The Olefin Synthesis from β-Hydroxyalkylphosphonates Induced by Fluorides or Relatively Weak Bases

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β-Hydroxyalkylphosphonates, which were prepared readily from alkylphosphonates and carbonyl compounds, were treated with a fluoride ion such as CsF or with relatively weak bases such as K_2CO_3 in *N*,*N*-dimethylformamide to give the corresponding olefins in good yields. One molar equivalent of water to bases is effective for increasing the yields of olefins. The stereochemistry of *erythro*-dimethyl (2-hydroxy-1-methyl-2-phenyl)ethylphosphonate was determined by X-ray crystallographic analysis. Use of *threo-isomer* gave (*E*)-olefin exclusively, while that of *erythro*-enriched isomer afforded predominantly (*Z*)-olefin, indicating that the present olefination proceeds stereospecifically in a manner of *syn*-elimination.

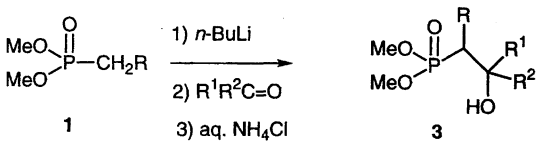
The Wittig reaction has widely been utilized as a useful method for olefin synthesis from carbonyl compounds.[1] On the other hand, the Horner–Emmons reaction[1a,1c,2] was developed as a synthetic improvement of the Wittig reaction incorporating the following feature: (1) Instead of phosphine oxides, which are by-products of the Wittig reaction, salts of phosphoric acid esters or phosphinic acids are very soluble in water, so that their removal is easy. (2) These carbanions are more nucleophilic than phosphorus ylides, because of less stabilization of carbanion. Such reagents are available for less reactive carbonyl compounds such as some of the ketones.

When phosphonates without any carbanion stabilizing group at α-position of the phosphorus atom were used, however, the yield of the olefin was quite low. In order to overcome such a difficulty, several modifications based on exchange of the ligand on the phosphorus atom have been reported. As the first approach, use of phosphonic diamides was disclosed by Corey and co-workers.[3a,3b,3e,3d] Then reactions using thiophosphates,[3c] diphenylphosphine oxides,[4] thiophosphinic amides,[5] and phosphinic amides[6] have been developed. Hannesian and co-workers reported the synthesis of optically active olefins using chiral phosphonic diamides.[7] In the course of our study on the Horner–Emmons reaction under neutral conditions,[8] we found that β-hydroxyalkylphosphonates could be treated with fluorides to give the corresponding olefins and reported preliminary results.[9] In this paper we wish to report full details of the present olefin formation reaction and its stereochemistry.

Results and Discussion

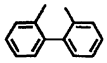
Preparation of β-Hydroxyalkylphosphonates. Sequential treatment of dimethyl alkylphosphonates (**1**) with 1.05—1.10 molar equivalent of *n*-BuLi (−78 °C, THF, 5 min), 1.05—1.10 molar equivalent of carbonyl compounds (**2**) (−78 °C, 5 min), and then aq NH_4Cl (−78 °C → r.t.) gave the corresponding β-hydroxyalkylphosphonates **3** in good yields, as shown in Table 1. In the reaction with enolizable carbonyl compounds, use of methylphosphonate **1a** gave the β-hydroxy phosphonates in better yields than that of ethylphosphonate **1b**, because of the steric bulkiness of the latter nucleophilic center (Entries 2 and 10). The reaction using **1a** and dibenzyl ketone afforded almost quantitatively the corresponding hydroxyalkylphosphonate **3b** (Entry 2), but the reaction using methyldiphenylphosphine oxide instead of **1a** gave the corresponding adduct **4** in 46% yield, indicating that the lithiomethylphosphonate has higher nucleophilicity than the lithiomethyl(diphenyl)phosphine oxide.

Table 1. Preparation of Dimethyl β-Hydroxyalkylphosphonates **3**



1 **3**

a: R= H
b: R=Me

Entry	1	3	R	R^1	R^2	Yields[a]/%
1	**1a**	**3a**	H	Ph	Ph	96
2	**1a**	**3b**	H	$PhCH_2$	$PhCH_2$	97
3	**1a**	**3c**	H	Me	Ph	95
4	**1a**	**3d**	H	n-$C_{11}H_{23}$	H	99
5	**1a**	**3e**	H	$-(CH_2)_5-$		95
6	**1a**	**3f**	H			97
7	**1a**	**3g**	H	p-$O_2NC_6H_4$	H	91
8	**1a**	**3h**	H	Ph	H	100
9	**1b**	**3i**	Me	Ph	Ph	100
10	**1b**	**3j**	Me	$PhCH_2$	$PhCH_2$	47

a) Isolated yields based on **1**.

Diastereoselective Formation of β-Hydroxyalkylphosphonates. The reaction using dimethyl ethylphosphonate (**1a**) and benzaldehyde gave a diastereomeric mixture of dimethyl (2-hydroxy-1-methyl-2-phenyl)ethylphosphonates (*erythro*- and *threo*-**3k**). The stereochemistry of *erythro*-**3k** was determined by X-ray crystallographic analysis. The crystal data are summarized in Tables 2, 3, 4, and 5 and the ORTEP drawing is shown in Fig. 1. Interestingly, although intramolecular hydrogen-bonding between the hydroxy group and the phosphoryl group was expected, only intermolecular hydrogen-bonding (P=O···H–O; O···H and O···O separations are 1.93 and 2.643(8) Å, respectively, with an O···H–O angle of 119°) was observed, in sharp contrast to the crystal structure of 2-(1*RS*,2*SR*)diphenylphosphinoyl-1-phenylpropan-1-ol.[4c] Bond lengths and bond angles were normal values.

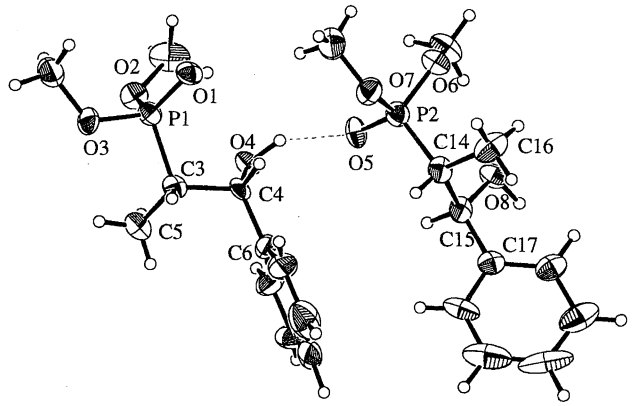
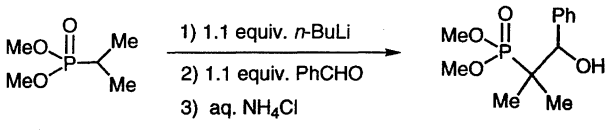


Fig. 1. ORTEP drawing of *erythro*-**3k** with thermal ellipsoid plots (30% probability). Selected bond Lengths (Å), bond angles (deg), and torsion angles (deg): P1–O1, 1.494(6); P1–O2, 1.576(7); P1–C3, 1.79(1); P2–O5, 1.502(6); P2–O6, 1.573 (7); P2–C14, 1.76(1); O1–P1–C3, 112.6(4); P1–C3–C5, 111.5(8); C3–C4–O4, 107.9(9); C3–C4–C6, 114.3(9); O5–P2–C14, 114.7(5); P2–C14–C16, 112.9(8); C14–C15–O8, 107.5(9); C14–C15–C17, 112(1); P1–C3–C4–O4, −57.1(9); P1–C3–C4–C6, 175.3(8); P2–C14–C15–O8, 60.7(10); P2–C14–C15–C17, −172.3(8).

