Angewandte Chemie

DOI: 10.1002/anie.200701255

Hydroformylation Catalysts

Catalysis by Design: Wide-Bite-Angle Diphosphines by Assembly of Ditopic Ligands for Selective Rhodium-Catalyzed Hydroformylation**

*David Rivillo, Henrik Gulyás, Jordi Benet-Buchholz, Eduardo C. Escudero-Adán, Zoraida Freixa, and Piet W. N. M. van Leeuwen**

Dedicated to Süd-Chemie on the occasion of its 150th anniversary

Diphosphines are powerful ligands in homogeneous catalysis.[1] Until a decade ago, the ligands, with very few exceptions,[2] contained a covalently bonded backbone holding the two phosphorus donors together. More recently, bidentate diphosphines have been assembled by strong[2] or weak[3] hydrogen-bond interactions, assembly metal interactions,[4] and ionic interactions.[5] All of these approaches are well-known in supramolecular chemistry and have recently been used in organometallic complexes.[6] Also, monophosphorus ligand systems without predetermined interactions turned out to be extremely effective in a number of cases,[7] as did mixed monophosphorus ligands.[8] A modular approach using monodentate ligands and their connectors[4,8,9] gives access to large libraries of new and potentially selective catalysts.

Many catalytic reactions carried out using catalysts with bidentate phosphorus ligands are highly sensitive to the bite angle of the diphosphine. There are rhodium-catalyzed hydroformylation,[10] nickel- and palladium-catalyzed hydrocyanation,[11] and palladium-catalyzed cross-coupling reactions[12] in which either the rate or the selectivity was considerably improved by the use of, for instance, Xantphos (4,5-bis(diphenylphosphino)-9,9-dimethyl-xanthene), which has a natural bite angle of approximately 110°.[13] In some cases, hydrogen-bonded bidentate ligand systems may suffice to give results that equal or surpass those of covalently bonded bidentate diphosphines.[2,3]

Herein, we focus on modular ditopic ligands that contain an anionic site and a soft donor phosphorus atom. The former will be used to bind a hard metal for assembling the bidentate phosphine ligand, while the latter binds a soft metal involved in catalysis.[4] We use this approach to prepare wide-bite-angle diphosphine ligands. The two fragments of the ditopic ligand, together with the hard metal (which can form a tetrahedral, square-planar, octahedral, or (bi)pyramidal coordination sphere) might give rise to a large variety of ligands, thus requiring a minimum of synthetic effort. In view of the strong bonds involved, these molecules should be more amenable to design by molecular mechanics than those containing weaker hydrogen bonds or nondirectional ionic interactions.

To this end, we synthesized the ditopic ligands **1**–**6** (Scheme 1). Ligands **1**–**3** are based on 3-diphenylphosphino-2-hydroxy-5-methylbenzaldehyde **13**, reported without the 5-methyl group by Börner and co-workers,[4a,b] who used it (assembled with an asymmetric diamine and $\mathrm{Ti(O}i\mathrm{Pr)_4}$ to give Salenophos) for asymmetric rhodium-catalyzed hydroformylation.

For the synthesis of **1**–**3**, the appropriate amines were treated with **13**. The ditopic ligands **4** and **6** are made by condensation of the corresponding aldehyde and 3-diphenylphosphinoaniline, and **5** is synthesized from 3-(diphenylphosphino)benzaldehyde. In general, the Schiff base condensation reactions were carried out in toluene heated at reflux in the presence of molecular sieves. The assembled bidentate phosphine ligands **7**–**12** were prepared by reaction of **1**–**6** with $[\mathrm{Zn\{N(SiMe_3)_2\}_2}]$ or $\mathrm{Ti(O}i\mathrm{Pr)_4}$ (see the Supporting Information). Molecular modeling calculations showed that in particular the assemblies **10**–**12** might be interesting as wide-bite-angle ligands. On the one hand, this approach allows screening of large numbers of catalysts, but on the other hand, sophisticated guesses must be made; indeed, **7**–**9** are less promising, as we will see below, both for structural and for reactivity reasons. Note that **8** and **9** are isostructural with SPANphos (SPANphos = 4,4,4′,4′6,6′-hexamethylspiro-2,2′-bichroman-8,8′-bis(diphenylphosphino)), which gave several wide-bite-angle complexes[14] in which the spiro carbon atom fragment $(\mathrm{CH_2})_2\mathrm{C(O)}_2$ has been replaced by the zinc fragment $(=\mathrm{NR})_2\mathrm{Zn(O)}_2$. For several of these bidentate phosphine assemblies, crystal structures were obtained. Figure 1 shows the X-ray structure of **12**.[15]

