Articles

Pyridyl *N*-Oxide Substituted Helically Chiral Poly(methacrylate)s in Asymmetric Organocatalysis

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ABSTRACT: Four pyridyl substituted helically chiral poly(methacrylate)s **poly-1**−**poly-4** were oxidized with *m*-CPBA, yielding four pyridyl *N*-oxide substituted polymers **poly-5**−**poly-8**. Poly[(3-pyridyl *N*-oxide)-dibenzosuberyl methacrylate] poly(3PyDBSMA-*N*O) **poly-5** was found to be quantitatively oxidized and showed a stable helical conformation. It was an active organocatalyst in the asymmetric allylation of benzaldehyde with allyltrichlorosilane.

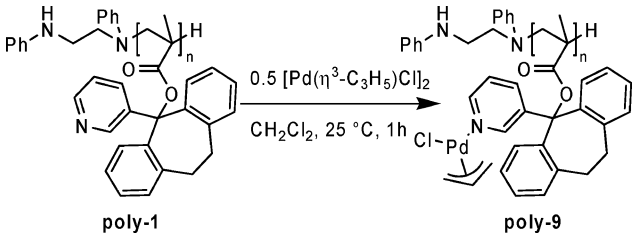
Introduction

Asymmetric catalysis is at the heart of contemporary organic chemistry.[1,2] Despite tremendous progress achieved in recent years, there remains plenty of room for further improvements. The immobilization of chiral catalysts to facilitate their removal from the reaction mixture and to allow for their repeated use is an active area of interest. To achieve these goals, soluble chiral polymers are promising candidates, especially if catalytic function and process advantages are combined. The reisolation of the chiral catalyst by precipitation or ultrafiltration should be easy, while all of the analytical and kinetical advantages of reactions in homogeneous phase should be maintained. Furthermore, one could take advantage of a number of beneficial effects related to the macromolecular state, like cooperativity or chiral amplification as observed in poly(isocyante)s.[3−5] This may allow for the synthesis of novel catalysts with properties not achievable with micromolecules.

In our group a new approach of using polymeric catalysts, whose asymmetric induction results exclusively from the helical secondary structure, was developed.[6] Following the work of Okamoto et al.,[7] chiral poly(methacrylate)s were prepared by helix sense selective anionic polymerization of sterically congested methacrylates. These single-handed helically chiral polymers were successfully converted to the corresponding palladium complexes, such as **poly-9** (Scheme 1).[6,8]

They proved to be active catalysts in allylic substitution reactions, thereby demonstrating the principal feasibility of helically chiral polymeric ligands devoid of any additional stereogenic elements in asymmetric transition metal catalysis.[6] The configuration of the product and the observed selectivity result exclusively from the helically chiral nature of the polymeric ligand. In the reaction of diphenylpropenyl acetate with dimethyl malonate, the substitution product was obtained with up to 60% *ee*.[6,8]

Scheme 1. Preparation of a Helically Chiral Palladium Complex



Chiral Lewis bases like amine *N*-oxides are able to catalyze the asymmetric allylation of aldehydes with allyltrichlorosilane.[9−11] We therefore anticipated that pyridyl *N*-oxide substituted helically chiral poly(methacrylate)s may function as macromolecular organocatalysts in the same reaction.

In this article we report on the synthesis and characterization of sterically congested, helically chiral pyridyl *N*-oxide substituted poly(methacrylate)s. First results of their application as chiral organocatalysts in the asymmetric allylation of benzaldehyde are presented.

Results and Discussion

There are two principal approaches to synthesize helically chiral poly(methacrylate)s containing pyridyl *N*-oxide groups: (i) polymerization of pyridyl *N*-oxide substituted methacrylates or (ii) *N*-oxidation of poly(methacrylate)s having pyridyl rings in the side chain. To obtain well-defined and completely *N*-oxidized polymers, approach i seemed more auspicious.

Moreover, Okamoto et al. found that the degree of methylation of different pyridyl substituted methacrylates is sensitive to the position of the nitrogen.[12] While both 3-pyridyl derivatives **1** and **2** (Scheme 2) could be methylated quantitatively with methyl iodide at room

