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Synergetic Effect of Randomly Methylated β-Cyclodextrin and a Supramolecular Hydrogel in Rh-Catalyzed Hydroformylation of Higher Olefins

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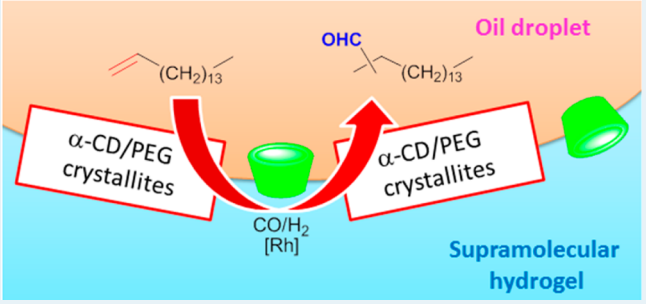
Supporting Information

ABSTRACT: A significant improvement in Rh-catalyzed hydroformylation of very hydrophobic alkenes was achieved using a biphasic catalytic system consisting of a substrate-containing organic phase and a catalyst-containing hydrogel phase [consisting of poly(ethylene glycol) 20000 (PEG20000) and α-cyclodextrin (α-CD)]. The catalytic performance of the Pickering emulsion that resulted from the formation of α-CD/PEG20000 crystallites at the oil droplet surface proved to be greatly dependent upon the presence of additives. We showed that controlled uploads of randomly methylated β-cyclodextrin (RAME-β-CD) within the supramolecular hydrogel could positively affect both the catalytic activity and chemoselectivity of the hydroformylation reaction. Conversely, no Pickering emulsion could be observed using excess RAME-β-CD, resulting in the subsequent degradation of the catalytic performance. Optical microscopy and optical fluorescence microscopy supported the catalytic results and allowed us to explain the role of RAME-β-CD. Indeed, controlled uploads of RAME-β-CD prevented the saturation of the oil droplet surface. RAME-β-CD acted as a fluidifier of the Pickering emulsion and accelerated the dynamics of exchange between the substrate-containing organic phase and the catalyst-containing hydrogel phase. Morever, RAME-β-CD acted as a receptor that participated in the conversion of the alkene by supramolecular means.



KEYWORDS: *hydrogel, cyclodextrins, Pickering emulsion, biphasic catalysis, hydroformylation*

Concurrently to their applications in biology,[1,2] medicine,[3,4] materials,[5−7] and sensing,[8−11] supramolecular hydrogels have emerged as a promising class of hydrophilic media for catalysis. Their main advantage lies in their easy preparation by physical binding between two complementary compounds through noncovalent interactions.[12−14] Moreover, the thermoresponsive properties of supramolecular hydrogels were of particular interest for catalytic applications. For example, their ability to deswell and swell reversibly to concentrate substrates and catalysts within the hydrogel matrix greatly accelerates the reaction rate.[15,16] Our group showed that supramolecular hydrogels proved to be especially effective as templates for *in situ* RuNPs syntheses and their subsequent use in hydrogenation reactions.[17] A hydrogel-based system capable of continuous self-monitoring and self-regulating behavior was also investigated, yielding very interesting results in four exothermic catalytic reactions.[18]

Recently, we demonstrated that supramolecular hydrogels consisting of poly(ethylene glycol) (PEG) and α-cyclodextrin (α-CD) could be advantageously used in the sol phase to convert organic substrates under aqueous biphasic conditions.[19] The α-CD/PEG combination led to nanosized columnar α-CD domains (crystallites) that formed Pickering emulsions (particle-stabilized emulsions) in the presence of hydrophobic alkenes. The existence of Pickering emulsions between the organic phase and the hydrogel compartment significantly improved the catalytic activity at the aqueous/organic interface. As such, very hydrophobic alkenes could be converted into aldehydes through hydroformylation of the terminal C═C double bonds under CO/H_2 pressure (50 bar), the water-soluble Rh catalyst being immobilized in the α-CD/PEG hydrogel phase. However, the catalytic activity regularly decreased with time as the Pickering emulsions became too stable with time. Actually, after 4 h, the organic droplet surface was saturated with α-CD/PEG crystallites and the conversion leveled off. To overcome the issue, we implemented successive depressurization/pressurization cycles to break the stable Pickering emulsions and recover dynamics of exchange at the aqueous/organic interface. For each cycle, 40−45% of the remaining substrate was sequentially converted. Full conversion could thus be obtained even for very hydrophobic alkenes (C12−C18). Although effective, the depressurization/pressur-

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ization technique was quite cumbersome and required a step-by-step procedure.

