generates acyl-catalyst intermediate **III**. Similar mechanisms have been observed in the neighboring group participation by carbonyl hydrates during the hydrolysis of carboxylate and phosphate esters. However these examples are stoichiometric reactions that are promoted by intramolecular carbonyl groups.[9–11] 3) Deacylation of the acyl-enzyme intermediate regenerates the catalysts. This process is mimicked by reaction of **III** with hydroxide to give tetrahedral intermediate **IV**, which then breaks down to yield hemithioacetal **V**. Dissociation of **V** releases the carboxylate anion and regenerates the 4-heterocyclohexanone catalyst.

We have performed two additional experiments to probe the validity of this proposed mechanism. First, we have synthesized control compound **8** in which the thiol group is blocked as the methyl thioether in order to determine if a thiol functionality in the substrate is necessary for catalysis. Comparison of entries 1 and 10 in Table 1 shows that the rate of hydrolysis of **8** in the presence of 600 mM catalyst is only sevenfold faster than the rate of hydrolysis of substrate **5** in the absence of catalyst. This comparison shows that a free thiol group in the substrate is required for catalysis. In addition, the results shows that the mechanism of the catalyzed reaction cannot involve simple intermolecular nucleophilic attack by the anion of the 4-heterocyclohexanone hydrate on the carbonyl of the amide substrate.

In a second experiment we have independently synthesized the acyl-catalyst intermediate **III** (Scheme 1) in which X = S, and we monitored its rate of hydrolysis under the reaction conditions. We find that this intermediate is hydrolyzed much faster than the amide substrates in any of the catalyzed reactions. These two observations are consistent with the mechanism proposed in Scheme 1, and they suggest that the rate-limiting step for the catalyzed reaction occurs before hydrolysis of intermediate **III**.

In conclusion, we have demonstrated that tetrahydropyranone (**4**) is an effective catalyst for the hydrolysis of amide substrates that contain an adjacent thiol functionality. The reaction displays two features that are most often associated with enzymatic systems. First, the substrate is bound to the catalyst through a preliminary equilibrium in order to decrease the entropic barrier to reaction. The catalysts employ reversible formation of a hemithioacetal to establish this equilibrium. We believe that formation of reversible covalent bonds of this type will prove to be a useful method for mediating the molecular recognition processes that are involved in catalysis and self-assembly. Reversible covalent bonds are complementary to the noncovalent interactions—such as hydrogen bonds, hydrophobic interactions, and electrostatic interactions—that are typically observed in biological recognition processes. A second similarity to enzymatic catalysis is that the reaction is catalyzed through the participation of neighboring groups. We are currently conducting experiments to characterize further the mechanism of the reaction, and also to explore the possibility of using 4-heterocyclohexanones to catalyze the cysteine-specific hydrolysis of peptides.

Received: August 17, 1998
Revised version: October 15, 1998 [Z 12293 IE]
German version: *Angew. Chem.* **1999**, *111*, 575 – 578

Keywords: amides · electrostatic interactions · enzyme mimetics · hydrolyses · synthetic proteases

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Highly Enantioselective Hydrogenation of Cyclic Enol Acetates Catalyzed by a Rh – PennPhos Complex**

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The growing demand for practical and effective chiral ligands and/or catalysts has fueled much recent progress in ligand design. Although benchmark ligands such as 2,2′-

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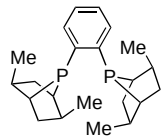
[**] This work was supported by a Camille and Henry Dreyfus New Faculty Award and Teaching Scholar Award, an ONR Young Investigator Award, a DuPont Young Faculty Award, Catalytica Pharmaceuticals, and DuPont Agrochemical Products. We acknowledge a generous loan of precious metals from Johnson Matthey Inc. and a gift of chiral GC columns from Supelco. PennPhos = *P,P′*-1,2-phenylenebis(*endo*-2,5-dialkyl-7-phosphabicyclo[2.2.1]heptanes).