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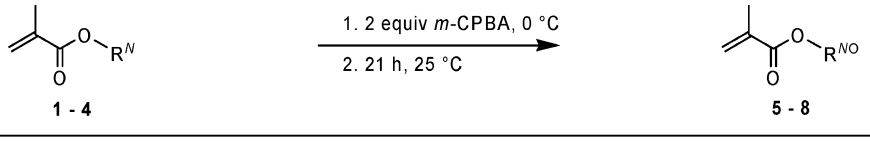
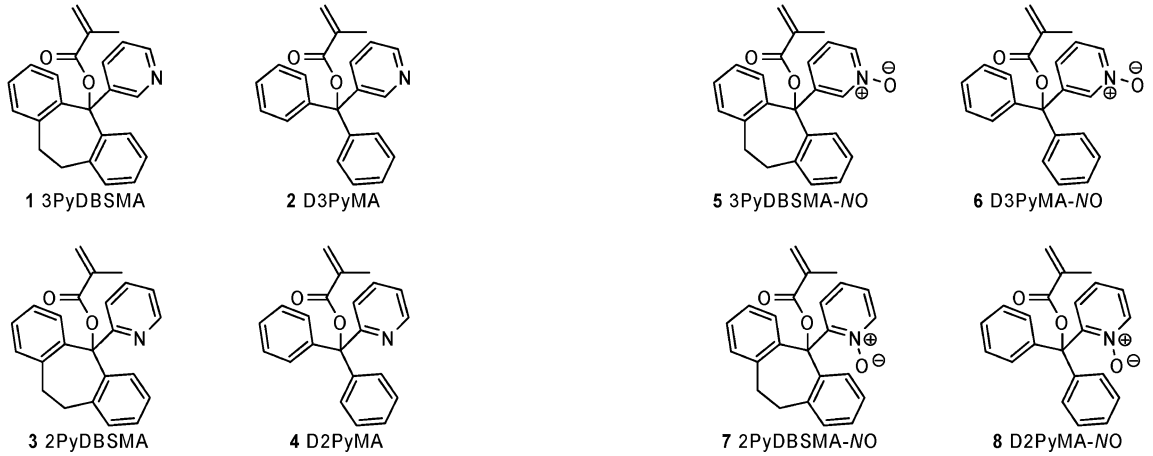
Scheme 2. Synthesis of Pyridyl *N*-Oxide Substituted Methacrylates 5−8





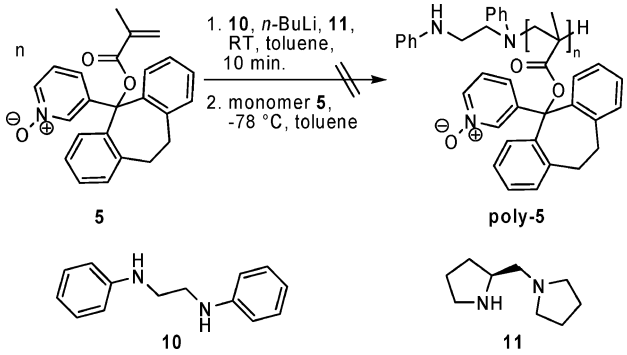
temperature, the complete methylation of the 2-pyridyl derivatives **3** and **4** (Scheme 2) failed even at elevated temperatures, which was attributed to a high sterical congestion of the nitrogens in the 2-position. From these results we expected the situation to be even worse with the highly congested polymers and thus decided to work with the monomers first. Furthermore, we hoped that *N*-oxidation may not be as sterically demanding as *N*-methylation, which in turn renders successful oxidation even in the 2-position possible.

We started our studies by synthesizing the methacrylates **1**−**4** following published procedures.[13−16] The oxidation of the pyridyl nitrogens was carried out according to Malkov's protocol[11] with 2 equiv of *m*-CPBA at room temperature for 21 h (Scheme 2). ^{1}H NMR analysis of the crude products **5**−**8** showed complete *N*-oxidation even with the 2-pyridyl derivatives **3** and **4** together with minor amounts of epoxidation products, indicating quantitative oxidation in all cases, thus confirming our expectation concerning the reduced steric demand of the oxidation reaction.

Guided by our experience with poly(3-pyridyldibenzosuberyl methacrylate) **poly-1** concerning its conformational stability and the accessibility of its N atom, we decided to focus our attention on the preparation of **poly-5**. Therefore, we isolated the corresponding monomer 3PyDBSMA-*N*O **5** from the reaction mixture of the oxidation reaction (90% yield). We next tried to prepare the desired polymer *N*-oxide by helix sense selective anionic polymerization of **5** using a chiral nonracemic base mixture prepared from DPEDA **10**, *n*-BuLi, and (+)-PMP **11** as initiator (Scheme 3, for abbreviations see experimental part). Unfortunately, after 67 h reaction time at −78 °C only monomer **5** could be isolated.

