PHIP Detection of a Transient Rhodium Dihydride Intermediate in the Homogeneous Hydrogenation of Dehydroamino Acids

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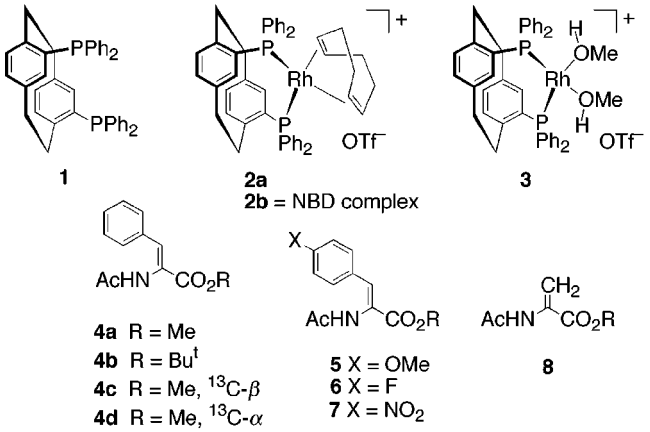
Since the first demonstrations[1] of effective asymmetric catalysis in the homogeneous hydrogenation of dehydroamino acid derivatives, mechanistic questions have been raised. Current information is based on a combination of incisive kinetic studies[2] and NMR characterization of reactive intermediates.[3] The anticipated rhodium dihydride has never been observed;[4] rather the reaction proceeds on to an alkylhydride which accumulates at low temperatures and is observable in some cases. This is the only post-H_2 addition intermediate to be characterized to date. With the recent advent of high-level DFT computations, detailed predictions can be made.[5] This further encourages the quest for experimental evidence.



The Rh catalyst derived from the PHANEPHOS ligand **1**[6] is unusually reactive, with turnover possible even at −40 °C. High reactivity coupled to good enantioselectivity provides an ideal case for characterizing the elusive Rh dihydride. The Rh complex **3,** prepared from precursor **2** in situ, bound dehydroamino acid esters rather weakly with MeOH displacement; at −40 °C the equilibrium constant was low for MAC (**4a**) binding but higher for the corresponding *tert*-butylamide **4b**.[7] In the latter case a typical enamide complex ^{31}P NMR spectrum was seen in CD_3-OD (δ 56.5 ppm, dd, $J_{RhP} = 175$ Hz, $J_{P1P2} = 22$ Hz; δ 35.0 ppm, dd, $J_{RhP} = 167$ Hz) as well as solvate **3** and a further species (the minor enamide complex? (5%)) at 48 and 39.5 ppm. No additional intermediates were observed under H_2 (−65 to −40 °C).

Para-enriched hydrogen offers considerable advantages for the NMR identification of transient intermediates.[8] The PHIP experiment carried out in situ (PASADENA conditions[9]) is especially powerful in this regard. When a solution of complex **2a** (ca. 0.23 mM) and a 5−10 molar excess of MAC in CD_3OD were reacted with para-H_2 (−10 to −25 °C), a single new transient was observed with signals in the M−H region at −1.9 and −18.9 ppm (Figure 1). Signals of the polarized hydrogenation product were concurrently detected at 4.6 and 3.15 ppm.[10]

A ^{31}P-INEPT($+\pi/4$) experiment showed polarization transfer only to the Rh solvate **3** at 63 ppm.[11]

The experiment was repeated with the para-substituted dehydroamino esters **5**, **6,** and **7**. In each case a similar transient species was seen but with significantly different chemical shifts. Pairs of these esters reacted to give two discrete species. Identical spectra were observed when the rapidly reduced bicycloheptadiene complex **2b** was employed in place of **2a**. The defining experiment was made with the ^{13}C-labeled ester **4c**, where an additional ^{13}C coupling of 86 Hz to the low-field Rh hydride was detected. The simulated spectrum is also shown in Figure 1. In addition to the expected polarization transfer to the $^{13}CH_2Ph$ of product at 38 ppm, a strong reactant signal was detected in the ^{13}C INEPT-($+\pi/4$) spectrum at 135 ppm, implying reversibility of enamide complexation in the observed transient.[12] With the α-^{13}C-labeled enamide **4d** weak ^{13}C coupling (ca 3 Hz) to the low-field hydride was observed. With the dehydroalanyl ester **8**, a distinct transient was observed, where the low field hydride was significantly shifted and displayed reduced coupling constants (Figure 2).

