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Furanoside diphosphines derived from D-(+)-xylose and D-(+)-glucose as ligands in rhodium-catalysed asymmetric hydroformylation reactions

Montserrat Diéguez,* Oscar Pàmies, Gemma Net, Aurora Ruiz* and Carmen Claver

Departament de Química Física i Inorgànica, Universitat Rovira i Virgili, Pl. Imperial Tàrraco 1, 43005 Tarragona, Spain

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Abstract—Chirality transfer by furanoside diphosphines **1**–**3** was investigated in the Rh-catalysed asymmetric hydroformylation of prochiral olefins. In general, they induced high regioselectivities with branched aldehydes and moderate enantioselectivities of up to 58%. Improved activities were seen when a methyl substituent was introduced at C-(5) of the sugar residue. Systematic variation of the configuration at C-(5) suggests that there is a cooperative effect between stereocentres, which results in a matched combination for ligand **3** with (*R*)-configuration at the C-(5) stereogenic centre. Introduction of a methyl substituent at C-(5) induces a strong coordination preference. The solution structures of the species formed under hydroformylation conditions were also investigated.

1. Introduction

Hydroformylation is one of the most widely studied homogeneous catalytic processes.[1] In recent years, asymmetric hydroformylation has attracted much attention as a potential tool for preparing enantiomerically pure aldehydes, which are important precursors for many fine chemicals.[1] Catalyst precursors based on $[Rh(acac)(CO)_2]$ modified with chiral phosphorus ligands are particularly well suited to enantioselective hydroformylation. Moderate to excellent enantioselectivities have previously been obtained in the hydroformylation of styrene using diphosphines,[2] diphosphinites,[3] diphosphite[4] and phosphine–phosphite[5] ligands. Recent theoretical studies with C_2-diphosphine ligands attributed the moderate enantioselectivities achieved to minor stereodifferentiation of the different coordination modes by the catalyst (Scheme 1).[6]

In situ spectroscopic studies on the most successful diphosphite and phosphine–phosphite ligands suggest that the presence of a single catalytically active species in solution is the key to controlling efficient chirality transfer.[4b,5] However, the mechanistic aspects of the asymmetric hydroformylation reaction are still not well enough understood to predict the type of ligand required to achieve high levels of enantioselectivity. In this context, the search for new efficient ligands which can be prepared from simple starting materials is still of great importance in catalysis research. Chiral auxiliaries from the chiral pool have attracted much attention. In recent studies sugar-derived ligands showed good conversions and excellent enantioselectivities in different types of catalytic reactions,[3,4c,7] e.g. hydrogenation, hydroformylation, hydrocyanation and allylic alkylation, which demonstrates their potential. One of the most successful families of sugar derivatives in asymmetric catalysis is the 1,2-protected furanoses derived from D-(+)-xylose and D-(+)-glucose (Scheme 2).[4c,7f,7g,8]

In this paper we describe the use of C_1-furanoside diphosphines **1**–**3** (Fig. 1) in the asymmetric hydroformylation of prochiral olefins. A feature of these ligands is that the two donor sites are different and can therefore match the coordination modes better, influencing their reactivity and achieving good enantioselec-

Scheme 1.

* Corresponding authors. Fax: (+34)-977559563; e-mail: dieguez@quimica.urv.es; aruiz@quimic.urv.es