To test whether the pyridyl *N*-oxide moiety is the reason for the failed polymerization, we tried to polymerize triphenylmethyl methacrylate with the aforementioned chiral base mixture in the presence of 1 equiv of pyridine *N*-oxide per monomer. After 4 h, we could only isolate a mixture of oligomers besides unreacted monomer, while the polymerization without addition of pyridine *N*-oxide, which was carried out in a parallel experiment, was almost quantitative. In a detailed study of the polymerization mechanism by Okamoto et al.,[17]

Scheme 3. Attempted Helix Sense Selective Polymerization of 3PyDBSMA-*N*O 5 Using a Chiral Base Mixture



it was found that the early steps in the chain propagation have to be stereoselectively directed by the chiral base, in our case PMP **11**. Those chains lacking complete stereoselection do not grow. We therefore speculate that the chiral base **11** is displaced by pyridine *N*-oxide. This way, an achiral complex results, the polymerization is not forced to proceed stereoselectively, and the oligomeric chains do not grow further. Moreover, the electronic properties and an increased bulkiness of the resulting complex may slow down the polymerization.

These results show that the initially preferred route to synthesize the desired polymers by polymerization of a methacrylate *N*-oxide is not feasible. Therefore, we tried the synthesis of pyridyl *N*-oxide substituted poly(methacrylate)s by oxidation of the corresponding polymers (approach ii).

Encouraged by the fact that the methacrylates **1**−**4** could be oxidized quantitatively, we prepared the four polymers **poly-1**−**poly-4** using the Okamoto protocol (Scheme 3, Table 1). All polymers were completely isotactic and showed high optical rotations comparable to the published data.[13−15,18]

Since the conformational stability of the helical secondary structure is crucial for the enantioselectivity of helically chiral catalysts, we recorded the optical rotation over a time period of 40 h (Figure 1, solid lines). As reported previously, polymers containing a dibenzo-

Table 1. Helix Sense Selective Polymerization of Methacrylates 1−4[a]

entry	monomer	polymer	*t* [h]	yield [%][b]	DP[c]	M_w/M_n[c]	tacticity[d]	$[\alpha]_D^{25}$ [e]
1	**1**	**poly-1**	64	55	24	1.14	>99% *mm*	+386
2	**2**	**poly-2**	24	66	31	1.16	>99% *mm*	+182
3	**3**	**poly-3**	40	84	27	1.21	>99% *mm*	+377
4	**4**	**poly-4**	4	89	48	1.13	>99% *mm*	+356

[a] All polymerizations were carried out with 1.0 g of monomer in toluene at −78 °C. The monomer/initiator ratio was 15:1. [b] Fraction insoluble in methanol and benzene/hexane. [c] Determined by GPC [poly(MMA) standard] after acidic hydrolysis and conversion to poly(MMA). [d] Determined by ^{1}H NMR analysis of the derived poly(MMA). [e] $c = 1$, $CHCl_3$/2,2,2-trifluoroethanol (9:1 by volume); measured immediately after isolation.

