The Phosphonate-Phosphate- and Phosphate-Phosphonate Rearrangement and Their Applications, 4[◇]

Deprotonation of Secondary Benzylic Phosphates – Configurationally Stabile Benzylic Carbanions with a Diethoxyphosphoryloxy Substituent and Their Rearrangement to Optically Active Tertiary α-Hydroxyphosphonates

Friedrich Hammerschmidt* and Susanne Schmidt

Institut für Organische Chemie der Universität Wien,
Währingerstraße 38, A-1090 Wien, Austria
Telefax: (internat.) +43-1-31367-2280

Received May 28, 1996

Key Words: Phosphate–Phosphonate rearrangement / Carbanions, benzylic, configurational stability of / α-Hydroxyphosphonates, tertiary, chiral, non-racemic / *t*-Butyl(phenyl)phosphinothioic acid, homochiral

Optically active alcohols (ee ≥ 98%) such as 1-phenylpropanol, 1-(2-naphthyl)ethanol, 1-tetralol, and 1-indanol were transformed into diethyl phosphates **7a–d**. *s*BuLi/TMEDA – induced phosphate–phosphonate rearrangement in diethyl ether furnished tertiary α-hydroxyphosphonates **8a–d** of high enantiomeric purity (ee 94–98%) in yields of 43–83% with retention of configuration. The enantiomeric excesses were determined by using homochiral *t*-butyl(phenyl)phosphinothioic acid as chiral solvating agent.

The synthesis of chiral, non-racemic secondary α-hydroxyphosphonates can be achieved by a variety of methods. The most general approaches are chemical resolution[1,2,3], enantioselective reduction of α-oxophosphonates[4], enantioselective addition of phosphite to aldehydes[5], diastereoselective addition of homochiral phosphorous acid derivatives to aldehydes[6], lipase-catalyzed resolution of α-acyloxyphosphonates[7], and enantioselective phosphate–phosphonate rearrangement[1]. The synthesis of tertiary α-hydroxyphosphonates, which are thermally and chemically more labile than their secondary counterparts, cannot be accomplished by the above-mentioned methods except by resolution[3]. In continuation of our investigations of the synthetic capabilities of the phosphate–phosphonate rearrangement, we are studying systematically its use to transform homochiral phosphates into homochiral α-hydroxyphosphonates.

The phosphate–phosphonate rearrangement[1,8] and its reverse process[9] are isomerization reactions characterized by a base-induced migration of a dialkoxyphosphoryl group from oxygen to carbon or carbon to oxygen (Scheme 1). A prerequisite for the rearrangement to occur is the deprotonation of phosphate **1** by strong bases such as *n*BuLi, *s*BuLi or LDA to generate dipole-stabilized[10] carbanion **2** with the lithium ion being part of a five-membered chelate ring. At least one of the substituents R^1 or R^2 should be a vinyl or phenyl group to facilitate proton removal. Intermediate **2** is a short-lived species and is configurationally stable[1,3] as proven for R^1 = Ph, R^2 = CH_3 and R^1 = Ph, R^2 = H, prior to rearrangement to lithiated hydroxyphosphonate **4** via **3**. On workup α-hydroxyphosphonate **5** is formed and isolated. The driving force for the reaction is that the Li–O bond is stronger than the C–Li bond, which outweighs the loss in energy in going from a P–O to a P–C bond. The rearrangement occurs with retention[1,3] of configuration at carbon. Intermediate **2** is related to carbanions with a carbamoyl[11] or acyl[12] group instead of the dialkoxyphosphoryl group. The reverse process, the phosphonate–phosphate rearrangement, is brought about by catalytic amounts[9] of base at room or higher temperature.

We have previously reported on the enantioselective phosphate–phosphonate rearrangement of benzyl phosphates to α-hydroxy(phenylmethyl)phosphonates[1]. This paper deals with the preparation of optically active tertiary α-hydroxyphosphonates from optically active alkyl aryl carbinols. Concomitantly, we wanted to study the microscopic configurational stability of the intermediate carbanions. So far only the rearrangement of the antipodes of diethyl 1-phenylethyl phosphate to the isomeric hydroxyphosphonates has been described as a single example of this approach[3].

The enantiomers of 1-phenylpropanol (**6a**), 1-(2-naphthyl)ethanol (**6b**), 1,2,3,4-tetrahydronaphth-1-ol (**6c**), and 1-indanol (**6d**), easily accessible with high optical purity (ee ≥ 98%) by lipase-catalyzed resolution[13] of the corresponding esters of acetic or chloroacetic acid, were used as starting materials. Racemic alcohols **6a** and **6d** were investigated as well. The most efficient procedure for the preparation of phosphates (±)-, (*R*)- and (*S*)-**7a** was the one given in Scheme 2. The alcohols were first transformed in dry THF at −78 °C into the potassium alkoxides with potassium bis(trimethylsilyl)amide, and these were then treated with di-

[◇] Part 3: Ref.[1].

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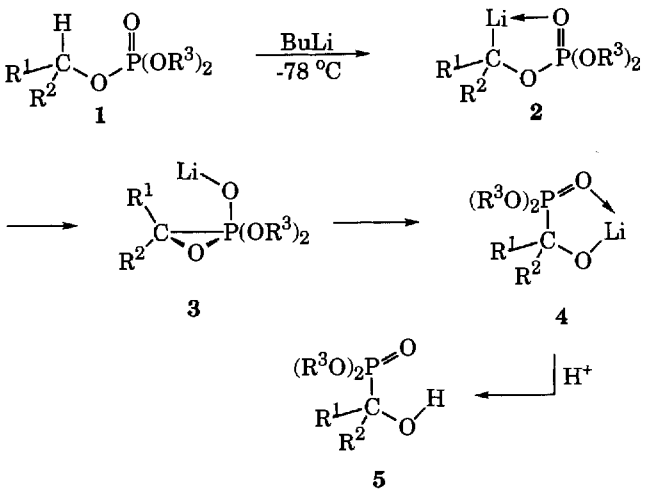
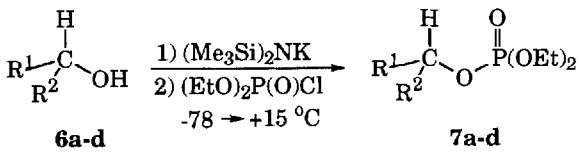
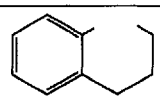
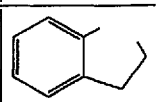
Scheme 1



