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Synthesis of Homochiral Pyridyl, Bipyridyl and Phosphino Derivatives of 2,2-Dimethyl-1,3-dioxolane: Use in Asymmetric Catalysis

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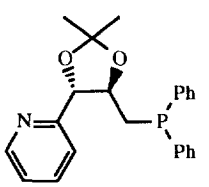
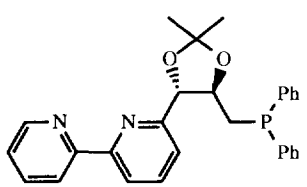
Abstract: Homochiral pyridyl, bipyridyl and phosphino derivatives of 2,2-dimethyl-1,3-dioxolane were prepared from L-(+)-tartrate. These compounds were assessed in metal catalyzed asymmetric addition of diethylzinc to benzaldehyde, hydroformylation of styrene, hydrocarboethoxylation of styrene and allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate.

Mixed bidentate pyridine-phosphine ligands are gaining increasing importance and the study of the catalytic activity of their metal complexes has been recently undertaken.[1] Few optically active examples of this class of substrates have been described and tested in asymmetric catalysis.[2] As part of our research aimed at the synthesis of pyridylphosphines in a recent communication we described the preparation of PYDIPHOS **1** as the first representative member of homochiral pyridylphosphines using L-(+)-tartaric acid as the starting point.[3]

In this article we give the results obtained in the synthesis of **1** and of the new bipyridine-phosphine **2**. Moreover, the enantioselectivity abilities of the three related ligands **1**, **2** and the P-oxide of PYDIPHOS (**3**) was evaluated in several types of asymmetric reactions catalyzed by transition metal complexes, namely in asymmetric addition of diethylzinc to benzaldehyde, hydroformylation of styrene, hydrocarboethoxylation of styrene and allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate.



1



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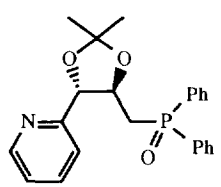
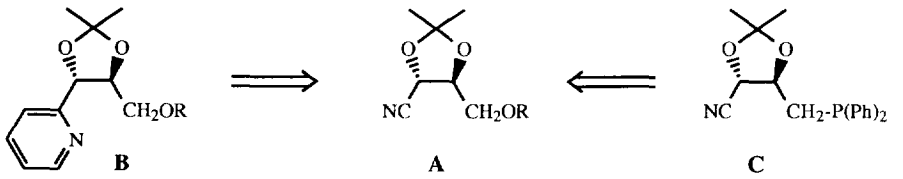


3

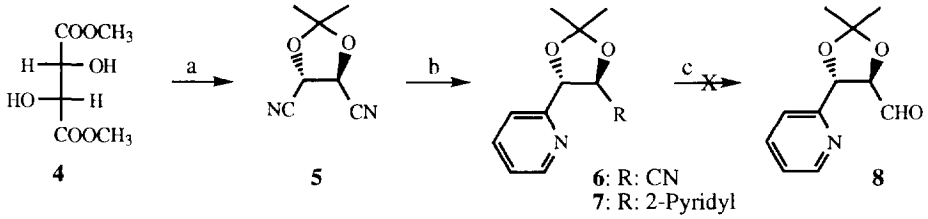
For the synthesis of **1** from L-(+)-tartaric acid the hydroxy-cyano derivative **A** was envisaged as the key intermediate from which the corresponding pyridine **B** could be obtained by the cobalt-catalyzed

cocyclotrimerization of acetylene with the cyano group and the diphenylphoshino group in **C** by elaboration of the hydroxy group.



Our investigations started with the dicyano compound **5**, which we prepared [4] as an intermediate in the synthesis of the dipyridine **7**, by a three reaction sequence from L-(+)-dimethyl tartrate **4** (Scheme 1). On this occasion we were interested in obtaining the compound of monoazaanellation of the dinitrile **5** so the reaction of cocyclotrimerization of acetylene with **5** in the presence of (π-cyclopentadienyl)cobalt 1,5-cyclooctadiene [CpCo(COD)] was carried out at 100 °C for 24h.[5] Under these conditions total conversion of the starting material was achieved and **6** was recovered after chromatographic purification in 41 % yield with the dipyridine **7** (25 %). The next step required the selective reduction of the cyano group to an aldehyde group which was performed with diisobutylaluminium hydride (DIBAH) at -78 °C. However, an unmanageable mixture of products was obtained.

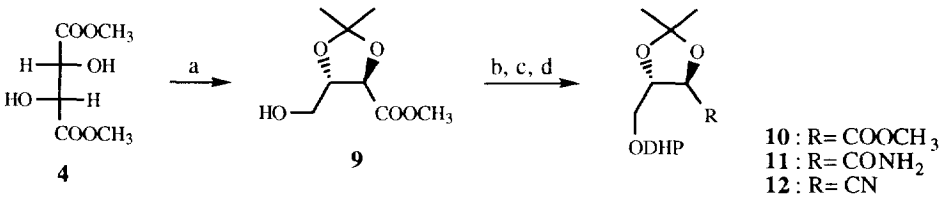
Scheme 1



a: Literature; b: CpCo(COD), acetylene, toluene, 100 °C, 14 atm, 24h; c: DIBAH, toluene, -78 °C

Next, we turned our attention to the hydroxyester **9** (Scheme 2) with the aim of obtaining the cyano group by following the well established sequence ester-amide-nitrile.[5] The hydroxy group of **9**, prepared according to a reported procedure,[6] was protected by its dihydropyranyl derivative. Treatment of the amide **11**, prepared by reaction of **10** with gaseous ammonia for 2 days in methanol, with *p*-toluenesulphonyl chloride in pyridine was expected to give the nitrile **12**. However, also in this case a complex mixture of products was obtained.

