The Synthesis of Non-Racemic Allylic Hydroxy Phosphonates via Alkene Cross Metathesis

Anyu He, Bingli Yan, Anchalee Thanavaro, Christopher D. Spilling,* and Nigam P. Rath

Department of Chemistry and Biochemistry, University of Missouri-St. Louis,

8001 Natural Bridge Road, St. Louis, Missouri 63121, USA.

cspill@umsl.edu

Supporting Information

<i>Table of Contents</i>	S1
General Experimental	S3
¹ H and ¹³ C NMR spectrum for 4a	S4
¹ H and ¹³ C NMR spectrum for 5a	S5
¹ H and ¹³ C NMR spectrum for 6a	S6
¹ H and ¹³ C NMR spectrum for 7a	S7
¹ H and ¹³ C NMR spectrum for 8	S8
¹ H and ¹³ C NMR spectrum for 2d	S9
¹ H and ¹³ C NMR spectrum for 2e	S10
¹ H and ¹³ C NMR spectrum for 2f	S11
¹ H and ¹³ C NMR spectrum for 2g	S12
¹ H and ¹³ C NMR spectrum for 3d	S13
¹ H and ¹³ C NMR spectrum for 4d	S14
¹ H and ¹³ C NMR spectrum for 5d	S15

^1H and ^{13}C NMR spectrum for 6d	S16
^1H and ^{13}C NMR spectrum for 7d	S17
^1H and ^{13}C NMR spectrum for 3e	S18
^1H and ^{13}C NMR spectrum for 3g	S19
^1H and ^{13}C NMR spectrum for 3h	S20
^1H and ^{13}C NMR spectrum for 3i	S21
^1H and ^{13}C NMR spectrum for 3k	S22
^1H and ^{13}C NMR spectrum for 3l	S23
^1H and ^{13}C NMR spectrum for 3m	S24
^1H and ^{13}C NMR spectrum for 3n	S25
^1H and ^{13}C NMR spectrum for 3o	S26
^{31}P NMR spectrum for the reaction of 2c with allyl acetate	S27
HPLC data for compound 2b	S28
HPLC data for compound 2d (from 2b)	S29
HPLC data for compound 8 (from rac 2a)	S30
HPLC data for compound 8 (from R- 2a)	S30
X-ray data tables for 8	S32

General Experimental: ^1H , ^{13}C and ^{31}P NMR spectra were recorded at 300, 75 and 121 MHz, respectively in CDCl_3 . ^1H NMR spectra are referenced to internal tetramethylsilane (TMS, $\delta=0.00$), ^{13}C NMR spectra to the center-line of CDCl_3 (77.23 ppm) and ^{31}P NMR spectra to external 85% H_3PO_4 . Coupling constants, J , are reported in Hz. Enantiomer ratios were measured by chiral stationary-phase HPLC on a (*S,S*)-Whelk-O 1 column or a Chiralpak AS column or by ^1H

NMR using Karfarski's quinine method.¹ Optical rotations were determined using a polarimeter set at 589 nm. (±) Dimethyl [1-hydroxy-2-propenyl] phosphonate **2a**,² (1*R*) Dimethyl [1-hydroxy-2-propenyl] phosphonate (**R**)**2a** (70% e.e.),² (1*R*) (2*E*) Dimethyl (1-hydroxy-3-phenyl-2-propenyl) phosphonate (**R**)**2b** (98% e.e.),^{2,3,4} (±) (2*E*) Dimethyl (1-hydroxy-2-butenyl) phosphonate **2c**,⁴ Dimethyl [1-(methoxycarbonyloxy)-2-propenyl] phosphonate **3a**,² (2*E*) Dimethyl [1-(methoxycarbonyloxy)-3-phenyl-2-propenyl] phosphonate **3b**,² and (2*E*) Dimethyl [1-(methoxycarbonyloxy)-2-butenyl] phosphonate (±)**3c**⁴ were prepared using previously published procedures.

1. Zymanczyk-Duda, E.; Skwarczynski, M.; Lejczak, B.; Karfarski, P. *Tetrahedron: Asymmetry* **1996**, 7, 1277.
2. Yan, B.; Spilling, C. D. *J. Org. Chem.* **2004**, 69, 2859.
3. Rowe, B. J.; Spilling, C. D. *Tetrahedron: Asymmetry* **2001**, 12, 1701; Blazis, V. J.; Koeller, K. J.; Spilling, C. D. *J. Org. Chem.* **1995**, 60, 931.
4. Rowe, B. J.; Spilling, C. D. *J. Org. Chem.* **2003**, 68, 9502

Column-S,S Whelk-O, EtOH:hexane (20:80), 1 mL/min, det 254 nm

Racemic

Retention time (min)	Area	% Area
6.97	5211	49.7
8.58	5281	50.3

R Isomer (95% e.e.)

Retention time (min)	Area	% Area	Ratio
6.88	503	2.5	39
8.38	19854	97.5	1

Racemic

Retention time (min)	Area	% Area
4.17	15318	48.2
4.65	16481	51.8

R Isomer (95% e.e.)

Retention time (min)	Area
3.5	impurity
4.17	10595
4.65	Not measured

Column-Chiralpak-AS, EtOH:hexane (20:80), 1 mL/min, det 210 nm

Dimer from Racemic 2a

Retention time (min)	Area	% Area
6.57	2886	23
7.50	9618	77

Isolated Crude from Dimerization of R-2a (70% e.e.)