Herein, we report on a more practical strategy that makes use of a randomly methylated β-cyclodextrin (RAME-β-CD) to fully hydroformylate hydrophobic alkenes with a very short reaction time in one go. We showed that addition of RAME-β-CD prevented the saturation of the oil droplet surface, resulting in a linear conversion of alkenes over time.

The catalytic system used in this study consisted of a rhodium precursor [$Rh(CO)_2(acac)$] and a water-soluble phosphane [TPPTS (sodium salt of the trisulfonated triphenylphosphane)] that stabilized the Rh catalyst in a supramolecular hydrogel (**H1**) [1/1 mixture of poly(ethylene glycol) with a molecular weight of 20000 (PEG20000) and α-CD].

The hydroformylation reactions were conducted under 50 bar of CO/H_2 at 80 °C. In Figure 1 are represented five

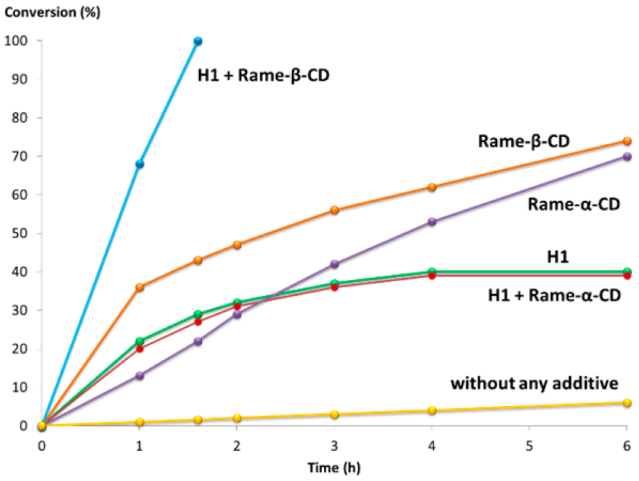

Figure 1. Effect of additives on the Rh-catalyzed hydroformylation of 1-hexadecene. Conditions: 1/5/140 Rh/TPPTS/1-hexadecene mixture, 80 °C, 50 bar of CO/H_2.

different kinetic curves relative to the hydroformylation of 1-hexadecene. Three of them describe the kinetic profiles of the constitutive components [hydrogel **H1**, randomly methylated α-cyclodextrin (RAME-α-CD), and RAME-β-CD]. Each of them led to a moderate conversion within 6 h (from 40 to 70%). The other two kinetic profiles reflected the conversion variations observed when a mixture of **H1** and RAME-α-CD (red curve) or RAME-β-CD (blue curve) was used as an aqueous medium. Ten equivalents of randomly methylated CDs with regard to the Rh catalyst was dissolved in **H1**.[20] When mixed with **H1**, RAME-α-CD did not alter the catalytic performance. Indeed, its availability at the aqueous/organic interface was significantly reduced because of its natural tendency to thread onto the PEG20000 chains (formation of polypseudorotaxanes).[21] Conversely, it clearly appeared that the **H1**/RAME-β-CD mixture led to a catalytic performance that was far better than that of the separated components or that of the **H1**/RAME-α-CD mixture. Indeed, an almost linear conversion variation was observed, and 100% 1-hexadecene was converted within 1.5 h. This constituted the best conversion ever for this substrate under aqueous biphasic conditions. Upon comparison to the catalytic performance obtained with the separated components, a synergetic effect resulted from the Pickering emulsion and the presence of RAME-β-CD within the hydrogel. Additionally, the chemoselectivity of the hydroformylation reaction was also positively affected by the **H1**/RAME-β-CD couple. From 64% without RAME-β-CD, the proportion of aldehydes increased to 77% in the presence of RAME-β-CD, an increase probably related to the well-known protecting ability of the CD cavity toward the terminal C═C bond (limitation of side isomerization reactions).[22] Note that the regioselectivity was not significantly altered by the presence of RAME-β-CD in the hydrogel (Supporting Information). The values of the linear/branched ratio obtained using the **H1**/RAME-β-CD mixtures were between those measured for the separated components, suggesting that the equilibria between the catalytic Rh species were not modified during the catalytic cycle. In this regard, the organic phase was recovered at room temperature once the reaction was complete to quantify any traces of Rh. No trace of Rh could be detected by ICP, thus demonstrating that the Rh catalyst was immobilized in the hydrogel phase. Other proof of the absence of Rh in the organic phase was given by the following experiment. After a reaction time of 3 h, an **H1**/RAME-β-CD catalytic system was cooled, and the organic phase was collected under nitrogen. Once an aliquot had been withdrawn for analysis, water (6 mL) and fresh 1-hexadecene (140 equiv with regard to Rh) were added to the organic phase. After reaction for an additional 3 h at 80 °C under 50 bar of CO/H_2, no conversion could be measured, indicative of the absence of Rh catalysts in the organic phase.[23]

