1024 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.34 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.35 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 2.24–2.32 (m, 2 H, CH_2), 2.79–2.85 (m, 2 H, PhC*H*$_2$), 3.14 (s, 3 H, CH_3S), 3.23 (s, 3 H, CH_3S), 3.99–4.05 (m, 1 H, PCHC*H*), 4.21 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.22 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 4.96–5.06 (m, 1 H, PCH), 7.18–7.30 (m, 5 H, CH_{Ar}).

^{13}C NMR ($CDCl_3$): δ = 16.20 (s, *C*H_3CH$_2$O), 16.27 (s, *C*H_3CH$_2$O), 30.24 (s, CH_2), 33.14 (d, $^3J_{C,P}$ = 3.5 Hz, CH_2), 38.91 (s, CH_3S), 39.36 (s, CH_3S), 63.93 (d, $^2J_{C,P}$ = 6.2 Hz, CH_3*C*H$_2$O), 64.02 (d, $^2J_{C,P}$ = 5.0 Hz, CH_3*C*H$_2$O), 74.84 (d, $^1J_{C,P}$ = 166.3 Hz, PCH), 78.08 (d, $^2J_{C,P}$ = 7.1 Hz, PCH*C*H), 126.17 (s, 2 × CH_{Ar}), 128.35 (s, CH_{Ar}), 128.42 (s, 2 × CH_{Ar}), 139.98 (s, C_{Ar}).

^{31}P NMR ($CDCl_3$): δ = 14.69.

Anal. Calcd for $C_{16}H_{27}O_9PS_2$: C, 41.91; H, 5.94. Found: C, 41.79; H, 5.97.

1,2-Di(methylsulfonyloxy)alkylphosphonic Acids 5a–e; General Procedure

A mixture of phosphonate **4** (0.01 mol) and bromotrimethylsilane (4.30 mL, 0.04 mol) in CH_2Cl_2 (50 mL) was left for 5 d at 25 °C. The solvent was evaporated under reduced pressure and the residue was dissolved in EtOH (10 mL) and stirred for 15 min. Evaporation of the solvent afforded crude **6**, which was used in the next step.

1,2-Di(methylsulfonyloxy)hexylphosphonic Acid (5a)

Yield: 95%; light yellow oil.

IR (film): 1216, 1024 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 0.92 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, C*H*$_3$CH$_2$), 1.29–1.41 (m, 2 H, CH_2), 1.44–1.55 (m, 2 H, CH_2), 1.92–2.04 (m, 2 H, CH_2), 3.19 (s, 3 H, CH_3S), 3.29 (s, 3 H, CH_3S), 4.94–5.08 (m, 2 H,, PCH, PCHC*H*).

^{13}C NMR (acetone-d_6): δ = 13.15 (s, CH_3), 17.26 (s, CH_2), 21.95 (s, CH_2), 25.94 (s, CH_2), 38.18 (s, CH_3S), 38.78 (s, CH_3S), 75.94 (d, $^1J_{P,C}$ = 164.7 Hz, PCH), 79.38 (d, $^2J_{P,C}$ = 5.5 Hz, PCH*C*H).

^{31}P NMR (acetone-d_6): δ = 13.65.

1,2-Di(methylsulfonyloxy)heptylphosphonic Acid (5b)

Yield: 95%; yellow oil.

IR (film): 1232, 1024 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 0.90 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3), 1.16–1.36 (m, 4 H, 2 × CH_2), 1.43–1.54 (m, 2 H, CH_2), 1.92–2.05 (m, 2 H, CH_2), 3.19 (s, 3 H, CH_3S), 3.29 (s, 3 H, CH_3S), 4.96–5.10 (m, 2 H, PCH, PCHC*H*).

^{13}C NMR (acetone-d_6): δ = 13.21 (s, CH_3), 18.77 (s, CH_2), 21.11 (s, CH_2), 25.46 (s, CH_2), 30.94 (s, CH_2), 38.76 (s, CH_3S), 39.32 (s, CH_3S), 74.79 (d, $^1J_{P,C}$ = 164.5 Hz, PCH), 78.86 (d, $^2J_{P,C}$ = 5.8 Hz, PCH*C*H).

^{31}P NMR (acetone-d_6): δ = 13.51.

1,2-Di(methylsulfonyloxy)-3-methylbutylphosphonic Acid (5c)

Yield: 94%; light yellow oil.