Table 2. Crystal Data of *erythro*-Dimethyl (2-Hydroxy-1-methyl-2-phenyl)ethylphosphonate (*erythro*-**3k**)

Formula	$C_{11}H_{17}PO_4$
Formula weight	244.23
Crystal color, habit	Colorless, Plate
Crystal dimensions(mm)	0.50 × 0.30 × 0.05
Crystal system	Monoclinic
Space group	*P*2/*a*
Z	8
a/Å	18.861(4)
b/Å	8.334(3)
c/Å	19.167(2)
V/Å^3	2646(1)
d_{calcd}/g cm^{-3}	1.226
β/deg	118.543(9)
F(000)	1040.00
μ/cm^{-1}	2.05
$2\theta_{max}$/deg	55.0
No. of reflections measured	5770
No. observations (I > 3.00σ(I))	1651
No. variables	289
R	0.077
R_w	0.041

In order to investigate stereoselectivity, the reactions under various conditions were examined; the results are summarized in Table 6. As shown in Table 6, all reactions except for that using potassiomethylphosphonate gave mainly *erythro*-**3k** and THF and lithiomethylphosphonate gave the best *erythro*-selectivity among the solvents and cations examined, respectively. Thus, use of THF and lithiomethylphosphonate at −98 °C afforded 85% diastereomeric excess (d.e.) and 98% chemical yield. A similar *erythro*-selectivity was first reported by Corey and Kwiatkowsky in the reaction using phosphonic diamides,[3a] and later by Warren et al. in that using diphenylpropylphosphine oxide.[4b] In the recent review, Clayden and Warren have proposed a new transition state based on the calculated structure of the lithiomethyl(diphenyl)phosphine oxide.[4a] On the other hand, *threo* isomer was mainly obtained by sequential treatment of **1a** with 1.1 molar equivalent of *n*-BuLi, benzaldehyde (1.1 molar equivalent), *n*-BuLi (5—15 molar equivalent), iodomethane (excess), and saturated aq NH_4Cl, as shown in Table 7. Diastereomeric excess of *threo*-**3k** was around 53—57% in THF, while it was > 99% in dimethoxymethane. The present solvent effect remains still unclear. Dimethyl (2-hydroxy-2-phenyl)ethylphosphonate (**3h**) and dimethyl (2-hydroxy-1,1-dimethyl-2-phenyl)ethylphosphonate (**3l**) were obtained as by-products in THF and dimethoxymethane, respectively, and *erythro*-**3k** could be removed by recrystallization, but **3h** and **3l** could not be separated even by chromatography. By-product **3l** was alternatively synthesized, as shown in the following equation (Eq. 1).



(1)

Olefin Synthesis from β-Hydroxyalkylphosphonates in the Presence of Weak Bases. In the course of our study on the fluoride ion-induced Horner–Emmons reaction, it has been found that β-trimethylsiloxyethylphosphonate **5a** was treated with CsF to give almost quantitatively 1,1-diphenylethylene (**6a**).[8] Although most of the olefin was considered to be formed via β-oxidoethylphosphonate **7a**, which was generated by an attack of fluoride ion on the Si, some amount of the olefin seemed to come from β-hydroxyalkylphosphonate **3a**, because water remaining in CsF must be responsible for the protodesilylation of **5a** giving **3a**.

Table 3. Atomic Coordinates and B_{iso}/B_{eq}

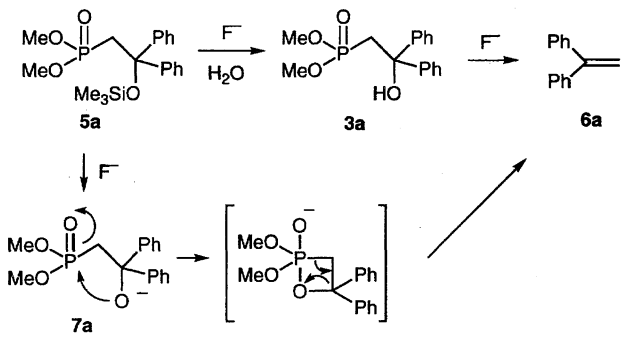
Atom	x	y	z	B_{eq}	Atom	x	y	z	B_{eq}
P(1)	0.5622(2)	0.4391(4)	0.3539(2)	4.03(9)	H(2)	0.5351	0.7733	0.3204	9.3762
P(2)	0.2147(2)	0.4888(4)	0.1443(2)	4.62(9)	H(3)	0.5410	0.8257	0.4006	9.3762
O(1)	0.5242(4)	0.4601(8)	0.2659(4)	4.7(2)	H(4)	0.7002	0.4681	0.3374	7.9386
O(2)	0.5735(4)	0.6005(9)	0.4009(4)	5.0(2)	H(5)	0.7176	0.5619	0.4138	7.9386
O(3)	0.6505(4)	0.3723(8)	0.3964(4)	5.2(2)	H(6)	0.7623	0.4020	0.4199	7.9386
O(4)	0.4010(4)	0.4752(8)	0.3497(4)	4.4(2)	H(7)	0.5220	0.1898	0.3650	4.8449
O(5)	0.2578(3)	0.5431(8)	0.2293(3)	4.9(2)	H(8)	0.4037	0.3110	0.2791	4.3037
O(6)	0.1695(4)	0.6296(9)	0.0849(4)	5.3(2)	H(9)	0.5352	0.3837	0.4876	8.2207
O(7)	0.2718(4)	0.4231(9)	0.1123(4)	5.9(2)	H(10)	0.6024	0.2683	0.4935	8.2207
O(8)	0.0553(4)	0.4861(8)	0.1451(4)	4.7(2)	H(11)	0.5216	0.1996	0.4834	8.2207
C(1)	0.5265(8)	0.742(1)	0.3638(7)	7.6(5)	H(12)	0.3738	0.0301	0.2707	8.2207
C(2)	0.7135(6)	0.461(2)	0.3908(6)	6.6(4)	H(13)	0.3046	−0.1689	0.2978	10.6562
C(3)	0.5123(6)	0.290(1)	0.3822(5)	4.1(3)	H(14)	0.2617	−0.1260	0.3919	11.4286
C(4)	0.4187(6)	0.314(1)	0.3346(5)	3.7(3)	H(15)	0.2866	0.1196	0.4595	10.1513
C(5)	0.5454(6)	0.285(1)	0.4713(6)	6.8(4)	H(16)	0.3608	0.3151	0.4345	7.4068
C(6)	0.3718(6)	0.190(2)	0.3487(7)	4.1(3)	H(17)	0.3679	0.4697	0.2847	6.9701
C(7)	0.3559(8)	0.047(2)	0.3088(8)	6.9(5)	H(18)	0.1206	0.8410	0.0640	7.9840
C(8)	0.315(1)	−0.070(2)	0.3238(10)	6.9(5)	H(19)	0.1106	0.7464	0.1285	7.9840
C(9)	0.2897(10)	−0.048(2)	0.378(1)	9.9(6)	H(20)	0.1931	0.8235	0.1487	7.9840
C(10)	0.3040(10)	0.097(2)	0.4207(10)	8.6(6)	H(21)	0.3119	0.6113	0.0827	7.7026
C(11)	0.3466(7)	0.215(2)	0.4061(9)	6.5(4)	H(22)	0.3625	0.4581	0.0923	7.7026
C(12)	0.1455(7)	0.773(1)	0.1081(6)	6.4(4)	H(23)	0.3710	0.5476	0.1669	7.7026
C(13)	0.3347(6)	0.519(2)	0.1133(6)	6.6(4)	H(24)	0.1835	0.2322	0.1477	5.4263
C(14)	0.1494(6)	0.324(1)	0.1258(6)	4.5(3)	H(25)	0.1396	0.3602	0.2276	5.5378
C(15)	0.1011(6)	0.344(2)	0.1722(5)	4.6(3)	H(26)	0.0574	0.3788	0.0114	7.9966
C(16)	0.0943(6)	0.291(1)	0.0351(6)	6.6(4)	H(27)	0.1255	0.2789	0.0088	7.9966
C(17)	0.0529(8)	0.198(2)	0.1675(7)	4.3(4)	H(28)	0.0632	0.1957	0.0279	7.9966
C(18)	−0.0293(9)	0.189(2)	0.1168(7)	5.5(4)	H(29)	−0.0563	0.2795	0.0829	6.5794
C(19)	−0.0740(10)	0.051(2)	0.1144(9)	8.1(5)	H(30)	−0.1317	0.0470	0.0787	9.7090
C(20)	−0.034(1)	−0.076(2)	0.162(1)	10.5(9)	H(31)	−0.0629	−0.1714	0.1599	13.5137
C(21)	0.046(1)	−0.067(3)	0.210(1)	9.8(8)	H(32)	0.0737	−0.1523	0.2455	12.4462
C(22)	0.0877(8)	0.063(2)	0.2134(8)	6.9(5)	H(33)	0.1450	0.0642	0.2492	8.2559
H(1)	0.4701	0.7178	0.3428	9.3762	H(34)	0.0087	0.4817	0.1601	18.8080

Table 4. Bond Lengths (Å) Involving the Nonhydrogen Atoms

Atom	Atom	Distance	Atom	Atom	Distance
P(1)	O(1)	1.494(6)	P(1)	O(2)	1.576(7)
P(1)	O(3)	1.566(6)	P(1)	C(3)	1.79(1)
P(2)	O(5)	1.502(6)	P(2)	O(6)	1.573(7)
P(2)	O(7)	1.571(7)	P(2)	C(14)	1.76(1)
O(2)	C(1)	1.45(1)	O(3)	C(2)	1.45(1)
O(4)	C(4)	1.45(1)	O(6)	C(12)	1.43(1)
O(7)	C(13)	1.42(1)	O(8)	C(15)	1.41(1)
C(3)	C(4)	1.57(1)	C(3)	C(5)	1.51(1)
C(4)	C(6)	1.47(1)	C(6)	C(7)	1.37(2)
C(6)	C(11)	1.41(1)	C(7)	C(8)	1.35(2)
C(8)	C(9)	1.35(2)	C(9)	C(10)	1.40(2)
C(10)	C(11)	1.38(2)	C(14)	C(15)	1.56(1)
C(14)	C(16)	1.57(1)	C(15)	C(17)	1.50(1)
C(17)	C(18)	1.38(1)	C(17)	C(22)	1.38(2)
C(18)	C(19)	1.41(2)	C(19)	C(20)	1.37(2)
C(20)	C(21)	1.35(2)	C(21)	C(22)	1.33(2)

