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Porphyrin Macrocyclic Catalysts for the Processive Oxidation of Polymer Substrates

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Natural proteins and enzymes have been widely used as blueprints for the construction of synthetic catalysts.[1] As mimics for the monooxygenase cytochrome P450, myriads of modifications have been introduced into the skeleton of catalytic porphyrins with the purpose to improve the degree of control over the catalytic reactions and to reach efficiencies comparable to that of natural enzymes.[2] For example, nitrogen containing axial ligands have been used to enhance the rate of oxidation catalysts by activating the manganese−oxygen bond of Mn(III) porphyrins;[3] electron donating or withdrawing groups of different nature have been added to the meso positions of these porphyrins to tune the electronic properties; i.e. the reactivity of the catalytic center;[4] and shape-selective or chiral binding pockets have been introduced to improve the chemo- and stereoselectivities of the reaction.[5] Furthermore, bulky substituents have been attached to the porphyrin to provide spatial shielding, thus preventing deactivation of the catalyst by dimerization reactions.[6]

We have previously reported on the synthesis and study of a diphenylglycoluril-appended porphyrin catalyst **Mn2** (Figure 1a).[7] Because of its open ring structure, this compound is capable of binding to a polymer chain, e.g. polybutadiene, and thread on it.[8] Kinetic studies have revealed that the catalyst can convert the double bonds of polybutadiene into epoxide functions while gliding along the polymer chain in a pseudorotaxane fashion[9] (Figure 1c). Because of this unique feature, this catalyst can be called a processive enzyme mimic.[10] In spite of the very promising results in terms of guest complexation, motion along the polymer chain, and oxidation of polymer substrates, the system has some drawbacks hampering its practical use as a processive catalyst. For instance, a large excess of a bulky coordinating ligand (a pyridine derivative) is required to efficiently shield the outer face of the catalyst, thereby facilitating the catalytic reaction to take place on the inside through a rotaxane mechanism. However, even at high concentrations of axial ligand, the outer face of the catalyst remained partially accessible, and as a result deactivation of the catalyst, probably by a dimerization reaction, still occurred. This led to premature stalling of the epoxidation process.

With this problem in mind, we decided to construct a new analogue of **Mn2** with ethylureapropoxy tails covalently attached to the outer *ortho*-positions of the porphyrin *meso*-phenyl groups (compound **Mn1**, Figure 1a). These tails are meant to protect the exposed face of the cavity and to prevent the destruction of the catalyst. Preliminary studies carried out with the zinc analogue of **Mn1** showed that the tails adopt a folded conformation over the porphyrin roof, with the urea moieties displaying a coordinative interaction with the zinc center (Figure 1b). We expected therefore that similar coordination behavior would be present in the case of the manganese derivative, thereby forcing the catalytic reaction to take place on the inside of the cage.

