Nanofiltration for Homogeneous Catalysis Separation: Soluble Polymer-Supported Palladium Catalysts for Heck, Sonogashira, and Suzuki Coupling of Aryl Halides

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The anionic polymerization of 4-methylstyrene results in a linear poly(4-methylstyrene), whose substoichiometric bromination with Br_2 converts a portion of 5−18% of the $-CH_3$ units into $-CH_2Br$ groups, which were then reacted with $(1-Ad)_2PH$ to synthesize a polymer loaded with sterically demanding and electron-rich $-CH_2P(1-Ad)_2$ groups as the respective air-stable phosphonium salt. Palladium complexes with the phosphinated polymer are efficient catalysts for carbon−carbon coupling reactions of the Sonogashira, Suzuki, and Heck type with aryl chlorides and bromides. The molecular weight of the respective phosphines in the range of 5−35 kDa does not have a significant effect on the catalytic performance. Such polymer-enlarged catalysts are suitable for separation over a solvent-resistant nanofiltration membrane composed of a dense poly(dimethylsiloxane) (PDMS) layer cast on a porous sublayer of poly(acrylonitrile) (PAN). The membrane displays virtually quantitative retention of the polymeric catalyst; furthermore palladium could not be found in the permeate; TXRF and spectrophotometric determinations are indicative of >99.95% retention of the catalyst. The activity of the catalyst retained in the retentate is almost unchanged, as shown by the high (typically >90%) and almost constant yields of the coupling reactions as well as by the constant turnover frequencies of the catalysts following the membrane separation experiments during up to nine cycles of Sonogashira and Suzuki reactions. For the Heck coupling the used polar aprotic solvents best suited for the catalytic reaction lead to rapid deterioration of the membranes tested.

Introduction

Following the development of suitable membranes for nonaqueous applications,[1,2] the utilization of ultra- and nanofiltration techniques has now become an attractive option for the separation of catalyst and product in homogeneous catalysis.[3−5] Membrane technology offers the possibility of continuously separating catalysts from the product in a nondestructive way and re-feeding the catalyst into the process.

Although homogeneous catalysts often display unmatched activities and selectivities, which can be easily tuned to meet the specific demands of a wide variety of substrates,[6] in industrial processes heterogeneous catalysis is still dominant. The decisive drawback of homogeneous catalysis results from the loss of the active catalyst during the isolation of products. Recovery of a (noble) metal catalyst is useful not only for obvious economic reasons but also because contamination of a product by heavy metal impurities is undesirable and must be limited to sub-ppm levels.[7] Consequently numerous approaches have been tested, aiming toward efficient recovery and reuse of the active catalyst utilizing various immobilization techniques of molecular catalysts on solid or colloidal supports,[8−10] encapsulation,[11] interphase chemistry,[12] and phase-tagging for biphasic catalysis[13−15] or ionic liquids.[16]

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Nonaqueous nanofiltration in combination with homogeneously catalyzed reactions has been applied primarily for the separation of molecular weight increased homogeneous catalysts for (enantioselective) hydrogenation reactions,[17] the Kharasch addition,[18] hydrovinylation,[19] allylic substitution,[20] and allylic amination[21] by attaching linear polymers or dendrimers to the ligands coordinating the catalytically active metal.[3,22] In some cases membranes with a correspondingly lower molecular weight cutoff have been applied to separate unmodified catalysts from the organic products. This approach has certain advantages since functional groups need not be attached to the catalyst; however, it also results in lower fluxes and modest (<99%) catalyst retention.[23,24]

We are interested in Pd-catalyzed carbon—carbon coupling reactions of the Heck, Sonogashira, and Suzuki type,[25] which are also used in fine chemicals synthesis, even though currently heterogeneous catalysts are preferred.[26] The application of nanofiltration techniques to such reactions appears to be limited to the pioneering work of Livingston, Vankelecom, et al., who reported on Heck coupling reactions on aryl iodides.[23,27] Nonetheless, it should be kept in mind that for such reactive substrates a number of highly competitive heterogeneous catalysts are known.[28]

Our motivation is to develop catalysts for the Heck,[29] Sonogashira,[30] and Suzuki[31] type coupling with activities high enough to compete with the best heterogeneous catalysts for such reactions. To allow a highly efficient separation of the catalyst from the coupling products with nanofiltration membranes, we adopted the concept of polymer-enlarged homogeneous catalysts.[32,33] In the present study we used hydrophobic membranes developed at GKSS which are resistant in a broad variety of organic solvents and are capable of separating low molecular weight components from organic solutions at reasonably high fluxes.[2]

Results and Discussion

Synthesis of the Soluble Polymer-Supported Phosphonium Salts. We decided to use linear poly-(*p*-methylstyrene) as a soluble polymeric support for carbon—carbon coupling catalyst.[34] Polystyrene appears to be ideal, since it does not contain functional groups that could interfere with the Pd-based catalyst. The purpose of the methyl group is twofold: First it is needed to increase the solubility of the respective polymer in nonpolar solvents, and second this group can be functionalized easily to allow the introduction of metal ligating groups.

