DOI: 10.1002/ejic.200800356

The Detection of PHIP Effects Allows New Insights into the Mechanism of Olefin Isomerisation during Catalytic Hydrogenation

Alessandra Viale,[a] Daniela Santelia,[a] Roberta Napolitano,[a] Roberto Gobetto,[a] Walter Dastrù,[a] and Silvio Aime*[a]

Keywords: Isomerization / Parahydrogen / Olefins / Hydrogenation / Catalysis

PHIP (parahydrogen-induced polarisation) effects in the ^{1}H NMR spectra of the products of Rh-complex-catalysed alkyne hydrogenation brings to light the fact that the *cis–trans* isomerisation of the formed olefin occurs through the formation of a σ-bonded intermediate stabilised by the reversible addition of a hydrogen molecule at the metal centre.

Introduction

It has been shown that under ordinary conditions hydrogen gas is a mixture of two kinds of molecules, known as ortho- and parahydrogen, that correspond to the triplet and the singlet state of the hydrogen molecule, respectively. The concentrations of the two species in equilibrium are determined by Boltzmann averaging and are accordingly temperature-dependent. At room temperature they are in a 3:1 ratio (due to the spin triplet/singlet ratio), but enrichment of the para isomer can be easily obtained.[1] Upon carrying out hydrogenation reactions with parahydrogen-enriched mixtures, the alteration of the spin-level populations yields dramatic changes in the ^{1}H NMR spectra of the hydrogenated products (parahydrogen-induced polarisation effect).[1–2]

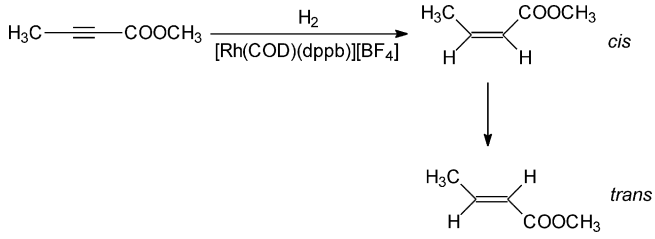
The use of the parahydrogen-induced polarisation (PHIP) effect in ^{1}H NMR spectra has proved to be extremely valuable to assess the occurrence of low-concentration reaction products, which are undetectable under ordinary conditions.[1–12] Moreover, information on the occurring reaction mechanism can be assessed by the simple appearance of a PHIP effect on a hydrogenation product even when the molecule contains chemically and magnetically equivalent protons.[13–15]

In this article, we aim to solve the basic problem of olefin isomerisation that takes place at Rh centres during hydrogenation of alkyne substrates. Our goal is to evaluate whether the use of parahydrogen can give new insights into the mechanism of the *cis–trans* isomerisation process occurring during catalytic hydrogenation with [Rh(diene)(diphos)]$^+$ complexes.[16,17]

[a] Dipartimento di Chimica IFM, University of Torino,
V. P. Giuria 7, 10125 Torino, Italy
Fax: +39 011 6707855
E-mail: silvio.aime@unito.it

Results and Discussion

The substrate chosen for the hydrogenation catalysed by [Rh(cyclooctadiene)(diphenylphosphanylbutane)][BF_4] was methyl 2-butynoate (**1**) (Scheme 1).



Scheme 1. Hydrogenation of methyl 2-butynoate (**1**) leads to a mixture of methyl *cis*- and *trans*-2-butenoate.

The reaction, which has been carried out in the NMR tube, quickly leads to methyl *trans*-2-butenoate. The hydrogenation reaction mechanism with [Rh(diene)(diphos)]$^+$ catalysts usually leads to the *cis* isomer, but due to fast-occurring *cis–trans* isomerisation, the predominant product is the *trans* isomer. However, when parahydrogen (50% para) is used, methyl *cis*-2-butenoate is clearly detected in the ^{1}H NMR spectrum by its enhanced signals (Figure 1a). The *trans* isomer is also polarised, but the intensities of the absorption/emission signals resulting from the PHIP effect are significantly lower than those observed for the *cis* isomer. It is noteworthy that in the completely relaxed spectrum the *trans* isomer is present in higher concentration (Figure 1b): thus the PHIP experiment highlights the fact that the *cis* isomer is formed in the first step of the catalytic hydrogenation, and then isomerisation to the *trans* form readily occurs.

