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# Solvent-Resistant Nanofiltration for Product Purification and Catalyst Recovery in Click Chemistry Reactions

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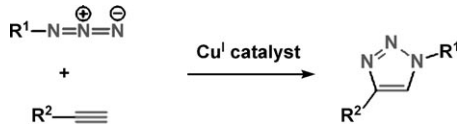
**Abstract:** The quickly developing field of "click" chemistry would undoubtedly benefit from the availability of an easy and efficient technology for product purification to reduce the potential health risks associated with the presence of copper in the final product. Therefore, solvent-resistant nanofiltration (SRNF) membranes have been developed to selectively separate "clicked" polymers from the copper catalyst and solvent. By using these solvent-stable cross-linked polyimide membranes in diafiltration, up to 98% of the initially present copper could be removed through the membrane together with the DMF solvent, the polymer product being almost completely retained. This paper also presents the first SRNF application in which the catalyst permeates through the membrane and the reaction product is retained.

**Keywords:** click chemistry · copper · polymers · product purification · solvent-resistant nanofiltration

## Introduction

The need for new and versatile materials with improved properties has recently led to the search for new synthetic routes. The so-called "click" chemistry receives particular attention as it is an easy and elegant synthetic approach to the coupling of chemical compounds. Of the different "click" reactions described by Sharpless and co-workers,[1] the copper(I)-catalysed Huisgen 1,3-dipolar cycloaddition reactions between azides and terminal alkynes are nowadays one of the most used (Scheme 1). The advantages of such reactions are numerous, namely, high selectivity and functional group tolerance, mild reaction conditions and quantitative yields. Furthermore, the possibility of tailoring the coupling molecules by easily introducing functions in the alkyne and azide at the required location has led to the rapid development of "click" chemistry in many applications.[2–5] In particular, in polymer and materials science, post-modifications using "click" reactions are an efficient and versatile approach to the end-functionalisation of polymers, the synthesis of block copolymers, hyperbranched and dendritic macromolecules and star-shaped polymers.[4–7]




Scheme 1. The copper(I)-catalysed Huisgen 1,3-dipolar cycloaddition reaction.

Owing to the potentially toxic contamination of "click" products, the effective removal of ligand-stabilised copper(I) catalysts from post-reaction solutions is of great importance to meet the specification limits for medicinal use in which significant levels of heavy metal residues are understandably unacceptable.[8] Active pharmaceutical ingredients are mostly synthesised in reactions that utilise homogeneous

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catalysts, which frequently present major separation challenges. Even though copper is considered an essential element with a clear nutritional value, the guidelines of the European Medicines Agency have set the permitted daily exposure (PDE) of patients to copper at 50 $\mu g\,kg^{-1}$ for oral doses and 10 $\mu g\,kg^{-1}$ for parenterally administered drugs.[9]

Recently, great interest has been shown in the development of metal-free strategies for the click reactions of azides and alkynes. Bertozzi and co-workers[10] synthesised strained cycloalkynes to enhance the reactivity of the alkynes, a strategy that was further improved by introducing electron-withdrawing substituents at the $\alpha$ position of the triple bond. Another approach makes use of substituted dibenzocyclooctynes.[11] Lutz recently summarised the research directed towards metal-free azide/alkyne cycloaddition reactions and concluded that the strategies developed will not replace the copper(I)-catalysed reactions in the near future.[12] However, a number of alternative "click" strategies have recently been reported in the search to avoid the use of a copper catalyst.[13] Of these, Diels–Alder "click" reactions,[14] thiol-based "click" reactions[15] and in particular hetero-Diels–Alder cycloaddition reactions[16] are of great interest. However, the copper(I)-catalysed azide/alkyne cycloaddition reaction is expected to remain by far the most widely applied "click" reaction due to the simple and readily available building blocks.[13]

Post-reaction purification technologies commonly used in the separation of homogeneous catalysts used in "click" chemistry include distillation,[17] extraction, ion-exchange,[18] adsorption[19] and the use of ionic liquids[20,21] or supercritical fluids.[22] These work-up methods are usually destructive and require an additional step to regain the catalyst prior to its reuse, which often leads to partial catalyst loss and thus additional cost. At present, hardly any industrially used separation technique is aimed at the recovery of homogeneous catalysts in their active form, but rather at obtaining a pure product whilst recovering the metal in a form that may be recycled to a catalyst.

