Origin of the selectivity and activity in the Rhodium-catalyzed asymmetric hydrogenation using supramolecular ligands

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General

General Procedure

All reactions were carried out under an argon atmosphere using standard Schlenk techniques. THF, pentane, hexane and diethyl ether were distilled from sodium benzophenone ketyl; CH$_2$Cl$_2$ was distilled from CaH$_2$ and toluene was distilled from sodium under nitrogen. NMR spectra were measured on a Bruker AMX 400 (400 MHz, 100 MHz and 162 MHz for $^1$H, $^{13}$C and $^{31}$P respectively), a Bruker DRX 500 (500 MHz, 126 MHz and 202 MHz for $^1$H, $^{13}$C and $^{31}$P respectively) or a Bruker DRX 300 (300 MHz, 75 MHz and 121 MHz for $^1$H, $^{13}$C and $^{31}$P respectively) at room temperature unless noted otherwise. NMR spectra are reported as chemical shifts in part per millions (ppm) relative to the solvent signal and converted to tetramethylsilane scale (CDCl$_3$: $^1$H, 7.26 ppm; $^{13}$C, 77.16 ppm; CD$_2$Cl$_2$: $^1$H, 5.32 ppm; $^{13}$C, 53.84 ppm). $^{31}$P NMR spectra were calibrated using 85% H$_3$PO$_4$ as an external chemical shift reference. Mass spectra were collected on an AccuTOF GC v 4g, JMS-T100GCV Mass spectrometer (JEOL, Japan). CD$_2$Cl$_2$ was dried over molecular sieves (4Å) and degassed by 3 freeze-pump-thaw cycles.

Materials.

All reagents were purchased from commercial suppliers and used without further purification.
except from substrate S1, S2, S3, S4, S5, S6 ligands L1 and L2 which were synthesized according to the published procedures.

**Synthesis**

**Synthesis of complex Rh(L1)(L2)(cod)BF4.** Ligand L1 (0.025 mmol, 1 equiv) and ligand L2 (0.025 mmol, 1 equiv) were placed in a dry-flamed Schlenk flask under an argon atmosphere. CD2Cl2 (0.3 ml) was dropped on them leading to a transparent solution. The commercially available [Rh(cod)2]BF4 salt was placed in another flamed-dry Schlenk flask under an argon atmosphere and was dissolved with 0.25 ml of CD2Cl2. The solution of the metal salt was added dropwise to the solution of ligands and the medium was stirred for 30 minutes at room temperature. The solution was transferred to the NMR tube under an argon atmosphere.

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5. Substrate S6 was prepared following the procedure described in ref. 2 and isolated from the crude reaction mixture by flash chromatography silica column.
8. [Rh(cod)2]BF4 was purchased from Strem Chemicals Inc. [www.strem.com](http://www.strem.com)
Figure S1. $^{31}$P NMR spectrum of complex Rh(L1)(L2)(cod)BF$_4$ in CD$_2$Cl$_2$ (121 MHz).

$\delta$(phosphoramidite) = 130.09 ppm (dd, $J_{P,Rh} = 242.3$ Hz; $J_{P,P'} = 31$ Hz); $\delta$(phosphine) = 34.03 ppm (dd, $J_{P,Rh} = 149.5$ Hz; $J_{P,P'} = 31$ Hz).

Figure S2. $^1$H NMR spectrum of complex Rh(L1)(L2)(cod)BF$_4$ in CD$_2$Cl$_2$ (400 MHz).
Figure S3. $^{13}$C NMR spectrum of complex Rh(L1)(L2)(cod)]BF$_4$ in CD$_2$Cl$_2$ (101 MHz).

Figure S4. COSY $^1$H-$^1$H NMR spectrum of complex Rh(L1)(L2)(cod)]BF$_4$ in CD$_2$Cl$_2$ (400 MHz).
Figure S5. NOESY $^1$H-$^1$H NMR spectrum of complex Rh(L1)(L2)(cod)BF$_4$ in CD$_2$Cl$_2$ (400 MHz).
**Figure S6.** HSQC $^{13}$C-$^1$H NMR spectrum of complex Rh(L1)(L2)(cod)]BF$_4$ in CD$_2$Cl$_2$ (400 MHz).

**HRMS (ESI):** found: 990.2643 [M]+ (calculated 990.2672).
Figure S7. Molecular structure of complex 1 in the racemic crystal (ellipsoids at 50% probability level). Hydrogen atoms (except H13), BF₄⁻ anion and disordered CH₂Cl₂ solvent molecules are omitted for clarity. Only one of two independent molecules is shown. The intramolecular H13…O12 distance is 2.05(3) Å.

\[ \text{[Cs₂H₅₅N₃O₅P₂Rh]}(\text{BF}_₄) + \text{disordered solvent, Fw = 1077.67,} ^9 \text{ yellow needle, 0.55} \times 0.26 \times 0.10 \text{ mm}^3, \text{triclinic, P-1 (no. 2), a = 14.1394(3), b = 15.0162(5), c = 28.9031(9) Å, } \alpha = 77.688(2), \beta = 87.174(1), \gamma = 78.469(1)^\circ, \text{ Z = 4, D}_x = 1.219 \text{ g/cm}^3, ^9 \text{ } \mu = 0.40 \text{ mm}^{-1}. ^9 \text{ 117189 Reflections were} \]

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^9 Derived values do not contain the contribution of the disordered solvent molecules.
measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator ($\lambda = 0.71073$ Å) at a temperature of 150(2) K up to a resolution of $(\sin \theta/\lambda)_{\text{max}} = 0.65$ Å$^{-1}$. The Eval15 software$^{10}$ was used for the integration of the intensities. Multiscan absorption correction and scaling was performed with SADABS$^{11}$ (correction range 0.68-0.75). 26994 Reflections were unique ($R_{\text{int}} = 0.030$), of which 21550 were observed [$I>2\sigma(I)$]. The structure was solved with Patterson superposition methods using SHELXT.$^{12}$ Least-squares refinement was performed with SHELXL-97$^{13}$ against $F^2$ of all reflections. The crystal structure contains large voids (1335 Å$^3$ / unit cell), filled with severely disordered CH$_2$Cl$_2$ solvent molecules. Their contribution to the structure factors was secured by back-Fourier transformation using the Squeeze routine$^{14}$ resulting in 351 electrons / unit cell. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in difference Fourier maps. N-H hydrogens and the C-H hydrogens of the cyclooctadiene double bonds were refined freely with isotropic displacement parameters. All other H-atoms were refined with a riding model. 1331 Parameters were refined with 94 restraints (distances and angles in BF$_4$). R1/wR2 [$I > 2\sigma(I)$]: 0.0388 / 0.1020. R1/wR2 [all refl.]: 0.0507 / 0.1063. S = 1.077. Residual electron density between -0.67 and 1.09 e/Å$^3$. Geometry calculations and checking for higher symmetry were performed with the PLATON program.$^{15}$

