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Realistic Energy Surfaces for Real-World Systems: An IMOMO CCSD(T):DFT Scheme for Rhodium-Catalyzed Hydroformylation with the 6-DPPon Ligand**

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Abstract: The hydroformylation of terminal alkenes is one of the most important homogeneously catalyzed processes in industry, and the atomistic understanding of this reaction has attracted enormous interest in the past. Herein, the whole catalytic cycle for rhodiumcatalyzed hydroformylation with the 6diphenylphosphinopyridine-(2H)-1-one (6-DPPon) ligand **1** was studied. This catalytic transformation is challenging to describe computationally, since two requirements must be met: 1) changes in the hydrogen-bond network must be modeled accurately and 2) bond-formation/bond-breaking processes in the coordination sphere of the rhodium center must be calculated accurately. Depending on the functionals used (BP86, B3LYP), the results were found to differ strongly. Therefore, the complete cycle was calculated by using highly accurate CCSD(T) computations for a PH₃ model ligand. By applying an

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Introduction

The hydroformylation of terminal alkenes is one of the most important industrial processes which relies on homogeneous catalysis.^[1] More than 9×10^6 t of oxo products are produced annually.^[2] The best regioselectivity for the frequently more desirable linear aldehyde can be obtained with rhodium catalysts modified with chelating diphosphine and diphosphite ligands.^[3] Despite their unique selectivities, the synthesis of these classic bidentate ligands can be difficult and may include many synthetic steps, and in some cases this makes

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- [**] 6-DPPon: 6-diphenylphosphinopyridine-(2*H*)-1-one; IMOMO: integrated molecular orbital plus molecular orbital.
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the ligands more expensive than the noble-metal source. As an alternative approach for efficient crafting of the microenvironment around the metal center, we^[4] and others^[5] recently introduced the concept of monodentate-to-bidentate ligand self-assembly. For this we studied the rather simple 6diphenylphosphino-(2*H*)-1-one system, which has hydrogenbonding capabilities between the pyridone and hydroxypyridine forms in the coordination sphere of a transition metal (Scheme 1).



Scheme 1. Self-organization of **1** in the coordination sphere of a late transition metal.

In previous studies we were able to show that the expected ligand-ligand interaction indeed occurs in a $[Cl_2Pt(1)_2]$ complex.^[6] The hydrogen bonds in the $[Cl_2Pt(1)_2]$ complex were intensively studied, and the enthalpic stabilization through hydrogen bonding was determined to be 14–15 kcal mol⁻¹.^[6a] Furthermore, we were able to demonstrate that this ligand system shows selectivity towards the linear aldehyde in rhodium-catalyzed hydroformylation similar to



Scheme 2. Results of the rhodium-catalyzed hydroformylation of 1-octene with PPh₃ (2), Xantphos (3) and 6-DPPon (1) ligands. Conditions: Rh:L:substrate = 1:20(10):7500, 80 °C, 10 bar, toluene.

those obtained with bidentate ligands such as Xantphos (3). The turnover frequencies (TOF) are even higher than those determined for the monodentate triphenylphosphine (2) under identical conditions (Scheme 2). Furthermore, we were able to detect hydrogen bonds in a competent intermediate of the catalytic transformation, namely, the rhodium acyl complex [(COR)Rh(1)₂(CO)₂] ($R = C_8 H_{17}$).^[7]

These results imply that for a realistic energy surface of the catalytic cycle the hydrogen-bond properties and the reaction energies for the elementary steps of the catalytic transformation must be predicted accurately. Density functional calculations are routinely applied to gain insight into the mechanisms of transition metal catalyzed transformations. In the last few years a growing number of DFT func-

tionals was developed (for exmeta-hybrid^[8] ample and double-hybrid functionals^[9]) to overcome the known shortcomings (reaction barriers, dispersion) of DFT calculations. However, the results of DFT calculations strongly depend on the chosen functional, and how appropriate a functional is to determine enthalpies is always questionable, since the performance of functionals normally depends on their parameterization.^[10] Furthermore, no systematic improvement of the accuracy of DFT calculations by applying larger basis sets is possible.^[11] We herein present an approach which is based on highlevel ab initio computations for a small model system. The accurate ab initio calculations allow standard DFT calculations of larger real-world systems to be corrected for their the light of experimental results. Finally, the two-layer integrated molecular orbital plus molecular orbital (IMOMO) method is introduced and validated.

