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Rhodium-Catalyzed Aqueous Biphasic Olefin Hydroformylation Promoted by Amphiphilic Cyclodextrins

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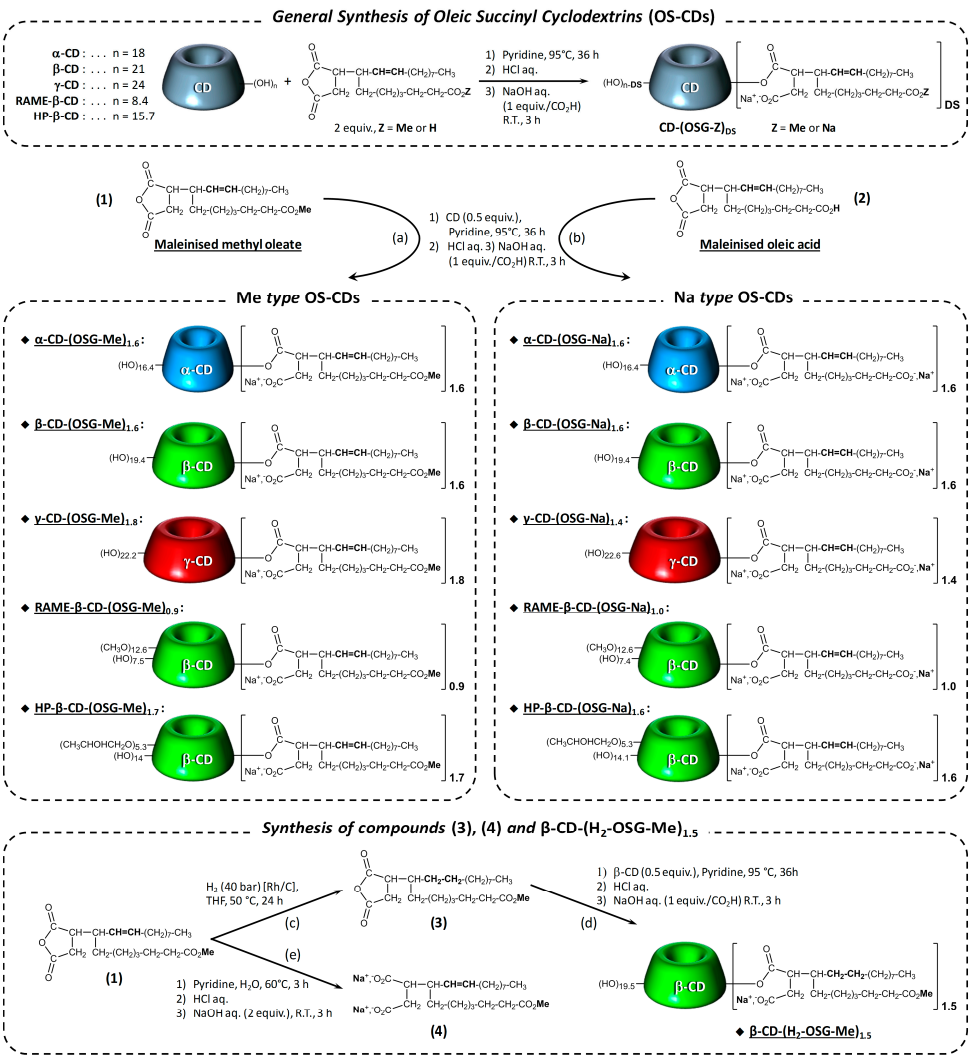
Abstract: Hydroformylation is an industrial process that allows for the production of aldehydes from alkenes using transition metals. The reaction can be carried out in water, and the catalyst may be recycled at the end of the reaction. The industrial application of rhodium-catalyzed aqueous hydroformylation has been demonstrated for smaller olefins (propene and butene). Unfortunately, larger olefins are weakly soluble in water, which results in very low catalytic activity. In an attempt to counteract this, we investigated the use of amphiphilic oleic succinyl-cyclodextrins (OS-CDs) synthesized from oleic acid derivatives and maleic anhydride. OS-CDs were found to increase the catalytic activity of rhodium during the hydroformylation of water-insoluble olefins, such as 1-decene and 1-hexadecene, by promoting mass transfer. Recyclability of the catalytic system was also evaluated in the presence of these cyclodextrins.