Alternatively, "click" catalysts can be heterogenised by covalent or non-covalent immobilisation on, for example, silica beads, polystyrene or mesoporous supports.[23–25] Another approach is the immobilisation of the catalyst onto soluble supports[26,27] that can be retained by ultra- or nanofiltration (NF) membranes. However, the use of heterogeneous catalysts results, in general, in slower reaction rates because the ligands do not match the optimal steric and electronic requirements achieved in homogeneous "click" reactions.[8,19]

With the recent development of polymeric membranes, solvent-resistant nanofiltration (SRNF)[28] appears to be a promising alternative that permits the use of homogeneous "click" catalysts and solves the problems arising from the presence of the catalyst in the product after reaction. Such an approach would not only allow the removal of copper from the post-reaction mixture, but also the recovery of the catalyst for reuse in subsequent reactions. The chemical stability and long-term performance of the membranes are crucial because "click" reactions are often carried out in polar aprotic solvents such as dimethylformamide (DMF). These solvents are particularly challenging for polymeric membranes because they are typically used to dissolve polymers prior to membrane formation by phase-inversion.

Much effort has been made in recent years to separate "off-the-shelf" homogeneous catalysts from their reaction mixtures by using SRNF membranes to recycle the catalyst and/or facilitate product purification. The SRNF-coupled recovery of transition-metal complexes has been amply reported in the literature,[17,29–36] for example, palladium coupling catalysts, the cobalt Jacobsen catalyst, ruthenium metathesis catalysts and rhodium hydroformylation catalysts. A hybrid process based on the combined use of a commercial polyimide (PI) membrane and adsorbents has been proposed for palladium removal from post-coupling reaction products.[37] The use of a commercial ceramic nanofiltration (NF) membrane has recently been reported to allow the recovery of "click"-synthesised dendritic phosphine ligands attached to a soluble support used in the palladium-catalysed coupling of aryl halides and phenylboronic acid.[38] However, the use of SRNF membranes to purify "click" products and recycle the unmodified copper catalyst has never been reported.

In this study SRNF was applied to different "click" post-reaction mixtures with DMF and THF as solvents with the objective of purifying the polymeric product and maximally recovering the catalyst. The recently developed cross-linked PI membranes[39,40] are excellent candidates because they are stable in polar aprotic solvents and allow easy tuning of their molecular weight cut-off (MWCO) by modifying the synthetic parameters. Several membranes were prepared and screened for their separation properties in the filtration of a typical "click" post-reaction mixture. The optimal membrane was then selected and applied in a diafiltration experiment in which the impurities, copper and any residual reagent, were progressively "washed out" together with the solvent. In contrast to earlier SRNF/catalysis studies in which the catalyst was always retained by the membrane,[28] in this work we envisaged the retention of the relatively large polymeric product and permeation of the catalyst. Such an approach has significant advantages because the purified product is also concentrated on the feed side of the membrane, which facilitates subsequent isolation, whereas the catalyst remains basically in its original environment, thus minimising deactivation processes due to increased concentration.

## Results and Discussion

**Membrane screening**: Three asymmetric PI membranes were prepared by phase inversion[41] and subsequently cross-linked with aromatic diamines to allow filtration in demanding solvents such as DMF and THF.[39] Phase inversion involves a controlled transformation of a polymeric solution into a solid film, which in this case was induced by immersion of a cast polymer film in a non-solvent bath (immer-