To gain insight into how the system proceeded, the amount of RAME-β-CD was varied from 5 to 40 equiv with regard to the Rh catalyst. Five hydroformylation reactions were conducted. The results were translated into a conversion spread (excess conversion value obtained with the **H1**/RAME-β-CD couple over the value measured with RAME-β-CD) as a function of the amount of RAME-β-CD (Figure 2). An optimal

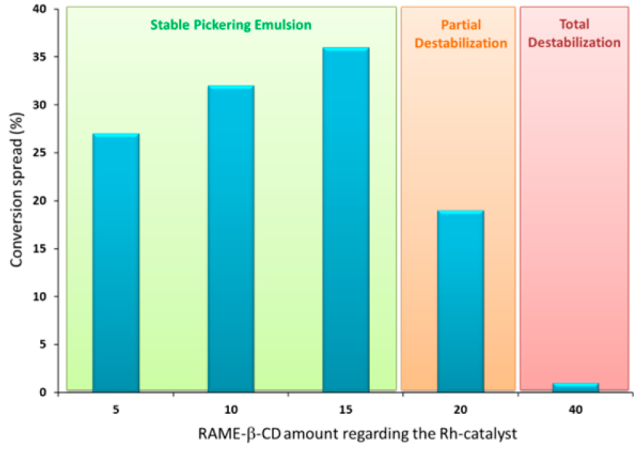

Figure 2. Variation of the conversion spread (excess conversion value obtained with the **H1**/RAME-β-CD couple over the value measured with RAME-β-CD) as a function of the amount of RAME-β-CD (with regard to the Rh catalyst) in the Rh-catalyzed hydroformylation of 1-hexadecene. Conditions: 1/5/140 Rh/TPPTS/1-hexadecene mixture, 80 °C, 50 bar of CO/H_2, t = 1 h.

conversion spread of 36% was obtained for 15 equiv of RAME-β-CD with regard to the Rh catalyst. Above that value, the spread drastically decreased, reaching a value of 2% when 40 equiv of RAME-β-CD was added to the hydrogel. Thus, excess RAME-β-CD significantly altered the catalytic performance of

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the system. More information about the catalytic system was obtained by optical microscopy measurements.

Using 15 equiv of RAME-β-CD with regard to the Rh catalyst, a well-dispersed oil in water (O/W) emulsion was observed at 80 °C (Figure 3a). With 20 equiv of RAME-β-CD,

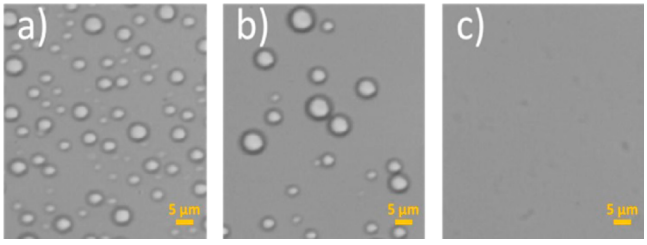

Figure 3. Optical microscopy performed at 80 °C of mixtures containing 1-hexadecene (1.2 mL), **H1** (6 mL), and (a) 15, (b) 20, and (c) 40 equiv of RAME-β-CD with regard to Rh.