Keywords: cyclodextrin; hydroformylation; water

1. Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of six (α-CD), seven (β-CD), or eight (γ-CD) α-D-glucopyranose units [1,2]. They form conical cylinders with an outer hydrophilic surface and inner hydrophobic surface. The inner surface forms a cavity and allows for the formation of an inclusion complex when it binds a hydrophobic substrate. To vary their size and shape, native CDs can be modified by substituting their hydroxyl groups with various other functional groups. These are referred to as mono- or polysubstituted CDs. Due to their ability to form inclusion complexes with a wide range of compounds, native and modified CDs have applications in various fields. These include analytical chemistry, agriculture, pharmaceuticals, foods, toilet products, and catalysis [3]. In the field of aqueous biphasic organometallic catalysis, CDs have mainly been employed as platforms for the production of water-soluble ligands using transition metals [4–13]. They have also been used as mass-transfer agents in order to increase the solubility of hydrophobic substrates in water [14,15]. For example, the use of CDs in rhodium-catalyzed hydroformylation in an aqueous/organic two-phase system was previously described [16–20]. Increases in catalytic potential were especially high for hydrophobic substrates, which shows the beneficial effect of CDs on mass transfer at the aqueous–organic interface. However, while the effect of CDs was experimentally observed in 1995 [21], their exact role was only clearly established about 10 years later. Indeed, a molecular-dynamics study by Sieffert and Wipff described the interactions occurring between olefins, the catalytic system, and CDs at the

aqueous–organic interface [22,23]. The study was performed in accordance with surface-tension measurements [24]. It was shown that the mass-transfer properties of CDs (and consequently the catalytic activity) were linked to surface excess, i.e., the number of CDs adsorbed per m^2 of interface. Modified CDs (mainly randomly methylated β-CD (RAME-β-CD)) increased the hydroformylation rate of olefins possessing eight to twelve carbons. However, CD efficiency was drastically reduced for larger olefins (>12 carbons) [25]. Indeed, the shape and size of the CD cavity did not allow for the binding of larger olefins, leading to lower catalytic activity. The construction of more sophisticated CDs, such as CD dimers or polymers, is therefore required to accommodate larger olefins with multivalent interactions [15]. For this reason, we evaluated the behavior of amphiphilic oleic succinyl-CDs (OS-CDs) synthesized from oleic acid derivatives and maleic anhydride in an aqueous hydroformylation reaction (Scheme 1). These CDs are easily synthetized, highly soluble in water, have low surface tension, and have low critical-aggregation concentration (CAC). The formation of aggregates could be useful in the solubilization of larger olefins in water. Surfactants have been used to facilitate hydroformylation reactions between water-soluble catalysts and larger olefins [26–30]. In this report, we showed that various OS-CDs were efficient in promoting the hydroformylation of water-insoluble olefins such as 1-decene and 1-hexadecene. The recyclability of the catalytic system was also evaluated in the presence of these CDs.



Scheme 1. Structure and synthesis of oleic succinyl-cyclodextrins (OS-CDs).