sion/precipitation). Owing to the miscibility of the solvent in the film and of water in the non-solvent bath, the latter diffuses into the polymer film and procures the solidification of the developing membrane structure. Crucial for the formation of a selective top layer, and thus for NF selectivity, is the short exposure of the cast film to the atmosphere (60 s in this case) prior to immersion in the coagulation bath because this allows partial evaporation of the solvents from the film surface.[41] The PI membranes prepared differ in polymer concentration and/or the NMP/THF solvent ratio of the dopes from which they are cast, as can be seen in Table 4 (see the Experimental Section). These membranes were screened by using different "click" post-reaction mixtures obtained from the reactions of typical alkynes and azides with DMF as the solvent (see Table 5 in the Experimental Section) to study their rejection properties. The screening was aimed at efficient purification and a high yield of the formed "click" polymer, that is, a maximal rejection of the product by the membrane combined with an as-complete-as-possible passage of the copper(I) catalyst to the permeate with the DMF solvent and any residual reagent.

Membranes M1 and M2 were selected for the filtration of the mixture obtained from the reaction between a relatively high molecular weight alkyne-functionalised polyurethane (8100 g mol$^{-1}$) and *N*-(2-azidoethyl)phthalimide (PHT-$N_3$) using CuBr/PMDETA (*N*,*N*,*N*′,*N*′,*N*″-pentamethylethylenetriamine) as the copper catalyst and DMF as the solvent [see Table 5, reaction (1)]. In the first instance, catalyst permeation through the membrane was simply observed visually by the appearance of a greenish blue colour in the permeate, whereas the presence of the cycloaddition product in the permeate was determined by $^1$H NMR spectroscopy. As shown in Table 1, membranes M1 and M2 are both sufficiently selective to reject all of the product as no polymer was detected in the permeates. However, a clear difference in permeate colour was observed during the filtration. Whereas for membrane M2, an intense blue permeate was obtained (Table 1, entry 2), filtration using membrane M1 resulted in a light blue filtrate (Table 1, entry 1), which suggests that the "in situ" generated copper catalyst (molecular weight of 317 g mol$^{-1}$) was partially retained as well as the polyurethane product. Complexation of copper by polyurethanes has been reported previously,[42] but this does not explain the difference in the colour of the permeate. The copper rejection depends on the MWCO of the membrane, that is, the denser membrane M1, cast from a more concentrated PI solution (see Table 4), partially rejects the catalyst complex, whereas the more open membrane M2 is less selective and allows full catalyst permeation. This behaviour could be expected because a higher concentration of PI in the precursor solution leads to a higher concentration at the polymer/non-solvent interface upon immersion. As a result, membranes with a denser surface structure and a lower porosity, and therefore a higher catalyst rejection, are obtained.[43,44] This difference in MWCO can also be seen in the permeate fluxes with membrane M2 exhibiting a much higher permeability than membrane M1 (Table 1).

Table 1. Membrane screening tests on "click" post-reaction mixtures in DMF.[a]

| | Membrane[b] | Reaction[c] | Permeability [L m$^{-2}$ h$^{-1}$ bar$^{-1}$] | Permeate colour | Product in permeate |
|---|---|---|---|---|---|
| 1 | M1 | 1 | 1.3 ± 0.2 | light blue | no |
| 2 | M2 | 1 | 3.2 + 0.5 | blue | no |
| 3 | M2 | 2 | 2.9 + 0.4 | dark blue | yes |

[a] Experiments were performed in duplicate (average performances are shown). Filtration conditions: 10 bar, room temperature. [b] See Table 4. [b] See Table 5.

Membrane M2 was also tested in the separation of the reaction mixture obtained after the cycloaddition reaction between a low-molecular-weight end-functionalised azido-PEO (1125 g mol$^{-1}$) and phenylacetylene in the presence of the CuBr/PMDETA catalyst, again using DMF as the solvent [see Table 5, reaction (2)]. In contrast to the filtrations carried out on the product mixture obtained from reaction (1), $^1$H NMR analysis revealed the presence of a significant amount of product in the permeate (Table 1, entry 3), which suggests that the relatively low molecular weight "clicked" polymer (1250 g mol$^{-1}$) could permeate through the membrane. On the other hand, the permeate was an intense blue, which demonstrates that membrane M2 allows permeation of the catalyst. To avoid product permeation, another end-functionalised azido-PEO with a molecular weight of around 2000 g mol$^{-1}$ (Table 5) was used in further reactions.