ethyl chlorophosphate to yield phosphates (±)-, (*R*)- and (*S*)-**7a** in yields of 83%, 76%, and 79%. They are stable enough to be purified by flash chromatography and bulb-to-bulb distillation under vacuum. The possible formation of tetraethyl pyrophosphate as side product was minimal and it could be removed by flash chromatography. Other methods[14] of esterification such as the use of pyridine as solvent and diethyl chlorophosphate at room temperature or at 40 °C, or diethyl bromophosphate or diethyl phosphite in combination with tetrabromomethane and pyridine, gave significantly lower yields of the desired products. The optimized procedure was also used for the preparation of phosphates (*R*)- and (*S*)-**6b–d** and (±)-**6d** in THF or diethyl ether in yields ranging from 59% to 81%. The lability of these products increased from **7b** to **7d** and none could be distilled without decomposition. Furthermore, **7b** and **7c** could be purified by flash chromatography, but **7d** could not; its crude product was used directly for the phosphate–phosphonate rearrangement.

Scheme 2



6, 7	a	b	c	d
R^1	Ph	2-Naphth		
R^2	Et	Me		

The deprotonation of phosphate **7a** was studied on a 1-mmol scale using a variety of conditions compiled in Table 1 (Scheme 3). When (*S*)-**7a** was treated in diethyl ether with 2 equivalents of *n*BuLi for 1 h at −78 °C and the reaction was quenched with 3 equivalents of acetic acid, the phosphonate (*R*)-**8a** could be isolated in just 6% yield (ee 76%) (Table 1, entry 1). The major portion of the starting material (*S*)-**7a** was recovered unchanged in 67% yield. Replacement of *n*BuLi by *s*BuLi and an increase in the reaction time to 2 h resulted in an increase of the yield up to 57%, 55%, and 69% (ee 95%, entries 2, 3, and 4). This strong base was then used for all further experiments. The phosphate–phosphonate rearrangement gave a lower yield in THF (entry 5) than in diethyl ether. The best conversions, 59%, 72%, and 71%, were obtained when a stoichiometric amount of TMEDA[15] relative to *s*BuLi was added as well, despite a reaction time of only 20 min (entries 6–8). The other phosphates, **7b–d**, were isomerized under the same conditions to give phosphonates **8b–d** (entries 9–15). Workup and purification have to be carried out under carefully controlled conditions. In particular, basic conditions[16] have to be avoided and solvents should not be removed at elevated temperatures, thus preventing the decomposition of phosphonate to the corresponding ketone and diethyl phosphite. Traces of ketone could be detected in crude phosphonates **8** and sometimes even in chromatographed samples. The ^{1}H-NMR spectra of **8b** recorded in $CDCl_3$ or C_6D_6 show for the hydroxyl group two doublets of different intensity and varying chemical shift, depending on the ee of the sample, but only one when recorded in [D_6]DMSO. The ^{1}H-NMR spectrum ($CDCl_3$) of racemic **8b** exhibits only one doublet for the OH group. This phenomenon is possibly due to the formation of diastereomeric dimers[17].

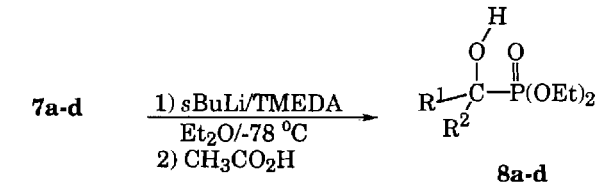
Table 1. Phosphate–phosphonate rearrangement of phosphates **7** to α-hydroxyphosphonates **8**

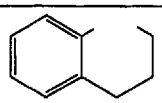
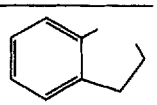
Entry	Start. mat.[a]	Product	Yield (%)	$[\alpha]_D^{20}$ (*c*)[b]	ee (%)[c]
1	(*S*)-(-)-**7a**	(*R*)-(+)-**8a**	6	+ 8.6 (1.1)	76
2	(±)-**7a**	(±)-**8a**	57		
3	(*R*)-(+)-**7a**	(*S*)-(-)-**8a**	55	-22.6 (2.0)	95
4	(*S*)-(-)-**7a**	(*R*)-(+)-**8a**	69	+24.9 (1.9)	95
5	(*R*)-(+)-**7a**	(*S*)-(-)-**8a**	25	-13.6 (2.2)	94
6	(±)-**7a**	(±)-**8a**	59		
7	(*R*)-(+)-**7a**	(*S*)-(-)-**8a**	72	-25.2 (2.0)	≥98
8	(*S*)-(-)-**7a**	(*R*)-(+)-**8a**	71	+26.3 (2.1)	≥98
9	(*S*)-(-)-**7b**	(*R*)-(+)-**8b**	79	+25.8 (2.1)	85
10	(*R*)-(+)-**7b**	(*S*)-(-)-**8b**	83	-10.2 (2.0)	38
11	(*S*)-(-)-**7c**	(*R*)-(+)-**8c**	51	+8.7 (2.0)	97
12	(*R*)-(+)-**7c**	(*S*)-(-)-**8c**	52	-9.0 (2.0)	98
13	(±)-**7d**	(±)-**8d**	47[d]		
14	(*R*)-(+)-**7d**	(*S*)-(+)-**8d**	45[d]	+19.7 (2.1)	≥98
15	(*S*)-(-)-**7d**	(*R*)-(-)-**8d**	54[d]	-19.2 (2.0)	≥98

[a] All reactions were carried out on a 1-mmol scale in diethyl ether as solvent except entry 5 (THF); entry 1: *n*BuLi, 1 h; entry 2: *s*BuLi, 2 h; entry 3: *s*BuLi, 1 h; entry 4: *s*BuLi, 1 h; entry 5: *n*BuLi, THF, 1 h; entries 6–15: *s*BuLi/TMEDA (1:1), 20 min, according to the General Procedure. – [b] In acetone, *c* = g/100 ml; concentrations were rounded to the nearest 0.1. – [c] Determined by ^{31}P-NMR spectroscopy using homochiral *t*-butyl(phenyl)phosphinothioic acid. – [d] Yield refers to alcohol.