Results and Discussion

Performance of the DFT functionals for the hydrogen-bond properties: In a previous work we presented the X-ray structure of symmetric pyridine dimer **1A**·**1A** (Figure 1).^[6a] This solid-state structure was used to evaluate the performance of the DFT functionals applied herein for predicting the geometries of the hydrogen bonds in the **1A**·**1A** dimer (Table 1). Both functionals describe the structural features



Figure 1. Overlay of the solid-state structure of the symmetric 6-DPPon dimer (1A·1A). and the DFT computed structures (blue: BP86/SDD-6-31G**, full color: B3LYP/SDD-6-31G**, black: X-ray.

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intrinsic drawbacks. We first validate the approach by considering a model system for which rigorous calculations at the CCSD(T) level are possible. Rhodium-catalyzed hydroformylation with the 6-diphenylphosphinopyridine-(2H)-1one (6-DPPon) ligand 1 was chosen as a case study. First, the accuracy of the functionals for describing hydrogen-bond energies is assessed by comparison to experimental results. Next, the results for the elementary steps of the catalytic transformation are discussed in



of the hydrogen-bond system in satisfactory agreement with the X-ray structure. BP86 slightly underestimates the distance between the two ligands by 0.05 Å. Furthermore, we were able to determine the free dimerization enthalpy of **1A** by NMR titration experiments.^[6a] The results of the calculations using the BP86 and



Scheme 3. Synthesis of $[HRh(1)_3(CO)]$ (4). The box marks the monomeric unit used for assessment of the DFT functionals.

Table 1. N=O distance and N=H=O angle in the symmetric $1A{\cdot}1A$ dimer.

	X-ray	BP86/6-31G**	B3LYP/6-31G**
NH•••O [Å] N−H•••O [°]	2.777(1) ^[a] 177.3(2) ^[a]	2.729 179.1	2.772 ^[a] 179.7 ^[a]

[a] Values taken from ref. [6a].

the B3LYP functional are in good agreement with the experiment (Table 2). This finding is consistent with previous studies by Perdew et al, who predicted the dissociation energy of ten hydrogen-bonded complexes with mean absolute errors (MAE) of 0.76 and 0.43 kcalmol⁻¹ for the BP86 and the B3LYP functional, respectively.^[12] For the study presented herein, this is important, since it suggests that changes in the hydrogen bond system during the catalytic transformation can also be expected to be described accurately.

Table 2. Free dimerization enthalpy of **1A** determined by NMR titration experiments and computed at the BP86 and B3LYP level of theory.

	NMR	BP86/6-31G**	B3LYP/6-31G**
$\Delta G [m kcal mol^{-1}]$	$-5.95 \pm 0.075^{[a]}$	-5.18	$-6.05^{[a]}$

[a] Values taken from ref. [6a].

Performance of the DFT functionals for rhodium complexes bearing 6-DPPon (1) ligands: We previously reported the synthesis of $[HRh(1)_3(CO)]$ (4).^[7] This complex, which is present as a dimer in solution and in the solid state, was characterized by X-ray analysis. To save CPU time we calculated only one monomeric unit and compared the structure obtained to that derived from X-ray analysis (Scheme 3). An overlay of the DFT calculated structures and the X-ray structure is shown in Figure 2. Clearly, both functionals predict the relative orientation of the heteroaromatic rings forming the hydrogen-bond network in close agreement with the solid-state structure (Figure 2).

Comparing the X-ray and DFT structures (Table 3) reveals that BP86 shows good agreement for the bond lengths at the rhodium center. For example, the rhodium–phosphorous bond lengths differ by only 0.04 Å. B3LYP overestimates the rhodium–phosphorus bond lengths by 0.08 Å, but the predicted rhodium–carbon bond length is in close agree-



Figure 2. Overlay of the solid-state structure of **4** and the DFT computed structures (blue: BP86/SDD-6-31G**, full color: B3LYP/SDD-6-31G**, black: X-ray).

Table 3. Equilibrium structure of $[HRh(1)_3(CO)]$ measured by X ray and calculated by DFT.

	X-ray	BP86/SDD-6-31G**	B3LYP/SDD-6-31G**
Rh–P1 [Å]	2.3023(7)	2.341	2.366
Rh–P2 [Å]	2.3027(6)	2.359	2.389
P1-Rh-P2 [°]	115.23(3)	113.98	115.08
Rh–CO [Å]	1.908(3)	1.902	1.913
NH•••N [Å]	2.892(3)	2.949	3.035
N–H•••N [°]	169(3)	167	165
OH•••O [Å]	2.657(4)	2.553	2.602
O−H•••O [°]	170(4)	169	168

ment to the X-ray structure. Furthermore, both functionals show good agreement for the P-Rh-P angle in comparison to the X-ray structure. The P-Rh-P angle was identified previously as an important parameter for the catalytic performance of bidentate phosphine ligands in rhodium-catalyzed hydroformylation.^[13]

The catalytic cycle: The generally accepted mechanism^[14] for rhodium catalyzed hydroformylation summarized in Scheme 4 consists of CO dissociation (step I), alkene coordination (step II), hydrometalation followed by CO coordination (steps III and IV) and migratory insertion (step V) leading to a rhodium acyl complex, which can undergo oxidative addition in the presence of H₂ (step VI). A final reductive elimination leads to a 16 valence electron (VE) species and concomitant formation of aldehyde (step VII).

