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Tetrahedron Letters 44 (2003) 2703–2707

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LETTERS

ROMPgel-supported tris(triphenylphosphine)rhodium(I) chloride: a selective hydrogenation catalyst for parallel synthesis

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Received 19 November 2002; accepted 6 February 2003

Abstract—ROMPgel-supported tris(triphenylphosphine)rhodium(I) chloride has been prepared and the immobilised catalyst has been effectively employed in selective hydrogenations of a variety of alkenes and terminal alkynes. © 2003 Elsevier Science Ltd. All rights reserved.

In parallel synthesis immobilized reagents[1] combine the advantages of simple purification, in that only filtration and washing are required to remove large excesses of reagents, with the ease of reaction monitoring associated with classical solution phase methodologies. As a result, immobilized reagents are ideal in the synthesis of compound libraries. In the last few years a range of solid-supported reagents has become available and there has been an ongoing effort to improve their loading and physical properties. Among the different solid supports, to which reagents can be attached, polymers derived from ring-opening metathesis (ROM) of norbornene and 7-oxanorbornene derivatives are particularly attractive. They can be prepared from readily available and highly functionalised monomers upon treatment with ruthenium carbenes.[2] The resulting polymers (ROMPgels) have high loadings and undergo significant swelling in various solvents.[3]

Catalytic hydrogenation is one the most important functional group interconversions and tris(triphenylphosphine)rhodium(I) chloride, Wilkinson's catalyst, is widely used for the reduction of unconjugated alkenes.[4] It is selective for sterically unhindered substrates, but the activity diminishes rapidly for more hindered compounds with tetrasubstituted alkenes being inert, a feature widely explored in selective hydrogenations. Despite its advantages, Wilkinson's catalyst suffers from one serious inherent disadvantage, namely the need to separate the catalyst from the product. This problem has been addressed by the attachment of the catalyst to polystyrene,[5] aluminosilicate,[6] alumina[7] and modified silica gel.[8] However, it has yet to be demonstrated that the resulting supported catalysts are generally applicable in parallel synthesis. An alternative to polymer supports has been the use of ionic liquids in biphasic systems.[9] Ionic liquids are immiscible with most organic solvents but show high affinity for metal complexes. Therefore, they can be efficiently employed in catalytic hydrogenations using the Osborn[10] complex or the Wilkinson catalyst.[11] In a biphasic ionic liquid/organic solvent system the metal complex is completely retained by the ionic liquid, while the reduction product can be recovered from the organic phase. Rhodium contamination in the products was thereby minimized. In addition, reaction rates and selectivities for hydrogenations performed in ionic liquids are often improved compared with conventional solvents.

We envisioned that ROMP methodology could be employed to prepare a novel supported Wilkinson catalyst, allowing fine-tuning of the polymer support in order to provide the best chemical environment for catalyst activity. We investigated the use of different ROM polymers, containing triarylphosphine **1**, imidazolium units **2** or a mixture of the two. The synthesis of ionic ROMPgels allowed us to explore the possibility of incorporating the advantages of ionic liquids into a solid supported reagent (Scheme 1).

ROMPgel-supported triphenylphosphine **5** was prepared as previously reported,[12] while the imidazolium hexafluorophosphate monomer **2** was obtained in three steps from commercially available starting materials (Scheme 2). *N*-Alkylimidazole **8** was prepared accord-

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Keywords: ROMPgels; catalytic hydrogenation; Wilkinson's catalyst; imidazolium salts; supported reagents.

