Supramolecular shuttle and protective agent: a multiple role of methylated cyclodextrins in the chemoselective hydrogenation of benzene derivatives with ruthenium nanoparticles†

Audrey Nowicki,[a] Yong Zhang,[a] Bastien Léger,[a] Jean-Paul Rolland,[b] Hervé Bricout,[c] Eric Monflier[c] and Alain Roucoux*[a]

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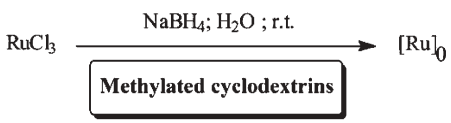
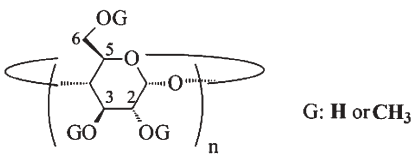
Efficient chemoselectivities have been obtained in the hydrogenation of benzene derivatives under biphasic liquid–liquid conditions using Ru(0) nanoparticles stabilized and controlled by the relevant choice of cavity and methylation degree of cyclodextrins.

Among active areas of research, total and partial hydrogenation of benzene derivatives still receive increasing interest, more particularly with the industrial demand for cyclohexane,[1] the most important precursor to adipic acid used to produce nylon-6,6, and for cyclohexene or cyclohexadiene as intermediates in organic synthesis. The process developed by Asahi Chemical Industry in Japan is an example of the selective formation of cyclohexene.[2] Generally, this catalytic transformation is carried out under drastic conditions (pressure and/or high temperature) using homogeneous or heterogeneous catalysts.[3] In the past few years, the concept of homogeneous arene hydrogenation catalysis has been reviewed since some catalysts originally assigned as homogeneous have proved to be precursors to heterogeneous (colloidal or nanoparticulate) catalysts.[4] Today, soluble noble metal nanoparticles are considered as reference in monocyclic arene catalytic hydrogenation under mild conditions and several stabilized systems have been reported.[5] Nevertheless, the development of modified nanoparticles for total, partial or selective arene hydrogenation remains an important challenge.

The use of colloidal metallic particles finely dispersed in water constitutes an original approach to biphasic liquid–liquid (water–hydrocarbon) systems, which continue to attract interest for economic and ecological reasons.[6] In such a catalytic system, the colloidal suspension must be stabilized by highly water soluble protective agents to avoid aggregation and to facilitate recycling. Recently, our laboratory has reported efficient hydrogenation of olefins and arenes by aqueous or organic suspensions of rhodium(0) and iridium(0) stabilized by hydroxyalkylammonium salts.[5,7] Following our studies on these reactions, we have investigated the stabilization of metal nanoparticles with cyclodextrins (CDs) as a protective agent and a potential host molecule for molecular recognition. This could be attractive as inclusion in a constrained environment could modify the reactivity and the selectivity of reactions. Indeed, CDs are water-soluble cyclic oligosaccharides formed of 6(α), 7(β) or 8(γ) glucopyranose units, exhibiting a hydrophobic internal cavity that can host a large variety of inorganic and organic compounds of appropriate size and shape. Molecular recognition of substrates by cyclodextrins is made possible by non-covalent interactions in the hydrophobic cavity of these cyclic sugar oligomers.[8] In this context, CDs and their derivatives such as the randomly methylated cyclodextrins (Me-CDs; Scheme 1) have already proved to be efficient inverse



Structure of the methylated cyclodextrin



Abbreviations	n	Carbon bearing the OCH_3 group	Average number of OH group substituted per glucopyranose unit
Me-α-CD	6	2, 3, 6	1.8
Me-β-CD (1.8)	7	2, 3, 6	1.8
Me-β-CD (0.7)	7	2	0.7
Me-γ–CD	8	2, 3, 6	1.8

Scheme 1 Preparation of Ru(0) nanoparticles in the presence of various methylated cyclodextrins.

[a]*UMR CNRS 6052 "Synthèses et Activations de Biomolécules", Ecole Nationale Supérieure de Chimie de Rennes, Institut de Chimie de Rennes, Avenue du Général Leclerc, 35700, Rennes, France. E-mail: Alain.Roucoux@ensc-rennes.fr; Fax: +33 (0)223 238 199*
[b]*UMR CNRS 6026 "Interactions Cellulaires et Moléculaires", Université de Rennes I, 35042, Rennes, France*
[c]*Laboratoire de Physico-chimie des Interfaces et Applications-FRE CNRS 2485, Faculté Jean Perrin, Université d'Artois, 62307, Lens Cedex, France*
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transfer catalysts and useful discriminating tools for substrate-selective reactions in aqueous organometallic catalysis.[9]