Several low dispersity poly(*p*-methylstyrenes) with a molecular weight of 5, 11, 20, and 35 kDa were prepared by anionic polymerization of *p*-methylstyrene.[35] These polymers were reacted with substoichiometric amounts of Br_2 to yield partially bromomethylated polymers with 5, 10, 15, or 18% of the $-CH_3$ groups converted to $-CH_2Br$ (Scheme 1). The bromination was found to exclusively occur at the p-CH_3 units, while the polymer backbone and the aromatic ring remain unchanged, as has previously been observed by Tsiang et al. for the bromination of a copolymer of methylstyrene, styrene, butene, and ethene.[36]

In this manner polymer **2** was prepared in various molecular masses and with different $-CH_2Br$ loadings: 5 kDa (5, 10, 15, and 18% $-CH_2Br$) and 11, 20, and 35 kDa each with 15% $-CH_2Br$.[37] The bromination approach was chosen as it allows the easy variation of the amount of reactive groups (and later the number of catalytically active centers) and since the $-CH_2Br$ unit is more reactive than $-CH_2Cl$ in polystyrenes obtained via chloromethylation of styrene,[38] copolymers of styrene and (CH_2Cl)-styrene,[39] or chlorination of poly(methylstyrene).[40]

A sterically demanding and electron-rich phosphine was chosen for loading onto the polymer since such

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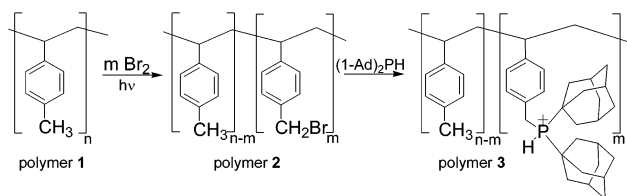(36) Tsai, C. Y.; Huang, C. P.; Tsiang, R. C. *J. Polym. Chem. A. Polym. Chem.* **1999**, *37*, 4108.

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Scheme 1

Table 1. Sonogashira Coupling of Aryl Bromides[a]

Entry	R	R'	Pd (mol%)	time (h)	yield (%)
1	CH₃CO	Ph	0.5	2	96
2	H	Ph	0.5	2.5	89
3	OCH₃	Ph	1	5	85
4	CH₃CO	Me₃Si	2	13	91
5	H	Me₃Si	2	16	87
6	OCH₃	Me₃Si	2	16	85
7	CH₃CO	n-C₆H₁₃	2	16	90
8	H	n-C₆H₁₃	3	16	85
9	OCH₃	n-C₆H₁₃	3	16	80

[a] Reaction conditions: 1.0 equiv aryl halide, 1.5 equiv acetylene, Pd(PhCN)$_2$Cl$_2$, polymeric phosphine (2 L/Pd), isolated yields after chromatography.

ligands are known to form highly efficient palladium catalysts with suitable metal sources.[41] The metal ligating $-$P(1-Ad)$_2$ group was attached to the polymer by reacting (1-Ad)$_2$PH and polymer **2** at 125 °C in xylene for 20 h (Scheme 1). In the ^{1}H NMR spectrum of polymer **3** the signal at 4.4 ppm corresponding to $-$CH$_2$Br was found to be missing and a new signal at 3.4 ppm is observed, which is assigned to the methylene protons of the $-$CH$_2$PH(1-Ad)$_2^+$ group. This suggests quantitative substitution of the $-$Br with the phosphine on the polymer. When performing this reaction on various polymers with $-$CH$_2$Br content of up to 18%, it was observed that only polymers with ≤15% $-$CH$_2$Br content can be quantitatively loaded with HP(1-Ad)$_2$. Attempts on 18% $-$CH$_2$Br polymer **2** result in incomplete phosphination, as evidenced by the presence of $-$CH$_2$Br groups, which is attributed to the precipitation of phosphonium salt polymer **3** from the xylene solution prior to completion of the reaction. However, we had no desire to aim for higher phosphine loading since we expect the catalyst performance to suffer from a higher concentration of metal ligating groups on the polymer. This argument arises because a Pd(PR$_3$)$_1$ complex is considered to be the catalytically most active species,[42,43] whose concentration will be decreased on high phosphine loading on the polymer.

The phosphonium salt polymer is air-stable[44] and conveniently used directly for catalysis since under the basic conditions needed for the coupling reactions it is deprotonated immediately to form the desired Pd complex.

Influence of the Nature of the Polymeric Phosphine on the Catalyst Performance. Prior to studying in detail the coupling reactions utilizing the polymer-based catalysts, we were interested in finding out whether the molecular mass of the polymer or its loading with $-$CH$_2$P(1-Ad)$_2$ groups has a significant influence on the catalyst performance. For this purpose we investigated a few representative Sonogashira coupling reactions. The respective phosphonium polymer **3**, Pd(PhCN)$_2$Cl$_2$, HN^{i}Pr$_2$, and the substrates (PhCCH and aryl bromide) were mixed in toluene to form the desired catalyst in situ, and the coupling reaction was carried out. The catalytic activity of polymer samples of 5 kDa loaded with 5, 10, and 15% of phosphine ligand

was tested by carrying out Sonogashira reactions on them. The three samples showed the same activity per $-$CH$_2$P(1-Ad)$_2$ group when activated substrates such as 4-bromoacetophenone and PhCCH were used, but with deactivated substrates (4-bromoanisol and 1-octyne) the 15% loaded polymer gave slightly better results. It seems that a 15% loading is low enough to avoid significant deactivation by chelation. Somewhat to our surprise the molecular mass of the polymer (5, 11, 20, or 35 kDa) with constant phosphine loading did not play a significant role in the catalytic activity.

Coupling Reactions. For each of the three different coupling reactions to be studied, the respective catalysts were optimized individually. The palladium catalyst is always formed in situ after combining a suitable metal source, the polymeric phosphine, a base, and the respective coupling partners.

Sonogashira Coupling. First the Sonogashira reaction was studied, and optimum reaction conditions utilizing the polymeric phosphine and (PhCN)$_2$PdCl$_2$ as the palladium source were looked for by performing a solvent/base screen. Among the solvents (THF, DMF, dioxane, DMA, DME, cyclohexane, toluene) and bases (Et$_3$N, Na$_2$CO$_3$, K$_3$PO$_4$, HN^{i}Pr$_2$) studied, the best results were observed in toluene solvent using HN^{i}Pr$_2$ as a base. This combination performed somewhat better than DMA/HN^{i}Pr$_2$, whereas in all other solvents the coupling yields were found to be low. The conditions are thus related to the one used by Buchwald, Fu, et al. for the Sonogashira coupling using a low molecular weight catalyst.[45]

The high efficiency of this catalyst is demonstrated for a number of coupling reactions, all of which are performed in excellent yields (Table 1). The acetylene substrates used display the typical reactivity order observed in Sonogashira coupling reactions: aryl-CCH > R$_3$SiCCH > alkyl-CCH. A subset of the reactions in Table 1 was chosen for nanofiltration experiments. The coupling reactions were conducted as described above, but after completion of the respective reaction the solution was filtered over a hydrophobic membrane

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Table 2. Sonogashira Coupling of Aryl Bromides Applying Nanofiltration[d]

R—⟨⟩—Br	acetylene	time (h)	conversion (%)/ cycle[47]							final yield/ cycle[c] (%)
			1	2	3	4	5	6	7	
R= CH$_3$CO[a]	PhC≡CH	2	98	98	95	89	85	80	80	86
H[a]	PhC≡CH	2.5	91	89	87	87	-	-	-	86
OCH$_3$[b]	PhC≡CH	5	87	84	84	80	-	-	-	81

[a] 0.5 mol % Pd. [b] 1.0 mol % Pd. [c] Yield after chromatographic purification averaged per cycle, conversions determined by GC. [d] Reaction conditions: 2.0 equiv aryl halide, 2.5 equiv acetylene, Pd(PhCN)$_2$Cl$_2$, polymeric phosphine (2 L/Pd).

composed of a dense poly(dimethylsiloxane) (PDMS) layer cast on a porous sublayer of poly(acrylonitrile) (PAN) as described in detail in the Experimental Section.[46] Following each membrane filtration experiment new reactants were added to the catalyst containing retentate and the next reaction was initiated. There was no need to add fresh CuI. This metal most likely forms a Cu-phosphine complex, which appears to be retained by the membrane. The results of the different catalytic cycles experiments are summarized in Table 2.

The coupling reactions result in excellent yields of product. The conversions were found to be between 80 and 95% and remain almost constant over the four to seven cycles studied. The final yields per cycle listed in Table 2 correspond to the average amount of product isolated after chromatographic purification of the combined crude products from each of the respective four cycles. The efficiency of catalyst recycling by nanofiltration and the absence of significant catalyst decomposition during the experiment are more convincingly demonstrated by determining the turnover frequencies (tof) of the catalyst[48] over the various cycles.[49] For the coupling of 4-bromoacetophenone and phenylacetylene the tof was found to be virtually constant (cycle (tof): cycle 1 (237 h^{-1}), cycle 2 (230 h^{-1}), cycle 3 (220 h^{-1}), cycle 4 (218 h^{-1})), indicative of excellent recyclability of the polymeric catalyst.

Suzuki Coupling. For the given combination of metal source Pd(OAc)$_2$ and polymeric phosphine ligand, the Suzuki reaction was optimized with respect to the use of solvent (acetonitrile, DMF, DMA, THF, dioxane, DME, toluene) and base (NaF, Na$_2$CO$_3$, K$_3$PO$_4$, HN^{i}Pr$_2$).

The best combination of solvent/base for the reaction of 4-bromoacetophenone and PhB(OH)$_2$ turned out to be toluene/K$_3$PO$_4$. The conditions closely resemble those in the seminal paper of Buchwald et al.[50] on Suzuki coupling reactions using low molecular weight phosphines.

Table 3. Suzuki Coupling of Aryl Bromides and Chlorides[a]

Entry	R	X	R'	Pd (mol%)	time (h)	yield (%)
1	H	Br	H	0.5	3	96
2	4-CO$_2$Et	Br	H	0.5	1	96
3	4-CH$_3$CO	Br	H	0.5	1	95
4	4-OCH$_3$	Br	H	0.5	0.5	87
5	4-CH$_3$CO	Br	2-CH$_3$	1	11	93
6	4-CH$_3$CO	Br	4-OCH$_3$	1	12	87
7	4-CH$_3$CO	Br	2,2'-CH$_3$	1	11	92
8	4-NO$_2$	Cl	H	1	16	86
9	2-CN	Cl	H	3	16	93
10	4-OCH$_3$	Cl	H	1	16	72
11	H	Cl	H	1	14	85
12	4-CH$_3$CO	Cl	H	1	14	94
13	4-CH$_3$CO	Cl	4-OCH$_3$	3	16	92

[a] Reaction conditions: 1.0 equiv aryl halide, 1.5 equiv boronic acid, Pd(OAc)$_2$, polymeric phosphine (2 L/Pd), yields correspond to isolated product after chromatographic purification.

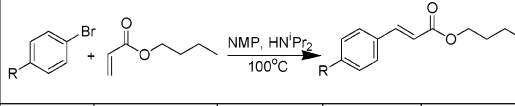### Table 4. Suzuki Coupling Applying Nanofiltration[d]

R	X	time (h)	conversion (%)/cycle									final yield/ cycle[c]
			1	2	3	4	5	6	7	8	9	
CH$_3$CO[a]	Br	1	99	97	97	98	95	95	93	90	90	95
OCH$_3$[a]	Br	7	91	90	88	88	-	-	-	-	-	88
CH$_3$CO[b]	Cl	14	95	95	92	90	-	-	-	-	-	90
H[b]	Cl	14	86	82	80	81	-	-	-	-	-	81

[a] 0.5 mol %. [b] 1.0 mol %, polymer (2 L/Pd). [c] Final yield after chromatographic purification. [d] Reaction conditions: 2.0 equiv aryl halide, 3.0 equiv boronic acid, Pd(OAc)$_2$, polymeric phosphine.

The results of the various coupling reactions are summarized in Table 3 and demonstrate the excellent activity of the catalyst used for the coupling reactions. The yields for the reactions of aryl bromides are between 87 and 96%, even for sterically demanding aryl boronic acids. For the coupling of aryl chlorides coupling yields are between 72 and 93%.

Again a subset of these reactions was chosen for nanofiltration and recycling experiments. The conversions for each cycle are high (80−99%) and remain almost constant over the reaction cycles (Table 4). Consequently the yields of purified coupling products are between 81 and 95% (calculated as the average of

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Table 5. Heck Coupling of Aryl Bromides[b]

Entry	R	Pd (mol%)	time (h)	yield (%)[a]
1	CH₃CO	0.5	16	87
2	H	0.5	16	84
3	OCH₃	0.5	16	80

[a] Yield after chromatographic purification, *E* isomer > 95%.
[b] Reaction conditions: 1.0 equiv aryl halide, 1.3 equiv *n*-butyl-acrylate, polymeric phosphine (2 L/Pd).

all individual reactions). Further evidence for the excellent recyclability of the Suzuki coupling is provided by determining the tof for a single set of reactions, here the coupling of 4-bromoacetophenone and PhB(OH)$_2$: cycle (tof): cycle 1 (290 h^{-1}), cycle 2 (305 h^{-1}), cycle 3 (300 h^{-1}), cycle 4 (300 h^{-1}).

The highly efficient recycling of a single batch of the soluble poly(methylstyrene) based catalyst by nanofiltration is convincingly demonstrated by performing a long-term experiment, in which the reaction is repeated nine times (Table 4). These data compare very favorably with those obtained by Buchwald et al. on the recycling of insoluble, cross-linked polystyrene-supported Suzuki catalysts, which already suffer a very significant loss in activity after the second or third recycling step.[51]

Heck Coupling. Using Pd(dba)$_2$ as a metal source together with the polymeric phosphine the Heck coupling of 4-bromoacetophenone and *n*-butylacrylate was optimized in a variety of solvent/base combinations (toluene, DMA, DME, NMP, and Et$_3$N, Hunig base, Cy$_2$NH, K$_2$CO$_3$). According to coupling yields NMP/HN^{i}Pr$_2$ turns out to be the best solvent/base combination. The results of the coupling experiments are listed in Table 5. The coupling yields for the three coupling reactions studied are 80–87% using relatively low concentration of catalyst (0.5 mol %).

However, on attempting the nanofiltration of the NMP solution, the membrane immediately suffered severe damage. This is not entirely surprising since it is well known that polar, aprotic solvents are detrimental to most polymeric membranes.[52] Unfortunately, we could not find a solvent that is tolerated by the polymeric membrane and still gives coupling yields nearly as good as those in NMP. According to publications from Hartwig et al.,[53] Beller et al.,[54] and Herrmann et al.[55] polar, aprotic solvents tend to give the best results for the Heck coupling, while Fu obtained high-activity catalysts in dioxane solvent.[56] However, in the case of our polymeric catalysts, the use of dioxane according to Fu gave only poor coupling yields even when using sterically more demanding amines as bases.

Table 6. Heck Coupling of Aryl Bromides Applying Nanofiltration[b]

	olefin	time (h)	(%)conversion / cycle				Final yield/cycle[a] (%)
			1	2	3	4	
CH₃CO	*n*-butylacrylate	16	87	77	51	29	55
H	*n*-butylacrylate	16	85	71	40	25	52

[a] Yield after chromatographic purification, *E* isomer > 95%.
[b] Reaction conditions: 1.5 equiv aryl bromide, 1.8 equiv *n*-butyl-acrylate, Pd(dba)$_2$ 0.5 mol %, polymer (2 L/Pd).

To still be able to perform nanofiltration experiments, we diluted the NMP solution after the reaction with a large amount of cyclohexane (which was evaporated prior to the next cycle). This solution containing less than 5 vol % of NMP could be filtered without immediate damage to the membrane. However, even when using this cumbersome procedure, the results are not entirely satisfying, as the coupling yields listed in Table 6 show that the catalyst performance suffers significantly after the second cycle. It is thus obvious that the solvents needed to realize high activity catalysts for Heck coupling reactions are not compatible with membranes presently available; newly developed, prototype membranes stable in aprotic polar solvents might be more suitable.[57]

Retention of the Catalyst. The performance of the chosen membrane−catalyst−solvent system for nanofiltration can be assessed in terms of catalyst performance, membrane stability, and catalyst rejection. The virtually quantitative retention of the catalyst in the retentate is essential for the usefulness of catalysis using nanofiltration. Thus for Sonogashira, Suzuki, and Heck coupling reactions, using poly(methylstyrene)-supported Pd catalysts, the absence of significant leaching of the catalyst into the permeate is indicated by the high yields of the catalytic transformations and the constant tof over the reaction cycles. Nonetheless a possible loss of polymer into the respective product in the permeate was checked, but we were not able to detect any polymer by ^{1}H NMR spectroscopy in the crude products. On the basis of these data we thus estimate the polymer leaching to be significantly smaller than 0.5%. Secondly, for the coupling reactions the amount of palladium lost into the permeate was determined by two independent methods: total reflection XRF and UV spectrophotometrically using the colorimetric reagent 4,4′-bis(dimethylamino)thiobenzophenone.[58] With both methods the amount of palladium in the permeate was found to be below the detection level of the respective analytical technique, and we thus conclude that the retention of the catalyst by the membrane is higher than 99.95%.

Summary and Conclusion

A polymer-enlarged catalyst formed from (1-Ad)$_2$P-substituted poly(methylstyrene), a suitable palladium source [Pd(PhCN)$_2$Cl$_2$, Pd(OAc)$_2$, or Pd(dba)$_2$], and a

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base (HN^iPr_2 or K_3PO_4 and the substrates) can be used to efficiently mediate carbon–carbon coupling reactions of the Suzuki, the Sonogashira, and the Heck type of aryl bromides and chlorides. Such catalysts were also studied in nanofiltration separation experiments. The linear 5000 Da polymer backbone is sufficiently large to be retained virtually quantitatively by a PDMS nanofiltration membrane. The leaching of the catalyst into the product containing permeate is very small (<0.05%); consequently the product is not contaminated with palladium. Furthermore the catalyst was reused up to nine times by using the catalyst containing retentate after filtration from the product. The efficient recyclability of the catalyst is evidenced by the constant and high yields of the coupling reaction for the Sonogashira and the Suzuki reaction and the virtually unchanged tof of these coupling reactions. In the case of the Heck coupling, however, the highly polar and aprotic solvents needed to realize high catalyst activities are detrimental to the integrity of polymeric membranes. In conclusion, for Sonogashira and Suzuki coupling reactions catalyst performance, membrane stability, and catalyst rejection are ideally met. In the case of Heck coupling reactions the applied membranes are not stable in the solvents typically used.

Experimental Section

General Methods. Aryl halides, acetylenes, and *n*-butyl-acrylate were used as received. All reactions and nanofiltration experiments were performed under an atmosphere of dry argon using standard Schlenk techniques. Column chromatography: silica MN60 (63–200 μm), tlc on Merck plates coated with silica gel 60, F254. Gas chromatography: Perkin-Elmer Autosystem. NMR spectroscopy: spectra recorded at 293 K with a Bruker Avance 500 (^{1}H NMR 500 MHz, ^{13}C NMR 125 MHz, ^{31}P NMR 203 MHz), a Bruker AC 300 (^{1}H NMR 300 MHz, ^{13}C NMR 75 MHz), or a Bruker AC 200 (^{1}H NMR 200 MHz, ^{31}P NMR 81 MHz) spectrometer. ^{1}H NMR spectra were referenced to residual protonated impurities in the solvent, ^{13}C NMR to the solvent signal (CDCl$_3$: $\delta_H = 7.24$ ppm, $\delta_C = 77.0$ ppm), and ^{31}P NMR to PMe$_3$ (38% in benzene $\delta = -62$ ppm) or aqeous H$_3$PO$_4$ as external standard. Molecular weights (M_n, M_w) were determined by GPC using a Jasco PU-980 pump and a Jasco UV-975 UV/vis detector equipped with PL Gel (type D and E, 300 × 7.5, particle size 5.0 μm) columns. Polystyrene standards in the range $M_n = 1600-76\,000$ were used for calibration. Starting materials were commercially available (PhB(OH)$_2$ was purchased from Merck) or prepared according to literature procedures: (1-Ad)$_2$PH,[59] Pd(PhCN)$_2$Cl$_2$, Pd(CH$_3$CN)$_2$Cl$_2$,[60] and arylboronic acids.[61] The coupling products obtained from Sonogashira, Suzuki, and Heck reactions were characterized by ^{1}H NMR spectroscopy; spectral data were found to be identical to those reported in the literature.[38c,45,50,62,63]

Nanofiltration Experiments. The membranes used for the nanofiltration experiments are composite membranes consisting of a porous poly(acrylonitrile) membrane with a selective layer of chemically and radiationally cross-linked poly(dimethylsiloxane) (PDMS).[46] Prior to the nanofiltration experiments the membranes were characterized by oxygen and nitrogen fluxes. All membranes possessed an oxygen/nitrogen

selectivity of 2.1, which is intrinsically for PDMS and indicates that the PDMS layer is defect-free. The pure toluene permeability of the membranes is about 11 L/h m² bar.

The nanofiltration experiments were performed in a glovebox under argon atmosphere with a stirred dead-end cell from Millipore with an effective membrane area of 13.9×10^{-4} m². Generally, dead-end cells are not optimized with respect to mass transfer but are very suitable for feasibility studies as performed in this study. The membranes were placed in the cell with the selective side upward. Afterward the cell was filled with the catalyst-containing solution and closed. Since swelling plays an important role in the application of polymeric membranes in nonaqueous solution, the membranes were preconditioned in toluene for about 30 min. After this time the solvent fluxes through the membranes appeared to be stable. Pure solvent fluxes were measured at 5 bar, while the fluxes with the catalyst-containing solutions were determined at 4–6 bar. Prior to filling the cell the reaction solutions were prefiltered over a Schlenk filter in order to remove salts. The salt was washed with the respective solvent, which was then added to the solution in the cell. This procedure was carried out three times. Permeate and retentate of the experiments were collected and analyzed as described above. Due to practical limitations (only one test cell could be placed in the glovebox), each catalytic cycle was performed with a fresh membrane stamp. The membrane separation tests for each catalytic cycle last approximately 2 h, during which the permeability of the membranes remained practically constant, indicating that the membranes were in the steady state and no membrane deterioration occurred.

Spectrophotometric Determination of Palladium (modified from ref 58). Determination of palladium using 4,4′-bis-(dimethylamino)thiobenzophenone was linear in the range 0–0.8 μg mL^{-1} with the coefficient of regression (R^2) of 0.9989 at pH 3.0–4.5. Test Sonogashira, Suzuki, and Heck reactions were carried out, and after the completion of reaction, the reaction solution was nanofiltered using the membrane cell. Toluene (cyclohexane/NMP in the case of Heck reaction) from the permeate of each of the reactions was evaporated to 2 mL and treated with 4,4′-bis(dimethylamino)thiobenzophenone solution (2 mL, 1 mM in ethanol) maintained at pH 3.5 with acetic acid. The final volume of the solution was made to 20 mL using ethanol, and the amount of Pd leached out in the permeate was determined photometrically at 523 nm.

Synthesis of Poly(*p*-methylstyrene) (polymer 1). Poly-(*p*-methylstyrene) was prepared by anionic polymerization.[5] *n*-Butyllithium (5 mmol, 1.85 mL of 2.7 M) was added to a stirred solution of *p*-methylstyrene (25 g, 0.2 mol), tmeda (1 mL), and cyclohexane (150 mL) under argon atmosphere. The color of the solution changed from colorless to dark red, indicating the formation of poly(*p*-methylstyrene) anions. The reaction mixture was allowed to stir for 90 min at room temperature before terminating the polymerization with 5 mL of methanol. The final polymer was precipitated in 2-propanol and dried under vacuum for 12 h. Yield: 24.5 g (97%), $M_n = 5260$, PDI = 1.05. For the synthesis of poly(*p*-methylstyrene) of M_n 11, 20, and 35 kDa, under the same experimental conditions 0.84, 0.46, and 0.26 mL of the initiator was used, respectively. Yields of the respective polymers were >95%. $M_n = 11\,110$, PDI = 1.04; $M_n = 20\,760$, PDI = 1.03; $M_n = 35\,046$, PDI = 1.09. ^{1}H NMR (CDCl$_3$): 1.3 (b, $-CH_2-$), 1.8 (b, $-CH$-Ph), 2.3 (b, Ph-CH_3), 6.4 (d, *o*-Ar*H*), 6.9 (d, *m*-Ar*H*).

Bromination of Polymer 1 to Give Polymer 2. The methyl groups of the poly(*p*-methylstyrene) were brominated by free radical photoinitiation.[5] Polymer **1** (7.0 g, 0.058 mol) was dissolved in cyclohexane (40 mL), K$_2$CO$_3$ (0.5 g) was added, and a constant temperature of the reaction vessel was maintained by water bath. Bromine liquid (0.57 mL, 3.77 mmol) was introduced, and the reaction was subjected to UV irradiation for 15 min. Afterward the reaction flask was cooled to room temperature, K$_2$CO$_3$ and KBr were filtered off, and the

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polymer was precipitated from the filtrate by adding 2-propanol (200 mL). The resulting polymer **2** was dried under vacuum for 10 h. Polymer **2** was characterized by NMR spectroscopy, and the percent loading of bromine on the methyl groups was found to be 15% with the yield of 96%. For 5, 10, and 18% bromination of the polymer, 0.19, 0.38, and 0.68 mL of bromine was added, respectively. Yields of the respective polymers were >95%. ¹H NMR (CDCl₃): 1.3 (b, −CH_2−), 1.8 (b, −CH-Ph), 2.3 (b, Ph-CH_3), 4.4 (s, Ph-CH_2Br), 6.4 (d, *o*-ArH), 6.9 (d, *m*-ArH). ¹³C NMR (CDCl₃): 142.6 (Ph, *ipso-C*), 134.8 (*p*-ArC), 127.7 (*o*-ArC), 128.7 (*m*-ArC), 45.9 (CH-Ph), 34.1 (−CH_2−), 27.1 (−CH_2Br), 21.2 (−CH_3).

Loading of Phosphine on Polymer 2 to Give Phosphinated Polymer 3. Polymer **2** (15% Br loaded, 7 g, 55 mmol) and (1-Ad)₂PH (11.5 mmol, 3.5 g) were dissolved in xylene (30 mL) and stirred at 125 °C. After 20 h, the reaction mixture was cooled to room temperature and poured into diethyl ether (120 mL). The precipitated polymer was filtered, washed with diethyl ether, and dried under vacuum. Yield: 8.5 g (90%). For the synthesis of 5 and 10% loaded phosphonium salt polymer the amount of (1-Ad)₂PH was varied accordingly. ¹H NMR (CDCl₃): 1.3 (b, −CH_2−), 1.7−2.45 (m, −CH-Ph, Ph-CH_3, −AdH), 3.4 (b, Ph-CH_2P(1-Ad)₂), 6.4 (d, *o*-ArH), 6.9 (d, *m*-ArH). ³¹P NMR (CDCl₃): 23.1. ¹³C NMR (CDCl₃): 142.5 (Ph, *ipso-C*), 134.8 (*p*-ArC), 128.7 (*m*-ArC), 127.7 (*o*-ArC), 45.0 (CH-Ph), 38.3, 37.2 (AdCH₂), 35.7 (CH_2P), 34.1 (−CH_2−), 32.1 (AdC), 27.8 (AdCH), 21.2 (−CH_3).

General Procedure for Sonogashira Reaction. In a Schlenk tube Pd(PhCN)₂Cl₂ (3.8 mg, 1.0 mol %), phosphinated polymer (15% loading with −P(1-Ad)₂, 100 mg, 2 mol % of ligand), CuI (3.0 mg, 1.5 mol %), and HN^{i}Pr₂ (1 mL) were dissolved in toluene (7 mL) with sonication. The respective aryl bromide (1 mmol) and acetylene (1.5 mmol) were added, and the reaction was stirred at 60 °C for a given time. After completion of the reaction, toluene was evaporated and the crude product was purified by column chromatography (cyclohexane/ethyl acetate) to obtain the respective pure products.