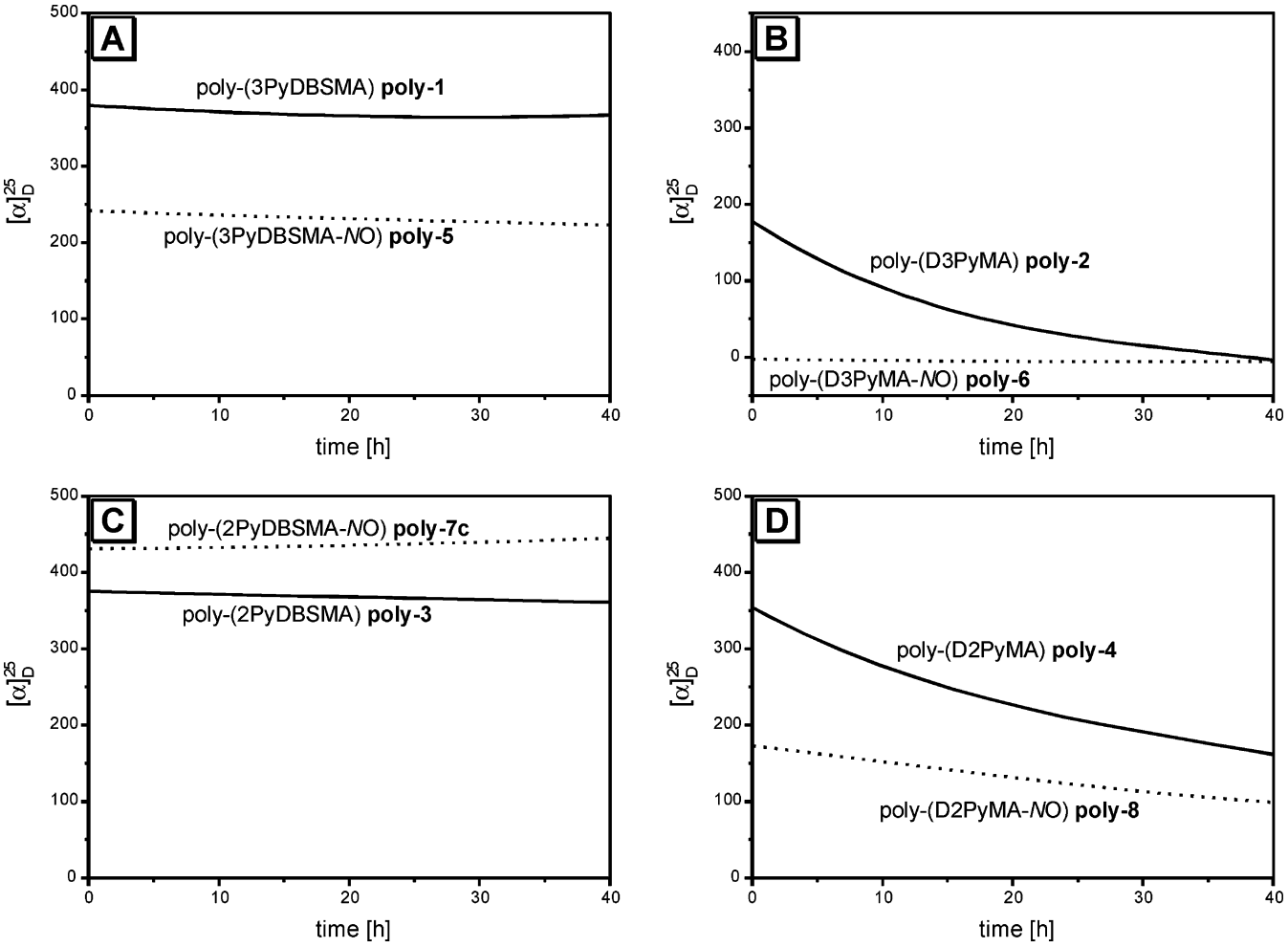


Figure 1. Change of optical rotation with time at room temperature in $CHCl_3$/2,2,2-trifluoroethanol (9:1 by volume): solid lines, nonoxidized polymers; dotted lines, oxidation products.

suberyl moiety (**poly-1** and **poly-3**, A and C) offer stable conformations due to their rigid lateral groups.[13,15] In contrast, optical rotations of those polymers lacking the ethylene linkage decrease rapidly (**poly-2** and **poly-4**, B and D), indicating a fast stereomutation leading to an equilibrium mixture of right- and left-handed helices.[19] Regarding the stereogenic centers in the vicinity of the chain ends, these helices are diastereomeric.[16] Small positive or negative optical rotations of polymer solutions after 40 h can be ascribed to this fact.

Despite the fact that from a stereochemical point of view only **poly-1** and **poly-3** were promising candidates for asymmetric catalysis, we oxidized *all* polymers to learn more about the structural preconditions for such a transformation (Table 2). Because of intense signal overlap in the aromatic section of the ^{1}H NMR spectra of the resulting poly(methacrylate)s, we could not directly analyze the degree of oxidation. Hence, we carried out an acidic cleavage of the ester groups with anhydrous HCl in methanol delivering poly(methacrylic acid) **poly-12** and the corresponding methyl ethers **13** and **14** of the lateral groups (Scheme 4, using **poly-5** as an example).[20] This method based on the analysis of small molecules with narrow lines offers the additional advantage to be more precise than analyzing polymer spectra with broad signals.

After purification of the methyl ethers **13** and **14** by extraction with ether, the pyridyl derivatives were analyzed by ^{1}H NMR spectroscopy. Figure 2 shows the sections of the ^{1}H NMR spectra of the cleavage products containing the protons next to the nitrogen in the pyridine rings.

In the case of **poly-5** (Table 2, entry 1) we found exclusively oxidized products (Figure 2A), demonstrating complete oxidation of the polymer. The optical rotation of this polymer was slightly reduced compared to **poly-1** but remained almost constant over a period of 40 h, as indicated in Figure 1A (dotted line).