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have good performance by predicting the hydrogen-bond strength compared to the experiment (Table 2), one would expect that the free-energy change of CO dissociation is in good agreement between the two functionals. However, the opposite is the case (Table 5). The E + zpv and ΔG values predicted by the BP86 and the B3LYP functional differ by more than 8 kcal mol⁻¹. However, since kinetic studies revealed an inverse first-order dependence of the TOF on the CO partial pressure, an accurate description of the energetics of this elementary step is desirable. Furthermore,

Scheme 4. Generally accepted mechanism for the rhodium-catalyzed hydroformylation of terminal alkenes.

We now focus on the individual elementary steps and introduce the IMOMO protocol used in the following, which will be validated for CO dissociation from the 18-VE complex [HRh(1_2 (CO)₂] (5) to furnish the 16-VE complex 6.

CO dissociation: Both DFT functionals employed herein predict *trans*-[HRh(1)₂(CO)] (*trans*-6) to be more stable than *cis*-[HRh(1)₂(CO)] (*cis*-6).^[15] Both functionals predict nearly identical structural changes on going from *eqeq*-5 to *trans*-6 (Figure 3). Regarding the changes in the hydrogenbond network, both functionals predict elongation of the NH···N bond by 0.5 Å, whereas the OH···O bond length remains unchanged at both levels of theory (Table 4).

Since both functionals predict similar (or identical) changes in the hydrogen-bond network and were proven to

Table 4. Changes in the N···N and O···O distance by going from *eqeq-5* to *trans-6*.

	BP86/SDD-6-31G**		B3LYP/SDD-6-31G**	
	eqeq-5	trans-6	eqeq-5	trans-6
NHN [Å]	2.90	3.40	2.96	3.51
OHO [Å]	2.57	2.59	2.63	2.63

	$E + zpv [kcal mol^{-1}]$	$\Delta G [ext{kcal mol}^{-1}]$
BP86/SDD-6-31G**	29.91	18.89
B3LYP/SDD-6-31G**	21.71	10.49



 $[HRh(1)_2(CO)_2]$ was identified as resting state of the catalytic transformation by in situ IR spectroscopy (Figure 4).

These results clearly indicate that CO dissociation may strongly contribute to the overall barrier of rhodium-catalyzed hydroformylation with the 6-DPPon (1) ligand.

The importance of this elementary step is also highlighted by the fact that, in a thorough investigation on the rate-determining step for hydroformylation with xanthene-based ligands, CO dissociation from the trigonal-bipyramidal [HRh-(PP)(CO)₂] complex was discussed to be rate-determining.^[16] We therefore performed high-level ab initio single-point calculations for a simplified model system in which the li-

Figure 3. Formation of *trans*-6 by CO dissociation from *eqeq*-5. The 3D figure shows an overlay of the BP86 (blue) and the B3LYP (full color) optimized structure.

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Figure 4. Changes in the IR spectrum after addition of 1-octene to preformed $[HRh(1)_2(CO)_2]$ at room temperature in toluene.

gands are replaced by PH_3 (Scheme 5). To obtain reliable geometries BP86 was used in conjunction with the smallcore ECP28MDF and the corresponding Dunning aug-ccpVTZ basis set (in the following denoted AVTZ), which was also used for all other atoms.



Scheme 5. Model reaction used for the ab initio calculations.

Since for the small system containing the PH_3 ligand CCSD(T) calculations above the triple- ζ level are also not suitable, additional MP2 calculations were used to extrapolate the CCSD(T) computations to the quadruple- ζ level (i.e., aug-cc-pwCVQZ). This level of theory is in the following denoted as CCSD(T)-MP2/AwCVQZ, the basis set re-

ferring to the largest basis used in the MP2 calculations. To determine whether the difference in predicting the reaction enthalpy of *eqeq*-5 to *trans*-6 may originate from an insufficient description of the Rh-CO bond strength, the model reaction was recalculated by using BP86/ SDD-6-31G** and B3LYP/ SDD-6-31G**. Furthermore, the DFT functionals were used in combination with the AVTZ basis set to investigate their basis-set dependence and together with the D3 correction of Grimme et al. to evaluate the importance of dispersion correction.^[17] To exclude shortcomings of the BP86 and the

Figure 5. Alkene coordination leading to *eqeq-7*. The 3D figure shows an overlay of the BP86 (blue) and the B3LYP (full color) optimized structures.