Several papers have reported the steric stabilization of metal nanoparticles with thiolated cyclodextrins as ligand[5b,10] (metal–S bond) and their use in catalytic reactions.[11] Nevertheless, to our knowledge, only two reports describe the catalytic hydrogenation of olefins using colloidal rhodium dispersions embedded by native cyclodextrins,[12] generating steric stabilization *via* hydrophobic interactions. More recently, the addition of native or cationic CDs to rhodium nanoparticles stabilized by TPPTS (triphenylphosphine trisulfonated sodium salt) has been reported, leading to high selectivities in the hydrogenation of unsaturated carboxylic acids.[13] Here we describe the hydrogenation of various arene derivatives under biphasic liquid–liquid (water–hydrocarbon) systems using ruthenium(0) colloids stabilized by classical Me-CDs (Scheme 1), which are modulated by the cavity and the substitution degree (SD). We show multiple role of cyclodextrins as i) stabilizer, ii) phase transfer agent and iii) suitable host molecule for selective hydrogenation controlled by the choice of the SD.

The catalytically active aqueous suspension is composed of metallic ruthenium(0) particles prepared by reducing ruthenium chloride with sodium borohydride in dilute aqueous solutions of methylated cyclodextrins. These ruthenium(0) aqueous suspensions are visually stable (no sedimentation). Since the particles are too large to be totally included in the cavity of α-, β-, γ-CDs, we could presume that the nanoparticles are embedded by several cyclodextrin molecules, avoiding aggregation. The molar ratio R = Ru/Me-CD has previously been optimized. Procedure investigation before and during the catalysis has established that R must be greater than 3. Nevertheless, the standard system has been defined as $R = 10$, which gives sufficient steric stabilization to maintain catalytic species within the aqueous phase, with good activities. Transmission electron microscopy (TEM) observations show that the average particle size was about 1.5 nm with 70% of the nanoparticles between 1 and 2.5 nm. The size distribution histogram was obtained on the basis of measurement of about 240 particles (see ESI†).

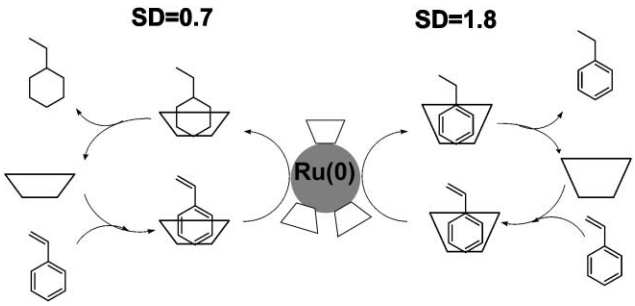
The so-obtained catalytic system (Ru–Me-CD–water) has been tested in the hydrogenation of various arene derivatives under biphasic conditions at room temperature and under atmospheric hydrogen pressure. The reaction was monitored by the volume of hydrogen consumed and gas chromatographic analysis. The results are summarised in Table 1.

Some interesting results in term of selectivity have been obtained. Indeed, the hydrogenation of aromatic rings depends on the type of Me-CD (α,β,γ) and also on the substitution degree (SD). Indeed, using Me-α-CD, the aromatic rings were not hydrogenated (entries 1, 5, 9) as they could form inclusion complex with the cyclodextrin, avoiding hydrogenation. Nevertheless, we observed regioselective hydrogenation of the exocyclic C–C double bond in the case of styrene (entry 5). In contrast, ruthenium nanocatalysts stabilized by Me-γ-CD (entries 4, 8, 12) show total hydrogenation of the aromatic rings. This phenomenon could be explained by the weaker interactions between substrates and cyclodextrins due to the larger cavity. In the case of Me-β-CDs, interesting selectivities have been obtained according to the substitution degree. Indeed, using Me-β-CD with a low substitution degree (SD = 0.7), the aromatic ring was hydrogenated (entries 2, 6, 10, 13, 15, 17). On the other hand, with the Me-β-CD possessing a higher substitution degree (SD = 1.8), benzene and toluene were hydrogenated (entries 3, 14), whereas all aromatic rings of substrates possessing an alkyl chain of more than two carbons were not hydrogenated (entries 7, 11, 16, 18). This difference of selectivity observed with the two kinds of methylated β-cyclodextrins with different substitution degrees could be explained by a deeper hydrophobic host cavity in the case of the more substituted cyclodextrin.[14] Indeed, the methylated β-CD with a high substitution degree presents methyl groups on the primary and the secondary faces whereas the methylated β-CD with a low substitution degree has essentially methyl groups on the secondary face. Consequently, the more substituted cyclodextrin can wrap

Table 1 Hydrogenation of benzene derivatives under biphasic conditions[a]

