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Synthesis of Nonracemic Allylic Hydroxy Phosphonates via Alkene Cross Metathesis

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Allylic hydroxy phosphonates and their derivatives can be interconverted by using cross metathesis with second generation Grubbs catalyst. The absolute stereochemistry of the starting phosphonate is conserved in the product. Cross metathesis reaction of the acrolein-derived phosphonate **2a** yields a series of functionalized allylic hydroxy phosphonates. However, the cross metathesis reaction is often accompanied by competing dimerization and alkene migration reactions leading to a reduction in yield. The cinnamaldehyde- and crotonaldehyde-derived phosphonates **2b** and **2c** were also examined. In general, the metathesis reactions of phosphonates **2b** and **2c** are considerably slower than those for phosphonate **2a** leading to mixtures. Several hydroxyl-protected derivatives of the phosphonate **2a** (methyl carbonate **3a**, acetate **4a**, *N*-tosyl carbamate **5a**, TBDMS **6a**, and acetoacetate **7a**) undergo metathesis without competing side reactions to give substituted allylic phosphonates in good to excellent yield.

Introduction

A major emphasis in the development of new organic reactions is the control of absolute stereochemistry via chiral catalysts.[1] For over 10 years there has been an interest in the asymmetric synthesis of hydroxy phosphonates,[2,3] precipitated not only by their biological activity,[4] but also because they are attractive precursors to other α- and γ-substituted phosphonates.[5−7] Allylic hydroxy phosphonates are particularly attractive because, like allylic alcohols, they participate in a number of stereoselective or stereospecific reactions leading to highly functionalized phosphonates.[7]

Although there are many attractive routes for the synthesis of hydroxy phosphonates,[2,3] nonracemic allylic hydroxy phosphonates are most conveniently generated by enzymatic kinetic resolution,[8] or asymmetric catalysis.[9] Both methods have attained varying levels of success, but a general, reproducible, high-yielding, and highly selective method is still unavailable. We reasoned that it would be easier to optimize reaction conditions to

(1) For examples see: *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley and Sons: New York, 1994. Cervinka, O. *Enantioselective Reactions in Organic Chemistry*; Ellis Horwood: New York, 1995. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Chiral Catalysis, Vol. 5; Academic Press: New York, 1985.

(2) For reviews of the asymmetric synthesis of hydroxy phosphonates see: (a) Wiemer, D. F. *Tetrahedron* **1997**, *53*, 16609. (b) Davies, S. R.; Mitchell, M. C.; Cain, C. P.; Devitt, P. G.; Taylor, R. J.; Kee, T. P. *J. Organomet. Chem.* **1998**, *550*, 29. (c) Gröger, H.; Hammer, B. *Chem. Eur. J.* **2000**, *6*, 943.

(3) For recent reports of the asymmetric synthesis of hydroxy phosphonates see: (a) Skropeta, D.; Schmidt R. R. *Tetrahedron*: *Asymmetry* **2003**, *14*, 265. (b) Pàmies, O.; Bäckvall, J.-E. *J. Org. Chem.* **2003**, *68*, 4815. (c) Zhang, Y.; Yuan, C.; Li, Z. *Tetrahedron* **2002**, *58*, 2973. (d) Burk, M. J.; Stammers, T. A.; Straub, J. A. *Org. Lett.* **1999**, *1*, 387. (e) Kolodiazhnyi, O. I.; Griskkun, E. V.; Sheiko, S.; Demchuk, O.; Thoennessen, H.; Jones, P. G.; Schmutzler, R. *Tetrahedron*: *Asymmetry* **1998**, *9*, 1645.

(4) For examples see: (a) Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E. *Tetrahedron Lett.* **1990**, *31*, 5587. (b) Stowasser, B.; Budt, K.-H.; Jian-Qi, L.; Peyman, A.; Ruppert, D. *Tetrahedron Lett.* **1992**, *33*, 6625.

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(6) For example see: (a) Zhu, J.; Lu, X. *Tetrahedron Lett.* **1987**, *28*, 1897. (b) Zhu, J.; Lu, X. *Chem. Commun.* **1987**, 1318. (c) Cooper, D.; Trippett, S. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2127. (d) Öhler, E.; Kotzinger, S. *Synthesis* **1993**, 497. (e) Öhler, E.; Kanzler, S. *Liebigs Ann.* **1997**, 1437. (f) Blackburn, G. M.; Kent, D. E. *Chem. Commun.* **1981**, 511. (g) Hammond, G. B.; de Mendonca *J. Fluorine Chem.* **1999**, 1. (h) Attolini, M.; Maffei, M.; Principato, B.; Peiffer, G. *Synlett* **1997**, 384.

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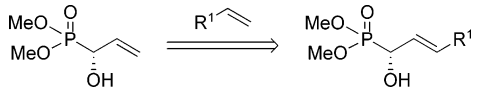
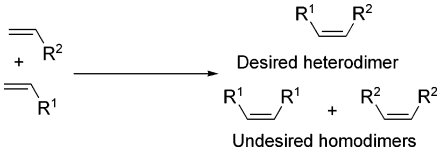
SCHEME 1. Proposed Cross Metathesis



SCHEME 2. A Generic Cross Metathesis Reaction



produce a single, structurally simple phosphonate in high enantiomeric excess, high yield, and large quantities, which would serve as a convenient precursor to more complex substituted allylic hydroxy phosphonates. This could conceivably be achieved by a cross metathesis reaction of an acrolein-derived phosphonate and an alkene (Scheme 1).

The cross metathesis reaction has become a powerful tool for alkene synthesis.[10] Potentially, three possible products can be obtained including the desired heterodimeric product and two undesired homodimeric products (Scheme 2). Examples of cross metathesis (CM) and ring closing metathesis (RCM) involving vinyl and allyl phosphonates and related compounds have been reported.[11,12] However, metathesis reactions involving interconversion of allylic hydroxy phosphonates remain to be explored.

The hydroxy phosphonates **2a**−**c** were prepared by the addition of dimethyl phosphite to the corresponding aldehyde. The nonracemic phosphonates were prepared by catalytic asymmetric phosphonylation, using dimethyl tartrate and titanium isopropoxide as the catalyst,[9a] whereas the racemic compounds were prepared with use of Et_3N.[13] The enantiomeric excess of the nonracemic phosphonates was determined by HPLC on a chiral stationary phase or ^{31}P NMR spectroscopy with quinine as the shift reagent.[9a,14] The hydroxy phosphonate **2a** was converted into the corresponding carbonate **3a**, acetate **4a**, *N*-tosylcarbamate **5a**, *tert*-butyldimethylsilyl **6a**, and acetoacetate **7a** derivatives with standard reaction conditions (Scheme 3).

The acrolein-derived phosphonate **2a** (Table 1, entry 1) rapidly underwent self-metathesis with the Grubbs second generation ruthenium benzylidene catalyst in CH_2Cl_2 even in the presence of other alkenes to give dimer **8** in good yield. The dimer is insoluble in CH_2Cl_2 and precipitated from the reaction solution. Fortunately, when the cross metathesis reaction was performed in chloroform with excess alkene, dimer formation was suppressed in favor of heterometathesis.

The acrolein-derived phosphonate **2a** was converted to substituted allylic hydroxy phosphonates **2b**,**d**−**g** by treatment with Grubbs second-generation catalyst and a terminal alkene in chloroform at 40−45 °C in modest yield (Table 1). The formation of the substituted products was always accompanied by the formation of varying amounts of dimer **8**. The trans geometry (cis <10%) of the products was confirmed by comparison of the spectroscopic data of allylic hydroxy phosphonates with known alkene geometry. In the ^{13}C NMR spectra, the signals for C-1 in the trans isomers (∼69 ppm) are downfield of the cis isomers (∼64 ppm). In the ^{31}P NMR, the signals for the trans isomers are upfield of the cis isomers by approximately 0.5 ppm.

