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**Bipyridine-functionalized amphiphilic Block Copolymers
as Support Materials for the Aerobic Oxidation of Primary Alcohols in
Aqueous Media**

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Abstract. Amphiphilic block copolymers with 4-methoxy-4'-alkoxybipyridine ligands in the hydrophobic block were synthesized by cationic ring-opening polymerization. The bipyridine moiety was either introduced directly as a 2-oxazoline monomer (**P1**) or by polymer-analogous coupling to a precursor poly(2-oxazoline) with chloropentyl side chains (**PP2-PP7**) to prepare the polymer ligands (**P2-P7**). The polymers were characterized by NMR and SEC measurements to determine polymer composition, molar masses and polydispersities. In water, these polymers form micelles with cmc values ranging from 1.8 to 22 $\mu\text{mol/L}$. SAXS and DLS measurements exhibited spherical particles with particles sizes of 8 to 21 nm. Polymers **P1 – P7** were finally utilized to carry out the aerobic oxidation of primary alcohols, including allylic, benzylic, and aliphatic derivatives at room temperature ($T=20^\circ\text{C}$) and ambient air in aqueous media indicating higher activities for **P2 – P7** compared to **P1** as a consequence of the different preparation methods. Moreover, product isolation and catalyst recycling can be easily accomplished by solvent extraction for five times without significant loss of activity.

Keywords: Amphiphilic Polymers – Green chemistry – Aerobic Oxidation – Polymer Micelles – Micellar Catalysis

Introduction

The selective oxidation of primary and secondary alcohols into the corresponding aldehydes or ketones is a key transformation in modern organic synthesis.¹⁻³ While in the past this reaction was carried out by the usage of stoichiometric amounts of inorganic oxidants such as KMnO_4 ,⁴ CrO_3 ,⁵ or dichromate,⁶ it is not surprising that there has been much research devoted to the replacement of these often hazardous or toxic agents by more environmentally friendly chemistry and more active catalysts.⁷⁻⁹ 2,2,6,6-Tetramethyl-piperidine-1-oxyl (TEMPO) radicals such as 4-methoxy-TEMPO (**1**) have been used extensively as a metal-free approach for the selective oxidation of alcohols to aldehydes and ketones.¹⁰ The strategy requires only catalytic amounts (typically, <10 mol%) of TEMPO and stoichiometric amounts of a co-oxidants, e.g., sodium hypochlorite,^{11,12} sodium chlorite,¹³ or oxone.¹⁴

Several TEMPO catalyst systems have been described that address also the problem of catalyst recovery and simplified product isolation. Some examples of support materials for TEMPO include silica,¹⁵ or multiwall CNTs,¹⁶ and more recently various nanoparticles based on Fe_3O_4 ,¹⁷ Merrifield resins,¹⁸ magnetic polystyrene particles,¹⁹ and TEMPO polymer-grafted silica nanoparticles have been successfully employed.²⁰ The nanoparticle approach allows very often simplified catalyst isolation and product separation while achieving good activities and thus represents an interesting alternative to homogeneous, soluble polymer supports based on poly(norbornene)²¹ or PEG.²²

On the other side some highly efficient catalysts for the aerobic oxidation of alcohols have been developed recently using either more expensive transition metal complexes based on water-soluble complexes of palladium(II) with phenanthroline-based ligands,^{23,24} water-soluble platinum(II) tetrasulfophthalocyanine catalysts,²⁵ water-soluble diruthenium complex $\text{Ru}_2(\text{m-OAc})_3(\text{m-CO}_3)$ ²⁶ or $\text{RuCl}_2(\text{PPh}_3)_3$ /TEMPO catalysts²⁷ and various Rh catalysts.²⁸ In 1984, Semmelhack and coworker reported the first aerobic oxidation of activated primary alcohols with a CuCl/TEMPO catalyst system which was able to oxidize allylic and benzylic

alcohols efficiently.²⁹ Despite many advances over the past decades, even the most versatile and active catalyst systems such as the CuCl/1,10-phenanthroline catalyst with dialkylazodicarboxylates as redox-active co catalyst required the use of pure O₂ as the oxidant and fluorobenzene as the solvent to obtain optimal results in a wide range of diversely functionalized primary and secondary allylic, benzylic, and aliphatic alcohols.³⁰

More recently, Stahl and coworker described a (bpy)Cu(I)/ nitroxyl co-catalyst system that enables the efficient and selective aerobic oxidation of a broad range of primary alcohols, including allylic, benzylic, and aliphatic derivatives, to the corresponding aldehydes.^{31,32} While many TEMPO-supported catalyst systems have been described in the literature¹⁵⁻²¹ there have been only few reports on the immobilization of bipyridine ligands to a homogenous polymer support for catalysis application.³³⁻³⁵ Another interesting feature for the development of environmentally friendly catalysts is a support material that is compatible with water and at the same time allows the conversion of hydrophobic substrates. Especially micelles based on block copolymers have been proven particularly successful in the past to provide hydrophobic cavities for the efficient catalytic transformation of hydrophobic substrates in aqueous media.³⁶⁻³⁸

Herein, we report the first synthesis of well-defined amphiphilic block copolymers modified with bipyridine ligands and their application in the Cu(I) / TEMPO based aerobic oxidation of alcohols in aqueous media.

Experimental

Materials. All chemicals were purchased commercially and used, unless otherwise noted, without further purification. Water-free dichloromethane and dimethylformamide were purchased from Acros Organics and dried over Al_2O_3 using a *M. Braun GmbH MB SPS 800*. Other water-free solvents were dried under standard procedures (acetonitrile and chlorobenzene, CaCl_2 ; isopropanol, Mg) and stored over molecular sieve 3 Å and argon atmosphere.

