Hybrid bidentate ligand for functional recognition: an application to regioselective C=C double bond hydrogenation

Frédéric Goettmann,[a] Pascal Le Floch*[b] and Clément Sanchez*[a]

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Regioselectivity increases in C=C double bond hydrogenation could be obtained for Lewis basic substrates on a Lewis acidic support by using a rhodium complex supported on a mesoporous solid.

Natural enzymes are more active and selective than any man made system.[1] One of the most fascinating properties of enzymes is their ability to orientate their substrate in order to discriminate similar active functions. For instance, the well-known Cytochrome P-450$_{CAM}$ is able to very selectively hydroxylate the 5-*exo* position of camphor. Here, regioselectivity relies on the binding of camphor to the OH group of tyrosine 96.[2] To transpose this concept to homogeneous catalysis, chemists have used van der Waals forces,[3–5] hydrogen bonding[6,7] or Lewis acid/base interactions,[8,9] showing that designing artificial mimics of enzyme sites requires fine molecular engineering. In the case of heterogeneous catalysts (with the intention of overcoming the usual separation problems of homogeneous systems[10]), such a strategy usually requires multi-step syntheses.[11,12] Herein, we wish to report on the use of a hybrid meso-organized catalytic system, based on a rhodium complex grafted onto mesoporous mixed zirconia/silica powders, in the catalytic hydrogenation of C=C double bonds. This material proved to be more selective than its homogenous counterpart. The Lewis acidic sites due to the zirconium atoms could positively interact with Lewis basic substrates, thus allowing discrimination between the double bonds in the substrate skeleton.

The main problem in the synthesis of a heterogeneous equivalent to enzymatic active sites is controlling the active and the binding site positions. To circumvent this obstacle, we propose to use the whole support surface as the binding function; the substrate bearing a specific function presenting a good affinity for the wall. Indeed, one could imagine that after grafting onto the surface, the substrate would be able to migrate until it meets a catalytic site, providing that available neighbouring sites exist. (Fig. 1)

We recently described hybrid catalytic systems called hybrid bidentate ligands (HBL),[13] in which the active complex is grafted as closely as possible to the surface.[14] A phosphanorbornadiene phosphonic acid derivative (1-phospha-4,5-dimethyl-3,6-diphenyl-norbornadienyl phosphonic acid **PNBDP**) grafted onto a zirconia-rich mesoporous material (**ZS20$_C$**) proved, once complexed to a rhodium(I) precursor, to be very active in the hydrogenation and hydroformylation of olefins.

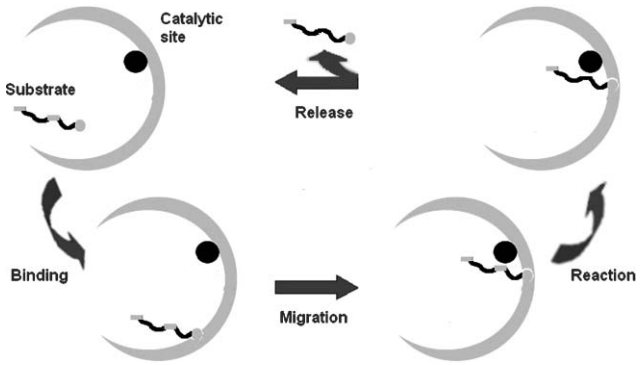
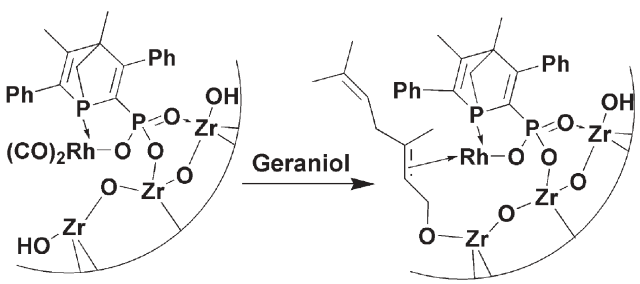


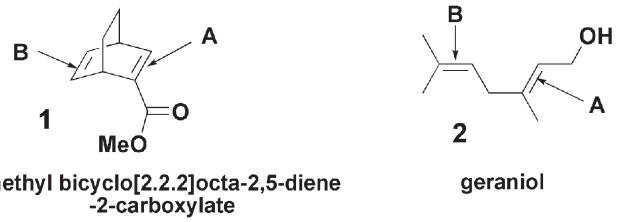
Fig. 1 Schematic representation of the concept of functional recognition, based on the support's wall properties. The substrate binds anywhere on the support, then migrates and meets the active site, where one of its reactive functions is better placed to react.