In addition to terminal olefins, metathesis of disubstituted olefins provided the corresponding products occasionally in higher yield. Phosphonate **2f** prepared utilizing *cis*-1,4-diacetoxy-2-butene (entry 7) provided the product in 61% yield, whereas a reaction utilizing allyl acetate (entry 6) gave less than a 30% yield. However, *trans*-stilbene (entry 3), a disubstituted olefin, was not as efficient as styrene (entry 2), a terminal alkene, in the formation of phosphonate **2b**. It was also observed that prolonged heating resulted in the formation of acyl phosphonate **9** as a new byproduct. The acyl phosphonate **9**, which exhibits a characteristic peak at 0.5 ppm in the ^{31}P NMR spectrum, probably arises via migration of the alkene from C(2)=C(3) to C(1)=C(2), followed by enol to ketone tautomerism.

Dimerization of the racemic acrolein phosphonate **2a** should, assuming the reaction rates are unaffected by stereochemistry, give a 50:50 mixture of the meso and RR/SS diastereoisomers, whereas the cross metathesis reaction of nonracemic acrolein phosphonate **2a** (70% ee, 85:15 R:S) is expected to give a mixture consisting of the meso diastereoisomer (26% y) and the RR/SS diastereoisomer (74% y, 97% ee). In practice, the racemic phosphonate **2a** typically gave a 75:25 mixture (by HPLC) of the meso and RR/SS diastereoisomers in the precipitated product isolated by filtration of the reaction mixture. The isolated dimer mixture (from racemic **2a)** was recrystallized from methanol to give pure meso diastereoisomer. Both the crude dimer mixture and the recrystallized meso isomer exhibited identical ^{31}P (24.5 ppm) and ^1H NMR spectra in DMSO solution. X-ray crystal data, obtained for several single crystals from a sample crystallized from MeOH, showed the presence of only the meso diastereoisomer (Figure 1). HPLC of samples of the crystallized (MeOH) or insoluble solid (CH_2Cl_2) and the corresponding solutions revealed that the RR/SS isomer is more soluble than the meso isomer in both methanol and CH_2Cl_2 since it remains in the mother liquor.

Alternatively, the nonracemic phosphonate (70% ee) gave a 25:75 mixture of meso to RR/SS diastereoisomers. Recrystallization of this mixture gave a solid predomi-

(10) For examples see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446. (b) Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58. (c) O'Leary, D. J.; Blackwell, H. E.; Washenfelder, R. A.; Miura, K.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 1091. (d) Crowe, W. E.; Zhang, Z. J. *J. Am. Chem. Soc.* **1993**, *115*, 10998. (e) Crowe, W. E.; Goldberg, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 5162. (f) Cossy, J.; BouzBouz, S.; Hoveyda, A. H. *J. Organomet. Chem.* **2001**, *624*, 327. (g) Chatterjee, A. K.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 1751.

(11) For examples see: (a) Chatterjee, A. K.; Choi, T.-L.; Grubbs, R. H. *Synlett* **2001**, 1034. (b) Lera, M.; Hayes, C. J. *Org. Lett.* **2001**, *3*, 2765. (c) Demchuk, O. M.; Pietrusiewicz, K. M.; Michrowska, A.; Grela, K. *Org. Lett.* **2003**, *5*, 3217.

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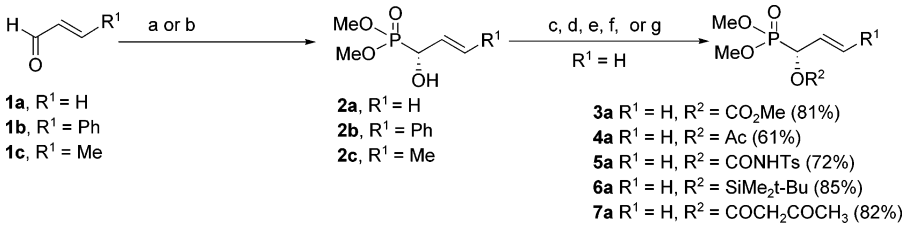
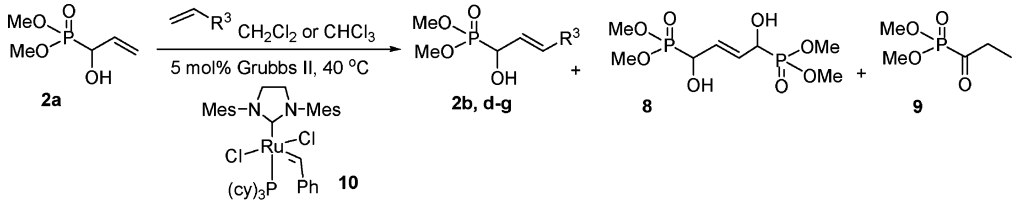
(14) Zymanczyk-Duda, E.; Skwarczynski, M.; Lejczak, B.; Karfarski, P. *Tetrahedron*: *Asymmetry* **1996**, *7*, 1277.

SCHEME 3. Preparation of Allylic Hydroxy Phosphonate Derivatives[a]



[a] Reagents and conditions: (a) dimethyl tartrate, Ti(O*i*Pr)$_4$, Et$_2$O, (MeO)$_2$P(O)H; (b) (MeO)$_2$P(O)H, Et$_3$N; (c) ClCO$_2$Me, Py, DMAP, CH$_3$CN; (d) AcCl, PVP, CH$_2$Cl$_2$; (e) TsNCO, CH$_2$Cl$_2$; (f) *t*-BuMe$_2$SiCl, imidazole, CH$_2$Cl$_2$; (g) diketene, DMAP, CH$_2$Cl$_2$:THF (1:1).

TABLE 1. Metathesis with Acrolein-Derived Phosphoate



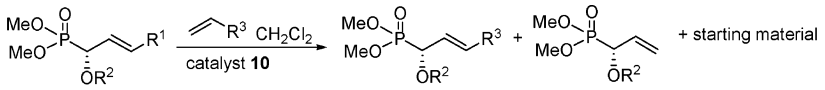
Entry	Alkene	Product	E.e. of **2a**	% Yield (e.e.)
1	**2a**	**8**	(±)	76[a] (±)
2		**2b**	70%	51[b] (70%)
3		**2b**	(±)	31[b] (±)
4		**2d**	(±)	57[b] (±)
5	TMS	**2e**	(±)	82[b] (±)
6	OAc	**2f**	(±)	<30[b] (±)
7	AcO OAc	**2f**	(±)	61[b] (±)
8		**2g**	70%	30[b] (70%)

[a] 5% catalyst **10**, CH$_2$Cl$_2$. [b] 5% catalyst **10**, CHCl$_3$, 5 equiv of alkene.

nating in the meso isomer (70:30) and a mother liquor containing an excess (12:88) of the RR/SS diastereoisomer. Attempted cross metathesis reaction with the meso dimer and 4-methyl-1-pentene or styrene in MeOH solution resulted in low conversion (<30%) over extended reaction times. In other solvents, little or no reaction was observed.