Measurements. ^1H (500.13 MHz) and ^{13}C NMR (100.63 MHz) spectra were recorded on a *Bruker DRX 500* spectrometer. GC-EI-HRMS measurements were performed on a *Thermo Electro* at 160 °C and 70 eV, as reference was used perfluorokerosene. Gel permeation chromatography (SEC) was carried out on a DMF (5 g/l LiBr) based SEC at 60 °C with PSS GRAM analytical 1000Å and 30Å columns equipped with a Knauer RI detector Smartline 2300 using linear polystyrene standards for the poly(2-oxazoline). Gas chromatography analyses were performed on a *Fisons 9000* equipped with a flame ionization detector FID/1177, capillary column CP-Sil 8, length 30 m, with helium as mobile phase and analysed with the program *EZChrom Elite*. Dynamic light scattering was carried out on a Malvern Zetasizer Nano-Z5 with a HeNe-Laser ($\lambda = 632$ nm). Fluorescence spectroscopy was recorded on a Perkin-Elmer LS 55 using a wavelength of $\lambda = 334$ nm and a 0.01 mM solution of pyrene in methanol. The analyses were carried out with the program FL WinLab. SAXS measurements were carried out with an Anton Paar SAXSess mc^2 Station using 5 mM polymer solutions and a copper anode. Imaging plates were used for detection and for analysis the software Optiquant and SAXSQuant 1D/2D.

Monomer Synthesis

Synthesis of 2-heptyl-2-oxazoline

To octanonitrile (24.57 ml, 154.94 mmol, 1 eq.) ethanolamine (11.24 ml, 185.93 mmol, 1.20 eq.) and Cd(OAc)₂·2H₂O (825.91 mg, 3.10 mmol, 0.02 eq.) was added. The solution was stirred 30 h at 130 °C and the product was purified by distillation (88 °C, 1.6 10⁻¹ mbar). After addition of CaH₂ the product was distilled again and yielded as colorless liquid (15.5 g, 91.57 mmol, 60 %).

¹H-NMR (500.13 MHz, CDCl₃): δ = 0.86 ppm (m, CH₃), 1.30 (m, CH₃CH₂CH₂CH₂CH₂CH₂), 1.61 (quin, *J* = 7.4 Hz, CH₃CH₂), 2.25 (t, *J* = 7.7 Hz, CCH₂), 3.80 (t, *J* = 9.4 Hz, CH₂N), 4.20 (t, *J* = 9.5 Hz, CH₂O).

¹³C-NMR (100.63 MHz, CDCl₃): δ = 14.0 ppm (CH₃), 22.6 (CH₃CH₂), 25.9 (CH₂CH₂CO), 27.9 (CH₂CH₂CH₂CH₃), 28.9 (CH₂CN), 29.2 (CH₂CH₂CH₂CN), 31.6 (CH₂CH₂CH₃), 54.3 (CH₂N), 67.1 (CH₂O), 168.6 (CO).

ESI-MS: M_{calculated} = 169.1467; M_{measured} = 170.1541 [M+H]⁺

Synthesis of M1

The synthesis was carried out according to *Litt et al.*³⁹ Starting from ε-caprolactone (10 g, 87.61 mmol, 1 eq.) **M1** was obtained after three steps with an overall yield of 66 %.

¹H-NMR (500.13 MHz, CDCl₃): δ = 1.47 ppm (m, CH₂CH₂CH₂Cl), 1.63 (quin, *J* = 7.6 Hz, CH₂CH₂C(O)N), 1.76 (quin, *J* = 7.2 Hz, CH₂CH₂O), 2.25 (t, *J* = 7.5 Hz, CH₂C(O)N), 3.5 (t, *J* = 6.7 Hz, NCH₂CH₂O), 3.78 (t, ³*J* = 9.7 Hz, CH₂Cl), 4.19 (t, *J* = 9.5 Hz, NCH₂CH₂O).

¹³C-NMR (100.63 MHz, CDCl₃): δ = 25.1 ppm (CH₂CH₂C(O)N), 26.3 (CH₂CH₂CH₂C(O)N), 27.6 (CH₂CH₂CH₂Cl), 32.1 (CH₂C(O)N), 44.7 (CH₂N), 54.3 (CH₂CH₂CH₂Cl), 67.1 (NCH₂CH₂O), 168.1 (C(N)O).

ESI-MS: M_{calculated} = 175.0764; M_{measured} = 176.0838 [M+H]⁺

Synthesis of ligand L2

To a solution of **L1** (500 mg, 2.31 mmol, 1 eq.) in 30 ml absolute acetic acid was given 48 % HBr_{aq} (0.31 ml, 2.77 mmol, 1.15 eq.) while stirring. After heating for reflux the solution was neutralized with aqueous ammonia solution up to pH 8-9 under ice bath cooling and stirred for 30 min at rt. The solution was extracted with dichloromethane (4x30 ml) and the organic layers were dried with MgSO_4 . The solvent was removed under reduced pressure and the residue was washed with a small amount of chloroform. **L2** was yielded as white crystals (328 mg, 1.62 mmol, 70 %).