2. Results and Discussion

OS-CDs synthesis was conducted in two steps as previously reported by our group [31,32]. The first step involved the alkenylation of maleic anhydride by methyl oleate and oleic acid, leading to the formation of maleinised methyl oleate or maleinised oleic acid, respectively. This step yielded a mixture of four regioisomers, with each regioisomer consisting of eight stereoisomers. The mixture is represented hereafter as a single compound (Scheme 1, compounds **1** and **2**). The second step involved the grafting of maleinised methyl oleate or maleinised oleic acid onto native CDs (α-, β-, or γ-CD), RAME-β-CD, and hydroxypropylated-β-CD (HP-β-CD). This was followed by the neutralization of carboxyl groups by sodium hydroxide. The obtained products were named CD-(OSG–Z)$_{DS}$, where CD corresponded to the nature of the cyclodextrin, OSG stood for Oleic Succinic Graft, Z indicated a methyl group or sodium atom (according to whether the reactant was methyl oleate or oleic acid), and DS was the degree of substitution.

Some physicochemical properties of OS-CDs are listed in Table 1.

Table 1. Physicochemical properties of OS-CDs.

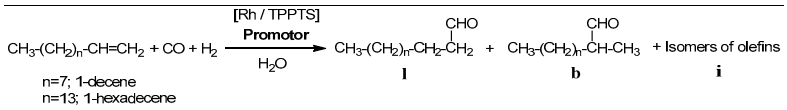
Entry	OS-CD	Solubility at 20 °C (mM)	CAC at 20 °C (μM)	Surface Tension [1] (mN/m)
1	α-CD-(OSG–Me)$_{1.6}$	52	15	33
2	α-CD-(OSG–Na)$_{1.6}$	121	206	36
3	β-CD-(OSG–Me)$_{1.6}$	28	11	39
4	β-CD-(OSG–Na)$_{1.6}$	158	94	38
5	γ-CD-(OSG–Me)$_{1.8}$	43	8	30
6	γ-CD-(OSG–Na)$_{1.4}$	176	190	39
8	RAME-β-CD-(OSG–Me)$_{0.9}$	247	24	32
9	RAME-β-CD-(OSG–Na)$_{1.0}$	288	18	35
10	HP-β-CD-(OSG–Me)$_{1.7}$	146	46	36
11	HP-β-CD-(OSG–Na)$_{1.6}$	178	54	52

[1] Surface tension value at the CAC concentration and at 20 °C.

The effect of these OS-CDs was studied in the rhodium-catalyzed hydroformylation of two olefins, 1-decene and 1-hexadecene. Catalysis experiments were conducted in an aqueous biphasic medium using Rh(acac)(CO)$_2$ as catalyst precursor and trisulfonated triphenylphosphine (TPPTS) as a ligand (Table 2). The reaction was carried out in an autoclave with a mechanical stirrer in order to elicit the maximum effect on mass transfer between the two layers. The pressure of syngas (CO:H$_2$ = 1:1) was 50 bar, the stirring rate was 1500 rpm, and the temperature was 80 °C. The first experiment was performed without a promotor, and therefore produced very little product in 6 h due to the very low water solubility of 1-decene and 1-hexadecene (Table 2, entries 1 and 9). The reaction was limited by mass transfer between the two layers. Among the modified CDs presented in Table 1, β-CD-(OSG–Me)$_{1.6}$ was chosen as the first promoter to be tested because it exhibited the best compromise between ease of synthesis and physicochemical properties. In addition, β-CD molecules are most appropriate for the functionalization of larger olefins [16]. Using an equivalent amount of β-CD-(OSG–Me)$_{1.6}$ and Rh, 100% of 1-decene and 65% of 1-hexadecene were converted in 4 and 6 h, respectively (Table 2, entries 2 and 10). Logically, the conversion rate significantly decreased with alkyl chain length. An identical catalytic experiment was also performed for 1-decene, and we found that conversion percentages at 0.5 and 2 h was 85% and 93%, respectively (Table 2, entries 4 and 3). The chemoselectivity of aldehydes was 61% and 52% (entries 2 and 10), and the main side products were isomeric olefins. With regard to regioselectivity, the linear/branched aldehyde ratios were 2.3 and 2.8 (entries 2 and 10). These results were compared to those obtained for β-CDs and RAME-β-CD (at equivalent levels of Rh), which are classically used CDs in aqueous organometallic catalysis (Table 2, entries 5, 6, 11, and 12). For β-CD and RAME-β-CD, conversion levels of 1-decene were 6% and 21% after 6 h (Table 2, entries 5 and 6), and 3% and 9% for 1-hexadecene (Table 2, entries 11 and 12), respectively. The superior conversion rates obtained using RAME-β-CD over β-CD were previously described [16]. The chemoselectivity and regioselectivity of RAME-β-CD were 90 and 2.1, respectively. In order to evaluate the role of each moiety, other control experiments were performed in the presence

