Substrate-Directed Diastereoselective Hydroformylations, Part 3[+]

# Substrate-Directed Diastereoselective Hydroformylation: Key Step for the Assembly of Polypropionate Subunits

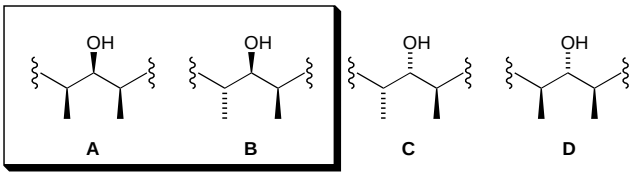
**Bernhard Breit,*[a,b] Mario Dauber,[a] and Klaus Harms[a]**

**Abstract:** Stereoselective hydroformylation of methallylic alcohols of types **3** and **4**, that employed the substrate-bound catalyst-directing *ortho*-diphenylphosphanylbenzoyl (*o*-DPPB) group, was used as a key step for the construction of bifunctionalized stereotriads, which are central building blocks of polyketide natural products. The required diastereomerically pure *syn*- and *anti*- starting methallylic alcohol systems **3** and **4** were obtained either by Cram-selective carbonyl reduction, Fráter alkylation, or by chelation-controlled carbonyl reduction. Enantiomerically pure stereotriad building blocks were derived from a combination of an Evans aldol addition and subsequent *o*-DPPB-directed stereoselective hydroformylation (→**24**). A crystal structure analysis for steretriad building block **24** confirmed the relative and absolute configuration of the stereogenic centers. Additionally, it provided evidence for a previously postulated preferred conformation of the catalyst-directing *o*-DPPB group as well as of the polyketide main chain.

**Keywords:** asymmetric synthesis · catalysis · hydroformylations · polyketides · structure elucidation

## Introduction

Polypropionates constitute an important class of natural products with a wide range of interesting biological activities.[1] Whereas nature makes use of the polyketide pathway to assembly these compounds,[2] the demand for a practical and flexible access to artificial polypropionate structures at will has culminated in a myriad of important new synthetic methods.[3] Among these a particularly useful approach is to divide sophisticated polypropionate chains into stereotriad units that consist of an alternating methyl—hydroxyl–methyl array. These units may be subsequently combined by means of fragment-coupling reactions to give more elaborate polyketide chains.[4] There are four different types of stereotriads (**A** to **D**) (there is a corresponding enantiomer for different end-groups for each of these stereotriads).

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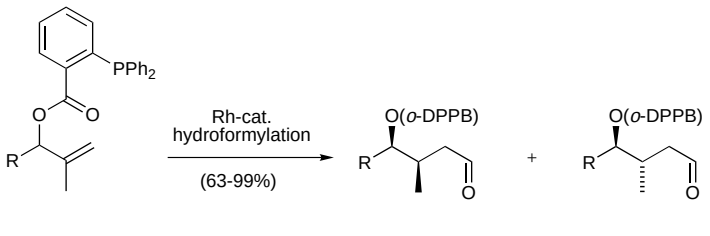
An attractive, although hitherto, unexplored route for the construction of such building blocks makes use of a stereoselective, transition metal catalyzed, carbon–carbon bond-forming process, such as the industrially important hydroformylation reaction.[5, 6] We have recently shown that stereoselectivity in the course of the hydroformylation can be controlled efficiently with the aid of a substrate-bound *catalyst-directing group*.[7, 8] By the use of the *ortho*-diphenylphosphanylbenzoate group (*o*-DPPB) as the catalyst-directing functionality of choice, methallylic alcohols were hydroformylated to afford the corresponding *syn*-aldehydes **2** in generally excellent yields and in diastereoselectivities of up to 96:4 (Scheme 1).[7]

Therefore, this reaction might be, in principle, suited for the construction of the stereotriads **A** and **B**. However, this would




**1** *syn*-**2** *anti*-**2**

up to

96 : 4

Scheme 1. Substrate-directed diastereoselective hydroformylation of methallylic *o*-DPPB esters **1**.

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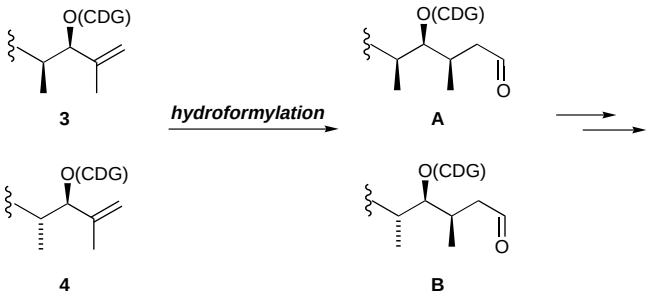
require a starting methallylic alcohol which possesses an additional stereogenic tertiary carbon atom adjacent to the alcohol-bearing stereocenter (see derivatives **3** and **4**, Scheme 2). Subsequent hydroformylation should complete the stereotriad, construct a new carbon–carbon bond, and




Scheme 2. Synthesis of the stereotriads **A** and **B** by hydroformylation.

would simultaneously introduce a synthetically valuable aldehyde functionality. Additionally, if the starting methallylic alcohol systems **3** and **4** were equipped with a suitable functional group (R), the resulting aldehyde-functionalized stereotriad building blocks **A** and **B** could undergo elaboration to enable extension of the polyketide chain into both directions of the main chain.

However, up to this point it was unclear as to what would be the influence of a second stereogenic center, directly neigboring the *o*-DPPB-substituted stereogenic center of a methallylic alcohol *o*-DPPB ester **1**, such as the case in derivatives **3** and **4**. An additional chiral element of this kind could have a significant impact on the reactive conformation of the methallylic alcohol derivatives, and hence, on the stereochemical outcome of the hydroformylation reaction.

We report here on the preparation and stereoselective hydroformylation of methallylic alcohol derivatives **3** and **4**, which provides efficient access to bifunctionalized stereotriad building blocks **A** and **B**.[9]

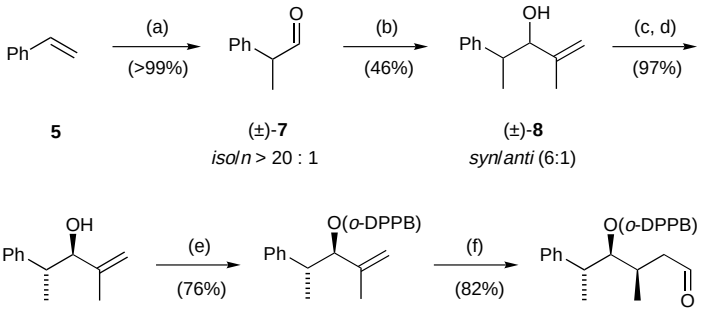
**Abstract in German:** *Die stereoselektive Hydroformylierung von Methallylalkoholen des Typs **3** und **4**, mittels der substratgebundenen Katalysator-dirigierenden ortho-Diphenylphosphanylbenzoyl- (o-DPPB-) Gruppe, konnte als Schlüsselschritt zum Aufbau bifunktionalisierter Stereotriaden des Typs **A** und **B**—zentrale Bausteine polyketider Naturstoffe—genutzt werden. Der Zugang zu den benötigten diastereomerenreinen syn- und anti-Ausgangsmethallylalkohol-Systemen **3** und **4** erfolgte via Cram-selektiver Carbonylreduktion, Fráter-Alkylierung bzw. mittels chelatkontrollierter Carbonylreduktion. Der Zugang zu enantiomerenreinen Stereotriadenbausteinen gelang durch Einsatz der Aldoladdition nach Evans und anschließender Kombination mit der o-DPPB-dirigierten stereoselektiven Hydroformylierung (→**28**). Die am Stereotriadenbaustein **24** durchgeführte Kristallstrukturanalyse bestätigte die absolute und relative Konfiguration der stereogenen Zentren sowie die erwartete Vorzugskonformation der Katalysator-dirigierenden o-DPPB-Gruppe und der Polyketidhauptkette.*

## Results and Discussion

**Construction of stereotriad B: Cram-selective reduction/*o*-DPPB-directed hydroformylation**: A potential synthetic access to the *anti*-methallylic alcohol system **4** could result from a Cram-selective reduction of a corresponding ketone that has a tertiary stereogenic carbon atom adjacent to the carbonyl group.[10]

This synthetic plan was realized starting from styrene (**5**) as the most basic building block. Thus, hydroformylation of styrene (**5**), with our recently developed, highly active and regioselective phosphabenzene (**6**)/rhodium catalyst, provided under mild reaction conditions [room temperature, $H_2$/CO (1:1, 20 bar)] the desired 2-phenylpropionaldehyde [(±)-**7**] in quantitative yields and excellent regioselectivity (*iso*/*n* ratio of >20:1).[11]

The subsequently performed carbonyl addition with 2-propenyl magnesium bromide proceeded in accord with the Felkin–Anh model and yielded preferentially the alcohol (±)-*syn*-**8**. However, diastereoselectivity of the Grignard addition was unsatisfactory (6:1) and the yield was only moderate (46%).[12] The resulting diastereomeric mixture of alcohols (±)-**8** was oxidized with PCC to provide the ketone (±)-**9**. Reduction with lithium aluminum hydride, again in accord with the Felkin–Anh model, afforded the desired alcohol (±)-*anti*-**8** in a diastereomeric ratio (*dr*) >9:1 (Scheme 3).