Scheme 2

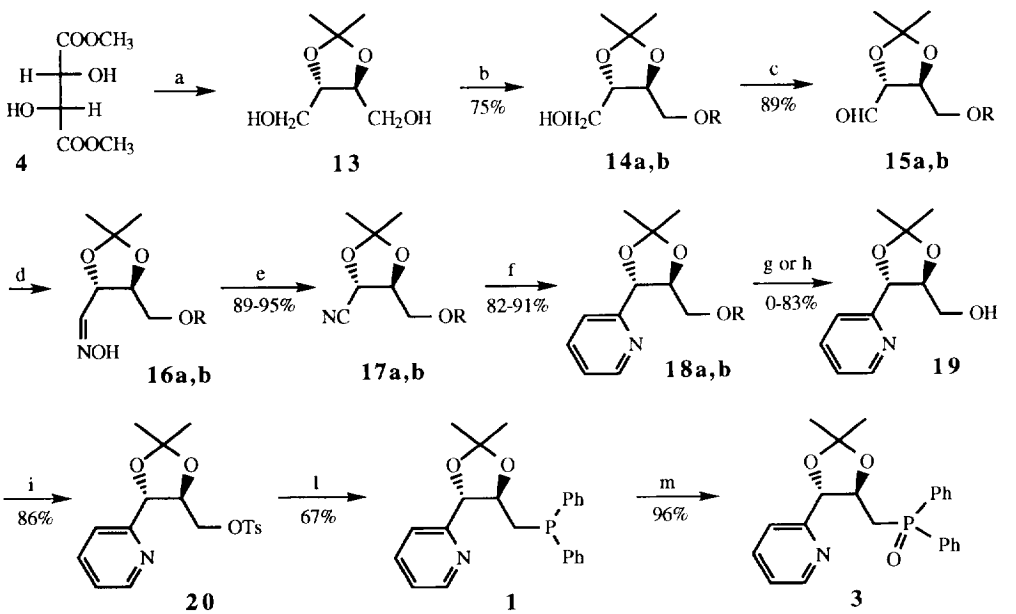


a: Literature; b: DHP, TsOH, CH_2Cl_2, 83 %; c: NH_3, MeOH, 2d, 89 %; d: TsCl, Py, 0 %.

These results prompted us to modifiy the synthetic approach and therefore the sequence aldehyde-oxime-nitrile was evaluated. The aldehyde **15a**[7] (Scheme 3) was converted into the nitrile **17a** *via* the formation of the corresponding oxime followed by dehydration with N,N'-carbonyldiimidazole. Cobalt catalyzed cocyclotrimerization of nitrile **17a** with acetylene afforded the pyridine **18a** in 62 % overall yield based on **15a**. Removal of the protecting group by hydrogen on Pd/C or PdO_2 at 1 and up to 5 atm failed.

The need to replace the benzyl group on the γ-hydroxyl function with a more easily removable protecting group was evident. Thus, the aldehyde **15b** was prepared by selective protection of the known diol **13**[8] with *tert*-butyldiphenylsilylchloride, followed by Swern's oxidation. Following the same reaction conditions as described above led to the pyridine **18b** in 60 % yield based on **13**. The hydroxy group was then easily deprotected using a 0.1 M solution of Bu_4NF in THF and converted into the tosylate **20**. Finally, nucleophilic displacement of the tosyl group with Na/K diphenylphosphide mixture gave PYDIPHOS **1** in 29% overall yield based on **13**. A similar result was obtained using a commercial solution of potassium diphenylphosphide in THF. Treatment of **1** with diluted hydrogen peroxide gave the P-oxide **3** in 96 % yield.

Scheme 3



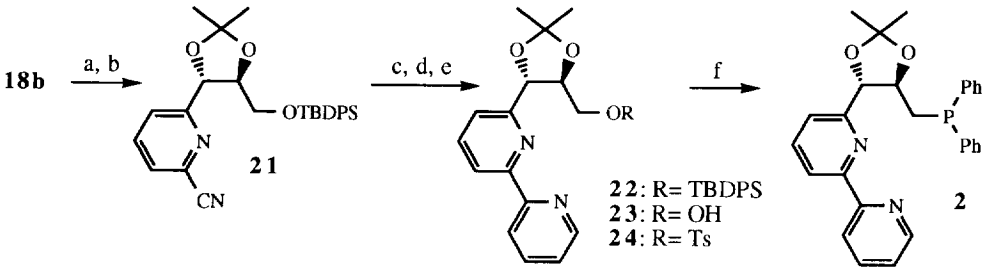
a: R= CH_2-Ph **b**: R= *t*-$BuPh_2Si$

a: Literature; b: NaH (1 equiv), *t*-$BuPh_2SiCl$ (TBDPSCl) or $BrCH_2Ph$; c: $(COCl)_2$, DMSO, Et_3N, -78 °C; d: $NH_2OH{\cdot}HCl$, 10% K_2CO_3; e: N,N'-carbonyldiimidazole; f: CpCo(COD), acetylene, toluene, 120 °C, 14 atm; g: Pd/C or PdO_2 from 1 to 5 atm; h: Bu_4NF, THF; i: TsCl, Et_3N, DMPA, CH_2Cl_2; l: Ph_3P, Na/K, dioxane; m: 5 % H_2O_2

