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# Chiral furanoside phosphite–phosphoroamidites: new ligands for asymmetric catalytic hydroformylation

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**Abstract**—We have designed a new series of phosphite–phosphoroamidites ligands **1**–**4** based on a furanoside backbone. These ligands were screened in the Rh-catalyzed asymmetric hydroformylation of styrene, inducing high regioselectivities with 2-phenylpropanal and moderate enantioselectivities (up to 65% e.e.). The results showed that the configuration of the stereogenic carbon atom C(3) at the ligand backbone had remarkable effects on the activity and enantioselectivity. Replacing the *tert*-butyl substituents with methoxy substituents at the *para* positions of the biphenyl moieties improved the enantioselectivities. We have also studied the solution structures of $HRh(PP)(CO)_2$ complexes. 

## 1. Introduction

In the last few years, asymmetric hydroformylation has attracted much attention as a potential tool for preparing enantiomerically pure aldehydes, which are important precursors for synthesizing fine chemicals.[1] Since the early seventies, transition metal complexes based on rhodium and platinum have been used as catalysts in asymmetric hydroformylation.[1] Although high enantioselectivities have been obtained with Pt/diphosphine catalysts, they suffer from low chemo- and regioselectivities.[2] In general, Rh/diphosphine catalysts show high catalytic activities and regioselectivities with branched aldehydes, but the e.e.s do not exceed 60%.[3] In the last decade significant improvements have been made in the rhodium-catalyzed asymmetric hydroformylation based on new diphosphite[4] and phosphine–phosphite[5] ligands. Recently, a new class of diphosphite ligands, derived from D-(+)-glucose, with sugar furanoside backbones have demonstrated their potential as catalytic ligands for asymmetric hydroformylation.[4c] Carbohydrates are particularly advantageous because they are inexpensive compounds and their modular nature makes the systematic introduction of different functionalities easy.[6]

In the last few years, a group of less electron-rich phosphorus compounds—phosphoroamidite ligands—have also demonstrated their potential utility in asymmetric hydrogenation[7] and copper-catalyzed addition of dialkylzinc to enones.[8] The combination of different functionalitites in a ligand has already proved beneficial to the enantiodiscrimination (Achiwa's idea).[9] In this context, it has been reported how phosphine–phosphite ligands used in and hydroformylation[5a] hydrogenation[10] remarkably improved enantioselectivity with respect to their diphosphine and diphosphite counterparts.

Following our interest in carbohydrate ligands, and bearing in mind Achiwa's idea, we have designed a new family of chiral bidentate phosphite–phosphoroamidite ligands **1**–**4** with xylofuranoside backbone (Fig. 1). These ligands have the potential advantages of both types of ligand. We have also investigated their use in the enantioselective rhodium-catalyzed asymmetric hydroformylation of styrene. Finally, we report the solution structures of the species formed under hydroformylation conditions.

To the best of our knowledge, only Agbossou et al. have reported the application of phosphite–phosphoroamidite ligands, having ephedrine and pyrrolidine backbones, in the asymmetric hydroformylation with modest enantioselectivities.[11]

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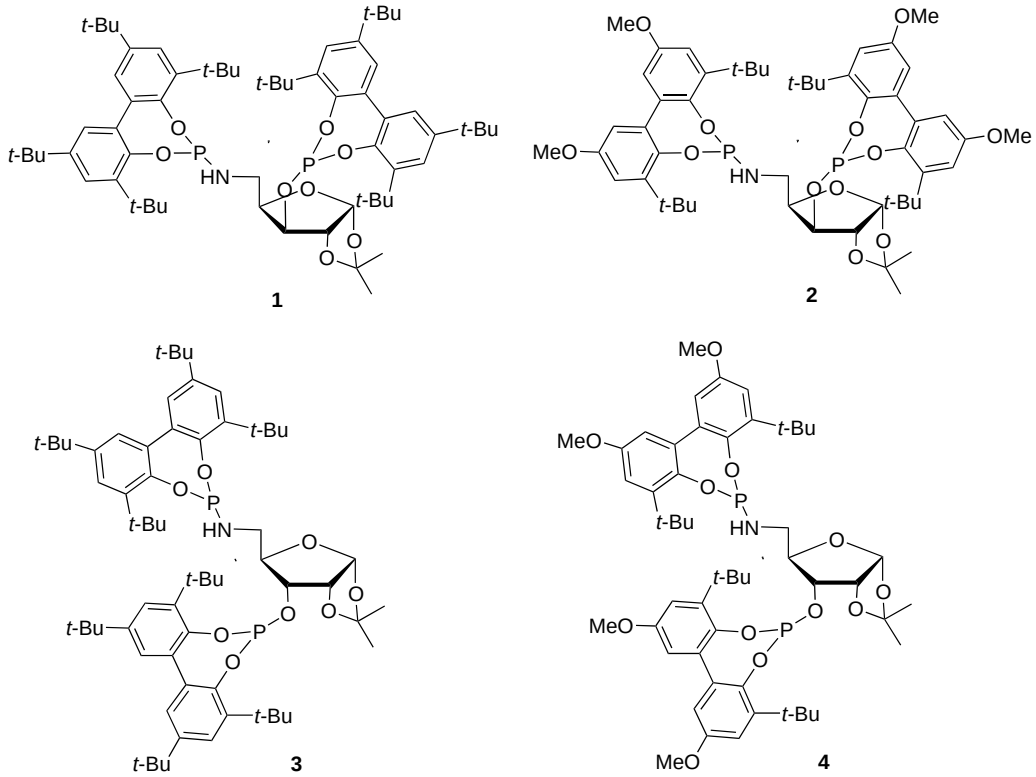