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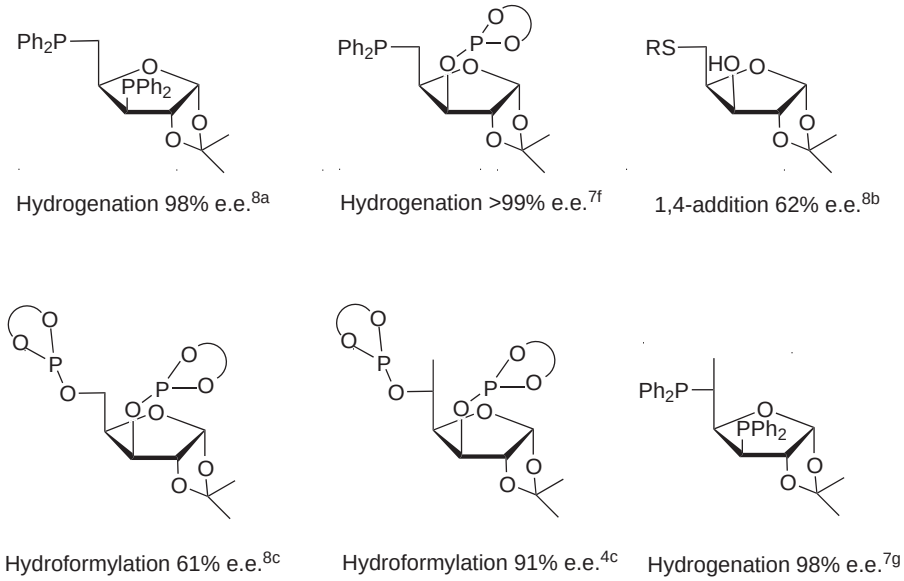


Scheme 2.

tivity.[9] Ligands **2** and **3** differ from ligand **1** at C-(5), where a new stereogenic centre was introduced allowing the effect of structural alterations at C-(5). The configuration at C-(5) was expected to be important to the course of the catalytic reaction because of its proximity to the metal centre.[7g]

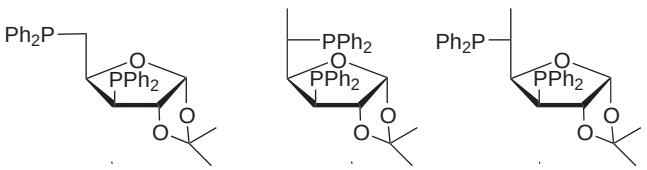


Figure 1.

2. Results and discussion

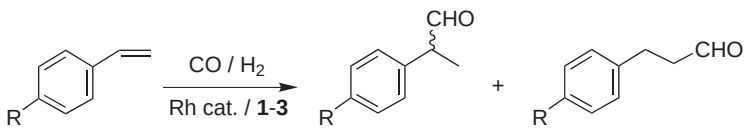
2.1. Hydroformylation of vinyl arenes

Diphosphine ligands **1**–**3** were tested in the rhodium-catalysed asymmetric hydroformylation of styrene and other vinyl arenes under different reaction parameters (Scheme 3).

Since other precursors were reported to give lower enantioselectivities,[5] the catalysts were prepared in situ from $[Rh(acac)(CO)_2]$ and the desired amount of diphosphine. In general, high ratios of branched aldehyde **5** to linear aldehyde **6** and moderate enantioselectivities were achieved (Table 1).

The effect of temperature, the ligand-to-metal ratio and the partial pressures of CO and H_2 on the enantioselectivity were investigated using ligand **1** (Table 1). Entries 1–3 indicate that an excess of diphosphine (2 equiv. with respect to Rh) was needed to prevent the formation of the active $[HRh(CO)_4]$ achiral species[10] and the modified active species containing the diphosphine as a monodentate ligand, which are known to lower the enantioselectivity of the reaction.[2]

Hydroformylation experiments under different partial pressures of CO and H_2 revealed that higher partial pressures of CO lead to lower initial turnover frequency (entries 2, 4 and 5). A comparison of entries 2, 4 and 5



4a	R = H	(*S*)-**5a**/(*R*)-**5a**	**6a**
b	R = OMe	(*S*)-**5b**/(*R*)-**5b**	**6b**
c	R = F	(*S*)-**5c**/(*R*)-**5c**	**6c**

Scheme 3. Hydroformylation of vinyl arenes **4a**–**4c**.

