Cyclodextrins or Calixarenes: What is the Best Mass Transfer Promoter for Suzuki Cross-Coupling Reactions in Water?

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Abstract: Cyclodextrins or calixarenes possessing extended hydrophobic host cavities and surface-active properties were found to be very efficient as mass transfer promoters for the palladium-mediated Suzuki cross-coupling reaction of 1-iodo-4-phenyl-benzene and phenylboronic acid in aqueous medium.

The cross-coupling rates were up to 92 times higher than those obtained without addition of any compound.

Keywords: calixarenes; cross-coupling; cyclodextrins; palladium; phase transfer catalysis

Introduction

The Suzuki–Miyaura reaction, the palladium-catalysed cross-coupling of organic halides with organoboron compounds, is one of the most important and powerful tools for the formation of carbon-carbon bonds.[1] Indeed, the availability of the reagents, the exceptional tolerance of functional groups and the mild reaction conditions contribute to the versatility of this reaction. From the standpoint of the separation and recycling of catalysts used in the Suzuki-type reactions, numerous approaches such as immobilisation of the catalyst on organic polymers or inorganic support materials[2] and the use of two-phase systems[3,4] have been reported in the literature. Among the different approaches, the aqueous-organic two-phase system where the catalyst is immobilised in the aqueous phase by a water-soluble phosphane appears the most attractive.[4] Actually, the phosphane allows one to stabilise the catalytic intermediates and water is a safe, non-toxic, environmentally friendly and cheap solvent compared to other immobilising phases. The main drawback of Suzuki cross-coupling reactions catalysed by water-soluble organometallic complexes is the phase-transfer limitation observed with water-insoluble substrates leading to very low reaction rates. In order to circumvent this crucial problem, the use of surfactants[5] or inverse phase-transfer catalysts such as cyclodextrins or calixarenes[6] has been described. The use of cyclodextrins or calixarenes is particularly interesting because these compounds allow one to use standard hydrosoluble ligands while avoiding the formation of an emulsion. Unfortunately, the results reported in the literature with these molecular receptors are rather disappointing. Indeed, native β-cyclodextrin, sulphonated calixarenes and amino-substituted calixarenes can only enhance the reaction rates by a factor of 2, 3 and 10, respectively.[6]

Our work in field of aqueous organometallic catalysis assisted by chemically modified cyclodextrins led us to think that the efficiency of these carrier molecules in the Suzuki cross-coupling reaction could be greatly increased by suitably modifying these compounds.[7] We report here the palladium-catalysed cross coupling of 1-iodo-4-phenylbenzene with phenylboronic acid in an aqueous solution of sodium carbonate in the presence of cyclodextrins (CD) or calixarenes possessing extended hydrophobic host cavities and surface-active properties (Scheme 1).
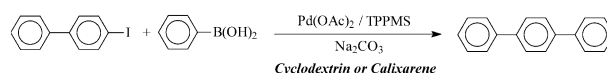
Scheme 1.

Results and Discussion

The sodium salt of the *meta*-substituted monosulfonated triphenylphosphane (TPPMS) ligand was preferred to the more classical sodium salt of the *meta*-substituted trisulfonated triphenylfosphane (TPPTS) ligand. Indeed, preliminary tests performed with iodobenzene as substrate clearly indicate that the catalyst prepared from TPPMS is more active than that prepared from TPPTS in water in the presence of an inorganic base. Similar behaviour was also observed by Miyaura and was attributed to the lower electron-donating ability of the TPPTS ligand.[4a, e] Although 1-bromo-4-phenylbenzene and 1-iodo-4-phenylbenzene are both very poorly soluble in water, 1-iodo-4-phenylbenzene was chosen as a model substrate to evaluate the efficiency of inverse
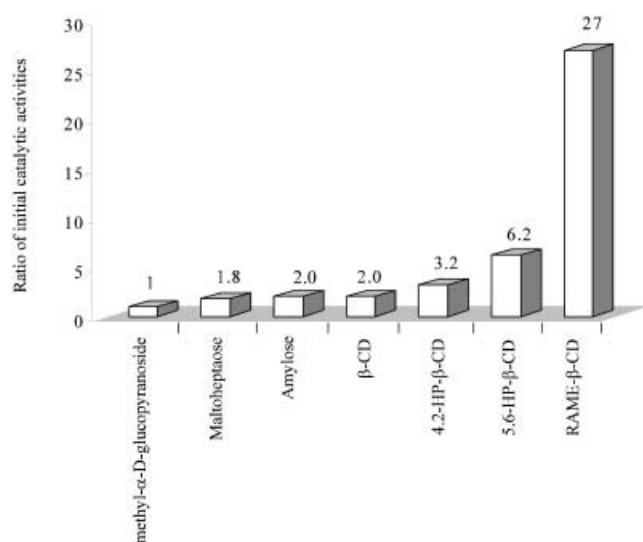
Figure 1.