Scheme 3. Reagents and conditions: a) $[Rh(CO)_2(acac)]$ (0.357 mol%), 2,4,6-triphenyl-$\lambda^3$-phosphinine (**6**, 0.714 mol%), $H_2$/CO (1:1, 20 bar), toluene, 25 °C, 22 h (>99%); b) BrMgC(Me)=$CH_2$, diethyl ether, −78 °C (46%); c) PCC on $Al_2O_3$, $CH_2Cl_2$, 25 °C, 8 h [→(±)-**9**] (99%); d) $LiAlH_4$, ether, −20 °C, 1 h (97%); e) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (0.1 equiv), $CH_2Cl_2$, 25 °C (76%); f) $[Rh(CO)_2(acac)]$ (0.7 mol%), $[P(OPh)_3]$ (2.8 mol%), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (82%).

The catalyst-directing *ortho*-diphenylphosphinobenzoate group [(*o*-DPPB (**10**)] was introduced under standard DCC/DMAP-esterification conditions (→(±)-**11**).[7b] Subsequent *o*-DPPB-directed stereoselective hydroformylation ($H_2$/CO 1:1 (20 bar), toluene, 90 °C) with 0.7 mol% of an optimized catalyst system consisting of $[Rh(CO)_2(acac)]$/4 $P(OPh)_3$ afforded the aldehyde-functionalized stereotriad **B** (±)-**12** (82% yield) as a single regioisomer with *dr* = 94:6, with respect to the newly formed stereocenter.



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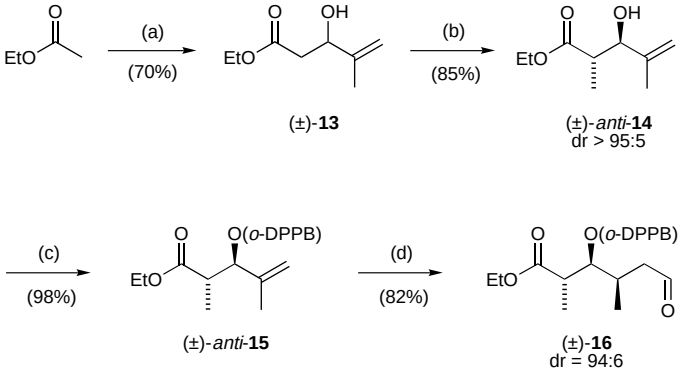
**Stereotriad B: Fráter-alkylation/*o*-DPPB-directed hydroformylation**: An alternative access to an *anti*-configured methallylic alcohol system **4** could provide the *anti*-selective introduction of a methyl group into the main chain. This plan was executed by the use of the well-established Fráter alkylation starting from an appropriate unsaturated $\beta$-hydroxy ester.[13]

Thus, the enolate of ethyl acetate was added to methacrolein to give the desired unsaturated $\beta$-hydroxy ester (±)-**13**.[14] This was transformed into the enolate with LDA (2.3 equiv) followed by treatment with excess methyl iodide in HMPT, according to the conditions of Fráter, to give the methallylic alcohol derivative (±)-*anti*-**14** in good yield and excellent diastereoselectivity (Scheme 4).



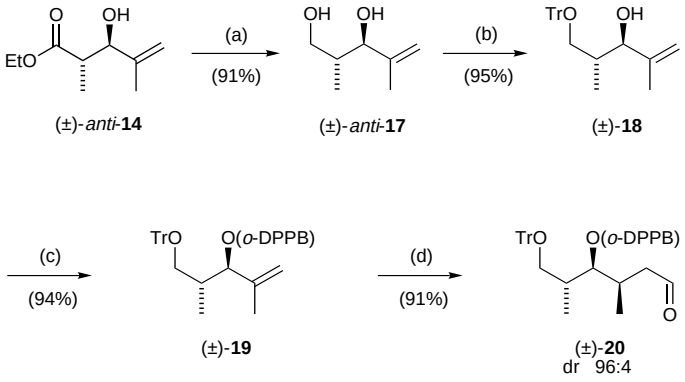

Scheme 4. Reagents and conditions: a) Following a procedure described in ref. [14] (70%); b) LDA (2.3 equiv), THF, $-50 \rightarrow -20\,^{\circ}C$ then MeI (excess), HMPT, $-20 \rightarrow 0\,^{\circ}C$ (85%); c) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (1 equiv), $CH_2Cl_2$, 25 °C (98%); d) $[Rh(CO)_2(acac)]$ (0.7 mol%), $[P(OPh)_3]$ (2.8 mol%), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (82%).

Introduction of the *o*-DPPB group by means of the DCC/DMAP esterification protocol (→(±)-*anti*-**15**) followed by hydroformylation, under the same conditions as described for (±)-**11**, yielded aldehyde (±)-**16** (82%, *dr* = 94:6, *syn*:*anti*). This reaction was performed on the 10 g scale which demonstrates the practicability of this methodology for large-scale preparation.

Aldehyde (±)-**16** represents an interesting bifunctionalized stereotriad **B** building block. The additional ester functionality may be subsequently transformed into an aldehyde functionality which itself may serve as a starting point for further polyketide chain elaborations which employ known methodologies, such as allylboration or aldol-type chemistry.[15]

Furthermore, the kinetic resolution of (±)-**13** by means of the Sharpless asymmetric epoxidation protocol has already been reported and hence, provides a potential access to the stereotriad building block **16** in an enantiomerically pure form.[14]

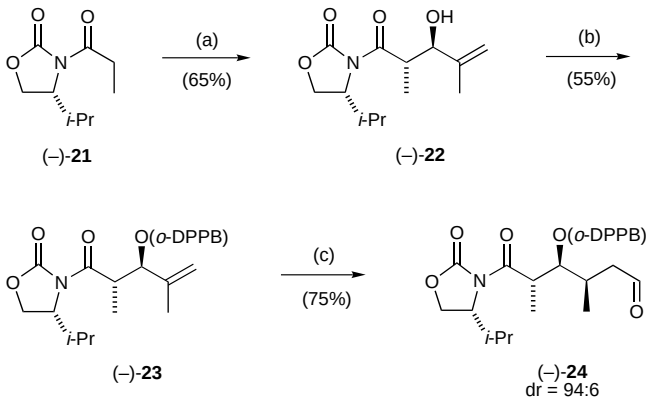
A primary alcohol, instead of an ester, could serve as an alternative latent aldehyde functionality: the alcohol could be transformed into an aldehyde by known oxidation methods. In order to explore the preparation of such a primary alcohol-functionalized stereotriad, the ester (±)-*anti*-**14** was reduced with lithium aluminum hydride to afford the diol (±)-*anti*-**17**. Chemoselective protection of the primary alcohol in the presence of a secondary allylic alcohol was achieved by means of standard trityl ether protection to give the alcohol (±)-**18**. The catalyst-directing *o*-DPPB group was introduced again with the DCC/DMAP coupling protocol [→(±)-**19**]. Subsequent hydroformylation (10 g scale) proceeded smoothly to provide the bifunctionalized stereotriad building block (±)-**20** in excellent yields (91%) and diastereomerically pure form (*syn*:*anti* = ≥96:≤4) according to NMR spectroscopy (Scheme 5).




Scheme 5. Reagents and conditions: a) $LiAlH_4$, diethyl ether, 0 °C (91%); b) TrCl, DMAP (5 mol%), pyridine, 4 d, 25 °C (95%); c) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (0.1 equiv), $CH_2Cl_2$, 25 °C (94%); d) $[Rh(CO)_2(acac)]$ (0.7 mol%), $[P(OPh)_3]$ (2.8 mol%), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (91%).

**Stereotriad B: Aldol addition/*o*-DPPB-directed hydroformylation**: As an entry into the synthesis of an enantiomerically pure stereotriad **B** building block, the combination was envisioned of an aldol addition reaction, which would have to control both relative and absolute configuration of the two newly formed stereogenic centers, with stereoselective hydroformylation (Scheme 6).

An aldol addition reaction, that fulfills the requirements described above, is a variant of the Evans chiral oxazolidinone method developed by Heathcock et al. which makes use of an additional bulky Lewis acid additive.[16] Thus, following a known procedure starting from the oxazolidinone (−)-**21**, the *anti*-methallylic alcohol (−)-**22** was obtained in fair yield (Scheme 6). After the attachment of the catalyst-directing *o*-DPPB group, the methallylic alcohol (−)-**23** was hydroformylated under our standard conditions to afford the enantiomerically pure stereotriad **B** aldehyde building block (−)-**24** in good yield and diastereoselectivity (*dr* = 94:6, *syn*:*anti*). The X-ray crystal structure analysis of aldehyde (−)-**24** confirmed the relative configuration of the new stereogenic centers formed in the course of this reaction sequence. Thus, in accord with the $^{13}C$ NMR spectroscopic data, a *syn*-relation between the stereogenic center at C3 and the oxygen-functionalized stereogenic center at C4 (Figure 1) was detected, which is the result of the *syn*-selective *o*-DPPB-directed hydroformylation.[7b] The stereogenic centers at C5 and C4 show an *anti*-relationship, which is the stereochemical result expected for the aldol addition method employed.[16]




Scheme 6. Reagents and conditions a) $n$Bu$_2$BOTf, $i$PrNEt$_2$, $-78\,^{\circ}$C, $CH_2Cl_2$, methacrolein, $Et_2AlCl$ following a procedure described in ref. [15] (65%); b) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (1 equiv), $CH_2Cl_2$, 25 °C (55%); c) [Rh(CO)$_2$(acac)] (0.7 mol%), [P(OPh)$_3$] (2.8 mol%), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (75%).