IR (film): 1216, 1016 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 1.03 (d, $^3J_{H,H}$ = 6.2 Hz, 3 H, CH_3), 1.09 (d, $^3J_{H,H}$ = 6.2 Hz, 3 H, CH_3), 2.30–2.42 (m, 1 H, CH), 3.21 (s, 3 H, CH_3S), 3.26 (s, 3 H, CH_3S), 4.85 (ddd, $^3J_{P,H}$ = 9.7 Hz, $^3J_{H,H}$ = 7.7 Hz, $^3J_{H,H}$ = 3.0 Hz, 1 H, PCH*C*H), 5.00 (dd, $^2J_{P,H}$ = 10.7 Hz, $^3J_{H,H}$ = 7.7 Hz, 1 H, PCH).

^{13}C NMR (acetone-d_6): δ = 15.89 (s, CH_3), 20.06 (s, CH_3), 28.79 [s, (CH_3)$_2$*C*H], 39.25 (s, CH_3S), 39.62 (s, CH_3S), 74.23 (d, $^1J_{P,C}$ = 164.8 Hz, PCH), 82.13 (d, $^2J_{P,C}$ = 5.7 Hz, PCH*C*H).

^{31}P NMR (acetone-d_6): δ = 13.93.

2-Cyclohexyl-1,2-di(methylsulfonyloxy)ethylphosphonic Acid (5d)

Yield: 96%; light yellow oil.

IR (film): 1264, 1024 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 1.18–1.32 (m, 6 H, 3 × CH_2), 1.43–1.84 [m, 5 H, C*H*(CH_2)$_5$, 2 × CH_2], 3.18 (s, 3 H, CH_3S), 3.22 (s, 3 H, CH_3S), 4.84–4.88 (m, 1 H, PCH*C*H), 5.05 (dd, $^2J_{P,H}$ = 12.5 Hz, $^3J_{H,H}$ = 7.5 Hz, 1 H, PCH).

^{13}C NMR (acetone-d_6): δ = 25.01 (s, CH_2), 26.02 [s, *C*H(CH_2)$_5$], 30.36 (s, 2 × CH_2), 31.49 (s, 2 × CH_2), 39.11 (s, CH_3S), 39.49 (s, CH_3S), 74.47 (d, $^1J_{P,C}$ = 164.9 Hz, PCH), 82.32 (d, $^2J_{P,C}$ = 5.1 Hz, PCH*C*H).

^{31}P NMR (acetone-d_6): δ = 14.22.

1,2-Di(methylsulfonyloxy)-4-phenylbutylphosphonic Acid (5e)

Yield; 92%; light yellow oil.

IR (film): 1244, 1048 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 2.21–2.35 (m, 2 H, CH_2), 2.76–2.91 (m, 2 H, PhC*H*$_2$), 3.22 (s, 3 H, CH_3S), 3.31 (s, 3 H, CH_3S), 5.11–5.14 (m, 1 H, PCHC*H*), 5.15 (dd, $^2J_{P,H}$ = 12.5 Hz, $^3J_{H,H}$ = 5.7 Hz, 1 H, PCH), 7.20–7.35 (m, 5H, CH_{Ar}).

^{13}C NMR (acetone-d_6): δ = 30.04 (s, CH_2), 32.97 (s, CH_2), 38.90 (s, CH_3S), 39.34 (s, CH_3S), 74.25 (d, $^1J_{C,P}$ = 164.8 Hz, PCH), 78.18 (d, $^2J_{C,P}$ = 7.1 Hz, PCH*C*H), 126.19 (s, 2 × CH_{Ar}), 128.15 (s, CH_{Ar}), 128.33 (s, 2 × CH_{Ar}), 139.74 (s, C_{Ar}).

^{31}P NMR (acetone-d_6): δ = 13.02.

(*E*)-Alk-1-enylmethanesulfonates 6a–e; General Procedure

To a solution of a corresponding phosphonic acid **5** (0.01 mol) in Et_2O (10 mL) was added aq sat. $NaHCO_3$ (5 mL). The mixture was stirred for 2 h at 25 °C. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography ($CHCl_3$–acetone, 7:3) affording pure **6**.

(*E*)-Hex-1-enyl Methanesulfonate (6a)

Yield: 80%; light yellow oil; R_f = 0.44.