The determination of the enantiomeric excesses of optically active phosphonates **8** is difficult. The tertiary, labile alcolhols cannot be esterified with homochiral acid derivatives. This problem could be circumvented by use of a homochiral solvating agent and ^{31}P-NMR spectroscopy. *t*-Butyl(phenyl)phosphinothioic acid, which can be obtained optically pure by chemical resolution[18] of the racemate with 1-phenylethylamine, was successfully applied to the determination of the enantiomeric excesses of phosphinic acid

Scheme 3



7, 8	a	b	c	d
R^1	Ph	2-Naphth		
R^2	Et	Me		

esters[18] and amides[17], phosphane oxides[19], sulfoxides[20], and N-oxides[21] by ^{1}H-NMR spectroscopy. Therefore, a sample of 5 mg of racemic **8a** and 2–2.5 equivalents of homochiral (S_P)-(−)-*t*-butyl(phenyl)phosphinothioic acid were dissolved in deuterated benzene. The ^{31}P-NMR spectrum (162 MHz) of the α-hydroxyphosphonate shows two singlets at δ = 24.01 and 23.99 of equal intensity for the two diastereomeric complexes. The shift difference of Δδ = 0.078 (13.0 Hz) is large enough to allow separate integration of the two signals. The ^{1}H-NMR spectrum at 400 MHz also shows well-separated signals for the diastereomeric complexes. The shift difference for the methyl group of $R^2 = C_2H_5$ for example is 0.062 ppm. The triplets for the methyl groups of the ethoxy residues are well separated. The ee values given in Table 1 were determined analogously by using homochiral (S_P)-(−)-*t*-butyl(phenyl)phosphinothioic acid and 5-mg samples of chiral, non-racemic α-hydroxyphosphonates **8a–d**. Anticipating the assignment of absolute configuration, the complexes with the (*R*)-configured α-hydroxyphosphonates **8** resonate at lower field than the complexes with the (*S*)-configured α-hydroxyphosphonates, the shift differences being 0.10, 0.033, and 0.024 for **8b**, **8c**, and **8d**. These results demonstrate unequivocally that this homochiral phosphinothioic acid is a chiral solvating agent for the convenient determination of the ee of tertiary α-hydroxyphosphonates. The results with secondary α-hydroxyphosphonates will be published separately. When this work was already finished, a paper by Lejczak et al. on the accurate assay of enantiopurity of secondary 1-hydroxy- and 2-hydroxyalkylphosphonate esters using homochiral *t*-butyl(phenyl)phosphinothioic acid was published[22].

Chiral, non-racemic phosphates afford optically active phosphonates. Assuming that here also the phosphate–phosphonate rearrangement proceeds with retention of configuration at the carbon atom, the phosphonates should have (*R*) or (*S*) configuration when starting from (*S*) or (*R*) phosphates, respectively (the change from *R* to *S* is brought about by a change of priorities according to the CIP system). In the case of (−)- and (+)-**7d** the sign of rotations does not change by going from phosphates **7d** to phosphonates **8d**, as is observed in the case of **8a–c** and for the rearrangement of diethyl 1-phenylethyl phosphate reported earlier[3]. One would expect similar behavior for the two cyclic structures **6c** and **6d**, but this is definitely not the case for **8d**. Therefore, CD spectra of (*S*)-**8a**, (*S*)-**8c** and (+)-**8d** were recorded (for data, see the Experimental section). The spectra of the two cyclic structures are virtually identical and very similar to the open structure **8a** and all three show a negative Cotton effect. So these should also have the same absolute configuration, that is (*S*).

The enantiomeric excesses of higher than 95% indicate that secondary benzylic phosphates can be transformed into phosphonates of the same optical purity. The α-hydroxyphosphonates (*R*)- and (*S*)-**8b** have enantiomeric excesses of 85% and 38%, respectively. (*R*)- and (*S*)-1-(2-naphthyl)-ethanol **6b**, used for the preparation of the phosphates (*R*)- and (*S*)-**7b**, had enantiomeric excesses of at least 98%, as determined by a comparison of their specific optical rotations with the values reported in the literature. The specific rotations of the phosphates (*R*)- and (*S*)-**7b** are already significantly different, $[\alpha]_D^{20} = -41.7$ (c = 2.24, acetone) for (*S*)-**7b** and $[\alpha]_D^{20} = +16.6$ (c = 1.905, acetone) for (*R*)-**7b**. The same relation holds for phosphonates (*R*)-**8b** with $[\alpha]_D^{20} = +25.8$ (c = 2.13, acetone) and (*S*)-**8b** with $[\alpha]_D^{20} = -10.2$ (c = 1.99, acetone). The most plausible explanation is the partial reacemization of phosphates **8b** under the conditions of phosphorylation of alcohols **6b**.