We supposed that this system could be an ideal support for testing our hypothesis. Indeed, as previously shown, the position of the grafted rhodium complex near the wall of the support is very well controlled. On the other hand, the Lewis acidic properties of zirconia are well known, and the naked **ZS20$_C$** material has recently been proved to act as an efficient hydroformylation catalyst, partly through its Lewis acidic binding sites.[15] We therefore investigated the use of this HBL in the regioselective hydrogenation of olefins. Note that the structure of the complex employed has been studied previously.[13] One could suggest the formation of a Zr–O–Rh bond as an alternative to the structure proposed in Scheme 1. However, solid state ^{31}P NMR data supported the formation of the depicted 5-membered metallacycle. Moreover, the presence of one available Lewis acidic site near the rhodium center was established during this study; the phosphorus



Scheme 1 Structure of the catalytic site and possible binding of a substrate.

[a]*Laboratoire de Chimie de la Matière Condensée de Paris, UMR CNRS 7574, Université Pierre et Marie Curie, 4 place Jussieu, 75005 Paris, France. E-mail: clems@ccr.jussieu.fr; Fax: (+33) 1-44-27-47-69*
[b]*Laboratoire Hétéroéléments et Coordination, UMR CNRS 7653 (DCPH), Département de Chimie, Ecole Polytechnique, 91128 Palaiseau cedex, France. E-mail: lefloch@poly.polytechnique.fr; Fax: (+33) 1-69-33-39-90*



methyl bicyclo[2.2.2]octa-2,5-diene -2-carboxylate

geraniol

Fig. 2 Structure of the substrates. The double bonds are labelled A or B depending one the distance to the Lewis basic function. The mono-hydrogenation products are hereafter labelled as A or B products when they are hydrogenated in the A or B positions, respectively.

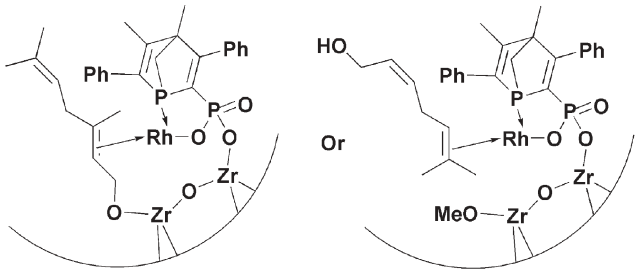


Fig. 3 Representation of the two possible paths for the coordination of geraniol to the rhodium center in the presence of methanol. In the left diagram, a methoxy moiety is coordinated to the zirconium center so that bond-B of geraniol can enter the rhodium coordination sphere.

atom of the phosphine moiety being coordinated through its lone pair to a zirconium atom prior to coordination to the $[Rh(CO)_2]$ fragment. The presence of this neighboring anchoring site could allow a substrate bearing a Lewis basic moiety to anchor itself near the rhodium complexes and thus control the regioselectivity, as depicted in Scheme 1 for geraniol.

The catalyst, (**[Rh(PNBDP)(CO)$_2$]@ZS20$_C$**), was prepared as previously described.[13] The mixed oxide was synthesized by spray drying an ethanolic sol of $ZrCl_4$ and $SiCl_4$ (molar ratio of 4 : 1) with cetyltrimethylammonium bromide (CTAB) as surfactant. After surfactant elimination, the powder exhibited a 230 m^2 g^{-1} specific surface area and an average pore diameter of about 20 Å. **PNBDP** was grafted under argon in toluene at 90 °C for 12 h, resulting in a 20 mass% organic charge. Solid state ^{31}P CP-MAS NMR and FT-IR confirmed the proposed structure of the catalyst.[13] Two model substrates, bearing a Lewis basic function like an ester or an alcohol, were chosen: methyl bicyclo[2.2.2]octa-2,5-diene-2-carboxylate (**1**) and geraniol (**2**) (Fig. 2). Hydrogenations were carried out in methanol at 50 °C under 10 bar of H_2 using 0.5 mol% of rhodium. The products were analyzed by ^1H NMR, and the results are summarized in Table 1. When required, the corresponding homogeneous catalyst, **[Rh(PNBDP)(CO)$_2$]**, was used for comparison.