$^1\text{H-NMR}$ (500.13 MHz, CDCl_3): δ = 3.91 ppm (s, CH_3O), 6.53 (dd, J = 7.2 Hz, CHCHCOCH_3), 6.88 (dd, J = 5.8 Hz, CHCHCOH), 7.11 (s, br, CCHCOH), 7.39 (s, CCHCOCH_3), 7.71 (d, J = 7 Hz, CHCHCOH), 8.42 (d, J = 5.8 Hz, CHCHCOCH_3).

$^{13}\text{C-NMR}$ (100.63 MHz, CDCl_3): δ = 55.5 ppm (CH_3O), 106.1 (2 x CCHCOR), 111.2 (2 x CHCHCOR), 150.2 (2 x CHCHCOR), 167.0 (2 x NCCH , 2 x COR).

ESI-MS: $M_{\text{calculated}} = 202.0742$; $M_{\text{measured}} = 203.0816$ [$\text{M}+\text{H}$] $^+$

Synthesis of monomer M2

To a solution of **L2** (1.00 g, 4.95 mmol, 1 eq.) in 20 ml dimethylformamide was given **M1** (1.04 g, 5.93 mmol, 1.2 eq.) and K_2CO_3 (0.82 g, 5.93 mmol, 1.2 eq.). After heating the mixture to 130 °C for 18 h the solvent was removed under reduced pressure. The residue was dissolved in water/dichloromethane, extracted with dichloromethane (4x30 ml) and the combined organic layers were dried with MgSO_4 . The solvent was removed and the residue was dissolved in boiled ethyl acetate and filtrated. The solvent was removed and the residue was recrystallized in ethyl acetate. Filtration and drying under reduced pressure gave **M2** as white crystals (1.58 g, 4.63 mmol, 94 %).

$^1\text{H-NMR}$ (500.13 MHz, CDCl_3): δ = 1.56 ppm (m, $\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 1.72 (m, $\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{N}$), 1.85 (m, $\text{CH}_2\text{CH}_2\text{O}$), 2.32 (t, J = 7.5 Hz, $\text{CH}_2\text{C}(\text{O})\text{N}$), 3.82 (t, J = 9.4 Hz, $\text{NCH}_2\text{CH}_2\text{O}$), 3.95

(s, CH_3O), 4.13 (t, $J = 6.4$ Hz, CH_2O), 4.22 (t, $J = 9.5$ Hz, $\text{NCH}_2\text{CH}_2\text{O}$), 6.83 (ddd, $J = 8/5.5/2.5$ Hz, 2 x CHCHC), 7.95 (dd, $J = 8.7/2.4$ Hz, 2 x CCHC), 8.46 (dd, $J = 5.5/3.3$ Hz, 2 x NCH).

^{13}C -NMR (100.63 MHz, CDCl_3): $\delta = 25.5$ ppm ($\text{CH}_2\text{CH}_2\text{CN}$), 25.6 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}$), 27.8 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 28.6 (CH_2CN), 54.3 (CH_2N), 55.3 (CH_3O), 67.2 ($\text{NCH}_2\text{CH}_2\text{O}$), 67.7 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$), 106.0 (CCHCOCH_3), 106.7 (CCHCOCH_2), 111.0 (CHCHCOCH_3), 111.3 (CHCHCOCH_2), 150.0 (2 x NCH), 157.7 (2 x CHNC), 166.0 (CHCOCH_2), 166.6 (CHCOCH_3), 168.3 (C(N)O).

ESI-MS: $M_{\text{calculated}} = 341.1739$; $M_{\text{measured}} = 342.1818$ $[\text{M}+\text{H}]^+$

Polymer Synthesis

All polymerizations were carried out in Schlenk tubes under inert atmosphere using freshly distilled and dried solvents. A typical procedure was as follows:

To 2-methyl-2-oxazoline (495.05 μl , 5.88 mmol, 22 eq.) in 7 ml acetonitrile was given methyltriflate (30.22 μl , 267.05 μmol , 1 eq.) at 0 °C. After stirring the mixture for 3 h at 120 °C, **M2** (273.52 mg, 801.15 μmol , 3 eq.), 3 ml chlorobenzene and 2-heptyl-2-oxazoline (188.34 μl , 1.07 mmol, 4 eq.) were added. The mixture was stirred for 24 h at 100 °C and terminated at rt by addition of piperidine (79.27 μl , 801.15 μmol , 3 eq.) for 12 h. After removal of the solvent, the residue was dissolved in 10 mL of chloroform and stirred with K_2CO_3 for 3 h. After filtration, **P1** was purified by precipitation in ice cold diethyl ether and dried under reduced pressure.

Polymer analogous coupling: To 2-methyl-2-oxazoline (495.05 μl , 5.88 mmol, 22 eq.) in 7 ml acetonitrile was given methyltriflate (30.22 μl , 267.05 μmol , 1 eq.) at 0 °C. After stirring the mixture for 3 h at 120 °C, **M1** (140.73 mg, 801.15 μmol , 3 eq.) and 2-heptyl-2-oxazoline (188.34 μl , 1.07 mmol, 4 eq.) were added. The mixture was stirred for 24 h at 100 °C and terminated at rt by addition of piperidine (29.1 μl , 293.76 μmol , 1.1 eq.) for 24 h. After

removal of the solvent, the residue was dissolved in 10 mL of chloroform and stirred with K_2CO_3 for 3 h. After filtration, polymer **PP2** was purified by precipitation in ice cold diethyl ether and dried under reduced pressure.

