Novel diphosphite derived from D-*gluco*-furanose provides high regio- and enantioselectivity in Rh-catalysed hydroformylation of vinyl arenes

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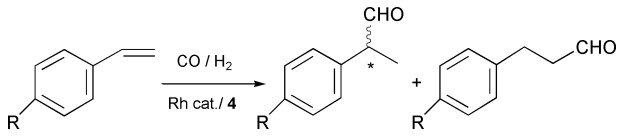
Both high enantioselectivity (91%) and high regioselectivity (98.8%) are achieved under mild reaction conditions in the Rh-catalysed hydroformylation of vinyl arenes with a new chiral diphosphite ligand derived from the readily available D-(+)-glucose.

Asymmetric hydroformylation has attracted much attention as a potential tool for preparing enantiomerically pure aldehydes. These are important as precursors for synthesising biologically active compounds, biodegradable polymers and liquid crystals.[1] In the last ten years, several studies have reported a remarkable improvement in the rhodium-catalysed asymmetric hydroformylation based on the use of diphosphite[2] or phosphine–phosphite[3] (Binaphos) ligands. At the moment, Binaphos is the only ligand with a wide scope in asymmetric hydroformylation, although its difficult preparation limits its application. Furthermore, its regioselectivy in 2-phenylpropanal is not completely satisfactory even under carefully optimised conditions.[3] More recently, perfluoroalkyl substituents at the aryl group of the Binaphos increased the regioselectivity, in the best case up to 96%, but high pressures and an excess of ligand were still needed for good enantioselectivities.[4] In this context, much research still needs to be done to find ligands that are readily available and provide both good regio- and enantioselectivities in asymmetric hydroformylation.

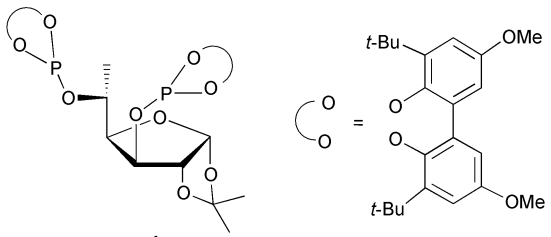
In the last few decades carbohydrates have been widely used in asymmetric synthesis.[5] Nevertheless their full potential in providing chiral ligands has scarcely been exploited[6] despite the accessibility and low cost of the carbohydrate synthons. In previous work on diphosphite ligands with a furanose backbone moderate results (up to 60% ee) in asymmetric hydroformylation of styrene have been reported.[7] Since these ligands had a phosphorus moiety bonded to a nonstereogenic center (C-5), we tested whether further modifying the ligand would improve enantioselectivities. With this purpose and following from our interest in using carbohydrates as a chiral source for preparing ligands,[7b,8] we designed a new diphosphite ligand **4** which was easily prepared from D-(+)-glucose. This ligand has the two phosphite moieties bonded to two stereogenic centers (C-3 and C-5) and has proven to be highly enantioselective and regioselective in the asymmetric hydroformylation of vinylarenes (Scheme 1).

Diphosphite **4**[9] was synthesised in 3 steps from 1,2-*O*-isopropylidene-3-*O*-acetyl-α-D-glucofuranose **5** as shown in Scheme 2. Diol **5** is easily prepared from D-(+)-glucose on a large scale by previously described highly effective methods.[10] Tosylation of **5** produced a good yield of the expected 5-tosyl derivative (88%).[11] Treatment with NaOMe at rt followed by reduction with lithium aluminium hydride produced crystalline 6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose **7** in 92% yield.[12]

Reacting diol **7** with two equiv. of 3,3′-di-*tert*-butyl-5,5′-dimethoxy-1,1′-biphenyl-2,2′-diyl phosphorochloridite[13] *in situ* formed in the presence of pyridine produced the desired diphosphite **4** in good overall yield.