Table 2. Oxidation of Pyridyl Substituted Poly(methacrylate)s Poly-1−Poly-4[a]

entry	polymer[b]	product	equiv of *m*-CPBA	yield [%]	oxidation level[c]	DP[d]	M_w/M_n[d]	$[\alpha]_D^{25}$[e]
1	**poly-1**	**poly-5**	1.2	100[f]	100	21	1.13	+241.5
2	**poly-3**	**poly-7a**	1.2	100[f]	42	24	1.17	+336.1
3	**poly-3**	**poly-7b**	2	89[g]	54	32	1.12	+431.0
4	**poly-3**	**poly-7c**	5	84[g]	65	33	1.10	+441.7
5	**poly-2**	**poly-6**	5	100[h]	100	32	1.09	−1.3
6	**poly-4**	**poly-8**	10	82[h]	37	49	1.09	+173.3

[a] Reaction time was 20 h. [b] Polymers are described in Table 1. [c] Determined by ^{1}H NMR analysis of the cleavage products after acidic hydrolysis. [d] Determined by GPC [poly(MMA) standard] after acidic hydrolysis and conversion to poly(MMA). [e] c = 1, $CHCl_3$/2,2,2-trifluorethanol (9:1 by volume). [f] Hexane-insoluble part. [g] Methanol-insoluble part. [h] Ether-insoluble part.

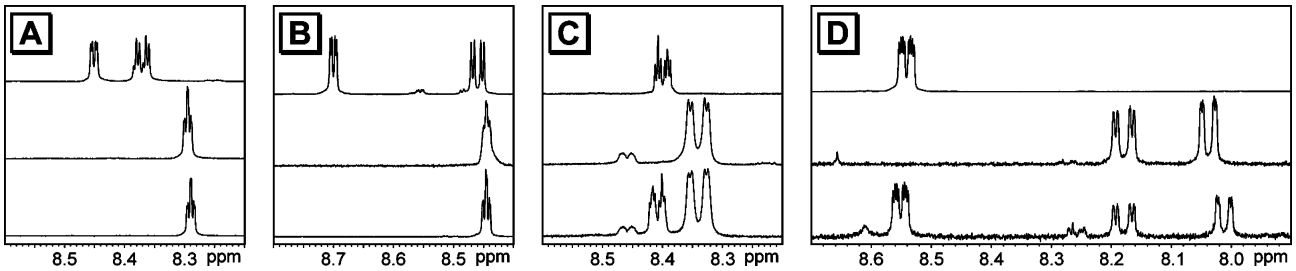
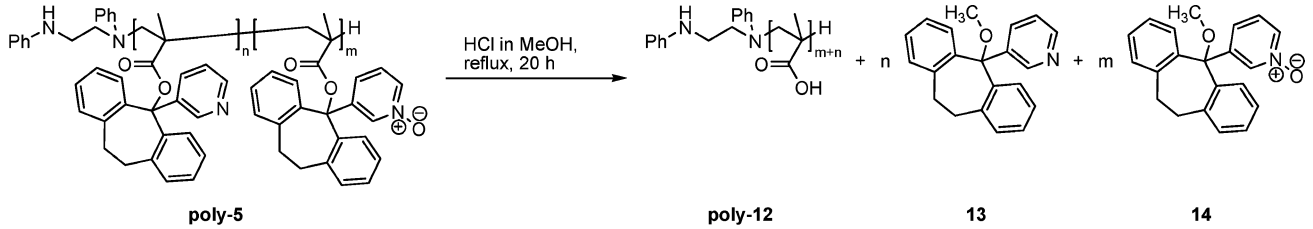


Figure 2. Downfield section of the ^{1}H NMR spectra of cleaved lateral groups showing signals of the protons next to the nitrogens: top traces, derived from the nonoxidized monomers; middle traces, derived from the oxidized monomers; bottom traces, derived from the oxidized polymers. (A) **1**, **5**, **poly-5**; (B) **2**, **6**, **poly-6**; (C) **3**, **7**, **poly-7c**; (D) **4**, **8**, **poly-8**.

