Substrate-Directed Diastereoselective Hydroformylations, 2[◇]

1,3-Asymmetric Induction in Stereoselective Rhodium-Catalyzed Hydroformylation of Homomethallylic Alcohols☆

Bernhard Breit

Fachbereich Chemie der Philipps-Universität Marburg,
Hans-Meerweinstraße, D-35043 Marburg, Germany
Fax: (internat.) +49(0)6421/28 8917
E-mail: breit@ps1515.chemie.uni-marburg.de

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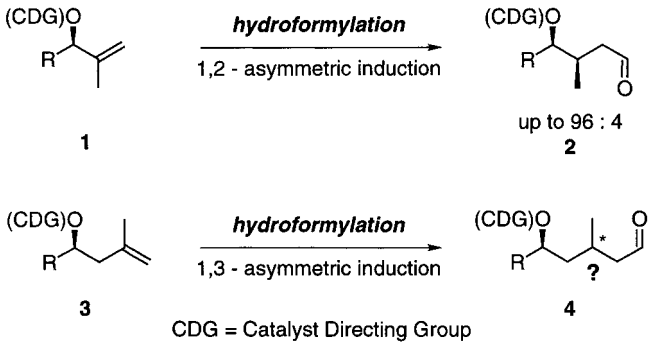
Introducing *ortho*-diphenylphosphanyl benzoyl as a substrate bound catalyst directing group (CDG) allows an efficient substrate-directed diastereoselective hydroformylation of acyclic homomethallylic alcohols **5**, making use of 1,3-asymmetric induction. The corresponding *anti*-aldehydes **10** were obtained as the major diastereomer in all cases, with diastereomer ratios of ca. 91:9 (*anti:syn*). Supporting evidence could be obtained for the ability of the *o*-DPPB group to act as a catalyst-directing group (CDG) via a reversible catalyst coordination. Finally, a model has been devised that rationalizes the origin of the 1,3-asymmetric induction. This model is based on a conformational analysis (NMR studies, MACROMODEL/MM3 calculations) of the homomethallylic substrates and indicates a relationship between the preferred substrate conformation and the experimentally determined stereoselectivities. In agreement with this model was the predicted significant improvement in stereoselectivity upon hydroformylation of the *anti*-homomethallylic alcohol derivative **15** (→ **21**).

Introduction

Transition metal catalyzed reactions have evolved into powerful tools for the construction of carbon backbones in modern organic synthesis. This is particularly due to their compatibility with multifunctionality in organic substrates, and their reliable operation under usually mild conditions. Some of these reactions also allow the generation of new stereocenters, either with the aid of a chiral catalyst[1] or by substrate-based asymmetric induction.[2] Despite its attractiveness with regard to synthetic efficiency, the latter approach is not frequently utilized in asymmetric synthesis.[3]

However, we recently found that the rational design of such processes becomes possible with the aid of a *catalyst-directing group* (CDG).[4] The role of such a group attached to the substrate is to precoordinate the catalytically active species, which should result in the selective positioning of the catalyst at one of two diastereotopic, e.g. olefin faces of a substrate. Based on this concept, the *ortho*-diphenylphosphanylbenzoate group (*o*-DPPB) has been developed as an effective catalyst-directing group for the stereoselective hydroformylation of methallylic alcohols **1**.[4][5] In this process, high 1,2-asymmetric induction gives rise to the formation of the *syn*-aldehydes **2** as the major diastereomers with diastereoselectivities of up to 96:4. A question then arose as to whether the same concept and catalyst-directing group would permit efficient 1,3-asymmetric induction. In this regard, acyclic homomethallylic alcohol derivatives **3** appeared to be a particularly interesting class of substrates, since their hydroformylation would furnish an acyclic building block **4** with hydroxy- and methyl-substituted stereocenters in a 1,3-relation. Such a structural motif is common within the polyketide class of natural products[6], and its stereoselective synthesis is therefore of considerable synthetic importance.



In this paper, full details are given on the use of the *o*-DPPB group as an efficient catalyst-directing group for the stereoselective rhodium-catalyzed hydroformylation of acyclic homomethallylic alcohols, giving rise to high 1,3-

[◇] For Part 1, see B. Breit, *Liebigs Ann.* **1997**, 1841−1851.

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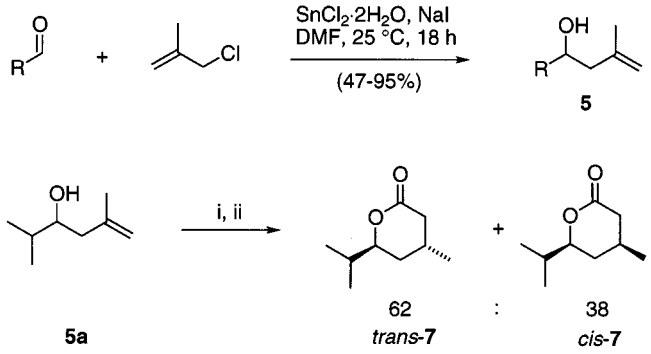
asymmetric induction.[7] Additionally, a model is described that rationalizes the stereochemical outcome of this reaction on the basis of calculated and experimentally determined preferred substrate conformations in solution.

Synthesis of Homomethallylic Alcohols and Exploratory Investigations

Homomethallylic alcohols **5** were prepared according to Imai's protocol.[8] In exploratory studies, the potential of the unprotected hydroxyl functionality of a homomethallylic alcohol to act as a catalyst-directing group was evaluated.

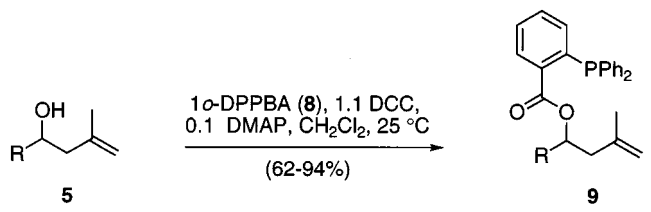


Reagents and conditions: i, 0.35 mol% [$Rh(CO)_2acac$], 7 mol% PPh_3, 20 bar H_2/CO (1 : 1), toluene, 90 °C, 23 h (25% conversion → **6**); ii, 2 PCC on Al_2O_3, CH_2Cl_2, 25 °C, 24 h (66%).

Thus, alcohol **5a** was subjected to hydroformylation conditions (90°C, toluene, 0.35 mol% $[Rh(CO)_2acac]$, 7 mol% PPh_3) for 24 h. A low conversion (25%) to the corresponding δ-lactols **6** was observed.[9] Subsequent oxidation of the lactols **6** with pyridinium chlorochromate (PCC) furnished the known lactones **7**,[10] as a 62:38 mixture of *trans*- and *cis*-**7**, indicating the inability of a hydroxyl group to act as an efficient catalyst-directing group. This result parallels observations made previously in the methallylic alcohol series.[4]

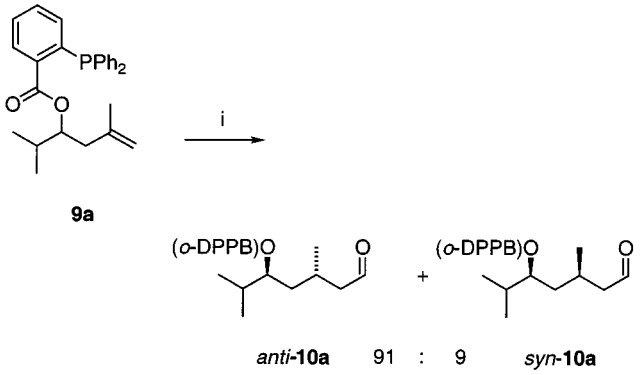
Synthesis and Hydroformylation of Homomethallylic *o*-DPPB Esters

At this stage it was decided to explore the potential of the recently developed catalyst-directing *o*-DPPB group to make more efficient use of the substrate-inherent chirality information. For this purpose, homomethallylic *o*-DPPB esters **9** were prepared from homomethallylic alcohols **5** and *ortho*-diphenylphosphanylbenzoic acid [*o*-DPPBA (**8**)] employing the DCC/DMAP esterification protocol.[11]



Hydroformylation of **9a** at 50°C furnished aldehyde **10a** in 91% yield with a diastereomer ratio of 91:9 (*anti*:*syn*).

Interestingly, a significant dependence of the diastereoselectivity on the reaction temperature was observed. Thus, reaction of *o*-DPPB ester **10a** at 90°C gave only a 70:30 ratio (Table 1, entry 3). Lowering the reaction temperature to 70°C and even further to 50°C improved the diastereomer ratio from 87:13 to 91:9 favoring the *anti*-aldehyde (Table 1, entries 1 and 2).



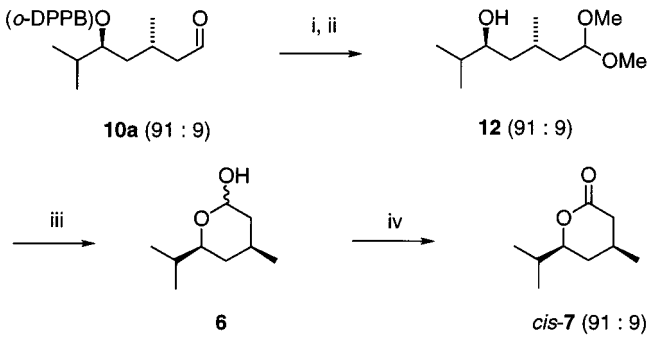
Reagents and conditions: i, 0.7 mol% $[Rh(CO)_2acac]$, 2.8 mol% $P(OPh)_3$, 20 bar H_2/CO (1 : 1), toluene, 50 °C, 72 h (93%).

Table 1. Temperature dependence of the diastereoselectivity of hydroformylation of **9a**

Entry	*T* [°C]	*t* [h]	Yield (%)[a]	*anti*:*syn*[b]
1	50	72	93	91:9
2	70	24	99	87:13
3	90	24	99	70:30

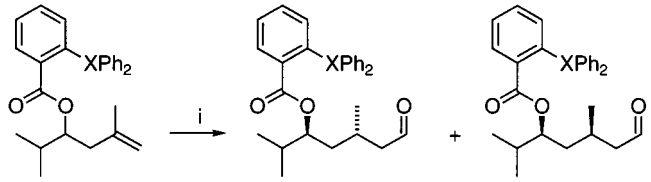
[a]Isolated yield after column chromatographic purification. – [b]Determined by NMR spectroscopic analysis of the crude product.

The relative configuration of the hydroformylation product **10a** was determined by transformation to the literature-known lactones **7**.[10] Thus, the aldehyde functionality in **10a** was protected as a dimethyl acetal (→ **11**). Subsequent alkaline hydrolysis furnished the alcohol **12** as well as *o*-DPPBA (**8**). Deprotection of the acetal employing lithium tetrafluoroborate in acetonitrile in the presence of 2% water furnished the δ-lactols **6**. Finally, PCC oxidation led to the known *cis*-lactone **7**.[10]



Reagents and conditions: i, MeOH, Bayer Lewatit® SPC 108, $MgSO_4$, 24 h, (→ **11**) (95%); ii, EtOH, KOH, 80 °C, 3 h (97%); iii, $LiBF_4$, CH_3CN, 2% H_2O, 24 h (quant.); PCC on Al_2O_3, CH_2Cl_2,18 h (98%).

In order to study the influence of the *o*-DPPB group on the stereoselectivity of the hydroformylation reaction, the benzoate **13** was prepared, which differs from the *o*-DPPB ester **9a** in that the phosphane moiety is replaced by a CH unit. Thus, derivative **13** should possess almost the same structural features as the corresponding *o*-DPPB ester **9a**, but should lack the ability to temporarily coordinate to the catalytically active transition metal center.[12]

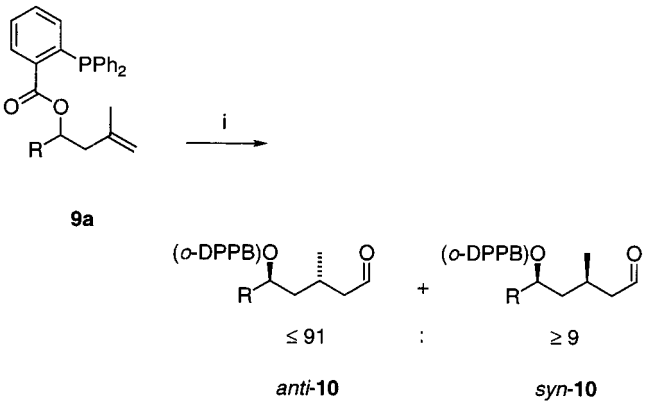


Reagents and conditions: i, 0.7 mol% $[Rh(CO)_2acac]$, 2.8 mol% $P(OPh)_3$, 20 bar H_2/CO (1 : 1), toluene (0.1 M), 50 ° (70 °C), 72 h.

