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Unprecedented Hydrogen Transfer from Water to Alkenes and Alkynes Mediated by Ti^{III} and Late Transition Metals

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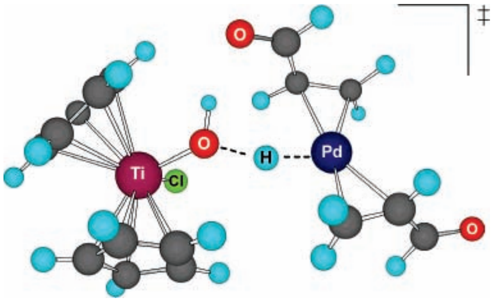
ABSTRACT



We describe how alkenes and alkynes can be hydrogenated under mild conditions by hydrogen transfer from water mediated by titanocene(III) and a substoichiometric quantity of one of the late transition metals usually employed as hydrogenation catalysts. This process proceeds presumably by H-atom transfer from Ti^{III}-coordinated water to the late transition metal partner (depicted in the drawing above), a mechanism in support of which we provide theoretical and experimental evidence.

The catalytic hydrogenation of alkenes and alkynes, one of the most important reactions in organic chemistry, is usually carried out with hydrogen gas.[1] Metal-promoted hydrogen transfer from accessible hydrogen donors has been widely used in the reduction of other functional groups.[2] Thus, hydrogen transfer from water, mediated by diiodosamarium[3] or titanocene(III),[4] can be successfully applied to the reduction of ketones. To the best of our knowledge, however, this procedure has not yet been extended to the hydrogenation of simple alkenes or alkynes. Here we present evidence to show that hydrogen transfer from water mediated by Ti^{III} and late transition metals can be used for the hydrogenation of alkenes and alkynes under mild conditions. More importantly, we also provide evidence for the hitherto unreported transfer of formal hydrogen atoms from Ti-aqua complexes to other transition metals via the homolytic cleavage of H−OH bonds.

We have recently observed that, in the presence of Cp_2TiCl,[5] water can be used as the H-atom source for the effective reduction of carbon radicals, presumably via aqua complex **1**.[6] On the basis of this observation we anticipated

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(1) (a) Smith, M. B.; March, J. *Advanced Organic Chemistry*, 5th ed.; Wiley: New York, 2001; pp 1002−1007. (b) Smith, M. B. *Organic Synthesis*, 2nd ed.; McGraw-Hill: New York, 2002; pp 369−382. (c) Carruthers, W.; Coldham, I. *Modern Methods of Organic Synthesis*, 4th ed.; Cambridge University Press: Cambridge, UK, 2004; pp 405−414.

(2) Samec, J. S. M.; Éll, A. H.; Áberg, J. B.; Privalov, T.; Eriksson, L.; Bäckval, J.-E. *J. Am. Chem. Soc.* **2006**, *128*, 14293−14305 and references therein.

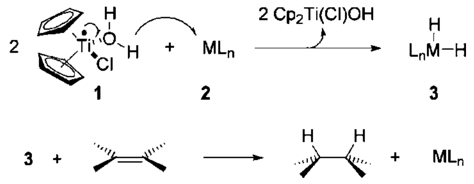
(3) (a) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698. For a recent overview on SmI_2 chemistry, see: (b) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351−10372.

(4) (a) Barrero, A. F.; Rosales, A.; Cuerva, J. M.; Gansäuer, A.; Oltra, J. E. *Tetrahedron Lett.* **2003**, *44*, 1079−1082. (b) Oller-López, J. L.; Campaña, A. G.; Cuerva, J. M.; Oltra, J. E. *Synthesis* **2005**, 2619−2622.