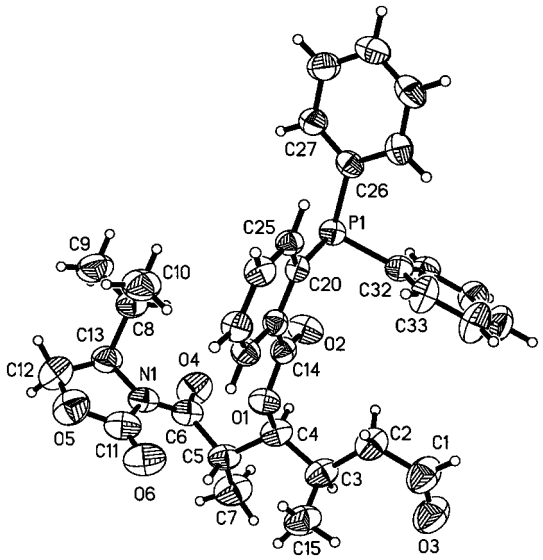


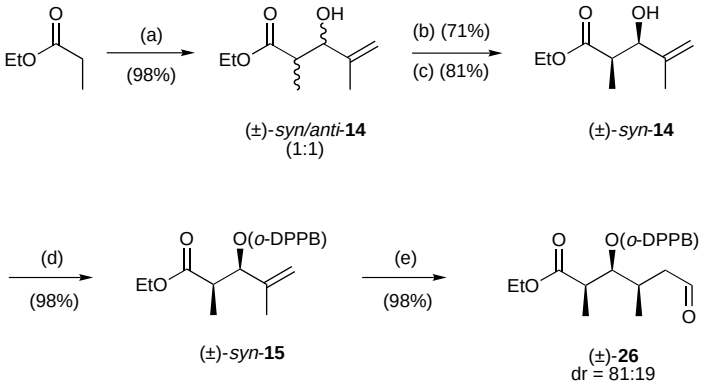

Figure 1. Structure of (–)-**24** in the solid state.

The *o*-DPPB ester function adopts the typical preferred conformation of a carboxylic ester of a secondary alcohol with a *syn*-coplanar arrangement of the carbonyl group and the C–H bond at C4 which results from the minimization of 1,3-allylic strain.[17] Such a preferred conformation was postulated earlier and has served as a structural basis for the design of the catalyst-directing *o*-DPPB group.[7a,b]

The all-*trans* conformation of the main chain is determined by the avoidance of repulsive *syn*-pentane interactions between the methyl groups at C3 and C5.[18]

**Stereotriad A: *syn*-Selective Zn(BH$_4$)$_2$-ketone reduction/*o*-DPPB-directed hydroformylation**: For the construction of an all-*syn* stereotriad (type **A**), a *syn*-methallylic alcohol system **3** was required as the starting point. One approach to such a *syn*-configured derivative could rely on the *syn*-selective reduction of ketones with heteroatom substituents in $\alpha$- or $\beta$-position which allow for a chelation-controlled intramolecular hydride transfer that employs $Zn(BH_4)_2$ as the reducing agent.[19]

Thus, ketone (±)-**25**, which was obtained by means of aldol addition of ethyl propionate and methacrolein [→(±)-*syn*/*anti*-**14** (1:1)] followed by PCC oxidation, was stereoselectively reduced with $Zn(BH_4)_2$ to give the alcohol (±)-*syn*-**14** ($dr > 95:5$). Hydroformylation of the corresponding *o*-DPPB ester (±)-*syn*-**15** gave the corresponding aldehyde (±)-**26** in good yields, however, with only moderate diastereoselectivity ($dr = 81:19$ *syn*:*anti*) (Scheme 7).




Scheme 7. Reagents and conditions: a) LDA, THF, $-78\,^{\circ}$C, then methacrolein (98%); b) PCC on $Al_2O_3$, $CH_2Cl_2$, 25 °C, 8 h [→(±)-**25**] (71%); c) $Zn(BH_4)_2$ (2.6 equiv), diethyl ether, 0 °C, 40 min (97%); d) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (0.1 equiv), $CH_2Cl_2$, 25 °C (98%); e) [Rh(CO)$_2$(acac)] (0.7 mol%), [P(OPh)$_3$] (2.8 mol%), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (98%).

Since the switch from the ester derivative (±)-*anti*-**15** to the primary alcohol derivative (±)-**19** provided an increase of diastereoselectivity in the course of the hydroformylation reaction, we became curious as to whether a similar structural change for the *syn*-diastereomer of (±)-**15** would provide a similar increase in the diastereoselectivity upon hydroformylation.

Therefore, the ester function in (±)-*syn*-**14** was reduced to a primary alcohol with lithium aluminum hydride to give the diol (±)-*syn*-**17** in good yields (Scheme 8). Selective protection of the primary alcohol in the presence of the secondary allylic alcohol was achieved as the pivaloate [→(±)-**27**]. After introduction of the catalyst-directing *o*-DPPB unit, hydroformylation of the resulting *o*-DPPB ester (±)-**28** afforded in good yield, and more importantly, excellent diastereoselectivity (*syn*:*anti* = 95:5) the all-*syn* stereotriad **A** building block (±)-**29**, which is well elaborated for polyketide chain extensions in both directions of the main chain (Scheme 8).

Hence, transformation of the ethyl ester function in (±)-*syn*-**15** into a sterically slightly more demanding $CH_2OPiv$-moiety, such as in (±)-**27**, turned out to be sufficient to improve the diastereoselectivity significantly from 81:19 for (±)-*syn*-**26** to 95:5 for (±)-**29**. This observation is in agreement with results obtained in the course of earlier studies on hydroformylation of simple methallylic alcohols.[7a,b] As a result of these studies, it was found that the diastereoselectivity in the course of the hydroformylation reaction is a function of the steric demand of the $\alpha$-substituent at the stereogenic center: the larger this substituent the higher the diastereoselectivity of the hydroformylation reaction.

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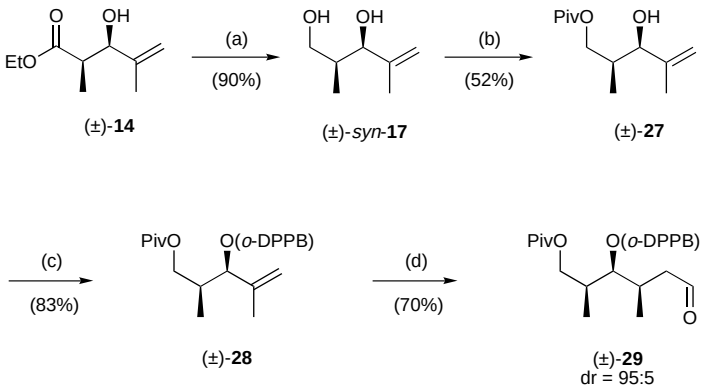


Scheme 8. Reagents and conditions: a) $LiAlH_4$, ether, 0 °C (90 %); b) PivCl, pyridine, 25 °C, 4 d (67 %); c) *o*-DPPBA (**10**, 1 equiv), DCC (1.1 equiv), DMAP (1 equiv), $CH_2Cl_2$, 25 °C (83 %); d) $[Rh(CO)_2(acac)]$ (0.7 mol %), $[P(OPh)_3]$ (2.8 mol %), $H_2$/CO (1:1, 20 bar), toluene, 90 °C, 24 h (70 %).

## Conclusions

We have demonstrated that *o*-DPPB-directed diastereoselective hydroformylation of functionalized methallylic alcohol derivatives can serve as a key step for the efficient construction of bifunctionalized stereotriad **A** and **B** building blocks in diastereomerically, and if desired, enantiomerically pure form. These building blocks are well elaborated for polyketide chain extensions in both directions of the main chain.

## 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 not corrected. $^1H$ and $^{13}C$ NMR spectra were recorded with Bruker ARX-200, Bruker AC-300, Bruker WH-400, and Bruker AMX-500 spectrometers with tetramethylsilane (TMS), chloroform ($CHCl_3$), or benzene ($C_6H_6$) as the internal standards. $^{31}P$ NMR spectra: recorded on a Bruker WH 400 (161.978 MHz) spectrometer with 85 % $H_3PO_4$ as the external standard. Melting points: Melting point apparatus by Dr. Tottoli (Büchi). Elemental analyses: CHN rapid analyzer (Heraeus). Flash chromatography: Silica gel Si 60 (40–63 μm from Merck). Hydroformylation reactions were performed in stainless-steel autoclaves (100 and 200 mL) equipped with magnetic stirrers. Gases: CO 2.0 (Messer-Griesheim), $H_2$ 3.0 (Messer-Griesheim).