there were fewer oil droplets that had larger diameters (Figure 3b), indicative of a smaller aqueous/organic interface. With 40 equiv of RAME-β-CD (Figure 3c), no oil droplet could be detected, suggesting that the Pickering emulsion was broken. In that case, the organic and aqueous phases coexisted separately. The extent of the aqueous/organic interface logically appeared to be directly connected to the catalytic performance. The higher the extent of the aqueous/organic interface, the better the conversion. Additionally, RAME-β-CD retained its ability to recognize 1-hexadecene and participated in its conversion by supramolecular means. Conversely, the same catalytic experiment conducted with an **H1**/RAME-γ-CD combination led to a poor conversion of 16%, an aldehyde selectivity of 64%, and a linear/branched aldehyde ratio of 2.7. These results were very similar to those observed using **H1** alone (22% conversion) or using an **H1**/RAME-α-CD combination (20% conversion). The conversion was far from that obtained using an **H1**/RAME-β-CD combination (68% conversion within 1 h). However, 1-hexadecene could be fully converted within 6 h using the **H1**/RAME-γ-CD combination, suggesting that RAME-γ-CD still acted as a fluidifier but not as a molecular receptor. We do believe that the lower affinity between the RAME-γ-CD cavity and the alkenes was responsible for this catalytic result. Indeed, contrary to RAME-β-CD whose cavity could accommodate the substrate, RAME-γ-CD was too wide to properly recognize 1-hexadecene, resulting in lower association constants with the substrate.

As demonstrated throughout our previous study,[8] the existence of an extended interface resulted from the presence of a Pickering emulsion. To confirm that Pickering emulsions were still active during the catalytic process, optical fluorescence microscopy was conducted at 80 °C on two samples containing the substrate (1.2 mL), hydrogel **H1** (6 mL), and 15 or 40 equiv of RAME-β-CD with regard to Rh (3 mg). DiI or DiO (2% by weight) was added to the mixture to stain the α-CD/PEG crystallites. The sample that contained 1-hexadecene, **H1**, and 15 equiv of RAME-β-CD produced crystallites that covered the oil droplet surface (Figure 4a,c). Accordingly, the presence of 15 equiv of RAME-β-CD probably altered the Pickering emulsion (as revealed by the improvement in the catalytic performance) but did not hamper the formation of α-CD/PEG crystallites on the oil droplet surface. Conversely, excess RAME-β-CD prevented the formation of α-

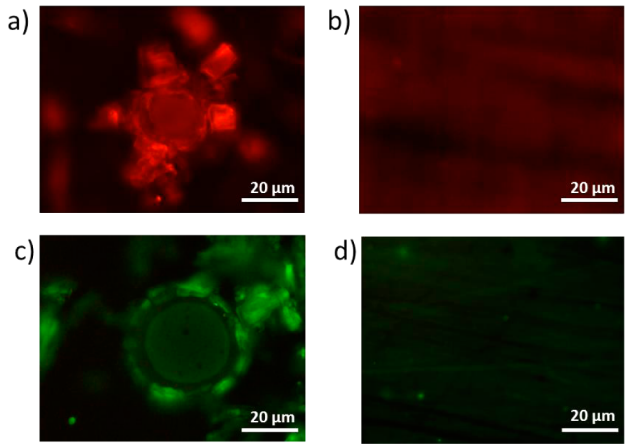

Figure 4. Optical fluorescence microscopy of mixtures containing 1-hexadecene (1.2 mL), **H1** (6 mL), and (a) 15 or (b) 40 equiv of RAME-β-CD with regard to Rh prepared at 80 °C and observed at 20 °C. DiI (a and b) and DiO (c and d) were used to stain the α-CD/PEG crystallites.

CD/PEG crystallites as none of them could be detected by optical fluorescence microcopy in that case (Figure 4b,d).