The cinnamyl **2b** and crotonyl **2c** phosphonates were examined to study the effect of allylic phosphonate substitution on the metathesis reaction. The cinnamyl phosphonate, in particular, was interesting because it can be recrystallized to >95% ee and, therefore, appeared to be a promising precursor for the synthesis of other hydroxy phosphonates of high enantiomeric excess.[7a,9a]

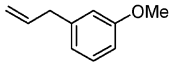
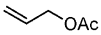
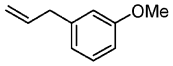
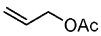
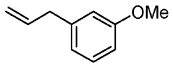
TABLE 2. Metathesis with Substituted Allylic Phosphonates



2b R^1 = Ph, R^2 = H
2c R^1 = Me, R^2 = H
3b R^1 = Ph, R^2 = CO_2Me
3c R^1 = Me, R^2 = CO_2Me

2 R^2 = H
3 R^2 = CO_2Me
for R^3 see table

2a R^2 = H
3a R^2 = CO_2Me

Entry	Phosphonate (R^1)	Phosphonate (R^2)	Alkene	Catalyst/ time	Product	% Yield (e.e.)
1	Ph (95% e.e) **2b**	H	 1.7 equiv	2.5% 12h	**2h**	50% conv[a] (>93%)
2	Ph (95% e.e.) **2b**	H	 5 equiv	5% 36h	**2d**	74% (95%)
3	Ph **2b**	H	 5 equiv.	5% 4 days	**2f**	NR
4	Ph **3b**	CO_2Me	 2 equiv.	5% 24h	**3h**	NR
5	Me **2c**	H	 3.75 equiv	3.75% 12h	**2d**	48%
6	Me **2c**	H	 5 equiv.	5% 12h	**2a** **2c** **2f**	20%[a] 24% 46%
7	Me **3c**	CO_2Me	 2 equiv.	5% 24h	**3a** **3c** **3h**	22%[a] 47% 36%

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

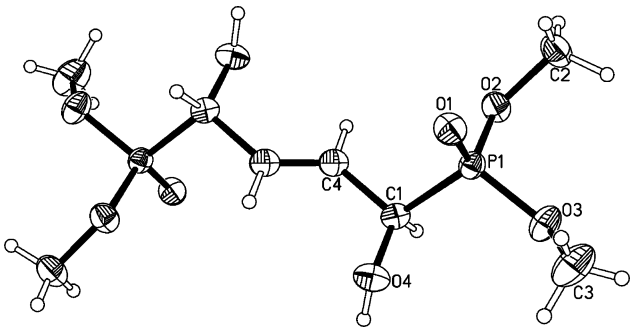
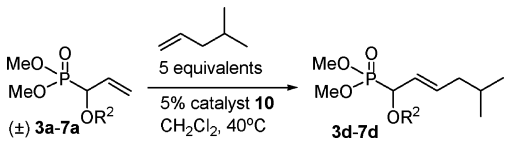


FIGURE 1. Projection view of the meso dimer with 50% thermal ellipsoids.

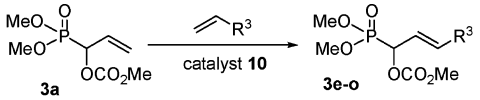
TABLE 3. Metathesis with Protected Acrolein Phosphonate Derivatives

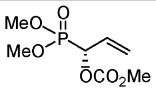
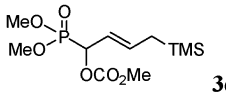
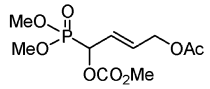
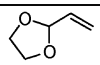
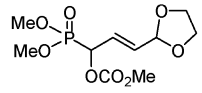
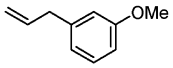
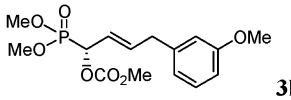
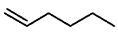
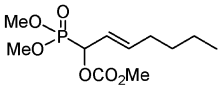
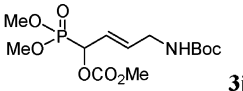
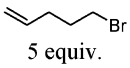
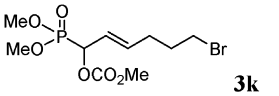
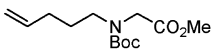
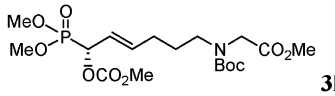
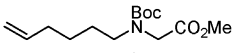
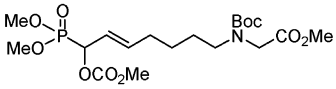
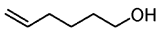
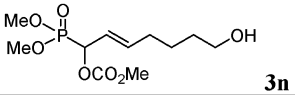
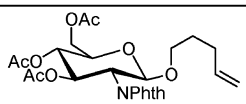
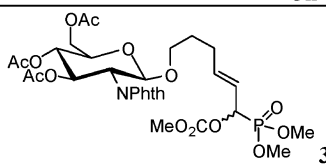


entry	protecting group (R^2)	% yield
1	CO_2Me **3**	92
2	Ac **4**	90
3	CONHTs **5**	88
4	$SiMe_2t$-Bu **6**	89
5	$COCH_2COCH_3$ **7**	82

In general, the metathesis reactions of phosphonates **2b** and **2c** (Table 2) are considerably slower than those for the acrolein phosphonate **2a**. Cross metathesis reaction of phosphonate **2b** with 1.7 equiv of 3-(3-methoxyphenyl)-propene (entry 1) stopped at approximately 50% conversion, presumably reaching equilibrium. However, reaction with 5 equiv of 4-methyl-1-pentene (entry 2) proceeded further and the product **2d** was isolated in 74% yield. In both reactions, there was no erosion of enantiomeric excess in the products. Allyl acetate (entry 3) was unreactive toward the phosphonate **2b** and the carbonate derivative **3b** (entry 4) was unreactive toward 3-(3-methoxyphenyl)propene and several other alkenes. The crotonyl phosphonate **2c** reacted with 4-methyl-1-pentene (entry 5) to give the phosphonate **2d** in 48% isolated yield. Unlike phosphonate **2b**, the crotonyl phosphonate **2c** showed some reactivity toward allyl acetate (entry 6) leading to mixtures of the starting material **2c**, the

TABLE 4. Metathesis with Carbonate Protected Acrolein Phosphonate Derivatives



Entry	Alkene	Product	Yield (e.e.)
1		--	NR
2	 5 equiv.	 **3e**	60%[b]
3		 **3f**	NR
4	 5 equiv.	 **3g**	32%[a]
5	 1.5 equiv.	 **3h**	68%[a] (69%)
6	 10 equiv.	 **3i**	97%[a]
7		 **3j**	10% conv
8	 5 equiv.	 **3k**	62%[a]
9	 2 equiv.	 **3l**	68%[c] (70%)
10	 2 equiv.	 **3m**	94%[c]
11	 2 equiv.	 **3n**	62%[d]
12		 **3o**	87%[e]

[a] 5% catalyst **10**, CH_2Cl_2. [b] 5% catalyst **10**, PhMe. [c] 7.5% total catalyst **10** added in 3 portions, CH_2Cl_2. [d] 5% total catalyst **10** added in 2 portions, CH_2Cl_2. [e] 5% catalyst **10**, CH_2Cl_2, 3 equiv of phosphonate **3a**.

expected product **2f**, and surprisingly the acrolein phosphonate **2a**. Similarly, reaction of the carbonate **3c** with 3-(3-methoxyphenyl)propene led to product mixtures (entry 7).

In an effort to optimize the cross metathesis reaction and suppress the unwanted side reaction, the cross metathesis reaction of several protected phosphonates **3a**−**7a** (Table 3) and 4-methylpent-1-ene was examined. Reaction of the protected phosphonates **3a**−**7a** and 4-methyl-1-pentene in CH_2Cl_2 with 5 mol % of Grubbs second generation catalyst gave the hetero-cross-metathesis products in high isolated yields (82−92%). The

homodimer of alkene was also formed; however, no homodimerization of the phosphonates or alkene bond migration was observed. Fortunately, the dimer of the alkene also entered into the metathesis reaction with the phosphonates **3a**−**7a**, so its formation had little consequence on the reaction outcome.

Since the carbonates are useful substrates for palladium-catalyzed additions,[6,7a,b] the carbonate derivative **3a** was examined more extensively. In general, the yields with terminal alkenes were good to excellent (Table 4). Only hetero-substituted allyl systems (e.g., entries 3, 4, and 7) failed to give satisfactory yields. Several functional groups including esters, alcohols, imide, carbamate, and halide could be incorporated into the phosphonates by using the metathesis reaction (entries 8−12). In all cases, the *E* isomer was predominant (>10:1). The signals for C-1 in the trans isomers in the ^{13}C NMR spectra are downfield of the cis isomers by approximately 5 ppm. Where examined, the enantiomeric excess of the starting material was preserved in the product, for example (Table 4, entry 5), the reaction of phosphonate **3a** (69% ee by HPLC) with 3-(3-methoxyphenyl)propene gave the substituted phosphonate **3h** (69% ee by HPLC) in 68% yield.

