Opposite Stereochemical Effects Exerted by $CeCl_3$ and $TiCl_4$ on the Lewis Acid Mediated Reduction of α-Alkyl-β-ketophosphine Oxides with Metallic Hydrides: A Highly Stereoselective Protocol for the Synthesis of *syn* and *anti* α-Alkyl-β-hydroxyphosphine Oxides

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Abstract: A general, highly efficient methodology for obtaining both *syn* and *anti* β-hydroxyphosphine oxides by reduction of the corresponding β-ketophosphine oxides is described. The nature of the Lewis acid was found to be pivotal in determining the outcome of these reactions. Strongly chelating $TiCl_4$ led to the *anti* isomer in high diastereoisomeric excess in noncoordinating solvents (CH_2Cl_2) at −78 °C with BH_3/py as reducing agent, while nonchelating $CeCl_3$ gave a high excess of the *syn* isomer in coordinating solvents (THF) at the same temperature with $LiBH_4$ as reducing agent. In the latter case, $CeCl_3$ is essential in achieving high yields and stereoselectivity, since it allows the reaction to be performed at low temperatures. Otherwise, higher temperatures (0 °C) are required, which lower both yields and selectivities. Moreover, each step of the protocol for the synthesis of stereodefined disubstituted olefins from alkylphosphine oxides (Warren's modification of the Horner procedure) has been optimized, and the optimized procedure has been applied to the synthesis of muscalure, the pheromone of the domestic fly.

Keywords
alkenes · asymmetric synthesis · natural products · Lewis acids · phosphane oxides

Introduction

In recent years, much attention has been paid to organocerium compounds.[1] For example, Luche's reduction of ketones ($NaBH_4$ in ethanol, at 0 °C in the presence of $CeCl_3 \cdot 7H_2O$)[2] is among the most commonly used methods for the chemoselective reduction of ketones in the presence of aldehyde groups[3] or for the almost exclusive 1,2-reduction of α,β-unsaturated carbonyl moieties.[4]

Organocerium compounds are highly efficient reagents for the nucleophilic transfer of an alkyl group to electrophilic centres,[5] since side reactions (proton abstraction,[6, 7] redox[8] and retroaldol processes[9]) are almost completely suppressed.

In many reactions, reasonably high asymmetric inductions have been observed when chiral centres are close to the prochiral carbonyl group.[10] When heteroatoms are bound to the β-carbon atom, the stereochemical outcome seems to be consistent with a chelation-controlled addition.[11] This interpretation is supported by the high coordination number generally shown by lanthanides: cerium chloride can accommodate seven water molecules in its coordination sphere.[1a]

We employed the above interpretation to account for the high stereoselectivity observed in the alkylation of β-ketophosphine oxides with $RCeCl_2$.[12] More recently, however, we found that β-hydroxyketones were alkylated with low stereoselectivity by organocerium reagents,[13] despite the presence of both an α-stereocentre and a β-heteroatom, set up for chelation in a six-membered ring as in the β-ketophosphine oxides. Moreover, cerium and lithium or magnesium compounds showed a very similar stereochemical outcome. The only advantage of the organocerium compounds were the much higher yields (>98% vs. 65–70% with Grignard or lithium reagents). There are many other examples of ambiguous results in the stereochemical outcome of organocerium reactions. For example, in the reduction of β-ketophosphine oxides under Luche's conditions a random stereoselectivity is observed.[14]

Owing to the richness of the synthetic applications of organocerium reagents, we have decided to start a systematic study to rationalise the role of the cerium. Our aim is to find a way of predicting with certainty the outcome of its reactions. For this purpose, we will examine here the reduction, with various reducing agents, of β-ketophosphine oxides with asymmet-

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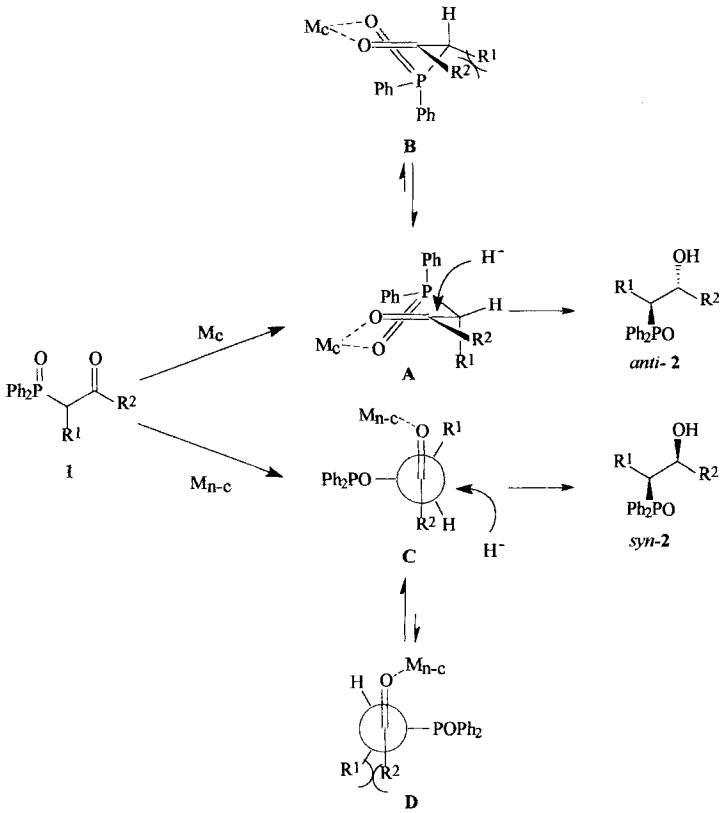
ric α-carbons in their racemic form, in the presence of either cerium(III) or titanium(IV) chloride. We chose this reaction for the following reasons:

1) It has been widely studied under Luche's conditions or with other reductive systems.[15]
2) The Lewis acidity of the metal atom can be easily exploited to tune this reaction, since this property governs the extent of chelation.[16] Thus, the most populated conformation of a chelated complex should be the half-chair with the R^1 substituent in the pseudo-axial position to minimise the steric strain with R^2 (Scheme 1, conformation **A**). The incoming hydride will attack from the less hindered side opposite to R^1 leading to the *anti* product. On the other hand, with nonchelating metals, the Felkin–Anh model predicts that the *syn* diastereomer will predominate when the diphenylphosphinoyl substituent is the largest group (Scheme 1, conformation **C**). Obviously, with increasing size of R^1 or particular shapes of R^2, other conformations may be preferred (see below).
3) The highly stereoselective syntheses of *syn* and *anti* β-hydroxyphosphine oxides would open up the way to stereoselective Horner olefinations. According to the Warren modification,[17] the NaH/DMF stereospecific elimination from the *syn* and *anti* derivatives leads to the (*E*) and (*Z*) alkenes, respectively. Recently, the Horner approach has received increasing attention, since it offers clear advantages over the classical Wittig and Wadsworth–Emmons procedures.[17, 18] However, general methods for the preparation of either *syn* or *anti* β-hydroxyphosphine oxides with high stereoselectivity are not yet available.



Scheme 1. Expected stereochemical control in the reduction of α-alkyl-β-ketophosphine oxides with hydrides (H^-) in the presence of chelating (M_c) or nonchelating (M_{n-c}) Lewis acids.

Results and Discussion

A series of α-alkyl-β-ketophosphine oxides **1** were synthesised with varying bulkiness of R^1 and R^2 groups. These compounds were reduced with hydrides or the borane/pyridine complex (BH_3/py) in the presence of titanium tetrachloride or cerium trichloride as the Lewis acid. We will first discuss the reaction with $TiCl_4$ since the ability of titanium salts to give chelation complexes is well documented.[19]

Reduction in the presence of $TiCl_4$: In a preliminary communication,[20] we found that the reduction of **1** in dichloromethane at low temperature with a 2 M THF solution of $LiBH_4$ (1 equiv) in the presence of $TiCl_4$ (1.2 equiv) led to the prevalent formation of *anti* β-hydroxyphosphine oxides (*anti*-**2**). This is clearly due to chelation by the metal atom, which creates a bridge between the oxygen atoms of the C=O and P=O groups. In the resulting six-membered cyclic intermediate, the most populated conformation **A** is preferentially attacked by the incoming hydride ion at the less hindered side opposite R^1 (Scheme 1). A solvent such as THF can compete with the substrate in coordinating the titanium atom, lowering its chelating effect. On the other hand, a very sluggish reaction is obtained with solid $LiBH_4$ in dichloromethane. Recently, DiMare reported that the BH_3/py system efficiently reduces ketones in the presence of titanium tetrachloride.[21] Actually, the β-ketophosphine oxide **1aa** ($R^1 = R^2 = Me$) is reduced by BH_3/py as efficiently as by $LiBH_4$/THF, but much more stereoselectively (Table 1). From a practical point of view, the $LiBH_4$/THF method requires a simpler workup. Consequently, when the stereoselectivity is very high (e.g. Table 1, entries 6, 10), this method is preferable.

The most relevant finding from data reported in Table 1 is that BH_3/py reductions always ensure a high stereoselectivity, regardless of the size of the R^1 and R^2 substituents. In a chelation-controlled reaction (Scheme 2), the minimum level of

Abstract in Italian: *In questo lavoro è riportata una soluzione assai valida alla sintesi stereoselettiva di α-alchil-β-idrossifosfinossidi a partire dai rispettivi β-chetofosfinossidi. L'isomero anti si ottiene usando come promotore un acido di Lewis con caratteristiche chelanti come il $TiCl_4$ e BH_3/py come riducente, mentre l'isomero sin viene ottenuto in presenza di un acido di Lewis non-chelante come il $CeCl_3$ e $LiBH_4$/THF come riducente. Il ruolo giocato dal cerio sulla stereochimica e sull'efficienza della reazione viene chiaramente evidenziato. Il Cerio infatti permette l'impiego di basse temperature (−78 °C) e ciò ovviamente favorisce una maggiore stereoselettività. Inoltre l'uso di $CeCl_3$ porta a rese significativamente maggiori. Infine sono stati migliorati tutti i passaggi della sintesi di olefine disostituite secondo la metodologia di Warren, per cui adesso è possibile ottenere in alte rese globali e con elevata stereochimica olefine a partire da alchilfosfinossidi. Questa metodologia multi stadio è stata applicata alla sintesi del muscalure, il feromone della mosca domestica.*

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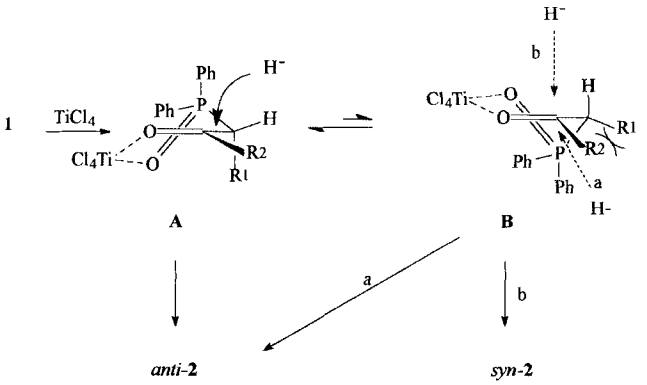
Table 1. Stereoselective reduction of β-ketophosphine oxides **1** to β-hydroxyphosphine oxides **2** in the presence of $TiCl_4$ at −78 °C.