B3LYP functional, we performed additional single-point calculations for the model system with the parameter-free hybrid PBE0 functional, the meta-GCA functional M06L, the global meta-hybrid M06 functional, and the long-range and dispersion-corrected ω B97X-D functional. The aug-ccpVTZ-PP (AVTZ) basis set was used for these calculations.

Indeed, comparison of the CCSD(T) and the DFT results shows that BP86 tends to overestimate the energy required for CO dissociation, whereas B3LYP in conjunction with the double-zeta basis set is in excellent agreement with the CCSD(T) calculations. Employing larger basis sets is of limited use (Table 6, entries 3 and 5). In combination with the AVTZ basis set, the B3LYP-D3, M06L and ω -B97X-D functionals show the smallest deviation from the energy calculated at the CCSD(T)-MP2 level of theory.

Alkene coordination: We next investigated alkene coordination leading to alkene complex *eqeq*-7 (Figure 5). Ethene

Table 6. Comparison of the results for the model reaction Model- $5 \rightarrow$ Model-6 calculated by CCSD(T)-MP2 and DFT.

	$\Delta E [m kcal mol^{-1}]$	$\Delta\Delta E [m kcal mol^{-1}]^{[c]}$
CCSD(T)-MP2/AwCVQZ ^[a]	20.99	-
CCSD(T)/AVTZ	21.73	-0.74
BP86/SDD-6-31G**	28.86	-7.86
BP86/AVTZ	26.08	-5.08
BP86-D3/AVTZ	28.86	-7.86
B3LYP/SDD-6-31G**	20.95	-0.05
B3LYP/AVTZ ^[a]	17.65	3.35
B3LYP-D3/AVTZ ^[a]	20.10	0.89
PBE0/AVTZ ^[a]	23.99	-2.99
M06-L/AVTZ ^[a]	22.62	-1.62
M06-L/AVTZ ^[b]	22.68	-1.68
M06/AVTZ ^[a]	16.34	4.65
M06/AVTZ ^[b]	16.60	4.39
ω -B97X-D/AVTZ ^[a]	19.38	1.62

[a] Single-point energy calculations on BP86/AVTZ optimized structures. [b] Single-point energy calculations on M06 L/AVTZ optimized structures. [c] $\Delta\Delta E = \Delta E_{CCSD(T)} - \Delta E_{DFT}$.

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was used as model substrate to decrease the number of possible conformers. On comparing the E + zpv values predicted at the DFT level, again a difference of 8 kcal mol⁻¹ was found between BP86 and B3LYP. Moreover, BP86 predicts the reaction to be exergonic, whereas B3LYP predicts an endergonic reaction (Table 7).

Table 7. E + zpv and ΔG values for the conversion of *trans*-6 to eqeq-7.

	$E + zpv [kcal mol^{-1}]$	$\Delta G [m kcal mol^{-1}]$
BP86/SDD-6-31G**	-15.51	-1.78
B3LYP/SDD-6-31G**	-8.12	5.45

To establish a realistic mechanistic picture of the rhodium-catalyzed hydroformylation with ligand 1, obtaining a realistic enthalpy for alkene coordination by means of computational chemistry is important, since kinetic experiments revealed a first-order dependence of the TOF on the concentration of 1-octene.[6a] Furthermore, many important homogenously catalyzed reactions start with coordination of an alkene to a late transition metal (e.g., rhodium-catalyzed hydrogenation^[18] and the Tsuji-Trost^[19] reaction). Establishing a methodology which would enable reliable prediction of the energetics of the addition of an unsaturated C-C bond to a transition metal seems therefore indispensable. Again, a model reaction in which the 6-DPPon ligand was replaced by PH₃ was investigated by means of ab initio calculations. Interestingly, by comparison between the CCSD(T) calculations and the DFT calculations, BP86/SDD-6-31G** is found to be in good agreement with the ab initio calculations (Table 8), whereas B3LYP underestimates the energy gained by alkene coordination by 8 kcal mol⁻¹.

Table 8. Comparison of the results for the model reaction Model- $6 \rightarrow$ Model-7 calculated by CCSD(T) and DFT.