In summary, the alkene cross metathesis reaction between acrolein-derived phosphonates and alkenes was successfully applied to the preparation of *E* allylic hydroxy phosphonates. The enantiomeric excess of the starting phosphonates was preserved in the products. The cinnamaldehyde- and crotonaldehyde-derived phosphonates **2b** and **2c** were also examined. In general, the metathesis reactions of phosphonates **2b** and **2c** are considerably slower than those for phosphonate **2a** leading to product mixtures. We are currently applying this chemistry to the synthesis of allylic hydroxy phosphonates as chiral building blocks for use in the asymmetric synthesis of natural products.

Experimental Section

Dimethyl [1-(Acetoxy)-2-propenyl]phosphonate (4a). Acetyl chloride (0.9 mL, 12.3 mmol) was added to a stirred suspension of poly(4-vinyl)pyridine (PVP) (0.97 g, 9.3 mmol) in CH_2Cl_2 (10 mL) at 0 °C, followed by addition of hydroxy phosphonate **2a** (1.02 g, 6.17 mmol). The reaction mixture was stirred at room temperature until the reaction was complete as indicated by TLC. The reaction mixture was filtered to remove the polymer and the solvent was evaporated in vacuo. The crude product was purified by chromatography (SiO_2, hexane:EtOAc, 1:1) to give the pure acetate **4a** as a colorless oil (0.78 g, 61%): IR (neat, NaCl) 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.88 (1H, m), 5.66 (1H, m), 5.35 (2H, m), 3.76 (3H, d, J_{HP} = 10.7 Hz), 3.74 (3H, d, J_{HP} = 10.7 Hz), 2.11 (3H, s); ^{13}C NMR ($CDCl_3$) δ 169.3 (d, J_{CP} = 7.6 Hz), 129.3 (d, J_{CP} = 4.4 Hz), 119.6 (d, J_{CP} = 11.6 Hz), 69.1 (d, J_{CP} = 168 Hz), 54.0 (d, J_{CP} = 7.0 Hz), 53.8 (d, J_{CP} = 6.4 Hz), 20.9; ^{31}P NMR ($CDCl_3$) δ 20.7; HRMS (FAB, MH$^+$) calcd for $C_7H_{14}O_5P$ 209.0579, found 209.0582.

Dimethyl[1-(*p*-Tolylsulfamylcarbonyloxy)-2-propenyl]-phosphonate (5a). To a solution of phosphonate **2a** (0.135 g, 1 mmol) in CH_2Cl_2 was added tosyl isocyanate (0.168 mL, 1.1 mmol) at room temperature. After being stirred for 2 h, the mixture was concentrated in vacuo to yield the crude product. Recrystallization from EtOAc/hexanes gave a white solid (0.262 g, 72%): IR (neat, NaCl) 1748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.93 (2H, d, J_{HH} = 8.4 Hz), 7.34 (2H, d, J_{HH} = 8.0 Hz), 5.80 (1H, m), 5.46 (1H, m), 5.35 (2H, m), 3.77 (3H, d, J_{HP} = 10.8 Hz), 3.75 (3H, d, J_{HP} = 10.8 Hz), 2.44 (3H, s); ^{31}P NMR ($CDCl_3$) δ 20.0; HRMS (FAB, MH$^+$) calcd for $C_{13}H_{19}NO_7PS$ 364.0620, found 364.0622. Anal. Calcd for $C_{13}H_{18}NO_7PS$: C, 42.98; H, 4.99. Found: C, 43.07; H, 5.06.

Dimethyl {1-[Dimethyl(*tert*-butyl)silyloxy]-2-propenyl}-phosphonate (6a). Imidazole (0.71 g, 10.4 mmol) was added to a stirred solution of phosphonate **2a** (1.08 g, 6.51 mmol) in anhydrous CH_2Cl_2 (10 mL). The solution was cooled to 0 °C and dimethyl(*tert*-butyl)silyl chloride (1.47 g, 9.76 mmol) was added. After 30 min at 0 °C, the reaction mixture was warmed to room temperature and stirred overnight. The solvent was evaporated in vacuo and the crude product was purified by chromatography (SiO_2, hexane:EtOAc, 1:1) to give the silyl ether **6a** as a colorless oil (1.55 g, 85%): ^{1}H NMR ($CDCl_3$) δ 5.93 (1H, m), 5.38 (1H, m), 5.22 (1H, m), 4.45 (1H, m), 3.71 (6H, d, J_{HP} = 10.4 Hz), 0.85 (9H, s), 0.05 (3H, s), 0.01 (3H, s); ^{13}C NMR ($CDCl_3$) δ 133.7 (d, J_{CP} = 3.8 Hz), 117.1 (d, J_{CP} = 12.0 Hz), 70.9 (d, J_{CP} = 169 Hz), 53.8 (d, J_{CP} = 7.3 Hz), 53.4 (d, J_{CP} = 7.1 Hz), 25.7, 18.3, −4.9, −5.2; ^{31}P NMR ($CDCl_3$) δ 22.8; HRMS(FAB, MH$^+$) calcd for $C_{11}H_{26}O_4PSi$ 281.1338, found 281.1339.

Dimethyl [1-(2-Keto-butanoyloxy)-2-propenyl]phosphonate (7a). Diketene (0.3 mL, 4.15 mmol) was added to a solution of hydroxy phosphonate **2a** (0.53 g, 3.19 mmol) in THF (5 mL) and CH_2Cl_2 (5 mL) at −20 °C, followed by addition of DMAP (0.009 g, 0.0013 mmol). The reaction mixture was stirred at −20 °C for 30 min. The mixture was allowed to warm to room temperature, and then it was stirred overnight. The reaction mixture was washed with 0.1% NaOH (twice) and the aqueous layer was re-extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated in vacuo. The crude product was purified by chromatography (SiO_2, hexane:EtOAc, 1:1) to give the acetoacetate **7a** as a pale yellow oil (0.66 g, 82%) (14% enol): IR (neat, NaCl) 1754, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.94 (1H, m), 5.75 (1H, m), 5.42 (2H, m), 3.81 (3H, d, J_{HP} = 10.7 Hz), 3.80 (3H, d, J_{HP} = 10.7 Hz), 3.57 (2H, s), 2.28 (3H, s); ^{13}C NMR ($CDCl_3$) δ 199.6, 165.4 (d, J_{CP} = 7.7 Hz), 128.6 (d, J_{CP} = 4.4 Hz), 120.0 (d, J_{CP} = 11.6 Hz), 69.7 (d, J_{CP} = 168 Hz), 54.0 (d, J_{CP} = 7.0 Hz), 53.7 (d, J_{CP} = 6.4 Hz), 49.8, 30.2; ^{31}P NMR ($CDCl_3$) δ 19.9 (86%), 20.5 (14%); HRMS (FAB, MH$^+$) calcd for $C_9H_{16}O_6P$ 251.0684, found 251.0687.

General Procedure for the Alkene Cross Metathesis Reaction. An oven-dried flask was charged with Grubbs second generation catalyst **10** (68 mg, 0.08 mmol) under an argon atmosphere. A solution of the phosphonate (0.550 g, 3.31 mmol) in freshly distilled solvent (usually CH_2Cl_2) was added, followed by addition of terminal or disubstituted olefin (0.5 to 10 equiv). The septum was then quickly replaced with a condenser connected to an argon bubbler. The flask was immersed in an oil bath preheated to 45 °C until the reaction was complete (monitored by ^{31}P NMR spectroscopy). The mixture was concentrated in vacuo and purified directly by silica gel chromatography or pretreated with DMSO[15] and then concentrated in vacuo and purified directly by silica gel chromatography. Quantities, experimental variations, yields, and characterization data are given below.