Table 5. Bond Angles (°) Involving the Nonhydrogen Atoms

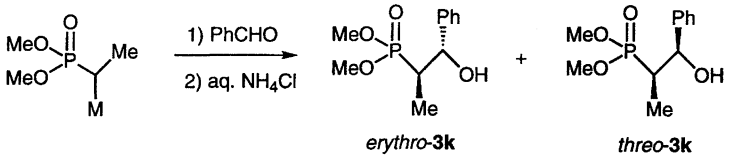
Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
O(1)	P(1)	C(14)	114.0(4)	O(1)	P(1)	O(3)	116.5(4)
O(1)	P(1)	C(3)	112.6(4)	O(2)	P(1)	O(3)	100.7(4)
O(2)	P(1)	C(3)	111.5(4)	O(3)	P(1)	C(3)	100.2(5)
O(5)	P(2)	O(6)	112.7(4)	O(5)	P(2)	O(7)	114.3(4)
O(5)	P(2)	O(14)	114.7(5)	O(6)	P(2)	O(7)	102.2(4)
O(6)	P(2)	C(14)	110.5(5)	O(7)	P(2)	C(14)	101.2(5)
P(1)	O(2)	C(1)	122.3(7)	P(1)	O(3)	C(2)	119.2(7)
P(2)	O(6)	C(12)	123.0(7)	P(2)	O(7)	C(13)	121.6(8)
P(1)	C(3)	C(4)	110.0(7)	P(1)	C(3)	C(5)	111.5(8)
C(4)	C(3)	C(5)	113.8(9)	O(4)	C(4)	C(3)	107.9(9)
O(4)	C(4)	C(6)	113.7(9)	C(3)	C(4)	C(6)	114.3(9)
C(4)	C(6)	C(7)	120(1)	C(4)	C(6)	C(11)	119(1)
C(7)	C(6)	C(11)	120(1)	C(6)	C(7)	C(8)	120(1)
C(7)	C(8)	C(9)	120(2)	C(8)	C(9)	C(10)	121(2)
C(9)	C(10)	C(11)	117(1)	C(6)	C(11)	C(10)	119(1)
P(2)	C(14)	C(15)	110.3(8)	P(2)	C(14)	C(16)	112.9(8)
C(15)	C(14)	C(16)	113.2(9)	O(8)	C(15)	C(14)	107.5(9)
O(8)	C(15)	C(17)	114.4(10)	C(14)	C(15)	C(17)	112(1)
C(15)	C(17)	C(18)	121(1)	C(15)	C(17)	C(22)	122(1)
C(18)	C(17)	C(22)	115(1)	C(17)	C(18)	C(19)	121(1)
C(18)	C(19)	C(20)	118(1)	C(19)	C(20)	C(21)	119(2)
C(20)	C(21)	C(22)	121(2)	C(17)	C(22)	C(21)	123(1)



(2)

This result prompted us to investigate the direct olefin formation from **3a** in the presence of fluoride ion. In fact, on heating with fluoride ion **3a** gave the corresponding olefin **6a** (Eq. 2). The results are shown in Table 8. Acetonitrile, 1,2-dimethoxyethane (DME), and *N*,*N*-dimethylformamide (DMF) can be effectively used as solvents for conversion of **3a** to **6a**. Among fluorides, CsF, KF, and Me_4NF can be used nicely, indicating that the kind of the counter cation is not so important. On the contrary, addition of an equimolar amount of water to the fluorides was very effective. A two phase system using toluene and benzene in the presence of phase transfer catalyst was also available, although the yield was around 50%. The additive water probably makes the surface area of the fluoride increase by the formation of their hydrate and/or controls basicity of the fluoride ion by hydro-

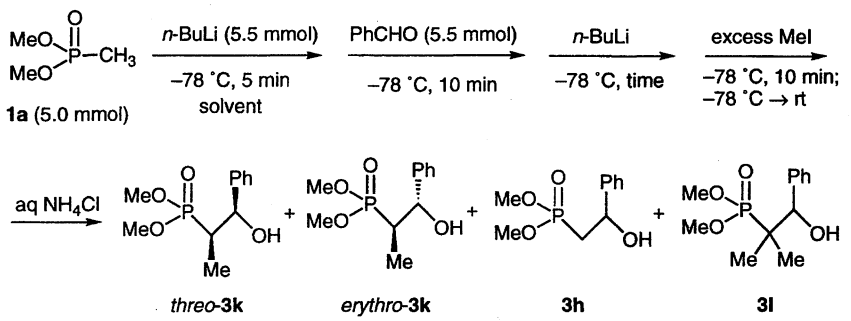
Table 6. Diastereomeric Excess (% d.e.) and Chemical Yields of **3k**



			% d.e.[a](Yields[b])/%		
Entry	M	Solvent	−78 °C	−98 °C	−120 °C
1	Li	THF	79 (96)	85 (98)	85 (79)
2	Li	THF–TMEDA	79 (98)	81 (98)	80 (62)
3	Li	THF–HMPA	74 (26)	—	—
4	Li	DME–TMEDA	61 (98)	—	—
5	Li	Et_2O	42 (94)	41 (96)	—
6	Li	$(MeO)_2CH_2$	48 (96)	50 (99)	—
7	Li	Toluene	38 (96)	31 (96)	—
8	Li	Hexane	5 (42)	—	—
9	K	THF	−1 (73)	—	—
10	MgCl	THF	64 (96)[c]	—	—
11	MgCl	THF–TMEDA	46 (90)[c]	—	—

a) Diastereomeric excess of *erythro*-**3k** was determined by ^{31}P NMR. b) Isolated yields based on **1b**. c) The temperature was raised from −78 °C to 5 °C.

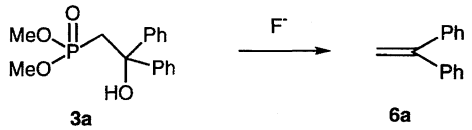
Table 7. Diastereomeric Excess (% d.e.) and Chemical Yields of **3k**



Entry	Solvent	*n*-BuLi/mmol	Time/min	% d.e.[a]	Yields[b]/%
1	THF	5.5	10	53	73[c]
2	THF	5.5	30	53	72[c]
3	THF	15.0	5	57	88[c]
4	$(MeO)_2CH_2$	15.0	5	>99	60[d]

a) Diastereomeric excess of *threo*-**3k** was obtained by ^{31}P NMR. b) Obtained by ^{31}P NMR. c) Compound **3h** was obtained. d) Compound **3l** was obtained instead of **3h**.

Table 8. Fluoride Ion Induced Olefin synthesis from **3a**



3a **6a**

Entry	**3a**/mmol	Fluorides	mmol	Solvent	Temp/°C	Time/h	Yields[a]/%
1	0.71	CsF	4.1	CH_3CN	Reflux	24	87
2	0.68	CsF	3.6	DME	Reflux	24	96
3	0.66	Me_4NF	1.6	DME	Reflux	48	44
4	1.78	CsF–H_2O	6.9	DMF	55	16	83
5	1.43	KF–H_2O	10.0	DMF	95	6	54
6	1.80	CsF–H_2O	6.6	DMF	90	5	85
7	1.77	CsF–H_2O SiO_2 (0.6 g)	7.2	DMF	90	24	74
8	1.20	*n*-Bu_4NBr KF (5 g) H_2O (5 ml)	0.8	Toluene	55	2	50
9	1.09	*n*-Bu_4NBr KF (5 g) H_2O (5 ml)	0.9	Benzene	Reflux	2	<50
10	1.03	KF (5 g) H_2O (5 ml)	1.03	Toluene	Reflux	24	<15
11	0.66	*n*-Bu_4NF	0.66	THF	r.t.	24	0

a) Isolated yields based on **3a**.

gen-bonding.

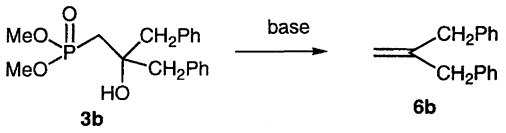
In order to elucidate whether double bond migration of the olefin occurs or not under the reaction conditions, the reaction using dibenzyl ketone adduct **3b** was carried out. The results are summarized in Table 9. Although the double-bond migrated olefin is thermodynamically more stable than the first product because of the presence of conjugation between the benzene ring and the ethylene moiety and an increase in the number of the substituents, no migrated olefin was obtained at all, indicating that this reaction is useful for the regioselective olefin synthesis (Entries 1—5 in Table 9).

