

Catalyst Immobilization

Reusable Catalysts Based on Dendrimers Trapped in Poly(*p*-xylylene) Nanotubes**

Jean-Pierre Lindner, Caren Röben, Armido Studer,* Michael Stasiak, Ramona Ronge, Andreas Greiner,* and Hans-Joachim Wendorff*

Organocatalysis has been intensively and successfully studied during the last few years.^[1] However, separation of the catalyst from the product can be problematic. Moreover, for economic reasons, catalyst recovery is highly desirable, in particular if expensive catalysts are used with high loading. In this regard, immobilized catalysts offer advantages over nonimmobilized systems. It is not surprising that different approaches to the immobilization of organocatalysts have been reported.^[2,3] Herein, we present reusable dendritic catalysts^[4] “bottled” in poly(*p*-xylylene) (PPX) nanotubes. Knoevenagel condensations and 2,2,6,6-tetramethylpiperidine-*N*-oxyl radical (TEMPO) mediated alcohol oxidations were studied as the first test reactions of these catalysts.^[5,6]

We have recently shown that catalysts can be immobilized into electrospun polymer nanofibers.^[7,8] Moreover, electrospun fibers can be used as templates for the preparation of nanotubes.^[9] The approach consists of depositing a PPX shell layer of [2.2]-*para*-cyclophane by chemical vapor deposition (CVD) onto an electrospun fiber, followed by removal of the core fiber. The layer thickness depends on the deposition time. Importantly, PPX is known to be partially crystalline and, therefore, is resistant to most common solvents.

We proposed to co-electrospin dendrimers with poly(ethylene oxide) (PEO). The nanofibers obtained would then be coated with PPX by CVD. Removal of the PEO by extraction should leave the dendrimers trapped inside the PPX tubes (Figure 1). For dendrimers of appropriate sizes, diffusion through the PPX tube should be fully suppressed. Hence, the tube can be considered as a nanoreactor and the catalytically active dendrimer should be freely soluble inside the tube. No detrimental activity effects that arise from immobilization should be observed.

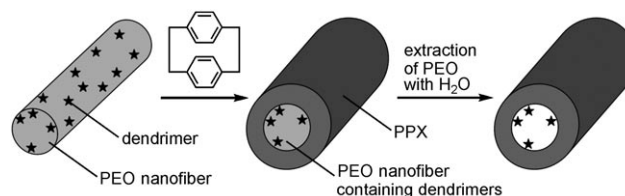


Figure 1. Concept of “bottling” dendritic catalysts in PPX nanotubes.

We used commercially available poly(amidoamine) (PAMAM) dendrimers^[4] of 4th (G4) and 5th generation (G5) in our studies. For production of PAMAM-containing PEO fibers, a solution of PAMAM in MeOH (10 wt% PAMAM, 0.3 mL) was added to an aqueous PEO solution ($M_w = 900\,000\text{ g mol}^{-1}$; 400 mg in 9.60 mL H₂O). This mixture was pumped through a metal capillary using a mechanical actuator connected to a voltage supply. The circular orifice of the capillary had a diameter of 0.45 mm, a circular counter-electrode with a diameter of 10 cm was located below the reservoir to result in a vertical arrangement of the electrodes, and fibers were collected on aluminum foil. The distance between the tip of the capillary and the counter-electrode was typically in the order of 20 cm and the applied voltage was 10 kV. PEO nanofibers bearing PAMAM dendrimers with a diameter of $(181 \pm 36)\text{ nm}$ were obtained (Figure 2). The

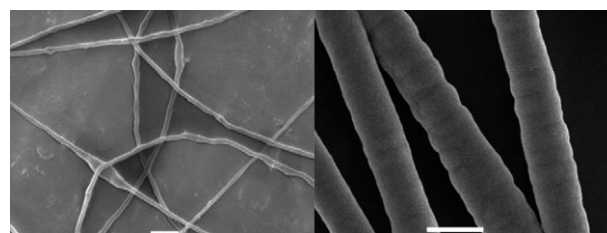


Figure 2. SEM images of PEO fibers containing PAMAM G5 before (left) and after coating with PPX by CVD (right; scale bars 1 μm).