Figure 2.

phase-transfer catalysts. Indeed, preliminary tests performed with a Pd/TPPMS catalytic system in an acetonitrile/water mixture (2/1) to avoid mass transfer limitation confirmed that the aryl iodide is much more reactive than the aryl bromide. So, with a reactive substrate such as 1-iodo-4-phenylbenzene and a highly active catalytic system such as that prepared from TPPMS, the limiting step of the reaction is expected to be the mass transfer in all cases.

The cross-coupling rate of 1-iodo-4-phenylbenzene with phenylboronic acid in a genuine two-phase system without a mass transfer promoter was very low. Indeed, the initial activity was $5 h^{-1}$ and the time required for complete conversion was 24 hours. The enhancements of catalytic activity obtained in the presence of cyclodextrins (CDs) are presented in Figure 1 and were measured as the ratio of the initial catalytic activity in the presence of added compound to the initial catalytic activity without addition of any compound.

Results obtained with methyl α-D-glucopyranoside and maltoheptaose (compounds which have the same subunits as the cyclodextrin but which do not possess a lipophilic host cavity) and with amylose (a linear polymer of D-glucose which can adopt helical conformations with six-seven glucose units per turn)[8] were also indicated.

The absence of effects of methyl α-D-glucopyranoside and maltoheptaose confirms that a process of molecular recognition must operate to perform the reaction and that enhancement of the catalytic activity observed with the CDs cannot be attributed to a co-solvent effect of these compounds. Moreover, the poor effect of amylose also suggests that the formation of stable inclusion complexes is crucial to achieve the cross-coupling reaction. Indeed, amylose is a linear oligosaccharide which cannot strongly encapsulate the organic compounds.[8] As already reported by Schatz et al.[6], the
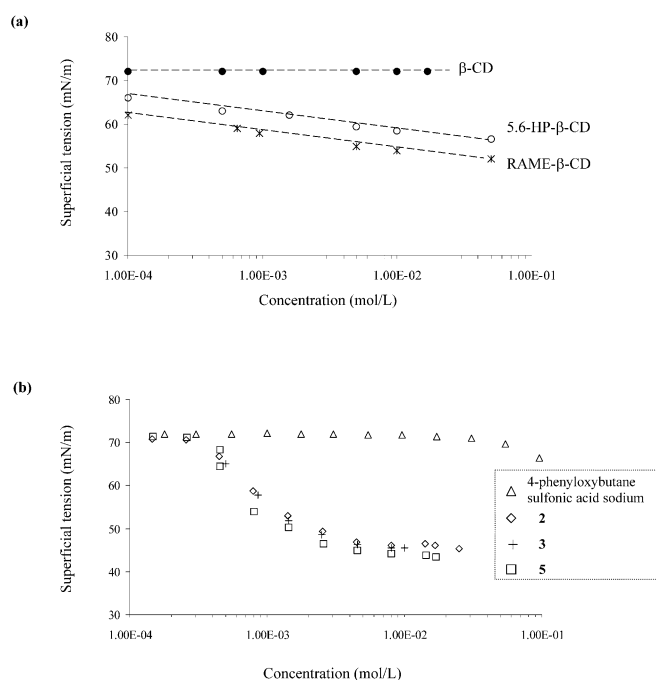
native β-CD did not increase notably the reaction rate. Actually, the latter is only increased by a factor of 2. Interestingly, the addition of a chemically modified CD into the reaction medium improved undoubtedly the catalytic activity. As shown in Figure 1, the best result was obtained with randomly methylated β-cyclodextrin (RAME-β-CD) that induced a rate enhancement of 27. With this methylated cyclodextrin, a quantitative conversion was achieved in 5 hours. The activity of the modified CD is strikingly dependent on the nature of the substituent group and on the degree of substitution of the CD. Thus, hydroxypropyl-CDs (HP-β-CD) exhibited a much lower activity than the RAME-β-CD and the HP-β-CD with an average substitution degree of 5.6 is more efficient than that with a substitution degree of 4.2.

