



Modular diphosphine ligands based on bisphenol A backbones

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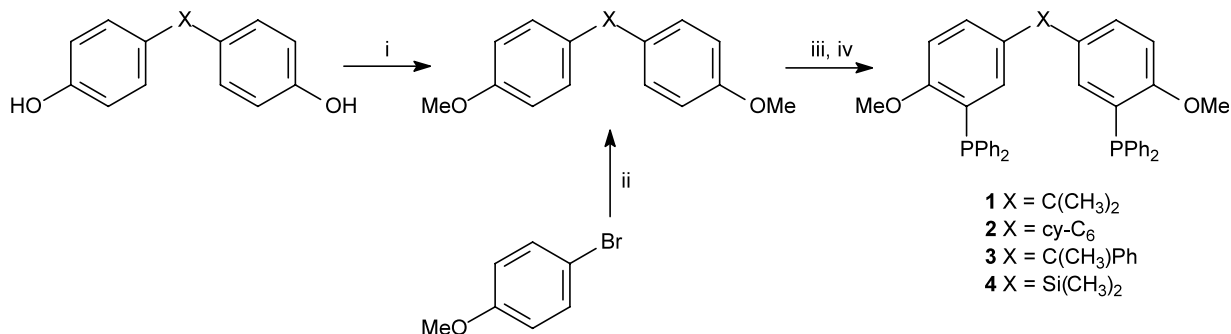
Abstract—A straightforward two-step synthesis is used to obtain new phosphorus-containing ligands based on readily available bisphenol A type backbones. Five diphosphine ligands have been prepared in good yields. An X-ray crystallographic study is presented for ligand **5**. Preliminary results on rhodium-catalyzed hydroformylation exemplify the use of these ligands for homogeneous catalysis. © 2003 Elsevier Science Ltd. All rights reserved.

Homogeneous catalysis has proven to be a very powerful tool for the synthesis of various intermediates and fine chemicals.¹ The success of homogeneous transition metal catalysts strongly depends on the ligands used. A large number of the ligands applied in such reactions are based on phosphorus donors and backbones such as biphenyl,² xanthene³ or norbornene.⁴ Frequently the starting materials are either expensive or not commercially available. In addition, structural variations and exchange of functional groups is not always easy in these systems while nowadays the aim is to create modular, highly variable ligand classes made from readily available materials.

We have selected bisphenol A and its derivatives as starting compounds for the development of modular

ligand classes. A broad variety of these bisphenols are commercially available at low cost since they are major components in epoxy resins.⁵ Generic structures are easily accessible by simple acid-catalyzed condensation of a ketone with two molecules of a phenol. Here we report the first examples of a new class of ligands based on bisphenol A type backbones. Their application in the rhodium-catalyzed hydroformylation of 1-octene exemplifies their use and potential for homogeneously catalyzed reactions.

Based on three derivatives of bisphenol A, we applied a simple, straightforward two-step synthetic route (Scheme 1). The approach was to use protected phenolic OH-groups as directing groups for the selective *ortho*-lithiation of both phenyl rings followed by reac-



Scheme 1. Synthetic methodology to generic ligands **1–4**. *Reagents and conditions:* (i) MeI, K₂CO₃, acetone, reflux 16 h, 85%; (ii) *n*-BuLi, TMEDA, –15°C, ether, 1 h, then SiCl₂Me₂, 72%; (iii) *n*-BuLi, TMEDA, –15°C, ether, 16 h, then ClPPh₂, hexanes, 0°C, 16 h, 60%.

Keywords: bisphenol A; terphenyl; modular backbone; diphosphine ligand; homogeneous catalysis; rhodium.