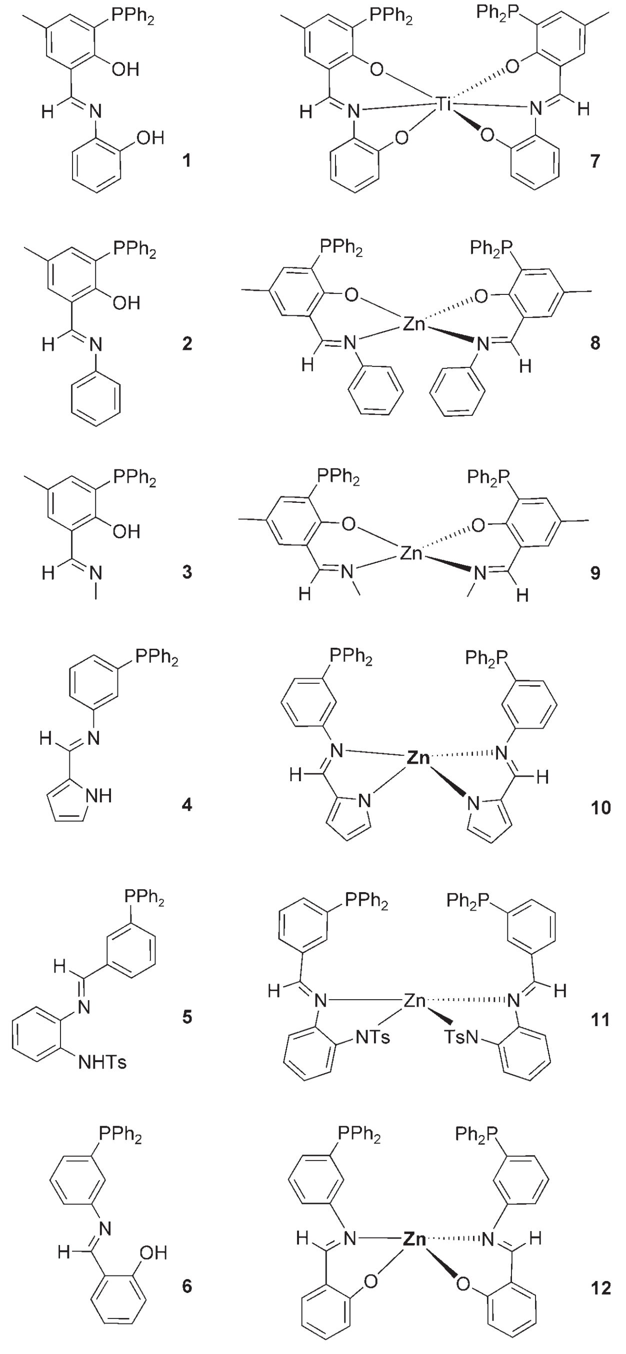
The coordination geometry of the zinc center in **12** is a distorted tetrahedron. The distance between the two phosphorous atoms is 7.7 Å, but this can be shortened without raising the energy by rotating the phenyl groups. The natural bite angle calculated by molecular mechanics (MM) for a complex with a rhodium or palladium center without configurational preference was approximately 110°. The corresponding $\mathrm{P}\cdots\mathrm{P}$ separations found in the preliminary crystal structures for **10** and **11** are 8 and 6.5 Å,[16] but these show the same flexibility as **12**. Preliminary crystal structures of **7** and **8**