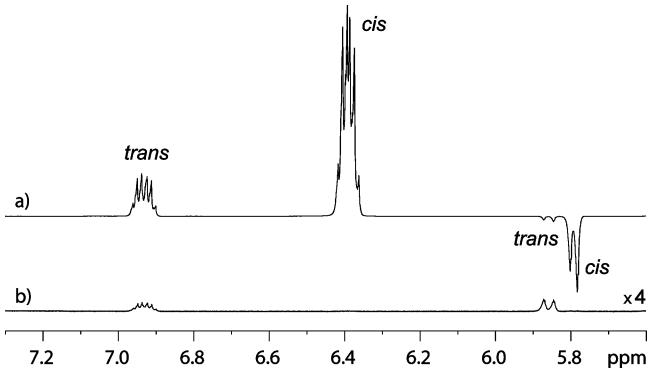
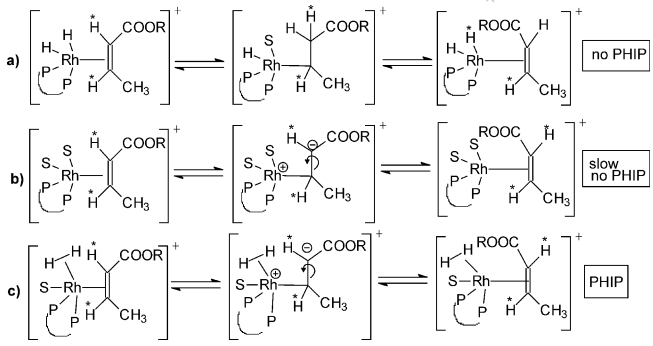


Figure 1. ^{1}H NMR spectra (600 MHz, [D$_6$]acetone, 298 K) of the reaction mixture of **1** and parahydrogen (50% enriched) in the presence of [Rh(COD)(dppb)][BF$_4$] as catalyst: (a) spectrum recorded 20 s after direct addition of parahydrogen into the NMR tube; (b) spectrum of the same reaction mixture recorded after 60 s.



Scheme 2. Possible pathways for the isomerisation process.

In order to evaluate the kinetic constant value for the isomerisation process, some experiments were carried out in Schlenk tubes, by stirring a reaction mixture containing the activated catalyst and methyl *cis*-2-butenoate exposed to a hydrogen/Ar (1:1) atmosphere. Pure hydrogen was not used in order to prevent hydrogenation of methyl 2-butenoate to methyl butyrate. The reaction was followed by ^{1}H NMR spectroscopy. The detailed procedure is reported in the experimental section. The measurement was carried out in acetone as well as in methanol solution, and showed that the isomerisation reaction proceeds by a first order kinetics, with rate constant values of $k_1 = 4.2 \times 10^{-2}$ s^{-1} and $k_1 = 3.1 \times 10^{-1}$ s^{-1} in acetone and methanol respectively.

The permanent presence of the PHIP effect during the isomerisation process indicates that the *cis–trans* transformation does not implicate the dissociation of hydrogen atoms. Two possible mechanisms for the olefin *cis–trans* isomerisation have been proposed for similar systems.[18–24] One involves the reversible addition of one hydrogen atom to the olefin (Scheme 2a), while in the second a polar σ-bonded intermediate of the type depicted in Scheme 2b is formed. In the latter the negative charge on the carbon atom is stabilised by electron-attracting groups, and the free rotation around the C–C bond leads to the observed *cis–trans* transformation, giving rise to the more stable *trans* isomer as the final product.

Obviously, the observation of the PHIP effect on the *trans* isomer rules out the occurrence of mechanism 2a. In fact, if this mechanism was the operating one, it would be unlikely that hydrogen elimination from the σ-alkyl intermediate invariably involves the same added hydrogen atom (this would be necessary in order to maintain the spin correlation in the resulting *trans* molecule).

