

PII: S0957-4166(96)00456-9

## Stereochemical Aspects of the Asymmetric Synthesis of Chiral $\alpha,\beta$ -Dihydroxy Phosphonates. Synthesis of $\alpha,\beta$ -Dihydroxy Phosphonic Acids

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Abstract: Stereocontrol in the asymmetric phosphonylation of aldehydes via organophosphorous esters has been obtained starting from chiral aldehydes. The nature of the O-protecting group is crucial to obtain, in terms of diastereoselectivity and chemical yields, the best results. An *ab initio* molecular orbital study on 2-silyloxy propanal and MM2 studies on 2-alkoxy propanal show the existence of stable cyclic and acyclic conformers, which are presumably responsible for the high *syn* diastereoselectivity observed in the addition of non-metal carrying phosphites. Copyright © 1996 Elsevier Science Ltd

#### Introduction.

Over the years the concept of bioisosterism has become a useful tool in medicinal chemistry. The prominent role of carboxylic acids in biological activity and molecular recognition has resulted in broad studies of carboxylic acid bioisosters. A wide variety of successful carboxylic acid bioisosters has been developed including sulphurous and phosphorous acids.<sup>1</sup> The synthesis of  $\alpha$ -substituted phosphonic acids has been an important area of research. In recent years, considerable interest has been focused on the synthesis of phosphonic acids, particularly the  $\alpha$ -substituted analogues which are an important class of compounds<sup>2</sup> with applications as antibiotics, antiviral agents and enzyme inhibitors.<sup>3</sup> Among the  $\alpha$ -functionalized phosphonic acids,  $\alpha$ -hydroxyphosponic acid derivatives are gaining interest in medicinal chemistry since they are potential inhibitors of enzymes such as protease, EPSP synthethase, and thyroxin specific protein kinase<sup>4</sup>, and since may may represent an interesting chiron for the preparation of the parent  $\alpha$ -aminophosphonic acids. Despite the number of papers which have appeared for the synthesis of  $\alpha$ -aminophosphonic acids, <sup>3a,5</sup> stereocontrolled syntheses of  $\alpha$ -hydroxyphosphonic acid derivatives have only recently begun to receive attention.<sup>6</sup>

Phosphonic acids are available by a number of methods: resolution, enzymatic techniques, or by utilising some aspects of asymmetric bond formation. One of the most useful methods is in the phosphonylation of aldehydes. Two related asymmetric procedures have been used to achieve carbonyl phosphonylation: one based on the Abramov reaction and the other based on the Pudovik reaction.<sup>7</sup>

## Results

 $\alpha,\beta$ -Dihydroxy phosphonic esters are easily prepared by the addition of trimethylsilyl diethylphosphite<sup>8</sup> 1a to  $\alpha$ -silyloxy or alkoxy-aldehydes 2a-2g in generally good yields and with variable diastereoselectivity. Recently, we have been involved in a program directed towards the use of chiral  $\alpha$ -silyloxy aldehydes as useful substrates for the EPC syntheses of biologically active compounds.<sup>9</sup> In the course of these studies, we have shown that a high asymmetric induction may be achieved by the correct choice of the *O*-protecting group. In this paper we report the results obtained in the asymmetric synthesis of  $\alpha,\beta$ -dihydroxy phosphonic esters with special emphasis to the factors controlling the diastereoselectivity of the reaction. In order to evaluate the effect of different parameters on the diastereoselectivity of the reaction, lactic aldehyde was chosen as the sample compound.

#### Determination of the diastereoselectivity

The first effect we have evaluated has been the influence of the O-protecting group of the hydroxy functionality of the aldehyde on the diastereoselectivity of the addition reaction. (Scheme and Table 1).<sup>10</sup> Scheme and Table 1: Diastereometic Ratio from R<sup>1</sup>



Exp	R <sup>1</sup>	Aldehyde	Products	Y%	Ratio
1	TES	2a	3a/4a <sup>10</sup>	55	63/37
2	TBDMS	2b	3b/4b	71	71/29
3	TIPS	2c	3c/4c	67	92/8
4	DPTBS	2d	3d/4d	66	90/10
5	<i>tert</i> -Bu	2e	3e/4e	23	86/14
6	Bn	25	3f/4f	79	33/67
7	Ме	2g	3g/4g	25	29/71

Changing the O-protecting group on the hydroxy functionality of the aldehyde showed an important effect on the diastereoselectivity. Upon increasing the steric hindrance of the Oprotecting group an increase of the syn diastereoselectivity is observed. The use of the hindered triisopropylsilyl<sup>11</sup> derivative showed the highest syn selectivity. Moreover, crossover experiments have determined that the relative reactivity of the  $\alpha$ silyloxy aldehyde is much higher than that of the corresponding  $\alpha$ -benzyloxy thus one such disclosing an activation by the silyl protecting group on the carbonyl function. (Chart 1). On the other hand, the diastereoselectivity of the reaction remained almost unchanged using different alkyl ester phosphites (Scheme and Table 2).



Ratio

92/8

93/7

85/15

91/9

91/9

85/15

89/11

89/11

Scheme and Table 2: Diastereomeric Ratio from R<sup>2</sup> R<sup>2</sup> Ex Phosp. Solv. Prod. Y% 1 Et 1a CH<sub>2</sub>Cl<sub>2</sub> 3c/4c 67 2 Et 1a 3c/4c 85 3 3h/4h 47 2c Мe 1b CH<sub>2</sub>Cl<sub>2</sub> 4 Me 1b 3h/4h 45 OTIPS 5 Bn 1c CH<sub>2</sub>Cl<sub>2</sub> 31/41 80 6 Bn 1C 31/41 80 7 *i*.Pr 1d CH<sub>2</sub>Cl<sub>2</sub> 3j/4j 61 3 *i*.Pr 1d 3/4j 51

The use of hindered silicon groups directly linked to the phosphite corresponds to a decrease of the diastereoselectivity with an increase of the steric hindrance of these groups (Scheme and Table 3).

In order to determine how the solvent dielectric constant might play a significant role in altering the relative rates of the syn anti ratio, the reaction of diethyltrimethylsilylphosphite 1a with triisopropylsilyloxyand benzyloxy-lactaldehyde, 2c and 2f, in a range of solvents was undertaken (Scheme and Table 4). Only a very negligible alteration in the syn anti ratio [87/13 in N-methylpropionamide (NMP) vs 88/12 in hexane] was observed (Table 4, entries 1, 9). The use of co-ordinating solvents (HMPA, THF, ether) resulted in slight reduction in selectivity but the chemical yields dropped. (Table 4, entries 4, 6, 7).

R<sup>3</sup> Phosphite Products Y% Ratio Exp 1 TMS 3c/4c 67 92/8 18 2 TES 3k/4k 74/26 1e 75 20 3 TBDMS 31/41 87 71/29 1f EtO, P TIPS 1a 3m/4m 89 64/36







i: -40°C, 3h. For work-up, see Experimental Section

Exp	R	Solvent	D.C.25°C 12	Y% a	Products	Ratio
1	TIPS	NMP	170.0	45	3c/4c	87/13
2	TIPS	DMF	38.3	95	3c/4c	81/19
3	TIPS	CH <sub>3</sub> CN	36.6	66	3c/4c	90/10
4	TIPS	HMPA	31.3	10	3c/4c	85/15
5	TIPS	CH <sub>2</sub> Cl <sub>2</sub>	8.93	83	3c/4c	90/10
6	TIPS	THF	7.52	34	3c/4c	84/16
7	TIPS	Et <sub>2</sub> O	4.26	37	3c/4c	86/14
8	TIPS	Toluene	2.38	91	3c/4c	87/13
9	TIPS	Hexane	1.88	63	3c/4c	88/12
10	TIPS	No Solvent	n.d	84	3c/4c	88/12
11	Bn	NMP	170.0	10	3f/4f	40/60
12	Bn	DMF	38.3	13	3f/4f	25/75
13	Bn	CH <sub>2</sub> Cl <sub>2</sub>	8.93	79	3f/4f	33/67
14	Bn	Hexane	1.88	58	3f/4f	37/63
15	Bn	No Solvent	n.d	28	3f/4f	48/52

n.d: not determined. The yield and diastereomeric ratio have been determined by 31P NMR on the crude reaction mixture. Increasing the reaction temperature (Scheme and Table 5) resulted in a decrease in selectivity, with reactions run at room or higher temperature showing the lowest selectivities whereas the highest one was reached at -78°C. The possibility that the syn and anti adducts were thermally interconvertible was eliminated by the following study: the pure syn adduct 3c was heated at temperature up to 80°C and then left to stand for one week in an attempt to equilibrate the addition products. No inter conversion was detected. At higher temperature (up 120°C), a retro-aldol type reaction takes place with concomitant extensive decomposition. (Chart 2).



Scheme and Table 5: Temperature effect on the diastereomeric ratio

a: The yield and diastereomeric ratio have been determined by <sup>31</sup>P NMR on the crude reaction mixture.

The high thermal stabilities observed in this reaction suggests that the syn anti ratio reported in Table 5 are a consequence of kinetic control during the addition process and are not the result of a thermal equilibration. Chart 2



Finally, in Table 6 are reported the results using other trialkylsilyloxy aldehydes as substrates. The data reported clearly shows that the R-group, directly linked to the chiral centre, plays a dramatic role in determining the diastereoselectivity and the yields of the reaction, the lowest being reached with highy hindered *t*-butyl group (Table 6, Exp. 6).

Scheme and Table 6: Silyloxy Phosphonylation of Aldehydes 2



#### Determination of the diastereomeric mixture.

In order to unequivocally establish the correct absolute configuration of the phosphonate esters reported, the corresponding cyclic carbonates<sup>13</sup> were prepared following the sequential reactions reported in Scheme 7a and 7b. The analysis of the H1-H2 coupling constants in the cyclic derivatives and, in dubious cases, NOE experiments allowed a straightforward determination of the configuration of the cyclic compounds and of their corresponding acyclic derivatives.

Relevant NMR data of the acyclic compounds are reported in Table 7. The analysis of these data shows that while the P-H2 and the P-CH3 values of the coupling constants are of the same magnitude, the H1-H2 coupling constant values are greater for the syn compound than for the anti, thus showing that both compounds prefer the same conformation in which the bulky phosphonyl group and the O-protecting group are antiperiplanar. Moreover it is interesting to note that the <sup>31</sup>P signal is always more compound.14 In deshielded in the syn conclusion these two effects are useful diagnostic tools for the determination of the relative configurations in the acyclic compounds.



6c, 7c, 8c: R=p-MeOPh; 5d, 6d, 7d, 8d: R=*i*-Pr; 5e, 6e, 7e, 8e: R=Pentyl.

Reagents and conditions: *i*: HF<sub>5%aq</sub>, CH<sub>3</sub>CN, r.t.; *ii*: Triphosgene, Pyridine, CH<sub>2</sub>Cl<sub>2</sub>, -78<sup>\*</sup>, 2h.