10.1021/ol070779i CCC: \$37.00

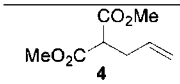
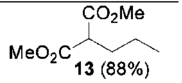
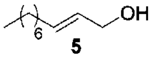
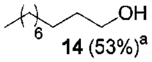
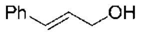
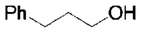
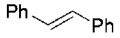
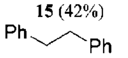
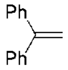
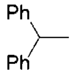
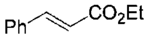
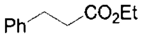
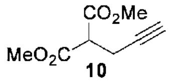
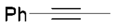
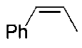
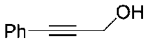
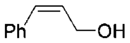
that this aqua complex might facilitate the H-atom transfer from water to late transition metals usually employed as hydrogenation catalysts (**2**) to give metal-dihydride species such as **3**.[7] These species could subsequently bring about alkene (and alkyne) hydrogenation as depicted in Scheme 1. In this way, formation of the expected hydrogenation products might additionally serve to prove the occurrence of H-atom transfers from Ti^{III}−aqua complexes to other transition metals, a phenomenon that has not been reported to date.

Scheme 1. Anticipated Hydrogen Transfer from Ti^{III}-Coordinated H_2O to Alkenes Catalyzed by Late Transition Metals



To check our hypothesis we treated a series of alkenes and alkynes with Cp_2TiCl (2.5 equiv),[5] H_2O (10 equiv), and a substoichiometric quantity (0.1 equiv) of different hydrogenation catalysts, including Pd/C, Pd/alumina, $Pd(dba)_2$,[8] Rh/alumina and Wilkinson, and Lindlar catalysts. All these experiments gave us the expected hydrogenation products (Table 1),[9] supporting the anticipated hydrogen-transfer process depicted in Scheme 1.

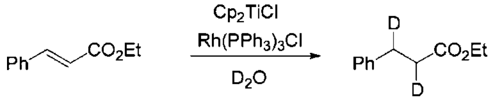
Table 1. H_2O/Cp_2TiCl-Based Hydrogenation of Alkenes and Alkynes Catalyzed by Late Transition Metals

substrate	catalyst	product (yield)
 **4**	Pd/C	 **13** (88%)
4	Pd/alumina	**13** (62%)
4	Rh/alumina	**13** (70%)
4	$Pd(dba)_2$	**13** (53%)
 **5**	Pd/C	 **14** (53%)[a]
 **6**	Pd/C	 **15** (56%)
6	$Pd(dba)_2$	**15** (42%)
 **7**	Pd/C	 **16** (37%)
7	Pd/alumina	**16** (38%)
7	$Pd(dba)_2$	**16** (99%)
 **8**	Pd/C	 **17** (27%)
 **9**	Wilkinson	 **18** (52%)
 **10**	Lindlar	**4** (79%)
 **11**	Lindlar	 **19** (61%)
 **12**	Lindlar	 **20** (69%)

[a] Besides **14** we obtained 15% decanal, presumably deriving from Pd-induced alkene isomerization.[7b]

Furthermore, when we treated ethyl cinnamate (**9**) with D_2O instead of H_2O we obtained the double-deuterated derivative **21** with a 75% incorporation of deuterium (Scheme 2), thus confirming that the incoming hydrogen atoms came from water. The results obtained with the Wilkinson catalyst also open up the possibility of using well-established rhodium chiral catalysts for enantioselective H_2O/Cp_2TiCl-based alkene hydrogenations.[10]

Scheme 2. Synthesis of Double-Deuterated Derivative **21**



The *cis* configuration of reduction products **19** and **20** coincided with that expected for conventional alkyne hydrogenation with the Lindlar catalyst.[1,7b] These results provided additional support for our hypothesis that the