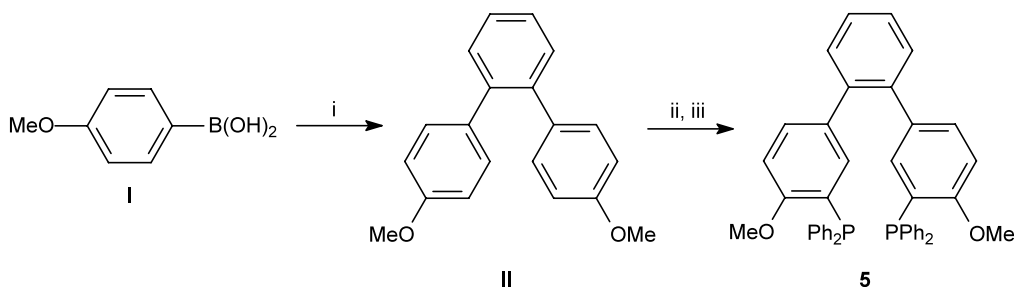
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tion with a suitable phosphorus compound, in this case ClPPh_2 . In this manner a wide range of phosphorus containing ligands is accessible. Using this method we obtained ligands **1–3** based on bisphenol A derived backbones.⁶

This modular approach allows for variation in rigidity, steric bulk and electronic properties of the ligands. Introduction of other P-containing groups is also an option, leading to, for instance, phosphonites.⁷ Taking advantage of the selective *ortho*-lithiation approach, and starting from 4-bromoanisole we also synthesized a silicon-bridged bisphenol ligand **4** as well as a ligand based on a terphenyl backbone, ligand **5**, which we have named Terphos (Scheme 2). In this latter case, the appropriate backbone, compound **II**, which was obtained in two steps via palladium-catalyzed Suzuki-coupling using 1,2-dibromobenzene, has been reported by Blake et al., with a yield of only 66% when using $\text{Ba}(\text{OH})_2$ as the base.⁸ We improved the yield of this

particular reaction to 85% using Na_2CO_3 as the base. Simple workup by filtration and evaporation of the solvent followed by washing of the crude product with methanol afforded the pure compounds in overall yields of 40–50%.

Ligand **5** could be crystallized from hot acetonitrile which gave crystals suitable for X-ray analysis.⁹ The molecular structure of **5** is depicted in Figure 1 together with selected bond lengths and angles. The terphenyl backbone has an approximately C_2 symmetry, the two peripheral aromatic rings being tilted at angles of 48.22(9) and 49.70(9)° with respect to the central ring. Because of the rotational freedom of the peripheral aryl rings of the terphenyl backbone, the diphenylphosphine groups are not constrained to any particular mutual orientation. The dihedral angles between the aromatic rings in the backbone are calculated to be 115.8 and 144.4° giving rise to the different spatial arrangements of the phosphorus atoms.



Scheme 2. Synthetic-route to ligand **5**. *Reagents and conditions:* (i) 1,2-dibromobenzene, Na_2CO_3 , $\text{Pd}(\text{PPh}_3)_4$, DME, H_2O , Δ , 16 h, 85%; (ii) *n*-BuLi, TMEDA, -40°C , Et_2O , 16 h; (iii) ClPPh_2 , hexanes, 0°C , 16 h, 60%.