1H -NMR (500.13 MHz, $CDCl_3$): δ = 0.85 ppm (s, $NC(O)C_6H_{12}CH_3$), 1.26 (s, $NC(O)CH_2CH_2C_4H_8CH_3$), 1.39-1.84 ($NC(O)CH_2C_3H_6CH_2Cl$ / $NC(O)CH_2CH_2C_5H_{11}$ / $NCH_2CH_2CH_2CH_2CH_2$), 2.00-2.20 ($NC(O)CH_3$), 2.31 (s, $NC(O)CH_2C_6H_{13}$ / $NC(O)CH_2C_4H_8Cl$), 2.90-3.05 (NCH_3), 3.45 (s, NCH_2CH_2N / CH_2Cl).

To **PP2** (1 eq. related to Cl-functionality) in dimethylformamide was given **L2** (1.2 eq.) and K_2CO_3 (1.2 eq.). After stirring the mixture for 36 h at 130 °C the solvent was removed. The residue was dissolved in dichloromethane, filtrated and the solvent was removed. The polymer was purified by precipitation in ice cold diethyl ether and dialyzed against ethanol (MWCO 1000) for 24 h. After removal of the solvent, polymer **P2** was again precipitated in ice cold diethyl ether and obtained a s a white powder after drying.

P1/P2: 1H -NMR (500.13 MHz, $CDCl_3$): δ = 0.85 ppm (s, $NC(O)C_6H_{12}CH_3$), 1.26 (s, $NC(O)CH_2CH_2C_4H_8CH_3$), 1.45-1.90 ($NC(O)CH_2C_3H_6CH_2OBiPy$ / $NC(O)CH_2CH_2C_5H_{11}$ / $NCH_2CH_2CH_2CH_2CH_2$), 2.00-2.20 ($NC(O)CH_3$), 2.31 (s, $NC(O)CH_2C_6H_{13}$ / $NC(O)CH_2C_4H_8OBiPy$), 2.90-3.05 (NCH_3), 3.45 (s, NCH_2CH_2N), 3.92 (s, CH_3O), 4.10 (s, CH_2OBiPy), 6.81 (s, 2 x $CHCHC$), 7.93 (s, 2 x $CCHC$), 8.43 (s, 2 x NCH).

Micellar catalysis with polymer-bound ligand

To polymer **P6** (50.83 mg, 10 μ mol, 0.01 eq.) in 2 ml acetonitrile (5 mM polymer solution) under inert atmosphere was added $CuBr$ (7.17 mg, 50 μ mol, 0.05 eq.). After stirring for 1 h at r.t. the solvent was removed and the polymer was dissolved in 2 ml water. *N*-methylimidazole (7.97 μ l, 100 μ mol, 0.1 eq.), TEMPO (7.81 mg, 50 μ mol, 0.05 eq.) and benzyl alcohol

(104 μl , 1 mmol, 1 eq.) were added to the solution. The solution was stirred at rt with a constant rate in an open flask for 3 h.

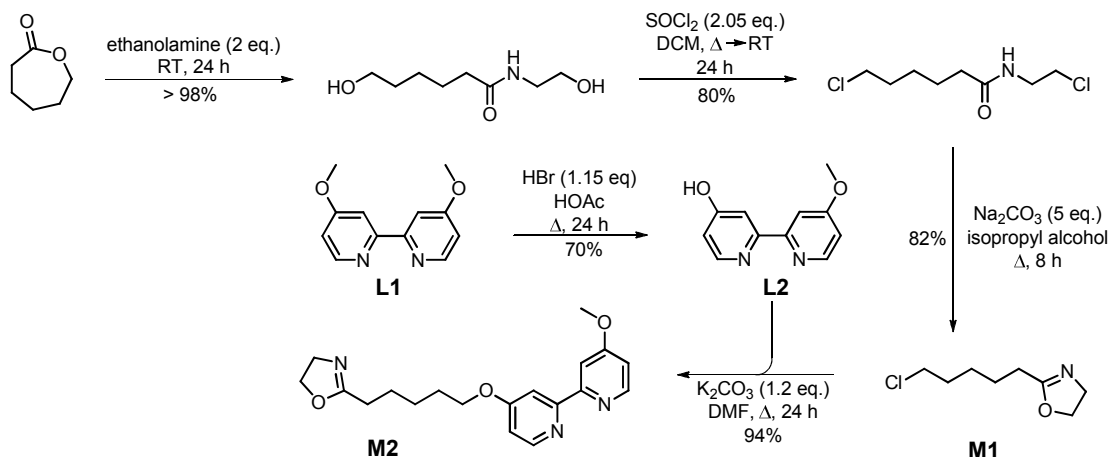
To isolate the product, the solution was extracted with diethyl ether (4x20 ml). The organic layers were dried with MgSO_4 and removed under reduced pressure. The product was purified via column chromatography (cyclohexane/ethyl acetate 5/1) and yielded with 94 %. The catalyst solution in water could be used for further runs by just adding *N*-methylimidazole and TEMPO again. For kinetics, 50 μl was taken out of the reaction solution and was frozen in liquid nitrogen. 30 μl of standard solution (200 μl *n*-undecane in 2 ml cyclohexane) and 500 μl diethyl ether were added. After extraction, MgSO_4 was added into the vial, the remaining solution was purged through a micro-column and the vial was washed with 500 μl diethyl ether again. The conversion was determined by gas chromatography.

