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## Rational Optimization of Supramolecular Catalysts for the Rhodium-Catalyzed Asymmetric Hydrogenation Reaction

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**Abstract:** Rational design of catalysts for asymmetric transformations is a longstanding challenge in the field of catalysis. In the current contribution we report a catalyst in which a hydrogen bond between the substrate and the catalyst plays a crucial role in determining the selectivity and the rate of the catalytic hydrogenation reaction, as is evident from a combination of experiments and DFT calculations. Detailed insight allowed *in silico* mutation of the catalyst such that only this hydrogen bond interaction is stronger, predicting that the new catalyst is faster. Indeed, we experimentally confirmed that optimization of the catalyst can be realized by increasing the hydrogen bond strength of this interaction by going from a urea to phosphine oxide H-bond acceptor on the ligand.

The asymmetric hydrogenation reaction is undoubtedly the most powerful asymmetric transformation for the fine chemical industry as it provides a rather general strategy to create chiral centers in organic molecules.<sup>[1]</sup> As the synthesis of the desired products cannot always be reached using the existing catalysts, the search for new methods and concepts has received considerable attention.<sup>[2]</sup> Combinatorial chemistry approaches and high throughput catalyst screenings have been demonstrated to be increasingly important.<sup>[3]</sup> For the generation of catalyst libraries based on chiral ligands, the use of supramolecular ligand building blocks that form bidentate ligands by self-assembly is a powerful strategy as the number of catalysts grows exponentially with the number of synthesized building blocks.<sup>[4]</sup> Next to interactions between the two ligand building blocks, hydrogen bonding between functional groups of the substrate and the ligands at the metal complex can contribute to catalyst selectivity.<sup>[5]</sup> One of the holy grails in the area of asymmetric hydrogenation, or more general in the field of catalysis, would be the rational design of transition metal catalysts. Although for several catalyst systems detailed knowledge on the reaction mechanism has been obtained,<sup>[6]</sup> prediction of the catalyst properties is still very challenging.<sup>[7]</sup> However, when the selectivity of a catalytic reaction is controlled by supramolecular interactions, further rational optimization could be performed, guided by theoretical prediction. Herein we report the first example of rational design of a catalyst for the asymmetric hydrogenation reaction by optimization of the supramolecular interactions between the substrate and the catalyst, leading to enhanced activity and superior selectivity in the hydrogenation of hydroxyl-functionalized diand trisubstituted alkenes. In order to allow a rational approach, the reaction mechanism of the supramolecular catalyst used was investigated by means of X-ray crystallography, NMR spectroscopy, kinetic studies, and DFT calculations of the

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reaction pathway. Subsequently, the relevant supramolecular interactions between the substrate and the catalyst were optimized in silico, resulting in the rational design of a second generation of catalysts. Catalytic and kinetic experiments with the newly prepared catalysts confirmed that both the activity and the selectivity is improved.



Scheme 1. The chemical structures of the ligand building blocks with H-bond acceptors (L1-L4) and H-bond donor (L5), and a typical example of a self-assembled bidentate ligands around a rhodium complex (6).

We previously reported the use of complex  $[Rh(L1)(L5)(cod)]BF_4$ as a new selective catalyst based on a self-assembled supramolecular hetero-bidentate ligand, formed by a single hydrogen bond between the NH group of a phosphoramidite and the urea carbonyl of a urea-functionalized phosphine.<sup>[8]</sup> This complex affords the highest enantioselectivity (>99% ee) reported up to now for the hydrogenation of methyl 2hydroxymethacrylate (and several of its derivatives), which upon hydrogenation forms the so-called "Roche ester", an important intermediate in the preparation of several biologically active compounds. Catalysis results show that hydrogen bonding between the catalyst and the substrate plays an important role achieving this high selectivity (Table 1).



