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FULL PAPER

Pillar[5]arenes as supramolecular hosts in aqueous biphasic rhodium-catalyzed hydroformylation of long alkyl-chain alkenes

Missipssa Benatmane,[a] Kévin Cousin,[b] Nérimel Laggoune,[a] Stéphane Menuel,[b] Eric Monflier,[b] Patrice Woisel,[a] Frédéric Hapiot*[b] and Jonathan Potier*[a]

Abstract: Aqueous biphasic catalysis continues to attract strong interest, especially when very hydrophobic substrates are concerned. Indeed, their insolubility in water strongly limit their transformation by water-soluble organometallic catalysts. To improve contacts between the substrate-containing organic phase and the catalyst-containing phase, one of the best solutions consists in using interfacial additives capable of supramolecularly recognize the substrate and/or the catalyst. In the present study, modified pillar[5]arenes are considered as interfacial additives and their performance is assessed in Rh-catalyzed hydroformylation of long alkyl-chain alkenes (higher olefins). Pillar[5]arenes substituted by carboxylate functions and methyl groups **P5A-(Me)$_{10-x}$-(CH$_2$COOMe)$_x$** are compared to pillar[5]arenes substituted by polyethylene glycol (PEG) chains (**P5A-(Me)$_5$-(PEG)$_5$** and **P5A-(PEG)$_{10}$**). Utilization of **P5A-(Me)$_{10-x}$-(CH$_2$COOMe)$_x$** leads to high conversion and regioselectivity (linear/branched aldehyde ratio) in Rh-catalyzed hydroformylation of 1-decene and 1-hexadecene. Compared with other interfacial additives such as modified cyclodextrins, the studied pillar[5]arenes show lower chemo-selectivity, similar catalytic activity and higher regioselectivity.

Introduction

The interest of chemists in Supramolecular Catalysis has recently been illustrated by reference publications. [1,2,3] Nowadays, countless examples support the efficacy of catalytic systems whose cohesion is ensured by weak interactions. Among them, those based on hydrogen bonding[4] and coordination chemistry[5,6] are the most popular, but systems based on other types of attractive interactions (ion-dipole, [7] electrostatic [8] or ionic hydrogen bond[9]) also proved to be successful to design effective catalysts. Of interest, catalytic systems that make use of hydrophobic effects proved to be especially suitable for the conversion of hydrophobic substrates under aqueous biphasic conditions. For example, appropriate hydrophobic substrates may enter into the cavity of supramolecular receptors, and favor contacts with the organometallic catalyst at the aqueous/organic interface.[10,11] Once the catalytic process is complete, the product is release in the organic phase and another substrate molecule gets into the host cavity. The concept has been widely exploited with cyclodextrins[12,13] (CDs), calixarenes[14,15,16] or cucurbiturils[17] as supramolecular hosts in various organometallic reactions, such as hydroformylation, carbon-carbon coupling, and cleavage of carbonates or urethanes (Tsuji-Trost reaction), to name only a few. It occurred to us that pillararenes, that consist of hydroquinone moieties linked together by methylene groups (Figure 1),[18,19] could also be good candidates to molecularly recognize organic substrates. Contrary to CDs and similarly to calix[n]arenes, their external surface is not hydrophilic and chemical modifications are required to increase their solubility in water.[20,21] Hence, how well the pillararenes will be substituted will play a huge role in determining their ability to adsorb at the aqueous/organic interface and subsequently interact with the substrate.

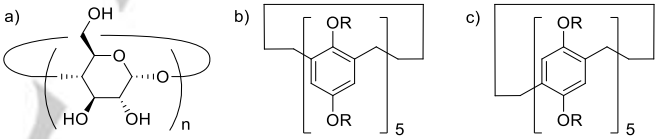

Figure 1. Structure of a) cyclodextrins, b) calixarenes, and c) pillararenes.

Astonishingly, there are less than a handful of reports on the use of pillararenes in organometallic catalysis. [22,23,24] To our knowledge, nothing has been reported so far on the use of pillararenes in aqueous biphasic catalysis. Herein is described the synthesis of water soluble pillar[5]arenes appropriately modified by both methyl and carboxyl groups or polyethylene glycol (PEG) chains. Their catalytic performance was assessed in Rh-catalyzed hydroformylation of higher olefins, a model reaction of industrial significance [25] that has been widely studied under biphasic conditions.[26] We show below that water soluble modified pillar[5]arenes are very efficient in this regards as they display excellent catalytic activity and better regioselectivity than CDs. We especially show that the number and the nature of the substituents should be accurately controlled and that the pillar[5]arene's cavity remains accessible to host higher olefins and favor their conversion into aldehydes at the aqueous/organic interface.

[a] M. Benatmane, Dr. N. Laggoune, Prof. P. Woisel, Dr. J. Potier
Univ. Lille, CNRS, INRA, ENSCL, UMR 8207 – UMET – Unité Matériaux et Transformations, F-59000 Lille, France. E-mail: jonathan.potier@univ-lille.fr
[b] K. Cousin, Dr. S. Menuel, Prof. E. Monflier, Prof. F. Hapiot
Univ. Artois, CNRS, Centrale Lille, ENSCL, Univ. Lille, UMR 8181, Unité de Catalyse et de Chimie du Solide (UCCS), F-62300 Lens, France.
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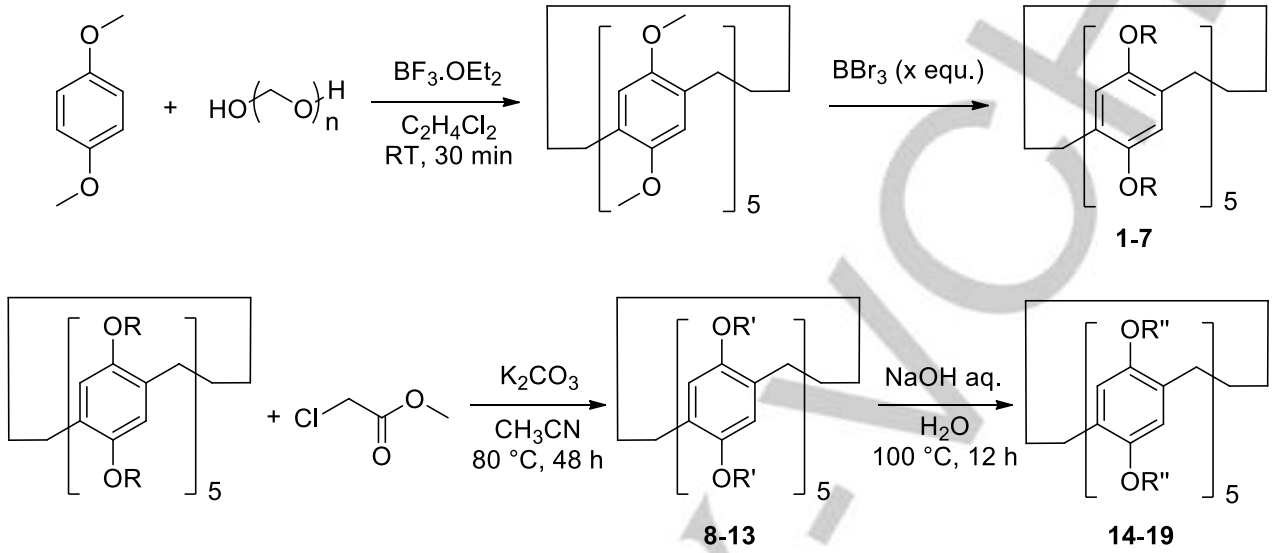
Results and Discussion