**(3*R**,4*S**)-(±)-2-Methyl-4-phenyl-pent-1-en-3-ol [(±)-*syn*-8] and (3*R**,4*R**)-(±)-2-Methyl-4-phenyl-pent-1-en-3-ol [(±)-*anti*-8]**: A solution of 2-phenylpropionaldehyde (±)-**7** (4.29 g, 32 mmol) in diethyl ether (10 mL) at −78 °C was added to a solution of isopropylmagnesium bromide [prepared from 2-bromopropene (4.84 g, 40 mmol) and magnesium (972 mg, 40 mmol)] in diethyl ether (40 mL). The mixture was allowed to warm to room temperature over a period of 6 h, and was then stirred at this temperature for a further 10 h. Subsequently, the reaction mixture was quenched by addition of saturated aqueous ammonium chloride solution (20 mL). The organic phase was separated and the aqueous phase was extracted with *tert*-butyl methyl ether (2 × 20 mL). The combined organic phases were dried ($Na_2SO_4$) and the solvent was evaporated in vacuo. The residue was prepurified by flash chromatography (petroleum ether/*tert*-butyl methyl ether 19:1 – 9:1 gradient). Subsequent bulb-to-bulb distillation (100 °C/5 × $10^{-3}$ mbar) furnished (±)-**8** (2.6 g, 46 %) as a colorless oil; *dr* = 6:1. *syn*:*anti*). Spectroscopic and analytical data correspond to those reported previously.[12]

**(4*RS*)-(±)-2-Methyl-4-phenyl-pent-1-en-3-one [(±)-9]**: PCC on $Al_2O_3$ (15.62 g, 15.62 mmol) was added to a solution of (±)-**9** (1.377 g, 7.91 mmol) in $CH_2Cl_2$ (50 mL). The mixture was stirred for 8 h at room temperature. Subsequently, the reaction mixture was filtered with $CH_2Cl_2$ (100 mL) through a plug of silica. The solvent was evaporated to give (±)-**9** (1.34 g, 99 %) as a pale yellow oil. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 1.36$ (d, $J =$ 7.1 Hz, 3 H, $CHCH_3$), 1.75 (s, 3 H, $CH_3$), 1.35 (q, $J = 6.8$ Hz, $CHCH_3$), 5.6 (s, 1 H, $=CH_2$), 5.89 (s, 1 H, $=CH_2$), 7.1 – 7.18 (m, 5 H, ArH); $^{13}C$ NMR (75.469 MHz, $CDCl_3$): $\delta = 18.16$, 19.27, 46.72, 125.09, 126.71, 127.47 (2 C), 128.88 (2 C), 141.80, 143.65, 202.01. MS (70 eV, EI); *m*/*z* (%): 174 (9.3) [$M^+$], 105 (100) [$C_6H_5$–$CH$=$CH_2^+$], 85 (63.8), 77 (33.8) [$C_6H_5^+$]; $C_{12}H_{14}O$: calcd 174.1045; found 174.1046 (HRMS).

**(3*R**,4*R**)-(±)-2-Methyl-4-phenyl-pent-1-en-3-ol [(±)-*anti*-8]**: Lithium aluminum hydride (235 mg, 6.2 mmol) was added to a solution of (±)-**9** (941 mg, 5.64 mmol) in diethyl ether (10 mL) at −20 °C. The reaction mixture was kept for 1 h at this temperature and was then carefully quenched with water (5 mL). The resulting mixture was allowed to warm to room temperature and then additional water (5 mL) and a Rochelle salt solution (20 %, 20 mL) were added. The mixture was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were dried ($Na_2SO_4$), the solvent was evaporated in vacuo, and the residue purified by flash chromatography (petrol ether/*tert*-butyl methyl ether 9:1) to afford (±)-*anti*-**8** (965 mg, 97 %) as a colorless oil; *dr* = 9:1, *anti*:*syn*). $^1H$ NMR (300 MHz, $CDCl_3$):$\delta = 1.14$ (d, $J = 7.05$ Hz, 3 H, $CHCH_3$), 1.18 (pseudo t, $J = 1.26$ Hz, 3 H, $CH_3$), 2.81 (dq, $J = 9.1$, 7.1 Hz, 1 H, $CHCH_3$), 4.06 (dd, $J =$ 9.1, 2.5 Hz, 1 H, OCH), 4.92 (m, 1 H, $=CH_2$), 4.95 (m, 1 H, $=CH_2$), 7.2 – 7.33 (m, 5 H, ArH); $^{13}C$ NMR (75.469 MHz, $CDCl_3$): $\delta = 16.63$, 18.50, 43.68, 81.42, 114.04, 126.80, 128.00 (2 C), 128.63 (2 C), 143.40, 145.24; $C_{12}H_{16}O$ (176.3): calcd C 81.77 H 9.15; found C 81.55 H 8.83.

**(1*R**)-(±)-1-[(1*R**)-1-Phenylethyl]prop-2-enyl 2-(diphenylphosphanyl)-benzoate [(±)-*anti*-11]**: *o*-DPPBA (**10**)[20] (606 mg, 1.98 mmol), DMAP (24 mg, 0.19 mmol), and DCC (449 mg, 2.18 mmol) were added successively to a solution of methallylic alcohol (±)-*anti*-**8** (697 mg, 1.98 mmol) in $CH_2Cl_2$ (4 mL), and the resulting mixture was stirred at room temperature until TLC analysis indicated complete consumption of the starting material (≈ 24 h). Subsequently, the reaction mixture was filtered through a plug of $CH_2Cl_2$-wetted Celite and washed with additional $CH_2Cl_2$. An appropriate amount of silica gel was added to the filtrate, which was then concentrated to dryness. Flash chromatography (petroleum ether/*tert*-butyl methyl ether 9:1) afforded the *o*-DPPB ester (±)-*anti*-**11** (697 mg, 76 %) as a colorless, highly viscous oil. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ (d, $J = 7.3$ Hz, 3 H, $CH_3$), 1.72 (s, 3 H, $CH_3$), 3.16 (m, 1 H, $CHCH_3$), 4.93 (d, $J = 1.0$ Hz, 1 H, $=CH_2$), 5.02 (s, 1 H, $=CH_2$), 5.56 (d, $J = 8.54$ Hz, HCO), 6.91 (m, 1 H, ArH), 7.19 – 7.44 (m, 17 H, ArH), 7.77 (m, 1 H, ArH); $^{13}C$ NMR (75.469 MHz, $CDCl_3$): $\delta = 18.49$, 18.59, 42.33, 82.01, 115.54, 126.66, 128.12 (2 C), 128.22, 128.46 (d, $J$(C,P) = 10.5 Hz, 4 C), 128.61 (2 C), 128.69 (2 C), 130.28 (d, $J$(C,P) = 2.5 Hz), 131.79, 133.97 (d, $J$(C,P) = 20.5 Hz, 2 C); 134.21 (d, $J$(C,P) = 20.7 Hz, 2 C), 134.32, 134.79 (d, $J$(C,P) = 18.8 Hz), 138.34 (d, $J$(C,P) = 12.1 Hz), 138.4 (d, $J$(C,P) = 12.6 Hz), 140.83 (d, $J$(C,P) = 27.5 Hz), 141.53, 143.14, 165.58 (d, $J$(C,P) = 2.3 Hz); $^{31}P$ NMR (161.978 MHz, $CDCl_3$): $\delta = -4.6$; $C_{31}H_{29}O_2P$ (464.5): calcd C 80.15, H 6.29; found C 79.95, H 5.98.

**(1*R**,2*S**)-(±)-2-Methyl-4-oxo-1-[(1*R**)-1-phenylethyl]butyl 2-(diphenylphosphanyl)benzoate [(±)-12]**: $P(OPh)_3$ (4.5 mg, $1.4 \times 10^{-2}$ mmol) was added, under the exclusion of air and moisture, to a solution of $[Rh(CO)_2(acac)]$ (0.9 mg, $3.5 \times 10^{-3}$ mmol) in toluene (3 mL) at 20 °C, and the resulting mixture was stirred at this temperature for 15 min. Subsequently, *o*-DPPB ester (±)-**11** (232 mg, 0.5 mmol) was added and the resulting solution was transferred by cannula into a stainless-steel autoclave, which had been evacuated and refilled with argon several times. The flask and cannula were rinsed with additional toluene (2 mL). The autoclave was heated to 90 °C, then pressurized successively with carbon monoxide (10 bar) and hydrogen (10 bar), and the reaction mixture was stirred under these conditions for 24 h. The autoclave was then cooled rapidly to 20 °C and the contents were filtered through a small plug of silica with *tert*-butyl methyl ether (30 mL). After evaporation of the solvent in vacuo, the crude product was analyzed by NMR spectroscopy to determine the diastereomer ratio. Subsequent flash chromatography (petroleum ether/*tert*-butyl methyl ether 9:1) afforded aldehyde (±)-**12** (203 mg, 82 %) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = ≥ 96: ≤ 4 (*syn*:*anti*). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta =$

0.92 (d, $J = 6.8$ Hz, $CH_3$), 1.28 (d, $J = 7.0$ Hz, 3H, $CH_3$), 1.92 (dd, $J = 18.0$, 8.0 Hz, 1H, $CH_2$), 2.27 (dd, $J = 18.0$, 5.7 Hz, 1H, $CH_2$), 2.56 (m, 1H, CH), 3.11 (m, 1H, CH), 5.27 (dd, $J = 9.3$, 2.7 Hz, HCO), 6.84 (m, 1H, ArH), 7.2–7.32 (m, 17H, ArH), 7.47 (m, 1H, ArH), 9.51 (s, 1H, CHO); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.47$, 19.12, 29.03, 42.11, 48.19, 80.24, 126.67, 127.85 (2C), 128.05, 128.59 (2C), 128.64 (d, $J$(C,P) = 7.4 Hz, 4C), 128.77 (2C), 130.18, 131.77, 133.99 (d, $J$(C,P) = 20.7 Hz, 2C), 134.0, 134.1 (d, $J$(C,P) = 23.0 Hz, 2C), 134.45 (d, $J$(C,P) = 21.1 Hz), 137.75 (d, $J$(C,P) = 13.1 Hz), 138.51 (d, $J$(C,P) = 11.5 Hz), 140.59 (d, $J$(C,P) = 27.2 Hz), 143.56, 166.43, 201.6; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.1$; $C_{32}H_{31}O_3P$ (494.6): calcd C 77.72, H 6.32; found C 77.70, H 6.19.