---

[*] D. Rivillo, Dr. H. Gulyás, Dr. J. Benet-Buchholz, E. C. Escudero-Adán, Dr. Z. Freixa, Prof. P. W. N. M. van Leeuwen
Institute of Chemical Research of Catalonia (ICIQ)
Av. Països Catalans 16, 43007 Tarragona (Spain)
Fax: (+34) 977-920-221
E-mail: pvanleeuwen@iciq.es
Homepage: http://www.iciq.es/english/grups_eng/vanleeuwen/entrada.htm

[**] Spanish MEC is kindly acknowledged for a "Ramón y Cajal" contract (Z. Freixa), project CTQ2005-03416/BQU and Consolider Ingenio 2010 (Grant N CSD2006_0003). Dr. Cristina Jiménez, Josep Maria López, Dr. Jonathan Barr, Susana Delgado and Enrique Cequier are acknowledged for technical support.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.



Scheme 1. Synthesized ligands.

show P···P distances of 6 and 8 Å, but since these compounds are more rigid, it may be more difficult to form bidentate complexes. Notably, complex **7** shows *trans* nitrogen ligands, which is not the case for the titanium complex reported by Börner and co-workers,[4b] as the nitrogen atoms form part of a 1,2-diphenyl-1,2-diaminoethane bridge. The new diphosphine ligands **7**–**12** react with a variety of common rhodium and palladium precursors ($[Rh(nbd)]^+$, [Rh(acac)], [PdMeCl]; nbd = 2,5-nobornadiene, acac = acetylacetonate) to both *cis* and *trans* complexes, which will be reported elsewhere.[16]

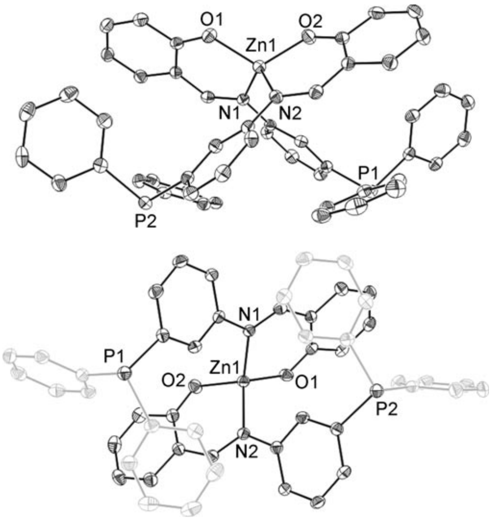


Figure 1. ORTEP plot of the molecular structure of **12** in two different projections. Thermal ellipsoids are set at the 50% probability level; hydrogen atoms are omitted for clarity. Selected interatomic separations [Å] and bond angles [°]: P1–P2 7.7; N1-Zn1-O1 97.45(8), O1-Zn-O2 117.20(8), N1-Zn1-N2 118.82(8), N2-Zn1-O2 98.05(8).

To study the effect of the assembly of monophosphine ligands **1**–**6** into diphosphine ligands **7**–**12** on the catalytic properties, all ligands were used in the rhodium-catalyzed hydroformylation of 1-octene (Table 1). Optimal phosphine-to-rhodium ratios (at 1 mM Rh) are different for mono- and diphosphines, and convenient average concentrations were used.[17] An incubation time of 3 h was used before 1-octene was added to the catalyst solution under pressure, as in situ IR spectroscopy measurements showed that in most cases the formation of $[HRh(CO)_2(phosphine)_2]$ from $[Rh(CO)_2(acac)]$ and the ligands took about 3 h at 80 °C and 20 bar of syn gas. Ditopic ligands **1**–**3** and their assemblies **7**–**9** gave poor

Table 1: Rhodium-catalyzed hydroformylation of 1-octene.[a]