Table 1. Hydroformylation of **4a**–**4c** with [Rh(acac)(CO)$_2$]/P-P (P-P = **1**–**3**)[a]

Entry	P-P	S	P-P/Rh	P_{CO}/P_{H2}	T (°C)	TOF[b]	% Conv[c]	% **5**[d]	% E.e.[e]
1	**1**	**4a**	1	1	80	87	82	84	6 (*S*)
2	**1**	**4a**	2	1	80	39	37	96	35 (*S*)
3	**1**	**4a**	4	1	80	37	36	96	34 (*S*)
4	**1**	**4a**	2	2	80	28	23	95	34 (*S*)
5	**1**	**4a**	2	0.5	80	58	52	95	33 (*S*)
6	**1**	**4a**	2	1	40	5	4	97	51 (*S*)
7	**1**	**4a**	2	1	40	5	58[f]	97	50 (*S*)
8	**1**	**4b**	2	1	80	38	33	95	38 (–)
9	**1**	**4c**	2	1	80	36	35	94	32 (+)
10	**2**	**4a**	2	1	80	50	45	96	29 (*S*)
11	**2**	**4a**	2	1	40	6	6	97	44 (*S*)
12	**3**	**4a**	2	1	80	54	48	97	39 (*S*)
13	**3**	**4a**	2	1	40	7	7	97	58 (*S*)
14	**3**	**4a**	2	0.5	40	12	10	97	57 (*S*)

[a] Reaction conditions: P = 30 bar, styrene (6.5 mmol), [Rh(acac)(CO)$_2$] (0.013 mmol), toluene (15 mL).
[b] TOF in mol substrate×Rh^{-1}×h^{-1} determined after 1 h reaction time by GC.
[c] % Conversion after 5 h.
[d] % Regioselectivity in **5**.
[e] The % e.e. of **5** was measured by GC.
[f] Determined after 72 h.

further shows that regio- and enantioselectivity are virtually unaffected by varying the partial pressure of CO.

Lowering the reaction temperature to 40°C increased the enantioselectivity (entry 6, 51% e.e.). The regio- and enantioselectivity of the reaction were also found to remain constant throughout the reaction, which shows that the catalyst was stable under the reaction conditions (entry 7).

Substituting different groups in the *para*-position of the substrate had no effect on the hydroformylation reaction with respect to the conversion or the regio- and enantioselectivity of the products (entries 8, 9 vs 2).

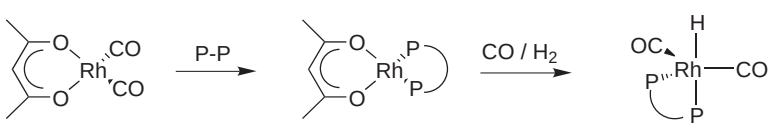
The other ligands were compared under 'standard' conditions, i.e. a ligand-to-rhodium ratio of 2 and a *syn* gas pressure of 30 bar. Activities improved when ligands **2** and **3** were used (entries 10 and 12 vs 2) in comparison to the use of ligand **1**. At 40°C with ligand **2**, having (*S*)-configuration at C-(5), gave (*S*)-**5a** with 44% e.e. (entry 11), while diastereomer **3** gave (*S*)-**5a** in 58% e.e. (entry 13). These results and those obtained with ligand **1** (entry 6) suggest that there is a cooperative effect between stereocentres, which results in a matched combination for ligand **3** and a mismatched combination for **2**.

In conclusion, catalytic precursors based on rhodium systems with C_1-furanoside diphosphines, which are readily available from the chiral pool, provide hydroformylated products with regioselectivities of up to 97% with e.e.s of up to 58%. These results are similar to those obtained with the most efficient diphosphine based catalytic systems previously reported.[2]

2.2. Solution structure of the species formed under hydroformylation conditions

To identify the intermediates formed during the hydroformylation process, we carried out a solution spectroscopic study of the catalytic species formed by adding two equivalents of the corresponding ligand to the catalyst precursor [Rh(acac)(CO)$_2$] in deuterated toluene and placing the resultant solution under 30 bar pressure with *syn* gas.

