

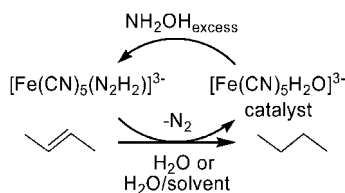
Hydrogen-Free Homogeneous Catalytic Reduction of Olefins in Aqueous Solutions

Carina Gaviglio and Fabio Doctorovich*

Departamento de Química Inorgánica, Analítica y Química Física/INQUIMAE-CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pabellón II, Piso 3, (C1428EHA) Buenos Aires, Argentina

doctorovich@qi.fcen.uba.ar

Received February 5, 2008



Herein we report a study involving the homogeneous catalytic reduction of unsaturated substrates in aqueous solutions or water–organic solvent mixtures. The reduction of olefins has been carried out in the presence of catalytic amounts of $[\text{Fe}(\text{CN})_5\text{NH}_3]^{3-}$ and excess of NH_2OH , which under mild reaction conditions can be used to reduce carbon–carbon saturations without affecting carbonyl functionalities and aromatic rings. To explore the scope of the catalytic reduction, a wide variety of representative unsaturated substrates have been examined. The steric effects of the substituents on the carbon–carbon multiple bond as well as the regioselectivity and stereoselectivity of the catalyst have been studied. The deuterium kinetic isotope effect on the catalytic reduction of double bonds in olefins has been analyzed, and no significant kinetic isotope effect was found. Among the great advantages of this novel procedure for catalytic reduction are that hydrogen and high pressures are not needed, the catalyst is inexpensive and easily prepared, and water as well as water–organic solvent mixtures can be used as reaction media.

Introduction

The reduction of unsaturated substrates is an important reaction in organic synthesis. The most commonly used method for reducing double and triple bonds involves homogeneous or heterogeneous catalytic hydrogenation. Among homogeneous catalysis,¹ asymmetric hydrogenation is a powerful way to produce compounds with high enantioselectivity.² Recent examples of iron catalysts for the hydrogenation of alkenes and carbonyl compounds can be mentioned,^{3,4,5c} as well as a family

of low-valent α -diimine iron complexes.⁶ Although catalytic hydrogenation is the method most often used, double bonds can be reduced by other reagents.

One of the most fundamental hydrides of nitrogen, diimide, also known as 1,2-diazene (N_2H_2) or diimine, is the nitrogen analogue of ethylene and formally isoelectronic with C_2H_4 , H_2CO , HNO and singlet O_2 . It is a short-lived species which has the ability to reduce multiple bonds^{7,8a} and becomes oxidized to N_2 . Currently, much attention has also been paid to diimide as a proposed intermediate on the reduction pathway of N_2 to NH_3 in the nitrogen cycle catalyzed by nitrogenase^{8b,9} and by a single molybdenum center.^{8c}

(1) Esteruelas, M. A.; Oro, L. A. *Chem. Rev.* **1998**, *98*, 577–588.
 (2) (a) Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5356–5362. (b) Roseblade, S. J.; Pfaltz, A. *Acc. Chem. Res.* **2007**, *40*, 1402–1411. (c) Minnaard, A. J.; Feringa, B. L.; Lefort, L.; De Vries, J. G. *Acc. Chem. Res.* **2007**, *40*, 1267–1277. (d) Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008–2022.
 (3) Sui-Seng, C.; Freutel, F.; Lough, A. J. Morris, R. H. *Angew. Chem., Int. Ed.* **2007**, *47*, 940–943.
 (4) Casey, C. P.; Guan, H. *J. Am. Chem. Soc.* **2007**, *129*, 5816–5817.
 (5) (a) Alluisetti, G. E.; Almaraz, A. E.; Amorebieta, V. T.; Doctorovich, F.; Olabe, J. A. *J. Am. Chem. Soc.* **2004**, *126*, 13432–13442. (b) Albertin, G.; Antoniutti, S.; Bacchi, A.; De Marchi, F.; Pelizzi, G. *Inorg. Chem.* **2005**, *44*, 8947–8954. (c) Hanna, T. E.; Keresztes, I.; Lobkovsky, E.; Chirik, P. *J. Inorg. Chem.* **2007**, *46*, 1675–1683.

(6) Bart, S. C.; Hawrelak, E. J.; Lobkovsky, E.; Chirik, P. *J. Organometallics* **2005**, *24*, 5518–5527.

(7) (a) For a general review for the diimide reduction see: (b) Pasto, D. J.; Taylor, R. T. *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1991; pp 91–155.

(8) (a) Smith, M. R., III.; Cheng, T. Y.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 8638–8642. (b) Lehnert, N.; Wiesler, B. E.; Tuczek, F.; Hennige, A.; Sellmann, D. *J. Am. Chem. Soc.* **1997**, *119*, 8869–8878. (c) Schrock, R. R. *Acc. Chem. Res.* **2005**, *38*, 955–962.