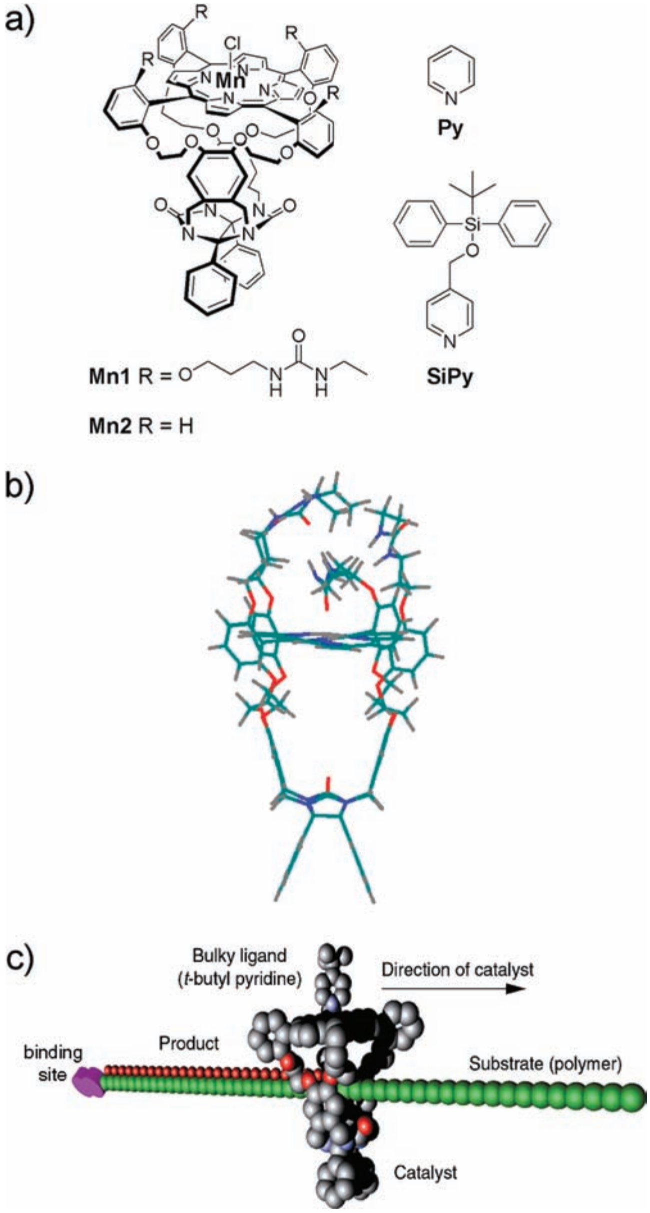

Figure 1. (a) Molecular structures of **Mn1**, **Mn2**, **Py**, and **SiPy**. (b) Computer-modeled structure of **Mn1** with one of the urea-functionalized tails coordinating to the manganese center. (c) Schematic representation of the processive catalytic epoxidation of polybutadiene by **Mn2**.

The synthesis of **Mn1** is outlined in Scheme 1. In the UV−vis spectrum of **Mn1** (see Supporting Information (SI)) the location of the absorption bands is clearly indicative of the occurrence of

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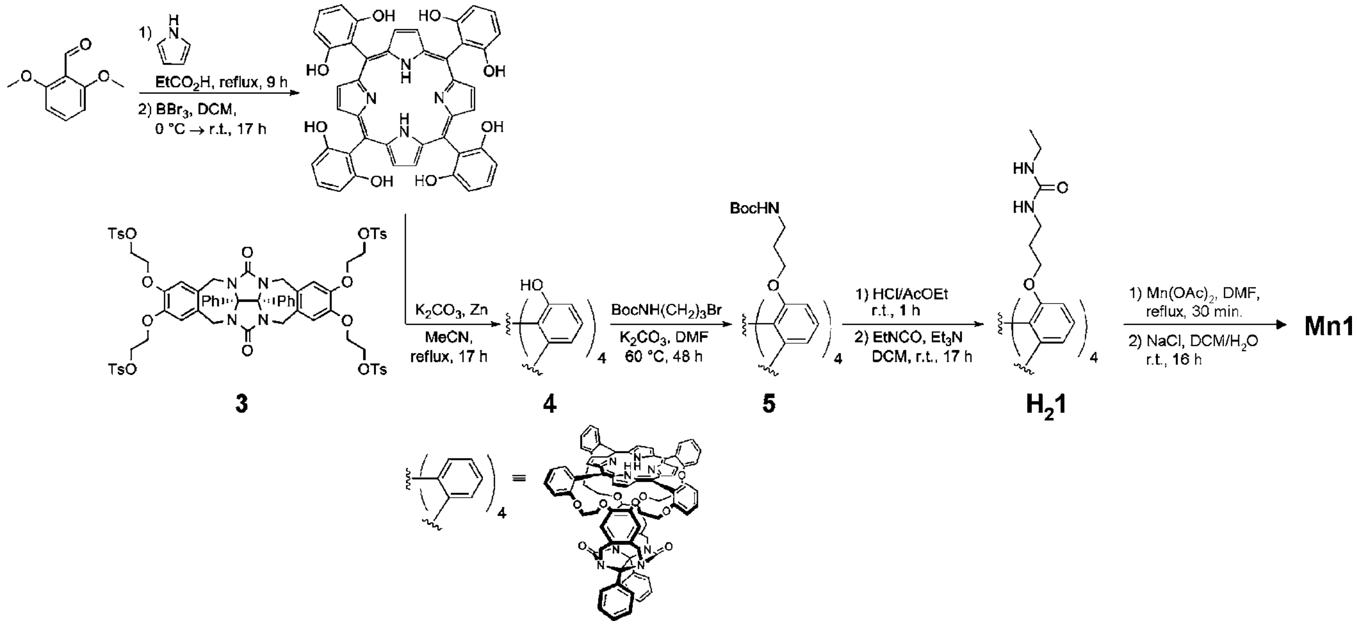
Scheme 1. Synthetic Route To Obtain Porphyrin Catalyst **Mn1**