Substrate	R <sub>1</sub>	R <sub>2</sub>	R₃	Conv (%)	ee (%)
S1⁵	ОН	Me	Н	100	99
S2 <sup>b</sup>	ОН	tBu	Н	100	99
S3 <sup>b</sup>	OH	Me	Ph⁴	83	96 <sup>[c]</sup> (S)
S4	OMe	Me	Ph⁴	67	25 (S)

[a]  $[Rh(1)(5)(cod)_2]= 0.2 \text{ mM}$ , [substrate] = 0.1 M, solvent:  $CH_2CI_2$ , reaction performed at 10 bar H<sub>2</sub> pressure at 25°C for 16 h [b] Results previously reported in [7]. [c] ee obtained for this substrate varies between 96 and 99%.[d] E isomer

In the context of further rational optimization by computational strategies we decided to study the origin of the high selectivity in detail. The X-ray analysis of  $[Rh(L1)(L5)(cod)]BF_4$  as the precatalyst as well as the solvento complex that is formed after hydrogenation of the cod (1,5-cyclooctadiene), confirmed the presence of the hydrogen bond between the PNH group of the phosphoramidite and the carbonyl group of the urea-functionalized phosphine, as predicted by the DFT computed structures. (These structures will be published in a full paper). The acetonitrile complex that was obtained after hydrogenation of the cod was also characterized in solution and in the solid state. This complex appeared to be sufficiently stable to allow further substrate coordination studies.

Upon addition of the trisubstituted alkene S3 to a solution of the solvento-complex in dichloromethane (see sup info), the substrate-catalyst complex A in which both the carbonyl and the alkene of the prochiral substrate are coordinated to the rhodium center was identified by NMR spectroscopy as the major species. Additional 2D <sup>1</sup>H-<sup>1</sup>H COSY experiments and DFT calculations revealed that the hydrogen bond between the substrate and the functional group is not with the ester group of L5, as previously proposed.<sup>[8]</sup> Instead, the OH group inserts in the existing hydrogen bond between L1 and L5, leading to the formation of two hydrogen bonds between the substrate and the complex. (Figure 1). This complex was found to be 5.45 kcal/mol more stable than the alternative complexes that were computed, and as such is the major catalyst-substrate species observed in solution. The binding of substrate S3 and S4, the methoxy protected analogue of S3 that cannot form hydrogen bonds, to the solvento-complex was also studied by UV-vis titrations. The binding of S3 was found to be 2 kcal/mol stronger than for S4 in line with the proposed hydrogen bond formation.



Figure 1. Optimized structure of the catalyst-substrate Rh(L1)(L5)(S3) (left) and the rate determining transition state of the hydride migration step (right) in which two hydrogen bonds are formed between the catalyst and S3

In order to further unravel the mechanism of the hydrogenation reaction with this complex as catalyst, *in situ* <sup>31</sup>P-NMR experiments were performed, indicating that the solventocomplex was the resting state of the reaction. As no hydrides could be detected when the complex was pressurized, the reaction follows the unsaturated pathway (as displayed in scheme 2), meaning substrate coordination is required prior to oxidative addition of molecular hydrogen.<sup>[9]</sup> Next, a series of kinetic experiments were performed, monitored by gas-uptake, to elucidate the kinetics of the reaction, which confirmed the earlier described reaction mechanism. The kinetic data obtained for both substrates **S3** and **S4** could be fitted using the Michaelis-Menten rate equation. constants obtained for these substrates again confirmed a stronger binding of S3 to the rhodium complex compared to S4. Interestingly, also Vmax appeared to be higher for S3, suggesting that the hydrogen bond also resulted in an overall lower energy barrier. This was further studied by computing the reaction pathways using DFT calculations. A detailed computational study of the different reaction pathways (unsaturated pathway, dihydride pathway and semi-dihydride pathway) revealed that the unsaturated pathway is energetically favored. Importantly, for the lowest energy pathway, the hydrogen bonds between the substrate and the ligands are present throughout the reaction. The rate-determining transition state is represented by the hydride migration step B (Scheme 2 and Fig. 3), in line with the kinetic studies, and is stabilized by the hydrogen bond to a larger extent than the substrate complex explaining the higher V<sub>max</sub> obtained for the substrate that can form hydrogen bonds. (Figure 1). Inspection of the structures in detail shows that the geometry of transition state is more suited to accommodate the hydrogen bonds as is reflected in the shorter NH-O and OH-carbonyl distances.