IR (film): 1648 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.91 (t, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3), 1.25–1.42 (m, 4 H, 2 × CH_2), 2.03 (tdd, $^3J_{H,H}$ = 7.5 Hz, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,H}$ = 1.2 Hz, 2 H, C*H*$_2$CH=), 3.04 (s, 3 H, CH_3S), 5.63 (dt, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*=CHO), 6.47 (dt, $^3J_{H,H}$ = 12.0 Hz, $^4J_{H,H}$ = 1.2 Hz, 1 H, OC*H*=CH).

^{13}C NMR ($CDCl_3$): δ = 13.51 (s, CH_3), 21.79 (s, CH_2), 26.37 (s, CH_2), 30.91 (s, *C*H$_2$CH=CH), 36.60 (s, CH_3S), 121.13 (s, *C*H=CHO), 135.01 (s, O*C*H=CH).

Anal. Calcd for $C_7H_{14}O_3S$: C, 47.17; H, 7.92. Found: C, 47.26; H, 7.89.

(*E*)-Hept-1-enyl Methanesulfonate (6b)

Yield: 75%; light yellow oil; R_f = 0.44.

IR (film): 1648 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.92 (t, $^3J_{H,H}$ = 6.7 Hz, 3 H, C*H*$_3$CH$_2$), 1.20–1.43 (m, 4 H, 2 × CH_2), 1.78–1.85 (m, 2 H, CH_2), 2.00 (tdd, $^3J_{H,H}$ = 7.5 Hz, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,H}$ = 1.2 Hz, 2 H, C*H*$_2$CH=CH), 3.06 (s, 3 H, CH_3S), 5.75 (dt, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.2 Hz, 1 H, C*H*=CHO), 6.42 (dt, $^3J_{H,H}$ = 12.0 Hz, $^4J_{H,H}$ = 1.2 Hz, 1 H, OC*H*=CH).

^{13}C NMR ($CDCl_3$): δ = 13.50 (s, *C*H$_3$CH$_2$), 21.74 (s, CH_2), 22.81 (s, CH_2), 26.33 (s, CH_2), 30.65 (s, *C*H$_2$CH=CH), 36.54 (s, CH_3S), 121.14 (s, *C*H=CHO), 135.11 (s, *C*H=CHO).

Anal. Calcd for $C_8H_{16}O_3S$: C, 49.97; H, 8.39. Found: C, 49.81; H, 8.43.

(*E*)-3-Methylbut-1-enyl Methanesulfonate (6c)
Yield: 70%; light yellow oil; R_f = 0.46.

IR (film): 1668 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.05 [d, $^3J_{H,H}$ = 6.7 Hz, 6 H, $(CH_3)_2CH$], 2.37 [dseptd, $^3J_{H,H}$ = 7.7 Hz, $^3J_{H,H}$ = 6.7 Hz, $^4J_{H,H}$ = 1.3 Hz, 1 H, $(CH_3)_2CH$], 3.04 (s, 3 H, CH_3S), 5.61 (dd, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.6 Hz, 1 H, C*H*=CHO), 6.47 (dd, $^3J_{H,H}$ = 12.0 Hz, $^4J_{H,H}$ = 1.3 Hz, 1 H, OC*H*=CH).

^{13}C NMR ($CDCl_3$): δ = 21.87 (s, CH_3CH), 22.11 (s, CH_3CH), 26.66 [s, $(CH_3)_2CH$], 36.35 (s, CH_3S), 127.58 (s, *C*H=CHO), 133.88 (s, O*C*H=CH).

Anal. Calcd for $C_6H_{12}O_3S$: C, 43.88; H, 7.37. Found: C, 43.59; H, 7.33.

(*E*)-2-Cyclohexylvinyl Methanesulfonate (6d)
Yield: 63%; light yellow oil; R_f = 0.54.

IR (film): 1664 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.04–1.26 (m, 6 H, 3 × CH_2), 1.65–1.76 (m, 4 H, 2 × CH_2), 1.97–2.09 [m, 1 H, C*H*$(CH_2)_5$], 3.03 (s, 3 H, CH_3S), 5.58 (dd, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*=CHO), 6.46 (dd, $^3J_{H,H}$ = 12.0 Hz, $^4J_{H,H}$ = 1.2 Hz, 1 H, OC*H*=CH).