intramolecular coordination of the urea functionalities located at the end of the porphyrin substituents to the porphyrin manganese center. When compared to its nonsubstituted counterpart **Mn2** in similar concentration conditions, **Mn1** shows a typical broadening of the Soret band, with a simultaneous blue shift and slight increase of the absorption maxima of the Q-bands. These features are typically observed in the UV−vis spectra of manganese porphyrins when an axial ligand binds to the metal center and are, in the case of **Mn1**, seemingly independent of the porphyrin concentration, which proves that the process of axial coordination is intramolecular. Additional evidence for this coordination comes from mass spectroscopic analysis. **Mn2** is characterized by the presence of a methanol adduct of the manganese porphyrin cation in the ESI-MS spectrum (100% isolation), which we attribute to axial coordination of methanol to the manganese center stabilized by inclusion inside the cavity of **Mn2**. Such an adduct is completely absent in the mass spectrum of **Mn1**, suggesting that binding of methanol to the manganese center is impossible, or at least unfavorable, presumably because of competition with the intramolecular binding of the urea functions in **Mn1**, while the chloride counterion is presumably coordinating inside the cavity.

Compound **Mn1** was tested as a catalyst in the epoxidation of polybutadiene (98% *cis*, average MW = 200.000 amu) in chloroform. The catalytic reactions were performed using iodosylbenzene as an oxidant, under conditions similar to those described in our previous studies with **Mn2**.[7] Pyridine (**Py**) and 4-{[(*tert*-butyldiphenylsilyl)oxy]methyl}pyridine (**SiPy**) (Figure 1a) were used as axial ligands. At given time intervals, the reaction mixtures were filtered to remove unreacted iodosylbenzene, and the filtrate was directly analyzed by ^{1}H NMR. The results are presented in Figure 2, and the values measured for the initial rates and *cis*/*trans* ratios of the reaction products are collected in Table 1. Experiments performed with manganese(III) 5,10,15,20-tetrakis-(*o*-methoxyphenyl) porphyrinato chloride (**MnTMPP**) as a reference catalyst are also included in Table 1 for comparison.

Figure 2 shows the differences between the catalytic reactions performed with **Mn1** and the reference compound **Mn2**. In the case of **Mn1**, independent of whether pyridine ligands were used in the reaction mixture or not, conversion of polybutadiene always proceeded to 100% completion following kinetics that could be fitted almost perfectly to a first-order substrate conversion reaction. In contrast, a substantial deviation from first-order was observed in all reactions performed with **Mn2**, and fitting of the kinetic curves required the use of eq 1, which includes a term (k_{bleach}) accounting for a bimolecular (second order) process of catalyst destruction, i.e. the detrimental formation of a μ-oxo dimer of the catalyst (see SI for more details about eq 1).

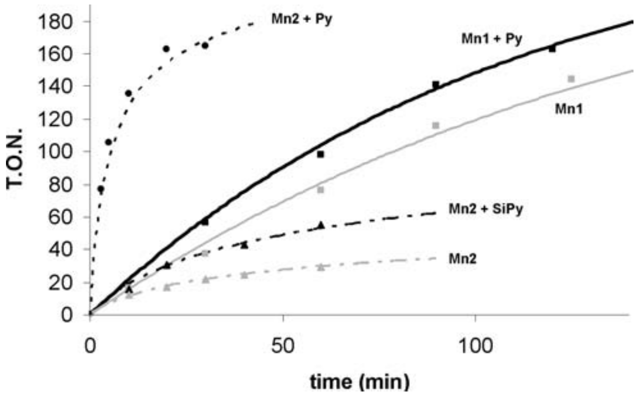


Figure 2. Kinetics of polybutadiene epoxidation by **Mn1** (full lines) and **Mn2** (dotted lines): first-order fit **Mn1**; first-order fit **Mn1**+**Py**; fit **Mn2** to eq 1; fit **Mn2**+**py** to eq 1; fit **Mn2** + **SiPy** to eq 1.