Next, the effect of an acid formed as a by-product on the yield of the olefin was examined. The reaction in the presence of potassium carbonate was carried out to give olefin **6b** in 77% yield (Entry 7). In the reaction of **3b** with the base without any fluoride ion, which was done as a control experiment, very interestingly, **6b** was obtained in almost the same yield (Entries 8—19). When a protic solvent such as ethanol and 1,2-ethanediol was used, the yield of **6b** was quite low (Entries 12 and 13), but methanol can be used as an additive instead of water (Entries 19 and 20). Among alkaline carbonates, Na_2CO_3 did not work (Entry 16), which can not be explained. This result prompted us to investigate the reaction using relatively weak organic bases (Entries 21—25). The reactions using DBU, triethylamine, and 2,6-lutidine gave the corresponding olefin in 51, <20, and 0% yields, respectively. Metal phenoxides were very effective, while metal alkoxides which are stronger bases than the phenoxides did not afford the olefin at all (Entries 25—29). Under the reaction conditions used for the olefin formation reaction using hydroxyalkyldiphenylphosphine oxides by Warren and coworkers,[4] i. e., NaH in DMF at room temperature or KOH in DMF, no olefin was obtained at all (Entry 29). It is interesting that the reaction using *t*-BuOCs afforded the starting ketone and phosphonate in 90% yield after the usual workup, in marked contrast to those using other bases (Entry 30).

Judging from the results as shown in Table 9, we find that relatively weak bases whose conjugate acids have pK_a around 10 (HCO_3^- 10.33, PhOH 9.98)[10] are very effective for the present olefin formation reaction. Strong bases probably underwent side reactions such as deprotonation of the proton on the carbon α to the phosphoryl group, followed by β-elimination of a hydroxide ion giving the corresponding vinylphosphonate,[3c] and retroaddition reaction affording the ketone and dimethyl methylphosphonate (see Footnote of Table 9), so the olefin could not be obtained.

As a fluoride ion is known to catalyze transesterification of phosphate triesters,[11] Path a as shown in Scheme 1 was thought at first to be operative for the mechanism: the formation of tetracoordinate 1,2-oxaphosphetane **8** by a fluoride ion-catalyzed intramolecular transesterification and spontaneous Wittig-type olefination to give olefin **6** and dimethyl phosphate (**9**), which is methanolysis product of metaphosphate.[12] From the facts that this type of transesterification is limited to aryl esters at least intermolecularly,[11] though there has been no report on intramolecular transesterification using alkyl esters and that relatively weak bases other than fluorides can be used, now we wish to propose another mechanism, as shown in Path b.[13] An increase in the strength of the hydrogen-bonding of the hydroxy group with the fluoride ion in order, going from the starting β-hydroxyalkylphosphonate **3** via intermediary pentacoordinate 2-hydroxy-1,2-oxaphosphetanes **10** to **9**, can be considered as a driving force of the present reaction. Several weak bases besides the

Table 9. Base Induced Olefin Synthesis from **3b**



3b **6b**

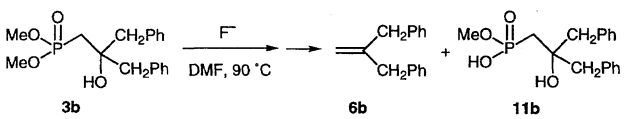
Entry	**3b**/mmol	Base	mmol	Solvent	Temp/°C	Time/h	Yields[a]/%
1	1.69	CsF	4.7	CH_3CN	Reflux	96	90
2	2.24	CsF	6.3	DMF	90	48	85
3	1.96	KF[b]–H_2O	11.0	DMF	110	24	74
4	1.00	CsF	3.2	DMF	65	48	50[c]
5	1.13	CsF–H_2O	3.8	DMF	65	48	81
6	1.11	CsF–H_2O	3.9	DMSO	90	48	85
7	1.97	CsF–H_2O K_2CO_3	3.9	DMF	90—100	96	77
8	1.97	K_2CO_3–H_2O	10.2	DMSO	80	100	73
9	2.03	K_2CO_3–H_2O	10.2	DMSO	100	24	76
10	1.97	K_2CO_3–$2H_2O$	9.8	DMSO	100	24	75
11	2.22	K_2CO_3–H_2O	14.3	DMF	100	24	71
12	2.33	K_2CO_3	14.5	EtOH	Reflux	14	28[d]
13	2.32	K_2CO_3	12.1	$HOCH_2CH_2OH$	95	14	13
14	2.25	K_2CO_3–H_2O	12.1	DMF	135	14	78
15	2.27	$KHCO_3$–H_2O	12.7	DMF	135	14	66
16	2.05	Na_2CO_3–H_2O	11.0	DMF	87	18	0[c]
17	2.02	K_2CO_3–H_2O	11.0	DMF	87	18	41[c]
18	2.07	Cs_2CO_3–H_2O	4.6	DMF	87	18	51[c]
19	1.08	K_2CO_3–MeOH	4.99	DMF	90	48	64
20	1.22	CsF–MeOH	5.52	DMF	90	48	56
21	1.05	DBU	5.0	DMF	100—105	14	56[c]
22	1.07	Et_3N	5.0	DMF	90—100	36	<20[c]
23	1.16	2,6-Lutidine	5.8	DMF	85	24	0
24	1.19	PhOLi	7.0	DMF	85—100	0.5	77
25	1.12	PhOK	3.1	DMF	90	1	72
26	1.91	MeOK	4.0	DMF	55	4	0[e]
27	2.85	*t*-BuOK	2.85	DMF	65	48	0[e]
28	0.94	KH	1.41	DMF	r.t.	12	0[e]
29	0.35	NaH	3.45	DMF	r.t.	12	0[e]
30	0.35	*t*-BuOCs	3.8	DMF	90	24	0[f]

a) Isolated yields based on **3b**. b) Freeze-dry KF was used. c) **3b** was recovered. d) Unidentified products were obtained. e) A complex mixture was obtained. The formations of the corresponding vinylphosphonate and $(MeO)_2P(O)Me$ were estimated from the ^{31}P NMR spectrum. f) $(PhCH_2)_2CO$ and $(MeO)_2P(O)Me$ were obtained.

fluoride ion seem to act similarly to shift the equilibration gradually to the products.

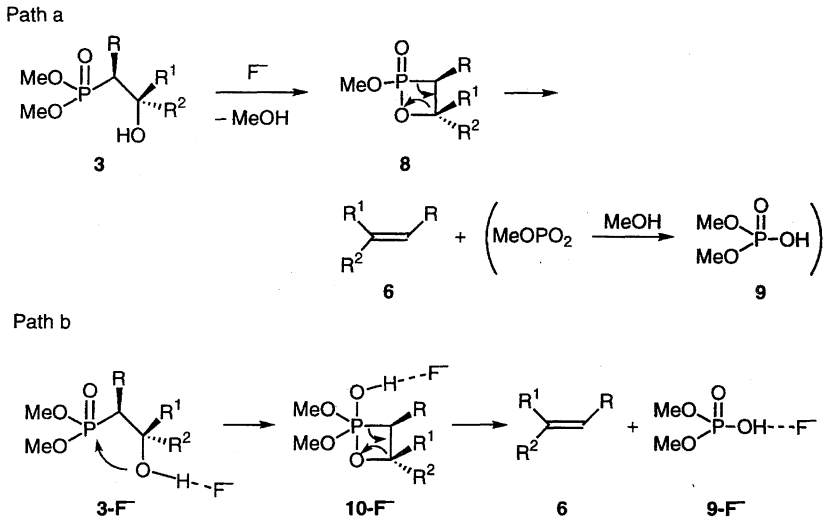
The present olefin formation reaction was applicable to various carbonyl adducts as shown in Table 10. The yields were moderate to good, but as shown in Entries 8 and 9, *p*-nitrobenzaldehyde adduct did not afford the corresponding olefin, but an unidentified product, indicating the limitation that this method can not be applied to β-hydroxyalkylphosphonates having a strong electron-withdrawing group.

Identification of the Side Reaction Product. The reaction using **3b** in the presence of CsF–H_2O in DMF was monitored by ^{31}P NMR spectroscopy to show disappearance of the starting material and the formation of some amount of the side reaction product **11b** (Eq. 3). The signal due to dimethyl phosphate (**9**), which seems to be formed together with the olefin, was not observed, probably because it was absorbed on the surface of the fluoride salts.[14] As **9** and **11b** were water-soluble, only olefin was obtained by treatment of the reaction mixture with water, followed by extraction with hexane and removal of the solvent, providing a synthetic merit of the present method. In order to determine the structure of the by-product, the aqueous layer was acidified with HCl, and then extracted with CH_2Cl_2. A small amount of the by-product was isolated, whose structure was estimated to be monoester **11b** from its NMR data. Finally it could be determined by the following alternative synthesis: Treatment of **3b** with NaI in acetonitrile, followed by acidification with HCl, afforded monoester **11b** in 97% yield (Eq. 4).[12] The spectral data of **11b** agreed with those of the by-product.



