The First Structure Determination of a Possible Intermediate in Ruthenium 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl Catalyzed Hydrogenation with a Prochiral Group Bound to Ruthenium. Stoichiometric Reaction of a Chiral Ruthenium–Carbon Bond with Dihydrogen Gas

Jason A. Wiles and Steven H. Bergens*

*Department of Chemistry, University of Alberta
Edmonton, Alberta T6G 2G2, Canada*

Victor G. Young

*X-ray Crystallographic Laboratory, 160 Kolthoff Hall
Chemistry Department, 207 Pleasant St. S.E.
The University of Minnesota
Minneapolis, Minnesota 55455*

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Complexes of Ru(II) and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) comprise the most effective catalyst systems developed for the enantioselective hydrogenation of prochiral olefins and ketones. Nearly 200 reports[1] describing these reactions, including several industrial syntheses, have appeared since the first examples were disclosed in 1985 and 1986.[2] Despite the intense study of these systems, there are no reports of structural characterization (even using spectroscopy)[3] of a species with a prochiral olefin or ketone bound to a Ru center. The structures of the catalytic intermediates (and therefore the origins of enantioselection) are speculative as they have been inferred from indirect methods—isotopic labeling, olefin isomerizations, and kinetic studies.[4] We now report the first isolation, structural characterization, and reaction with dihydrogen gas of the major Ru-containing species present in

solution during hydrogenation of (*Z*)-methyl α-acetamidocinnamate (MAC) catalyzed by a Ru–BINAP compound. We recently reported the synthesis and the catalytic activity of [Ru-((*R*)-BINAP)(H)(MeCN)(sol)$_2$](BF$_4$) (**1**, sol = MeOH or THF).[5] Compound **1** catalyzed the hydrogenation of MAC in methanol solutions to generate *N*-acetylphenylalanine methyl ester (MACH$_2$) in 86% ee (*R*) (eq 1).[5] This enantioselectivity is comparable to those of other Ru–BINAP complexes.[1a,4e]
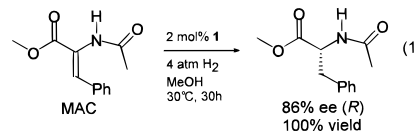
We found that the stoichiometric reaction between MAC and **1** in acetone at room temperature resulted in rapid formation of a predominant species (**2**, >99%) in solution (eq 2). ^{31}P NMR spectra recorded under conditions similar to those of the catalytic reaction (ambient temperature, 2 mol % of **1**, MeOH solution, pressure H$_2$ ≈ 2 atm) showed that **2** was the predominant species in solution during the catalytic hydrogenation.[6] NMR suggested
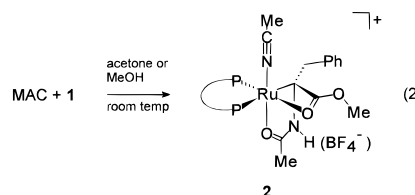
that **2** resulted from transfer of the hydride in **1** to the β-olefinic carbon of MAC and transfer of Ru to the α-carbon to form a 5-membered metallacycle. Further, the signal in the ^{13}C{^{1}H} NMR spectrum of **2** for the α-carbon showed *cis*- and *trans*-coupling (δ 67.3, $^2J_{CPcis}$ = 3.9 Hz, $^2J_{CPtrans}$ = 42.2 Hz) to the phosphorus nuclei, suggesting that the α-carbon was coordinated to Ru in the plane containing the phosphine groups. The ^{13}C signals for the amido and the ester carbonyl groups were also coupled to the phosphorus nuclei, suggesting that these groups were coordinated to Ru as well. Rh(III) and Ir(III) alkyl hydride compounds that are related to **2** have been spectroscopically characterized by Halpern and Brown.[7,8]

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* Author to whom correspondence should be addressed at (403)-492-9703 (voice), (403)-492-8231 (fax), or Steve.Bergens@UAlberta.CA (e-mail).