Hydroformylation of the homomethallylic esters **9a** and **13** furnished the aldehydes **10a** and **14**, respectively. The *o*-DPPB derivative **9a** could be reacted at 50°C, whereas the phosphane-lacking derivative **13** required a slightly higher reaction temperature of 70°C for hydroformylation to proceed smoothly, indicating a rate-enhancing effect of the intramolecular phosphane ligand.[12] The stereochemical outcome of these two reactions proved to be most interesting. Thus, *o*-DPPB ester **9a** gave predominantly the *anti*-aldehyde **10a** in a diastereomer ratio of 91:9. In contrast, the phosphane-free system **13** furnished preferentially the *syn*-aldehyde **14** in a diastereomer ratio of 71:29.[12] Evidently, the homomethallylic substrate has an inherent ability (presumably of spatial origin) to direct the rhodium catalyst to the diastereotopic olefin face, which leads to the formation of the *syn*-aldehyde. However, the *o*-DPPB group is capable of overruling these sterically-based directing effects, giving rise to the formation of the opposite diastereomer. This result underlines the ability of the *o*-DPPB group to act as a *catalyst-directing group* (CDG) by reversible coordination of the catalyst, and is in agreement with similar observations that have been made with the corresponding methallylic alcohol *o*-DPPB esters (**1** → **2**).[4]

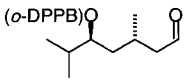
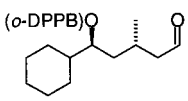
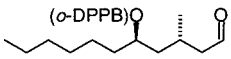
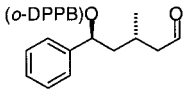
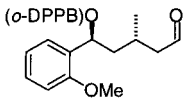
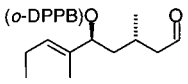
To check whether the diastereoselectivity shows a dependence on the nature of the substituent R at the stereogenic center in the hydroformylation of the homomethallylic alcohol *o*-DPPB esters **9**, the hydroformylation of the homomethallylic *o*-DPPB esters **9b**–**f** was investigated (see Table 2).

In all cases, hydroformylation was found to proceed smoothly to give the corresponding aldehydes **10** in good to excellent yields and with *anti*-diastereoselectivities of up to 91%. Surprisingly, and in striking contrast to previous results on the hydroformylation of methallylic *o*-DPPB esters[4], no significant influence of the substituent R on the diastereoselectivity could be detected. Thus, primary and secondary alkyl as well as aryl substituents were tolerated



Reagents and conditions: i, 0.7 mol% $[Rh(CO)_2acac]$, 2.8 mol% $P(OPh)_3$, 20 bar H_2/CO (1 : 1), toluene, 30-50 °C, (72-90%).

Table 2. Results of the substrate-directed diastereoselective hydroformylation of homomethallylic *o*-DPPB esters **9**

Entry	Major diastereomer (*anti*-**10**)	*T* [°C]	*t* [h]	Yield (%)[a]	*anti* : *syn*[b]
1	 **10a**	50	72	93	91 : 9
2	 **10b**	50	72	90	91 : 9
3	 **10c**	30	168	81	90 : 10
4	 **10d**	30	120	72	90 : 10
5	 **10e**	30	240	78	90 : 10
6	 **10f**	30	168	85	90 : 10

[a] Isolated yield after column chromatographic purification. – [b] Determined by NMR spectroscopic analysis of the crude product.

and gave diastereomer ratios of ca. 91:9, irrespective of the nature of R. The hydroformylation of the alkenyl-substituted derivative **9f**, in which a 1,1-disubstituted alkene could be reacted chemo-, regio- and stereoselectively in the presence of a trisubstituted alkene to give the *anti*-aldehyde **10f** in 85% yield and with a diastereomer ratio of 90:10 (Table 2, entry 6) was particularly interesting.

A comparison of the NMR spectra of the aldehydes **10** revealed characteristic differences between the *anti*- (major) and *syn*- (minor) diastereomers. Thus, the ^{13}C-NMR resonances of the methyl carbons at C3 are shifted to higher field in *anti*-**10a**−**f** relative to those in *syn*-**10a**−**f** (see Table 3). The same holds for the ^{13}C-NMR resonances of the oxygen-substituted carbon atom C1. Accordingly, with the derivatization of *anti*-**10a** to the known cis-δ-lactone **7** as a point of reference, ^{13}C-NMR spectroscopy allows the assignment of *anti*- and *syn*-configuration, respectively.

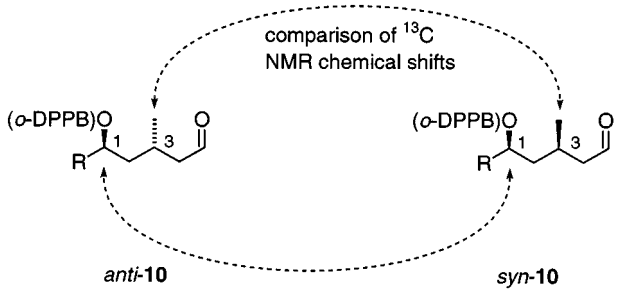


Table 3. Comparison of selected NMR data of *anti*- and *syn*-aldehydes **10**

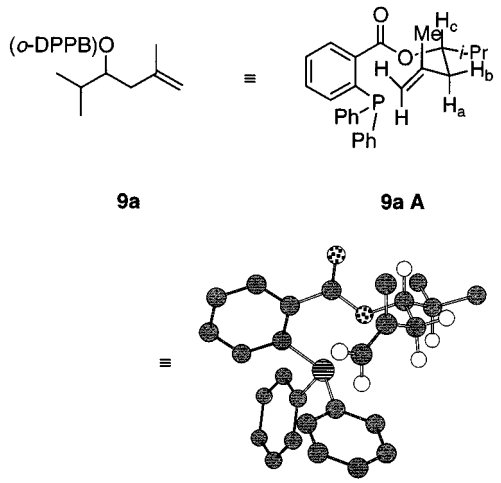
Compound	R	^{13}C NMR resonances of C1, δ		^{13}C NMR resonances of methyl-C at C 3, δ	
		anti	*syn*	*anti*	*syn*
10a	*i*-Pr	77.07	77.15	19.32	20.60
10b	*c*-Hex	76.57	76.69	19.49	20.53
10c	*n*-Hex	73.20	73.40	19.65	20.54
10d	Ph	75.03	75.44	19.84	20.27
10e	*o*-MeOC$_6$H$_4$	69.74	69.79	19.74	20.54
10f	(*E*)-EtCH=CMe	78.16	79.10	19.76	19.92
21	*i*-Pr	79.60	79.90	19.98	20.12

Preferred Substrate Conformation and Model for 1,3-Asymmetric Induction

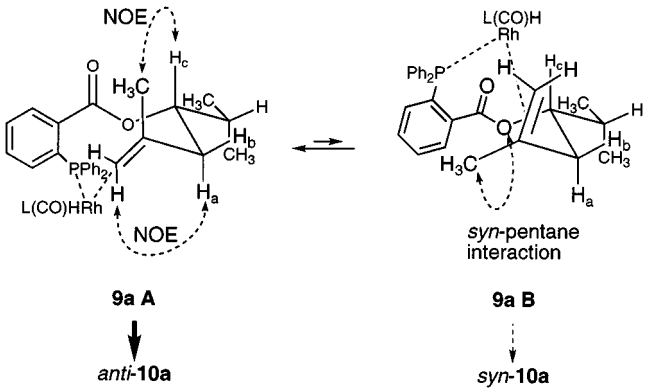
The aforementioned investigations showed that hydroformylation of the homomethallylic *o*-DPPB esters **9** led to diastereomer ratios of about 90:10, almost independently of the nature of the substituent at the stereogenic center. From this, it could be assumed that the observed 1,3-asymmetric induction stemmed from a conformational preference inherent to the homomethallylic system itself. This hypothesis was further supported by the strong temperature dependence that was observed on hydroformylation of derivative **9a** (see Table 1).

To gain further insight, the preferred conformation of the homomethallylic *o*-DPPB ester **9a** in solution at 25°C was examined by NMR techniques.[14] Thus, H_a showed a large vicinal coupling constant of 9.0 Hz to H_c, whereas coupling between H_b and H_c was smaller (4.1 Hz). Furthermore, the 2D-NOESY spectra revealed a strong NOE contact between the protons of the methyl substituent at the olefin and H_c, as well as between one of the olefinic protons and H_a. Both the vicinal coupling constants as well as the observed NOE contacts showed compound **9a** to have the preferred conformation **9aA**.[15] This is in agreement with MACROMODEL/MM3 calculations, which indicate **9aA** to be the preferred conformation at ambient temperature (ca. 60% populated at 25°C, see Figure 1).[16]

Figure 1. Energetically most stable conformation **A** of **9a** according to MACROMODEL/MM3 (ca. 60% populated at 25°C)



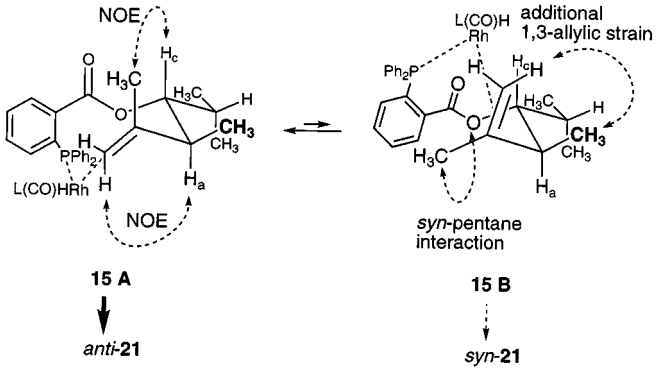
Scheme 1. Preferred conformation **A** and minor conformation **B** of **9a**; the indicated coordination of the rhodium catalyst is hypothetical



If one assumes a coordination of the rhodium catalyst between the catalyst-directing group and the alkene as indicated (Scheme 1), hydroformylation would furnish the *anti*-aldehyde *anti*-**10a**, as was indeed found experimentally. The less preferred conformation **9aB** (about 5 kJ/mol less stable than conformation **9aA** according to MACROMODEL/MM3) should give rise to complexation of the opposite diastereotopic alkene face, i.e. to the formation of the corresponding *syn*-aldehyde (*syn*-**10a**). According to the MACROMODEL/MM3 calculations, conformation **B** is populated to an extent of about 10% at 25°C. All other conformations of **9a** (ca. 30% at 25°C) do not permit a chelating bidentate binding mode of the olefin and *o*-DPPB group. Assuming that the intramolecular process involving precoordination of the catalyst by the *o*-DPPB group is the only reaction pathway in operation,[17] other conformations can be neglected.

The question then arises as to the nature of the underlying reasons for conformation **9aA** being energetically favored compared to conformation **9aB**. The only argument one could put forward is the avoidance of a repulsive *syn*-pentane interaction[18] between the oxygen substituent and the methyl substituent at the olefin. Such a destabilizing interaction reaches a maximum in conformation **9aB**, but is minimized in conformation **9aA**. Thus, the observed reaction pathway via conformer **9aA** to the *anti* major diastereomer *anti*-**10a** might be preferred due to the avoidance of this repulsive *syn*-pentane interaction. On the other hand, if this assumption is correct, the incorporation of an additional conformational destabilizing (repulsive) interaction in conformer **9aB** only, should disfavor conformer **B** even more compared to conformer **A**, and ultimately, should give rise to higher *anti*-diastereoselectivity in the course of the hydroformylation reaction. Such an additional repulsive interaction could result from incorporation of additional 1,3-allylic strain[19] into conformer **B**. Such an interaction would arise if H_b in **9a** were to be replaced by a methyl substituent.

Scheme 2. Preferred conformation **A** and minor conformation **B** of **15**; the indicated coordination of the rhodium catalyst is hypothetical

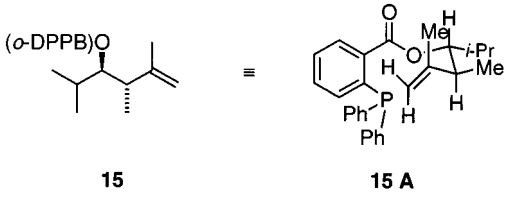


Substitution of H_b by a methyl group leads to the homomethallylic *o*-DPPB ester **15**, in which the oxygen-bearing- and the methyl-substituted stereocenters have an *anti* relation. MACROMODEL/MM3 force field calculations indicate that the homomethallylic *o*-DPPB ester **15** has the expected preferred conformation **15A**, which is populated to an extent of about 74% at 25°C (see Figure 2).[16] In other words, according to the force field calculations, compound **15**, bearing the additional methyl substituent, shows an enhanced conformational preference for conformer **A**.