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(5) Bis(cyclopentadienyl)titanium(III) chloride, generated in situ by stirring commercial Cp_2TiCl_2 with Mn dust in THF, exists as an equilibrium mixture of the monomer Cp_2TiCl and the dinuclear species $(Cp_2TiCl)_2$; see: (a) Enemærke, R. J.; Larsen, J.; Skrydstrup, T.; Daasbjerg, K. *J. Am. Chem. Soc.* **2004**, *126*, 7853−7864. (b) Daasbjerg, K.; Svith, H.; Grimme, S.; Gerenkamp, M.; Mück-Lichtenfeld, C.; Gansäuer, A.; Barchuck, A.; Keller, F. *Angew. Chem., Int. Ed.* **2006**, *45*, 2041−2044. (c) Gansäuer, A.; Barchuk, A.; Keller, F.; Schmitt, M.; Grimme, S.; Gerenkamp, M.; Mück-Lichtenfeld, C.; Dassbjerg, K.; Svith, H. *J. Am. Chem. Soc.* **2007**, *129*, 1359−1371. For clarity's sake we represent this complex as Cp_2TiCl. For recent reports on the synthetic applications of this single-electron-transfer reagent, see: (d) Barrero, A. F.; Oltra, J. E.; Cuerva, J. M.; Rosales, A. *J. Org. Chem.* **2002**, *67*, 2566−2571. (e) Barrero, A. F.; Rosales, A.; Cuerva, J. M.; Oltra, J. E. *Org. Lett.* **2003**, *5*, 1935−1938. (f) Rosales, A.; Oller-López, J. L.; Justicia, J.; Gansäuer, A.; Oltra, J. E.; Cuerva, J. M. *Chem. Commun.* **2004**, 2628−2629. (g) Justicia, J.; Rosales, A.; Buñuel, E.; Oller-López, J. L.; Valdivia, M.; Haïdour, A.; Oltra, J. E.; Barrero, A. F.; Cárdenas, D. J.; Cuerva, J. M. *Chem. Eur. J.* **2004**, *10*, 1778−1788. (h) Justicia, J.; Oltra, J. E.; Cuerva, J. M. *J. Org. Chem.* **2004**, *69*, 5803−5806. (i) Justicia, J.; Oller-López, J. L.; Campaña, A. G.; Oltra, J. E.; Cuerva, J. M.; Buñuel, E.; Cárdenas, D. J. *J. Am. Chem. Soc.* **2005**, *127*, 14911−14921. (j) Justicia, J.; Oltra, J. E.; Cuerva, J. M. *J. Org. Chem.* **2005**, *70*, 8265−8272. (k) Estévez, R. E.; Oller-López, J. L.; Robles, R.; Melgarejo, C. R.; Gansäuer, A.; Cuerva, J. M.; Oltra, J. E. *Org. Lett.* **2006**, *8*, 5433−5436. For recent reviews see: (l) Gansäuer, A.; Lauterbach, T.; Narayan, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 5556−5573. (m) Cuerva, J. M.; Justicia, J.; Oller-López, J. L.; Oltra, J. E. *Top. Curr. Chem.* **2006**, *264*, 63−91.

(6) Cuerva, J. M.; Campaña, A. G.; Justicia, J.; Rosales, A.; Oller-López, J. L.; Robles, R.; Cárdenas, D.; Buñuel, E.; Oltra, J. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 5522−5526.

(7) For homogeneous hydrogenation catalysts see: (a) Takaya, H.; Noyori, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 8, pp 443−469. For heterogeneous catalysts, see: (b) Siegel, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 8, pp 417−442.

(8) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 1065−1066.

(9) For detailed experimental procedures see the Supporting Information.

(10) For a Nobel Lecture including outstanding rhodium chiral catalysts see: Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008−2022.

process took place via H-atom transfer to the transition metal (as depicted in Scheme 1) and not through electron transfer from Ti^{III} to the alkyne followed by proton transfer, which would presumably have led to *trans* alkenes, as occurs in alkyne reduction by dissolving metals.[11]

Once we were confident about hydrogen transfer from water, we carried out new experiments to gain more information about the unprecedented mechanism presumably involved in this process. Thus, when we treated **4** with Cp_2TiCl and water in the absence of any hydrogenation catalyst the starting alkene was recovered unchanged, thus confirming the indispensable hydrogen-carrier role played by the transition-metal catalyst in Scheme 1. Furthermore, the recovery of the unchanged starting alkene when we treated **4** with Pd/C, Mn dust, and water in the absence of titanium confirmed that not only a late transition metal but also the titanium−aqua complex was essential for the process, thus providing new support in favor of the successive hydrogen transfer from **1** to **2** and from **3** to the corresponding alkene (or alkyne) set out in Scheme 1.