Entry	Ligand L	L/Rh	Conv. [%][b]	Linear aldeh. [%][c]	l/b	Isom. [%][c]	TOF $\times 10^{-3}$[d]
1	**4**	4	100	59	2.9	20	1.5
2	**4**	20	100	70	3.2	8	1.2
3	**10**	2	98	76	5.1	9	0.9
4	**10**	10	91	79	6.1	8	0.9
5	**5**	20	100	68	3.4	12	0.9
6	**11**	2	100	71	3.5	9	0.8
7	**11**	10	92	81	13[e]	13	0.8
8	**6**	4	100	62	2.8	16	1.4
9	**6**	20	100	68	3.6	13	1.2
10	**12**	2	100	74	4.9	11	1.5
11	**12**	10	95	84	21	12	0.9
12	PPh_3[f]	20	98	65	2.5	9	1.8
13	Xantphos[g]	2.2	–	97	54	0.5	0.8

[a] Conditions: $T = 80$ °C, $CO/H_2 = 1$, $P(CO/H_2) = 10$ bar, [Rh] = 1 mM in toluene, substrate/Rh = 670. [b] Percentage of 1-octene converted determined at 2 h of reaction. [c] Percentage of linear aldehyde and isomerization from the total of reaction products calculated after 2 h. [d] Average turnover frequency in mol mol^{-1} h^{-1} determined at 40% alkene conversion. [e] l/b ratio evolves during reaction (25–11; 0.4–3 h). [f] Data from reference [3a]. [g] Data from reference [10].

catalysts (not shown in Table 1), most likely because of formation of salen complexes or phosphinophenolate complexes of rhodium. In situ IR spectroscopy of **4** showed bands at 2074 and 2009 $\mathrm{cm^{-1}}$, which indicate the presence of a dicarbonyl rhodium(I) species, in accordance with literature data of similar complexes.[18]

Ligands **4**–**6** show catalytic performance close to that of $\mathrm{PPh_3}$ (Table 1, entry 12) in terms of both selectivity and rate. Isomerization decreases when more ligand is used (Table 1, entries 1 and 2), and the linear/branched ratio goes up. Consistently, ligands **4**–**6** give higher l/b ratios than $\mathrm{PPh_3}$ (e.g. 3.4 for Table 1, entry 5 vs. 2.5 for entry 12), which may point to an intramolecular interaction between the two salen or salen-like fragments through hydrogen-bond interactions. The assembled bidentate diphosphines **10**–**12** with their calculated natural bite angles of 110–120° indeed gave higher l/b ratios than the corresponding monodentate ligands. The initial linear/branched ratio for **11** was as high as 25 (Table 1, entry 7). Ligand **12** gave a more stable system with a l/b ratio of 21. The rates are about half those of the monodentate ligands, which is also true for Xantphos (Table 1, entry 13) compared to $\mathrm{PPh_3}$; Xantphos typically gives higher l/b ratios (25–60). Isomerization remains relativly high for **10**–**12**, which may be due to the low pressure applied or to the presence of other $\mathrm{Rh^I}$ species. Indeed, the in situ high-pressure IR spectra of complexes of **10** show the same species as with **4** in low concentrations. The in situ IR spectra of **6** and **12** both show the characteristic bands for a $\mathrm{[HRh(CO)_2(arylphosphine)_2]}$ species at 2044, 1987 (broad, two peaks), and 1956 $\mathrm{cm^{-1}}$ (**6** shows a few more absorptions), but in the spectrum of **12**, the intensity of the bisequatorial diphosphine species (2044 and 1987 $\mathrm{cm^{-1}}$) is considerably stronger (fulfilling our expectations), at the expense of the equatorial–apical species (1987 and 1956 $\mathrm{cm^{-1}}$). These findings nicely explain the increased preference for the formation of linear aldehyde with ligand **12**.[17]

In summary, we have extended the number of ditopic ligands that bind with their hard donor atoms N and O to an assembly metal (herein zinc and titanium) and to a soft metal such as rhodium(I) through their P donor atom. While the class of compounds is not new, we have shown that by proper selection, catalytically active and selective species can be generated in a facile manner. MM calculations have shown that assembly by tetrahedral zinc centers may lead to wide-bite-angle diphosphine ligands. It was found that the assemblies indeed give high selectivities for linear product in the rhodium-catalyzed hydroformylation of 1-octene. The method presented herein is extremely versatile, as both the building blocks of the ditopic ligands and the assembly metal can be varied extensively. The synthesis of the diphosphine ligands usually involves only three steps. Furthermore, the assembly metal fragments can be modified by additional donor molecules or additional anionic fragments, which could be used to make the ligands chiral.