Tetramethyl (1,4-Dihydroxybut-2-enyl)-1,4-diphosphonate (8). Hydroxy phosphonate **2a** (0.550 g, 3.31 mmol) and Grubbs catalyst (0.068 g, 0.08 mmol) in CH_2Cl_2 (3 mL) for 15 h at 40 °C gave, after filtration, the diphosphonate **8** as a white solid (0.381 g, 76% yield): mp 200−203 °C (MeOH); ^{1}H NMR (d_6-DMSO) δ 5.90 (1H, br s), 5.83 (1H, m), 4.53 (1H, m), 3.67 (3H, d, J_{HP} = 10.1 Hz); ^{13}C NMR (d_6-DMSO) δ 127.5 (app t, J_{CP} = 5.3 Hz), 68.2 (dd, J_{CP} = 164, 3.7 Hz), 53.0 (app t, J_{CP} = 3.0 Hz), 52.6 (app t, J_{CP} = 3.1 Hz); ^{31}P NMR (DMSO) δ 24.5. Anal. Calcd for $C_8H_{18}O_8P_2$: C, 31.60; H, 5.96. Found: C, 30.69; H, 5.95.

Dimethyl [1-Hydroxy-5-methyl-2-hexenyl]phosphonate (2d). Hydroxy phosphonate **2a** (0.255 g, 1.53 mmol), 4-methyl-1-pentene (1.0 mL, 7.67 mmol), and Grubbs catalyst (0.0651 g, 0.0766 mmol) in $CHCl_3$ (3 mL) for 24 h at 40 °C

(15) Ahn, Y. M.; Yang, K. L.; Georg, G. I. *Org. Lett.* **2001**, *3*, 1411.

gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the hydroxy phosphonate **2d** as a colorless oil (0.19 g, 57%) (*E*:*Z*, 12:1): IR (neat, NaCl) 3298 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.88 (1H, m), 5.59 (1H, m), 4.47 (1H, dd, J_{HH} = 7.0 Hz, J_{HP} = 10.4 Hz), 3.82 (3H, d, J_{HP} = 10.4 Hz), 3.81 (3H, d, J_{HP} = 10.4 Hz), 1.98 (2H, m), 1.67 (1H, m), 0.90 (3H, d, J_{HH} = 6.7 Hz), 0.89 (3H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 134.7 (d, J_{CP} = 13.1 Hz), 125.2 (d, J_{CP} = 3.9 Hz), 69.5 (d, J_{CP} = 161 Hz), 53.8 (d, J_{CP} = 7.1 Hz), 41.9 (d, J_{CP} = 1.5 Hz), 28.4 (d, J_{CP} = 2.9 Hz), 22.5, 22.4; ^{31}P NMR ($CDCl_3$) δ 24.9; HRMS (EI, M^+) calcd for $C_9H_{19}O_4P$ 222.1021, found 222.1017.

Dimethyl [1-Hydroxy-4-(trimethylsilyl)-2-butenyl]-phosponate (2e). Hydroxy phosphonate **2a** (0.251 g, 1.51 mmol), allyl trimethylsilane (1.2 mL, 7.57 mmol), and Grubbs catalyst (0.0643 g, 0.0757 mmol) in $CHCl_3$ (5 mL) at 40 °C for 23 h gave after chromatography (SiO_2, hexane:EtOAc, 1:1) the hydroxy phosphonate **2e** as a colorless oil (0.313 g, 82%) (*E*:*Z*, 10.7:1): IR (neat, NaCl) 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.86 (1H, m), 5.42 (1H, m), 4.42 (1H, dd, J_{HH} = 7.5 Hz, J_{HP} = 8.5 Hz), 3.81 (6H, d, J_{HP} = 10.4 Hz), 1.55 (2H, dd, J_{HH} = 8.3 Hz, J_{HP} = 3.3 Hz), 0.02 (9H, s); ^{13}C NMR ($CDCl_3$) δ 133.3 (d, J_{CP} = 13.7 Hz), 122.3 (d, J_{CP} = 4.1 Hz), 69.8 (d, J_{CP} = 162 Hz), 53.7 (d, J_{CP} = 7.1 Hz), 53.6 (d, J_{CP} = 7.2 Hz), 23.6, −1.8; ^{31}P NMR ($CDCl_3$) δ 25.4; HRMS(FAB, M^+) calcd for $C_9H_{21}O_4PSi$ 252.0947, found 252.0938.

Dimethyl (1-Hydroxy-4-acetoxy-2-butenyl)phosphonate (2f). Hydroxy phosphonate **2a** (1.01 g, 6.08 mmol), *cis*-1,4-diacetoxy-2-butene (2.09 g, 12.17 mmol), and Grubbs catalyst (0.125 g, 0.15 mmol) in $CHCl_3$ (3 mL) for 24 h at 40 °C gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the hydroxy phosphonate **2f** as a light brown oil (0.88 g, 61%): IR (neat, NaCl) 3299, 1739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.01 (2H, m), 4.57 (3H, m), 3.82 (6H, d, J_{HP} = 10.4 Hz), 2.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 171.1, 128.6, 127.5 (d, J_{CP} = 12.7 Hz), 68.8 (d, J_{CP} = 161 Hz), 64.4, 54.3 (d, J_{CP} = 6.9 Hz), 54.1 (d, J_{CP} = 7.4 Hz), 21.3; ^{31}P NMR ($CDCl_3$) δ 24.6.

Dimethyl [1-Hydroxy-3-(1,3-dioxan-1-yl)prop-2-enyl]-phosphonate (2g). Hydroxy phosphonate **2a** (0.30 g, 1.81 mmol), 2-vinyl-1,3-dioxalane (0.362 mL, 3.62 mmol), and Grubbs catalyst (0.042 g, 0.05 mmol) in $CHCl_3$ (3 mL) for 9 h at 40 °C gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the hydroxy phosphonate **2g** as a light brown oil (0.12 g, 30%) (*E*:*Z*, 7.8:1): ^1H NMR ($CDCl_3$) δ 6.00 (2H, m), 5.33 (1H, m), 4.59 (1H, m), 3.90 (4H, m), 3.81 (3H, d, J_{HP} = 10.4 Hz), 3.80 (3H, d, J_{HP} =10.3 Hz); ^{13}C NMR ($CDCl_3$) δ 130.4 (d, J_{CP} = 3.5 Hz), 129.0 (d, J_{CP} = 11.9 Hz), 103.0 (d, J_{CP} = 1.9 Hz), 68.3 (d, J_{CP} = 161 Hz), 65.11, 65.08, 54.2 (d, J_{CP} = 7.1 Hz), 53.9 (d, J_{CP} = 7.4 Hz); ^{31}P NMR ($CDCl_3$) δ 24.3.

Dimethyl [1-Hydroxy-5-methyl-2-hexenyl]phosphonate (2d) from (1*R*),(2*E*)-Dimethyl (1-Hydroxy-3-phenyl-2-propenyl)pPhosphonate (2b). Phosphonate **2b** (>95% ee, 0.3 g, 1.24 mmol), 4-methyl-1-pentene (0.521 g, 6.19 mmol), and Grubbs catalyst (0.051 g, 0.062 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 36 h gave, after chromatography (SiO_2, hexane:EtOAc 4:1, then hexane:EtOAc 1:1), the phosphonate **2d** as a colorless oil (0.202 g, 74%, >95% ee) (*E*:*Z*, 12.5:1).

Dimethyl [1-Hydroxy-5-methyl-2-hexenyl]phosphonate (2d) from Dimethyl (1-Hydroxy-2*E*-butenyl)Phosphonate (2c). Phosphonate **2c** (0.3 g, 2.22 mmol), 4-methyl-1-pentene (0.701 g, 8.33 mmol), and Grubbs catalyst (0.069 g, 0.084 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 12 h gave, after chromatography (SiO_2, hexane:EtOAc, 4:1, then hexane:EtOAc, 1:1), the phosphonate **2d** as a colorless oil (0.176 g, 48%) (*E*:*Z*, 14.3:1).