Entry	1	R^1	R^2	Reducing agent	2	*anti*/*syn* [a]	Yield (%) [b]
1	**1aa**	Me	Me	$LiBH_4$/THF [c]	**2aa**	75/25	>98
2	**1aa**	Me	Me	BH_3/py [d]	**2aa**	90/10	>98
3	**1ab**	Me	Ph	$LiBH_4$/THF	**2ab** [e]	90/10	98
4	**1ab**	Me	Ph	BH_3/py	**2ab**	>99/1	>98
5	**1ac**	Me	*c*-C_6H_{11}	$LiBH_4$/THF	**2ac** [e]	98/2	97
6	**1cd**	*c*-C_6H_{11}	Pr	$LiBH_4$/THF	**2cd** [e]	97/3	95
7	**1dc**	Pr	*c*-C_6H_{11}	BH_3/py	**2dc**	92/8	>98
8	**1de**	Pr	Bu	$LiBH_4$/THF	**2de** [e]	87/13	95
9	**1de**	Pr	Bu	BH_3/py	**2de**	92/8	>98
10	**1df**	Pr	-≡-Ph	$LiBH_4$/THF	**2df** [e]	98/2	90
11	**1ga**	CH_2Ph	Me	$LiBH_4$/THF	**2ga** [e]	75/25	96
12	**1ga**	CH_2Ph	Me	BH_3/py	**2ga**	97/3	>98
13	**1gb**	CH_2Ph	Ph	$LiBH_4$/THF	**2gb** [e]	98/2	95
14	**1gf**	CH_2Ph	-≡-Ph	$LiBH_4$/THF	**2gf** [e]	96/4	92
15	**1gh**	CH_2Ph	*i*Pr	$LiBH_4$/THF	**2gh** [e]	94/6	92
16	**1ie**	C_5H_{11}	Bu	BH_3/py	**2ie**	>99/1	>98
17	**1ih**	C_5H_{11}	*i*Pr	BH_3/py	**2ih**	>99/1	>98
18	**1jk**	C_8H_{17}	$C_{13}H_{27}$	BH_3/py	**2jk**	92/8	>98

[a] Determinated by ^1H NMR spectroscopy. [b] Calculated on the mixture of diastereomers. [c] By adding a 2 M solution of $LiBH_4$ in THF to the CH_2Cl_2 solution of **1**/$TiCl_4$ complex at −78 °C. [d] By adding the BH_3/py complex to the CH_2Cl_2 solution of **1**/$TiCl_4$ complex at −78 °C. [e] See ref. [20].



Scheme 2. Chelation control in the $TiCl_4$-mediated reduction of α-alkyl-β-ketophosphine oxides.

stereoselectivity should be observed when R^1 and R^2 are methyl, since this is the sterically least demanding alkyl group. An *anti*/*syn* ratio of 90/10 is obtained in this unfavourable case under our experimental conditions. With more bulky R^1 and R^2 groups, the conformational equilibrium will shift towards conformation **A** and the *anti*/*syn* ratio will thus increase.

The method described above is the first general protocol for the stereoselective preparation of β-hydroxyphosphine oxides, which are intermediates for the synthesis of stereodefined olefins. The method based on the addition of lithium salts of alkylphosphine oxides to aldehydes fails when R^1 is as large as the Ph_2PO group (i.e. with α-branched alkyl groups).[17] Moreover, this reaction always gives lower stereoselectivities than our procedure. The alternative method based on the Luche's reduction of α-alkyl-β-ketophosphine oxides only gives good stereoselection when a secondary alkyl substituent is present in the α-position. In fact, straight-chain alkyl groups reverse the selectivity.[17]

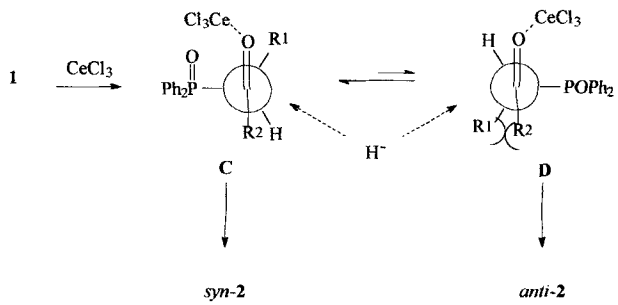
Reduction in the presence of $CeCl_3$: We first tested the reduction of **1aa** in the presence of $CeCl_3$ with the reducing system BH_3/py/CH_2Cl_2, which was highly efficient with $TiCl_4$. Unfortunately, no reaction was observed, and at −78 °C the starting material was quantitatively recovered after 2 h (Table 2, entry 1). Prolonged reaction times and higher reaction temperatures were also ineffective. A complex between cerium(III) chloride and β-ketophosphine oxide was formed, since the addition of the substrate to a suspension of the cerous salt resulted in a clear solution after about 1 h. Unfortunately, the paramagnetism of cerous salt prevented useful NMR information on the structure of this complex from being obtained.[22]

Table 2. Stereoselective reduction of β-ketophosphine oxides **1** to β-hydroxyphosphine oxides **2** with $LiBH_4$ in the presence of $CeCl_3$ in THF at −78 °C [a], unless specified otherwise.

Entry	1	R^1	R^2	2	*syn*/*anti* [b]	Yield (%) [c]
1	**1aa**	Me	Me	**2aa** [d]	n.r.	n.r.
2	**1aa**	Me	Me	**2aa** [e]	75/25	>98
3	**1aa**	Me	Me	**2aa**	91/9	>98
4	**1ab**	Me	Ph	**2ab**	98/2	>98
5	**1ac**	Me	*c*-C_6H_{11}	**2ac**	97/3	>98
6	**1cd**	*c*-C_6H_{11}	Pr	**2cd**	20/80	80
7	**1dc**	Pr	*c*-C_6H_{11}	**2dc**	>99/1	>98
8	**1de**	Pr	Bu	**2de** [c]	87/13	>98
9	**1de**	Pr	Bu	**2de**	96/4	>98
10	**1df**	Pr	-≡-Ph	**2df**	50/50	95
11	**1ga**	CH_2Ph	Me	**2ga** [e]	86/14	>98
12	**1ga**	CH_2Ph	Me	**2ga**	96/4	>98
13	**1gb**	CH_2Ph	Ph	**2gb**	98/2	94
14	**1ge**	CH_2Ph	-≡-Ph	**2ge**	55/45	95
15	**1gh**	CH_2Ph	*i*Pr	**2gh**	95/5	>98
16	**1ie**	C_5H_{11}	Bu	**2ie**	>99/1	>98
17	**1ih**	C_5H_{11}	*i*Pr	**2ih**	>99/1	>98
18	**1jk**	C_8H_{17}	$C_{13}H_{27}$	**2jk**	90/10	>98

[a] By adding a 2 M solution of $LiBH_4$ in THF to the THF solution of **1**/$CeCl_3$ complex at −78 °C. [b] Determined by ^1H NMR spectroscopy. [c] Calculated on the mixture of diastereomers. [d] By adding the BH_3/py complex to the CH_2Cl_2 solution of **1**/$CeCl_3$ complex at −78 °C. [e] By adding a 2 M solution of $LiBH_4$ in THF to the CH_2Cl_2 solution of **1**/$CeCl_3$ complex at −78 °C.

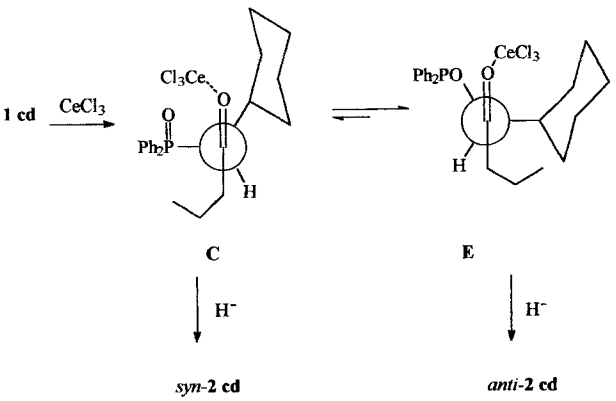
The reduction of the β-ketophosphine oxide proceeded successfully when a 2 M THF solution of lithium borohydride was employed under the same experimental conditions as those used with titanium tetrachloride. The reaction was rapid and gave the expected β-hydroxyphosphine oxide in almost quantitative yield, but with reversed selectivity with respect to the $TiCl_4$ reaction (75/25 *syn*/*anti* ratio; Table 2, entry 2). With increasing length of the straight-chain alkyl groups R^1 and R^2, the *syn*/*anti* ratio increases (entries 9, 16). These findings strongly support an open-chain mechanism, and the Felkin–Anh model explains the stereochemical outcome of the reaction (Scheme 3). The



Scheme 3. Nonchelation control in the $CeCl_3$-mediated reduction of α-alkyl-β-ketophosphine.

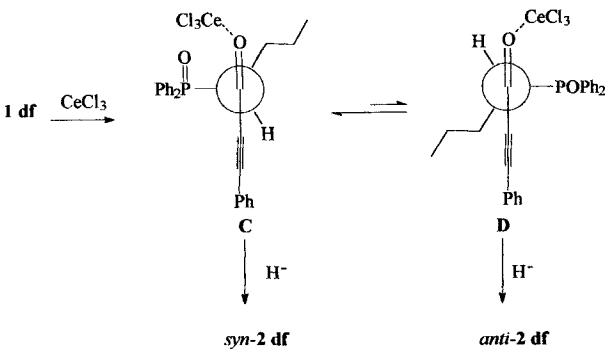
sterically demanding alkyl chains favour conformation **C** over **D**, leading to higher *syn*/*anti* ratios. The same steric effects favour conformation **A** over **B** in the chelation-controlled mechanism and thus the *anti* isomer (Scheme 2). Also, with the mechanism shown in Scheme 3, the use of coordinating solvents should give better results: in THF the *syn*/*anti* ratio rises to 91/9 (Table 2, entry 3). Therefore THF is the best solvent to ensure almost quantitative yields and high diastereoselectivities. The equilibrium between conformations **C** and **D** is completely shifted to the left when the steric demand of R^1 is lower than that of the Ph_2PO group (R^1 = linear alkyl chain). Obviously, bulky R^2 moieties have the same positive effect on the conformational equilibrium. However, in the present case this effect is not evident, since a high diastereoselectivity is even observed when R^1 and R^2 are both methyl groups.