**Figure 1.**

## 2. Results and discussion

### 2.1. Ligand design

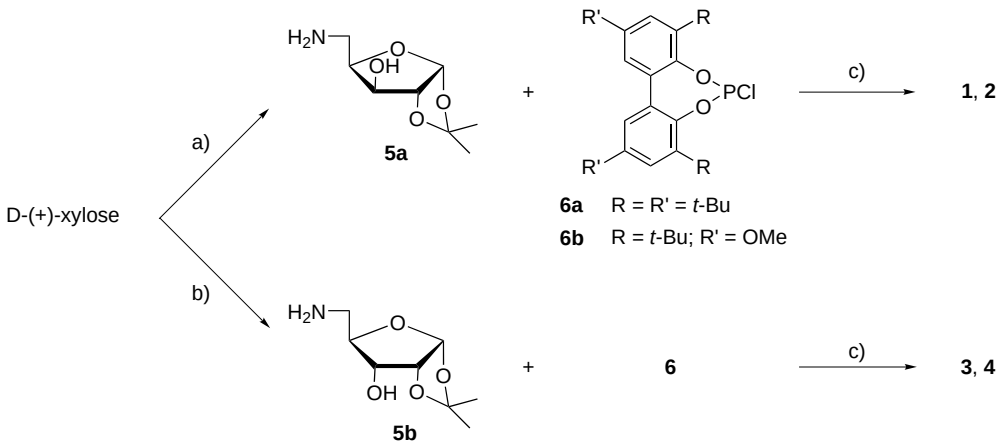
Ligands **1**–**4** consist of a chiral 1,2-*O*-protected furanoside backbone, which determines their underlying structure, and one amine group at C(5). Several phosphoric acid biphenol esters are attached to this basic framework (Scheme 1).

We investigated how the different groups attached to the *para* positions of the bisphenol moieties affected enantioselectivity using ligands **1** and **2**, which have the same configuration at C(3).

We also investigated the influence of the stereogenic carbon atom C(3) by comparing diastereomeric ligands **3** and **4** with ligands **1** and **2**, which have the opposite configuration at C(3) but have the same substituents on the biphenyl moieties.

### 2.2. Synthesis of the chiral phosphite–phosphoroamidite ligands

The new ligands **1**–**4** were synthesized very efficiently in one step from the corresponding amino alcohols **5a**[12] and **5b**,[13] which were easily prepared on a large scale from inexpensive D-(+)-xylose (Scheme 1). Reacting aminoalcohols **5** with 2 equiv. of the desired in situ formed phosphorochloridite **6** (either 3,3′-di-*tert*-butyl-




**Scheme 1.** Synthesis of ligands **1**–**4**. (a) Ref. 12; (b) Ref. 13; (c) Py, toluene, 100°C.

5,5′-di-methoxy-1,1′-biphenyl-2,2′-diyl phosphorochloridite or 3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl phosphorochloridite) in the presence of pyridine produced ligands **1**–**4** in good overall yield.

All of the ligands were stable during purification on neutral alumina under an atmosphere of argon and they were isolated as solids. They were stable at room temperature and are fairly robust towards hydrolysis. The $^{1}H$ and $^{13}C$ NMR spectra agree with those expected for these $C_1$ ligands (see Section 4).

### 2.3. Asymmetric hydroformylation of styrene

The phosphite–phosphoroamidite ligands **1**–**4** were then tested in the rhodium-catalyzed asymmetric hydroformylation of styrene under different reaction conditions. The catalysts were prepared in situ by adding 1 equiv. of the corresponding phosphite–phosphoroamidite ligand to $Rh(acac)(CO)_2$ as a catalyst precursor, since other precursors were reported to be less enantioselective.[5a] The styrene hydroformylation results are given in Table 1. Hydrogenated or polymerized products of styrene were not observed.

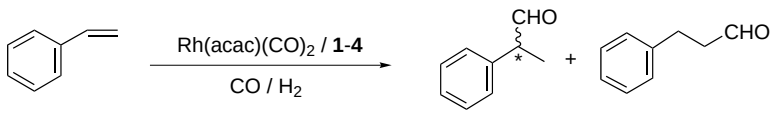
The effects of different reaction parameters were investigated for the catalytic precursor containing ligand **1**. After identical catalyst preparation, hydroformylation experiments were carried out under different partial pressures of CO and $H_2$ (entries 1–3). Higher partial pressures of $H_2$ clearly led to higher initial turnover frequencies. Moreover, comparing entries 1–3 shows that regio- and enantioselectivity were not affected by varying the partial pressure of $H_2$.

Varying the ligand-to-rhodium ratio showed that these catalyst systems are highly stable under hydroformylation conditions and no excess of ligand is needed (entry 4). This is an important advantage over the most successful catalysts based on diphosphites[4a,b] and phosphine–phosphite,[5] which need larger excesses of ligand.

When ligand **2** with methoxy groups instead of *tert*-butyl groups in the *para* positions of the biphenyl moieties was used, the activity and enantioselectivity was higher than with the catalyst system Rh/**1** (entry 1 versus 5). These results are in line with the beneficial *para* methoxy effect observed in enantioselectivity using diphosphite ligands.[4a,c,14]

Ligands **3** and **4**, whose configuration at C(3) is opposite to those of ligands **1** and **2**, followed the same trend as catalyst precursors Rh/**1** and Rh/**2** but activities were higher and the product enantiomeric excesses were smaller (entries 6 and 7). A monodentate coordination of the ligand may explain their higher activities[15] but this can be excluded from the spectroscopic data obtained under hydroformylation conditions (vide infra). A more plausible explanation is that the conformation adopted by ligands **3** and **4** probably causes less steric hindrance at the rhodium complexes than the $[HRh(CO)_2$ (ligands **1** or **2**)], and therefore, they are more reactive and less enantioselective. Moreover, unlike when related diphosphite ligands are used,[14b] the sense of the asymmetric induction is not controlled by the absolute configuration of stereogenic carbon atom C(3). Therefore, irrespective of the configuration of C(3) of the ligand, the absolute configuration of the major enantiomer of the product aldehyde is always *S*.