PAMAM dendrimers are probably not well-dispersed in the PEO fibers, as indicated in Figure 1. It is likely that the dendrimers will be preferentially located at the surface of the fiber material.^[8a] However, since most of the PEO will be extracted later in the process (see below), it is not important to know the exact distribution of the dendrimer within the PEO fiber. CVD of [2.2]-*para*-cyclophane eventually resulted in core-shell fibers (the coat thickness could be adjusted from 50 to 230 nm, see the Supporting Information). Removal of most of the core PEO fiber material was achieved by

[*] J.-P. Lindner, C. Röben, Prof. Dr. A. Studer
Organisch-Chemisches Institut, Westfälische Wilhelms-Universität
Corrensstrasse 40, 48149 Münster (Germany)
Fax: (+49) 281-833-6523
E-mail: studer@uni-muenster.de

Dr. M. Stasiak, R. Ronge, Prof. Dr. A. Greiner, Prof. Dr. H.-J. Wendorff
Fachbereich Chemie Philipps-Universität Marburg
Hans-Meerwein Strasse, 35032 Marburg (Germany)
Fax: (+49) 6421-282-5573
E-mail: greiner@staff.uni-marburg.de
wendorff@staff.uni-marburg.de

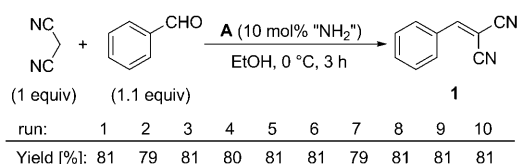
[**] We thank the DFG for supporting our work within the priority program “organocatalysis”. We thank Dr. Wilhelm Hemme for conducting solid-state NMR measurements.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.200903448>.

extraction of the core-shell fibers with water to give tubes **A** containing PAMAM.^[10]

We first studied the leaching behavior of PAMAM G4 from core-shell fibers (coat thickness about 230 nm).^[11] To this end, the core-shell material was immersed in water for two minutes. After removal of the fiber material, the H₂O solution was analyzed by applying the classical ninhydrin test, and the resulting solution was analyzed by UV/Vis spectroscopy (see the Supporting Information). This procedure was repeated several times. Disappointingly, PAMAM G4 seemed to be too small and diffusion through the PPX layer occurred.^[12] After 200 minutes, no further leaching was observed. Elemental analysis revealed that only 6% of the initially added PAMAM G4 remained in the tube system. Therefore, we switched to the core-shell system that contained the larger^[12] PAMAM G5 (coat thickness around 220 nm). Pleasingly, we did not identify any PAMAM G5 in the water solution (after three days). We tested DMSO as an additional solvent as it is commonly used in organocatalysis and it dissolves PAMAM. These studies were performed on tube material after PEO core fiber extraction with water. A negative ninhydrin test confirmed that PAMAM G5 in DMSO remained entrapped in the PPX tube (thickness 220 nm, for three days). The same result was obtained for leaching studies with EtOH as a solvent. Moreover, we found that even for a tube material with a thickness of only 50 nm, PAMAM G5 was not extracted with DMSO. In addition, elemental analysis showed that all the added PAMAM G5 (within experimental error) remained in the tube material. We can therefore conclude that PAMAM G5 entrapped in PPX tubes should be well-suited to act as a recyclable catalyst.^[13]

As a first test experiment to study the catalytic activity of the tube material, we investigated the PAMAM-catalyzed Knoevenagel condensation of malonodinitrile with benzaldehyde to dinitrile **1** (Scheme 1).^[14] Reactions were performed



Scheme 1. Knoevenagel reactions catalyzed by system **A** and corresponding yields.

by immersing the tube material **A** as a catalyst containing PAMAM (with 10 mol% NH₂ function) into a solution of benzaldehyde, EtOH (1.1 equivalents), and malonodinitrile at 0 °C for 3 hours (Figure 3).^[15] System **A** proved to be active and **1** was isolated in 81% yield. Catalyst recovery was readily achieved by removal of the tube material from the solvent, followed by rinsing with dichloromethane. Catalyst **A** was successfully reused for another nine runs without any activity loss (yields 79–81%). As mentioned above, our entrapping strategy should not result in any detrimental effects on the intrinsic catalyst reactivity, as PAMAM G5 is probably freely