Comp	R	<b>R</b> <sup>1</sup>	$\delta H_1[J_{H_1-H_2}]$	δ H <sub>2</sub> [J <sub>P-H2</sub> ]	δ P <sub>1</sub> [J <sub>P-CH3</sub> ]	δ C <sub>2</sub> [J <sub>P-C1</sub> ]	δ C <sub>3</sub> [J <sub>P-C2</sub> ]
			$\delta H_{1'} [J_{H_{1'}-H_{2'}}]$	$\delta H_2[J_{P-Hz}]$	δ P <sub>1'</sub> [J <sub>P-CH3</sub> ]	$\delta C_{2'}[J_{P-C_{1'}}]$	δ C <sub>3'</sub> [J <sub>P-Cz</sub> ]
3c'	CH <sub>3</sub>	TMS	3.88 [5.10]	4.0	20.83[4.47]	73.86[167.15]	70.29[3.87]
4c'	CH3	TMS	4.12[1.04]	4.30[3.84]	19.16	75.84[165.12]	68.86[15.60]
3c	CH3	Н	3.61[6.44]	4.31[6.70]	20.40[5.70]	72.69[162.31]	68.32[5.32]
4c	CH <sub>3</sub>	Η	4.05[2.90]	4.33[5.56]	19.22[5.83]	72.78[162.46]	68.38[5.43]
3n'	Ph	TMS	4.22[6.70]	5.31[8.90]	19.08	74.96[165.52]	75.87[8.14]
4n'	Ph	TMS	4.62[3.10]	5.48[3.10]	17.49	75.81[163.90]	75.00[13.01]
3n	Ph	Η	4.19[7.00]	5.34[7.00]	19.22	73.32[157.45]	75.02[0.00]
4n	Ph	Н	4.52[3.80]	5.47[5.75]	18.00	73.72[161.12]	74.31[9.55]
30'	p-MeOPh	TMS	4.23[7.05]	5.32[8.80]	19.72	75.11[165.39]	75.50[8.61]
40'	p-MeOPh	TMS	4.65[3.10]	5.50[3.10]	18.09	76.03[146.87]	74.27[3.46]
30	p-MeOPh	H	4.20[7.20]	5.32[7.20]	20.23	73.46[164.51]	74.49[7.39]
40	p-MeOPh	Η	4.55[3.80]	5.45[5.60]	17.82	73.78[161.32]	73.82[9.71]
3p'	i-Pr	TMS	4.02[4.65]	3.75[26.80]	21.30	72.73[166.06]	78.26[4.41]
4p'	i-Pr	TMS	4.13[1.42]	4.00[7.50]	20.12	76.30[161.86]	77.30[13.15]
3p	i-Pr	Η	3.78[6.20]	4.15	21.64	65.71[165.86]	73.31[2.98]
4p	i-Pr	Η	4.13	4.00	19.81	73.00[159.69]	76.10[8.21]
3q'	Pentyl	TMS	3.95	3.95	20.82	72.58[167.22]	73.94[3.18]
4q'	Pentyl	TMS	4.10	4.10	19.53	75.41[180.44]	73.90[3.80]
3q	Pentyl	H	3.78[3.54]	4.15	21.09	68.93[162.67]	71.34[3.80]
4q	Pentyl	H	4.02[2.92]	4.13	19.61	72.40[158.27]	73.27[7.39]
3r	Cyclohex	Н	4.03 [4.24]	3.74[11.52]	24.30	67.28[167.80]	73.57[4.00]
4r	Cyclohex	Н	3.86 [3.20]	3.92[9.39]	23.70	71.54[157.60]	74.11[0.00]

#### Preparation of the sodium salts of the 1,2-dihydroxy phosphonic acids.

Finally the conversion of phosphonate esters to phosphonic acids was achieved by hydrolysis with HCl at reflux (Scheme 8. See also experimental section).



Reagents and conditions: *ir.* HCl 1N; Reflux *ir.* Dowex50X8 (Na<sup>+</sup> Form). Reagent and Conditions: *i*: H<sub>2</sub>/Pd/C, 10%; *ii*: Dowex50X8(Na<sup>+</sup> form)

Hydrolysis of 3n by this method gave extensive isomerization and decomposition of the starting ester. In order to obtain the corresponding disodium salt, the dibenzyl derivative 3t was prepared starting from dibenzyl triethylphosphite 1c and mandelic aldehyde 2h following the phosphonylation procedure (Method B). The resulting dibenzylphosphite was converted into desired phosphonic acid by hydrogenolysis with Pd/C 10%. (Scheme 9).

#### Discussion

The most popular approach in explaining the facial diastereoselectivity of a given reaction examines the partitioning of the reaction mechanism via a chelated transition state, which gives the syn isomer, and an unchelated one of comparable activation energy, which affords a preponderant amount of the anti diastereomer. This partition has been named by Reetz<sup>15</sup> chelation and non chelation control. <sup>16</sup> From this point of view an important role is played, by the metal present, in case it is in the reaction medium, in the reaction medium. Scantly co-ordinating metals give rise to a poor diastereocontrol of the reaction while strong chelating metals usually generate high diastereocontrol. In our case, no metal is present in the reaction medium, nevertheless a high syn stereocontrol is achieved.<sup>17</sup>

In the addition of phosphites derivatives to the  $sp^2$  carbon atom, at the freezing of the tricoordinated form of diethylphosphite by means of O-silylation<sup>18</sup> results in a promoting of the nucleophilic reactivity of the phosphonylating reagent *via* a concerted [3+2] cycloaddition reaction as suggested by Evans<sup>50</sup>. In considering this reaction mechanism, it is tempting to





postulate a chelated transition state (Chart 3), in which the aldehyde and diethyltrimethylsilylphosphite are coordinated by the silicon atom and react in a concerted manner. It is known that pentacoordinate organosilicon compounds<sup>19</sup> exhibit enhanced reactivity compared to their tetracoordinate analogues.<sup>20</sup> Recently, we have demonstrated by *ab initio* calculations the existence of a cyclic conformer in the  $\alpha$ -silyloxy-*N*trimethylsilylimine derivatives.<sup>21</sup> In addition, a recent paper by Gung<sup>22</sup> has shown that the most stable conformer of 3-silyloxy propanal has a cyclic structure, where the silicon atom is 3.1 Å from the carbonyl oxygen atom. These facts point out an attractive electrostatic interaction between the silicon and the carbonyl oxygen atom. In this light we performed *ab initio* calculations on the silyloxy-lactaldehyde 2n (Fig. 1) in which the silyl group is SiH<sub>3</sub>. These calculations clearly show the presence of only two stable conformers, one of linear all-*trans* geometry *aa* (anti-anti) (see Fig. 1 and Table 8)  $2n_{aa}$  and the other one of cyclic-planar geometry *ss* (syn-syn see Fig. 1 and Table 8)  $2n_{ss}$ . The energy difference between  $2n_{ss}$  and the straight chain conformer  $2n_{aa}$  is -10.5 KJ/mol, thus emphasising a higher stability of the conformer  $2n_{ss}$ . This conformer is

characterized by a silicon carbonyl-oxygen distance of 2.8 Å and a corresponding bond order of  $0.124 e^{-}$ . These values are of the same magnitude of those found for the imine derivatives.<sup>21</sup> The current results show that the association of the silicon and the carbonyl is preferred and that this attractive interaction might be responsible for the pre-association of the two reactants required in the mechanism suggested for the uncatalysed silicon-directed aldol condensation. Moreover, the calculated stability of the cyclic conformer with respect to the acyclic one may be invoked to explain the high syn diastereoselectivity observed when the starting aldehyde used is the silyloxy one. In fact in this case the nucleophile is forced to attack from the less hindered diastereotopic face of the cyclic conformer  $2n_{ss}$ , thus generating the syn diastereomer (Fig. 1).

What is more intriguing is to try to explain the increase of the syn-diastereoselectivity on the increasing the bulkiness of the silyloxy group, since it is well know that higher steric hindrance on the silicon group doesn't allow, to some extent, the formation of a chelated complex.<sup>15,16</sup> Surprisingly, analysis of the data in Table 1 (Table 1, Entry 5) shows that, with very bulky alkoxy groups, which essentially means in the absence of any possible chelated species, a very high syn diastereoselectivity is once again present. MM2 force field calculations were performed to get a better insight on the conformational preferences of such a compound. From these calculations it turns out that the more stable aldehyde-conformer ag (anti-gauche)  $2e_{ag}$  (Fig. 1 and Table 8) is that in which the polar groups are antiperiplanar to each other, but the strong non bonded steric interaction forces the *tert*-butyl group to accommodate itself perpendicularly to the carbonyl plain on the opposite side of the methyl group. Under these conditions, the nucleophile will attack, according to the Burgi-Dünitz trajectory<sup>23</sup>, from the methyl face, since the other face is more crowded.

		2n <sub>se</sub>	2n <sub>as</sub>	2e <sub>ag</sub>
	d 1-2	1.209	1.207	1.209
6	d 2-3	1.506	1.515	1.525
H <sub>2</sub> C, R	d 3-4	1,413	1.433	1.424
5	d 4-5	1.644	1.637	1.437
-34	d 3-6	1.536	1.527	1.540
1 2	a 1-2-3	123.1	123.3	123.9
. 2	a 2-3-4	110.8	105.1	110.0
	a 3-4-5	139.1	134.4	118.2
2n <sub>se</sub> , 2n <sub>sa</sub> : R= SiH <sub>3</sub> ,	a 2,3,6	109.6	111.0	110.2
2e <sub>ag</sub> : R= <i>tert</i> - Bu	t 1,2,3,4	-0.5	198.3	173.0
	t 2,3,4,5	0.6	194.1	-94.8
	t 1,2,3,6	120.9	-40.1	-69.9

Table 8: Selected data for the structures 2nss, 2nas and 2eag

d: Bond distances in Å. a: Bond angles in degrees. t: torsional angles in degree.

In our case, the bigger the nucleophile, the more this situation is true. Further confirmation of this mechanistic hypothesis comes from the benzyloxy and the methoxy groups, which are less sterically demanding than the *tert*-butoxy group. In these cases, a relatively high *anti* diastereoselectivity (Table 1, entries 6 and 7) is observed. As a matter of fact force field calculations on the benzyloxy- and the methoxy-aldehyde derivatives 2f and 2g show that both *aa* and *ag* conformers are present. (Table 9). However, with the silyloxy group *the predominance of the syn diastereomer is always taking place*. The rational of this behaviour may be found assuming the possibility that two different mechanistic pathways are involved. In the first one, with the silicon group bearing the small substituent, the formation of a cyclic conformer is allowed and the *syn* isomer is preferentially produced. In the second one, the bulkiness of the silyl-substituent forbids the formation of the cyclic conformer but forces the silyl- oxy group to accommodate itself as in the case of the*t*-butoxy group. As a result of this steric situation the *syn* conformer is *always* preferentially produced. Finally, when the *R*-group directly linked to the stereogenic center is particularly hindered, a complete loss of diastereoselectivity and a

decrease in the reactivity must be expected. As a matter of fact the data reported in Table 6 (Table 6, Entries 3, 5,6) fully in accord with these expectations. In conclusion, it must be stressed that, in all of the cases examined, a [2+3] cycloaddition reaction takes place according to the small solvent dependence on the rates of the *syn/anti* ratio. This behaviour strongly supports the Evans' hypothesis<sup>50</sup> that the rate determining step involves cyclic transition states possessing little charge separation.





The diastereoselectivity of the reaction strongly depends on the population of conformers present, which, in turn, is strictly bound to the very nature of the O-protecting groups.

Figure 1. Chem 3D of structures  $2n_{ss}$  and  $2n_{aa}$  from optimised *ab initio* co-ordinates and of structure 2eag from MM2 co-ordinates



#### Conclusion

From the results reported, it appears clear that the syn selectivity of this reaction increases as the  $\alpha$ -oxygen becomes more and more crowded. Of course, without more sophisticated and elaborate investigations, we cannot provide a transition-state drawing to fully explain these results. However, from our preliminary studies, we can anticipate that the chelation is always associated with syn diastereoselectivity while non-chelation gives the anti as well as thesyn diastereomer depending on the very nature of the substrate. Be that as it may, the experimental facts carry two important messages: 1. A very high syn diastereoselectivity has been achieved without the use of co-reagents such as chelating Lewis acid; 2. The diastereofacial selectivity can be

varied or reversed without changing any chiral centres or backbone functionality. Simple protecting group alterations are enough to vary or reverse a given diastereofacial selectivity. In our opinion the head implication of our results is : it is generally assumed that improvements of a poor diastereofacial synthesis require a change in the backbone functionality or the chiral centres, notwithstanding this is a rather difficult task. The results presented in this paper demonstrate that simply changing the very nature of the protecting groups is sufficient to improve stereoselectivity without major modifications of the reactants, or without adding extra reactants and to provide an avenue for solving, in some extent, stereochemical problems.