Initially, displacement of two carbon monoxide molecules by the ligand caused the formation of a mononuclear [Rh(acac)(P-P)] **7a**–**7c** species (Scheme 4, Table 2).[11] Under these hydroformylation conditions

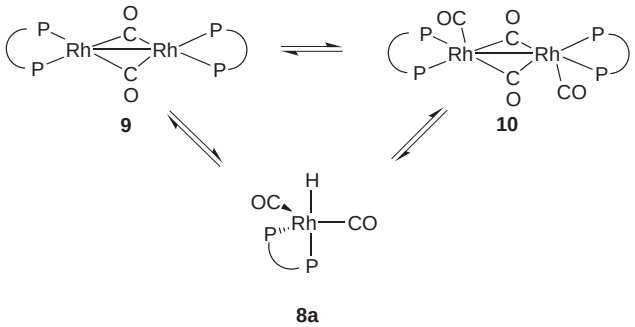


Scheme 4.

Table 2. Selected $^{31}P\{^1H\}$ and ^1H NMR data for species **7** and **8**[a]

						Hydride			
	δ(P)	J\{P-Rh\}	δ(P)	J\{P-Rh\}	J\{P-P\}	δ(H)	J\{H-P\}	J\{H-P\}	J\{H-Rh\}
7a	35.04	183.6	44.52	188.9	73.3				
7b	37.32	179.8	43.45	189.3	69.9				
7c	39.31	183.2	48.67	187.6	71.2				
8a	8.02	120.4	18.75	107.7	44.4	−8.58	34.5	84.3	11.1
8b	21.31	122.0	27.43	100.6	51.9	−8.36	19.7	102.2	11.6
8c	22.43	119.3	28.56	102.4	54.8	−8.42	18.2	100.9	11.3

[a] Chemical shifts (δ) in ppm and coupling constants (J) in Hz.



Scheme 5.

7a–**7c** reacted rapidly to form the hydridorhodium dicarbonyl species **8a**–**8c**, which are known to be responsible for the catalytic activity.[1]

At 25°C, the $^{31}P\{^1H\}$ NMR spectrum of solution containing ligand **1** showed two broad doublets at 3.61 ($^1J_{P\text{-}Rh}=145$ Hz) and 6.74 ppm ($^1J_{P\text{-}Rh}=149$ Hz) attributed to inactive dimers **9** and **10** (Scheme 5), which have a Rh–Rh bond and two CO groups that bridge the metal atoms. Dimer **10** has an additional terminal CO group on each rhodium centre. Similar compounds have previously been reported for other diphosphine systems, with very similar rhodium–phosphorus coupling constants (around 145 Hz).[12] After heating the solution to 80°C, the $^{31}P\{^1H\}$ NMR spectrum showed two new doublets of doublets at 8.02 and 18.75 ppm. These correspond to the mononuclear hydride–rhodium complex **8a** (Table 2, Scheme 5).

The ^1H NMR spectrum of this solution in the hydride region revealed a doublet of doublets of doublets (Table 2, Fig. 2), which is indicative of hydride coupling with rhodium and the two non-equivalent phosphorus atoms. The phosphorus–hydride coupling constants are characteristic of a hydrido-rhodium dicarbonyl species with equatorial-axially coordinating diphosphines.[12a,d] Small *cis*-phosphorus–hydride coupling constants of between 1 and 20 Hz are reported in $HRh(PP)(CO)_2$ complexes with bis-equatorially coordinating diphosphine. In contrast, a coupling constant of 106 Hz in trigonal bipyramidal $HRh(CO)_2$(DPEphos) has been found for an apical phosphine.[13,14] The intermediate values for the phosphorus–hydride coupling constants indicate that there is an equilibrium between the two equatorial–axial diastereoisomers in fast exchange in the NMR time-scale. Interestingly, taking into reference the typical values of $^2J_{P\text{-}H}$ for phosphines in equatorial and axial positions,[12a,d] it seems clear that one diastereoisomer is much more stable under these conditions. Moreover, as in related systems containing chiral diphosphines such as Bdpp, there is an equilibrium between mono- and binuclear species.[12a,d]