When R^1 is an α-branched alkyl group such as cyclohexyl, the *anti* isomer prevails (Table 2, entry 6); this demonstrates that the steric demand of this group is higher than that of the diphenylphosphinoyl moiety. In the Felkin model, the larger group is cyclohexyl and **E** is the most populated conformation (Scheme 4). Moreover, the steric effect prevails over the Coulombic repulsion between the electronegative Ph_2PO and the incoming hydride in conformation **E**.[23] It should be noted that conformation **E** of the Felkin model corresponds to the most stable chelate conformer **A** (Scheme 2) as far as the molecular arrangement around the $C_\alpha-C_{C=O}$ bond is concerned.



Scheme 4.

Finally, the cylindrical symmetry of alkynyl groups in R^2 position reduces the unfavourable steric interactions between the two substituents R^1 and R^2 in conformation **D** (Scheme 5).



Scheme 5.

The hypothesis of "nonperpendicular attack" (owing to the destabilising interactions arising from the out-of-phase overlap with the oxygen atom and from the four-electron interaction with the HOMO of the substrate, the nucleophile approaches the carbonyl at an angle of 109° rather than 90°) predicts that attack will be preferred at conformation **C** for steric reasons.[23a, b] However, the electronic effects that open up the approach angle to 109° with respect to the carbonyl group, also apply to the same extent to the triple bond. These effects cancel out, and perpendicular attack occurs, accounting for the poor efficiency of the diastereomeric induction (Table 2, entries 10, 14).

If the cerium atom is not able to chelate, is its presence essential for high yields and stereoselectivities? In Table 3, the comparison between the reaction of phosphine oxide **1aa** with $LiBH_4$ in the presence and in the absence of cerium trichloride is reported. The reaction with $LiBH_4$ alone was slower (2 h vs. 10 min in THF at −78 °C) and the yields were lower with respect to the same reaction carried out with $CeCl_3$, but the stereochemical outcome was exactly the same.

Table 3. Stereoselective reduction of a selection of β-ketophosphine oxides **1** to β-hydroxyphosphine oxides **2** with $LiBH_4$, in the presence and in the absence of $CeCl_3$, in THF at various temperatures.

Entry	1	T (°C)	2	Lewis acid	Yield (%) [a]	*syn*/*anti* [b]
1	**1aa**	−78	**2aa**	$CeCl_3$ [c]	>98	91/9
2	**1aa**	−78	**2aa**	none [d]	85 [e]	90/10
3	**1de**	−78	**2dc**	$CeCl_3$ [c]	>98	96/4
4	**1de**	−78	**2de**	none	n.r. [e,f]	n.r.
5	**1de**	0	**2de**	$CeCl_3$ [c]	>98	87/13
6	**1de**	0	**2de**	none [d]	60 [e,g]	87/13
7	**1cd**	−78	**2cd**	$CeCl_3$ [c]	80	20/80
8	**1cd**	−78	**2cd**	none [d]	n.r. [e,h]	n.r.
9	**1cd**	0	**2cd**	$CeCl_3$ [c]	>98	50/50
10	**1cd**	0	**2cd**	none [d]	n.r. [e,i]	n.r.

[a] Calculated on the mixture of diastereomers. [b] Determined by ^1H NMR spectroscopy. [c] By adding a 2 M solution of $LiBH_4$ in THF to the THF solution of **1**/$CeCl_3$ complex. [d] By adding a 2 M solution of $LiBH_4$ in THF to the THF solution of **1**. [e] Formation of insoluble polymeric products was observed. [f] 88% of starting material recovered. [g] Together with 10% starting material. [h] 92% of starting material recovered. [i] 70% of starting material recovered.

When the alkyl chains R^1 and R^2 were longer than methyl, as in **1de**, no reaction occurred at −78 °C in the absence of $CeCl_3$ (Table 3, entry 4). Reduction with short reaction times could be obtained at 0 °C, but to the detriment of the diastereoisomeric ratio (Table 3, entry 6). Moreover, the yields were lower since an insoluble polymer was formed. At 0 °C in the presence of $CeCl_3$, high yields were obtained but the same low stereoselectivity was observed (Table 3, entry 5). For the reaction of phosphine oxide **1cd**, lower stereoselection was observed at 0 °C than at −78 °C. At the lower temperature, a prevalence of the *anti* isomer was observed, as seen above, while at 0 °C a *syn*/*anti* ratio of 1/1 was obtained. These reactions do not proceed without $CeCl_3$.

In conclusion, the presence of the cerous salt is essential to obtain both high yields and high stereochemical efficiency, since the reaction can then be carried out at lower temperatures. According to the Boltzmann's law, the population of the more stable conformer increases as temperatures decrease.

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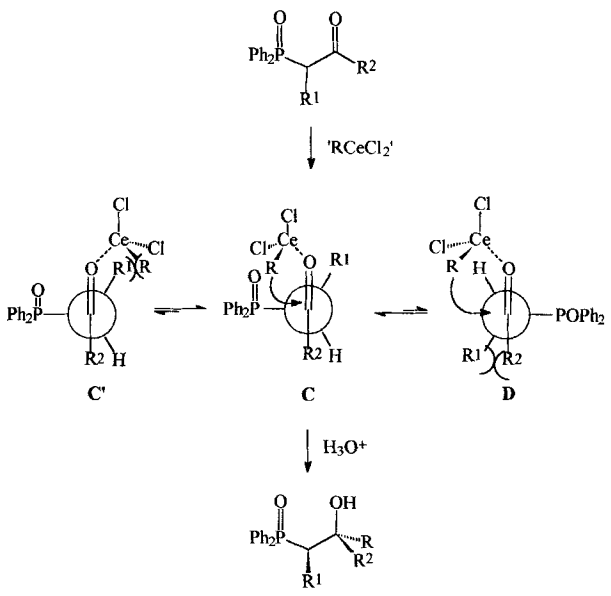
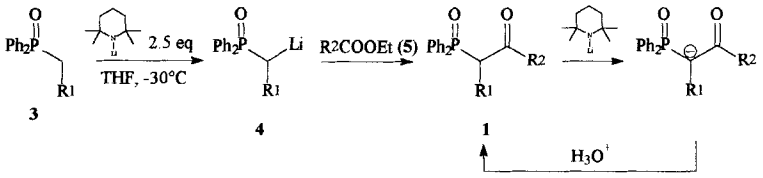
The reduction of β-ketophosphine oxides has been widely studied under the Luche's conditions or with sodium borohydride in ethanol.[17] As expected under the latter conditions, the reduction affords the *syn* isomer in a mechanism that is not chelation-controlled; however, the stereoselectivity is much lower than that reported in this paper, owing to the much higher temperature employed. Under the Luche's conditions ($CeCl_3$/$NaBH_4$/ethanol), the presence of cerium shifts the stereoselectivity towards the *anti* diastereomer, but the trend with varying bulkiness of the R^1 groups is similar to that observed under our conditions. Thus, the *syn* isomer prevails with unbranched R^1 alkyl group and the *anti* isomer with branched R^1 (e.g. the reduction of **1ab** and **1cd** led to *syn*/*anti* ratios of 70/30 and 4/96, respectively,[14c, 17] vs. 98/2 and 20/80 observed in the present work). In our opinion, in contrast to the interpretation of the authors, the reaction under the Luche's conditions also proceeds through a nonchelation-controlled mechanism. The higher proportion of *anti* isomer in the case of **1ab** can be easily accounted for, since the *syn*/*anti* ratio can be influenced by the temperature, the polarity of the solvent and the size of the Lewis acid.[24] It is improbable that the reaction proceeds with a different mechanism in a very polar and coordinating solvent such as ethanol.



Scheme 6.



Scheme 7. Synthesis of α-alkyl-β-ketophosphine oxides.

It should be noted that the addition of organocerium compounds to β-ketophosphine oxides follows the opposite stereochemical course to the present one. We previously attributed these results to a chelation-controlled mechanism.[12] The reluctance of the cerium atom to give a chelated, six-membered transition state, demonstrated by the present work, casts doubt on this interpretation. Based on an open-chain mechanism or simple Lewis acid catalysis, a convincing explanation for the experimental results can be given. Assuming a coordination of the cerium to the oxygen atom of the carbonyl moiety, the alkyl group bound to the cerium atom must attack the carbonyl atom from the Ph_2PO side to minimise the steric repulsions with the R^1 group, that is, conformation **C** should prevail over **C′** (Scheme 6). Alternatively, the alkyl transfer should occur in the less populated conformation **D** in which the small hydrogen atom is closest to the incoming alkyl group. In both cases, the product with *syn* relationship between the incoming alkyl group R and the Ph_2PO group is obtained (Scheme 6).

Synthesis of α-alkyl-β-ketophosphine oxides: There are various methods to prepare α-alkyl-β-ketophosphine oxides. Direct alkylation of the monoanion of unsubstituted β-ketophosphine oxides with alkyl iodides suffers from the drawbacks that the reaction only proceeds smoothly with short alkyl chains (R^1 = Me, Et) or highly reactive derivatives (e.g. benzyl bromides), and that O-alkylation can compete.[25]

It is more convenient to prepare these compounds from the reaction of lithium derivatives of alkyldiphenylphosphine oxides **3** with the appropriate ester **5** (Scheme 7). However, in the previously reported procedure,[26] 2 equiv of **4**, produced by the metallation of **3** with a slight excess of BuLi (1.2 equiv), are required for 1 equiv of ester **5**, because 1 equiv of **4** is consumed in the irreversible abstraction of the very acidic α proton of the α-alkyl-β-ketophosphine oxide **1**. Under these conditions, the nucleophilic BuLi cannot be used in large excess, since it can add to the ester **5**. The fast enolization of ketone **1** prevents it from undergoing a further nucleophilic addition of **4**, but serious difficulties arise in the separation of **1** and **3**.

We modified this methodology[20] by simply metallating **3** with 2.5 equiv of a strong nonnucleophilic base, such as lithium tetramethylpiperidide (LiTMP). Its presence does not interfere with the ester and **1** can be deprotonated or **3** re-metallated by the excess of LiTMP, so that α-alkyl-β-ketophosphine oxides **1** are obtained in high yields based on **3** (Scheme 7). This procedure has proved to be very efficient in preparing a large variety of α-alkyl-β-ketophosphine oxides (Table 4), but completely fails when R^1 is a branched alkyl substituent.