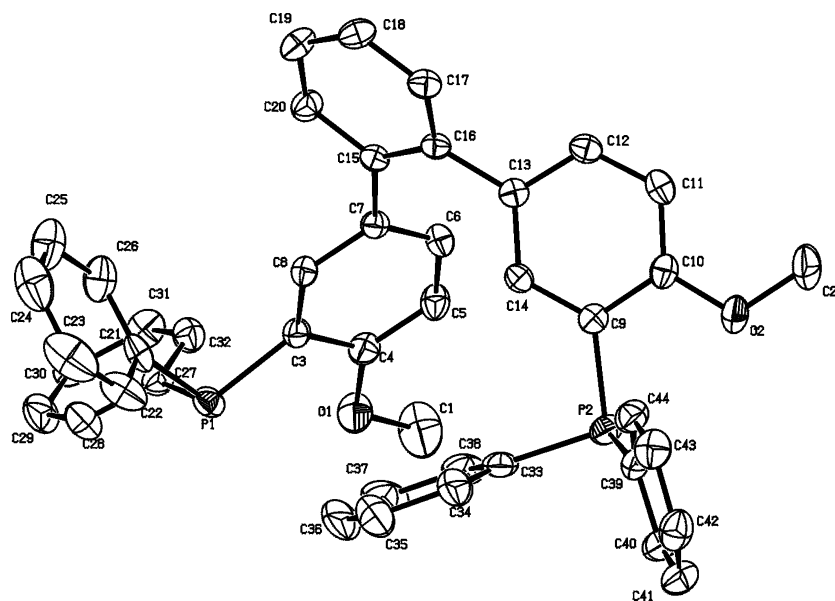


Figure 1. Ortep drawing of the crystal structure of ligand **5** (Terphos). Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths (Å): $\text{P}_1\text{--C}_3$ 1.8322(19), $\text{P}_2\text{--C}_9$ 1.8362(19), $\text{O}_1\text{--C}_1$ 1.431(3), $\text{O}_2\text{--C}_2$ 1.433(3). Selected bond angles ($^\circ$): $\text{C}_3\text{--P}_1\text{--C}_{21}$ 101.85(9), $\text{C}_3\text{--P}_1\text{--C}_{27}$ 105.36(8), $\text{C}_{21}\text{--P}_1\text{--C}_{27}$ 101.13(9), $\text{C}_9\text{--P}_2\text{--C}_{33}$ 101.81(9), $\text{C}_9\text{--P}_2\text{--C}_{39}$ 104.56(9), $\text{C}_{33}\text{--P}_2\text{--C}_{39}$ 100.62(9), $\text{C}_1\text{--O}_1\text{--C}_4$ 117.83(18), $\text{C}_2\text{--O}_2\text{--C}_{10}$ 116.34(16), $\text{C}_7\text{--C}_{15}\text{--C}_{16}$ 124.69(16), $\text{C}_{13}\text{--C}_{16}\text{--C}_{15}$ 125.16(16).

Our approach is not comparable to earlier work on the synthesis of ligands based on bisphenol A type backbones. To the best of our knowledge there are only two reports so far in the literature using bisphenol A as a building block for phosphorus ligands; however, they deal with the functionalization of the phenolic OH-groups¹⁰ and the formation of phosphite-bridged macrocycles.¹¹

To illustrate the applicability of the new phosphorus ligands in homogeneous catalysis, we chose the rhodium catalyzed hydroformylation of 1-octene as an example (Scheme 3). The catalysis was carried out under typical hydroformylation conditions, 20 bar of syngas (CO/H₂ 1:1) and a temperature of 80°C.

There is a direct influence of the flexibility and steric crowding of the central-atom in the backbone skeleton on the activity of the corresponding catalyst. The least rigid ligand **1** (entry 1, Table 1) gave a TOF of 735 h⁻¹. The activity was improved to a TOF of 1029 h⁻¹ when a cyclohexyl-moiety was present in the backbone of ligand **2** (entry 2) while with ligand **3** the activity increased further to a TOF of 1418 h⁻¹ (entry 3). Selectivity for the terminal aldehyde is moderate with a linear to branched (l/b) ratio of about 3. This is expected as these ligands are not optimized to obtain a high regioselectivity, as far as rigidity, bulkiness and bite-angle are concerned. For ligand **4** (entry 4) the activity was unexpected since it was thought to resemble ligand **1**.

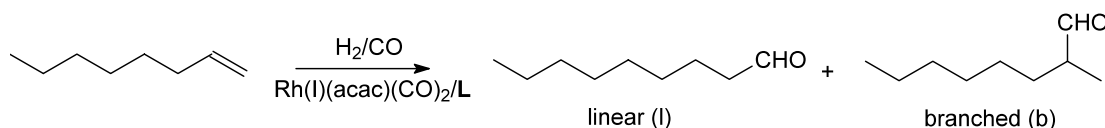
Ligand **5** turned out to give the highest activity, with a turnover frequency up to nearly 3500 h⁻¹ which leads to a conversion of nearly 22% after 15 min (entry 5). No side reactions such as hydrogenation and isomerization

of the substrate occurred. Furthermore, the catalytic system based on Terphos (ligand **5**) shows the typical behavior expected for diphosphine ligands concerning the influence of temperature, pressure and CO/H₂ ratio (entries 6–9).