Results and Discussion

Synthesis of amphiphilic, bipyridine functionalized block copolymers

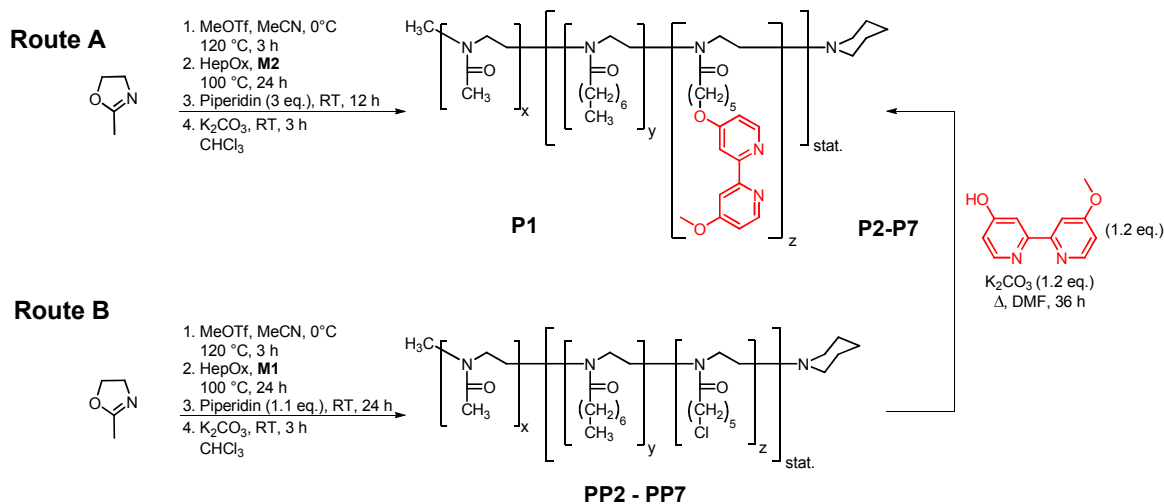
The cationic ring-opening polymerization of 2-oxazolines provides a versatile monomer system for the synthesis of amphiphilic block copolymers with different architecture, composition and functionalization.^{40,41} Two different approaches can be utilized to incorporate the bipyridine units into polyoxazolines, either (i) directly via suitable bipyridine-containing monomers⁴² or (ii) in a polymer-analogous fashion by coupling of the bipyridine moiety to a precursor polymer as has been demonstrated for other ligands before.⁴³ While the first approach is clearly more elegant, the post-analogous modification of a precursor polymer has been proven to be very useful when the ligand may interfere with the cationic polymerization procedure.⁴³ Therefore, we decided to develop a monomer synthesis route that allows the examination of both approaches of bipyridine introduction into the polymer. The synthesis of the monomers **M1** and **M2** is shown in Scheme 1. As a ligand we chose the 4-methoxy-4'-alkoxybipyridine system which has recently shown to be more active in the aerobic oxidation of primary alcohols than the bipyridine ligands.⁴⁴

The synthesis of (2-(5-chloropentyl)-2-oxazoline) monomer **M1** was carried out according to a literature procedure⁴⁵ starting from ϵ -caprolactone and its ring-opening reaction with ethanolamine. Overall yield for the three step synthesis was 66 %. The bipyridine-containing monomer **M2** was prepared by reacting **M1** with the deprotonated bipyridine derivative **L2** in a Williamson ether synthesis to give **M2** in 94 % yield.



Scheme 1 Synthesis of the 2-oxazoline monomers **M1** and **M2**.

The structure and composition of **M2** were confirmed by ^1H and ^{13}C NMR spectroscopy and mass spectrometry. Characteristic are the two methylene groups of the oxazoline ring at 3.82 (-N- CH_2 -) and 4.22 ppm (-O- CH_2 -) and the signals at 6.83, 7.95 and 8.46 ppm can be clearly assigned to the protons of the bipyridine unit.



Scheme 2 Synthesis of the bipyridine-containing poly(2-oxazoline)s **P1-P7**. A: Direct introduction of the bipyridine unit by polymerization of **M2**. B: Post-analogous coupling of the bipyridine moiety to the polymer precursor **PP2-PP7** in a Williamson ether synthesis (indirect method).

Two approaches were pursued to prepare catalytically active polymer scaffolds (see Scheme 2). In the first approach (Route A), we prepared the amphiphilic block copolymer by consecutive cationic polymerization of 2-methyl-2-oxazoline to form the hydrophilic block and a mixture of **M2** / HepOx to form the hydrophobic block. The polymerization was terminated with piperidine. The polymer structure of **P1** was analyzed by ^1H NMR spectroscopy (see Figure 1) that confirmed the successful introduction of **M2** into the hydrophobic block with the signals **12** - **14** corresponding to the bipyridine unit between 6.9 to 8.5 ppm.

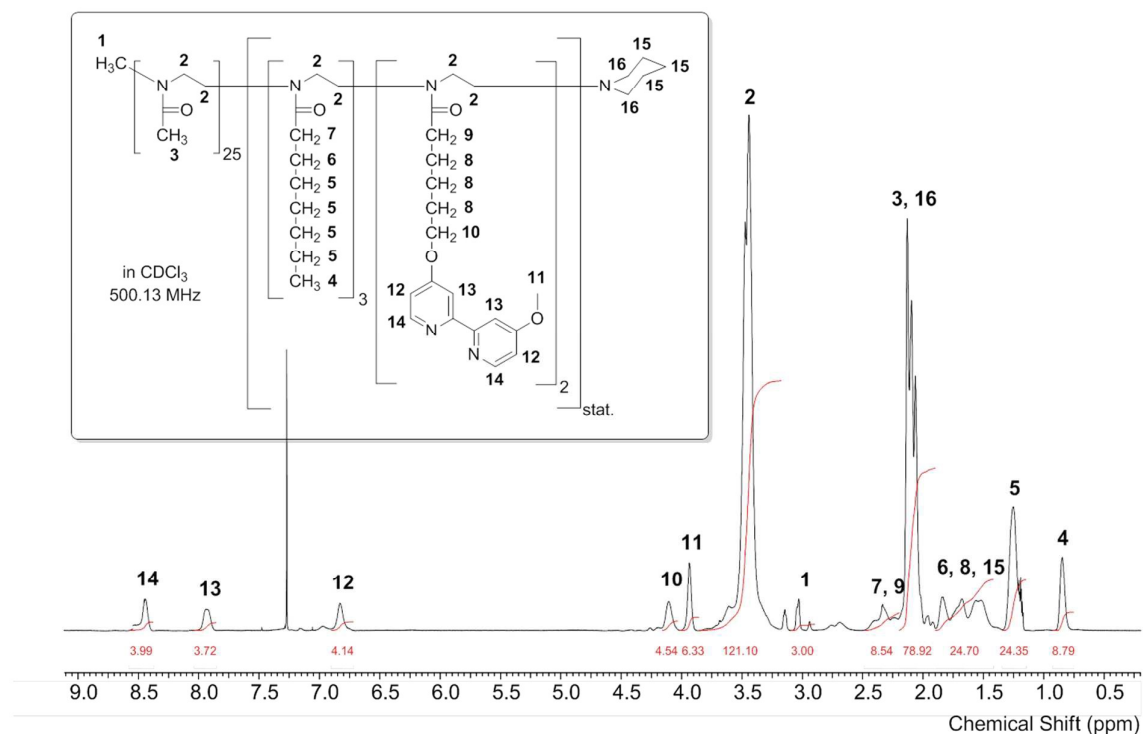


Fig.1 ^1H -NMR (CDCl_3 , 500.13 MHz) of the bipyridine-containing copolymer **P1**.

Moreover, ^1H NMR spectroscopy was used to analyze copolymer composition and molar mass by end group analysis (see Table 1). Size exclusion chromatography of **P1**, however, resulted in a bimodal curve and a polydispersity index of $\bar{M}_w / \bar{M}_n = 1.34$. The bimodal shape of the SEC curve for **P1** can be explained by a partial termination of the cationic chain

end by the bipyridine unit during polymerization (see Figure 2). As a consequence, part of the bipyridine moieties may not be available anymore for the formation of the active catalyst in **P1**.

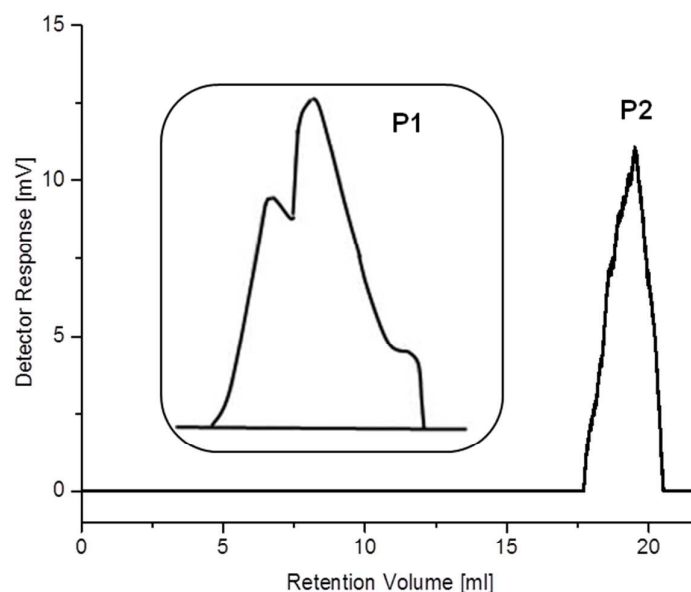


Fig. 2 SEC curve for **P1** (direct polymerization) and **P2** (polymer-analogous introduction of the bipyridine ligand).

Therefore, all other polymers **P2** – **P7** were prepared in a two-step approach, by synthesizing first a polymer precursors (**PP2** – **PP7**) with **M1** in the hydrophobic block, that were then reacted in a polymer-analogous fashion with the bipyridine moiety **L2** to give the final polymer ligands **P2** – **P7** (see Scheme 2, Route B). By using this methodology we prepared two sets of polymer ligands that contained either a mixture of 2-heptyl-2-oxazoline and the 4-methoxy-4'-pentoxy-2,2'-bipyridine ligand in the side chain of the hydrophobic block (**P2** – **P4**) or only the bipyridine moiety as the hydrophobic unit (**P5** – **P7**). Narrow PDI values of 1.09 – 1.20 suggest a living polymerization process that was further validated by mono-modal SEC curves for all polymer **P2** to **P7** as can be seen for **P2** in Figure 2. All polymers **P2** – **P7**

were characterized by ^1H NMR spectroscopy to determine their composition and molecular weight by endgroup analysis (see Table 1).

Table 1 Analytical data of the polymers **P1** – **P7**.