Scheme 2. Proposed catalytic cycle for the supramolecular rhodiumcatalyzed asymmetric hydrogenation reaction of hydroxyl-functionalized alkenes

From this mechanistic study it is clear that hydrogen bonds between the substrate and the ligands play a crucial role in determining both the selectivity and the activity. With this knowledge in mind, we wondered if it would be possible to generate a better catalyst based on rational design by targeting these interactions. As phosphine-oxides are known to be the strongest hydrogen bond acceptors, we aimed for replacing urea-phosphine building block L1 in the complex for a phosphine-oxide analogue. DFT-optimized structures of catalyst substrate complexes based on building block L2 and L3 showed that ligand L3 forms complexes that are structurally most similar to the parent complex (see fig 2). Clearly, the phosphine oxide takes the role of the urea group: forming a hydrogen bond with the OH-group of the substrate. Additionally, we could further

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optimize the strength of the hydrogen bond by changing the substituents on the phosphine oxide group for methyl groups. NMR studies on a solution of complex Rh(L3)(L5)(cod)BF<sub>4</sub> and Rh(L4)(L5)(cod)BF<sub>4</sub> showed that indeed complexes are formed that are very similar to that of Rh(L1)(L5)(cod)BF<sub>4</sub>. In line with a stronger binding between the ligands, a large shift of the NH in <sup>1</sup>H NMR was observed with the bis-phosphine monoxide ligands (BPMO). Importantly, 2D COSY NMR experiments showed that the hydrogen bonds between the catalyst and the substrate in complex [Rh(L3)(L5)(S3)]BF<sub>4</sub> are similar to those found for the analogues urea-based system.



Figure 2. Rational optimization of supramolecular interactions in a transition metal catalysts. The crucial hydrogen bond acceptor (urea of L1) in the catalyst-substrate complex A (left structure) is replaced by a phosphineoxide (L3, complex C, right) without changing the basic structure of catalystsubstrate complex.

To confirm that the stronger hydrogen bond also translates in better catalysis, we computed the reaction pathway of the hydrogenation of substrate **S3** by complex Rh(L3)(L5)BF<sub>4</sub> using DFT methods. As for the first generation catalyst, the energy profile of the reaction displays an uphill profile and the rate-determining step is also represented by the hydride migration transition state structure **D**. The calculated pathways of the hydrogenation of substrate **S3** by complex [Rh(L1)(L5)]BF<sub>4</sub> and [Rh(L3)(L5)]BF<sub>4</sub> are plotted on the same graph in Figure 3 and it is clear that the predicted overall energy barrier is lower by 2.34 kcal mol<sup>-1</sup> for [Rh(L3)(L5)]BF<sub>4</sub>. Therefore, the stronger hydrogen bond acceptor, by going from the urea to the phosphine oxide group, is predicted to provide faster catalysis.



Figure 3. Normalized energy profiles of the unsaturated pathways for the urea-based supramolecular catalyst (blue path) and the phosphine oxidebased supramolecular catalyst Rh(L3)(L5) (red path).