Useful methods for the generation of this transfer hydrogenation agent *in situ* include hydroxylamine and ethyl acetate,¹⁰ oxidation of hydrazine with one of several oxidants,^{11,12} decomposition of an azodicarboxylic acid,¹³ thermal decomposition of an anthracene–diimide adduct,¹⁴ and elimination of HX from an acid hydrazide.¹²

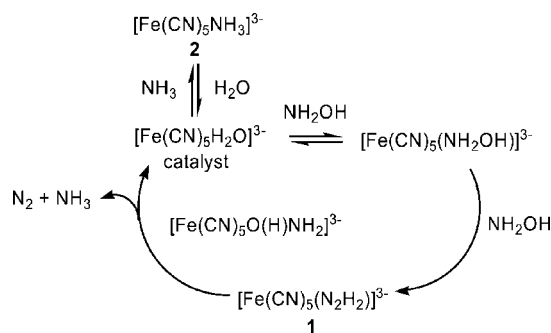
Diimide is also capable of reacting with itself to form the disproportionation products, hydrazine and nitrogen. Therefore, the common procedures for reduction with this unstable reducing agent involve *in situ* generation of diimide in the presence of the molecule to be reduced. In general, diimide reacts with greater stereospecificity than most hydrogenation catalysts.^{7,12,15} This stereospecificity is believed to derive from a concerted dihydrogen transfer mechanism.^{7,12,16} Presently, this species is widely known as a *cis*-specific reducing agent.^{7,12,17} Consequently, diimide has great synthetic utility due to its ability to stereospecifically reduce olefinic bonds.^{7,12,18} Symmetrical multiple bonds such as carbon–carbon multiple bonds are reduced much more readily by diimide than are unsymmetrical unsaturated bonds of the type of C≡N, C=O, N=O, S=O.^{7,12,19} Also, diimide does not produce hydrogenolysis of single bonds such as S–S or C–Br.¹² Heteroatom bonds like N–N, N–O, and O–O, which often suffer reductive cleavage under catalytic hydrogenation conditions, remain intact during diimide reductions. On the other hand, as it was previously mentioned, it is highly unstable in its free state but can be stabilized by coordination to metal complex fragments.^{5,8,9}

Compared with traditional procedures using finely divided metals and high hydrogen pressures, homogeneous catalytic reduction of alkenes and alkynes in aqueous solutions, which generates no organic solvent waste, is environmentally and economically attractive.

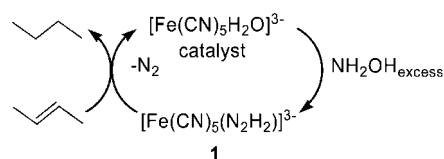
The present work discusses the homogeneous catalytic reduction of alkenes and alkynes in aqueous solution and solvent mixtures under mild conditions, by *in situ* generation of the diimide complex $[\text{Fe}(\text{CN})_5(\text{N}_2\text{H}_2)]^{3-}$ (**1**).

As shown in Scheme 1, our previously reported work^{5a} describes how coordinated diimide (**1**) can be generated by the

SCHEME 1. Generation of Coordinated Diimide



SCHEME 2. Proposed Catalytic Cycle



reaction of $[\text{Fe}(\text{CN})_5\text{H}_2\text{O}]^{3-}$, produced by aqution of $[\text{Fe}(\text{CN})_5\text{NH}_3]^{3-}$ (**2**), with an excess of NH_2OH . In the absence of olefin, coordinated diimide disproportionates spontaneously, producing N_2 and NH_3 .

However, in the present work we will show that in the presence of a double or triple C–C bond, diimide acts as a reducing agent, producing the corresponding saturated C–C bond in a *syn* stereospecific arrangement (Scheme 2).

This reduction can be carried out under mild conditions (atmospheric pressure, temperature range = 25–100 °C, and pH = 9), in aqueous solutions or solvent mixtures, and without the use of hydrogen gas. The reduced product can be obtained quantitatively in all cases by adding the appropriate amount of hydroxylamine. Although this environmentally attractive method is ideal for water-soluble olefins, it can be extended to nonsoluble ones by the use of solvent mixtures. It is important to remark that very few methods^{7,20} are known which are efficient for the reduction of olefins, mild, and can be carried out in water without the use of H_2 gas.

Results and Discussion

Catalytic Behavior in Aqueous Solutions. The diimide-bound complex $[\text{Fe}(\text{CN})_5(\text{N}_2\text{H}_2)]^{3-}$ (**1**) resulted from aqution of the catalyst precursor $[\text{Fe}(\text{CN})_5(\text{NH}_3)]^{3-}$ (**2**) and subsequent reaction of the catalyst $[\text{Fe}(\text{CN})_5(\text{H}_2\text{O})]^{3-}$ with an excess of NH_2OH .^{5a} Compound **1** was studied as an *in situ* reducing agent of unsaturated substrates. Results for the reduction of maleic acid (**3**) under different reaction conditions are shown in Table 1.