With compound **1** in hand we examined the possibility of preparing its pyridyl derivative **2**. This new bipyridine-phosphine was obtained starting from the pyridine **18b** and following the reaction sequences reported in Scheme 4. Regiospecific introduction of a cyano group into the 6-position of the pyridine **18b** was obtained by treatment of its N-oxide derivative with trimethylsilylcarbonitrile and dimethylcarbamyl chloride in

CH_2Cl_2 for 6 days (83 % yield based on **18b**)[9]. Cocyclotrimerization of cyanopyridine **21** with acetylene in the presence of CpCo(COD) afforded the dipyridine **22** in 86 % yield. From this intermediate the bipyridyl-phosphine **2** was obtained in three steps using an experimental procedure analogous to that described for compound **1**. However, in this case the nucleophilic displacement of the tosyl group of **24** with Na/K diphenylphosphide mixture gave a complex mixture from which **2** was recovered in low yield (15 %) after three repeated chromatographic separations.

Scheme 4

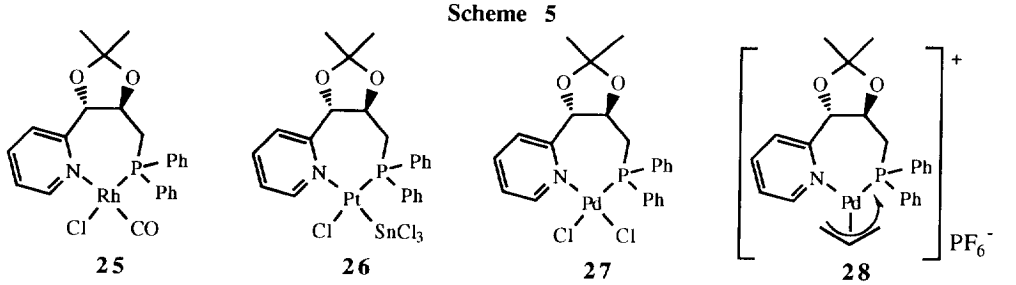


a: MCPA, $CHCl_3$, 24h; b:$(CH_3)_2NCOCl$, $(CH_3)_3SiCN$, CH_2Cl_2, r.t., 6d, 83%; c: CpCo(COD), acetylene, toluene,120 °C, 13 atm, 86%; d:Bu_4NF, THF, 97%; e: TsCl, Et_3N, DMPA, CH_2Cl_2, 75%; f: Ph_3P, Na/K, dioxane,67%.

ENANTIOSELECTIVE REACTIONS.

With the three related compounds **1-3** in hand, the performance of these ligands was evaluated in several types of asymmetric reactions catalyzed by transition metal complexes, namely in asymmetric addition of diethylzinc to benzaldehyde, hydroformylation of styrene, hydrocarboethoxylation of styrene and allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. These reactions were carried out using either preformed metal-complexes **25-28**[10] (Scheme 5) or *in situ* formed complexes between pro-catalysts and ligands **1-3**.

Scheme 5



Asymmetric addition of diethylzinc to benzaldehyde.

Chiral pyridine ligands, namely pyridyl alcohols and amines, have been used as effective ligands in the catalyzed enantioselective addition of alkylzinc compounds to aldehydes leading to a diverse array of secondary alcohols of high enantiomeric purity.[11] We now examined the enantioselective addition of diethylzinc to benzaldehyde using ligands **2**, **1** and its P-oxide **3**, though, to our knowledge, no data has been so far reported for the use of chiral phosphine derivatives in this catalytic process.[12] All catalysts gave 1-phenyl-1-propanol in good yield but with low enantioselectivity.

Table 1. Asymmetric Addition of Diethylzinc to Benzaldehyde[a]

C_6H_5-CHO $\xrightarrow{Zn(C_2H_5)_2 / L^*}$ C_6H_5-$\overset{*}{C}$H-C_2H_5 (OH)

Ligand	Time (h)	Conv.[b] (%)	$[\alpha]^{25}_D$, (*c*, solvent)	Ee (%)[c]	Conf.
1	15	99	+10 (3, $CHCl_3$)	21	R
2	21	88	-2.4 (4, $CHCl_3$)	5	S
3	22	84	+1.1 (3, $CHCl_3$)	2	R

[a]Reaction carried out at room temperature in hexane/toluene with a molar ratio Et_2Zn/aldehyde/ligand= 2/1/0.06. [b]GLC yield of the crude products.[c]Determined from the specific rotation of (S)-1-phenylpropanol: $[\alpha]^{25}_D$ -47.6 ($CHCl_3$): Kitamura, M., Suga, S., Kawai, R., Noyori, R. *J. Am. Chem. Soc.*, **1986**, *108*, 6071.

Hydroformylation of styrene.