^{13}C NMR ($CDCl_3$): δ = 25.47 (s, CH_2), 25.56 (s, 2 × CH_2), 32.50 (s, 2 × CH_2), 36.10 [s, *C*H$(CH_2)_5$], 36.50 (s, CH_3S), 126.55 (s, *C*H=CHO), 134.21 (s, O*C*H=CH).

Anal. Calcd for $C_6H_{12}O_3S$: C, 52.92; H, 7.89. Found: C, 53.00; H, 7.93.

(*E*)-4-Phenylbut-1-enyl Methanesulfonate (6e)
Yield: 74%; light yellow oil; R_f = 0.40.

IR (film): 1640 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.31–2.40 (m, 2 H, CH_2CH=), 2.73 (t, $^3J_{H,H}$ = 7.2 Hz, 2 H, PhCH_2), 2.92 (s, 3 H, CH_3S), 5.62 (dt, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*=CHO), 6.43 (dt, $^3J_{H,H}$ = 12.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, OC*H*=CH), 7.14–7.29 (m, 5 H, CH_{Ar}).

^{13}C NMR ($CDCl_3$): δ = 28.57 (s, CH_2), 35.24 (s, *C*H_2CH=), 36.65 (s, CH_3S), 119.97 (s, *C*H=CHO), 126.09 (s, 2 × CH_{Ar}), 128.37 (s, 3 × CH_{Ar}), 135.71 (s, *C*H=CHO), 140.51 (s, C_{Ar}).

Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.24. Found: C, 58.46; H, 6.20.

α-Hydroxy Aldehydes 8a–e; General Procedure
To a solution of a corresponding alk-1-enyl mesylate **6** (5.0 mmol) in acetone (4 mL) and *t*-BuOH (16 mL) were added NMO (0.64 g, 5.5 mmol) and OsO_4 (4 mg, 0.016 mmol) and the resulting mixture was stirred at 25 °C for 3 d. H_2O (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The corresponding crude product was used in the next step (see below).

(*R*)- and (*S*)-α-Hydroxyhexanals 8a
AD-mix-α or AD-mix-β (2.0 g), $K_2OsO_4·H_2O$ (4.5 mg, 0.8 mol%) were dissolved in *t*-BuOH–H_2O (1:1, 15 mL) at 25 °C. $MeSO_2NH_2$ (0.19 g, 2.0 mmol) was added to the mixture at 0 °C, followed by hex-1-enyl mesylate (**6a**; 0.36 g, 2.0 mmol). The mixture was stirred at 25 °C for 3 d. H_2O (10 mL) was added and the resulting mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The corresponding crude product was used in the next step (see below).

Ethyl (*E*)-4-Hydroxyalk-2-enoates 10a–e; (*E*)-4-Hydroxyoct-2-enenitrile (13); Diethyl (*E*)-3-Hydroxyhept-1-enylphosphonate (14); General Procedure
To a solution of NaH (0.12 g, 0.5 mmol) in THF (10 mL) were added **9**, **11**, or **12** (0.5 mmol) and the α-hydroxy aldehyde **8** and the resulting mixture was stirred at 25 °C for 20 h. H_2O (20 mL) was added and the solvent was evaporated under reduced pressure. The residue was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography to give pure **10a–e**, **13**, and **14**, respectively.

Ethyl (*E*)-4-Hydroxyoct-2-enoate (10a)[11]
Yield: 66%; light yellow oil; R_f = 0.29 (hexane–EtOAc, 4:1).

IR (film): 1648 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.91 (t, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3CH$_2$), 1.30 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH$_2$O), 1.26–1.39 (m, 4 H, 2 × CH_2), 1.52–1.61 (m, 2 H, CH_2), 4.21 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$CH_2O), 4.31 (tdd, $^3J_{H,H}$ = 6.7 Hz, $^3J_{H,H}$ = 5.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, C*H*OH), 6.03 (dd, $^3J_{H,H}$ = 15.7 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, O=CC*H*=CH), 6.95 (dd, $^3J_{H,H}$ = 15.7 Hz, $^3J_{H,H}$ = 5.0 Hz, 1 H, C*H*=CHC=O).

(*R*)-10a
$[\alpha]_D^{20}$ –21.59 (*c* = 1.00, $CHCl_3$).

(*S*)-10a
$[\alpha]_D^{20}$ +18.19 (*c* = 1.00, $CHCl_3$).