#### **Experimental Section**

General: Melting points are uncorrected. All reactions were conducted under an argon atmosphere. THF was distilled from Na/benzophenone ketyl and CH<sub>2</sub>Cl<sub>2</sub> was distilled from P<sub>2</sub>O<sub>5</sub>. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded at 300 and 75 MHz in CDCl<sub>3</sub>, unless otherwise stated, using TMS or residual CHCl<sub>3</sub> as internal reference or in D<sub>2</sub>O using dioxane as external reference. <sup>31</sup>P-NMR (121.5 MHz) was taken in CDCl<sub>3</sub> or D<sub>2</sub>O using 85% H<sub>3</sub>PO<sub>4</sub> as an external reference with broad-band <sup>1</sup>H-NMR decoupling.

Ab initio calculations were performed at the SCF/3-21G\* level using the Gaussian 92 program<sup>24</sup>. MM3 calculations were performed using the MM3(92) program.<sup>25</sup> For both calculations, geometries were fully optimised by gradient techniques and the final minima were checked by frequency analysis.

#### General Procedure for the Synthesis of $\alpha$ -Silyloxy Aldehydes from Hydroxy Esters.

To a solution of  $\alpha$ -hydroxy ester (30 mmol) and imidazole (60 mmol) in anhydrous DMF (30 mL) cooled with ice-water were added 30 mmol of the appropriate silyl-chloride. After ten minutes the bath was removed and the reaction was left at room temperature for three hours. The mixture was poured into ice-water and extracted with hexane (3x50 mL). The organic layers were washed with brine (2x50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in vacuo to give the  $\alpha$ -silyloxy ester in almost quantitative yields and sufficiently pure for further elaboration. To a solution of the appropriate ester (20 mmol) in anhydrous ether (80 mL) was added dropwise diisobutylaluminiumhydride (DIBAH) (30 mmol, 30 mL, 1 M sol. in hexane ) by a side arm at -78 °C. After being stirred at the same temperature for the time required to consume the starting ester (from 15 min to 2 hr) the mixture was poured into ice water and extracted with ether. The organic layer was washed twice with diluted cold hydrochloric acid, brine, and then dried and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/ethyl acetate 9/1) or distilled to give the target aldehyde.

Aldehydes 2a, 2b, 2c, 2d, 2e, 2f and 2h were prepared according to the literature procedure.<sup>9b,29</sup> Synthesis of 2-Methoxy Lactate<sup>28</sup>

To a solution of 100 mmol (11.5 mL) of commercially available (S)-ethyl lactate and Ag<sub>2</sub>O (200 mmol, 46g) in DMF (60 mL) was added dropwise methyl iodide (7.5 mL, 120 mmol), leaving the temperature to rise 46°C. The temperature was kept at this value for the entire addition, freezing by ice-water-bath and heathed for 6 hr at 50°C. The mixture was stirred at r.t. overnight. The mixture filtered, the residue washed with ethyl acetate and the organic layers washed with HCl 1N. The solvent was removed in vacuo and the residue was purified by distillation to give the 2-methoxy-ethyl-lactate (Kp760=142°C) (Y%=28).Spectral data as follow:

IR (Film) 1734 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.22 (q, 2H, J=7.3); 3.86 (q, 1H, J=6.8); 3.39 (s, 3H); 1.40 (d, 3H, J=6.8); 1.29 (t, 3H, J=7.1). <sup>13</sup>C NMR 172.87, 76.17, 60.56, 57.44, 18.23, 14.06.

#### 2-Methoxylactaldehyde 2g.

To a solution of 2-methoxyethyl lactate (13.6 mmol, 1.8g) in ether (15 mL) was added DIBAH (1.3 eq, 18mmol, 3.2 mL) in ether (15 mL) at -78°C. The reduction was complete in 30min and sodium fluoride (72 mmol, 3.02 gr) was added at -78°C followed by water (3eq, 0.97ml). The reaction was stirred at r.t. for 30 min. A white precipitate occurred. The mixture was filtered and the residue washed with ether. The solvent was removed by bubbling argon-stream through the solution. The residue was used as such for the preparation of the corresponding phosphonate.

IR (Film) 1730 cm<sup>-1</sup>; <sup>1</sup>H NMR 9.65 (d, 1H, J=1.7); 3.87 (m, 1H); 3.45 (s, 3H); 1.29 (d, 3H, J=6.6). 2-(Triisopropylsilyloxy)-2-(p-methoxyphenyl)-ethanal 2i. IR (CHCl<sub>3</sub>) 1730, 1511, 1172, 1034 cm<sup>-1</sup>; <sup>1</sup>H NMR 9.47 (d, 1H, J=2.66), 7.33 (d, 2H, J=8.30), 6.90 (d, 2H, J=8.65), 5.01 (d, 1H, J=2.66), 3.80 (s, 3H), 1.03 (m, 21H). <sup>13</sup>C NMR 199.37, 159.82, 128.99, 127.74, 114.23, 79.70, 55.23, 17.80, 12.10. MS m/z 293 (M<sup>+</sup>-29), 279 (M<sup>+</sup>-43). Anal Calcd for C18H<sub>30</sub>O<sub>3</sub>Si: C, 67.03; H, 9.38. Found: C, 66,70; H, 9.36.

## (-)-(S)-2-(Triisopropylsilyloxy)-3-methyl-butanal 2j.

 $[\alpha]_D^{20}$  =-22.63 (c 1.01, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 1730, 1464, 1107, 1065 cm<sup>-1</sup>; <sup>1</sup>H NMR 9.62 (d, 1H, J=2.70), 3.85 (dd, 1H, J=2.70, 4.74), 2.00 (m, 1H, J=4.74, 6.96), 1.04 (m, 21H), 0.96 (t, 6H, J=6.96). <sup>13</sup>C NMR 205.34, 82.07, 32.87, 17.94, 17.14, 12.39. MS m/z 215 (M<sup>+</sup>-43), 172. Anal Calcd for C<sub>14</sub>H<sub>30</sub>O<sub>2</sub>Si: C, 65.05; H, 11.69. Found: C, 65.31; H, 11.74.

## 2-Triisopropylsilyloxy heptanal 2k.

To a solution of 3-hydroxy-1-octene (30 mmol) and imidazole (60 mmol) in anhydrous DMF (30 mL) cooled with ice-water TIPSCI (30 mmol) was added. After ten minutes the bath was removed and the reaction was left at room temperature for three hours. The mixture was poured into ice-water and extracted with hexane (3x50 mL). The organic layers were washed with brine (2x50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in vacuo to give the 3-(triisopropylsilyloxy)-1-octene in almost quantitative yields. Spectral data as follow.

IR (CHCl<sub>3</sub>) 2958, 1464, 1265, 1091, 1065, 995 cm<sup>-1</sup>; <sup>1</sup>H NMR 6.68 (m, 1H), 5.04 (m, 2H), 4.18 (m, 1H), 1.50 (m, 2H), 1.25 (m, 6H), 1.03 (s, 21H), 0.85 (m, 3J). <sup>13</sup>C NMR 142.04, 113.57, 74.24, 38.38, 32.01, 24.33, 22.67, 18.13, 14.02, 12.49. MS m/z 284 (M<sup>+</sup>), 245 (M<sup>+</sup>- 43), 216. Anal Calcd for C<sub>17</sub>H<sub>36</sub>OSi: C, 71.75; H, 12.75. Found: C, 71.40; H, 12.70.

A solution of 3-triisopropylsilyloxy-1-octene (10 mmol) in methylene chloride was ozonized at -78°C. When the solution became deep-blue, after removing the excess of ozone by flushing with nitrogen, the mixture was treated with DMS (3 mL) and left overnight. The solvent was removed in vacuo and the resulting 2triisopropylsilyloxy aldehyde purified by flash chromatography. (Y%=60)

IR (CHCl<sub>3</sub>) 1730, 1465, 1424, 1047, cm<sup>-1</sup>; <sup>1</sup>H NMR 9.62 (d, 1H, J=2.20), 4.05 (dt, 1H, J=2.20, 5.90), 1.65 (m, 2H), 1.30 (m, 6H), 1.05 (s, 21H), 0.88 (m, 3H). <sup>13</sup>C NMR 204.94, 77.66, 33.49, 31.87, 23.61, 22.44, 17.83, 13.92, 12.23. MS m/z 257 (M<sup>+</sup>-29), 243 (M<sup>+</sup>- 43), 213. Anal Calcd for C<sub>16</sub>H<sub>34</sub>O<sub>2</sub>Si: C, 67.01; H, 11.96. Found: C, 66.89; H, 11.92.

# General procedure for the synthesis of $\alpha$ -tert -butyldimethylsilyloxy aldehydes from the corresponding cyanhydrins<sup>27</sup>.

To a solution of 10 mmol (10 equiv) of aldehyde and 12 mmol (1.2 equiv) of TBDMSCN in anhydrous methylene chloride under argon were added 0.3 mmol of anhydrous ZnI<sub>2</sub>. The mixture was stirred at 25°C overnight. The protected cyanohydrins were purified by bubble to bubble distillation (Yields are reported in brackets for each example).

## 2-tert-Butyldimethylsilyloxy-2-cyclohexyl-acetonitrile 21'.

(Y=86%). <sup>1</sup>H NMR 4.19 (d, 1H, J=6.6); 1.85-1.60 (m, 6H); 1.25-1.03 (m, 5H); 0.92 (s, 9H); 0.19 (s, 3H0; 0.13 (s, 3H). <sup>13</sup>C NMR 119.4, 66.93, 49.18, 27.96, 26.05, 25.52, 18.05, -5.35, -5.56. MS m/z 253 (M<sup>+</sup>), 211, 196; 169, 114, 75.

### 2-tert-Butyldimethylsilyloxy-3,3-dimethyl butyrronitrile 2m'.

(Y=90%). IR (Film) 2959, 2933, 2886, 2861, 1473, 1466 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.01 (s, 1H), 1.03 (s, 9H); 0.93 (s, 9H); 0.21 (s, 3H). <sup>13</sup>C NMR 119.2, 71.1, 36.0, 25.45, 24.90, 18.00, -5.30, -6.60. MS m/z 227 (1) (M<sup>+</sup>), 212 (1), 171 918), 143 (100), 115 (6), 99 (4), 75 (65).

General Procedure for the reduction of  $\alpha$ -silyloxycynhydrins.

To a solution of 6 mmol (6 equiv) of cyanhydrine in anhydrous *tert*-butylmethyl ether under argon at -78°C was added DIBAH (7.2 mL of a 1 M solution in hexane). The mixture was stirred at the same temperature for 1 h. The reaction mixture is poured into 50 mL of water containing 20 g of sodium potassium tartrate. After stirring for 25 min, the mixture is extracted with ether, the organic layer dried (Na<sub>2</sub>SO<sub>4</sub>) and chromatographed (Cyclohexane/ether 96/4). (Yields are reported in brackets for each example).

2-tert-Butyldimethylsilyloxy-2-cyclohexyl-acetaldehyde 21.

(Y=70%). IR (Film) 1736 cm<sup>-1</sup>; <sup>1</sup>H NMR 9.59 (d, 1H, J=2.2); 3,71 (dd, 1H, J=2.2; J=5.0) 1.73-1.60 (m, 6H); 1.25-1.10 (m, 5H); 0.91 (s, 9H); 0.06 (s, 6H). <sup>13</sup>C NMR 204.9, 81.7, 41.1, 29.0, 27.2, 26.2, 26.1, 25.9, 25.7, 18.2, -4.6, -5.1. MS m/z 227 (M<sup>+</sup>-29), 199, 169, 155, 117, 75. Anal Calcd for C<sub>14</sub>H<sub>28</sub>O<sub>2</sub>Si: C, 65.57; H, 11.00. Found: C, 65.62; H, 11.03.