of 1.6 equivalents (with respect to rhodium) of oleic moiety (**4**) or the combination of 1 + 1.6 equivalents of β-CD + (**4**). The term "1.6 equivalents" corresponds to the mean number of grafts on CDs, i.e., the DS of β-CD-(OSG–Me)$_{1.6}$. Conversion percentages in the presence of compound **4** and β-CD + compound **4** were increased to 20% and 45% for 1-decene, and to 10% and 23% for 1-hexadecene, respectively. However, these values were lower than those obtained for β-CD-(OSG–Me)$_{1.6}$ (Table 2, entries 7–8 and 13–14 compared to 2 and 10). In both cases, chemoselectivity was 53% and regioselectivity between 2.5 and 2.7. Regardless of the used olefin (1-decene or 1-hexadecene), conversion efficiency was higher in the presence of β-CD-(OSG–Me)$_{1.6}$ than β-CD, RAME-β-CD, compound **4**, or a combination β-CD + compound **4**. Nevertheless, chemoselectivity was lower in the presence of β-CD-(OSG–Me)$_{1.6}$. This was comparable to systems without CDs (Table 2, entries 1 and 9). The formation of aggregates with β-CD-(OSG–Me)$_{1.6}$ did not prevent an isomerization reaction. In contrast, RAME-β-CD formed inclusion complexes with the substrate, which prevented isomerization of the double bond [33].

Table 2. Rhodium-catalyzed hydroformylation of 1-decene and 1-hexadecene in presence of various promotors.[1]



Entry	Substrate	Promotor	Promotor (/Rh)	Time (h)	Conversion [2] (%)	Selectivity [3] (%)	l/b
1	$C_{10}H_{20}$	(-)	(-)	6	3	65	2.7
2	$C_{10}H_{20}$	β-CD-(OSG–Me)$_{1.6}$	1	4	100	61	2.3
3	$C_{10}H_{20}$	β-CD-(OSG–Me)$_{1.6}$	1	2	93	59	2.4
4	$C_{10}H_{20}$	β-CD-(OSG–Me)$_{1.6}$	1	0.5	85	58	2.6
5	$C_{10}H_{20}$	β-CD	1	6	6	80	2.6
6	$C_{10}H_{20}$	RAME-β-CD	1	6	21	90	2.1
7	$C_{10}H_{20}$	(**4**)	1.6	6	20	53	2.7
8	$C_{10}H_{20}$	β-CD + (**4**)	1 + 1.6	6	45	53	2.5
9	$C_{16}H_{32}$	(-)	(-)	6	1	62	2.7
10	$C_{16}H_{32}$	β-CD-(OSG–Me)$_{1.6}$	1	6	65	52	2.8
11	$C_{16}H_{32}$	β-CD	1	6	3	78	2.4
12	$C_{16}H_{32}$	RAME-β-CD	1	6	9	90	2.1
13	$C_{16}H_{32}$	(**4**)	1.6	6	10	53	2.7
14	$C_{16}H_{32}$	β-CD + (**4**)	1 + 1.6	6	23	53	2.5
15	$C_{16}H_{32}$	β-CD-(H_2–OSG–Me)$_{1.6}$	1	6	68	58	2.6
16	$C_{16}H_{32}$	β-CD-(OSG–Me)$_{1.6}$ [4]	1	6	63	50	2.8
17	$C_{16}H_{32}$	β-CD-(OSG–Me)$_{1.6}$ [5]	1	6	67	51	2.8