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11 G. M. Sheldrick, SADABS and TWINABS, Universität Göttingen, Germany, 2008.
Synthesis of complex Rh(L1)(PPh3)(cod)BF4. Ligand L1 (0.025 mmol, 1 equiv) and triphenylphosphine (0.025 mmol, 1 equiv) were placed in a dry-flamed Schlenk flask under an argon atmosphere. CD₂Cl₂ (0.3 ml) was dropped on them leading to a transparent solution. The commercially available [Rh(cod)₂]BF₄ salt was placed in another flamed-dry Schlenk flask under an argon atmosphere and was dissolved with 0.25 ml of CD₂Cl₂. The solution of the metal salt was added dropwise to the solution of ligands and the medium was stirred for 30 minutes at room temperature. The solution was transferred to the NMR tube under an argon atmosphere.
Figure S8. $^{31}$P NMR spectrum of the mixture of complex Rh(L1)$_2$(cod)]BF$_4$, Rh(PPh$_3$)$_2$(cod)]BF$_4$ and Rh(L1)(LPPh3)(cod)]BF$_4$ in CD$_2$Cl$_2$ (121 MHz).

Figure S9. $^1$H NMR spectrum of the mixture of complex Rh(L1)$_2$(cod)]BF$_4$, Rh(PPh$_3$)$_2$(cod)]BF$_4$ and Rh(L1)(LPPh3)(cod)]BF$_4$ in CD$_2$Cl$_2$ (400 MHz).
**Figure S10.** COSY $^1$H-$^1$H NMR spectrum of the mixture of complex Rh(L1)$_2$(cod)BF$_4$, Rh(PPh$_3$)$_2$(cod)BF$_4$ and Rh(L1)(LPPh3)(cod)BF$_4$ in CD$_2$Cl$_2$ (400 MHz).

**Preparation and characterization of solvate complex 2**

**Preparation of solvate complex in deuterated dichloromethane.** A solution of 0.04 mmol of complex 1 in 0.6 ml of CD$_2$Cl$_2$ was transferred to a high pressure HNMR tube under an argon atmosphere. The tube was cooled down to -90°C in a Dewar containing a mixture of ethanol/liquid N$_2$. The sample was purged 3 times with 3 bar of hydrogen and then pressurized to 5 bar. Then, the sample was shaken manually for 2 hours, taking care that the temperature did not exceed -70°C. The solution was degassed by mean of 4 freeze-pump-thaw cycles and warmed up to room temperature yielding a red colored solution.
**Figure S11**: $^{31}$P NMR spectrum of complex 2 ([Rh(L$_1$)(L$_2$)$_2$]) in CD$_2$Cl$_2$ (162 MHz).

At high concentration (c = 0.065 M), 2 sets of doublet of doublet (δ P$^1$ 132.17 ppm, $^{1}J_{P,Rh} = 294.9$ Hz, $^{2}J_{P,P'} = 44.8$ Hz; δ P$^2$ 131.05 ppm, $^{1}J_{P,Rh} = 291.6$ Hz, $^{2}J_{P,P'} = 44.3$ Hz; δ P$^3$ 51.63 ppm, $^{1}J_{P,Rh} = 208.1$ Hz, $^{2}J_{P,P'} = 44.8$ Hz; δ P$^4$ 49.35 ppm, $^{1}J_{P,Rh} = 214.2$ Hz, $^{2}J_{P,P'} = 44.5$ Hz) were observed. Crystals suitable for X-ray analysis were obtained from the solution and the solid state structure revealed an unusual dimeric complex 2 in which both the urea carbonyl group of the phosphine and the ester carbonyl group of the phosphoramidite coordinated to another rhodium center (Figure S11).
X-ray crystal structure determination of complex 2 \([\text{[Rh}(L_1)(L_2)]_2(\text{BF}_4)_2]\)

**Figure S12.** Molecular structure of complex 2 in the racemic crystal (ellipsoids at 30% probability level). Hydrogen atoms (except H13), BF₄ anions and disordered CH₂Cl₂ solvent molecules are
omitted for clarity. The intramolecular H13…O43 distance is 2.55 Å and the N13-H13…O43 angle is 101 °. Symmetry code $i$: 1-x, -y, -z.

\[ \text{[C}_{92}\text{H}_{86}\text{N}_{6}\text{O}_{10}\text{P}_{4}\text{Rh}_{2}]\text{(BF}_{4}\text{)}_{2} + \text{disordered solvent, Fw} = 1938.98, \] yellow needle, 0.34 x 0.11 x 0.07 mm$^3$, monoclinic, P2₁/n (no. 14), a = 14.1446(5), b = 25.4077(11), c = 15.6384(5) Å, $\beta = 94.839(2)$ °, \[ V = 5600.1(4) \text{Å}^3, Z = 2, D_\text{x} = 1.150 \text{g/cm}^3, \mu = 0.41 \text{mm}^{-1}. \] 57099 Reflections were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator ($\lambda = 0.71073$ Å) at a temperature of 150(2) K up to a resolution of (sin $\theta/\lambda_{\text{max}} = 0.65$ Å$^{-1}$. The Eval15 software$^{10}$ was used for the integration of the intensities. Multiscan absorption correction and scaling was performed with SADABS$^{11}$ (correction range 0.66-0.75). 12886 Reflections were unique (R$_{\text{int}} = 0.053$), of which 9231 were observed \[ {I}>2\sigma(I) \]. The structure was solved with Direct Methods using SIR-2011.$^{16}$ Least-squares refinement was performed with SHELXL-2013$^{12}$ against F$^2$ of all reflections. The crystal structure contains large voids (1811 Å$^3$ / unit cell), filled with severely disordered solvent molecules. Their contribution to the structure factors was secured by back-Fourier transformation using the Squeeze routine$^{14}$ resulting in 751 electrons / unit cell.

Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Disorder in the binaphthyl moiety was not resolved. All hydrogen atoms were introduced in calculated positions and refined with a riding model. 562 Parameters were refined with 120 restraints (to approximate isotropic behavior in the binaphthyl moiety). R1/wR2 \[ [I > 2\sigma(I)] : 0.0569 / 0.1433. \] \[ R1/wR2 [all refl.]: 0.0827 / 0.1571. S = 1.048. \] Residual electron density between -1.15 and 2.08 e/Å$^3$. Geometry calculations and checking for higher symmetry were performed with the PLATON program.$^{15}$

Preparation and characterization of acetonitrile solvato complex 2′

A freshly prepared solution of solvate complex 2 (C = 0.03 M) in deuterated dichloromethane was charged into a 5 mm NMR tube under inert glovebox atmosphere and 15µl of acetonitrile was added to the solution. The sample was manually shaken for 5 minutes at room temperature and placed in the NMR spectrometer for analysis.