Synthesis of modified pillar[5]arenes

Pillar[5]arenes are chosen as potentially interesting molecular receptors because the size of their cavity can advantageously accommodate the linear alkyl chain of higher olefins.[21] However, pillar[5]arenes being insoluble in water, substitution of their macrocyclic structure by hydrophilic groups is required. Three different water soluble pillar[5]arenes were synthesized and compared in the present study.



Scheme 1. Synthesis of water soluble pillar[5]arenes **P5A-(Me)$_{10-x}$-(CH$_2$COONa)$_x$**. R = H or CH$_3$. R' = CH$_2$COOCH$_3$ or CH$_3$. R''= CH$_2$COONa or CH$_3$.

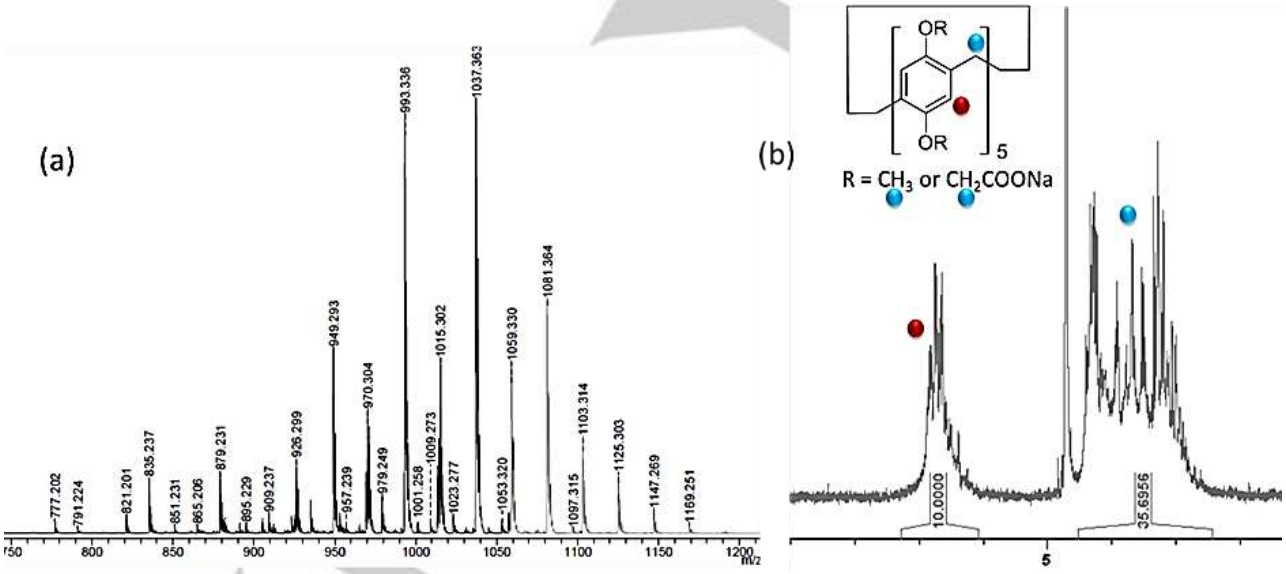
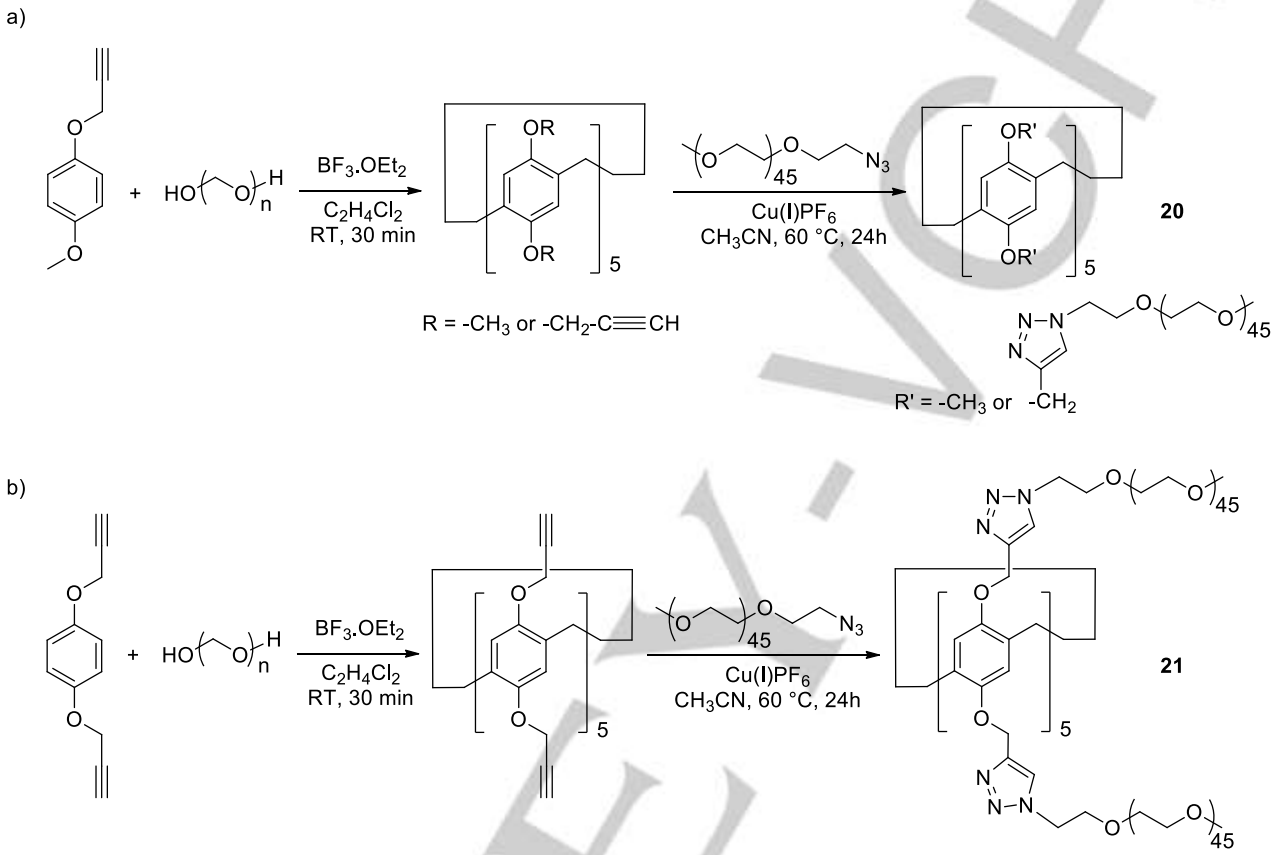