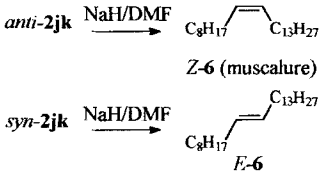
Table 4. Synthesis of β-ketophosphine oxides **1** from the reaction of the anions derived from alkylphosphine oxides **3** with esters **5** in THF at −78 °C.

Entry	3	R^1	5	R^2	Product	Yield (%) [a]
1	**3a**	Me	**5a**	Me	**1aa**	75
2	**3a**	Me	**5b**	Ph	**1ab**	88 [b]
3	**3a**	Me	**5c**	c-C_6H_{11}	**1ac**	87 [b]
4	**3c**	c-C_6H_{11}	**5d**	Pr	**1cd**	n.r. [c]
5	**3d**	Pr	**5c**	c-C_6H_{11}	**1dc**	88
6	**3d**	Pr	**5e**	Bu	**1de**	77 [b]
7	**3d**	Pr	**5f**	-≡-Ph	**1df**	79 [b]
8	**3g**	CH_2Ph	**5a**	Me	**1ga**	90 [b]
9	**3g**	CH_2Ph	**5b**	Ph	**1gb**	90 [b]
10	**3g**	CH_2Ph	**5f**	-≡-Ph	**1gf**	75 [b]
11	**3g**	CH_2Ph	**5h**	*i*Pr	**1gh**	85 [b]
12	**3i**	C_5H_{11}	**5e**	Bu	**1ie**	90
13	**3i**	C_5H_{11}	**5h**	*i*Pr	**1ih**	89
14	**3j**	C_8H_{17}	**5k**	$C_{13}H_{27}$	**1jk**	85

[a] Yields of crystallized product from diethyl ether. [b] See ref. [20]. [c] 85% of starting material recovered.

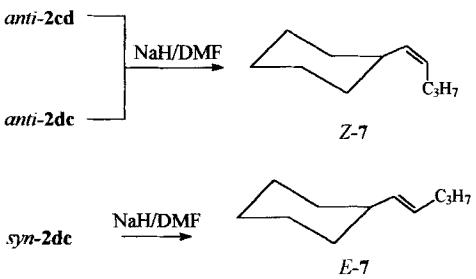
Synthesis of stereodefined disubstituted alkenes: α-Alkyl-β-hydroxyphosphine oxides are key intermediates in the synthesis of stereodefined substituted olefins, since they can undergo facile stereospecific elimination of diphenylphosphinoate anion in basic media.

The procedure proposed by Warren (KH in DMF)[27] for the synthesis of disubstituted alkenes is very efficient in most cases, except when the substituent at the α position is a phenyl[15] or a benzyl group.[20] So we focused our attention on the synthesis of muscalure ((*Z*)-**6**),[28] the pheromone of the domestic fly, from *anti*-**2jk** and of its (*E*) isomer from *syn*-**2jk**. For this purpose, the reaction mixtures obtained from reduction of **1jk** with $TiCl_4/BH_3$/py and $CeCl_3/LiBH_4$, respectively (Tables 1 and 2, entries 18), were submitted, without purification, to elimination according to Warren's procedure. Muscalure was obtained in 95% yield and with 93:7 diastereomeric purity; the corresponding values for (*E*)-**6** were 98% and 92:8 (Scheme 8).



Scheme 8. Synthesis of muscalure and its (*E*) isomer.

We also examined the syntheses of (*E*)- and (*Z*)-1-cyclohexyl-1-pentene, since different strategies can be adopted here (Scheme 9). The (*Z*) isomer can be obtained both from *anti*-**2cd** or *anti*-**2dc** (Table 1, entries 6, 7) in high yields and high geometrical purity. However, the route from compound **2dc** is preferable, since its precursor **1dc** is much more readily available than **1cd**. The (*E*) isomer can be prepared only from *syn*-**2dc**, because the synthesis of *syn*-**2cd** is not stereoselective and the separation from its isomer is very difficult.



Scheme 9. Synthesis of (*Z*)- and (*E*)-1-cyclohexyl-1-pentene.

Conclusion

A general, highly efficient multistep methodology has been described for obtaining both *syn* and *anti* β-hydroxyphosphine oxides, which are key intermediates for the synthesis of stereodefined olefins according to the Warren modification of the Horner procedure. The nature of the Lewis acid was found to be pivotal in determining the outcome of these reactions. Strongly chelating $TiCl_4$ led largely to the *anti* isomer with BH_3/py as reducing agent, while nonchelating $CeCl_3$ gave a high excess of the *syn* isomer with $LiBH_4$ as reducing agent, except in some particular cases (branched α-alkyl substituents, alkynyl ketones).

Moreover, a synthesis of β-ketophosphine oxides has been described, which is more efficient than those previously reported. This combined with the above reductions gives β-hydroxyphosphine oxides in high yield and purity, from readily available and cheap starting materials, in two reaction steps. We wish to underline that this methodology might be applicable to many analogous systems, and studies in this direction are in progress.

In this paper, it has been clearly demonstrated that the cerium trichloride cannot participate in chelation when a six-membered transition state is involved. This does not necessarily apply when larger or smaller rings are involved.

Finally, it should be noted[29] that cerous salts have been employed under the Luche's conditions. Only one report is known in which the anhydrous cerium trichloride is employed together with lithium aluminium hydride in THF. This reaction should be studied in more detail, since this paper demonstrates that it could have wide applications.

Experimental Section

NMR spectra were recorded at 300 MHz on a Varian Gemini 300. ^{1}H NMR shifts are given in ppm from Me_4Si in $CDCl_3$. Coupling constants are given in Hz. Flash chromatography was performed on Merck silica gel (0.040–0.063 mm) with Et_2O as the eluent. THF was dried by refluxing it over sodium until the blue colour of benzophenone ketyl persisted and distilling it into a receiver under nitrogen atmosphere. $CeCl_3 \cdot 7H_2O$ (Aldrich) was dried according to Imamoto's procedure.[16b] CH_2Cl_2 was filtered on alumina before use. Alkyldiphenylphosphine oxides **3** were prepared according to the literature procedure.[15] Products **3a,c,d** are known.[15] Selected spectral data of previously unknown alkyldiphenylphosphine oxides follow.

(2-Phenylethyl)diphenylphosphine oxide (3g): ^{1}H NMR: $\delta = 2.50-2.65$ (m, 2H, PCH_2-CH_2Ph), 2.80–3.00 (m, 2H, PCH_2CH_2Ph), 7.20–7.80 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 32.0$ (CH_2, $^1J_{CP} = 70$), 27.7 (CH_2); M.p. 73±1 °C. $C_{20}H_{19}PO$ (306.3): calcd C 78.42, H 6.25, P 10.11; found C 78.40, H 6.25, P 10.10.

Hexyldiphenylphosphine oxide (3i): ^{1}H NMR: $\delta = 0.84$ (t, 3H, CH_3, $J_{HH} = 7.1$), 1.20–1.30 (m, 4H, CH_2), 1.30–1.45 (m, 2H, CH_2), 1.50–1.70 (m, 2H, CH_2), 2.20–2.35 (m, 2H, CH_2P), 7.40–7.80 (m, 10H, Ph_2PO); ^{13}C NMR: $\delta = 30.8$ (CH_2), 30.77 (CH_2, $^1J_{CP} = 38.7$), 29.0 (CH_2), 22.4 (CH_2), 21.3 (CH_2), 14.0 (CH_3); M.p. 56±1 °C. $C_{18}H_{23}PO$ (286.3): calcd C 75.50, H 8.10, P 10.82; found C 75.40, H 8.10, P 10.85.

Nonyldiphenylphosphine oxide (3j): ^{1}H NMR: $\delta = 0.85$ (t, 3H, CH_3, $J_{HH} = 7.1$), 1.15–1.35 (m, 10H, $5CH_2$), 1.35–1.45 (m, 2H, CH_2), 1.55–1.70 (m, 2H, CH_2), 2.20–2.35 (m, 2H, CH_2P), 7.40–7.90 (m, 10H, Ph_2PO); ^{13}C NMR: $\delta = 31.5$ (CH_2, $^1J_{CP} = 38$), 31.0 (CH_2), 30.8 (CH_2), 30.4 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 22.6 (CH_2, $^2J_{CP} = 11$), 21.7 (CH_2), 14.1 (CH_3); M.p. 58±1 °C. $C_{21}H_{29}PO$ (328.4): calcd C 76.80, H 8.90, P 9.43; found C 76.90, H 8.90, P 9.40.

General procedure for the synthesis of α-alkyl-β-ketophosphine oxides: BuLi (2.5 equiv, solution 1.6 M in hexanes) was added to 2,2,6,6-tetramethylpiperidine (2.5 equiv, solution in THF) at −30 °C. After 30 min **3** (1 equiv, solution in THF) was added, and the mixture turned red immediately. After 1 h the mixture was cooled to −78 °C, and the ester **5** (3 equiv, solution in THF) was added. Two hours later, the reaction was allowed to reach room temperature and then quenched with dilute HCl (10%) and extracted with Et_2O. The

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organic layer was dried over $MgSO_4$, filtered and evaporated, and the product crystallised from Et_2O. Yields of pure products are reported in Table 4. Compounds **1aa**; **1ab**; **1ac**; **1cd**; **1dc** were recognized by comparison with literature data.[15, 17] Selected spectral data of previously unknown α-alkyl-β-ketophosphine oxides follow.

4-Diphenylphosphinoylnonan-5-one (1de): ^{1}H NMR: $\delta = 0.78$ (t, 3H, CH_3, $J_{HH} = 7.5$), 0.84 (t, 3H, CH_3, $J_{HH} = 7.5$), 1.10–1.45 (m, 6H, $3CH_2$), 1.50–1.75 (m, 1H, PCHCH_2), 2.05–2.25 (m, 1H, PCHCH_2), 2.35–2.60 (m, 2H, CH_2C=O), 3.55–3.70 (m, 1H, PCH, $J_{HH} = 3.0$, $J_{HH} = 11.6$, $J_{HP} = 14.4$), 7.40–7.90 (m, 10H, Ph_2P=O); ^{13}C NMR: $\delta = 207.5$ (C=O), 56.8 (CH, $^1J_{CP} = 56$), 43.7 (CH_2), 29.7 (CH_2), 28.9 (CH_2), 25.3 (CH_2), 22.0 (CH_2), 13.8 (CH_3), 13.7 (CH_3); M.p. 118±1 °C. $C_{21}H_{27}PO_2$ (342.4): calcd C 73.66, H 7.95, P 9.05; found C 73.70, H 8.00, P 9.00.