	$\Delta E [m kcal mol^{-1}]$	$\Delta\Delta E [m kcal mol^{-1}]^{[c]}$
CCSD(T)-MP2/AwCVQZ ^[a]	-17.62	-
CCSD(T)/AVTZ	-18.14	0.53
BP86/SDD-6-31G**	-17.30	-0.32
BP86/AVTZ	-14.20	-3.42
BP86-D3/AVTZ	-19.33	1.71
B3LYP/SDD-6-31G**	-9.90	-7.72
B3LYP/AVTZ ^[a]	-6.27	-11.35
B3LYP-D3/AVTZ ^[a]	-10.75	-6.87
PBE0/AVTZ ^[a]	-15.38	-2.23
M06-L/AVTZ ^[a]	-13.56	-4.02
M06-L/AVTZ ^[b]	-13.61	-4.07
M06/AVTZ ^[a]	-9.65	-7.97
M06/AVTZ ^[b]	-9.68	-7.94
ω-B97X-D/AVTZ ^[a]	-13.13	-4.49

[a] Single-point energy calculations on BP86/AVTZ optimized structures. [b] Single-point energy calculations on M06 L/AVTZ optimized structures. [c] $\Delta\Delta E = \Delta E_{CCSD(T)} - \Delta E_{DFT}$

Since the B3LYP functional was shown to be in excellent agreement with the CCSD(T)-MP2/AwCVQZ calculations for the first elementary step (CO dissociation) the results presented herein show that benchmarking the performance

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of DFT functionals against only one elementary step of a catalytic transformation can be misleading. This can also be seen from the fact that, in combination with the AVTZ basis set, the PBE0 functional displays the smallest deviation of the energetics of the alkene coordination from the CCSD(T)-MP2/AwCVQZ compound calculation (Table 8). The M06L and ω-B97X-D functionals, which were found to predict the CO dissociation rather accurately with respect to the CCSD(T)-MP2/AwCVQZ calculations (Table 6), show deviations of about 4 kcalmol⁻¹ for alkene coordination. However, by comparing the performance of the BP86 and B3LYP functionals with the D3-corrected variants, it is obvious that the dispersion correction can indeed partially solve the problem of predicting the rhodium-ethene binding. The popular M06 functional shows deviations of 4.7 kcalmol⁻¹ for CO dissociation and 8.0 kcalmol⁻¹ for alkene coordination from the CCSD(T)-MP2/AwCVQZ calculations. In summary, we were not able to identify a DFT functional which leads to reliable results for both CO dissociation and alkene coordination.

The CCSD(T):DFT IMOMO scheme: Following earlier work of Morokuma et al., we decided that quantitative information about the intrinsic error of the DFT calculations for a specific elementary step of the catalytic cycle can be used to design a two-layer IMOMO scheme.^[20] The idea of an IMOMO calculation is to split the investigated system into two layers which are treated by different methods and basis sets.^[21] The model complex serves as high layer and is treated with a high-level ab initio method [here CCSD(T)], whereas the real-world system, treated at the DFT level, can be regarded as the low layer (Scheme 6). The IMOMO



Scheme 6. Schematic representation of the two-layer IMOMO extrapolation scheme used herein.

energy is then obtained by three independent methods [Eq. (1)].

$$\Delta E_{\text{IMOMO(CCSD(T):DFT)}} = \Delta E_{\text{real world (DFT)}} + (\Delta E_{\text{Model (CCSD(T))}} - \Delta E_{\text{Model (DFT)}})$$
(1)

Since the BP86 and B3LYP functionals in combination with a double- ζ basis set were shown to have a good performance for the hydrogen-bond properties and the structural features of a the [HRh(1)₃(CO)] complex, we used these efficient combinations of functionals and basis sets for the de-

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scription of the real-world system. The IMOMO scheme which uses CCSD(T) single-point calculations extrapolated with MP2 to the aug-cc-pwCVQZ basis set on BP86/aug-cc-pVTZ optimized structures on the model system in combination with DFT calculations using SDD-6-31G** on the real-world system is in the following designated CCSD(T)-MP2:DFT. By applying this IMOMO method to the "real-world" CO dissociation step (Scheme 3), excellent agreement between BP86 and B3LYP was achieved.

Applying the IMOMO scheme reduces the difference in the predicted energy and enthalpy changes for CO dissociation from eqeq-**5** between the two functionals is from more than 8 kcal mol⁻¹ to less than 1 kcal mol⁻¹ (Table 9). By ap-

Table 9. E+zpv and ΔG values for the conversion of *eqeq*-5 to *trans*-6 obtained with DFT and IMOMO methods.