Except for entries 7 and 8, in all cases the reactions were carried out up to the complete consumption of **1**, easily followed thanks to its characteristic orange color ($\lambda_{\text{max}} = 440 \text{ nm}$, $\epsilon \approx 4500 \text{ M}^{-1} \text{ cm}^{-1}$) which bleaches upon consumption.

Upon treatment of **3** at 25 °C with a catalytic amount of **2** (8 mol %), 38% yield of succinic acid (**4**) was obtained (Table 1, entry 1). Remarkably, performing the reaction at 60 °C and at 100 °C resulted in formation of **4** in higher yield, 60% (entry 2) and 68% (entry 3), respectively; showing that at higher

(9) (a) Barney, B. M.; McClead, J.; Lukoyanov, D.; Laryukhin, M.; Yang, T.; Dean, D. R.; Hoffman, B. M.; Seefeldt, L. C. *Biochemistry* **2007**, *46*, 6784–6794. (b) McKenna, C. E.; Simeonov, A. M.; Eran, H.; Bravo-Leerabhandh, M. *Biochemistry* **1996**, *35*, 4502–4514.

(10) Wade, P. A.; Amin, N. V. *Synth. Commun.* **1982**, *12*, 287–291.

(11) (a) Kondo, K.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1977**, *42*, 3727–3730. (b) Furst, A.; Berlo, R. C.; Hooton, S. *Chem. Rev.* **1965**, *65*, 51–68. (c) Corey, E. J.; Mock, W. L.; Pasto, D. J. *Tetrahedron Lett.* **1961**, *11*, 347–352.

(12) Back, R. A. *Rev. Chem. Intermed.* **1984**, *5*, 293–323.

(13) (a) van Tاملen, E. E.; Dewey, R. S.; Timmons, R. J. *J. Am. Chem. Soc.* **1961**, *83*, 3725–3726. (b) Hünig, S.; Müller, H. R.; Thier, W. *Tetrahedron Lett.* **1961**, *11*, 353–357.

(14) Corey, E. J.; Mock, W. L. *J. Am. Chem. Soc.* **1962**, *84*, 685–686.

(15) Miller, C. E. *J. Am. Chem. Soc.* **1965**, *42*, 254–259.

(16) (a) Garbisch, E. W.; Schilderout, S. M.; Patterson, D. B.; Sprecher, C. M. *J. Am. Chem. Soc.* **1965**, *87* (13), 2932–2944. (b) Hünig, S.; Müller, H. R.; Thier, W. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 271–382. (c) van Tاملen, E. E.; Timmons, R. J. *J. Am. Chem. Soc.* **1962**, *84*, 1067–1068. (d) Hünig, S.; Müller, H. R. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 213–214. (e) Corey, E. J.; Pasto, D. J.; Mock, W. L. *J. Am. Chem. Soc.* **1961**, *83*, 2957–2958. (f) van Tاملen, E. E.; Dewey, R. S.; Lease, M. F.; Pirkle, W. H. *J. Am. Chem. Soc.* **1961**, *83*, 4302.

(17) (a) Tang, H. R.; McKee, M. L.; Stanbury, D. M. *J. Am. Chem. Soc.* **1995**, *117*, 8967–8973. (b) Ra, C. S.; Park, G. *Bull. Korean Chem. Soc.* **2004**, *25*, 1463–1464. (c) McKee, M. L.; Squillacote, M. E.; Stanbury, D. M. *J. Phys. Chem.* **1992**, *96*, 3266–3272. (d) Stanbury, D. *Inorg. Chem.* **1991**, *30*, 1293–1296. (e) Pasto, D. J.; Chipman, D. M. *J. Am. Chem. Soc.* **1979**, *101*, 2290–2296. (f) Siegel, S.; Foreman, M.; Fisher, R. P.; Johnson, S. E. *J. Org. Chem.* **1975**, *40*, 3599–3601.

(18) (a) McKee, M. L. *J. Phys. Chem.* **1993**, *97*, 13608–13614. (b) Okuyama, T.; Toyoshima, K.; Fueno, T. *J. Org. Chem.* **1980**, *45*, 1604–1608.

(19) Dürckheimer, W. *Liebigs Ann. Chem.* **1969**, *721*, 240–243.

(20) Corey, E. J.; Mock, W. L.; Pasto, D. J. *Tetrahedron Lett.* **1961**, *11*, 347–352.

TABLE 1. Tuning the Conditions for the Catalytic Reduction of Maleic Acid by Diimide^a

Entry	3 (mmol)	2 (mmol)	NH ₂ OH (mmol)	T (°C)	4 (yield [%]) ^b
1	0.25	0.02	1.25	25	38
2	0.25	0.02	1.25	60	60
3	0.25	0.02	1.25	100	68
4	0.25	0.02	2.5	60	90
5	0.25	0.02	2.5	100	95
6	0.25	0.02	5	100	100 ^d , 96 ^c
7	0.25	0.02	12.5	25	100
8	0.25	0.002	12.5	25	18
9	0.25	0.2	12.5	25	31
10	0.25	0	1.25	25	0

^a All reactions were run in aqueous borax buffer (3 mL). ^b Relative yields determined by ¹H NMR analysis of crude reaction mixtures. ^c Isolated yield.

temperature the reduction is favored over the competitive reactions of disproportionation and decomposition of diimide.