To extend the scope of the phosphate–phosphonate rearrangement, a kinetic resolution of (±)-**7a** with two different homochiral bases was also tested. When racemic phosphate **7a** was treated with 0.65 equivalents of *s*BuLi and (−)-sparteine[11] in diethyl ether at −78 °C and the reaction was quenched after 40 min with 7 equivalents of acetic acid, the α-hydroxyphosphonate (*R*)-(+)-**8a** was obtained in 36% yield with an ee of just 5% {$[\alpha]_D^{20} = +1.33$ (c = 1.955, acetone)}. The yield for the same reaction with (*R*)-lithium *N*-(1-phenylethyl)-*N*-isopropylamide[1] as base with a reaction time of 1 h was 17% and the ee was 6% {$[\alpha]_D^{20} = +1.53$ (c = 1.825, acetone)}. The enantioselectivity is too low to be of relevance.

Conclusions

The data presented provide further evidence of the potential of the phosphate–phosphonate rearrangement for the synthesis of α-hydroxyphosphonates from benzylic phosphates. The ease of deprotonation of benzylic phosphates with *s*BuLi/TMEDA is noteworthy. The intermediate diethoxyphosphoryloxy-substituted carbanions with either a phenyl or a 2-naphthyl residue are configurationally stable for their lifetime. Hoffmann et al. studied the microscopic and macroscopic configurational stability of benzylic carbanions with a variety of substituents, but not with a naphthyl residue[23]. Recently, Hoppe et al. reported that a tertiary benzylic carbanion with a naphthyl, a methyl and a carbamoyloxy substituent macroscopically rapidly racemizes at −78 °C in the presence of TMEDA[24]. Configurational stability at a synthetically useful degree is restored in the absence of TMEDA. The carbanions with a diethoxyphosphoryloxy group are not chemically stable, but are supposed to isomerize, as soon as they are formed, to

α-hydroxyphosphonates. The diethoxyphosphoryloxy group acts as an intramolecular electrophile which quenches the carbanion as soon as it is formed. It is thus ideally suited to act as an internal clock to determine the microscopic configurational stability of even labile carbanions. This aspect will be the subject of further investigations. *s*BuLi, TMEDA, and diethyl ether exert a positive effect on the reaction rate. The bidendate ligand TMEDA, which is sometimes considered to display no effect[15] on reactions conducted in THF, might in combination with the P=O bond disaggregate the *s*BuLi in diethyl ether. The ligation of the lithium cation to the P=O bond will fix the base near the carbon atom from which the proton has to be removed (proximity effect[25]). Additionally, it will increase the positive charge on the phosphorus atom, resulting in an increased acidity of the hydrogen atom and an easier attack of the carbanionic center in the course of the rearrangement.

We thank the *Fonds zur Förderung der wissenschaftlichen Forschung* (projects no. 10566 CHE, 6537C, and 8208C) for support and *Amano* for a gift of lipase SAM II. We are very much indepted to Prof. *M. Mikolajczyk* (Lodz, Poland) for samples of homochiral *t*-butyl(phenyl)phosphinothioic acid.

Experimenal

TLC: Merck precoated TLC plates (0.25 mm), silica gel 60, F_{254}; detection: UV and/or dipping the TLC plates into a solution of $(NH_4)_6Mo_7O_{24}\cdot 4\ H_2O$ (24 g) and $Ce(SO_4)_2\cdot 4\ H_2O$ (1 g) in 10% H_2SO_4 (500 ml) in water followed by heating with a hot gun. – ^{1}H- and ^{13}C-NMR spectra (*J* modulated) were recorded with a Bruker AM 400 WB at 400.13 and 100.61 MHz in $CDCl_3$, unless indicated otherwise; internal standard TMS. ^{31}P-NMR spectra were recorded in C_6D_6, unless indicated otherwise, with the same spectrometer at 161.97 MHz; external standard H_3PO_4 (85%). In order to obtain undistorted ^{31}P signal intensities for an accurate integration, adequate relaxation times were used without irradiation during this period to avoid NOE enhancements. – IR spectra were measured with a Perkin-Elmer 1600 FT-IR spectrophotometer. Liquid samples were measured neat between NaCl windows. Solid samples were dissolved in CH_2Cl_2 and applied to a silicon plate[26]. The solvent was allowed to evaporate before recording the IR spectra. – CD: Circulardigraph I. S. A. Jobin-Yvon CDC (200–350 nm, 5 scans, 0.1-cm cell). – Flash chromatography: Merck silica gel 60, 0.040–0.063 mm; eluents: petroleum ether (boiling range 60–95°C), ethyl acetate and dichloromethane. – Optical rotation: Perkin-Elmer polarimeter 141 (1-dm cell). – Melting points were measured with a Reichert Thermovar instrument and are uncorrected. – Reactions were carried out in dry solvents under argon. THF was distilled from potassium and diethyl ether from lithium aluminum hydride. TMEDA was refluxed for 5 h with CaH_2, distilled and stored over molecular sieve (4 Å). – Optically active alcohols (ee ≥ 98%) were prepared by enzymatic resolution[13] of their esters using lipase SAM II (from *Pseudomonas sp.*; *Amano*). The hydrolyses were stopped at conversions of 45%. Ester and alcohol were separated by flash chromatography. The ester was again hydrolyzed enzymatically until the consumption of base was neglibile. The ester was isolated and hydrolyzed with KOH in methanol. Alcohols **7b** and **7d** were recrystallized.

General Procedure for the Phosphate–Phosphonate Rearrangement of Phosphates **7**: A stirred solution of 1 mmol of phosphate **7a–c** or one third of the crude product of **7d** and 0.23 g (0.30 ml, 2 mmol) of TMEDA in 8 ml of dry diethyl ether was cooled to −78°C under argon. After the dropwise addition of 1.54 ml (2 mmol) of a 1.3 M solution of *s*BuLi in cyclohexane, stirring was continued for 20 min. The reaction was quenched with 3.5 ml (7 mmol) of a 2 M solution of acetic acid in diethyl ether. The cooling bath was removed and the solution was concentrated in a rotary evaporator (bath temperature 20°C). The residue was taken up in 10 ml of water and the solution was extracted four times with CH_2Cl_2. The combined organic phases were washed with water, dried with Na_2SO_4 and concentrated in vacuo (water bath temperature 20°C). The product was purified by flash chromatography to yield crystalline hydroxyphosphonate **8**.