As can be seen, the hydrogenation reaction is totally regioselective in the case of compound **1** (Table 1, entry 1), whereas the homogeneous catalyst only yields 80% of the same product (Table 1, entry 2). Indeed, bicyclodienes like barreledienes or norbornadiene are known to act as bidentate ligands towards rhodium(I) fragments.[16,17] Therefore, both double bonds can be hydrogenated. With the heterogeneous catalyst, one can propose that the binding of the ester moiety to the surface efficiently protects the double bond in the A-position, preventing its coordination to rhodium. One could of course suggest that the observed selectivity doesn't rely on the coordination of the substrate to the zirconium oxide surface but instead on the increased steric hindrance around the metallic centre due to the grafting of the complex. Indeed, in substrate **1**, double bond B is the least hindered and the most hydrogenated. However, the case of geraniol (substrate **2**) contradicts this assumption. We found that the heterogeneous catalyst is much more active than the homogeneous one (5% conversion, Table 1, entry 6),† while attempts to increase regioselectivities by enhancing the steric hindrance usually resulted in activity losses. Moreover, the observed regioselectivities strongly depend on the experimental conditions. In methanol, the reaction is totally selective towards the A-product at 60% conversion. Increasing the reaction time results in hydrogenation of the second double bond (B-product) but no traces of the B-compound could be detected. This indicates that hydrogenation of bond A is much faster than that of bond B, even if neither of them is clearly less sterically hindered. An explanation of this behaviour could be that geraniol and methanol compete to complex the zirconium surface, since both are alcohols. It would therefore be possible for a geraniol molecule to enter the coordination sphere of the rhodium centre without being bonded to the surface, while a methoxy moiety would occupy the molecular recognition position on the zirconium centre (Fig. 3). However, hydrogenation of a geraniol molecule that is not bonded to the surface seems to be far less favourable, as at 60%

Table 1 Catalytic hydrogenation of methyl bicyclo[2.2.2]octa-2,5-diene-2-carboxylate (**1**) and geraniol (**2**)[a]

					Products (%)		
					Monohydrogenation		
Entry	Substrate	Catalyst	Reaction time/h	Conversion (%)	A product	B product	Dihydrogenation
1	**1**	Heterogeneous	24	100	0	100	0
2	**1**	Homogeneous	24	100	10	80	10
3	**2**	Heterogeneous	24	60	100	0	0
4	**2**	Heterogeneous	72	100	30	0	70
5	**2**[b]	Heterogeneous	72	100	70	0	30
6	**2**	Homogeneous	72	5	50	0	50

[a] The catalysts used were: **[Rh(PNBDP)(CO)$_2$]@ZS20$_C$** (referred to as heterogeneous) and **[Rh(PNBDP)(CO)$_2$]** (referred to as homogeneous). For monohydrogenations, product A refers to that in which the double bond located nearest to the Lewis basic group was hydrogenated and B to the other one. [b] The solvent used was toluene.

conversion, only A-product is detected. It is only when almost all the A-bonds have reacted that hydrogenation of the B-bonds starts, yielding dihydrogenation products. In order to confirm this hypothesis, we decided to employ a solvent that has a much lower affinity for Lewis acids than alcohols, such as toluene. As expected, a much higher selectivity towards the A-product (70%) was obtained at 100% conversion (Table 1, entry 5). As geraniol is in large excess compared with the number of the Lewis acidic binding sites, it is a likely assumption that all of these sites are occupied either by a geraniol molecule or a hydrogenated molecule. This strongly hinders a non-grafted molecule from entering the rhodium coordination sphere, even at 100% conversion; thereby accounting for the observed regioselectivity.

This work shows that the use of a HBL in rhodium-catalyzed C=C double bond hydrogenation results in an increased regioselectivity compared with the corresponding homogeneous equivalent. This increase in selectivity, together with the increased activity, could rely on the complexation of the Lewis basic substrate onto the Lewis acidic zirconia wall. To fully validate the proposed mechanism, a full *in situ* FT-IR study might allow the detection of the binding of the substrate to the support. A further step would be to find substrates where the bond that is ideally placed for reacting is, simultaneously, the most difficult to reduce, in order to favour unexpected regioselectivities. Direct conversion of citral to citronellol would exemplify this new concept. We also believe that this simple concept could be extended to other catalytic processes of synthetic relevance. Importantly, applying this strategy to synthesizing molecular imprinted devices[18] would probably strengthen the interaction between the substrates and the cavities, improving the level of molecular control.

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Notes and references

† The activity of the homogeneous complex in the case of geraniol is remarkably low. This feature is however consistent with previous reports on the poor activity of Rh–PNBDP complexes in the hydrogenation of protic substrates.[19]

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