4-Diphenylphosphinoyl-1-phenyl-1-heptyn-3-one (1df): ^{1}H NMR: $\delta = 0.90$ (t, 3H, CH_3, $J_{HH} = 7.3$), 1.30–1.60 (m, 2H, CH_2CH_3), 1.80–1.95 (m, 1H, $CH_2CH_2CH_3$), 2.25–2.45 (m, 1H, $CH_2CH_2CH_3$), 3.83 (m, 1H, CHP, $J_{HH} = 3.0$, $J_{HH} = 11.7$, $J_{HP} = 13.0$), 7.25–7.90 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 184.0$ (C=O), 94.3 (C), 88.4 (C), 58.7 (CH, $^1J_{CP} = 56.1$), 28.7 (CH_2), 22.0 (CH_2, $^2J_{CP} = 12.2$), 13.8 (CH_3); M.p. 160±1 °C. $C_{25}H_{23}PO_2$ (386.4): calcd C 77.70, H 6.00, P 8.02; found C 77.60, H 6.00, P 8.00.

2-Diphenylphosphinoyl-1-phenylbutan-3-one (1ga): ^{1}H NMR: $\delta = 2.05$ (s, 3H, CH_3), 2.95–3.10 (m, 1H, CH_2Ph, $J_{HH} = 14.4$, $J_{HH} = 3.2$, $J_{HP} = 10.2$), 3.30–3.50 (m, 1H, CH_2Ph, $J_{HH} = 14.4$, $J_{HH} = 11.8$, $J_{HP} = 5.5$), 3.90–4.05 (m, 1H, CH-P, $J_{HH} = 3.2$, $J_{HH} = 11.8$, $J_{HP} = 12.2$), 7.00–7.92 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 204.2$ (C=O), 58.8 (CH, $^1J_{CP} = 55$), 32.5 (CH_2), 31.9 (CH_3); M.p. 167±1 °C. $C_{22}H_{21}PO_2$ (348.4): calcd C 75.85, H 6.08, P 8.89; found C 75.80, H 6.10, P 8.85.

1,3-Diphenyl-2-Diphenylphosphinoylpropan-1-one (1gb): ^{1}H NMR: $\delta = 3.15$–3.35 (m, 1H, CH_2Ph, $J_{HH} = 13.8$, $J_{HH} = 2.6$, $J_{HP} = 10.3$), 3.50–3.70 (m, 1H, CH_2Ph, $J_{HH} = 13.8$, $J_{HH} = 11.4$, $J_{HP} = 4.8$), 4.75–4.90 (m, 1H, PCHCH_2Ph, $J_{HH} = 2.6$, $J_{HH} = 11.4$, $J_{HP} = 15.7$), 7.10–8.00 (m, 20H, 4Ph); ^{13}C NMR: $\delta = 197.7$ (C=O), 54.4 (CH, $^1J_{CP} = 54.5$), 34.2 (CH_2); M.p. 168±1 °C. $C_{27}H_{23}PO_2$ (410.5): calcd C 79.01, H 5.65, P 7.55; found C 79.10, H 5.65, P 7.60.

1,5-Diphenyl-4-diphenylphosphinoyl-1-pentyn-3-one (1gf): ^{1}H NMR: $\delta = 3.15$–3.40 (m, 1H, CH_2Ph, $J_{HH} = 14.7$, $J_{HH} = 2.8$, $J_{HP} = 10.1$), 3.55–3.75 (m, 1H, CH_2Ph, $J_{HH} = 14.7$, $J_{HH} = 11.5$, $J_{HP} = 4.9$), 4.10–4. 30 (m, 1H, CHPO, $J_{HH} = 11.5$, $J_{HH} = 2.8$, $J_{HP} = 12.7$), 7.10–8.00 (m, 20H, 4Ph); ^{13}C NMR: $\delta = 182.8$ (C=O), 94.9 (C), 88.6 (C), 60.5 (CH, $^1J_{CP} = 53.2$), 32.3 (CH_2); M.p. 169±1 °C. $C_{29}H_{23}PO_2$ (434.5): calcd C 80.17, H 5.34, P 7.13; found C 80.10, H 5.35, P 7.10.

2-Diphenylphosphinoyl-4-methyl-1-phenylpentan-3-one (1gh): ^{1}H NMR: $\delta = 0.36$ (d, 3H, CH(CH_3)$_2$, $J_{HH} = 7.3$), 0.60 (d, 3H, CH(CH_3)$_2$, $J_{HH} = 6.5$), 2.05–2.25 (m, 1H, CH(CH$_3$)$_2$), 2.90–3.10 (m, 1H, CH_2Ph, $J_{HH} = 13.6$, $J_{HH} = 2.2$, $J_{HP} = 12.1$), 3.24–3.42 (m, 1H, CH_2Ph, $J_{HH} = 13.6$, $J_{HH} = 11.6$, $J_{HP} = 4.6$), 4.05–4.22 (m, 1H, CHPO, $J_{HH} = 2.2$, $J_{HH} = 11.6$, $J_{HP} = 16.0$), 7.05–8.02 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 210.2$ (C=O), 58.5 (CH, $^1J_{CP} = 53$), 43.5 (CH), 33.9 (CH_2), 17.4 (CH_3), 17.0 (CH_3); M.p. 147±1 °C. $C_{25}H_{25}PO_2$ (388.4): calcd C 77.30, H 6.49, P 7.97; found C 77.40, H 6.45, P 8.00.

6-Diphenylphosphinoylundecan-5-one (1ie): ^{1}H NMR: $\delta = 0.78$ (t, 3H, CH_3, $J_{HH} = 7.3$), 0.81 (t, 3H, CH_3, $J_{HH} = 7.4$); 1.05–1.45 (m, 10H, $5CH_2$), 1.55–1.65 (m, 1H, CHCH_2(CH$_2$)$_3$CH$_3$), 2.05–2.15 (m, 1H, CHCH_2(CH$_2$)$_3$CH$_3$), 2.35–2.55 (m, 2H, CH_2C=O), 3.55–3.65 (m, 1H, PCH, $J_{HH} = 3.0$, $J_{HH} = 11.6$, $J_{HP} = 13.0$), 7.4–7.9 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 207.5$ (C=O, $^2J_{CP} = 3$), 57.0 (CH, $^1J_{CP} = 57$), 43.5(CH_2), 31.2(CH_2), 28.4 (CH_2, $^2J_{CP} = 13$), 26.7 (CH_2), 25.1 (CH_2), 22.2 (CH_2), 21.9 (CH_2), 13.8 (CH_3), 13.7 (CH_3); M.p. 103±1 °C. $C_{23}H_{31}PO_2$ (370.5): calcd C 74.57, H 8.43, P 8.36; found C 73.50, H 8.40, P 8.40.

4-Diphenylphosphinoyl-2-methylnonan-3-one (1ih): ^{1}H NMR: $\delta = 0.76$ (d, 3H, CH(CH_3)$_2$, $J_{HH} = 6.6$), 0.77 (t, 3H, CH_3, $J_{HH} = 7.2$), 0.92 (d, 3H, CH(CH_3)$_2$, $J_{HH} = 7.1$), 1.05–1.30 (m, 6H, $CH_2(CH_2)_3CH_3$), 1.55–1.70 (m, 1H, PCHCH_2(CH$_2$)$_3$CH$_3$), 2.00–2.15 (m, 1H, CHCH_2(CH$_2$)$_3$CH$_3$), 2.50–2.60 (m, 1H, CH(CH$_3$)$_2$), 3.70–3.85 (m, 1H, PCH, $J_{HH} = 2.7$, $J_{HH} = 11.3$, $J_{HP} = 16.8$), 7.45–7.90 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 211.5$–211.44 (C=O, $^2J_{CP} = 3$), 56.0 (CH, $^1J_{CP} = 55$), 42.4 (CH), 31.6 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 27.5 (CH_2), 22.4 (CH_2), 18.6 (CH_3), 17.4 (CH_3), 14.0 (CH_3); M.p. 132±1 °C. $C_{22}H_{29}PO_2$ (356.5): calcd C 74.13, H 8.20, P 8.69; found C 74.20, H 8.20, P 8.70.

9-Diphenylphosphinoyltricosan-10-one (1jk): ^{1}H NMR: $\delta = 0.83$ (t, 3H, CH_3, $J_{HH} = 6.9$), 0.86 (t, 3H, CH_3, $J_{HH} = 6.5$), 1.05–1.40 (m, 34H, $(CH_2)_6CH_3$, $(CH_2)_{11}CH_3$), 1.60–1.75 (m, 1H, CHCH_2(CH$_2$)$_6$CH$_3$), 2.05–2.25 (m, 1H, CHCH_2(CH$_2$)$_6$CH$_3$), 2.35–2.55 (m, 2H, COCH_2-(CH$_2$)$_{11}$CH$_3$), 3.50–3.65 (m, 1H, PCH, $J_{HH} = 3.0$, $J_{HH} = 11.6$, $J_{HP} = 13.4$), 7.40–7.90 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 207.5$ (C=O), 57.1 (CH, $^1J_{CP} = 56.5$), 43.7 (CH_2), 31.8 (CH_2, $^2J_{CP} = 13.4$), 14.1 (CH_3), 14.0 (CH_3); M.p. 62±1 °C. $C_{35}H_{55}PO_2$ (538.8): calcd C 78.02, H 10.29, P 5.75; found C 78.00, H 10.25, P 5.75.

Synthesis of *anti*-α-alkyl-β-hydroxyphosphine oxides 2 from reduction of α-alkyl-β-ketophosphine oxides 1 with metallic hydrides in presence of $TiCl_4$.

$TiCl_4$/$LiBH_4$ method—general procedure: $TiCl_4$ (1.3 mmol, solution 1 M in CH_2Cl_2) was added to a solution of **1** (1 mmol) in CH_2Cl_2 (5 mL) at −30 °C. The reaction mixture turned orange. After 1 h the mixture was cooled to −78 °C and $LiBH_4$ (1.5 mmol, solution 2 M in THF) was added. Two hours later, the reaction was allowed to warm to room temperature. It was then quenched with dilute HCl (10%) and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered and evaporated giving *anti*-α-alkyl-β-hydroxyphosphine oxides **2** contaminated only by a minor amount of the *syn* diastereoisomer. Diastereomeric purity, determined by NMR analysis, and yields are reported in Table 1.

$TiCl_4$/BH_3/py method—general procedure: $TiCl_4$ (1.3 mmol, solution 1 M in CH_2Cl_2) was added to a solution of **1** (1 mmol) in CH_2Cl_2 (5 mL) at −30 °C. The reaction mixture turned orange. After 1 h the mixture was cooled to −78 °C and BH_3/py (1.5 mmol) was added. Two hours later, the reaction was allowed to warm to room temperature. It was then quenched with dilute HCl (10%), extracted with Et_2O, dried over $MgSO_4$, filtered and evaporated. The crude product was submitted to flash chromatography on a short silica-gel column (Et_2O as eluent) to give *anti*-α-alkyl-β-hydroxyphosphine oxides **2** contaminated only by a minor amount of the *syn* diastereoisomer. Diastereomeric purity, determined by NMR analysis, and yields are reported in Table 1. Elemental analyses of unknown products were performed on diastereomeric mixtures.