Figure 2. MALDI-TOF (a) and ^{1}H NMR spectra (D$_2$O, 25 °C) (b) of **P5A-(Me)$_{6.3}$-(CH$_2$COONa)$_{3.7}$** (compound **14**).

Synthesis of pillar[5]arenes substituted by methyl and sodium carboxylated methyl groups

Persubstituted pillar[5]arenes **P5A-(Me)$_{10}$** (compound **1**) are prepared according to a procedure from the literature (Scheme 1).[27] **1** is then subjected to partial demethylation with BBr$_3$ (x equiv. with respect to **1** with x≤10) in chloroform for 12 h at room temperature. Depending on the amount of BBr$_3$, six different pillar[5]arenes **P5A-(Me)$_{10-x}$-(H)$_x$** (compounds **2**-**7**) with various degrees of substitution in hydroxyl groups are obtained (3.7, 5.7, 7.8, 8.6, 9.2 and 10). Subsequent reaction with methyl chloroacetate in acetonitrile in the presence of potassium carbonate at 80 °C for 48 h affords pillar[5]arenes randomly substituted by both methyl and methyl carboxymethyl groups (**P5A-(Me)$_{10-x}$-(CH$_2$COOMe)$_x$** with x being the number of methyl carboxymethyl groups distributed on both sides of the macrocycle, compounds **8**-**13**). Further saponification of the ester functions under basic conditions (NaOH in water at 100 °C for 12 h) leads to the corresponding pillar[5]arenes featuring methyl and sodium carboxylmethyl groups randomly substituted onto the cyclic structure **P5A-(Me)$_{10-x}$-(CH$_2$COONa)$_x$** (compounds **14**-**19**).

The synthesized modified pillar[5]arenes are characterized by NMR spectroscopy. **1** shows three signals at 6.77, 3.77 and 3.65 ppm relative to aromatic protons (10H), methylene bridge (10H) and methoxy groups (30H), respectively. Reaction with BBr_3 offers partially demethylated compounds **2**-**7** as confirmed by the decrease in intensity of the signal relative to the methoxy groups and the presence of numerous peaks at 6.5 and 3.8 ppm relative to aromatic protons and randomly distributed methoxy groups, respectively (ESI). For the characterization of final water soluble pillar[5]arenes, MALDI-TOF and NMR study in water were coupled to determine the proportion of methoxy and carboxylate groups (Figure 2).



Scheme 2. Syntheses of water soluble pillar[5]arenes **20** and **21**.

Synthesis of water soluble P5A substituted by PEG chains

Pillar[5]arenes substituted by PEG chains featuring an average number of 45 ethyleneoxy units have also been considered as additives as PEG chains are well-known to help partitioning organic substrates within aqueous biphasic systems.[28,29] The synthesis of the studied PEG-substituted pillar[5]arenes is inspired by chemical modification of pillar[5]arenes described in the literature.[30,31] *Para*-propargyloxy anisole reacts with paraformaldehyde to afford pillar[5]arenes substituted by an equal number of methyl and propargyl groups (Scheme 2a). Subsequent copper-catalyzed alkyne-azide cycloaddition (CuAAC) with PEG chains end-functionalized by azide in acetonitrile at 60 °C for 24 h produces pillar[5]arenes **20** which is substituted by five methyl groups and five PEG-triazolylmethyl moieties. Similarly, *para*-dipropargyloxy benzene condenses with paraformaldehyde to yield pillar[5]arenes persubstitued by propargyl groups (Scheme 2b). Subsequent CuAAC gives the expected pillar[5]arene **21** persubstituted by ten PEG-triazolylmethyl moieties.[32]

Table 1. Synthesized compounds.

P5A-(R)$_{10-x}$-(R')$_x$	R	R'	x
1	Me	-	0
2	Me	H	3.7
3	Me	H	5.7
4	Me	H	7.8
5	Me	H	8.6
6	Me	H	9.2
7	-	H	10
8	Me	CH_2COOMe	3.7
9	Me	CH_2COOMe	5.7
10	Me	CH_2COOMe	7.8
11	Me	CH_2COOMe	8.6
12	Me	CH_2COOMe	9.2
13	-	CH_2COOMe	10
14	Me	CH_2COONa	3.7
15	Me	CH_2COONa	5.7
16	Me	CH_2COONa	7.8
17	Me	CH_2COONa	8.6
18	Me	CH_2COONa	9.2
19	-	CH_2COONa	10
20	Me	PEG	5
21	-	PEG	10

Surface tension

Surface tension measurements were carried out at the air/water interface to establish correlation between the catalytic results and the surface adsorption of modified pillar[5]arenes (Figure 3). In all cases, no clear CMC is identified. A slight decrease in the surface tension with the concentration is observed showing the capability of the modified pillar[5]arenes to adsorb at the interface layer without forming micelles. Concerning compounds 14-19, the decrease in the surface tension is more marked with the addition of carboxylate functions (Figure 3.a). Indeed, the surface tension evolves from 63 to 37 mN.m^{-1} at the catalytic concentration (red dotted line) for pillar[5]arenes featuring 3.7 and 8.6 carboxylate functions, respectively. Higher carboxylate substitution degree leads to lower surface tension. For example, adsorption of the very hydrophilic pillar[5]arenes (x = 10) at the interface is very weak as the surface tension is only reduced from 72 mN.m^{-1} for pure water to 59 mN.m^{-1} at 0.032 mol.L^{-1}. Surface tension assays of 20 and 21 were performed in lower concentration ranges (Figure 3.b) because their molar weight is 5 to 10 times higher than 14-19. The concentrations applied in catalysis were still considered in this study. The two pillar[5]arenes do not show any significant change in surface tension with the concentration, 21 being slightly more adsorbed than 20 in the catalytic concentration range (47 and 49 mN.m^{-1}, respectively).