Figure S13. $^{31}$P NMR spectrum of complex 2′, \([\text{Rh}(L_1)(L_2)(\text{acetonitrile})_2\text{BF}_4]\), in CD$_2$Cl$_2$ / CD$_3$CN (162 MHz).
Figure S14. $^1$H NMR spectrum of the complex $2'$, ([Rh(L$_1$)(L$_2$)(acetonitrile)$_2$]BF$_4$) in CD$_2$Cl$_2$ / CD$_3$CN (400 MHz).


X-ray crystal structure determination of complex $2'$ ([Rh(L$_1$)(L$_2$)(acetonitrile)]BF$_4$)

[C$_{50}$H$_{49}$N$_5$O$_5$P$_2$Rh](BF$_4$), Fw = 1051.60, pale yellow block, 0.31 × 0.09 × 0.04 mm$^3$, triclinic, P-1 (no. 2), a = 12.6207(4), b = 13.6039(4), c = 15.2008(6) Å, α = 72.598(2), β = 83.301(1), γ = 76.784(2)*, V = 2421.13(15) Å$^3$, Z = 2, D$_x$ = 1.442 g/cm$^3$, μ = 0.49 mm$^{-1}$. 39473 Reflections were measured on a Bruker Kappa ApexII diffractometer with sealed tube and Triumph monochromator (λ = 0.71073 Å) at a temperature of 150(2) K up to a resolution of (sin θ/λ)$_{max}$ = 0.65 Å$^{-1}$. The Eval15 software$^{10}$ was used for intensity integration. Multiscan absorption correction and scaling was performed with SADABS$^{11}$ (correction range 0.68-0.75). 11120 Reflections were unique (R$_{int}$ = 0.045), of which 8668 were observed ([I>2σ(I)]. The structure was solved with Direct Methods using SHELXS-97.$^{13}$ Least-squares refinement was performed with SHELXL-2012$^{14}$ against F$^2$ of all
reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in difference Fourier maps. The N-H hydrogens were refined freely with isotropic displacement parameters. All other hydrogen atoms were refined with a riding model. 634 Parameters were refined with no restraints. R1/wR2 [I > 2σ(I)]: 0.0342 / 0.0731. R1/wR2 [all refl.]: 0.0549 / 0.0796. S = 1.014. Residual electron density between -0.53 and 0.57 e/Å³. Geometry calculations and checking for higher symmetry were performed with the PLATON program.15

Figure S15. Molecular structure of complex 2⁺ in the racemic crystal (ellipsoids at 50% probability level). Hydrogen atoms (except H4N) and BF₄⁻ anion are omitted for clarity. The intramolecular H4N…O12 distance is 2.24(3) Å
Preparation of the catalyst-substrate adduct 3

To a freshly prepared solution of solvate complex 2 (C = 0.03 M) in deuterated dichloromethane was directly added 3 equivalents of substrate S3 under inert glovebox atmosphere. The sample was manually shaken for 15 minutes at room temperature and placed in the NMR spectrometer for analysis.

Figure S16. $^1$H NMR spectrum of the catalyst-substrate complex 3 in CD$_2$Cl$_2$ (400 MHz).
Figure S17. $^{31}$P NMR spectrum of the catalyst-substrate complex 3 in CD$_2$Cl$_2$ (162 MHz).
Figure S18. $^{13}$C NMR spectrum of the catalyst-substrate complex 3 in CD$_2$Cl$_2$ (100 MHz).

Figure S19. $^{13}$C NMR spectrum of the catalyst-substrate complex 3a in CD$_2$Cl$_2$ (100 MHz): carbonyl region. (■ = ester of group of the phosphoramidite, ● = ester group of substrate S3 non-coordinated, ▲ = ester group of substrate S3 coordinated, ○ = urea group of the phosphine).
Figure S20. $^1$H-$^1$H COSY NMR spectrum of catalyst-substrate complex 3 (400 MHz)
Figure S21. $^1$H-$^1$H NOESY NMR spectrum of catalyst-substrate complex 3 (400 MHz)
Figure S22. HSQC $^{13}$C-$^1$H NMR spectrum of catalyst-substrate complex 3 (400 MHz)
1H NMR spectra of product P3 and P4

Figure S23. $^1$H NMR spectrum of product P3 in acetone-$d_6$. The yield is calculated by integration of the aromatic peaks of product P3 (7.29-7.23 ppm) and the aromatic peaks of substrate S3 (7.6-7.45 ppm, not present in this spectrum)
Figure S24. $^1$H NMR spectrum of product P4 in acetone-$d_6$. The yield is calculated by integration of the aromatic peaks of product P4 (7.29-7.22 ppm) and the aromatic peaks of substrate S4 (7.61 +7.47 ppm)

**Determination of absolute configurations of products P3 and P4**

**Determination of the absolute configuration of product P3.** The absolute configuration of product P3 was determined using Vibrational Circular Dichroism (VCD).\cite{Nafie2011}

**a) Preparation of the VCD sample:** A 4 ml vial equipped with a magnetic Teflon stirring bar was charged with 500 μl of a 1 mM of S-[Rh(L₁)(L₂)(cod)]BF₄ (complex 1) and 57.6 mg of (E)-methyl 2-

(hydroxymethyl)-3-phenylacrylate (S3) in 2 ml of dry dichloromethane. The reaction vessel was prepared in a glovebox under a N\textsubscript{2} atmosphere and placed in a stainless steel autoclave. The charged autoclave was purged 3 times with 5 bar of dihydrogen and then pressurized at 10 bar H\textsubscript{2}. The reaction mixture was stirred at 25°C for 16 hours. After catalysis the pressure was released. The conversion was determined by \textsuperscript{1}H NMR (95% conversion) and the enantiomeric purity was determined by chiral HPLC (98 % ee). The reaction mixture was purified by flash chromatography on silica gel (ethylacetate/hexane, 4:6) to give the product as a colorless liquid. A 5 mM solution of product P3 in DCM and DCM-d\textsubscript{2} was prepared for VCD measurements.

b) Experimental methods for the VCD measurements: Samples were prepared in DCM and DCM-d\textsubscript{2} with concentrations of 5 mM of product P3. The solutions were prepared under inert conditions and inserted in sealed infrared cells with 3 mm thick CaF\textsubscript{2} windows separated by 500 \textmu m and 1 mm Teflon spacers, for DCM and DCM-d\textsubscript{2}, respectively. Fourier-transform infrared (FTIR) and VCD spectra (with spectral resolution of 2 and 4 cm\textsuperscript{-1}, respectively) were obtained with a Bruker Vertex 70 spectrometer in combination with a PMA 50 module. The photoelastic modulator (PEM) was set to a center frequency of 1500 cm\textsuperscript{-1} for quarter-wave retardation. Baseline corrections were accounted for with spectra of pure dry DCM and DCM-d\textsubscript{2}, respectively. VCD spectra were obtained after four hours of averaging.
c) **Computational Methods for the simulation of the VCD spectrum of the S- and R-Product P3:**

Density functional theory (DFT) calculations were carried out with Gaussian 09. Groundstate geometry optimizations and harmonic vibrational frequencies were computed using the B3LYP hybrid functional and the 6-31G(d,p) basis set. An implicit solvent model has been employed, including a polarizable continuum model (PCM) accounting for the dielectric constant of DCM.