To verify our prediction, the performance of various rhodium complexes based on self-assembled ligands, using hydrogen bond donor L5 and one of the hydrogen bond acceptors from L1-L4, was evaluated in the asymmetric hydrogenation of substrate S3 by monitoring the reaction rate by gas-uptake experiments (Table 2). In line with the prediction from the computational studies, the reaction is much faster when the phosphine oxide-based catalyst [Rh(L3)(L5)]BF<sub>4</sub> is applied, compared to the parent [Rh(L1)(L5)]BF4 and also the selectivity significantly improved (entry 1 vs 2). Using L5 in combination with L2 results in lower activity, as in this complex the geometry is not suited to form the optimal hydrogen bond (calculated structure in supporting information). In contrast, when  $[Rh(L4)(L5)]BF_4$  is applied the activity is even higher, as in this case the geometry of the hydrogen bond is the same, but the dimethyl phosphine oxide is a stronger hydrogen bond acceptor as the methyl groups are more electron donating than the phenyl groups. Interestingly, experiments performed at 45°C resulted in a drop in selectivity for [Rh(L1)(L5)]BF4 to 93% ee, while the phosphine oxide-based catalyst [Rh(L3)(L5)]BF4 still produced the product in 96% ee.

 Table 2. Hydrogenation of substrate S3 by complexes [Rh(L1)(L5)],

 [Rh(L2)(L5)], [Rh(L3)(L5)] and [Rh(L4)(L5)].<sup>[a]</sup>

Entry	Complex	Conv. [%] <sup>b</sup>	TOF <sup>c</sup>	ee <sup>d</sup> [%]
1	Rh( <b>L1)(L5)(</b> cod)BF <sub>4</sub>	98	875	96
2	Rh( <b>L3</b> )(L5)(cod)BF <sub>4</sub>	100	3644	>99
3	Rh( <b>L2)(L5)(</b> cod)BF <sub>4</sub>	39	335	96
4	Rh( <b>L4)(L5)(</b> cod)BF <sub>4</sub>	99	4561	>99

[a] Reagents and conditions: [Rh] = 0.2 mM, S/C ratio =  $1000, 25^{\circ}$ C, 20 hours, pH<sub>2</sub> = 10 bar. [b] determined by <sup>1</sup>H NMR [c] turnover frequencies calculated at 15% conversion [d] determined by HPLC.

In conclusion, whereas previously it has been demonstrated that the inclusion of hydrogen bonding in catalyst development can lead to unprecedented selectivity in catalysis by appropriate substrate organization at the metal complex<sup>[5]</sup>, we now show for the first time the successful in silico optimization of such catalyst The rational approach relies on mechanistic understanding of the role of the hydrogen bonds, and subsequent in silico optimization of this specific interaction. In the current example, new supramolecular bidentate ligands were used, in which the urea functional group was replaced by the stronger hydrogen bond acceptor phosphine oxide in one of the building blocks. According to DFT calculations and experiments two hydrogen bonding interactions between the catalyst and the substrate exist. Increasing the strength of this hydrogen bond interaction results in a reaction pathway with a lower overall energy barrier, which as a consequence results in higher reaction rates found experimentally. In addition, the product is also produced in higher selectivity (>99% ee) with the rationally optimized catalyst. The development of catalysts by rational approaches is based on long-standing established parameters such as steric effects, electronic effects and bite angle effects.<sup>[10]</sup> The flourishing number of supramolecular strategies implies that non-covalent interactions should also be taken into account in the design of a catalyst. This work highlights the potential of catalyst fine-tuning

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by means of modification of the supramolecular interactions that can be used as a new tool to improve catalyst performance.

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Keywords: Supramolecular ligands • ligand design • asymmetric hydrogenation • dft calculations • Catalyst prediction