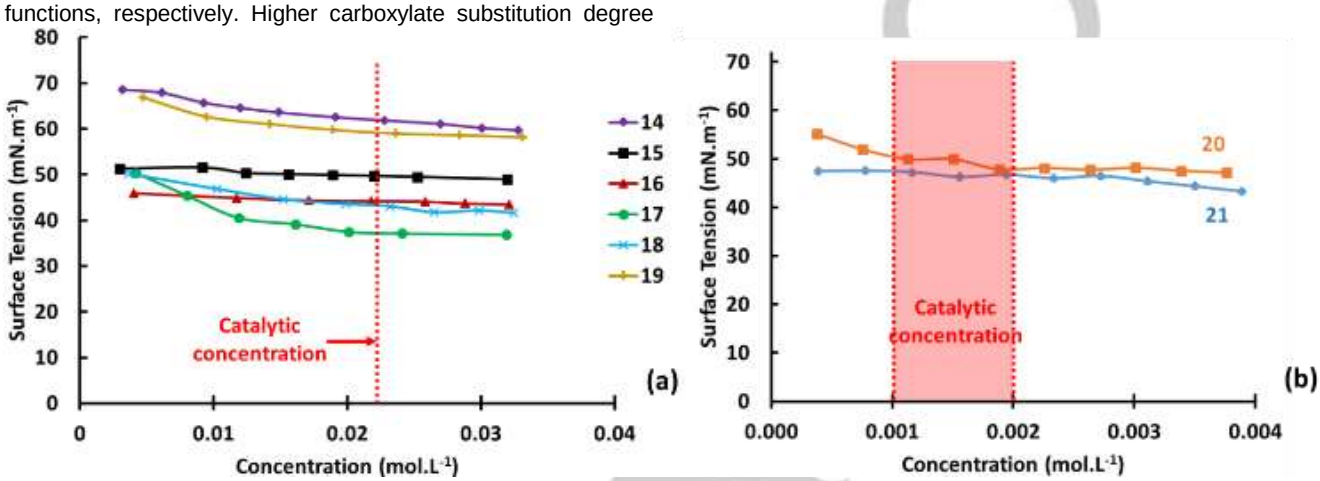


Figure 3. Surface tension measurements at 20 °C of a) compounds **14**-**19**, and b) compounds **20** and **21**.

Rh-catalyzed hydroformylation of higher olefins

Hydroformylation of 1-decene

While the Rh-catalyzed hydroformylation of lower alkenes has been well described in the literature,[33,34] hydroformylation of higher olefins remains a challenge (because of obvious insolubility issues), not only in terms of catalytic activity but also in terms of chemo- and regioselectivities. In the following paragraph are summarized results obtained in rhodium-catalyzed hydroformylation of 1-decene and 1-hexadecene with compounds **14-21** as interfacial additives. The results are also compared to the randomly methylated β-CD (**RAME-β-CD**), one of the best molecular receptors in aqueous biphasic catalysis so far.

In an initial exploratory study to assess the potential of modified pillar[5]arenes in aqueous biphasic catalysis, the performance of **14**-**19** is evaluated in Rh-catalyzed hydroformylation of 1-decene. The reaction is performed under 50 bar of CO/H_2 (1:1) at 80 °C in water, $Rh(CO)_2(acac)$ as a metal precursor (acac = acetylacetonate) and the sodium salt of the trisulfonated triphenylphosphine (TPPTS) as a ligand. Table 2 summarizes the catalytic results. The conversion in carbon-carbon double bonds is increased up to 85% with increasing the number of sodium carboxylate methyl groups (x) up to ca. 8, then goes down for higher carboxylate substitution degrees (Figure 4). Thus, as observed for randomly modified CDs,[35] the substrate conversion is highly related to the pillar[5]arene substitution degree. This may be partly related to surface tension properties. Indeed, the best results are obtained for pillar[5]arenes displaying good adsorption capability at the aqueous/organic interface (Figure 3). However, the surface tension at the aqueous/organic interface is not fully responsible for the observed results as the highest conversion is obtained with **16** whose adsorption is slightly lower than the most surface active pillar[5]arene (**17**). This results tend to prove that the availability of the cavity is as important as the adsorption capability of the macrocycle. Indeed, when the pillar[5]arene has too many carboxylate functions, the hydrophobic substrate has more difficulties to be recognized and its conversion decreases. This assertion is confirmed with **19**. While it shows the same adsorption ability than **14**, its effectiveness in catalysis is more than twice as low (Table 2, entries 1 and 6). Accordingly, while **19** adsorbs properly at the interface, it proves inappropriate to recognize hydrophilic substrates. Additionally, its strong anionic character probably repels the anionic TPPTS-based catalyst, resulting in lower probability of contacts between the small proportion of **19**-included substrate and the catalyst. A similar behavior was reported for cyclodextrins highly substituted by sulfobutyl groups.[36]

Interestingly, conversion and chemoselectivity follows an opposite trend. The aldehyde selectivity slightly decreases for x from 3.7 to 5.7, then increases with increasing x. The highest aldehyde selectivity is observed with **19**. This is consistent with the suggestion that contacts between the Rh-catalyst and the substrate included into the cavity of **19** are more constrained than with other **P5A** derivatives substituted both with methyl and carboxymethyl groups. In other words, **19** orient the included

substrate to react through a more selective pathway when approaching the Rh-catalyst. However, it should be noted that the "protecting" effect of the cavity towards side-reactions is lower than what is observed with **RAME-β-CD** (98% aldehyde selectivity under the same experimental conditions, entry 12), suggesting a not-so-deep inclusion of 1-decene into the pillar[5]arene's cavity.