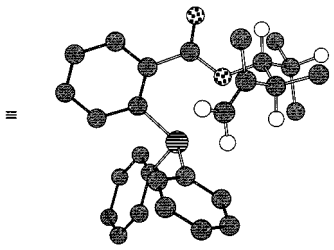
On the other hand, substitution of H_a by a methyl group (→**16**) should give rise to an additional repulsive 1,3-allylic strain in conformer **16A**, which would destabilize this conformation (see Scheme 3). Consequently, for derivative **16**, neither conformation **A** nor conformation **B** would be significantly favored. According to our model, this should result in a low diastereoselectivity upon hydroformylation of the *syn*-homomethallylic *o*-DPPB ester **16**.

This prediction was confirmed by a conformational analysis (MACROMODEL/MM3) of derivative **16**. Thus, neither conformer **16A** nor conformer **16B** was shown to be significantly populated at ambient temperature (percentage of both conformers of all populated conformations at 25°C amounts to < 10%).[16] Interestingly, the calculation indicated conformer **16C** to be the major populated species at 25°C at a level of 87% (see Figure 3).

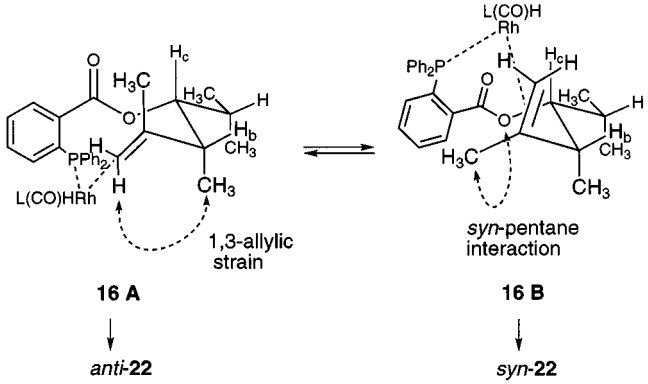
Figure 2. Energetically most stable conformation **A** of **15** according to MACROMODEL/MM3 (ca. 74% populated at 25°C)



15 **15 A**



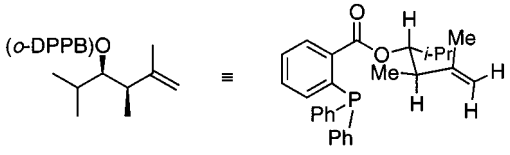
Scheme 3. Repulsive interactions in conformation **A** and conformation **B** of **16**; the indicated coordination of the rhodium catalyst is hypothetical



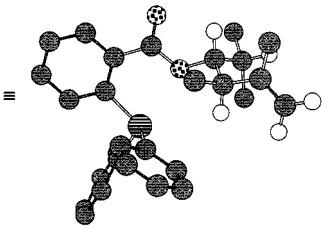
16 A **16 B**

anti-**22** *syn*-**22**

Figure 3. Energetically most stable conformation **C** of **16** according to MACROMODEL/MM3 (ca. 87% populated at 25°C)

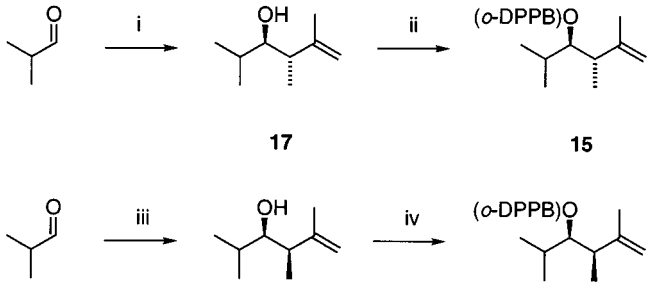


16 **16 C**



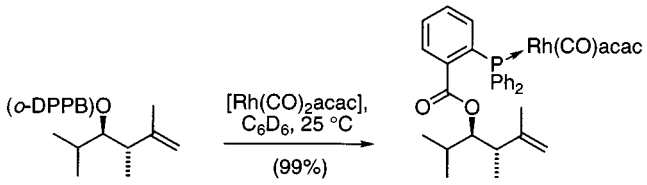
A conformer such as **16C** does not permit the required chelating binding mode of the phosphane and olefin. Therefore, conformation **16C** can be neglected as a reactive conformation for the *o*-DPPB-directed hydroformylation reaction, even though it is significantly populated.

The corresponding *anti*-homomethallylic alcohol **17** (*dr* ≥ 95:5) was obtained according to Moise and Szymoniak employing a Ti(III) allylating reagent prepared from [Cp_2TiCl_2], isoprene and 2 equiv. of isopropylmagnesium bromide.[20] Stereoselective synthesis of the *syn*-diastereomer **19** was achieved in moderate yield starting from isovaleraldehyde and the known allylstannane **18**[21]. Esterification with *o*-DPPBA employing the DCC/DMAP protocol gave the corresponding *o*-DPPB esters **15** and **16**.



Reagents and conditions: i, 1.25 equiv. isoprene, 0.8 equiv. [Cp_2TiCl_2], 2 equiv. *i*-PrMgBr, THF, 25 °C (42%); ii,1 equiv. *o*-DPPBA (**8**), 1.1 equiv. DCC, 1 equiv. DMAP, CH_2Cl_2, 25 °C (70%); iii, *E*-MeHC=C(Me)CH_2SnBu_3 (**18**), 2 $BF_3 \cdot OEt_2$, CH_2Cl_2, -78 °→10 °C, (28%); iv, 1 equiv. *o*-DPPBA (**8**), 1.1 equiv. DCC, 1 equiv. DMAP, CH_2Cl_2, 25 °C (47%).

At first, it had to be verified that *anti*-derivative **15** did indeed populate conformation **15A** in solution, as was predicted by our model and MACROMODEL/MM3 calculations. These investigations had to be performed on a suitable model system, which needed to be as similar as possible to the situation in the course of the hydroformylation reaction. The rhodium complex **20**, which was obtained from **15** by reaction with [$Rh(CO)_2$acac] in benzene at room temperature, was considered to be an appropriate model system.



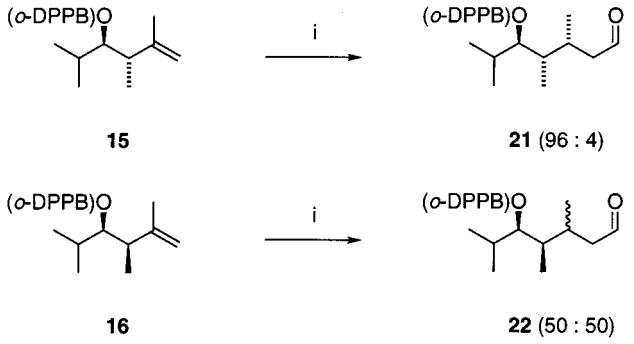
15 **20**

The structure of **20** was confirmed by NMR spectroscopy. Thus, the ^{31}P-NMR resonance of **20** is shifted downfield by about 60 ppm (**20**: δ = 54.8) compared to that of the free phosphane **15** (δ = −4.1), as expected for an η^1-coordination of a triarylphosphane to a rhodium(I) central atom. Furthermore, the ^{31}P-NMR resonance shows a characteristic splitting to a doublet, with a typical $^1J_{P,Rh}$ coupling constant of 189.1 Hz, indicating that the P atom resides in the direct neighborhood of the rhodium nucleus.[22] The ^{13}C-NMR spectrum reveals the presence of a carbonyl ligand by a typical resonance at low field (δ =

189.6) and a characteristic splitting to a doublet of doublets ($^1J_{C,Rh}$ = 76.1 Hz, $^2J_{C,P}$ = 25.4 Hz).[23]

To determine the preferred conformation of the rhodium complex **20** in solution, 2D NOESY and selective proton-decoupling experiments were performed. Thus, NOE′s and vicinal coupling constants were observed for the rhodium complex **20** similar to those found in the case of **9a** (see Scheme 2). Consequently, compound **20** can be assigned the same preferred conformation **A** in solution at room temperature as **9a**, although it is impossible to determine the differences in conformer populations between **9a** and **15/20** on the basis of these experimental data.

However, of major interest was the influence of the additional methyl substituents attached to the *o*-DPPB esters **15** and **16** on the stereochemical outcome of the hydroformylation reaction. When **15** was hydroformylated at 50°C, the *anti*-aldehyde **21** was obtained in 91% yield with a diastereomer ratio of 96:4. This is a significantly higher diastereoselectivity than was found in the absence of the additional methyl substituent (compare **9a** → **10a**, 91:9) and is therefore fully consistent with the proposed model. Accordingly, hydroformylation of the *syn*-derivative **16** proceeded in a stereorandom fashion, also as predicted by this model.



Reagents and conditions: i, 0.7 mol% $[Rh(CO)_2acac]$, 2.8 mol% $P(OPh)_3$, 20 bar H_2/CO (1 : 1), toluene, 50 °C, **21** (91%) **22** (92%).

This work was supported by the *Fonds der Chemischen Industrie*, the *Otto Röhm Gedächtnisstiftung*, and by the *Deutsche Forschungsgemeinschaft* (SFB 260). The author thanks Prof. *R. W. Hoffmann* for his continuous support, the companies *BASF* and *Degussa* for their gifts of chemicals, and *M. Dauber* for his skillful experimental assistance.

Experimental Section

General: Reactions were performed in flame-dried glassware either under argon (purity > 99.998%) or under nitrogen. The solvents were dried by standard procedures, distilled, and stored under nitrogen. All temperatures quoted are uncorrected. − ^{1}H-, ^{13}C-NMR spectra: Bruker ARX-200, Bruker AC-300, Bruker WH-400, Bruker AMX-500 with tetramethylsilane (TMS), chloroform ($CHCl_3$) or benzene (C_6H_6) as internal standards. − ^{31}P-NMR spectra: Bruker WH 400 (161.978 MHz) with 85% H_3PO_4 as external standard. − Melting points: Melting point apparatus by Dr. Tottoli (Büchi). − Elemental analyses: CHN rapid analyzer (Heraeus). − Flash chromatography: Silica gel Si 60, E. Merck AG, Darmstadt, 40−63 μm. − Hydroformylation reactions were performed in 100 or 200 ml stainless steel autoclaves equipped with magnetic stirrers. − Gases: Carbon monoxide 2.0 (Messer-Griesheim), hydrogen 3.0 (Messer-Griesheim).

General Procedure for the Preparation of Homomethallylic Alcohols **5**:[8] To a magnetically stirred solution of the appropriate aldehyde (50 mmol) and 4.95 g (55 mmol) of methallyl chloride in 100 ml of DMF, was added 16.9 g (75 mmol) of tin dichloride dihydrate followed by 11.24 g (75 mmol) of sodium iodide. The reaction mixture was stirred for 18 h at room temp., and then a mixture of 50 ml of 25% aq. NH_4F solution and 100 ml of *tert*-butyl methyl ether was added. The mixture was stirred vigorously and then the layers were allowed to separate. The aqueous phase was reextracted with two 80 ml portions of *tert*-butyl methyl ether. The combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and the residue was purified by distillation to give the alcohol **5** as a colorless liquid.

2,5-Dimethylhex-5-en-3-ol (**5a**): From 3.6 g (50 mmol) isobutyraldehyde was obtained 5.28 g (85%) of **5a** (b.p. 60°C/40 mbar). Spectroscopic and analytical data were identical to those reported previously.[24]

1-Cyclohexyl-3-methylbut-3-en-1-ol (**5b**): From 5.61 g (50 mmol) cyclohexane carbaldehyde was obtained 6.12 g (73%) of **5b** (b.p. 125°C/50 mbar). Analytical data were identical to those reported previously.[25] − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.1−2.0 (m, 11 H, *c*-Hex), 1.8 (s, 3 H, CH_3), 2.1 (dd, *J* = 12.5 Hz, 10.0 Hz, 1 H, CH_2), 2.3 (d, *J* = 12.5 Hz, 1 H, CH_2), 3.5 (m, 1 H, OCH), 4.85 (br s, 1 H, OH), 4.93 (s, 1 H, =CH_2), 5.02 (s, 1 H, =CH_2). − ^{13}C NMR (50.329 MHz, $CDCl_3$): δ = 22.1, 26.1, 26.2, 26.6, 28.0, 29.0, 42.9, 43.3, 72.4, 113.2, 143.2.