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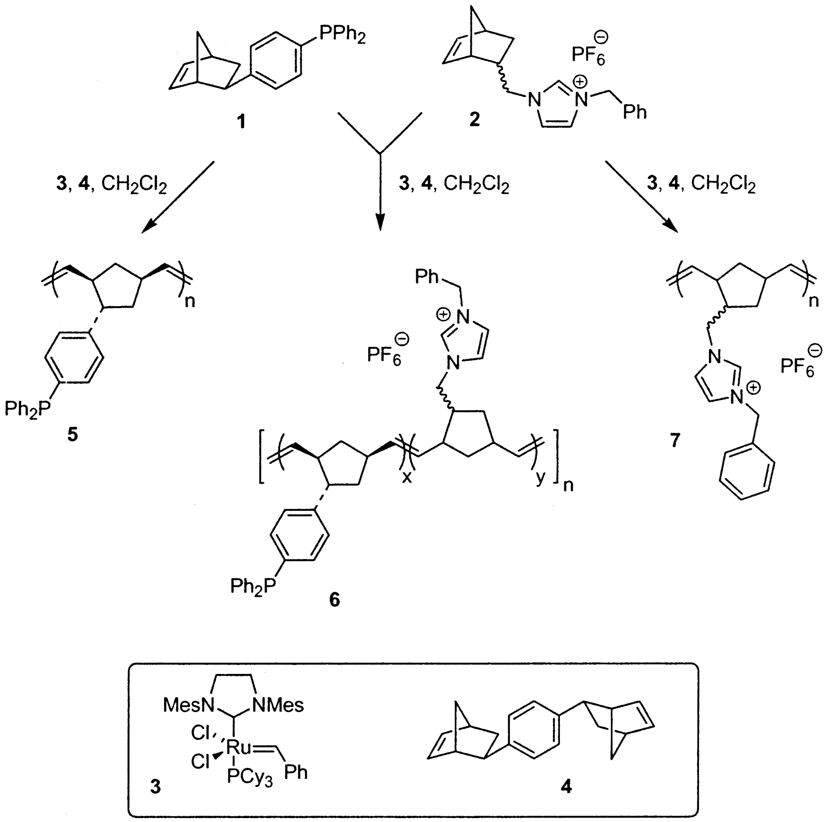
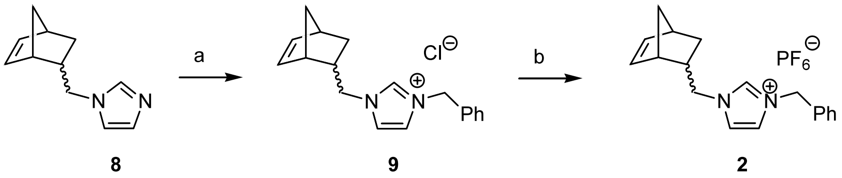
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00351-4



Scheme 1.



Scheme 2. *Reagents and conditions*: (a) BnCl, PhMe, reflux, 24 h; (b) KPF_6, CH_2Cl_2, rt, 12 h.

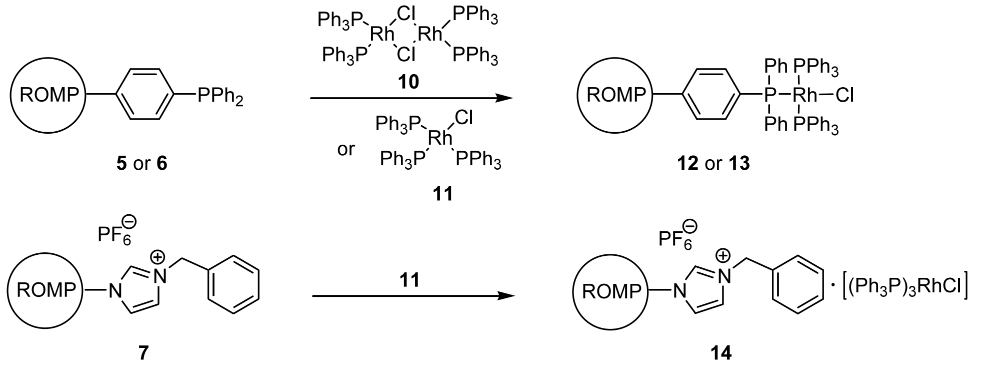
ing to a reported procedure[13] and allowed to react with benzyl chloride in toluene to give the imidazolium chloride **9** in 78% yield. Ion exchange using potassium hexafluorophosphate in dichloromethane gave the salt **2** in quantitative yield.