Two factors can account for the higher efficiency of chemically modified CDs.[7] The first is the surface-active behaviour of these cyclodextrins.[9] Indeed, contrary to native β-CD, HP-β-CD and RAME-β-CD are hydrotrope compounds that allow a decrease in the surface tension without formation of micellar aggregates as shown in Figure 2a. This property allows an increase of the interfacial area and, consequently, of the mass transfer between the aqueous and organic phases. The second factor, and the most important, is the presence of a deep hydrophobic host cavity. Indeed, attachment of methyl or hydroxypropyl groups to the β-CD extends the cavity of the β-CD. Thus, these cyclodextrins have much more important lipophilic domains and cavity volumes approximately 10–20% larger than native β-CD due to the increase in the height of the CD
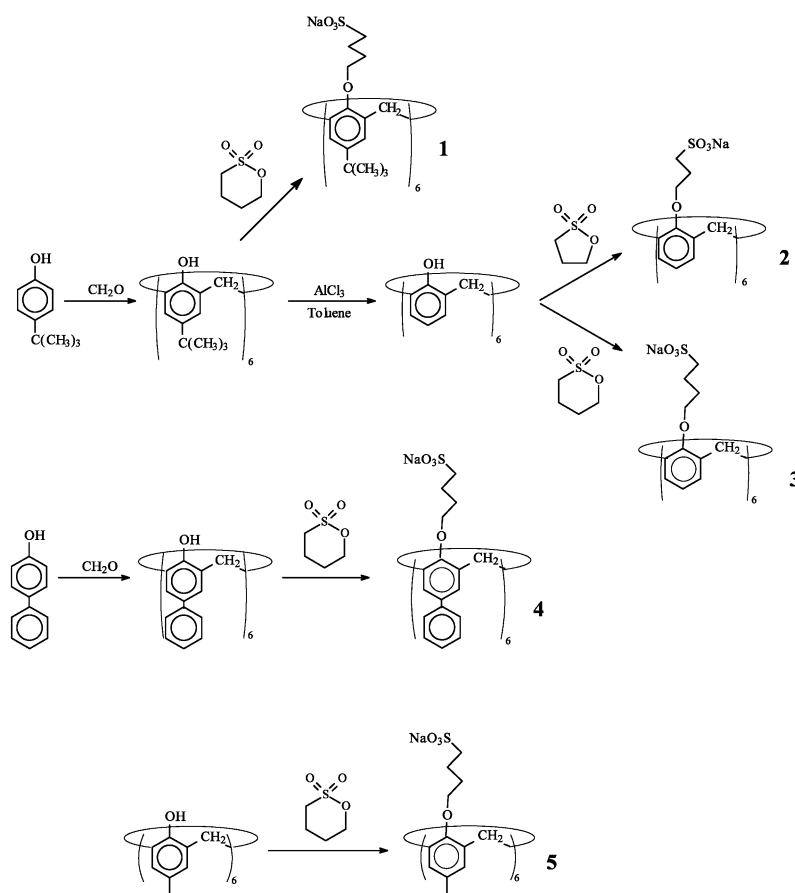
Scheme 2.

torus.[10,11] This gives rise to CDs that accommodate more easily highly hydrophobic substrates such as the 1-iodo-4-phenylbenzene.[10,11]