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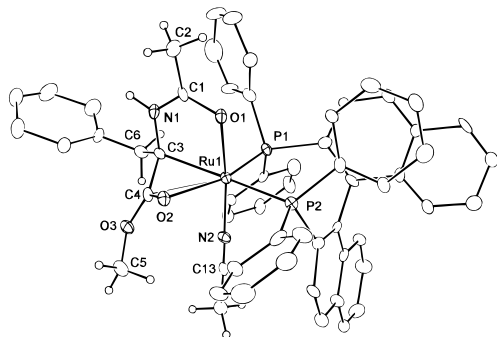
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Figure 1. The solid state structure of **2** as determined by X-ray diffraction. The positions of the hydrogen atoms are based on geometries of the parent carbon atoms. Non-hydrogen atoms are represented at the 20% probability level. Selected bond lengths (Å) are as follows: Ru(1)−N(2), 2.009(9); Ru(1)−P(1), 2.269(3); Ru(1)−P(2), 2.369(3); C(3)−C(6), 1.526(14).

Figure 1 shows the solid state structure of **2** as determined by X-ray diffraction.[9] The positions of the signals in the ^{13}C CP/MAS NMR spectrum of **2** were nearly identical to those in the solution spectrum, implying that the solid state structure was representative of the solution structure. As predicted from the NMR data, MACH was bonded to the Ru center via the α-carbon and the amido and ester groups. Similar tridentate bonding of MACH to a metal center was identified spectroscopically at low temperatures by Brown *et al.* for [Rh-(DIPAMP)(MACH)H](BF₄) (DIPAMP is (*R,R*)-1,2-bis[(*o*-methoxyphenyl)phenylphosphino]ethane).[7] We note that the amido group of **2** occupied a coordination site *cis* to both phosphines and that the ester group was coordinated in the plane containing the phosphines. Molecular models indicated that exchange of coordination sites by the ester and amide groups would result in severe steric repulsions between an equatorial phenyl group of (*R*)-BINAP and the benzyl group of MACH for both absolute configurations around C(3). The bonding of the enolate of MACH to Ru resembled that of an η^3-oxo allyl group in two ways. First, the geometry around the α-carbon of MACH was intermediate between that of an sp³ and an sp² carbon center.[10] Second, the distance between Ru and the carbonyl carbon of the ester group (Ru(1)−C(4) 2.353(9) Å) was comparable to the ruthenium−oxygen (2.260(7)Å (Ru(1)−O(2)), 2.075(7) Å (Ru(1)−O(1)) and to the ruthenium−carbon (2.257 (10) Å (Ru(1)−C(3)) bond lengths.

The absolute configuration at the α-carbon was *S*. Stereospecific replacement of Ru by a hydrogen atom would generate (*R*)-MACH₂, which has the same absolute configuration as the

major enantiomer of the catalytic hydrogenation. The stoichiometric reaction of **2** with dihydrogen gas under conditions similar[11] to those of the catalytic hydrogenation resulted in formation of MACH₂ and [Ru((*R*)-BINAP)(H)(η^6-MACH₂)]⁺ (**3**), in which MACH₂ was bonded to Ru as an η^6-arene ligand.[12,13] MACH₂ was liberated from **3** by refluxing in MeCN solution (to generate [Ru((*R*)-BINAP)(H)(MeCN)₃]⁺) (eq 3).
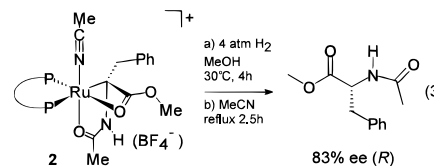
The ee of the combined portions of MACH₂ was 83% (*R*).[14] Assuming that direct reaction of **2** with dihydrogen gas results in a stereospecific replacement of Ru by hydrogen,[15] these results imply that formation of **2** was to some extent reversible under the conditions of the catalytic hydrogenation.[16,17]

Hydrogenolysis of the bond between [Ru(BINAP)] and a chiral carbon center has been proposed as a key step in several catalytic hydrogenations and may be the enantioselective step of the present catalytic hydrogenation.[4] Further investigation is required to determine if **2** is an actual intermediate in the catalytic cycle and if the chiral interactions in **2** are relevant to the origins of enantioselection. We note, however, that formation of compound **2** was rapid relative to the overall rate of the catalytic hydrogenation, that **2** was likely the predominant species in solution during catalysis, and that the rate of reaction of **2** with dihydrogen gas was comparable to that of the catalytic reaction.[18]

Supporting Information Available: Experimental and X-ray crystallographic details (42 pages). See any current masthead page for ordering and Internet access instructions.