All the experiments summarized in Table 1, however, were performed in the presence of an excess of Mn dust.[5] This metal shows a considerable standard reduction potential (−1.185 V)[12] and, therefore, we also considered the possibility of an alternative mechanism via the generation of H_2 by a slow reaction between Mn(0) and water, despite the results of a control experiment in the absence of titanium (see above) which suggested that this was not the case. In this scenario we performed an additional experiment that definitively excluded the possibility of a hydrogenation process deriving from H_2 generation via a reaction between Mn and water. We generated Cp_2TiCl by stirring Cp_2TiCl_2 and Mn dust in THF.[5] Subsequently stirring was stopped, all excess manganese precipitated, and the Mn^0-free supernatant solution of Cp_2TiCl was transferred to a second flask in which, after the addition of H_2O and Pd/C, **4** underwent hydrogenation to **13**. It is therefore unlikely that the hydrogenation of **4** derives from the generation of H_2 under these conditions. In fact, the additional possibility of H_2 generation via a reaction between Cp_2TiCl and water was ruled out by Barden and Schwartz when they stated that, "Inexpensive and easy to prepare green titanocene chloride, $[Cp_2Ti^{III}Cl]_2$, readily hydrolyzes to give blue $[Cp_2Ti^{III}(H_2O)]^+$ which is stable in water in the absence of oxygen."[13] In this context we have recently provided evidence to support the idea that the structure of the species generated from Cp_2TiCl and water probably has the form shown in **1**.[6] Over the last 5 years we have been working with this species and, in agreement with Barden and Schwartz, have never observed the evolution of hydrogen gas or any other sign of decomposition.[4,5d,k,6] Finally, the unlikely possibility of H_2 being generated via a reaction between Pd/C and water can also be ruled out in the light of the failure of **4** to hydrogenate in the control experiment made in the absence of titanium (see above).

Under these circumstances, the H-atom transfer from **1** to **2** depicted in Scheme 1 seemed to be the most plausible mechanism to rationalize the hydrogenation reactions summarized in Table 1. Nevertheless, we could not find any precedent for this crucial transfer, so we made a computational study to explore the feasibility of this process. To this end we studied the H-atom transfer from Ti-coordinated water to Pd under homogeneous conditions, using $Pd(acrolein)_2$ as a model for $Pd(dba)_2$, in order to avoid the considerable difficulties inherent in theoretical studies of systems involving metals in a heterogeneous phase. Thus, by means of calculations at the DFT level we could locate a transition state (Figure 1) that showed moderate activation energy (17.3 kcal mol^{-1}),[14] suggesting that this H-atom transfer could be the rate-limiting step in the overall hydrogenation process. For the D_2O analogue of **1** we calculated a substantially higher energy barrier, suggesting an isotope effect of more than 7 at 298 K, in accordance with experimental observations.[15]

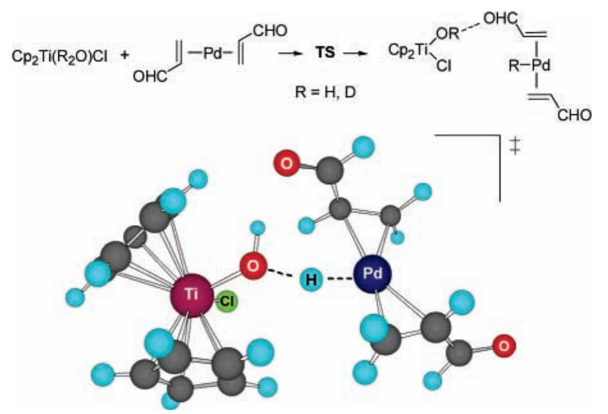

Figure 1. Calculated transition state for the H-atom tranfer from **1** to $Pd(acrolein)_2$ (DFT level, see the Supporting Information).

The concordance between theoretical calculations and experimental observations about a strong isotope effect is another solid argument in support of the mechanism depicted in Scheme 1, especially because hydrogenation processes with hydrogen gas show K_H/K_D ratios near 1.[16]

Finally, a second H-atom transfer to the Pd(I) intermediate would afford a Pd dihydride derivative such as that represented in **3**.