Entry	Substrate	Cyclodextrin (SD)[b]	Product (conv. [%])[c]	Time/h	TOF/h^{-1} [d]
1	benzene	Me-α-CD	—	—	—
2		Me-β-CD (0.7)	cyclohexane (100)	4	25
3		Me-β-CD (1.8)	cyclohexane (100)	4	25
4		Me-γ-CD	cyclohexane (100)	10	10
5	styrene	Me-α-CD	ethylbenzene (100)	10	10
6		Me-β-CD (0.7)	ethylcyclohexane (100)	11	9
7		Me-β-CD (1.8)	ethylbenzene (100)	11	9
8		Me-γ-CD	ethylcyclohexane (100)	24	4
9	ethylbenzene	Me-α-CD	—	—	—
10		Me-β-CD (0.7)	ethylcyclohexane (100)	11	9
11		Me-β-CD (1.8)	—	—	—
12		Me-γ-CD	ethylcyclohexane (100)	11	9
13	toluene	Me-β-CD (0.7)	methylcyclohexane (100)	6	17
14		Me-β-CD (1.8)	methylcyclohexane (100)	6	17
15	propylbenzene	Me-β-CD (0.7)	propylcyclohexane (100)	11	9
16		Me-β-CD (1.8)	—	—	—
17	allylbenzene	Me-β-CD (0.7)	propylcyclohexane (100)	12	8
18		Me-β-CD (1.8)	propylbenzene (100)	3	34

[a] *Conditions:* catalyst (1.5×10^{-5} mol), cyclodextrin (1.5×10^{-4} mol), substrate (1.5×10^{-3}mol), hydrogen pressure (1 bar), temperature (20 °C), stirred at 1500 min^{-1}, 10 mL water. [b] SD (substitution degree) defined as average number of hydroxyl group substituted per glucopyranose unit. [c] Determined by GC analysis. [d] Turnover frequency defined as number of mol of consumed H_2 per mol of ruthenium per hour.



Scheme 2 Proposed selective mechanism of styrene hydrogenation.

more efficiently the aromatic rings and avoid their hydrogenation. Moreover, the group of Fenyvesi has recently established the association constants of Me-β-CD (with SD = 1.9) for various benzene derivatives.[15] This work reports that the stability of the complex increases with the carbon number of the substituent on the aromatic ring, namely benzene (110 M^{-1}) < toluene (144 M^{-1}) < ethylbenzene (320 M^{-1}), thus showing a significant value for the ethyl group.

Finally, we could presume that Me-CDs play several essential roles in arene hydrogenation by ruthenium nanocatalysts. Firstly, CDs act as a steric stabilizer of the colloidal suspension *via* hydrophobic–hydrophobic interactions between Ru nanoparticles and cyclodextrins[16] or *via* interactions between Ru nanoparticles and hydroxyl groups of native cyclodextrins, as previously reported for gold nanoparticles.[17] In our catalytic system, we have established that 3 equivalents of Me-CDs per mole of metal were enough to stabilize the colloidal suspension. Secondly, cyclodextrins act also as a supramolecular shuttle between the organic phase and the surface of the water-soluble nanoparticles by forming inclusion complexes with the substrate, which come close to the nanoparticle surface. The driving forces contributing to the inclusion complex formation are the different types of interactions in terms of the van der Waals interaction, hydrogen-bonding interactions, and hydrophobic forces.[18] The orientations and the positions of the included guests in the host cavity are strongly sensitive to the shapes, sizes and polarities of the substituent groups. The transport function of CDs justifies the necessity to have an excess of CDs in the media. In our case, 7 equivalents of Me-CDs could play this role and no good catalytic activity was observed when only 3 equivalents of CDs were used. This phenomenon has been proved by additive studies. Firstly, we have shown no hydrogenation reaction with *ortho*-xylene by Ru–Me-α-CD (R = 10), a substrate known to interact very weakly with the α-CD.[19] Secondly, we added 5 eq. Me-β-CD (1.8) to a previously stabilized Ru–Me-α-CD (R = 5) catalytic system (in previous experiments, we have observed that stabilization with Me-α-CD was better with R = 5, this kind of CD being less hydrophilic). In that case, the hydrogenation of *ortho*-xylene was carried out with 100% conversion in 1,2-dimethylcyclohexane in 15 hours. We could undoubtly presume that only the Me-β-CD plays the role of supramolecular carrier as the substrate does not fit tightly within Me-α-CD. The proposed mechanism is presented in Scheme 2.

In conclusion, new aqueous colloidal solutions of Me-CD protected Ru(0) nanoparticles could be easily prepared by reduction of $RuCl_3$. These nanoparticles present interesting activity for the hydrogenation in two liquid phases of various arene derivatives under mild conditions. For the first time, we report a nanoheterogeneous system stabilized by various methylated cyclodextrins which have proved to be a discriminating tool for aromatic ring hydrogenation. The selective hydrogenation between reducible exocyclic functions such as C=C double bonds and aromatic groups was easily controlled by the choice of the substitution degree. These preliminary results may be extended to other substrates and under hydrogen pressure to increase turnover activities.

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