Compounds *anti*-**2aa**,[15] *anti*-**2ab**,[30] and *anti*-**2ac**[15] are known and were recognized by comparison with literature data. We report the ^{13}C NMR data here, since this is very useful for stereochemical assignment.

(*R,*S**)-3-Diphenylphosphinoylbutan-2-ol** (*anti*-**2aa**): ^{13}C NMR: $\delta = 64.75$ (CH, $^2J_{CP} = 3.2$), 36.9 (CH, $^1J_{CP} = 70.5$), 20.6 (CH_3, $^2J_{CP} = 13.2$), 5.2 (CH_3).

(*R,*S**)-2-Diphenylphosphinoyl-1-phenylpropan-1-ol** (*anti*-**2ab**): ^{13}C NMR: $\delta = 70.8$ (CH, $^2J_{CP} = 3.7$), 38.5 (CH, $^1J_{CP} = 68$), 5.4 (CH_3).

(*R,*S**)-2-Diphenylphosphinoyl-1-cyclohexylpropan-1-ol** (*anti*-**2ac**): ^{13}C NMR: $\delta = 73.7$ (CH, $^2J_{CP} = 3.6$), 40.2 (CH, $^3J_{CP} = 11.5$), 32.8 (CH, $^1J_{CP} = 71$), 29.9 (CH_2), 28.7 (CH_2), 26.4 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 5.6 (CH_3, $^2J_{CP} = 5.4$).

(*R,*S**)-1-Cyclohexyl-1-diphenylphosphinoylpentan-2-ol** (*anti*-**2cd**): ^{1}H NMR: $\delta = 0.74$ (t, 3H, CH_3, $J_{HH} = 7.2$), 0.9–2.1 (m, 15H, 7-CH_2 + 1-CH), 2.17 (brd, 1H, CHPO, $J_{HP} = 9.8$), 3.95–4.10 (m, 1H, CHOH, $J_{HP} = 13$, $J_{HH} = 7.5$), 4.20 (d, 1H, OH, $J_{HH} = 1.5$), 7.30–7.85 (m, 10H, 2Ph). ^{13}C NMR: $\delta = 71.3$ (CH, $^2J_{CP} = 3.1$), 47.2 (CH, $^1J_{CP} = 68$), 37.5 (CH_2, $^3J_{CP} = 12.3$), 36.6 (CH), 34.5 (CH_2), 33.5 (CH_2), 33.4 (CH_2), 27.4 (CH_2), 26.1 (CH_2), 19.7 (CH_2), 14.0 (CH_3). $C_{23}H_{31}PO_2$ (370.5): calcd C 74.57, H 8.43, P 8.36; found C 74.50, H 8.40, P 8.40.

(*R,*S**)-1-Cyclohexyl-2-diphenylphosphinoylpentan-1-ol** (*anti*-**2dc**): ^{1}H NMR: $\delta = 0.72$ (t, 3H, $(CH_2)_2CH_3$, $J_{HH} = 7.0$), 0.80–1.95 (m, 14H, 7-CH_2), 2.05–2.20 (m, 1H, CH-Chx), 2.35–2.45 (m, 1H, CHPO), 3.55–3.70 (brt, 1H, CHOH, $J_{HP} = 10.2$, $J_{HH} = 10.1$), 4.27 (brs, 1H, OH), 7.40–7.95 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 74.3$ (CH, $^2J_{CP} = 12.2$), 40.3 (CH, $^3J_{CP} = 12.2$), 38.0 (CH, $^1J_{CP} = 69.6$), 29.6 (CH_2), 29.1 (CH_2), 26.1 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 23.6 (CH_2), 23.5 (CH_2, $^2J_{CP} = 6.1$), 14.3 (CH_3). $C_{23}H_{31}PO_2$ (370.5): calcd C 74.57, H 8.43, P 8.36; found C 74.55, H 8.45, P 8.35.

(*R,*S**)-4-Diphenylphosphinoylnonan-5-ol** (*anti*-**2de**): ^{1}H NMR: $\delta = 0.69$ (t, 3H, CH_3, $J_{HH} = 7.3$), 0.83 (t, 3H, CH_3, $J_{HH} = 6.8$), 1.00–1.75 (m, 9H, CH_2), 1.75–1.95 (m, 1H, CH_2), 2.15–2.25 (m, 1H, CH-P), 3.95–4.05 (m, 1H, CH-OH), 4.25 (brs, 1H, OH), 7.30–7.95 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 69.9$ (CH, $^2J_{CP} = 3.6$), 41.1 (CH, $^1J_{CP} = 68.9$), 34.7 (CH_2, $^2J_{CP} = 13$), 28.2 (CH_2), 23.9 (CH_2, $^3J_{CP} = 7.2$), 23.7 (CH_2), 22.5 (CH_2), 14.2 (CH_2), 14.0 (CH_3). $C_{21}H_{29}PO_2$ (344.4): calcd C 73.23, H 8.49, P 8.99; found C 73.20, H 8.45, P 9.00.

(*R,*S**)-4-Diphenylphosphinoyl-1-phenyl-1-heptyn-3-ol** (*anti*-**2df**): ^{1}H NMR: $\delta = 0.85$ (t, 3H, CH_3, $J_{HH} = 7.1$), 1.25–1.40 (m, 1H, CH_2CH_3), 1.50–1.65 (m, 1H, CH_2CH_3), 1.65–1.80 (m, 1H, $CH_2CH_2CH_3$), 1.90–2.05 (m, 1H, $CH_2CH_2CH_3$), 2.75–2.85 (m, 1H, CHPO, $J_{HH} = 2.8$), 5.05–5.20 (m, 1H, CHOH, $J_{HP} = 17$, $J_{HOH} = 5.2$, $J_{HH} = 2.8$), 7.25–7.90 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 88.2$ (C, $^3J_{CP} = 14$), 85.7 (C), 62.5 (CH), 43.4 (CH, $^1J_{CP} = 67.6$), 27.1 (CH_2), 22.27 (CH_2, $^2J_{CP} = 7.3$), 14.1 (CH_3). $C_{25}H_{25}PO_2$ (388.4): calcd C 77.29, H 6.49, P 7.98; found C 77.20, H 6.45, P 8.00.

(*R,*S**)-2-Diphenylphosphinoyl-1-phenylbutan-3-ol** (*anti*-**2ga**): ^{1}H NMR: $\delta = 1.20$ (d, 3H, CH_3, $J_{HH} = 6.3$), 2.60–2.70 (m, 1H, PCHCH_2Ph), 2.90–3.10 (m, 1H, PCHCH_2Ph, $J_{HP} = 4.1$, $J_{HH} = 15.3$, $J_{HH} = 15.4$), 3.20–3.35 (m, 1H, PCHCH_2Ph, $J_{HP} = 13.7$, $J_{HH} = 15.4$, $J_{HH} = 5.8$), 4.25–4.40 (m, 1H, CH-OH, $J_{HP} = 12.3$, $J_{HCH3} = 6.3$, $J_{HOH} < 1$, $J_{HH} < 1$), 4.4 (brs, 1H, OH), 6.80–7.95 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 65.9$(CH), 45.0 (CH, $^1J_{CP} = 68$), 27.7 (CH_2), 21.8 (CH_3, $^2J_{CP} = 13$). $C_{22}H_{23}PO_2$ (350.4): calcd C 75.41, H 6.62, P 8.84; found C 75.45, H 6.60, P 8.80.

(*R,*S**)-1,3-Diphenyl-2-diphenylphosphinoylpropan-1-ol** (*anti*-**2gb**): ^{1}H NMR: $\delta = 2.70$–3.20 (m, 3H, PCHCH_2Ph), 4.96 (brs, 1H, OH), 5.63 (d, 1H, CHOH, $J_{HP} = 9.7$), 6.06 (d, 2H, $J_{HH} = 7.0$) and 6.65–8.05 (m, 18H, 4Ph); ^{13}C NMR: $\delta = 71.2$ (CH), 47.5 (CH, $^1J_{CP} = 66.2$), 26.6 (CH_2). $C_{27}H_{25}PO_2$ (412.5): calcd C 78.62, H 6.11, P 7.51; found C 78.70, H 6.10, P 7.50.

(*R,*S**)-1,5-Diphenyl-4-diphenylphosphinoyl-1-pentyn-3-ol** (*anti*-**2gf**): ^{1}H NMR: $\delta = 2.90$–3.25 (m, 3H, $CHCH_2$Ph), 4.90–5.00 (m, 1H, CHOH, $J_{HOH} = 5.8$, $J_{HH} = 2.2$, $J_{HP} = 18$); 5.4 (d, 1H, OH, $J_{HOH} = 5.8$), 6.80–7.90 (m, 20H, 4Ph); ^{13}C NMR: $\delta = 88.1$ (C, $^3J_{CP} = 13$), 86.7 (C), 62.7 (CH), 45.7 (CH, $^1J_{CP} = 67$), 31.5 (CH_2). $C_{29}H_{25}PO_2$ (436.5): calcd C 79.80, H 5.77, P 7.10; found C 79.90, H 5.75, P 7.10.

(*R,*S**)-2-Diphenylphosphinoyl-4-methyl-1-phenylpentan-3-ol** (*anti*-**2gh**): ^{1}H NMR: $\delta = 0.68$ (d, 3H, $CH(CH_3)_2$, $J_{HH} = 6.7$), 0.94 (d, 3H, $CH(CH_3)_2$, $J_{HH} = 6.5$), 1.75–1.90 35 (m, 1H, $CH(CH_3)_2$), 2.80–3.30 (m, 3H, CH_2Ph and CHPO), 3.60 (brt, 1H, CHOH, $J_{HH} = 10.6$, $J_{HP} = 10.6$), 4.4 (brs, 1H, OH), 6.75–7.90 (m, 15H, 3Ph); ^{13}C NMR: $\delta = 76.1$ (CH), 40.9 (CH, $^1J_{CP} = 68.5$), 31.1 (CH, $^3J_{CP} = 12.6$), 27.4 (CH_2), 19.8 (CH_3), 19.1 (CH_3). $C_{25}H_{27}PO_2$ (390.4): calcd C 76.90, H 6.97, P 7.93; found C 76.85, H 7.00, P 8.00

(*R,*S**)-6-Diphenylphosphinoylundecan-5-ol** (*anti*-**2ie**): ^{1}H NMR: $\delta = 0.73$ (t, 3H, CH_3, $J_{HH} = 7.0$), 0.86 (t, 3H, CH_3, $J_{HH} = 7.1$), 0.95–1.75 (m, 13H, CH_2), 1.80–2.00 (m, 1H, PCHCH_2(CH_2)$_3$CH_3); 2.15–2.20 (m, 1H, PCH), 3.95–4.10 (m, 1H, CHOH), 4.25 (s, 1H, OH), 7.40–7.90 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 69.9$ (CH), 41.3 (CH, $^1J_{CP} = 69$), 34.6 (CH_2, $^2J_{CP} = 13$), 31.7 (CH_2), 30.3 (CH_2, $^2J_{CP} = 16.5$), 28.1 (CH_2), 22.5 (CH_2), 22.0 (CH_2), 21.4 (CH_2), 13.9 (CH_3), 13.7 (CH_3). $C_{23}H_{33}PO_2$ (372.5): calcd C 74.16, H 8.93, P 8.32; found C 74.20, H 8.90, P 8.30.