Though the enantioselective hydroformylation of styrene can be performed today with enantiomeric excesses >90 %,[13] the search for new catalysts is of current interest. The preformed Rhodium(I) catalyst **25** afforded, under mild conditions, low yields of hydrotropaldehyde having only about 30% ee (Table 2, run 1), while with *in situ* formed Rh(I)-complex with ligands **1** much higher catalytic activity was observed, but practically no asymmetric induction (run 2).[14] Similar results were obtained with *in situ* formed Rh(I)-complexes with ligands **2** and **3** (runs 3,4)[14]. It is possible that in both cases the concentration of catalytically active species bearing the chiral ligands are very low and cannot compete under *oxo*-conditions with more effective unmodified Rh-carbonyl complexes present in the reaction medium.

The hydroformylation reaction runs sluggishly in the presence of preformed Platinum(II) catalyst **26** but, giving only 31 % ee (run 5). Contrary to expectations for Pt(II)-complexes[15] the presence of ligand **1** in the complex **26** shifts the regioselectivity towards the formation of branched aldehyde. An attempt to increase the ee % of the hydropaldehyde by trapping it as diethylacetal using triethylorthoformate[16] as co-solvent failed to give any *oxo*-product (run 6).

Table 2. Hydroformylation of styrene[a]

C_6H_5-CH=CH_2 $\xrightarrow[\text{catalyst}]{CO/H_2;\ \text{benzene}}$ C_6H_5-$\overset{*}{C}$H(-CH_3)-CHO + C_6H_5-CH_2-CH_2-CHO

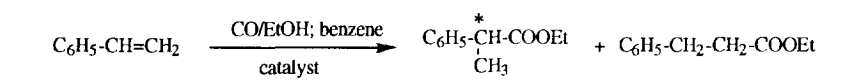
Run	Catalytic precursor	Pressure atm	Temp. °C	Time h	Conv. %	Yield %	Aldehydes b/l	% Ee[d] (conf.)
1	PydiphosRh(CO)Cl	85	30	21	30	15	90/10	28(R)
2[b]	$Rh(CO)_2$(acac)/Pydiphos	90	30	20	80	70	95/5	1(R)
3[b]	$Rh(CO)_2$(acac)/diPydiphos	90	30	1	98	95	97/3	1(R)
4[b]	$Rh(CO)_2$(acac)/Pydiphos-P-oxide	90	30	5	99	95	95/5	1(R)
5	PydiphosPt($SnCl_3$)Cl	90	60	18	20	12	70/30	31(R)
6[c]	PydiphosPt($SnCl_3$)Cl	100	120	170	5	--	--	--

[a]The reaction was carried out in benzene (20 ml) using 3.12 g (0.03 mol) of styrene, the degassed solution was introduced in a stirred stainless steel vessel pressurized at the desired pressure with CO/H_2=1/1 gas mixture; catalyst substrate 1:300. [b]Catalytic precursor prepared *in situ* using a ratio ligand/Pd=2.5/1. [c]Experiment carried out in the presence of triethylorthoformate using *o*-dichlorobenzene as solvent.[16] [d]Determined by ^{1}H-NMR using Eu(hfc)$_3$ as chiral shift reagent.[16]

Hydrocarboethoxylation of styrene.

The data reported in Table 3 for asymmetric hydroesterification[17] experiments give some indications: i) when using only preformed Pd-complex **27** the catalytic activity was satisfactory and the enantioselectivity appreciable (run 2); ii) *in situ* formed complexes between $PdCl_2$ and ligands **1** and **2** exhibited very poor activity and optical enantioselectivity (runs 1,3). These results strongly suggest that complexation of ligands **1** and **2** to Pd(II) in a chelating manner is rather difficult under the reaction conditions used. The fact that in all experiments only the branched ethyl ester is produced seems to indicate that both pyridylphosphines act as monodentate ligands.[18]

Table 3. Hydrocarboethoxylation of styrene[a]



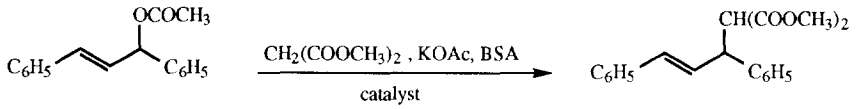
Run	Catalytic precursor	Pressure atm	Temp. °C	Time h	Conv. %	Yield %	Esters b/l	% Ee[c] (conf.)
1[b]	$PdCl_2$/Pydiphos	110	100	40	5	4	100/0	2 (R)
2	(Pydiphos)$PdCl_2$	105	100	240	90	77	100/0	20 (R)
3	$PdCl_2$/diPydiphos	120	100	24	20	12	100/0	3 (R)

[a]The reaction was carried out in benzene/ethanol (20/5 ml) using 3.12 g of styrene, the degassed solution was introduced in the stirred stainless steel vessel pressurized at the desired pressure with CO; catalyst/substrate 1:300. [b]Catalyst precursor prepared *in situ* using a ratio ligand/Pd=2.5/1. [c]Determined from the specific rotation of (+)(S)-1-phenylpropanoate: $[\alpha]^{21}_D$ +71.2 (neat): Praceius, H. *Liebigs Ann. Chem.*, **1960**, *634*, 18.

Allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate

Palladium-catalyzed allylic substitution is a versatile, widely used process in organic synthesis.[19] C_2 symmetric nitrogen ligands such as chiral semicorrines and bis-dihydrooxazoles have proved to be effective in the palladium-catalyzed enantioselective allylic substitution process.[20] More recently heterobidentate ligands without C_2 symmetry, namely sulphur and phosphorus derivatives of oxazolines gave very good results showing that the selectivity in metal-catalyzed reactions can be controlled by steric and stereoelectronic factors.[21]

Table 4. Allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate[a]



Run	Catalyst	Catalyst/substrate	Time, h	Yield, %	% Ee[b](conf.)
1	[(Pydiphos)Pd(η^3-C_3H_5)]PF_6	2.5/100	24	95	9 (R)
2[c]	[Pd(η^3-C_3H_5)Cl]$_2$/Pydiphos	2.5/100	13	99	7 (R)

[a]Reaction of 1,3-diphenyl-2-propenyl acetate (0.4 mmol) with dimethyl malonate (1.2 mmol), N,O-bis(trimethylsilyl)acetamide (BSA) (1.2 mmol) and potassium acetate (3 % mol) in 2 ml of CH_2Cl_2 at r.t. [b]Determined by ^{1}H-NMR using Eu(hfc)$_3$ as chiral shift reagent. [c]Ligand/Pd = 2/1

The effectiveness of Pydiphos was examined for its ability to provide asymmetric induction in palladium catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. Allylic substitutions were carried out as described in Table 4. We employed Trost's procedure, which used a mixture of dimethyl malonate and N,O-bis(trimethylsilyl)acetamide (BSA) and catalytic amount of KOAc.[22] As catalysts we used either the palladium π-allyl complex **28** prepared by treating a solution (CH_2Cl_2) of Pydiphos and the complex [Pd(η^3-C_3H_5)Cl]$_2$ with a silver salt or the complex generated *in situ* by mixing [Pd(η^3-C_3H_5)Cl]$_2$ and Pydiphos (2 equiv/Pd). In both cases the complexes were found to be effective catalysts giving the substitution compound in an essentially quantitative yield. However low enantioselectivity was obtained.

In summary, the synthesis of chelating ligands of the desired type has been achieved and their catalytic activity demonstrated. Further studies for the synthesis of new pyridine-phosphine ligands are in progress.

EXPERIMENTAL SECTION

General. Boiling points are uncorrected. Melting points were determined on a Buchi 510 capillary apparatus and are uncorrected. The ^1H NMR (300 MHz) spectra were obtained with a Varian VXR-300 spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter in a 1 dm tube. Elemental analyses were performed on a Perkin-Elmer 240 B analyzer.

(4S,5S)-4-Hydroxymethyl-5-[(*tert*-butyldiphenylsilyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 14b. Sodium hydride (4.8 g, 0.1 mol, 50% suspension in oil) was suspended in THF (150 ml) after being washed with hexane. A solution of 4,5-bis(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (**13**)[8] (16.2 g, 0.1 mol) in THF (50 ml) was added to this mixture at room temperature and stirred for 45 min by which time a large amount of an opaque white precipitate had formed. The *tert*-butyldimethylsilyl chloride (27.5 g, 0.1 mol) was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (300 ml), washed with 10% aqueous K_2CO_3 (24 ml) and brine (30 ml) , dried (Na_2SO_4) and concentrated in vacuo. The resulting oil was purified by chromatography on silica gel (hexane:ethyl acetate/7:3) to give pure **14b**: 30.0 g (75 %); $[\alpha]^{28}_D$ -0.77 (*c* 2.7, $CHCl_3$); ^1H-NMR ($CDCl_3$) δ 7.67 (m, 4H), 7.41 (m, 6H), 4.07 (m, 1H), 3.98 (m, 1H), 3.85-3.60 (m, 4H), 1.17 (broad, 1H), 1.42 (s, 3H), 1.39 (s, 3H), 1.06 (s, 9H); *Elem. Anal.*, found % (calcd. for $C_{23}H_{32}O_4Si$) C, 68.86 (68.96); H, 8.15 (8.05).

(4S,5S)-4-Cyano-5-[(*tert*-butyldiphenylsilyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 17b. A solution of dimethyl sulfoxide (9.84 g, 126 mmol) in anhydrous CH_2Cl_2 (28 ml) was added dropwise to a solution of oxalyl chloride (7.9 g, 63.1 mmol) in CH_2Cl_2 (150 ml) at -78 °C. After stirring for 5 min a solution of **14b** (19.2 g, 47.9 mmol) in CH_2Cl_2 (60 ml) was added. The cloudy mixture was stirred at -78 °C for 15 min and Et_3N (24.3 g, 240 mmol) was added dropwise. The resulting solution was warmed to room temperature and stirred for 1h. The mixture was poured into H_2O (100 ml) and the organic phase separated, washed with H_2O, concentrated and the residue taken up with Et_2O. The aqueous phases were extracted with Et_2O. The combined ethereal phases were washed with H_2O (3x70 ml) and brine (50 ml). The dried solution (Na_2SO_4) concentrated under reduced pressure gave **15b** which was used in the next step without further purification.

A solution of hydroxylamine hydrochloride (3.75 g, 54 mmol) in 10% Na_2CO_3 (24 ml) was added to a solution of **15b** in methanol (100 ml). The mixture was stirred for 24 h. The methanol was evaporated and the residue taken up CH_2Cl_2. The organic layer was washed with H_2O, dried (Na_2SO_4) and concentrated under reduced pressure to give **16b** which was used in the next step without further purification.