When the reduction was done with double the amount of NH₂OH in comparison with the previous experiments, 90% yield of **4** was obtained at 60 °C (entry 4), and 95% was obtained at 100 °C (entry 5). Quantitative yield of **4** was obtained when the reaction was performed with a ratio of NH₂OH/**3** = 20 at 100 °C (entry 6), and at room temperature a ratio of NH₂OH/**3** = 50 was needed (entry 7). Investigating the catalytic effect of **2**, showed that at room temperature only 18% yield of **4** was obtained (entry 8) with 0.8 mol % of **2** in comparison with the quantitative yield of **4** (entry 7) with 8 mol % of **2**. Interestingly, further increase in the amount of **2** to 80 mol % reduced the yield to 31% as compared to 8 mol % (entries 9 and 7), probably due to the formation of dimeric species.^{5a} These results showed the optimal ratio of the catalyst to be around 8 mol %. The experiments showed that the catalyst is efficient under very mild conditions (25 °C). However, the conditions used on entries 4 and 5 were chosen as the most appropriate to study the reduction of another unsaturated substrates, due to the faster reaction rates (at 60 °C the reaction is completed in ~3 h, and at 100 °C it only takes 3 min to completion). Control experiments (blanks) confirmed that no reduction was observed in the absence of **2** (entry 10).

Extending the Scope of the Catalyst to Solvent Mixtures. The effect of various solvents on the catalytic reduction of substrate **3** was investigated to extend the reaction to alkenes and alkynes which are not soluble in water (Table 2).

As the catalyst is very soluble and stable in aqueous buffer solution, 90% yield of **4** was obtained in water (Table 2, entry 1). Remarkably, performing the reduction in aqueous phosphate buffer/dioxane gave also a high yield (88%, entry 2) and in phosphate buffer/ethanol the yield was still very good (75%, entry 3). On the other hand, in phosphate buffer/CH₃CN the yield was lower (entry 4) and in phosphate buffer/DMSO or phosphate buffer/DMF it was even lower (entries 5 and 6). No reduction was observed in phosphate buffer/acetone (entry 7). Probably, in entries 4–6 lower yields were obtained due to the ability of these coordinating solvents to block the catalytic site.

TABLE 2. Solvent Screening for the Catalytic Reduction of Maleic Acid by Diimide^a

entry	medium	4 (yield [%]) ^b
1	H ₂ O	90
2	H ₂ O/dioxane	88
3	H ₂ O/ethanol	75
4	H ₂ O/CH ₃ CN	44
5	H ₂ O/DMSO	19
6	H ₂ O/DMF	8
7	H ₂ O/acetone	0

^a Reaction conditions: **3** (0.25 mmol); **2** (0.02 mmol); NH₂OH (2.5 mmol); T = 60 °C; solvent mixtures (aqueous phosphate buffer/solvent = 1:1; total volume = 3 mL). ^b Relative yields determined by ¹H NMR analysis of crude reaction mixtures.

In the case of acetone (entry 7), it inhibits the formation of **1** due to the competitive production of the oxime (CH₃)₂C=NOH by reaction with NH₂OH. These results clearly indicate that dioxane and ethanol are the cosolvents of choice for this reaction, and as we will show later, a wide variety of organic substrates can be reduced with these solvent mixtures (aqueous phosphate buffer/dioxane and aqueous phosphate buffer/ethanol), extending in this way the scope of the catalyst without affecting the efficiency of the reaction.

Substrate Scope. After initial catalyst and solvent screening the substrate scope was investigated. A number of relative reactivity studies have been carried out on a wide variety of representative alkyl- and aryl-substituted olefins with different types of solubility. An appropriate selection of data is presented in Table 3.

In order to compare these 13 substrates, the reaction conditions were similar in all cases, except where noted (exact reaction conditions for each case are included in the Supporting Information). It is worth mentioning that in all cases quantitative yield of hydrogenated product could be obtained by adding more NH₂OH and/or raising the reaction temperature. We show experimental conditions to obtain quantitative yield of hydrogenated product for substrates **3** and **6**.