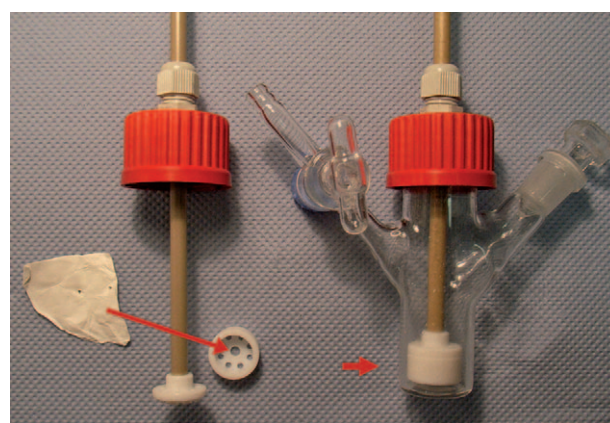
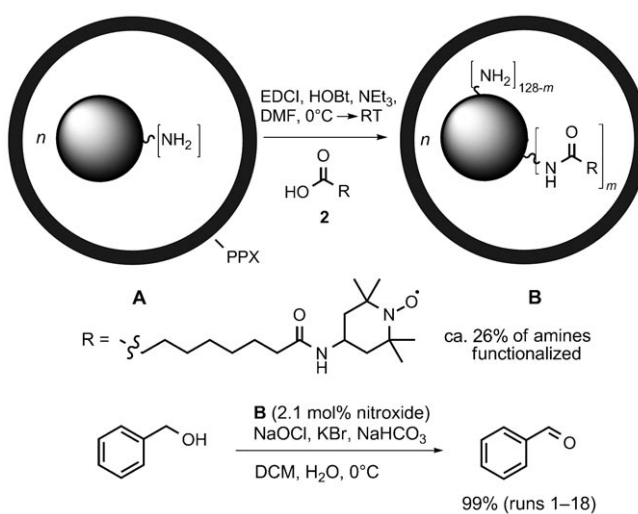


Figure 3. PPX tube mat used as catalyst and apparatus used for catalytic studies.

soluble inside the PPX tube. In fact, with “free” PAMAM G5 as a catalyst under otherwise identical conditions a similar yield (79%) was obtained.

We next planned to use tube system **A** as a platform for the preparation of another recyclable catalyst. This goal should be readily achieved by conjugation of the entrapped PAMAM G5 with the desired catalytically active moiety. Conjugation should lead to an enlargement of the dendrimer diameter, and it is therefore expected that leaching will not be a problem for the conjugated system. To this end, we reacted a tube system of type **A** with acid **2** by using EDCI/HOBt/NEt₃ (EDCI = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, HOBt = 1-hydroxy-1*H*-benzotriazole) for acid activation (Scheme 2). The tube material was then thoroughly washed and dried to provide catalyst system **B**, in which about 26% of the amines were conjugated by TEMPO moieties (determined gravimetrically).

As a test reaction, we studied the oxidation of benzyl alcohol to benzaldehyde under typical oxidation conditions.^[16] We were very pleased that **B** was active and



Scheme 2. Conjugation of PAMAM G5 inside the tube and use of catalyst system **B** in the oxidation of benzyl alcohol.

benzaldehyde was formed quantitatively by using around 2.1 mol% of nitroxide. Moreover, **B** was successfully reused 17 times without loss of activity (quantitative yield as determined by GC analysis).^[17]

In conclusion, we have presented a new method for preparation of PPX nanotubes that contain PAMAM dendrimers trapped inside the tubes. Our approach uses electrospinning, a technique that is frequently applied in materials science.^[7] Electrospinning equipment is cheap and readily available, and the tube material of our catalyst systems was prepared by CVD of commercially available *para*-cyclophane. PAMAM G5 entrapped in PPX nanotubes showed activity as a recyclable catalyst in a Knoevenagel reaction. More importantly, PAMAM was successfully chemically modified inside the tube by amide C–N bond formation. This reaction allowed the synthesis of TEMPO-conjugated PAMAM derivatives, which were active as reusable catalysts in the TEMPO/bleach oxidation of benzyl alcohol. Thus, our approach should be very general, and essentially any catalyst can be “bottled” into PPX nanotubes through conjugation of PAMAM.