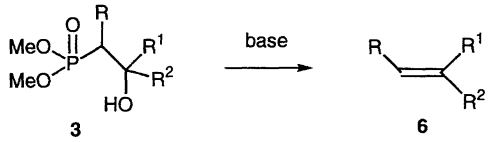
3b **6b** **11b**

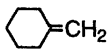
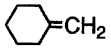
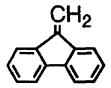
(3)



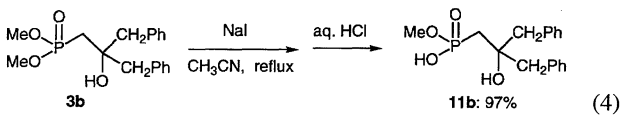
Scheme 1. Plausible mechanisms of the present olefin formation.

Table 10. Synthesis of Other Olefins



Entry	3	mmol	Base	mmol	Temp/°C	Time/h	Olefin	Yields[a]/%
1	**3c**	5.19	$CsF–H_2O$	14.0	80	9	$PhMeC=CH_2$	76
2	**3c**	3.87	$K_2CO_3–H_2O$	21.1	85	40	$PhMeC=CH_2$	75
3	**3d**	1.21	$CsF–H_2O$	4.2	100	48	$n\text{-}C_{11}H_{23}CH=CH_2$	62
4	**3d**	2.97	$K_2CO_3–H_2O$	23.4	130	48	$n\text{-}C_{11}H_{23}CH=CH_2$	41
5	**3e**	7.38	$CsF–H_2O$	21.7	100	48		46
6	**3e**	8.63	$K_2CO_3–H_2O$	56.0	110	48		52
7	**3f**	3.26	$CsF–H_2O$	12.2	85	24		100
8	**3g**	0.41	$CsF–H_2O$	1.58	85	8	$p\text{-}O_2NC_6H_4CH=CH_2$	0
9	**3g**	2.36	$KHCO_3–H_2O$	15.4	80	24	$p\text{-}O_2NC_6H_4CH=CH_2$	0
10	**3i**	1.44	$K_2CO_3–H_2O$	7.9	45—50	48	$Ph_2C=CHMe$	91
11	**3j**	2.70	$CsF–H_2O$	7.0	92	48	$(PhCH_2)_2C=CHMe$	78
12	**3j**	3.08	CsF	7.2	105	48	$(PhCH_2)_2C=CHMe$	70

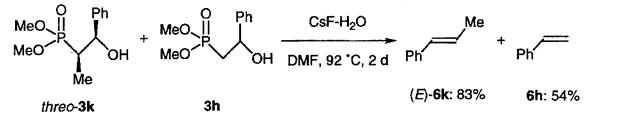
a) Isolated yields based on **3**.



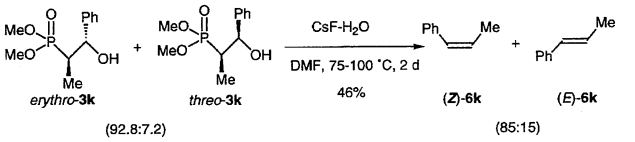
(4)

Stereospecific Olefin Formation from *erythro*- and *threo*-Dimethyl (2-Hydroxy-1-methyl-2-phenyl)ethylphosphonates (*erythro*- and *threo*-3k). In order to clarify the stereochemistry of the present olefin formation reaction, the reactions using *erythro*- and *threo*-dimethyl (2-hydroxy-1-methyl-2-phenyl)ethylphosphonates were carried out. Threo isomer (>99% d.e.) was contaminated with dimethyl (2-hydroxy-2-phenyl)ethylphosphonate (**3h**) and could not be isolated in a pure state. A mixture (3 : 1) of *threo*-**3k** and **3h** was treated with $CsF–H_2O$ in DMF at 92 °C for 2 d to give (*E*)-*β*-methylstyrene and styrene in 83 and 54% yields based on **3k** and **3h**, respectively, as shown in the following equation (Eq. 5). Only (*E*)-olefin was exclusively obtained. On the other hand, an *erythro*-enriched mixture of **3k** (85.6% d.e.) must be used, because *erythro*-**3k** could not be purified in practical scale, while single crystals for X-ray analysis were obtained. A similar treatment at 75—100 °C for 2 d gave a mixture (46%) of (*Z*)- and (*E*)-**6k** in a ratio of 85 : 15 (Eq. 6). Although the yield of the olefin formation was moderate, stereospecificity from *erythro*-**3k** is calculated to be 97.7% if *threo*-**3k** gave (*E*)-**6k** in the same yield as shown in the case of *threo*-**3k**, see Experimental. The higher chemical yield and stereospecificity from *threo*-isomer than those from *erythro*-isomer were also ob-

served in the system of β-hydroxyalkyldiphenylphosphine oxides.[4] These results indicate that the present olefin formation proceeds stereospecifically in a manner of *syn*-elimination, which is a common feature of such types of olefin formation reactions under neutral and basic conditions.[4,15]



(5)



(6)

Experimental

Melting points are uncorrected. ^{1}H NMR spectra were measured with a JOEL FX-90Q (90 MHz) and Bruker AM-500 (500 MHz) spectrometer using tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were taken with a Bruker AM-500 (125 MHz) spectrometer using TMS as internal standard. ^{31}P NMR spectra were recorded with a JEOL FX-90Q (36.3 MHz) spectrometer using 85% H_3PO_4 as external standard. Mass spectra were measured at 70 eV with a JEOL 300-D or JEOL JMS-SX102A mass spectrometer. Dry column chromatography (DCC) was carried out using ICN silica DCC 60A. Elemental analyses were performed by the Microanalytical Laboratory of the Department of Chemistry, Faculty of Science, The University of Tokyo.

General Procedure for the Synthesis of β-Hydroxyalkylphosphonates. To a solution of alkylphosphonates (10—50 mmol) in tetrahydrofuran (THF) (50—150 mL) was added *n*-BuLi (hexane solution, 1.05—1.10 molar equivalent) at −78 °C under argon atmosphere. After we stirred the solution for 5 min at −78 °C, we added to it a solution of carbonyl compounds (1.05—1.10 molar equivalent) in THF (10—50 mL) at −78 °C. Stirring was continued for 5 min and the reaction was quenched with aq NH_4Cl. The solvent was evaporated and the residue was extracted with CH_2Cl_2 several times. Combined extracts were dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue was recrystallized from appropriate solvent or distilled with Kugelrohr to give almost pure samples of the corresponding β-hydroxyalkylphosphonates. The results are summarized in Table 1.

Dimethyl (2-Hydroxy-2,2-diphenyl)ethylphosphonate (3a): Mp 102.0—103.0 °C (EtOH); ^{1}H NMR ($CDCl_3$, 500 MHz) δ=2.89 (d, J_{HP}=17.7 Hz, 2H, PC$\underline{H}_2$), 3.36 (d, J_{HP}=11.0 Hz, 6H, P(OC$\underline{H}_3$)$_2$), 4.93 (br s, 1H, O$\underline{H}$), 7.18—7.22 (m, 1H, *p*-H), 7.28—7.32 (m, 2H, *m*-H), and 7.46—7.51 (m, 2H, *o*-H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=37.81 (d, J_{CP}=136.6 Hz, P$\underline{C}$H$_2$), 52.12 (d, J_{CP}=6.2 Hz, P(O$\underline{C}$H$_3$)$_2$), 75.27 (d, J_{CP}=4.2 Hz, $\underline{C}$HOH), 125.63 (s, *o*-C), 126.98 (s, *p*-C), 128.08 (s, *m*-C), and 146.15 (d, J_{CP}=10.4 Hz, *ipso*-C); ^{31}P NMR ($CDCl_3$) δ=31.36; MS (70 eV) *m/z* 306 (M^+; 18%), 229 (40), 197 (6.5), 193 (13), and 125 (100). Found: C, 62.54; H, 6.29%. Calcd for $C_{16}H_{19}O_4P$: C, 62,74; H, 6.25%.

Dimethyl (2-Benzyl-2-hydroxy-3-phenyl)propylphosphonate (3b): Mp 140—141 °C (EtOH–hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ=1.93 (d, J_{HP}=18.9 Hz, 2H, PC$\underline{H}_2$), 2.93 (s, 4H, PhC$\underline{H}_2$), 3.49 (br s, 1H, OH), 3.69 (d, J_{HP}=11.0 Hz, 6H, P(OC$\underline{H}_3$)$_2$), and 7.21—7.32 (m, 10H, C_6H_5); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=33.22 (d, J_{CP}=136.5 Hz, PCH$_2$), 46.70 (d, J_{CP}=8.3 Hz, CH$_2$Ph), 52.12 (d, J_{CP}=6.2 Hz, OCH$_3$), 72.67 (d, J_{CP}=4.2 Hz, COH), 126.44 (s, *p*-C), 127.98 (s, *m*-C), 10.80 (s, *o*-C), and 136.87 (s, *ipso*-C); ^{31}P NMR ($CDCl_3$) δ=32.47; MS (70 eV) *m/z* 334 (M^+; 0.41%), 316 (7.1), 243 (100), and 211 (11.4). Found: C, 64.49; H, 6.96%. Calcd for $C_{18}H_{23}O_4P$: C, 64.66; H, 6.93%.