1,1'-Carbonyldiimidazole (7.53 g, 46.5 mmol) in anhydrous CH_2Cl_2 (70 ml) was added dropwise to a solution of **16b** in anhydrous CH_2Cl_2 (50 ml). The mixture was stirred for 1 h and the solvent evaporated. The residue was chromatographed on silica gel (hexane:ethyl acetate/7:3) to give pure **17b**: 16.85 g (89 %); $[\alpha]^{26}_D$ -3.65 (*c* 2.5, cyclohexane); ^{1}H-NMR ($CDCl_3$) δ 7.66 (m, 4H), 7.41 (m, 6H), 4.72 (d, 1H), 4.44 (m, 1H), 3.82 (dd, 1H), 3.73 (dd, 1H), 1.51 (s, 3H), 1.44 (s, 3H), 1.07 (s, 9H); *Elem. Anal.*, found % (calcd. for $C_{23}H_{29}NO_3Si$) C, 69.86 (69.84); H, 7.27 (7.39); N, 3.57 (3.54).

(4S,5S)-4-(2-Pyridyl)-5-[(*tert*-butyldiphenylsilyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 18b. (π-Cyclopentadienyl)cobalt-1,5-cyclooctadiene (500 mg) was placed in a stainless-steel autoclave (200 ml). The autoclave was rocked and the air removed (0.1 atm). A solution of **17b** (16.7 g, 42.3 mmol) in air-free toluene (100 ml) was introduced by suction. The reaction vessel was pressurized with acetylene up to 14 atm. and then rocked and heated at 120 °C. After 24 h the autoclave was cooled and the residual gas released. The reaction mixture was filtered and the solvent removed. The residue was chromatographed on silica gel (hexane:ethyl acetate/7:3) to give pure **18b**: 18.1 g (94 %); $[\alpha]^{26}_D$ -2.60 (*c* 3.1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.53 (d, 1H), 7.67 (m, 4H), 7.51-7.13 (m, 9H), 5.16 (d, 1H), 4.16 (m, 1H), 4.02 (dd, 1H), 3.94 (dd, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.03 (s, 9H); *Elem. Anal.*, found % (calcd. for $C_{27}H_{33}NO_3Si$) C, 72.66 (72.44); H, 7.53 (7.43); N, 3.23 (3.13).

(4S,5S)-4-(2-Pyridyl)-5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane, 19. A 1 M solution of *n*-Bu_4NF in THF (36 ml) was added dropwise at 0 °C to a solution of **18b** (16 g, 35.8 mmol) in THF (40 ml), and the solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (benzene:acetone/8:2) to give pure **19**: 6.2 g (83 %); $[\alpha]^{21}_D$ +57.66 (*c* 2.2, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.48 (d, 1H), 7.72 (t, 1H), 7.58 (d, 1H), 7.21 (m, 1H), 4.92 (d, 1H), 4.87 (broad, 1H), 4.06-3.84 (m, 3H), 1.51 (s, 3H), 1.46 (s, 3H); *Elem. Anal.*, found % (calcd. for $C_{11}H_{15}NO_3$) C, 63.30 (63.14); H, 7.43 (7.23); N, 6.53 (6.69).

(4S,5S)-4-(2-Pyridyl)-5-[(tolylsulfonyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 20. *p*-Toluenesulfonyl chloride (7.35 g, 39.5 mmol) in anhydrous CH_2Cl_2 (100 ml) was added at 0 °C to a solution of **19** (5.48 g, 26.2 mmol), Et_3N (7.4 ml, 52.4 mmol), 4-(dimethylamino)pyridine (373 mg, 3.3 mmol) in anhydrous CH_2Cl_2 (70 ml). The resulting solution was stirred at 0 °C for 10 min and then at room temperature for 5 h. The reaction mixture was poured into a 10% $NaHCO_3$ solution, the organic phase separated, washed with H_2O, dried on Na_2SO_4 and the solvent removed under reduced pressure. The residue was taken up with Et_2O, the solid formed separated and the solvent evaporated to give **20** (8.2 g) which was used in the next step without further purification: ^{1}H-NMR ($CDCl_3$) δ 8.42 (d, 1H), 7.86-7.09 (m, 7H), 4.81 (d, 1H), 4.61 (d, 1H), 4.25 (dd, 1H), 4.13 (m, 1H), 2.41 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H).

(4S,5R)-4-(2-Pyridyl)-5-(diphenylphosphino)methyl-2,2-dimethyl-1,3-dioxolane, 1. Potassium (0.4 g, 10 mmol) and sodium (100 mg, 4.3 mmol) were melted together under dry argon. Dry, air-free dioxane (20 ml) was added followed by triphenylphosphine (1.31 g, 5 mmol) and the mixture stirred vigorously for 12 h. A solution of **20** (1.82 g, 5 mmol) in anhydrous dioxane (10 ml) was added to the yellow suspension of potassium diphenylphosphide which was formed. The suspension was stirred for 30 min, the solvent removed under reduced pressure and the residue purified by flash chromatography (petroleum ether:ethyl acetate/7:3) to give pure **1**: 1.26 g (67 %); $[\alpha]^{21}_D$ -48.0 (*c* 7, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.45 (d, 1H), 7.57 (t, 1H), 7.38-7.09 (m, 12H), 4.80 (d, 1H), 3.96 (m, 1H), 2.70 (m, 1H), 2.40 (m, 1H), 1.45 (s, 3H), 1.39 (s, 3H). ^{31}P-NMR ($CDCl_3$) δ −21.85. *Elem. Anal.*, found % (calcd. for $C_{23}H_{24}NO_2P$) C, 73.31 (73.19); H, 6.53 (6.41); N, 3.65 (3.71).