**Ethyl (3*R**,4*S**)-(±)-3-hydroxy-2,4-dimethylpent-4-enoate [(±)-*anti*-14]**: *n*BuLi (1.66 M in hexane, 32.7 mL, 54 mmol) was added dropwise to a solution of diisopropylamine (5.49 g, 54.24 mmol) in THF (15 mL) at 0 °C. The reaction mixture was cooled to −50 °C and a solution of hydroxy ester (±)-**13** (3.9 g, 24.65 mmol) in THF (5 mL) was added dropwise. During the addition the temperature was allowed to rise to −20 °C (thermometer in reaction medium). The reaction mixture was stirred for a further 30 min at this temperature. Subsequently, a solution of methyl iodide (41 g, 289 mmol) in HMPT (5 mL) was added at such a rate that the temperature of the reaction mixture rose to 0 °C. After the mixture was stirred for a further 5 min at 0 °C it was allowed to warm to room temperature and subsequently quenched with saturated aqueous ammonium chloride solution (20 mL). The mixture was extracted with *tert*-butyl methyl ether (3 × 60 mL), the combined organic phases were dried ($Na_2SO_4$), and the solvent was removed in vacuo. Flash chromatography furnished (±)-*anti*-**14** (3.59 g, 85%) as a slightly yellow oil; *dr* = 15:1, *anti*:*syn*, detected by GC). $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 1.09$ (d, $J = 7.2$ Hz, 3H, CHC$H_3$), 1.26 (t, $J = 7.1$ Hz, 3H, $CH_2CH_3$), 1.70 (br s, 3H, $CH_3$), 2.64 (dq, $^3J = 8.0$ Hz, 7.2 Hz, 1H, C$H$CH$_3$), 2.72 (d, $J = 5.1$ Hz, 1H, OH), 4.14 (m, 1H, HCO), 4.16 (q, $J = 7.1$ Hz, 2H, $OCH_2$), 4.92, 4.96 (m, 1H, each =$CH_2$); $^{13}$C NMR (50.329 MHz, $CDCl_3$): $\delta = 14.0$, 14.2, 16.8, 43.0, 60.5, 77.8, 113.6, 144.3, 175.7. Analytical data correspond to those reported previously.[60]

**Ethyl (2*R**,3*S**)-(±)-2,4-dimethyl-3-[2-(diphenylphosphanyl)benzoyloxy]-pent-4-enoate [(±)-*anti*-15]**: The procedure was analogous to that for the preparation of the methallylic *o*-DPPB ester(±)-**11**: Reaction of (±)-*anti*-**14** (3.5 g, 20 mmol), DMAP (2.4 g, 20 mmol), DCC (6.13 g, 21 mmol), and *o*-DPPBA (**10**)[20] (6.13 g, 20 mmol) in $CH_2Cl_2$ (120 mL) gave (±)-*anti*-**15** (9.026 g, 98%) as a colorless, highly viscous oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.10$ (d, $J = 7.1$ Hz, 3H, $CH_3$), 1.17 (t, $J = 7.0$ Hz, 3H, $CH_3$), 1.62 (s, 3H, $CH_3$), 2.85 (m, 1H, C$H$CH$_3$), 4.08 (q, $J = 7.0$ Hz, 2H, $OCH_2$), 4.95 (s, 1H, =$CH_2$), 5.06 (s, 1H, =$CH_2$), 5.55 (d, $J = 9.4$ Hz, 1H, OCH), 6.94 (m, 1H, ArH), 7.25–7.48 (m, 12H, ArH), 8.1 (m, 1H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.58$, 14.0, 17.4, 42.2, 60.49, 79.28, 116.4, 128.6, 128.24 (d, $J$(C,P) = 7.2 Hz, 4C), 128.29 (2C), 130.6, 131.78, 133.67 (d, $J$(C,P) = 20.5 Hz, 2C), 133.83 (d, $J$(C,P) = 20.8 Hz, 2C), 134.25 (signal for C1′, expected to be a doublet at $\delta \approx 134$, is obscured by the signals at $\delta =$ 133.83 and 134.25), 137.93 (d, $J$(C,P) = 11.8 Hz), 138.04 (d, $J$(C,P) = 12.7 Hz), 139.7, 140.61 (d, $J$(C,P) = 27.8 Hz), 164.8, 173.46; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.8$; $C_{28}H_{29}O_4P$ (460.5): calcd C 73.03, H 6.35; found C 72.95, H 6.45.

**Ethyl (2*R**,3*R**,4*S**)-(±)-2,4-dimethyl-3-[2-(diphenylphosphanyl)benzoyloxy]-6-oxohexanoate [(±)-16]**: The procedure was analogous to that for the hydroformylation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-*anti*-**15** (9 g, 20 mmol), $[Rh(CO)_2acac]$ (36 mg, 0.14 mmol), and $P(OPh)_3$ (174 mg, 0.56 mmol) in toluene (12 mL) for three days gave (±)-**16** (7.88 g, 82%) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = 94:6 (*syn*:*anti*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.75$ (d, $J = 6.8$ Hz, $CH_3$), 1.04 (t, $J = 7.1$ Hz, 3H, $CH_3$), 1.16 (d, $J = 6.1$ Hz, $CH_3$), 1.86 (ddd, $J = 18.0$, 7.9, 1.2 Hz, 1H, $CH_2$), 2.2 (dd, $J = 18.0$, 5.7 Hz, 1H, $CH_2$), 2.35 (m, 1H, CH), 2.77 (m, 1H, CH), 3.91 (q, $J = 7.2$ Hz, 2H, $OCH_2$), 5.17 (dd, $J = 9.4$, 2.8 Hz, 1H, HCO), 6.84 (m, 1H, ArH), 7.96 (m, 1H, ArH), 9.43 (s, 1H, CHO); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.14$, 14.03, 14.07, 28.34, 42.4, 47.72, 60.73, 77.46, 128.21, 128.52 (d, $J$(C,P) = 7.2 Hz, 4C), 128.62, 128.74, 130.73, 132.13, 133.49 (d, $J$(C,P) = 17.6 Hz), 133.83 (d, $J$(C,P) = 20.7 Hz, 2C), 134.16, 134.31 (d, $J$(C,P) = 21.1 Hz, 2C), 137.66 (d, $J$(C,P) = 13.0 Hz), 138.46 (d, $J$(C,P) = 11.4 Hz), 141.27 (d, $J$(C,P) = 28.1 Hz), 165.86 (d, $J$(C,P) = 2.9 Hz), 173.59, 200.98; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -3.8$; $C_{29}H_{31}O_5P$ (490.5): calcd C 71.01, H 6.37; found C 70.81, H 6.24.

**(2*R**,3*R**)-(±)-2,4-Dimethylpent-4-en-1,3-diol [(±)-*anti*-17]**: (±)-*anti*-**14** (2.6 g, 15.3 mmol) in THF (3 mL) was added to a suspension of lithium aluminum hydride (745 mg, 19.9 mmol) in THF (45 mL) at room temperature. The reaction mixture was refluxed for 1 h. After cooling to room temperature the reaction mixture was quenched by successive additions of water (0.77 mL), aqueous NaOH solution (15%, 0.77 mL), and a second portion of water (0.77 mL). The resulting mixture was dried by addition of $Na_2SO_4$, then it was filtered and the residue washed thoroughly with *tert*-butyl methyl ether. The solvent was removed in vacuo and the remaining crude product purified by column chromatography (petroleum ether/*tert*-butyl methyl ether 7:3) to give (±)-*anti*-**17** (1.788 g, 91%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.7$ (d, $J = 7.0$ Hz, $CH_3$), 1.65 (s, 3H, $CH_3$), 1.82 (m, 1H, CH), 3.44 (d, $J = 2.6$ Hz, 1H, OH), 3.6 (m, 3H, $CH_2OH$), 3.88 (dd, $J = 8.5$, 1.8 Hz, 1H, HCO), 4.82 (m, 1H, =$CH_2$), 4.87 (m, 1H, =$CH_2$); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.65$, 16.77, 37.04, 67.75, 82.57, 113.96, 146.01; $C_7H_{14}O_2$ (130.1868): calcd C 64.58, H 10.84; found: C 64.63, H 11.13.

**(3*R**,4*R**)-(±)-2,4-Dimethyl-5-(triphenylmethoxy)pent-1-en-3-ol [(±)-18]**: Chlorotriphenylmethane (3.71 g, 13.3 mmol) was added to a solution of (±)-*anti*-**17** (1.575 g, 12.1 mmol) and DMAP (74 mg, 0.61 mmol) in pyridine (50 mL). The mixture was stirred for 4 d at room temperature. Silica gel was added and the solvent evaporated to dryness. Subsequent flash chromatography (petroleum ether/*tert*-butyl methyl ether) furnished (±)-**18** (4.268 g, 95%) as a colorless viscous oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 7.0$ Hz, 3H, $CH_3$), 1.71 (s, 3H, $CH_3$), 1.95 (m, 1H, CH), 3.2 (m, 1H, $CH_2O$), 3.36 (dd, $J = 9.3$, 4.2 Hz, 1H, $CH_2O$), 3.5 (d, $J = 2.7$ Hz, 1H, OH), 3.9 (dd, $J = 8.1$, 2.2 Hz, 1H, HCO), 4.84 (m, 1H, =$CH_2$), 4.88 (s, 1H, =$CH_2$), 7.2–7.37 (m, 11H, ArH), 7.45–7.52 (m, 4H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 14.28$, 16.92, 36.30, 67.71, 80.72, 87.37, 112.89, 126.97 (3C), 127.83 (6C), 128.58 (6C), 143.72 (3C), 146.9; $C_{26}H_{28}O_2$ (372.5): calcd C 83.83, H 7.58; found C 83.69, H 7.78.