  1433-7851/99/3804-0516 $ 17.50+.50/0

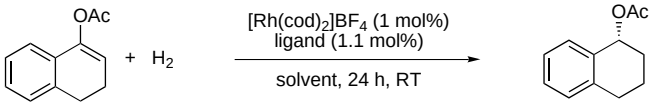
bis(diphenylphosphanyl)-1,1′-binaphthyl (BINAP) and 1,2-bis(phospholano)benzene (DuPhos) have shown broad utilities for catalytic asymmetric hydrogenation,[1] changes in the steric and electronic properties of the substrates sometimes lead to unexpected results. In our continuing effort to develop a general asymmetric hydrogenation of ketones, we became interested in exploring a related reaction, the enantioselective hydrogenation of readily accessible enol acetates,[2] as an attractive alternative to direct hydrogenation of unfunctionalized ketones. An advantage that may accrue for enol acetate substrates is chelation, which can restrict the mobility of metal substrates and could therefore promote high enantioselectivities upon asymmetric hydrogenation.[3a–f] While good to excellent enantioselectivities have been achieved upon asymmetric hydrogenation of some acyclic enol esters[3] (e.g., Rh–DuPhos-catalyzed hydrogenation of enol acetates bearing electron-withdrawing carboxylate groups[3i]), the asymmetric hydrogenation of cyclic enol acetates has not been reported. Recently we have developed a new family of electron-rich and conformationally rigid chiral bisphosphanes, *P*,*P*′-1,2-phenylenebis(*endo*-2,5-dialkyl-7-phosphabicyclo[2.2.1]heptanes) (PennPhos); an example is (*R*,*S*,*R*,*S*)-Me-PennPhos. A Rh–PennPhos complex was demonstrated to be an effective enantioselective catalyst for hydrogenation of simple ketones.[4c] Herein we report the first highly enantioselective hydrogenation of cyclic enol acetates catalyzed by a Rh–PennPhos complex.



(*R*,*S*,*R*,*S*)-Me-PennPhos

We initially chose the hydrogenation of 3,4-dihydronaphth-1-yl acetate for optimization studies in this series (Table 1). The reaction was carried at room temperature under an initial hydrogen pressure of 1.7 bar for 24 h. The catalyst was generated in situ by stirring a solution of $[Rh(cod)_2]BF_4$ (cod = 1,5-cyclooctadiene) as the Rh precursor and the ligand, and a substrate:[Rh]:ligand ratio of 1:0.01:0.011 was used.

Table 1. Rhodium-catalyzed asymmetric hydrogenation of 3,4-dihydronaphth-1-yl acetate.[a]



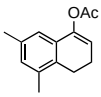
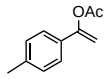
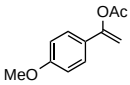
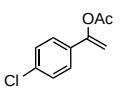
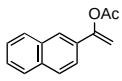
Entry	Ligand	Solvent	Conversion [%]	*ee* [%] (config.)[a]
1	(*R*,*S*,*R*,*S*)-Me-PennPhos	toluene	64	98.3 (*R*)
2	(*R*,*S*,*R*,*S*)-Me-PennPhos	CH_2Cl_2	100	86.8 (*R*)
3	(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	98.7 (*R*)
4	(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	100	99.1 (*R*)
5[c]	(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	99.2	98.3 (*R*)
6	(*R*)-BINAP	THF	2.4	18.0 (*R*)
7	(*R*)-BINAP	MeOH	1.9	3.1 (*R*)
8	(*R*,*R*)-Me-DuPhos	THF	1.3	12.3 (S)
9	(*R*,*R*)-Me-DuPhos	MeOH	–[d]	–[d]

[a] For details, see text and the Experimental Section. [b] Enantiomeric excesses were determined by gas chromatography using a Supelco Chiral Select 1000 column. The absolute configurations were determined from the optical rotation. [c] $[\{Rh(cod)Cl\}_2]$ was used as the catalyst precursor. [d] No reaction.