Table 2. Aqueous biphasic hydroformylation of 1-decene using modified pillar[5]arenes and RAME-β-CD[a]

Entry	Additive	Eq./Rh	Conv. (%)	Sel. Ald (%)[b]	Sel. Iso (%)[c]	l/b[d]
1	**14**	10	74	71	29	2.6
2	**15**	10	76	65	35	2.4
3	**16**	10	85	66	34	2.4
4	**17**	10	76	67	33	2.5
5	**18**	10	51	69	31	2.5
6	**19**	10	33	78	22	4.1
7	**20**	0.5	96	81	19	2.4
8	**20**	0.75	100	92	8	2.4
9	**PEG45**	3.75	13	57	43	2.5
10	**21**	0.75	83	77	23	2.6
11	**PEG45**	7.50	16	59	41	2.5
12	**RAME-β-CD**	10	97	98	2	1.7
13	**-**	10	5	59	41	2.8

[a] Conditions: 1-decene (307 µL, 1.63 mmol), $Rh(CO)_2(acac)$ (3 mg, 0.012 mmol), TPPTS (33 mg, 0.058 mmol), water (6 mL), 3 h, 80 °C, 50 bar CO/H_2 (1/1), 1500 rpm. [b] aldehyde selectivity. [c] selectivity in isomerized products. [d] linear to branched aldehydes ratio.

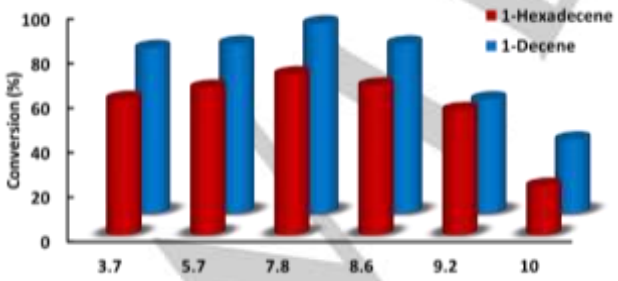


Figure 4. Variation of the conversion in hydroformylation of 1-decene and 1-hexadecene with the average number of carboxymethyl groups onto compounds **14**-**19**.

The regioselectivity, for its part, is higher than that measured with RAME-β-CD. The linear to branched (l/b) ratio is especially high using **19** as molecular receptor (l/b of 4.1 vs 1.8 for RAME-β-CD). The point one learns from this information is that the studied pillar[5]arenes do not interact with the TPPTS ligand, as confirmed by 2D T-ROESY analysis (Figure 5). Indeed, inclusion of TPPTS into the receptor's cavity usually results in the shift of the equilibriums between the catalytic species towards low phosphane-coordinated rhodium species responsible for the formation of branched aldehydes.[37] This is typically what is observed with RAME-β-CD. In the present case, as TPPTS does not interact with the cavity of compounds **14**-**19**, equilibriums are not altered and linear aldehydes are mainly formed.

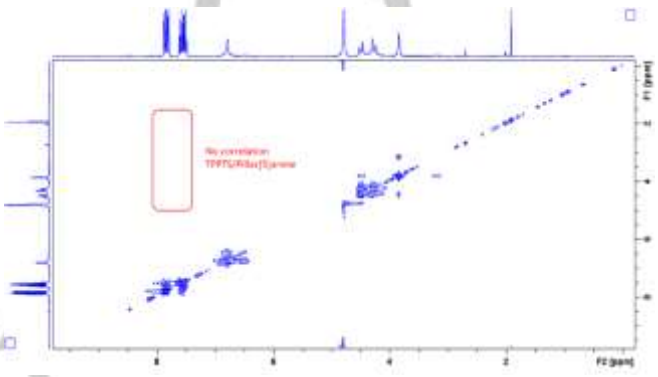


Figure 5. 2D T-ROESY NMR spectrum (D_20, 25 °C) of TPPTS/**15** mixture (1:1).

The l/b ratios measured with **14**-**19** are rather high and agree well with those obtained in former studies on homogeneous and biphasic hydroformylation.[25] This constitutes a major advantage over modified β-CDs. Basically, **14**-**19** better compare with modified α-CDs (smaller cavity than β-CDs).[38]

To get deeper insight into the performance of modified pillar[5]arenes under aqueous biphasic conditions, a series of experiments is performed using **20** or **21** as both molecular receptors and interfacial additives (Table 2). The recognition capability of the pillar[5]arene's cavity and the amphiphilic nature of the PEG chains are combined to speed up the hydroformylation of 1-decene into the corresponding linear and branched aldehydes. As expected, the use of PEG-derived pillar[5]arenes leads to higher conversions under the same experimental conditions because of the ability of PEG to better partition 1-decene between the two phases within the interfacial layer. 96% of 1-decene are converted within 3 h using 0. 5 equiv. of **20** with respect to Rh (Table 2, Entry 7), a conversion surpassing any of the conversions obtained with **14**-**19** (85% at best). Complete conversion of the carbon-carbon double bonds is achieved using 0.75 equiv. of **20** with respect to Rh (Table 2, entry 8). To our delight, the aldehyde selectivity is also increased to 92% while the l/b ratio remained constant at 2.4. Conversely, persubstitution of the pillar[5]arene macrocycle by PEG-triazolylmethyl moieties has a detrimental effect on both the conversion and the aldehyde selectivity (Table 2, entry 10), probably because the recognition of the substrate within the cavity is hampered by the bulky PEG-triazolylmethyl substituents. Comparison with PEG45 (blank runs realized with PEG45 mol% equivalent to PEG-based pillararenes) highlights the pillararene/PEG combination in hydroformylation of 1-decene as conversions are multiplied by a factor up to 8 (Table

2, compare entries 8 et 9 and entries 10 et 11). The result also favorably compares with **RAME-β-CD** (97% conv., Table 2, entry 12). However, as observed above with compounds **14**-**19**, the chemoselectivity measured with **20** is lower than with **RAME-β-CD** (81% vs 98% aldehyde selectivity), indicative of the lowest ability of **20** to protect the substrate against isomerization. The regioselectivity (l/b of 2.4), for its part, is in the range of what is classically observed under aqueous biphasic conditions without receptor/ligand interaction (l/b~2.5).