Addition of the second-generation Grubbs catalyst **3** (1 mol%) to the imidazolium monomer **2** afforded the ionic ROMPgel **7** in 94% yield. The triphenylphosphine/imidazolium co-polymer **6** was obtained simply by adding the above-mentioned catalyst to a 2:3 mixture of the corresponding monomers. For simplicity ROMPgel **6** is depicted as a block co-polymer, however the structure is probably random (Scheme 1). The cross linker **4** (10 mol%) was used in the synthesis of both ROMPgels **6** and **7**.

Tris(triphenylphosphine)rhodium(I) chloride (**11**) was anchored to the ROMPgels **5**, **6** and **7** by heating a suspension of the polymer and either of the rhodium complexes **10** or **11** in dichloromethane for 18 h (Scheme 3). In the case of polymers containing triphenylphosphine groups, attachment of the catalyst was achieved by ligand displacement, giving rise to the proposed structures **12** and **13**. In the case of polymer **7**, we investigated the possibility of supporting the Wilkinson catalyst through non-bonding interactions with the ionic ROMPgel (Scheme 3).

The resulting polymeric rhodium complex catalysts were screened for their ability to catalyse the hydrogenation of terminal alkenes (Table 1). When the catalysts **12** and **13** were compared, using the same weight percentage of polymer to substrate, the catalyst **12** turned out to be significantly more active than **13**. This clearly shows that, unfortunately, the ionic moiety does not have the desired rate-enhancing effect on the catalytic reduction. The polymer **14**, obtained by heating the ionic ROMPgel **7** to reflux in the presence of Wilkinson catalyst **11**, showed no activity.

The conditions for catalytic hydrogenation using the best-performing polymer **12** were further optimised.[14] To prevent the backbone double bonds interfering with



Scheme 3.

the catalyst, the polymer **12** was exposed to hydrogen (50 psi, 1:1 THF:ethanol, 48 h, 20°C). This procedure is likely to reduce backbone double bonds, which are accessible to the rhodium complexes, thereby preventing competitive reduction in the presence of a substrate. The reductive step also proved efficient in washing out loosely bound rhodium complexes. As determined by ICP–AES the resulting polymer contained 6.86% rhodium, which corresponds to a loading of 0.66 mmol/g. The phosphorous to rhodium ratio was found to be 2.78.

To compensate for the reduced diffusion rate of large substrates, i.e. steroids, generally encountered in transformations with supported reagents/catalysts a fixed mass percentage of 100% of polymer **13** to substrate was used. In this way a number of alkenes/alkynes were selectively reduced and obtained in high yield and purity (Table 2).

In a typical experiment, a degassed (N_2) mixture of THF and ethanol (1:1, 2 ml) was added to the substrate (0.040 g) and the polymer **13** (0.040 g) under nitrogen. The nitrogen was replaced with hydrogen, the reaction mixture connected to a hydrogen source and shaken vigorously. When the reaction had gone to completion the resulting mixture was filtered, the polymer washed repeatedly with dichloromethane and diethyl ether, and the combined filtrates concentrated in vacuo. As can be seen from Table 2, the ROMPgel-supported catalyst **13** is selective and allows for reduction of terminal alkenes and alkynes in the presence of more hindered alkenes. Most noteworthy is the selective reduction of a ring alkene in the presence of a *trans*-disubstituted alkene. Also, alkenes can be reduced in the presence of other functionalities such as ketones, esters, amides and nitro groups. In all cases the products are obtained in good to excellent yields and purities.

In conclusion, ROMPgel-supported tris(triphenylphosphine)rhodium(I) chloride has been prepared by loading the complex **10** onto ROMP-supported triphenylphosphine, and the immobilised catalyst has been utilised for selective hydrogenation of alkenes.