Compared with toluene (Table 1, entry 1) and CH_2Cl_2 (entry 2), THF (entry 3) and MeOH (entry 4) are better solvents for the asymmetric hydrogenation reaction catalyzed by Rh–(*R*,*S*,*R*,*S*)-Me-PennPhos. Up to 99 % *ee* was achieved for the hydrogenation of 3,4-dihydronaphth-1-yl acetate in MeOH using $[Rh(cod)_2]BF_4$ as the catalyst precursor and a PennPhos as the ligand (entry 4), which is the benchmark for this transformation. The neutral Rh precursor $[\{Rh(cod)Cl\}_2]$ is also effective (entry 5), although the enantiomeric excess is slightly lower than that resulting from reaction with the cationic precursor $[Rh(cod)_2]^+$. Interestingly, Rh–BINAP as well as Rh–DuPhos complexes are not effective catalysts for hydrogenation of 3,4-dihydronaphth-1-yl acetate in terms of enantioselectivity and activity (entries 6–8). In contrast to the excellent *ee* values obtained in the Rh–DuPhos-catalyzed hydrogenation of electron-deficient enol acetates with carboxylate groups in the α position,[3i] poor enantioselectivities were observed with the electron-rich cyclic enol acetate used in the present study (entries 8 and 9).

Under optimized conditions, several cyclic enol acetates as well as acyclic enol acetates were hydrogenated with Rh–diphosphane catalysts (Table 2). The enol acetate derived

Table 2. Rhodium-catalyzed asymmetric hydrogenation of enol acetates.[a]

Entry	Substrate	Ligand	Solvent	Conversion [%]	*ee* [%] (config.)[b]
1		(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	100	99.1 (*R*)
2		(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	100	98.2 (*R*)
3		(*R*)-BINAP	MeOH	5.0	66.1 (*R*)
4		(*R*,*R*)-Me-DuPhos	MeOH	4.9	69.4 (*R*)
5		(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	100	>99 (*R*)
6		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	98.5 (*R*)
7		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	84.8 (*R*)
8		(*R*,*S*,*R*,*S*)-Me-PennPhos	MeOH	100	83.5 (*R*)
9		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	80.9 (*R*)
10		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	83.9 (*R*)
11		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	83.0 (*R*)
12		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	80.9 (*R*)
13		(*R*,*S*,*R*,*S*)-Me-PennPhos	THF	100	82.0 (*R*)

[a] For details, see text and the Experimental Section. [b] Enantiomeric excesses were determined by gas chromatography using a Supelco Chiral Select 1000 column. The absolute configurations were determined from the optical rotation.

  1433-7851/99/3804-0517 $ 17.50+.50/0

from 1-indanone was also reduced in high enantioselectivity using the Rh–(*R*,*S*,*R*,*S*)-Me-PennPhos complex (entry 2) while *ee* values achieved with either Rh–BINAP or Rh–Me-DuPhos complexes were significantly lower (entries 3 and 4). Hydrogenation of a substituted 3,4-dihydronaphth-1-yl acetate gave outstanding enantioselectivities with the Rh–(*R*,*S*,*R*,*S*)-Me-PennPhos catalytic system (entries 5 and 6). The highly enantioselective hydrogenation of five- and six-membered ring enol acetates provides a practical route for the syntheses of the corresponding chiral secondary alcohols.