[1] Experiment conditions: Rh(acac)(CO)$_2$, 21 μmol (1 eq.); trisulfonated triphenylphosphine (TPPTS), 5 eq.; substrate, 500 eq.; water, 6 mL; temperature, 80 °C; pressure, 50 bar CO/H_2 (1:1); stirring rate, 1500 rpm. [2] Olefin conversion. [3] Aldehyde selectivity—(moles of aldehydes)/(moles of converted olefins) × 100. [4] Experiment conducted using aqueous phase of Experiment 10 (first recycling). [5] Experiment conducted using the aqueous phase of Experiment 16 (second recycling).

After proving that β-CD-(OSG–Me)$_{1.6}$ was able to facilitate the hydroformylation of 1-decene and 1-hexadecene, other control experiments were performed with 1-hexadecene. This substrate was more challenging to functionalize in an aqueous medium.

Given that the oleic moiety of β-CD-(OSG–Me)$_{1.6}$ contains a carbon–carbon double bond that can be hydroformylated, the structure of this OS-CD was analyzed after applying hydroformylation conditions without an added substrate (experiment conditions of Table 2, 1 equivalent of OS-CD per rhodium atom, no 1-decene or 1-hexadecene, and reaction time = 6 h). The aqueous phase was recovered and analyzed using matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS). By the end of this catalytic test, 16% of carbon–carbon double bonds in CD grafts were hydroformylated (as proven by the appearance of a new peak at 1581, i.e., β-CD-(OSG–Me)$_1$ + H + CHO + Na^+ on the MALDI-MS spectrum) (Figure 1). Among the mixture of CDs, only CDs bearing one graft (β-CD-(OSG–Me)$_1$) were hydroformylated. This result may have been due to greater accessibility to the C–C double bond in the organometallic complex. Thus, in CDs bearing two, three, or four grafts, hydroformylation of unsaturated grafts rarely took place. The same MALDI-MS analysis was

performed after Experiment 10 (Table 2), which led to the hydroformylation of 65% of 1-hexadecene in 6 h. In this experiment, only 6% of carbon–carbon double bonds in CD grafts were hydroformylated. Therefore, the presence of the olefin substrate decreased the hydroformylation of β-CD-(OSG–Me)$_{1.6}$.