The key role played by the presence of a deep host cavity led us to envisage the synthesis of carriers which present a more extended hydrophobic host cavity. As the synthesis of more hydrophobic CDs is arduous and time-consuming,[12] we then turned our attention to calixarenes. Calixarenes are cyclic oligomers made up of benzene units as cyclodextrins are made up of glucose units but a large variety of a hydrophilic or hydrophobic substituents can be easily attached on the upper or lower rim of the arene rings.[13]

Although numerous water-soluble calixarenes have been described in the literature,[14] we did not find any water-soluble calixarenes that present a well identified hydrophobic host cavity, i.e., calixarenes where polar groups are located on the lower rim and a long way from the rim of the arene rings. Fortunately, we were able to obtain such calixarenes in 2 or 3 steps from commercially available phenol derivatives or calixarenes according to Scheme 2.

This series of calixarenes bearing hydrogen, methyl, *tert*-butyl or phenyl group on the upper rim has been designed to modulate the CH/π and π/π interactions

that are, besides hydrophobic and electrostatic interactions, the main interactions responsible for the formation of inclusion complexes. To the best of our knowledge, no calixarene synthesised in this work has ever been described in the literature. We only note that Shinkai et al. have reported the synthesis of an analogue of **1**, i.e., 5,11,17,23,29,35-hexa(*tert*-butyl)-37,38,39,40,41,42-hexakis(3-sulfonatopropyloxy) calix[6]-arene.[15] As calixarenes **1** to **5** present a distinct hydrophobic and hydrophilic part like conventional surfactant, we sought to investigate the surface activity of these compounds. Due to the poor solubilities in water of calixarenes **1** and **4** ($<10^{-5}$ and $<10^{-3}$ mol/L, respectively), only the surfactant behaviour of calixarenes **2**, **3** and **5** could be studied by surface tension measurements. The linear decreases in surface tension with log(c) until a minimum value indicates undoubtedly a surfactant behaviour for calixarenes **2**, **3** and **5** (Figure 2b). Although these calixarenes have different structures, the critical micellar concentrations and the surface tensions above the critical micellar concentration were similar for the three calixarenes: *ca.* $2\ 10^{-3}$ mol/L and 42–45 mN/m, respectively. For comparison purpose, the effect on the surface tension of 4-phenyloxybutanesulfonic acid sodium salt, a non-cyclic
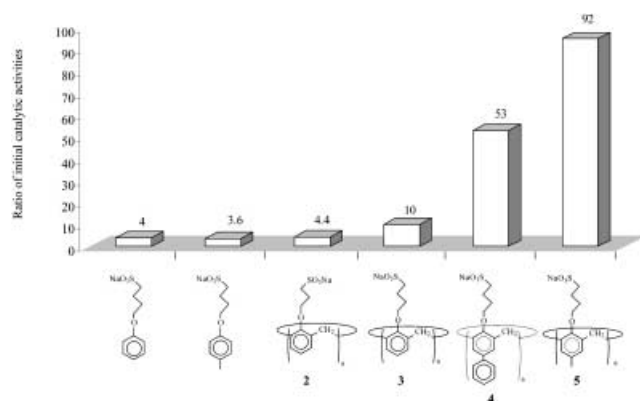
Figure 3.

analogue of **3**, was also measured. No significant change in the surface tension was observed with this compound, suggesting that the arrangement of the aromatic ring in the calixarene makes the formation of a monolayer at the air-water interface easier.

The effect of calixarenes **2**, **3**, **4** and **5** on the cross-coupling rate is presented in Figure 3. The water solubility of calixarene **1** was so poor that no experiment was conducted with this calixarene. Control experiments conducted with non-cyclic analogues of **3** and **5** were also performed to confirm the importance of the cavity for the rate enhancement. The percentage by weight of non-cyclic analogue in the aqueous phase was equal to that of the corresponding calixarene.