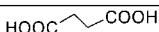
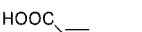
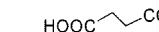


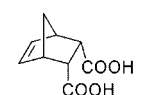
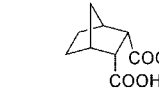
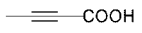
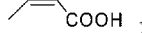
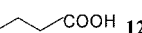
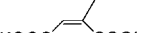
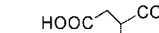
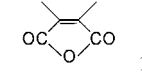
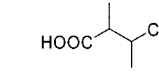
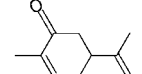
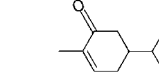
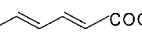
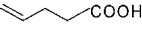
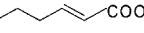
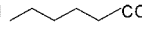
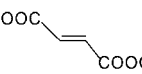
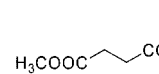
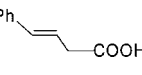
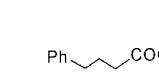
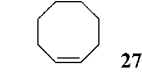
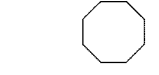
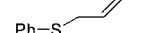
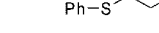
As it was previously mentioned, stereochemical studies on the reduction of alkenes and alkynes have led to the suggestion that *cis*-diimide is the reactive hydrogen-transfer reagent.^{7,12,16} Pasto et al. has reported that *trans* double bonds are more reactive than *cis* double bonds.⁷ In our system, the reduction of **3** (*cis*) was compared against fumaric acid (**5**, *trans*) under exactly the same reaction conditions. The product yield obtained from the reduction of **3** was 91% (compare to 95%, entry 1), while from **5** it was 42% (Table 3, entry 2). On the contrary as it has been reported with free diimide,^{7,16b} a higher yield of reduction for the *cis*-configuration substrate is obtained with our selective catalyst probably due to the steric hindrance produced by the presence of the [Fe(CN)₅]³⁻ moiety.

Comparing **5** and cinnamic acid (**6**), both compounds have the same degree but different types of substitution at the unsaturated bond. In order to obtain practically the same amount of reduction in both cases, a higher reaction temperature (90 °C) was needed for **6** (entry 3) as compared to **5** (60 °C, entry 2); this can be attributed to steric effects of the phenyl substituent.

Deuterium-labeling studies were carried out on substrate **8** (entry 4). The product was analyzed by NMR spectroscopy showing that the hydrogen transfer occurs in a concerted *syn* stereospecific manner, as previously observed for free diimide.^{7,12,16}

The ¹H NMR spectrum of the reduction carried out in H₂O shows the signals corresponding to H_a and H_b at 1.55 and 1.39

TABLE 3. Scope of the Catalytic Reduction Depicted in Scheme 1^a

Entry	Substrate	Products (yield [%]) ^b
1	 3	 4 (95 %), (96 %) ^c
2	 5	 4 (42 %)
3	 6	 7 (44 %), (93 %) ^c
4	 8	 9 (94%)
5	 10	 11 (19 %)  12 (36 %)
6	 13	 14 (36 %)
7	 15	 16 (7 %)
8	 17	 18 (38 %) ^d
9	 19	 20 (29 %)  21 (3 %)  22 (40 %)
10	 23	 24 (86 %)
11	 25	 26 (55 %)
12	 27	 28 (21 %)
13	 29	 30 (8 %)

^a General reaction conditions: all reactions were run in 3 mL of solution, substrate (0.25 mmol), **2** (0.025 mmol), NH₂OH (2.5 mmol), medium: aqueous borax buffer, or aqueous borax buffer/ethanol = 1:1, or phosphate buffer in D₂O/*p*-dioxane-*d*₈ = 1:1 (see Supporting Information for details).
^b Relative yields determined by ¹H NMR analysis of crude reaction mixtures (except where noted). ^c Isolated yield, 5 and 12.5 mmol of NH₂OH were used in entries 1 and 3, respectively. ^d Yield determined by gas chromatography with an internal standard.

ppm, respectively (Figure 1a). When the reduction is carried out in D₂O, the signal at 1.39 ppm (which overlaps with the signal corresponding to the methylene on the bridge) disappears, and the double of doublets observed at 1.55 ppm shifts to 1.64 ppm and loses the geminal coupling, becoming a doublet (Figure 1b). The ²D NMR spectrum shows only one signal at 1.37 ppm corresponding to deuterium atoms located in a *syn* arrangement (Figure 1b, inset). NOESY experiments indicate that the hydrogen atoms transferred by diimide are located in the *exo* positions (H_b), being the attack from the other face (*endo*) sterically more hindered by the presence of the carboxyl groups.

The alkyne 2-butyric acid (**10**) was reduced with formation of the corresponding alkene and alkane (entry 5). Only the *cis*-2-butyric acid (**11**) (³J_{HH_{cis}} = 11.6 Hz) was obtained. This

result reinforces the previous one with regard to the *syn* stereoselectivity. On the other hand, the higher alkane yield indicates that the intermediate alkene is more reactive than the starting alkyne, as usually observed in a variety of organic reactions.