	$E + zpv [kcal mol^{-1}]$	$\Delta G [ext{kcal mol}^{-1}]$
BP86/SDD-6-31G**	29.91	18.89
B3LYP/SDD-6-31G**	21.71	10.49
CCSD(T)-MP2:BP86	22.06	11.03
CCSD(T)-MP2:B3LYP	21.28	10.37

plying the CCSD(T)-MP2:DFT IMOMO scheme to the real-world reaction for alkene coordination, a difference of less than 0.3 kcal mol⁻¹ for the E+zpv and ΔG values is predicted with CCSD(T)-MP2:BP86 and CCSD(T)-MP2:B3LYP (Table 10, entries 3 and 4). Furthermore, both functionals now predict that alkene coordination is exothermic and exergonic.

Table 10. E + zpv and ΔG values for the conversion of *trans*-6 to *eqeq*-7 obtained with DFT and IMOMO methods.

	$E + zpv [kcal mol^{-1}]$	$\Delta G [m kcal mol^{-1}]$
BP86/SDD-6-31G**	-15.51	-1.78
B3LYP/SDD-6-31G**	-8.12	5.45
CCSD(T)-MP2:BP86	-15.83	-2.10
CCSD(T)-MP2:B3LYP	-15.84	-2.27

The IMOMO energy surface: The individual reaction enthalpies and activation energies of the elementary steps of the catalytic cycle calculated at the BP86/SDD-6-31G**, B3LYP/SDD-6-31G**, CCSD(T)-MP2:BP86, and CCSD(T)-MP2:B3LYP levels are summarized in Table 11.^[22]

On applying the IMOMO method presented herein, the average difference in the predicted reaction enthalpies between CCSD(T)-MP2:BP86 and CCSD(T)-MP2:B3LYP is 0.9 kcalmol⁻¹, as opposed to 5.4 kcalmol⁻¹ when the pure DFT functionals are applied. More importantly, the maximum difference is reduced from 8.4 to 2.1 kcalmol⁻¹. The free-energy surfaces derived from the IMOMO and DFT calculations are depicted in Figure 6.

Interestingly, the largest differences between the pure GGA and the hybrid DFT functional were observed in the early steps of the catalytic transformation (e.g., CO dissociation, alkene coordination, CO coordination to 8), in which the type of π -accepting ligands change. These findings clearly indicate that the DFT functionals studied herein have

Table 11. Reaction enthalpies and activation energies of the individual steps of the catalytic transformation as displayed in Scheme 4. All values are Gibbs free energies $[kcal mol^{-1}]$.^[a]

Reaction	BP86	B3LYP	CCSD(T):BP86	CCSD(T):B3LYP
eqeq-5→trans-6	18.89	10.49	11.03	10.54
trans-6→TS-1	10.34	11.00	7.21	6.85
trans-6→eqeq-7	-1.78	5.45	-2.10	-2.27
eqeq-7→TS-2	11.83	13.02	12.15	12.20
eqeq-7→cis-8	1.99	-1.33	0.99	2.37
$cis-8 \rightarrow eqeq-9$	-11.59	-4.67	-4.89	-5.67
eqeq-9→TS-3	8.07	9.81	13.29	12.91
eqeq-9→trans-10	-0.77	-3.34	2.10	3.39
trans-10→TS-4	9.57	13.01	9.54	7.93
<i>trans</i> -10 \rightarrow <i>eqeq</i> -11	1.48	3.43	5.65	3.55
eqeq-11→TS-5	10.04	11.25	8.10	7.96
eaea-11 \rightarrow trans-6 ^[b]	-21.01	-28.52	-23.13	-23.55

[a] The given energies and enthalpies are referred to the sum of the energies and enthalpies of *eqeq*-5 and the substrates. [a] With concomitant formation of the product, in this case propanal.

problems in accounting for π -backdonation effects. Furthermore, the BP86 functional predicts ethene coordination to be rate-determining. However, with the IMOMO method, independent of the DFT functional, hydrometalation is predicted to be rate-determining.