Hydroformylation of 1-hexadecene

The use of modified pillararenes and cyclodextrins is then extended to Rh-catalyzed hydroformylation of 1-hexadecene, a much more hydrophobic olefin (Table 3).

Table 3. Aqueous biphasic Rh-catalyzed hydroformylation of 1-hexadecene with modified pillar[5]arenes and cyclodextrins.[a]

Entry	Additive	Eq./Rh	Conv (%)	Sel. Ald (%)[b]	Sel. Iso. (%)[c]	l/b[d]
1	**14**	10	61	56	44	2.3
2	**15**	10	66	56	44	2.5
3	**16**	10	72	55	45	2.4
4	**17**	10	67	56	44	2.4
5	**18**	10	56	55	45	2.5
6	**19**	10	22	55	45	2.5
7	**20**	0.75	58	53	47	2.6
8	**PEG45**	3.75	12	45	55	2.5
9	**21**	0.75	50	49	51	2.6
10	**PEG45**	7.5	15	47	53	2.5
11	**RAME-β-CD**	10	56	65	35	1.5
12	**-**	10	4	30	70	2.5

[a] Conditions: 1-hexadecene (468 µL, 1.63 mmol), $Rh(CO)_2(acac)$ (3 mg, 0.012 mmol), TPPTS (33 mg, 0.058 mmol), water (6 mL), 3 h, 80 °C, 50 bar CO/H_2 (1/1), 1500 rpm. [b] aldehyde selectivity. [c] selectivity in isomerized alkenes. [d] linear to branched aldehydes ratio.

Here again, the number of carboxylate and methyl groups determines the ability of compounds **14**-**19** to convert the substrate into aldehyde. As previously observed for 1-decene (Figure 4), the maximum in conversion of 1-hexadecene is observed for **16** (Table 3, entry 3). The latter displays a fine balance of carboxylate and methyl groups to ensure both adsorption at the aqueous/organic interface and molecular recognition of 1-hexadecene. The chemo- and regioselectivities remain constant irrespective of the substitution degree, indicative of the absence of interaction between host and ligands throughout the catalytic process. **20** proves slightly more effective to convert 1-hexadecene than **21**. Indeed, **20** is more prone to include the substrate because it is less encumbered than **21** and permits highest accessibility to the cavity (entries 6 and 7). The advantages of **P5A** derivatives over PEG45 (Table 3, entries 8 and 10) and **RAME-β-CD** (Table 3, entry 11) are also significant for 1-hexadecene both in terms of conversion and selectivity. As described above, the linear to branched ratio is especially high compared to **RAME-β-CD** because of the absence of interaction between **P5A** derivatives and TPPTS.

Reusability of the catalytic system

To assess the viability of the studied system over several catalytic runs, we performed additional experiments as follows. Rh-catalyzed hydroformylation of 1-decene is carried out using compounds **14**-**19** as interfacial additive and molecular receptor under the catalytic conditions described in Table 2. Once the product resulting from Run 1 has been recovered, the catalyst-containing solution is reused over four additional consecutives runs. Satisfyingly, both conversions and selectivities remain constant, indicative of the robustness of the studied catalytic system under aqueous biphasic conditions (Figure 6).

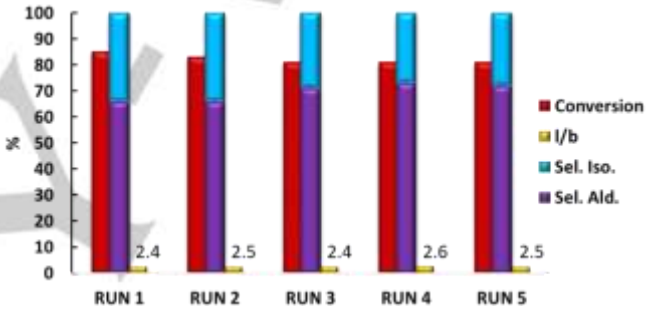


Figure 6. Reusability of the aqueous 16-containing solution in Rh-catalyzed hydroformylation of 1-decene. Conditions: see Table 2.

Conclusions

In this study, we developed the synthesis of pillar[5]arenes substituted by both methyl and carboxylate groups or PEG chains. The modified pillar[5]arenes adsorb differently at the air/aqueous interface depending on the substitution degree. Their ability to favor the conversion of hydrophobic substrate under biphasic conditions was assessed in Rh-catalyzed hydroformylation of terminal alkenes. The main advantage of modified pillar[5]arenes over cyclodextrins lies in their ability to reduce the surface tension, recognize the substrate, and above all prevent interaction with ligands stabilizing the organometallic species in water. While a decrease of the linear to branched aldehyde ratio is usually observed with cyclodextrins as interfacial additive, the proportion of linear and branched aldehydes is high (l/b up to 4.1) using modified pillar[5]arenes substituted by both methyl and carboxylate groups or PEG chains in comparison with reactions carried out under homogeneous conditions. However, the chemoselectivity is modest (aldehyde selectivity up to 92%), possibly because of the lower ability of modified pillararenes to protect the substrate against isomerization. Additionally, the pillar[5]arene-based catalytic system is robust as it is reusable over five consecutives catalytic runs. Experiments are currently

on-going to widen their utilization to other organometallic catalytic reactions.

Experimental Details

Synthesis of P5A-(Me)$_{10}$ (1)
In a 250 mL round flask were dissolved 1,4-dimethoxybenzene (5.52g, 40 mmol) and paraformaldehyde (3.72g, 120 mmol) in 1,2-dichloroethane (40 mL). Then, boron trifluoride diethyl etherate [$BF_3.O(C_2H_5)_2$] (6.25 mL, 40 mmol) was added to the solution and the mixture was stirred at room temperature for 30 min. Addition of methanol (200 mL) resulted in the precipitation of solids. After filtration, the latter were purified by silica gel column chromatography using a CH_2Cl_2/petroleum spirit mixture (60/40). **1** was obtained in 80% yield (4.86 g) as a pale yellow powder.

Synthesis of P5A-(Me)$_{10-x}$-(H)$_x$ (2-7)
In a 250 mL round flask was dissolved **P5A-(Me)$_{10}$ (**3 g, 3.95 mmol) in 200 mL of anhydrous $CHCl_3$. The solution was degassed by bubbling with nitrogen. Then, BBr_3 was added in well-defined quantity to obtain the desired degree of substitution in hydroxyl groups (see Table S1). The solution was then stirred at room temperature for 15 h under nitrogen. The reaction was stopped by addition of pure water (200 mL). After decantation, the organic layer was washed with 0.5 M aqueous hydrochloric acid, dried with Na_2SO_4 and evaporated to yield compounds **2**-**7** as pale yellow powders (Yields: 85-90%).