Received: June 25, 2009

Revised: August 31, 2009

Published online: October 23, 2009

Keywords: dendrimers · electrospinning · organocatalysis · oxidation · polymers

- [1] For recent reviews on organocatalysis, see: *Chem. Rev.* **2007**, 107(12) (special issue).
- [2] For the immobilization of catalysts, see: a) J. M. Fraile, J. I. García, J. A. Mayoral, *Chem. Rev.* **2009**, 109, 360; b) A. F. Trindade, P. M. P. Gois, C. A. M. Afonso, *Chem. Rev.* **2009**, 109, 418; c) R. Akiyama, S. Kobayashi, *Chem. Rev.* **2009**, 109, 594.
- [3] For the immobilization of organocatalysts, see: a) M. Benaglia, A. Puglisi, F. Cozzi, *Chem. Rev.* **2003**, 103, 3401; b) M. Benaglia, *New J. Chem.* **2006**, 30, 1525; c) F. Cozzi, *Adv. Synth. Catal.* **2006**, 348, 1367; d) M. Gruttadauria, F. Giacalone, R. Noto, *Chem. Soc. Rev.* **2008**, 37, 1666.
- [4] a) R. van Heerbeek, P. C. J. Kamer, P. W. N. M. Van Leeuwen, J. N. H. Reek, *Chem. Rev.* **2002**, 102, 3717; b) B. Helms, J. M. J. Fréchet, *Adv. Synth. Catal.* **2006**, 348, 1125; c) E. de Jesús, J. C. Flores, *Ind. Eng. Chem. Res.* **2008**, 47, 7968.
- [5] For a review, see: T. Vogler, A. Studer, *Synthesis* **2008**, 1979.
- [6] For the immobilization of TEMPO, see: C. Bolm, T. Fey, *Chem. Commun.* **1999**, 1795; A. Dijkman, I. W. C. E. Arends, R. A. Sheldon, *Chem. Commun.* **2000**, 271; T. Fey, H. Fischer, S. Bachmann, K. Albert, C. Bolm, *J. Org. Chem.* **2001**, 66, 8154; A. Dijkman, I. W. C. E. Arends, R. A. Sheldon, *Synlett* **2001**, 102; S. Weik, G. Nicholson, G. Jung, J. Rademann, *Angew. Chem.* **2001**, 113, 1489; *Angew. Chem. Int. Ed.* **2001**, 40, 1436; R. Ciriminna, C. Bolm, T. Fey, M. Pagliaro, *Adv. Synth. Catal.* **2002**, 344, 159; I. A. Ansari, R. Gree, *Org. Lett.* **2002**, 4, 1507; M. L. Testa, R. Ciriminna, C. Hajji, E. Z. Garcia, M. Ciclosi, J. S. Arques, M. Pagliaro, *Adv. Synth. Catal.* **2004**, 346, 655; P. Ferreira, E. Phillips, D. Rippon, S. C. Tsang, W. Hayes, *J. Org. Chem.* **2004**, 69, 6851; G. Pozzi, M. Cavazzini, S. Quici, M. Benaglia, G. Dell’Anna, *Org. Lett.* **2004**, 6, 441; P. Ferreira, W. Hayes, E. Phillips, D. Rippon, S. C. Tsang, *Green Chem.* **2004**, 6, 310; M. Gilhespy, M. Lok, X. Baucherel, *Chem. Commun.* **2005**, 1085; N. Jiang, A. Ragauskas, *Tetrahedron Lett.* **2005**, 46, 3323;
- O. Holczknecht, M. Cavazzini, S. Quici, I. Shepperson, G. Pozzi, *Adv. Synth. Catal.* **2005**, 347, 677; M. Benaglia, A. Puglisi, O. Holczknecht, S. Quici, G. Pozzi, *Tetrahedron* **2005**, 61, 12058; F. Geneste, C. Moinet, S. Ababou-Girard, F. Solal, *New J. Chem.* **2005**, 29, 1520; J. Kubota, T. Ido, M. Kuroboshi, H. Tanaka, T. Uchida, K. Shimamura, *Tetrahedron* **2006**, 62, 4769; D. J. Vugts, L. Veum, K. al-Mafraji, R. Lemmens, R. F. Schmitz, F. J. J. de Kanter, M. B. Groen, U. Hanefeld, R. V. A. Orru, *Eur. J. Org. Chem.* **2006**, 1672; A. Gheorghe, E. Cuevas-Yañez, J. Horn, W. Bannwarth, B. Narsaiah, O. Reiser, *Synlett* **2006**, 2767; A. Gheorghe, A. Matsuno, O. Reiser, *Adv. Synth. Catal.* **2006**, 348, 1016; J. Luo, C. Pardin, W. D. Lubell, X. X. Zhu, *Chem. Commun.* **2007**, 2136; B. P. Mason, A. R. Bogdan, A. Goswami, D. T. McQuade, *Org. Lett.* **2007**, 9, 3449; B. Karimi, A. Biglari, J. H. Clark, V. Budarin, *Angew. Chem.* **2007**, 119, 7348; *Angew. Chem. Int. Ed.* **2007**, 46, 7210; A. Gheorghe, T. Chinnusamy, E. Cuevas-Yañez, P. Hilgers, O. Reiser, *Org. Lett.* **2008**, 10, 4171; A. P. Dobbs, M. J. Penny, P. Jones, *Tetrahedron Lett.* **2008**, 49, 6955; M. A. Subhani, M. Beigi, P. Eilbracht, *Adv. Synth. Catal.* **2008**, 350, 2903; A. Schätz, R. N. Grass, W. J. Stark, O. Reiser, *Chem. Eur. J.* **2008**, 14, 8262; M. Kuroboshi, K. Goto, H. Tanaka, *Synthesis* **2009**, 903.