*(±)-, (R)-(+)- and (S)-(−)-Diethyl 1-Phenylpropyl Phosphate [(±)-, (R)-(+)- and (S)-(−)-***7a***]:* A solution of 0.409 g (3 mmol) of **6a** in 15 ml of dry THF was stirred under argon at −78°C and 7.8 ml (3.9 mmol, 1.3 equiv.) of a 0.5 M solution of potassium bis(trimethylsilyl)amide in toluene was added by means of a syringe. After 30 min, 0.777 g (0.65 ml, 4.5 mmol, 1.5 equiv.) of diethyl chlorophosphate was added dropwise. The reaction mixture was allowed to warm up in the cooling bath from −78°C to +15°C within 17 h. Water (1 ml) was added and stirring was continued for 30 min. The solvent was removed in a rotary evaporator (water bath temperature 20°C). The residue was taken up in 20 ml of water and the solution was extracted four times with 10 ml of CH_2Cl_2. The combined organic phases were washed with water, dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography [CH_2Cl_2/ethyl acetate (19:1)] and bulb-to-bulb distillation (105–106°C/0.01 mm) to give phosphate **7a**, R_f = 0.64 [CH_2Cl_2/ethyl acetate (6:4)] as a colorless liquid.

(±)-**7a**: 0.678 g (83%); (*R*)-(+)-**7a**: 0.624 g (76%), $[\alpha]_D^{20}$ = +42.4 (*c* = 1.86, acetone); (*S*)-(−)-**7a**: 0.645 g (79%), $[\alpha]_D^{20}$ = −43.6 (*c* = 2.065, acetone). – IR (NaCl): $\tilde{\nu}$ = 2979 cm^{-1}, 1274, 1036, 1007, 997. – ^{1}H NMR: δ = 0.90 (t, *J* = 7.4 Hz, 3H, CH_3), 1.12 (dt, *J* = 7.1, 1.0 Hz, 3H, OCH_2CH_3), 1.25 (dt, *J* = 7.1, 1.0 Hz, 3H, OCH_2CH_3), 1.86 (m, 1H, CCH_2CH_3), 2.00 (m, 1H, CCH_2CH_3), 3.85 (m, 2H, OCH_2), 3.97 and 4.07 (2 m, 2H, OCH_2), 5.20 (q, *J* = 7.1 Hz, 1H, PhCH), 7.34 (m, 5H, H_{arom}). – ^{13}C NMR: δ = 9.59 (CH_2CH_3), 15.82 (d, J_{PC} = 7.6 Hz, OCH_2CH_3), 15.95 (d, J_{PC} = 7.8 Hz, OCH_2CH_3), 30.87 (d, J_{PC} = 6.1 Hz. CCH_2), 63.67 (d, J_{PC} = 6.1 Hz, OCH_2), 63.45 (d, J_{PC} = 5.3 Hz, OCH_2), 81.83 (d, J_{PC} = 6.1 Hz, CHOP), 126.45, 128.04 and 128.27 ($C_{arom}H$), 140.36 (d, J_{PC} = 3.0 Hz, C_{arom}). – $C_{13}H_{21}O_4P$ (272.28): calcd. C 57.35, H 7.77; found C 56.69, H 7.62.

*(R)-(+)- and (S)-(−)-Diethyl 1-(2-Naphthyl)ethyl Phosphate [(R)-(+)- and (S)-(−)-***7b***]:* These phosphates were prepared from 0.517 g (3 mmol) of (*R*)-(+)- or (*S*)-(−)-**6b** by the procedure used for the synthesis of **7a**, except that dry diethyl ether and 0.624 g (0.52 ml, 3.6 mmol) of diethyl chlorophosphate were used. When the bath temperature had reached +15°C, 5 ml of a saturated aqueous solution of NaCl was added and the mixture was vigorously shaken in a separating funnel. Then 15 ml of diethyl ether was added followed by a sufficient amount of water to dissolve precipitated salts. The organic phase was separated, washed with water, dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography [CH_2Cl_2/ethyl acetate (19:1)] to give a viscous oil. Bulb-to-bulb distillation of this oil in vacuo was not possible; R_f = 0.37 [CH_2Cl_2/ethyl acetate (19:1)].

(*R*)-(+)-**7b**: 0.549 g (59%), $[\alpha]_D^{20}$ = +16.6 (*c* = 1.905, acetone); (*S*)-(−)-**7b**: 0.749 g (81%), $[\alpha]_D^{20}$ = −41.7 (*c* = 2.24, acetone). – IR (NaCl): $\tilde{\nu}$ = 2982 cm^{-1}, 1392, 1370, 1270, 1032, 949. – ^{1}H NMR: δ = 1.15 (dt, *J* = 7.1, 1.0 Hz, 3H, OCH_2CH_3), 1.28 (dt, *J* = 7.1, 1.0 Hz, 3H, OCH_2CH_3), 1.71 (d, *J* = 6.4 Hz, 3H, $ArCCH_3$), 3.93 (m, 2H, OCH_2), 4.07 (m, 2H, OCH_2), 5.65 (quint, *J* = 6.9 Hz, 1H,

ArCH), 7.50 and 7.83 (2 m, 7H, H_{arom}). – ^{13}C NMR: δ = 15.91 (d, J_{PC} = 7.0 Hz, OCH_2CH_3), 16.02 (d, J_{PC} = 7.0 Hz, OCH_2CH_3), 24.17 (d, J_{PC} = 5.2 Hz, CH_3), 63.54 (d, J_{PC} = 6.1 Hz, OCH_2), 63.60 (d, J_{PC} = 6.1 Hz, OCH_2), 76.78 (d, J_{PC} = 5.7 Hz, ArCH), 123.70, 124.79, 126.14, 126.24, 127.63, 128.04 and 128.35 ($C_{arom}H$), 133.08 (d, J_{PC} = 3.1 Hz, $C_{arom}COP$), 139.02 and 139.09 (C_{arom}). – $C_{16}H_{21}O_4P$ (308.31): calcd. C 62.33, H 6.87; found C 62.02, H 7.04.