**(1*R**,2*R**)-(±)-1-[1-Methyl-2-(triphenylmethoxy)ethyl]prop-2-enyl 2-(diphenylphosphanyl)-benzoate [(±)-19]**: The procedure was analogous to that for the preparation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-**18** (5.448 g, 14.6 mmol), DMAP (179 mg, 1.46 mmol), DCC (3.322 g, 16.1 mmol), and *o*-DPPBA (**10**,[20] 4.472 g, 14.6 mmol) in $CH_2Cl_2$ (30 mL) gave (±)-**19** (9.025 g, 94%) as a colorless, highly viscous oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.9$ Hz, 3H, $CH_3$), 1.58 (s, 3H, $CH_3$), 2.1 (m, 1H, CH), 3.0 (dd, $J = 8.9$, 6.3 Hz, 1H, $OCH_2$), 3.1 (dd, $J = 8.9$, 3.8 Hz, 1H, $OCH_2$), 4.82 (d, $J = 1.4$ Hz, 1H, =$CH_2$), 4.9 (s, 1H, =$CH_2$), 5.25 (d, $J = 8.7$ Hz, 1H, OCH), 6.88 (m, 1H, ArH), 7.1–7.48 (m, 27H, ArH), 7.84 (m, 1H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 14.6$, 18.27, 36.10, 64.57, 80.19, 86.52, 115.26, 141.23, 126.9–144.4 all Aryl-C, 165.66 (d, $J$(C,P) = 2.5 Hz); $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.6$; $C_{45}H_{41}O_3P$ (660.8): calcd C 81.80, H 6.25; found C 81.64, H 6.54.

**(1*R**,2*S**)-(±)-2-Methyl-1-[(1*S**)-methyl-2-(triphenylmethoxy)ethyl]-4-oxo-butyl 2-(diphenylphosphanyl)benzoate [(±)-20]**: The procedure was analogous to that for the hydroformylation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-**19** (8.518 g, 12.9 mmol), $[Rh(CO)_2acac]$ (23.8 mg, 0.092 mmol), and $P(OPh)_3$ (114 mg, 0.368 mmol) in toluene (30 mL) for three days gave (±)-**20** (8.084 g, 91%) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = ≥ 96: ≤ 4 (*syn*:*anti*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.6$ Hz, 3H, $CH_3$), 1.09 (d, $J = 6.6$ Hz, 3H, $CH_3$), 1.9 (dd, $J = 17.6$, 8.3 Hz, 1H, $CH_2$), 2.1 (m, 1H, CH), 2.22 (dd, $J = 17.6$, 5.1 Hz, 1H, $CH_2$), 2.46 (m, 1H, CH), 2.96 (pseudo t, $J = 8.3$ Hz, 1H, $OCH_2$), 3.15 (dd, $J = 8.7$, 3.0 Hz, 1H, $OCH_2$), 4.97 (dd, $J = 9.0$, 2.3 Hz, 1H, OCH), 6.92 (m, 1H, ArH), 7.12–7.46 (m, 27H, ArH), 7.76 (m, 1H, ArH), 9.46 (s, 1H, CHO); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.50$, 14.86, 28.86, 36.04, 48.02, 64.94, 78.27, 86.63, 126.90 (3C), 127.74 (6C), 128.18, 128.48 (2C), 128.57 (d, $J$(C,P) = 6.9 Hz, 4C), 128.81 (6C), 130.80, 132.00, 133.58 (d, $J$(C,P) = 16.9 Hz), 133.83 (d, $J$(C,P) = 20.4 Hz, 2C), 134.22, 134.36 (d, $J$(C,P) = 21.6 Hz, 2C), 137.92 (d, $J$(C,P) = 13.5 Hz), 138.53 (d, $J$(C,P) = 20.9 Hz), 141.18 (d, $J$(C,P) = 28.1 Hz), 144.17 (3C), 166.19, 201.44; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -3.5$; $C_{46}H_{43}O_4P$ (690.8): calcd C 79.98, H 6.27; found C 79.74, H 6.20.

**(1*R*,2*S*)-(−)-2-Methyl-3[(4*R*)-isopropyl-2-oxazolidin-3-yl]-3-oxo-1-(prop-2-enyl)propyl-2-(diphenylphosphanyl)benzoate [(−)-23]**: The procedure was analogous to that for the preparation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of oxazolidinone (−)-**22**[16] (5.225 g, 20.4 mmol), DMAP (2.495 g, 20.4 mmol), DCC (4.63 g, 22.44 mmol), and *o*-DPPBA (**10**, 6.249 g, 20.4 mmol) in $CH_2Cl_2$ (40 mL) gave ester (−)-**23** (6.14 g, 55%) as a colorless, highly viscous oil. $[\alpha]_D = -28.1$ ($c = 4.0$, $CH_2Cl_2$); $^1$H NMR



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(300 MHz, $CDCl_3$): $\delta = 0.56$ (d, $J = 6.9$ Hz, 3H, $CH_3$), 0.78 (d, $J = 7.0$ Hz, 3H, $CH_3$), 1.04 (d, $J = 7.0$ Hz, 3H, $CH_3$), 1.61 (s, 3H, $CH_3$), 2.2 [m, 1H, C*H*$(CH_3)_2$], 4.11 (dd, $J = 9.2$, 3.0 Hz, 1H), 4.20 (pseudo t, $J = 8.9$ Hz, 1H), 4.38 (m, 2H), 4.92 (s, 1H, $=CH_2$), 5.06 (s, 1H, $=CH_2$), 5.60 (d, $J = 10.2$ Hz, 1H, OCH), 6.88 (m, 1H, ArH), 7.17–7.35 (m, 12H, ArH), 8.02 (m, 1H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 14.23$, 14.37, 17.35, 17.93, 28.17, 39.25, 58.60, 63.00, 80.04, 117.41, 128.03, 128.26 (d, $J$(C,P) = 7.0 Hz, 2C), 128.31 (d, $J$(C,P) = 6.6 Hz, 2C), 128.44 (2C), 130.67 (d, $J$(C,P) = 2.5 Hz), 131.78, 133.77 (d, $J$(C,P) = 20.5 Hz, 2C), 133.81 (d, $J$(C,P) = 20.8 Hz, 2C), 134.27 (d, $J$(C,P) = 19.0 Hz), 134.22, 138.00 (d, $J$(C,P) = 12.2 Hz), 138.10 (d, $J$(C,P) = 12.3 Hz), 139.84, 140.75 (d, $J$(C,P) = 28.0 Hz), 153.75, 164.73 (d, $J$(C,P) = 2.3 Hz), 174.13; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.8$; $C_{32}H_{34}NO_5P$ (543.6): calcd C 70.71, H 6.30, N 2.58; found C 70.40, H 6.36, N 2.50.

**(1*S*,2*R*)-(−)-2-Methyl-1-[(1*S*)-methyl-3-oxo-propyl]-3-[(4*R*)-isopropyl-2-oxazolidin-3-yl]-3-oxopropyl 2-(diphenylphosphanyl)benzoate [(−)-24]**: The procedure was analogous to that for the hydroformylation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of ester (−)-**23** (543 mg, 1 mmol), $[Rh(CO)_2acac]$ (1.9 mg, $7.1 \times 10^{-3}$ mmol), and $P(OPh)_3$ (8.8 mg, $2.84 \times 10^{-2}$ mmol) in toluene (5 mL) for 24 h gave the aldehyde (−)-**24** (430 mg, 75%) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = 94:6 (*syn*:*anti*). Single crystals suitable for X-ray diffraction were obtained from a saturated solution of (−)-**24** in $CDCl_3$ at room temperature. M.p. 177 °C; $[\alpha]_D = -77.7$ ($c = 2.0$, $CH_2Cl_2$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.50$ (d, $J = 6.9$ Hz, 3H, $CH_3$), 0.69 (d, $J = 7.0$ Hz, 3H, $CH_3$), 0.82 (d, $J = 6.8$ Hz, 3H, $CH_3$), 1.11 (d, $J = 6.8$ Hz, 3H, $CH_3$), 1.82 (ddd, $J = 18.1$, 8.0, 1.0 Hz, 1H, $CH_2$), 2.04 (m, 1H, CH), 2.20 (dd, $J = 18.1$, 5.7 Hz, 1H, $CH_2$), 2.41 (m, 1H, CH), 4.05 (dd, $J = 9.1$, 2.9 Hz, 1H), 4.16 (pseudo t, $J = 9.0$ Hz, 1H), 4.28 (m, 2H), 5.40 (dd, $J = 10.1$, 2.2 Hz, 1H, HCO), 6.84 (m, 1H, ArH), 7.13–7.33 (m, 12H, ArH), 7.9 (m, 1H, ArH), 9.37 (s, 1H, CHO); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 12.89$, 14.12, 14.47, 17.87, 27.97, 28.03, 39.54, 47.87, 58.72, 63.04, 77.50, 127.85, 128.28 (d, $J$(C,P) = 7.2 Hz, 2C), 128.35 (d, $J$(C,P) = 6.3 Hz, 2C), 128.58 (2C), 130.55, 131.92, 133.32 (d, $J$(C,P) = 17.1 Hz), 133.57 (d, $J$(C,P) = 20.5 Hz, 2C), 134.11, 134.25 (d, $J$(C,P) = 21.2 Hz, 2C), 137.70 (d, $J$(C,P) = 14.0 Hz), 138.31 (d, $J$(C,P) = 10.6 Hz), 141.38 (d, $J$(C,P) = 28.7 Hz), 153.62, 165.48, 173.80, 200.90; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -3.6$; $C_{33}H_{36}NO_6P$ (573.6): calcd C 69.10, H 6.33, N 2.44 found C 68.90, H 6.50, N 2.40.