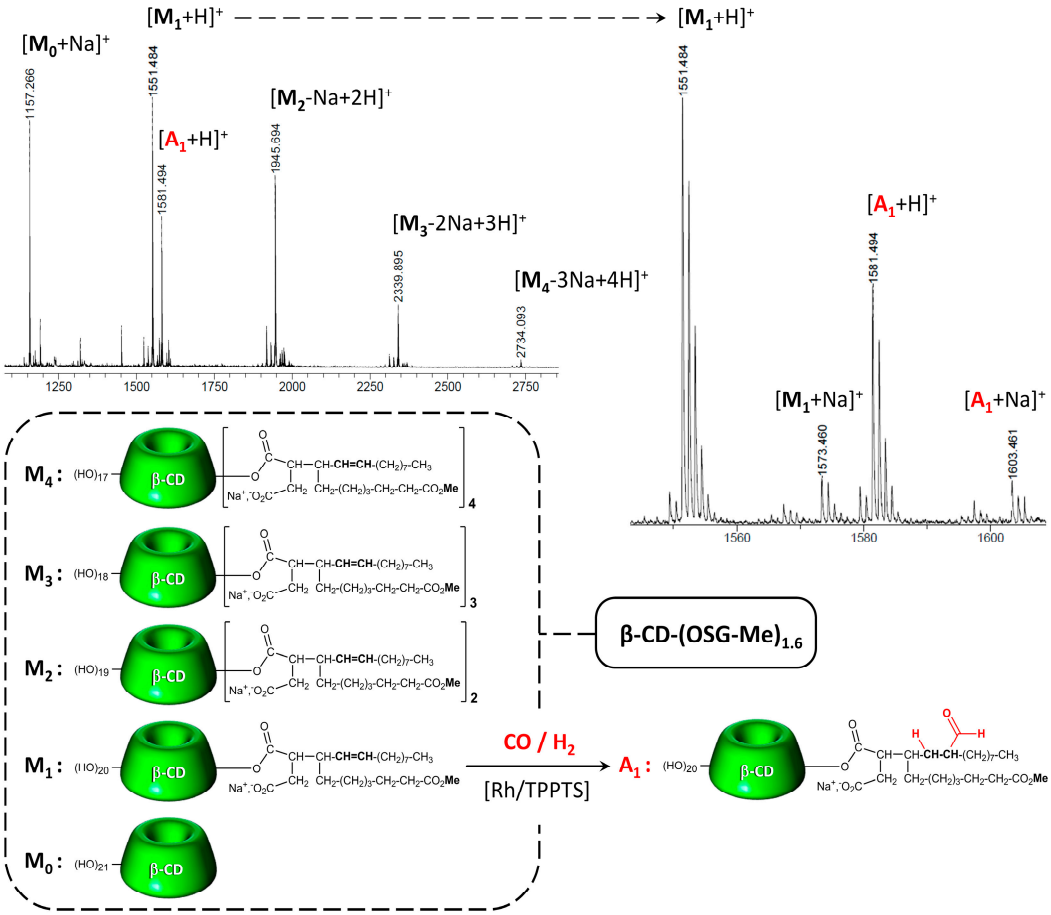


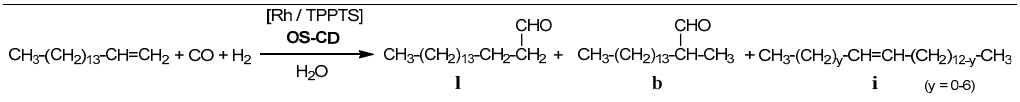
Figure 1. Matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) spectrum of β-CD-(OSG–Me)$_{1.6}$ after treatment with Rh(acac)(CO)$_2$/TPPTS catalytic system (1 and 5 molar equivalents with respect to CD). Experiment conditions: pressure, 50 bar of CO/H$_2$ (1:1); solution, 6 mL H$_2$O for every 21 μmol of cyclodextrin (CD); temperature, 80 °C; time, 6 h.

To confirm if the presence of a carbon–carbon double bond in the graft was detrimental to catalytic activity, a catalytic test was performed using β-CD-bearing hydrogenated arms (Scheme 1, β-CD-(H$_2$-OSG–Me)$_{1.6}$). To synthesize β-CD-(H$_2$–OSG–Me)$_{1.6}$, compound **1** was hydrogenated to give compound **3**, which was then grafted onto β-CD. In the presence of β-CD-(H$_2$–OSG–Me)$_{1.6}$, the conversion percentage, chemoselectivity, and regioselectivity of 1-hexadecene were 68%, 58%, and 2.6, respectively. This was compared to 65%, 52%, and 2.8 in the presence of β-CD-(OSG–Me)$_{1.6}$ (Table 2, entries 15 and 10). Therefore, saturation of the oleic arm did not significantly modify the course of hydroformylation.

The recyclability of the catalytic system and of β-CD-(OSG–Me)$_{1.6}$ was investigated by reusing the aqueous catalytic phase obtained after Experiment 10 in successive hydroformylation runs (Table 2, entries 10, 16, and 17). Although β-CD-(OSG–Me)$_{1.6}$ concentration was 380 times higher than its CAC, decantation occurred at the end of the reaction. This allowed for isolation of the aqueous layer of the reaction product. This layer was reloaded with 1-hexadecene and reused with the same experimental conditions. The aqueous layer was then used for two further runs and similar conversion percentages were obtained (Table 2, 65%, 63%, and 67% for entries 10, 16, and 17, respectively). Chemoselectivity and regioselectivity were unchanged.