(R)-(+)- and (S)-(−)-Diethyl (1,2,3,4-Tetrahydro-1-naphthyl) Phosphate[14] *[(R)-(+)- and (S)-(−)-**7c**]:* These phosphates were prepared from 0.445 g (3 mmol) of (*R*)-(−)- or (*S*)-(+)-**6b** by the procedure used for the synthesis of **7a**. The crude products were purified by flash chromatography [petroleum ether/ethyl acetate (65:35)] to give viscous oils, which could not be subjected to bulb-to-bulb distillation in vacuo; R_f = 0.22 [petroleum ether/ethyl acetate (65:35)].

(*R*)-(+)-**7c**: 0.689 g (81%), $[\alpha]_D^{20}$ = +18.4 (*c* = 1.96, acetone); (*S*)-(−)-**7c**: 0.627 g (73%), $[\alpha]_D^{20}$ = −17.9 (*c* = 1.92, acetone). – IR (NaCl): $\tilde{\nu}$ = 2983 cm^{-1}, 2939, 1261, 1033, 983. – ^1H NMR: δ = 1.29 (dt, *J* = 7.4, 1.0 Hz, 3H, CH_3), 1.34 (dt, *J* = 7.4, 1.0 Hz, 3H, CH_3), 1.81 (m, 1H, CCH_2C), 2.02 (m, 2H, CCH_2C), 2.19 (m, 1H, CCH_2C), 2.79 (m, 2H, $ArCH_2$), 4.09 (m, 4H, OCH_2CH_3), 5.50 (quint, *J* = 3.6 Hz, 1H, CHOP), 7.10, 7.21 and 7.48 (3 m, 5H, H_{arom}). – ^{13}C NMR: δ = 16.02 (d, J_{PC} = 6.1 Hz, CH_3), 16.19 (d, J_{PC} = 6.1 Hz, CH_3), 18.21 and 28.76 (CCH_2C), 30.42 (d, J_{PC} = 3.0 Hz, CCH_2C), 63.54 (d, J_{PC} = 3.6 Hz, OCH_2), 63.59 (d, J_{PC} = 3.6 Hz, OCH_2), 74.57 (d, J_{PC} = 6.1 Hz, CHOP), 125.99, 128.30, 128.97 and 129.74 ($C_{arom}H$), 134.50 (d, J_{PC} = 6.9 Hz, $C_{arom}CH$), 137.52 ($C_{arom}CH_2$). – $C_{14}H_{21}O_4P$ (284.29): calcd. C 59.15, H 7.45; found C 58.88, H 7.68.

(±)-, (R)-(+)- and (S)-(−)-Diethyl 1-Indanyl Phosphate[14] *[(±)-, (R)-(+)- and (S)-(−)-**7d**]:* These phosphates were prepared from 0.403 g (3 mmol) of (±)-, (*R*)-(−)- or (*S*)-(+)-**6c** by the procedure used for the synthesis of **7b**. The products decomposed on flash chromatography or bulb-to-bulb distillation in vacuo. The crude phosphates, which are brownish-colored liquids containing some tetraethyl pyrophosphate (^1H NMR), were therefore coevaporated twice with benzene in a rotary evaporator, dried in vacuo (0.1 mm) and used for phosphate–phosphonate rearrangement without further purification; R_f = 0.26 [petroleum ether/ethyl acetate (65:35)].

(±)-**7d**: 0.878 g; (*R*)-(+)-**7d**: 0.744 g, $[\alpha]_D^{20}$ = +14.6 (*c* = 2.22, acetone); (*S*)-(−)-**7d**: 0.931 g, $[\alpha]_D^{20}$ = −16.0 (*c* = 2.04, acetone). – IR (NaCl): $\tilde{\nu}$ = 2982 cm^{-1}, 1480, 1261, 1032, 982. – ^1H NMR: δ = 1.31 (dt, *J* = 7.3, 1.0 Hz, 3H, CH_3), 1.35 (dt, *J* = 7.3, 1.0 Hz, 3H, CH_3), 2.27 (m, 1H, CH_2), 2.49 (m, 1H, CH_2), 2.99 (AB part of an ABXY system, J_{AB} = 16.2 Hz, *J* = 2 × 8.4, 6.4, 4.9 Hz, 2H, $ArCH_2$), 4.10 (m, 4H, OCH_2), 5.58 (dt, *J* = 6.4, 3.9 Hz, 1H, ArCH), 7.26 (m, 3H, H_{arom}), 7.52 (d, *J* = 7.4 Hz, 1H, H_{arom}). – ^{13}C NMR: δ = 16.04 (d, J_{PC} = 5.8 Hz, CH_3), 16.09 (d, J_{PC} = 6.5 Hz, CH_3), 29.91 (CH_2), 33.67 (d, J_{PC} = 4.2 Hz, CH_2), 63.61 (d, J_{PC} = 5.9 Hz, OCH_2), 81.88 (d, J_{PC} = 5.8 Hz, CHOP), 124.78, 125.40, 126.67 and 129.11 ($C_{arom}H$), 140.96 (d, J_{PC} = 5.8 Hz, $C_{arom}CH$), 143.95 ($C_{arom}CH_2$).