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(9) Crystals suitable for structure determination by X-ray diffraction were obtained by liquid−liquid diffusion of diethyl ether into a 1,2-dichloroethane solution of **3** at room temperature. Crystal data: $M = 1145.93$; monoclinic, space group $P2_1$; $a = 15.3846(1)$ Å, $b = 18.9635(3)$ Å, $c = 21.8056(1)$ Å, $\beta = 101.856(1)°$, $V = 6225.98(11)$ Å³, $Z = 4$, $d_{calcd} = 1.223$ g cm⁻³; crystal size $0.45 \times 0.25 \times 0.12$ mm; μ(Mo Kα) = 0.359 mm⁻¹. Data were measured using a Siemens SMART Platform CCD diffractometer with Mo Kα radiation ($\lambda = 0.710$ 73 Å; q range for data collection of 1.35−25.10°); 16 214 independent reflections (10 610 with $F_o^2 > 2s(F_o^2)$) were measured. The structure was solved via direct methods (SHELXTL-V5.0). Full-matrix, least-squares refinement on F^2 (SHELXTL-V5.0) yielded $R_1 = 0.0685$ $F_o^2 > 2s(F_o^2)$), and $wR_2 = 0.1733$ (all data).

(10) Bond angles (deg) around C(3) with estimated standard deviations: C(4)−C(3)−C(6), 118.1(8); N(1)−C(3)−C(4), 111.1(9); N(1)−C(3)−C(6), 114.6(8); Ru(1)−C(3)−N(1), 99.7(6); Ru(1)−C(3)−C(6), 132.7(7); Ru-(1)−C(3)−C(4), 73.9(5).

(11) The dihydrogen gas pressure, temperature, and solvent were the same as those for the catalytic reaction, but the [**2**] for the stoichiometric reaction was ∼3 times higher than the initial [**1**] for the catalytic reaction.

(12) The remainder of the ruthenium compounds were unidentifiable, and presumably resulted from decomposition of **1** under these conditions in the absence of MAC.

(13) Compound **3** was identified by NMR spectroscopy. We synthesized the (*S*)-MACH₂ and the (*rac*)-MACH₂ η^6-arene adducts for comparison. See the Supporting Information for NMR data.

(14) The ee was determined by separating MACH₂ from [Ru((*R*)-BINAP)(H)(MeCN)₃]⁺ by chromatography in ethyl acetate over silica gel, followed by use of Eu(tfc)₃ shift reagent in chloroform-d_1.

(15) We are investigating the reaction of **2** with acid in MeOH, with dideuterium gas in MeOH, with dihydrogen gas in MeOH-d_4, and with para-enriched dihydrogen gas. We point out that solvolysis of the ruthenium−carbon bond may also have occurred under these conditions.

(16) A mechanism involving reversible formation of an intermediate similar to **2** was proposed to account for the isomerization of (*E*)-2-(benzoylamino)cinnamic acid to (*Z*)-2-(benzoylamino)cinnamic acid observed during a hydrogenation catalyzed by Ru₂Cl₄[(*R*)-BINAP]₂NEt₃.[4e]

(17) Low-temperature reactions between **1** and MAC resulted in observation of two isomers of [Ru((*R*)-BINAP)(H)(η^3-MAC)(MeCN)]⁺ (MAC is bonded through the amide carbonyl group and through an olefin−ruthenium π-bond) and one other compound. We are investigating the solution structures and kinetics of these compounds in order to further understand the mechanism of this hydrogenation.

(18) The stoichiometric reaction was 92% complete after 1.25 h.