**Table 1.** Asymmetric hydroformylation of styrene catalyzed by $Rh(acac)(CO)_2$/phosphite–phosphoroamidite **1**–**4**[a]




| Entry | Ligand | TOF[b] | Conv[c] (%) | 2-PP[d] (%) | E.e.[e] (%) |
|---|---|---|---|---|---|
| 1 | **1** | 30 | 68 | 97 | 35 (*S*) |
| 2[f] | **1** | 21 | 46 | 97 | 36 (*S*) |
| 3[g] | **1** | 15 | 35 | 97 | 35 (*S*) |
| 4[h] | **1** | 31 | 69 | 97 | 36 (*S*) |
| 5 | **2** | 35 | 83 | 96 | 55 (*S*) |
| 6 | **3** | 51 | 100 | 96 | 15 (*S*) |
| 7 | **4** | 52 | 100 | 96 | 19 (*S*) |
| 8[i] | **1** | 4 | 10 | 97 | 45 (*S*) |
| 9[i] | **2** | 5 | 12 | 97 | 65 (*S*) |

[a] Reaction conditions: $T=40°C$, $P=10$ bar, styrene (13 mmol), $Rh(acac)(CO)_2$ (0.0135 mmol), ligand/Rh = 1.1, toluene (15 mL), $P_{CO}/P_{H2}=0.5$.
[b] TOF in mol styrene×mol $Rh^{-1}$×$h^{-1}$ determined after 1 h reaction time by GC.
[c] % Conversion of styrene after 24 h.
[d] Regioselectivity in 2-phenylpropanal.
[e] % E.e. measured by GC.
[f] $P_{CO}/P_{H2}=1$.
[g] $P_{CO}/P_{H2}=2$.
[h] Ligand/Rh = 2.
[i] $T=20°C$.

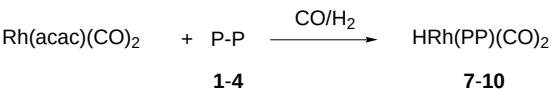
Lowering the temperature to 20°C resulted in increased enantioselectivity (up to 65%) with good regioselectivity for 2-phenylpropanal (up to 97%) (entries 8 and 9). These results represent a remarkable improvement with respect to the best enantioselectivities (19% e.e.) reported by Agbossou et al. using phosphite–phosphoroamidite ligands in the Rh-catalyzed hydroformylation of styrene.[11b]

### 2.4. Characterization of $HRh(PP)(CO)_2$ complexes

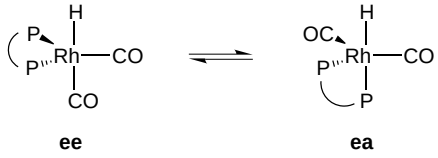
Hydridorhodium phosphite–phosphoroamidite dicarbonyl complexes denoted as $HRh(PP)(CO)_2$ **7–10**, which are known to be responsible for the catalytic activity, have been prepared to elucidate the solution structures of these catalysts.[1] The complexes were prepared in situ under hydroformylation conditions (10 bar, 40°C) by adding 1 equiv. of phosphite–phopshoroamidite ligand **1–4** to the catalyst precursor $Rh(acac)(CO)_2$ (Scheme 2). NMR spectroscopy under atmospheric conditions showed no detectable decomposition of the complexes. Table 2 shows the selected data for complexes **7–10**.

At room temperature, the $^{31}P\{^1H\}$ NMR spectra of complexes **7**, **9** and **10** showed the expected eight-line spectrum due to the two non-equivalent coordinated phosphorus atoms and a rhodium atom (ABX system). The $^{31}P\{^1H\}$ NMR spectrum of complex **8**, showed a doublet at 164.7 ppm due to the $^{31}P$–$^{103}Rh$ coupling. The fact that there is a doublet, not the expected eight-line spectra, was caused by the coincidental isochronicity of the two phosphorus atoms in fluxional behavior. This was confirmed by measuring the low-temperature $^{31}P$ $\{^1H\}$ NMR spectrum.[16]

For all complexes, the $^1H$ NMR spectra in the hydride region revealed a double triplet, due to the coupling with rhodium and the two phosphorus atoms. The fact that there was a double triplet instead of the expected double double doublet was caused by the coincidence of the phosphorus-hydride coupling constants. The values of the phosphorus-hydride coupling constants are relatively large for a pure bis-equatorial (**ee**) coordination.[17] There are two explanations for this; first, the formation of a distorted TBP hydridorhodium dicarbonyl species with **ee** coordinating ligands[14a,17b] and second, a fast equilibrium mixture of bis-equatorially and equatorial–axial (**ea**) species, which gives averaged signals in the NMR spectra (Scheme 3).[18] Evidence for the latter should be supplied by the HP-IR spectra because of the faster time-scale and lower detection limit of this technique compared to the NMR.[18] If an equilibrium between two isomers occurs, two sets of carbonyl frequencies originating from the two isomers should be observed. In general, the carbonyl bands of the **ea** isomer are found at lower wavenumbers than those of the **ee** isomer.[17b] The infra red spectra of complexes **7–10** showed four carbonyl absorption bands in the 2100–1900 $cm^{-1}$ region, which can be attributed to a mixture of **ee** and **ea** isomers (Table 3).[17a] The relative intensities of the absorption bands obtained from the HP-IR indicate that the proportion of **ea** species are rather lower than the **ee** species, which is in agreement with the observed phosphorous-hydride coupling constants. The large values of the phosphorous–phosphorous coupling constants for $HRh(PP)(CO)_2$ complexes are further evidence of the dominant role of the **ee** species in the mentioned equilibrium.[4c]




**Scheme 2.** Synthesis of $HRh(PP)(CO)_2$ complexes **7–10**.




**Scheme 3.** Equilibrium between equatorial–equatorial (**ee**) and equatorial–axial (**ea**) species.

**Table 3.** Selected HP-IR data ($cm^{-1}$) for complexes **7–10**

| Complex | $\nu_1$ (**ee**) | $\nu_2$ (**ea**) | $\nu_3$ (**ee**) | $\nu_4$ (**ea**) |
|---|---|---|---|---|
| **7** | 2078 (s) | 2056 (w) | 2024 (s) | 2001 (w) |
| **8** | 2076 (s) | 2055 (w) | 2022 (s) | 1999 (w) |
| **9** | 2077 (s) | 2057 (w) | 2021 (s) | 2001 (w) |
| **10** | 2076 (s) | 2056 (w) | 2023 (s) | 2000 (w) |

## 3. Conclusions

A series of new phosphite–phosphoroamidite ligands with a furanoside backbone have been easily synthesized in a few steps from commercial D-(+)-xylose. These ligands were employed in the asymmetric Rh-catalyzed hydroformylation of styrene. The results show that the type of substituents at the *para* positions in the