Similar screening was also carried out on post-reaction mixtures obtained under the same reaction conditions but with THF as solvent. In this case, the membrane was invariably coloured blue after filtration, which indicates a strong adsorption of the catalyst on the PI membrane surface. Therefore DMF was used as the solvent in all further experiments.

Based on this qualitative preliminary study, membrane M2 was selected as the most promising membrane for copper permeation. To overcome the limited rejection of this membrane for relatively low molecular weight products (Table 1, entry 3) and to further improve its catalyst separation efficiency (Table 1, entry 2), a new membrane was prepared. This new membrane M3 was obtained by increasing the co-solvent/solvent (THF/NMP) weight ratio of the PI membrane precursor solution from 1:5 (M2) to 1:3 (see Table 4). A higher concentration of volatile co-solvent is known to induce a thicker and/or denser top layer during the evaporation step prior to immersion of the cast film in the coagulation bath.[41,43,44] Filtration experiments on fresh "click" reaction post-mixtures in DMF were carried out with membrane M3 for two reactions with different copper concentrations. To validate the filtration process, the molecular weight of the end-functionalised azido-PEO (2000 g mol$^{-1}$) was chosen such that the final "click" product has a molecular weight well above the expected MWCO of

the membrane, that is, around 1000 g mol$^{-1}$, based on a rejection greater than 95% for the dye rose Bengal (1017 g mol$^{-1}$). This azido-PEO was treated with two different alkyne compounds, namely, phenylacetylene [see Table 5, reaction (3)] and 3,5-bis(hydroxymethyl)-1-propargyloxybenzene [PBM; see Table 5, reaction (4)], which have recently been used in "click" chemistry research.[39] DMF was used as the solvent in all the reactions (Table 2) and the copper catalyst was formed in situ using different concentrations of CuBr/PMDETA, that is, 0.1 and 0.5 equiv relative to the alkyne. Catalyst and product rejections were quantitatively determined by UV/Vis absorbance measurements and gravimetric analysis, respectively.

Table 2. Screening of the reaction conditions for the "click" coupling of azido-PEO (2000 g mol$^{-1}$) with phenylacetylene (entries 1 and 2) and PBM (entry 3).[a]

| | Reaction[b] | CuBr/ PMDTA[c] [equiv] | Permeability [L m$^{-2}$ h$^{-1}$ bar$^{-1}$] | Catalyst rejection [%] | Product rejection [%] |
|---|---|---|---|---|---|
| 1 | 3a | 0.1 | 0.40 ± 0.13 | 52 ± 10 | 93 ± 2 |
| 2 | 3b | 0.5 | 0.9 ± 0.4 | 52 ± 6 | 93 ± 3 |
| 3 | 4a | 0.1 | 0.67 ± 0.03 | 45 ± 7 | 96 ± 2 |

[a] Filtration conditions: membrane M3, 10 bar, room temperature; data are the average of two experiments. [b] See Table 5. [c] Relative to the alkyne compound, see Table 5.

Regardless of the copper concentration used, filtration of the post-reaction mixtures resulting from the cycloaddition reactions between azido-PEO and phenylacetylene (Table 2, entries 1 and 2) gave similar results with regard to catalyst (52%) and product (93%) retention. Product rejections were slightly higher (96%) when the azido-PEO was treated with PBM. In comparison with the mixture obtained from reaction (4), and rather unexpectedly, the permeate flux was higher for the filtration of the mixture from reaction (3) with a lower substrate/catalyst loading. Overall, the catalyst rejections clearly show that a single filtration is not sufficient to remove the copper to below the threshold concentration limit.

Based on its elevated product rejection and superior permeability, reaction (3b) (Table 2, entry 2) was selected for further filtration experiments with membrane M3, with the aim of further reducing the copper content in the retained product.

