Acylation of Alkyl Halides and Amino Aldehydes with a Phosphane Oxide-Based d^1-Synthon

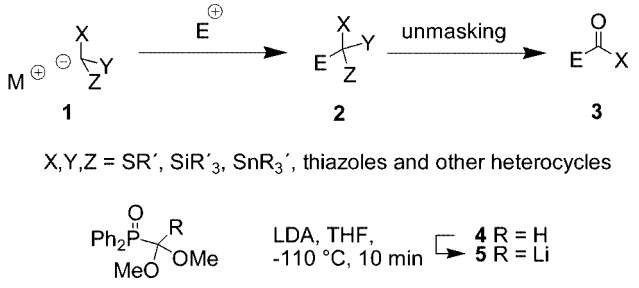
Marco Brünjes,[a] Christof Kujat,[a] Holger Monenschein,[a] and Andreas Kirschning*[a]

Keywords: Aldehydes / Acylation / Dihydroxylations / Mechanistic studies / Horner−Wittig reactions

Alkyl iodides and α-amino aldehydes can be homologated to the corresponding methyl esters and β-amino methyl esters, including β-amino-α-hydroxy methyl esters, using lithiated (dimethoxymethyl)diphenylphosphane oxide. The primary α,α-(dimethoxy)diphenylphosphane oxides obtained by this Horner–Wittig type process collapse to give the target esters under proton-catalyzed conditions in the presence of water. Detailed and carefully conducted mechanistic studies revealed that the diphenylphosphane oxide group is activated by protonation, and acts as the initial leaving group in this process. In the cases of adducts derived from the reaction of the phosphane oxide-stabilized anion with α-amino aldehydes, homologation to the β-amino- and β-amino-α-hydroxy methyl esters can be achieved by KO*t*Bu-mediated elimination to the intermediate *O*,*O*-ketene acetals. These may either be allowed to react with water under acidic conditions to yield the β-amino methyl esters, or may be treated under the Sharpless asymmetric dihydroxylation conditions to directly furnish the β-amino-α-hydroxy methyl esters.

Introduction

Homologation of electrophiles using various d^1-synthons is a key transformation in organic synthesis.[1] Appropriate substitution of the nucleophilic carbanion **1** with two or three heteroatoms (X, Y, Z) (Scheme 1) leads to masked formyl anion equivalents. In the presence of electrophiles, these carbanions can be used for the preparation of masked aldehydes, carboxylic acids or esters **2**, which subsequently have to be unmasked to give the desired carbonyl compounds **3**. The most commonly used heteroatoms for these d^1-synthons are sulfur,[2] and to a lesser extent silicon,[3] the latter being used in some cases in connection with oxygen substituents;[4] tin can be used in tin-metal exchange.[5] Additionally, the carbanion can be stabilized by nitrogen[6] which is often part of a heterocycle, namely benzothiazole[7] or 2-(trimethylsilyl)thiazole.[8] The simplest d^1-synthon, however, is the cyanide anion. Liberation of the carbonyl group from the primary adducts, including cyanides, is still a major challenge in all these methods.



Scheme 1. Formyl anion synthons

Recently, we reported on a formate carbanion equivalent **5** which is stabilized by phosphorous and serves as a d^1-synthon.[9] We demonstrated that anion **5** rapidly reacts with aldehydes, including carbohydrate-based ones, to yield 2-hydroxy-1-diphenylphosphane oxides, which, on treatment with KO*t*Bu, undergo elimination to give the corresponding alkenes,[10] in this case *O*,*O*-ketene acetals. These highly reactive intermediates yield α-hydroxy esters under the Sharpless asymmetric dihydroxylation conditions.[11]

Based on the observations that anion **5** can be used for the formylation of aldehydes, we extended these studies to the homologation of alkyl halides and alkyl triflates, as well as to the important group of α-amino aldehydes. The alkylation is particularly noteworthy here, as the ester functionality can be liberated from the intermediate phosphane oxide adducts under very mild acidic conditions.[12] Therefore, we also tried to shed light onto the proton-induced mechanism of the collapse of the α,α-(dimethoxy)diphenylphosphane oxides.

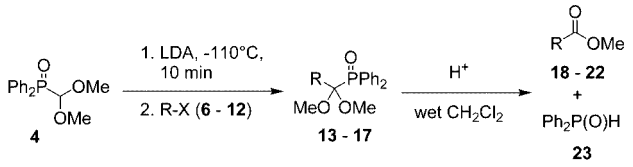
Results and Discussion

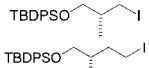
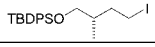
Alkylation of lithiated phosphane oxide **5** is initiated by the deprotonation of (dimethoxymethyl)diphenylphosphane

[a] Institut für Organische Chemie, Universität Hannover, Schneiderberg 1B, 30167 Hannover, Germany
Fax: (internat.) + 49-(0)511-7623011
E-mail: andreas.kirschning@oci.uni-hannover.de

oxide (**4**),[13] which is achieved at −110 °C within a few minutes, using LDA as a base (Scheme 1). Addition of primary alkyl halides **6**, **7** and **9**−**12**, or octyl triflate (**8**), yielded the phosphane oxides **13**−**17** (Table 1). These phosphane oxides can either be isolated by chromatography, or can be transformed into the corresponding carboxylic esters **18**−**22** using traces of acid in wet dichloromethane.[12] As a by-product, phosphane oxide **23** was formed instead of the hydroxy tautomer, as determined from the P,H coupling constant (J = 480 Hz).

Table 1. Formylation of alkyl halides and octyl triflate[a]



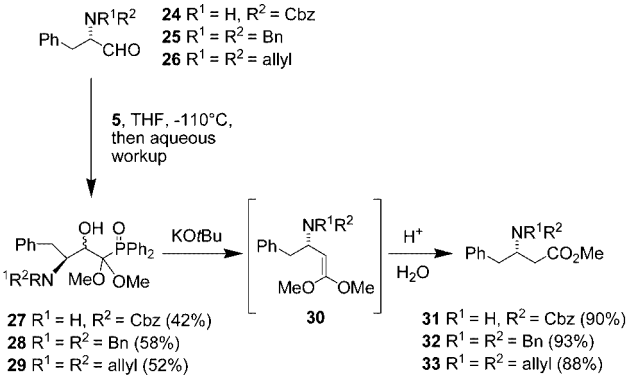
Alkyl iodide	R–X	phosphane oxide (yield in %)[b]	methyl ester (yield in %)[b]
6	$CH_3(CH_2)_6CH_2Br$	**13** (30)	**18** (98, 66)[c]
7	$CH_3(CH_2)_6CH_2I$	**13** (75)	
8	$CH_3(CH_2)_6CH_2OTf$	**13** (87)	
9	CH_2=CH-CH_2Br	**14** (76)	**19** (98)[d]
10	$PhCH_2Br$	**15** (94)	**20** (94)
11		**16** (18)	**21** (98)
12		**17** (55)[e]	**22** (87)

[a] For details, refer to the Exp. Sect. [b] All yields refer to isolated pure products after chromatographic purification or crystallization. [c] Transformations were quantitative; reduced yields are due to the volatile character of the products. [d] Due its volatile character, the yield of **19** was determined from its crude ^{1}H NMR spectrum. [e] Not optimized.

In contrast to octyl iodide (**7**) and octyl triflate (**8**), the corresponding bromide **6** reacts only sluggishly with lithiated phosphane oxide **5**. Only when the bromide is activated, such as in allyl bromide **9** and benzyl bromide **10**, were good yields for the phosphane oxide adducts **13** and **14** observed. However, the situation changes when some steric hindrance arising from nearby branching is introduced into the electrophile. This becomes evident for alkyl iodides **11** and **12**. Here, the isolated yields for phosphane oxides **16** and **17** are low to moderate, with a substantial increase when the methyl branching-point is shifted from the 2- to the 3-position. We ascribed these reduced yields to the instability of the anion **5**[14] when extended reaction-times were required, or when the reaction temperature had to be raised above −100 °C in order to increase the reaction rate. The liberation of the ester functionality in this two-step process is particularly mild. The likely mechanism will be discussed in detail below.

In the next phase of the project, α-amino aldehydes were tested as highly versatile electrophiles in reactions with anion **5**. The importance of this reaction is due to the fact that homologation yields β-amino esters, which are important precursors for peptide synthesis with β-amino acids.[15] In fact, along with strategies based on asymmetric methods, the chiral pool approach, starting from α-amino acids, is still an important route towards enantiomerically pure β-amino acids. One of the most versatile homologation protocols for carboxylic acids is the Arndt−Eistert reaction.[16] In this case, the mixed anhydrides of protected α-amino acids are treated with diazomethane. The resulting α-azido ketone is subjected to the reaction conditions of the Wolff rearrangement, which yields the corresponding β-amino acids. Secondly, α-amino acids can be converted into the corresponding primary iodides, which are homologated by treatment with cyanide to yield α-amino nitriles.[17a] Thirdly, asparagine has served as a chiral building block for the preparation of β-amino acids. In this case, asparagine was transformed into perhydropyrimidin-4-one, which was diastereoselectively alkylated.[18] Synthetic strategies towards β-amino-α-hydroxy esters are of pharmaceutical relevance in the case of phenylisoserine which is present in the side-chain of the anti-tumor drug paclitaxel.[19]

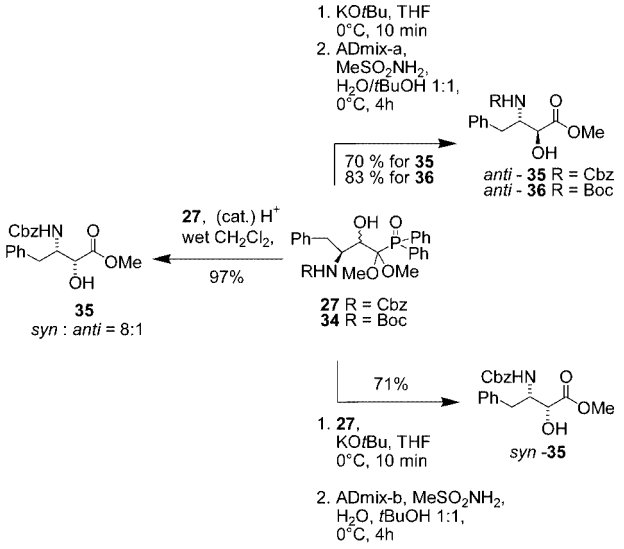
As shown in Scheme 2, lithiated phosphane oxide **5** reacts with α-amino aldehydes **24**−**26** to give the phosphane oxide adducts **27**[12] −**29**, in moderate isolated yields. KO*t*Bu-mediated elimination gave ketene acetal **30**, which was treated with an aqueous solution of 1 M HCl until the pH value was adjusted to 5. This treatment furnished the β-amino esters **31**−**32** in very good yields. Surprisingly, the intermediate *O*,*O*-ketene acetal **30** survived isolation as a crude product. In fact, we did not observe formation of α,β-unsaturated esters which could arise directly from β-elimination of the *O*,*O*-ketene acetal **30**. The enantiomeric purity of compounds **31** was determined by comparison of the [α] value with those reported in the literature.[17b]



Scheme 2. Preparation of β-amino esters by homologation of α-amino aldehydes (Z = Cbz = benzyloxycarbonyl)

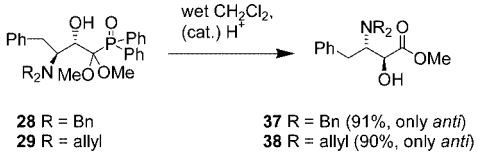
Based on these results, we envisaged the preparation of β-amino-α-hydroxy esters. When Cbz-protected phosphane oxide adduct **27** was treated with acidic wet dichloromethane, collapse of the α,α-dimethoxyphosphane oxide group occurred, resulting in the preferential formation of the *syn*-configured amino-hydroxy ester (2*R*,3*S*)-*anti*-**35**, in excellent yield (Scheme 3). It is very likely that this product ratio reflects the initial diastereomeric mixture of adducts **27**

formed on addition of anion **5** to the chiral aldehyde. This is helpful, as the diastereoselectivity of this addition could not unequivocally be determined at the stage of the phosphane oxide.