In conclusion, we have described a two-step synthetic route to a new and modular class of phosphorus containing ligands, based on bisphenol A derived skeletons. As a first introduction four diphosphine ligands were prepared in good yields. Based on the same methodology, we used a new terphenyl backbone to obtain a fifth ligand, Terphos. For this ligand the X-ray structure is presented. In the rhodium-catalyzed hydroformylation of 1-octene high activities were obtained, especially for ligand **5**. For this new class of ligands we are currently investigating the coordination with various transition metals and the activity in other catalytic reactions. The family will be extended by introduction of other phosphorus containing groups.

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Scheme 3. Hydroformylation of 1-octene.

Table 1. Hydroformylation of 1-octene catalyzed by [Rh(acac)(CO)₂]/**1–5**^a

Entry	Ligand	Time (min)	Temperature (°C)	<i>p</i> (bar)	Conversion (%) ^b	Sel. _{aldehyde} (%) ^b	l/b ratio ^b	TOF (h ⁻¹) ^c
1	1	60	80	20	18.8	97.9	2.8	735
2	2	60	80	20	26.8	99.0	2.9	1029
3	3	60	80	20	35.4	99.2	2.7	1418
4	4	60	80	20	31.6	99.3	2.9	1250
5	5	15	80	20	21.8	98.1	3.0	3485
6	5	60	80	30	40.0	97.6	2.9	1615
7	5	60	70	20	20.3	98.4	3.0	800
8	5	60	60	20	8.3	98.3	3.0	325
9	5	60	60	20 ^d	15.8	98.9	2.4	620

^a Reaction conditions: 1-octene (31.0 mmol), [Rh(acac)(CO)₂] (0.39 mM), decane (12.5 mmol), toluene (12.7 mL), 1-octene:Rh=4000:1, preformation time 1 h, L:Rh=6:1.

^b Determined by GC.

^c TOF in mol 1-octene·mol Rh⁻¹ h⁻¹ determined by GC.

^d *p*(H₂):*p*(CO)=3:1.

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9. Crystal data for **5**: [C₄₄H₃₆O₂P₂], *M_w* = 658.67 g mol⁻¹, triclinic space group *P* $\bar{1}$ (no. 2), *Z* = 2 in cell with the following dimensions: *a* = 9.4589(1) Å, *b* = 0110.8619(2) Å, *c* = 18.4500(3) Å, α = 80.1013(7)°, β = 76.3222(6)°, γ = 78.9500(10)°, *V* = 1791.68(5) Å³, *D_{calcd}* = 1.221 g cm⁻³, 435 parameters, 0 restraints, *R*(*F*) = 0.0467 [*I* > 2σ(*I*)], *wR*(*F*²) = 0.1193, *S* = 1.03, Δ_{*p*}max/Δ_{*p*}min = 0.39/−0.34 e Å⁻³. The data were collected at 150 K for a single crystal (0.27 × 0.15 × 0.09 mm³) on a Nonius Kappa CCD diffractometer with rotating anode (λ(Mo Kα) = 0.71073 Å). Of μ = 0.158 mm⁻¹, 28679 measured reflections, and 8182 were unique reflections (2θ_{max} = 27.5, *R*_{int} = 0.058). An absorption correction was considered unnecessary. The structure was solved by direct methods using SHELXS-97,^{9a} and refined on *F*² by least-squares procedures using SHELXL-97.^{9b} All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were constrained to idealized geometries and allowed to ride on their carrier atoms with an isotropic displacement parameter related to the equivalent displacement parameter of their carrier atoms. Structure validation and molecular graphics preparation were performed with the PLATON package.^{9c} CCDC 198081 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk). (a) Sheldrick, G. M. SHELXS-97. University of Göttingen, Germany, 1997. (b) Sheldrick, G. M. SHELXL-97. University of Göttingen, Germany, 1997. (c) Spek, A. L. PLATON, A Multipurpose Crystallographic Tool, Utrecht University, The Netherlands, 2002.
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