2-Methyldec-1-en-4-ol (**5c**): From 5.7 g (50 mmol) 1-heptanal was obtained 6.9 g (81%) of **5c**. Spectroscopic and analytical data were identical to those reported previously.[26]

3-Methyl-1-phenylbut-3-en-1-ol (**5d**): From 5.3 g (50 mmol) benzaldehyde was obtained 5.76 g (71%) of **5d** (b.p. 118°C/12 mbar). Spectroscopic and analytical data were identical to those reported previously.[8]

1-(2-Methoxy)phenylbut-3-en-1-ol (**5e**): From 6.8 g (50 mmol) 2-methoxybenzaldehyde was obtained 4.45 g (47%) of **5e** (b.p. 129−134°C/8 mbar). Spectroscopic and analytical data were identical to those reported previously.[27]

(E)-2,5-Dimethylocta-1,5-dien-4-ol (**5f**): From 4.9 g (50 mmol) 2-methyl-2-pentenal was obtained 7.37 g (95%) of **5f** (b.p. 65°C/40 mbar). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.6 Hz, 3 H, CH_2CH_3), 1.55 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.8 (s, 1 H, OH), 1.96 (m, 2 H), 2.17 (d, *J* = 7.0 Hz, 2 H, H at C3), 4.05 (t, *J* = 6.6 Hz, 1 H, OCH), 4.73 (d, *J* = 1.0 Hz, 1 H, =CH_2), 5.36 (t, *J* = 7.2 Hz, 1 H, =CH). − ^{13}C NMR (50.329 MHz, $CDCl_3$): δ = 11.3, 13.89, 20.74, 22.18, 44.24, 74.58, 113.24, 128.14, 135.84, 142.64. − $C_{10}H_{18}O$ (154.3): calcd. C 77.87, H 11.76; found C 77.78, H 11.74.

Hydroformylation of (RS)-(±)-2,5-Dimethylhex-5-en-3-ol [(±)-**5a**]: To a solution of 2 mg (7.7×10^{-3} mmol) of $[Rh(CO)_2(acac)]$ in 2 ml of toluene at 20°C (exclusion of air and moisture), 40.5 mg (1.55×10^{-1} mmol) PPh_3 was added and the mixture was stirred for 15 min. at 20°C. Then, 278 mg (2.17 mmol) (±)-**5a** was added and the resulting solution was cannulated into a stainless steel autoclave, which had been repeatedly evacuated and refilled with argon. The flask and the cannula were rinsed with an additional 1 ml of toluene. The autoclave was heated to 90°C, then pressurized

successively with carbon monoxide (10 bar) and hydrogen (10 bar), and the reaction solution was stirred under these conditions for 23 h. Thereafter, the autoclave was cooled rapidly to 20°C and depressurized. The degree of conversion was determined to be 25% by GC. The solvent was evaporated and the residue was subjected to PCC oxidation conditions without further purification.

cis/trans-(±)-4-Methyl-6-isopropyl-3,4,5,6-tetrahydro-2H-pyran-2-one (**7**): To a solution of the aforementioned residue in 10 ml CH_2Cl_2, 4 g of PCC on Al_2O_3 (1 mmol/g) was added and the suspension was stirred for 12 h at room temp. The reaction mixture was then filtered through silica gel with a further 50 ml of CH_2Cl_2, the solvent was evaporated, and the residual product was analyzed by NMR to determine the diastereomer ratio [62:38 (*trans*:*cis*)]. Yield of lactones after purification by flash chromatography with petroleum ether/*tert*-butyl methyl ether (4:1): 56 mg (66% of theoretical). Spectroscopic and analytical data matched those reported previously.[10]

General Procedure for Synthesis of o-DPPB Esters: To a solution of 1 equiv. of the appropriate homomethallylic alcohol in CH_2Cl_2 (0.5 M), 1 equiv. of *o*-DPPBA **8**,[28] 0.1 equiv. of DMAP and 1.1 equiv. of DCC were successively added, and the resulting mixture was stirred at room temperature until TLC analysis indicated complete consumption of the starting material. Then, the reaction mixture was filtered through a plug of CH_2Cl_2-wetted Celite, which was subsequently washed with further CH_2Cl_2. An appropriate amount of silica gel was added to the filtrate, and the solvent was removed. Flash chromatography with petroleum ether/*tert*-butyl methyl ether (9:1) furnished the *o*-DPPB esters **9**, usually as slightly yellow to colorless, highly viscous oils.

(1RS)-(±)-3-Methyl-1-isopropylbut-3-enyl 2-(Diphenylphosphanyl)benzoate (**9a**): From 1.28 g (10 mmol) of homomethallylic alcohol (±)-**5a**, 3.218 g (77%) of (±)-**9a** was obtained as a colorless, viscous oil. – ^{1}H NMR (500 MHz, C_7D_8): δ = 0.80 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.84 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.61 (br s, 3 H, CH_3), 1.69 (m, 1 H, CH), 2.06 (dd, *J* = 14.1, 4.1 Hz, 1 H, CH_2), 2.21 (dd, *J* = 14.1, 9.0 Hz, 1 H, CH_2), 4.68 (s, 1 H, =CH_2), 4.7 (s, 1 H, =CH_2), 5.17 (d pseudo t, *J* = 9.2, 4.5 Hz, 1 H, OCH), 6.96 (m, 1 H, Ar H), 7.05–7.1 (m, 8 H, ArH), 7.32 (m, 4 H, ArH), 8.14 (m, 1 H, ArH).

Table 4. Temperature dependence of selected vicinal proton-proton coupling constants of **9a** in [D_8]toluene (400 MHz)

Temperature [K]	Vicinal coupling constants [Hz] of the sp^3 CH_2 unit of **9a**
298	9.0/4.1
303	9.0/4.1
323	8.7/4.3
343	8.5/4.5
363	8.4/4.6

^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.48, 18.68, 22.28, 31.39, 39.81, 76.86, 113.18, 128.03, 128.35 (d, $J_{C,P}$ = 7.8 Hz, 2 C), 128.38 (d, $J_{C,P}$ = 6.9 Hz, 2 C), 128.48 (2 C), 130.4 (d, $J_{C,P}$ = 2.3 Hz), 131.65, 133.9 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.05 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.15, 134.56 (d, $J_{C,P}$ = 17.8 Hz), 138.23 (d, $J_{C,P}$ = 11.7 Hz), 138.33 (d, $J_{C,P}$ = 12.5 Hz), 140.82 (d, $J_{C,P}$ = 27.6 Hz), 141.86, 166.09. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = –3.9. – $C_{27}H_{29}O_2P$ (416.5): calcd. C 77.86, H 7.02; found C 77.75, H 7.15.

(1RS)-(±)-1-Cyclohexyl-3-methylbut-3-enyl 2-(Diphenylphosphanyl)benzoate (**9b**): From 0.841 g (5 mmol) of homomethallylic alcohol (±)-**5b**, 1.436 g (63%) of (±)-**9b** was obtained as a colorless, viscous oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.8–1.9 (m, 11 H), 1.6 (s, 3 H, CH_3), 2.17 (m, 2 H, H at C2), 4.6 (s, 2 H, =CH_2), 4.97 (d pseudo t, *J* = 8.1, 5.3 Hz, 1 H, OCH), 6.81 (m, 1 H, ArH), 7.17–7.3 (m, 12 H, ArH), 7.59 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 22.24, 24.98, 26.04, 26.27, 27.76, 29.07, 39.9, 41.3, 76.54, 113.13, 127.94, 128.3 (d, $J_{C,P}$ = 6.5 Hz, 4 C), 128.44 (2 C), 130.48 (d, $J_{C,P}$ = 1.96 Hz), 131.59, 133.86 (d, $J_{C,P}$ = 20.83 Hz, 2 C), 134.02 (d, $J_{C,P}$ = 20.9 Hz, 2 C), 134.05, 134.37 (d, $J_{C,P}$ = 17.7 Hz), 138.13 (d, $J_{C,P}$ = 9.9 Hz), 138.28 (d, $J_{C,P}$ = 12.5 Hz), 140.76 (d, $J_{C,P}$ = 27.9 Hz), 141.91, 166.08. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = –3.8. – $C_{30}H_{27}O_2P$ (456.6): calcd. C 78.92, H 7.29; found C 78.64, H 7.17.

(1RS)-(±)-1-Methallylheptanyl 2-(Diphenylphosphanyl)benzoate (**9c**): From 0.851 g (10 mmol) of homomethallylic alcohol (±)-**5c**, 1.834 g (80%) of (±)-**9c** was obtained as a colorless, viscous oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.5 Hz, 3 H, CH_3), 1.17–1.29 (m, 8 H), 1.47 (m, 2 H), 1.65 (s, 3 H, CH_3), 2.13 (dd, *J* = 14.4, 5.7 Hz, 1 H, H at C2), 2.25 (dd, *J* = 14.2, 7.3 Hz, 1 H, H at C2), 4.65 (d, *J* = 1.0 Hz, 1 H, =CH_2), 4.69 (pseudo t, *J* = 1.7 Hz, 1 H, =CH_2), 5.15 (m, 1 H, OCH), 6.88 (m, 1 H, ArH), 7.2–7.4 (m, 12 H, ArH), 8.05 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 14.18, 22.57, 22.69, 25.4, 29.25, 31.79, 34.05, 42.88, 73.56, 113.34, 128.2, 128.52 (d, $J_{C,P}$ = 5.2 Hz, 4 C), 128.62 (2 C), 130.65 (d, $J_{C,P}$ = 2.6 Hz), 131.78, 134.06 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.11 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.33, 134.99 (d, $J_{C,P}$ = 18.8 Hz), 138.38 (d, $J_{C,P}$ = 12.0 Hz), 138.44 (d, $J_{C,P}$ = 12.3 Hz), 140.47 (d, $J_{C,P}$ = 27.4 Hz), 141.88, 166.47. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = –4.1. – $C_{30}H_{35}O_2P$ (458.6): calcd. C 78.58, H 7.69; found C 78.36, H 7.73.

(1RS)-(±)-3-Methyl-1-phenylbut-3-enyl 2-(Diphenylphosphanyl)benzoate (**9d**): From 1.62 g (10 mmol) of homomethallylic alcohol (±)-**5d**, 4.22 g (94%) of (±)-**9d** was obtained as a colorless, viscous oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69 (s, 3 H, CH_3), 2.5 (dd, *J* = 14.0, 6.1 Hz, 1 H, CH_2), 2.72 (dd, *J* = 14.0, 8.0 Hz, 1 H, CH_2), 4.69 (s, 1 H, =CH_2), 4.75 (s, 1 H, =CH_2), 6.15 (dd, *J* = 8.0, 6.2 Hz, 1 H, OCH), 6.96 (m, 1 H, ArH), 7.29–7.44 (m, 17 H, ArH), 8.16 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 22.49, 44.43, 74.88, 113.8, 126.72, 127.75 (2 C), 128.08 (2 C), 128.33, 128.35 (d, $J_{C,P}$ = 7.1 Hz, 4 C), 128.42, 128.48, 130.61 (d, $J_{C,P}$ = 2.5 Hz), 131.77, 133.87 (d, $J_{C,P}$ = 20.6 Hz, 2 C), 133.94 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.24, 134.56 (d, $J_{C,P}$ = 18.9 Hz), 138.02 (d, $J_{C,P}$ = 12.5 Hz), 138.18 (d, $J_{C,P}$ = 11.8 Hz), 140.06, 140.53 (d, $J_{C,P}$ = 27.7 Hz), 140.83, 165.73. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = –4.1. – $C_{30}H_{27}O_2P$ (450.5): calcd. C 79.98, H 6.04; found C 79.85, H 5.91.

(1RS)-(±)-1-(2-Methoxyphenyl)-3-methylbut-3-enyl 2-(Diphenylphosphanyl)benzoate (**9e**): From 0.961 g (5 mmol) of homomethallylic alcohol (±)-**5e**, 1.78 g (74%) of (±)-**9e** was obtained as colorless crystals, m.p. 130°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.6 (s, 3 H, CH_3), 2.46 (dd, *J* = 14.0, 8.6 Hz, 1 H, CH_2), 2.51 (dd, *J* = 14.0, 4.8 Hz, 1 H, CH_2), 3.78 (s, 3 H, OCH_3), 4.59 (s, 1 H, =CH_2), 6.49 (dd, *J* = 8.3, 5.3 Hz, 1 H, OCH), 6.8–6.9 (m, 3 H, ArH), 7.17–7.45 (m, 14 H, ArH), 8.15 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 22.57, 44.15, 55.53, 69.93, 110.62, 113.35, 120.63, 126.6, 128.33, 128.52 (d, $J_{C,P}$ = 7.1 Hz, 4 C), 128.56 (2 C), 128.63, 129.25, 130.79 (d, $J_{C,P}$ = 2.2 Hz), 131.91, 133.96 (d, $J_{C,P}$ = 20.5 Hz, 2 C), 134.16 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.48, 134.9 (d, $J_{C,P}$ = 18.5 Hz), 138.34 (d, $J_{C,P}$ = 12.9 Hz), 138.44 (d, $J_{C,P}$ = 11.6 Hz), 140.74 (d, $J_{C,P}$ = 27.7 Hz), 141.77, 156.31, 165.7. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = –4.4. – $C_{31}H_{29}O_3P$ (480.5): calcd. C 77.48, H 6.08; found C 77.46, H 6.33.