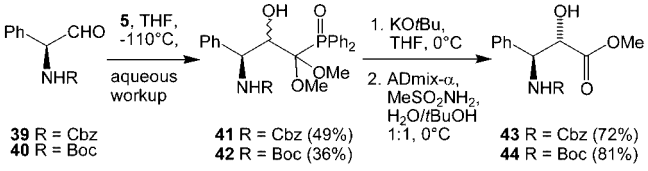
Scheme 3. Synthetic routes towards benzylisoserine methyl esters

An alternative route proceeds via the intermediate *O*,*O*-ketene acetals (refer to Scheme 2), which are dihydroxylated under typical asymmetric Sharpless conditions. The elimination product derived from the Cbz-protected phosphane oxide **27** was treated with with ADmix-α, giving *anti*-configured (2*S*,3*S*)-aminohydroxy ester **35** in good overall yield, and with excellent selectivity ($dr > 15{:}1$). Likewise, the Boc-protected derivative **34**, which had been prepared according to Scheme 2 in 32% isolated yield, was transformed into the (2*S*,3*S*)-methyl ester **36** in this manner. Furthermore, phosphane oxides **28** and **29**, whose amino functionalities were protected with a benzyl group and an allyl group, respectively, were converted into the corresponding (2*S*,3*S*)-configured β-amino-α-hydroxy-amino esters **37** and **38** using the acidic degradation conditions described above. The 2,3-*anti*-configured isomers were obtained with high enantiomeric excess as single diastereomers, as determined by comparison of their ^{13}C NMR spectra, and the [α] values of the corresponding *N*-deprotected methyl esters, with those data reported in the literature.[20] This reflects the stereochemical outcome of the nucleophilic attack of anion **5** on aldehydes **25** and **26**, respectively (Scheme 2), which is in sharp contrast to the stereochemical outcome for the Z-protected amino aldehyde **24** (refer to Scheme 2). It is evident that adduct **29** is not suitable for the dihydroxylation route, as it contains two additional terminal double bonds. Attempts to obtain a β-amino-α-hydroxy ester (such as **37**) from the dibenzylamino derivative **28** via the corresponding *O*,*O*-ketene acetal **30** were unsuccessful, as this latter intermediate turned out to be unreactive under the Sharpless dihydroxylation conditions. Steric hindrance around the double bond is possibly responsible for this unreactivity. In the case of the *N*,*N*-dibenzylated methyl ester **37**, *N*-deprotection, and preparation of the hydrochloride salt of the resulting methyl ester allowed us to determine the absolute configuration around the nitrogen-bearing stereogenic center, by direct comparison of the [α] values.



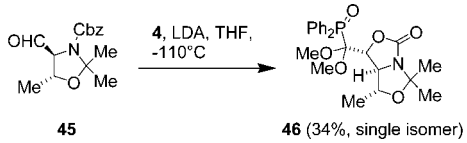
Sdheme 4. Proton-catalyzed degradation of phosphane oxides **28** and **29**

Likewise, aldehydes **39** and **40**, derived from phenylglycine, yielded adducts **41** and **42**, which were subjected to the dihydroxylation route via the corresponding *O*,*O*-ketene acetals (Scheme 5). As a result of this sequence, the phenylisoserine esters **43** and **44** were prepared as single isomers.



Scheme 5. Synthetic routes towards phenylisoserine methyl esters **43** and **44**

Finally, the threonine-derived aldehyde **45**[21] gave the bicyclic oxazolidinone **46** in 34% yield as a single isomer. Here, the diastereoselective addition of lithiated phosphane oxide **4** is followed by intramolecular attack of the intermediate alkoxy anion on the Cbz protecting group (Scheme 6). The configuration of the newly formed stereogenic center was elucidated by determination of the coupling-constant ($J_{H,H} = 4.6$ Hz) and by comparison with the related oxazolidinones, studied in detail by the groups of Dondoni[22] and Luly.[23]



Scheme 6. Formylation of the *N*,*O*-protected threonine-derived aldehyde **45**

The contrasting diastereomeric preferences in the primary addition to the protected α-amino aldehydes can be rationalized by assuming a Felkin−Anh-chelate transition state **I** for the Cbz- and Boc-protected amino aldehydes (Figure 1). In contrast, for the stereochemical outcome of *N*,*N*-dibenzylated and allylated amino aldehydes **25** and **26**, the Felkin−Anh transition state model **II** can explain the selectivity.[24] Finally, conformational analysis of amino al-

dehyde **45** in the transition state with the approaching nucleophile using MacroModel® Version 7.0 (MMFFs forcefield in $CHCl_3$)[25] suggested that application of the Cornforth model **III** may help to rationalize the 1,2-*anti* configuration of the primary addition product.[26]

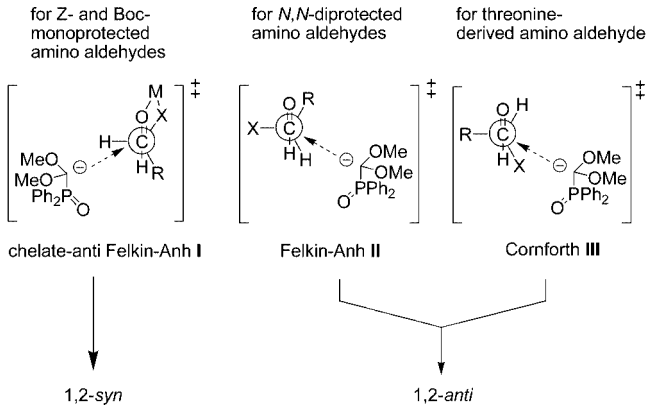
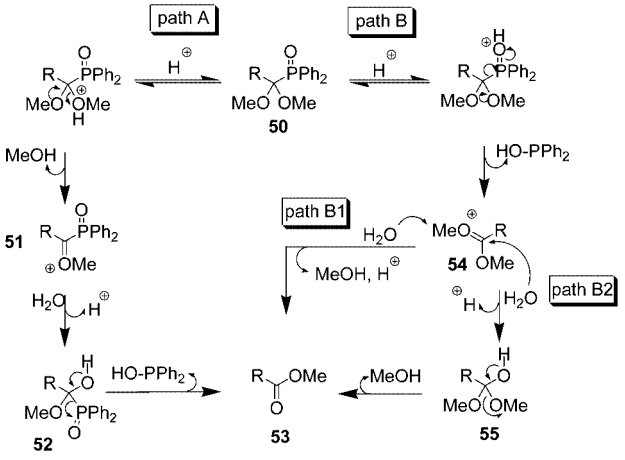


Figure 1. Proposed transition-states **I**−**III** for nucleophilic attack on *N*-protected α-amino aldehydes

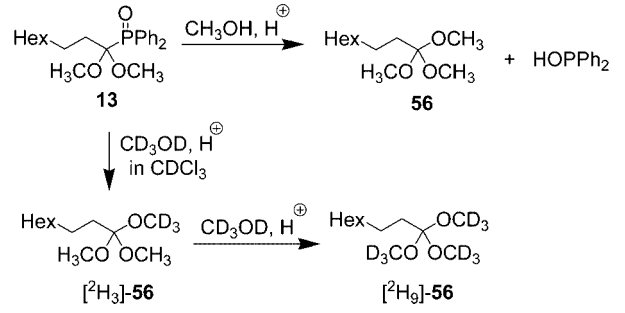
At this point, it can be speculated as to how the solvolysis of adducts **13**−**17** occurs. The proton-induced fragmentation proceeds under very mild conditions, in essentially quantitative yield. To the best of our knowledge, the protonated diarylphosphane oxide moiety has not previously been described as a good leaving group. In our system, the presence of two excellent donor groups at the α-position may strongly facilitate this process.

Dichloromethane that has been washed with aqueous 2 N hydrochloric acid can serve as the proton source. In contrast, anhydrous conditions do not initiate the fragmentation. Based on these observations, two plausible major reaction pathways for the acid-induced fragmentation can be discussed (Scheme 7). In principle, they differ in the choice of the leaving group in the initial protonation step. Mechanistic pathway A is characterized by initial protonation of the acetal functionality, followed by removal of one methoxy group to give oxonium cation **51**. This intermediate is then trapped by water to furnish hemiacetal **52**, which collapses to the ester **53**. Alternatively, the diphenyl phosphane oxide functionality can serve as a leaving group after protonation of the oxygen-phosphorous double bond (path B). At the stage of intermediate **54**, it is not clear whether water traps the intermediate cation (path B2), again affording a labile intermediate **55**, which spontaneously collapses to the ester **53**, or whether water nucleophilically attacks the activated methyl group in **54** (path B1), thereby directly liberating the ester. At this point, it should be noted that the mechanism of choice is determined by the relative rates k_1/k_2 rather than by the protonation states of the two Lewis basic sites.



Scheme 7. Possible mechanisms for the proton-catalyzed fragmentation of the phosphane oxides **50**

First, investigations into differentiation of the major mechanistic pathways A and B were conducted. If the phosphane oxide moiety is protonated, it can leave. The resulting oxonium cation **54** can be trapped by nucleophiles, such as methanol, leading to the formation of ortho ester **56**. However, the ortho ester cannot be formed if methanol is the initial leaving group and an oxonium cation **51** is the first intermediate. In fact, when we carried out the protonation in the presence of methanol, ortho ester **56** was formed in 65% yield (Scheme 8).



Scheme 8. Acid-catalyzed degradation of the phosphane oxide **13** in methanol (Hex = hexyl)

This experiment was repeated in an NMR tube using deuterated methanol in $CDCl_3$ and a catalytic amount of trifluoroacetic acid. Eleven ^1H NMR spectra were recorded within 20 h (Table 2 and Figure 2). Integration of the relevant signals [aromatic H at δ = 8.08 ppm (4 H) for **13** (position **1**); OCH_3 at δ = 3.32 ppm (6 H) for **13** (position **2**); H-2 at δ = 1.82 ppm (2 H) for **13** (position **3**)] clearly shows that exchange of the methoxy groups only occurs after the diphenylphosphane oxide group has left, as the integrals for the aromatic groups and methoxy groups in **13** remain in the same ratio throughout the experiment. Once the phosphane oxide has been removed, the ortho ester is formed, and it rapidly exchanges with the deuterated methanol. These experimental results exclude path A.

Table 2. Relative integrals of protons at δ = 8.08 ppm (position **1**), at δ = 3.32 ppm (position **2**) and at δ = 1.82 ppm (position **3**) (also refer to Figure 2)

Recording time[min][a] At δ = 8.08 ppm	Relative integrals at δ = 3.32 ppm	Relative integrals at δ = 1.82 ppm	Relative integrals
0	1.00	1.00	1.00
10	0.79	0.77	0.82
18	0.74	0.74	0.75
40	0.59	0.58	0.61
63	0.47	0.47	0.49
77	0.42	0.42	0.44
115	0.30	0.31	0.31
140	0.23	0.25	0.25
205	0.13	0.15	0.15
250	0.09	0.11	0.11
350	0.06	0.07	0.07
1200	0.00	0.00	0.00

[a] For details, refer to the text, Figure 2 and the Exp. Sect.