Poly-mer	Polymer Composition ^a	$M_{\text{N NMR}}$ (g·mol ⁻¹) ^b	$M_{\text{N SEC}}$ (g·mol ⁻¹) ^c	PDI ^c	cmc (x 10 ⁻⁶ mol·l ⁻¹) ^d	d_{DLS} (nm) ^e	d_{SAXS} (nm) ^f
P1	Me ₂₅ Hep ₃ BiPy ₂	3450	3490	1.34	7.9	11.01	n. d.
P2	Me ₂₆ Hep ₃ BiPy ₂	3530	4010	1.09	7.9	8.04	11.68
P3	Me ₃₇ Hep ₂ BiPy ₂	4310	4440	1.18	22	10.74	13.12
P4	Me ₄₀ Hep ₅ BiPy ₄	5770	4660	1.15	1.8	12.48	13.38
P5	Me ₂₀ BiPy ₃	2850	3030	1.09	18	11.86	13.90
P6	Me ₃₈ BiPy ₅	5080	3230	1.20	20	16.11	n. d.
P7	Me ₅₀ BiPy ₁₀	7839	4940	1.18	3.1	21.16	19.08

^a Polymer composition as determined by ^1H NMR analysis; Me = 2-methyl-2-oxazolin; Hep = 2-heptyl-2-oxazolin; BiPy = 4-methoxy-4-pentoxy-2,2-bipyridine units. ^b Determined by ^1H NMR endgroup analysis in CDCl_3 . ^c Determined by SEC analysis in DMF / 5 g/l LiBr with linear PS standards; ^d With pyrene (0.01 mM in MeOH). ^e by DLS measurements in water (0.5 - 1 mM) at room temperature. ^f By SAXS measurements in water (1 - 5 mM) at room temperature.

2.2 Characterization of Micellar Aggregates

The study of aggregate formation was guided by two considerations. First, we wanted to make sure that micellar aggregates were formed at the polymer concentrations used in the catalytic experiments. In addition, we were interested in finding out if there is any correlation between copolymer composition, aggregate size and catalytic activity. Critical micelle concentration (cmc) was determined for each copolymer **P1** – **P7** by pyrene solubilization experiments resulting in cmc values of 3.1 to 20 $\mu\text{mol/L}$ which is in a typical range for amphiphilic poly(oxazoline) block copolymers.^{36,43} Aggregate size and shape of the polymers **P1** - **P7** formed in water was further analyzed by DLS and SAXS measurements at a similar polymer concentration of 5 mM polymer solutions that were also used in the subsequent catalysis

experiments. The results are summarized in Table 1, column 6-8. The hydrodynamic radii of the polymer micelles were in the range of 8 to 21 nm which is typical for micellar aggregates based on poly(2-oxazoline)s with a similar molar mass and block copolymer composition and a rather bulky, hydrophobic side chain.^{36,43} Moreover it was noticed that polymers (**P5-P7**) that contained only bipyridine units in the hydrophobic block formed larger aggregates with diameter of 12 to 21 nm compared to polymers (**P2-P4**) where the hydrophobic block was composed of a mixture of heptyl side chains and bipyridine units with 8 to 12.5 nm. SAXS measurements confirmed the size of the micellar aggregates and showed that all particles displayed a spherical shape (data not shown here).

2.3 Application of the Polymer Micelles in the Aerobic Oxidation of Primary Alcohols

The homogeneous, aerobic oxidation of primary alcohols catalyzed by a (bpy)Cu(I) / nitroxyl co-catalyst system has witnessed great interest recently due to their high activity and selectivity for a broad range of primary alcohols.^{31,32} Although homogeneous catalysts have many advantages, catalyst immobilization is a well known methodology to allow efficient catalyst separation and to obtain metal-free products.⁴⁶⁻⁵¹ Moreover, with the increasing interest in *Green Chemistry Processing* the replacement of expensive, toxic and flammable organic solvents by water as the preferred solvent is highly desirable due to economically and safety related process engineering reasons.⁵²⁻⁵⁵

In the first set of experiments we studied the effect of polymer-ligand preparation, **P1** (direct polymerization) and **P2** (polymer-analogous introduction of the bipyridine ligand) on catalytic activity. Cu(I)Br was chosen as the copper source due to its higher stability in aqueous media compared to [Cu(MeCN)₄]OTf which is preferred in organic media. The active catalyst was prepared by dissolution of the polymer-ligand in acetonitrile (5 mM polymer solution) before CuBr was added in stoichiometric amounts with respect to the bipyridine units to the solution. After 1 h stirring, the solvent was removed and the Cu-

polymer complex was dissolved in water before *N*-methylimidazole, TEMPO and benzyl alcohol were added to the mixture. As can be seen from Figure 3A, the synthetic route of polymer-ligand preparation had a strong effect on catalytic activity. With **P1** a nearly quantitative conversion of benzyl alcohol to benzaldehyde was obtained after 7 h whereas with **P2** it was possible to obtain this after only 3 h. The results confirm our previous findings from the SEC analysis of **P1** and **P2**. The polymerization of **M2** leads to a partial termination of the polymerization reaction in **P1** due to the nucleophilic character of the bipyridine units. As a result less ligand is available for the formation of an active complex thus leading to a reduced activity.