No binuclear species were detected by HPNMR for solutions containing ligands **2** and **3**. Therefore, at room temperature, the $^{31}P\{^1H\}$ NMR spectrum of these solutions showed two doublets of doublets. These were attributed to complexes **8b** and **8c**, respectively (Table 2). The spectrum also contained a doublet of doublets of doublets in the hydride region (Table 2), again indicating hydride coupling with rhodium and the two non-equivalent phosphorus atoms. Moreover, the $^2J_{P\text{-}H}$ values and the VT NMR indicate that there is no equatorial–axial exchange of phosphorus. This contrasts with the equilibrium usually reported for equatorial–axial diphosphine chelates.[12a,d]

In conclusion, ligands **1**–**3** take advantage of their C_1-symmetry to reduce their coordination modes in the $[HRh(PP)(CO)_2]$ complexes. The introduction of a methyl substituent at C-(5) induces a strong coordination preference, therefore ligands **2** and **3** have only one diastereoisomer under hydroformylation conditions. However, this strong coordination preference affects the enantioselectivity minimally. Enantioselectivity is, however, affected by the configuration of the stereocentres in the ligand, which produce a matched combination for ligand **3**.

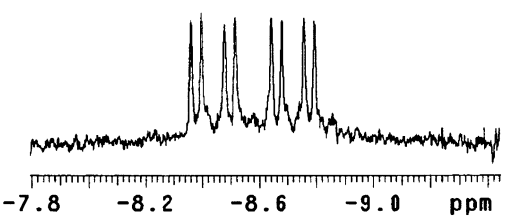


Figure 2. ^1H HPNMR of the solution of $[Rh(acac)(CO)_2]$/**1** in the hydride region under hydroformylation conditions.

3. Experimental

3.1. General techniques

All syntheses were performed by standard Schlenk techniques under a nitrogen or argon atmosphere. $[Rh(acac)(CO)_2]$[15] and ligands **1**–**3**[7g,8a] were prepared by previously described methods. Solvents were purified by standard procedures. All other reagents were commercially available and used as supplied. ^1H and $^{31}P\{^1H\}$ NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. Chemical shifts were relative to $SiMe_4$ (^1H) as internal standard or H_3PO_4 (^{31}P) as external standard. 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 of hydroformylation products were measured using a Hewlett–Packard HP 5890A gas chromatograph (split/splitless injector, J&W Scientific, FS-Cyclodex b-I/P 50 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 100 kPa He, F.I.D. detector) after oxidation of the aldehyde to the corresponding carboxylic acid; the absolute configuration of the **5a** products were then assigned by comparing the retention times with enantiomerically pure (*S*)-(+)-2-phenylpropionic and (*R*)-(−)-2-phenylpropionic acids.

3.2. Hydroformylation of styrene and derivatives

In a typical experiment the autoclave was purged three times with CO, then filled with a solution of $[Rh(acac)(CO)_2]$ (3.5 mg, 0.0135 mmol) in toluene (10 mL). Diphosphine (0.027 mmol, P-P/Rh ratio of 2) and styrene or styrene derivative (6.5 mmol) were added. After pressurising to the desired pressure with *syn* gas and heating the autoclave to the reaction temperature, the reaction mixture was stirred. During the reaction several samples were taken from the autoclave. After the desired reaction time, the autoclave was cooled to room temperature and depressurised and the reaction mixture was analysed by gas chromatography.

3.3. In situ HPNMR characterisation of $[HRh(CO)_2(PP)]$

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 P/Rh = 2) in toluene-d_8 (1.5 mL). The HPNMR tube was purged twice with CO and pressurised to the appropriate pressure of CO/H_2. After shaking the sample until the desired temperature was reached, the solution was analysed.