Mechanism 2b involves a Rh$^{\mathrm{I}}$ centre, where the coordination sites formerly occupied by the cyclooctadiene ligand (which is promptly eliminated as cyclooctene upon reaction with H_2) are occupied by two solvent molecules, while in mechanism 2c the two vacant sites are occupied by one solvent and one hydrogen molecule.[25] If the operating mechanism was 2b, hydrogen would not have any role in the isomerisation process, and isomerisation would take place at the same rate both in the presence and in the absence of H_2. In contrast, the reaction rate should be affected by the presence of H_2 if mechanism 2c was the operating one. Therefore, in order to distinguish between the occurrence of mechanisms 2b and 2c, the kinetic rate constant measurement was repeated under the same experimental conditions used before, but by replacing hydrogen with an inert gas (Ar). It was found that isomerisation does not take place at all in the absence of H_2. This leads to the conclusion that H_2 has an active role in the isomerisation process, possibly as depicted in Scheme 2c. It is known that the positive charge which is formed on the metal upon the metal-olefin linkage π→σ bond transformation is stabilised by reversible hydrogen molecule coordination at the Rh centre[26,27] (Scheme 2c) competing against solvent coordination. In this regard, the difference between the two kinetic constant values determined in methanol and acetone solution may be due to a greater coordinative capability of acetone with respect to methanol in the present system, slowing down hydrogen coordination. In fact, even if methanol is usually considered as a better coordinating solvent with respect to acetone, it has been reported that in some cases they could show opposite behaviour, depending on many factors such as hard-soft character of both the solvent and the metal ion, other ligands already present at the metal, and a possible second coordination sphere effect.[28,29]

The rate of hydrogen binding at the Rh centre in the olefin complex should therefore determine the *cis–trans* isomerisation process. It is noteworthy that, effectively, the para–ortho conversion in the presence of the catalyst used in this work is four orders of magnitude slower than the *cis–trans* isomerisation process carried out under the same experimental conditions (in methanol solution, $k_{\mathrm{para-ortho}} = 4.2 \times 10^{-5}$ s^{-1}).[30] Thus, if the proposed 2c mechanism for olefin isomerisation is correct, one can conclude that only a very minor number of interactions at the metal centre results in a net para–ortho transformation. In other words, the polarisation of parahydrogen decreases at a rate which is considerably lower than the binding of H_2 molecules to the metal centres, i.e. the lifetime of the Rh–H_2 interactions is very short and does not significantly affect the ortho/para ratio. This appears to be consistent with recent findings reporting the observation of a PHIP effect on molecules

which are parahydrogenated with heterogeneous catalysts.[31] Obviously, the spin relaxations induced in systems with long molecular correlation times (here represented by the immobilised catalysts) are largely diminished by the short lifetime of the H_2 molecules at the metal centres. These considerations may be relevant for the exploitation of PHIP effects in heterogeneous catalysis.[31]

Conclusions

The detection of the PHIP effect in conjunction with kinetic measurements allowed to get more insight into the mechanism of olefin isomerisation during catalytic alkyne hydrogenation. It was found that hydrogen coordination is necessary but no H-scrambling takes place between the coordinated H_2 molecule and the H atoms on the coordinated olefin. The isomerisation step involves an intermediate containing one solvent and one hydrogen molecule bound to the Rh centre, whereas the organic fragment is freely rotating at the Rh–C σ-bond.

Experimental Section

^{1}H NMR PHIP spectra were recorded with a Bruker Avance-600 spectrometer operating at 600 MHz. ^{1}H NMR spectra for kinetic evaluations were recorded with an EX-400 JEOL spectrometer operating at 400 MHz.

Para-enriched hydrogen (50%) was prepared by storing H_2 with Fe_2O_3 at 77 K for one hour.

Parahydrogenation reactions were carried out in a 5-mm NMR tube equipped with a Young valve. The catalyst [Rh(COD)(dppb)][BF_4] (10 mM in [D_6]acetone) was activated by reaction with normal hydrogen, the tube was then opened, and the substrate methyl 2-butynoate (**1**) (100 mM) was quickly added. The tube was frozen, and parahydrogen (1.2 atm) was introduced (corresponding to 3.8 atm at room temp.); the sample was then warmed to room temp., shaken for ten seconds and introduced into the spectrometer. Single-scan ^{1}H NMR spectra (with 45° pulses) were recorded at different times (from 20 to 120 s) after the introduction of the sample in the spectrometer.