(E)-(1RS)-(±)-1-Methallyl-2-methylpent-2-enyl 2-(Diphenylphosphanyl)benzoate (**9f**): From 0.771 g (5 mmol) of homomethal-

lylic alcohol (±)-**5f**, 1.37 g (62%) of (±)-**9f** was obtained as a colorless, viscous oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.9 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.58 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.97 (m, 2 H, CH_2CH_3), 2.25 (dd, *J* = 14.0, 6.3 Hz, 1 H, CH_2), 2.39 (dd, *J* = 14.0, 8.0 Hz, 1 H, CH_2), 4.65 (s, 1 H, =CH_2), 4.68 (s, 1 H, =CH_2), 5.47 (m, 2 H, OCH and =CH), 6.9 (m, 1 H, ArH), 7.26–7.39 (m, 12 H, ArH), 8.06 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 11.9, 13.94, 20.98, 22.93, 41.49, 78.49, 113.34, 128.25, 128.52 (d, $J_{C,P}$ = 7.25 Hz, 4 C), 128.64, (2 C) 130.68 (d, $J_{C,P}$ = 2.3 Hz), 131.12, 131.82, 132.11, 134.05 (d, $J_{C,P}$ = 20.7 Hz, 2 C), 134.14 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.36, 135.03 (d, $J_{C,P}$ = 18.6 Hz), 138.37 (d, $J_{C,P}$ = 13.7 Hz), 138.34 (d, $J_{C,P}$ = 11.5 Hz), 140.57 (d, $J_{C,P}$ = 27.3 Hz), 141.6, 165.9. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.2. – $C_{29}H_{31}O_2P$ (442.5): calcd. C 78.71, H 7.06; found C 78.50, H 6.82.

Hydroformylation of Homomethallylic o-DPPB Esters (**9**). – *General Procedure:* To a solution of 0.9 mg (3.5×10^{-3} mmol) [$Rh(CO)_2(acac)$] in 3 ml toluene at 20°C (exclusion of air and moisture), 4.5 mg (1.4×10^{-2} mmol) $P(OPh)_3$ was added and the resulting mixture was stirred at this temperature for 15 min. Subsequently, *o*-DPPB ester **9** (0.5 mmol) was added and the resulting solution was cannulated into a stainless steel autoclave, which had been repeatedly evacuated and refilled with argon. The flask and cannula were rinsed with a further 2 ml of toluene. The autoclave was heated to the appropriate temperature, then pressurized successively with carbon monoxide (10 bar) and hydrogen (10 bar), and the reaction mixture was stirred under these conditions until TLC indicated complete consumption of the starting material. The autoclave was then cooled rapidly to 20°C and the contents were filtered through a small plug of silica with 30 ml of *tert*-butyl methyl ether. After evaporation of the solvent in vacuo, the crude product was analyzed by NMR to determine the degree of conversion and the diastereomer ratio. Subsequent flash chromatography with petroleum ether/*tert*-butyl methyl ether (9:1) furnished the aldehydes **10** as highly viscous oils.

(1R,3R*)-(±)-1-Isopropyl-3-methyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**10a**]: From 208 mg (0.5 mmol) **9a**, 208 mg (93%) of *anti*-**10a** was obtained. Reaction temperature 50°C. Reaction time 72 h. Diastereomer ratio 91:9 (*anti:syn*). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 [d, *J* = 6.8 Hz, 6 H, $CH(CH_3)_2$], 0.8 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.24 (ddd, *J* = 14.0, 10.1, 2.6 Hz, 1 H, H at C2), 1.51 (ddd, *J* = 14.0, 10.2, 3.7 Hz, 1 H, H at C2), 1.72 [m, 1 H, $CH(CH_3)_2$], 1.88 (m, 1 H, H at C3), 2.16 (ddd, *J* = 16.3, 7.3, 2.4 Hz, 1 H, H at C4), 2.18 (ddd, *J* = 16.3, 6.4, 2.3 Hz, 1 H, H at C4), 4.96 (ddd, *J* = 10.1, 5.5, 2.4 Hz, 1 H, H at C1), 6.87 (m, 1 H, ArH), 7.2–7.34 (m, 12 H, ArH), 8.07 (m, 1 H, ArH), 9.59 (pseudo t, *J* = 2.2 Hz, 1 H, CHO-*anti*), [9.42 (dd, *J* = 3.1, 1.1 Hz, CHO-*syn*)]. – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.8, 18.29, 19.32, 24.71, 32.09, 38.11, 51.31, 76.84, 128.14, 128.35 (d, $J_{C,P}$ = 7.2 Hz, 2 C), 128.39 (d, $J_{C,P}$ = 7.4 Hz, 2 C), 128.54 (2 C), 130.61 (d, $J_{C,P}$ = 2.3 Hz), 131.84, 133.74 (d, $J_{C,P}$ = 21.1 Hz, 2 C), 134.02 (d, $J_{C,P}$ = 21.5 Hz, 2 C), 134.19 (signal for C1′ expected as a doublet at ca. 134.1 is obscured by the signals at 134.02 and 134.19), 138.04 (d, $J_{C,P}$ = 12.8 Hz), 138.14 (d, $J_{C,P}$ = 11.2 Hz), 140.55 (d, $J_{C,P}$ = 27.7 Hz), 166.5 (d, $J_{C,P}$ = 2.6 Hz), 202.29 (CHO-*anti*), [202.52 (CHO-*syn*)]. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −3.9. – $C_{28}H_{31}O_3P$ (446.5): calcd. C 75.32, H 7.00; found C 74.99, H 7.21.

(1R,3R*)-(±)-1-Cyclohexyl-3-methyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**9b**]: From 228 mg (0.5 mmol) **9b**, 219 mg (90%) of *anti*-**10b** was obtained. Reaction temperature 50°C. Reaction time 72 h. Diastereomer ratio 91:9 (*anti:syn*). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82–1.76 (m, 13 H), 0.88 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.87 (m, 1 H), 2.13 (ddd, *J* = 11.5, 6.5, 2.2 Hz, 2 H, H at C4), 5.02 (ddd, *J* = 10.1, 5.9, 2.5 Hz, H at C1), 6.91 (m, 1 H, ArH), 7.27–7.46 (m, 12 H, ArH), 7.95 (m, 1 H, ArH), 9.68 (pseudo t, *J* = 2.3 Hz, 1 H, CHO-*anti*), [9.48 (dd, *J* = 3.2, 1.1 Hz, CHO-*syn*)]. – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 19.49, 24.96, 26.08, 26.14, 26.41, 28.28, 28.97, 38.66, 42.18, 51.58, 76.61, 128.31, 128.53 (d, $J_{C,P}$ = 7.3 Hz, 2 C), 128.56 (d, $J_{C,P}$ = 7.0 Hz, 2 C), 128.73 (2 C), 130.91 (d, $J_{C,P}$ = 2.3 Hz), 132.02, 133.95 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.27 (d, $J_{C,P}$ = 20.7 Hz, 2 C), 134.38 (d, $J_{C,P}$ = 18.0 Hz), 134.41, 138.28 (d, $J_{C,P}$ = 12.8 Hz), 138.37 (d, $J_{C,P}$ = 12.8 Hz), 140.77 (d, $J_{C,P}$ = 27.7 Hz), 166.68, 202.67 (CHO-*anti*), [202.86 (CHO-*syn*)]. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −3.7. – $C_{31}H_{35}O_3P$ (486.6): calcd. C 76.52, H 7.00; found C 76.37, H 7.28.

(1R,3R*)-(±)-1-Hexyl-3-methyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**10c**]: From 229 mg (0.5 mmol) **9c**, 198 mg (81%) of *anti*-**10c** was obtained. Reaction temperature 30°C. Reaction time 168 h. Diastereomer ratio 90:10 (*anti:syn*). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 0.9 (d, *J* = 6.9 Hz, 3 H, $CHCH_3$), 1.15–1.6 (m, 12 H), 2.0 (m, 1 H), 2.17 (ddd, *J* = 16.1, 7.4, 2.1 Hz, 1 H, H at C4), 2.26 (ddd, *J* = 16.0, 6.2, 2.0 Hz, 1 H, H at C4), 5.12 (m, 1 H, H at C1), 6.89 (m, 1 H, ArH), 7.24–7.5 (m, 12 H, ArH), 8.08 (m, 1 H, ArH), 9.66 (pseudo t, *J* = 2.34 Hz, 1 H, CHO-*anti*), [9.53 (m, CHO-*syn*)]. – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 14.18, 19.65, 22.6, 24.89, 25.4, 29.22, 31.76, 35.09, 41.55, 51.38, 77.32, 128.32, 128.55 (d, $J_{C,P}$ = 7.2 Hz, 2 C), 128.59 (d, $J_{C,P}$ = 7.5 Hz, 2 C), 128.72 (2 C), 130.87 (d, $J_{C,P}$ = 2.5 Hz), 132.0, 133.95 (d, $J_{C,P}$ = 20.6 Hz, 2 C), 134.15 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.44, 134.79 (d, $J_{C,P}$ = 19.0 Hz), 138.33 (d, $J_{C,P}$ = 12.5 Hz), 138.45 (d, $J_{C,P}$ = 11.5 Hz), 140.37 (d, $J_{C,P}$ = 27.9 Hz), 166.74, 202.42 (CHO-*anti*), [202.5 (CHO-*syn*)]. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −3.9. – $C_{31}H_{37}O_3P$ (488.6): calcd. C 76.21, H 7.63; found C 75.91, H 7.75.

(1R,3R*)-(±)-3-Methyl-5-oxo-1-phenylpentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**10d**]: From 225 mg (0.5 mmol) **9d**, 173 mg (72%) of *anti*-**10d** was obtained. Reaction temperature 30°C. Reaction time 120 h. Diastereomer ratio 90:10 (*anti:syn*). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.67 (ddd, *J* = 14.1, 8.5, 4.6 Hz, 1 H, H at C2), 2.11 (ddd, *J* = 14.0, 9.5, 4.5 Hz, 1 H, H at C2), 2.2–2.4 (m, 3 H), 6.16 (dd, *J* = 9.5, 4.5 Hz, 1 H, H at C1), 7.07 (m, 1 H, ArH), 7.22–7.5 (m, 17 H, ArH), 8.25 (m, 1 H, ArH), 9.74 (pseudo t, *J* = 1.9 Hz, 1 H, CHO-*anti*), [9.62 (dd, *J* = 2.6, 1.5 Hz, CHO-*syn*)]. – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 19.84, 25.21, 43.77, 51.16, 75.04, 125.58, 126.82 (2 C), 128.18 (2 C), 128.48, 128.77 (d, $J_{C,P}$ = 7.2 Hz, 2 C), 128.86 (d, $J_{C,P}$ = 7.2 Hz, 2 C), 129.27 (2 C), 131.14 (d, $J_{C,P}$ = 2.6 Hz), 132.25, 134.12 (d, $J_{C,P}$ = 20.5 Hz, 2 C), 134.32 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.69, 134.82 (d, $J_{C,P}$ = 18.9 Hz), 138.14 (d, $J_{C,P}$ = 12.4 Hz), 138.3 (d, $J_{C,P}$ = 11.5 Hz), 140.51 (d, $J_{C,P}$ = 28.9 Hz), 140.7, 166.43, 202.09. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.3. – $C_{31}H_{29}O_3P$ (480.5): calcd. C 77.48, H 6.08; found C 77.16, H 6.18.