**d) Assignment of the absolute configuration (AC) of product P3:** Comparison of experimental and calculated infrared absorption and VCD spectra for the compound are shown in Figure S26. Measurements of pure DCM and DCM-d$_2$ were performed in the same experimental conditions for baseline subtraction. The infrared absorption spectrum of the compound obtained in DCM-d$_2$ complements the one with DCM due to the shift of its infrared absorption bands. A similar complimentary evaluation can be done for the VCD spectra to facilitate the assignment. The band around 1700 cm$^{-1}$ is clearly visible in the spectrum with DCM, while in DCM-d$_2$ is cut off by solvent absorption. Taking in consideration this band, and through comparison with the quantum-chemical predicted VCD spectrum, one assigns the AC of the compound as the S enantiomer. Moreover, the spectrum obtained with DCM-d$_2$ solution unveils spectral features in the fingerprint region, below 1200 cm$^{-1}$. Two bands (a +/- bisignate signal) are visible and easily assigned to the S-enantiomer by comparison with the calculated spectrum. We can therefore confidently assign the absolute configuration of the compound as the S enantiomer.
Figure S26. FTIR/VCD spectra for the determination of the absolute configuration of product P3. Top: Overlay of the FTIR spectra of the calculated R-isotope (red line), product P3 in DCM-d$_2$ (black line), DCM-d$_2$ (grey line), product P3 in DCM (dotted black line), DCM (dotted grey line). Bottom: simulated VCD spectrum of the R-product (red line), simulated VCD spectrum of the S-product (dotted red line), measured VCD spectrum of product P3 in DCM-d$_2$ (black line), measured VCD spectrum of product P3 in DCM (dotted black line).
Determination of the absolute configuration of product P4. In order to determine the absolute configuration of the hydrogenation product P4, an analytical derivatization was performed on the hydrogenation product P3. Experimental procedure: 0.62 mmol of S-product P3 (97% ee, 120 mg) was placed in a dry-flamed Schlenk flask under an argon atmosphere. Ag₂O (5eq, 3.1 mmol), Mg₂SO₄ (30 mg) and 2 ml of dry dichloromethane were added to the Schlenk flask and the reaction mixture was stirred for 3 hours at room temperature. Iodomethane (5eq, 186 μl) was added at 0°C and the reaction mixture was stirred overnight. Filtration of the reaction mixture and evaporation of the solvents under vacuum afford a colorless liquid. The derivatized product was directly analyzed by GC. Overlay of the spectrum of the GC analysis of product P4 with the spectrum of the GC spectrum of the derivatized S-product P3 clearly indicates that the S-enantiomer is obtained in the hydrogenation reaction of both substrates S3 and S4.

Coordination chemistry with substrates S4

**Figure S27.** $^{31}p$ NMR spectrum of the catalyst-substrate complex 4 in CD₂Cl₂ (162 MHz).
**In situ NMR experiment**

To a solution of 0.005 mmol of complex 1 in 1 ml of CD$_2$Cl$_2$ was added 50 equivalents of substrate S3 (0.25 mmol, 48mg). The solution was transferred to a high pressure HNMR tube under an argon atmosphere. The tube was flushed 3 times with hydrogen and pressurized to 5 bar H$_2$. The high pressure NMR tube was shaken manually and a $^{31}$P NMR spectrum was recorded overnight.
**Figure S28.** *In situ* $^{31}$P NMR spectrum of the hydrogenation of substrate S3 by complex 1 in CD$_2$Cl$_2$ under 5 bar H$_2$ (162 MHz).

**UV-vis experiments**

**Determination of the binding constants of substrates S3 and S4 on solvate complex 2 using UV-Vis titrations**

UV-Vis titration was performed by preparation of several aliquots of the solvate complex 2 at same concentration ($C = 5.10^{-4}$ M) and various substrate concentrations (5, 10, 20, 40, 60 and 150...
equivalents). The samples were prepared in an inert atmosphere glovebox by dilution of a concentrated solution of catalyst-substrate complex by a solution of solvate catalyst of same concentration. 30 minutes after the preparation, the aliquots were transferred into a 1 mm path septum-capped cuvette using micropipettes. No isobestic points were recorded. The evolution of the absorbance at 390 nm was used to calculate the binding constants. The association constants were determined using the non-linear least-squares curve fitting method for titration with no dilution. This was carried out on the data fitting software package Origin 8.0.
Table S1: (a) spectral changes observed of solutions of solvate complex \(2 ([2] = 5.10^{-4} \text{M})\) containing various concentrations of substrate \(S3\) at 24°C. (b) Fitting process and \(Keq\).

\[
Keq = 137.28 \text{ M}^{-1}
\]

Table S2: (a) spectral changes observed of solutions of solvate complex \(2 ([2] = 5.10^{-4} \text{M})\) containing various concentrations of substrate \(S4\) at 24°C. (b) Fitting process and \(Keq\).

\[
Keq = 62 \text{ M}^{-1}
\]
**Stopped-flow experiments**

**Determination of association rate constants using stopped-flow UV-Vis methods**

The experiments were carried out on an OLIS stopped-flow apparatus equipped with a thermostatic spectrophotometer. The solution of solvate complex 2 was prepared according to the protocol described in the experimental part “preparation of solvate complex 2”. The preparation of the finale solutions was realized by appropriate dilutions of the solvate complex and the substrates. The gas-tight syringes were loaded in an inert atmosphere glove box and positioned on the stopped flow apparatus which was previously flushed with N₂. The reaction was monitored spectroscopically at 390 nm. The measurement was performed until the equilibrium was reached. To avoid inaccuracies due to the preparation of the sample, the measurements for substrate S₃ and S₄ were done successively and with the same freshly prepared stock-solution of solvate complex 2. Three kinetic traces were obtained for each temperature conditions with a typical standard deviation of the slope of the pseudo-first-order section of ± 10% of the mean value.

First, the measured data of the stopped-flow measurements (plotted with the absorbance in time) were smoothed, to minimize the noise inherent in the integral measurements (to capture important patterns in the data, while leaving out noise), with the Origin 8.0 software. To avoid artefacts, the correctness of the model used was evaluated and confirmed by the analysis of the regular residuals of the fitting. The evolution in time of the catalyst-substrate complex 3 was calculated based on the final absorbance observed at the equilibrium ($A_{\text{max}}$), for which

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corresponds the concentration of the complex at the equilibrium. The concentration at the equilibrium was determined by solving the quadratic polynomial equation deduced from the expression of the equilibrium constant (left, Table S3). By plotting the rate of formation of catalyst-substrate complex in function of the concentration of the solvate complex, the reaction rate constant was determined by the slope the linear part of the plot (Table S3).