(*R,*S**)-4-Diphenylphosphinoyl-2-methylnonan-3-ol** (*anti*-**2ih**): ^{1}H NMR: $\delta = 0.60$ (t, 3H, $(CH_2)_4CH_3$, $J_{HH} = 6.9$), 0.74 (d, 3H, $CH(CH_3)_2$, $J_{HH} = 6.7$), 0.88 (d, 3H, $CH(CH_3)_2$, $J_{HH} = 7.6$), 0.85–1.20 (m, 6H, $3CH_2$), 1.45–1.65 (m, 1H, $CH(CH_3)_2$), 1.70–1.90 (m, 2H, CH_2), 2.25–2.35 (m, 1H, PCH), 3.40–3.55 (m, 1H, CHOH, $J_{HH} = 8.0$, $J_{HP} = 10.8$), 4.3 (brs, 1H, OH), 7.35–7.80 (m, 10H, 2Ph); ^{13}C NMR: $\delta = 75.9$ (CH, $^2J_{CP} = 3.5$), 38.8 (CH, $^1J_{CP} = 70$), 31.9 (CH_2), 31.2 (CH, $^3J_{CP} = 13$), 30.1 (CH_2, $^3J_{CP} = 5$), 22.0 (CH_2), 21.4(CH_2), 19.6 (CH_3), 19.2 (CH_3), 13.8 (CH_3). $C_{22}H_{31}PO_2$ (358.5): calcd C 73.72, H 8.72, P 8.64; found C 73.75, H 8.75, P 8.60.

(*R,*S**)-9-Diphenylphosphinoyltricosan-10-ol** (*anti*-**2jk**): ^{1}H NMR: $\delta = 0.83$ (t, 3H, CH_3, $J_{HH} = 7$), 0.87 (t, 3H, CH_3, $J_{HH} = 7$), 1.05–1.90 (m, 38H, $(CH_2)_7CH_3$, $(CH_2)_{12}CH_3$), 2.10–2.20 (m, 1H, PCH), 3.95–4.05 (m, 1H, CHOH), 4.3 (brs, 1H, OH), 7.40–7.90 (m, 10H, Ph); ^{13}C NMR: $\delta = 69.9$ (CH, $^2J_{CP} = 4$), 41.3 (CH, $^1J_{CP} = 69$), 34.9 (CH_2, $^2J_{CP} = 13$), 31.8 (CH_2, $^2J_{CP} = 7$). $C_{35}H_{57}PO_2$ (540.8): calcd C 77.73, H 10.62, P 5.73; found C 77.70, H 10.65, P 5.75.

Synthesis of *syn*-α-alkyl-β-hydroxyphosphine oxides 2 from reduction of α-alkyl-β-ketophosphine oxides with metallic hydrides in presence of $CeCl_3$.

$CeCl_3$/BH_3/py in CH_2Cl_2: Dried $CeCl_3$ (1.3 mmol) was suspended in 5 mL of CH_2Cl_2 and left to stir overnight at room temperature. At this temperature a solution of **1aa** (1 mmol) in 5 mL of CH_2Cl_2 was added and left to stir until the mixture became opalescent. After 1 h the mixture was cooled to −78 °C and BH_3/py (1.5 mmol) was added. Four hours later, the reaction was allowed to warm to room temperature. It was then quenched with dilute HCl (10%) and extracted with Et_2O. Starting material **1aa** was almost quantitatively recovered.

$CeCl_3$/$LiBH_4$ in CH_2Cl_2—general procedure: Dried $CeCl_3$ (1.3 mmol) was suspended in 5 mL of CH_2Cl_2 and left to stir overnight at room temperature. At this temperature a solution of **1** (1 mmol) in 5 mL of CH_2Cl_2 was added and left to stir until the mixture became opalescent. Then it was cooled to −78 °C and $LiBH_4$ (3 mmol, solution 2 M in THF) was added. Two hours later, the reaction was allowed to reach room temperature and then quenched with dilute HCl (10%) and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered and evaporated to give *syn*-α-alkyl-β-hydroxyphosphine oxides **2** contaminated only by a minor amount of the *anti* diastereoisomer. Diastereomeric purity was determined by NMR analysis. This procedure was applied only to α-alkyl-β-ketophosphine oxides **1aa,de,ga.** Diastereomeric purity of *syn*-**2aa,de,ga** and yields are reported in Table 2.

$CeCl_3$/$LiBH_4$ in THF—general procedure: Dried $CeCl_3$ (1.3 mmol) was suspended in 5 mL of THF and left to stir overnight at room temperature. At this temperature a solution of **1** (1 mmol) in 10 mL of THF was added and left to stir until the mixture became clear. Then it was cooled to −78 °C and $LiBH_4$ (3 mmol, solution 2 M in THF) was added. Two hours later, the reaction was allowed to reach room temperature and then quenched with dilute HCl (10%) and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered and evaporated to give *syn*-α-alkyl-β-hydroxyphosphine oxides **2** contaminated only by a minor amount of the *anti*-diastereoisomer except in the reaction of **1cd,df,gf**. Our attempts to separate the two diastereomers of **2cd** and **2df** were unsuccessful. Diastereomeric purity, determined by NMR analysis, and yields are reported in Table 2. Elemental analyses of unknown products were performed on diastereomeric mixtures.

Compounds *syn*-**2aa**,[15] *syn*-**2ab**,[30] and *syn*-**2ac**[15] are known and were recognized by comparison with literature data. We report the ^{13}C NMR data here, since this is very useful for stereochemical assignment.

(*R,*R**)-3-Diphenylphosphinoylbutan-2-ol** (*syn*-**2aa**): ^{13}C NMR: $\delta = 67.3$ (CH), 39.0 (CH, $^1J_{CP} = 69.9$), 20.7 (CH_3, $^2J_{CP} = 4.9$), 9.9 (CH_3).

(*R,*R**)-2-Diphenylphosphinoyl-1-phenylpropan-1-ol** (*syn*-**2ab**); ^{13}C NMR: $\delta = 75.8$ (CH, $^2J_{CP} = 3.6$), 39.4 (CH, $^1J_{CP} = 68$), 13.1 (CH_3).

(*R,*R**)-2-Diphenylphosphinoyl-1-cyclohexylpropan-1-ol** (*syn*-**2ac**): ^{13}C NMR: $\delta = 76.3$ (CH, $^2J_{CP} = 5.0$), 40.2 (CH, $^3J_{CP} = 9.0$), 34.7 (CH, $^1J_{CP} = 70$), 30.4 (CH_2), 26.7 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 25.2 (CH_2), 12.7 (CH_3).

(*R,*R**)-1-Cyclohexyl-1-diphenylphosphinoylpentan-2-ol** (*syn*-**2cd**): The reaction of **1cd** with $CeCl_3$/$LiBH_4$ gave a 2:8 mixture of *syn*-**2cd** and *anti*-**2cd**. Our attempts to separate the two diastereomers were unsuccessful. NMR signals that do not overlap are reported. ^{1}H NMR: $\delta = 0.69$ (t, 3H, CH_3, $J_{HH} = 7.3$). ^{13}C NMR: $\delta = 71.1$ (CH), 47.6 (CH, $^1J_{CP} = 68$), 41.2 (CH_2, $^3J_{CP} = 3.5$), 38.8 (CH), 29.7 (CH_2), 13.8 (CH_3). $C_{23}H_{31}PO_2$ (370.5): calcd C 74.57, H 8.43, P 8.36; found C 74.55, H 8.45, P 8.35.

(*R,*R**)-1-Cyclohexyl-2-diphenylphosphinoylpentan-1-ol** (*syn*-**2dc**): ^{1}H NMR: $\delta = 0.72$ (t, 3H, $(CH_2)_2CH_3$, $J_{HH} = 7.0$), 0.60–1.90 (m, 14H, $7CH_2$), 1.95–2.05 (m, 1H, CH-Chx), 2.55–2.65 (m, 1H, CHPO), 3.50–3.70 (m, 1H, CHOH, $J_{HP} = 21.8$, $J_{HOH} = 8.0$, $J_{HH} = 4.6$, $J_{HH} = 7.7$), 4.37 (d, 1H, OH, $J_{HOH} = 8.0$), 7.40–7.95 (10H, 2Ph); ^{13}C NMR: $\delta = 77.15$ (CH, $^2J_{CP} = 5.3$), 41.66 (CH, $^3J_{CP} = 4.6$), 38.7 (CH, $^1J_{CP} = 68.5$), 30.4(CH_2), 29.4 (CH_2), 28.4 (CH_2), 26.3 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 21.3 (CH_2,

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$^2J_{CP}$ = 10.5), 13.9 (CH_3). $C_{23}H_{31}PO_2$ (370.5): calcd C 74.57, H 8.43, P 8.36; found C 74.60, H 8.45, P 8.30.

(*R,*R**)-6-Diphenylphosphinoyl-nonan-5-ol** (*syn*-**2de**): ^{1}H NMR: δ = 0.75 (t, 3H, CH_3, J_{HH} = 6.9), 0.77 (t, 3H, CH_3, J_{HH} = 6.9), 1.05–1.75 (m, 10H, 5CH_2), 2.35–2.50 (m, 1H, C*H*P), 3.80–4.00 (m, 1H, C*H*OH), 4.25 (br s, 1H, OH), 7.40–7.85 (m, 10H, 2Ph); ^{13}C NMR: δ = 72.4 (CH, $^2J_{CP}$ = 3.3), 42.5 (CH, $^1J_{CP}$ = 68), 36.3 (CH_2, $^2J_{CP}$ = 6), 28.6 (CH_2), 28.4 (CH_2), 22.4 (CH_2), 21.82 (CH_2, $^3J_{CP}$ = 10), 14.0 (CH_3), 13.9 (CH_3). $C_{21}H_{29}PO_2$ (344.4): calcd C 73.23, H 8.49, P 8.99; found C 73.20, H 8.50, P 9.00.