#### 2-tert-Butyldimethylsilyloxy-3,3-dimethyl butyrraldehyde 2m.

(Y=73%). IR (Film) 1734 cm<sup>-1</sup>; <sup>1</sup>H NMR 9.61 (d, 1H, J=3.3); 3.48 (d, 1H, J=3.3); 0.97 (s, 9H); 0.94 (s, 9H); 0.06 (s, 3H); 0.02 (s, 3H). <sup>13</sup>C NMR 204.7, 84.2, 35.8, 25.7, 25.7, 18.2, -4.5, -5.1. MS m/z 215 (M<sup>+</sup>-15) (1), 201 (32), 173 (100); 159 (2), 129 (6), 115 (75). 73 (100). Anal Calcd for C<sub>12</sub>H<sub>26</sub>O<sub>2</sub>Si: C, 62.54; H, 11.37. Found: C, 62.79; H, 11.41.

## General Procedure for the synthesis of phosphonates

Method A: To a solution of commercially available diethyl- or dimethyl-trimethylsilylphosphite (10 mmol) in methylene chloride (130 mL) was added the aldehyde. The reaction mixture was stirred for 3 hrs at -78°C, and then the reaction was allowed to reach r.t. (1 h). A saturated solution of NH4Cl in water was added and the mixture and extracted with methylene chloride. The organic extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to give the crude adducts constituted by a mixture of 1-TMS-protected and 1-hydroxy phosphonates. This mixture was dissolved in methanol (50 mL), citric acid was added (1.92g, 10 mmol) and the reaction was stirred overnight. Methanol was removed under vacuum, hexane (10 ml) was added and the mixture stirred for 30 min. After removal of the precipitate, the solvent was removed in vacuum. The residue was purified by flash chromatography (Ethyl acetate/Cyclohexane) to give the diastereomeric mixture of 1-hydroxy-2-silyloxy phosphonates in diastereomeric ratios and yields reported in the tables reported in the text.

Method B: To a stirred and cooled (0°C) solution of diethyl, dimethyl, dibenzylphosphite or diisopropylphosphite (10 mmol) in anhydrous methylene chloride (130 mL), under argon atmosphere, were added TEA (1.6 mL, 12 mmol) and TMSCl (1.68 mL, 12 mmol). After 45 min the solution was cooled at -78°C and the aldehyde (10 mmol) in methylene chloride (5 mL) was added. From this point the reaction mixture was processed as described in Method A.

Method C: To a solution of LiHMDSA at 0°C (50 mL, 1M sol in THF) was added dropwise the diethyl phosphite (50 mmol) dissolved in THF (30 mL). The reaction mixture was left, under stirring at r.t., for 45 min, then cooled to 0°C and the corresponding trialkylsilylchloride (60 mmol) in THF (20 mL) was added. The resulting mixture was stirred overnight at r.t., THF was removed under vacuo and the residue was distilled in vacuo to give the trialkylsilyl-diethylphosphite in almost quantitative yield. This phosphite was used for the preparation of phosphonates as described in method A.

The yields and the diastereomeric ratios of phosphonates are reported in the respective tables where the interested reader is directed.

#### Triethylsilyloxydiethyl phosphonic ester 1e.

Kp4.1mmHg= 82-84\*C IR (Film) 2974, 2940, 2878, 1459, 1443, 1386, 1241, 1097, 1061, 1032. cm<sup>-1</sup>; <sup>1</sup>H NMR 3.86 (m, 4H); 1.23 (t, 3H, J=7.10); 0.98 (t, 9H, J=8.0), 0.66 (q, 6H, J=7.7). <sup>13</sup>C NMR 56.47 (d, J=9.2), 16.86, 16.86 (d, J=4.4), 6.47, 5.72. <sup>31</sup>P -4.63. MS m/z (M<sup>+</sup>), 252, 224, 196, 169, 149, 109, 103. *tert*- Butyldimethylsilyloxydiethyl phosphonic ester 1f.

Kp4.1mmHg=70-71<sup>°</sup>C. IR (Film) 2972, 2950, 2930, 2864, 2868, 1465, 1386, 1031, 978 cm<sup>-1</sup>; <sup>1</sup>H NMR 3.85 (m, 4H); 1.24 (t, 3H, J=7.05); 1.08 (m, 21H). <sup>13</sup>C NMR 56.33 (d, J=9.2), 17.61, 16.86 (d, J=4.7), 12.57. <sup>31</sup>P -6.12. MS m/z 398 (M<sup>+</sup>), 294, 252, 223, 210, 195, 177, 159, 123, 103, 89, 75.

#### Triisopropylsilyloxydiethyl phosphonic ester 1g.

 $\begin{array}{l} Kp_{0.56mmHg} = 71^{\circ}C. \ IR \ (Film) \ 2972, \ 2950, \ 2930, \ 2864, \ 2868, \ 1465, \ 1386, \ 1031, \ 978, \ 926, \ 882 \ cm^{-1}; \ ^{1}H \\ NMR \ 3.85 \ (m, \ 4H); \ 1.24 \ (t, \ 3H, \ J=7.05); \ 1.08 \ (m, \ 21H). \ ^{13}C \ NMR \ 56.33 \ (d, \ J=9.2), \ 17.61, \ 16.86 \ (d, \ J=4.7), \ 12.57. \ ^{31}P \ -6.12. \ MS \ m/z \ 398 \ (M^+), \ 294, \ 252, \ 223, \ 210, \ 195, \ 177, \ 159, \ 123, \ 103, \ 89, \ 75. \end{array}$ 

(+)-(15, 25)1-Trimethylsilyloxy-2-triethylsilyloxy-propyl-phosphonic acid diethyl ester 3a.  $[\alpha]_D^{20} = +2.78$  (c 1.80, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 1252, 1095, 1052, 1030 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.12 (m, 4H), 4.00 (ddq, 1H, J=5.84, 6.24, 14.92), 3.76 (dd, 1H, J=5.84, 8.20), 1.30 (t, 6H, J=7.08), 1.26 (d, 3H, J=6.24), 0.95 (t, 9H, J=7.50), 0.60 (q, 6H, J=7.50), 0.13 (s, 9H). <sup>13</sup>C NMR 74.30 (d, J=165.25), 69.32 (d, J=6.64), 62.29 (d, J=7.12), 61.82 (d, J=6.78), 20.10 (d, J=4.68), 16.48 (d, J=5.97), 16.45 (d, J=5.90), 6.81, 4.97, 0.19.  $^{31}P$  20.62. MS m/z 398 (M<sup>+</sup>), 383, 369, 240, 157, 129.

(-)-(1*R*, 2*S*) 1-Trimethylsilyloxy-2-triethylsilyloxy-propyl-phosphonic acid diethyl ester 4a.  $[\alpha]_D^{20} = -2.25 \ (c \ 0.89, CHCl_3)$ . IR (CHCl\_3) 1250, 1093, 1054, 1034 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.13 (m, 5H), 4.00 (dd, 1H, J=1.92, 12.02), 0.94 (t, 6H, J=7.08), 1.22 (d, 3H, J=6.20), 0.94 (t, 9H, J=7.90), 0.58 (q, 6H, J=7.90), 0.13 (s, 9H). <sup>13</sup>C NMR 75.42 (d, J=165.19), 68.44 (d, J=14.17), 62.76 (d, J=7.32), 61.87 (d, J=6.91),18.03, 16.49 (d, J=5.63), 16.37 (d, J=6.11), 6.75, 4.77, 0.12. <sup>31</sup>P 19.31. MS m/z 398 (M<sup>+</sup>), 383, 369, 240, 157, 129.

(+)-(15,25)2-tert-Butyldimethylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3b.  $[\alpha]_D^{20} = +9.01 (c \ 0.91, CHCl_3);$  IR (CHCl\_3) 3460, 1230, 1049, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.07 (m, 5h), 3.52 (ddd, 1H, J=4.80, 6.70, 7.40), 2.95 (dd, 1H, J=6.70, 11.60), 1.31 (m, 9H), 0.78 (s, 9H), 0.02(s, 3H), 0.01 (s, 3H). <sup>13</sup>C NMR 72.46 (d, J=162.02), 67.74 (d, J=4.37), 62.37 (d, J=7.22), 61.93 (d, J=6.93), 25.60, 20.96 (d J=7.69), 17.81, 16.26 (d, J=5.70), -4.46, -4.99. <sup>31</sup>P 20.28. MS m/z 311 (M<sup>+</sup>-15), 269. Anal Calcd for C<sub>13</sub>H<sub>31</sub>O<sub>5</sub>PSi: C, 47.83; H, 9.57. Found: C, 47.95; H, 9.59.

(+)-(1*R*,2*S*)2-*tert*-Butyldimethylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 4b  $[\alpha]_D^{20} = +5.56 \ (c \ 3.85, CHCl_3);$  IR (CHCl\_3) 3460, 1253, 1052, 1028 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.17 (m, 5H); 3.88 (dd, 1H, J=3.85, 9.05); 2.78 (bs, 1H); 1.33 (dt, 6H, J=7.04); 0.29 (d, 3H, J=6.30); 0.88 (s, 9H); 0.07 (s, 6H). <sup>13</sup>C NMR 72.74 (d, J=159.08), 68.83 (d, J=6.36), 62.54 (d, J=7.03), 62.32 (d, J=6.93), 25.75, 18.64 (d, J=2.47), 18.00, 16.42 (d, J=5.51), -4.56, -4.90. <sup>31</sup>P 19.96. MS m/z 311 (M<sup>+</sup>-15), 269. Anal Calcd for C<sub>13</sub>H<sub>31</sub>O<sub>5</sub>PSi: C, 47.83; H, 9.57. Found: C, 48.02; H, 9.60.

(+)-(1S, 2S) 2-Triisopropylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3c.  $[\alpha]_D^{20} = +6.25 \ (c \ 1.38, CHCl_3); IR \ (CHCl_3) \ 3580, 1244, 1050, 1028, 955 \ cm^{-1}; \ ^1H \ NMR \ 4.31 \ (ddq, 1H, J=6.44, 6.70, 6.70); 4.15 \ (m, 4H); 3.61 \ (dt, 1H, J=4.90, 6.44); 3.00 \ (dd, 1H, J=4.90, 16.10); 1.30 \ (m, 9H), 1.05 \ (m, 21H). \ ^{13}C \ NMR \ 72.69 \ (d, J=162.31), \ 68.32 \ (d, J=5.32), 62.73 \ (d, J=7.19), 62.42 \ (d, J=6.84), 21.23 \ (d, J=5.70), 18.10, 18.00, 16.35 \ (d, J=5.79), 12.74. \ ^{31}P \ 20.40. \ MS \ m/z \ 325 \ (M^+-43), 186. \ Anal Calcd for C_{16}H_{37}O_5PSi: C, 52.15; \ H, 10.12. \ Found: C, 51.90; \ H, 10.16.$ 

(+)-(1*R*, 2*S*) 2-Triisopropylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 4c.  $[\alpha]_D^{20} = +1.75$  (c 0.80, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 3580, 1244, 1050, 1028, 955 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.33 (m, 1H); 4.20 (m, 4H); 4.05 (dt, 1H, J=4.20, 11.18); 2.60 (dd, 1H, J=4.20, 22.30); 1.33 (m, 9H); 1.05 (m, 21H). <sup>13</sup>C NMR 72.78 (d, J=162.46), 68.38 (d, J=5.43), 62.54 (d, J=7.19), 62.18 (d, J=6.78), 21.32 (d, J=5.83), 18.01, 17.93, 16.34 (d, J=5.70), 12.60. <sup>31</sup>P 19.22. MS m/z 325 (M<sup>+</sup>-43), 186. Anal Calcd for C<sub>16</sub>H<sub>37</sub>O<sub>5</sub>PSi: C, 52.15; H, 10.12. Found: C, 51.99; H, 10.14.