1 a R = H; **b** R = F; **c** R = OMe (*R*)-**2**/(*S*)-**2** **3**

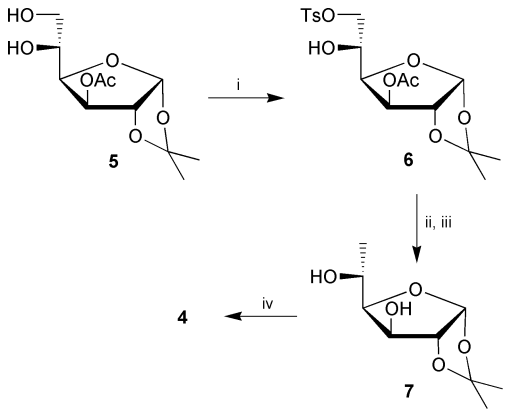


4

Scheme 1

Ligand **4** was used in the rhodium-catalysed asymmetric hydroformylation of styrene and other vinylarenes.[14] Results are given in Table 1. In no cases were hydrogenated or polymerised products observed.

Varying the ligand-to-rhodium ratio shows that it is not necessary to have excess ligand to obtain good regio- and enantioselectivities (entries 1–2). This contrasts with Rh–Binaphos systems, for which a large excess of ligand is needed.[3,4] Moreover, activities were best at low P_{CO}–P_{H2} ratios



5 **6** **4** **7**

Scheme 2 Synthesis of ligand **4**: (i) TsCl, pyridine, CH_2Cl_2, 16h, −20 to 25 °C, 88%; (ii) NaOMe, CH_2Cl_2, 1 h, 25°C, quantitative; (iii) $LiAlH_4$, THF, 60 °C, 92%; (iv) phosphorochloridite, pyridine, toluene, 100 °C, 71%.

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Table 1 Asymmetric hydroformylation catalysed by [Rh(acac)$(CO)_2$]/**4**[a]

Entry	Substrate	P_{CO}–P_{H2}	T/°C	TOF[b]	%Conv (time/h)[c]	%Regio[d]	%Ee[e]
1	**1a**	1	40	98	98 (10)	97.8	78 (*S*)
2[f]	**1a**	1	40	97	96 (10)	97.7	78 (*S*)
3	**1a**	0.5	40	174	100 (6)	97.9	78 (*S*)
4	**1a**	0.5	20	18	83 (48)	98.6	90 (*S*)
5	**1b**	0.5	20	17	80 (48)	98.8	89 (+)
6	**1c**	0.5	20	16	81 (48)	98.6	91 (−)

[a] Reaction conditions: P = 10 bar, styrene (13 mmol), [Rh(acac)$(CO)_2$] (0.013 mmol), toluene (15 mL), PP/Rh = 1.1. [b] TOF in mol styrene × Rh^{-1} × h^{-1} determined after 1 h reaction time by GC. [c] % Conversion of styrene measured by GC. [d] % Regioselectivity defined as **2**/(**2** + **3**). [e] % Ee measured by GC. [f] PP/Rh = 2.

(entry 3). This is in line with detailed kinetic studies on rhodium-catalysed hydroformylation with bulky phosphites reported by van Leeuwen *et al.*, who showed that the rate-determining step is the oxidative addition of H_2 to the acyl–rhodium complex.[15] Comparing entries 1 and 3 also shows that regio- and enantioselectivities are not affected by varying the partial pressure of CO. A remarkable increase in enantioselectivities (up to 91%, entries 4–6) combined with excellent regioselectivities (up to 98.8%) were found by lowering the reaction temperature. There were no changes in the enantioselectivities over time, which indicates that no decomposition of the catalyst took place.

Results were similar when **4** was used in the asymmetric hydroformylation of the substituted vinylarenes **1b** and **1c**. The presence of different substituents in the *para* position does not seem to affect the conversion or the regio- and enantioselectivities of the hydroformylation.

In conclusion, a novel chiral diphosphite **4**, derived from readily available D-(+)-glucose, is a highly efficient ligand for the asymmetric rhodium-catalysed hydroformylation of vinyl arenes under mild reaction conditions and without an excess of ligand. The combination of excellent regio- and enantioselectivities (up to 98.8 and 91% respectively) in simple unoptimised reactions and the low cost of the ligand make this catalyst system attractive for further investigation of its potential use for the industrial preparation of biologically active compounds in asymmetric hydroformylation. Studies of the scope and mechanistic aspects of the catalytic process are currently in progress.

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Notes and references

1 (*a*) M. Beller, B. Cornils, C. D. Frohning and V. W. Kohlpainter, *J. Mol. Catal.*, 1995, **104**, 17; (*b*) F. Agboussou, J. F. Carpentier, A. Mortreux, *Chem. Rev.*, 1995, **95**, 2485.