A very low acceleration of the cross-coupling rate was observed when the monomeric counterpart of calixarene **3** and **5** was added to the reaction medium, indicating that these compounds modify the polarity of the aqueous phase and thus increase the solubility of 1-iodo-4-phenylbenzene. Surprisingly, although calixarenes **2** and **3** are much more surface active than the RAME-β-CD ($\gamma = 56$ mN/m for RAME-β-CD against $42 - 45$ mN/m for **2** and **3** at $C = 10^{-2}$ mol/L), the reaction rates did not increase outstandingly and remained largely lower than that observed with the RAME-β-CD. This result confirms that the most important factor governing the efficiency of the carrier in our experimental conditions is not the surface properties of the carrier but its capacity to bind strongly to the 1-iodo-4-phenylbenzene. The first significant result was obtained with the calixarene **4** that allowed an increase in the rate by a factor of 53 (time required for complete conversion in the presence of **4**: 2 hours). By comparing the structures of calixarenes **3** and **4**, the beneficial effect of **4** could be rationalized by invoking additional π/π aromatic interactions between the calixarene and the aromatic rings of the substrate. Unfortunately, the reasons why the rate increased with calixarene **4** are more delicate to discuss as a slurry was clearly observed in the course of reaction indicating that a part of the calixarene was not totally soluble. The result

obtained with calixarene **5** is quite remarkable. This calixarene induced a rate enhancement of 92 and is more efficient than calixarenes **3** and **2** by a factor of 9.2 and 21, respectively. Furthermore, a quantitative conversion was achieved in 35 minutes. In the case of calixarene **5**, a comparison of the result with those obtained with **2** and **3** is meaningful as this calixarene is totally soluble in the reaction medium. The differences of reactivity observed under identical experimental conditions originate presumably from molecular recognition processes involving calixarenes and the water-insoluble 1-iodo-4-phenylbenzene and could reflect the different binding ability of calixarenes towards 1-iodo-4-phenylbenzene. Indeed, these three calixarenes have similar effects on the surface tension (see Figure 2b) and the non-cyclic analogue of **3** and **5** have poor effects on the reaction rates. The additional CH/π-interaction of the methyl group at the upper rim towards the aromatic moiety of 1-iodo-4-phenylbenzene could explain the higher binding strength of calixarene **5**.[16] The difference of reactivity observed between **2** and **3** also suggests that an extended hydrophobic cavity increases the molecular recognition, confirming our initial approach. ^{1}H NMR studies are currently under way in our laboratory to study inclusion properties of the new calixarenes **2**, **3** and **5**.

Finally, the possibility to recover quantitatively the catalytic system was investigated by performing three consecutive runs with the RAME-β-CD or the calixarene **5**. Contrary to the methylated β-cyclodextrin, separation of the aqueous layer from the organic layer in the case of calixarenes **5** was troublesome. Indeed, a complete phase separation required $3 - 4$ hours with **5** vs. 5 minutes with RAME-β-CD. In all cases, a decrease of $20 - 30\%$ in the initial activity was observed between each run. As the organic phases were colourless and the ^{31}P{H} and ^{1}H NMR analyses did not indicate the presence of TPPMS or mass transfer promoter in the organic phase, this decrease in the initial activity does not seem to be related to leaching of the catalyst or mass transfer promoter from the aqueous to organic phase but to the decay of the palladium/TPPMS catalyst. This assumption was fully supported by the fact that palladium black aggregates were clearly observed at the aqueous/organic interface during recycling experiments. So, if consecutive runs are envisaged with cyclodextrins or calixarenes possessing extended hydrophobic host cavities and surface-active properties, the use of much more stable water-soluble catalytic systems such as those described by Miyaura et al. will be necessary.[4a, e]

Conclusion

We have demonstrated that the efficiency of cyclodextrins and calixarenes in the Suzuki cross-coupling reaction can be greatly increased by finely designing the

structure of the carrier. From the point of view of reactivity, these results and the few works reported in the literature[6,17] reinforce the idea that calixarenes are better than cyclodextrins to overcome mass transfer limitation in aqueous organometallic catalysis. Indeed, contrary to cyclodextrins, calixarenes can be more easily tuned to accommodate the substrate. Nevertheless, in the view of punctual use in the laboratory or in large-scale industrial applications, the methylated β-cyclodextrins are the best candidates in so far as they are cheap, non-toxic, biodegradable and commercially available in bulk.