(+)-(15,25)2-tert-Butyldiphenylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3d. m.p.= 120-2 °C.  $[\alpha]_D^{20}$  = +2.47 (c 0.81, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 3612, 3440, 1240, 1112, 1047, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.75 (m, 4H); 7.40 (m, 6H); 4.25 (ddq, 1H, J=5.50, 7.00, 7.00); 4.15 (m, 4H); 3.72 (ddd, 1H, J=5.50, 6.20, 7.90); 2.95 (dd, 1H, J=6.20, 13.80); 1.30 (dt, 3H); 1.12 (d, 3H, J=7.00); 1.10 (s, 9H). <sup>13</sup>C NMR 135.84, 133.98, 132.96, 129.83, 129.67, 127.68, 127.48, 72.90 (d, J=161.18), 69.59 (d, J=5.49), 62.55 (d, J=7.25), 62.20 (d, J=6.92), 26.88, 20.71 (d, J=6.46), 19.30, 16.35 (d, J=5.43). <sup>31</sup>P 20.22. MS m/z 393 (M<sup>+</sup>-57), 315. Anal Calcd for C<sub>23</sub>H<sub>35</sub>O<sub>5</sub>PSi: C, 61.31; H, 7.83. Found: C, 61.50; H, 7.85.

(+)-(1*R*, 2*S*)2-*tert*-Butyldiphenylsilyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 4d m.p.= 78-80 °C.  $[\alpha]_D^{20} = +2.12$  (*c* 0.81, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3612, 3440, 1240, 1112, 1047, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.70 (m, 4H); 7.40 (m, 6H); 4.20 (ddq, 1H, J= 2.90, 6.40, 7.30); 4.10 (m, 4H); 3.93 (ddd, 1H, J=2.90, 5.10, 11.00); 2.55 (dd, 1H, J=5.10, 19.00); 1.25 (m, 9H, J=6.40); 1.10 (s, 9H). <sup>13</sup>C NMR 135.86, 135.77, 133.70, 133.48, 129.93, 129.84, 127.82, 127.68, 72.61 (d, J=158.98), 69.88 (d, J=8.17), 62.60 (d, J=6.83), 62.38 (d, J=6.84), 26.99, 19.25, 18.05, 16.43 (d, J=5.60), 16.39 (d, J=5.79). <sup>31</sup>P 19.35. MS m/z 393 (M<sup>+</sup>-57), 315, 223. Anal Calcd for C<sub>23H35</sub>O<sub>5</sub>PSi: C, 61.31; H, 7.82. Found: C, 61.13; H, 7.80. (syn) 2-*tert*-Butoxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3e

IR (Film) 3350, 2980, 2935, 1392, 1358, 1232, 1196, 1053, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.14 (m, 4H); 3.97 (m, 1H); 3.58 (t, 1H, J=6.6); 1.35 (m, 6H); 1.31 (d, 3H; J=6.1); 1.26 (s, 9H). <sup>13</sup>C NMR 74.99, 71.70 (d, J=162.2). 66.70 (d, J=4.9); 62.72 (d, J=6.9); 62.15 (d; J=6.5), 28.65, 20.93, 20.87, 16.36. <sup>31</sup>P 23.41.

(anti) 2-tert-Butoxy-1-hydroxy-propyl-phosphonic acid diethyl ester 4e.

IR (Film) 3350, 2980, 2935, 1392, 1358, 1232, 1196, 1053, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.14 (m, 4H); 3.93 (m, 2H); 1.35 (m, 6H); 1.31 (d, 3H; J=6.1); 1.26 (s, 9H). <sup>13</sup>C NMR 74.45; 72.70 (d, J=157.6), 67.35 (d, J=8.0), 62.20 (d, J=7.0), 61.87 (d, J=7.5), 28.22, 20.93, 20.87, 17.58. <sup>31</sup>P 22.69.

(syn) 2-Benzyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3f.<sup>29</sup>

<sup>1</sup>H NMR 7.35 (m, 5H, Ar); 4.68 (d, 1H, J=11.2); 4.53 (d, 1H, J=11.2); 4.15 (m, 4H); 4.00 (m, 1H); 3.76 (dd, 1H, J=4.6, 9.2); 1.34 (d, 3H, J=6.3); 1.27 (t, 6H, J=7.4). <sup>31</sup>P 23.16.

(anti) 2-Benzyloxy-1-hydroxy-propyl-phosphonic acid diethyl ester 4f.29

<sup>1</sup>H NMR 7.35 (m, 5H, Ar); 4.62 (d, 1H, J=11.5); 4.52 (d, 1H, J=11.5); 4.15 (m, 4H); 4.05 (dd, 1H4.3, 9.5); 3.90 (m, 1H); 1.37 (d, 3H, J=6.4); 1.30 (t, 6H, J=7.1). <sup>31</sup>P 23.36.

(syn) 2-Methoxy-1-hydroxy-propyl-phosphonic acid diethyl ester 3g.

IR (CDCl<sub>3</sub>) 3320, 2985, 2965, 2930, 2910, 2830, 1445, 1390, 1260, 1090 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.19 (4H, m), 3.67 (m, 2H); 3.40 (s, 3H); 1.33 (m, 9H). <sup>13</sup>C NMR 75.58 (d, J=3.2), 71.78 (d, J=164.4), 62.54 (m), 56.57, 16.48, 16.37, 15.35 (d, J=8.5) <sup>31</sup>P 23.68. MS m/z 226 (M<sup>+</sup>), 139, 89. Anal Calcd for C<sub>8</sub>H<sub>19</sub>O<sub>5</sub>P: C,42.48; H,8.47. Found: C, 42.54; H, 8.49.

(anti) 2-Methoxy-1-hydroxy-propyl-phosphonic acid diethyl ester. 4g

IR (CDCl<sub>3</sub>) 3320, 2985, 2980, 2930, 2910, 2830, 1445, 1390, 1260, 1090 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.20 (m, 4H); 4.02 (dd, 1H, J=4.2, J=9.6); 3.69 (m, 1H); 3.36 (s, 3H); 1.34 (m, 9H). <sup>13</sup>C NMR 76.85, (d, J=6), 70.08 (d, J=157.8), 62.54 (m), 56.44, 16.48, 16.37, 14.64 (d, J=3.7). <sup>31</sup>P 24.30. MS m/z 226 (M<sup>+</sup>), 139, 89.

(+)-(1S, 2S) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid dimethyl ester 3h.  $[\alpha]_{365}^{20}$  =+19.0 (c, 1.92 CHCl<sub>3</sub>),  $[\alpha]_D^{20}$  = +6.00 (c, 1.92 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3400, 1728, 1616, 1461, 1243, 1058, 1034. cm<sup>-1</sup>; <sup>1</sup>H NMR 4.33 (m, 1H); 3.80 (d, 1H, J=1.7); 3.75 (d, 3H, J=1.7); 3.65 (dd, 1H, J=5.6, 6.72); 2.86 (bs, 1H, OH); 1.33 (d, 3H, J=6.14); 1.06 (m, 21H). <sup>13</sup>C NMR 72.62 (d, J=161.08), 68.22 (d, J=5.1), 53.11 (d, J=7.11), 52.78 (d, J=6.7), 21.28 (d, J=6.63), 18.01, 17.94, 12.68. <sup>31</sup>P 22.64. (+)-(1R, 2S) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid dimethyl ester 4h.  $[\alpha]_{365}^{20}$  =+17.1 (c, 1.46 CHCl<sub>3</sub>),  $[\alpha]_D^{20}$  = +5.0 (c, 1.46 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3400, 1728, 1616, 1461, 1243, 1058, 1034 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.30 (m, 1H); 4.05 (dd, 1H, J=3.0, 10.5); 3.83 (d, 3H, J=4.1); 3.78 (d, 3H, J=4.1); 2.45 (bs, 1H, OH); 1.34 (d, 3H, J=6.26); 1.05 (m, 21H). <sup>13</sup>C NMR 72.80 (d, J=159.3), 68.78 (d, J=7.84), 53.24 (d, J=7.03), 52.82 (d, J=6.7), 18.15, 18.02, 12.42. <sup>31</sup>P 21.82.

(+)-(1*S*, 2*S*) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid dibenzyl ester 3i.  $[\alpha]_D^{20} = +4.06 \ (c, 1.62 \ \text{CDCl}_3). \ [\alpha]_{355}^{20} = +11.4 \ (c, 1.62 \ \text{CDCl}_3) \ \text{IR} \ (\text{CHCl}_3) \ 3450, 1241, 1050, 1028 \ \text{cm}^{-1}; \ ^{1}\text{H}$ NMR 7.33 (s, 10H); 5.06 (m, 4H); 4.32 (ddq, 1H, J=5.84. 7.84, 6.16); 3.69 (ddd, 1H, J=5.84. 5.84, 3.7); 3.07 (dd, 1H, J=3.7, 14.4); 1.33 (d, 3H, J=6.16); 1.04 (bs, 21H) . \ ^{13}\text{C} \ \text{NMR} \ 136.42 \ (d, J=6.5), \ 136.30 \ (d, J=5.85); 128.52, 128.49, 128.36, 128.31, 128.03, 73.33 \ (J=160.8), \ 68.35 \ (d, J=5.3), \ 68.13 \ (d, J=7.0), \ 67.75 \ (J=6.74), \ 21.41 \ (d, J=6.2), \ 18.0, \ 17.9, \ 12.7. \ \ ^{31}\text{P} \ 21.09 \ \text{MS} \ \text{m/z} \ 492 \ (\text{M}^+). \ \text{Anal Calcd for} \ C\_{26}H\_{41}O\_5\text{PSi:} \ C, \ 63.38; \ H, \ 8.38. \ \text{Found: C, } 63.18; \ H, \ 8.42.

(+)-(1*R*, 2*S*) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid dibenzyl ester 4i.  $[\alpha]_{365}^{20}$  = +5.05 (*c*, 0.93 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3450, 1241, 1050, 1028 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.34 (m, 10H); 5.07 (m, 4H); 4.31 (ddq, 1H, J=2.82, 5.8, 6.34); 4.08 (dd, 1H, J=2.82, 10.74); 2.35 (bs, 1H, OH); 1.35 (d, 3H, J=6.34); 1.03 (m, 21H). <sup>13</sup>C NMR 136.30 (d, J=5.4), 135.61 (d, J=6.0), 128.60, 128.49, 128.34, 128.31, 127.95, 73.36 (d, J=159.0), 68.10 (d, J=6.9), 67.79 (d, J=6.71), 67.25 (d, J=5.7), 18.12, 17.98, 12.35. <sup>31</sup>P 20.12 . MS m/z 492 (M<sup>+</sup>).

(syn) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid diisopropyl ester 3j. IR (Film) 3300, 2978, 2942, 2867, 1466,1386, 1376, 1240, 1206, 1178, 1133, 1106, 1062 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.75 (m, 2H); 4.27 (m, 1H); 3.53 (t, 1H. J=6.6); 1.34 (m, 15H); 1.08 (m, 21H). <sup>13</sup>C NMR 73.04 (d, J=163.8), 71.25 (d, J=7.3); 70.88 (d, J=7.0), 68.52 (d, J=5.7), 24.02, 23.90, 21.49 (d, J=5.3), 18.02, 12.65.  $^{31}P$  21.23 .

(anti) 1-Hydroxy-2-triisopropylsilyloxy-propyl-phosphonic acid diisopropyl ester 4j.

IR (Film) 3300, 2978, 2942, 2867, 1466,1386, 1376, 1240, 1206, 1178, 1133, 1106, 1062, 1008, 988 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.75 (m, 2H); 4.27 (m, 1H); 3.93 (dd, 1H. J=11.3, 2.6), 1.35 (m, 15H); 1.08 (m, 21H). <sup>31</sup>P 20.32 (syn) 1-Triethylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester. 3k

IR (Film) 2950, 2850, 1465, 1262, 1240, 1120, 1099, 1054, 1080, 963 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.34-3.95 (m, 6H); 1.38 (d, 3H, J=6.3); 1.29 (m, 6H); 1.06 (s, 21H); 0.96 (m, 9H0; 0.65 (m, 6H). <sup>13</sup>C NMR 73.45 (d, J=166.4), 70.51, 61.90 (d, J=67), 61.65 (d, J=67), 19.12 (d, J=4.8), 18.06, 16.52, 16.45, 12.49, 6.69, 4.75. <sup>31</sup>P 23.59 . MS m/z 482 (M<sup>+</sup>), 467, 439, 411, 381, 353, 295, 282, 187, 159, 115.