Scheme 4. Acidic Cleavage and Methoxylation of the Lateral Groups

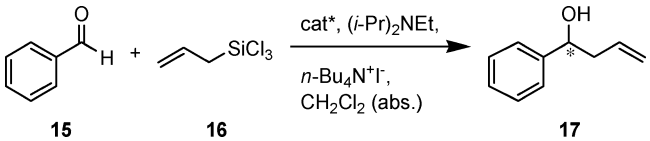


Contrasting the results with **poly-1**, the oxidation of the more hindered **poly-3** with a 2-pyridyl group close to the dibenzosuberyl moiety could not be achieved quantitatively under the same conditions (Table 2, entry 2), again confirming our considerations concerning the relative reactivities of the monomers and polymers toward the oxidation agent (see above). To achieve complete oxidation, we increased the amounts of *m*-CPBA (Table 2, entries 3 and 4). But even with 5 equiv of *m*-CPBA, the maximum oxidation level was 65% (**poly-7c**, Figure 2C). Nevertheless, the resulting polymer exhibits a constantly high optical rotation (Figure 1C, dotted line), indicating a stable single-handed helical structure. Interestingly, this time the optical rotation is even higher as compared to the nonoxidized polymer **poly-3**. The change in magnitude of the optical rotation in both cases relative to the nonoxidized polymers may be ascribed to conformational changes within the lateral groups, as is also discussed for other poly(methacrylate)s.[21]

The oxidation of the polymers **poly-2** and **poly-4** missing the ethylene linkage within the monomeric units resulting in a less stable conformation was carried out using higher amounts of *m*-CPBA, hoping that a fast oxidation will restrain the flexibility of the polymer and lead to a stable helical conformation. Unfortunately, the decay of optical rotation is faster than expected; indeed, it was even faster than with the parent compound. Using **poly-2**, we obtained a fully oxidized product **poly-6** (Table 2, entry 5; Figure 2B) but with a rotatory power close to zero (Figure 1B, dotted line), indicating that the oxidized lateral groups do not stabilize the conformation and/or racemization was complete before the oxidation took part. Like **poly-3**, the sterically hindered **poly-4** was only partially oxidized even with 10 equiv of *m*-CPBA after 20 h (Table 2, entry 6; Figure 2D). Furthermore, **poly-8** showed merely low optical activity, which is comparable to the value the nonoxidized polymer **poly-4** shows after 20 h in solution (Figure 1D, dotted line). Moreover, this rapid deterioration of optical activity indicates that the helical conformation of **poly-8** is not stable.

Since **poly-5** was the only completely oxidized polymer being conformationally stable at the same time, we chose this polymer to study its properties as an organocatalyst in the allylation of benzaldehyde **15** with allyltrichlorosilane **16** (Scheme 5).

Scheme 5. Asymmetric Allylation of Benzaldehyde 15 with Allyltrichlorosilane 16



To exclude any background reaction, we first tried to use the nonoxidized precursor polymer **poly-1** as a catalyst[11] and found, as expected, that it is inactive (Table 3, entries 1 and 2). This lack of reactivity demonstrates the necessity of pyridyl *N*-oxide units in the polymer. With the *N*-oxidized polymer **poly-5** (Table 3, entries 3 and 4), we observed moderate catalytic activity. Furthermore, modest enantiomeric enrichments in the allylation product **17** (14.3−19.1% *ee*) were detected by GC on a chiral stationary phase. The higher

Table 3. Asymmetric Allylation of Benzaldehyde 15 with Allyltrichlorosilane 16[a]

entry	catalyst	*T* [°C]	yield [%][b]	*ee* [%][c]	config[d]
1	**poly-1**	0	0		
2	**poly-1**	25	0		
3	**poly-5**	0	56.3	19.1	*R*
4	**poly-5**	25	44.9	14.3	*R*

[a] Catalyses were performed with 10 mol % of *N*-oxide and pyridine units, respectively; reaction time was 40 h. [b] Isolated yields. [c] Determined by chiral GC. [d] Determined by the sign of optical rotation.[22]

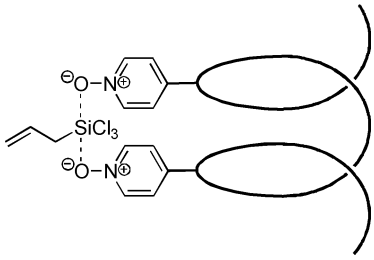


Figure 3. Wind spanning complex between silicon and two pyridyl *N*-oxide groups.

yield at 0 °C compared to 25 °C may be ascribed to the formation of a thermodynamically stable chelate complex between the silicon and two oxygens (Figure 3), which may be disturbed at higher temperatures. This speculation is in accordance with Denmark's results, indicating that activation via two Lewis basic ligands leads to higher reactivity than activation with only one ligand.[23]

Even if the enantioselectivities are only moderate, the results clearly show the principal suitability of helically chiral pyridyl *N*-oxide substituted poly(methacrylate)s for asymmetric organocatalysis.