Experimental Section

General Remarks

The ^{1}H and ^{13}C NMR spectra were recorded at 300.13 and 75.46 MHz, respectively, on a Bruker Avance 300 DPX instrument. IR spectra were recorded on a Vector 22 Bruker spectrometer. Elemental analyses were performed by the Department of Micro-Analyses at the University of Artois using an EA 1110 CHNS Thermoquest instrument. Gas chromatographic analyses were carried out on a Shimadzu GC-17A gas chromatograph equipped with a methyl silicone capillary column (25 m × 0.25 mm) and a flame ionisation detector (GC:FID). The interfacial tension measurements were performed using a KSV Instruments digital tensiometer (Sigma 70) with a platinium plate. The precision of the force transducer of the surface tension apparatus was 0.1 mN/m. The experiments were performed at $25 \pm 0.5\,^{\circ}$C controlled by a thermostatted bath Lauda (RC6 CS). The samples were freshly prepared by dissolving the desired amount of mass transfer promoter in ultrapure water (Fresenius Kabi, France).

Palladium acetate was purchased from Aldrich. β-cyclodextrin (β-CD), hydroxypropyl-β-cyclodextrins (HP-β-CD) and methylated β-cyclodextrin (RAME-β-CD) were purchased from Aldrich or Cyclolab (Budapest, Hungary) and dried before use. The RAME-β-CD was a mixture of methylated β-CDs, in which 12.6 hydroxy groups of the twenty-one have been methylated. HP-β-CDs were mixtures of 2-hydroxypropylated-β-CDs: 4.2 hydroxy groups of the twenty-one have been hydroxypropylated for the 4.2-HP-β-CD and 5.6 hydroxy groups of the twenty-one for the 5.6-HP-β-CD. The sodium salt of the monosulfonated triphenylphosphane (TPPMS) was synthesised as reported by Chatt et al.[18] 1-Iodo-4-phenylbenzene was prepared by a Sandmeyer reaction starting from 4-phenylaniline and potassium iodide.[19] 5,11,17,23,29,35-Hexamethyl-37,38,39,40,41,42-hexahydroxy-calix[6]arene was purchased from Synchem and used without further purification. 5,11,17,23,29,35-Hexa(*tert*-butyl)-37,38,39,40,41,42-hexahydroxycalix[6]arene was prepared by the base-catalysed condensation of *p-tert*-butylphenol with formaldehyde according to published procedures.[20] The *tert*-butyl groups were removed by an aluminium chloride-catalysed alkyl group transfer to give the 37,38,39,40,41,42-hexahydroxycalix[6]arene.[21] The 5,11,17,23,29,35-hexaphenyl-37,38,39,40,41,42-hexahydroxycalix[6]arene was synthes-

ised according to a procedure analogous to that described by Gutsche et al.[22]

Typical Procedure for Sulfonation of *para*-Substituted Calix[6]arene

To a 1-L, three-necked flask containing calix[6]arene (4 mmol) dissolved in 600 mL of dry THF under a nitrogen atmosphere was added an excess of NaH (12 equiv., powder). The mixture was stirred at room temperature for 30 min. The sultone (10 equiv.) was then introduced and the solution stirred at room temperature for 5 hours. Another excess of NaH (12 equiv.) and sultone (10 equiv.) was then introduced and the mixture was stirred for an additional 5 h. This was repeated three times allowing total substitution of the hydroxy groups. The precipitate formed was filtered off and successively washed with THF and EtOH. The solid was recrystallised several times from EtOH/H$_2$O (until ^{1}H NMR spectroscopy showed complete removal of excess starting sultone) to yield a white solid.