Received: March 21, 2007

Keywords: ditopic ligands · homogeneous catalysis · hydroformylation · supramolecular catalysis · wide bite angles

---

[1] Z. Freixa, P. W. N. M. van Leeuwen, *Dalton Trans.* **2003**, 1890 – 1901.

[2] P. W. N. M. van Leeuwen, C. F. Roobeek, R. L. Wife, J. H. G. Frijns, *J. Chem. Soc. Chem. Commun.* **1986**, 31 – 33.

[3] a) B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608 – 6609; b) L. K. Knight, Z. Freixa, P. W. N. M. van Leeuwen, J. N. H. Reek, *Organometallics* **2006**, *25*, 954 – 960; c) P. A. Duckmanton, A. J. Blake, J. B. Love, *Inorg. Chem.* **2005**, *44*, 7708 – 7710.

[4] a) A. Kless, R. Kadyrov, A. Boerner, J. Holz, H. B. Kagan, *Tetrahedron Lett.* **1995**, *36*, 4601 – 4602; b) A. Kless, C. Lefeber, A. Spannenberg, R. Kempe, W. Baumann, J. Holz, A. Boerner, *Tetrahedron* **1996**, *52*, 14599 – 14606; c) J. M. Takacs, D. S. Reddy, S. A. Moteki, D. Palencia, H. Wu, *J. Am. Chem. Soc.* **2004**, *126*, 4494; d) D. H. Leung, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2007**, *129*, 2746 – 2747; e) X. Sun, D. W. Johnson, D. L. Caulder, R. E. Powers, K. N. Raymond, E. H. Wong, *Angew. Chem.* **1999**, *111*, 1386 – 1390; *Angew. Chem. Int. Ed.* **1999**, *38*, 1303 – 1307; f) F. Lam, J. X. Xu, K. S. Chan, *J. Org. Chem.* **1996**, *61*, 8414 – 8418; g) S. Chikkali, D. Gudat, M. Niemeyer, *Chem. Commun.* **2007**, 981 – 983.

[5] H. Gulyás, J. Benet-Buchholz, E. C. Escudero-Adán, Z. Freixa, P. W. N. M. van Leeuwen, *Chem. Eur. J.* **2007**, *13*, 3424 – 3430.

[6] T. S. Koblenz, H. L. Dekker, C. G. de Koster, P. W. N. M. van Leeuwen, J. N. H. Reek, *Chem. Commun.* **2006**, 1700 – 1702.

[7] a) C. Claver, E. Fernandez, A. Gillon, K. Heslop, D. J. Hyett, A. Martorell, A. G. Orpen, P. G. Pringle, *Chem. Commun.* **2000**, 961 – 962; b) M. van den Berg, A. J. Minnaard, E. P. Schudde, J. van Esch, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *J. Am. Chem. Soc.* **2000**, *122*, 11539 – 11540; c) M. T. Reetz, G. Mehler, *Angew. Chem.* **2000**, *112*, 4047 – 4049; *Angew. Chem. Int. Ed.* **2000**, *39*, 3889 – 3890.

[8] a) M. T. Reetz, T. Sell, A. Meiswinkel, G. Mehler, *Angew. Chem.* **2003**, *115*, 814 – 817; *Angew. Chem. Int. Ed.* **2003**, *42*, 790 – 793; b) D. Peña, A. J. Minnaard, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Org. Biomol. Chem.* **2003**, *1*, 1087 – 1089; c) M. T. Reetz, X. Li, *Angew. Chem.* **2005**, *117*, 3019 – 3021; *Angew. Chem. Int. Ed.* **2005**, *44*, 2959 – 2962; d) M. Kuil, P. E. Goudriaan, P. W. N. M. van Leeuwen, J. N. H. Reek, *Chem. Commun.* **2006**, 4679 – 4681; e) V. F. Slagt, P. W. N. M. van Leeuwen, J. N. H. Reek, *Angew. Chem.* **2003**, *115*, 5777 – 5781; *Angew. Chem. Int. Ed.* **2003**, *42*, 5619 – 5623.