(4S,5R)-4-(2-Pyridyl)-5-(diphenylphosphino)methyl-2,2-dimethyl-1,3-dioxolane P-oxide, 3. A solution of 5% hydrogen peroxide (20 ml) was added to a cooled (0 °C) solution of **1** (0.5 g, 1.33 mmol) in CH_2Cl_2 (50 ml) and then stirred vigorously at room temperature for 0.5 h. The organic phase was separated, dried (Na_2SO_4) and the solvent evaporated to give **3** as a oil: 0.5 g (96 % yield); $[\alpha]^{25}_D$ +21.04 (*c* 2, $CHCl_3$); ^{31}P-NMR ($CDCl_3$) δ 30.83. IR ν (P=O) 1260 cm^{-1} *Elem. Anal.*, found % (calcd. for $C_{23}H_{24}NO_3P$) C, 70.32 (70.22); H, 6.23 (6.15); N, 3.55 (3.56).

(4S,5S)-4-(6-Cyanopyridin-2-yl)-5-[(*tert*-butyldiphenylsilyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 21. 3-Chloroperbenzoic acid (16.8 mmol) was added to a cold solution of compound **18b** (6.26 g, 14 mmol) in CH_2Cl_2 (150 ml.). The mixture was stirred at room temperature for 24h, and then treated with 10% K_2CO_3. The organic layer was separated and the aqueous phase extracted with $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and the solvent evaporated. The solid residue was washed with *n*-hexane to give the N-oxide of **18b** (6.25 g) which was used in the next step without further purification. Dimethylcarbamyl chloride (1.44 g, 13.5 mmol) was added dropwise to a solution of N-oxide of **23** (6.25 g, 13.5 mol) and trimethylsilylcyanide (1.59 g, 14.8 mmol) in CH_2Cl_2 (100 mL). The solution was stirred at room temperature for 5 days, then 10% K_2CO_3 was added and stirring continued for 15 minutes. The organic phase was separated, dried (Na_2SO_4) and the solvent evaporated. The residue was chromatographed on silica gel (hexane: ethyl acetate/7:3) to give **21**: 4 g (63 % yield); ^{1}H-NMR ($CDCl_3$) δ 7.86-7.30 (m, 13H), 5.17 (d, 1H), 4.13-3.93 (m, 3H), 1.58 (s, 1H), 1.52 (s, 1H), 1.04 (s, 9H). *Elem. Anal.*, found % (calcd. for $C_{28}H_{32}N_2O_3Si$) C, 71.30 (71.15); H, 6.70 (6.83); N, 5.83 (5.93).

(4S,5S)-4-[6-(2-Pyridyl)pyridin-2-yl]-5-[(*tert*-butyldiphenylsilyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 22. The procedure reported for the preparation of **18b** was followed. From **21** (2.36 g, 5 mmol) after 48 h at 120 °C compound **22** was isolated after chromatography on silica gel (hexane: ethyl acetate/7:3): 1.46 g (56 % yield); $[\alpha]^{25}_D$ +4.96 (*c* 2.4, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.65 (d, 1H), 8.32 (d, 1H), 8.25 (d, 1H), 7.81 (t, 1H), 7.71 (m, 4H), 7.53 (d, 1H), 7.45-7.23 (m, 8H), 5.20 (d, 1H), 4.25-3.95 (m, 3H), 1.60 (s, 3H), 1.56 (s, 3H), 1.05 (s, 9H). *Elem. Anal.*, found % (calcd. for $C_{32}H_{36}N_2O_3Si$) C, 73.45 (73.25); H, 6.70 (6.92); N, 5.33 (5.34).

(4S,5S)-4-[6-(2-Pyridyl)pyridin-2-yl]-5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane, 23. The procedure reported for the preparation of **19** was followed. From **22** (1.8 g, 3.45 mmol) compound **23** was isolated after chromatography on silica gel (hexane:ethyl acetate/8:2): 0.95 g (97 %); $[\alpha]^{25}_D$ +131.4 (*c* 2.6, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.65 (d, 1H), 8.30 (d, 1H), 8.22 (d, 1H), 7.88 (t, 1H), 7.62 (d,1H), 7.37-7.27 (m, 2H), 5.05 (d, 1H), 4.56 (broad, 1H), 4.18-4.01 (m, 3H), 1,57 (s, 3H), 1.51 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{16}H_{18}N_2O_3$) C, 67.11 (67.12); H, 6.44 (6.34); N, 9.63 (9.78).

(4S,5S)-4-[6-(2-Pyridyl)pyridin-2-yl]-5-[(tolylsulfonyl)oxy]methyl-2,2-dimethyl-1,3-dioxolane, 24. The procedure reported for the preparation of **20** was followed. From **23** (1 g, 3.5 mmol) compuound **24** was isolated after chromatography on silica gel (hexane: ethyl acetate/7:3): 1.15 g (75 %); ^{1}H-NMR ($CDCl_3$) δ 8.66 (m, 1H), 8.34 (m, 2H), 7.90-7.70 (m, 4H), 7.47 (d, 1H), 7.40-7.31 (m, 1H), 7.29-7.23 (m, 2H), 4.94 (d, 1H), 4.69 (dd, 1H), 4.43 (dd, 1H), 4.25 (m, 1H), 2.38 (s, 3H), 1.50 (s, 3H), 1.47 (s, 3H). *Elem. Anal.*, found % (calcd. for $C_{23}H_{24}N_2O_5S$) C, 62.80 (62.71); H, 5.50 (5.49); N, 6,33 (6.36).