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(9) The PHIP experiments were conducted under strictly oxygen-free conditions inside the NMR probe in CD_3OD, on a Bruker AC200 system with a proton resonance frequency of 200 MHz. Para-enriched hydrogen was obtained as described (Woelk, K.; Bargon, J. *Z. Phys. Chem.* **1993**, *180*, 65−93), but enrichment took place at 25 K. Phase cycling was used to allow 4, 8, or 16 accumulations and to suppress "normal" NMR signals. Simulations were conducted with the help of the program PHIP++ written by T. Greve (Ph.D. Thesis, 1996, University of Bonn, Institute of Physical and Theoretical Chemistry). Assignments were confirmed by ^{31}P decouplings.

(10) With sequential pulses of para-enriched H_2, the transient hydride and polarized product eventually disappeared together. After completion of the hydrogenation a new species was observed whose stucture is under current investigation. That a Rh solvent dihydride is possible is highlighted by the recent characterization of an analogue (Gridnev, I. D.; Higashi, N.; Asakura, K.; Imamoto, T. *J. Am. Chem. Soc* **2000**, *122*, 7183−94).

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(12) The observation of excited reactant implies that the observed dihydride **9** is formed reversibly with respect to enamide dissociation, although by itself this is not informative of the mechanism of reversal.

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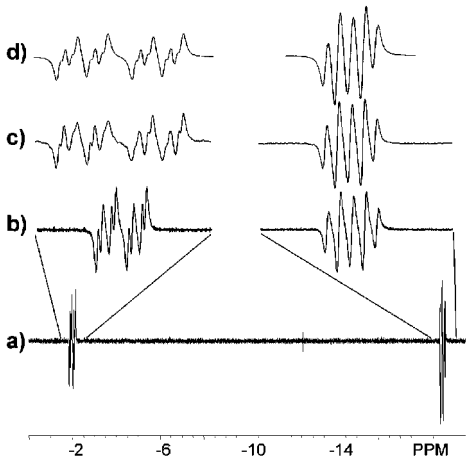

Figure 1. (a) PHIP NMR spectrum of the transient hydride detected while hydrogenating MAC (**4a**) using **3** as the catalyst. (b) Zoom of the hydrido signals. (c) Hydrido signals detected while hydrogenating β-^{13}C-labeled MAC. (d) Computer simulation of spectrum c:[9] δ_H (200 MHz, CD_3OD) −1.97 (^{1}H, ddddd, −4.3 (J_{HH}), 5.8, 34 (J_{HP}), 13.4 (J_{HRh}), 85.8 (J_{HC}), LW = 8.3 Hz); −18.92 (^{1}H, dddd, −4.3 (J_{HH}), 10.8, 23.8 (J_{HP}), 11.0 (J_{HRh}), LW = 7.2 Hz).

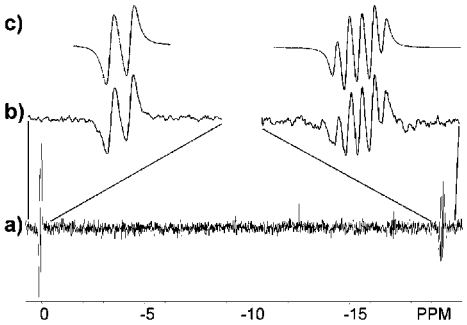

Figure 2. (a) PHIP NMR spectrum of the transient hydride detected while hydrogenating **8**. (b) Zoom of the hydrido signals. (c) Computer simulation of spectrum a:[9] δ_H (200 MHz, CD_3OD,) 0.07 (^{1}H, dddd, −1 (J_{HH}), 1, 17.5 (J_{HP}), 1 (J_{HRh}), LW = 12 Hz); −19.5 (^{1}H, dddd, −1 (J_{HH}), 11.8, 24 (J_{HP}), 11 (J_{HRh}), LW = 10 Hz), with absolute accuracy of *J*-values limited by the extent of line-broadening.