Several acyclic enol acetates were also hydrogenated with the Rh–(*R*,*S*,*R*,*S*)-Me-PennPhos catalyst (entries 7–13). The enantioselectivities were lower than those achieved with cyclic enol acetates. Modifying the steric or electronic properties of these acyclic enol acetates had only small effects on the enantioselectivities (observed ranging from 80 to 85% *ee*). For the enol acetate derived from acetophenone, the enantioselectivity obtained with Rh–(*R*,*S*,*R*,*S*)-Me-PennPhos (entries 7 and 8) was comparable to those obtained with Rh–DuPhos compounds (77% *ee* in THF catalyzed by [Rh(Me-DuPhos)(cod)]BF_4, 89% *ee* in MeOH with [Rh(Me-DuPhos)(cod)]OTf,[3f] OTf = trifluormethanesulfonate). Further modification of the Rh–PennPhos structure may lead to practical catalysts for the hydrogenation of electron-rich acyclic enol acetates.

The rationale for the highly enantioselective hydrogenation of cyclic enol acetates is not clear. Phosphabicyclo[2.2.1]heptanes are electron-rich and conformationally rigid ligands with a well-defined deep chiral pocket. Our previous work has shown that this novel motif imparts valuable properties to this catalytic system.[4] Since enol acetates are likely to be chelating substrates, the constrained geometry of the cyclic enol acetates may enhance recognition toward chiral transition metal complexes compared with acyclic enol acetates.

Experimental Section

All reactions and manipulations were performed in a nitrogen-filled glovebox or using standard Schlenk techniques. Toluene and THF were distilled from sodium benzophenone ketyl under nitrogen. CH_2Cl_2 was distilled from CaH_2. MeOH was distilled from Mg under nitrogen. The chiral PennPhos ligand was prepared as previously described.[4c] Gas chromatography was carried out on Helwett-Packard 5890 and 6890 gas chromatographs using the Chiral Select 1000 column (15 m × 0.25 mm (inner diameter), carrier gas: He (1 mL min^{-1})).

General procedure for the asymmetric hydrogenation: To a solution of [Rh(cod)$_2$]BF_4 (5.0 mg, 0.012 mmol) in MeOH (10 mL) in a glovebox was added (*R*,*S*,*R*,*S*)-Me-PennPhos (0.15 mL of a 0.1M solution in MeOH, 0.015 mmol). After the mixture was stirred for 30 min, the enol acetate (1.2 mmol) was added. The hydrogenation was performed at room temperature under 1.7 bar of hydrogen for 24 h. After the hydrogen was released, the reaction mixture was passed through a short silica gel column to remove the catalyst. The enantiomeric excess was measured by capillary GC without any further purification. The absolute configurations of the products were determined by comparing the observed optical rotations with those of chiral acetates made from readily available secondary alcohols.

Received: August 27, 1998 [Z12345IE]
German version: *Angew. Chem.* **1999**, *111*, 578–580

Keywords: alcohols · asymmetric catalysis · enols · hydrogenations · rhodium

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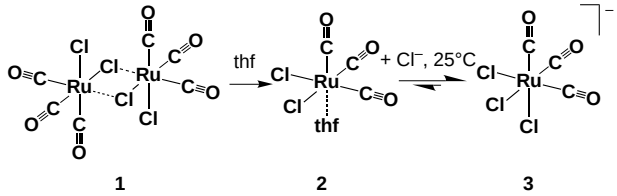
Reactions of a Transient Carbonyl(chloro)(hydrido)ruthenium(II) Complex with Ethylene, Alkynes, and CO; Chemistry of the New Anion $[Ru_2(CO)_4Cl_5]^-$**

Matthieu Faure, Luc Maurette, Bruno Donnadieu, and Guy Lavigne*

Dedicated to Professor Helmut Werner on the occasion of his 65th birthday

In spite of the high interest in halide salts as promoters for a variety of carbon–carbon bond-forming reactions,[1–4] little is known about the reactivity of simple carbonyl(halo)ruthenium(II) complexes such as the interconvertible species **1**–**3** (Scheme 1).[5]



1 **2** **3**

Scheme 1.

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[**] This work was supported by the CNRS. We thank Prof. Herbert D. Kaesz, Prof. John Bradley, and Dr Noël Lugan for helpful discussions.

  1433-7851/99/3804-0518 $ 17.50+.50/0