#### References

- a) N. B. Johnson, I. C. Lennon, P. H. Moran, J. A. Ramsden, Acc. [1] Chem. Res. 2007, 40, 1291-1299; b) H. Shimizu, I. Nagasaki, K. Matsumura, N. Sayo, T. Saito, Acc. Chem. Res. 2007, 40, 1385-1393; c) L. A. Saudan, Acc. Chem. Res. 2007, 40, 1309-1319; d) D. J. Ager, A. H. M. de Vries, J. G. de Vries, Chem. Soc. Rev. 2012, 41, 3340-3380; e) P. Etayo, A. Vidal-Ferran, Chem. Soc. Rev. 2013, 42, 728; f) M. Beller and C. Bolm, Eds. Transition Metals for Organic Synthesis; Wiley-VCH: Weinheim, 2004.
- [2] a) B. Cornils, W.A. Herrmann, J. of Catal. 2003, 216, 23-31; b) W.A. Herrmann, Angew. Chem. Int. Ed. 2002, 41, 1290-1309; c) J. Meeuwissen, J. N. H. Reek, Nat. Chem. 2010, 2, 615-621; d) G.L. Hamilton, E.J. Kang, M. Mba, F.D. Toste, Science, 2007, 317, 496-499; e) P. W. N. M. van Leeuwen, Homogeneous Catalysis: Understanding the Art; Kluwer Academic Publishers: Dordrecht, 2004; f) . F. Hartwig, Organotransition Metal Chemistry: From Bonding to Catalysis; University Science Books: Sausalito, 2009; g) T. P. Yoon, Science 2003. 299. 1691-1693.
- For reviews on high throughput screening, see: (a) W. Tang, X. Zhang, [3] Chem. Rev. 2003, 103, 3029; b) C. Jäkel, R. Paciello, Chem. Rev. 2006. 106. 2912-2942; c) C. Gennari, U. Piarulli, Chem. Rev., 2003. 103, 3071-3100. For the use of mixture of monodentate ligands, see: d) M.T. Reetz, T. Sell, A. Meiswinkel, G. Mehler, Angew. Chem. Int. Ed. 2003, 42, 7, 790; e) D. Pena, A.J. Minnaard, J.A.F. Boogers, A.H.M. de Vries, J.G. de Vries, B.L. Feringa, Org. Bio. Chem., 2003, 1, 1-87-1089; f) M. T. Reetz, O. Bondarev, Angew. Chem. Int. Ed. 2007, 46,4523-4526; g) A.J. Minnaard, B.L. Feringa, L. Lefort, J.G. de Vries, Acc Chem. Res. 2007, 40, 1267-1277.
- For reviews, see: a) M. J. Wilkinson, P. W. N. M. van Leeuwen, J. N. H. [4] Reek, Org., Biomol. Chem. 2005, 3, 2371-2383; b) B. Breit, Angew. Chem. Int. Ed. 2005, 44, 6816-6825; c) A. J. Sandee, J. N. H. Reek, Dalton Trans. 2006, 3385-3391; d) R. Bellini, J. I. van der Vlugt and J. N. H. Reek, Isr. J. Chem., 2012, 52, 613-629; e) S. Carboni, C. Gennari, L. Pignataro and U. Piarulli, Dalton Trans., 2011, 40, 4355-4373; f) P. E. Goudriaan, P. W. N. M. van Leeuwen, M.-N. Birkholz and J. N. H. Reek, Eur. J. Inorg. Chem., 2008, 2939–2958; g) M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, Chem. Soc. Rev. 2014, 43, 1660-1733. For some supramolecular ligands in asymmetric hydrogenation see: h) L. Pignataro, S. Carboni, M. Civera, R. Colombo, U. Piarulli, C. Gennari, Angew. Chem. Int. Ed. 2010, 49, 6633-6637; i) L. Pignataro, M. Boghi, M. Civera, S. Carboni, U. Piarulli, C. Gennari, Chem. Eur. J. 2012, 18, 1383-1400; j) 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. Int. Ed. 2006, 45, 1223-1227; k) M. N.