Conclusions

Four different pyridyl substituted, helically chiral poly(methacrylate)s have been *N*-oxidized by *m*-CPBA. From the analysis of the acidolysis products of the resulting polymers, quantitative *N*-oxidation was observed for the 3-pyridyl substituted polymers **poly-5** and **poly-6** although only **poly-5** maintained its helicity on the same time scale as compared with its unoxidized precursor **poly-1**. The helix sense selective polymerization of *N*-oxidized monomers failed.

Poly-5 was found to be an active organocatalyst in the allylation reaction of benzaldehyde with allyltrichlorosilane, although the enantiomeric excess observed in the product was rather low (19% *ee*). This insufficient selectivity may be traced back to an inefficient chirality transfer from the helical polymer backbone to the lateral triaryl units. From the elegant work of Mislow[24,25] and Kessler,[26,27] it is known that Ar3ZX systems exist in a number of isomeric forms due to the simultaneous occurrence of central, planar, and helical chirality (in the most unsymmetrical case). In **poly-5** the maximum number of isomers is 16 (two different aryl rings, none of them C2-symmetric)[24] which are equilibrating diastereomeric conformers due to the helicity of the polymer backbone. Facing this great many of diastereomeric conformations, a nonuniform microenvironment at the catalytically active sites may be a consequence, which in turn is expected to be detrimental for highly asymmetric inductions. On the other hand, this analysis of the problem may be the clue to circumvent it. If the number of conformational diastereomers can be reduced to be only two or three and if one assumes that one of these isomers reacts faster than the other(s), then the asymmetric induction from each repeating unit should be uniform and high enantiomeric excesses may result. The stereochemical control of two tropos axes[28,29] in biphenol derived phosphonates by a centrochiral core is a successful example for the feasibility of this concept.[30] Work along these lines using biphenol substituted polyisocyanates and functionalized polyquinoxalines is in progress.

Experimental Section

Materials and General Procedures. *N*,*N*′-Diphenylethylenediamine **10** (DPEDA),[31] (+)-(*S*)-1-(2-pyrrolidinomethyl)-pyrrolidine **11** ((+)-PMP),[32,33] poly(3PyDBSMA) **poly-1**,[13] poly(D3PyMA) **poly-2**,[14] poly(2PyDBSMA) **poly-3**,[15] and poly-(D2PyMA) **poly-4**[18] were prepared according to published procedures. After the reaction times compiled in Table 1 the resulting polymers were isolated following the published procedures. All other reagents and solvents were purchased from commercial sources and used as received unless otherwise noted.

Diethyl ether (Et_2O), tetrahydrofuran (THF), toluene, and benzene were distilled from sodium/benzophenone, and dichloromethane (CH_2Cl_2) was distilled from calcium hydride (all under argon) just before use. Argon (4.8) was deoxygenized by a Cu catalyst and then passed through 4 Å molecular sieve, blue gel, sulfuric acid (concentrated), phosphorus pentoxide on silica (Sicapent), and finally potassium hydroxide to remove water and acidic contaminations. Preparations of air-sensitive materials were carried out using standard Schlenk and vacuum line techniques.

Spectroscopic Techniques. NMR spectra were recorded on a Bruker DRX 500 or an ARX 300. Gel permeation chromatography (GPC) was carried out at 30 °C, with JASCO HPLC pumps, MZ-Gel Sdplus 10E3 Å and 10E5 Å GPC columns connected in series with exclusion sizes of 70 000 and 4 000 000; flow 1.0 mL min^{-1}, using THF as eluent, JASCO UV detector UV 975. Specific optical rotations were determined on a Perkin-Elmer polarimeter 241 with Haake D8 thermostat in 1 dm cuvettes. Chiral GC was performed with a Fisons Instruments GC-8360 gas chromatograph using a Resteck RT-γDEXsa (0.25 mm i.d. × 30 m × 0.25 μm) with nitrogen as carrier gas at a flow rate of 1 mL min^{-1} and isothermal conditions at 135 °C.

General Procedure for the Oxidation of Pyridyl Substituted Methacrylates. A solution of 2 equiv of 50% *m*-CPBA in 1 mL $mmol^{-1}$ dichloromethane was added slowly via syringe to a solution of the monomer in dichloromethane (10 mL $mmol^{-1}$) at 0 °C. After stirring for 20 h at ambient temperature, the reaction mixture was extracted three times with 35 mL $mmol^{-1}$ $NaHCO_3$ solution, washed with 10 mL $mmol^{-1}$ saturated NaCl solution, and dried over Na_2SO_4. After removal of the solvent under reduced pressure ^{1}H NMR analysis of the crude product was carried out. Only **5** was further purified; **6**−**8** were analyzed as crude product.