**Product purification by diafiltration**: Because full purification of the final "click" polymer formed in reaction (3b) (see Table 5) could not be achieved in a single filtration with membrane M3, a post-reaction diafiltration was carried out in which a progressive "washing out" of the lower molecular weight compounds, that is, the copper catalyst, was anticipated, thus achieving a higher purity of the retained "click" product. This was realised by adding fresh solvent (DMF) to the feed reservoir after the permeation of approximately 50% of the initial post-reaction mixture. This discontinuous dilution of the retentate with DMF was repeated four times in such a way that the feed volume of each new filtration was always equal to the initial feed volume (50 mL). In all five filtrations, the same sample of membrane was used. The diafiltration process is schematically shown in Figure 1 and the fluxes and separation efficiencies of the five successive membrane filtrations are summarised in Table 3.

Approximately 50 mL of the reaction mixture (product yield 92%) was poured into the filtration cell. This solution (Feed 1), with an initial copper concentration of 258 ppm, as

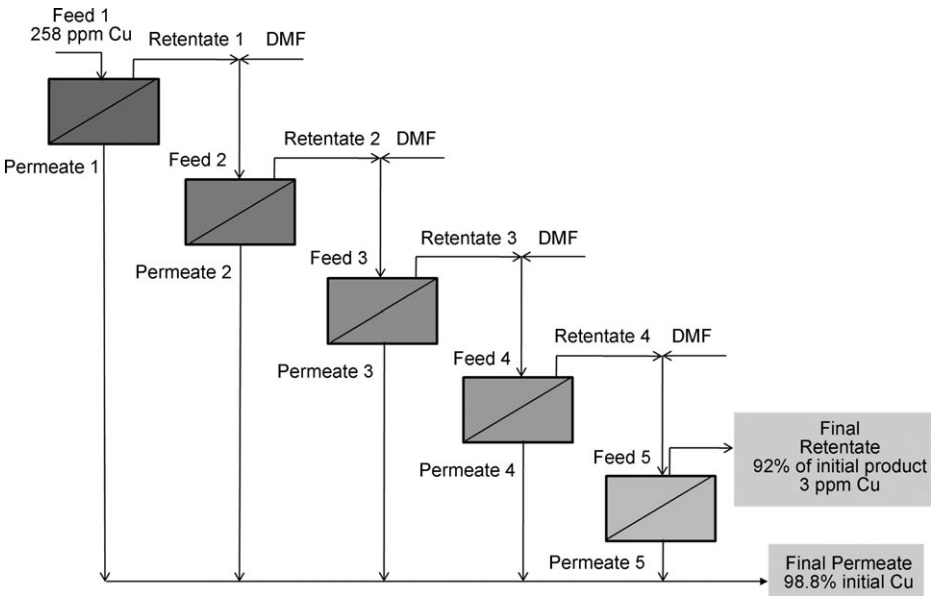



Figure 1. Schematic overview of the diafiltration process for reaction (3b). Filtration conditions: membrane M3, 10 bar, room temperature.

Table 3. Permeabilities, product rejections and retentate copper concentrations of the five successive filtrations of the diafiltration process of the product mixture obtained from reaction (3b).[a]

| Sample | Permeability [L m$^{-2}$ h$^{-1}$ bar$^{-1}$] | Polymer product rejection [%] | Copper conc. in the retentate [ppm] |
|---|---|---|---|
| Feed | – | – | 258 |
| Filtr. 1 | 1.1 | 96 | 118 |
| Filtr. 2 | 1.9 | 96 | 69 |
| Filtr. 3 | 1.9 | 100 | 28 |
| Filtr. 4 | 1.9 | 100 | 13 |
| Filtr. 5 | 2.4 | 100 | 3 |

[a] Filtration conditions: membrane M3, 10 bar, room temperature.