Table S4 and Table S5 summarize de data of the temperature dependence experiments for substrate S3 and S4 (top) and the corresponding Eyring plot for the determination of ΔH and ΔS (bottom).
Table S3. Left: evolution of the absorbance in time upon addition of substrate S3 to solvate complex 2 and determination of [3] eq. Right: plot of rate = f ([2]) and determination of the reaction rate constant at 23°C.

\[ K_{eq} = \frac{x}{([2]_0 - x)([S3]_0 - x)} \]

With \([2]_0 = 0.00025 \text{ M}, [S3]_0 = 0.0375 \text{ M} \) and \( K_{eq} = 137 \text{ M}^{-1} \)

\[ x = 2.090758 \times 10^{-4} \text{ M} = [3]_{eq} \Leftrightarrow A_{max} \]

\[ -\frac{d[2]}{dt} = \frac{d[3]}{dt} = k_{obs}[2] \]

\[ k_{obs} = k_1 [S3] \]

\( k_{obs} \) is given by the slope of the curve
Table S4. Top: kinetic data for the association of solvate complex 2 with substrate S3. Bottom: Eyring plot.

<table>
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<th>T (K)</th>
<th>$k_{on}$ (s$^{-1}$)</th>
<th>error</th>
<th>$k_1$ (M$^{-1}$.sec$^{-1}$)</th>
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<tr>
<td>283</td>
<td>0.245</td>
<td>0.0408</td>
<td>6.553</td>
<td>1.088</td>
<td>1.880</td>
<td>0.023</td>
<td>-3.765</td>
</tr>
<tr>
<td>293</td>
<td>0.486</td>
<td>0.0356</td>
<td>12.965</td>
<td>0.949</td>
<td>2.562</td>
<td>0.044</td>
<td>-3.117</td>
</tr>
<tr>
<td>295</td>
<td>0.514</td>
<td>0.0301</td>
<td>13.707</td>
<td>0.804</td>
<td>2.617</td>
<td>0.046</td>
<td>-3.069</td>
</tr>
<tr>
<td>303</td>
<td>1.032</td>
<td>0.0212</td>
<td>27.536</td>
<td>0.565</td>
<td>3.315</td>
<td>0.090</td>
<td>-2.398</td>
</tr>
<tr>
<td>313</td>
<td>1.557</td>
<td>0.0173</td>
<td>41.536</td>
<td>0.463</td>
<td>3.726</td>
<td>0.132</td>
<td>-2.019</td>
</tr>
</tbody>
</table>

$\ln k/T = f(1/T)$

- $y = -5321x + 15.038$
- $R^2 = 0.9871$
**Table S5.** Top: kinetic data for the association of solvate complex 2 with substrate S4. Bottom: Eyring plot.

<table>
<thead>
<tr>
<th>T (K)</th>
<th>k_{on} (s^{-1})</th>
<th>error</th>
<th>k_{i} (M^{-1}.sec^{-1})</th>
<th>error</th>
<th>Ln k</th>
<th>k/T</th>
<th>ln k/T</th>
</tr>
</thead>
<tbody>
<tr>
<td>283</td>
<td>0.0601</td>
<td>0.0082</td>
<td>1.603</td>
<td>0.220</td>
<td>0.472</td>
<td>0.005</td>
<td>-5.173</td>
</tr>
<tr>
<td>293</td>
<td>0.1634</td>
<td>0.0019</td>
<td>4.358</td>
<td>0.050</td>
<td>1.472</td>
<td>0.014</td>
<td>-4.208</td>
</tr>
<tr>
<td>295</td>
<td>0.1987</td>
<td>0.0046</td>
<td>5.299</td>
<td>0.122</td>
<td>1.667</td>
<td>0.017</td>
<td>-4.019</td>
</tr>
<tr>
<td>303</td>
<td>0.732</td>
<td>0.0487</td>
<td>19.541</td>
<td>1.301</td>
<td>2.972</td>
<td>0.064</td>
<td>-2.741</td>
</tr>
<tr>
<td>313</td>
<td>1.9197</td>
<td>0.1109</td>
<td>51.1928</td>
<td>2.958</td>
<td>3.935</td>
<td>0.163</td>
<td>-1.810</td>
</tr>
</tbody>
</table>

\[ y = -10316x + 31.135 \]
\[ R^2 = 0.9853 \]
Table S6. Stopped-flow data obtained for the reaction between solvate complex 2 and substrate \( S_3 \) and \( S_4 \).

<table>
<thead>
<tr>
<th>Substrate</th>
<th>T (°C)</th>
<th>( k_1 ) (M(^{-1}).s(^{-1}))</th>
<th>( \Delta H ) (kcal mol(^{-1}))</th>
<th>( \Delta S ) (cal.M(^{-1}).K(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( S_3 )</td>
<td>10</td>
<td>6.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>12.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>13.70</td>
<td>10.5</td>
<td>-17.3</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>27.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>41.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( S_4 )</td>
<td>10</td>
<td>1.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>4.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>5.29</td>
<td>20.4</td>
<td>14.6</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>19.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>51.19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gas uptake experiments

The experiments were carried out in the AMTEC SPR16 equipment\(^{19}\) consisting of 16 parallel reactors equipped with internal temperature and pressure sensors, and a mass flow controller. The apparatus is suited for monitoring gas uptake profiles during the catalytic reactions. Prior to catalytic experiments, the autoclaves were heated to 110°C and flushed with argon (22 bar) five times. Next the reactors were cooled to room temperature and flushed again with argon (22 bar) five times. Then, the autoclaves were charged with solutions of the rhodium catalysts, substrate,

\(^{19}\) www.amtec-chemnitz.de
product (if necessary) in CH₂Cl₂ (8ml). The reactors were pressurized with hydrogen and heated up to 25°C. The pressure was kept constant during the whole reaction, and the gas uptake was monitored and recorded for every reactor. After catalysis, the pressure was reduced to 2.0 bar and samples were taken for further analysis. Conversions were determined by NMR analysis of the final reaction mixtures. Enantiomeric excess was determined by GC or HPLC. All the measured data of the gas consumption in time were smoothed, to minimize the noise inherent in the integral measurements (to capture important patterns in the data, while leaving out noise),¹⁰ with the Origin 8.0 software, applying exponential model or similar. To avoid artefacts, the correctness of the model was evaluated and confirmed by the analysis of the regular residuals of the fitting. The smoothed data were used to determine initial TOF’s.

1. Hydrogenation of substrate S3 by complex 1– different initial substrate concentration

1) Conditions: [S3] = 0.1 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 10 bar, 25°C.
2) Conditions: \([S3] = 0.15 \, \text{M}, \, [\text{Rh(L1)(L2)}] = 0.2 \, \text{mM}\) in \(\text{CH}_2\text{Cl}_2\) (8 ml), pressure \(\text{H}_2\) 10 bar, 25°C.
3) Conditions: $[S3] = 0.2$ M, $[\text{Rh(L1)(L2)}] = 0.2$ mM in CH$_2$Cl$_2$ (8 ml), pressure H$_2$ 10 bar, 25°C.