Ethyl (*E*)-4-Hydroxynon-2-enoate (10b)
Yield: 64%: light yellow oil; R_f = 0.29 (hexane–EtOAc, 4:1).

IR (film): 1660 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.91 (t, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3CH$_2$), 1.28 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH$_2$O), 1.26–1.39 (m, 4 H, 2 × CH_2), 1.52–1.61 (m, 5 H, 2 × CH_2, OH), 4.20 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$CH_2O), 4.30 (tdd, $^3J_{H,H}$ = 6.7 Hz, $^3J_{H,H}$ = 5.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, C*H*OH), 6.05 (dd, $^3J_{H,H}$ = 15.7 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, O=CC*H*=CH), 6.94 (dd, $^3J_{H,H}$ = 15.7 Hz, $^3J_{H,H}$ = 5.0 Hz, 1 H, C*H*=CHC=O).

^{13}C NMR ($CDCl_3$): δ = 13.71 (CH_3CH_2), 13.96 (CH_3CH_2O), 17.48 (CH_2), 22.21 (CH_2), 27.31 (CH_2), 36.00 (CH_2), 60.20 (CH_2O), 70.87 (CHOH), 119.25 (O=C*C*H=CH), 150.03 (*C*H=CHC=O), 166.25 (C=O).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.73; H, 10.10.

Ethyl (*E*)-4-Hydroxy-5-methylhex-2-enoate (10c)[11]
Yield: 63%; light yellow oil; R_f = 0.25 (hexane–EtOAc, 4:1).

^1H NMR ($CDCl_3$): δ = 0.95 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3CH), 0.96 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3CH), 1.30 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH$_2$O), 2.37 [sept d, $^3J_{H,H}$ = 6.7 Hz, $^3J_{H,H}$ = 5.2 Hz, 1 H, $(CH_3)_2CH$], 4.10 (ddd, $^3J_{H,H}$ = $^3J_{H,H}$ = 5.2 Hz, $^4J_{H,H}$ = 1.7 Hz, 1 H, C*H*OH), 4.21 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$CH_2O), 6.05 (dd, $^3J_{H,H}$ = 15.7 Hz, $^4J_{H,H}$ = 1.7 Hz, 1 H, O=CC*H*=CH), 6.96 (dd, $^3J_{H,H}$ = 15.7 Hz, $^3J_{H,H}$ = 5.2 Hz, 1 H, C*H*=CHC=O).

Ethyl (*E*)-4-Cyclohexyl-4-hydroxybut-2-enoate (10d)[11]
Yield: 62%; light yellow oil; R_f = 0.29 (hexane–EtOAc, 3:1).

IR (film): 1724, 1660 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.00–1.29 (m, 4 H, 2 × CH_2), 1.30 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH$_2$O), 1.45–1.51 (m, 6 H, 3 × CH_2), 1.63–1.76 [m, 1 H, C*H*$(CH_2)_5$], 4.00–4.10 (m, 2 H, C*H*OH, OH), 4.21 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$CH_2O), 6.02 (dd, $^3J_{H,H}$ = 15.7 Hz,

$^4J_{H,H}$ = 1.0 Hz, 1 H, O=CC*H*=CH), 6.96 (dd, $^3J_{H,H}$ = 15.7 Hz, $^3J_{H,H}$ = 5.2 Hz, 1 H, C*H*=CHC=O).

Ethyl (*E*)-4-Hydroxy-6-phenylhex-2-enoate (10e)
Yield: 61%; light yellow oil; R_f = 0.42 (hexane–EtOAc, 4:1).

IR (film): 1724, 1648 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3CH$_2$O), 1.27–1.38 (m, 2 H, CH_2), 3.00 (br s, 1 H, OH), 4.10 (q, $^3J_{H,H}$ = 7.0 Hz, 2 H, CH$_3$CH_2O), 4.15–4.26 (m, 1 H, C*H*OH), 6.07 (dd, $^3J_{H,H}$ = 15.7 Hz, $^4J_{H,H}$ = 1.0 Hz, 1 H, O=CC*H*=CH), 6.98 (dd, $^3J_{H,H}$ = 15.7 Hz, $^3J_{H,H}$ = 5.5 Hz, 1 H, C*H*=CHC=O), 7.18–7.29 (m, 5 H, CH_{Ar}).