**Table 2.** Selected $^1H$ and $^{31}P$ NMR data for $HRh(PP)(CO)_2$ complexes **7–10**[a]

| Complex | PP | $\delta$ $P_1$ | $\delta$ $P_2$ | $^1J_{Rh-P1}$ | $^1J_{Rh-P2}$ | $^2J_{P1-P2}$ | $\delta$ H | $^2J_{H-P}$ | $^2J_{H-P}$ | $^1J_{H-Rh}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **7** | **1** | 161.2 | 164.3 | 234.3 | 224.3 | 271.0 | −10.52 (dt) | 10.5 | 10.5 | 3.3 |
| **8** | **2** | 164.7 | 164.7 | 229.2 | 229.2 | – | −10.30 (dt) | 8.1 | 8.1 | 3.3 |
| **9** | **3** | 162.6 | 166.2 | 234.8 | 232.1 | 278.5 | −10.67 (dt) | 9.8 | 9.8 | 3.2 |
| **10** | **4** | 166.2 | 168.9 | 239.1 | 228.3 | 271.8 | −10.34 (dt) | 8.8 | 8.8 | 3.6 |

[a] Prepared in toluene-$d_8$. NMR spectra recorded under atmospheric conditions at room temperature. $\delta$ in ppm. Coupling constants in Hz.

biphenyl moieties and the configuration of the stereogenic center at C(3) of the ligand backbone had remarkable effects on the activity and enantioselectivity of the hydroformylation reaction. The enantiomeric excess for these diasteroisomeric ligands was higher for ligand **3**, which had *para*-methoxy substituents in the biphenyl moieties and (*S*)-configuration at C(3). Although the enantioselectivities achieved with these ligands are similar to those of related diphosphite ligands, their behavior is different. Therefore, unlike the results with related diphosphite ligands, the sense of the asymmetric induction is not controlled by the absolute configuration of the stereogenic carbon atom C(3).

We have characterized the rhodium complexes formed under hydroformylation conditions by the NMR technique and in situ IR spectroscopy. Our results show that the most stable bis-equatorial diastereomers of hydridorhodium dicarbonyl complexes **7**–**10** are in equilibrium with equatorial–axial species. Based on the encouraging results obtained by using these new types of furanoside ligands, further research into more active and stereoselective catalysts is now in progress, exploiting the advantage that these sugar ligands can be so easily modified.

## 4. Experimental

### 4.1. General comments

All syntheses were performed using standard Schlenk techniques under argon atmosphere. Solvents were purified by standard procedures. All syntheses were performed using standard Schlenk techniques under argon atmosphere. Solvents were purified by standard procedures. Compounds and **5b**[12] and **5b**[13] phosphorochloridites **6**[19] were prepared by previously described methods. All other reagents were used as commercially available. Elemental analyses were performed on a Carlo Erba EA-1108 instrument. $^{1}H$, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra were recorded on a Varian Gemini 400 MHz spectrometer. Chemical shifts are relative to $SiMe_4$ ($^{1}H$ and $^{13}C$) as internal standard or $H_3PO_4$ ($^{31}P$) as external standard. All the NMR spectra were recorded using $CDCl_3$ as solvent except in the case of HPNMR were toluene-$d_8$ were used. All assignments in NMR spectra were determined by COSY and HETCOR spectra. Gas chromatographic analyses were run on a Hewlett–Packard HP 5890A instrument (split/splitless injector, J&W Scientific, Ultra-2 25 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 150 kPa He, F.I.D. detector) equipped with a Hewlett–Packard HP 3396 series II integrator. Hydroformylation reactions were carried out in a home-made 100 mL stainless steel autoclave. Enantiomeric excesses were measured after oxidation of the aldehydes to the corresponding carboxylic acids on a Hewlett–Packard HP 5890A gas chromatograph (split/splitless injector, J&W Scientific, FS-Cyclodex β-I/P 50 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 100 kPa He, F.I.D. detector). Absolute configuration was determined by comparing the retention times with enantiomerically pure (*S*)-(+)-2-phenylpropionic and (*R*)-(−)-2-phenylpropionic acids. Optical rotations were measured at 20°C on a Perkin–Elmer 241 MC Polarimeter. The specific rotations are given in deg $cm^3$ $g^{-1}$ $dm^{-1}$ units.

### 4.2. 3,5-Bis[(3,3′,5,5′-tetra-*t*-butyl-1,1′-biphenyl-2,2′-diyl)phosphite]-5-amine-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose 1

In situ formed phosphorochloridite **6a** (2.2 mmol) was dissolved in toluene (5 mL) to which pyridine (0.36 mL, 4.6 mmol) was added. 5-Amine-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose **5a** (0.19 g, 1 mmol) was azeotropically dried with toluene (3×1 mL) and dissolved in toluene (10 mL), to which pyridine (0.18 mL, 2.3 mmol) was added. The diol solution was transferred slowly over 30 min to the solution of phosphorochloridite **6a** at room temperature. The reaction mixture was stirred under reflux overnight and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam which was purified by flash chromatography (eluent: toluene/$NEt_3$ 100/1, $R_f$ 0.9) to produce a white powder (0.86 g, 81%). Anal. calcd for $C_{64}H_{93}NO_8P_2$: C, 72.08; H, 8.79; N, 1.31. Found: C, 72.02; H, 8.43; N, 1.52%. $[\alpha]_D^{20}=-11.2$ (*c* 1.0, $CH_2Cl_2$). $^{31}P\{^{1}H\}$ NMR: $\delta$ 144.8 (b), 145.1 (s). $^{1}H$ NMR: $\delta$ 1.18 (s, 3H, $CH_3$), 1.34 (s, 9H, $CH_3$, *t*-Bu), 1.36 (s, 9H, $CH_3$, *t*-Bu), 1.37 (s, 9H, $CH_3$, *t*-Bu), 1.39 (s, 9H, $CH_3$, *t*-Bu), 1.42 (s, 3H, $CH_3$), 1.46 (s, 18H, $CH_3$, *t*-Bu), 1.47 (s, 9H, $CH_3$, *t*-Bu), 1.48 (s, 9H, $CH_3$, *t*-Bu), 2.87 (m, 1H, H-5), 3.05 (m, 1H, H-5′), 3.42 (dt, 1H, NH, $J_{H\text{-}P}=31.2$ Hz, $J=7.2$ Hz), 4.21 (m, 1H, H-4), 4.35 (b, 1H, H-2), 4.60 (dd, 1H, H-3, $^{3}J_{3\text{-}P}=9.2$ Hz, $^{3}J_{3\text{-}4}=2.8$ Hz), 5.63 (d, 1H, H-1, $^{3}J_{1\text{-}2}=3.2$ Hz), 7.2–7.5 (m, 8H, CH=). $^{13}C$ NMR: $\delta$ 26.5 ($CH_3$), 26.8 ($CH_3$), 31.2 ($CH_3$, *t*-Bu), 31.4 ($CH_3$, *t*-Bu), 31.7 ($CH_3$, *t*-Bu), 34.4 (C, *t*-Bu), 34.9 (C, *t*-Bu), 35.5 (C, *t*-Bu), 35.6 (C, *t*-Bu), 35.7 (C, *t*-Bu), 39.2 (d, C-5, $J_{5\text{-}P}=6.4$ Hz), 76.8 (d, C-3, $J_{3\text{-}P}=3.4$ Hz), 80.8 (m, C-4), 84.5 (C-2), 105.0 (C-1), 111.9 ($CMe_2$), 124.2 (CH=), 124.3 (CH=), 124.6 (CH=), 126.5 (CH=), 126.6 (CH=), 126.8 (CH=), 126.9 (CH=), 132.6 (C), 132.7 (C), 133.2 (C), 139.8 (C), 140.3 (C), 140.4 (C), 145.8 (C), 146.2 (C), 146.9 (C), 147.2 (C).