Other OS-CDs presented in Table 1 were also evaluated for their capacity to act as mass-transfer promotors in the functionalization of 1-hexadecene (Table 3, entries 1–10). While the nature of CDs did not significantly influence chemoselectivity or regioselectivity (51–66 and 1.8–3.0, respectively), conversion percentages were deeply impacted—values varied from 9% to 94%. In fact, two trends emerged, one for Me-type OS-CDs possessing a methyl ester group (one sodium carboxylate group per graft, Table 3, entries 1–5), and another for Na-type OS-CDs (two sodium carboxylate groups per graft, Table 3, entries 6–10). Conversion percentages were largely higher for Me-type OS-CDs compared with Na-type OS-CDs. The tensioactive behavior of Me-type OS-CDs was more marked, given that disodium dicarboxylate derivatives have a higher CAC than that of their ester counterparts. In addition, for Na-type OS-CDs, the presence of two sodium carboxylate groups in the graft may have caused electronic repulsions between anionic groups of CDs and sulfonate groups of water-soluble phosphine. This phenomenon may have reduced catalytic activity by preventing the meeting of organometallic species and substrates. β-CD derivatives yielded a higher conversion percentage than that of α-CD derivatives. α-CD derivatives, in turn, yielded higher conversion percentages than γ-CD derivatives (Table 3, entries 1–3 and 6–8). For RAME-β-CD and HP-β-CD derivatives (Table 3, entries 4–5 and 9–10), variations in conversion percentages were significant for Me-type OS-CDs, while similar conversation percentages were obtained for Na-type OS-CDs. The best result was obtained using RAME-β-CD-$(OSG–Me)_{0.9}$ (Table 3, entry 4). This CD performed 10 times better than RAME-β-CD in terms of conversion percentage, and its regioselectivity was also slightly higher, but its chemoselectivity was significantly lower. In fact, the modes of action of these two CDs were different. RAME-β-CD formed inclusion complexes with the substrate, preventing isomerization of the double bond. In the case of RAME-β-CD-$(OSG–Me)_{0.9}$, the formation of aggregates facilitated binding of the substrate and catalyst but did not prevent the isomerization reaction.

Table 3. Rhodium-catalyzed hydroformylation of 1-hexadecene in presence of various CDs. [1]



Entry	Promotor	Eq/Rh	Conversion [2] (%)	Selectivity [3] (%)	l/b
1	α-CD-$(OSG–Me)_{1.6}$	1	57	61	2.5
2	β-CD-$(OSG–Me)_{1.6}$	1	65	52	2.8
3	γ-CD-$(OSG–Me)_{1.6}$	1	39	51	3.0
4	RAME-β-CD-$(OSG–Me)_{0.9}$	1	94	53	2.5
5	HP-β-CD-$(OSG–Me)_{1.7}$	1	66	55	2.5
6	α-CD-$(OSG–Na)_{1.6}$	1	15	62	2.9
7	β-CD-$(OSG–Na)_{1.6}$	1	22	58	1.8
8	γ-CD-$(OSG–Na)_{1.4}$	1	9	65	2.9
9	RAME-β-CD-$(OSG–Na)_{1.0}$	1	31	62	2.6
10	HP-β-CD-$(OSG–Na)_{1.6}$	1	32	66	2.6
11	RAME-β-CD	1	9	90	2.1
12	RAME-β-CD	10	18	90	2.2

[1] Experiment conditions: $Rh(acac)(CO)_2$, 21 μmol (1 eq.); TPPTS, 5 eq.; substrate, 500 eq.; water, 6 mL; temperature, 80 °C; pressure, 50 bar CO/H_2 (1:1); stirring rate, 1500 rpm; reaction time, 6 h. [2] 1-hexadecene conversion. [3] Aldehyde selectivity—(moles of aldehydes)/(moles of converted olefins) × 100.