(anti) 1-Triethylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester 4k. IR (Film) 2950, 2850, 1465, 1262, 1240, 1120, 1099, 1054, 1080, 963 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.20 (m, 6H); 1.29 (m, 9H); 1.06 (s, 21H); 0.96 (m, 9H); 0.65 (m, 6H). <sup>13</sup>C NMR 75.80 (d, J=163.2), 68.97 (d, J=15.5), 62.08-61.90 (m), 18.02, 17.84, 16.37, 12.34, 6.69, 4.75. <sup>31</sup>P 21.94. MS m/z 482 (M<sup>+</sup>), 467, 439, 411, 381, 353, 295, 282, 187, 159, 115.

(syn) 1-*tert*-Butyldimethylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester. 31

IR (Film) 2956, 2867, 1473, 1464, 1252, 1119, 1099, 1031, 962 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.11 (m, 6H); 1.28 (m, 6H); 1.06 (s, 21H); 0.89 (s, 9H); 0.13 (s, 6H). <sup>13</sup>C NMR 73.33 (d, J=166.0), 70.48, 61.97 (d, J=6.6); 61.43 (d, J=7.1), 25.68, 19.07 (d, J=5.3), 18.07, 17.87, 16.48, 16.34, 12.46, -4.73, -5.22. <sup>31</sup>P 23.62. MS m/z (467, M<sup>+</sup>-15), 439, 425, 353, 282, 251, 195.

(anti) 1-*tert*-Butyldimethylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester 41.

IR (Film) 2956, 2867, 1473, 1464, 1252, 1119, 1099, 1031, 962 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.20 (m, 5H); 3.96 (dd, 1H, J=4.4, 7.1); 1.37 (d, 3H, J=6.3) 1.28 (m, 6H); 1.06 (s, 21H); 0.92 (s, 9H); 0.08 (s, 6H). <sup>13</sup>C NMR 75.80 (d, J=162.5), 68.96 (d, J=16.3), 61.84 (m), 25.75, 19.07, 17.98, 17.87, 16.48, 16.36, 12.29, -4.73, -5.22. <sup>31</sup>P 21.96. MS m/z (467, M<sup>+</sup>-15), 439, 425, 353, 282, 251, 195.

(syn) 1-Triisopropylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester 3m IR (Film) 2945, 2868, 1445, 1262, 1122, 1099, 1064, 1031, 962, 883 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.18 (m, 6H); 1.41 (d, 3H, J=6.2); 1.29 (m, 9H); 1.06 (m, 39H) . <sup>13</sup>C NMR 73.69 (d, J=166.4), 70.78, 61.76 (d, J=6.5), 61.06 (d, J=7.0), 18.78 (d, J=4.4), 18.04, 17.97, 16.48, 16.41, 12.57, 12.42. <sup>31</sup>P 23.84. MS m/z 524 (M<sup>+</sup>), 481, 437, 409, 381, 363, 324, 281, 251, 195, 181, 157, 117.

(anti)-1-Triisopropylsilyloxy-2-triisopropylsilyloxy-propyl-phosphonic acid diethyl ester 4m IR (Film) 2945, 2868, 1445, 1262, 1122, 1099, 1064, 1031, 962, 883 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.18 (m, 6H); 1.29 (m, 12H); 1.06 (m, 39H) . <sup>13</sup>C NMR 76.16 (d, J=156), 69.4 (d, J=15.6), 62.03 (d, J=7.0), 61.59 (d, J=7.5), 18.05, 17.97, 17.85, 16.54, 16.33, 12.66, 12.35. <sup>31</sup>P 22.45 . MS m/z 524 (M<sup>+</sup>), 481, 437, 409, 381, 363 , 324 , 281 , 251, 195 , 181, 157, 117 .

(+)-(15,25)1-Hydroxy-2-triisopropylsilyloxy-2-phenylethyl-phosphonic acid diethyl ester 3n m.p. 106-8 °C.  $[\alpha]_D^{20}$  = +37.36 (c 0.53, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3450, 1241, 1050, 1028 cm<sup>-1</sup>; <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) 7.50 (m, 2H); 7.12 (m, 3H); 5.34 (dd, 1H, J=7.00, 7.00); 4.66 (dd, 1H, J=3.50, 11.60); 4.19 (ddd, 1H, J=5.50, 7.00, 7.00); 3.97 (m, 2H); 3.73 (m, 2H); 1.10 (m, 21H); 1.00 (t, 3H, J=7.08); 0.89 (t, 3H, J=7.08). <sup>13</sup>C NMR 141.04 (d, J=2.16), 128.25, 128.00, 127.70, 75.02, 73.32 (d, J=157.45), 62.59 (d, J=6.78), 61.84 (d, J=6.92), 17.89, 17.74, 16.26 (d, J=5.90), 16.11 (d, J=6.15), 12.40. <sup>31</sup>P 19.22. MS m/z 388 (M+-43), 263, 249. Anal Calcd for C<sub>21</sub>H<sub>39</sub>O<sub>5</sub>PSi: C, 58.57; H, 9.12. Found: C, 58.81; H, 9.15.

(+)-(1*R*,2*S*)1-Hydroxy-2-triisopropylsilyloxy-2-phenylethyl-phosphonic acid diethylester 4n m.p.= 98-100 °C.  $[\alpha]_D^{20}$  = +32.64 (*c* 1.25, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3460, 1228, 1047, 1030 cm<sup>-1</sup>; <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) 7.68 (m, 2H); 7.15 (m, 3H); 5.47 (dd, 1H, J=3.80, 5.75); 4.52 (dd, 1H, J=3.80, 9.45); 3.85 (m, 4H); 3.57 (m, 1H); 1.05 (m, 21H); 1.00 (t, 3H, J=7.08); 0.92 (t, 3H, J=7.08). <sup>13</sup>C NMR 139.37, 128.21, 128.03, 127.72, 74.31 (d, J=9.55), 73.72 (d, J=161.12), 62.45 (d, J=7.05), 62.26 (d, J=6.92), 17.94, 17.83, 16.28

(d, J=7.46), 16.15 (d, J=5.96), 12.22. <sup>31</sup>P 18.00. MS m/z 388 (M<sup>+</sup>-43), 263, 249. Anal Calcd for  $C_{21}H_{39}O_5PSi: C, 58.58; H, 9.13.$  Found: C, 58.38; H, 9.16.

## (syn) 1-Hydroxy-2-triisopropylsilyloxy-2-(p-methoxy)phenylethyl-phosphonic acid diethyl ester 30.

m.p.=60-2°C. IR (CHCl<sub>3</sub>) 1513, 1245, 1048, 1031 cm<sup>-1</sup>; <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) 7.47 (d, 2H); 6.79 (d, 2H); 5.32 (dd, 1H, J=7.20, 7.20); 4.62 (dd, 1H, J=5.20, 12.50); 4.20 (ddd, 1H, J=5.20, 7.20, 7.60); 4.05 (m, 2H); 3.80 (m, 2H); 3.30 (s, 3H); 1.10 (m, 24H); 0.92 (t, 3H). <sup>13</sup>C NMR 159.61, 133.21 (d, J=4.22), 128.88, 113.37, 74.49 (d, J=7.39), 73.46 (d, J=164.51), 62.57 (d, J=6.71), 61.84 (d, J=6.85), 55.20, 17.92, 17.77, 16.27 (d, J=7.32), 16.14 (d, J=6.17), 12.39. <sup>31</sup>P 20.23. MS m/z 417 (M<sup>+</sup>-43), 294. Anal Calcd for C<sub>22</sub>H<sub>41</sub>O<sub>6</sub>PSi: C, 57.36; H, 8.97. Found: C, 57.20; H, 9.00.

(anti) 1-Hydroxy-2-triisopropylsilyloxy-2-(p-methoxy)phenylethyl-phosphonic acid diethyl ester 40.

m.p. 52-4°C. IR (CHCl<sub>3</sub>) 1513, 1248, 1047, 1033 cm<sup>-1</sup>; <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) 7.65 (d, 2H); 6.85 (d, 2H); 5.45 (dd, 1H, J=3.80, 5.60); 4.55 (ddd, 1H, J=3.80, 6.60, 9.05); 4.15 (dd, 1H, J=6.60, 10.30); 3.90 (m, 4H); 3.30 (s, 3H); 1.10 (m, 21H); 1.00 (dt, 6H). <sup>13</sup>C NMR 159.43, 131.58 (d, J=1.86), 129.31, 113.11, 73.82 (d, J=9.71), 73.78 (d, J=161.32), 72.18, 62.47 (d, J=6.98), 62.19 (d, J=6.91), 55.22, 17.95, 17.84, 16.31 (d, J=5.84), 16.20 (d, J=5.69), 12.22. <sup>31</sup>P 17.82. MS m/z 417 (M<sup>+</sup>-43), 294. Anal Calcd for C<sub>22</sub>H<sub>41</sub>O<sub>6</sub>PSi: C, 57.37; H, 8.97. Found: C, 57.28; H, 8.95.

(+)-(1S, 2S) 1-Hydroxy-2-triisopropylsilyloxy-3-methylbutyl-phosphonic acid diethyl ester 3p

 $[\alpha]_D^{20} = +3.15$  (c 0.73 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 3540, 1259, 1090, 1048, 1028 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.15 (m, 5H); 3.78 (ddd, 1H, J=2.40, 6.20, 8.50); 3.18 (dd, 1H, J=2.40, 7.94); 2.00 (m, 1H); 1.30 (t, 6H, J=6.90); 1.08 (m, 21H); 0.96 (d, 3H, J=6.84); 0.86 (d, 6H, J=6.90. <sup>13</sup>C NMR 73.31 (d, J=2.98), 65.71 (d, J=165.86), 62.42 (d, J=7.19), 61.88 (d, J=7.19), 33.76 (d, J=12.34), 18.12, 18.03, 17.91, 16.35 (d, J=4.00), 12.88. <sup>31</sup>P 21.64. MS m/z 353 (M<sup>+</sup>-43), 217. Anal Calcd for C<sub>18</sub>H<sub>41</sub>O<sub>5</sub>PSi: C, 54.51; H, 10.42. Found: C, 54.70; H, 10.45.

(-)-(1R, 2S) 1-Hydroxy-2-triisopropylsilyloxy-2-methylbutyl-phosphonic acid diethyl ester 4p

 $[\alpha]_D^{20} = -6.46$  (c 1.78 CHCl<sub>3</sub>). IR(CHCl<sub>3</sub>) 3440, 1242, 1043, 1023 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.13 (m, 5H); 4.00 (m, 1H); 2.73 (dd, 1H, J=3.25, 20.40); 2.17 (m, 1H, J=2.40, 6.80); 1.27 (t, 6H, J=7.08); 1.03 (m, 21H); 0.97 (t, 6H, J=6.80). <sup>13</sup>C NMR 76.10 (d, J=8.21), 73.00 (d, J=159.69), 62.45 (d, J=7.32), 62.30 (d, J=8.07), 31.33, 21.43, 18.08, 17.18, 16.28 (d, J=5.83), 12.85. <sup>31</sup>P 19.81. MS m/z 353 (M<sup>+</sup>-43), 217. Anal Calcd for C<sub>18</sub>H<sub>41</sub>O<sub>5</sub>PSi: C, 54.51; H, 10.42. Found: C, 54.30; H, 10.39.

(syn) 1-Hydroxy-2-triisopropylsilyloxy-heptyl-phosphonic acid diethyl ester 3q.