5,11,17,23,29,35-Hexa(*tert*-butyl)-37,38,39,40,41,42-hexakis(4-sulfonatobutyloxy)calix[6]arene (1): Yield: 1.3 g (0.6 mmol, 16%). ^{1}H NMR (DMSO-d_6): δ = 7.66 – 6.75 (m, 2H, ArH), 3.85 (m, 2H, Ar-CH$_2$-Ar), 3.34 (m, 2H, O-CH$_2$-), 2.75 (2H, S-CH$_2$), 1.9 (m, 4H, -CH$_2$-CH$_2$-), 1.5 – 0.8 (m, CH$_3$); ^{13}C {^{1}H} NMR: δ = 155.2, 136.5, 133.6, 125.1 (C Ar), 74.6 (O-CH$_2$), 52.1 (S-CH$_2$), 33.4 [C(CH$_3$)$_3$], 31.3 (Ar-CH$_2$-Ar), 31.9 [C(CH$_3$)$_3$], 28.6 (O-CH$_2$-CH$_2$), 25.7 (S-CH$_2$-CH$_2$); IR: ν = 3104, 2954 – 2877, 1645, 1470, 1198, 1019, 845, 657 cm^{-1}; anal. calcd. for C$_{90}$H$_{126}$Na$_6$O$_{24}$S$_6$ · 6 H$_2$O: C 53.25, H 6.35; found: C 53.74, H 6.71.

37,38,39,40,41,42-Hexakis(3-sulfonatopropyloxy)calix[6]-arene (2): Yield: 1.6 g (1.1 mmol, 22.7%). ^{1}H NMR (D$_2$O): δ = 6.74 (s, 2H, *m*-ArH), 6.62 (s, 1H, *p*-ArH), 3.91 (s, 2H, Ar-CH$_2$-Ar), 3.53 (s, 2H, O-CH$_2$-), 2.85 (s, 2H, S-CH$_2$), 1.8 (s, 2H, -CH$_2$-); ^{13}C {^{1}H} NMR: δ = 155.5, 145.9, 139.9, 124.9 (C Ar), 74.1 (O-CH$_2$), 51.7 (S-CH$_2$), 31.3 (Ar-CH$_2$-Ar), 26.2 (C-CH$_2$-C); IR: ν = 3103, 2930 – 2850, 1641, 1468, 1204, 1022, 850, 645 cm^{-1}; anal. calcd. for C$_{60}$H$_{66}$Na$_6$O$_{24}$S$_6$ · 6 H$_2$O: C 44.78, H 4.88; found: C 44.81, H 4.93.

37,38,39,40,41,42-Hexakis(4-sulfonatobutyloxy)calix[6]-arene (3): Yield: 2.0 g (1.2 mmol, 29.4%). ^{1}H NMR (D$_2$O): δ = 6.76 (s, 2H, *m*-ArH), 6.63 (s, 1H, *p*-ArH), 3.92 (s, 2H, Ar-CH$_2$-Ar), 3.53 (s, 2H, O-CH$_2$-), 2.72 (s, 2H, S-CH$_2$), 1.65 (s, 4H, -CH$_2$-); ^{13}C {^{1}H} NMR: δ = 155.6, 136.3, 133.8, 125.7 (C Ar), 74.0 (O-CH$_2$), 51.5 (S-CH$_2$), 31.2 (Ar-CH$_2$-Ar), 29.7 (O-CH$_2$-CH$_2$), 21.4 (S-CH$_2$-CH$_2$); IR: ν = 3100, 2930 – 2853, 1644, 1467, 1202, 1028, 850, 645 cm^{-1}; anal calcd. for C$_{66}$H$_{78}$Na$_6$O$_{24}$S$_6$ · 6 H$_2$O: C 46.81, H 5.35; found: C 46.09, H 5.17.

5,11,17,23,29,35-Hexaphenyl-37,38,39,40,41,42-hexakis(4-sulfonatobutyloxy)calix[6]arene (4): Yield: 1.8 g (0.8 mmol, 21.4%). ^{1}H NMR (DMSO-d_6): δ = 7.70 – 6.90 (m, 2H, ArH), 4.34 (s, 2H, Ar-CH$_2$-Ar), 3.87 (s, 2H, O-CH$_2$-), 2.74 (s, 2H, S-CH$_2$), 1.92 (s, 4H, -CH$_2$-CH$_2$-); ^{13}C {^{1}H} NMR: δ = 159 – 122 (C Ar), 74.0 (O-CH$_2$), 52.3 (S-CH$_2$), 40.8 (Ar-CH$_2$-Ar), 30.3 (O-CH$_2$-CH$_2$), 26.8 (S-CH$_2$-CH$_2$); IR: ν = 3101, 2952 – 2851, 1646, 1468, 1201, 1024, 847, 653 cm^{-1}; anal. calcd. for C$_{102}$H$_{102}$Na$_6$O$_{24}$S$_6$ · 6 H$_2$O: C 57.00, H 5.34; found: C 57.54, H 5.18.