determined by UV/Vis spectroscopy, was then filtered at 10 bar until approximately half of the initial feed had permeated through the membrane. The filtrate (Permeate 1) was collected and analysed for copper content by UV/Vis spectroscopy and the presence of polymer by both gravimetry and $^1$H NMR spectroscopy. Subsequently, the remaining solution (Retentate 1) was depressurised and diluted with fresh DMF back to its initial volume. This new mixture (Feed 2) was filtered again through the same membrane. After the second filtration of approximately half of Feed 2, only 3.67 mg of the initial 14.17 mg of copper remained in the retentate (Retentate 2), which is a 75% reduction (Figure 2). With product selectivities of up to 96%, only 4% of the polymer was lost through the membrane (Permeate 2), in agreement with the rejections found in the screening test (Table 2, entry 2). In the three subsequent filtrations, no further product loss was observed (Table 3). After five filtrations and four dilutions, 92% of the total polymer present in Feed 1 was thus recovered in the retentate (Figure 1). A gradual and almost complete removal of copper was detected (Table 3) such that only 3 ppm was detected in the final retentate, which means that 98.8% of the initial catalyst had been removed (Figure 2). This final copper concentration of the product mixture is well below the copper residue limit (15 ppm) prescribed by the European Medicines Agency,[9] which demonstrates the feasibility of the proposed diafiltration process. As anticipated from the screening tests, no copper fouling on the membrane surface was observed.

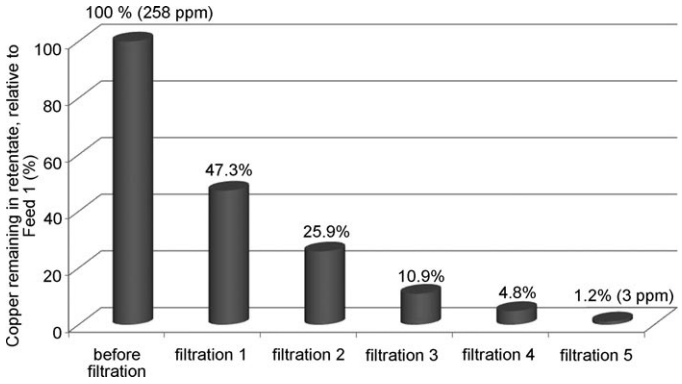



Figure 2. Evolution of the concentration of copper upon diafiltration of the product mixture of reaction (3) (see Table 5). Filtration conditions: membrane M3, 10 bar, room temperature.

In parallel with the progressive removal of copper, a significant increase in the permeability of DMF was observed, from 1.1 $L m^{-2} h^{-1} bar^{-1}$ in the first filtration to 2.4 $L m^{-2} h^{-1} bar^{-1}$ in the last filtration (Table 3). This rather unexpected increase in flux cannot be explained by a gradual degradation of the membrane in the solvent medium because the polymer rejection increased during the diafiltration process. Thus, it is possible that a swelling of the membrane took place during the extended exposure to DMF, also overnight under non-pressurised conditions.

The ratio between the mass of the "click" product and the mass of copper in the initial reaction mixture (Feed 1) was found to be 68. After the five-step diafiltration experiment, the same ratio in Retentate 5 was 5806, an 85-fold increase compared with the value in Feed 1. As a result of the favourable product/copper selectivity, high flux and good DMF stability throughout the entire diafiltration process, the cross-linked PI membrane allows the separation of "clicked" polymer compounds from the copper catalyst and thus is an efficient tool for product purification.

## Conclusions

SRNF has been presented as a powerful tool for separating "click" reaction mixtures, leading to an efficient purification of polymeric products. The cross-linked PI membranes permitted permeation of the ligand-stabilised copper(I) catalyst, whereas the products were almost fully retained. This is the first report of SRNF in which the catalyst is the permeating species and the product is retained. After an initial screening, the most promising membrane was used in a diafiltration experiment involving five consecutive filtrations and intermediate dilutions with DMF. This allowed removal of almost 99% of the initial copper with a metal content in the final product stream of no more than 3 ppm. As a result of the favourable product/copper selectivity, elevated flux and excellent DMF stability, the developed membranes offer a robust alternative to the current, generally limited technologies used for purifying "click" products. Membranes with tailor-made MWCOs offer a powerful and general solution for post-reaction product work-up, thus responding to one of the most important issues in the burgeoning field of "click" chemistry.