**Conversion**

- Experimental
- Fitted

**Residual Residuals**
4) Conditions: \([S3] = 0.25 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml}), \text{ pressure H}_2 10 \text{ bar, 25°C.} \)
2. Hydrogenation of substrate S3 by complex 1 – different hydrogen pressure

1) Conditions: \([S3] = 0.2 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM}\) in \(\text{CH}_2\text{Cl}_2\) (8 ml), pressure \(\text{H}_2\) 20 bar, 25°C.

![Conversion graph](image)

![Regular residuals](image)
2) Conditions: [S3] = 0.2 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 30 bar, 25°C.
3) Conditions: \([S_3] = 0.2 \text{ M, } [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 \text{ (8 ml), pressure H}_2 \text{ 40 bar, 25°C.}

![Conversion graph](image1)

![Regular residuals graph](image2)
3. Hydrogenation of substrate S4 by complex 1 – different initial substrate concentration

1) Conditions: [S4] = 0.1 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 10 bar, 25°C.

conversion

regular residuals
2) Conditions: [S4] = 0.15 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 10 bar, 25°C.
3) Conditions: [S4] = 0.2 M, [Rh(L1)(L2)] = 0.2 mM in CH2Cl2 (8 ml), pressure H2 10 bar, 25°C.
4) Conditions: \([S4] = 0.25 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM}\) in \(\text{CH}_2\text{Cl}_2\) (8 ml), pressure \(\text{H}_2\) 10 bar, 25°C.
4. Hydrogenation of substrate S4 by complex 1 – different hydrogen pressure

1) Conditions: [S4] = 0.2 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 20 bar, 25°C
2) Conditions: \([S4] = 0.2 \text{ M}, \ [\text{Rh(L1)(L2)}] = 0.2 \text{ mM} \) in \(\text{CH}_2\text{Cl}_2\ (8 \text{ ml})\), pressure \(\text{H}_2\) 30 bar, 25°C

### Conversion

![Conversion Graph](image)

- **Experimental**
- **Fitted**

### Regular Residuals

![Regular Residuals Graph](image)
3) Conditions: \([S4] = 0.2 \text{ M, } [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml})\), pressure \(H_2 40 \text{ bar, } 25^\circ\text{C}\)

conversion

regular residuals
5. Michaelis-Menten

In order to test the Michaelis-Menten kinetic model with a competitive product inhibition (equation 2) for experiments with different initial substrate concentrations of S3 and S4 (under otherwise identical conditions of pressure, temperature and catalyst concentration), the initial data (without smoothing) were used, to avoid the data deflection due to amplifying of the fitting errors. The numerical differentiation was performed, and all datasets from 4 different experiments were simultaneously fitted to the equation 2. The global fitting with parameter sharing method was applied using the data fitting software Origin 8.0. The maximum reaction rate $V_{max}$, the Michaelis-Menten constant $K_{MM}$ and the inhibition constant $K_i$ were set as shared free parameters for fitting, while the initial substrate concentration was set as fixed parameter for each dataset. Analysis of the regular residuals of the fitting confirmed the goodness of the fit.

1. Hydrogenation of substrate S3 by complex 1 – different initial substrate concentration

The raw data from 4 independent gas uptake experiments at different initial substrate concentration were fitted to the Michaelis-Menten equation. Three parameters were estimated during the global data fitting procedure: the maximum reaction rate $V_{max} = 0.38701\pm0.036 \ M*h^{-1}$, the Michaelis constant $K_{mm} = 0.04282\pm0.01892 \ M$, and the inhibition constant $K_i = 0.01449\pm0.00557M$. 

A) Conditions: \([S3] = 0.1 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM}\) in \(\text{CH}_2\text{Cl}_2\) (8 ml), pressure \(\text{H}_2\) 10 bar, 25°C.
B) Conditions: \([S3] = 0.15 \text{ M}, \text{[Rh(L1)(L2)]} = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml}), \text{ pressure H}_2 \text{ 10 bar, 25°C.} \)
C) Conditions: \([S3] = 0.2 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2\ (8 \text{ ml}), \text{ pressure } H_2 10 \text{ bar, } 25^\circ\text{C.} \)
D) Conditions: \([S_3] = 0.25 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml}), \text{ pressure H}_2 10 \text{ bar, 25}^\circ\text{C.} \)
2. Hydrogenation of substrate S4 by complex 1 – different initial substrate concentration

The raw data from 4 independent gas uptake experiments at different initial substrate concentration were fitted to the Michaelis-Menten equation. Three parameters were estimated during the global data fitting procedure: the maximum reaction rate $V_{\text{max}} = 0.1581 \pm 0.00977 \text{M}^{-1} \text{h}^{-1}$, the Michaelis constant $K_{\text{m}} = 0.06002 \pm 0.01375 \text{M}$, and the inhibition constant $K_{i} = 0.00424 \pm 0.00074 \text{M}$. 

![Graph showing the relationship between substrate concentration and reaction rate for different initial substrate concentrations.](image-url)
A) Conditions: $[S4] = 0.1 \text{ M}, [\text{Rh(L1)(L5)}] = 0.2 \text{ mM}$ in $\text{CH}_2\text{Cl}_2$ (8 ml), pressure $\text{H}_2$ 10 bar, 25°C.
B) Conditions: \([S4] = 0.15 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml}), \text{ pressure H}_2 10 \text{ bar, 25°C.}

**regular residuals**

**rate**

- fitted values
C) Conditions: [S4] = 0.2 M, [Rh(L1)(L2)] = 0.2 mM in CH₂Cl₂ (8 ml), pressure H₂ 10 bar, 25°C.

**regular residuals**

![regular residuals graph]

**rate**

![rate graph]
D) Conditions: \([S4] = 0.25 \text{ M}, [\text{Rh(L1)(L2)}] = 0.2 \text{ mM in CH}_2\text{Cl}_2 (8 \text{ ml}), \text{ pressure H}_2 10 \text{ bar, 25°C.}\)

- **regular residuals**
  - Scatter plot showing regular residuals.