(1R,3R*)-(±)-1-(2-Methoxyphenyl)-3-methyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**10e**]: From 240 mg (0.5 mmol) **9e**, 199 mg (78%) of *anti*-**10e** was obtained. Reaction temperature 30°C. Reaction time 240 h. Diastereomer ratio 90:10 (*anti:syn*). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.58 (ddd, *J* = 14.0, 8.4, 4.4 Hz, 1 H, H at C2), 1.84 (ddd, *J* = 14.0, 8.8, 5.1 Hz, 1 H, H at C2), 2.0–2.22 (m, 2 H), 2.38 (m, 1 H), 3.74 (s, 3 H, OCH_3), 6.45 (dd, *J* = 8.7, 4.4 Hz, 1 H, HCO), 6.79 (d, *J* = 7.9 Hz, 1 H, ArH), 6.84 (t, *J* = 7.7 Hz, 1 H, ArH), 6.94 (m, 1 H, ArH), 7.1–7.43 (m, 14 H, ArH), 8.15 (m, 1

H, ArH), 9.64 (pseudo t, J = 2.1 Hz, 1 H, CHO-*anti*), [9.54 (dd, J = 3.0, 1.5 Hz, CHO-*syn*)]. − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 19.71, 25.13, 42.98, 51.0, 55.48, 69.71, 110.53, 120.74, 126.33, 128.41, 128.54 (d, $J_{C,P}$ = 7.1 Hz, 4 C), 128.6 (2 C), 128.64, 129.42, 130.93 (d, $J_{C,P}$ = 2.8 Hz), 131.99, 133.91 (d, $J_{C,P}$ = 20.5 Hz, 2 C), 134.11 (d, $J_{C,P}$ = 20.7 Hz, 2 C), 134.54, 134.92 (d, $J_{C,P}$ = 19.6 Hz), 138.1 (d, $J_{C,P}$ = 12.8 Hz), 138.3 (d, $J_{C,P}$ = 11.4 Hz), 140.6 (d, $J_{C,P}$ = 27.1 Hz), 155.94, 166.12 (d, $J_{C,P}$ = 2.2 Hz), 202.6 (CHO-*anti*), [202.83 (CHO-*syn*)]. − ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.6. − $C_{32}H_{31}O_4P$ (510.6): calcd. C 75.28, H 6.12; found C 74.94, H 6.10.

(1R,3R*)-(±)-[(E)-1-Methylbut-1-enyl]-3-methyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**10f**]: From 221 mg (0.5 mmol) **9f**, 201 mg (85%) of *anti*-**10f** was obtained. Reaction temperature 30°C. Reaction time 168 h. Diastereomer ratio 90:10 (*anti:syn*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.9 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 1.4 (m, 2 H), 1.7 (m, 1 H), 1.95 (m, 2 H), 2.16 (ddd, J = 16.3, 8.2, 2.6 Hz, 1 H, H at C4), 2.34 (ddd, J = 16.2, 5.3, 3.4 Hz, 1 H, H at C4), 5.41 (m, 2 H, =CH and H at C1), 6.91 (m, 1 H, ArH), 7.24−7.43 (m, 12 H, ArH), 8.07 (m, 1 H, ArH), 9.67 (pseudo t, J = 2.3 Hz, 1 H, CHO-*anti*), [9.6 (dd, J = 2.6, 1.7 Hz, CHO-*syn*)]. − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 11.81, 13.76, 19.76, 20.82, 24.9, 39.74, 50.8, 78.16, 128.21, 128.43 (d, $J_{C,P}$ = 7.1 Hz, 4 C), 128.54 (2 C), 130.65 (d, $J_{C,P}$ = 2.6 Hz), 130.9, 131.8, 132.14, 133.87 (d, $J_{C,P}$ = 20.5 Hz, 2 C), 134.03 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.3, 134.7 (d, $J_{C,P}$ = 19.0 Hz), 138.08 (d, $J_{C,P}$ = 12.8 Hz), 138.2 (d, $J_{C,P}$ = 11.8 Hz), 140.4 (d, $J_{C,P}$ = 27.3 Hz), 166.09, 202.3. − ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.2. − $C_{30}H_{33}O_3P$ (472.6): calcd. C 76.41, H 6.84; found C 76.26, H 6.90.

Determination of Relative Configuration of anti-**10a**. − *(1R*,3R*)-(±)-1-Isopropyl-3-methyl-5-dimethoxypentyl 2-(Diphenylphosphanyl)benzoate* (*anti*-**11**): To a solution of 515 mg (1.15 mmol) of **10a** in 5 ml dry methanol were added 150 mg of Bayer Lewatit® SPC 108 and 200 mg of $MgSO_4$. After magnetic stirring at room temp. for 24 h, the reaction mixture was filtered through basic alumina. Evaporation of the solvent afforded 537 mg (95%) of *anti*-**11** as a colorless, viscous oil. Diastereomer ratio 91:9 (*anti:syn*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.74 (d, J = 6.2 Hz, 9 H, 3 CH_3), 1.19−1.63 [m, 6 H, H at C2, C3, C4 and $CH(CH_3)_2$], 3.2 (s, 6 H, OCH_3), 4.35 (pseudo t, J = 5.5 Hz, 1 H, H at C5), 4.92 (m, 1 H, H at C1), 6.83 (m, 1 H, ArH), 7.2−7.32 (m, 12 H, ArH), 8.0 (m, 1 H, ArH). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.93, 18.54, 19.57, 25.87, 32.08, 38.43, 40.36, 52.48, 52.68, 77.22, 103.24, 128.15, 128.48 (d, $J_{C,P}$ = 7.3 Hz, 4 C), 128.6 (2 C), 130.57 (d, $J_{C,P}$ = 2.1 Hz), 131.79, 133.94 (d, $J_{C,P}$ = 20.7 Hz, 2 C), 134.15 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.29, 134.75 (d, $J_{C,P}$ = 18.3 Hz), 138.34 (d, $J_{C,P}$ = 11.8 Hz), 138.4 (d, $J_{C,P}$ = 12.7 Hz), 140.83 (d, $J_{C,P}$ = 27.7 Hz), 166.51. − ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.2. − $C_{30}H_{37}O_4P$ (492.6).

(3R,6R*)-(±)-3,6-Dimethyl-5-hydroxyheptanone Dimethyl Acetal* (*anti*-**12**): To a solution of 401 mg (0.81 mmol) *anti*-**11** in 5 ml of ethanol, 3 ml of a saturated ethanolic potassium hydroxide solution was added at room temp. The resulting mixture was heated to reflux for 3 h, cooled to room temp., and concentrated. The residue was transferred to a separatory funnel with 50 ml of water and extracted with three 30 ml portions of *tert*-butyl methyl ether. The combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and the residue was purified by flash chromatography with petroleum ether/*tert*-butyl methyl ether (4:1) to furnish 160 mg (97%) of *anti*-**12** as a yellow oil. Diastereomer ratio 91:9 (*anti:syn*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.9 [d, J = 6.8 Hz, 6 H, $CH(CH_3)_2$], 0.95 [d, J = 6.6 Hz, 3 H, $CH(CH_3)_2$], 1.22 (ddd, J = 14.0, 9.5, 2.7 Hz, 1 H, H at C5), 1.42 (ddd, J = 14.0, 10.0, 4.1 Hz, 1 H, H at C5), 1.46−1.8 (m, 5 H, H at C2, C3, C7 and OH), 3.31 (s, 6 H, 2 OCH_3), 3.44 (m, 1 H, H at C6), 4.48 [pseudo t, J = 6.0 Hz, 1 H, $CH(OCH_3)_2$]. − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.16, 18.59, 19.63, 26.05, 34.1, 40.26, 41.45, 52.37, 52.45, 74.25, 103.02. − $C_{11}H_{24}O_3$ (204.3): calcd. C 64.67, H 11.84; found C 64.90, H 11.61.

cis-(±)-4-Methyl-6-isopropyl-3,4,5,6-tetrahydro-2H-pyran-2-one (*cis*-**7**): To a solution of 175 mg (0.86 mmol) *anti*-**12** in 2.5 ml of dry acetonitrile and 50 µl water, 84 mg (0.9 mmol) of lithium tetrafluoroborate was added at room temp. After magnetic stirring for 18 h, the reaction mixture was diluted with 30 ml of diethyl ether, washed with 10 ml of satd. aq. sodium bicarbonate solution, and dried (Na_2SO_4) to give 162 mg of lactols **6** as a pale-yellow oil. Lactols **6** were used directly in the subsequent oxidation step without further purification.

To a magnetically stirred solution of lactols **6** in 5 ml CH_2Cl_2 at room temp., 1.72 g (1.72 mmol) of PCC on Al_2O_3 (1 mmol/g) was added and the suspension was stirred for 24 h. The reaction mixture was then filtered through silica gel with a further 50 ml of CH_2Cl_2, the solvent was evaporated, and the residue was purified by flash chromatography with petroleum ether/*tert*-butyl methyl ether (4:1) to afford 131 mg (98% both steps) of the lactone *cis*-**7** as a colorless oil. Spectroscopic and analytical data matched those reported previously.[10]

Control Experiments Addressing the Role of the o-DPPB Group: (1RS)-(±)-3-Methyl-1-isopropylbut-3-enyl 2-(Diphenylmethyl)benzoate [(±)-**13**]: According to the General Procedure described for the preparation of the homomethallylic *o*-DPPB esters **9**, reaction of 256 mg (2 mmol) of homomethallylic alcohol (±)-**5a**, 577 mg (2 mmol) 2-diphenylmethylbenzoic acid[29], 24 mg (0.2 mmol) DMAP and 433 mg (2.1 mmol) DCC in 10 ml CH_2Cl_2 afforded 476 mg (50%) of (±)-**13** as a colorless, viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 [d, J = 6.8 Hz, 6 H, $CH(CH_3)_2$], 1.68 (s, 3 H, CH_3), 1.70 [m, 1 H, $CH(CH_3)_2$], 2.19 (m, 2 H, CH_2), 4.66 (s, 2 H, $=CH_2$), 5.05 (d pseudo t, J = 7.8, 5.3 Hz, 1 H, HCO), 6.64 (s, 1 H, $CHPh_2$), 6.99−7.38 (m, 13 H, ArH), 7.8 (dd, J = 7.6, 1.2 Hz, 1 H, ArH). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.30, 18.55, 22.21, 31.43, 39.82, 76.27, 113.09, 126.06, 126.13, 128.10, 129.67, 130.08, 130.89, 131.02, 141.9, 143.87, 143.91, 144.37, 167.34. − $C_{28}H_{30}O_2$ (398.5): calcd. C 84.38, H 7.59; found C 84.44, H 7.46.

(1R,3S*)-(±)-1-Isopropyl-3-methyl-5-oxopentyl 2-(Diphenylmethyl)benzoate* [(±)-*syn*-**14**] *and (1R*,3R*)-(±)-1-Isopropyl-3-methyl-5-oxopentyl 2-(Diphenylmethyl)benzoate* [(±)-*anti*-**14**]: According to the General Procedure described for the hydroformylation of *o*-DPPB esters **9**, reaction of 199 mg (0.5 mmol) **13** afforded 118 mg (55%) of *syn*-**14** and *anti*-**14**. Diastereomer ratio 71:29 (*syn:anti*). Spectroscopic data of the mixture of diastereomers are given, with signals of the minor diastereomer in []. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (m, 9 H, CH_3), 1.5−2.5 (m, 6 H, CH, CH_2), 4.98 (m, 1 H, OCH), 6.98−7.4 (m, 13 H, ArH), 7.88 (m, 1 H, ArH), 9.53 (m, 1 H, CHO), 6.78, 6.82 (each s, together 1 H, $CHPh_2$). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.4 [17.73], 18.59 [18.44], 20.73 [19.59], 24.99 [24.72], 31.82 [32.24], 37.98 [38.16], 51.93 [51.87], 76.44 [76.16], 120.13 [120.20], 126.26, 128.3, 129.8, 130.3, 132.0, 132.5, 143.93, 144.0, 144.75, 167.5, 202.34. − $C_{29}H_{32}O_3$ (428.6): calcd. C 81.27, H 7.59; found C 80.81, H 7.57.

(1R,3S*)-(±)-5,5-Dimethoxy-1-isopropyl-3-methylpentyl 2-(Diphenylmethyl)benzoate* [(±)-*syn*-**11b**] *and (1R*,3R*)-(±)-5,5-Dimethoxy-1-isopropyl-3-methylpentyl 2-(Diphenylmethyl)benzoate* [(±)-*anti*-**11b**]: To a solution of 200 mg (0.467 mmol) of **14** in 2 ml of dry methanol, 50 mg of Bayer Lewatit® SPC 108 and 100 mg

of $MgSO_4$ were added at room temp. After magnetic stirring at room temp. for 24 h, the reaction mixture was filtered through basic alumina. Evaporation of the solvent afforded 220 mg (99%) of **11b** as a colorless, viscous oil. Diastereomer ratio 71:29 (*syn:anti*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.8−0.9 (m, 9 H, CH_3), 1.35−1.8 (m, 6 H, CH, CH_2), 3.25, 3.26, 3.30, 3.32 (each s, together 6 H, OCH_3), 4.45 (m, 1 H, OCH), 5.06 [m, 1 H, *H*C(OMe)$_2$], 6.77, 6.82 (each s, together 1 H, C*H*Ph$_2$), 7.07−7.31 (m, 13 H, ArH), 7.9 (m, 1 H, ArH). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 17.0 [17.26], 18.39 [18.23], 20.44 [19.51], 26.14 [25.74], 31.25 [31.89], 38.12 [38.22], 51.82 [51.75], 52.57 [52.27], 76.79 [76.26], 102.79 [103.0], 126.05, 128.09, 129.63, 130.0, 130.9, 131.03, 143.84, 143.9, 144.39, 144.56 [144.64], 167.31 [167.39]. − $C_{31}H_{38}O_4$ (474.6): calcd. C 78.45, H 8.06; found C 78.40, H 7.98.