IR (CHCl<sub>3</sub>) 3450, 1250, 1048, 1030 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.15 (m, 5H); 3.78 (ddd, J=3.50, 7.80, 7.80); 2.83 (dd, 1H, J=7.80, 7.80); 1.73 (m, 1H); 1.55 (m, 1H); 1.28 (m, 12H); 1.05 (m, 21H); 0.85 (m, 3H). <sup>13</sup>C NMR 71.34 (d, J=3.53), 68.93 (d, J=162.67), 62.09 (d, J=7.19), 61.75 (d, J=7.05), 34.09 (d, J=8.88), 31.61, 24.04, 22.26, 17.84, 17.76, 16.12 (d, J=5.63), 13.63, 12.67. <sup>31</sup>P 21.09. MS m/z 381 (M<sup>+</sup>-43), 307, 243. Anal Calcd for C<sub>20</sub>H<sub>45</sub>O<sub>5</sub>PSi: C, 56.57; H, 10.68. Found: C, 56.44; H, 10.70.

(anti) 1-Hydroxy-2-triisopropylsilyloxy-heptyl-phosphonic acid diethyl ester 4q.

IR (CHCl<sub>3</sub>) 3480, 1248, 1047, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.13 (m, 5H); 4.02 (ddd, 1H, J=2.90, 5.40, 8.30); 2.59 (dd, 1H, J=5.40, 17.40); 1.80 (m, 1H); 1.54 (m, 1H); 1.30 (m, 12H); 1.05 (m, 21H); 0.85 (m, 3H). <sup>13</sup>C NMR 73.27 (d, J=7.39), 72.40 (d, J=158.27), 62.46 (d, J=6.99), 62.24 (d, J=6.63), 32.61, 32.03, 25.42, 22.50, 18.07, 16.40 (d, J=5.56), 16.34, 13.95, 12.65. <sup>31</sup>P 19.61. MS m/z 381 (M<sup>+</sup>-43), 308, 244. Anal Calcd for C<sub>20</sub>H<sub>45</sub>O<sub>5</sub>PSi: C, 56.57; H, 10.68. Found: C, 56.75; H, 10.70.

(syn) 2-tert-Buthyldimethylsilyloxy-2-cyclohexyl-1-hydroxy-ethyl-phosphonic acid diethyl ester 3r.

IR (CDCl<sub>3</sub>) 3350, 2930, 2856, 1718, 1450, 1252, 1229, 1202, 1113, 1093, 1049, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.16 (m, 4H); 4.03 (dd, 1H, J=4.2, 10.2); 3.74 (dt, 1H, J=11.5, 4.2, 4.2); 1.92 (m, 1H); 1.65 (m, 5H); 1.31 (m,

6H); 1.19 (m, 5H); 0.91 (s, 9H); 0.14 (s, 3H), 0.12 (s, 3H). <sup>13</sup>C NMR 73.57 (d, J=4.0), 67.28 (d, J=162.8), 62.38 (m), 43.79, 30.55, 29.65, 28.29, 28.03, 25.38, 25.96, 24.94, 16.40, -4.26, -4.52. <sup>31</sup>P 24.40. MS m/z 227 (M<sup>+</sup>-167), 199, 117.

## (anti) 2-tert-Butyldimethylsilyloxy-2-cyclohexyl-1-hydroxy-ethyl-phosphonic acid diethyl ester 4r.

IR (CDCl<sub>3</sub>) 3350, 2930, 2856, 1718, 1450, 1252, 1229, 1202, 1113, 1093, 1049, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.16 (m, 4H); 3.92 (dt, 1H, J=9.4, 3.2, 3.2); 3.86 (dd, 1H, J=3.2, 6.5); 1.92 (m, 1H); 1.63 (m, 5H); 1.31 (m, 6H); 1.19 (m, 5H); 0.91 (s, 9H); 0.14 (s, 3H), 0.12 (s, 3H). <sup>13</sup>C NMR 74.11, 71.54 (d, J=157.6), 62.38 (m), 42.86, 29.24, 28.87, 28.17, 26.55; 26.43; 25.71; 24.90; 16.51, -4.06, -4.62. <sup>31</sup>P 23.93. MS m/z 227 (M<sup>+</sup>-167), 199, 117.

### Competitive kinetic experiment.

Following the general procedure described for the synthesis of phosphonates (Method A), a mixture of (S)triisopropylsilyloxy lactaldehyde (1.0 eq) 2c, (S)-benzyloxylactaldehyde 2f (1.0 eq) and phosphite 1a (1 eq), were reacted under the reaction conditions described (CH<sub>2</sub>Cl<sub>2</sub>, -78 °C, 3h). At -78 °C, a saturated solution of ammonium chloride was added. The reaction mixture was extracted with methylene chloride and the solvent was removed. The residue was treated with citric acid in MeOH overnight, the methanol was removed and hexane (10 ml) was added. After 30 min stirring, the mixture was filtered, the solvent removed and the residue purified by flash chromatography to give phosphonates 3c and 4c in 36% yield. No traces of the corresponding 3f and 4f derivatives could be detected.

## General Synthesis of 1,2-Dihydroxy phosphonates.

To a solution of 1-hydroxy-2-silyloxyphosphonic ester (10mml) in acetonitrile (6 mL) was added a solution of 5%  $HF_{aq}$ . The resulting solution was stirred at r.t. for 30 min. monitoring by t.l.c. At complete consumption of the starting material, the solvent was removed in vacuo. The residue, containing essentially the target compound, was used as such for the synthesis of cyclic carbonates (see below).

Synthesis of 1,2-Dihydroxy-propyl-phosphonic acid from 1-*tert*-butoxy-2-hydroxy-propyl-phosphonic acid<sup>30</sup>

To a solution of the esters 3e and 4e (50 mg, 0.19 mmol) in methylene chloride (2 mL) under argon at 0°C was added TiCl<sub>4</sub> (0.31 mL, 0.28 mmol). The reaction mixture was immediately worked-up by treating it with a few drops of NH<sub>4</sub>Cl solution and extracting several times with methylene chloride. After drying with MgSO<sub>4</sub> and removal of the solvent in vacuo, the target was obtained in quantitative yields.

(syn) 1,2-Dihydroxy-propyl-phosphonic-acid diethyl ester. 5a

<sup>1</sup>H NMR 4.19 (m, 5H), 3.69 (dd, 1H, J=3.0, 8.0); 1.32 (m, 9H). <sup>31</sup>P 24.33

(anti) 1,2-Dihydroxy-propyl-phosphonic-acid diethyl ester. 7a

<sup>1</sup>H NMR 4.19 (m, 4H); 4.06 (m, 1H); 3.81 (dd, 1H, J=5.1, 7.3); 1.32 (m, 9H). <sup>31</sup>P 24.33

General Procedure for the Synthesis of Cyclic Carbonates.

To a solution of 1,2-dihydroxy phosphonate (10 mmol) in pyridine (12 mL) at -70°C was added dropwise triphosgene (1g, 3.33 mmol) in methylene chloride (30 mL). The resulting solution was stirred at -70°C for 30 min.and the temperature was allowed to reach spontaneously r.t.. A saturated solution of ammonium chloride was added and the mixture extracted with methylene chloride. The organic layers were washed with diluted HCl (1 N), 5% sodium bicarbonate<sub>aq</sub> and the organic layers were dried over sodium sulphate. The crude reaction mixture was purified by flash chromatography to give the cyclic derivative in 60-70% yields.

(-)-(15, 55)-5-Methyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 6a.

 $[\alpha]_D^{20}$ =-30.49 (c 1.22 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 1811, 1244, 1077, 1042, 1025 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.93 (m, 1H, J=6.22, 7.50, 14.00); 4.22 (m, 5H); 1.53 (d, 3H, J=6.22); 1.37 (t, 6H). <sup>13</sup>C NMR 153.44 (d, J=6.03), 75.90 (d, J=171.71), 74.59, 63.99 (d, J=6.83), 63.71 (d, J=6.83), 19.89, 19.74, 16.25 (d, J=5.51). <sup>31</sup>P 12.29. MS m/z 223 (M<sup>+</sup>-15), 193, 178, 138, 136. Anal Calcd for C<sub>8</sub>H<sub>15</sub>O<sub>6</sub>P: C, 40.34; H, 6.35. Found: C, 40.50 H, 6.38.

(+)-(1R, 5S)-5-Methyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 8a.

 $[\alpha]_D^{20}$  = +20.00 (c 1.28 CHCl<sub>3</sub>). IR(CHCl<sub>3</sub>) 1812, 1251, 1042, 1029 cm<sup>-1</sup>; <sup>1</sup>H NMR 5.03 (m, 1H, J=6.60, 8.30, 21.50); 4.75 (dd, 1H, J=2.40, 8.30); 4.20 (m, 4H, J=7.08); 1.65 (d, 3H, J=6.60); 1.35 (t, 6H, 7.08). <sup>13</sup>C NMR 153.50 (d, J=6.14), 74.98, 73.72 (d, J=169.87), 64.06 (d, J=7.12), 63.56 (d, J=6.85), 16.39 (d, J=5.63), 16.27 (d, J=5.97). <sup>31</sup>P 10.79. MS m/z 238 (M<sup>+</sup>), 193, 167, 136. Anal Calcd for C<sub>8</sub>H<sub>15</sub>O<sub>6</sub>P: C, 40.34; H, 6.35. Found: C, 40.18; H, 6.33.

(-)-(1S, 5S)-5-Phenyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 6b.

 $[\alpha]_D^{20} = -18.50 \ (c \ 1.20 \ CHCl_3)$ . IR (CHCl\_3) 1825, 1823, 1251, 1045, 1025 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.40 (s, 5H); 5.80 (dd, 1H, J=7.04, 15.00); 4.60 (d, 1H, J=7.04); 4.25 (m, 4H); 1.35 (m, 6H). <sup>13</sup>C NMR 153.36 (d, J=6.44), 135.81 (d, J=7.69), 129.82, 129.20, 125.68, 78.59, 76.89 (d, J=171.35), 64.35 (d, J=7.05), 64.02 (d, J=6.84), 16.40 (d, J=5.54), 16.37 (d, J=5.49). <sup>31</sup>P 12.15. MS m/z 300 (M<sup>+</sup>), 256, 161, 136. Anal Calcd for C<sub>13H17</sub>O<sub>6</sub>P: C, 52.00; H, 5.71. Found: C, 52.15; H, 5.73.

(+)-(1R, 5S)-5-Phenyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 8b.

 $[\alpha]_D^{20}$  =+ 64.76 (c 1.05 CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>) 1831, 1807, 1251, 1041 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.40 (s, 5H); 5.95 (dd, 1H, J=8.50, 20.00); 5.05 (dd, 1H, J=3.55, 8.50); 3.80 (m, 4H); 1.15 (dt, 3H). <sup>13</sup>C NMR 153.61 (d, J=6.74), 132.19 (d, J=4.83), 129.56, 128.28, 126.91, 79.09, 75.24 (d, J=172.41), 63.66 (d, J=6.94), 63.12 (d, J=6.84), 16.22 (d, J=5.62), 16.12 (d, J=5.16). <sup>31</sup>P 9.79. MS m/z 300 (M<sup>+</sup>), 240, 161, 136. Anal Calcd for C<sub>13H17</sub>O<sub>6</sub>P: C, 52.00; H, 5.71. Found: C, 52.21; H, 5.73.

*Trans*-5(4-Methoxy-Phenyl)-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 6c. <sup>1</sup>H NMR 7.31 (d, 2H, J=8.84); 6.94 (d, 2H, J=8.84); 5.74 (dd, 1H, J=7.40, 15.00); 4.61 (d, 1H, J=7.40); 4.23 (m, 4H); 3.80 (s, 3H); 1.34 (m, 6H). <sup>31</sup>P 12.12. MS m/z 330 (M<sup>+</sup>), 287 (M<sup>+</sup>-43 CO<sub>2</sub>), 191. Anal Calcd for C<sub>14</sub>H<sub>19</sub>O<sub>7</sub>P: C, 50.91; H, 5.80. Found: C, 51.05; H, 5.82.