(*R,*R**)-4-Diphenylphosphinoyl-1-phenyl-1-heptyn-3-ol** (*syn*-**2df**)**:** The reaction of **1df** with $CeCl_3$/$LiBH_4$ gave a 1:1 mixture of *syn*-**2df** and *anti*-**2df.** Our attempts to separate the two diastereomers were unsuccessful. The ^{1}H NMR signals of the two products almost completely overlap. ^{13}C NMR signals are distinguishable: δ = 88.95 (C, $^3J_{CP}$ = 7.9), 86.6 (C), 62.5 (CH, $^2J_{CP}$ = 3.2), 42.6 (CH, $^1J_{CP}$ = 68.5), 28.4 (CH_2), 21.4 (CH_2, $^2J_{CP}$ = 9.9), 13.9 (CH_3). $C_{25}H_{25}PO_2$ (388.4): calcd C 77.29, H 6.49, P 7.98; found C 77.30, H 6.50, P 8.00.

(*R,*R**)-2-Diphenylphosphinoyl-1-phenylbutan-3-ol** (*syn*-**2ga**): ^{1}H NMR: δ = 1.12 (d, 3H, CH_3, J_{HH} = 6.6), 2.65–3.15 (m, 3H, PC*H*-CH_2Ph), 3.85–4.05 (m, 1H, C*H*-OH), 4.15 (d, 1H, OH, J_{HOH} = 8.5), 7.00–7.95 (m, 15H, 3Ph); ^{13}C NMR: δ = 68.0 (CH, $^2J_{CP}$ = 3.4), 45.4(CH, $^1J_{CP}$ = 66.5), 32.3 (CH_2), 23.7 (CH_3). $C_{22}H_{23}PO_2$ (350.4): calcd C 75.41, H 6.62, P 8.84; found C 75.40, H 6.60, P 8.85.

(*R,*R**)-1,3-Diphenyl-2-diphenylphosphinoylpropan-1-ol** (*syn*-**2gb**): ^{1}H NMR: δ = 2.75–2.85 (m, 1H, C*H*CH_2Ph), 2.95–3.25 (m, 2H, C*H*CH_2Ph), 4.95–5.10 (m, 1H, C*H*OH, J_{HOH} = 8.2, J_{HH} = 3.6, J_{HP} = 24); 5.77 (d, 1H, OH, J_{HOH} = 8.2), 6.80–7.90 (m, 20H, 4Ph); ^{13}C NMR: δ = 73.31 (CH, $^2J_{CP}$ = 4.4), 46.0 (CH, $^1J_{CP}$ = 66.1), 32.9 (CH_2). $C_{27}H_{25}PO_2$ (412.5): calcd C 78.62, H 6.11, P 7.51; found C 78.60, H 6.10, P 7.55.

(*R,*R**)-1,5-Diphenyl-4-diphenylphosphinoylpentyn-3-ol** (*syn*-**2gf**)**:** ^{1}H NMR: δ = 2.60–2.80 (m, 1H, C*H*CH_2Ph), 2.90–3.10 (m, 1H, C*H*CH_2Ph), 3.15–3.35 (m, 1H, C*H*CH_2Ph), 4.65–4.90 (m, 1H, C*H*OH, J_{HOH} = 9.9, J_{HH} = 3.3, J_{HP} = 24); 5.32 (d, 1H, OH, J_{HOH} = 9.9), 6.80–8.10 (m, 20H, 4Ph); ^{13}C NMR: δ = 89.3 (C), 87.6 (C), 61.7 (CH, $^2J_{CP}$ = 5), 44.1 (CH, $^1J_{CP}$ = 67.7), 32.5 (CH_2). $C_{29}H_{25}PO_2$ (436.5): calcd C 79.80, H 5.77, P 7.10; found C 79.85, H 5.80, P 7.10.

(*R,*R**)-2-Diphenylphosphinoyl-4-methyl-1-phenylpentan-3-ol** (*syn*-**2gh**): ^{1}H NMR: δ = 0.47 (d, 3H, CH(CH_3)$_2$, J_{HH} = 6.6), 0.80 (d, 3H, CH(CH_3)$_2$, J_{HH} = 6.5), 1.55–1.70 (m, 1H, C*H*(CH$_3$)$_2$), 2.75–3.10 (m, 3H, PC*H* and CH_2Ph), 3.25–3.40 (m, C*H*OH, J_{HH} = 3.3, J_{HH} = 9.0, J_{HOH} = 9.0, J_{HP} = 23.4), 4.61 (d, 1H, OH, J_{HOH} = 9.0), 7.05–7.95 (m, 15H, 3Ph); ^{13}C NMR: δ = 78.5 (CH, $^2J_{CP}$ = 5.5), 41.45 (CH, $^1J_{CP}$ = 66.3), 34.0 (CH_2), 32.42 (CH, $^3J_{CP}$ = 3.7), 19.6 (CH_3), 19.1 (CH_3). $C_{25}H_{27}PO_2$ (390.4): calcd C 76.90, H 6.97, P 7.93; found C 76.90, H 7.00, P 7.90.

(*R,*R**)-6-Diphenylphosphinoyl-undecan-5-ol** (*syn*-**2ie**): ^{1}H NMR: δ = 0.77 (t, 3H, CH_3, J_{HH} = 7.1), 0.78 (t, 3H, CH_3, J_{HH} = 7.1), 0.85–1.55 (m, 13H, CH_2), 1.60–1.80 (m, 1H, PCHCH_2(CH$_2$)$_3$CH$_3$); 2.40–2.50 (m, 1H, PCH), 3.85–4.05 (m, 1H, C*H*OH), 4.19 (d, 1H, OH, J_{HOH} = 6.8), 7.40–7.90 (m, 10H, 2Ph); ^{13}C NMR: δ = 72.48 (CH, $^2J_{CP}$ = 3), 43.7 (CH, $^1J_{CP}$ = 68.5), 36.35 (CH_2, $^2J_{CP}$ = 5), 31.6 (CH_2), 28.4 (CH_2), 28.3 (CH_2), 26.5 (CH_2), 22.4 (CH_2), 22.2 (CH_2), 13.9 (CH_3). $C_{23}H_{33}PO_2$ (372.5): calcd C 74.16, H 8.93, P 8.32; found C 74.10, H 8.95, P 8.30.

(*R,*R**)-4-Diphenylphosphinoyl-2-methyl-nonan-3-ol** (*syn*-**2ih**): ^{1}H NMR: δ = 0.69 (t, 3H, (CH$_2$)$_4$CH_3, J_{HH} = 7.4), 0.70 (d, 3H, CH(CH_3)$_2$, J_{HH} = 6.8), 0.86 (d, 3H, CH(CH_3)$_2$, J_{HH} = 6.6), 0.90–1.15 (m, 6H, 3CH_2), 1.30–1.55 (m, 2H, CH_2), 1.60–1.70 (m, 1H, C*H*(CH$_3$)$_2$), 2.45–2.55 (m, 1H, PCH), 3.50–3.65 (m, 1H, C*H*OH, J_{HOH} = 7.1, J_{HH} = 6.6, J_{HH} = 12.6, J_{HP} = 18), 4.40 (d, 1H, OH, J_{HOH} = 7.1), 7.35–7.80 (m, 10H, 2Ph); ^{13}C NMR: δ = 77.75 (CH, $^2J_{CP}$ = 5), 40.25 (CH, $^1J_{CP}$ = 69), 31.8 (CH_2), 31.6 (CH), 27.9 (CH_2, $^2J_{CP}$ = 9), 27.5 (CH_2), 22.3(CH_2), 20.1 (CH_3), 17.5 (CH_3), 14.0 (CH_3). $C_{22}H_{31}PO_2$ (358.5): calcd C 73.72, H 8.72, P 8.64; found C 73.70, H 8.75, P 8.65.

(*R,*R**)-9-Diphenylphosphinoyltricosan-10-ol** (*syn*-**2jk**): ^{1}H NMR: δ = 0.85 (t, 3H, CH_3, J_{HH} = 7), 0.90 (t, 3H, CH_3, J_{HH} = 7), 1.05–1.70 (m, 38H, (CH_2)$_7$CH$_3$, (CH_2)$_{12}$CH$_3$), 2.40–2.50 (m, 1H, PCH), 3.85–4.00 (m, 1H, C*H*OH), 4.2 (br s, 1H, OH), 7.40–7.90 (m, 10H, 2Ph); ^{13}C NMR: δ = 72.1 (CH), 42.9 (CH, $^1J_{CP}$ = 68.4), 36.3 (CH_2), 31.7 (CH_2, $^2J_{CP}$ = 12). $C_{35}H_{57}PO_2$ (540.8): calcd C 77.73, H 10.62, P 5.73; found C 77.70, H 10.60, P 5.70.

Reduction of α-alkyl-β-ketophosphine oxides 1aa, 1de, 1cd with $LiBH_4$ in THF—general procedure: A solution of **1** (1 mmol) in 10 mL of THF was cooled to the desired temperature and $LiBH_4$ (3 mmol, solution 2 M in THF) was added. The reaction was left to stir at this temperature for four hours and then quenched with dilute HCl (10%) and extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered and evaporated. The crude product was submitted to flash chromatography on a short silica-gel column (Et_2O as eluent) in order to remove a undefined polymeric insoluble material. The residual collected material was submitted to NMR analysis. Data are reported in Table 3.

Synthesis of (*Z*)-9-tricosene (muscalure, (*Z*)-**6**): Compound *anti*-**2jk** (2 mmol) was dissolved in anhydrous DMF (5 mL), trated with an excess of KH and heated at 50 °C for 30 min. The mixture was cooled, 5 mL of pentane added, and the resulting solid removed by filtration and washed with pentane. The organic mother liquor was washed with water, dried and concentrated to dryness. The olefin (*Z*)-**6** was obtained in 95% yield and in 93% stereomeric purity.

Synthesis of (*E*)-9-tricosene: Olefin (*E*)-**6** was obtained from *sin*-**2jk** in 98% yield and in 92% stereomeric purity following the same procedure as for the synthesis of muscalure.

Synthesis of (*Z*)-1-cyclohexyl-1-pentene: Olefin (*Z*)-**7** was obtained from *anti*-**2cd** and *anti*-**2dc** in 96% and 97% yields and in 97% and 92% stereomeric purities, respectively, following the same procedure as for the synthesis of muscalure. Selected ^{13}C NMR data: δ = 136.1 (CH), 127.7 (CH), 36.3 (CH), 29.5 (CH_2).

Synthesis of (*E*)-1-cyclohexyl-1-pentene: Olefin (*E*)-**7** was obtained from *sin*-**2dc** in 98% yield and in 98% stereomeric purity following the same procedure as for the synthesis of muscalure. Selected ^{13}C NMR data: δ = 136.6 (CH), 127.4 (CH), 40.7 (CH), 33.3 (CH_2).

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