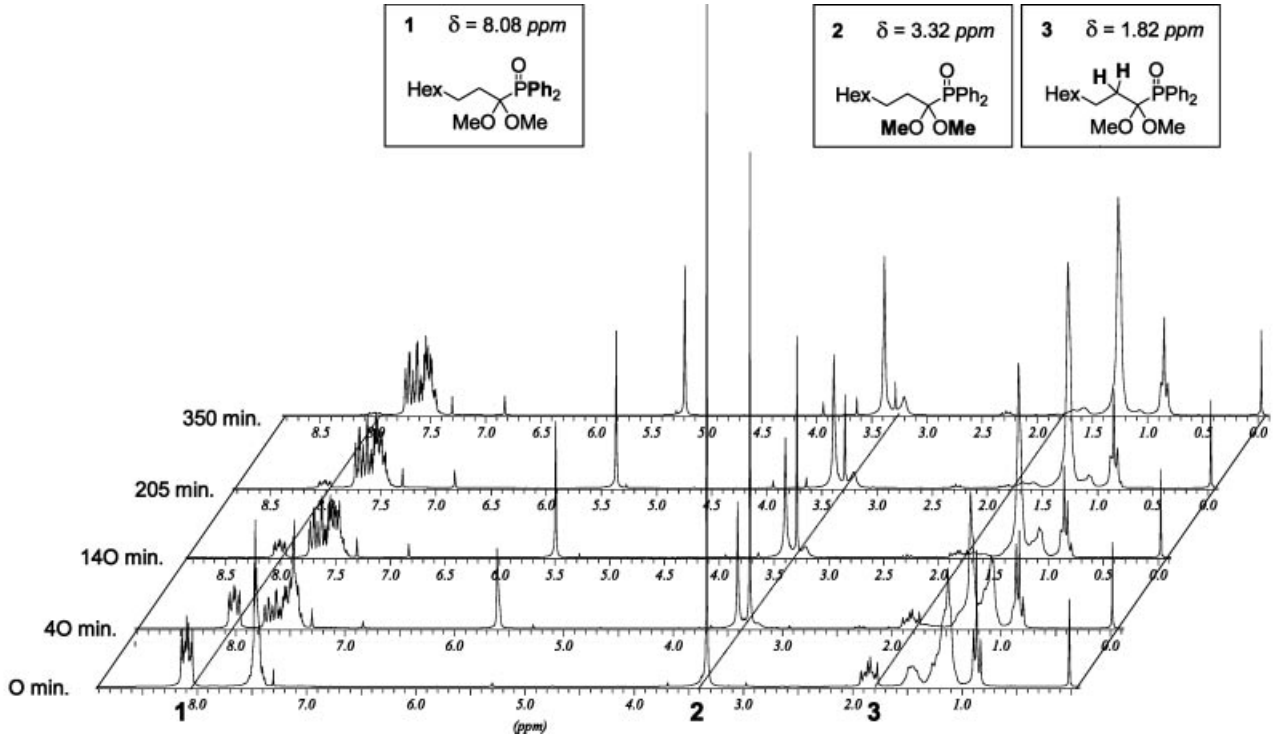
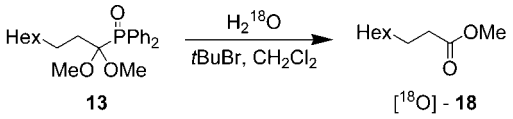


Figure 2. Acid-catalyzed degradation of the phosphane oxide **13** in deuterated methanol, as followed by ^{1}H NMR spectroscopy

Next, we had to distinguish the two possible pathways of mechanism B. This can be achieved because in route B2, the oxygen atom of water is incorporated into the ester functionality. This is not the case for route B1. Hence, the solvolytic step was carried out under refluxing conditions in the presence of *tert*-butyl bromide and ^{18}O-labeled water (96% purity). The bromide was used in order to generate traces of HBr and avoid contamination of the reaction mixture with unlabeled H_2O. After isolation of the ester **18** (90% yield), the mass spectrum (HRMS: *m*/*z* for $C_{10}H_{20}{}^{16}O^{18}O$; calcd. $[M]^+$ 174.1506; found 174.1495) clearly revealed the incorporation of one ^{18}O-atom. This result was further verified by recording a ^{13}C NMR spectrum, and carefully analyzing the chemical shift of the ester carbon atom. It is well established that carbonyl groups which contain an [^{18}O]-oxygen atom are shifted upfield (0.02−0.06 ppm) with respect to the corresponding unlabeled carbonyl group.[28] In the current case, we observed the same result as is shown in Figure 2.

All these experiments strongly suggest that pathway B2 is the relevant one in operation. This notion is further supported by the observation that the β-keto compound **60**, which can be prepared by treatment of benzoyl chloride with lithiated phosphane oxide **5**, cannot be transformed



Scheme 9. Acid-catalyzed degradation of the phosphane oxide **13** in the presence of ^{18}O-labeled water

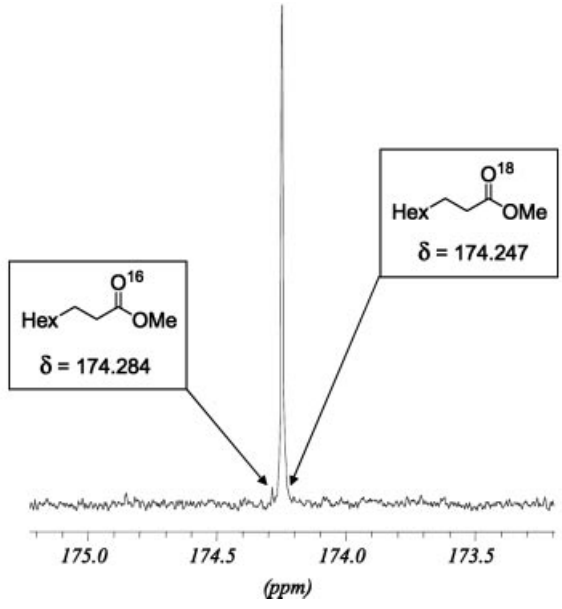
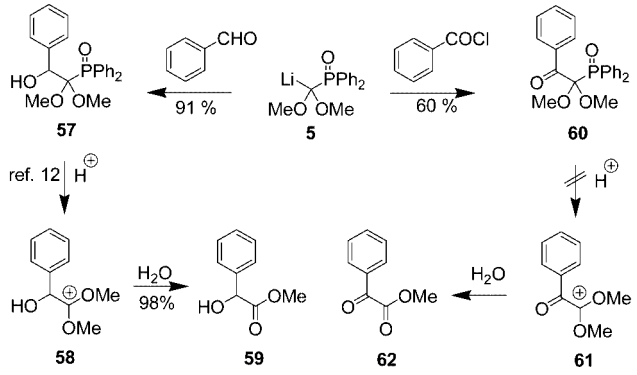


Figure 3. ^{13}C NMR spectrum of [^{18}O]-labeled ester **18**

into α-keto ester **62** by treatment with acid, even when 2.5 equivalents of HCl (0.05 N) at 40 °C were used (Scheme 10). This can be rationalized by the fact that formation of the intermediate α-keto carbenium ion **61** is highly disfavoured, despite the fact that two stabilizing methoxy groups are present. The keto group, which is an additional Lewis base, could trap the proton. However, product **57**, which originates from the reaction of lithiated phosphane oxide **5** with benzaldehyde, also contains an additional Lewis base. And it is transformed into the corresponding mandelic methyl ester **59** under conditions just as mild as those described for the alkylation products **13**−**17**. Indeed, the intermediate carbenium ion **58**, which is generated when pathway B is



Scheme 10. Attempted proton-induced degradation of the β-ketophosphane oxide **60**

under operation, is stabilized by the adjacent hydroxy group.

Conclusion

In summary, we have shown that lithiated (dimethoxymethyl)diphenylphosphane oxide is an excellent nucleophilic acylating C_1-building block in the reaction with primary alkyl iodides. The advantage of this acylating agent comes from the ease and mildness of liberation of the ester functionality. Our mechanistic findings, and the existence of phosphane oxide adduct **50**, broaden the synthetic scope of this formylating concept, as intermediate **54** may also be trapped by other nucleophiles, including carbon nucleophiles.

Experimental Section

General Remarks and Starting Materials: ^1H and ^{13}C NMR spectra were measured with Avance 200/DPX (Bruker) with 200 MHz (50 MHz), Avance 400/DPX (Bruker) 400 MHz (100 MHz) and Avance 500/DRX (Bruker), respectively, using tetramethylsilane as the internal standard. If not otherwise noted, $CDCl_3$ is the solvent for all NMR experiments. Mass spectra were recorded with a type LCT-spectrometer (Micromass). The products obtained from the labeling experiments were analyzed with a type VG autospec (Micromass). Optical rotations [α] were collected with a Polarimeter 341 (Perkin−Elmer) at a wavelength of 589 nm. GC was carried out with a HPGC series 5890 Hewlett−Packard equipped with a column RTX-50 (30 m) and a FID detector 19231 D/E. Chiral GC was conducted with a HPGC series 5890 Hewlett−Packard equipped with a FID detector 19231 D/E and a column: heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin (25 m); gas: helium; conditions: isothermal, $p_{(column)}$ = 175 kPa, p_{He} = 3.5 bar, p_{H_2} = 1.5 bar, flow rate. Furher details can be found in ref.[9b].

All solvents used were of reagent grade and were dried further. Reactions were monitored by TLC on silica gel 60_{P254}, and detected either by UV absorption or by staining with H_2SO_4/4-methoxybenzaldehyde in ethanol. Flash column chromatography was performed on silica gel 60 (230−400 mesh). Except for iodides **11**, **12**, as well as octyl triflate (**8**)[29a] all starting halides are commercially available. Alkyl iodides **11** and 12 were obtained from the corresponding alcohols by the standard Appel protocol.[29b] Amino aldehydes **24**, **39**, **40** and **45** were prepared from the corresponding amino alcohols according to ref.[30] while the analoguous aldehydes **25** and **26** were obtained by the Parikh−Doering procedure.[31] Phosphane oxides **4** and **57** were prepared as described before.[9,13] Methyl esters **18**−**21** are known or are commercially available. The preparation of **34** is described in ref.[32] The spectroscopic and physical data of compounds **35**,[12] **36**[33] and **59**[9] are listed in the literature.

Lithiation of the Phosphane Oxide 4 and Formation of the Anion 5: (Dimethoxymethyl)phosphane oxide (1.93 g, 7 mmol) in dry THF (20 mL) was added to a solution of lithiumdiisopropyl amide (6 mmol) in dry THF (40 mL) at −110 °C under nitrogen.

General Procedure for the Reaction of Lithiated Phosphane Oxide 5 with Alkyl Halides and Alkyl Triflates: Two minutes after the formation of the dark red anion **5**, the respective alkylating agent (0.33

equiv.) in dry THF (2.5 mL/mmol electrophile) was added dropwise, followed directly by aqueous hydrolysis (25 mL/mmol electrophile) at −110 °C. The mixture was warmed to room temperature, concentrated in vacuo and extracted with dichloromethane (4 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography.

1-(Diphenylphosphinoyl)-1,1-dimethoxynonane (13): By treatment of octyl bromide (6) (386 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound 13 (235 mg, 0.61 mmol, 30%) was prepared. By treatment of octyl iodide (7) (528 mg, 2.2 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound **13** (638 mg, 1.64 mmol, 75%) was prepared. By treatment of octyl triflate (8) (300 mg, 1.1 mmol) with lithiated phosphane oxide **5** (3.4 mmol), the title compound **13** (385 mg, 1.0 mmol, 87%) was prepared. ^{1}H NMR (400 MHz, TMS, δ = 0.0 ppm): δ = 0.85 (t, J = 7.1 Hz, 3 H, 9-H), 1.05−1.27 (m, 10 H), 1.42 (m, 2 H), 1.82 (m, 2 H), 3.32 (s, 6 H, OMe), 7.40−7.50 (m, 6 H), 8.04−8.10 (m, 4 H) ppm. ^{13}C NMR (100 MHz, TMS, δ = 0.0 ppm): δ = 14.0 (C-9), 22.6 (C-8), 23.1 (d, $J_{P,C}$ = 1.9 Hz, C-3), 2 × 29.0, 30.0, 31.7 (C-4 − C-7), 33.8 (d, $J_{P,C}$ = 13.2 Hz, C-2), 50.7 (d, $J_{P,C}$ = 6.9 Hz, OMe), 105.2 (d, $J_{P,C}$ = 114.6 Hz, C-1), 128.1 (d, $J_{P,C}$ = 11.3 Hz), 131.3 (d, $J_{P,C}$ = 3.0 Hz), 131.9 (d, $J_{P,C}$ = 8.6 Hz), 133.1 (d, $J_{P,C}$ = 89.0 Hz) ppm. HRMS ($C_{46}H_{66}NaO_6P_2$): calcd. 799.4232 [2M + Na]$^+$, found 799.4204.