The number of substituents at the unsaturated carbon atoms plays a significant role in the reduction yield. Upon treatment of **3** with a catalytic amount of **1** (8 mol %) a high yield of **4** was obtained (entry 1). Performing the reduction of the trisubstituted alkene methylmaleic acid (**13**) under the same experimental conditions resulted in formation of **14** in lower yield (entry 6), while a notably substantial difference was observed for the tetrasubstituted alkene 2,3-dimethylmaleic anhydride (**15**) as it was not efficiently reduced (entry 7). In

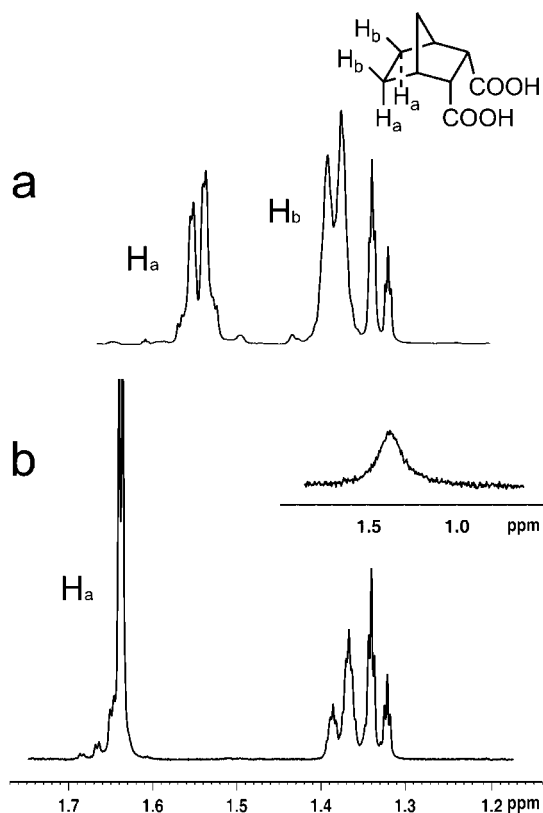


FIGURE 1. NMR spectra for the reduction of the norbornene derivative **8** (crude reaction mixture). (a) ¹H NMR spectrum for the reaction carried out in H₂O. (b) ¹H NMR spectrum for the reaction carried out in D₂O. Inset: ²D NMR spectrum.

general, as the degree of alkyl substitution on the double bond of an alkene increases, the reduced product yield decreases, presumably due to steric factors.

Upon reduction of *R*-(-)-carvone (**17**), only product **18** was obtained (entry 8). Reduction is sensitive to steric hindrance explaining the selectivity for reaction with the exocyclic disubstituted double bond but not the internal trisubstituted double bond. The high selectivity observed in this case can be attributed to an important steric hindrance promoted by the diimide coordination to the bulky moiety [Fe(CN)₅]³⁻.

The reduction of the conjugated diene 2,4-hexadienoic acid (**19**) was selective toward the α,β unsaturation (entry 9). This result was unexpected since α,β unsaturations are generally less reactive than γ,δ unsaturations.

Substrates **23** and **25** which are insoluble in aqueous solution, were successfully reduced in an aqueous phosphate buffer/dioxane = 1:1 solvent mixture. The conditions used in the case of the reduction of *cis*-cyclooctene (**27**) were the same as the previous ones except for the use of deuterated solvents. The steric hindrance presented by the ring is observed for substrate **27** where the obtained yield is only 21% (entry 12). The reduced product **26** was obtained in lower yield in comparison to **24** probably due to steric effects of the phenyl substituent (entries 11 and 10). These last three cases demonstrate that the scope of the reaction can be extended to substrates that are not soluble in aqueous solutions.

Sulfur is a major poison to noble metal catalysts in hydrogenation processes. In order to study the sulfur resistance of our catalyst, the reduction of allyl phenyl sulfide (**29**) was investigated. The hydrogenated product **30** was obtained in low yield (entry 13) probably due to poisoning of the catalytic site.

As it was mentioned previously, reduced product yields could be increased by addition of more NH₂OH. Consequently, the catalyst can be reused several times by adding more NH₂OH; this could be useful for laboratory synthesis and also in industrial processes. The reduction of **3** at 353 K presented turnover numbers (TONs) of at least 200 and turnover frequencies (TOFs) of 4 h⁻¹.

Kinetic Studies of the Catalytic Reduction of Cinnamic Acid. The kinetics for the reaction of cinnamic acid (**6**), [Fe(CN)₅NH₃]³⁻ and NH₂OH were measured in borax aqueous buffer, pH 9.3 at 30 °C, under an excess of NH₂OH with respect to [Fe(CN)₅NH₃]³⁻ and cinnamic acid (see Experimental Section for details). The amount of **1** was ~80% with respect to the precursor **2** throughout the reaction. Under these reaction conditions, the concentration of coordinated diimide (**1**) remains approximately constant throughout the measurements ([**1**] ≈ 1.4 × 10⁻⁴ M). A pseudo-first-order reaction rate in cinnamic acid was found with an observed rate constant $k_{\text{obs}} = 2.4 \times 10^{-5} \pm 1.7 \times 10^{-6} \text{ s}^{-1}$ at 30 °C.