*(±)-, (R)-(+)- and (S)-(−)-Diethyl (1-Hydroxy-1-phenylpropyl)phosphonate [(±)-, (R)-(+)- and (S)-(−)-**8a**]:* These α-hydroxyphosphonates were prepared according to the General Procedure and the products were purified by flash chromatography using CH_2Cl_2/ethyl acetate (6:4; R_f = 0.43) as eluent. (±)-**8a**: 0.16 g (59%), m.p. 67–72°C (diethyl ether/petroleum ether, b.p. 40°C); (*R*)-(+)-**8a**: 0.193 g (71%), $[\alpha]_D^{20}$ = +26.3 (*c* = 2.06, acetone), ee ≥ 98%; (*S*)-(−)-**8a**: 0.197 g (72%), $[\alpha]_D^{20}$ = −25.2 (*c* = 1.95, acetone), ee ≥ 98%. – IR [Si, of (±)-**8a**]: $\tilde{\nu}$ = 3281 cm^{-1}, 3060, 1495, 1227, 1054, 1027, 967. – CD [EtOH, of (*S*)-**8a**]: λ (Δε) = 217 (−7.93). – ^1H NMR: δ = 0.77 (t, *J* = 7.4 Hz, 3H, CCH_2CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.26 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 2.16 and 2.28 (2 sept, *J* = 7.4 Hz, 2H, CCH_2CH_3), 2.77 (d, *J* = 5.9 Hz, 1H, OH), 3.76 and 3.93 (2 m, 2H, OCH_2CH_3), 4.10 (quint, *J* = 7.1 Hz, 2H, OCH_2CH_3), 7.27, 7.36 and 7.57 (3 m, 5H, H_{arom}). – ^{13}C NMR: δ = 6.24 (d, J_{PC} = 11.5 Hz, CCH_2CH_3), 16.24 (d, J_{PC} = 5.3 Hz, OCH_2CH_3), 16.35 (d, J_{PC} = 5.4 Hz, OCH_2CH_3), 30.21 (d, J_{PC} = 4.7 Hz, CCH_2CH_3), 63.00 (d, J_{PC} = 7.6 Hz, OCH_2), 63.22 (d, J_{PC} = 7.6 Hz, OCH_2), 76.52 [d, J_{PC} = 157.2 Hz, C(OH)P], 126.21 (d, J_{PC} = 4.6 Hz, $C_{arom}H$), 127.10 (d, J_{PC} = 3.1 Hz, $C_{arom}H$), 127.99 (d, J_{PC} = 3.1 Hz, $C_{arom}H$), 138.43 (C_{arom}). – ^{31}P NMR: δ = 24.93. – $C_{13}H_{21}O_4P$ (272.28): calcd. C 57.35, H 7.77; found C 57.61, H 7.63.

*(R)-(+)- and (S)-(−)-Diethyl [1-Hydroxy-1-(2-naphthyl)-ethyl]phosphonate [(R)-(+)- and (S)-(−)-**8b**]:* These α-hydroxyphosphonates were prepared according to the General Procedure and the products were purified by flash chromatography using CH_2Cl_2/ethyl acetate (6:4; R_f = 0.31) as eluent. (*R*)-(+)-**8b**: 0.244 g (79%), $[\alpha]_D^{20}$ = +25.8 (*c* = 2.13, acetone), ee 85%; (*S*)-(−)-**8b**: 0.256 g (83%), $[\alpha]_D^{20}$ = −10.2 (*c* = 1.99, acetone), ee 38%. – IR [Si, of (*S*)-(−)-**8a**]: $\tilde{\nu}$ = 3283 cm^{-1}, 2982, 1227, 1049, 1025, 967. – ^1H NMR [of (*S*)-(−)-**8b**]: δ = 1.18 (t, *J* = 7.1 Hz, 3H, CH_3), 1.26 (t, *J* = 6.9 Hz, 3H, CH_3), 1.92 (d with a shoulder at higher field, *J* = 15.3 Hz, 3H, $ArCCH_3$), 3.35 and 3.41 (2 d, integration ratio 2.4:1, *J* = 6.4 Hz, 1H, OH), 3.93 (m, 2H, OCH_2), 4.11 (m, 2H, OCH_2), 7.47, 7.73, 7.84 and 8.18 (4 m, 7H, H_{arom}). – ^1H NMR [of (*S*)-(−)-**8b**, [D$_6$]DMSO]: δ = 1.08 (t, *J* = 7.1 Hz, 3H, CH_3), 1.18 (t, *J* = 7.1 Hz, 3H, CH_3), 1.77 (d, *J* = 5.3 Hz, 3H, $ArCCH_3$), 3.85 and 4.00 (2 m, 4H, OCH_2), 6.55 (d, *J* = 10.3 Hz, 1H, OH), 7.49, 7.70, 7.89 and 8.05 (4 m, 7H, H_{arom}). – ^{13}C NMR [of (*S*)-(−)-**8b**]: δ = 16.33 (d, J_{PC} = 5.9 Hz, CH_3), 16.39 (d, J_{PC} = 5.9 Hz, CH_3), 26.14 and 26.16 (2 d, different intensity, J_{PC} = 3.5 Hz, $ArCCH_3$), 63.34 (d, J_{PC} = 7.4 Hz, OCH_2), 73.76 [d, J_{PC} = 158.7 Hz, C(OH)P], 124.08 (d, J_{PC} = 3.0 Hz, $C_{arom}H$), 124.72 (d, J_{PC} = 6.1 Hz, $C_{arom}H$), 126.00 (s, 2 $C_{arom}H$), 127.46 (d, J_{PC} = 1.5 Hz, $C_{arom}H$), 127.53 (d, J_{PC} = 1.9 Hz, $C_{arom}H$), 128.31 (d, J_{PC} = 1.0 Hz, $C_{arom}H$), 132.59 (d, J_{PC} = 1.5 Hz, C_{arom}), 132.99 (d, J_{PC} = 2.4 Hz, C_{arom}), 138.44 and 138.46 (2 s, different intensity, $C_{arom}H$). – ^{31}P NMR [of (*S*)-(−)-**8b**]: δ = 24.89 and 24.91 (integration ratio ≈ 1:2). – ^{31}P NMR [of (*S*)-(−)-**8b**, $CDCl_3$]: δ = 24.50. – $C_{16}H_{21}O_4P$ (308.31): calcd. C 62.33, H 6.87; found C 62.13, H 6.96.