1-(Diphenylphosphinoyl)-1,1-dimethoxy-3-butene (14): By treatment of allyl bromide **9** (242 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound **14** (478 mg, 1.51 mmol, 76%) was prepared. ^{1}H NMR (400 MHz, TMS, δ = 0.0 ppm): δ = 2.71 (ddt, J = 11.3, 7.0, 1.6 Hz, 2 H, 2-H), 3.35 (s, 6 H, OMe), 4.90 (ddt, J = 17.1, 1.6, 1.5 Hz, 1 H, 4-H), 4.93 (ddt, J = 10.3, 1.6, 1.5 Hz, 1 H, 4-H′), 5.86 (ddt, J = 17.1, 10.3, 7.0 Hz, 1 H, 3-H), 7.39−7.52 (m, 6 H), 8.02−8.11 (m, 4 H) ppm. ^{13}C NMR (100 MHz, TMS, δ = 0.0 ppm): δ = 38.5 (d, $J_{P,C}$ = 13.4 Hz, C-2), 51.1 (d, $J_{P,C}$ = 6.9 Hz, OMe), 104.3 (d, $J_{P,C}$ = 115 Hz, C-1), 117.7 (C-4), 128.2 (d, $J_{P,C}$ = 11.3 Hz), 131.4 (d, $J_{P,C}$ = 2.9 Hz), 131.9 (d, $J_{P,C}$ = 3.5 Hz, C-3), 132.0 (d, $J_{P,C}$ = 8.8 Hz), 132.6 (d, $J_{P,C}$ = 89.7 Hz) ppm. HRMS ($C_{20}H_{24}NNaO_3P$): calcd. 380.1392 [M + CH_3CN + Na]$^+$, found 380.1408.

1-(Diphenylphosphinoyl)-1,1-dimethoxy-2-phenylethane (15): By treatment of benzyl bromide **10** (342 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol) the title compound **15** (731 mg, 1.87 mmol, 94%) was prepared. ^{1}H NMR (400 MHz, TMS, δ = 0.0 ppm): δ = 3.28 (d, $J_{P,H}$ = 8.5 Hz, 2 H, PhCH_2), 3.32 (s, 6 H, OMe), 7.05−7.13 (m, 3 H), 7.15−7.22 (m, 2 H), 7.34−7.47 (m, 6 H), 7.92−8.01 (m, 4 H) ppm. ^{13}C NMR (100 MHz, TMS, δ = 0.0 ppm): δ = 39.5 (d, $J_{P,C}$ = 15.1 Hz, PhCH_2), 51.7 (d, $J_{P,C}$ = 6.33 Hz, OMe), 104.9 (d, $J_{P,C}$ = 114.4 Hz, C-1), 126.5, 127.6, 128.1 (d, $J_{P,C}$ = 11.3 Hz), 131.2, 131.3 (d, $J_{P,C}$ = 2.9 Hz), 132.0 (d, $J_{P,C}$ = 8.6 Hz), 132.8 (d, $J_{P,C}$ = 89.3 Hz), 134.8 (d, $J_{P,C}$ = 5.9 Hz) ppm. HRMS ($C_{22}H_{24}O_3P$): calcd. 367.1463 [M + H]$^+$, found 367.1472.

(*S*)-4-(*tert*-Butyldiphenylsiloxy)-1-(diphenylphosphinoyl)-1,1-dimethoxy-3-methylbutane (16): By treatment of (*R*)-3-[(*tert*-butyl)-diphenylsiloxy]-1-iodo-2-methylpropane (**11**) (210 mg, 0.48 mmol) with lithiated phosphane oxide **5** (1.7 mmol), the title compound **16** (51 mg, 0.09 mmol, 18%) was prepared. ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ppm): δ = 0.91 (d, J = 6.8 Hz, 3 H, Me), 0.98 (s, 9 H, *t*Bu), 1.60 (ddd, J = 14.8, 12.4, 6.7 Hz, 1 H, 2-H), 2.07 (ddd, J = 14.8, 11.3, 4.9 Hz, 1 H, 2-H′), 2.37 (m, 1 H, 3-H), 3.27 (s, 3 H, OMe), 3.32 (s, 3 H, OMe′), 3.38 (dd, J = 9.6, 5.2 Hz, 1 H, 4-H), 3.45 (dd, J = 9.6, 5.5 Hz, 1 H, 4-H′), 7.30−7.48 (m, 12 H), 7.55−7.62 (m, 4 H), 8.03−8.11 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.0 ppm): δ = 18.5 (Me), 19.3 (*t*Bu), 26.8 (*t*Bu), 30.6 (d, $J_{P,C}$ = 3.1 Hz, C-3), 36.9 (d, $J_{P,C}$ = 13.4 Hz, C-2), 50.5 (d, $J_{P,C}$ = 7.7 Hz, OMe), 50.8 (d, $J_{P,C}$ = 6.5 Hz, OMe′), 68.9 (C-4), 105.5 (d, $J_{P,C}$ = 114.1 Hz, C-1), 2 × 127.5 (TBDPS), 128.2 (d, $J_{P,C}$ = 11.3 Hz), 129.3 (TBDPS), 129.4 (TBDPS), 131.2 (d, $J_{P,C}$ = 2.9 Hz), 2 × 131.9 (d, $J_{P,C}$ = 8.6 Hz), 133.3 (d, $J_{P,C}$ = 88.4 Hz), 133.4 (d, $J_{P,C}$ = 88.0 Hz), 133.9, 134.0 (2 × TBDPS), 2 × 135.6 (TBDPS) ppm. HRMS ($C_{35}H_{43}NaPO_4Si$): calcd. [M + Na]$^+$ 609.2566, found 609.2553.

(*S*)-5-[*tert*-Butyl)diphenylsiloxy]-1-(diphenylphosphinoyl)-1,1-dimethoxy-4-methylpentane (17): By treatment of (*S*)-4-[(*tert*-butyl)-diphenylsiloxy]-1-iodo-3-methylbutane (**12**) (37 mg, 0.082 mmol) with lithiated phosphane oxide **5** (0.27 mmol), the title compound **17** (27 mg, 0.045 mmol, 55%) was prepared. ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ppm): δ = 0.73 (d, J = 6.6 Hz, 2 H, Me), 1.01 (s, 9 H, *t*Bu), 1.28 (m, 1 H, 3-H), 1.40 (m, 1 H, 3-H′), 1.56 (m, 1 H, 4-H), 1.71−1.95 (m, 2 H, 2-H), 3.26 (dd, J = 9.9, 6.7 Hz, 1 H, 5-H), 3.30 (s, 6 H, OMe), 3.33 (dd, J = 9.9, 5.5 Hz, 1 H, 5-H′), 7.31−7.50 (m, 12 H, Ph), 7.55−7.62 (m, 4 H, Ph), 7.98−8.08 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.6 (Me), 19.2 (*t*Bu), 26.5 (d, $J_{P,C}$ = 1.9 Hz, C-3), 26.9 (*t*Bu), 31.5 (d, $J_{P,C}$ = 13.4 Hz, C-2), 36.3 (C-4), 50.7 (d, $J_{P,C}$ = 6.9 Hz, OMe), 50.8 (d, $J_{P,C}$ = 6.5 Hz, OMe′), 68.6 (C-5), 105.2 (d, $J_{P,C}$ = 114.4 Hz, C-1), 2 × 127.5 (TBDPS), 128.2 (d, $J_{P,C}$ = 11.1 Hz, C arom.), 129.4 (TBDPS), 131.3 (d, $J_{P,C}$ = 2.9 Hz), 2 × 131.9 (d, $J_{P,C}$ = 8.6 Hz), 133.0 (d, $J_{P,C}$ = 89.1 Hz), 133.0 (d, $J_{P,C}$ = 88.9 Hz), 2 × 134.0 (TBDPS), 2 × 135.6 (TBDPS) ppm. HRMS ($C_{36}H_{45}NaO_4PSi$): calcd. [M + Na]$^+$ 623.2722, found 623.2712.

General Procedure for the Reaction of Lithiated Phosphane Oxide 5 with Aldehydes: Two minutes after the formation of the dark red anion **5**, the respective aldehyde (0.33 equiv.) in dry THF (2.5 mL/mmol electrophile) was added dropwise, followed directly by aqueous hydrolysis. Once the mixture had warmed up to room temperature it was concentrated in vacuo. The resulting aqueous suspension was extracted with dichloromethane (3 ×), the combined organic layers were dried with $MgSO_4$ and the solvents evaporated. The residue was purified by column chromatography (on silica gel using a mixture of petroleum ether/ethyl acetate as eluent unless otherwise stated).

(2*RS*,3*S*)-3-[(Benzyloxycarbonyl)amino]-1-(diphenylphosphinoyl)-1,1-dimethoxy-4-phenyl-2-butanol (27): By treatment of benzyl (1*S*)-(1-formyl-2-phenylethyl)carbamate (**24**) (567 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound **27** (470 mg, 0.84 mmol, 42%) was prepared. Spectroscopic and physical data of 27 were in accordance with those reported before.[12]

(2*S*,3*S*)-3-Dibenzylamino-1-(diphenylphosphinoyl)-1,1-dimethoxy-4-phenyl-2-butanol (28): By treatment of (2*S*)-2-dibenzylamino-3-phenylpropionaldehyde (**25**) (658 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound **28** (703 mg, 1.16 mmol, 58%) was prepared. Colorless crystals, m.p. 65 °C. $[\alpha]_D^{20}$ = +54.5 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 2.96 (dd, J = 14.7, 4.1 Hz, 1 H, 4-H′), 3.03 (dd, J = 14.7, 11.3 Hz, 1 H, 4-H), 3.29 [d, J = 14.3 Hz, 2 H, N(CH_2Ph)′], 3.30 (m, 1 H, 3-H), 3.31 (s, 3 H, OMe′), 3.40 (s, 3 H, OMe), 3.82 [d, J = 14.3 Hz, 2 H, N(CH_2Ph)], 4.48 (m, 2 H, 2-H, OH), 6.40−7.87 (m, 25 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77 ppm): δ = 32.9 (C-4), 50.1 (d, $J_{P,C}$ = 8.2 Hz, OMe′), 53.1 (d, $J_{P,C}$ = 3.6 Hz, OMe′), 53.4 [2 × , N(CH_2Ph)$_2$], 57.6 (d, $J_{P,C}$ = 3.1 Hz, C-3), 72.8 (d, $J_{P,C}$ = 12.1 Hz, C-2), 103.5 (d, $J_{P,C}$ = 107.3 Hz, C-1), 125.4, 126.3, 127.4, 127.7, 128.1, 128.2, 128.7,

128.9, 129.9, 131.2, 131.8, 131.9, 132.1, 132.4, 132.5 (25 × , C arom.), 3 × 140.1, 2 × 140.5 (5 × , C arom.) ppm. HRMS ($C_{38}H_{41}NO_4P$): calcd. 606.2773 $[M + H]^+$, found 606.2796.