### 4.3. 3,5-Bis[(3,3′-bis-*t*-butyl-5,5′-bis-methoxy-1,1′-biphenyl-2,2′-diyl)phosphite]-5-amine-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose 2

Treatment of in situ formed phosphorochloridite **6b** (2.2 mmol) and **5a** (0.19 g, 1 mmol) as described for compound **1** afforded phosphite–phosphoroamidite **2**, which was purified by flash chromatography (eluent: toluene/$NEt_3$ 100/1, $R_f$ 0.9) to produce a white powder (0.68 g, 71%). Anal. calcd for $C_{52}H_{69}NO_{12}P_2$: C, 64.92; H, 7.23; N, 1.46. Found: C, 64.99; H, 7.30; N, 1.50%. $[\alpha]_D^{20}=-91.1$ (*c* 1.0, $CH_2Cl_2$). $^{31}P\{^{1}H\}$ NMR: $\delta$ 144.0 (s), 145.9 (s). $^{1}H$ NMR: $\delta$ 1.22 (s, 3H, $CH_3$), 1.30 (s, 9H, $CH_3$, *t*-Bu), 1.37 (s, 3H, $CH_3$), 1.39 (s, 9H, $CH_3$, *t*-Bu), 1.41 (s, 9H, $CH_3$, *t*-Bu), 1.44 (s, 9H, $CH_3$, *t*-Bu),

2.63 (m, 1H, H-5), 2.97 (m, 1H, H-5′), 3.43 (dt, 1H, NH, $J_{H\text{-}P}=36.4$ Hz, $J=7.6$ Hz), 3.76 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.83 (s, 3H, OMe), 4.28 (m, 1H, H-4), 4.47 (b, 1H, H-2), 4.60 (dd, 1H, H-3, $^3J_{3\text{-}P}=10.4$ Hz, $^3J_{3\text{-}4}=2.8$ Hz), 5.72 (d, 1H, H-1, $^3J_{1\text{-}2}=3.6$ Hz), 6.66 (m, 2H, CH=), 6.72 (m, 2H, CH=), 6.90 (m, 2H, CH=), 6.96 (m, 2H, CH=). $^{13}$C NMR: $\delta$ 26.0 ($CH_3$), 26.5 ($CH_3$), 30.5 ($CH_3$, *t*-Bu), 30.9 ($CH_3$, *t*-Bu), 31.2 ($CH_3$, *t*-Bu), 35.0 (C, *t*-Bu), 35.2 (C, *t*-Bu), 35.4 (C, *t*-Bu), 38.5 (m, C-5), 55.3 (OMe), 55.4 (OMe), 55.5 (OMe), 55.6 (OMe), 76.1 (d, C-3, $J_{3\text{-}P}=6.1$ Hz), 80.2 (m, C-4), 84.0 (C-2), 105.0 (C-1), 111.8 ($CMe_2$), 112.4 (CH=), 112.9 (CH=), 113.2 (CH=), 113.9 (CH=), 114.0 (CH=), 114.3 (CH=), 133.1 (C), 133.9 (C), 141.8 (C), 142.2 (C), 142.3 (C), 142.5 (C), 154.8 (C), 155.2 (C), 155.5 (C), 156.0 (C).

### 4.4. 3,5-Bis[(3,3′,5,5′-tetra-*t*-butyl-1,1′-biphenyl-2,2′-diyl)phosphite]-5-amine-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose 3

Treatment of in situ formed phosphorochloridite **6a** (2.2 mmol) and **5b** (0.19 g, 1 mmol) as described for compound **1** afforded phosphite–phosphoroamidite **3**, which was purified by flash chromatography (eluent: toluene/$NEt_3$ 100/1, $R_f$ 0.9) to produce a white powder (0.84 g, 79%). Anal. calcd for $C_{64}H_{93}NO_8P_2$: C, 72.08; H, 8.79; N, 1.31. Found: C, 72.12; H, 8.83; N, 1.42%. $[\alpha]_D^{20}=-26.7$ (*c* 0.3, $CH_2Cl_2$). $^{31}P\{^1H\}$ NMR: $\delta$ 143.2 (s), 150.2 (s). $^1$H NMR: $\delta$ 1.29 (s, 3H, $CH_3$), 1.34 (s, 9H, $CH_3$, *t*-Bu), 1.36 (s, 27H, $CH_3$, *t*-Bu), 1.42 (s, 9H, $CH_3$, *t*-Bu), 1.44 (s, 9H, $CH_3$, *t*-Bu), 1.47 (s, 18H, $CH_3$, *t*-Bu), 1.52 (s, 3H, $CH_3$), 2.90 (m, 1H, H-5), 3.30 (m, 2H, NH, H-5′), 4.06 (m, 1H, H-4), 4.17 (m, 1H, H-3), 4.21 (m, 1H, H-2), 5.55 (d, 1H, H-1, $^3J_{1\text{-}2}=3.2$ Hz), 7.1–7.5 (m, 8H, CH=). $^{13}$C NMR: $\delta$ 26.7 ($CH_3$), 26.9 ($CH_3$), 31.3 (d, $CH_3$, *t*-Bu, $J_{C\text{-}P}=1.5$ Hz), 31.4 (d, $CH_3$, *t*-Bu, $J_{C\text{-}P}=3.0$ Hz), 31.5 (d, $CH_3$, *t*-Bu, $J_{C\text{-}P}=3.0$ Hz), 31.6 (d, $CH_3$, *t*-Bu, $J_{C\text{-}P}=1.5$ Hz), 31.7 ($CH_3$, *t*-Bu), 31.8 ($CH_3$, *t*-Bu), 34.8 (C, *t*-Bu), 34.9 (C, *t*-Bu), 35.5 (C, *t*-Bu), 41.8 (d, C-5, $J_{5\text{-}P}=22.4$ Hz), 74.5 (d, C-3, $J_{3\text{-}P}=5.3$ Hz), 78.9 (d, C-2, $J_{2\text{-}P}=2.3$ Hz), 79.4 (t, C-4, $J_{4\text{-}P}=3.8$ Hz), 103.5 (C-1), 113.5 ($CMe_2$), 124.1 (CH=), 124.3 (CH=), 124.5 (CH=), 126.4 (CH=), 126.7 (CH=), 126.9 (CH=), 128.4 (CH=), 129.3 (CH=), 132.8 (C), 133.2 (C), 140.2 (C), 140.3 (C), 140.4 (C), 140.5 (C), 145.9 (C), 146.0 (C), 146.8 (C), 146.9 (C).