Retention time (min)	Area	% Area
6.45	2211	75
7.43	728	25

Recrystallized product from Dimerization of R-2a

Retention time (min)	Area	% Area
6.52	462	17
7.43	2320	83

Mother liquor from Recrystallization of Dimerization Product of R-2a

Retention time (min)	Area	% Area
6.47	7834	82
7.45	1748	18

Table 1. Crystal data and structure refinement for cds14502.

Identification code	s14502/lt	
Empirical formula	C ₈ H ₁₈ O ₈ P ₂	
Formula weight	304.16	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 20.1094(14) Å	α = 90°.
	b = 7.4334(5) Å	β = 120.158(4)°.
	c = 10.5575(7) Å	γ = 90°.
Volume	1364.53(16) Å ³	
Z	4	
Density (calculated)	1.481 Mg/m ³	
Absorption coefficient	0.347 mm ⁻¹	
F(000)	640	
Crystal size	0.30 x 0.30 x 0.28 mm ³	
Theta range for data collection	2.34 to 29.97°.	
Index ranges	-28 ≤ h ≤ 27, -10 ≤ k ≤ 10, -14 ≤ l ≤ 14	
Reflections collected	16236	
Independent reflections	1882 [R(int) = 0.0172]	
Completeness to theta = 29.97°	94.4 %	
Absorption correction	None	
Max. and min. transmission	0.9091 and 0.9031	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	1882 / 0 / 118	
Goodness-of-fit on F ²	1.099	
Final R indices [I > 2σ(I)]	R1 = 0.0383, wR2 = 0.1077	
R indices (all data)	R1 = 0.0437, wR2 = 0.1125	
Largest diff. peak and hole	0.606 and -0.384 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for cds14502. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
P(1)	1269(1)	2379(1)	1048(1)	22(1)
O(1)	1262(1)	396(1)	1001(1)	28(1)
O(2)	634(1)	3327(2)	-383(1)	28(1)
O(3)	1129(1)	3158(2)	2284(1)	32(1)
O(4)	2736(1)	2724(2)	2628(1)	30(1)
C(1)	2139(1)	3420(2)	1283(2)	24(1)
C(2)	-164(1)	2796(3)	-993(2)	35(1)
C(3)	1269(2)	2115(3)	3542(2)	48(1)
C(4)	2236(1)	3044(2)	-26(2)	26(1)

Table 3. Bond lengths [$\text{\AA}$] and angles [$^\circ$] for cds14502.

P(1)-O(1)	1.4747(11)
P(1)-O(2)	1.5719(10)
P(1)-O(3)	1.5772(11)
P(1)-C(1)	1.8131(14)
O(2)-C(2)	1.4522(19)
O(3)-C(3)	1.438(2)
O(4)-C(1)	1.4181(17)
C(1)-C(4)	1.5146(19)
C(4)-C(4)#1	1.315(3)
O(1)-P(1)-O(2)	115.23(6)
O(1)-P(1)-O(3)	113.12(6)
O(2)-P(1)-O(3)	103.54(6)
O(1)-P(1)-C(1)	115.01(6)
O(2)-P(1)-C(1)	101.69(6)
O(3)-P(1)-C(1)	106.96(6)
C(2)-O(2)-P(1)	119.19(10)
C(3)-O(3)-P(1)	122.17(12)
O(4)-C(1)-C(4)	114.49(12)
O(4)-C(1)-P(1)	104.72(9)
C(4)-C(1)-P(1)	110.70(9)
C(4)#1-C(4)-C(1)	123.18(17)

Symmetry transformations used to generate equivalent atoms:

#1 $-x+1/2, -y+1/2, -z$

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for cds14502. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	24(1)	22(1)	21(1)	1(1)	12(1)	1(1)
O(1)	28(1)	22(1)	33(1)	0(1)	14(1)	-1(1)
O(2)	25(1)	33(1)	25(1)	6(1)	12(1)	2(1)
O(3)	44(1)	31(1)	29(1)	4(1)	24(1)	6(1)
O(4)	29(1)	28(1)	25(1)	2(1)	7(1)	-4(1)
C(1)	26(1)	24(1)	22(1)	-1(1)	11(1)	-2(1)
C(2)	23(1)	44(1)	33(1)	4(1)	12(1)	1(1)
C(3)	72(2)	52(1)	30(1)	9(1)	34(1)	5(1)
C(4)	28(1)	26(1)	24(1)	0(1)	13(1)	-4(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for cds14502.

	x	y	z	U(eq)
H(1)	2057(10)	4840(20)	1194(19)	23(4)
H(2A)	-190(15)	1650(30)	-1110(30)	54(7)
H(2B)	-445(16)	3430(30)	-1850(30)	62(7)
H(2C)	-337(16)	2890(40)	-250(30)	61(7)
H(3A)	1010(30)	2630(50)	3840(50)	118(15)
H(3B)	1230(20)	860(50)	3390(40)	101(11)
H(3C)	1780(30)	2350(50)	4260(50)	130(18)
H(4)	1865(12)	3640(30)	-980(20)	36(5)
H(4A)	3073(16)	3600(40)	3130(30)	61(7)

Projection view with 50% thermal ellipsoids

Crystal Packing with H-bonds: