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Assessment of the Reusability of Pd Complexes Supported on Fluorous Silica Gel as Catalysts for Suzuki Couplings

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A thorough investigation of different perfluoro-tagged Pd complexes supported on fluorous silica gel (FSG) as catalysts for Suzuki reactions is presented. The rates of reaction upon recycling of the supported complexes were measured in order to determine the reusability of the catalysts. Perfluoro-tagged and untagged complexes adsorbed on FSG and unmodified silica gel were also compared. While with dimethoxyethane (DME) as a solvent the catalytic activity decreased upon reuse, significant activity was retained with recycled catalysts for reactions in water. With catalyst loadings of 0.001 mol-%, TONs as high as 526000 were obtained.

Introduction

Since the seminal work of Horváth and Rábai, fluorous catalysis has received ever growing attention as a strategy for the separation and recovery of catalysts.[1–6] This concept is based on the phenomenon that perfluorinated solvents exhibit a temperature-dependent immiscibility with many organic solvents, which allows for the formation of liquid–liquid biphasic systems. Since the solubility of organic compounds in perfluorinated solvents can be increased by the attachment of perfluoroalkyl chains, the so-called "fluorous tags", compounds labelled in this way, in our context catalysts, can be selectively separated from other compounds by simple liquid–liquid extraction. As an alternative, the isolation or separation of the catalyst can be performed by chromatography on a plug of fluorous silica gel (FSG), which is silica gel that has been modified with perfluoroalkyl entities.[7,8]

We have recently reported another approach, in which we have used perfluoro-tagged Pd–phosphane complexes physisorbed on FSG for catalysis of C–C couplings in organic solvents and water. The separation of the catalyst was performed by simple filtration and it was possible to re-use the supported catalyst several times.[9,10] Here we present a more detailed kinetic study and a comparison of different catalysts, involving perfluoro-tagged diphosphane complexes and different support materials.

Results and Discussion

While in our initial investigations of perfluoro-tagged Pd catalysts on fluorous silica gel we employed the yield of consecutive runs as a criterion for the reusability of the catalyst, we soon recognized that yields alone are insufficient to evaluate the recycling of catalysts. Assuming that the reaction times are rather long but that the reaction is finished after a short period of time and that there would be a partial loss of catalytic activity in each cycle, it would take longer reaction times in the following cycles to complete the reaction but this would still give the impression that the catalyst is completely recyclable. This common misunderstanding has been treated in detail by Gladysz.[11]

We therefore set out to investigate the rate of reaction in repetitive cycles in addition to the conversion, since this should provide a good measure of the efficiency of catalyst reuse and therefore allow different pre-catalysts to be easily compared. In these studies we employed a number of palladium complexes with monodentate and bidentate phosphane ligands (Figure 1).

Complexes **1a**–**e** and the required ligands were prepared according to our previously published procedures.[12–14] The straightforward synthesis of the bidentate phosphanes according to Scheme 1 started from perfluoroalkyl-tagged aryl bromide **6**.[15] For the preparation of methylene-bridged diphosphane **7a** and ethylene-bridged diphosphane **7b** lithium–halogen exchange, followed by condensation with the appropriate bidentate chlorophosphane, gave the diphosphanes in 57% and 67% yields, respectively.

The propylene-bridged diphosphane **7c** was prepared according to a modified procedure of Curran et al. (Scheme 2).[16] Thus, aryl bromide **6** was converted into the corresponding aryllithium derivative, which was treated with freshly distilled Et_2NPCl_2. The phosphoramidite intermediate was hydrolysed with concentrated aqueous hydrogen chloride to give diarylphosphane oxide **8** in 67% yield. Alkylation of diarylphosphane oxide **8** with 1,3-dibromopropane, and subsequent reduction with trichlorosilane

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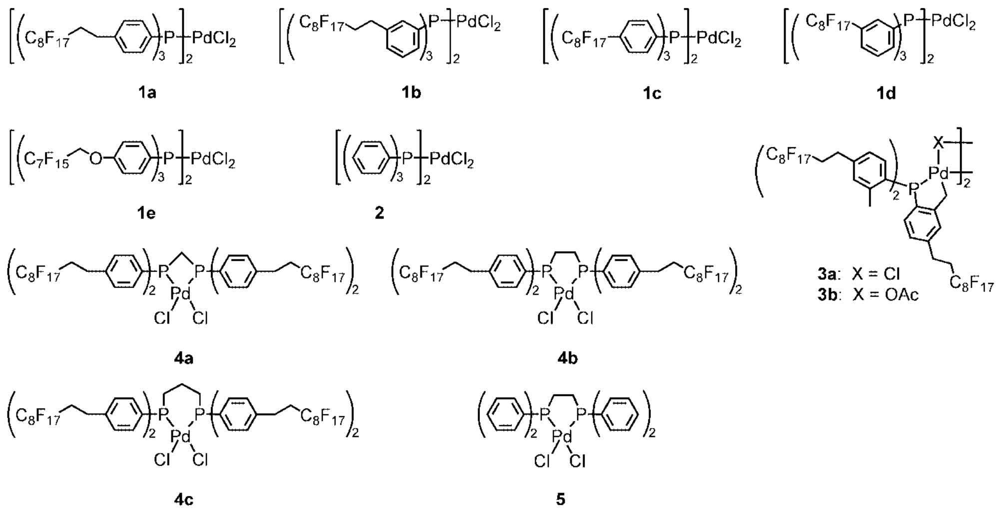
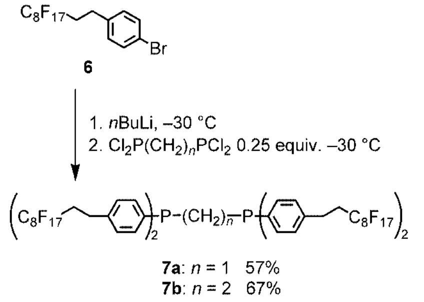
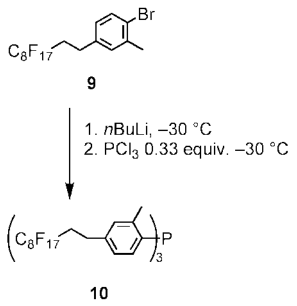


Figure 1. Palladium complexes employed in this study.



Scheme 1. Synthesis of bidentate phosphanes **7a** and **7b**.



Scheme 3. Synthesis of phosphane **10**.

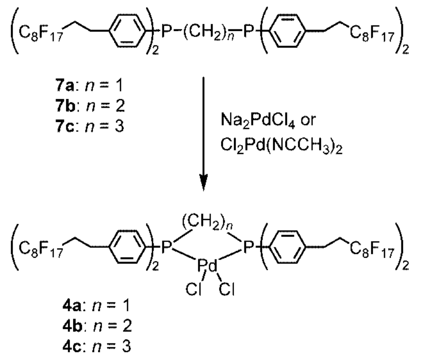
and triethylamine, provided the perfluoro-tagged propylene-bridged diphosphane **7c** in an isolated yield of 55%.

The synthesis of the perfluoro-tagged phosphane **10** was carried out with a yield of 58% as described by Genêt (Scheme 3).[15]

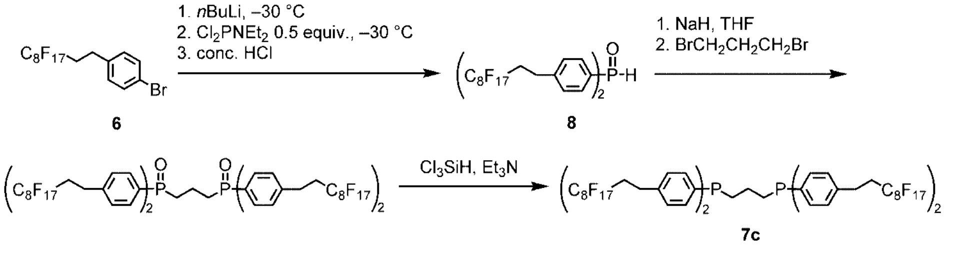
Palladium complexes **4a**–**c** of bidentate ligands were prepared by addition of a solution of Na_2PdCl_4 or $[PdCl_2(CH_3CN)_2]$ to a solution of bidentate ligand in THF at room temperature (Scheme 4).

The perfluoro-tagged palladacyclic complexes **3a** and **3b** were prepared according to the procedure of Hermann (Scheme 5).[17]

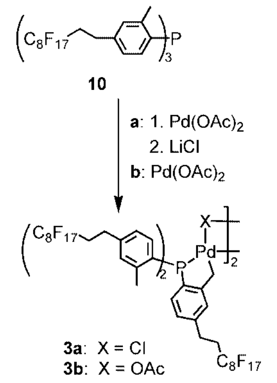
In our initial experiments we investigated the Suzuki coupling of 4-nitrobromobenzene and phenylboronic acid with different Pd complexes on FSG as catalyst (Scheme 6).



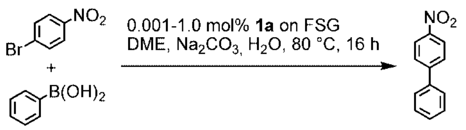
Scheme 4. Synthesis of palladium complexes **4a**–**c**.



Scheme 2. Synthesis of bidentate phosphane **7c**.



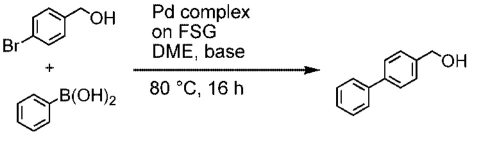
Scheme 5. Synthesis of palladacyclic complex **3a** and **3b**.



Scheme 6. Suzuki coupling of 4-bromonitrobenzene and phenylboronic acid.

However, this substrate combination proved not to be suitable for two reasons: the reaction is very fast, and hence precise sampling is difficult to perform, and secondly, reliable automated workup cannot be ensured due to the tendency of the product to crystallise. Nevertheless, these early experiments showed that the rate of reaction is proportional to the catalyst loading, as one would expect.

Therefore, we switched to a less-active substrate combination of 4-bromobenzyl alcohol and phenylboronic acid (Scheme 7). The former is almost two orders of magnitude less reactive than 4-bromonitrobenzene as starting material. Furthermore, the product of the reaction, 4-phenylbenzyl alcohol is better soluble, thus allowing for reliable automated workup. As a measure of the activity of the catalyst, we chose the apparent rate constant, k_{app}.



Scheme 7. Suzuki coupling of 4-bromobenzyl alcohol and phenylboronic acid.

The reaction follows a first-order rate law of the form

$$\mathrm{d}[\mathrm{S}]/\mathrm{d}t = -k_{\mathrm{app}}\cdot[\mathrm{S}]\cdot n_{\mathrm{Pd}}/V_{\mathrm{rxn}} \tag{1}$$

where [S] is the substrate concentration at a given time, n_{Pd} is the molar amount of pre-catalyst and V_{rxn} is the reaction volume. The ratio $n_{\mathrm{Pd}}/V_{\mathrm{rxn}}$ is used instead of the palladium concentration because the latter is not known. Thus, $n_{\mathrm{Pd}}/V_{\mathrm{rxn}}$ is a substitute, which equals [Pd] only in the case that all Pd precatalyst is indeed dissolved. Equation (1) can be transformed by integration into

$$(\ln[\mathrm{S}]_0 - \ln[\mathrm{S}])\cdot V_{\mathrm{rxn}}/n_{\mathrm{Pd}} = k_{\mathrm{app}}\cdot t \tag{2}$$

where $[\mathrm{S}]_0$ is the initial concentration of the substrate. According to Equation (2), the apparent rate constant, k_{app}, can be obtained from a logarithmic plot of [S] vs. t.

To carry out the experiments, we employed a Chemspeed Automated Synthesis Workstation, which allowed us to carry out reactions in parallel. The reactions were run on a 0.3-mmol scale in a reaction volume of 3 mL. Aliquots of the reaction mixture were withdrawn by the robotic synthesiser and subsequently analysed by HPLC.

Three consecutive runs were performed automatically with the same catalyst for every experiment. Palladium complexes **1a**–**e** and **3a** of perfluoro-tagged monodentate phosphanes and complexes **4a**–**c** of bidentate phosphanes on FSG were used with a catalyst loading of 0.1 mol-%. Additionally, untagged complex **2** on FSG as well as on unmodified silica gel (SG) and complexes **1a** and **4a**–**c** on SG were used for comparison. Different from the previous experiments, potassium carbonate was used as a base in these experiments and the amounts of base and water were reduced in order to avoid the formation of two distinct liquid phases in the reaction mixture, which would add further complexity to the reaction system. In contrast to earlier experiments with the very reactive 4-bromonitrobenzene, differences in the reactivity of the pre-catalysts in terms of conversion and rate of reaction, as illustrated in Table 1, became recognizable with 4-bromobenzyl alcohol as substrate.

Table 1. Comparison of different supported catalysts, 4-bromobenzyl alcohol (0.3 mmol), phenylboronic acid (0.33 mmol), 0.1 mol-% Pd, K_2CO_3 (0.6 mmol), DME, 80 °C, 16 h.

Entry	Complex	Support	Conversion[a] [%]	Cumulative TON[b]	k_{app}[a] [L mol^{-1} min^{-1}]
1	**2**	SG	63 (16, 10)	893	90 (1, 0)
2	**2**	FSG	82 (18, 4)	1042	313 (7, 0)
3	**1a**	SG	61 (19, 9)	886	67 (6, 1)
4	**1a**	FSG	71 (36, 13)	1205	111 (10, 1)
5	**1b**	FSG	44 (32, 27)	1029	35 (6, 1)
6	**1c**	FSG	40 (26, 8)	747	35 (1, 0)
7	**1d**	FSG	36 (4, 3)	422	39 (0, 0)
8	**1e**	FSG	70 (31, 7)	1073	76 (3, 1)
9	**3a**	SG	62 (54, 38)	1545	18 (14, 3)
10	**3a**	FSG	67 (37, 19)	1226	24 (9, 3)
11	**4a**	SG	66 (60, 35)	1607	39 (18, 8)
12	**4a**	FSG	66 (64, 50)	1809	27 (23, 15)
13	**4b**	SG	53 (13, 5)	700	25 (2, 1)
14	**4b**	FSG	75 (55, 49)	1786	42 (15, 8)
15	**4c**	SG	62 (48, 27)	1376	22 (13, 6)
16	**4c**	FSG	70 (35, 26)	1310	41 (10, 7)

[a] Values for recycling in brackets. [b] (mol product)/(mol Pd complex).

When comparing the FSG-supported perfluoro-tagged complexes, the highest cumulative turnover number of approx. 1800 was achieved with **4a** and **4b** as pre-catalysts, while the other perfluoro-tagged complexes gave TONs in the range of 1000–1300; only **1c** and **1d** yielded lower TONs. This order of reactivity was not reflected by the respective rates of reaction. In the initial run, the highest rate constants, k_{app}, were observed for complexes **1a** and **1e**; the rate constants for the other catalysts were smaller by roughly a factor 3. The differences in the yields arise less from differences in the rate of reaction but rather from the degree to which activity is lost upon recycling. While all complexes exhibit a decrease of k_{app}, this is less marked for **4a** and **4b**; in the other cases k_{app} drops by a factor of 5–20 upon reuse of the supported catalyst. As one might expect, the loss of activity observed for the untagged complex **2** is even more pronounced (Figure 2).

These results are certainly not as clear-cut as we would have desired, but nevertheless it is possible to sketch a general picture of these catalyst systems, which partly revises our previous conclusions.[9] Of the pre-catalysts examined, only the ones with bidentate phosphane ligands, namely **4a**, show a limited reusability in DME as organic solvent. For all complexes, the rates of reaction as well as the final conversion decrease more or less sharply when the complexes are reused. The probable causes for this loss of catalytic activity could be catalyst deactivation or leaching of the complex. We had already observed in our earlier work that the activity of the catalyst decreases to a larger degree than expected with less-reactive substrates.[9] This effect could be reduced by the addition of additional ligand, which is a hint that decomposition might occur at the stage of the Pd^0 intermediate. Extensive leaching, on the other hand, seems to be an unlikely reason for the decrease of activity, since, based on the palladium content, we found less than 2% of the total catalyst amount in the product.[9]

We briefly compared four different organic solvents and bases using 0.1 mol-% **1a** on FSG as pre-catalyst. The results did not deviate notably from the ones reported above. Of the solvents used, we obtained the highest TONs with

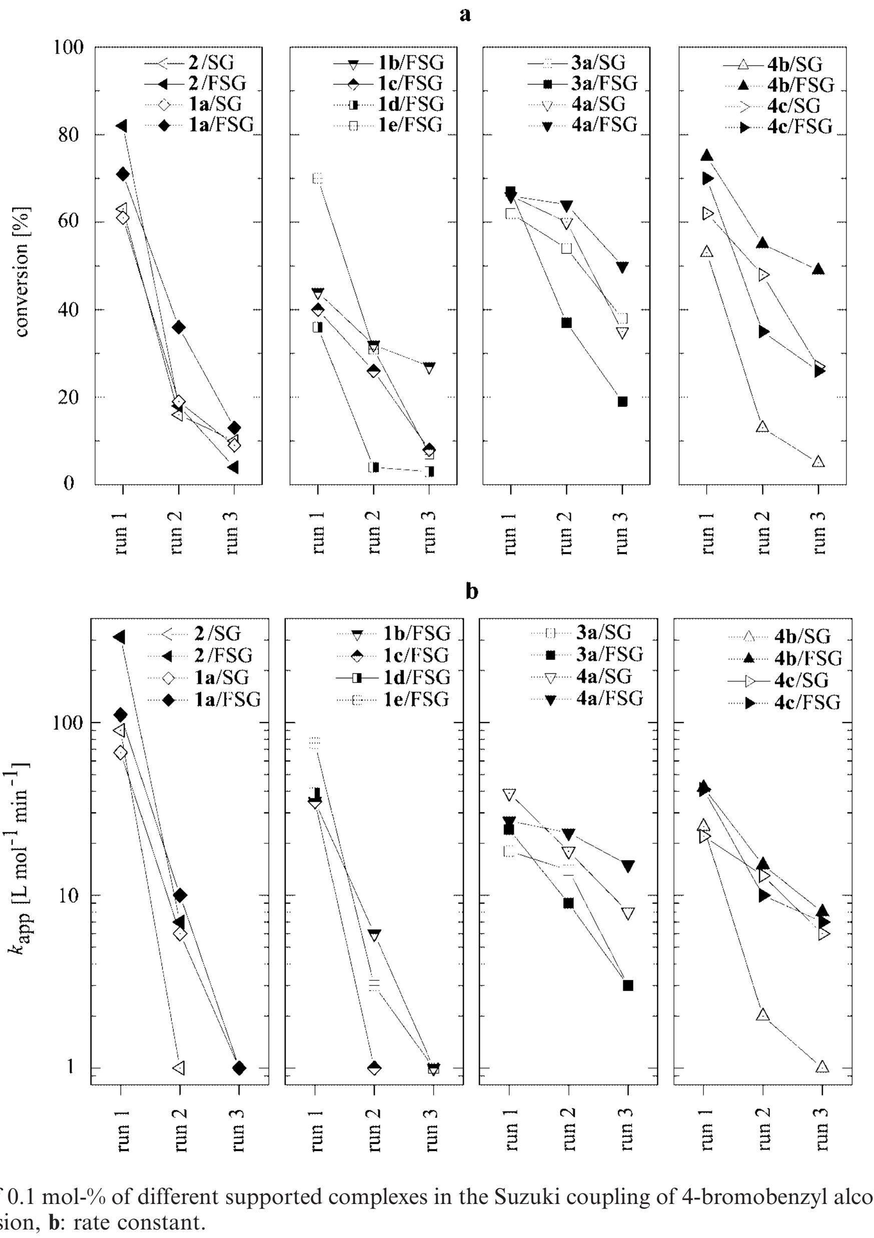


Figure 2. Comparison of 0.1 mol-% of different supported complexes in the Suzuki coupling of 4-bromobenzyl alcohol and phenylboronic acid in DME. **a**: conversion, **b**: rate constant.

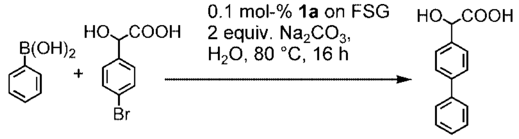
ethanol; toluene and DME gave slightly lower conversions, while in acetonitrile we observed only low conversion. Cs_2CO_3, CsF, NaOAc and LiOH were employed as bases. Except for NaOAc, which resulted in low activity, all bases were equally well suited. Generally, the rate of reaction dropped significantly upon recycling of the complex (Scheme 8).

We also turned our attention to Suzuki couplings of polar substrates in water as the solvent, since we felt that an increase in the solvent polarity might influence the catalyst

Table 2. Comparison of different supported catalysts, 4-bromomandelic acid (0.3 mmol), phenylboronic acid (0.33 mmol), 0.1 mol-% Pd, Na_2CO_3 (0.6 mmol), water, 80 °C, 16 h. Values are averages of at least two independent experiments.

Entry	Complex	Pd [mol-%]	Support	Conversion[a] [%]	Cumulative TON[b]	k_{app} [a] [L mol^{-1} min^{-1}]
1	**1a**	0.001	FSG	27 (71, 54, 37, 22, 7)	217388	121 (1341, 1315, 921, 345, 68)
2	**1a**	0.01	FSG	4 (76, 84, 85, 85, 69)	40382	6 (416, 422, 424, 373, 141)
3	**1a**	0.1	FSG	99 (91, 88, 79, 80, 76)	5130	288 (37, 33, 31, 31, 22)
4	**1a**	1	FSG	98 (98, 95, 90, 83, 87)	551	51 (14, 8, 4, 4, 3)
5	**1b**	0.1	FSG	88 (62, 83, 84, 86, 82)	4846	108 (23, 23, 24, 29, 33)
6	**1c**	0.1	FSG	94 (76, 83, 82, 74, 73)	4820	112 (32, 24, 23, 25, 23)
7	**1e**	0.1	FSG	85 (90, 89, 88, 85, 75)	5120	44 (50, 42, 38, 34, 22)
8	**1a**	0.1	SG	88 (89, 87, 86, 84, 82)	5170	50 (46, 33, 27, 31, 34)
9	**2**	0.1	FSG	90 (91, 90, 86, 85, 72)	5135	75 (58, 47, 38, 31, 21)
10	**2**	0.1	SG	52 (95, 95, 91, 85, 77)	4953	53 (68, 55, 38, 32, 33)
11[c]	**1a**	0.001	FSG	1 (8, 6, 8, 8, 2)	32317	13 (130, 87, 153, 155, 20)
12[c]	**1a**	0.01	FSG	1 (45, 38, 39, 21, 17)	16114	1 (72, 87, 81, 44, 36)
13[c]	**1a**	0.1	FSG	58 (93, 93, 85, 90, 88)	5071	69 (67, 71, 72, 71, 70)
14[c]	**1a**	0.1	SG	77 (94, 87, 85, 86, 75)	5048	21 (90, 52, 62, 44, 42)
15[c]	**2**	0.1	FSG	69 (97, 96, 96, 97, 88)	5431	17 (106, 89, 123, 67, 63)
16[c]	**2**	0.1	SG	56 (86, 98, 97, 94, 85)	5297	11 (95, 105, 92, 64, 48)
17[c]	**1e**	0.1	FSG	24 (96, 95, 97, 99, 86)	4970	5 (90, 69, 82, 60, 51)
18[c]	**1a**	1	FSG	60 (98, 98, 96, 99, 96)	547	1 (7, 8, 11, 8, 10)
19	**1a**	0.01	FSG	4 (41, 82)	12799[d]	7 (285, 471)
20	**1a**	0.01	SG	85 (90, 94)	26939[d]	535 (586, 752)
21	**2**	0.01	FSG	10 (86, 85)	18072[d]	12 (452, 482)
22	**2**	0.01	SG	84 (84, 74)	24150[d]	568 (332, 270)
23[e]	**1a**	0.01	FSG	94 (88, 85)	26715[d]	885 (418, 459)
24[e]	**1a**	0.01	SG	61 (47, 46)	15376[d]	688 (403, 315)
25[e]	**2**	0.01	FSG	17 (2, 1)	2031[d]	47 (1, 1)
26[e]	**2**	0.01	SG	24 (6, 2)	3169[d]	30 (8, 2)
27[e]	**4a**	0.1	FSG	93 (92, 92, 82, 86, 82)	5263	108 (58, 56, 31, 30, 26)
28[e]	**4a**	0.01	FSG	55 (89, 85, 84, 87, 84)	44669	81 (588, 428, 188, 495, 227)
29[e]	**4a**	0.001	FSG	82 (85, 88, 81, 81, 68)	483997	5093 (4546, 4507, 2446, 3963, 1810)
30[e]	**4a**	0.1	SG	95 (94, 92, 92, 91, 90)	5541	57 (45, 40, 36, 31, 37)
31[e]	**4a**	0.01	SG	96 (98, 92, 86, 84, 83)	54034	1613 (1079, 561, 421, 378, 347)
32[e]	**4a**	0.001	SG	32 (41, 29, 22, 26, 19)	169058	1 (1243, 533, 214, 388, 213)
33[e]	**4b**	0.1	FSG	89 (92, 90, 82, 86, 85)	5242	62 (59, 47, 30, 28, 30)
34[e]	**4b**	0.01	FSG	77 (90, 88, 84, 86, 84)	50966	696 (492, 392, 176, 371, 260)
35[e]	**4b**	0.001	FSG	86 (83, 91, 91, 84, 63)	497535	4664 (3137, 3170, 3254, 1926, 702)
36[e]	**4b**	0.1	SG	92 (96, 91, 89, 87, 86)	5395	62 (59, 47, 30, 28, 30)
37[e]	**4b**	0.01	SG	85 (98, 95, 84, 77, 75)	51362	696 (492, 392, 176, 371, 260)
38[e]	**4b**	0.001	SG	49 (32, 36, 65, 27, 58)	266682	4664 (3137, 3170, 3254, 1926, 702)
39[e]	**5**	0.01	FSG	32 (45, 41, 45, 32, 45)	23919	136 (181, 54, 171, 118, 180)
40[e]	**5**	0.001	FSG	1 (3, 4, 4, 19, 4)	36278	28 (50, 80, 21, 42, 48)
41[e]	**5**	0.01	SG	48 (45, 43, 35, 14, 33)	21713	154 (199, 25, 107, 9, 104)
42[e]	**5**	0.001	SG	37 (6, 3, 32, 3, 34)	114459	74 (91, 24, 1365, 10, 77)
43[e]	**4c**	0.1	FSG	98 (96, 92, 91, 96, 87)	5593	52 (68, 49, 34, 43, 26)
44[e]	**4c**	0.01	FSG	96 (79, 77, 79, 79, 79)	48936	485 (356, 293, 192, 271, 259)
45[e]	**4c**	0.001	FSG	89 (83, 70, 63, 50, 33)	389054	5678 (2721, 2636, 1722, 1108, 611)
46[e]	**4c**	0.1	SG	98 (92, 88, 87, 85, 83)	5335	52 (49, 38, 10, 28, 34)
47[e]	**4c**	0.01	SG	98 (97, 89, 89, 88, 76)	53687	1307 (702, 407, 417, 371, 288)
48[e]	**4c**	0.001	SG	82 (68, 65, 44, 48, 34)	341896	3026 (1628, 1906, 1402, 1082, 462)
49[e]	**3a**	0.1	FSG	98 (98, 97, 97, 94, 93)	5775	136 (97, 73, 44, 44, 62)
50[e]	**3a**	0.01	FSG	43 (87, 85, 85, 81, 89)	47059	82 4(89, 401, 433, 312, 397)
51[e]	**3a**	0.001	FSG	53 (53, 36, 36, 28, 28)	234607	2644 (2020, 863, 720, 498, 404)
52[e]	**3a**	0.1	SG	99 (98, 96, 93, 91, 92)	5690	85 (110, 73, 41, 38, 41)
53[e]	**3a**	0.01	SG	92 (95, 93, 84, 83, 85)	53236	807 (820, 510, 396, 356, 408)
54[e]	**3a**	0.001	SG	86 (88, 93, 94, 78, 87)	525865	1381 (3839, 4177, 5349, 3221, 4369)

[a] Values for recycling in brackets. [b] (mol product)/(mol Pd complex). [c] Filtration experiment. [d] Cumulative TON over three runs. [e] Pre-wetting of support.



Scheme 8. Suzuki coupling of bromomandelic acid and phenylboronic acid.

reactivity, reusability and leaching. Indeed, we observed a markedly different behaviour of the catalyst in initial experiments. With 4-bromomandelic acid as a water-soluble substrate with a reactivity similar to 4-bromobenzyl alcohol, high cross-coupling yields were obtained even after the fifth recycling of the catalyst. The results for different catalyst loadings and different catalysts, as well as for a number of substrates, were communicated recently (Table 2).[10]

In addition, we measured the rates of reactions for these examples. Upon comparing the rate constants, k_{app}, for the coupling of 4-bromomandelic acid and phenylboronic acid in water with catalyst loadings between 0.001 and 1.0 mol-% of **1a** we observed a striking dependence of k_{app} on the catalyst loading (Figure 3, **b**). For 0.1 mol-% **1a**, k_{app} starts out at a value significantly higher than the analogous value for the reaction in DME and remains on a fairly constant lower level for five reuses of the catalyst. Similarly, for 1.0 mol-% **1a**, k_{app} starts at a high value, which slowly decreases until it levels-off in the fourth run. In contrast to this, the reaction with 0.01 mol-% **1a** is unexpectedly slow in the first run, but upon reuse of the catalyst k_{app} jumped to a high level, where it remains until the fifth run. A similar behaviour was observed for 0.001 mol-% **1a**: the reaction is slow in the first run but a high value of k_{app} is observed in the second and third runs and decreases in the following reuses. The most prominent observation is that the levels of reactivity differ by roughly one order of magnitude, which is the result of the rate of reaction being largely independent of the initial pre-catalyst loading. Since it is safe to assume that the same catalytic species is formed regardless of the amount of pre-catalyst, the most obvious interpretation of the results is that, independent of the amount of pre-catalyst, approximately the same amount of catalytic species is formed upon recycling. Although this is surprising at first sight, a comparable phenomenon has been reported recently in the case of a so-called ligand-free Heck reaction.[18]

We also compared the perfluoro-tagged complexes **1a**, **1b**, **1c** and **1e**, and the untagged complex **2** at a loading of 0.1 mol-% on FSG. The conversions exhibit an almost random variation within a range of 85–100% in the first run, decreasing to 70–80% in the sixth run (Figure 4, **a**). While the rate constants, k_{app}, show a spread of nearly one order of magnitude in the first run, the following order of activity can be observed in the second, third and fourth runs: **2** ≈ **1e** > **1a** > **1c** ≈ **1b**, although the differences are small considering the variation of the results of single experiments (Figure 4, **b**). In the fifth and sixth runs the differences in reactivity are no longer significant.

Similarly, complexes **1a** and **2** were compared on FSG and unmodified SG as support. Again, in terms of conversion a difference could be hardly detected. In terms of the rate of reaction, however, **2** is slightly more active than **1a** upon recycling, and no influence of the support is obvious (Figure 5).

For this set of pre-catalysts (complexes **1a** and **2** on FSG and unmodified SG) we also carried out a filtration experiment, where we filtered the hot reaction mixture and monitored the conversion in the filtrate (Figure 6). In the first run, the conversions and the rates of reaction were significantly lower than in the analogous experiments without filtration. In the following runs, however, the conversions

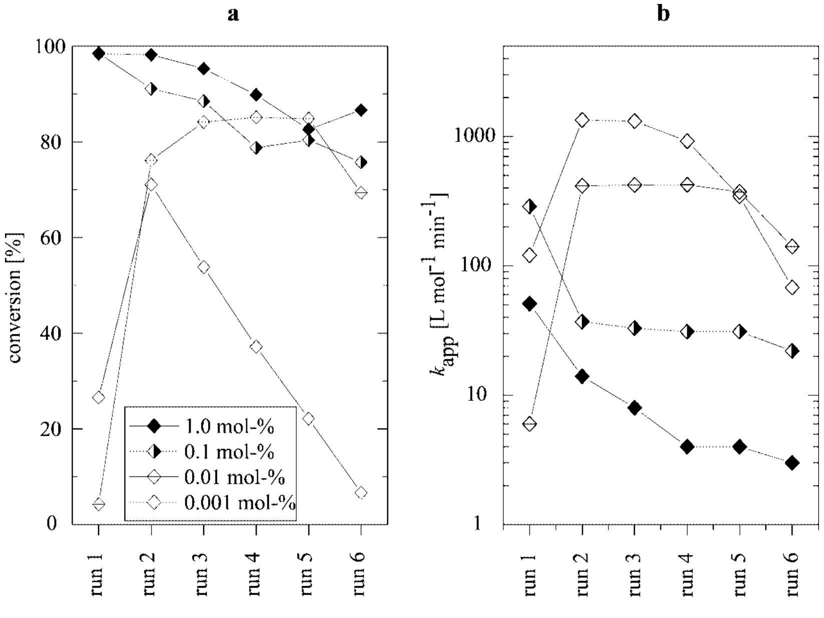


Figure 3. Suzuki coupling of 4-bromomandelic acid and phenylboronic acid in water with different amounts of complex **1a** on FSG. **a**: conversion, **b**: rate constant.

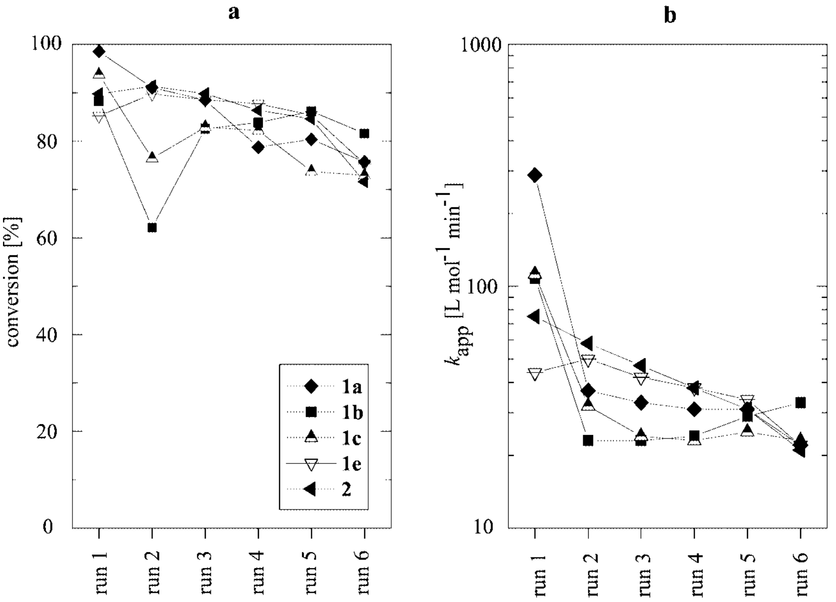


Figure 4. Comparison of different supported complexes in the coupling of 4-bromomandelic acid and phenylboronic acid in water with 0.1 mol-% Pd. **a**: conversion, **b**: rate constant.

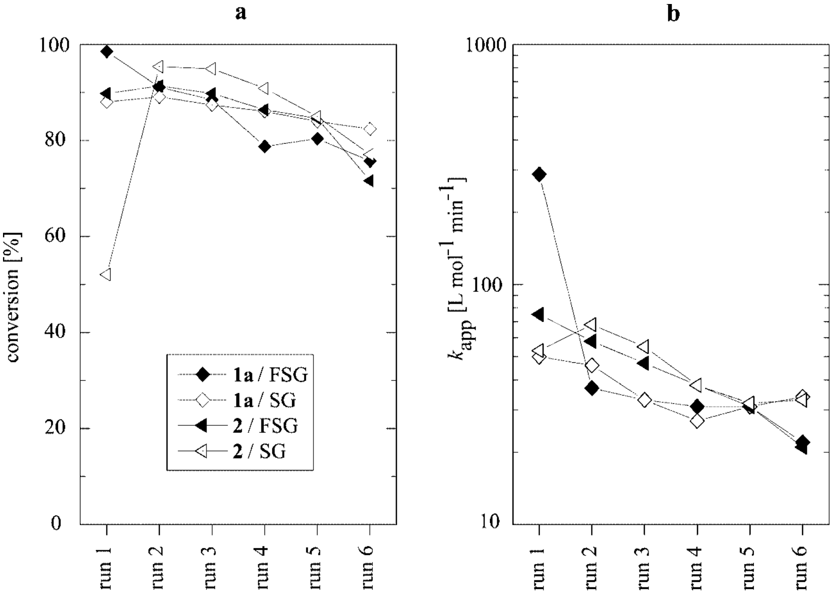


Figure 5. Comparison of perfluoro-tagged and untagged complexes on FSG and SG in the coupling of 4-bromomandelic acid and phenylboronic acid in water with 0.1 mol-% Pd. **a**: conversion, **b**: rate constant.

were in the usual range again, and the rate constants were even higher than in the analogous series. No significant systematic influence of either the fluorous tag or the support material is apparent. This result is strongly in favour of a homogeneously dissolved catalytic species, and is in accordance with the already reported results of a three-phase test.[10]

A puzzling result, however, is the observation that the reactions are slower with fresh complex than with reused catalyst, as had already been observed for smaller catalyst loadings of 0.01 and 0.001 mol-%. The most obvious explanation would be a slow catalyst-activation step, which generates the catalytically active species from the Pd complex. This should lead to an activation period or at least to non-first-order kinetics in the first run. In the event, we did not observe any activation period,[19] and the conversions closely followed first-order kinetics.

Since we suspected that insufficient wetting of the solid support might be the reason for lower conversions and rates of reaction in the first run, a further series of experiments was performed with pre-wetting of the supported complex. Thus, the support was shaken with a small amount of methanol and then filtered prior to the actual first cross-coupling reaction. We speculated that this procedure would remove the air from the pores of the support and cover it with a film of methanol, which should facilitate the subsequent

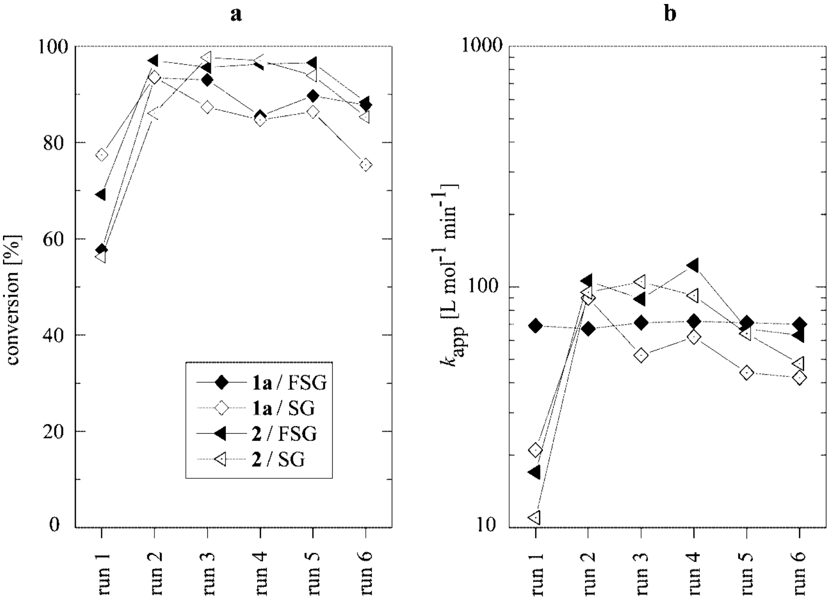


Figure 6. Filtration experiment with perfluoro-tagged and untagged complexes on FSG and SG in the coupling of 4-bromomandelic acid and phenylboronic acid in water with 0.1 mol-% Pd. **a**: conversion, **b**: rate constant.

wetting of the support by the aqueous reaction mixture. Again, complexes **1a** and **2** on FSG and SG were used as catalyst sources for these comparative experiments, but this time with an initial loading of 0.01 mol-% (Figure 7). In the control experiments without pre-wetting, both catalysts on FSG gave low conversions in the first runs, while with SG as support the conversion was above 80% already in the initial run. In the following runs the yields were in the range between 75 and 95% and no influence of the support or pre-catalyst was apparent. The same picture also arises from the rates of reaction. The complexes on FSG were 50 times slower than the complexes on SG during the first run. In the second and third runs, however, the rate constants were similar for all four catalyst support combinations. In the pre-wetting experiment the reactivities were completely altered. The conversion with the perfluoro-tagged complex **1a** on FSG was already high in the first run and decreased slightly to 85% in the third run. The conversions for the same complex on SG were considerably lower and remained in the range between 50 and 60%. The unmodified complex **2** on either support led only to low conversions of between 0 and 20%. Also, in terms of the rate of reaction the influence of the perfluoro tag is clearly visible. The rate constant in the first run for the perfluoro-tagged complex **1a** is 20 times larger than for complex **2**, independent of the support. This difference increased further upon recycling of the catalyst. Clearly, the pre-wetting procedure is beneficial only for the perfluoro-tagged complex on FSG, but is detrimental for the unmodified complex. A possible explanation for this observation could be that wetting of the FSG with water is indeed facilitated by washing it with methanol, whereas the unmodified complex is largely washed off the support, thus leading to low catalytic activities.

On the basis of these results, we carried out several experiments using bidentate perfluoro-tagged complexes **4a**–**c** as pre-catalysts. All three complexes were tested with Pd loadings of 0.001, 0.01 and 0.1 mol-% on both FSG and SG using the pre-wetting procedure. A few experiments with the corresponding unmodified ligands were carried out for comparison.

For complex **4a**, high conversions were generally obtained in the range of 80 to 100%, the only exception being the lowest catalyst loading on SG. The cumulative TON over six runs for 0.001 mol-% **4a** on FSG was 484000, which is 2.5 times the TON for the monodentate complex **1a** (Figure 8). With regard to the rate constants, the same phenomenon as for complex **1a** was observed: the rate constants decreased only slightly upon recycling, and decreasing the catalyst loading by one order of magnitude increased k_{app} by approximately one order of magnitude. Except for the lowest catalyst loading on SG, which gave a lower rate of reaction, there is no influence of the support material. The rates are slightly higher than with the monodentate complex **1a**. The only pronounced difference was seen for the lowest catalyst loading of 0.001 mol-% **4a**, where k_{app} was larger by a factor of 4 and remained at a high level through all six runs, in contrast to **1a**. Due to the pre-wetting, the results were more regular for the initial run, with the only exception being that for 0.01 mol-% **4a** on FSG, where a lower activity was initially observed.

Very similar results were obtained for complex **4b** (Figure 9): the yields remained at a high level of 75–95% over six runs, again with the exception of the lowest catalyst loading on SG. The rates of reaction were similar to the ones observed for **4a**. Although less clear-cut, the same pattern emerges, with lower loadings giving higher values of

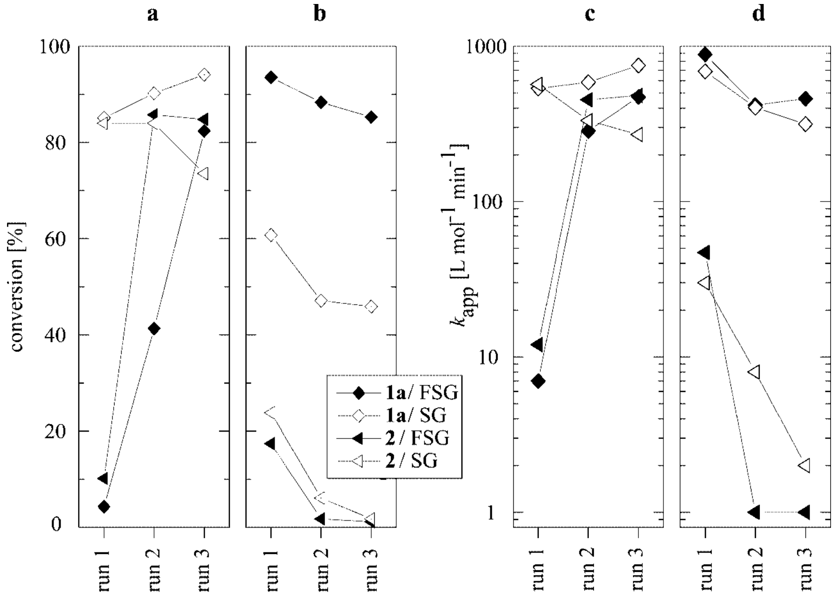


Figure 7. Influence of pre-wetting of the supported complex on the coupling of 4-bromomandelic acid and phenylboronic acid in water with 0.1 mol-% Pd. Comparison of perfluoro-tagged and untagged complexes on FSG and SG. **a**: conversion without pre-wetting; **b**: conversion with pre-wetting with MeOH; **c**: rate constant without pre-wetting; **d**: rate constant with pre-wetting with MeOH.

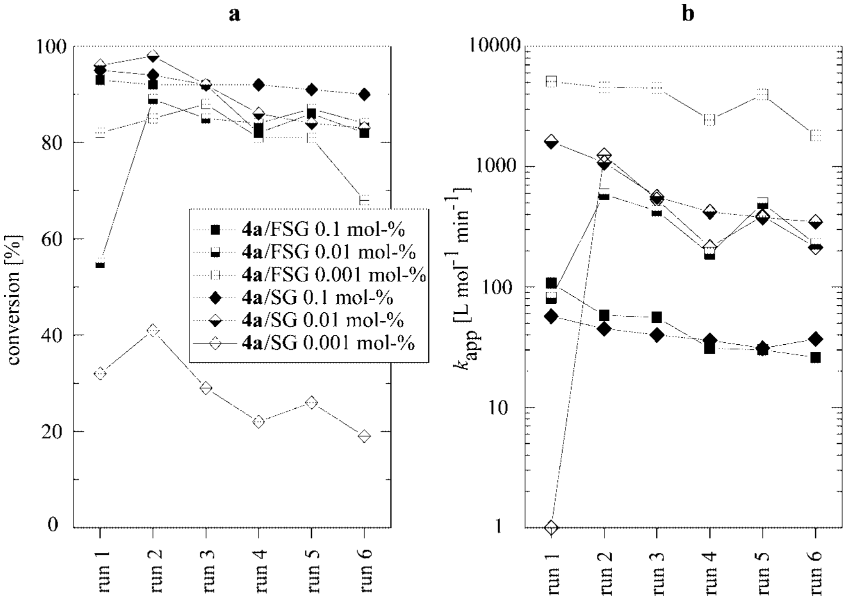


Figure 8. Suzuki coupling of 4-bromomandelic acid and phenylboronic acid in water with different amounts of complex **4a** on FSG and SG with pre-wetting of the support with MeOH. **a**: conversion, **b**: rate constant.

k_{app} and no influence of the support material. Much lower conversions were obtained for the corresponding untagged complex **5**, and the rates of reactions were lower with a larger random variation. This, again, is in accordance with our initial investigation of the influence of the pre-wetting with methanol.

The results for complex **4c** were similar to the ones obtained with **4a** and **4b**. The conversions remained above 80%, and only with the lowest catalyst loading did the conversion decrease from approx. 85% in the first run to 40% in the last run, which still led to a cumulated TON of 389000, almost twice as much as for the monodentate complex **1a** (Figure 10).

In general, the reactions exhibit a considerably different behaviour depending on whether water or DME is used as solvent. In organic solvents there is a significant decrease of activity upon recycling of the catalyst, while for very active substrates, although the yields of cross-coupling product remained high, the rates of reaction clearly decreased. For less reactive substrates a drop in yield as well as rate of reaction was obvious when the catalyst was recycled. This could be a combined result of catalyst leaching and catalyst decom-

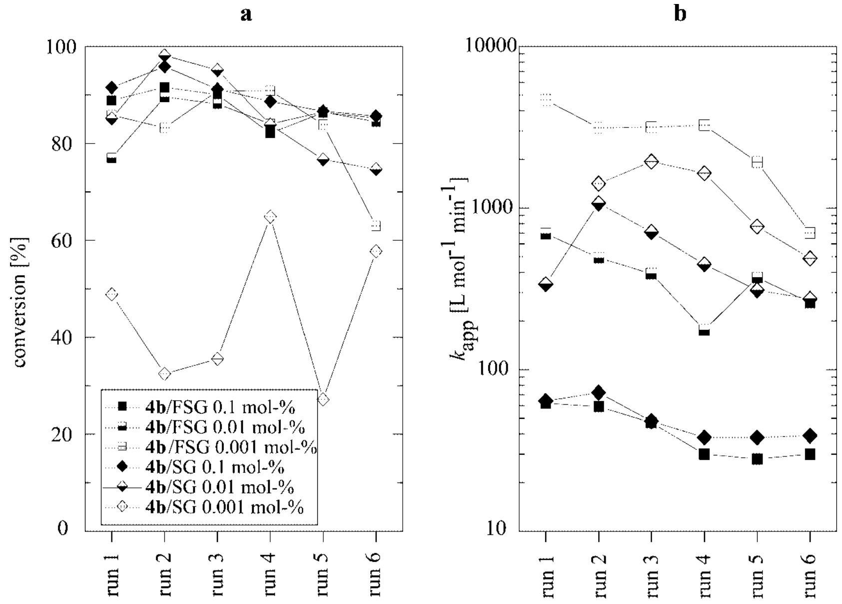


Figure 9. Suzuki coupling of 4-bromomandelic acid and phenylboronic acid in water with different amounts of complex **4b** on FSG and SG with pre-wetting of the support with MeOH. **a**: conversion, **b**: rate constant.

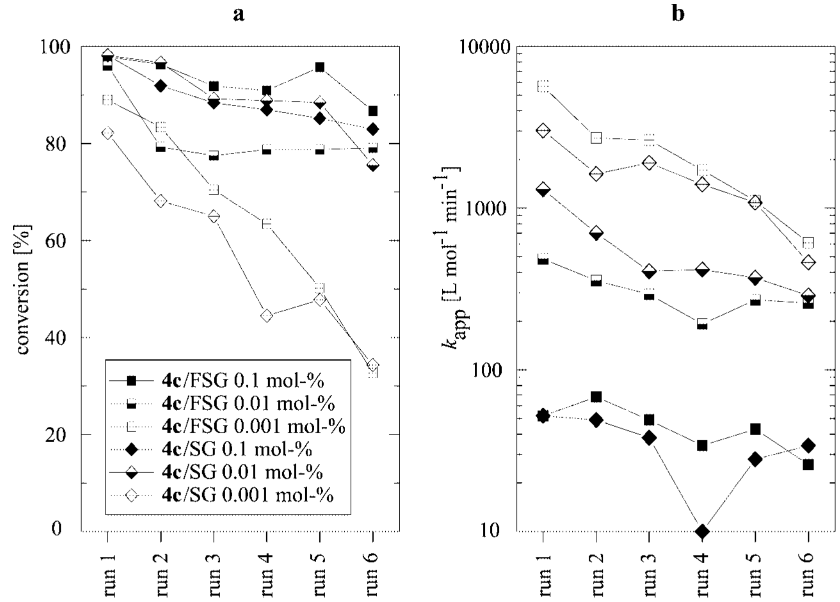


Figure 10. Suzuki coupling of 4-bromomandelic acid and phenylboronic acid in water with different amounts of complex **4c** on FSG and SG with pre-wetting of the support with MeOH. **a**: conversion, **b**: rate constant.

position, but since the Pd content of the products were small, the latter process seems to be the most relevant one.

In water as solvent a completely different behaviour was observed. The conversion to cross-coupling product remained high over six runs, and the rate of reaction decreased only slightly for catalyst loadings of 0.01 mol-% or above. Surprisingly, the rates of reaction showed only a small dependence on the catalyst loading, which results in increasing observed rate constants with lower catalyst loading. The conclusion from this observation is that the amount of actual catalytically active species is almost independent of the initial pre-catalyst loading. Furthermore, the influence of the support material (FSG or SG) and the nature of the pre-catalyst is small. Only with 0.001 mol-% of complexes **4a** and **4b** were significantly higher rates of reaction and conversions observed in comparison to the complexes with monodentate ligands. Filtration experiments and a three-phase test clearly indicated that the catalytic reaction occurs homogeneously in solution and not heterogeneously on the surface of the support material. These results lead us to the assumption that the homogeneously dissolved catalytic species no longer contains phosphane ligands and is rather solvated by water molecules or anions in the reaction mixture. Comparable ligand-free Pd catalysts have been reported for Heck reactions with so called homeopathic catalyst loadings.[18] Therefore no significant difference between perfluoro-tagged complexes and untagged complex **2** is observed. Likewise, the nature of the support does not exert a detectable influence. We surmise that different phosphane ligands only exert an influence on the stability of the insoluble Pd reservoir. The process of conversion of the initial complex into such a reservoir is not well understood. However, the wetting of the support seems to play an important role, at least for lower catalyst loadings, since low activities are sometimes observed with the very hydrophobic FSG as support. Pre-wetting with methanol to remove air from the pores and cover the surface with a hydrophilic film alleviates this problem for perfluoro-tagged complexes. A very interesting aspect of the catalyst activation appears to be the influence of pre-wetting with methanol on untagged complex **2**. While **2** without pre-wetting yields high conversions and reaction rates upon reuse of the support, washing with methanol prior to the first reaction largely removes the catalytic activity. This latter observation can clearly be interpreted as the result of washing the pre-catalyst off the support. However, since methanol was also employed in the work-up in-between the reactions, it is obvious that the complex is converted into a catalyst reservoir, which more strongly adheres to the support regardless of whether it is FSG or SG. However, on the basis of these results we cannot distinguish whether the catalyst is truly recycled or the support acts only as a Pd reservoir.

Conclusions

We have investigated a set of different perfluoro-tagged Pd complexes with mono- and bidentate ligands on FSG or SG as support as reusable catalysts for the Suzuki cross-coupling reaction in organic solvents and water. In organic solvents the activity decreases upon recycling, therefore the catalyst is clearly not reusable under these conditions, which we attribute to catalyst decomposition rather than catalyst leaching. In water, the behaviour is completely different: significantly higher cumulative TONs are observed, and the activity remains at a high level upon reuse of the supported complex. This clearly indicates, once again, that yields obtained in repetitive cycles alone are not appropriate to judge the reusability of catalysts. Instead, it becomes obvious that the rates of reaction have also to be investigated in order to assess the true potential of a catalytic system. Although reusability of catalysts is frequently claimed, thorough investigations including rates of reaction are rarely published. While in our case it still remains debatable whether the catalytic species itself is truly recycled in the Suzuki reactions in water, the high turnover numbers and the low Pd leaching open interesting practical opportunities for Suzuki couplings of polar substrates in water as the sole reaction medium.

Experimental Section

General: All reagents and solvents were obtained from either Fluka or Aldrich and were used without further purification. 1-Bromo-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)benzene (**6**) and 1-bromo-4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-2-methylbenzene (**10**) were prepared according to the literature.[15] Methylenebis(dichlorophosphane) ($Cl_2PCH_2PCl_2$) was prepared according to the literature.[20] ($C_6F_{13}CH_2CH_2$–)FSG was prepared from SG (particle size: 100–300 µm; pore size: 500 Å; specific surface: 70–90 $m^2 g^{-1}$), obtained from Grace, and ($C_6F_{13}CH_2CH_2$)Si(OEt)$_3$ as described earlier.[21] Melting points were measured with an IA9000 apparatus from Electrothermal Engineering Ltd. and are uncorrected. NMR Spectra: chemical shifts δ are given in ppm relative to Si(CH$_3$)$_4$ (δ = 0 ppm) for ^{1}H NMR, CHCl$_3$ (δ = 77 ppm) for ^{13}C NMR and 85% aq. H$_3$PO$_4$ (δ = 0 ppm) for ^{31}P NMR. MS: Finnegan MAT8200 (EI), MAT312 (CI) and TSQ7000 (ESI) mass spectrometers. HPLC: Agilent 1100 system with binary pump, sample changer, column oven and diode array detector.

1,2-Bis{bis[4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl]phosphanyl}methane (7a): Under argon, a solution of *n*-butyllithium (8.0 mL, 2.5 M in hexane) was added dropwise to a solution of **6** (12.12 g, 20.096 mmol) in anhydrous THF/Et$_2$O (1:1, 40 mL) keeping the bath temperature below –30 °C. The yellow-green solution was stirred for 10 min, after which freshly distilled Cl$_2$PCH$_2$PCl$_2$ (1.09 g, 5.005 mmol) dissolved in 3 mL of anhydrous THF was added dropwise at –30 °C and the resulting purple mixture was stirred at room temperature for 3 h. The solution was filtered through SiO$_2$ under argon, eluting with anhydrous Et$_2$O (3 × 30 mL). The solvent was removed under reduced pressure to afford a pale-yellow solid (10.4 g, 90%). The compound (containing around 7% of oxide) could be recrystallised from Et$_2$O/MeOH to give the product as a white powder (7.51 g, 65% yield) or purified by column chromatography [silica gel 0.063–0.2 mm, cyclohexane/ethyl acetate (10:1), R_f = 0.32] under argon to give **7a** (6.19 g, 57%). M.p. 89 °C. ^{1}H NMR (300 MHz, C$_6$F$_6$/C$_6$D$_6$ capillary): δ = 2.8 (t, $^2J_{P,H}$ = 1.5 Hz, 2 H, C*H*$_2$-P), 2.28–2.42 (m, 8 H, C*H*$_2$-Ar), 2.89–2.96 (m, 8 H, C*H*$_2$-CF$_2$), 7.2–7.38 (m, 16 H, Ar) ppm. ^{13}C NMR [75 MHz, C$_6$D$_6$/C$_6$F$_6$, 1:1 (*v*/*v*)]: δ = 28.2 (t, $^1J_{C,P}$ = 24.2 Hz, *C*H$_2$-P), 32.6 (t, $^2J_{C,F}$ = 22.0 Hz, *C*H$_2$CF$_2$), 104.8–123.4 (m, C$_8$F$_{17}$), 128.4 (d, $^3J_{C,P}$ = 6.3 Hz, *m*-C, Ar), 133.4 (d, $^2J_{C,P}$ = 18.2 Hz, *o*-C, Ar), 137.2 (d, $^1J_{C,P}$ = 12.3 Hz, *C*-P, Ar), 139.8 (s, *p*-C, Ar) ppm. ^{31}P NMR (162 MHz, C$_6$F$_6$/C$_6$D$_6$ capillary): δ = –22.2 ppm. MS (ESI-dir.): *m*/*z* (%) = 2168 (20) [M$^+$], 2216 (35), 2215 (68), 1750 (44), 1749 (100), 1283 (21), 1167 (16), 596 (23).

1,2-Bis{bis[4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl]phosphanyl}ethane (7b): Under argon, a solution of *n*-butyllithium (8.0 mL, 2.5 M in hexane) was added dropwise to a solution of **6** (12.12 g, 20.096 mmol) in anhydrous THF/Et$_2$O (1:1, 40 mL) keeping the bath temperature below –30 °C. The yellow-green solution was stirred for 10 min, after which freshly distilled Cl$_2$PCH$_2$CH$_2$PCl$_2$ (from ABCR; 1.16 g, 5.005 mmol) dissolved in 3 mL anhydrous THF was added dropwise at –30 °C and the resulting purple mixture was stirred at room temperature for 3 h. The solution was filtered through SiO$_2$ under argon, eluting with anhydrous Et$_2$O (3 × 30 mL). The solvents were removed under reduced pressure to afford 10.4 g of a pale-yellow solid (10.7 g, 92%). The product (containing around 9% of oxide) could be purified by column chromatography [silica gel 0.063-0.2 mm, cyclohexane/ethyl acetate (10:1), R_f = 0.34] under argon to give **7b** (7.32 g, 67% yield). M.p. 82 °C. ^{1}H NMR (300 MHz, C$_6$F$_6$/C$_6$D$_6$ capillary): δ = 2.1 (s, 4 H, C*H*$_2$P), 2.3–2.5 (m, 8 H, C*H*$_2$-Ar), 2.8–3.1 (m, 8 H, C*H*$_2$-CF$_2$), 7.2–7.4 (m, 16 H, Ar) ppm. ^{13}C NMR [75 MHz, C_6D_6/C_6F_6, 1:1 (*v*/*v*)]: δ = 26.3 (s, $C\mathrm{H_2}$-Ar), 27.4–29.2 (m, P-$C\mathrm{H_2}$), 32.6 (t, $^3J_{C,F}$ = 22.1 Hz, $C\mathrm{H_2CF_2}$), 104.5–123.3 (m, C_8F_{17}), 128.4 (d, $^3J_{C,P}$ = 6.4 Hz, *m*-C, Ar), 133.3 (d, $^2J_{C,P}$ = 18.6 Hz, *o*-C, Ar), 137.2 (d, $^1J_{C,P}$ = 12.1 Hz, I-P, Ar), 140.1 (s, *p*-C, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = –13.8 ppm. MS (ESI-dir.): *m*/*z* (%) = 2182 (32) [M$^+$], 2230 (25), 2229 (58), 1954 (14), 1876 (12), 1749 (44), 1748 (100), 1283 (11), 1187 (16), 596 (19).

Bis[4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl]phosphane Oxide (8): A solution of *n*-butyllithium (4.0 mL, 2.5 M in hexane) was added dropwise, under argon, to a solution of **6** (6.06 g, 10.048 mmol), cooled to –40 °C, in anhydrous Et_2O (70 mL) keeping the bath temperature below –35 °C. The yellow-green solution was stirred for 10 min. Then, freshly distilled Et_2NPCl_2 (871 mg, 5.005 mmol) dissolved in 10 mL of anhydrous Et_2O was added slowly dropwise at –35 °C. The resulting purple mixture was warmed to 0 °C over 30 min and was further stirred at room temperature overnight. The reaction was monitored by ^{31}P NMR spectroscopy (δ = –4.2 ppm). Concentrated aqueous hydrogen chloride (3.0 mL, 36 mmol) was then added and the mixture was stirred at room temperature for an additional 3 h. Water (50 mL) was added, the ethereal layer was separated and the aqueous layer was further extracted with diethyl ether (3 × 50 ml). The combined diethyl ether layers were washed with brine and dried with $MgSO_4$. Diethyl ether was removed under reduced pressure and the residue was purified by column chromatography (silica gel 0.063-0.2 mm, cyclohexane/ethyl acetate, 10:1), to give the product (3.64 g, 66.5%). ^{1}H NMR (300 MHz, C_6F_6/C_6D_6 capillary): δ = 2.28–2.49 (m, 8 H, $\mathrm{C}H_2$-Ar), 2.78–3.22 (m, 8 H, $\mathrm{C}H_2$-CF_2), 7.4 (dd, *J* = 8.2 Hz, 2.1 Hz, 4 H), 7.7 (dd, *J* = 13.6 Hz, 8.2 Hz, 4 H), 8.12 (d, $^1J_{P,H}$ = 483.1 Hz, 1 H, P-*H*) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 22.8 ppm.

1,2-Bis{bis[4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl]phosphanyl}propane (7c): Sodium hydride (0.133 g, 60% suspension in oil, 3.33 mmol) was added at room temperature, under argon, to a solution of **8** (3.9 g, 3.33 mmol) in 20 mL of dry THF. The resulting mixture was stirred at room temperature for 30 min. A solution of 1,3-dibromopropane (336.1 mg, 1.665 mmol) in THF (2 mL) was then added slowly. After stirring at room temperature for 4 h, water (2 mL) was added. The THF was partially removed in vacuo and the residue was extracted with benzotrifluoride (BTF; 3 × 10 mL). The combined BTF layers were dried with $MgSO_4$, the solvent was removed under reduced pressure and the residue was dried under vacuum overnight. [^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 21.36 ppm]. The residue was then redissolved in BTF (50 mL) and trichlorosilane (2.4 mL) and triethylamine (3.5 mL) were added under argon. The mixture was refluxed for 8 h, and the reaction was monitored by ^{31}P NMR spectroscopy. The reaction mixture was then cooled to room temperature and 50 mL of 30% sodium hydroxide aqueous solution (previously degassed with argon) was added. The resulting mixture was stirred at room temperature under argon until both layers were clear. The organic layer was separated and the aqueous layer was further extracted with BTF (3 × 30 mL). The combined organic layers were dried with $MgSO_4$, the solvent was removed under reduced pressure, and the residue was dried under vacuum overnight and purified by column chromatography (silica gel 0.063–0.2 mm, cyclohexane/ethyl acetate, 10:1), to give **7c** (2.01 g, 55%) as a white solid. M.p. 78 °C. ^{1}H NMR (300 MHz, C_6F_6/C_6D_6 capillary): δ = 1.64 (m, 2 H, $\mathrm{C}H_2\mathrm{CH_2P}$), 2.23 (t, *J* = 7.5 Hz, 4 H, $\mathrm{CH_2C}H_2\mathrm{P}$), 2.38 (tt, *J* = 18.2, 9.3 Hz, 8 H, $\mathrm{C}H_2$-Ar), 2.89–2.96 (m, 8 H, $\mathrm{C}H_2$-CF_2), 7.18 (d, *J* = 7.5 Hz, 8 H, Ar), 7.33–7.39 (m, 8 H, Ar) ppm. ^{13}C NMR [75 MHz, C_6D_6/C_6F_6, 1:1 (*v*/*v*)]: δ = 22.3 (t, $^2J_{C,P}$ = 16.4 Hz, $\mathrm{CH_2}C\mathrm{H_2CH_2}$), 26,3 (s, $C\mathrm{H_2}$-Ar), 29.5 (t, $^1J_{C,P}$ = 14.3 Hz, P-$C\mathrm{H_2}$), 32.7 (t, $^2J_{C,F}$ = 22.1 Hz, $C\mathrm{H_2CF_2}$), 104.6–123.2 (m, C_8F_{17}), 128.6 (d, $^3J_{C,P}$ = 6.4 Hz, *m*-C, Ar), 133.2 (d, $^2J_{C,P}$ = 18.6 Hz, *o*-C, Ar), 137.1 (d, $^1J_{C,P}$ = 12.1 Hz, C-P, Ar), 139.9 (s, *p*-C, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = –18.1 ppm.

Tris[4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-2-methyl]phosphane (10): A solution of *n*-butyllithium (4.0 mL, 2.5 M in hexane) under argon was added dropwise to a solution of **9** (6.17 g, 10 mmol) in anhydrous THF/Et_2O (1:1, 40 mL) keeping the bath temperature below –30 °C. The yellow-green solution was stirred for 15 min. Then, freshly distilled PCl_3 (456 mg, 3.3 mmol) in 10 mL of THF was added dropwise. The reaction was monitored by ^{31}P NMR spectroscopy. The solution was filtered through silica gel under argon, eluting with anhydrous Et_2O (3 × 30 mL). The solvents were removed under reduced pressure and the product, which contained approx. 10% of oxide, was purified by column chromatography [silica gel 0.063–0.2 mm, cyclohexane/ethyl acetate (10:1), R_f = 0.36] under argon to give the title compound (3.14 g, 58% yield). M.p. 76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32–2.52 (m, 6 H, $\mathrm{C}H_2$-Si), 2.5 (s, 9 H, $\mathrm{C}H_3$), 2.88–2.96 (m, $\mathrm{C}H_2$-CF_2), 6.7 (dd, *J* = 7.8, 4.2 Hz, 3 H, H^5), 7.0 (d, *J* = 7.8 Hz, 3 H, H^6), 7.1 (d, *J* = 3.4 Hz, 3 H, H^3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1 (d, $^3J_{C,P}$ = 21.2 Hz, $C\mathrm{H_3}$), 26.1 (s, $C\mathrm{H_2}$-Ar), 32.7 (t, $^2J_{C,F}$ = 22.1 Hz, $C\mathrm{H_2CF_2}$), 125.9 (s, C^5, Ar), 130.2 (s, C^3, Ar), 132.6 (d, $^1J_{C,P}$ = 10.6 Hz, C^1, Ar), 133.4 (s, C^6), 139.6 (s, C^4, Ar), 143.2 (d, $^2J_{C,P}$ = 26.6 Hz, C^2, Ar) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = –30.44 ppm.

General Procedure for Preparation of $PdCl_2$ Complexes 4a–c of Bidentate Ligands. Method A: A solution of Na_2PdCl_4 (264.77 mg, 0.90 mmol) in 50 mL of MeOH was added dropwise, at room temperature, to a solution of perfluoro-tagged bidentate phosphane (0.922 mmol) in 200 mL of THF. The reaction mixture was then stirred at room temperature for a further 12 h. The precipitated yellow Pd complex was separated by filtration and washed with distilled water (2 × 20 mL), MeOH (2 × 20 mL) and Et_2O (2 × 10 mL).

Method B: A solution of $[PdCl_2(CH_3CN)_2]$ (233.47 mg, 0.90 mmol) in 50 mL of CH_2Cl_2 was added dropwise, at room temperature, to a solution of perfluoro-tagged bidentate phosphane (0.922 mmol) in 200 mL of THF. The reaction mixture was then stirred at room temperature for a further 12 h. The precipitated yellowish Pd complex was separated by filtration and washed with CH_2Cl_2 (2 × 20 mL) and Et_2O (2 × 10 mL).

[{Bis[*P*,*P*′-{4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl}phosphanyl]methane-*P*,*P*′}dichloropalladium(II)] (4a): Yellow solid. Yield: 1.94 g, (92%). ^{1}H NMR (400 MHz, C_6F_6/C_6D_6 capillary): δ = 2.3–2.5 (m, 8 H, $\mathrm{C}H_2$-Ar), 2.9–3.2 (m, 8 H, $\mathrm{C}H_2$-CF_2), 4.3 (t, $^2J_{P,H}$ = 11.2 Hz, 2 H, P-$\mathrm{C}H_2$-P), 7.1–8.2 (m, 16 H, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = –54.2 ppm.* MS (ESI-dir.): *m*/*z* (%) = 2343 (9) [M]$^+$, 2325 (9) [M – F + H]$^+$, 2307 (21) [M – Cl]$^+$, 2243 (15), 2242 (62), 2241 (100), 1617 (16), 700 (14), 699 (32), 671 (31), 663 (22). $C_{65}H_{34}Cl_2F_{68}P_2Pd$ (2346.1): calcd. C 33.28, H 1.46, P 2.64; found C 33.26, H 1.57, P 2.48. * cf. ^{31}P NMR chemical shift of the Pd complex of bis(diphenylphosphanyl)methane (δ = –53.7 ppm).[22]

[{Bis[*P*,*P*′-{4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl}phosphanyl]ethane-*P*,*P*′}dichloropalladium(II)] (4b): Yellow solid. Yield: 1.91 g, (90%). ^{1}H NMR (400 MHz, C_6F_6/C_6D_6 capillary): δ = 2.2–2.5 (m, 8 H, $\mathrm{C}H_2$-Ar and 4 H P-$\mathrm{C}H_2$), 2.8–3.1 (m, 8 H, $\mathrm{C}H_2$-CF_2), 7.0–8.1 (m, 16 H, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 62.2 ppm. MS (ESI-dir.): *m*/*z* (%) = 2357 (8) [M]$^+$, 2341 (13) [MH – F + H]$^+$, 2323 (91) [M –

Cl]$^+$, 2215 (100) [M – Pd – Cl – H]$^+$, 1749 (27), 1659 (22), 1617 (34), 1179 (12), 1151 (13), 699 (65), 672 (25), 671 (55), 537 (45). $C_{66}H_{36}Cl_2F_{68}P_2Pd$ (2360.2): calcd. C 33.59, H 1.54, P 2.62; found C 33.43, H 1.60, P 2.29.

[{Bis[*P*,*P*′-{4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)phenyl}phosphanyl]propane-*P*,*P*′}dichloropalladium(II)] (4c): Yellow solid. Yield: 1.84 g, (86%). ^{1}H NMR (400 MHz, C_6F_6/C_6D_6 capillary): δ = 1.8–2.6 [m, 6 H, P-$(CH_2)_3$ and 8 H, CH_2-Ar], 2.89–3.25 (m, 8 H, CH_2-CF_2), 7.12–8.07 (m, 16 H, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 11.4 ppm. MS (ESI-dir.): *m*/*z* (%) = 2371 (7) [M]$^+$, 2354 (12) [M – F + H]$^+$, 2337 (41) [M – Cl]$^+$, 2310 (100), 1334 (38), 1333 (27), 1306 (19), 1300 (16), 1276 (26), 1228 (36), 1201 (47). $C_{67}H_{38}Cl_2F_{68}P_2Pd$ (2374.2): calcd. C 33.90, H 1.61, P 2.61; found C 34.32, H 1.71, P 2.49.

Preparation of *trans*-[Di(μ-acetato)bis{4-[bis{(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)(2-methyl)phenyl}phosphanyl]benzyl-*P*,*C*}dipalladium(II)] (3b): A solution of $Pd(OAc)_2$ (134.7 mg, 0.600 mmol) in 20 mL of THF was added dropwise to a solution of **10** (1.0 g, 0.609 mmol) in 20 mL of THF and the reaction mixture was stirred for 12 h. The resulting yellow-green solid was filtered and washed with distilled water (2 × 10 mL), MeOH (2 × 10 mL) and Et_2O (2 × 10 mL). The product was dried in vacuo. Yield: 965 mg (89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.98 (s, 6 H, CH_3), 2.15 (br. s, 6 H, CH_3), 2.32–2.52 (m, 6 H, CH_2-Si and m, 2 H, CH_aH_b-Pd), 2.82–2.95 (m, 6 H, CH_2-CF_2; m, 2 H, CH_aH_b-Pd; s, 6 H, CH_3), 6.5–7.15 (br. m, 18 H, Ar) ppm. ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 29.7 ppm. MS (ESI-dir.): *m*/*z* (%) = 3995 (5), 3234 (5), 2570 (5), 1822 (8) [1/2 MH + O]$^+$, 1821 (9) [1/2 M + O]$^+$, 1805 (4) [1/2 M]$^+$, 1722 (26), 1700 (10), 1669 (14), 1641 (25), 1640 (30), 1639 (13), 1623 (15), 1622 (45), 1618 (39), 1617 (75), 1547 (46), 1546 (100), 1545 (48), 1522 (44), 1521 (44), 1502 (34), 1501 (21), 1500 (19). $C_{106}H_{62}F_{102}O_4P_2Pd_2$ (3614.3): calcd. C 35.23, H 1.78, P 1.71; found C 35.62, H 1.97, P 1.71.

Preparation of *trans*-[Bis{4-[bis{(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)(2-methyl)phenyl}phosphanyl]benzyl-*P*,*C*}di(μ-chloro)dipalladium(II)] (3a): A solution of LiCl (6.35 mg, 0.15 mmol) in MeOH (10 mL) was added dropwise to a solution of **3b** (216.8 mg, 0.06 mmol) in THF/Et_2O (1:1, 40 mL). A yellow-green solid precipitated immediately and the reaction mixture was stirred for an additional 2 h. The yellow-green solid was filtered, washed with water (2 × 10 mL), MeOH (2 × 10 mL) and Et_2O (2 × 10 mL), and dried under vacuum. Yield: 196.9 g, (92%). ^{31}P NMR (162 MHz, C_6F_6/C_6D_6 capillary): δ = 26.44 ppm. MS (ESI-dir.): *m*/*z* (%) = 3563 (4) [M]$^+$, 2570 (4), 1798 (8) [1/2 MH + O]$^+$, 1797 (7) [1/2 M + O]$^+$, 1781 (5) [1/2 M]$^+$, 1724 (13), 1723 (10), 1670 (12), 1641 (25), 1639 (20), 1639 (11), 1622 (14), 1621 (45), 1618 (12), 1617 (39), 1616 (65), 1563 (18), 1547 (46), 1546 (100), 1545 (48), 1522 (42), 1521 (43), 1502 (33), 1501 (22), 1500 (18). $C_{102}H_{58}Cl_2F_{102}P_2Pd_2$ (3567.1): calcd. C 34.35, H 1.64, P 1.74; found C 34.65, H 1.79, P 1.53.

Typical Preparation of Supported Complexes: Palladium complex **1a** (30.5 mg, 9.03 μmol) was dissolved in BTF (2 mL). The yellow solution was diluted with diethyl ether (300 mL) and FSG (3020 mg) was added. The solvent was removed by rotary evaporation. Diethyl ether (300 mL) was added to the dry FSG and the solvent was again removed by rotary evaporation. This was repeated once more. Drying in vacuo gave the FSG-supported complex (3040 mg) as a pale-yellow, free-flowing solid with a calculated loading of 2.97 μmol g^{-1}. The other complexes employed in this study were supported on FSG or SG in a similar manner. Supported complexes were prepared with palladium loadings of 0.03, 0.3, 3 and 30 μmol g^{-1}.

Typical Procedure for Recycling Experiments in DME: A stock solution of the substrates in DME (3 mL, containing 0.3 mmol of 4-bromobenzyl alcohol and 0.33 mmol of phenylboronic acid) and an aqueous solution of potassium carbonate (0.5 mL, 0.6 mmol) were added to the FSG-supported catalyst (100 mg) under argon. The reaction mixture was shaken with a frequency of 900 min^{-1} at 80 °C for 16 h. Aliquots (20 μL) of the solution were withdrawn after 15, 30, 45, 60, 75, 90, 105, 120, 240, 480 and 960 min, and the conversion was measured by HPLC analysis. The reaction mixture was then cooled to 20 °C and filtered. The FSG was washed with DME (2 × 2 mL), water (2 × 2 mL) and DME (2 × 2 mL). The immobilized catalyst was reused as such in further experiments. All manipulations were carried out automatically (Automated Synthesis Workstation ASW 2000, Chemspeed Ltd., Augst, Switzerland).

HPLC Analysis: Separations were carried out on a C-18 column (Zorbax SB, 3 μm, 4.6 × 50 mm) with water/acetonitrile (1:1, *v*/*v*) as isocratic eluent and detection at 210 nm. Conversions were calculated from the ratio of the peak areas of 4-bromobenzyl alcohol and 4-phenylbenzyl alcohol corrected for the extinction coefficients.

Calculation of Rate Constants: $\ln(1 - x)$, where x is the conversion, was plotted against time. The slope, K, was calculated by linear regression. The apparent rate constant was calculated as $k_{app} = -K\,V_{rxn}/n_{Pd}$, where n_{Pd} is the molar amount of pre-catalyst and V_{rxn} is the reaction volume [see Equation (2)].

Typical Procedure for Recycling Experiments in Water: An aqueous stock solution of the substrates (3 mL, containing 0.3 mmol of 4-bromomandelic acid, 0.33 mmol of phenylboronic acid and 0.6 mmol of Na_2CO_3) was added to the FSG-supported catalyst (100 mg containing 0.003, 0.03, 0.3 or 3 μmol of Pd complex) under argon. The reaction mixture was shaken with a frequency of 900 min^{-1} at 80 °C for 16 h. Aliquots (20 μL) of the solution were withdrawn after 15, 30, 45, 60, 75, 90, 105, 120, 240, 480 and 960 min, and the conversion was measured by HPLC analysis. The reaction mixture was then cooled to 20 °C and filtered. The FSG was washed with methanolic HCl (2 × 1 mL, 1 M, MeOH/H_2O, 11:1), MeOH (2 × 1 mL) and water (2 × 1 mL). The immobilized catalyst was reused as such in further experiments. All manipulations were carried out automatically.

HPLC Analysis: Separations were carried out on a C-18 column (Zorbax SB, 3 μm, 4.6 × 50 mm) with water/acetonitrile/formic acid (70:30:0.2, *v*/*v*) as isocratic eluent and detection at 210 nm. Conversions were calculated from the ratio of the peak areas of 4-bromomandelic acid and 4-phenylmandelic acid corrected for the extinction coefficients.

Typical Procedure for Filtration Experiments: The experiments were carried out as described above for the recycling experiments in water with the modification that the reaction mixture was filtered (suction filtration) after withdrawal of the second sample. The following samples were withdrawn from the filtrate.

Typical Procedure for Experiments with Pre-wetting of the Support: The experiments were carried out as described above for the recycling experiments in water with the modification that the supported complex was shaken with methanolic HCl (2 × 1 mL, 1 M, MeOH/H_2O, 11:1) and MeOH (2 × 1 mL) and filtered prior to the first reaction.

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