Dimethyl[1-(Methoxycarbonyloxy)-5-methyl-2-hexenyl]-phosphonate (3d). Phosphonate **3a** (3.0 g, 13.4 mmol), 4-methyl-1-pentene (8.5 mL, 67 mmol), and Grubbs catalyst (0.568 g, 0.67 mmol) in CH_2Cl_2 (30 mL) at 40 °C for 20 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **3d** as a pale yellow oil (3.43 g, 92%) (*E*:*Z* 11.8:1): IR (neat, NaCl) 1754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.92 (1H, m), 5.53 (1H, m), 5.43 (1H, dd, J_{HH} = 7.8 Hz, J_{HP} = 12.4 Hz), 3.81 (3H, d, J_{HP} = 10.7 Hz), 3.80 (3H, s), 3.79 (3H, d, J_{HP} = 10.7 Hz), 1.97 (2H, m), 1.65 (1H, m), 0.87 (6H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, J_{CP} = 9.9 Hz), 137.9 (d, J_{CP} = 12.5 Hz), 121.5 (d, J_{CP} = 4.0 Hz), 73.2 (d, J_{CP} = 170 Hz), 55.5, 53.9 (d, J_{CP} = 7.2 Hz), 53.8 (d, J_{CP} = 6.6 Hz), 41.8 (d, J_{CP} = 1.2 Hz), 28.2 (d, J_{CP} = 2.6 Hz), 22.4; ^{31}P NMR ($CDCl_3$) δ 20.5; HRMS(EI, M^+) calcd for $C_{11}H_{21}O_6P$ 280.1076, found 280.1074.

Dimethyl [1-Acetoxy-5-methyl-2-hexenyl]phosphonate (4d). The acetoxy phosphonate **4a** (0.255 g, 1.23 mmol), 4-methyl-1-pentene (0.8 mL, 6.13 mmol), and Grubbs catalyst (0.052 g, 0.0613 mmol) in CH_2Cl_2 (4.5 mL) at 40 °C for 24 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **4d** as a colorless oil (0.291 g, 90%) (*E*:*Z*, 9.5:1): IR (neat, NaCl) 1751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.87 (1H, m), 5.65 (1H, dd, J_{HH} = 7.8 Hz, J_{HP} = 12.6 Hz), 5.51 (1H, m), 3.79 (3H, d, J_{HP} = 10.6 Hz), 3.78 (3H, d, J_{HP} = 10.6 Hz), 2.12 (3H, s), 1.96 (2H, m), 1.65 (1H, m), 0.87 (6H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 169.4 (d, J_{CP} = 7.8 Hz), 137.4 (d, J_{CP} = 12.6 Hz), 121.9 (d, J_{CP} = 4.1 Hz), 69.2 (d, J_{CP} = 170 Hz), 53.8 (d, J_{CP} = 7.0 Hz), 53.7 (d, J_{CP} = 6.4 Hz), 41.8 (d, J_{CP} = 1.4 Hz), 28.2 (d, J_{CP} = 2.7 Hz), 22.4, 21.0; ^{31}P NMR ($CDCl_3$) δ 21.6; HRMS(EI, MH^+) calcd for $C_{11}H_{22}O_5P$ 265.1205, found 265.1205.

Dimethyl [1-(*p*-Tolylsulfamylcarbonyloxy)-5-methyl-2-hexenyl]phosphonate (5d). Phosphonate **5a** (0.251 g, 0.692 mmol), 4-methyl-1-pentene (0.9 mL, 6.92 mmol), and Grubbs catalyst (0.0294 g, 0.0345 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 22 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **5d** as a colorless oil (0.256 g, 88%) (*E*:*Z*, 10:1): IR (neat, NaCl) 1754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.94 (2H, d, J_{HH} = 8.3 Hz), 7.33 (2H, d, J_{HH} = 8.3 Hz), 5.83 (1H, m), 5.42 (2H, m), 3.76 (3H, d, J_{HP} = 10.7 Hz), 3.74 (3H, d, J_{HP} = 10.7 Hz), 2.45 (3H, s), 1.92 (2H, m), 1.59 (1H, m), 0.83 (3H, d, J_{HH} = 6.6 Hz), 0.82 (3H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 149.8 (d, J_{CP} = 10.7 Hz), 145.2, 139.2 (d, J_{CP} = 12.8 Hz), 135.9, 129.8, 128.6, 120.9 (d, J_{CP} = 3.7 Hz), 71.5 (d, J_{CP} = 174 Hz), 54.2 (d, J_{CP} = 6.8 Hz), 54.0 (d, J_{CP} = 6.8 Hz), 41.8 (d, J_{CP} = 1.2 Hz), 28.2 (d, J_{CP} = 2.4 Hz), 22.4, 22.3, 22.0; ^{31}P NMR ($CDCl_3$) δ 20.3; HRMS (FAB, MH^+) calcd for $C_{17}H_2N_7O_7PS$ 420.1246, found 420.1249.

Dimethyl {1-[Dimethyl(*tert*-butyl)silyloxy]-5-methyl-2-hexenyl}phosphonate (6d). Phosphonate **6a** (0.255 g, 0.909 mmol), 4-methyl-1-pentene (0.6 mL, 4.55 mmol), and Grubbs catalyst (0.0386 g, 0.0454 mmol) in anhydrous CH_2Cl_2 (4.5 mL) at 40 °C for 24 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **6d** as a colorless oil (0.272 g, 89%) (*E*:*Z*, 10:1): ^1H NMR ($CDCl_3$) δ 5.81 (1H, m), 5.57 (1H, m), 4.47 (1H, dd, J_{HH} = 6.4 Hz, J_{HP} = 14.0 Hz), 3.79 (3H, d, J_{HP} = 10.3 Hz), 3.78 (3H, d, J_{HP} = 10.3 Hz), 1.98 (2H, m), 1.66 (1H, m), 0.92 (9H, s), 0.90 (3H, d, J_{HH} = 6.7 Hz), 0.89 (3H, d, J_{HH} = 6.7 Hz), 0.12 (3H, s), 0.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 133.5 (d, J_{CP} = 13.0 Hz), 126.5 (d, J_{CP} = 3.9 Hz), 70.9 (d, J_{CP} = 171 Hz), 53.9 (d, J_{CP} = 7.2 Hz), 53.5 (d, J_{CP} = 7.1 Hz), 41.8 (d, J_{CP} = 2.0 Hz), 28.5 (d, J_{CP} = 3.2 Hz), 25.9, 22.5, 22.4, 18.5, −4.5, −4.9; ^{31}P NMR ($CDCl_3$) δ 23.7; HRMS (FAB, MH^+) calcd for $C_{15}H_{34}O_4SiP$ 337.1964, found 337.1960.

Dimethyl[1-(2-Keto-butanoyloxy)-5-methyl-2-hexenyl]-phosphonate (7d). Phosphonate **7a** (3 g, 12 mmol), 4-methyl-1-pentene (4.6 mL, 36 mmol), and Grubbs catalyst (0.509 g, 0.6 mmol) in CH_2Cl_2 (30 mL) at 40 °C for 20 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **7d** as a pale yellow oil (2.99 g, 82%) (*E*:*Z*, 10:1): IR (neat, NaCl) 1754, 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.84 (1H, m), 5.44 (1H, m), 3.72 (3H, d, J_{HP} = 10.7 Hz), 3.71 (3H, d, J_{HP} = 10.7 Hz), 3.45 (2H, s), 2.2 (3H, s), 1.90 (2H, m), 1.56 (1H, m), 0.80 (6H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 199.8, 165.7 (d, J_{CP} = 8.0 Hz), 138.2 (d, J_{CP} = 12.6 Hz), 121.4 (d, J_{CP} = 4.1 Hz), 70.0 (d, J_{CP} = 171 Hz), 53.9 (d, J_{CP} = 6.5 Hz), 53.8 (d, J_{CP} = 6.0 Hz), 50.1, 41.8, 30.3, 28.2 (d, J_{CP} = 2.5 Hz), 22.4; ^{31}P NMR ($CDCl_3$) δ 20.9; HRMS (EI, MH^+) calcd for $C_{13}H_{24}O_6P$ 307.1310, found 307.1311.