(2*S*,3*S*)-3-Diallylamino-1-(diphenylphosphinoyl)-1,1-dimethoxy-4-phenyl-2-butanol (29): By treatment of (2*S*)-2-diallylamino-3-phenylpropionaldehyde (**26**) (1.60 g, 7.0 mmol) with lithiated phosphane oxide **5** (21 mmol), the title compound 29 (1.84 g, 3.64 mmol, 52%) was prepared. Colorless crystals, m.p. 76 °C. $[\alpha]_D^{20}$ = +23.2 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 2.76−2.84 [m, 3 H, N(CH_2CHCH$_2$)$_2$′, 4-H′], 2.98 (dd, *J* = 14.4, 3.4 Hz, 1 H, 4-H), 3.11 [dddd, *J* = 14.8, 5.0, 1.8, 1.8 Hz, 2 H, N(CH_2CHCH$_2$)$_2$], 3.42 (s, 3 H, OMe′), 3.44 (ddd, *J* = 10.7, 3.4, 1.3 Hz, 1 H, 3-H), 3.47 (s, 3 H, OMe), 3.98 (br. s, 1 H, O*H*), 4.23 (dd, *J* = 10.7, 5.8 Hz, 1 H, 2-H), 4.80−4.88 [m, 4 H, N(CH$_2$CHCH_2)$_2$], 5.40 [dddd, *J* = 17.1, 10.3, 6.8, 5.0 Hz, 2 H, N(CH$_2$C*H*CH$_2$)$_2$], 6.85−8.12 (m, 15 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77 ppm): δ = 32.9 (C-4), 51.3 (d, $J_{P,C}$ = 6.9 Hz, OMe′), 2 × 52.6 [2 × t, N(*C*H$_2$CHCH$_2$)$_2$], 53.0 (d, $J_{P,C}$ = 5.6 Hz, OMe), 59.5 (d, $J_{P,C}$ = 2.9 Hz, C-3), 74.8 (d, $J_{P,C}$ = 13.0 Hz, C-2), 104.1 (d, $J_{P,C}$ = 108.5 Hz, C-1), 2 × 115.4 [2 × t, N(CH$_2$CH*C*H$_2$)$_2$], 125.1, 127.4, 128.1, 128.3, 128.7, 128.8, 129.5, 132.0, 132.1, 132.2, 132.3 (17 × d, C arom.), 2 × 137.7 [2 × d, N(CH$_2$*C*HCH$_2$)$_2$], 141.2 (C arom.) ppm. HRMS ($C_{30}H_{37}NO_4P$): calcd. 506.2460 $[M + H]^+$, found 506.2458.

Benzyl (1*S*,2*RS*)-[3-(Diphenylphosphinoyl)-2-hydroxy-3,3-dimethoxy-1-phenylpropyl]carbamate (41): By treatment of benzyl (2*S*)-(2-oxo-1-phenylethyl)carbamate (**39**) (808 mg, 3.0 mmol) with lithiated phosphane oxide **5** (9 mmol), the title compound **41** (801 mg, 1.47 mmol, 49%) was prepared. colorless oil. ^{1}H NMR (200 MHz, TMS, δ = 0 ppm): δ = 3.33 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 4.24 (ddd, $J_{P,H}$ = 11.8, *J* = 6.8, 1.4 Hz, 1 H, 2-H), 4.81 (br. s, 2 H, PhCH_2O), 5.00 (d, *J* = 6.8 Hz, 1 H, 1-H), 5.17 (br. s, 1 H, NH), 6.28 (br. s, 1 H, OH), 7.13−7.60 (m, 16 H, H arom.), 7.75−8.10 (m, 4 H, H arom.) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, δ = 77 ppm): δ = 52.6 ($J_{P,C}$ = 6.8 Hz, OMe), 52.6 ($J_{P,C}$ = 5.3 Hz, OMe), 60.4 (NCH), 66.3 (Ph*C*H$_2$O), 77.5 (d, $J_{P,C}$ = 11.7 Hz, C-2), 103.2 (d, $J_{P,C}$ = 108.9 Hz, C-3), 126.5, 127.0, 127.7, 128.1, 128.3, 128.5, 128.7, 131.6, 131.8, 131.9, 132.0, 132.2, 132.5, 132.7 (C arom.), 130.6, 130.8, 136.6, 142.5 (C arom.), 155.4 (N*C*O) ppm. $C_{31}H_{32}NO_6P$ (545.56): calcd. C 68.25, H 5.91, N 2.57; found C 68.33, H 5.86, N 2.39.

***tert*-Butyl (1*S*,2*RS*)-[3-(Diphenylphosphinoyl)-2-hydroxy-3,3-dimethoxy-1-phenylpropyl]carbamate (42):** By treatment of *tert*-butyl (2*S*)-(2-oxo-1-phenylethyl)carbamate (**40**) (470 mg, 2.0 mmol) with lithiated phosphane oxide **5** (6 mmol), the title compound **42** (368 mg, 0.72 mmol, 36%) was prepared. Colorless oil. ^{1}H NMR (200 MHz, TMS = 0 ppm): δ = 1.29 (s, 9 H, *t*Bu), 3.42 (s, 3 H, OMe), 3.44 (s, 3 H, OMe), 4.22 (ddd, $J_{P,H}$ = 9.2, *J* = 5.6, 1.8 Hz, 1 H, 2-H), 4.86 (m, 1 H, 1-H), 4.98 (d, *J* = 6.8 Hz, 1 H, NH), 5.96 (d, *J* = 5.6 Hz, 1 H, OH), 7.13−8.18 (m, 15 H, H arom.) ppm. $C_{28}H_{34}NO_6P$ (511.54): calcd. C 65.74, H 6.70, N 2.74; found C 65.56, H 6.75, N 2.48.

(1*R*,4*S*,7*R*)-1-[(Diphenylphosphinoyl)dimethoxymethyl]-5,5,7-trimethyl-dihydro-oxazolo[3,4-*c*]oxazol-3-one (46): By treatment of the benzyl (4*S*,5*R*)-4-formyl-2,2,5-trimethyloxazolidine-3-carboxylate **45** (500 mg, 1.8 mmol) with lithiated phosphane oxide **5** (5.4 mmol), the title compound 46 (367 mg, 0.61 mmol, 34%) was prepared. Colorless crystals, m.p. 62 °C. $[\alpha]_D^{20}$ = −23.0 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 1.26 (d, *J* = 6.0 Hz, 3 H, 7-Me), 1.44 (s, 3 H, 5-Me′), 1.56 (s, 3 H, 5-Me), 3.37 (s, 3 H, OMe′), 3.46 (s, 3 H, OMe), 3.62 (dd, *J* = 8.6, 6.0 Hz, 1 H, 7-H), 4.46 (dd, *J* = 4.6, $J_{P,H}$ = 12.7 Hz, 1 H, 1-H), 4.80 (dd, *J* = 8.6, 4.6 Hz, 1 H, 4-H), 8.18−7.42 (m, 10 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, $CDCl_3$, δ = 77 ppm): δ = 16.7 (7-Me), 23.6 (5-Me′), 28.9 (5-Me), 50.5 (d, $J_{P,C}$ = 7.9 Hz, OMe′), 52.8 (d, $J_{P,C}$ = 5.2 Hz, OMe), 64.2 (C-4), 76.2 (d, $J_{P,C}$ = 14.6 Hz, C-1), 77.3 (C-7), 93.9 (C-5), 102.1 [d, $J_{P,C}$ = 110.4 Hz, *C*(OMe)$_2$], 127.9, 128.2, 128.3, 128.5, 128.6, 128.7, 130.7, 130.8, 131.8, 131.9 (10 × d, C arom.), 132.5, 133.4 (2 × , C arom.), 154.7 (s, C-3) ppm. HRMS ($C_{23}H_{28}NO_6P$): calcd. 468.1552 $[M + Na]^+$, found 468.1551.

General Procedure for the Acid-Catalyzed Hydrolysis of α,α-(Dimethoxy)diphenylphosphane Oxides: The α,α-(dimethoxy)diphenylphosphane oxide was dissolved in acidic wet dichloromethane which had been prepared in the following manner: 200 mL of dichloromethane and 10 mL 2 N HCl were stirred for 10 min. The aqueous phase was separated and the acidity (1.5 mmol/L) of the organic phase was determined by titration with 0.1 N NaOH. After the reaction of α,α-(dimethoxy)diphenylphosphane oxide with this acidic solution was complete, the reaction mixture was concentrated in vacuo and, if necessary, final purification was achieved by column chromatography.

Methyl Nonanoate (18): By treatment of the phosphane oxide **13** (103 mg, 0.265 mmol) in dichloromethane prepared according to general procedure, the title compound **18** (30 mg, 0.174 mmol, 66%) was obtained. The transformation proceeded quantitatively. The reduced yield is ascribed to the volatile character of ester **18**. The physical and spectroscopic data were in accordance with those reported in the literature.[34]

Methyl But-3-enoate (19): By treatment of the phosphane oxide **14** (40 mg, 0.126 mmol) in deuterated chloroform (1 mL) and hydrochloric acid (20 μL, 6 M) in the NMR tube, the title compound **19** was prepared in quantitative yield as judged by ^{1}H NMR spectroscopy. The reaction was not further worked up because of the volatile character of the title compound 19. The NMR data data were in accordance with those reported in the literature.[35]

Methyl 2-Phenylacetate (20): By treatment of the phosphane oxide **15** (148 mg, 0.40 mmol) in dichloromethane prepared according to general procedure, the title compound **20** (57 mg, 0.38 mmol, 94%) was obtained. The physical and spectroscopic data were in accordance with those reported in the literature.[36]

Methyl (*S*)-4-[(*tert*-Butyl)diphenylsilyloxy)-3-methylbutyrate (21): By treatment of phosphane oxide **16** (52 mg, 89 μmol) in dichloromethane prepared according to general procedure, the title compound **21** (33 mg, 88 μmol, > 98%) was obtained. Colorless oil. $[\alpha]_D^{20}$ = −5.4 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.62 ppm): δ = 0.98 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.05 (s, 9 H, *t*Bu), 2.18 (dd, *J* = 14.7, 8.3 Hz, 1 H, 2-H), 2.22 (m, 1 H, 3-H), 2.62 (dd, *J* = 14.7, 5.3 Hz, 1 H, 2-H′), 3.49 (dd, *J* = 9.9, 6.3 Hz, 1 H, 4-H), 3.58 (dd, *J* = 9.9, 5.2 Hz, 1 H, 4-H′), 3.65 (s, 3 H, OCH_3), 7.34−7.45 (m, 6 H, TBDPS), 7.68−7.62 (m, 4 H, TBDPS) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.0 ppm): δ = 16.6 (CH_3), 19.3 (*t*Bu), 26.8 (*t*Bu), 33.0 (C-3), 38.0 (C-2), 51.4 (OMe), 68.1 (C-4), 127.6, 129.6, 133.7, 135.6 (4 × TBDPS), 173.6 (s, *C*OOMe) ppm.