[9] X.-B. Jiang, L. Lefort, P. E. Goudriaan, A. H. M. de Vries, P. W. N. M. van Leeuwen, J. G. de Vries, J. N. H. Reek, *Angew. Chem.* **2006**, *118*, 1245 – 1249; *Angew. Chem. Int. Ed.* **2006**, *45*, 1223 – 1227.

[10] M. Kranenburg, Y. E. M. van der Burgt, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **1995**, *14*, 3081 – 3089.

[11] M. Kranenburg, P. C. J. Kamer, P. W. N. M. van Leeuwen, D. Vogt, W. Keim, *J. Chem. Soc. Chem. Commun.* **1995**, 2177 – 2778.

[12] a) M. C. Harris, O. Geis, S. L. Buchwald, *J. Org. Chem.* **1999**, *64*, 6019 – 6022; b) Y. Guari, D. S. van Es, J. N. H. Reek, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Tetrahedron Lett.* **1999**, *40*, 3789 – 3790.

[13] C. P. Casey, G. T. Whiteker, *Isr. J. Chem.* **1990**, *30*, 299 – 304.

[14] C. Jiménez-Rodríguez, F. X. Roca, C. Bo, J. Benet-Buchholz, E. C. Escudero-Adán, Z. Freixa, P. W. N. M. van Leeuwen, *Dalton Trans.* **2006**, 268 – 278.

[15] X-ray structure determination: Crystals of **12** were obtained by slow diffusion of cyclohexane into dichloromethane at room temperature. Although the measured crystal was stable under atmospheric conditions, it was prepared under inert conditions and immersed in perfluoropolyether for manipulation. Measurements were made on a Bruker–Nonius diffractometer equipped

with an APPEX 2 4 K CCD area detector, a FR591 rotating anode with $\text{Mo}_{K\alpha}$ radiation, Montel mirrors as monochromator, and a Kryoflex low-temperature device ($T=-173$ °C). Full-sphere data collection was used with ω and ϕ scans. Programs used: Data collection Apex2V. 1.0–22 (Bruker-Nonius 2004), data reduction Saint+ Version 6.22 (Bruker-Nonius 2001), and absorption correction SADABS V. 2.10 (2003). For structure solution and refinement, SHELXTL Version 6.10 (Sheldrick, 2000) was used. Crystal data for **12** at 100 K: $C_{50}H_{38}N_2O_2P_2Zn_1$, 826.13 g mol^{-1}, orthorhombic, space group *Pbca*, $a=15.8553(14)$, $b=18.3592(18)$, $c=26.862(2)$ Å, $V=7819.2(12)$ Å^3, $Z=8$, $\rho_{calcd}=1.404$ Mg m^{-3}, $R_1=0.0495$ (0.1014), $wR2=0.1059$ (0.1278), for 7205 reflections with $I>2\sigma(I)$ (for 11 564 reflections [R_{int}: 0.1609] with a total measured of 91 491 reflections), goodness-of-fit on $F^2=1.000$, largest difference peak (hole) = 0.568 (−0.835) e Å^{-3}. CCDC-641173 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[16] D. Rivillo, H. Gulyás, J. Benet-Buchholz, E. C. Escudero-Adán, Z. Freixa, P. W. N. M. van Leeuwen, unpublished results.

[17] a) P. W. N. M. van Leeuwen, C. P. Casey, G. T. Whiteker, *Catalysis by Metal Complexes*, *Vol. 22*, Kluwer, Dordrecht, **2000**, chap. 4, pp. 63–105; b) L. A. van der Veen, P. H. Keeven, G. C. Schoemaker, J. N. H. Reek, P. C. J. Kamer, P. W. N. M. van Leeuwen, M. Lutz, A. L. Spek, *Organometallics* **2000**, *19*, 872–883.

[18] J. H. H. Ho, D. St Clair Black, B. A. Messerle, J. K. Clegg, P. Turner, *Organometallics* **2006**, *25*, 5800–5810.