5,11,17,23,29,35-Hexamethyl-37,38,39,40,41,42-hexakis(4-sulfonatobutyloxy)calix[6]arene (5): Yield: 1.3 g (0.7 mmol, 18%). ^{1}H NMR (D$_2$O): δ = 6.69 (s, 2H, ArH), 3.82 (s, 2H, Ar-

CH$_2$-Ar), 3.50 (s, 2H, O-CH$_2$-), 2.67 (s, 2H, S-CH$_2$), 1.64 (s, 4H, -CH$_2$-CH$_2$-), 2.12 (s, CH$_3$); ^{13}C {^{1}H} NMR: $\delta = 155.2$, 136.5, 133.6, 125.1 (C Ar), 74.6 (O-CH$_2$), 52.1 (CH$_2$-S), 31,0 (Ar-CH$_2$-Ar), 28.6 (O-CH$_2$-CH$_2$), 25.7 (S-CH$_2$-CH$_2$), 20.2 (ArCH$_3$); IR: $\nu = 3100$, 2930 – 2853, 1644, 1467, 1202, 1028, 850, 645 cm^{-1}; anal. calcd. for C$_{72}$H$_{90}$Na$_6$O$_{24}$S$_6 \cdot$ 6 H$_2$O: C 48.65, H 5.77; found: C 48.54, H 5.75.

Palladium Catalytic Solution

In a 20-mL Schlenk tube, Pd(OAc)$_2$ (5 mg, 0.022 mmol) was dissolved in 5 mL distilled water. To the yellow solution was added the TPPMS phosphane (9 equiv./Pd) as a powder. The solution was bubbled under nitrogen and the mixture was then vigorously stirred at room temperature until the phosphane was completely solubilised (*ca.* 30 min.)

Catalytic Experiments

In a 100-mL Schlenk tube were placed 1-iodo-4-phenylbenzene (140 mg, 0.5 mmol), phenylboronic acid (79 mg, 0.65 mmol), the inverse phase-transfer catalyst (calixarene or cyclodextrin) (0.2 mmol), sodium carbonate (159 mg, 1.5 mmol), dodecane (internal reference for GC analysis, 115 mg, 0.67 mmol), 5 mL toluene and 19 mL distilled water. The solution was bubbled under nitrogen (10 min.), stirred vigorously (700 rpm) and heated to 80 °C under a nitrogen atmosphere. 1 mL of the palladium catalytic solution was then transferred under a nitrogen atmosphere by cannula into the 100-mL Schlenk tube. Samples were then taken at regular time intervals and analyzed by GC. These analyses allow us to draw a curve depicting the conversion as a function of time. From the slope of the curve at the initial time, the initial catalytic activity was calculated as the mole number of 1-iodo-4-phenylbenzene transformed per hour and per mole of palladium. In all experiments, 4 – 6% of the homo-coupling product of phenylboronic acid (biphenyl) was observed. This percentage was independent of the mass transfer promoter employed.

Recycling Experiments

The first batch was carried out as described above. After 20 minutes (calixarene **5**) or 3 hours (RAME-β-CD) of reaction time, the Schlenk tube was cooled to room temperature. After 15 minutes (RAME-β-CD) or 5 hours (calixarene **5**), the aqueous and organic phases were separated and a new water/toluene mixture (2 mL/5 mL) containing 1-iodo-4-phenylbenzene (0.5 mmol), dodecane (0.67 mmol), phenylboronic acid (0.65 mmol), sodium carbonate (1.5 mmol) was introduced into the Schlenk tube. The resulting mixture was then heated to 80 °C under a nitrogen atmosphere and the next cycle was performed.

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