(3-Pyridyl *N*-oxide)dibenzosuberyl Methacrylate 5. With 1.90 g of 50% *m*-CPBA (5.49 mmol) and 976 mg (2.745 mmol) of (3-pyridyl)dibenzosuberyl methacrylate **1**, 1.4 g of crude product was obtained. Isolation of the product was carried out by flash chromatography on silica gel using ethyl acetate/methanol (5:1 by volume), yielding 918 mg (90%) of **5**. ^{1}H NMR ($CDCl_3$, 300 K, δ in ppm) δ 1.961 (dd, 3H, J = 1.5, 1.0 Hz, CH_3), 3.11−3.19 (m, 4H, CH_2−CH_2), 5.675 (dq, 1H, J = 1.5, 1.0 Hz, C=CH_2), 6.258 (dq, 1H, J = 1.0, 1.0 Hz, C=CH_2), 7.05−7.20 (m, 8H, ArH), 7.28−7.38 (m, 2H, ArH), 8.018 (ddd, 1H, J = 6.3, 1.8, 1.1 Hz, PyH), 8.395 (td, 1H, J = 1.7, 0.6 Hz, PyH). ^{13}C NMR data ($CDCl_3$, 300 K, δ in ppm) δ 18.55 (*C*H_3), 35.79 (*C*H_2−*C*H_2), 86.74 (Ar$_3$*C*−O), 124.68 (Ar), 125.35 (Py), 126.50 (H_2*C*=C), 127.05 (Ar), 128.24 (Ar) 128.88 (Ar), 130.58 (Ar), 136.87 (H_2C=*C*), 137.44 (Py), 137.61 (Py), 139.80 (Ar), 140.70 (Ar), 148.01(Py), 164.50 (*C*OO).

General Procedure for the Oxidation of Pyridyl Substituted Poly(methacrylate)s. A solution of 50% *m*-CPBA in 3.5 mL $mmol^{-1}$ dichloromethane was added slowly via syringe to a solution of the polymer in dichloromethane (10 mL $mmol^{-1}$ monomer units) at 0 °C. After stirring for 20 h at ambient temperature, the reaction mixture was poured onto 70 mL $mmol^{-1}$ ice cold hexane, methanol, or diethyl ether. The precipitate was isolated and dried, yielding a white solid. Molar ratios and solvent for workup are listed in Table 2. To analyze the oxidation level, 50 mg of the resulting polymer was refluxed with 3 mL of saturated anhydrous HCl in methanol for 20 h. After neutralization with 1 *m* NaOH in methanol, evaporation of the solvent, extraction of the cleaved side groups with diethyl ether from the aqueous solution, and drying over Na_2SO_4, a white solid was isolated. By ^1H NMR analysis of the cleaved side groups the oxidation level was determined.

Synthesis of Poly[(3-pyridyl-*N*-oxide)dibenzosuberyl methacrylate] Poly(3PyDBSMA-*N*O) Poly-5. Using 316 mg (0.915 mmol) of 50% *m*-CPBA and 270 mg of poly(3-pyridyldibenzosuberyl methacrylate) (0.759 mmol pyridine units) **poly-1**, precipitation from 50 mL of ice cold hexane yielded 283 mg (quant) of a white solid. To analyze the oxidation level, 50 mg of the polymer was hydrolyzed, yielding 17 mg of a white solid, containing exclusively the oxidized product **14**.

General Procedure for the Asymmetric Allylation. Benzaldehyde (41 μL, 400 μmol) **15**, catalyst (41 μmol, ~10 mol % *N*-oxide or pyridyl units), ethyldiisopropylamine (350 μL, 2 mmol), and tetrabutylammonium iodide (175.9 mg, 476 μmol) were dissolved in 2 mL of dichloromethane and adjusted at the temperature listed in Table 3. Allyltrichlorosilane (84.1 mg, 479 μmol) **16** was added, and the resulting mixture was stirred for 40 h at that temperature. After this time, TLC analysis of the reaction mixture showed no further conversion. The reaction was quenched by addition of 1 mL of aqueous saturated $NaHCO_3$ solution, and the product was extracted three times with 10 mL of ethyl acetate. The combined organic layers were washed with 10 mL of saturated NaCl solution and dried over Na_2SO_4, and finally the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on 20 g of silica gel (15−40 μm) using petroleum ether/ethyl acetate (20:1 by volume). Enantiomeric excess was analyzed by chiral GC: R_t(*R*-**17**) = 32.7 min, R_t-(*S*-**17**) = 34.9 min, and R_t(PhCHO) = 9.6 min.

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