Kinetic Isotope Effect on the Catalytic Reduction. The kinetic isotope effect for deuterium substitution on the catalytic reduction of double bonds in substrate **6** has been studied. No noticeable isotope effect was found. The observed rate constant $k_{\text{obs}}^{\text{D}} = 2.8 \times 10^{-5} \pm 1.5 \times 10^{-6} \text{ s}^{-1}$ (D₂O) is almost equal to $k_{\text{obs}}^{\text{H}} = 2.4 \times 10^{-5} \pm 1.7 \times 10^{-6} \text{ s}^{-1}$ (H₂O), both obtained under the same experimental conditions. This fact indicates that the rate-determining step in the reaction does not involve N–H bond rupture, but is probably related to the formation of the transfer hydrogenation agent **1**. The absence of kinetic isotope effect was also confirmed by determining relative spectroscopic yields of product by ¹H NMR in the reduction of **3** under identical reaction conditions (except for the deuterium content of the solvent). Substrate **3** was chosen in order to do the reaction in aqueous medium avoiding the use of solvent mixture. The obtained yields were almost identical, 67% and 65% in H₂O and D₂O, respectively. These results are in contrast with the KIE of 1.9 informed by Tang et al. for fumaric acid.^{17a}

Conclusions

A versatile and selective homogeneous catalyst for the reduction of unsaturated substrates has been developed. This procedure is an example of the use of a soluble transition metal complex for the catalytic transfer of hydrogen to an olefin. A great advantage of the new catalyst is that the reduction of a wide variety of substrates can be done in water under mild conditions. Another important benefit is that solvent mixtures can be used for substrates which are not soluble in aqueous solution, broadening in this way the scope of the reaction. According to the type of substrate, an increase in reaction temperature favors the obtained yield of saturated product. The last effect can also be achieved by increasing the ratio of NH₂OH, an inexpensive and easily handled reagent.

We have also found that the reduction is sensitive to steric congestion. As the degree of substitution at the unsaturated moiety increases, the relative rate of reduction decreases; the same fact is observed as the substituents become more voluminous. As a result, the iron catalyst has been found useful for the selective saturation of unhindered double bonds in polyolefinic substances, such as carvone. Additionally, hydrogen addition occurs in a stereoselective *syn* arrangement.

It has to be mentioned that unsaturations may be reduced even in the presence of functional groups such as keto and aromatic rings, which are not reduced.

An important benefit of this method is that the reduction is done in the absence of hydrogen gas and high pressures, avoiding the inconvenience and expense of using gaseous hydrogen. Diimide reductions can be carried out in simple, readily available laboratory equipment, in contrast to catalytic hydrogenation, which demands handling of hydrogen gas and often requires rather expensive high-pressure equipment. It may also be noted that this catalyst precursor (**2**) is easily synthesized²¹ and that all the reagents are inexpensive in comparison with the usual noble metal catalysts.²² In conclusion, the results convincingly show that saturated substrates produced by this chemistry should be very useful for the synthesis of a wide variety of compounds.

Experimental Section

Synthesis of $\text{Na}_3[\text{Fe}(\text{CN})_5\text{NH}_3]\cdot 3\text{H}_2\text{O}$ (2**).** **2** was prepared according to literature procedures²¹ with only a slight modification. To a mixture of powdered $\text{Na}_2[\text{Fe}(\text{CN})_5\text{NO}]\cdot 2\text{H}_2\text{O}$ (50 mg) and anhydrous sodium acetate (16.7 mg) was added 200 μL of a concentrated NH_4OH solution was added. The mixture was stirred until dissolution. The solution was left below 10 °C overnight in a vial closed with a septum, and a needle was connected to it for the release of gases. The yellow precipitate formed was filtered. It was purified by dissolution in a 0.1 M NH_3 solution and by precipitation with ethanol giving 30.6 mg of **2** in 56% yield.

General Procedure for the Catalytic Reduction of Unsaturated Substrates (Tables 1–3). The reactions were studied in buffer solutions (0.2 M in phosphates for pH 8 or 0.1 M in borax for pH 9.3). A buffered solution of **2** was added to a buffered solution of NH_2OH previously neutralized before each experiment. After stirring the mixture at room temperature for 45 min the unsaturated substrate dissolved in aqueous buffer solution, or in a mixture of aqueous buffer solution and the corresponding solvent, was added to it (see Scheme 1). The reactions were done at different temperatures, in most cases until consumption of NH_2OH , and indirectly followed spectrophotometrically at 440 nm by measuring the disappearance of the absorbance due to **1**.

Except for reactions done in deuterated solvents and for reduction of **15**, in all cases the solvent was evaporated, the crude reaction mixture was dissolved in deuterated solvent, and ^1H NMR was used to identify the reduced product.

Internal standards were used in ^1H NMR to quantify spectroscopically the obtained yields in the reduction of **3** and **6**. At the same time, relative spectroscopically determined yields of product versus substrate were checked in both cases, and comparable results were obtained. Consequently, for the rest of the substrates, relative spectroscopically yields were determined. Regarding substrate **15**, it was quantified by gas chromatography with an internal standard and identified by electrospray mass spectrometry. Representative examples of isolation procedures are as follows.