2 (*a*) J. E. Babin and G. T. Whiteker, WO 93/03839, US 911, 518, 1992; (*b*) G. J. H. Buisman, L. A. van deer Veen, A. Klootwijk, W. G. J. de Lange, P. C. J. Kamer, P. W. N. M. van Leeuwen and D. Vogt, *Organometallics*, 1997, **16**, 2929.

3 K. Nozaki, N. Sakai, T. Nanno, T. Higashijima, S. Mano, T. Horiuchi and H. Takaya, *J. Am. Chem. Soc.*, 1997, **119**, 4413.

4 G. Franciò and W. Leitner, *Chem. Commun.*, 1999, 1663.

5 (*a*) S. Hanessian in *Total Synthesis of Natural Products: The "Chiron" Approach*, Pergamon Press, vol. 3, London 1983; (*b*) J. S. Penne in *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, John Wiley & Sons, New York, 1995.

6 (*a*) H. U. Blaser, *Chem. Rev.*, 1992, **92**, 935; (*b*) H. Brunner and W. Zettlmeier in *Handbook of Enantioselective Catalysis*, VCH, Weinheim, 1993; (c) T. V. RajanBabu and T. A. Ayers, *Tetrahedron Lett.*, 1994, **35**, 4295; (*d*) M. T. Reetz and T. Neugebauer, *Angew. Chem., Int. Ed.*, 1999, **38**, 179; (*e*) T. V. RajanBabu, B. Radetich, K. K. You, T. A. Ayers, A. L. Casalnuovo and J. C. Calebrese, *J. Org. Chem.*, 1999, **64**, 3429 and references cited therein; (*f*) K. Yonehara, T. Hashizume, K. Mori, K. Ohe and S. Uemura, *Chem. Commun.*, 1999, 415

7 (*a*) G. J. H. Buisman, M. E. Martin, E. J. Vos, A. Klootwijk, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Tetrahedron: Asymmetry*, 1995, **6**, 719; (*b*) O. Pàmies, G. Net, A. Ruiz and C. Claver, *Tetrahedron: Asymmetry*, 2000, **11**, 1097.

8 (*a*) O. Pàmies, G. Net, A. Ruiz, C. Bó, J. M. Poblet and C. Claver, *J. Organomet. Chem.*, 1999, **586**, 125; (*b*) O. Pàmies, M. Diéguez, G. Net, A. Ruiz and C. Claver, *J. Chem. Soc., Dalton Trans.*, 1999, 3439; (*c*) O. Pàmies, G. Net, A. Ruiz and C. Claver, *Tetrahedron: Asymmetry*, 1999, **10**, 2007; (*d*) O. Pàmies, M. Diéguez, G. Net, A. Ruiz and C. Claver, *Organometallics*, 2000, **19**, 1488; (*e*) O. Pàmies, G. Net, A. Ruiz and C. Claver, *Eur. J. Inorg. Chem.*, in the press.

9 *Selected data for* **4**: δ_P (CD_2Cl_2, 233 K) 144.6 (d, 1P, J_{P-P} = 30.9 Hz), 145.1 (d, 1P, J_{P-P} = 30.9 Hz).

10 O. T. Schmidt in *Methods in Carbohydrate Chemistry*, eds. R. L. Whistler and M. L. Wolfrom, Academic Press, New York, 1963, Vol. II.

11 Compound **6** was preprared by a minor modification of the procedure described in M. Nakjima and S. Takahashi, *Agric. Biol. Chem.*, 1967, **31**, 1079.

12 J. Hiebl and E. Zbiral, *Monatsh. Chem.*, 1990, **121**, 691.

13 3,3′-di-*tert*-butyl-5,5′-dimethoxy-1,1′-biphenyl-2,2′-diyl phosphorochloridite is easily prepared in one step from the corresponding biphenol as described in (*a*) G. J. H. Buisman, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Tetrahedron: Asymmetry*, 1993, **4**, 1625. The corresponding biphenol is easily prepared on large scale in the same way as the related 4,4′,6,6′-tetra-*tert*-butyl-2,2′-biphenol described in (*b*) T. Jongsma, M. Fossen and P. W. N. M. van Leeuwen, *J. Mol. Catal.*, 1993, **83**, 17.

14 The standard hydroformylation procedure is described in ref. 8*d*.

15 A. van Rooy, E. N. Orij, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Organometallics*, 1995, **14**, 34.