The above calculations provided theoretical evidence in support of the mechanism depicted in Scheme 1. There is a

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[11] Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 4th ed.; Kluwer Academic/Plenum Publishers: New York, 2001; Part B, p 295.

[12] *Handbook of Chemistry and Physics*, 85th ed.; Lide, D. R. Ed.; CRC Press; Boca Raton, FL, 2004; p 8-25.

[13] Barden, M. C.; Schwartz, J. *J. Am. Chem. Soc.* **1996**, *118*, 5484−5485. The sentence referred to in this report can be understood to mean that the reaction between Cp_2TiCl and H_2O generates the cationic $[Cp_2Ti(H_2O)]^+$species and the corresponding chloride counterion, but not H_2. Moreover, if the $[Cp_2Ti(H_2O)]^+$ species is "stable in the absence of oxygen", this obviously means that under these conditions, which were employed in all our experiments, this species does not decompose to give H_2 or any other product.

[14] For detailed calculation procedures see the Supporting Information.

[15] Cp_2TiCl-mediated hydrogenation of **4** with a 1:1 mixture of D_2O and H_2O gave **13**, whereas deuterium-labeled products were not detected.

[16] Siegel, S.; Ohrt, D. W. *Chem. Commun.* **1971**, 1529−1530.

precedent proposal for a H-atom transfer from a metal−aqua complex to another transition metal,[17] the simplest atom transfer between two metals described. To the best of our knowledge, however, this is the first time that this transfer is supported by both theoretical and experimental evidence.

In conclusion, we demonstrate here for the first time that alkenes and alkynes can be hydrogenated under mild conditions by hydrogen transfer from water mediated by titanocene(III) and a substoichiometric quantity of one of the late transition metals usually employed as hydrogenation catalysts. This process proceeds presumably by H-atom transfer from Ti^{III}-coordinated water to the late transition metal partner. At the moment, we are analyzing the effects of temperature and solvents on the process and studying the potential hydrogen transfer from theoretically predicted Zr^{III}− and Hf^{III}−aqua complexes[6] to different transition metals, including recently developed gold catalysts.[18] Moreover, bearing in mind that the calculated dissociation energy of the O−H bond of aqua complex **1** (49.4 kcal mol^{-1})[6] is considerably lower than that of H_2 (104.2 kcal mol^{-1}),[19] we are exploring the possibility of taking advantage of this complex to facilitate hydrogen transfer from water to metal−organic frameworks used for chemical hydrogen storage.[20]

Acknowledgment. We thank the Spanish MEC for financial support (Projects CTQ2005-08402 and CTQ2004-02040) and for fellowships to A.G.C. and R.E.E, and the “Centro de Computación Científica-UAM” for computation time. We are also grateful to our English colleague Dr. J. Trout (University of Granada) for revising our English text.

Supporting Information Available: Experimental procedures, spectroscopic data for new compounds, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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[17] H-atom transfer from Zn-coordinated water to Pd has been previously proposed on the basis of experimental evidence; see: Mukhopadhyay, S.; Rothenberg, G.; Wiener, H.; Sasson, Y. *New J. Chem.* **2000**, *24*, 305−308.

[18] Corma, A.; Serna, P. *Science* **2006**, *313*, 332−334.

[19] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987; p 161.

[20] (a) Rowsell, J. L. C.; Millward, A. R.; Park, K. S.; Yaghi, O. M. *J. Am. Chem. Soc.* **2004**, *126*, 5666−5667. (b) Peterson, V. K.; Liu, Y.; Brown, C. M.; Kepert, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 15578−15579. (c) Dinca, M.; Dailly, A.; Liu, Y.; Brown, C. M.; Neumann, D. A.; Long, J. R. *J. Am. Chem. Soc.* **2006**, *128*, 16876−16883. (d) Foster, P. M.; Eckert, J.; Heiken, B. D.; Parise, J. B.; Yoon, J. W.; Jhung, S. H.; Chang, J. S.; Cheetham, A. K. *J. Am. Chem. Soc.* **2006**, *128*, 16846−16850.