### 4.5. 3,5-Bis[(3,3′-bis-*t*-butyl-5,5′-bis-methoxy-1,1′-biphenyl-2,2′-diyl)phosphite]-5-amine-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose 4

Treatment of in situ formed phosphorochloridite **6b** (2.2 mmol) and **5b** (0.19 g, 1 mmol) as described for compound **1** afforded phosphite–phosphoroamidite **4**, which was purified by flash chromatography (eluent: toluene/$NEt_3$ 100/1, $R_f$ 0.9) to produce a white powder (0.69 g, 73%). Anal. calcd for $C_{52}H_{69}NO_{12}P_2$: C, 64.92; H, 7.23; N, 1.46. Found: C, 65.01; H, 7.27; N, 1.51%. $[\alpha]_D^{20}=-40.2$ (*c* 0.3, $CH_2Cl_2$). $^{31}P\{^1H\}$ NMR: $\delta$ 143.5 (s), 149.3 (s). $^1$H NMR: $\delta$ 1.29 (s, 3H, $CH_3$), 1.31 (s, 9H, $CH_3$, *t*-Bu), 1.38 (s, 9H, $CH_3$, *t*-Bu), 1.40 (s, 3H, $CH_3$), 1.44 (s, 9H, $CH_3$, *t*-Bu), 1.46 (s, 9H, $CH_3$, *t*-Bu), 2.68 (m, 1H, H-5), 3.27 (m, 1H, H-5′), 3.35 (m, 1H, NH), 3.78 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.12 (m, 1H, H-4), 4.32 (m, 2H, H-2, H-3), 5.64 (d, 1H, H-1, $^3J_{1\text{-}2}=3.6$ Hz), 6.75 (m, 2H, CH=), 6.79 (m, 2H, CH=), 6.93 (m, 2H, CH=), 7.00 (m, 2H, CH=). $^{13}$C NMR: $\delta$ 26.2 ($CH_3$), 26.8 ($CH_3$), 30.4 ($CH_3$, *t*-Bu), 30.7 ($CH_3$, *t*-Bu), 31.2 ($CH_3$, *t*-Bu), 35.2 (C, *t*-Bu), 35.4 (C, *t*-Bu), 35.5 (C, *t*-Bu), 35.6 (C, *t*-Bu), 40.2 (m, C-5), 55.4 (OMe), 55.5 (OMe), 55.6 (OMe), 74.2 (m, C-3), 78.3 (C-2), 80.0 (m, C-4), 103.2 (C-1), 112.1 ($CMe_2$), 113.1 (CH=), 113.2 (CH=), 113.6 (CH=), 113.9 (CH=), 114.0 (CH=), 114.2 (CH=), 133.4 (C), 133.6 (C), 141.9 (C), 142.0 (C), 142.2 (C), 142.3 (C), 155.2 (C), 155.4 (C), 155.5 (C).

### 4.6. Hydroformylation experiments

In a typical experiment, the autoclave was purged three times with CO. The solution was formed from $Rh(acac)(CO)_2$ (0.013 mmol) and phosphite–phosphoroamidite (0.015 mmol) in toluene (10 mL). After pressurizing to the desired pressure with syn gas and heating the autoclave to the reaction temperature, the reaction mixture was stirred for 16 h to form the active catalyst. The autoclave was depressurized and a solution of styrene (13 mmol) in toluene (5 mL) was brought into the autoclave and pressurized again. During the reaction several samples were taken from the autoclave. After the desired reaction time, the autoclave was cooled to room temperature and depressurized. The reaction mixture was analyzed by gas chromatography.

### 4.7. High-pressure IR experiments

These experiments were performed in an SS 316 50 mL autoclave equipped with IRTRAN windows (ZnS, transparent up to 70 $cm^{-1}$, 10 mm i.d. optical path length 0.4 mm), a mechanical stirrer, a temperature controller, and a pressure device. In a typical experiment a degassed solution of $Rh(acac)(CO)_2$ (0.013 mmol) and phosphite–phosphoroamidite (0.015 mmol) in methyltetrahydrofuran (15 mL) was introduced into the high-pressure IR autoclave. The autoclave was purged twice with CO and pressurized to 10 bar of $CO/H_2$ and heated to 40°C.

### 4.8. In situ HP-NMR hydroformylation experiments

In a typical experiment, a sapphire tube ($\phi=10$ mm) was filled under argon with a solution of $Rh(acac)(CO)_2$ (0.030 mmol) and ligand (molar ratio PP/Rh = 1.1) in toluene-$d_8$ (1.5 mL). The HP-NMR tube was purged twice with CO and pressurized to the appropriate pressure of $CO/H_2$. After a reaction time of 16 h shaking at the desired temperature, the solution was analyzed.