P5A-(Me)$_{10-x}$-(CH_2COOMe)$_x$ (8-13)
In a 250 mL two-necked round flask were introduced compounds **2-7** (2.50 g, 1 eq.), K_2CO_3 (20 eq.), and anhydrous acetonitrile (180 mL). After degassing, methyl chloroacetate (10 eq.) was injected and the mixture was stirred under reflux for 48 h. After filtration of excess K_2CO_3, the solvent was evaporated and the product was recrystallized in chloroform/diethyl ether. **8-13** were obtained in 55-60% yield as pale yellow powders.

P5A-(Me)$_{10-x}$-(CH_2COONa)$_x$ (14-19)
In a 100 mL round flask was prepared a saturated solution of NaOH (12 mL) in ethanol (40 mL). Compounds **8**-**13** (1.5 g) was then introduced and the mixture was heated to reflux and stirred for 15 h. The product was precipitated with aqueous hydrochloric acid (50 mL) and filtered to obtain **P5A-(Me)$_{10-x}$-(CH_2COOH)$_x$**. The expected methyl carboxymethylated derivatives **14**-**19** were obtained by stirring **P5A-(Me)$_{10-x}$-(CH_2COOH)$_x$** in aqueous NaOH (1 eq.) at room temperature for 5 h. After lyophilisation, the crude product was washed with ethanol/water (6:4) mixture and pure acetone. Yellow pale powders were obtained in all cases (Yields: 70-75%).

P5A-(Me)$_5$-(PEG)$_5$ and **P5A-(PEG)$_{10}$ (20** and **21)**
In a two-necked round flask were dissolved **P5A-(Me)$_5$-(propargyl)$_5$ (**13.4 mg, 0.016 mol, 1 eq.) and 182 mg of PEG_{45}-N_3 (0.09 mol, 5.5 eq., prepared following a literature procedure[39]) in anhydrous acetonitrile (5 mL) under nitrogen. Then, $Cu(MeCN)_4PF_6$ (35 mg, 0.09 mol, 5.5 eq.) was added and the mixture was stirred under nitrogen at 60 °C for 48 h. The solvent was evaporated under vacuum and the resulting compound **20** was purified by dialysis in water. The same procedure was applied for the synthesis of **21** using 11 eq. of PEG_{2000}-N_3 (364 mg) and $CuPF_6$ (70 mg). The products were obtained as white powders in *ca.* 70% yield.

Catalytic experiment
In a typical experiment, $Rh(CO)_2(acac)$ (3 mg, 0.012 mmol) was degassed three times by vacuum–N_2 cycles and dissolved in a degassed solution of P5A derivative (0.058 mmol) in water (6 mL). The resulting solution was stirred at 1500 rpm at room temperature until all of the rhodium complexes were dissolved (2 h). The substrate (1.63 mmol) was poured into an autoclave and N_2-purged. The catalytic solution was then cannulated under nitrogen into the autoclave. Once the desired temperature was reached, the autoclave was pressurized under CO/H_2 (1:1) pressure (typically 50 bar) and the solution was vigorously stirred (1500 rpm). When the reaction was complete, the apparatus was cooled down to room temperature and depressurized. The products were analyzed by ^1H and ^{13}C NMR experiments. All runs were performed at least twice in order to ensure reproducibility.

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Keywords: Pillararenes • aqueous biphasic catalysis • hydroformylation • molecular recognition • inclusion complexes

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Entry for the Table of Contents

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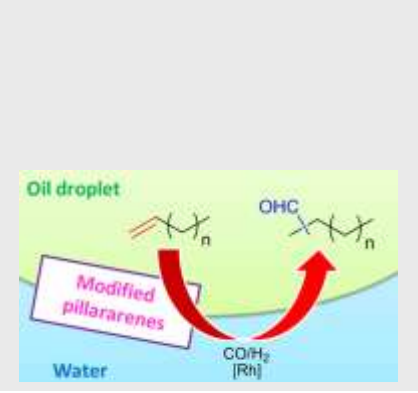
Modified pillar[5]arenes are interesting interfacial additives in Rh-catalyzed hydroformylation of long alkyl-chain alkenes



Missipssa Benatmane, Kévin Cousin, Nérimel Laggoune, Stéphane Menuel, Eric Monflier, Patrice Woisel, Frédéric Hapiot and Jonathan Potier**

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[1] M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1660-1733.
[2] M. Raynal, P. Ballester, A. Vidal-Ferran, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2014**, *43*, 1734-1787.
[3] S. S. Nurttila, P. R. Linnebank, T. Krachko, J. N. H. Reek, *ACS Catal.* **2018**, *8*, 3469-3488.
[4] L. Diab, T. Šmejkal, J. Geier, B. Breit, *Angew. Chem. Int. Ed.* **2009**, *48*, 8022-8026.
[5] C. García-Simón, R. Gramage-Doria, S. Raoufmoghaddam, T. Parella, M. Costas, X. Ribas, J. N. H. Reek, *J. Am. Chem. Soc.* **2015**, *137*, 2680-2687.
[6] N. C. Thacker, S. A. Motekia, J. M. Takacs, *ACS Catal.* **2012**, *2*, 2743-2752.
[7] M. Vaquero, L. Rovira, A. Vidal-Ferran, *Chem. Commun.* **2016**, *52*, 11038-11051.
[8] K. Ohmatsu, Y. Hara and T. Ooi, *Chem. Sci.* **2014**, *5*, 3645-3650.
[9] X.-X. Lu, H.-S. Tang, C.-C. Ko, J. K.-Y. Wong, N. Zhu, V. W.-W. Yam, *Chem. Commun.* **2005**, 1572‑1574.
[10] F. Hapiot, E. Monflier, *Catalysts* **2017**, *7*, 173.
[11] F. Hapiot, S. Menuel, M. Ferreira, B. Léger, H. Bricout, S. Tilloy, E. Monflier, *ACS Sustain. Chem. Eng.* **2017**, *5*, 3598-3606.
[12] F. Hapiot, S. Menuel, H. Bricout, S. Tilloy, E. Monflier, *Appl. Organomet. Chem.* **2015**, *29*, 580-587.
[13] F. Hapiot, H. Bricout, S. Menuel, S. Tilloy, E. Monflier, *Catal. Sci. Technol.* **2014**, *4*, 1899-1908.
[14] F. Hapiot, J. Lyskawa, H. Bricout, S. Tilloy, E. Monflier, *Adv. Synth. Catal.* **2004**, *346*, 83-89.
[15] L. Monnereau, D. Sémeril, D. Matt, L. Toupet, *Adv. Synth. Catal.* **2009**, *351*, 1629-1636.
[16] J. Tomasek, M. Seßler, H. Gröger, J. Schatz, *Molecules* **2015**, *20*, 19130-19141.
[17] Y.-H. Wang, H. Cong, F.-F. Zhao, S.-F. Xue, Z. Tao, Q.-J. Zhu, G. Wei, *Catal. Commun.* **2011**, *12*, 1127-1130.
[18] T. Ogoshi, S. Kanai, S. Fujinami, T. Yamagishi, Y. Nakamoto, *J. Am. Chem. Soc.* **2008**, *130*, 5022-5023.