General Procedure for Sonogashira Reaction with Nanofiltration. Pd(PhCN)₂Cl₂ (3.8 mg, 0.5 mol %), CuI (5.0 mg, 1.5 mol %), HN^{i}Pr₂ (1 mL), and phosphinated polymer (100 mg, 1 mol %) were dissolved in toluene (20 mL) with sonification. The respective aryl bromide (2 mmol) and PhC≡CH (0.306 mg, 3 mmol) were added, and the reaction was stirred at 60 °C for a given time. The progress of the reaction was monitored by GC. Finally the reaction mixture was filtered from the insoluble ammonium salt, which in turn was washed twice with toluene (2 × 10 mL). The combined solutions were poured into the nanofiltration cell (glovebox) and filtered (by applying 4 bar of N₂ pressure) down to a minimum volume of 5 mL. Another 10 mL of fresh toluene was added to the membrane cell and again filtered to the minimum volume of 5 mL.[64] The remaining retentate was transferred back into the reaction flask. The nanofiltration cell was rinsed twice with fresh toluene (10 mL) to collect back the catalyst and the catalyst solution transferred to the reaction flask. HN^{i}Pr₂ (1 mL) and two substrates were added for the next reaction cycle. This procedure was repeated to perform four reaction cycles. The permeates collected from the four cycles were combined and evaporated. The residue was purified by column chromatography (cyclohexane/ethyl acetate) to obtain the respective pure products.

General Procedure for the Suzuki Reaction. In a Schlenk tube, Pd(OAc)₂ (3.3 mg, 1.5 mol %) and phosphinated polymer (150 mg, 15% loading with −P(1-Ad)₂, 3 mol % of ligand) were dissolved in toluene (7 mL). Aryl halide (1.0 mmol), aryl boronic acid (1.5 mmol), and K₃PO₄ (2 mmol, 420

mg) were added to the solution and stirred at 100 °C until the reactants were consumed. After cooling, the volatiles were evaporated. The residue was purified by column chromatography (cyclohexane/ethyl acetate) to obtain the respective pure product.

General Procedure for Suzuki Reaction with Nanofiltration. Pd(OAc)₂ (2.2 mg, 0.5 mol %) and phosphinated polymer (100 mg, 1 mol %) were dissolved in toluene (20 mL). The respective aryl halide (2 mmol), phenylboronic acid (3 mmol), and K₃PO₄ (4 mmol, 840 mg) were added, and the reaction was stirred at 100 °C. The progress of the reaction was monitored by GC. Finally the reaction mixture was filtered from the insoluble salts and then washed twice with toluene (2 × 10 mL). The combined solutions were poured into the nanofiltration cell (glovebox) and filtered (by applying 4 bar of N₂ pressure) down to a minimum volume of 5 mL. Another 10 mL of fresh toluene was added to the membrane cell and again filtered to the minimum volume of 5 mL. The procedure was repeated two times to ensure that only a minimum amount of coupling product is left in the retentate. The remaining retentate was transferred back into the reaction flask. The nanofiltration cell was rinsed twice with fresh toluene (10 mL) to collect back the catalyst and the catalyst solution transferred to the reaction flask. K₃PO₄ (840 mg) and the two substrates were added for the next reaction cycle. This procedure was repeated to carry out four reaction cycles. The permeates collected from the four cycles were combined and evaporated, and the crude product was purified by column chromatography (cyclohexane/ethyl acetate) to obtain the respective pure products.

General Procedure for the Heck Reaction. In a Schlenk tube, Pd(dba)₂ (2.6 mg, 0.5 mol %) and phosphinated polymer (50 mg, 15% loading with −P(1-Ad)₂, 1 mol % of ligand) were dissolved in NMP (5 mL). Aryl bromide (1.0 mmol), *n*-butylacrylate (1.3 mmol, 166 mg), and HN^{i}Pr₂ (0.5 mL) were added to the solution and stirred at 100 °C until the reactants were consumed. After cooling the volatiles were evaporated. The residue was purified by column chromatography (cyclohexane/ethyl acetate) to obtain the respective pure product.

General Procedure for Heck Reaction with Nanofiltration. To the solution of Pd(dba)₂ (4.0 mg, 0.5 mol %) and phosphinated polymer (75 mg, 1 mol %) in NMP (1.5 mL) were added HN^{i}Pr₂ (0.4 mL), butyl acrylate (1.8 mmol, 230 mg), and the respective aryl bromide (1.5 mmol), and the reaction was stirred at 100 °C. After completion, the reaction mixture was diluted to 45 mL by adding cyclohexane. After a first filtration to remove the ammonium salt, the solution was filtered through the nanofiltration membrane by applying 4 bar of N₂ pressure. The ammonium salt was washed with cyclohexane (20 mL), which was added to the cell and filtered. The retentate (7 mL) was poured back into the reaction flask, and the filtration cell was rinsed with cyclohexane (10 mL). The cyclohexane was removed from the reaction mixture. Fresh NMP (1.5 mL), HN^{i}Pr₂ (0.4 mL), and the two substrates were added to the reaction flask for the next cycle, and a similar procedure was used for the next three cycles. The solvent retentate obtained from the four cycles was poured into water and extracted with diethyl ether. The crude product obtained on evaporating the solvent was purified by column chromatography (cyclohexane/ethyl acetate = 9:1).

(64) Minor modifications to the general procedure were required when determining tof and conversion of the coupling products: The procedure was repeated two times to ensure that only a minimum amount of coupling product is left in the retentate.