Dimethyl (2-Hydroxy-2-phenyl)propylphosphonate (3c): Bp 120—125 °C/0.05 Torr (Kugelrohr) (1 Torr=133.322 Pa) ^{1}H NMR ($CDCl_3$, 500 MHz) δ=1.63 (d, J_{HP}=1.8 Hz, 3H, CC$\underline{H}_3$), 2.36 (t, J=J_{HP}=15.3 Hz, 1H, PC$\underline{H}$H′), 2.48 (dd, J=15.3 Hz, J_{HP}=17.7 Hz, PCH$\underline{H}$′), 3.21 (d, J_{HP}=11.0 Hz, 3H, P(OC$\underline{H}_3$) (OCH$_3$)′), 3.67 (d, J_{HP}=11.0 Hz, 3H, P(OCH$_3$)(OC$\underline{H}_3$)′), 4.25 (br s, 1H, OH), 7.22—7.26 (m, 1H, *p*-H), 7.32—7.38 (m, 2H, *m*-H), and 7.45—4.52 (m, 2H, *o*-H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=31.59 (d, J_{CP}=12.5 Hz, CCH$_3$), 38.73 (d, J_{CP}=136.5 Hz, PCH$_2$), 51.39 (d, J_{CP}=6.2 Hz, P(O$\underline{C}$H$_3$)(OCH$_3$)′), 51.97 (d, J_{CP}=6.2 Hz, P(OCH$_3$)(OCH$_3$)′), 71.46 (s, COH), 124.30 (s, *m*-C), 126.40 (s, *p*-C), 127.74 (s, *o*-C), and146.83 (d, J_{CP}=6.3 Hz, *ipso*-C); ^{31}P NMR ($CDCl_3$) δ=31.28; HRMS (70 eV) Found: *m/z* 244.0842. Calcd for $C_{11}H_{17}O_4P$: M, 244.0862.

Dimethyl 2-Hydroxytridecylphosphonate (3d): Mp 60.0—60.5 °C (Et_2O); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=0.7—2.1 (m, 25H, PC$\underline{H}_2$, $C_{11}\underline{H}_{23}$), 3.30 (br s, 1H, OH), 3.76 (d, J_{HP}=11.0 Hz, 3H, P(OC$\underline{H}_3$) (OCH$_3$)′), 3.77 (d, J_{HP}=10.7 Hz, 3H, P(OCH$_3$) (OC$\underline{H}_3$)′), and 3.2—4.2 (m, 1H, CHOH); ^{13}P NMR ($CDCl_3$) δ=33.19; MS (70 eV) *m/z* 308 (M^+; 1.6%), 290 (12), 177 (12), 166 (6.2), 154 (100), and 124 (50). Found: C, 58.49; H, 10.71%. Calcd for $C_{15}H_{33}O_4P$: C, 58.42; H, 10.79%.

Dimethyl (1-Hydroxy-1-cyclohexyl)methylphosphonate (3e): Bp 135 °C/0.05 Torr; ^{1}H NMR ($CDCl_3$, 500 MHz) δ= 1.24—1.33 (m, 1H, C(CH$_2$CH$_2$)$_2$C$\underline{H}$H′), 1.39—1.47 (m, 2H, C(CH$_2$C$\underline{H}$H′)$_2$CH$_2$), 1.47—1.55 (m, 3H, C(CH$_2$CH$_2$)$_2$CH$\underline{H}$′), C(C$\underline{H}$H′CH$_2$)$_2$CH$_2$), 1.64—1.77 (m, 4H, C(CH$_2$CH$\underline{H}$′)$_2$CH$_2$, C(CH$\underline{H}$′CH$_2$)$_2$CH$_2$), 2.03 (d, J_{HP}=23.2 Hz, 2H, PCH$_2$), 3.75 (d, J_{HP}=11.0 Hz, 6H, P(OC$\underline{H}_3$)(OCH$_3$)′), 3.87 (s, 1H, OH), and 3.75 (d, J_{HP}=11.0 Hz, 6H, P(OC$\underline{H}_3$)(OCH$_3$)′); ^{13}C{^{1}H} NMR ($CDCl_3$) δ= 21.94 (s, C(CH$_2$CH$_2$)$_2$$\underline{C}H_2$), 25.20 (s, C(CH$_2$$\underline{C}H_2$)$_2CH_2$), 36.63 (d, J_{CP}=136.6 Hz, PCH$_2$), 38.60 (d, J_{CP}=10.3 Hz, C($\underline{C}$H$_2$CH$_2$)$_2$CH$_2$), 51.94 (d, J_{CP}=6.2 Hz, P(OCH$_3$)$_2$), and 69.30 (s, J_{CP}=4.2 Hz, COH); ^{31}P NMR ($CDCl_3$) δ=32.86; HRMS (70 eV) Found: *m/z* 222.1047. Calcd for $C_9H_{19}O_4P$: M, 222.1022.

Dimethyl (9-Hydroxy-9-fluorenyl)methylphosphonate (3f): Mp 169—170°C (EtOH–hexane); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.53 (d, J_{HP}=17.6 Hz, 2H, PCH$_2$), 3.56 (d, J_{HP}=11.0 Hz, 6H, P(OC$\underline{H}_3$)$_2$), 4.37 (br s, 1H, OH), and 7.2—7.7 (m, 8H, –$C_6\underline{H}_4$–$C_6\underline{H}_4$–); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=35.68 (d, J_{CP}=136.6 Hz, P$\underline{C}$H$_2$), 52.12 (d, J_{CP}=6.2 Hz, O$\underline{C}$H$_3$), 78.89 (s, $\underline{C}$OH), 119.87 (s), 124.03 (s), 127.80 (s), 129.10 (s), 138.97 (s), and 148.03 (d, J_{CP}=6.3 Hz, *ipso*-C); ^{31}P NMR ($CDCl_3$) δ=30.07. HRMS (70 eV) Found: *m/z* 304.0854. Calcd for $C_{16}H_{17}O_4P$: M, 304.0864. Found: C, 62.93; H, 5.69%. Calcd for $C_{16}H_{17}O_4P$: C, 63.16; H, 5.69%.

Dimethyl 2- Hydroxy- 2- (4- nitrophenyl)ethylphosphonate (3g): Mp 125—126 °C (EtOH–hexane); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.0—2.3 (m, 2H, PCH$_2$), 3.73 (d, J_{HP}=11.0 Hz, 3H, P(OC$\underline{H}_3$)(OCH$_3$)′), 3.77 (d, J_{HP}=10.7 Hz, 3H, P(OCH$_3$)(OC$\underline{H}_3$)′), 4.71 (br s, 1H, OH), 5.0—5.4 (m, 1H, C$\underline{H}$OH), and 7.5—8.3 (m, 4H, C_6H_4); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=34.79 (d, J_{CP}=138.8 Hz, PCH$_2$), 52.50 (d, J_{CP}=6.3 Hz, P(O$\underline{C}$H$_3$)(OCH$_3$)′), 52.79 (d, J_{CP}=6.3 Hz, P(OCH$_3$)(O$\underline{C}$H$_3$)′), 67.80 (d, J_{CP}=4.2 Hz, $\underline{C}$HOH), 123.71 (s), 126.32 (s), 147.33 (s), 150.88 (d, J_{CP}=16.6 Hz, *ipso*-C); ^{31}P NMR ($CDCl_3$) δ=35.72; MS (70 eV) *m/z* 275 (M^+; 0.7%) and 124 (100). HRMS (70 eV) Found: *m/z* 275.0528. Calcd for $C_{10}H_{14}NO_6P$:

M, 275.0558. Found: C, 43.94; H, 4.92; N, 5.23%. Calcd for $C_{10}H_{14}NO_6P$: C, 43.62; H, 5.13; N, 5.09%.

Dimethyl (2-Hydroxy-2-phenyl)ethylphosphonate (3h): Mp 65.5—66.0 °C (Et_2O); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.0—2.4 (m, 2H, PC$\underline{H}_2$), 3.647 (d, J_{HP}=10.8 Hz, 3H, P(OC$\underline{H}_3$)(OCH$_3$)′), 3.654 (d, J_{HP}=11.0 Hz, 3H, P(OCH$_3$)(OC$\underline{H}_3$)′), 4.41 (br s, 1H, O$\underline{H}$), and 7.1—7.5 (m, 5H, C_6H_5); ^{31}P NMR ($CDCl_3$) δ=31.55. HRMS (70 eV) Found: *m/z* 230.0699. Calcd for $C_{10}H_{15}O_4P$: M, 230.0706.

