Self-Assembly of Bidentate Ligands for Combinatorial Homogeneous Catalysis Based on an A–T Base-Pair Model[3]

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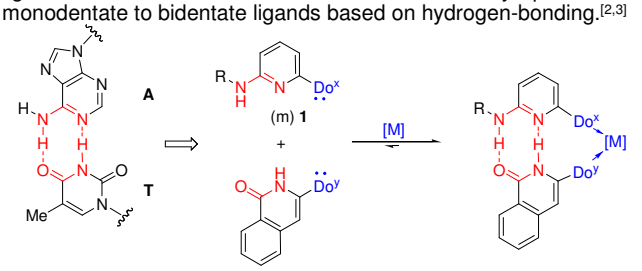
Introduction

Selectivity control in homogeneous metal complex catalysis relies in many cases on tailor-made bidentate ligands. The quest for the ultimate ligand giving rise to a catalyst with optimal activity and selectivity is a difficult task. Since rational design still does not allow to predict the ligand of choice for a given reaction and substrate, methods for combinatorial synthesis of ligand libraries have become an additional strategy.[1] However, the rate determining step in catalyst development is in most cases the time-consuming ligand synthesis.

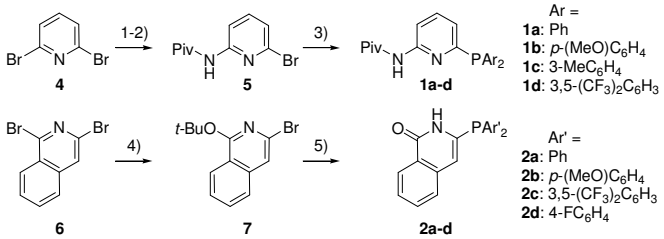
Results

We herein report on an alternative approach to generate bidentate ligand libraries that relies on a self-assembly process of monodentate to bidentate ligands based on hydrogen-bonding.[2,3]



Scheme 1: An A–T base-pair model (highlighted in red) as a platform for the self-assembly of monomeric to mixed bidentate ligands.

Basis for success of this concept is the use of an A–T base-pair analogous platform – the aminopyridine **1** / isoquinolone **2** self-assembling system. Synthesis of the ligands was straightforward starting from simple heterocyclic precursors (Scheme 2).



Scheme 2: Synthesis of monodentate aminopyridines **1** and isoquinolones **2**: 1) NH_4OH, 190 °C, 5 h; 2) pivaloylchloride, NEt_3, CH_2Cl_2, 0 °C → RT; 3) *n*-BuLi (2 equiv), THF, – 100 °C, then $ClPR_2$, – 100 °C → RT; 4) KO*t*-Bu (1.1 equiv), toluene, 80 °C, 1 h; 5) *n*-BuLi (1 equiv), THF, – 100 °C, then $ClPR_2$, – 100 °C → RT, then H_2O (1 equiv) and formic acid excess (50–75%).

Mixing of one equivalent of 6-diphenylphosphino-*N*-pivaloyl-2-aminopyridine (6-DPPAP; **1a**) with one equivalent of 3-diphenylphosphinoisoquinolone (3-DPICon; **2a**) in the presence of $[PtCl_2(1,5\text{-cod})]$ gave the heteroleptic complex *cis*-[(**1a**,**2a**)$PtCl_2$] in quantitative yield. From solution ^{31}P-NMR

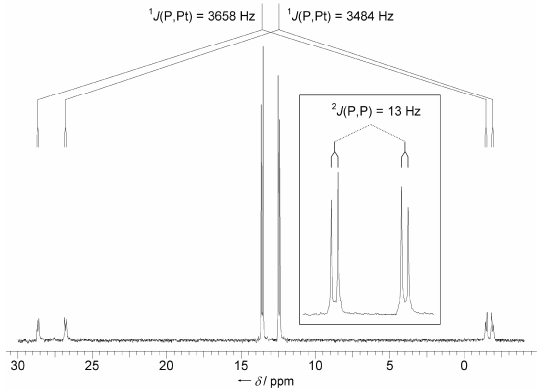


Figure 1: ^{31}P-NMR spectrum of *cis*-[(**1a**,**2a**)$PtCl_2$] in $CDCl_3$ solution.