Kinetic measurements were carried out as follows: Inside a Schlenk tube, equipped with a rubber septum, [Rh(COD)(dppb)][BF_4] (15 mg) was suspended in deuterated solvent (CD_3OD or [D_6]-acetone, 2.5 mL), this suspension was frozen and degassed, and H_2 (1 atm) was introduced into the tube. The resulting mixture was stirred at room temp. until complete dissolution of the catalyst: this indicated the activation of the catalyst by hydrogenation of the COD ligand. The clear orange solution was then frozen again, and H_2 was replaced with a 1:1 mixture of H_2 and Ar, or with Ar alone, depending on the type of measurement. The tube was warmed up to room temp., then a solution of methyl *cis*-2-butenoate (22 mg) in CD_3OD or [D_6]acetone (0.5 mL) was added by a syringe. Aliquots of 0.25 mL were taken at successive times and were analysed by ^{1}H NMR spectroscopy. Concentrations of the *cis* and *trans* isomers were determined by integration of the spectra, and were reported as a function of time for the evaluation of the kinetic constants.

Synthesis of 1: Compound **1** was prepared by esterification of 2-butynoic acid: 2-butynoic acid (0.9 g, 10.6 mmol) in methanol (20 mL) was added to a solution of sulfuric acid (96%, 0.45 mL) in methanol (10 mL). The mixture was stirred for four days at room temp. Then water (25 mL) was added, and the ester was extracted with diethyl ether (3 × 20 mL). The organic solution was washed with water, a saturated aqueous solution of sodium carbonate and water again; then it was dried with sodium sulfate. The product was filtered, and the solvent was evaporated under vacuum. The yield was 67%. ^{1}H NMR (400 MHz, [D_6]acetone): δ = 1.99 (s, 3 H), 3.70 (s, 3 H) ppm. ^{13}C NMR (150 MHz, [D_6]acetone): δ = 153.38 (s), 85.02 (s), 71.73 (s), 51.56 (q), 1.99 (q) ppm.

Synthesis of Methyl *cis*-2-Butenoate: Inside a three-necked flask equipped with valves for connection to a vacuum pump, a manometer and a hydrogen reservoir, sodium 2-butynoate (1.16 g) was dissolved in methanol (15 mL). A mixture of Pd/$BaSO_4$ (20 mg), quinoline (20 mg) and water (3 μL) was added, the flask was frozen in liquid N_2 and degassed, then it was warmed to room temp., and hydrogen (1.2 atm) was introduced. The reaction mixture changed colour from brown to black, indicating that hydrogenation had started. The mixture was stirred up to the end of hydrogen consumption (about 2 h). Then it was filtered, and the solvent was removed under vacuum. The residue was dissolved in water (10 mL), HCl (37%, 0.8 mL) was added, and the obtained *cis*-2-butenoic acid was extracted with diethyl ether (4 × 7 mL). The ether solution was desiccated with sodium sulfate, filtered and dried under vacuum. *cis*-2-Butenoic acid was then dissolved in methanol (20 mL), and sulfuric acid (96%) (0.2 mL) was added. The solution was stirred at room temp. for four days. Then water (20 mL) was added, and the ester was extracted with diethyl ether (3 × 20 mL). The organic solution was washed with water, a saturated aqueous solution of sodium carbonate and water again; then it was dried with sodium sulfate. The product was filtered, and the solvent was evaporated under vacuum. The yield was 60%. ^{1}H NMR (400 MHz, [D_6]acetone): δ = 2.09 (d, 3 H), 3.65 (s, 3 H), 5.77 (dd, 1 H); 6.38 (m, 1 H) ppm. ^{13}C NMR (150 MHz, [D_6]acetone): δ = 167.14 (s), 146.6 (d), 121.2 (d), 51.2 (q), 15.0 (q) ppm.