**Crystal structure determination of (−)-24**: $C_{33}H_{36}NO_6P$, $M_r = 573.60$; orthorhombic, space group: $P2_12_12_1$; $a = 891.9(1)$, $b = 1554.3(1)$, $c = 2179.6(1)$ pm , $V = 3021.5(2)$ Å$^3$, $\rho_{calcd} = 1.261$ g cm$^{-3}$; $Z = 4$, $F(000) = 1216$, $\mu(Cu_{K\alpha}) = 1.174$ mm$^{-1}$, $\lambda = 154.178$ pm, $T = 213(2)$ K, crystal dimensions: $0.4 \times 0.2 \times 0.2$ mm. A total of 5657 reflections were collected (Enraf Nonius CAD4) with $\omega$ scans in the range $3.5 < 2\theta < 65°$, 5128 of these were unique ($R_{int} = 0.0521$). The structure was solved by direct methods.[21] Full-matrix least-squares refinement[22] was based on $F^2$, with all non-hydrogen atoms anisotropic and with hydrogens included in calculated positions with isotropic temperature factors 1.2 times ($CH_3$ 1.5 times) that of the $U_{eq}$ of the atom to which they were bonded. The isopropyl group was disordered. The refinement converged at $R1 = 0.0611$ (for 4468 reflections with $I > 2\sigma(I)$) and $wR2 = 0.1782$ (all unique data) [$w = (\sigma^2F_o^2 + (0.0940\,P)^2 + 1.2635\,P)^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$]; final $GOF = 1.059$; largest peak and hole in the final difference Fourier: 0.208/ − 0.443 e Å$^{-3}$.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-115078 ((−)-**24**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

**Ethyl (3*R**,4*S**)-(±)-3-hydroxy-2,4-dimethylpent-4-enoate and ethyl (3*R**,4*R**)-(±)-3-hydroxy-2,4-dimethylpent-4-enoate [(±)-*syn*/*anti*-14]**: A solution of *n*BuLi in hexane (1.6 M, 77 mL, 125 mmol) was added to a solution of diisopropylamine (12.65 g, 125 mmol) in THF (150 mL) at room temperature. The resulting reaction mixture was cooled to −78 °C followed by the dropwise addition of a solution of ethyl propionate (11.74 g, 115 mmol) in THF (15 mL). After stirring for 30 min at −78 °C methacrolein (8.06, 115 mmol) in THF was added. After stirring for 35 min at −78 °C the reaction was quenched by addition of saturated aqueous $NH_4Cl$ solution (100 mL). The organic phase was separated and the aqueous phase was extracted with *tert*-butyl methyl ether ($3 \times 100$ mL). The combined organic phases were dried ($Na_2SO_4$) and the solvent removed in vacuo to give (±)-**14** (21.5 g, 98%) as a mixture of diastereomers (*syn*:*anti* ≈ 1:1) in analytically pure form as a yellow oil. $C_9H_{16}O_3$ (172.2): calcd C 62.77, H 9.36; found C 62.83, H 9.31.

**Ethyl (4*RS*)-(±)-2,4-dimethyl-3-oxopent-4-enoate [(±)-25]**: PCC on $Al_2O_3$ (40 g, 40 mmol) was added to a solution of (±)-*syn*/*anti*-**14** (3.44 g, 20 mmol) in $CH_2Cl_2$ (50 mL), and the resulting reaction mixture was stirred for 48 h at room temperature. Subsequently, the reaction mixture was filtered through silica gel with $CH_2Cl_2$ (100 mL) and the solvent was removed in vacuo. Flash chromatography of the residue (petroleum ether/*tert*-butyl methyl ether 9:1) gave (±)-**25** (2.42 g, 71%) as a pale yellow oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (q, $J = 7.3$ Hz, 3H, $CH_3$), 1.30 (d, $J = 7.2$ Hz, 3H, $CH_3$), 3.40 (q, $J = 7.1$ Hz, 1H, C*H*$CH_3$), 4.07 (q, $J = 7.0$ Hz, 2H, $OCH_2$), 5.78 (m, 1H, $=CH_2$), 5.93 (s, 1H, $=CH_2$); $^{13}$C NMR (50.329 MHz, $CDCl_3$): $\delta = 13.66$, 13.90, 18.26, 47.20, 61.63, 125.17, 143.68, 170.93, 197.22; $C_9H_{14}O_3$ (170.2): calcd C 63.51, H 8.29; found C 63.22, H 8.39.

**Ethyl (3*R**,4*R**)-(±)-3-hydroxy-2,4-dimethylpent-4-enoate [(±)-*syn*-14]**: An ethereal solution of $Zn(BH_4)_2$ (0.625 M, 48 mL, 30 mmol) was added at 0 °C to a magnetically stirred solution of the enone (±)-**25** (1.954 g, 11.5 mmol) in diethyl ether (40 mL).[19] After the mixture was stirred for 40 min at 0 °C, water (4.5 mL) was added. The mixture was stirred for a further 40 min at 0 °C and then warmed to room temperature. The resulting mixture was dried ($MgSO_4$), filtered, and the solvent removed in vacuo. Flash chromatography of the residue furnished (±)-*syn*-**14** (1.6 g, 81%) as a colorless oil; *dr* = ≥ 96: ≤ 4 (*syn*:*anti*). $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 1.10$ (d, $J = 7.0$ Hz, 3H, $CH_3$), 1.24 (t, $J = 6.9$ Hz, 3H, $CH_3$), 1.68 (s, 3H, $CH_3$), 2.6 (m, 2H, CH and OH), 4.13 (q, $J = 6.9$ Hz, 2H, $OCH_2$), 4.35 (d, $J = 2.0$ Hz, 1H, OCH), 4.9 (s, 1H, $=CH_2$), 4.97 (s, 1H, $=CH_2$); $^{13}$C NMR (50.329 MHz, $CDCl_3$): $\delta = 10.82$, 14.08, 19.36, 42.23, 60.64, 74.84, 112.0, 143.92, 175.76; $C_9H_{16}O_3$ (172.2): calcd C 62.77, H 9.36; found C 62.82, H 9.61.

**Ethyl (2*R**,3*R**)-(±)-2,4-dimethyl-3-[2-(diphenylphosphanyl)benzoyloxy]pent-4-enoate (44)**: The procedure was analogous to that for the preparation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-*syn*-**14** (603 mg, 3.5 mmol), DMAP (43 mg, 0.35 mmol), DCC (794 mg, 3.85 mmol), and *o*-DPPBA (**10**,[20] 1.072 g, 3.5 mmol) in $CH_2Cl_2$ (7 mL) gave (±)-*syn*-**15** (1.37 g, 98%) as a colorless, highly viscous oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.06$ (d, $J = 8.0$ Hz, 3H, $CH_3$), 1.16 (t, $J = 7.1$ Hz, 3H, $CH_3$), 1.71 (s, 3H, $CH_3$), 2.85 (pseudo quintet, $J = 7.0$ Hz, 1H, CH), 4.02 (q, $J = 7.1$ Hz, 2H, $OCH_2$), 4.90 (s, 1H, $=CH_2$), 4.96 (s, 1H, $=CH_2$), 5.7 (d, $J = 6.3$ Hz, HCO), 6.96 (m, 1H, ArH), 8.14 (m, 1H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 11.23$, 13.94, 18.68, 42.1, 60.47, 77.71, 113.9, 128.12, 128.26 (d, $J$(C,P) = 7.2 Hz, 2C), 128.3 (d, $J$(C,P) = 6.7 Hz, 2C), 128.43 (2C), 130.56 (d, $J$(C,P) = 2.4 Hz), 131.89, 133.67 (d, $J$(C,P) = 20.6 Hz, 2C), 133.91 (d, $J$(C,P) = 20.75 Hz, 2C), (C1′, expected at $\delta \approx 134$ as a doublet, is obscured by the signals at $\delta = 133.67 - 133.91$), 134.30, 137.93 (d, $J$(C,P) = 11.4 Hz), 137.97 (d, $J$(C,P) = 12.5 Hz), 140.55, 140.95 (d, $J$(C,P) = 28.0 Hz), 164.99 (d, $J$(C,P) = 2.3 Hz), 172.98; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.3$; $C_{28}H_{29}O_4P$ (460.5): calcd C 73.03, H 6.35; found C 72.95, H 6.45.