- **rate**
  - Scatter plot showing rate vs. \([S4] / \text{M}\).
Determination of the reaction rate constant of the reaction $k_{cat}$

At high concentration of substrate and under the standard conditions (10 bar H$_2$, [sub] = 0.1 M, [Rh]=0.2 mM, ratio S/C=500 at 298 K), the coordination of the substrate is fast and thus the concentration of the catalyst-substrate complex is considered constant over a considerable time span (i.e. at the beginning of the reaction). This condition allows for the quasi-steady state approximation (QSSA) to be applied and the Michaelis-Menten constant $K_{MM}$ can be estimated as:

$$K_{MM} = \frac{k_{-1} + k_{cat}}{k_1}$$

and

$$k_{cat} = (K_{MM} \cdot k_1) - k_{-1}$$

In order to determine the rate constants of the reaction $k_{cat}$ for S3 and S4, the values of $k_{-1}$ and $k_1$ have been calculated. The Michaelis-Menten constants $K_{MM}$ are obtained directly from the gas uptake experiments by fitting of the reaction rate to the Michaelis-Menten equation.

a) Determination of the reaction rate constant $k_1$ at 298 K

The reaction rate constant $k_1$ at 298 K is calculated from the Eyring equation obtained by the stopped-flow experiments performed at different temperatures (see Table S4). For substrate S3, the Eyring equation obtained from the temperature experiments is:

$$\ln(k/T) = -5321/T + 15.038$$

Therefore, at T=298K
\[ \ln k = 2.879 \]

and

\[ k_1 = 17.79 \text{ M}^{-1} \text{ sec}^{-1} \text{ at 298 K for substrate } S3 \]

The same calculation was done from the Eyring equation associated to \( S4 \) (table S5) to obtain the reaction rate constant \( k_1 \) for substrate \( S4 \): \( k_1 = 9.15 \text{ M}^{-1} \text{ sec}^{-1} \text{ at 298 K} \).

b) **Determination of the reverse reaction rate constant \( k_{-1} \)**

\( K_{eq} \) and \( k_1 \) are obtained from the binding titration and the stopped-flow experiments respectively. Therefore, the reverse reaction rate constants \( k_{-1} \) is calculated directly from the relation between the equilibrium constant of a reaction and the associated reaction rate constants:

\[ K_{eq} = \frac{k_1}{k_{-1}} \]

and

\[ k_{-1} = \frac{k_1}{K_{eq}} \]

\( k_{-1} = 0.1295 \text{ sec}^{-1} \text{ for substrate } S3 \text{ at 298 K} \)

\( k_{-1} = 0.1475 \text{ sec}^{-1} \text{ for substrate } S4 \text{ at 298 K} \)

c) **Determination of the rate constant of the reaction \( k_{cat} \)**

The rate constant of the reaction \( k_{cat} \) is obtained from the estimated Michaelis-Menten equation using the values of \( K_{MM}, k_1 \) and \( k_{-1} \) at 298 K:
\[ k_{\text{cat}} = (K_{\text{MM}} \cdot k_1) - k_{-1} \]

\[ k_{\text{cat}} = 0.616 \text{ sec}^{-1} \text{ for substrate S3} \]

\[ k_{\text{cat}} = 0.401 \text{ sec}^{-1} \text{ for substrate S4} \]

**DFT Calculations**

*(for energies and coordinates, see supporting information part B)*

The geometry optimizations were carried out with the Turbomole program\(^\text{21}\) coupled to the PQS Baker optimizer\(^\text{22}\) at the ri-DFT level\(^\text{23}\) using the BP86\(^\text{24}\) functional and the resolution-of-identity (ri) method. The def2-TZVP basis set was used for the geometry optimizations of all stationary points. As the conventional DFT functionals usually lacks dispersion interactions, empirical dispersions forces were taken into account using Grimme's version 3 dispersions corrections.\(^\text{25}\)

All minima (no imaginary frequencies) and transition states (one imaginary frequency) were characterized by numerically calculating the Hessian matrix. ZPE and gas-phase thermal corrections (entropy and enthalpy at 298 K, 1 bar) from these analyses were calculated.


1. Construction of a potential energy surface

In order to take into account the influence of both steric hindrance and hydrogen bond interactions, we decided to compute the full system, using the coordinates of the crystal structures obtained as a starting point for subsequent geometry optimizations.26 Also, since other weak interactions can have an influence on the proposed H-bond effect, empirical dispersions forces were taken into account using Grimme’s version 3 dispersion corrections.27 To assess the method of calculation, we compared the results of optimization of the precatalyst at several levels of theory (BP86 and b3-lyp, with and without dispersion corrections) with the structure obtained by X-ray crystallography. The overlay of the solid-state structure with the structures optimized by DFT shows a good agreement between the different assessed methods and the X-ray structure (Figure S29).

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26 Preliminary calculations were performed on a simplified model in which the BINOL group had been replaced by a five-membered ring and both phenyl groups on the phosphine were replaced by methyl groups. However, this model was not accurate enough for such supramolecular systems and did not give consistent results at the BP86 level.

Figure S29. Overlay of the solid-state structure of supramolecular complex 1 and the DFT optimized structures (black: X-ray, blue: BP86/disp3, purple: b3-lyp/disp3).

Typical bond lengths and angles of the X-ray structures and the optimized geometries using different levels of theory are reported in Table S7. Among the different methods evaluated, the basis set BP86 with additional dispersion corrections gives the most accurate bond lengths compared to the X-ray structure, even though those values seem slightly overestimated when compared with the X-ray structure. The length of the hydrogen bond between the two ligands varies importantly with the different methods of calculation. It is clear from Table S7 that the hydrogen bond calculated with BP86 is shorter than the length determined in the solid state, while of the same order with b3-lyp. Due to the inaccuracy of X-ray analysis in determining the
position of hydrogen atoms (as diffraction by the electron in the bond is measured rather than the position of the hydrogen atom), a normalization of the N-H bond length is necessary. In fact, the N-H bond determined by X-ray diffraction is systematically too short, and as a consequence the hydrogen bond is too long.\textsuperscript{28} The normalization of the X-ray hydrogen bond length brings the corrected value to 1.909\AA.\textsuperscript{29} The H-bond length calculated at the b3-lyp/disp 3 level gives also a close value compared to the X-ray. However, the large deviation in the H-bond angle makes this method less reliable in the evaluation of H-bond effects. This conclusion is supported by other reports describing the underestimation of the hydrogen bond strength at the b3-lyp level.\textsuperscript{30} The same assessment of the method has been done on the acetonitrile-solvate complex, leading to the same conclusions. After evaluation of the different methods, calculations at the DFT-D3 BP86 def2-TZVP level appeared the most suitable to describe the current supramolecular system.\textsuperscript{31}

\textsuperscript{28} T. Steiner, Crystallography Reviews 2003, 9, 2-3, 177-228.
\textsuperscript{29} The normalization has been effected by correction of the X-ray value with the average systematic error observed in the literature in the comparison between X-ray and neutron diffraction results for hydrogen bonds (0.1\AA). For articles see: (a) G. A. Jeffrey, L. Lewis, Carbohyd. Res., 1978, 60, 179-182; (b) R.Taylor, O.Kennard, Acta Cryst., 1983, B39, 133.
\textsuperscript{31} In addition to the dispersion forces correction, the size of the optimized structures required to integrate a multiple grid m4 in the calculations. This additional grid size did not change significantly the energy of the optimized structures but enabled to obtain a more accurate gradient optimization and faster convergence of calculations.
**Table S7.** Length and angles of important bonds around the metal center in the complex 1.