(4S,5R)-4-[6-(2-Pyridyl)pyridin-2-yl]-5-(diphenylphosphino)methyl-2,2-dimetyl-1,3-dioxolane, 2. The procedure reported for the preparation of **1** was followed. From **24** (1.15 g, 2.67 mmol) compound **2** was isolated after three repeated purifications by flash chromatography (petroleum ether:ethyl acetate/7:3): 0.18 g (15 % yield); $[\alpha]^{25}_D$ +98.8 (*c* 2, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 8.60 (d, 1H), 8.26 (d,

1H), 8.17 (d, 1H), 7.77-7.57 (m, 6H), 7.44-7.17 (m, 8H), 4.89 (d, 1H), 4.37 (dt, 1H), 3.07 (dt, 1H), 2.80 (m, 1H), 1.37 (s, 3H), 1.32 (s, 3H). ^{31}P-NMR ($CDCl_3$) δ –22.3. *Elem. Anal.*, found % (calcd. for $C_{28}H_{27}N_2O_2P$) C, 74.03 (73.99); H, 6.10 (5.99), N, 6.23 (6.16).

Addition of diethylzinc to benzaldehyde: general procedure. A solution of ligands **1-3** (0.37 mmol) in toluene (5 ml) was cooled at 0 °C. A 1M solution of diethylzinc in hexane (12.4 ml, 12.4 mmol) was added over a period of 5 min. The mixture was stirred at room temperature for 20 min, cooled at 0 °C, added with benzaldehyde (0.6 ml, 0.647 g, 6.1 mmol) and then stirred at room temperature for the appropiate time (see Table 1). The reaction mixture was quenched with 10% H_2SO_4 (10 ml) and extracted with ether. The organic layer was washed with 10% H_2SO_4, saturated $NaHCO_3$, and dried (Na_2SO_4). The solvent was evaporated and the residue purified by flash chromatography to afford pure (GLC) 1-phenylpropanol.

Hydroformylation of styrene: general procedure. A mixture of the styrene (3.12 g, 0.03 mol) and the rhodium or platinum complex (0.1 mmol) [alternatively a solution of ligands **1** or **2** and $Rh(CO_2)(acac)$ with a ratio ligand/Rh=2.5/1 in benzene was used] in benzene (20 ml) was introduced in a 150 ml stainless steel reaction vessel and pressurized to 85-100 atm (see Table 2) with synthesis gas (CO/H_2=1/1). After the appropiate time at 30-120 °C (Table 2) the reaction was completed. The solvent was evaporated and the residue distilled under reduced pressure to give a mixture of 2-phenylpropanal and 3-phenylpropanal. The mixture was submitted to ^{1}H-NMR analysis. The conversion was calculated on the basis of the integration of the starting material and product signals. The branched to normal ratios were estimated by the integrations of aldehyde proton signals. The enantiomeric excess was determined from ^{1}H-NMR using $Eu(hfc)_3$ as chiral shift reagent.[16]

Hydrocarboethoxylation of styrene: general procedure. A mixture of the styrene (3.12 g, 0.03 mol) and the palladium complex (0.1 mmol) [alternatively a solution of ligands **1** or **2** and $PdCl_2$ with a ratio ligand/Pd=2.5/1 in benzene was used] in benzene/ethanol (20/5 ml) was introduced in a 150 ml stainless steel reaction vessel and pressurized at the appropiate pressure (see Table 3) with CO. After the proper time (Table 3) at 100 °C the reaction was completed. The solvent was evaporated and the residue distilled under reduced pressure give pure 2-phenylpropanoate. The enantiomeric excess was determined from the optical rotation of (+)(S)-ethyl 2-phenylpropanoate (Table 4).

Allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate: general procedure. A solution of Pydiphos (**1**) (76 mg, 0.2 mmol, 5 mol %) and $[\{Pd(\eta^3\text{-}C_3H_5)Cl\}_2]$ (4 mg, 2.5 mol %) in dry CH_2Cl_2 (2 ml) was stirred at room temperature for 15 min [alternatively a solution of $[(Pydiphos)Pd(\eta 3\text{-}C_3H_5)]PF_6$ (0.1 mmol, 2.5 mol %) in CH_2Cl_2 was used]. This solution was treated successively with a solution of *rac*-(E)-1,3-diphenyl-2-propenyl acetate (0.4 mmol) in CH_2Cl_2 (1 ml), dimethyl malonate (1.2 mmol), N,O-bis(trimethylsilyl)acetamide (1.2 mmol) and anhydrous potassium acetate (3 mol %). The reaction mixture was stirred for the appropiate time (see Table 4) until conversion was complete as shown by TLC analysis [light petroleum:ether/3:1]. The reaction mixture was diluted with ether (25 ml), washed with ice-cold saturated aqueous ammonium chloride. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography [light petroleum:ether/3:1] to afford dimethyl 1,3-diphenylprop-2-enylmalonate. The enantiomeric excess was determined from the ^{1}H-NMR spectrum in the presence of enantiomerically pure shift reagent $Eu(hfc)_3$; splitting of the signals for one of the two methoxy groups was observed.

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