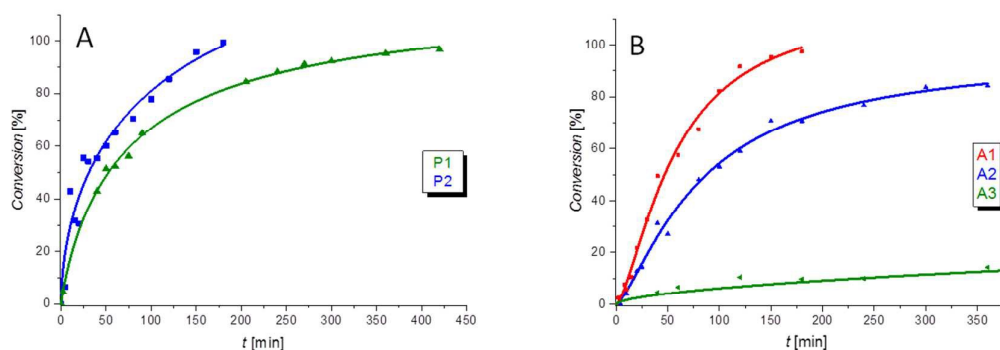
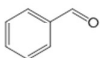
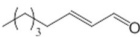
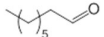


Fig. 3 A Oxidation of benzyl alcohol (5 mol % Cu(I)Br; 5 mol % ligand, 5 mol % TEMPO, 10 mol % NMI, solvent, at RT, air) with **P1** and **P2** in water. **B**: Comparison of the conversion of representative benzylic (**A1**), allylic (**A2**) and aliphatic alcohol (**A3**) under micellar catalytic conditions with **P6**.

In the next set of experiments we studied the conversion of different benzylic, allylic and aliphatic alcohols under micellar catalytic conditions with **P6** as the catalyst support. As can be seen from Figure 3B, benzyl alcohol was completely converted after 180 min, while the conversion of allylic alcohol and aliphatic alcohol was considerable slower with 70 % and 10 %, respectively. This gradual decrease in reactivity from benzylic and allylic to aliphatic alcohols is in excellent agreement with the results reported in the literature from homogeneous oxidation experiments.^{31,32}

Table 2 Oxidation of different primary alcohols under micellar catalytic conditions.

$$\text{R-CH}_2\text{-OH} \xrightarrow[\text{H}_2\text{O, rt, air}]{\begin{array}{l} 5 \text{ mol\% CuBr} \\ 5 \text{ mol\% Ligand P6} \\ 5 \text{ mol\% TEMPO} \\ 10 \text{ mol\% NMI} \end{array}} \text{R-CHO}$$

Solvent	aldehyde	Time (h)	Conversion (%) ^a	Yield (%) ^b	TOF (h ⁻¹) ^c
H ₂ O		3	98	94	13.3
H ₂ O		6	82	80	8.2
H ₂ O		60	51	45	0.3

^a Determined by GC. ^b Determined by NMR after work-up and isolation. ^c After 50 % of the given conversion, determined by GC.

Although polymers **P2** – **P7** varied in size (d = 8 to 21 nm) and composition of the hydrophobic polymer block no significant difference in catalytic activity was observed (see Table 3) which again underlines the robustness and flexibility of the polymeric carrier system.

Table 3 Effect of the polymer composition on the oxidation of benzyl alcohol in water under micellar catalytic conditions.

Polymer	Polymer Composition	Conversion (%) ^a	TOF (h ⁻¹) ^b
P1	Me ₂₅ Hep ₃ BiPy ₂	82	13.5
P2	Me ₂₆ Hep ₃ BiPy ₂	99	16.7
P3	Me ₃₇ Hep ₂ BiPy ₂	95	16.3
P4	Me ₄₀ Hep ₅ BiPy ₄	94	10.9
P5	Me ₂₀ BiPy ₃	98	11.3
P6	Me ₃₈ BiPy ₅	98	13.3
P7	Me ₅₀ BiPy ₁₀	88	11.6

^a Determined by GC. ^b After 50 % of the given conversion, determined by GC.

The main advantage of the polymer-supported catalyst system besides working in aqueous media is the possibility of catalyst recycling. Separation of the catalyst and the product is feasible by simple extraction of the aqueous solution. Therefore, we used diethyl ether as extracting solvent to isolate the product(s) while the polymer bound bipyridine Cu catalyst remains in the aqueous phase. Only TEMPO and NMI had to be given to the aqueous polymer phase after every extraction step. In contrast, the use of low molecular weight surfactants with a catalyst that is not bound to the surfactant, leads often to catalyst leaching and recycling is not possible by simple extraction.⁵⁶⁻⁵⁹ As can be seen in Figure 4, the catalyst system shows no significant decrease in reactivity in 5 cycles.

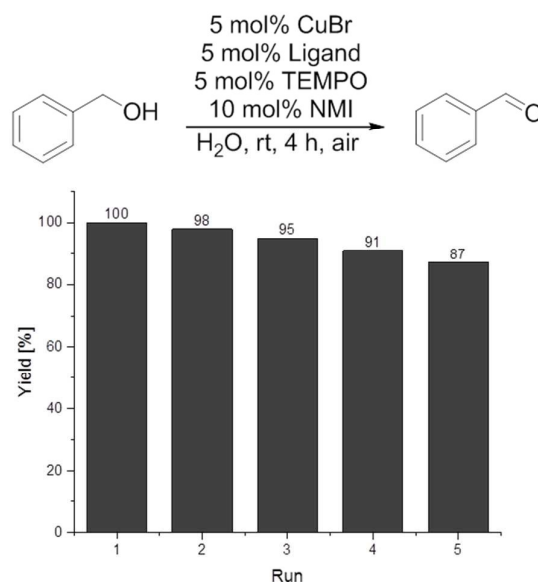


Fig. 4 Recycling experiments for the oxidation of benzyl alcohol in H₂O in the presence of **P6**.

Conclusion

In summary, we developed a route to well-defined bipyridine-supported amphiphilic block copolymers for the micellar catalytic aerobic oxidation of benzylic, allylic and aliphatic primary alcohols. Successful recycling makes these polymer supports very attractive for the preparation of various aldehydes under environmental benign reaction conditions.

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