<table>
<thead>
<tr>
<th></th>
<th>X-ray</th>
<th>BP86</th>
<th>BP86/disp3</th>
<th>b3-lyp&lt;sup&gt;a&lt;/sup&gt;</th>
<th>b3-lyp/disp3&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-P1 [Å]</td>
<td>2.26</td>
<td>2.299</td>
<td>2.246</td>
<td>2.312</td>
<td>2.256</td>
</tr>
<tr>
<td>Rh-P2 [Å]</td>
<td>2.313</td>
<td>2.370</td>
<td>2.320</td>
<td>2.403</td>
<td>2.350</td>
</tr>
<tr>
<td>P1-Rh-P2 [°]</td>
<td>92.06</td>
<td>93.41</td>
<td>90.93</td>
<td>93.73</td>
<td>91.36</td>
</tr>
<tr>
<td>Rh-C1 [Å]</td>
<td>2.228</td>
<td>2.229</td>
<td>2.230</td>
<td>2.252</td>
<td>2.263</td>
</tr>
<tr>
<td>Rh-C2 [Å]</td>
<td>2.267</td>
<td>2.290</td>
<td>2.307</td>
<td>2.339</td>
<td>2.357</td>
</tr>
<tr>
<td>H…O [Å]</td>
<td>2.009 (uncorrected)</td>
<td>1.909 (normalized)</td>
<td>1.959</td>
<td>1.822</td>
<td>2.012</td>
</tr>
<tr>
<td>NH…O [°]</td>
<td>169.65</td>
<td>171.32</td>
<td>172.56</td>
<td>171.89</td>
<td>174.25</td>
</tr>
</tbody>
</table>

<sup>a</sup> At the b3-lyp level, the size of the calculations was too large to calculate a Hessian, and it was therefore not possible to check unequivocally that the optimized structures are minima. However, the criteria of convergence of the optimizations are considered to be reliable enough in assigning these structures as minima.
2. Unsaturated pathway

Figure S30. Energy profile of the unsaturated pathways from diastereoisomers 2 and 8 (free energies at 298 K in kcal mol\(^{-1}\)).

3. Dihydride pathway

The observation of hydride species at high pressure and the possible crossover between the different reactions mechanisms has led us to investigate the dihydride pathway. Therefore, we have computed the coordination and oxidative addition of hydrogen to the solvate complex 1 (Figure S31). The approach of molecular hydrogen can occur on two sites of the solvate complex (trans to the phosphoramidite ligand or trans to the phosphine ligand) and was found to be barrierless in both cases.\(^{32}\) Each of the two \(\sigma\)-hydrogen solvate complexes 17 and 18 can undergo

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\(^{32}\) The approach of dihydrogen on the solvate complex 1 was simulated both by a dissociative process (removal of the dichloromethane molecule and subsequent approach of dihydrogen) and by an associative process (approach of the dihydrogen from the upper face of the solvate complex 1 followed by the displacement of the dichloromethane molecule and complete coordination of dihydrogen). Both simulations led to the conclusion that this step is barrierless.
oxidative addition leading in both cases to two dihydride solvate complexes (structures 19, 20, 21 and 22), depending on the position of the apical hydrogen.

**Figure S31.** Energy profile of dihydride pathway (free energies at 298 K in kcal mol\(^{-1}\)).

For the calculated paths (TS12, TS13, TS14 and TS15), this step requires an amount of energy ranging between 7 and 12 kcal mol\(^{-1}\). The uphill energy profile of the reaction explains why we did not observe the formation of hydrides in the NMR experiments under standard conditions (1-10 bar H\(_2\)).

4. **Semi-dihydride pathway**

We also investigated the possibility of the semi-dihydride pathway that was previously suggested by other groups.\(^{33}\) In this mechanism, the substrate is coordinated only through the carbonyl

group when the square planar complex undergoes the oxidative addition of hydrogen to yield a non-chelating dihydride Rh(III) octahedral species in which the double bond of the substrate is not bound to the metal center (Figure S32).

![Energy profile of the semi-dihydride pathway (free energies at 298 K in kcal mol⁻¹).](image)

**Figure S32.** Energy profile of the semi-dihydride pathway (free energies at 298 K in kcal mol⁻¹).

As can be seen from figure S32, the solvate complex 1 is stabilized upon coordination of the carbonyl group of the substrate (structures 23 and 24). The coordination of hydrogen is followed by the oxidative addition step. The oxidative addition from the σ-hydrogen species 25 and 26 can lead to two octahedral dihydride complexes, depending on the apical position of the hydride. Interestingly, the energy differences between the σ-hydrogen species 25 and 26, and the energies of the transition states (TS16, TS17, TS18 and TS19) are of the same order of magnitude as the oxidative addition step calculated for the dihydride pathway. This means that the coordination of the substrate doesn’t significantly affect the energy required in the oxidative
addition step between the semi-hydride pathway and the dihydride pathway. Therefore, hydrogen bonds do not seem to affect this oxidative addition step.

5. Overview on the mechanisms

To get insight in the reaction mechanism, the energy profile of the lowest route for the unsaturated pathway, the dihydride pathway and the semi-hydride pathway have been plotted on the same graph (Figure S33). Starting from the solvate complex 1, the catalytic system undergoes an energetically disfavored process when directly reacting with molecular hydrogen (Figure S33, red line). On the other hand, upon coordination of the substrate to the solvate complex 1, the system produces a stable catalyst-substrate complex. Both these results are in agreement with experimental observations that identified the substrate-catalyst complex 2 as the resting state of the reaction.
Figure S33. Overall energy profile of various routes in the hydrogen bond assisted reaction mechanism for the supramolecular asymmetric hydrogenation (free energies at 298 K in kcal mol\(^{-1}\)).

Upon comparing the unsaturated pathway with the semi-dihydride route one can conclude that 24 and 2 may be in equilibrium, but the route from 2 via TS16 to form 30 is associated with a higher energy barrier than the route to form dihydride 5. It was not possible to calculate the energy required in the coordination of the double bond in structure 24. However, this step might occur via a dissociative process of the dichloromethane molecule and therefore involves a low energy barrier leading to fast equilibrium between the structures 23 and 24 (see Figure S33), and the diasteromer 2. Also, we could not calculate the energy required during the coordination of the double bond in non-chelating octahedral species 27, 28, 29, 30 (values from the literature estimate the energy required in this step between 9 and 14 kcal mol\(^{-1}\)). Since the semi-dihydride
path and the unsaturated path are in equilibrium via diasteromer 2 and that the energy required for the coordination of the double bond in the non-chelating Rh(III) species 27, 28, 29, 30 are most likely to be higher in energy than TS3, the unsaturated pathway is favored over the semi-dihydride path. Hence, in light of the results obtained experimentally and the DFT study of the energy profile of the reaction, we conclude that the unsaturated pathway is the dominant pathway.