- [7] For reviews on electrospinning, see: a) D. Li, Y. Xia, *Adv. Mater.* **2004**, 16, 1151; b) A. Greiner, J. H. Wendorff, *Angew. Chem.* **2007**, 119, 5770; *Angew. Chem. Int. Ed.* **2007**, 46, 5670.
- [8] a) M. Stasiak, C. Röben, N. Rosenberger, F. Schleth, A. Studer, A. Greiner, J. H. Wendorff, *Polymer* **2007**, 48, 5208; b) M. Stasiak, A. Studer, A. Greiner, J. H. Wendorff, *Chem. Eur. J.* **2007**, 13, 6150; c) C. Röben, M. Stasiak, B. Janza, A. Greiner, J. H. Wendorff, A. Studer, *Synthesis* **2008**, 2163.
- [9] M. Bognitzki, H. Hou, M. Ishaque, T. Frese, M. Hellwig, C. Schwarte, A. Schaper, J. H. Wendorff, A. Greiner, *Adv. Mater.* **2000**, 12, 637.
- [10] We performed solid-state NMR studies to investigate the material obtained after water extraction. We found that around 15–20% of the initial added PEO remained in the tube material (representative NMR spectra are shown in the Supporting Information). The PEO used has a broad molecular weight distribution and we believe that the longest chains were not extracted. We would like to point out that it is well-established in terms of theory and experiments that, other than the diffusion of three-dimensional particles such as dendrimers, the diffusion of flexible polymer chains through polymer matrices is not controlled by their hydrodynamic radius but follows reptational motions (i.e., along the length of the chain) so that even rather long chain molecules are able to pass through polymer membranes, see: K. Kremer, G. S. Grest, *J. Chem. Phys.* **1990**, 92, 5057.
- [11] Leaching studies with water were performed on core-shell fibers prior to removal of the PEO fibers, in order to make sure that leaching that occurs during core fiber extraction will also be taken into account.
- [12] Diameter: 4.5 nm for PAMAM G4 (14242 g mol⁻¹) and 5.4 nm for PAMAM G5 (28965 g mol⁻¹), see: a) J. Li, L. T. Piehler, D. Qin, J. R. Baker, Jr., D. A. Tomalia, *Langmuir* **2000**, 16, 5613; b) A. Sharma, M. Rao, R. Miller, A. Desai, *Anal. Biochem.* **2005**, 344, 70.
- [13] We also conjugated the dendrimers inside the tubes by adding isothiocyanates containing fluorescein (see the Supporting Information). Gravimetry showed that around 57% of the amino groups were dye-functionalized. These mats showed the typical color. However, for the G4 system after extraction, gravimetry showed that dye functionalization was not successful, thus further indicating that only very small amounts of G4 are present in the system. Unfortunately, confocal fluorescence microscopy did not allow us to learn about the distribution of the dye-loaded catalysts within the tube system.

- [14] G. R. Krishnan, K. Sreekumar, *Eur. J. Org. Chem.* **2008**, 4763.
- [15] We found that the background reaction was slow (7%) under the applied conditions. The “background yield” was also obtained by using the G4 system after water extraction, thus further supporting that only very small amounts of G4 dendrimers remained in the tubes after extraction.
- [16] P. Lucio Anelli, C. Biffi, F. Montanari, S. Quici, *J. Org. Chem.* **1987**, 52, 2559.
- [17] The morphology of the tube material altered over time as partial decomposition of the PPX tube material probably occurred under the strongly oxidizing conditions. This explanation is supported by the observation that morphology change was not observed for system **A** while studying the Knoevenagel condensation.
-