[19] M. Xue, Y. Yang, X. Chi, Z. Zhang, F. Huang, *Acc. Chem. Res.* **2012**, *45*, 1294-1308.
[20] H. Zhang, Y. Zhao, *Chem. Eur. J.* **2013**, *19*, 16862-16879.
[21] T. Ogoshi, T.-a. Yamagishi, Y. Nakamoto, *Chem. Rev.* **2016**, *116*, 7937-8002.
[22] X.-D. Xiao, Y.-L. Bai, J.-Q. Liu, J.-W. Wang, *Tetrahedron Lett.* **2016**, *57*, 3385-3388.
[23] Y. Liu, B. Lou, L. Shangguan, J. Cai, H. Zhu, B. Shi, *Macromolecules* **2018**, *51*, 1351-1356.
[24] X.-D. Xiao, J.-Q. Liu, Y.-L. Bai, R.-H. Wang, J.-W. Wang, *J. Inclusion Phenom. Macrocycl. Chem.* **2017**, *87*, 29-36.
[25] A. Börner, R. Franke, Hydroformylation: Fundamentals, Processes, and Applications in Organic Synthesis, Wiley-VCH, **2016**.
[26] See for example: a) J. M. Dreimann, H. Warmeling, J. N. Weimann, K. Künnemann, A. Behr, A. J. Vorholt, *AIChE J.* **2016**, *62*, 4377-4383; b) M. Zagajewski, J. Dreimann, M. Thönes, A. Behr, *Chem. Eng. Process.* **2016**, *99*, 115-123; c) B. Bibouche, D. Peral, D. Stehl, V. Söderholm, R. Schomäcker, R. von Klitzing, D. Vogt, *RSC Adv.* **2018**, *8*, 23332-23338; d) M. Illner, D. Müller, E. Esche, T. Pogrzeba, M. Schmidt, R. Schomäcker, G. Wozny, J.-U. Repke, *Ind. Eng. Chem. Res.* **2016**, *55*, 8616-8626; e) H. Warmeling, D. Janz, M. Peters, A. J. Vorholt, *Chem. Eng. J.* **2017**, 330, 585-595; f) S. Chen, E. Manoury, F. Gayet, R. Poli, *Polymers* **2016**, 8, 26; g) A. Riisager, B. E. Hanson, *J. Mol. Catal. A-Chem.* **2002**, *189*, 195-202; h) M. Li, H. Y. Fu, M. Yang, H. J. Zheng, Y. E. He, H. Chen, X. J. Li, *J. Mol. Catal. A-Chem.* **2005**, *235*, 130-136; P. J. Baricelli, M. Rodriguez, L. G. Melean, M. M. Alonso, M. Borusiak, M. Rosales, B. Gonzalez, K. C. B. de Oliveira, E. V. Gusevskaya, E. N. dos Santos, *Appl. Catal. A: Gen.* **2015**, *490*, 163-169.
[27] T. Ogoshi, T. Aoki, K. Kitajima, S. Fujinami, T.-a. Yamagishi, Y. Nakamoto, *J. Org. Chem.* **2011**, *76*, 328-331.
[28] H. D. Willauer, J. G. Huddleston, R. D. Rogers, *Ind. Eng. Chem. Res.* **2002**, *41*, 1892-1904.
[29] J. Chen, S. K. Spear, J. G. Huddleston, J. D. Holbrey, R. P. Swatloski, R. D. Rogers, *Ind. Eng. Chem. Res.*, **2004**, *43*, 5358-5364.
[30] H. Zhang, X. Ma, K. T. Nguyen, Y. Zhao, *ACS Nano* **2013**, *7*, 7853-7863.
[31] E.-R. Janeček, U. Rauwald, J. Del Barrio, M. Cziferszky, O. A. Scherman, *Macromol. Rapid Commun.* **2013**, *34*, 1547-1553.
[32] H. Deng, X. Shu, X. Hu, J. Li, X. Jia, C. Li, *Tetrahedron Lett.* **2012**, *53*, 4609-4612.
[33] E. G. Kuntz, *Chemtech* **1987**, *17*, 570-575.
[34] L. Obrecht, P. C. J. Kamer, W. Laan, *Catal. Sci. Technol.* **2013**, *3*, 541-551.
[35] F.-X. Legrand, M. Sauthier, C. Flahaut, J. Hachani, C. Elfakir, S. Fourmentin, S. Tilloy, E. Monflier, *J. Mol. Catal. A: Chem.* **2009**, *303*, 72-77.
[36] D. Kirschner, T. Green, F. Hapiot, S. Tilloy, L. Leclercq, H. Bricout, E. Monflier, *Adv. Synth. Catal.* **2006**, *348*, 379-386.
[37] L. Caron, S. Tilloy, E. Monflier, J.-M. Wieruszeski, Guy Lippens, D. Landy, S. Fourmentin, G. Surpateanu, *J. Incl. Phenom. Macrocycl. Chem.* **2000**, *38*, 361-379.
[38] L. Leclercq, M. Sauthier, Y. Castanet, A. Mortreux, H. Bricout, E. Monflier, *Adv. Synth. Catal.* **2005**, *347*, 55-59.
[39] E.-R. Janeček, U. Rauwald, J. del Barrio, M. Cziferszky, O. A. Scherman, *Macromol. Rapid Commun.* **2013**, *34*, 1547-1553.