(3R,6S*)-(±)-3,6-Dimethyl-5-hydroxy-1-heptanone Dimethyl Acetal* [(±)-*syn*-**12**] *and (3R*,6R*)-(±)-3,6-Dimethyl-5-hydroxy-1-heptanone Dimethyl Acetal* [(±)-*anti*-**12**]: To a solution of 190 mg (0.81 mmol) **11b** in 2 ml of ethanol, 2 ml of a saturated ethanolic sodium hydroxide solution was added at room temp. The resulting mixture was heated to reflux for 3 h, cooled to room temp., and concentrated. The residue was transferred to a separatory funnel with 20 ml of water and was extracted with three 30 ml portions of *tert*-butyl methyl ether. The combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and the residue was purified by flash chromatography with petroleum ether/*tert*-butyl methyl ether (4:1) to furnish 80 mg (98%) of **12** as a 71:29 (*syn*:*anti*) mixture of diastereomers in the form of a yellow oil. Spectroscopic data of *syn*-**9** are as follows. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.8−0.96 (m, 9 H, 3 CH_3), 1.24−1.8 (m, 6 H, CH, CH_2), 2.0 (br m, 1 H, OH), 3.25 (s, 3 H, OCH_3), 3.26 (s, 3 H, OCH_3), 3.4 (d pseudo t, *J* = 8.2, 4.8 Hz, 1 H, HCO), 4.42 [m, 1 H, *H*C(OMe)$_2$]. − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 16.87, 18.72, 21.18, 25.96, 33.60, 38.60, 41.59, 52.47, 52.58, 73.77, 103.36. − Analytical data were identical to those of *anti*-**12**.

(3R,4R*)-*(±)-*2,4,5-Trimethylhex-5-en-3-ol* (**17**)[20]: To a suspension of 1.0 g (4.03 mmol) [Cp_2TiCl_2] in 20 ml of THF, 4.48 ml (8.06 mmol) of a 1.8 M solution of *i*-PrMgBr in Et_2O and 0.5 ml (5 mmol) isoprene were simultaneously added dropwise by means of syringes. After stirring the resulting mixture for 30 min. at room temp., 361 mg (5 mmol) of isobutyraldehyde was added dropwise. The reaction mixture was allowed to stir for a further 60 min. at room temp. and then 20 ml of satd. aq. $NaHCO_3$ solution was added. The organic phase was separated and the aqueous phase was extracted with two 20 ml portions of *tert*-butyl methyl ether. The combined organic phases were dried (Na_2SO_4), and filtered through a plug of Celite with a further 50 ml of *tert*-butyl methyl ether. The solvent was evaporated and the residue was subjected to flash chromatography with petroleum ether/*tert*-butyl methyl ether (9:1) to furnish 238 mg (42%) of **17** as a colorless oil. Diastereomer ratio according to NMR analysis ≥ 95:5 (*anti:syn*). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.8 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.9 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.97 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.5 (d, *J* = 2.6 Hz, 1 H, OH), 1.64 (s, 3 H, CH_3), 1.7 [m, 1 H, C*H*(CH$_3$)$_2$], 2.2 (m, 1 H, H at C3), 3.2 (m, 1 H, H at C4), 4.77 (s, 1 H, =CH_2), 4.88 (m, 1 H, =CH_2). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 14.0, 15.6, 18.4, 20.7, 29.0, 45.4, 76.2, 112.9, 148.0. − $C_9H_{18}O$ (142.2). Analytical data were identical to those reported previously.[30]

(3R,4R*)-(±)-2,4,5-Trimethylhex-5-en-3-ol* (**19**): To a solution of 634 mg (8.79 mmol) isobutyraldehyde in 15 ml of CH_2Cl_2 at −78°C, was added 2.49 g (17.58 mmol) of borontrifluoride−ether followed by 3.16 g of the methallylstannane **18**.[21] The reaction mixture was allowed to warm to −10°C over a period of 2 h and then 10 ml of water was added. The organic phase was separated and the aqueous phase was extracted with two 20 ml portions of CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), the solvent was removed in vacuo, and the residue was purified by filtration through a plug of silica (5 × 3 cm) with 200 ml petroleum ether/*tert*-butyl methyl ether (9:1). Flash chromatography of the resulting crude product with petroleum ether/*tert*-butyl methyl ether (19:1) furnished 350 mg (28%) of **19** as a colorless oil. Diastereomer ratio according to NMR analysis ≥ 95:5 (*syn:anti*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.88 (d, *J* = 6.6 Hz, 3 H, CH_3), 0.96 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.63 [m, 2 H, C*H*(CH$_3$)$_2$ and OH], 1.64 (s, 3 H, CH_3), 2.24 (m, 1 H, H at C3), 3.15 (m, 1 H, H at C4), 4.7 (s, 1 H, =CH_2), 4.77 (m, 1 H, =CH_2). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 12.96, 16.59, 19.41, 20.63, 30.04, 43.4, 76.93, 111.06, 148.17. − $C_9H_{18}O$ (142.2). Analytical data were identical to those reported previously.[30]

(1R,2S*)-(±)-1-Isopropyl-3-methylbut-3-enyl 2-(Diphenylphosphanyl)benzoate* (**15**): According to the General Procedure for the preparation of the homomethallylic *o*-DPPB esters **9** (exception: 1 equiv. of DMAP was used), the reaction of 318 mg (2.236 mmol) of homomethallylic alcohol **17** afforded 670 mg (70%) **15** as a colorless, viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.83 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.88 (d, *J* = 7.1 Hz, 3 H, CH_3), 1.51 (s, 3 H, =C−CH_3), 1.88 [m, 1 H, C*H*(CH$_3$)$_2$], 2.5 (pseudo t, *J* = 7.1 Hz, 1 H, H at C3), 4.55 (s, 1 H, =CH_2), 4.64 (s, 1 H, =CH_2), 4.89 (dd, *J* = 8.1, 4.8 Hz, 1 H, OCH), 6.86 (m, 1 H, ArH), 7.2−7.34 (m, 12 H, ArH), 8.04 (m, 1 H, ArH). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 16.15, 16.33, 19.0, 19.97, 29.38, 43.46, 79.86, 112.66, 128.04, 128.4 (d, $J_{C,P}$ = 6.8 Hz, 2 C), 128.46 (d, $J_{C,P}$ = 6.9 Hz, 2 C), 128.55 (2 C), 130.5 (d, $J_{C,P}$ = 1.7 Hz), 131.75, 133.96 (d, $J_{C,P}$ = 21.1 Hz, 2 C), 134.17, 134.25 (d, $J_{C,P}$ = 21.7 Hz, 2 C) (signal for C1′ expected at ca. 134 is obscured by the signals at 134.17 and 134.25), 138.4 (d, $J_{C,P}$ = 11.5 Hz), 138.47 (d, $J_{C,P}$ = 13.1 Hz), 141.57 (d, $J_{C,P}$ = 28.2 Hz), 146.84, 165.87 (d, $J_{C,P}$ = 3.0 Hz). − ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.1. − $C_{28}H_{31}O_2P$ (430.5): calcd. C 78.12, H 7.26; found C 78.25, H 7.42.

(1R,2R*)-(±)-1-Isopropyl-3-methylbut-3-enyl 2-(Diphenylphosphanyl)benzoate* (**16**): According to the General Procedure for the preparation of the homomethallylic *o*-DPPB esters **9** (exception: 1 equiv. of DMAP was used), the reaction of 495 mg (3.48 mmol) of homomethallylic alcohol **19** afforded 703 mg (47%) of **16** as a colorless, viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.84 (d, *J* = 6.7 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.82 [m, 1 H, C*H*(CH$_3$)$_2$], 2.47 (m, 1 H, C*H*CH$_3$), 4.66 (m, 1 H, =CH_2), 4.71 (s, 1 H, =CH_2), 4.99 (dd, *J* = 8.2, 4.3 Hz, 1 H, H at C1), 6.9 (m, 1 H, ArH), 7.23−7.36 (m, 12 H, ArH), 8.1 (m, 1 H, ArH). − ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 15.45, 16.39, 19.7, 19.9, 29.71, 43.4, 80.11, 111.94, 128.08, 128.42 (d, $J_{C,P}$ = 7.4 Hz, 4 C), 128.47 (2 C), 130.53, 131.79, 134.04, 134.07 (d, $J_{C,P}$ = 20.9 Hz, 4 C), 134.26 (signal for C1′ expected at ca. 134 is obscured by the signals at 134.07 and 134.26), 138.26 (d, $J_{C,P}$ = 12.1 Hz, 2 C), 141.26 (d, $J_{C,P}$ = 28.2 Hz), 147.05, 166.31. − ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −4.1. − $C_{28}H_{31}O_2P$ (430.5): calcd. C 78.12, H 7.26; found C 77.86, H 7.10.

Rhodium(I)-carbonyl-(η^1)-P-{(1R,2S*)-(±)-1-Isopropyl-3-methylbut-3-enyl 2-(Diphenylphosphanyl)benzoate}acetylacetonate* (**20**): To a solution of 47 mg (0.183 mmol) of [Rh(CO)$_2$acac] in 1 ml C_6D_6, 79 mg (0.183 mmol) of **15** was added at room temp. Gas evolution was observed and the solution turned intensely yellow. After stirring for 1 h at room temp., completion of the reaction was checked by ^{31}P-NMR spectroscopy. The solvent was then eva-

porated in vacuo to furnish 120 mg (99%) of the rhodium complex **20** as a yellow glass. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.64 (d, J = 6.8 Hz, 3 H, CH_3), 0.76 (d, J = 6.7 Hz, 3 H, CH_3), 0.81 (d, J = 7.0 Hz, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.77 (m, 1 H, H at C5), 1.97 (s, 3 H, CH_3), 2.47 (m, 1 H, H at C3), 4.55 (s, 1 H, $=CH_2$), 4.61 (s, 1 H, $=CH_2$), 4.82 (dd, J = 7.9, 5.0 Hz, 1 H, OCH), 5.26 (s, 1 H, CHacac), 6.89 (ddd, J = 11.7, 7.7, 1 Hz, 1 H, ArH), 7.22–7.8 (m, 12 H, ArH), 8.18 (m, 1 H, ArH). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 16.08, 16.41, 18.87, 19.6, 26.33, 27.43, 29.24, 43.28, 79.6, 100.15, 112.39, 127.8–136.0 (all aryl-C), 146.82, 163.9, 184.64, 187.03, 189.56 (dd, $J_{C,Rh}$ = 76.1 Hz, $J_{C,P}$ = 25.4 Hz, RhCO). – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = 54.8 (d, $J_{P,Rh}$ = 189.1 Hz). – $C_{34}H_{38}O_5PRh$ (660.6).

(1R,2S*,3R*)-(±)-2,3-Dimethyl-1-isopropyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* (**21**): According to the General Procedure for the hydroformylation of the homomethallylic *o*-DPPB esters **9**, the reaction of 215 mg (0.5 mmol) of **15** afforded 210 mg (91%) of **21** as a colorless, viscous oil. Diastereomer ratio 96:4 (*anti:syn*). Relative configuration of **21** was assigned on the basis of characteristic carbon-13 NMR chemical shifts (see Table 3). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.62 (d, J = 6.6 Hz, 3 H, CH_3), 0.65 (d, J = 7.0 Hz, 3 H, CH_3), 0.74 (d, J = 6.8 Hz, 3 H, CH_3), 0.78 (d, J = 6.7 Hz, 3 H, CH_3), 1.67 (m, 2 H), 1.86 (m, 1 H), 2.06 (ddd, J = 13.0, 6.2, 2.2 Hz, 1 H, H at C4), 2.17 (ddd, J = 12.7, 7.0, 2.4 Hz, 1 H, H at C4), 4.89 (dd, J = 9.5, 3.3 Hz, 1 H, H at C1), 6.85 (m, 1 H, ArH), 7.18–7.5 (m, 12 H, ArH), 8.07 (m, 1 H, ArH), 9.56 (pseudo t, J = 2.3 Hz, 1 H, CHO). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 9.97, 13.84, 15.32, 20.08, 27.27, 29.29, 38.15, 49.77, 79.77, 128.27, 128.5 (d, $J_{C,P}$ = 7.3 Hz, 2 C), 128.53 (d, $J_{C,P}$ = 7.1 Hz, 2 C), 128.68 (2 C) 130.7, 132.02, 133.9 (d, $J_{C,P}$ = 20.8 Hz, 2 C), 134.27 (d, $J_{C,P}$ = 21.1 Hz, 2 C), 134.36 (signal for C1′ expected as a doublet at ca. 134 is obscured by the signals at 134.27 and 134.36), 138.03 (d, $J_{C,P}$ = 12.0 Hz), 138.07 (d, $J_{C,P}$ = 11.0 Hz), 141.12 (d, $J_{C,P}$ = 28.0 Hz), 166.26, 202.84. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −3.6. – $C_{29}H_{33}O_3P$ (460.6): calcd. C 75.63, H 7.22; found C 75.71, H 7.34.