Dimethyl (2-Hydroxy-1-methyl-2,2-diphenyl)ethylphosphonate (3i): Mp 113—114 °C (Et_2O); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=1.24 (dd, J_{HP}=17.6 Hz, J=7.5 Hz, 3H, PCHC$\underline{H}_3$),2.99 (d, J_{HP}=10.8 Hz, 3H, P(OC$\underline{H}_3$)(OCH$_3$)′), 3.59 (d, J_{HP}=10.8 Hz, 3H, P(OCH$_3$)(OC$\underline{H}_3$)′), 3.0—3.8 (m, 1H, PC$\underline{H}$), 5.31 (br s, 1H, OH), and 7.1—7.7 (m, 10H, C_6H_5); ^{31}P NMR ($CDCl_3$) δ=35.72; MS (70 eV) *m/z* 320 (M^+; 0.28%), 202 (5.5), 201 (9.7), 105 (17.2), 92 (21.3), and 32 (100). Found: C, 63.47; H, 6.77%. Calcd for $C_{17}H_{21}O_4P$: C, 63.74; H, 6.61%.

Dimethyl (2-Benzyl-2-hydroxy-1-methyl-3-phenyl)propylphosphonate (3j): Mp 94.7—95.5 °C (Et_2O); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=1.23 (dd, J_{HP}=17.7 Hz, J=7.4 Hz, 3H, PCHC$\underline{H}_3$), 1.8—2.3 (m, 1H, PC$\underline{H}$), 2.6—3.3 (m, 4H, C$\underline{H}_2$Ph), 3.62 (d, J_{HP}=10.5 Hz, 3H, P(OC$\underline{H}_3$)(OCH$_3$)′), 3.77 (d, J_{HP}=10.5 Hz, 3H,P(OCH$_3$)-(OC$\underline{H}_3$)′), 4.39 (br s, 1H, OH), and 7.2—7.9 (m, 10H C_6H_5); ^{31}P NMR ($CDCl_3$) δ=36.13; MS (70 eV) *m/z* 348 (M^+; 0.55%), 330 (13.5), 257 (71), 210 (94), 119 (79), and 91 (100). Found: C, 65.35; H, 6.95%. Calcd for $C_{19}H_{25}O_4P$: C, 65.51; H, 7.23%.

Preparation of (2-Benzyl-2-hydroxy-3-phenyl)propyldiphenylphosphine Oxide (4). To a solution of methyldiphenylphosphine oxide[16] (0.675 g, 3.14 mmol) in THF (30 mL) was added *n*-BuLi (3.15 mmol) solution at −78 °C. After 5 min a solution of dibenzyl ketone (0.659 g, 3.14 mmol) in THF (10 mL) was added to the solution at the same temperature and the reaction was quenched with aq NH_4Cl after 5 min. The usual workup gave (2-benzyl-2-hydroxy-3-phenyl)propyldiphenylphosphine oxide (**4**) in 46% yield.

4: Mp 214.2—214.8 °C (EtOH); ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.44 (d, J_{HP}=10.3 Hz, 2H, PC$\underline{H}_2$), 2.6—3.1 (m, 4H, C$\underline{H}_2$Ph), 4.49 (s, 1H, OH), and 6.9—7.7 (m, 20H, $C_6\underline{H}_5$); ^{31}P NMR ($CDCl_3$) δ=32.39; MS (70 eV) *m/z* 408 ($M^+ - H_2O$; 20%), 335 (100), 215 (20), and 201 (63). Found: C, 79.07; H, 6.49%. Calcd for $C_{28}H_{27}O_2P$: C, 78.85; H, 6.38%.

Diastereoselective Synthesis of Dimethyl (2-Hydroxy-1-methyl-2-phenyl)ethylphosphonate. To a solution of dimethyl ethylphosphonate (**1b**) (0.69 g, 5.0 mmol) in THF (25 mL) was added *n*-BuLi solution (5.5 mmol) at −78 °C and the mixture was stirred for 5 min. To the cooled reaction mixture at appropriate temperature was added a solution of benzaldehyde (0.58 g, 5.5 mmol) in THF (10 mL) for 15—20 min and the mixture was stirred for 5—10 min. Then the reaction was quenched with a mixture of aq NH_4Cl and THF. After the usual workup, a diastereomeric mixture of *erythro*- and *threo*-dimethyl (2-hydroxy-1-methyl-2-phenyl)ethylphosphonates (**3k**) was obtained. The ratio was determined by ^{31}P NMR spectroscopy. The integral ratios obtained under the following two measuring conditions agreed with each other, so the latter conditions (2) were used. Measuring conditions (1): Data points: 16 K; Spectral Width: 200 Hz; Pulse Delay: 1 min; Flip Angle: 36°; Irradiation mode: Gated proton decoupling without NOE. (2): Data points: 16 K; Spectral Width: 3000 Hz; Pulse Delay: 3 s; Flip Angle: 36°; Irradiation Mode: Proton-noise decoupling. *N,N,N′,N′*-Tetramethylethylenediamine (TMEDA) and hexamethylphosphoric triamide (HMPA) were used as additives.

The diastereomeric excess of the *erythro* isomer (% d.e.) and chemical yields are summarized in Table 6.

Preparation of Potassium 1-(Dimethoxyphosphinoyl)-ethanide. To a solution of *t*-BuOK freshly prepared by the reaction of potassium metal (0.382 g, 9.8 mmol) with excess *t*-BuOH, followed by removal of the alcohol by heating at 100 °C in vacuo for 2 h, in THF (10 mL) was added *n*-BuLi (hexane solution) (5.5 mmol) at −78 °C, and the mixture was stirred for 5 min.[17] To the solution was slowly added a solution of dimethyl ethylphosphonate (**1b**) (0.69 g, 5 mmol) in THF (15 mL) and the mixture was stirred at −78 °C for 5 min.

Preparation of 1-(Dimethoxyphosphinoyl)ethylmagnesium Chloride. A suspension (0.5 M, 1 M=1 mol dm^{-3}) of magnesium chloride was prepared by the reaction of magnesium turnings (1.34 g, 55 mmol) with 1,2-dichloroethane (4.95 g, 50 mmol) in THF (100 mL). The suspension (11 mL, 5.5 mmol) was added to a solution of lithium 1-(dimethoxyphosphinoyl)ethanide prepared from dimethyl ethylphosphonate (**1b**) (0.69 g, 5 mmol) and *n*-BuLi (5.5 mmol) in THF (15 mL), at −78 °C. The reaction mixture was allowed to warm to room temperature and then stirred for 30 min.

***threo* Selective Synthesis.** To a solution of dimethyl methylphosphonate (**1a**) (0.62 g, 5.0 mmol) in THF (25 mL) was added *n*-BuLi (5.5 mmol) at −78 °C. After 5 min a solution of benzaldehyde (0.58 g, 5.5 mmol) in THF (10 mL) was added to the solution and to the reaction mixture was added *n*-BuLi (5.5—15.0 mmol) after stirring for 10 min. After an appropriate period, excess iodomethane was added to the solution at −78 °C. After stirring at the same temperature for 10 min, the reaction mixture was allowed to warm to room temperature and then treated with aq NH_4Cl. A similar reaction using dimethoxymethane instead of THF as solvent was carried out. The results are summarized in Table 7.

When THF was used, *threo*-**3k** was mainly obtained along with *erythro*-**3k** and benzaldehyde adduct **3h**, *erythro*-**3k** was removed by recrystallization from Et_2O. However, **3h** could not be removed even by chromatography. When dimethoxymethane was used, another by-product, dimethyl (2-hydroxy-1,1-dimethyl-2-phenyl)ethylphosphonate (**3l**), was formed, which could not be separated from *threo*-**3k**, neither. Therefore, *threo*-**3k** (>99% d.e.) was obtained as mixtures with **3h** or **3l** in ratios of 3 : 1 and 3 : 2, respectively.

Alternative Synthesis of By-product 3l. To a solution of dimethyl isopropylphosphonate (0.691g, 4.53 mmol) in THF (20 mL) was added *n*-BuLi (5.40 mmol) at −78 °C. After we stirred this for 15 min we added a solution of benzaldehyde (0.5 mL) to it for 2 min. The reaction mixture was stirred for 30 min. Then it was allowed to warm to room temperature and was treated with aq NH_4Cl. After the usual workup, the residue was recrystallized from ether to give dimethyl (2-hydroxy-1,1-dimethyl-2-phenyl)ethylphosphonate (**3l**) (0.95 g, 81%).