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References

1. See for instance: (a) Pruett, R. L. *Adv. Organomet. Chem.* **1979**, *17*, 1. (b) Agboussou, F.; Carpentier, J. F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485. (c) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal. A* **1995**, *104*, 17. (d) Gladiali, S.; Bayón, J. C.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *6*, 1453. (e) Frohhning, C. D.; Kohlpaintner, Ch. W. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B.; Herrmann, W. A., Eds.; Springer-Verlag: New York, 1996; pp. 29–90. (f) *Rhodium Catalysed Hydroformylation*; van Leeuwen, P. W. N. M., Claver, C., Eds.; Kluwer Academic Press: Dordrecht, 2000.
2. Diéguez, M.; Pereira, M. M.; Masdeu-Bultó, A. M.; Claver, C.; Bayón, J. C. *J. Mol. Catal. A: Chem.* **1999**, *143*, 111 and references cited therein.
3. RajanBabu, T. V.; Ayers, T. A. *Tetrahedron Lett.* **1994**, *35*, 4295.
4. (a) Babin, J. E.; Whiteker, G. T. WO 93/03839 US 911, 518, 1992; (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. Commun.* **2000**, 1607.
5. Nozaki, K.; Sakai, N.; Nanno, T.; Higashijima, T.; Mano, S.; Horiuchi, T.; Takaya, H. *J. Am. Chem. Soc.* **1997**, *119*, 4413.
6. Gleich, D.; Herrmann, W. A. *Organometallics* **1999**, *18*, 4354 and references cited therein.
7. (a) Brunner, H.; Zettlmeier, W. *Handbook of Enantioselective Catalysis*; VCH: Weinheim, 1993; (b) Selke, R. *J. Organomet. Chem.* **1989**, *370*, 241; (c) RajanBabu, T. V.; Casalnuovo, A. L. *Pure Appl. Chem.* **1994**, *94*, 149; (d) Yonehara, K.; Hashizuma, T.; Mori, K.; Ohe, K.; Uemura, S. *Chem. Commun.* **1999**, 415; (e) Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179; (f) Pàmies, O.; Diéguez, M.; Net, G.; Ruiz, A.; Claver, C. *Chem. Commun.* **2000**, 2383; (g) Diéguez, M.; Pàmies, O.; Ruiz, A.; Castillón, S.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 4701.
8. (a) Pàmies, O.; Net, G.; Ruiz, A.; Claver, C. *Eur. J. Inorg. Chem.* **2000**, 2011; (b) Pàmies, O.; Net, G.; Ruiz, A.; Claver, C.; Woodward, S. *Tetrahedron: Asymmetry* **2000**, *11*, 871; (c) 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; (d) Pàmies, O.; Net, G.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 1097; (e) Pàmies, O.; Diéguez, M.; Net, G.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 4377.

9. Inoguhi, K.; Sakuraba, S.; Achiwa, K. *Synlett* **1992**, 169.
10. Garland, M.; Pino, P. *Organometallics* **1991**, *10*, 1693.
11. (a) Sakai, N.; Nozaki, K.; Mashima, K.; Takaya, H. *Tetrahedron: Asymmetry* **1992**, *3*, 583; (b) Buisman, G. J. H.; Vos, E. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1995**, 409.
12. (a) Castellanos-Páez, A.; Castillón, S.; Claver, C.; van Leeuwen, P. W. N. M.; de Lange, W. G. J. *Organometallics* **1998**, *17*, 2543 and references cited therein; (b) Evans, D.; Yagupsky, G.; Wilkinson, G. *J. Chem. Soc. (A)* **1968**, *1*, 2660; (c) Yagupsky, M.; Brown, C. K.; Yagupsky, G.; Wilkinson, G. *J. Chem. Soc. (A)* **1970**, 937; (d) Pàmies, O.; Net, G.; Widhalm, M.; Ruiz, A.; Claver, C. *J. Organomet. Chem.* **1999**, *587*, 136.
13. DPEphos stands for 2,2′-bis(diphenylphosphino)diphenyl ether.
14. van der Veen, L. A.; Boele, M. D. K.; Bregman, F. R.; Kamer, P. C.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J.; Schenk, H. *J. Am. Chem. Soc.* **1998**, *120*, 11616.
15. (a) Gallay, J.; de Mountouzon, D.; Poilblanc, R. *J. Organomet. Chem.* **1972**, *38*, 179; (b) Bonati, F.; Wilkinson, G. *J. Chem. Soc.* **1964**, 3156.