[1] R. Eisenberg, *Acc. Chem. Res.* **1991**, *24*, 110–116.
[2] D. Canet, C. Aroulanda, P. Mutzenhardt, S. Aime, R. Gobetto, *Concepts Magn. Reson. Part A* **2006**, *28*, 321–330.
[3] S. B. Duckett, C. L. Newell, R. Eisenberg, *J. Am. Chem. Soc.* **1994**, *116*, 10548–10556.
[4] S. B. Duckett, G. K. Barlow, M. G. Partridge, B. A. Messerie, *J. Chem. Soc., Dalton Trans.* **1995**, 3427–3429.
[5] J. Bargon, J. Kandels, P. J. Kating, *J. Chem. Phys.* **1993**, *98*, 6150–6153.
[6] J. Bargon, J. Kandels, P. J. Kating, A. Thomas, K. Woelk, *Tetrahedron Lett.* **1990**, *31*, 5721–5724.
[7] C. R. Bowers, D. P. Weitekamp, *Phys. Rev. Lett.* **1986**, *57*, 2645–2648.
[8] C. R. Bowers, D. H. Jones, N. D. Kurur, J. A. Labinger, M. G. Pravica, D. P. Weitekamp, *Adv. Magn. Reson.* **1990**, *14*, 269–291.
[9] S. Aime, R. Gobetto, F. Reineri, D. Canet, *J. Chem. Phys.* **2003**, *119*, 8890–8896.
[10] R. Gobetto, L. Milone, F. Reineri, L. Salassa, A. Viale, E. Rosenberg, *Organometallics* **2002**, *21*, 1919–1924.
[11] J. Natterer, J. Bargon, *Prog. Nucl. Magn. Reson. Spectrosc.* **1997**, *31*, 293–315 and references cited therein.
[12] S. B. Duckett, C. J. Sleigh, *Prog. Nucl. Magn. Reson. Spectrosc.* **1999**, *34*, 71–92 and references cited therein.
[13] S. Aime, R. Gobetto, D. Canet, *J. Am. Chem. Soc.* **1998**, *120*, 6770–6773.
[14] S. Aime, W. Dastrù, R. Gobetto, A. Viale, D. Canet, *J. Phys. Chem. A* **1999**, *103*, 9702–9705.
[15] S. Aime, D. Canet, W. Dastrù, F. Reineri, A. Viale, *J. Phys. Chem. A* **2001**, *105*, 6305–6310.

[16] J. Halpern, D. P. Riley, A. S. C. Chan, J. J. Pluth, *J. Am. Chem. Soc.* **1977**, *99*, 8055–8057.
[17] J. Halpern, *Inorg. Chim. Acta* **1981**, *50*, 11–19.
[18] L. D. Field, A. J. Ward, *J. Organomet. Chem.* **2003**, *681*, 91–97.
[19] M. G. Musolino, G. Apa, A. Donato, R. Pietropaolo, *Catal. Today* **2005**, *100*, 467–471.
[20] L. L. Padolik, F. Ungvary, A. Wojcicki, *J. Organomet. Chem.* **1992**, *424*, 319–329.
[21] P. M. Henry, *Acc. Chem. Res.* **1973**, *6*, 16–24.
[22] M. T. Chicote, M. Green, J. L. Spencer, F. Gordon, A. Stone, J. Vicente, *J. Organomet. Chem.* **1977**, *137*, C8–C10.
[23] J. Ashley-Smith, M. Green, D. C. Wood, *J. Chem. Soc. A* **1970**, 1847–1852.
[24] P. Michelin Lausarot, G. A. Vaglio, M. Valle, *Gazz. Chim. Ital.* **1979**, *109*, 127–130.
[25] In Scheme 2c, hydrogen is indicated as η^2-coordinated rather than as a dihydride in order to account for the strong solvent effect observed on the reaction rate, which suggests insertion of a solvent molecule into the first coordination sphere of the metal.
[26] G. J. Kubas, *Acc. Chem. Res.* **1988**, *21*, 120–128.
[27] G. J. Kubas, *PNAS* **2007**, *104*, 6901–6907.
[28] G. Gritzner, *J. Mol. Liq.* **1997**, *73–74*, 487–500.
[29] J. A. Davies, F. R. Hartley, S. G. Murray, *J. Chem. Soc., Dalton Trans.* **1980**, 2246–2249.
[30] J. M. Brown, L. R. Canning, A. J. Downs, A. M. Forster, *J. Organomet. Chem.* **1983**, *255*, 103–111.
[31] I. V. Koptyug, K. V. Kovtunov, V. Burt, V. Anwar, V. Hilty, S. I. Han, A. Pines, R. Z. Sagdeev, *J. Am. Chem. Soc.* **2007**, *129*, 5580–5586.

Received: April 8, 2008
Published Online: August 22, 2008