Succinic Acid (4**).** The general procedure was followed using **2** (6.5 mg, 0.02 mmol), NH_2OH (347.5 mg, 5 mmol) and **3** (29.0 mg, 0.25 mmol) with aqueous borax buffer (3 mL) as solvent for

10 min at 100 °C. Quantitative formation of **4** was observed. The solvent was evaporated, and the crude reaction mixture was dissolved in 0.5 mL of water (pH \approx 3). The resulting aqueous phase was extracted with diethyl ether (5 \times 5 mL). The combined organic layers were dried with MgSO_4 , and the solvent was removed *in vacuo* giving 28.3 mg of **4** in 96% yield. ^1H NMR (500 MHz, D_2O) δ 2.37 (s, 4H, 2 CH_2). Mp = 184–187 °C.

Hydrocinnamic Acid (7**).** The general procedure was followed using **2** (6.5 mg, 0.02 mmol), NH_2OH (868.6 mg, 12.5 mmol) and **6** (37.0 mg, 0.25 mmol) with aqueous borax buffer/ethanol = 1:1 (total volume = 3 mL) as solvent for 15 min at 100 °C. Quantitative formation of **7** was observed. The solvent was evaporated, and the crude reaction mixture was extracted with chloroform (5 \times 5 mL). The solvent was removed *in vacuo* giving 28.3 mg of **4** in 93% yield. ^1H NMR (200 MHz, CDCl_3) δ 7.23–7.06 (m, 5H, Ar), 2.87 (t, J = 7.6 Hz, 2H, CH_2), 2.58 (t, J = 7.6 Hz, 2H, CH_2). Mp = 46–49 °C.

Procedure for the Determination of TONs and TOFs for Maleic Acid. The reaction was studied in borax buffer solution at 353 K. A buffered solution of **2** (3.0×10^{-4} mg, 9.1×10^{-7} mmol) was added to a buffered solution of NH_2OH (10.4 mg, 0.15 mmol) previously neutralized. After stirring the mixture at room temperature for 45 min the unsaturated substrate **3** (0.9 mg, 7.5×10^{-3} mmol) dissolved in borax buffer solution was added to it. After 2 h of reaction, a second addition of buffered solution of NH_2OH (10.4 mg, 0.15 mmol) previously neutralized was added in order to regenerate the reducing agent **1**, and 1 h later a new addition of unsaturated substrate **3** (0.9 mg, 7.5×10^{-3} mmol) was annexed. In this way, after consecutive additions of NH_2OH (10.4 mg, 0.15 mmol) previously neutralized and of unsaturated substrate **3** (0.9 mg, 7.5×10^{-3} mmol), the catalyst is preserved, and relatively large TONs (200) can be obtained.

Kinetics. Rate measurements of reduction of cinnamic acid were done in spectrophotometric cells at 30 °C, by measuring the disappearance of the absorbance due to cinnamic acid at 268 nm ($\epsilon_{268\text{nm}} = 18579 \pm 699 \text{ M}^{-1} \text{ cm}^{-1}$). These reactions were carried out in borax aqueous buffered solutions at pH 9.3, under an excess of NH_2OH ($[\text{NH}_2\text{OH}] = 9.02 \text{ mM}$) with respect to $[\text{Fe}(\text{CN})_5\text{NH}_3]^{-3}$ ($[[\text{Fe}(\text{CN})_5\text{NH}_3]^{3-}] = 180 \mu\text{M}$) and cinnamic acid ($[\text{CA}] = 24 \mu\text{M}/48.1 \mu\text{M}$). Absorbance values at fixed wavelength (268 nm) were registered as a function of time. The observed rate constants (k_{obs}) for the spontaneous decay process due to the reduction of cinnamic acid by $\text{Na}_3[\text{Fe}(\text{CN})_5(\text{N}_2\text{H}_2)]$ were determined by initial rates showing that all kinetics were pseudo-first-order with respect to cinnamic acid concentration. In order to investigate the deuterium kinetic isotope effect for the reduction of olefins, the reaction was conducted in a fully deuterated medium using D_2O as the solvent.

Acknowledgment. We gratefully acknowledge financial support from ANPCyT, CONICET and UBA. We thank Prof. Gerardo Burton for some provided substrates and Rosana Misico for useful discussions related to NMR. We wish to particularly acknowledge Professors José A. Olabe and Valentín Amorebieta for their initial input.

Supporting Information Available: General considerations, reactions conditions for Table 3, selected NMR and MS spectra, kinetic studies of the catalytic reduction of cinnamic acid, kinetic isotope effect on the catalytic reduction. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO800302V

(21) Kenney, D. J.; Flynn, T. P.; Gallini, J. B. *J. Inorg. Nucl. Chem.* **1961**, *20*, 75–81.

(22) Jardine, F. H. *Prog. Inorg. Chem.* **1981**, *28*, 63–202.