Table 1. Initial Turnover Frequencies (T.O.F.) and *Cis*/*Trans* Product Ratios Found in the Various Catalyzed Epoxidation Experiments

	axial ligand					
	—[a]		SiPy		Py	
porphyrin catalyst	initial T.O.F.[b]	*cis*/ *trans*	initial T.O.F.[b]	*cis*/ *trans*	initial T.O.F.[b]	*cis*/ *trans*
Mn1	120	30/70	120	30/70	150	30/70
Mn2	95	30/70	180	30/70	5200	97/3
MnTMPP	73	60/40	270	85/15	330	85/15

[a] In the absence of axial ligand. [b] In h^{-1}; extrapolated from the slope of the tangent to the catalytic curve at the origin.

$$[\mathrm{P}] = [\mathrm{S}]_0\{1 - (1 + [\mathrm{Cat}]_0 \cdot k_{\mathrm{bleach}} \cdot t)(-k_{\mathrm{cat}}/k_{\mathrm{bleach}})\} \tag{1}$$

Moreover, an additional series of experiments carried out with a large excess (8000 equiv with respect to catalyst) of substrate at low concentrations of the porphyrin catalyst (see SI) and in the absence of axial ligand showed that the conversion was almost complete after 96 h for **Mn1**, whereas the oxidation process stalled after a turnover number (T.O.N.) of 1800 for **Mn2**. These results strongly suggest that the urea tails of the catalyst have a beneficial shielding effect and increase the stability of **Mn1**. The shielding effect was confirmed by the fact that additional batches of substrate could be successfully converted.[11]

As can be seen in Table 1, the use of an axial ligand in the epoxidation reactions leads to remarkable differences between **Mn1** and the other catalysts. For the reference catalyst **MnTMPP**, the activation of the metal center by a pyridine ligand results in an enhancement of its catalytic activity by a factor of 4 to 5 depending on the type of pyridine ligand (Table 1, entry 3).

In the case of **Mn2** the use of the bulky **SiPy** ligand, which coordinates to the outside of the catalyst, gives a small yet significant double enhancement of the initial turnover frequency (T.O.F.) (Table 1, entry 2). In contrast, addition of a **SiPy** ligand to **Mn1** does not affect the catalytic reaction at all. The turnover frequencies in the presence or absence of this ligand were identical within experimental error (Table 1, entry 1). This indicates that no complexation takes place between **SiPy** and the manganese center of **Mn1**, presumably as the result of intramolecular coordination of the urea tails to this center.

The use of the smaller **Py** ligand as a promoter of the catalytic reaction led to an even more pronounced difference in behavior between **Mn1** and **Mn2**. In the latter case, **Py** binds to the inside of the porphyrin cavity, forcing the oxidation reaction to take place on the outside, which is more accessible to the polymeric substrate. This different arrangement of the catalytic complex leads to striking differences in the activity and stereoselectivity of the reaction, with the initial TOF being enhanced by a factor of more than 50 compared to the TOF in the absence of an axial **Py** ligand. Also the stereoselectivity of the reaction changes dramatically, i.e. in the direction of the *cis*-epoxide product (*cis*/*trans* ratio changes from 30:70 to 97:3) (Table 1, entry 2). Such changes are not observed in the case of **Mn1**: under analogous reaction conditions, only a very limited rate enhancement of the reaction rate was measured (TOF changes by a factor of 1.5), while no change in the *cis/trans* selectivity was found (Table 1, entry 1). This is clear evidence that the binding of **Py** in the cavity of **Mn1** is prevented. We attribute the latter to a competition between this ligand and the urea moieties of the tails for binding to the manganese center. The presence of four urea groups covalently anchored to the porphyrin cage complex results in a high effective molarity of these groups, efficiently counterbalancing the normally 2 to 3 orders of magnitude higher binding of **Py** inside the cavity of the catalyst.[7] The marginal enhancement for **Mn1** is probably unrelated to any binding of **Py** to the porphyrin cage, but presumably the result of slight changes in the polarity of the medium due to the addition of the non-negligible amounts of **Py** (up to 2 vol %). From the data above it can be concluded that in the case of **Mn1** the epoxidation reaction is efficiently and exclusively directed toward the inside of the cage catalyst. In other words, when **Mn1** is used as a catalyst, the oxidation of polybutadiene will only occur after the formation of an initial rotaxane intermediate, which is favorable for a processive sequence of reaction steps.

In conclusion, we have shown that the attachment of ethylureapropoxy tails to the outside of the cavity containing porphyrin complex is a suitable procedure not only to increase the stability of the catalyst, viz. by preventing degradation via dimerization but also to force the catalytic reaction to take place within the cavity of the catalyst in a pseudorotaxane fashion. We expect that these features can be advantageously used in the future development of efficient processive catalysts.

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Supporting Information Available: Experimental procedures, derivation of eq 1, UV−vis spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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