***erythro*-Dimethyl (2-Hydroxy-1-methyl-2-phenyl)ethylphosphonate (*erythro*-3k) (85.6% d.e.):** Mp 63.0—65.2 °C (Et_2O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ=1.02 (dd, J_{HP}=16.3 Hz, J=7.3 Hz, 3H, PCHC$\underline{H}_3$), 2.20 (ddq, J=7.3 Hz, J=2.4 Hz, J_{HP}=20.8 Hz, 1H, PC$\underline{H}$), 3.73 (br s, 1H, OH), 3.74 (d, J_{HP}=10.4 Hz, 6H, P(OC$\underline{H}_3$)$_2$), 5.29 (dd, J=2.4 Hz, J_{HP}=9.2 Hz, 1H, C$\underline{H}$OH), 7.21—7.26 (m, 1H, *p*-H), and 7.30—7.36 (m, 4H, *o*-H and *m*-H); ^{13}C{^{1}H} NMR ($CDCl_3$) δ=6.33 (s), 38.44 (d, J_{CP}=136.5 Hz), 52.29 (d, J_{CP}=8.3 Hz), 52.89 (d, J_{CP}=6.2 Hz), 74.60 (d, J_{CP}=4.2 Hz), 125.66 (s), 127.01 (s), 127.95 (s), and 141.83 (d, J_{CP}=16.6 Hz); ^{31}P NMR ($CDCl_3$) δ=35.64. HRMS (70 eV) Found: *m/z* 244.0844. Calcd for $C_{11}H_{17}O_4P$: M, 244.0864. Found: C, 53.88; H, 7.18%. Calcd for $C_{11}H_{17}O_4P$: C, 54.10; H, 7.02%.

***threo*-3k (as a 3 : 1 mixture with 3h):** ^{1}H NMR ($CDCl_3$, 500 MHz) δ=0.88 (dd, J_{HP}=17.7 Hz, J=7.3 Hz, 3H, PCHC$\underline{H}_3$), 2.20—

2.31 (m, 1H, PCH), 3.72 (d, J_{HP}=11.0 Hz, 3H, P(OCH$_3$)(OCH$_3$)′), 3.79 (d, J_{HP}=11.0 Hz, 3H, P(OCH$_3$)(OCH$_3$)′), 4.41 (brs, 1H, OH), 4.73 (dd, J=9.5 Hz, J=10.7 Hz, 1H, CHOH), and 7.24—7.37 (m, 5H, C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ=11.57 (d, J_{CP}=6.2 Hz), 38.69 (d, J_{CP}=136.6 Hz), 52.53 (d, J_{CP}=6.3 Hz), 52.61 (d, J_{CP}=6.3 Hz), 74.50 (s), 126.75 (s), 127.37 (s), 128.21 (s), and 141.0 (d, J_{CP}=14.6 Hz); ^{31}P NMR ($CDCl_3$) δ=35.34.

Dimethyl (2-Hydroxy-1,1-dimethyl-2-phenyl)ethylphosphonate (3l): ^{1}H NMR ($CDCl_3$, 500 MHz) δ=0.94 (d, J_{HP}=17.7 Hz, 3H, PCCH$_3$CH$_3'$), 1.12 (d, J_{HP}=16.5 Hz, 3H, PCCH$_3$CH$_3'$), 3.79 (d, J_{HP}=11.0 Hz, 3H, P(OCH$_3$)(OCH$_3$)′), 3.81 (d, J_{HP}=8.6 Hz, 3H, P(OCH$_3$)(OCH$_3$)′), 4.10 (br s, 1H, OH), 4.92 (d, J_{HP}=9.2 Hz, 1H, CHOH), and 7.24—7.37 (m, 5H, C_6H_5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ=15.19 (s), 20.93 (d, J_{CP}=6.3 Hz), 40.49 (d, J_{CP}=134.5 Hz), 52.57 (d, J_{CP}=6.3 Hz), 53.37 (d, J_{CP}=6.3 Hz), 76.11 (s), 127.55, 127.83, 128.11, and 138.50 (d, J_{CP}=14.5 Hz); ^{31}P NMR ($CDCl_3$) δ=38.5. HRMS (70 eV) Found: *m/z* 258.1012. Calcd for $C_{12}H_{19}O_4P$: M, 258.1021.

X-Ray Crystallographic Analysis of *erythro*-3k. Single crystals for X-ray crystallographic analysis were grown in Et_2O. The intensity data ($2\theta<55°$) were collected at 293 K on a Rigaku AFC7R diffractometer with graphite monochromated Mo $K\alpha$ radiation (λ = 0.71609 Å and the structure was solved by direct methods (SHELXS86). The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1651 observed reflections [$I>3.00\sigma(I)$] and 289 variable parameters with R (R_w) = 0.077 (0.041). Crystal data are shown in Table 1 and atomic coordinates, bond lengths, and bond angles are summarized in Tables 2, 3, 4, and 5. Full details were deposited as Document No. 70049 at the Office of the Editor of Bull. Chem. Soc. Jpn.

General Procedure for Weak Base-Induced Olefin Synthesis. A mixture of β-hydroxyalkylphosphonates (**3**) (0.41—8.83 mmol) and base (1.0—7.9 molar equivalents) with or without an equimolar amount of water in solvent (ca. 0.1 mol dm^{-3} solution of **3**) was heated under appropriate conditions. When DMF and DMSO were used as solvent, the reaction mixture was diluted with water and the organic layer was extracted five times with ether. The ethereal solution was twice washed with water. When some solvent other than DMF and DMSO was used, the solvent was evaporated. Water and CH_2Cl_2 were added to the residue; then the organic layer was extracted several times with CH_2Cl_2. These ethereal and CH_2Cl_2 solutions were dried over anhydrous $MgSO_4$. After removal of the solvent, the corresponding olefin was obtained in an almost pure state, unless otherwise noted in a footnote in a Table. The results from the reactions using dimethyl (2-hydroxy-2,2-diphenyl)-ethylphosphonate (**3a**) and fluorides, those using dimethyl (2-benzyl-2-hydroxy-3-phenyl)propylphosphonate (**3b**) and various bases, and those using various β-hydroxyalkylphosphonates (**3c—j**) and bases, are summarized in Tables 8, 9, and 10, respectively.

Alternative Synthesis of the Side Reaction Product. A solution of **3b** (3.16 g, 9.46 mmol) and NaI (7.5 g, 50 mmol) in CH_3CN (100 mL) was refluxed overnight.[12] After removal of the solvent under reduced pressure, aq K_2CO_3 was added. The aqueous layer was washed four times with CH_2Cl_2, and acidified with HCl. The resulting precipitates were extracted with CH_2Cl_2 and the organic layer was dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was recrystallized from ether to give methyl (2-benzyl-2-hydroxy-3-phenyl)propylphosphonate (**11b**) (2.94 g, 97%).

11b: Mp 100.9—102.5 °C (decomp) (Et_2O); ^{1}H NMR (D_2O, 90 MHz) δ=1.6 (d, J_{HP}=17 Hz, 2H, PCH$_2$), 2.4—2.7 (br s, 4H, CH$_2$Ph), 3.2 (d, J_{HP}=10 Hz, 3H, POCH$_3$), and 6.6—7.1 (m, 10H, C_6H_5); ^{31}P NMR (D_2O) δ=20.39. Found: C, 63.56; H, 6.31%. Calcd for $C_{17}H_{21}O_4P$: C, 63.74; H, 6.61%.

Reactions Using *threo*-3k and *erythro*-Enriched Mixture. A 3 : 1 mixture (0.597 g) of *threo*-**3k** (1.86 mmol) and **3h** (0.62 mmol) was treated with CsF (0.86 g, 5.66 mmol) and H_2O (5.66 mmol) in DMF (24 mL) at 92 °C for 2 d. To the reaction mixture was added water and the organic layer was extracted with ether. Ethereal solution was dried over anhydrous $MgSO_4$. After removal of the solvent, ^{1}H NMR of the residue showed the formation of (*E*)-β-methylstyrene (**6k**) (1.55 mmol, 83%) and styrene (**6h**) (0.33 mmol, 54%). No (*Z*)-isomer was observed.

A similar reaction using *erythro*-enriched mixture (2.387 g, 85.6% d.e.), CsF (4.7 g, 31 mmol), and water (31 mmol) in DMF (60 mL) at 70—100 °C for 2 d afforded a mixture (0.535 g, 46%) of (*Z*)- and (*E*)-β-methylstyrenes (**6k**) in a ratio of 85 : 15.

The fraction of (*Z*)-**6k** formed from *erythro*-**3k**=46×0.85. The fraction of (*E*)-**6k** formed from *threo*-**3k**=83×0.072, because the fraction of (*E*)-**6k** from *thero*-**3k** is 83%. The fraction of (*E*)-**6k** formed from *erythro*-**3k**=46×0.15−83×0.072. Stereospecificity from *erythro*-**3k**=100×46×0.85/(46×0.85+46×0.15−83×0.072)=97.7%.

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