^{13}C NMR ($CDCl_3$): δ = 14.84 (*C*H$_3$CH$_2$O), 28.57 (Ph*C*H$_2$), 28.97 (CH_2), 31.11 (CH_2), 32.69 (CH_2), 60.22 (CH_2O), 69.87 (CHOH), 120.25 (*C*H=CHC=O), 126.09 (2 × CH_{Ar}), 128.98 (3 × CH_{Ar}), 135.71 (*C*H=CHC=O), 140.14 (C_{Ar}), 149.01 (O=C*C*H=CH), 168.98 (C=O).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.50; H, 7.69.

(*E*)-4-Hydroxyoct-2-enenitrile (13)
Yield: 60%; light yellow oil; R_f = 0.25 (hexane–EtOAc, 4:1).

IR (film): 2225, 1664 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.92 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_3), 1.22–1.40 (m, 4 H, 2 × CH_2), 1.51–1.63 (m, 3 H, CH_2, OH), 4.32 (tdd, $^3J_{H,H}$ = 7.2 Hz, $^3J_{H,H}$ = 4.0 Hz, $^4J_{H,H}$ = 2.0 Hz, 1 H, CH), 5.68 (dd, $^3J_{H,H}$ = 16.2 Hz, $^4J_{H,H}$ = 2.0 Hz, 1 H, NCC*H*=CH), 6.77 (dd, $^3J_{H,H}$ = 16.2 Hz, $^3J_{H,H}$ = 4.0 Hz, 1 H, NCCH=C*H*).

^{13}C NMR ($CDCl_3$): δ = 13.83 (*C*H$_3$CH$_2$), 22.39 (CH_2), 27.14 (CH_2), 35.99 (CH_2), 70.86 (CH), 98.49 (CN), 117.36 (NC*C*H=CH), 156.90 (CNCH=*C*H).

Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.15. Found: C, 68.87; H, 9.48; N, 10.10.

(*R*)-13
$[\alpha]_D^{20}$ –21.45 (*c* = 1.30, $CHCl_3$).

(*S*)-13
$[\alpha]_D^{20}$ +18.11 (*c* = 1.30, $CHCl_3$).

Diethyl (*E*)-3-Hydroxyhept-1-enylphosphonate (14)[2]
Yield: 59%; light yellow oil; R_f = 0.27 (EtOAc).

IR (film): 1662, 1256, 1040 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.91 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_3), 1.34 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, 2 × CH_3CH$_2$O), 1.34–1.43 (m, 4 H, 2 × CH_2), 1.54–1.60 (m, 2 H, CH_2), 4.07 (dq, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.0 Hz, 4 H, 2 × CH$_3$CH_2O), 4.24–4.30 (m, 1 H, C*H*OH), 5.93 (ddd, $^2J_{P,H}$ = 21.0 Hz, $^3J_{H,H}$ = 17.0 Hz, $^4J_{H,H}$ = 1.5 Hz, 1 H, PC*H*=CH), 6.79 (ddd, $^3J_{P,H}$ = 22.5 Hz, $^3J_{H,H}$ = 17.00 Hz, $^3J_{H,H}$ = 4.0 Hz, 1 H, PCH=C*H*).

^{13}C NMR ($CDCl_3$): δ = 13.84 (s, CH_3), 16.20 (d, $^3J_{P,C}$ = 6.4 Hz, *C*H$_3$CH$_2$O), 22.45 (s, CH_2), 27.36 (s, CH_2), 36.03 (d, $^4J_{P,C}$ = 1.6 Hz,, CH_2), 61.69 (d, $^2J_{P,C}$ = 5.6 Hz, CH$_3$*C*H$_2$O), 71.37 (d, $^3J_{P,C}$ = 21.2 Hz, CHOH), 114.64 (d, $^1J_{P,C}$ = 188.6 Hz, P*C*H=CH), 155.62 (d, $^2J_{P,C}$ = 4.4 Hz, PCH=*C*H).

^{31}P NMR ($CDCl_3$): δ = 19.33.

Anal. Calcd for $C_{11}H_{23}O_4P$: C, 52.79; H, 9.26. Found: C, 52.94; H, 9.21.

(*R*)-14
$[\alpha]_D^{20}$ –21.89 (*c* = 1.45, $CHCl_3$).

(*S*)-14
$[\alpha]_D^{20}$ +18.25 (*c* = 1.45, $CHCl_3$).

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