## Experimental Section

**Synthesis of "click" reagents**: 3,5-Bis(hydroxymethyl)-1-propargyloxybenzene (PBM),[45] *N*-(2-azidoethyl)phthalimide (PHT-$N_3$)[46] and azidopoly(ethylene oxide) (azido-PEO) (1125 and 2000 $g mol^{-1}$)[47] were synthesised as reported in the literature. Polyurethane PU-PBM-50 (8100 $g mol^{-1}$) was synthesised from 1 equiv of PBM and 1 equiv of hexamethylene diisocyanate (HDI) according to Fournier and Du Prez.[46]

Copper(I) bromide (CuBr, 99.99%), *N*,*N*,*N*′,*N*′,*N*″-pentamethylethylenetriamine (PMDETA, 99+%), phenylacetylene (98%), tetrahydrofuran (THF, 99+%) and dimethylformamide (DMF, 99+%) were used as received. All reagents were obtained from commercial suppliers and used without further purification.

**Preparation of the SRNF membranes**: Integrally skinned asymmetric SRNF membranes were prepared from Lenzing P84 polyimide (PI) dope solutions by the phase-inversion technique. The polymer was purchased from Evonik Fibres (Austria) and dissolved in THF/NMP (*N*-methylpyrrolidinone, 99%) in a 1:5 or 1:3 solvent weight ratio. The three casting solutions with the compositions indicated in Table 4 were cast as 250 μm thick films on a non-woven support (Novatex 2471, Freudenberg, Germany) using an automatic film applicator (Braive Instruments, Belgium). The nascent films were then exposed to ambient air for 60 s to allow solvent evaporation from the surface and subsequently immersed in a deion-

Table 4. Composition of the casting solutions of the PI membranes.

| Membrane | P84 [wt%] | NMP [wt%] | THF [wt%] | THF/NMP |
|---|---|---|---|---|
| M1 | 21.5 | 65.4 | 13.1 | 1:5 |
| M2 | 19.0 | 66.7 | 13.3 | 1:5 |
| M3 | 19.0 | 60.7 | 20.3 | 1:3 |

ised water bath at room temperature in which solidification of the membrane structure took place.[28,41]

Chemical cross-linking was achieved by immersing the PI membranes in a 10 wt% *p*-xylylenediamine (99%) solution in methanol (99%) for 24 h.[39] After cross-linking, the membranes were extensively rinsed with methanol to wash out the cross-linker and then treated by solvent exchange by immersion in 2-propanol (IPA, 99%) for 3 h and subsequently in a toluene/2-methyl-4-pentanone/mineral oil (P3, Pfeiffer; 40:40:20 v/v/v) solution for 3 days.[48] Finally, the membranes were dried for 1 h at 60 °C and stored until use.

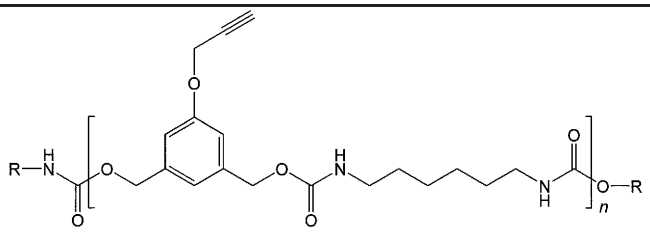
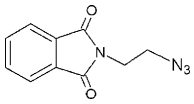
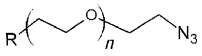
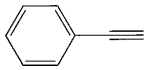
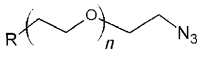
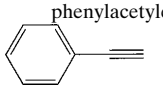
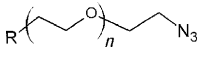
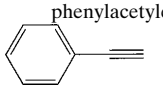
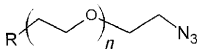
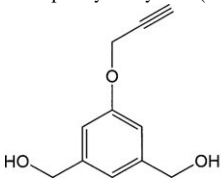
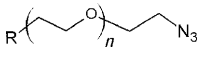
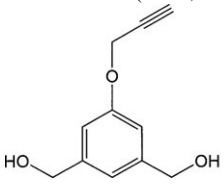
**"Click" reactions**: "Click" coupling reactions were carried out for 14 h at room temperature using DMF and occasionally THF as the solvent. In all cases 1 equiv of the polymeric compound and 2 equiv of the organic compound were mixed together with the catalyst based on CuBr and the ligand PMDETA. The structures and molecular weights of the reacting compounds and the equivalents of copper salt and ligand are summarised in Table 5.