Comparison to the experimentally determined barrier: the energetic-span model: The kinetics discussed herein makes it seem difficult to identify a single step of the rhodium-catalyzed hydroformylation as rate-determining step. However, the experimentally found inverse first-order dependence on the alkene concentration and first-order dependence on the 1-octene concentration can be rationalized in terms of the energetic-span concept introduced by Shaik et al.^[23] The $[HRh(1)_2(CO)_2]$ complex, which was identified as resting state of the catalytic transformation by means of in situ IR spectroscopy, can then be regarded as the TOF-determining intermediate (TDI) and the transition state of the hydrometalation would represent the TOF-determining transition state (TDTS). On going from the $[HRh(1)_2(CO)_2]$ complex to the transition state for hydrometalation, one molecule of CO leaves the cycle, whereas one molecule 1-octene enters the cycle, and this explains the experimentally found dependence on the substrate concentrations. Both DFT functionals (BP86 and B3LYP) predict a ΔG^{\dagger} value of 28.9 kcal mol⁻¹ for ethene as substrate. In contrast, calculations based on the IMOMO method lead to a barrier of 20-21 kcal mol^{-1} (21.07 kcal mol⁻¹ at the CCSD(T)-MP2:BP86 and 20.47 kcalmol⁻¹ at the CCSD(T)-MP2:B3LYP level). For a direct comparison with the experimentally determined energetics, the energetic-span model was used to translate the measured TOFs into free activation energies [Eq. (2)],^[25]

$$TOF = (k_{\rm B}T/h)e^{-\Delta G^{TS}/RT} [\text{octene}] / [CO]$$
(2)

where $k_{\rm B}$ denotes the Boltzmann constant and *h* Planck's constant. Herein, $\Delta G^{\rm TS}$ represents the energetic span of the catalytic transformation.

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Figure 6. Gibbs free-energy surface calculated at the BP86/SDD-6-31G**, B3LYP/SDD-6-31G**, CCSD(T)-MP2:BP86, and CCSD(T)-MP2:B3LYP levels of theory.

To account for the difference between ethene and 1octene, the TDTS was reoptimized with propene as smallest model substrate for a monosubstituted alkene. The results at different temperatures are listed in Table 12. Indeed, both functionals overestimate the experimentally found barrier by 8–9 kcalmol⁻¹. The uncorrected PES displayed in Figure 6 clearly shows that BP86 overestimates the energetic span because the energy required for CO dissociation is overestimated. In case of the B3LYP functional, alkene coordination is predicted to be endergonic, and this results in overestimation of the overall barrier. In stark contrast, the IMOMO methods show the desired chemical accuracy with deviations of 1 kcalmol⁻¹ from the experimentally determined values.^[24]

Comparison to the experimentally determined TOF of the 6-DPPon (1) and Xantphos (3) ligands: The accuracy of the

Table 12. Experimental free activation barriers derived from the energetic-span model and the barriers computed by the pure DFT functionals and the IMOMO method. Propene was used as model substrate for the experimentally used 1-octene.

BP86

32.90

32.97

33.04

 ΔG^{TS} [kcal mol⁻¹]

CCSD(T)-

25.03

25.10

25.18

MP2:BP86

B3LYP

33.57

33.65

33.72

IMOMO method makes it seem possible to predict the cata-
lytic potential of given transition metal/ligand combinations.
To prove this, we compared the 6-DPPon (1) ligand with the
Xantphos ligand (3). Since experimental and computational
data suggest that the same rate-determining states account
for the TOF in the case of Xantphos-catalyzed hydroformy-
lation, ^[13,21c] the TDI and TDTS were reoptimized with this
ligand (Scheme 7).
A survey of a difference that we could a manage of a difference that 12 the

As expected from the results presented in Table 12, the pure GGA functional BP86 and hybrid functional B3LYP deliver completely unrealistic TOFs (0.03 and 0.01, and 0.01 and 0.001, respectively, as opposed to the experimentally observed TOFs of 3359 for the 6-DPPon (1) catalyst and 726 for the Xantphos (3) catalyst, see Table 13.

Conversely, by applying the CCSD(T)-MP2:DFT method, realistic TOFs were calculated for both catalyst systems (Table 13). Taking into account the exponential dependence of the TOF on the ΔG^{TS} values, the observed deviation between experiment and theory is surprisingly small. Therefore, the CCSD(T):DFT IMOMO method presented herein is a promising step towards in silico catalyst design.

Conclusion

We have provided a comprehensive computational investigation of the catalytic cycle of rhodium-catalyzed hydrofor-

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 $3359 \pm 240 \quad 24.84 \pm 0.05$

Exptl

 23.91 ± 0.02

 24.36 ± 0.09

Т

60

70

80

TOF

 1527 ± 39

 2375 ± 319

[°C] [h⁻¹]

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CCSD(T)-

25.09

25.16

25.24

MP2:B3LYP

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Table 13. Experimental free activation barriers and TOFs of the 6-DPPon (1) and Xantphos (3) ligands in comparison to the values computed with the pure DFT functional and the IMOMO method. Propene was used as model substrate for the experimentally used 1-octene.