Methyl (*S*)-5-[(*tert*-Butyl)diphenylsilyloxy)-4-methylpentanoate (22): By treatment of phosphane oxide **17** (20 mg, 33 μmol) in dichloromethane prepared according to general procedure, the title compound **22** (11 mg, 29 μmol, 87%) was obtained. Colorless oil. $[\alpha]_D^{20}$ = −2.8 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (400 MHz, $CDCl_3$, δ = 7.26 ppm): δ = 0.92 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.05 (s, 9 H, *t*Bu), 1.48 (dddd, *J* = 13.4, 9.0, 7.7, 6.4 Hz, 1 H, 3-H), 1.67 (m, 1 H, 4-

H), 1.81 (dddd, J = 13.4, 9.3, 6.7, 5.7 Hz, 1 H, 3-H′), 2.28 (ddd, J = 15.6, 9.0, 6.7 Hz, 1 H, 2-H), 2.33 (ddd, J = 15.6, 9.3, 6.4 Hz, 1 H, 2-H′), 3.46 (dd, J = 9.9, 5.9 Hz, 1 H, 5-H), 3.49 (dd, J = 9.9, 5.8 Hz, 1 H, 5-H′), 3.66 (s, 3 H, OCH_3), 7.33−7.45 (m, 6 H, TBDPS), 7.68−7.62 (m, 4 H, TBDPS) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.0 ppm): δ = 16.5 (CH_3), 19.3 (*t*Bu), 26.9 (*t*Bu), 28.4 (C-3), 31.8 (C-2), 35.2 (C-4), 51.4 (OMe), 68.5 (C-4), 127.6, 129.5, 2 × 133.9, 2 × 135.6 (6 × TBDPS), 174.3 (s, *C*OOMe) ppm. HRMS ($C_{23}H_{32}O_3NaSi$): calcd. $[M + Na]^+$ 407.2018, found 407.2023.

Methyl (3*S*)-3-[(Benzyloxycarbonyl)amino]-4-phenylbutyrate (31): Phosphane oxide **27** (70 mg, 0.125 mmol) in THF (3 mL) under nitrogen was treated with potassium *tert*-butoxide (1.1 equiv.) in THF (2 mL/mmol) at 0 °C. After 15 min, the solution was concentrated in an ice-bath under reduced pressure to a volume of appoximately 1 mL. The intermediate ketene acetal was treated with an aqueous solution of 1 N HCl until the pH value was adjusted to **5**. The mixture was extracted with dichloromethane and the combined organic layers were dried ($MgSO_4$) and purified by column chromatography to give the title compound 31 (27 mg, 0.083 mmol, 66%). Spectroscopic data of 31 were in accordance with those reported before.[36] Colorless oil. $[\alpha]_D^{20}$ = −15.2 ($CHCl_3$, c = 1.0). HRMS ($C_{19}H_{21}NO_4$): calcd. 350.1368 $[M + Na]^+$, found 350.1374.

Methyl (3*S*)-3-Dibenzylamino-4-phenylbutyrate (32): Phosphane oxide **28** (95 mg, 0.157 mmol) in 3 mL THF under nitrogen was treated with potassium *tert*-butoxide (1.1 equiv.) in THF (2 mL/mmol) at 0 °C. After 15 min, the solution was concentrated in an ice-bath under reduced pressure to a volume of appoximately 1 mL. The intermediate ketene acetal was treated with with an aqueous solution of 1 N HCl until the pH value was adjusted to 5. The mixture was extracted with dichloromethane and the combined organic layers were dried ($MgSO_4$) and purified by column chromatography to give the title compound **32** (55 mg, 0.147 mmol, 93%). Colorless oil. $[\alpha]_D^{20}$ = −1.5 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 2.31 (dd, J = 14.1, 6.0 Hz, 1 H, 2-H′), 2.53 (dd, J = 13.4, 8.9 Hz, 1 H, 4-H′), 2.62 (dd, J = 14.1, 8.7 Hz, 1 H, 2-H), 3.10 (dd, J = 13.4, 5.6 Hz, 1 H, 4-H), 3.43 (dddd, J = 8.9, 8.7, 6.0, 5.6 Hz, 1 H, 3-H), 3.58 [d, J = 13.7 Hz, 2 H, N(CH_2Ph)′], 3.54 (s, 3 H, OMe), 3.73 [d, J = 13.7 Hz, 2 H, N(CH_2Ph)], 7.04−7.29 (m, 15 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77 ppm): δ = 35.8 (t, C-2), 36.1 (t, C-4), 51.3 (q, OMe), 53.4 [2 × t, N(*C*H_2Ph)$_2$], 57.6 (d, C-3), 126.1, 126.9, 128.1, 128.3, 128.9, 129.3 (15 × d, C arom.), 139.4, 139.5 (3 × s, C arom.), 172.7 (s, C-1) ppm. HRMS ($C_{25}H_{27}NO_2$): calcd. 374.2120 $[M + H]^+$, found 374.2108.

Methyl (3*S*)-3-Diallylamino-4-phenylbutyrate (33): Phosphane oxide **29** (168 mg, 0.33 mmol) in 4 mL THF under nitrogen was treated with potassium *tert*-butoxide (1.1 equiv.) in THF (2 mL/mmol) at 0 °C. After 15 min, the solution was concentrated in an ice-bath under reduced pressure to a volume of appoximately 1 mL. The intermediate ketene acetal was treated with an aqueous solution of 1 N HCl until the pH value was adjusted to 5. The mixture was extracted with dichloromethane and the combined organic layers were dried ($MgSO_4$) and purified by column chromatography to give the title compound 33 (80 mg, 0.293 mmol, 88%). Colorless oil. $[\alpha]_D^{20}$ = −28.2 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 2.27 (dd, J = 14.3, 5.9 Hz, 1 H, 2-H′), 2.39 (dd, J = 13.3, 9.2 Hz, 1 H, 4-H′), 2.45 (dd, J = 14.3, 9.2 Hz, 1 H, 2-H), 2.93 (dd, J = 13.3, 5.1 Hz, 1 H, 4-H), 3.03 [dddd, J = 14.3, 7.1, 1.2, 1.2 Hz, 2 H, N(CH_2CHCH$_2$)$_2$′], 3.23 [dddd, J = 14.3, 5.2, 1.7, 1.7 Hz, 2 H, N(CH_2CHCH$_2$)$_2$], 3.51 (dddd, J = 9.2, 9.2, 5.9, 5.1 Hz, 1 H, 3-H), 3.58 (s, 3 H, OMe), 5.19 [m, 4 H, N(CH$_2$CHCH_2)$_2$], 5.72 [dddd, J = 17.2, 10.1, 7.1, 5.2 Hz, 2 H, N(CH$_2$C*H*CH$_2$)$_2$], 7.12−7.30 (m, 5 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77 ppm): δ = 35.7 (t, C-4), 36.7 (t, C-2), 51.2 (q, OMe), 2 × 52.5 [2 × t, N(*C*H_2CHCH$_2$)$_2$], 58.4 (d, C-3), 2 × 116.4 [2 × t, N(CH$_2$CH*C*H$_2$)$_2$], 128.3, 2 × 128.6, 128.7, 129.2 (5 × d, C arom.), 2 × 137.2 [2 × d, N(CH$_2$*C*HCH$_2$)$_2$], 139.6 (s, C arom.), 172.7 (s, C-1) ppm. HRMS ($C_{17}H_{23}NO_2$): calcd. 274.1807 $[M + H]^+$, found 274.1813.

Methyl (2*R*,3*S*)-3-[(Benzyloxycarbonyl)amino]-2-hydroxy-4-phenylbutyrate (35): By treatment of phosphane oxide **27** (56 mg, 0.1 mmol) in dichloromethane prepared according to general procedure, the title compound **35** (33.3 mg, 97 μmol, 97%) was obtained. The diastereomeric ratio was determined by ^{1}H NMR sprectroscopy to be 8:1 in favour of the 2*R*,3*S*- over the 2*S*,3*S*-isomer.

(2*R*,3*S*)-35:[12] Colorless crystals, m.p. 97 °C (CH_2Cl_2). $[\alpha]_D^{23}$ = +7.9 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ = 0 ppm): δ = 2.89 (dd, J = 13.2, 7.1 Hz, 1 H, 4-H′), 2.97 (dd, J = 13.2, 8.9 Hz, 1 H, 4-H), 3.16 (br. s, 1 H, O*H*), 3.70 (s, 3 H, OMe), 4.08 (d, J = 1.8 Hz, 1 H, 2-H), 4.33 (dddd, J = 8.9, 8.0, 7.1, 1.8 Hz, 1 H, 3-H), 5.04 (s, 2 H, PhCH_2O), 5.09 (d, J = 8.0 Hz, 1 H, NH), 7.38−7.20 (m, 10 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, $CDCl_3$, δ = 77 ppm): δ = 38.3 (t, C-4), 52.9 (q, OMe), 54.7 (d, C-3), 66.8 (t, Ph*C*H_2O), 70.1 (d, C-2), 126.7, 127.9, 128.1, 128.5, 128.6, 129.4 (10 × d, C arom.), 136.3, 137.2 (2 × s, C arom.), 155.7 (s, N*C*O$_2$), 174.1 (s, C-1) ppm. HRMS ($C_{19}H_{21}NO_5$): calcd. 366.1317 $[M + Na]^+$, found 366.1326.

Methyl (2*S*,3*S*)-3-Dibenzylamino-2-hydroxy-4-phenylbutyrate (37): By treatment of phosphane oxide **28** (60.6 mg, 0.1 mmol) in dichloromethane prepared according to general procedure, the title compound 37 (35.4 mg, 91 μmol, 91%) was obtained as pure *anti*-configured isomer. Colorless oil. $[\alpha]_D^{20}$ = +35.8 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, $CDCl_3$, TMS, δ = 0 ppm): δ = 2.80 (dd, J = 13.9, 7.6 Hz, 1 H, 4-H′), 3.02 (dd, J = 13.9, 7.0 Hz, 1 H, 4-H), 3.12 (br. s, 1 H, O*H*), 3.41 (ddd, J = 7.6, 7.0, 2.5 Hz, 1 H, 3-H), 3.51 (s, 3 H, OMe), 3.65 [d, J = 14.0 Hz, 2 H, N(CH_2Ph)′], 3.81 [d, J = 14.0 Hz, 2 H, N(CH_2Ph)], 4.49 (br. s, 1 H, 2-H), 7.28−7.04 (m, 15 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, $CDCl_3$, δ = 77 ppm): δ = 32.0 (t, C-4), 52.3 (q, OMe), 54.6 [2 × t, N(*C*H_2Ph)$_2$], 62.2 (d, C-3), 69.7 (d, C-2), 126.1, 126.9, 128.0, 128.1, 128.8, 129.5 (15 × d, C arom.), 139.6, 139.0 (3 × s, C arom.), 174.9 (s, C-1) ppm. HRMS ($C_{25}H_{27}NO_3$): calcd. 390.2069 $[M + H]^+$, found 390.2082. The material was subjected to the hydrogenation conditions (Pd/C, H_2) described in ref.[20] in order to prove its stereochemical purity. The analytical and spectroscopic data of the hydrochloride of methyl (2*S*,3*S*)-3-amino-2-hydroxy-4-phenylbutanoate were identical with those reported in the literature.[20]

Methyl (2*S*,3*S*)-3-Diallylamino-2-hydroxy-4-phenylbutyrate (38): By treatment of phosphane oxide **29** (50.5 mg, 0.1 mmol) in dichloromethane prepared according to general procedure, the title compound 38 (26 mg, 90 μmol, 90%) was obtained as pure *anti*-configured isomer. Colorless oil. $[\alpha]_D^{20}$ = +7.6 ($CHCl_3$, c = 1.0). ^{1}H NMR (400 MHz, $CDCl_3$, TMS = 0 ppm): δ = 2.81 (dd, J = 13.8, 8.2 Hz, 1 H, 4-H′), 2.87 (dd, J = 13.8, 6.3 Hz, 1 H, 4-H), 3.13 [dddd, J = 14.4, 6.9, 1.2, 1.2 Hz, 2 H, N(CH_2CHCH$_2$)$_2$′], 3.19 [dddd, J = 14.4, 5.7, 1.5, 1.5 Hz, 2 H, N(CH$_2$CHCH$_2$)$_2$], 3.26 (br. s, 1 H, OH), 3.59 (s, 3 H, OMe), 3.46 (ddd, J = 8.2, 6.3, 3.6 Hz, 1 H, 3-H), 5.16−5.08 [m, 4 H, N(CH$_2$CHCH$_2$)$_2$], 4.24 (br. s, 1 H, 2-H), 5.73 [dddd, J = 17.1, 10.2, 6.9, 5.7 Hz, 2 H, N(CH$_2$C*H*CH$_2$)$_2$], 7.28−7.15 (m, 5 H, H arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, $CDCl_3$, δ = 77 ppm): δ = 31.9 (t, C-4), 52.1 (q, OMe), 2 × 53.7 [2 × t, N(*C*H_2CHCH$_2$)$_2$], 63.6 (d, C-3), 70.6 (d, C-2), 2 × 117.0 [2 × t, N(CH$_2$CH*C*H$_2$)$_2$],

126.1, 128.1, 129.5 (5 × d, C arom.), 2 × 136.7 [2 × d, $N(CH_2CHCH_2)_2$], 139.3 (s, C arom.), 174.6 (s, C-1) ppm. HRMS ($C_{17}H_{23}NO_3$): calcd. 290.1756 $[M + H]^+$, found 290.1754.