**Filtration experiments**: Filtration experiments were carried out at room temperature on circular membranes of 12.6 $cm^2$ using a stainless steel dead-end filtration cell. Approximately 50 mL of post-reaction mixture was poured into the cell, magnetically stirred at 500 rpm and pressurised to 10 bar with nitrogen gas. In the screening tests, permeate samples were only taken for analysis after the initial non-equilibrium conditions during which the permeates were discarded. Permeabilities ($L\,m^{-2}\,h^{-1}\,bar^{-1}$) were determined gravimetrically.

In the diafiltration experiment, the permeate was collected immediately after pressurisation until approximately half of the initial feed volume (50 mL) had permeated. After filtration, the retentate was depressurised and approximately 25 mL of fresh DMF was added after which the new feed was filtered again. These discontinuous filtration/dilution cycles, with a constant feed volume at the start of each filtration, were repeated until the desired degree of purification had been achieved.

Product and catalyst rejections (%) were calculated as $(1-C_p/C_f)\times 100$, in which $C_f$ and $C_p$ refer to the solute concentration of the initial feed and of the permeate, respectively. Catalyst concentrations were analysed on a Perkin–Elmer Lambda 12 UV/Vis spectrophotometer at 697 nm. The concentration of "click" products was gravimetrically determined after evaporation of the solvent from the difference in the weight of the empty

Table 5. Reaction conditions for the copper(I)-catalysed 1,3-dipolar cycloaddition reactions in DMF.

| Reaction | Polymeric compound | Organic compound | CuBr [equiv] | PMDETA [equiv] |
|---|---|---|---|---|
| 1 |  PU-PBM-50 (8100 $g\,mol^{-1}$) |  PHT-$N_3$ (206 $g\,mol^{-1}$) | 0.1 | 0.1 |
| 2 |  azido-PEO (1125 $g\,mol^{-1}$) |  phenylacetylene (133 $g\,mol^{-1}$) | 0.1 | 0.1 |
| 3a |  azido-PEO (2000 $g\,mol^{-1}$) |  phenylacetylene (133 $g\,mol^{-1}$) | 0.1 | 0.1 |
| 3b |  azido-PEO (2000 $g\,mol^{-1}$) |  phenylacetylene (133 $g\,mol^{-1}$) | 0.5 | 0.5 |
| 4a |  azido-PEO (2000 $g\,mol^{-1}$) |  3,5-bis(hydroxymethyl)-1-propargyloxybenzene (PBM; 192 $g\,mol^{-1}$) | 0.1 | 0.1 |
| 4b |  azido-PEO (2000 $g\,mol^{-1}$) |  3,5-bis(hydroxymethyl)-1-propargyloxybenzene (PBM; 192 $g\,mol^{-1}$) | 0.5 | 0.5 |

sample container and the weight after evaporation of the solvent. If this weight difference was less than 0.001 g it was considered that no product was present in the sample. Because the maximum amount of copper catalyst at the beginning of the reaction was 32 mg and, on the basis that most of it had been removed, it can be assumed that the weight difference was due only to the presence of the "click" product.

$^1$H NMR spectroscopy was used to identify the presence of the "click" polymer in the samples. The $^1$H NMR spectra were recorded in $CDCl_3$ and [$D_6$]DMSO at room temperature on a Bruker Avance 300 spectrometer at 300 MHz.

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