**4.8.1. [HRh(CO)$_2$1] 7**. $^{31}$P{$^1$H} NMR: $\delta$ 161.2 (dd, 1P, $^1J_{P\text{-}Rh}$ = 234.3 Hz, $^2J_{P\text{-}P}$ = 271.0 Hz), 164.3 (dd, 1P, $^1J_{P\text{-}Rh}$ = 224.3 Hz, $^2J_{P\text{-}P}$ = 271.0 Hz). $^1$H NMR: $\delta$ −10.52 (dt, 1H, $^1J_{Rh\text{-}H}$ = 3.3 Hz, $^2J_{P\text{-}H}$ = 10.5 Hz), 0.81 (s, 3H, $CH_3$), 1.03 (s, 9H, $CH_3$, *t*-Bu), 1.04 (s, 9H, $CH_3$, *t*-Bu), 1.05 (s, 9H, $CH_3$, *t*-Bu), 1.14 (s, 9H, $CH_3$, *t*-Bu), 1.24 (s, 3H, $CH_3$), 1.37 (s, 9H, $CH_3$, *t*-Bu), 1.47 (s, 9H, $CH_3$, *t*-Bu), 1.51 (s, 9H, $CH_3$, *t*-Bu), 1.53 (s, 9H, $CH_3$, *t*-Bu), 2.52 (m, 2H, H-5, H-5′), 3.58 (m, 1H, H-4), 3.67 (m, 1H, NH), 4.19 (d, 1H, H-2, $^3J_{2\text{-}1}$ = 3.2 Hz), 4.86 (m, 1H, H-3), 5.28 (d, 1H, H-1, $^3J_{1\text{-}2}$ = 3.2 Hz), 6.8–7.5 (m, 8H, CH=). $^{13}$C NMR: $\delta$ 26.1 ($CH_3$), 26.9 ($CH_3$), 31.3 ($CH_3$, *t*-Bu), 31.4 ($CH_3$, *t*-Bu), 31.5 ($CH_3$, *t*-Bu), 31.6 ($CH_3$, *t*-Bu), 31.7 ($CH_3$, *t*-Bu), 32.6 ($CH_3$, *t*-Bu), 33.4 ($CH_3$, *t*-Bu), 34.5 (C, *t*-Bu), 34.6 (C, *t*-Bu), 34.7 (C, *t*-Bu), 35.7 (C, *t*-Bu), 38.7 (m, C-5), 77.2 (m, C-3), 82.1 (m, C-4), 84.5 (C-2), 105.0 (C-1), 111.8 ($CMe_2$), 124.1 (CH=), 124.3 (CH=), 125.5 (CH=), 126.1 (CH=), 126.4 (CH=), 126.7 (CH=), 127.6 (CH=), 128.2 (CH=), 133.4 (C), 133.5 (C), 133.7 (C), 140.2 (C), 140.6 (C), 146.2 (C), 146.3 (C), 146.6 (C), 146.9 (C).

**4.8.2. [HRh(CO)$_2$2] 8**. $^{31}$P{$^1$H} NMR: $\delta$ 164.7 (d, 2P, $^1J_{P\text{-}Rh}$ = 229.2 Hz). $^1$H NMR: $\delta$ −10.30 (dt, 1H, $^1J_{Rh\text{-}H}$ = 3.3 Hz, $^2J_{P\text{-}H}$ = 8.1 Hz), 0.98 (s, 3H, $CH_3$), 1.44 (s, 3H, $CH_3$), 1.52 (s, 9H, $CH_3$, *t*-Bu), 1.61 (s, 9H, $CH_3$, *t*-Bu), 1.66 (s, 1H, $CH_3$, *t*-Bu), 2.08 (m, 2H, H-5, H-5′), 3.28 (s, 3H, OMe), 3.30 (s, 3H, OMe), 3.33 (s, 3H, OMe), 3.42 (s, 3H, OMe), 3.84 (m, 1H, NH), 4.50 (d, 1H, H-2, $^3J_{2\text{-}1}$ = 3.6 Hz), 4.53 (m, 1H, H-4), 5.08 (m, 1H, H-3), 5.61 (d, 1H, H-1, $^3J_{1\text{-}2}$ = 3.6 Hz), 6.66 (m, 4H, CH=), 7.10 (m, 4H, CH=). $^{13}$C NMR: $\delta$ 26.1 ($CH_3$), 26.8 ($CH_3$), 31.4 ($CH_3$, *t*-Bu), 32.6 ($CH_3$, *t*-Bu), 33.2 ($CH_3$, *t*-Bu), 35.6 (C, *t*-Bu), 35.7 (C, *t*-Bu), 36.2 (C, *t*-Bu), 36.3 (C, *t*-Bu), 38.9 (m, C-5), 54.9 (OMe), 55.0 (OMe), 77.4 (m, C-3), 82.2 (m, C-4), 84.5 (C-2), 105.0 (C-1), 111.8 ($CMe_2$), 113.2 (CH=), 113.6 (CH=), 114.4 (CH=), 114.5 (CH=), 114.7 (CH=), 114.8 (CH=), 115.7 (CH=), 115.9 (CH=), 134.1 (C), 134.3 (C), 142.4 (C), 142.5 (C), 142.6 (C), 156.0 (C), 156.4 (C), 156.7 (C).

**4.8.3. [HRh(CO)$_2$3] 9**. $^{31}$P{$^1$H} NMR: $\delta$ 162.6 (dd, 1P, $^1J_{P\text{-}Rh}$ = 234.8 Hz, $^2J_{P\text{-}P}$ = 278.5 Hz), 166.2 (dd, 1P, $^1J_{P\text{-}Rh}$ = 232.1 Hz, $^2J_{P\text{-}P}$ = 278.5 Hz). $^1$H NMR: $\delta$ −10.67 (dt, 1H, $^1J_{Rh\text{-}H}$ = 3.2 Hz, $^2J_{P\text{-}H}$ = 9.8 Hz), 1.01 (s, 3H, $CH_3$), 1.04 (s, 9H, $CH_3$, *t*-Bu), 1.05 (s, 9H, $CH_3$, *t*-Bu), 1.15 (s, 9H, $CH_3$, *t*-Bu), 1.21 (s, 3H, $CH_3$), 1.25 (s, 9H, $CH_3$, *t*-Bu), 1.52 (s, 9H, $CH_3$, *t*-Bu), 1.55 (s, 18H, $CH_3$, *t*-Bu), 1.57 (s, 9H, $CH_3$, *t*-Bu), 2.71 (m, 2H, H-5, H-5′), 3.29 (m, 1H, NH), 3.34 (m, 1H, H-4), 4.10 (m, 1H, H-2), 4.24 (m, 1H, H-3), 5.21 (d, 1H, H-1, $^3J_{1\text{-}2}$ = 3.6 Hz), 6.8–7.5 (m, 8H, CH=).