(1R,2R*,3R*)-(±)-2,3-Dimethyl-1-isopropyl-5-oxopentyl 2-(Diphenylphosphanyl)benzoate* [(±)-*anti*-**22**] *and (1R*,2R*,3S*)-(±)-2,3-Dimethyl-1-isopropyl-5-oxopentyl 2-(Diphenylphosphanyl)-benzoate* [(±)-*syn*-**22**]: According to the General Procedure for the hydroformylation of the homomethallylic *o*-DPPB esters **9**, the reaction of 215 mg (0.5 mmol) of **15** afforded 212 mg (92%) of **21** as a colorless, viscous oil. Diastereomer ratio 50:50 (*anti:syn*). Spectroscopic data of the 1:1 mixture of *anti*- and *syn*-**22** are as follows. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.8 (m, 24 H, all CH_3), 1.65 [m, 2 H, C*H*$(CH_3)_2$], 1.8–2.2 (m, 6 H), 2.4 (m, 2 H, H at C4), 4.9 (m, 2 H, H at C1), 6.88 (m, 2 H, ArH), 7.2–7.37 (m, 24 H, ArH), 8.1 (m, 2 H, ArH), 9.49 (dd, J = 2.6, 1.5 Hz, 1 H, CHO), 9.61 (dd, J = 2.8, 1.1 Hz, 1 H, CHO). – ^{13}C NMR (75.469 MHz, $CDCl_3$): δ = 10.39, 11.02, 15.92, 17.49, 17.92, 18.46, 19.33, 19.46, 29.39, 29.73, 30.05, 30.18, 38.15, 39.07, 47.36, 49.0, 79.85, 80.23, 128.1–141.7 (all aryl-C), 166.15, 166.26, 202.5, 202.56. – ^{31}P NMR (161.978 MHz, $CDCl_3$): δ = −3.8, −3.9. – $C_{29}H_{33}O_3P$ (460.6): calcd. C 75.63, H 7.22; found C 75.43, H 7.16.

☆ Dedicated to Professor *R. W. Hoffmann* on the occasion of his 65th birthday.

[1] See for example: [1a] M. Sakai, S. Mano, K. Nozaki, H. Takaya, *J. Am. Chem. Soc.* **1993**, *115*, 7033–7034. – [1b] F. Agbossou, J.-F. Carpentier, A. Mortreux, *Chem. Rev.* **1995**, *95*, 2485–2506. – [1c] B. M. Trost, *Acc. Chem. Res.* **1996**, *29*, 355–364. – [1d] M. Shibasaki, H. Sasai, T. Arai, *Angew. Chem.* **1997**, *109*, 1290–1311; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1236–1256.

[2] A. H. Hoveyda, D. A. Evans, G. C. Fu, *Chem. Rev.* **1993**, *93*, 1307–1370.

[3] For successful exceptions see: [3a] A. H. Hoveyda, Z. Xu, *J. Am. Chem. Soc.* **1991**, *113*, 5079–5080. – [3b] A. H. Hoveyda, Z. Xu, J.-P. Morken, A. F. Houri, *ibid.* **1991**, *113*, 8950–8952. – [3c] A. F. Houri, M. T. Didiuk, Z. Xu, N. R. Horan, A. H. Hoveyda, *ibid.* **1993**, *115*, 6614–6624. See also refs.[4][5][7]. For substrate directed transition metal catalysed reduction processes see: J. M. Brown, *Angew. Chem.* **1987**, *99*, 169–182; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 190–203; D. A. Evans, G. C. Fu, A. H. Hoveyda, *J. Am. Chem. Soc.* **1992**, *114*, 6671–6679; K. Burgess, M. J. Ohlmeyer, *Chem. Rev.* **1991**, *91*, 1179–1191.

[4] [4a] B. Breit, *Angew. Chem.* **1996**, *108*, 3021–3023; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2835–2837. – [4b] B. Breit, *Liebigs Ann.* **1997**, 1841–1851. – [4c] B. Breit in *Organic Synthesis via Organometallics* (Eds.: G. Helmchen, J. Dibo, D. Flubacher, B. Wiese), Vieweg, Braunschweig, **1997**, 139–146.

[5] For a review on stereoselective hydroformylations, see: [5a] P. Eilbracht in *Houben-Weyl, Methods of Organic Synthesis, E 21, Stereoselective Synthesis,* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1995**, p. 2488–2557. – For substrate-directed diastereoselective hydroformylation of cyclic systems, see: – [5b] S. D. Burke, J. E. Cobb, *Tetrahedron Lett.* **1986**, *27*, 4237–4240. – [5c] W. R. Jackson, P. Perlmutter, E. E. Tasdelen, *J. Chem. Soc., Chem. Commun.* **1990**, 763–764.

[6] See for example: [6a] *FK506*: H. Tanaka, A. Kuroda, H. Marusawa, H. Hatanaka, T. Kino, T. Goto, M. Hashimoto, T. Taga, *J. Am. Chem. Soc.* **1987**, *109*, 5031–5033; T. Kino, H. Hatanaka, M. Hashimoto, M. Nishiyama, T. Goto, M. Okuhara, M. Kohsaka, H. Aoki, H. Imanaka, *J. Antibiot.* **1987**, *40*, 1249. – [6b] *Aplyronine A*/*B*/*C*: K. Yamada, M. Ojika, T. Ishigaki, Y. Yoshida, H. Ekimoto, M. Arakawa, *J. Am. Chem. Soc.* **1993**, *115*, 11020–11021. – [6c] *Palytoxin*: J. K. Cha, W. J. Christ, J. M. Finan, H. Fujioka, Y. Kishi, L. L. Klein, S. S. Ko, J. Leder, W. W. McWhorter, Jr., K.-P. Pfaff, M. Yonaga, D. Uemura, Y. Hirata, *J. Am. Chem. Soc.* **1982**, *104*, 7369–7371. – [6d] *Herbimycin*: S. Omura, A. Nakagawa, N. Sadakane, *Tetrahedron Lett.* **1979**, 4323–4326. – [6e] *Side chain of Maitotoxin*: M. Sasaki, N. Matsumori, T. Maruyama, T. Nonomura, M. Murata, K. Tachibana, T. Yasumoto, *Angew. Chem.* **1996**, *108*, 1782–1785; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1672. – [6f] *AAL-toxin TA1*: A. T. Bottini, D. G. Gilchrist, *Tetrahedron Lett.* **1981**, *22*, 2719–2722. – [6g] *Fumonisin B1*: S. C. Bezuidenhout, W. C. A. Gelderblom, C. P. Gorst-Allman, R. M. Horak, W. F. O. Marasas, G. Spiteller, R. Vleggaar, *J. Chem. Soc., Chem. Commun.* **1988**, 743–745.

[7] Parts of this work have been published previously as a preliminary communication: B. Breit, *J. Chem. Soc., Chem. Commun.* **1997**, 591–592.

[8] T. Imai, S. Nishida, *Synthesis* **1993**, 395–399.

[9] Employing a catalyst system consisting of 0.35 mol% $[Rh(CO)_2acac]$, 2.8 mol% $P(OPh)_3$ under similar hydroformylation conditions (conversion of **5a** after 24 h at 90°C: quantitative) gave a complicated mixture of different products,which contained only minor amounts of the lactols **6**.

[10] B. Bardili, H. Marschall-Weyerstahl, P. Weyerstahl, *Liebigs Ann. Chem.* **1985**, 275–300.

[11] G. Höfle, W. Steglich, H. Vorbrüggen, *Angew. Chem.* **1978**, *90*, 602–615; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 569–583.

[12] Compare similar studies in ref.[4].

[13] For determination of the relative configuration of the aldehydes **14**, they were transformed in a similar manner as the *o*-DPPB derivative **10a** via the corresponding dimethyl acetal **11b** into the alcohol **12** (*syn*:*anti*, 71:29). For details, see the Experimental Section.

[14] For the combined use of vicinal coupling constants, 2D NOESY and MM3 force field calculations to determine preferred conformations of acyclic molecules in solution, see: R. Göttlich, C. Kahrs, J. Krüger, R. W. Hoffmann, *J. Chem. Soc., Chem. Commun.* **1997**, 247–251; R. Göttlich, U. Schopfer, M. Stahl, R. W. Hoffmann, *Liebigs Ann.* **1997**, 1757–1764; R. J. Smith, D. H. Williams, J. C. J. Barna, I. R. McDermott, K. D. Haegele, F. Piriou, J. Wagner, W. Higgins, *J. Am. Chem. Soc.* **1985**, *107*, 2849–2857; D. Neuhaus, M. P. Williamson, "The Nuclear Overhauser Effect in Structural and Conformational Analysis", VCH, New York **1989**, pp 412; *ibid*, Chapter 11.

[15] On going from 30°C to 90°C, the vicinal coupling constants for H_aH_c and H_bH_c change from 9.0/4.1 Hz to 8.4/4.6 Hz (400

MHz, [D_8]toluene, digital resolution: 0.125 Hz/pt). These data indicate a change in conformer populations for **10a** on going to higher temperatures, which is reflected in the temperature dependence of the diastereoselectivities of the hydroformylation reaction.

[16] MACROMODEL: F. Mohadi, N. G. J. Richardson, W. C. Guida, R. Liskamp, M. Lipto, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440−467. A Boltzmann distribution over all low energy conformers (E_{rel} < 25 kJ·mol^{-1} above the most stable conformer) resulted in the conformer population reported, whereas different conformers of the PPh_2 unit and the isopropyl substituent with identical conformation of the main chain have been combined additively.

[17] The intramolecular *o*-DPPB-directed hydroformylation has been shown to be at least 15 times faster than a corresponding intermolecular hydroformylation process (see ref.[4]).

[18] R. W. Hoffmann, *Angew. Chem.* **1992**, *104*, 1147−1157; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1124.

[19] R. W. Hoffmann, *Chem. Rev.* **1989**, *89*, 1841−1860.

[20] J. Szymoniak, S. Pagneux, D. Felix, C. Moise, *Synlett* **1996**, 46−48.

[21] S. Weigand, R. Brückner, *Synthesis* **1996**, 475−482.

[22] S. Berger, S. Braun, H.-O. Kalinowski, *NMR-Spektroskopie von Nichtmetallen*, Bd. 3, Thieme, Stuttgart, **1993**, Chapter 3.3.11.1, p. 164−166.

[23] Compare [Rh(acac)(PPh_3)(CO)]: ^{13}C NMR (CH_2Cl_2): δ = 189.5 ($^1J_{C,Rh}$ = 74.8 Hz, $^1J_{C,P}$ = 24.8 Hz) ; see L. J. Todd, J. R. Wilkinson, *J. Organomet. Chem.* **1974**, *77*, 1-25; and L. S. Bresler, N. A. Buzina, Y. S. Varshavsky, N. V. Kiseleva, T. G. Cherkasova, *J. Organomet. Chem.* **1979**, *171*, 229−235.

[24] B. Ragonnet et, M. Santelli, M. Bertrand, *Bull. Soc. Chim. Fr.* **1973**, 3119−3121.

[25] G. P. Boldrini, L. Lodi, E. Tagliavini, C. Tarasco, C. Trombini, A. Umani-Ronchi, *J. Org. Chem.* **1987**, *52*, 5447−5452.

[26] L. S. Hegedus, S. D. Wagner, E. L. Waterman, K. Siirala-Hansen, *J. Org. Chem.* **1975**, *40*, 593−598.

[27] R. Dran, T. Prange, *C. R. Hebd. Seances Acad. Sci. Ser. C* **1966**, *262*, 492−494.

[28] J. E. Hoots, T. B. Rauchfuss, D. A. Wrobleski, H. C. Knachel, *Inorg. Synth.* **1982**, *21*, 175−179.

[29] W. Wykypiel, J.-J. Lohmann, D. Seebach, *Helv. Chim. Acta* **1981**, *64*, 1337−1346.

[30] Y. Gao, H. Urabe, F. Sato, *J. Org. Chem.* **1994**, 59, 5521−5523. [97394]