General Procedure for the KO*t*Bu-Induced Formation of *O*,*O*-Ketene Acetals and Asymmetric Dihydroxylation: The diphenylphosphane oxide adducts were dissolved in absolute THF (10 mL/mmol) under nitrogen and treated with potassium *tert*-butoxide (1.1 equiv.) in THF (2 mL/mmol) at 0 °C. After 15 min, the solution was concentrated in an ice-bath under reduced pressure to a volume of appoximately 1 mL. A suspension of "ADmix" [1 mol % $(DHQ)_2$-PHAL for ADmix-α or $(DHQD)_2$-PHAL for ADmix-β] in water (5 mL/mmol) and *tert*-butanol (5 mL/mmol) was prepared at room temperature, cooled to 0 °C and added to the pre-cooled ketene acetal. After addition of methanesulfonic acid amide (1.02 equiv.), the suspension was vigorously stirred for 4 h at 0 °C, and then reduced with sodium sulfite (1.5 g/mmol). Stirring was continued for 30 min at 0 °C, and after a further 15 min at room temperature, water (5 mL/mmol) and dichloromethane (20 mL/mmol) were added. The aqueous layer was extracted with dichloromethane (3 ×), and the combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure and purified by column chromatography on silica gel.

Methyl (2*S*,3*S*)- and (2*R*,3*S*)-3-[(Benzyloxycarbonyl)amino]-2-hydroxy-4-phenylbutyrate (35): By treatment of phosphane oxide **27** (559 mg, 1 mmol) in THF with potassium *tert*-butoxide and ADmix-α or ADmix-β, respectively, in dichloromethane, the title compound (2*S*,3*S*)-**35** (240 mg, 0.7 mmol, 70% for ADmix-α), and (2*R*,3*S*)-**35** (244 mg, 0.71 mmol, 71% for ADmix-β) was obtained according to the general procedure. Spectroscopic data for (2*R*,3*S*)-**35** are described above.

(2*S*,3*S*)-35:[12] Colorless crystals, m.p. 120 °C (CH_2Cl_2). $[\alpha]_D^{23}$ = +73.6 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.8 (m, 2 H, 4-H), 3.22 (s, 1 H, OH), 3.57 (s, 3 H, OMe), 4.34 (m, 1 H, 2-H), 4.41 (m, 1 H, 3-H), 5.05 (s, 2 H, $PhCH_2O$), 5.12 (d, *J* = 8.8 Hz, 1 H, NH), 7.40−7.14 (m, 10 H, H arom.) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 35.6 (t, C-4), 52.7 (q, OMe), 54.6 (d, C-3), 66.8 (t, $PhCH_2O$), 72.2 (d, C-2), 129.4, 128.5, 128.4, 128.1, 128.0, 126.7 (s, *C* aromat.), 136.8, 136.3 (s, *C* aromat.), 155.9 (s, NCO_2), 173.0 (s, C-1) ppm. HRMS ($C_{19}H_{21}NO_5$): calcd. 366.1317 $[M + Na]^+$, found 366.1319.

Methyl (2*S*,3*S*)-(*tert*-Butyloxycarbonyl)amino-2-hydroxy-4-phenylbutyrate (36): By treatment of phosphane oxide **27** (525 mg, 1 mmol) in THF with potassium *tert*-butoxide and ADmix-α according to the general procedure, the title compound **36** (256 mg, 0.83 mmol, 83%) was obtained.

36: Colorless crystals, m.p. 105 °C. $[\alpha]_D^{22.5}$ = +15.8 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (200 MHz, TMS = 0 ppm): δ = 1.38 (s, 9 H, *t*Bu), 2.79 (d, *J* = 7.6 Hz, 2 H, $PhCH_2$), 3.31 (d, *J* = 5.8 Hz, 1 H, OH), 3.60 (s, 3 H, COO*Me*), 4.33 (m, 2 H, NC*H*, C*H*OH), 4.85 (d, *J* = 7.6 Hz, 1 H, NH), 7.14−7.35 (m, 5 H, H arom.) ppm. ^{13}C NMR (50 MHz, $CDCl_3$ = 77 ppm): δ = 28.2 (q, *t*Bu), 35.7 (t, $PhCH_2$), 52.6 (q, COO*Me*), 54.3 (d, N*C*H), 72.5 (d, *C*HOH), 79.8 (s, *t*Bu), 126.6, 128.4, 129.5 (d, C arom.), 137.0 (s, C arom.), 155.5 (s, *C*O-O*t*Bu), 173.1 (s, *C*OOMe) ppm. $C_{16}H_{23}NO_5$ (309.36): calcd. C 62.12, H 7.49, N 4.53; found C 62.18, H 7.68, N 4.36.

Methyl (2*S*,3*S*)-3-(Benzyloxycarbonyl)amino-2-hydroxy-3-phenylpropanoate (43): By treatment of **41** (545 mg, 1.0 mmol) in THF with potassium *tert*-butoxide and ADmix-α according to the general procedure, the title compound **43** (236 mg, 0.72 mmol, 72%) was obtained. Colorless crystals, m.p. 102 °C. $[\alpha]_D^{22.2}$ = +16.8 ($CHCl_3$, *c* = 0.5). ^{1}H NMR (200 MHz, TMS, δ = 0 ppm): δ = 2.89 (d, 1 H, OH), 3.69 (s, 3 H, OMe), 4.61 (dd, *J* = 6.8, 3.5 Hz, 1 H, 2-H), 5.08 (2 × d, *J* = 12.1 Hz, 2 H, $PhCH_2O$), 5.17 (dd, *J* = 8.8, 3.5 Hz, 1 H, 3-H), 5.87 (d, *J* = 8.8 Hz, 1 H, NH), 7.19−7.37 (m, 10 H, H arom.) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, δ = 77 ppm): δ = 52.5 (q, OMe), 56.9 (d, C-3), 67.0 (t, $PhCH_2O$), 73.1 (d, C-2), 126.7, 127.3, 127.8 128.1, 128.2, 128.4, 128.6 (d, C arom.), 136.2, 138.8 (s, C arom.), 155.5 (s, N*C*OO), 172.1 (s, *C*OOMe) ppm. $C_{18}H_{19}NO_5$ (329.35): calcd. C 65.64, H 5.81, N 4.25; found C 65.76, H 5.85, N 4.40.

Methyl (2*S*,3*S*)-3-(*tert*-Butoxycarbonyl)amino-2-hydroxy-3-phenylpropanoate (44): By treatment of **42** (511 mg, 1.0 mmol) in THF with potassium *tert*-butoxide and ADmix-α according to general procedure, the title compound **44** (239 mg, 0.81 mmol, 81%) was obtained. Colorless crystals, m.p. 81 °C. $[\alpha]_D^{22.5}$ = +25.8 ($CHCl_3$, *c* = 1.0). ^{1}H NMR (200 MHz, TMS, δ = 0 ppm): δ = 1.43 (s, 9 H, *t*Bu), 2.89 (d, *J* = 6.2 Hz, 1 H, OH), 3.70 (s, 3 H, OMe), 4.60 (dd, *J* = 6.2, 3.6 Hz, 1 H, 2-H), 5.10 (dd, *J* = 8.0, 3.6 Hz, 1 H, 3-H), 5.61 (d, *J* = 8.0 Hz, 1 H, NH), 7.20−7.38 (m, 5 H, H arom.) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, δ = 77 ppm): δ = 28.3 (q, *t*Bu), 52.6 (q, OMe), 56.7 (d, C-3), 73.3 (d, C-2), 79.9 (s, *t*Bu), 127.2, 128.1, 128.5 (d, C arom.), 136.7 (s, C arom.), 155.0 (s, *C*OO*t*Bu), 172.3 (s, *C*OOMe) ppm. $C_{15}H_{21}NO_5$ (295.33): calcd. C 61.00, H 7.17, N 4.74; found C 60.87, H 7.01, N 4.77.

Degradation of Phosphane Oxide 13 in the Presence of Methanol: Phosphane oxide **13** (50 mg, 0.13 mmol) was dissolved in $CDCl_3$ (1 mL) in a NMR tube, and fifteen drops of MeOH and and two drops of TFA were added. The reaction was followed by recording NMR spectra. After 3 days, the 1,1,1-trimethoxynonane **56** was formed in 65% yield, while 22% starting material **13** was still present. In addition, methyl ester **18** (13%) was formed, which was ascribed to the presence of traces of water. ^{1}H NMR (400 MHz, TMS, δ = 0 ppm): δ = 3.23 (s, 9 H, OMe), 1.36−1.21 (m, 12 H, 3-H−8-H), 1.73 (m, 2 H, 2-H), 0.88 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, δ = 77.0 ppm): δ = 115.8 (C-1), 49.2 (OMe), 31.7, 30.2, 2 × 29.4, 29.1, 22.6, 22.5 (C-2 − C-8), 13.9 (C-9) ppm.

Acid-Promoted Hydrolysis in the Presence of $H_2{}^{18}O$: Phosphane oxide **13** (190 mg, 0.49 mmol) was dissolved in dry dichloromethane (4 mL) under nitrogen. After the addition of $H_2{}^{18}O$ (40 μL, 2 mmol; 96% purity) and *tert*-butyl bromide (50 mg, 0.36 mmol), the reaction was refluxed for 90 min. After cooling and removal of the solvent, the product was purified by flash column chromatography (petroleum ether/ethyl acetate, 4:1) to yield [^{18}O]-**18** (77 mg, 0.44 mmol; 90%). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.6, 24.9, 2 × 29.1, 29.2, 31.8, 34.1, 51.4, 174.247 (s, C^{18}OOMe), 174.285 (s, COOMe) ppm. HRMS ($C_{10}H_{20}O^{16}O^{18}$): calcd. 174.1506 $[M]^+$, found 174.1495.

2-(Diphenylphosphinoyl)-2,2-dimethoxy-1-phenylethanone (60): Lithiated phosphane oxide **5** (7 mmol) in THF (10 mL) was treated with benzoyl chloride (281 mg, 2 mmol) in THF (5 mL) at −110 °C, followed directly by aqueous hydrolysis. The mixture was warmed to room temperature, concentrated in vacuo, and extracted with dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography to yield the ethanone 60 (457 mg, 1.2 mmol; 60%). Light yellow crystals; m.p. 134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.46 (s, 6 H, OMe), 7.35−7.53 (m, 9 H, Ph, PhCO), 8.01−8.07 (m, 4 H, Ph), 8.25−8.28 (m, 2 H, PhCO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.5 (d, $J_{P,C}$ = 7.1 Hz, OMe), 108.7 (d, $J_{P,C}$ = 95.7 Hz, C-2), 127.7 (PhCO), 128.2

(d, $J_{P,C}$ = 11.9 Hz, Ph), 131.2 (d, $J_{P,C}$ = 92.8 Hz, Ph), 131.3 (PhCO), 131.8 (d, $J_{P,C}$ = 3.1 Hz, Ph), 132.2 (d, $J_{P,C}$ = 9 Hz, Ph), 133.1, 135.5 (2 × PhCO), 193.6 (d, $J_{P,C}$ = 12.1 Hz, C-1) ppm. HRMS ($C_{22}H_{21}O_4PNa$): calcd. 403.1075 $[M + Na]^+$, found 403.1068.