Birkholz, N. V. Dubrovina, H. Jiao, D. Michalik, J. Holz, R. Paciello, B. Breit, A. Borner, Chem. Eur. J. 2007, 13, 5896-5907; I) FA. J. Sandee, A. M. van der Burg, J. N. H. Reek, Chem. Commun. 2007, 864-866; m) J. Meeuwissen, M. Kuil, A. M. van der Burg, A. J. Sandee, J. N. H. Reek, Chem. Eur. J. 2009, 15, 10272-10279; n) C. Chen, Z. Zhang, S. Jin, X. Fan, M. Geng, Y. Zhou, S. Wen, X. Wang, L.W. Cheng, X.-Q.

- for reviews see; a) P. Dydio, J.N.H. Reek, Chem. Sci. 2014, 5, [5] 2135-2145 b) H.J. Davis, R.J. Phipps, Chem. Sci, 2017, 8, 864-877. For some examples see c) T. Šmejkal, D. Gribkov, J. Geier, M. Keller, B. Breit, Chem. Eur. J. 2010, 16, 2470-2478; d) P. Dydio. C. Rubay, T. Gadzikwa, M. Lutz, J. N. H. Reek, J. Am. Chem. Soc. 2011, 133, 17176-17179. e) P. Dydio, W. Dzik, M Lutz, B. de Bruin, J.N.H. Reek, Angew. Chem. Int. Ed. 2011, 50, 396-400 f) W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek and B. de Bruin, J. Am. Chem. Soc., 2010, 132, 10891-10902;g) P. Fackler, S. M. Huber, T. Bach, J. Am. Chem. Soc., 2012, 134, 12869- 12878. h) S. Das, C. D. Incarvito, R. H. Crabtree and G. W. Brudvig, Science, 2006, 312, 1941-1943 i) P. Dydio and J. H N. Reek, Angew. Chem., Int. Ed., 2013, 52, 3878-3882
- (a) J. M. Brown, P. A. Chaloner, J. Chem. Soc. Chem. Commun. 1978, [6] 32; (b) J. M. Brown, P. A. Chaloner, Tetrahedron Lett. 1978, 19, 1877; (c) J. M. Brown, P.A. Chaloner, J. Chem. Soc., Chem. Commun. 1979, 613; (d) J. M. Brown, P.A. Chaloner, J. Chem. Soc., Chem. Commun. 1980, 344; (e) J. M. Brown, P.A. Chaloner, R. Glaser, S. Geresh, Tetrahedron, 1980, 36, 815; (f) J. Halpern, D. P. Riley, A. S. C. Chan, J. J. Pluth, J. Am. Chem. Soc. 1977, 99, 8055; (g) A.S. C. Chan, J. Halpern, J. Am. Chem. Soc., 1980, 102, 838; (h) A. S. C. Chan, J. J. Pluth, J. Halpern, J. Am. Chem. Soc. 1980, 102, 5952; (i) J. Halpern, Science, 1982, 217, 401.
- a) C. Poree, F. Schoenbeck, Acc. Chem. Res. 2017, 50, 605 608 ; b) [7] K. N. Houk, F. Liu, Acc. Chem. Res. 2017, 50, 539 - 543; For a recent contribution in this field see: Y. Guan, S.E. Wheeler Angew. Chem. Int. Ed., 2017, 56, 12, 9101-9105.
- [8] P.-A. R. Breuil, F. W. Patureau, and J. N. H. Reek, Angew. Chem. Int. Ed., 2009, 48, 12, 2162-2165.
- I. D. Gridnev, T. Imamoto, Chem. Comm., 2009, 7447-7464. [9]
- a) C. A. Tolman, Chem. Rev. 1977, 77, 313-348. b) C. P. Casey, G. T. [10] Whiteker, Isr. J. Chem. 1990, 30, 299-304; c) P. W. N. M. van Leeuwen P. C. J. Kamer, J. N. H. Reek, P. Dierkes, Chem. Rev. 2000, 100, 2741-2769. d) C. A. Tolman, J. Am. Chem. Soc. 1970, 92, 2953-2956

Dong, X. Zhang, Angew. Chem. Int. Ed. 2017, 56, 6808-6812.

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