*(R)-(+)- and (S)-(−)-Diethyl (1-Hydroxy-1,2,3,4-tetrahydro-1-naphthyl)phosphonate [(R)-(+)- and (S)-(−)-**8c**]:* These α-hydroxyphosphonates were prepared according to the General Procedure and the products were purified by flash chromatography using CH_2Cl_2/ethyl acetate (1:1, R_f = 0.31) as eluent. (*R*)-(+)-**8c**: 0.146 g (51%), $[\alpha]_D^{20}$ = +8.7 (*c* = 1.95, acetone), ee 97%; (*S*)-(−)-**8c**: 0.147 g (52%), $[\alpha]_D^{20}$ = −9.0 (*c* = 1.975, acetone), ee 98%. – IR (Si): $\tilde{\nu}$ = 3301 cm^{-1}, 2979, 2935, 1450, 1391, 1226, 1052, 1025, 966. – CD [EtOH, of (*S*)-(−)-**8b**]: λ (Δε) = 224 (−2.59), 266 (−0.41), 274 (−0.34). – ^1H NMR: δ = 1.12 (t, *J* = 6.9 Hz, 3H, CH_3), 1.31 (t, *J* = 6.9 Hz, 3H, CH_3), 1.89 (m, 1H, CH_2), 2.05 (m, 2H, CH_2), 2.38 (m, 1H, CH_2), 2.81 (m, 2H, CH_2), 3.10 (d, *J* = 6.9 Hz, 1H, OH), 3.79 and 4.01 (2 m, 2H, OCH_2), 4.13 (m, 2H, OCH_2), 7.10, 7.21 and 7.88 (3 m, 4H, H_{arom}). – ^{13}C NMR: δ = 16.26 (d, J_{PC} = 5.3 Hz, CH_3), 16.44 (d, J_{PC} = 6.1 Hz, CH_3), 18.85 (d, J_{PC} = 4.6 Hz, CH_2), 29.45 (CH_2), 33.59 (d, J_{PC} = 1.5 Hz, CH_2), 63.02 (d, J_{PC} = 6.9 Hz, OCH_2), 63.29 (d, J_{PC} = 7.6 Hz, OCH_2), 72.16 [d, J_{PC} = 161.0 Hz, C(OH)P], 126.03 (d, J_{PC} = 2.3 Hz, $C_{arom}H$), 128.05 (d, J_{PC} = 2.3 Hz, $C_{arom}H$), 128.32 (d, J_{PC} = 3.8 Hz, $C_{arom}H$), 129.07 ($C_{arom}H$), 135.44 (d, J_{PC} = 3.1 Hz, C_{arom}), 138.00 (d, J_{PC} = 6.9 Hz, C_{arom}). – ^{31}P NMR: δ = 24.93. – $C_{14}H_{21}O_4P$ (284.29): calcd. C 59.15, H 7.45; found C 58.87, H 7.63.

*(±)-, (R)-(−)- and (S)-(+)-Diethyl (1-Hydroxy-1-indanyl)-phosphonate [(±)-, (R)-(−)- and (S)-(+)-**8d**]:* These α-hydroxyphosphonates were prepared according to the General Procedure and the products were purified by flash chromatography using CH_2Cl_2/ethyl acetate (1:1; R_f = 0.26) as eluent. (±)-**8d**: 0.127 g (47%, based on **6d**), m.p. 76−78°C (diethyl ether/petroleum ether, b.p. 40°C); (**R**)-(−)-**8d**: 0.147 g (54%, based on **6d**), $[\alpha]_D^{20}$ = −19.2 (*c* = 1.98, acetone), ee ≥ 98%; (*S*)-(+)-**8d**: 0.122 g (45%, referring to **6d**), $[\alpha]_D^{20}$ = +19.7 (*c* = 2.115, acetone), ee ≥ 98%. − IR [Si, of (*S*)-(+)-**8d**]: $\tilde{\nu}$ = 3265 cm^{-1}, 2987, 1391, 1266, 1203, 1070, 1103, 1026, 965. − CD [EtOH, of (*S*)-(+)-**8d**]: λ (Δε) = 222 (−1.80), 267 (−0.33), 273 (−0.30). − ^1H NMR: δ = 1.14 (t, *J* = 7.1 Hz, 3H, CH_3), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3), 2.20 (m, 1H, CH_2), 2.77 (m, 1H, CH_2), 2.99 (m, 2H, CH_2), 3.49 (d, *J* = 5.9 Hz, 1H, OH), 3.87 (m, 1H, OCH_2), 4.06 (m, 3H, OCH_2), 7.24 and 7.60 (2 m, 4H, H_{arom}). − ^{13}C NMR: δ = 16.28 (d, J_{PC} = 5.4 Hz, CH_3), 16.44 (d, J_{PC} = 5.7 Hz, CH_3), 30.08 (d, J_{PC} = 3.7 Hz, CH_2), 37.24 (d, J_{PC} = 5.8 Hz, CH_2), 63.02 (d, J_{PC} = 7.3 Hz, OCH_2), 63.29 (d, J_{PC} = 7.1 Hz, OCH_2), 81.33 [d, J_{PC} = 166.6 Hz, C(OH)P], 124.73 (d, J_{PC} = 1.0 Hz, $C_{arom}H$), 125.15 (d, J_{PC} = 2.3 Hz, $C_{arom}H$), 126.71 (d, J_{PC} = 2.3 Hz, $C_{arom}H$), 129.02 (d, J_{PC} = 2.2 Hz, $C_{arom}H$), 141.61 (d, J_{PC} = 3.2 Hz, C_{arom}), 144.26 (d, J_{PC} = 8.5 Hz, C_{arom}). − ^{31}P NMR: δ = 25.04. − $C_{13}H_{19}O_4P$ (270.27): calcd. C 57.77, H 7.09; found C 58.03, H 7.25.

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