Cis-5(4-Methoxy-Phenyl)-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 8c. <sup>1</sup>H NMR 7.33 (d, 2H); 6.90 (d, 2H); 5.88 (dd, 1H, J=8.55, 19.40); 5.00 (dd, 1H, J=3.63, 8.55); 3.90 (m, 4H); 3.80 (s, 3H); 1.15 (m, 6H). <sup>31</sup>P 9.76. MS m/z 330 (M<sup>+</sup>), 287 (M<sup>+</sup>-43 CO<sub>2</sub>), 191. Anal Calcd for  $C_{14}H_{19}O_7P$ : C, 50.91; H, 5.80. Found: C, 50.98; H, 5.81.

(-)-(15, 55)-5-Isopropyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 6d.

 $[\alpha]_D^{20} = -38.60 \ (c \ 1.45 \ CHCl_3). \ IR \ (CHCl_3) \ 1812, \ 1261, \ 1162, \ 1080, \ 1045, \ 1029 \ cm^{-1}; \ ^1H \ NMR \ 4.60 \ (dt, \ 1H, \ J=5.40, \ 5.60, \ 15.60); \ 4.45 \ (d, \ 1H, \ J=5.40); \ 4.24 \ (m, \ 4H); \ 1.96 \ (m, \ 1H); \ 1.35 \ (t, \ 6H, \ J=7.08); \ 1.00 \ (d, \ 3H, \ J=6.64); \ 0.99 \ (d, \ 3H, \ J=6.86). \ ^{13}C \ NMR \ 153.62 \ (d, \ J=4.12), \ 81.87, \ 72.48 \ (d, \ J=171.83), \ 64.17 \ (d, \ J=7.05), \ 63.93 \ (d, \ J=6.92), \ 32.19 \ (d, \ J=9.08), \ 16.98, \ 16.39 \ (d, \ J=5.56), \ 16.28. \ ^{31}P \ 13.11. \ MS \ m/z \ 266 \ (M^+), \ 111. \ Anal \ Calcd \ for \ C_{10}H_{19}O_6P: \ C, \ 45.12; \ H, \ 7.19. \ Found: \ C, \ 44.98; \ H, \ 7.22.$ 

(+)-(1R, 5S)-5-Isopropyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 8d.

 $[\alpha]_{D}^{20}$ =+52.00 (*c* 1.15, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 1832, 1810, 1259, 1246, 1163, 1067, 1049, 1033 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.77 (dd, 1H, J=1.40, 7.40); 4.43 (ddd, 1H, J=7.40, 9.84, 30.40); 2.38 (m, 1H); 1.35 (t, 6H, J=7.08); 1.10 (d, 3H, J=6.54); 1.03 (d, 3H, J=6.54).<sup>13</sup>C NMR 153.58 (d, J=2.31), 84.86, 74.53 (d, J=165.86), 63.97 (d, J=7.19), 63.45 (d, J=7.05), 28.75 (d, J=4.00), 19.40, 18.74, 16.31 (d, J=5.63) . <sup>31</sup>P 11.20. MS m/z 223 (M<sup>+</sup>-43). Anal Calcd for C<sub>10</sub>H<sub>19</sub>O<sub>6</sub>P: C, 45.11; H, 7.19. Found: C, 45.20; H, 7.20.

Trans-5-Pentyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 6e.

IR (CHCl<sub>3</sub>) 1813, 1811, 1249, 1246, 1077, 1043, 1025 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.80 (m, 1H); 4.34 (d, 1H, J=6.80); 4.23 (m, 4H); 1.75 (m, 2H); 1.33 (m, 12H); 0.90 (m, 3H). <sup>13</sup>C NMR 153.53 (d, J=6.29), 78.04, 74.66 (d, J=171.72), 72.97, 64.13 (d, J=6.92), 63.85 (d, J=6.78), 34.53 (d, J=7.93), 31.11, 23.98, 22.31, 16.40 (d, J=5.49), 13.82. <sup>31</sup>P 12.43. MS m/z 279 (M<sup>+</sup>-15), 167. Anal Calcd for  $C_{12}H_{23}O_6P$ : C, 48.98; H, 7.88. Found: C, 49.17; H, 7.91.

Cis-5-Pentyl-2-oxo-[1,3]dioxolan-4-yl-phosphonic acid diethyl ester 8e.

IR (CHCl<sub>3</sub>) 1810, 1250, 1043, 1031 cm<sup>-1</sup>; <sup>1</sup>H NMR 4.95 (m, 1H); 4.74 (d, 1H, J=6.20); 4.18 (m, 4H); 2.10-1.75 (m, 2H); 1.30 (m, 12H); 0.85 (m, 3H). <sup>13</sup>C NMR 153.55 (d, J=5.83), 79.21, 73.74 (d, J=169.39), 64.05 (d, J=7.12), 63.52 (d, J=6.78), 31.17, 30.30 (d, J=4.27), 25.80, 22.37, 16.40 (d, J=5.49), 13.86. <sup>31</sup>P

10.82. MS m/z 266 (M<sup>+</sup>-28), 234 (M<sup>+</sup>-60),167, 157, 137. Anal Calcd for  $C_{12}H_{23}O_6P$ : C, 48.98; H, 7.88. Found: C, 49.20; H, 7.90.

#### Synthesis of 1,2-Dihydroxy phosphonic Acids Disodium salts.

General Procedure: 1,2-Dihydroxy phosphonic ester (10 mmol) was dissolved in HCl 6N (25 mL). The resulting solution was refluxed for 6 hr until the disappearance of the starting material. The residue was washed with ether and the water was eliminated by lyophilization. The residue was dissolved in 10 mL of Millipore purified water and was treated with Dowex 50WX8 (Na<sup>+</sup> form) (1.00 g) with gentle occasional stirring. After 2.5 hr extra resin (1 g) was added. The mixture was left to stand for 15 min, decanted, the resin was washed with purified water and the aqueous layers were collected. The combined solution was lyophilised to give the phosphonic acids as sodium salts in essentially quantitative yields starting from 1-hydroxy-2-silyloxyphosphonic esters.

## (+)-(1S, 2S) 1,2-Dihydroxy-propyl-phosphonic-acid disodium salt. 9a

 $[\alpha]_{365}^{20}$  =+23.12 (c 10.22, H<sub>2</sub>O). <sup>1</sup>H NMR 3.85 (m, 1H); 3.40 (dd, 1H, J=5.65, 9.70); 1.02 (d, 3H, J=6.35). <sup>13</sup>C NMR 73.61 (d, J=153.28), 68.65 (d, J=5.45), 19.98 (d, J=6.35). <sup>31</sup>P 19.18. Anal Calcd for C<sub>3</sub>H<sub>7</sub>O<sub>5</sub>Na<sub>2</sub>P: C, 18.01; H, 3.53. Found: C, 17.95; H, 3.54.

(-)-(15, 25)1,2-Dihydroxy-3-methyl-butyl-phosphonic-acid disodium salt. 9b

 $[\alpha]_{345}^{20}$  =-4.65 (c 3.87, H<sub>2</sub>O). <sup>1</sup>H NMR 3.68 (dd, 1H, J=3.40, 11.12); 3.42 (m, 1H); 1.78 (m, 1H), 0.81 (d, 3H, J=6.90); 0.77 (d, 3H, J=6.90). <sup>13</sup>C NMR 77.42 (d, J=2.04), 69.66 (d, J=153.12), 30.72 (d, J=8.87), 19.67, 18.65. <sup>31</sup>P 19.33. Anal Calcd for C<sub>5</sub>H<sub>11</sub>O<sub>5</sub>Na<sub>2</sub>P: C, 26.32; H, 4.86. Found: C, 26.28; H, 4.88.

#### (syn) 1,2-Dihydroxy-heptyl-phosphonic-acid disodium salt. 9c

<sup>1</sup>H NMR 3.70 (m, 1H); 3.44 (dd, 1H, J=4.30, 10.25); 1.40 (m, 2H); 1.13 (m, 6H); 0.70 (m, 3H). <sup>13</sup>C NMR 72.35 (d, J=3.17), 71.87 (d, J=152.38), 33.52 (d, J=7.82), 31.95, 25.61, 22.87, 14.26. <sup>31</sup>P 18.60. Anal Calcd for  $C_7H_{15}O_5Na_2P$ : C, 32.82; H, 5.90. Found: C, 32.71; H, 5.92.

(syn) 2-Cyclohexyl-1,2-Dihydroxy-ethyl-phosphonic-acid disodium salt 9d

IR(CHCl<sub>3</sub>) 3465, 1520, 1423, 1229, 1046 cm<sup>-1</sup>; <sup>1</sup>H NMR 3.81 (dd, J=12.0, 1H, 3.40); 3.43 (dt, 1H, J=7.38, 3.40); 1.5 (m, 5 H); 1.0 (m, 6H). <sup>31</sup>P 22.36. Anal. Calc. for C<sub>8</sub>H<sub>15</sub>Na<sub>2</sub>PO<sub>5</sub>: C, 35.83; H, 5.64; Found: C, 35.72; H, 5.65.

# (+)-(1S, 2S)1-Hydroxy-2-triisopropylsilyloxy-2-phenylethyl-phosphonic acid dibenzyl ester 3t

 $(Y=45\%) [\alpha]_D^{20} =+17.51$  (c=1.93, CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 3465, 1520, 1423, 1229, 1046 cm<sup>-1</sup>; <sup>1</sup>H NMR 7.25 (m, 15H); 5.14 (dd, 1H, J=7.10, 7.20); 5.00 (m, 2H); 4.75 (m, 1H); 4.07 (ddd, 1H, J=4.40, 6.90, 7.10); 3.53 (dd, 1H, J=4.40, 18.10); 1.00 (m, 21H). <sup>13</sup>C NMR 140.85 (d, J=4.38), 136.31 (d, J=5.98), 136.01 (d, J=5.93), 128.26, 128.22, 128.05, 127.96, 127.81, 127.77, 127.63, 74.93 (d, J=7.98), 73.77 (, J=163.54), 68.03 (d, J=6.67), 67.19 (d, J=6.83), 17.82, 17.67, 12.33. MS m/z 511 (M<sup>+</sup>-43), 264, 250, 171. Anal Calcd for C<sub>31</sub>H<sub>43</sub>O<sub>5</sub>PSi: C, 67.12; H, 7.82. Found: C, 67.05; H, 7.79.

#### (+)-(1S, 2S)1,2-Dihydroxy-2-phenyl-ethyl-phosphonic-acid disodium salt 9e

Dibenzyl ester 3t was hydrogenated over Pd/C 10% in methanol under hydrogen pressure of (25-30 psi) in a Parr apparatus. The residue was filtered through Celite and the solvent was removed in vacuo. To the residue was added water, the mixture was washed with ether and lyophilised. The crude acid was purified as its sodium salt to an ion-exchange resin as described above.

 $[\alpha]_{355}^{20}$  =+106.90 (c 1.45 in H<sub>2</sub>O).<sup>1</sup>H NMR 7.25 (m, 5H); 4.88 (t, 1H, J=3.95); 3.71 (dd, 1H, J=3.95, 10.60). <sup>13</sup>C NMR 142.03 (d, J=6.54), 129.41, 128.76, 127.64, 74.15 (d, J=3.17), 73.55 (d, J=151.90). <sup>31</sup>P 17.52. Anal Calcd for C<sub>8</sub>H<sub>9</sub>O<sub>5</sub>Na<sub>2</sub>P: C, 36.65; H, 3.46. Found: C, 36.52; H, 3.47.

Acknowledgements: This project was partially supported by Progetto Strategico "Tecnologie Chimiche Innovative" C.N.R.-Rome and M.P.I. (Fondi 40%). R.C thanks *GlaxoWellcome Italia* Verona for financial support.

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(Received in UK 19 September 1996)