Acknowledgements

We thank Merck KGaA (to L.T.), the Norwegian Research Council (to E.Å.), the EPSRC for their support of this research, Glaxo SmithKline for the generous endowment (to A.G.M.B), the Royal Society and Wolfson Foundation for a Royal Society–Wolfson Research Merit Award (to A.G.M.B), and the Wolfson Foundation for establishing the Wolfson Centre for Organic Chemistry in Medical Science at Imperial College.

Table 1.

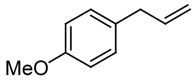
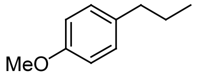
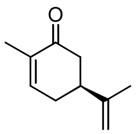
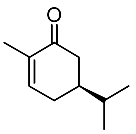
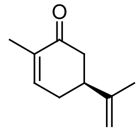
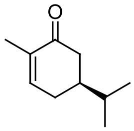
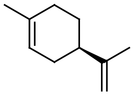
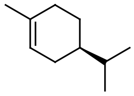
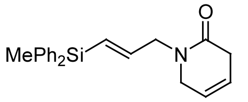
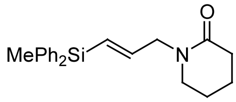
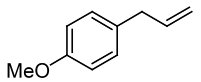
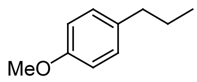
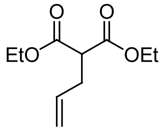
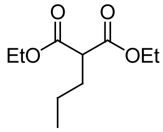
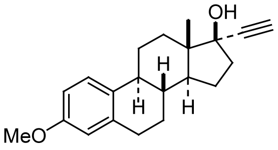
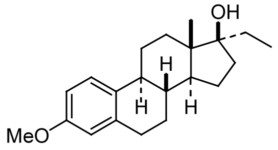
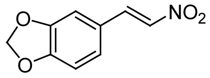
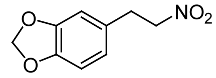
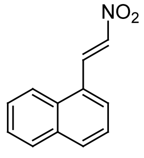
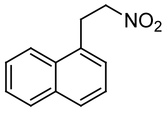
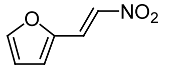
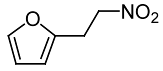
Entry	Substrate	Product	Catalyst	Time [h]	Conversion [%]
1			**12**	12	>95
2			**13**	12	61
3			**14**	12	–
4			**12**	12	>95
5			**13**	12	32
6			**14**	12	–

Table 2. Selective hydrogenation of alkenes/alkynes using ROMPgel-supported $(PPh_3)_3RhCl$ **13**

Substrate	Product	Pressure	Time	Yield (purity)[a]
		1 atm	12 h	94% (> 95%)
		1 atm	24 h	74% (90%)
		1 atm	24 h	98% (90%)
		1 atm	12 h	100% (95%)
		1 atm	12 h	100% (95%)
		1 atm	24 h	98% (95%)
		50 psi	3 days	68% (95%)
		50 psi	3 days	70% (95%)
		50 psi	3 days	75% (70%)[b]

[a] Yields refer to isolated products. Purities as judged by ^1H and ^{13}C NMR spectra, and GC-MS. [b] The product contained 30% of the starting material.

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13. Kent, M. S.; Saunders, R. US Patent 5,603,985, 1997; *Chem. Abstr.* **1997**, *126*, 225990.
14. *Preparation of polymer* ***12***: To ROMP-supported triphenylphosphine **5** (0.454 g, 1.1 mmol) was added the dimer **10** (0.783 g, 0.6 mmol) and CH_2Cl_2 (20 ml) and the mixture was heated to 50°C for 18 h (without stirring). At this time the reaction mixture was exposed to air and filtered. The polymer was washed repeatedly with CH_2Cl_2 and diethyl ether and dried under reduced pressure to give the ROMP-supported Wilkinson's catalyst **12** (0.611 g).