What structural evidence does these experiments reveal? The H−H coupling of −4.3 Hz is small compared to that of typical PHIP-observed Rh dihydrides.[13] The unusual chemical shift of the low-field signal, its strong C_β−H coupling, and the absence of a *trans* H−Rh−P *J*-coupling[14] (J_{HP} = 5.8, 34 Hz) suggest an agostic hydride bonded to rhodium and C_β. By contrast, the high-field signal is normal for a hydrogen *trans* to oxygen. It is a reasonable working assumption that the characteristic chelate coordination remains in place during dihydrogen addition. The differences between complexes **9a** and **9b** are best interpreted as due to a dynamic agostic methyl group in the latter case, with rapid interchange between the Rh−H and C−H sites.[15]

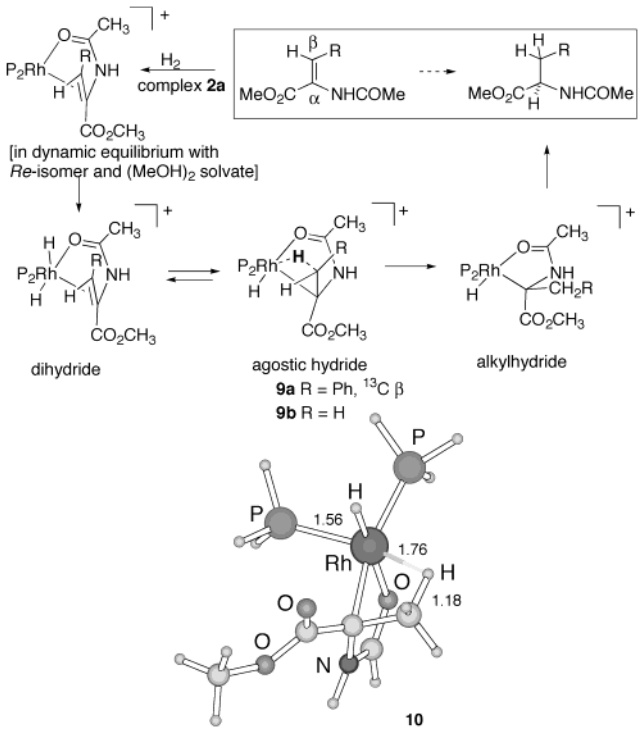

Figure 3. Pathway to the agostic dihydride species, and the DFT-predicted structure of a simple model compound **10**.

In DFT calculations on the simple $(PH_3)_2Rh$ complex,[5] reaction proceeds through an η^2-dihydrogen complex to a classical dihydride. The thermodynamically favored Rh diastereomer of this dihydride has a low-energy pathway to an agostic species closely resembling our intermediate **9**, although this is not on the computationally preferred pathway of hydrogenation. Our own DFT calculations[16] on the model dehydroamino ester indicate that structure **10** of Figure 3 is a significant minimum with a 60 kJ mol^{-1} barrier to formation and a 130 kJ mol^{-1} barrier to breakdown; in our case the computed Rh−H bond length at 1.76 Å is much shorter than in the prior calculations[5] (2.12 Å) due to our choice of functional. Sample geometry optimizations on Rh(III) complexes indicated that the best *structures* are obtained at the local density approximation level, which parallels earlier observations for high oxidation state and/or ionic transition metal complexes.[17]

We envisage the agostic hydride species described here as being the direct precursor of an alkylhydride. Quite probably further transformation involves the ligation of a solvent molecule. The reversibility implied by observation of excited reactant, the weak binding of enamide, and the possible observation of a PHIP-excited solvate on completion of reaction warrant caution in interpretation of the detailed mechanistic significance at this stage.

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