These observations from the catalytic results and the optical microscopies echoed recent results we obtained on CD-based catalytic micellar systems. Indeed, we showed that the addition of RAME-β-CD in an aqueous medium could have a beneficial impact on the catalytic performances of phosphane-based aggregates in the Rh-catalyzed hydroformylation reaction[24] and in the Pd-catalyzed cleavage of allyl carbonates (Tsuji−Trost reaction).[25] The exchanges between the hydrophobic substrate-containing aggregate core and the catalyst-containing aqueous phase were then greatly favored, resulting in an improvement in the catalytic performance. In the study presented here, RAME-β-CD played a similar role and accelerated the dynamics of exchange in the Pickering emulsion, i.e., between the organic phase and the catalyst-containing hydrogel. In fact, RAME-β-CD adsorbed at the aqueous/organic interface and inserted itself between the α-CD/PEG crystallites to prevent the saturation phenomenon of the oil droplet surface observed in our previous work.[19] Accordingly, while asymptotic kinetic profiles were obtained without RAME-β-CD, the conversion variation became linear in its presence (Figure 1). The reaction could be performed in one go and no longer required a step-by-step procedure.

Given the aforementioned results obtained with 1-hexadecane as the substrate, the study was extended to other relevant substrates. First, the length of the substrate alkyl chain was varied. Within only 1 h, 100% 1-dodecene and 88% 1-tetradecene were already converted (Table 1, runs 1 and 2, respectively). Logically, the conversion regularly decreased when the substrate hydrophobicity increased. However, even half of the very hydrophobic 1-octadecene was hydroformylated under the same experimental conditions (Table 1, run 4). Note that the regular decrease in conversion observed when an increase in the length of the alkyl chain indirectly confirmed the absence of catalytic species in the organic phase.[23] Similar catalytic activities would have been observed otherwise. Increasing the length of the substrate alkyl chain also affected the aldehyde selectivity because of a poor fit between the substrate and the RAME-β-CD cavity (Supporting Information). Interestingly, biobased substrates could also be hydro-

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Table 1. Rh-Catalyzed Hydroformylation of Higher Olefins Using Pickering Emulsions in the Presence of RAME-β-CD[a]

run	substrate	conversion (%)	selectivity[b] (%)	l/b[c]
1	1-dodecene	100	94	1.8
2	1-tetradecene	88	83	1.9
3	1-hexadecene	68	77	2.0
4	1-octadecene	46	65	1.7
5	methyl 10-undecenoate	100	98	1.7
6[d]	methyl oleate	25	55	–

[a]Catalytic conditions: substrate (1.63 mmol), $Rh(CO)_2(acac)$ (3 mg, 0.012 mmol), TPPTS (33 mg, 0.058 mmol), α-CD (600 mg, 0.61 mmol), PEG (0.36 mg, monomer/α-CD stoichiometric ratio), RAME-β-CD (228 mg, 0.18 mmol), 6 mL of H_2O, 80 °C, 50 bar of CO/H_2, t = 1 h. Conversions and selectivities were determined by ^1H and ^{13}C nuclear magnetic resonance measurements. [b]Aldehyde selectivity. [c]Linear/branched aldehyde ratio. [d]t = 7 h.

formylated, which is indicative of the efficacy of the studied catalytic system and the wide range of hydrophobic substrates amenable to this process. As such, methyl 10-undecenoate underwent a total conversion within 1 h with a very high aldehyde chemoselectivity of 98% (Table 1, run 5). As expected, the internal C=C bond of methyl oleate was more difficult to functionalize than terminal ones (Table 1, run 6).

In summary, we found a simple and elegant solution to a saturation problem encountered in biphasic Rh-catalyzed hydroformylation of very hydrophobic alkenes mediated by Pickering emulsions that consisted of an olefin-containing organic phase and a catalyst-containing hydrogel phase. While RAME-α-CD proved to be ineffective because of the threading onto PEG chains, RAME-β-CD and RAME-γ-CD appeared to be efficient fluidifiers at the aqueous/organic interface, preventing the covering of oil droplets by α-CD/PEG crystallites. When added in a controlled quantity, RAME-β-CD had the added advantage of retaining its interfacial properties and participated in the conversion of the substrate by supramolecular means. As such, we obtained the best conversion ever for higher olefins under aqueous biphasic conditions using a hydrogel/RAME-β-CD combination. Beneficial effects on both the catalytic activity and the chemoselectivity arose from the presence of RAME-β-CD. Although this study focused on higher levels of olefin hydroformylation, we believe that this work is not restricted to this reaction and could be extended to other catalytic systems that make use of Pickering emulsions in aqueous media.

■ ASSOCIATED CONTENT

Supporting Information

Preparation of the hydrogels, details of catalytic experiments, and results of optical microscopy and optical fluorescence microscopy. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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