Dimethyl [1-(Methoxycarbonyloxy)-4-(3-methoxyphenyl)-2-butenyl]phosphonate (3h).[7a] Phosphonate **3a** (1.5 g,

6.7 mmol), 3-(3-methoxyphenyl)propene (1.49 g, 10.0 mmol), and Grubbs catalyst (0.284 g, 0.335 mmol) in CH_2Cl_2 (10 mL) at 40 °C for 12 h gave, after chromatography (SiO_2, CH_2Cl_2:EtOAc, 1:4), the phosphonate **3h** as a pale yellow oil (1.56 g, 68%): IR (neat, NaCl) 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20 (1H, t, J_{HH} = 7.8 Hz), 6.74 (3H, m), 6.07 (1H, m), 5.65 (1H, m), 5.49 (1H, dd, J_{HH} = 7.9 Hz, J_{HP} = 13 Hz), 3.81 (3H, s), 3.79 (6H, d, J_{HP} = 11 Hz), 3.78 (3H, s), 3.42 (2H, m); ^{13}C NMR ($CDCl_3$) δ 160.0, 154.9 (d, J_{CP} = 9.5 Hz), 140.7 (d, J_{CP} = 2.3 Hz), 136.4 (d, J_{CP} = 12.3 Hz), 129.7, 122.1 (d, J_{CP} = 3.9 Hz), 121.1, 114.4, 112.0, 72.9 (d, J_{CP} = 169 Hz), 55.6, 55.3, 55.1 (d, J_{CP} = 7.1 Hz), 53.9 (d, J_{CP} = 6.5 Hz), 38.8 (d, J_{CP} = 1.3 Hz); ^{31}P NMR ($CDCl_3$) δ 20.7; HRMS (EI, M^+) calcd for $C_{15}H_{21}O_7P$ 344.1025, found 344.1027.

Dimethyl [4-(1,3-Dioxan-1-yl)-1-(methoxycarbonyloxy)-2-butenyl]phosphonate (3g). Phosphonate **3a** (0.26 g, 1.16 mmol), 2-vinyl-1,3-dioxolane (0.6 mL, 5.81 mmol), and Grubbs catalyst (0.0493 g, 0.058 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 20 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), the phosphonate **3g** as a pale yellow oil (0.11 g, 32% yield): IR (neat, NaCl) 1758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.03 (1H, m), 5.87 (1H, m), 5.56 (1H, ddd, J_{HH} =1.4, 5.6 Hz, J_{HP} = 15.3 Hz), 5.30 (1H, dd, J_{HH} = 5.2 Hz, J_{HP} = 1.9 Hz), 3.95 (2H, m), 3.88 (2H, m), 3.80 (3H, s), 3.79 (6H, d, J_{HP} = 10.6 Hz); ^{13}C ($CDCl_3$) δ 154.7 (d, J_{CP} = 8.7 Hz), 131.1 (d, J_{CP} = 11.0 Hz), 126.1 (d, J_{CP} = 3.8 Hz), 102.3 (d, J_{CP} = 1.8 Hz), 71.7 (d, J_{CP} = 167 Hz), 65.1, 65.0, 55.7, 54.3 (d, J_{CP} = 7.1 Hz), 54.0 (d, J_{CP} = 6.5 Hz); ^{31}P NMR ($CDCl_3$) δ 18.8; HRMS (FAB, MH^+) calcd for $C_{10}H_{18}O_8P$ 297.0739, found 297.0735.

Dimethyl [1-(Methoxycarbonyloxy)-2-hexenyl]phosphonate (3i). Phosphonate **3a** (0.3 g, 1.34 mmol), 1-hexene (1.13 g, 13.4 mmol), and Grubbs catalyst (0.055 g, 0.067 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 22 h gave, after chromatography (SiO_2, hexane then hexane:EtOAc, 4:1), the phosphonate **3i** as a pale yellow oil (0.362 g, 97%) (*E*:*Z*, 10:1): IR (neat, NaCl) 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.95 (1H, m), 5.54 (1H, m), 5.43 (1H, dd, J_{HH} = 7.8 Hz, J_{HP} = 12.5 Hz), 3.82 (3H, d, J_{HP} = 10.6 Hz), 3.81 (3H, s), 3.81 (3H, d, J_{HP} = 10.6 Hz), 2.09 (2H, m), 1.35 (4H, m), 0.88 (3H, t, J_{HH} = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, J_{CP} = 9.9 Hz), 139.2 (d, J_{CP} = 12.5 Hz), 120.3 (d, J_{CP} = 3.8 Hz), 73.2 (d, J_{CP} = 171 Hz), 55.4, 54.0 (d, J_{CP} = 7.0 Hz), 53.8 (d, J_{CP} = 6.5 Hz), 32.2 (d, J_{CP} = 1.0 Hz), 30.8 (d, J_{CP} = 2.4 Hz), 22.3, 14.0; ^{31}P NMR ($CDCl_3$) δ 20.4; HRMS (FAB, MH^+) calcd for $C_{11}H_{22}O_6P$ 281.1154, found 281.1157.

Dimethyl [1-(Methoxycarbonyloxy)-4-(trimethylsilyl)-2-butenyl]phosphonate (3e). Phosphonate **3a** (0.3 g, 1.34 mmol), allyltrimethylsilane (0.76 g, 6.69 mmol), and Grubbs catalyst (0.055 g, 0.067 mmol) in toluene (5 mL) at 75 °C for 37 h gave, after chromatography (SiO_2, hexane:EtOAc 3:1), the phosphonate **3e** as a pale yellow oil (0.224 g, 60%) (*E* only): IR (neat, NaCl) 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.97 (1H, m), 5.37 (2H, m), 3.80 (6H, d, J_{HP} = 10.7 Hz), 3.79 (3H, s), 3.79 (6H, d, J_{HP} = 10.7 Hz), 1.56 (2H, dd, J_{HH} = 8.3 Hz, J_{HP} = 2.7 Hz), 0.00 (9H, s); ^{13}C NMR ($CDCl_3$) δ 155.0 (d, J_{CP} = 11.0 Hz), 137.4 (d, J_{CP} = 13.2 Hz), 118.3 (d, J_{CP} = 3.8 Hz), 73.8 (d, J_{CP} = 174 Hz), 55.4, 53.8 (d, J_{CP} = 7.0 Hz), 53.7 (d, J_{CP} = 6.4 Hz), 23.8, −1.8; ^{31}P NMR ($CDCl_3$) δ 20.9; HRMS (FAB, M_2H^+) calcd for $C_{22}H_{47}O_{12}P_2Si_2$ 621.2081, found 621.2070.

Dimethyl [6-Bromo-1-(methoxycarbonyloxy)-2-hexenyl]phosphonate (3k). Phosphonate **3a** (0.3 g, 1.34 mmol), 5-bromo-1-pentene (0.998 g, 6.69 mmol), and Grubbs catalyst (0.055 g, 0.067 mmol) in CH_2Cl_2 (5 mL) at 40 °C for 26 h gave, after chromatography (SiO_2, hexane then hexane:EtOAc, 4:1), the phosphonate **3k** as a pale yellow oil (0.285 g, 62%): IR (neat, NaCl) 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.90 (1H, m), 5.62 (1H, m), 5.44 (1H, ddd, J_{HH} = 7.4, 0.7 Hz, J_{HP} = 13.0 Hz), 3.81 (3H, d, J_{HP} = 10.6 Hz), 3.81 (3H, s), 3.80 (3H, d, J_{HP} = 10.6 Hz), 3.39 (2H, t, J_{HH} = 6.6 Hz), 2.27 (2H, m), 1.95 (2H, m); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, J_{CP} = 9.9 Hz), 136.3 (d, J_{CP} = 12.3 Hz), 120.1 (d, J_{CP} = 4.0 Hz), 73.0 (d, J_{CP} = 171 Hz), 55.6, 54.0 (d, J_{CP} = 7.1 Hz), 53.9 (d, J_{CP} = 6.4 Hz), 32.9, 31.5 (d, J_{CP} = 2.6 Hz), 30.8 (d, J_{CP} = 1.0 Hz); ^{31}P NMR ($CDCl_3$) δ 20.1; HRMS (FAB, MH^+) calcd for $C_{10}H_{19}O_6BrP$ 345.0103, found 345.0101.