**Ethyl (2*R**,3*S**,4*R**)-(±)-2,4-dimethyl-3-[2-(diphenylphosphanyl)benzoyloxy]-6-oxohexanoate [(±)-26]**: The procedure was analogous to that for the hydroformylation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-*syn*-**15** (460 mg, 1 mmol), $[Rh(CO)_2(acac)]$ (1.9 mg, $7.1 \times 10^{-3}$ mmol), and $P(OPh)_3$ (8.8 mg, $2.84 \times 10^{-2}$ mmol) in toluene (5 mL) for 24 h gave (±)-**26** (481 mg, 98%) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = 81:19 (*syn*:*anti*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.9$ (d, $J = 6.8$ Hz, $CH_3$), 1.05 (d, $J = 6.9$ Hz, $CH_3$), 1.09 (t, $J = 7.1$ Hz, $CH_3$), 2.02 (ddd, $J = 17.0$, 8.1, 1.7 Hz, 1H, $CH_2$), 2.27 (dd, $J = 17.3$, 5.0 Hz, 1H, $CH_2$), 2.32 (m, 1H, CH), 2.74 (dq, $J = 8.9$, 6.8 Hz, 1H, CH), 4.06 (q, $J = 7.1$ Hz, 2H, $OCH_2$), 5.25 (dd, $J = 8.9$, 3.1 Hz, HCO), 6.9 (m, 1H, ArH), 7.2–7.4 (m, 12H, ArH), 8.1 (m, 1H, ArH), 9.5 (m, 1H, CHO-*syn*), minor diastereomer: [9.56 (m, CHO-*anti*)]; $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 13.9$ (2C), 14.0, 30.03, 42.13, 47.88, 60.73, 77.26, 128.15, 128.47 (d, $J$(C,P) = 7.2 Hz, 4C), 128.66 (d, $J$(C,P) = 3.2 Hz, 2C), 130.61 (d, $J$(C,P) = 1.9 Hz), 132.22, 133.30 (d, $J$(C,P) = 19.0 Hz), 133.87 (d, $J$(C,P) = 20.8 Hz, 2C), 134.09 (d, $J$(C,P) = 21.0 Hz, 2C), 134.3, 137.61 (d, $J$(C,P) = 12.5 Hz), 138.07 (d, $J$(C,P) = 11.9 Hz), 141.45 (d, $J$(C,P) = 28.3 Hz), 166.0, 173.32, 200.65, minor diastereomer: [11.33, 16.84, 30.03, 41.38, 46.24, 60.79, 77.58, aryl-C from 128.1–141.5, 165.9, 173.37, 201.23]; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -3.3$; $C_{29}H_{31}O_5P$ (490.5): calcd C 71.01, H 6.37; found C 70.86, H 6.57.

**(2*R**,3*R**)-(±)-2,4-Dimethylpent-4-en-1,3-diol [(±)-*syn*-17]**: A solution of (±)-**14** (398 mg, 2.3 mmol) in diethyl ether (1 mL) was added dropwise at 0 °C to a magnetically stirred suspension of lithium aluminum hydride (114 mg, 3 mmol) in diethyl ether (5 mL). The reaction mixture was stirred for a further 60 min at 0 °C followed by successive careful addition of water (0.12 mL), an aqueous NaOH solution (15%, 0.12 mL), and a second portion of water (0.35 mL). The resulting mixture was dried ($Na_2SO_4$), filtered, and the residue washed extensively with *tert*-butyl methyl ether. The solvent was removed in vacuo followed by flash chromatographic purification of the residue with petroleum ether/*tert*-butyl methyl ether to give (±)-*syn*-**17** (270 mg, 90%) as a colorless oil. Spectroscopic and analytical data correspond to those reported previously.[18b]

**3-Hydroxy-2,4-dimethylpent-4-enyl (2*R**,3*S**)-(±)-2,2-dimethylpropionate [(±)-27]**: Pivalic acid chloride (561 mg, 4.65 mmol) and pyridine (664 mg, 8.4 mmol) were added at 0 °C to a magnetically stirred solution of (±)-*syn*-**17** (550 mg, 4.2 mmol) in $CH_2Cl_2$ (30 mL). The reaction mixture was allowed to warm to room temperature and stirred for a further four days. Subsequently, saturated aqueous $NaHSO_4$ solution (50 mL) was added, followed by dilution of the resulting mixture with $CH_2Cl_2$ (50 mL). The organic phase was separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 30 mL). The combined organic phases were dried ($Na_2SO_4$) and the solvent was removed in vacuo. Purification of the residue by flash chromatography (petroleum ether/*tert*-butyl methyl ether 9:1) furnished the pivaloate (±)-**27** (603 mg, 67%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 10.85$ (d, $J = 6.9$ Hz, 3H, $CH_3$), 1.13 [s, 9H, $C(CH_3)_3$], 1.64 (s, 3H, $CH_3$), 1.95 (m, H at C2), 3.81 (dd, $J = 10.9$, 6.0 Hz, 1H, $CH_2$), 3.96 (br s, 1H, OH), 4.05 (dd, $J = 10.9$, 7.2 Hz, 1H, $CH_2$), 4.84 (s, 1H, =$CH_2$), 4.92 (s, 1H, =$CH_2$); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 10.62$, 18.54, 27.15 (3C), 35.47, 38.79, 66.67, 75.31, 111.42, 145.68, 178.61; $C_{12}H_{22}O_3$ (214.3): calcd C 67.26, H 10.35; found C 67.49, H 10.58.

**(2*R**,3*R**)-(±)-2,4-Dimethyl-3-[2-diphenylphosphanyl)benzoyloxy]pent-4-enyl-2,2-dimethylpropionate [(±)-28]**: The procedure was analogous to that for the preparation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of (±)-**27** (662 mg, 2.2 mmol), DMAP (269 mg, 2.2 mmol), DCC (499 mg, 2.42 mmol), and *o*-DPPBA (**10**,[20] 674 mg, 2.2 mmol) in $CH_2Cl_2$ (5 mL) gave (±)-**28** (914 mg, 83%) as a colorless, highly viscous oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 6.8$ Hz, 3H, $CH_3$), 1.21 [s, 9H, $C(CH_3)_3$], 1.75 (s, 3H, $CH_3$), 2.23 (m, 1H, CH), 3.91 (dd, $J = 11.0$, 6.2 Hz, 1H, $CH_2$), 4.0 (dd, $J = 11.0$ Hz, 6.3 Hz, 1H, $CH_2$), 4.92 (s, 1H, =$CH_2$), 4.96 (s, 1H, =$CH_2$), 5.38 (d, $J = 6.0$ Hz, 1H, HCO), 6.98 (m, 1H, ArH), 8.15 (m, 1H, ArH); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta = 12.11$, 18.89, 27.21 (3C), 34.67, 38.8, 65.85, 78.21, 113.77, 128.24, 128.43 (d, $J$(C,P) = 7.0 Hz, 4C), 128.55 (d, $J$(C,P) = 2.3 Hz, 2C), 130.52 (d, $J$(C,P) = 2.4 Hz), 131.97, 133.83 (d, $J$(C,P) = 20.5 Hz, 2C), 133.91, 134.34 (d, $J$(C,P) = 22.7 Hz, 2C), 134.42 (d, $J$(C,P) = 19.0 Hz), 138.05 (d, $J$(C,P) = 12.8 Hz), 138.07 (d, $J$(C,P) = 11.5 Hz), 140.82 (d, $J$(C,P) = 27.8 Hz), 141.11, 165.49 (d, $J$(C,P) = 2.3 Hz), 178.31; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -4.4$; $C_{31}H_{35}O_4P$ (502.6): calcd C 74.08, H 7.02; found C 73.98, H 6.76.

**(2*R**,3*R**,4*S**)-(±)-2,4-Dimethyl-3-[2-(diphenylphosphanyl)benzoyloxy]-6-oxohexyl-2,2-dimethylpropionate (29)**: The procedure was analogous to that for the hydroformylation of the methallylic *o*-DPPB ester (±)-**11**: Reaction of the ester (±)-**28** (502 mg, 1 mmol), $[Rh(CO)_2(acac)]$ (1.9 mg, $7.1 \times 10^{-3}$ mmol), and $P(OPh)_3$ (8.8 mg, $2.84 \times 10^{-2}$ mmol) in toluene (6 mL) for 24 h gave (±)-**29** (373 mg, 70%) as a colorless, highly viscous oil; *dr* (between controlling and newly formed stereogenic center) = 95:5 (*syn*:*anti*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.8$ Hz, 3H, $CH_3$), 0.88 (d, $J = 6.8$ Hz, $CH_3$), 1.15 [s, 9H, $C(CH_3)_3$], 2.01 (ddd, $J = 17.6$, 8.0, 1.6 Hz, 1H, $CH_2$), 2.1 (m, 1H, CH), 2.22 (dd, $J = 17.6$, 5.5 Hz, 1H, $CH_2$), 2.39 (m, 1H, CH), 3.85 (dd, $J = 11.2$, 5.8 Hz, 1H, $OCH_2$), 3.94 (dd, $J = 11.2$, 5.5 Hz, 1H, $OCH_2$), 4.99 (dd, $J = 7.5$, 3.8 Hz, 1H, HCO), 6.89 (m, 1H, ArH), 8.05 (m, 1H, ArH), 9.47 (s, 1H, CHO); $^{13}$C NMR (75.469 MHz, $CDCl_3$): $\delta =$ 13.24, 14.23, 27.1 (3C), 29.34, 34.5, 38.76, 47.89, 65.89, 77.6, 128.13, 128.43 (d, $J$(C,P) = 6.7 Hz, 2C), 128.53 (d, $J$(C,P) = 8.0 Hz, 2C), 128.63 (2C),130.51 (d, $J$(C,P) = 2.0 Hz), 132.11, 133.34 (d, $J$(C,P) = 17.2 Hz), 133.87 (d, $J$(C,P) = 20.8 Hz, 2C), 134.10 (d, $J$(C,P) = 21.4 Hz, 2C), 134.24, 137.64 (d, $J$(C,P) = 12.5 Hz), 138.05 (d, $J$(C,P) = 11.5 Hz), 141.38 (d, $J$(C,P) = 28.2 Hz), 166.16 (d, $J$(C,P) = 3.0 Hz), 178.3, 200.78; $^{31}$P NMR (161.978 MHz, $CDCl_3$): $\delta = -3.8$; $C_{32}H_{37}O_5P$ (532.6): calcd C 72.16, H 7.00; found C 72.17, H 6.81.

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