Ligand	$TOF[h^{-1}]$					ΔG^{TS} [kcal mol ⁻¹]				
	Expt1 ^[a]	BP86	B3LYP	CCSD(T)- MP2:BP86	CCSD(T)- MP2:B3LYP	Exptl ^[a]	BP86	B3LYP	CCSD(T)- MP2:BP86	CCSD(T)- MP2:B3LYP
6-DPPon (1)	3359 ± 240	0.03	0.01	2028	1913	24.84 ± 0.05	33.04	33.72	25.18	25.24
Xantphos (3)	726 ± 40	0.002	0.001	140	218	25.91 ± 0.04	34.94	35.25	27.17	26.77

[a] Conditions: Rh:L:substrate = 1:20(10):7500, 80 °C, 10 bar, toluene.



Scheme 7. The rate-determining states for hydroformylation with the 6-DPPon (1) and Xantphos (3) ligands.

imaginary frequency. All discussed reaction energetics were calculated under standard conditions (1 bar ideal gas for all species and 298.15 K).

Model system: To obtain reliable energies for a model system in which ligand 1 was replaced by PH₃, we performed coupled cluster calculations including double excitation and approximate triple excitations [CCSD(T)]. However, these calculations require large basis sets to display the desired accuracy. For the model system, CCSD(T) calculations at the quadruple- ζ level are also not feasible. Therefore, the following scheme based on the nearly identical convergence behavior of CCSD(T) and MP2 towards

mylation with the 6-DPPon (1) ligand using an CCSD(T)-MP2:DFT IMOMO method. The calculations were supported by analysis of previously determined turnover frequencies within the framework of the energetic-span model. Calculations based on the IMOMO scheme yield excellent agreement with the experimental results for two popular DFT functionals (BP86 and B3LYP). This may be related to the observation that DFT calculations on the geometries and hydrogen-bond strengths in the ligand backbone lead to favorable agreement with experimental results. Furthermore, by applying the IMOMO methodology, the predicted activation barrier is now found to be in excellent agreement with the experimentally determined activation barrier for the 6-DPPon (1) and Xantphos (3) ligands. In summary, we have documented that IMOMO schemes can be used to reach the chemical accuracy of high-level ab initio methods for real-world systems, which suggests that this methodology may be useful for computer-aided catalyst design. Furthermore, the IMOMO scheme is rather modular and can be easily modified for specific cases. For example, if dispersion interactions in the real world system are important, DFT can be replaced by DFT-D3 as low-layer method.

Experimental Section

Real-world system: All intermediates and transition states containing ligand **1** of the catalytic cycle were fully optimized with the BP86^[26,27] and B3LYP^[28] functionals. The Stuttgart–Dresden relativistic core potential^[29] in conjunction with the D95 double-zeta basis set^[30] (SDD) was used for rhodium. The full-electron 6-31G** basis set^[31] was used for all other atoms.^[32] Thermodynamic corrections were calculated at the same level of theory from a harmonic vibrational analysis. Transition states and minimum structures were identified by the presence or absence of one

formed by using the BP86 functional together with the Stuttgart-Köln full relativistic ECP28MDF core potential^[33] and the corresponding augcc-pVTZ-PP33 basis set for Rh. The standard aug-cc-pVTZ basis set was used for all other atoms.^[34] 2) An MP2 single-point energy calculation with the cc-pwCVDZ basis set (cc-pwCVDZ-PP¹⁸ for Rh) including core valence functions was performed. 3) An additional MP2 single-point energy calculation with the aug-cc-pwCVQZ basis set (aug-cc-pwCVQZ-PP for Rh) including diffuse and core valence functions was performed. 4) To account for correlation effects beyond second-order perturbation theory a coupled-cluster calculation with single and double substitutions and with inclusion of perturbative triple excitations [CCSD(T)] together with cc-pwCVDZ basis set was performed. 5) The final single-point energy was obtained by the equation CCSD(T)/cc-pwCVDZ+MP2/augcc-pwCVQZ-MP2/cc-pwCVDZ. Using additional MP2 calculations to extrapolate CCSD(T) to the quadruple-ζ limit is an established procedure.^[36] To check for a possible multiconfigurational character in case of the CCSD(T) calculations, the largest T2 amplitudes were investigated and found to be less than 0.1.^[37] Additional single-point calculations for the model system were performed with the parameter-free hybrid PBE0^[37] functional, the meta-GCA M06L^[8] and meta-hybrid M06^[8] functionals, and long-range and dispersion-corrected wB97X-D^[39] functional. The aug-cc-pVTZ-PP basis set was used for these calculations. The D3 calculations were performed with the ORCA program package,^[40] and all other calculations by using the Gaussian 09 suite of programs.^[41]

the basis set limit was applied: 1) Geometry optimizations were per-

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