Dimethyl [(*N*-(*tert*-Butoxycarbonyl)-*N*-(methyl 2-acetate)-6-amino-1-(methoxycarbonyloxy)-2-hexenyl]-phosphonate (3*l*). Phosphonate **3a** (0.5 g, 2.2 mmol), alkene (1.15 g, 4.46 mmol), and Grubbs catalyst (0.078, 0.036, and 0.056 mmol at 0, 16, and 40 h, respectively) in toluene (5 mL) at 75 °C for 52 h gave, after DMSO addition[15] (24 h) and chromatography (SiO_2, hexane then hexane:EtOAc, 4:1), the phosphonate **3*l*** as a pale yellow oil (0.692 g, 68%): IR (neat, NaCl) 1755, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.95 (1H, m), 5.56 (1H, m), 5.43 (1H, m), 3.93 (1H, s), 3.84 (1H, s), 3.81 (6H, br s), 3.78 (3H, s), 3.72 (3H, s), 3.25 (2H, m), 2.11 (2H, m), 1.62 (2H, m), 1.46 and 1.41 (9H, s); ^{13}C NMR ($CDCl_3$) (reported as rotomer pairs) δ 170.8 and 170.7, 155.9 and 155.3, 154.9 (d, J_{CP} = 9.8 Hz), 137.9 and 137.7 (d, J_{CP} = 12.6 Hz), 121.2 (app m), 80.5 and 80.4, 73.1 and 73.0 (d, J_{CP} = 170 Hz), 55.5, 54.0 (d, J_{CP} = 7.2 Hz), 53.9 (d, J_{CP} = 6.7 Hz), 52.15 and 54.12, 49.6 and 48.95, 48.2 and 48.1, 29.8, 28.5 and 28.4, 27.6 and 27.3; ^{31}P NMR ($CDCl_3$) δ 20.3; HRMS (FAB, MH^+) calcd for $C_{18}H_{33}O_{10}NP$ 454.1842, found 454.1834.

Dimethyl [*N*-(*tert*-Butoxycarbonyl)-*N*-(methyl 2-acetate)-7-amino-1-(methoxycarbonyloxy)-2-heptenyl]-phosphonate (3m). Phosphonate **3a** (0.5 g, 2.2 mmol), alkene (1.21 g, 4.46 mmol, 2 equiv), and Grubbs catalyst (0.075 and 0.036 mmol at 0 and 17 h, respectively) in toluene (5 mL) at 75 °C for 31 h gave, after DMSO addition[15] (24 h) and chromatography (SiO_2, hexane:EtOAc 5:1 then hexane:EtOAc 1:1), the phosphonate **3m** as a pale yellow oil (0.94 g, 90%): IR (neat, NaCl) 1755, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.92 (1H, m), 5.52 (1H, m), 5.42 (1H, m), 3.91 (1H s), 3.82 (1H, s), 3.79 (6H, br s), 3.77 (3H, s), 3.71 (3H, s), 3.24 (2H, m), 2.10 (2H, m), 1.43 (4H, m), 1.39 and 1.33 (9H, s); ^{13}C NMR ($CDCl_3$) (reported as rotomer pairs) δ 170.8 and 170.7, 155.9 and 155.3, 154.9 (d, J_{CP} = 9.9 Hz), 138.4 (m), 120.8 (m), 80.3 and 80.2, 73.1 (d, J_{CP} = 170 Hz), 55.5, 54.0 (d, J_{CP} = 8.7 Hz), 53.9 (d, J_{CP} = 6.6 Hz), 52.1, 49.3 and 48.6, 48.2 and 48.1, 32.2, 28.5 and 28.4, 27.9 and 27.7, 25.8; ^{31}P NMR ($CDCl_3$) δ 20.3; HRMS (FAB, MH^+) calcd for $C_{19}H_{35}O_{10}NP$ 468.1999, found 468.2011.

Dimethyl [7-Hydroxy-1-(methoxycarbonyloxy)-2-heptenyl]phosphonate (3n). Phosphonate **3a** (1.0 g, 4.5 mmol), 5-hexenol (0.89 g, 8.9 mmol), and Grubbs catalyst (0.18 g, 0.22 mmol, 5%) in CH_2Cl_2 (10 mL) at 40 °C for 30 h gave, after chromatography (SiO_2, hexane then hexane:EtOAc, 4:1), the phosphonate **3n** as a pale yellow oil (0.28 g, 62%) (*E*:*Z*, 27:1): IR (neat, NaCl) 3439, 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.95 (1H, m), 5.55 (1H, m), 5.42 (1H, ddd, J_{HH} = 7.7, 0.7 Hz, J_{HP} = 12.5 Hz), 3.80 (3H, d, J_{HP} = 10.6 Hz), 3.80 (3H, s), 3.79 (3H, d, J_{HP} = 10.6 Hz), 3.60 (2H, t, J_{HH} = 6.1 Hz), 2.13 (2H, m), 1.97 (1H, s), 1.53 (4H, m); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, J_{CP} = 9.9 Hz), 138.7 (d, J_{CP} = 12.5 Hz), 120.7(d, J_{CP} = 3.9 Hz), 73.1 (d, J_{CP} = 171 Hz), 62.5, 55.5, 54.0 (d, J_{CP} = 7.1 Hz), 53.9 (d, J_{CP} = 6.5 Hz), 32.2 (d, J_{CP} = 0.9 Hz), 32.1, 24.8 (d, J_{CP} = 2.5 Hz); ^{31}P NMR ($CDCl_3$) δ 20.4; HRMS (FAB, MH^+) calcd for $C_{11}H_{22}O_7P$ 297.1103, found 297.1106.

Carbohydrate Phosphonate (3o). Phosphonate **3a** (0.081 g, 0.36 mmol, 3 equiv), *O*-pentenyl glycoside (0.06 g, 0.12 mmol) in CH_2Cl_2 (2 mL), and Grubbs catalyst (5.1 mg, 0.006 mmol) at 40 °C for 24 h gave, after chromatography (SiO_2, hexane:EtOAc, 1:1), a diastereoisomeric mixture of phosphonates **3o** as a colorless oil (0.073 g, 87%): IR (neat, NaCl) 1750, 1716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.86 (2H, dd, J_{HH} = 3.1, 5.5 Hz), 7.74 (2H, dd, J_{HH} = 3.1, 5.4 Hz), 5.76 (2H, m), 5.33 (3H, m), 5.16 (1H, t, J_{HH} = 9.8 Hz), 4.31 (2H, m), 4.16 (1H, dd, J_{HH} = 1.9, 12.3 Hz), 3.75−3.88 (11H, m), 3.43 (1H, m), 2.10 (3H, s), 2.02 (3H, s), 1.90 (2H, m), 1.85 (3H, s), 1.55 (2H, m); ^{13}C NMR ($CDCl_3$) δ 170.9, 170.3, 169.7, 167.8, 154.8 (2), 137.4(m), 134.6, 131.5, 123.8, 121.0 (m), 98.3, 72.9 (m), 72.0, 70.9, 69.2, 62.2, 55.5, 54.8, 53.9 (2), 53.8 (d, J_{CP} = 5.9 Hz), 53.7 (d, J_{CP} = 6.0 Hz), 28.6, 28.5 (2), 20.9, 20.8, 20.6; ^{31}P NMR ($CDCl_3$) δ 20.22, 20.20; HRMS (FAB, MH^+) calcd for $C_{30}H_{39}NO_{16}P$ 700.2007, found 700.2016.

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Supporting Information Available: General experimental, ^{1}H and ^{13}C NMR spectra for compounds **4a**, **5a**, **6a**, **7a**, **8**, **2d**, **2e**, **2f**, **3d**, **4d**, **5d**, **6d**, **7d**, **3e**, **3g**, **3h**, **3i**, **3k**, **3*l***, **3m**, **3n**, and **3o**, HPLC data for compounds (+)**2b**, (**R**)**2b**, (+)**2d**, **(R)2d**, and **8**, and X-ray data for **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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