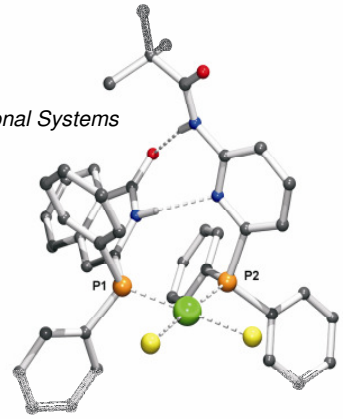


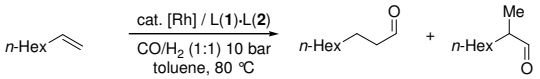
Figure 2: PLATON plot of the structure of *cis*-[(**1a**,**2a**)$PtCl_2$] in the solid state (H atoms bound to carbon are omitted for clarity). Selected interatomic distances [Å] and angles [°]: Pt-P1 2.2486(5), Pt-P2 2.2437(5), NH···N 2.932(2), O···HN 2.977(2); P1-Pt-P2 102.896(18), N-H···N 163(2) O···H-N 172(2). Green Pt, yellow Cl, orange P, blue N, red O.

data (Figure 1) and from the X-ray crystal structure of *cis*-[(**1a**,**2a**)$PtCl_2$] (Figure 2) it is clear that the two *cis*-coordinated phosphine ligands form the expected hydrogen-bonding network reminiscent of the Watson Crick base pairing of A and T in DNA.

The heterodimeric ligands based on this platform operate as bidentate ligands throughout the rhodium catalyzed hydroformylation of terminal alkenes. This is shown by comparison with hydroformylation in presence of only **1a** or **2a**, which gives rather low regioselectivities (**l**:**b** ≈ 75:25) as expected for mono-dentate phosphines.

From a self-assembled 4x4 library a catalyst operating with outstanding activity and regioselectivity upon hydroformylation of terminal alkenes was identified (Table 1).[3]

Table 1: 4x4 ligand matrix of aminopyridine **1a–d** / isoquinolone **2a–d** derived self-assembled bidentate ligands in the [Rh]-catalyzed hydroformylation of 1-octene.[a]



linear **b**ranched

	L(**1**)			
L(**2**)	**1a**	**1b**	**1c**	**1d**
2a	2425 h^{-1}[b] 94:6[c]	1040 h^{-1} 94:6	2732 h^{-1} 96:4	2559 h^{-1} 95:5
2b	2033 h^{-1} 93:7	1058 h^{-1} 92:8	1281 h^{-1} 96:4	1772 h^{-1} 94:6
2c	3537 h^{-1} 94:6	1842 h^{-1} 93:7	1808 h^{-1} 96:4	2287 h^{-1} 94:6
2d	7439 h^{-1} 96:4	2695 h^{-1} 95:5	7465 h^{-1} 94:6	**8643 h^{-1}** **96:4**

[a] Reaction conditions: $[Rh(CO)_2(acac)]$, [Rh]:L(**1**):L(**2**):1-octene = 1:10:10:7500, 10 bar CO/H_2 (1:1), toluene, c_0 (1-octene) = 2.91 M, 5 h.
Catalyst preformation: 5 bar CO/H_2 (1:1), 30 min, RT→80 °C.
[b] Turnover frequency (TOF) was calculated as (mol aldehydes)x(mol catalyst)$^{-1}$x(t [h])$^{-1}$ at 20–30% conversion, determined by GC analysis.
[c] Regioselectivity: linear to branched determined by GC analysis. The best TOF and regioselectivity are highlighted in red.

Conclusion

The first bidentate-phosphine-ligand library for homogeneous metal-complex catalysis, based on self-assembly through hydrogen bonding, was realized on the basis of an A–T base-pair analogous platform – the aminopyridine **1** / isoquinolone **2** system. From a 4x4 library generated by self-assembly a catalyst operating with outstanding activity and regioselectivity upon hydroformylation of terminal alkenes was identified. Application of this general principle and related libraries to asymmetric catalysis is a logical step.

Literature

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Acknowledgments

This work was supported by the Fonds der Chemischen Industrie, the Alfried Krupp Award for young university teachers of the Krupp foundation (to B.B.), and BASF. We thank Dr. M. Keller for the X-ray crystal structure analysis and G. Leonhardt-Lutterbeck and N. Stöcks for technical assistance.