**4.8.4. [HRh(CO)$_2$4] 10**. $^{31}$P{$^1$H} NMR: $\delta$ 166.2 (dd, 1P, $^1J_{P\text{-}Rh}$ = 239.1 Hz, $^2J_{P\text{-}P}$ = 271.8 Hz), 168.9 (dd, 1P, $^1J_{P\text{-}Rh}$ = 228.3 Hz, $^2J_{P\text{-}P}$ = 271.8 Hz). $^1$H NMR: $\delta$ −10.34 (dt, 1H, $^1J_{Rh\text{-}H}$ = 3.6 Hz, $^2J_{P\text{-}H}$ = 8.8 Hz), 0.99 (s, 3H, $CH_3$), 1.32 (s, 3H, $CH_3$), 1.44 (s, 9H, $CH_3$, *t*-Bu), 1.47 (s, 9H, $CH_3$, *t*-Bu), 1.52 (s, 9H, $CH_3$, *t*-Bu), 1.56 (s, 9H, $CH_3$, *t*-Bu), 2.19 (m, 2H, H-5, H-5′), 3.30 (s, 3H, OMe), 3.31 (s, 3H, OMe), 3.33 (s, 6H, OMe), 3.52 (m, 1H, NH), 3.98 (m, 1H, H-4), 4.26 (m, 1H, H-2), 4.98 (m, 1H, H-3), 5.47 (d, 1H, H-1, $^3J_{1\text{-}2}$ = 3.6 Hz), 6.5–7.5 (m, 8H, CH=).

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## References

1. (a) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpainter, V. W. *J. Mol. Catal.* **1995**, *104*, 17; (b) Agboussou, F.; Carpentier, J.-F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485; (c) Gladiali, S.; Bayón, J.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *7*, 1453; (d) *Rhodium Catalyzed Hydroformylation*; van Leeuwen, P. W. N. M.; Claver, C; Dordrecht: Kluwer, Academic Press, 2000.
2. (a) Stille, J. K.; Su, H.; Brechot, P.; Parrinello, G.; Hegedus, L. S. *Organometallics* **1991**, *10*, 1183; (b) Consiglio, G.; Nefkens, S. C. A.; Borer, A. *Organometallics* **1991**, *10*, 2046.
3. Diéguez, M.; Pereira, M. M.; Masdeu-Bultó, A. M.; Claver, C.; Bayón, J. C. *J. Mol. Catal. A: Chemical* **1999**, *143*, 111 and references cited therein.
4. (a) Babin, J. E.; Whiteker, G. T. Union Carbide Chem. Plastics Techn. Co., WO 93/03839, **1993** [Chem. Abs. **1993**, *119*, P159872h]; (b) Buisman, G. J. H.; van deer Veen, L. A.; Klootwijk, A.; de Lange, W. G. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Organometallics* **1997**, *16*, 2929; (c) Diéguez, M.; Pàmies, O.; Ruiz, A.; Castillón, S.; Claver, C. *Chem. Eur. J.* **2001**, *7*, 3086.
5. (a) Nozaki, K.; Sakai, N.; Nanno, T.; Higashijima, T.; Mano, S.; Horiuchi, T.; Takaya, H. *J. Am. Chem. Soc.* **1997**, *119*, 4413; (b) Franciò, G.; Leitner, W. *Chem. Commun.* **1999**, 1663.
6. (a) Penne, J. S. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; John Wiley & Sons: New York, 1995; (b) Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach*; Pergamon Press: London, 1983; Vol. 3.
7. (a) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539; (b) Franciò, G.; Faraone, F.; Leitner, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 1428; (c) Huttenloch, O.; Spieler, J.; Waldmann, H. *Chem. Eur. J.* **2001**, *7*, 671.
8. Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346 and references cited therein.
9. Inoguhi, K.; Sakuraba, S.; Achiwa. K. *Synlett* **1992**, 169. Achiwa's idea is that two different donor sites can *a priori* match the intermediates better and so influence their reactivity and enantioselectivity positively.
10. Pàmies, O.; Diéguez, M.; Net, G.; Ruiz, A.; Claver, C. *Chem. Commun.* **2000**, 2383.
11. (a) Lot, O.; Suisse, I.; Mortreux, A.; Agbossou, F. *J. Mol. Catal.* **2000**, *164*, 125; (b) Naili, S.; Suisse, I.; Mortreux, A.; Agbossou-Niedercorn, F.; Nowogrocki, G. *J. Organomet. Chem.* **2001**, *628*, 114.
12. Ewing, D. F.; Goethals, G.; Mackenzie, G.; Martin, P.; Ronco, G.; Vanbaelinghem, L.; Villa, P. *J. Carbohydr. Chem.* **1999**, *18*, 441.

13. Ewing, D. F.; Goethals, G.; Mackenzie, G.; Martin, P.; Ronco, G.; Vanbaelinghem, L.; Villa, P. *Carbohydr. Res.* **1999**, *321*, 190.
14. (a) Buisman, G. J. H.; Martin, M. E.; Vos, E. J.; Klootwijk, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1995**, *6*, 719; (b) Pàmies, O.; Net, G.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 1097.
15. van Rooy, A.; Orij, E. N.; Kamer, P. C. J.; van den Aardweg, F.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Chem. Commun.* **1991**, 1096.
16. Broad signals were observed when the temperature was lowered. We were not able to resolve these signals, nor when the temperature was lowered to −80°C.
17. (a) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741 and references cited therein; (b) van der Slot, S. C.; Kamer, P.; C:, J.; van Leeuwen, P. W. N. M.; Fraanje, J.; Goubitz, K.; Lutz, M.; Spek, A. L. *Organometallics* **2000**, *19*, 2504.
18. van der Veen, L. A.; Boele, M. D. K.; Bregman, F. R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J.; Schenk, H.; Bo, C. *J. Am. Chem. Soc.* **1998**, *120*, 11616.
19. Buisman, G. J. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1993**, *4*, 1625.