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie. We thank Dr. Gerald Dräger for helpful discussions, and C. Jasper and Y. Shili for expert preparative assistance. Benjamin Oelze is thanked for the forcefield calculations. This project is part of the joint initiative "Biologisch aktive Naturstoffe − Chemische Diversität" at the University of Hannover.

[1] [1a] A. Dondoni, L. Colombo, in *Advances in the Use of Synthons in Organic Chemistry* (Ed.: A. Dondoni), JAI Press Ltd., London, **1993**, vol. 1, 1−49. [1b] D. J. Ager, in *Umpoled Synthons* (Ed.: T. A. Hase), Wiley Interscience, New York, **1987**, 19−72.

[2] Selected examples of sulfur-stabilized d^1-synthons: [2a] E. J. Corey, D. Seebach, *Angew. Chem.* **1965**, *77*, 1134−1135; *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 1075−1976. [2b] G. Guanti, L. Banfi, A. Guaragna, E. Narisano, *J. Chem. Soc., Chem. Commun.* **1986**, 138−140. [2c] K. Ogura, T. Tsuruda, K. Takahashi, H. Iida, *Tetrahedron Lett.* **1986**, *27*, 3665−3668.

[3] [3a] T. Mandai, M. Yamaguchi, Y. Nakayama, J. Otera, M. Kawada, *Tetrahedron Lett.* **1985**, *26*, 2675−2678. [3b] A. de Groot, B. J. Hansen, *Synth. Commun.* **1983**, *13*, 985−990. [3c] J. Otera, *Synthesis* **1988**, 95−102.

[4] [4a] L. Colombo, M. Di Giacomo, G. Brusotti, E. Milano, *Tetrahedron Lett.* **1995**, *36*, 2863−2866. [4b] D. J. Ager, M. B. East, *J. Org. Chem.* **1986**, *51*, 3983−3992. [4c] J.-P. Quintard, P. Elissondo, D. Mouko-Mpegna, *J. Organomet. Chem.* **1983**, *251*, 175−187. [4d] J.-P. Quintard, P. Elissondo, B. Jousseaume, *Synthesis* **1984**, 495−498.

[5] [5a] P. Magnus, G. Roy, *Organometalics* **1982**, *1*, 553−559. [5b] J. Yoshida, S. Matsunaga, S. Isoe, *Tetrahedron Lett.* **1989**, *30*, 219−222. [5c] D. J. Ager, J. E. Gano, S. I. Parekh, *J. Chem. Soc., Chem. Commun.* **1989**, 1256−1258.

[6] [6a] A. R. Katritzky, Y.-X. Cheng, K. Yannakopoulou, P. Lue, *Tetrahedron Lett.* **1989**, *30*, 6657−6660. [6b] A. R. Katritzky, M. Drewniak-Deyrup, X. Lan, F. Brunner, *Heterocycl. Chem.* **1989**, *26*, 829−836.

[7] [7a] E. J. Corey, D. L. Boger, *Tetrahedron Lett.* **1978**, *19*, 5−8. [7b] H. Chikashita, M. Ishibaba, K. Ori, K. Itoh, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3637−3648.

[8] [8a] A. Dondoni, *Pure Appl. Chem.* **1990**, *62*, 643−652. [8b] A. Dondoni, in *Modern Synthetic Methods* (Ed.: R. Scheffold), Helvetica Chimica Acta Basel, **1992**, 377−437 and references cited therein.

[9] [9a] A. Kirschning, G. Dräger, A. Jung, *Angew. Chem.* **1997**, *109*, 253−255; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 253−255. [9b] H. Monenschein, G. Dräger, A. Jung, A. Kirschning, *Chem. Eur. J.* **1999**, *5*, 2270−2280.

[10] Reviews on the Horner−Wittig reaction: [10a] J. Clayden, S. Warren, *Angew. Chem.* **1996**, *108*, 261−291; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 241−270. [10b] B. E. Maryanoff, A. B. Reitz, *Chem. Rev.* **1989**, *89*, 863−927.

[11] Reviews of asymmetric dihydroxylation: [11a] D. J. Berrisford, C. Bolm, K. B. Sharpless, *Angew. Chem.* **1995**, *107*, 1159−1171; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1050−1064. [11b] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483−2547. [11c] R. A. Johnson, K. B. Sharpless, in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH Publishers, New York, **1993**, 227−272.

[12] H. Monenschein, M. Brünjes, A. Kirschning, *Synlett* **2002**, *3*, 525−527.

[13] T. A. M. van Schaik, A. V. Henzen, A. van der Gen, *Tetrahedron Lett.* **1983**, *24*, 1303−1306.

[14] For the stability of the lithiated phosphane oxide **5**, refer to ref.[9b].

[15] Reviews on the preparation of β-amino acid derivatives: [15a] P. A. Magriotis, *Angew. Chem. Int. Ed.* **2001**, *40*, 4377−4379. [15b] M. Liu, M. P. Sibi, *Tetrahedron* **2002**, *58*, 7991−8035.

[16] [16a] D. Seebach, M. Overhand, F. N. M. Kühnle, B. Martinone, L. Oberer, U. Hommel, H. Widmer, *Helv. Chim. Acta* **1996**, *79*, 913−941. [16b] E. P. Ellmermer-Müller, D. Brössner, N. Maslouh, A. Takó, *Helv. Chim. Acta* **1998**, *81*, 59−65. [16c] c. G. Guichard, S. Abele, D. Seebach, *Helv. Chim. Acta* **1998**, *81*, 187−206.

[17] [17a] R. Caputo, E. Cassano, L. Longobardo, G. Palumbo, *Tetrahedron* **1995**, *51*, 12337−12350. [17b] J. Podlech, D. Seebach, *Liebigs Ann. Org. Bioorg. Chem.* **1995**, *7*, 1217−1228.

[18] [18a] F. J. Lakner, K. S. Chu, G. R. Negrete, J. P. Konopelski, *Org. Synth.* **1996**, *73*, 201−214. [18b] E. Juaristi, M. Balderas, E. García-Pérez, *Tetrahedron: Asymmetry* **1996**, *7*, 2233−2246. [18c] E. Juaristi, M. Balderas, Y. Ramírez-Quirós, *Tetrahedron: Asymmetry* **1998**, *9*, 3881−3888. [18d] E. Juaristi, H. López-Ruiz, D. Madrigal, Y. Ramírez-Quirós, J. Escalante, *J. Org. Chem.* **1998**, *63*, 4706−4710. [18e] J. E. Semple, O. E. Levy, N. K. Minami, T. D. Owens, D. V. Siev, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2305−2309.

[19] Recent advances in the synthesis of phenylisoserine: [19a] M. V. Voronkov, A. V. Gontcharov, Z.-M. Wang, *Tetrahedron Lett.* **2003**, *44*, 407−409. [19b] R. Caputo, G. Cecere, A. Guadagna, G. Palumbo, S. Pedatella, *Eur. J. Org. Chem.* **2002**, 3050−3054. [19c] S. H. K. Reddy, S. Lee, A. Datta, G. I. Georg, *J. Org. Chem.* **2001**, *66*, 8211−8214. [19d] M. Bruncko, G. Schlingloff, K. B. Sharpless, *Angew. Chem.* **1997**, *109*, 1580−1583; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1483−1486. [19e] K. C. Nicolaou, S. Natajaran, H. Li, N. F. Jain, R. Hughes, M. E. Solomon, J. M. Ramanjulu, C. N. C. Boddy, M. Takayanagi, *Angew. Chem.* **1998**, *110*, 2872−2878, *Angew. Chem. Int. Ed.* **1998**, *37*, 2708−2714.

[20] M. Seki, K. Matsumoto, *Synthesis* **1999**, *6*, 924−926.

[21] The serine analogue of **45** is commonly named as "Garner aldehyde": P. Garner, S. Ramakant, *J. Org. Chem.* **1986**, *51*, 2609.

[22] A. Dondoni, D. Perrone, *Synthesis* **1993**, 1162−1176.

[23] J. R. Luly, J. F. Dellaria, J. J. Plattner, J. L. Sonderquist, N. Yi, *J. Org. Chem.* **1987**, *52*, 1487−1492.

[24] [24a] M. Reetz, *Angew. Chem.* **1991**, *103*, 1559−1573; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1531−1546. [24b] M. Reetz, M. W. Drewes, A. Schmitz, *Angew. Chem.* **1987**, *99*, 1186−1188; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1141−1143.

[25] The Cornforth model is based on dipole minimization between the C−X bond and the adjacent carbonyl group: [25a] J. W. Cornforth, R. H. Cornforth, K. K. Mathew, *J. Chem. Soc.* **1959**, 112−127. [25b] M. N. Paddon-Row, N. G. Rondan, K. N. Houk, *J. Am. Chem. Soc.* **1982**, *104*, 7162−7166. [25c] A. S. Cieplak, K. B. Wiberg, *J. Am. Chem. Soc.* **1992**, *114*, 9226−9227. [25d] G. Frenkin, K. F. Köhler, M. T. Reetz, *Tetrahedron* **1994**, *50*, 11197−11204.

[26] The starting geometries were minimized using the MMFF ForceField within MacroModel. These minimized conformations were used as input for a Monte Carlo search to find the global minimum. All minimizations were calculated in chloroform as a solvent model to complete convergence. Monte Carlo searches were run until the global minimum was found more than once. The minimized conformation relevant for the Cornforth model was more stable than the first conformation which leads to the *syn*-configured addition product by about ΔE = 5.64 kJ/mol.

[27] [27a] J. G. Dingwall, J. Ehrenfreund, R. G. Hall, *Tetrahedron* **1989**, *45*, 3787−3808. [27b] V. V. Moska, A. I. Maikova, A. I. Razomov, *J. Gen. Chem. U. S. S. R.* **1969**, *39*, 2391−2399.

[28] An illustrative example is presented in: G. Udvarnoki, T. Henkel, R. Machinek, J. Rohr, *J. Org. Chem.* **1992**, *57*, 1274−1276.
[29] [29a] Yuang Shili, Diplomarbeit, University of Hannover, **2003**. [29b] Christof Kujat, Diplomarbeit, University of Hannover, **2003**.
[30] [30a] S. Steurer, J. Podlech, *Eur. J. Org. Chem.* **1999**, 1551−1560. [30b] M. Brünjes, G. Sourkouni-Argirusi, A. Kirschning, *Adv. Synth. Catal.* **2003**, *345*, 635−642.
[31] T. T. Tidwell, *Synthesis* **1990**, 857−870.
[32] Holger Monenschein, Diplomarbeit, Technische Universität Clausthal, **1998**.
[33] W. Yuan, B. Munoz, C.-H. Wong, J. Z. Haeggstroem, A. Wetterholm, B. Samuelsson, *J. Med. Chem.* **1993**, 211−220.
[34] B. J. Rawlings, P. B. Reese, S. E. Ramer, J. C. Vederas, *J. Am. Chem. Soc.* **1989**, *111*, 3382−3390.
[35] [35a] A. Kleversaat, H. Laatsch, G. Rak, *Liebigs Ann. Chem.* **1986**, *4*, 741−750. [35b] G. Esteban, M. A. Lopez-Sanchez, E. Martinez, J. Plumet, *Tetrahedron* **1998**, *54*, 197−212.
[36] S. Caddick, C. A. M. Afonso, S. X. Candeias, P. B. Hitchcock, K. Jenkins, L. Murtagh, D. Pardoe, A. G. Santos, N. R. Treweeke, R. Weaving, *Tetrahedron* **2001**, *57*, 6589−6606.

Received October 7, 2003