3. Materials and Methods

3.1. General Remarks

Organic compounds, alkenes, and dicarbonylacetylacetonato rhodium (I) were purchased from Acros Organics, Sigma-Aldrich, and Strem Chemicals, respectively. They were purchased in their purest form and were used without further purification. The sodium salt tris (3-sodium sulfonatophenyl) phosphane (TPPTS–P(*m*-$C_6H_4SO_3Na)_3$) was synthesized using a method reported by B. Cornils et

al. [34]. The purity of TPPTS was carefully controlled. In particular, ^{1}H and ^{31}P NMR analysis indicated that TPPTS was only sulfonated in the metaposition, and less than 1% of its oxide was present. Ultrapure water was used in all experiments (Fresenius Kabi, Paris, France). The carbon monoxide/hydrogen mixture (1:1) was used directly from cylinders (>99.9% pure, Air Liquide, Loos, France). β-CD was a generous gift from Roquette Frères (Lestrem, France). Pharmaceutical-grade RAME-β-CD (Cavasol® W7 M) was purchased from Wacker Chemie GmbH and was unmodified. All high-pressure hydroformylation experiments were carried out in a 25 mL stainless-steel autoclave supplied by Parr. NMR spectra were recorded with a Bruker DRX300 spectrometer operating at 300 MHz for ^{1}H nuclei. $CDCl_3$ (99.50% isotopic purity) was purchased from Euriso-Top. Mass spectra were recorded on a MALDI-TOF/TOF Bruker Daltonics Ultraflex II in positive reflectron mode with 2,5-DHB as a matrix.

3.2. General Procedure for Rhodium-Catalyzed Hydroformylation Experiments

The preparation of the catalyst and alkene was performed under nitrogen using standard Schlenk techniques. All liquid reagents were degassed by bubbling nitrogen for 15 min or using 2 freeze–pump–thaw cycles before use. $Rh(acac)(CO)_2$ (21 μmol), TPPTS (105 μmol), and promotor (21 μmol) were dissolved in 6 mL of degassed water in an inert atmosphere. The resulting aqueous and organic phases contained alkenes (10.5 mmol), and were charged under an inert atmosphere into a 25 mL autoclave. Mechanical stirring using a multipaddle unit was then started (1500 rpm), and the reactor was heated up to 80 °C. As soon as this temperature was reached, the autoclave was pressurized with 50 bar of CO/H_2 (1:1). The addition of CO/H_2 was considered to be the beginning of the reaction. After the reaction, the autoclave was cooled, and the organic layer obtained after decantation was analyzed using ^{1}H NMR.

4. Conclusions

In this study, various OS-CDs were used to facilitate the aqueous biphasic rhodium-catalyzed hydroformylation of 1-decene and 1-hexadecene. In the case of 1-hexadecene, the best catalytic activity was obtained in the presence of RAME-β-CD-$(OSG–Me)_{0.9}$. Although the hydroformylation of oleic grafts in OS-CDs was observed, this did not have a detrimental effect on catalytic activity. The aqueous phase of the catalyst was recycled twice without loss of activity. The observed chemoselectivity was rather weak, but this could be explained by the formation of OS-CD aggregates that increased catalytic activity without preventing the isomerization reaction. In the case of amphiphilic CDs, the presence of a cavity did not prevent isomerization of the substrate's double bond. These new amphiphilic CDs could be used in biphasic aqueous organometallic processes that are less demanding in their selectivity, such as hydrogenation reactions or carbon–carbon coupling.

Author Contributions: H.B., E.M., and S.T. conceived and designed the experiments; A.C. and H.B. performed the experiments; H.B., E.M., and S.T. analyzed the data; F.D.-P. contributed reagents/materials and analysis; E.M. and S.T. wrote the paper. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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