Communications to the Editor

Pseudo-Generational Effects Observed for a Series of Hyperbranched Polymers When Applied as Epoxidation Catalysts

X. Zheng, I. R. Oviedo, and Lance J. Twyman*

Department of Chemistry, The University of Sheffield, Brook Hill, Sheffield S2 7HF, U.K.

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The architecture of dendritic polymers (i.e., dendrimers and hyperbranched polymers) can be exploited for a variety of applications.[1] One of the key properties of these molecules is their ability to isolate a functional group at their core or center. Being able to isolate a core enables us to precisely control the environment around that core, which leads to enhanced solubilization and/or stabilization. This is a particularly useful property with respect to catalysis, where controlling the local environment enables beneficial effects to be observed. For example, making the core more or less polar than the bulk solvent can encourage substrate access, which in turn can lead to enhanced rates.[2] Although some related work using hyperbranched polymers has recently been published,[3] this property has been most extensively study using dendrimers.[4] Because of steric crowding (at the core or periphery), the catalytic ability or rate often decreases as the dendrimers become larger. However, in some cases the rate is actually observed to increase as the dendrimer becomes larger (tailing off when the size eventually becomes too big).[5] The enhanced catalytic ability of these core functionalized dendrimers has led to favorable comparisons with biological catalysts, i.e., as synthetic enzymes. Despite these encouraging results, the application of dendrimers is often limited by their lengthy and sometimes complicated synthetic procedures. Although hyperbranched polymers (HBPs) are much simpler to synthesize, their application to areas that require site isolation has been limited. One of the reasons limiting their application is related to the difficulty in synthesizing HBPs with functional cores.[6] The main challenge is to ensure that each and every hyperbranched molecule in a polydisperse mix possess a core unit. This is an essential requirement if we wish to compare a particular property with a series of HBPs of different molecular weight (i.e., catalysis). Recently, we described an efficient process that utilized a reversible/equilibrium procedure that overcame this problem. This method was recently exploited for the construction of porphyrin cored HBPs and their application as mimics for the oxygen binding and storage proteins hemoglobin and myoglobin.[7]

For the work described in this paper, we were interested to test porphyrin cored HBPs as mimics for cytochrome P450, an enzyme responsible for a variety of biological oxidation reactions.[8] As well as studying the catalytic potential of these macromolecules, we were also interested in determining whether or not any generational effects could be observed when a series of HBPs of differing molecular weight were used (i.e., pseudo-generations). Specifically, we wanted to know whether the environment around the catalytic core, provided by the bulk polymer, would lead to an advantageous effect on the catalytic reaction.

The HBPs selected for our study were the same porphyrin cored hyperbranched polyarylester systems previously reported in our heamoglobin/myoglobin studies.[7a] Tetra(acetoxyphenyl)porphyrin (TAPP) was reacted with an excess of the AB_2 monomer 3,5-diacetoxybenzoic acid under reversible transesterification condition to give the HBP **1** shown in Scheme 1.[7b] Iron was inserted within the porphyrin core by reacting polymer **1** with 10 equiv of $FeCl_2$ in the presence of 5 equiv of 2,6-lutidine in THF (Scheme 1). The solution was refluxed for 4 h and subsequently exposed to air to convert the Fe(II) porphyrin to the Fe(III) porphyrin. Purification was achieved by filtration through Celite (to remove excess $FeCl_2$), followed by trituation from concentrated THF into MeOH to give the porphyrin cored HBP **2** as shown in Scheme 1.

Iron insertion to give **2** was confirmed by UV/vis spectroscopy, which showed a broad Soret peak at 418 nm and two Q bands at 508 and 563 nm. As expected, the ^{1}H NMR spectrum of **2** was very broad due to the paramagnetic effect of high-spin Fe(III) in the porphyrin core. GPC analysis of **1** and **2** showed that the polymer had not been degraded during metal insertion, with M_n values of 9700 (PD 3.3) and 10 200 (PD 2.9) being recorded for the free base porphyrin and Fe(III) porphyrin cored HBPs, respectively. When dual detection was carried out, using an RI and UV detector (set to 418 nm), it was shown that both detection peaks were superimposed and completely overlapped. This confirms that the porphyrin core was distributed over the whole molecular weight range of the hyperbranched polymer. Fractionation followed by UV spectroscopy and mass spectrometry analysis confirmed that the porphyrin cored was distributed *evenly* across the complete molecular weight range of the hyperbranched polymer.[6]

To evaluate the catalytic efficiency of the hyperbranched polymer and to determine whether the catalytic rate could occur at a reasonable velocity, we first chose to study the epoxidation of a simple alkene (1-octene) using iodosylbenzene as the oxygen donor and the bulk polymer **2** as the catalyst (along with *N*-dodecane as an internal standard).[8] The epoxidation of 1-octene epoxidation under these conditions yields an epoxide plus other oxidation byproduct, as shown in Scheme 2.[9] The molar ratio between bulk HBP catalyst **2** and iodosylbenzene was 1:50, with excess alkene substrate used to inhibit the side reactions.[10] Iodosylbenzene was added to a sealed reactor vial, and after the reactor vial was evacuated and flushed with nitrogen, a solution of 1-octene and HBP **2** in DCM was added (along with a known amount of an internal standard). Aliquots were taken out at various times and after filtration were analyzed by GC. The relationship between the reaction time and the yield of products (assessed by following the formation of iodobenzene) is shown in Figure 1. The yield of oxidation products

* Corresponding author. E-mail: l.j.twyman@sheffield.ac.uk.

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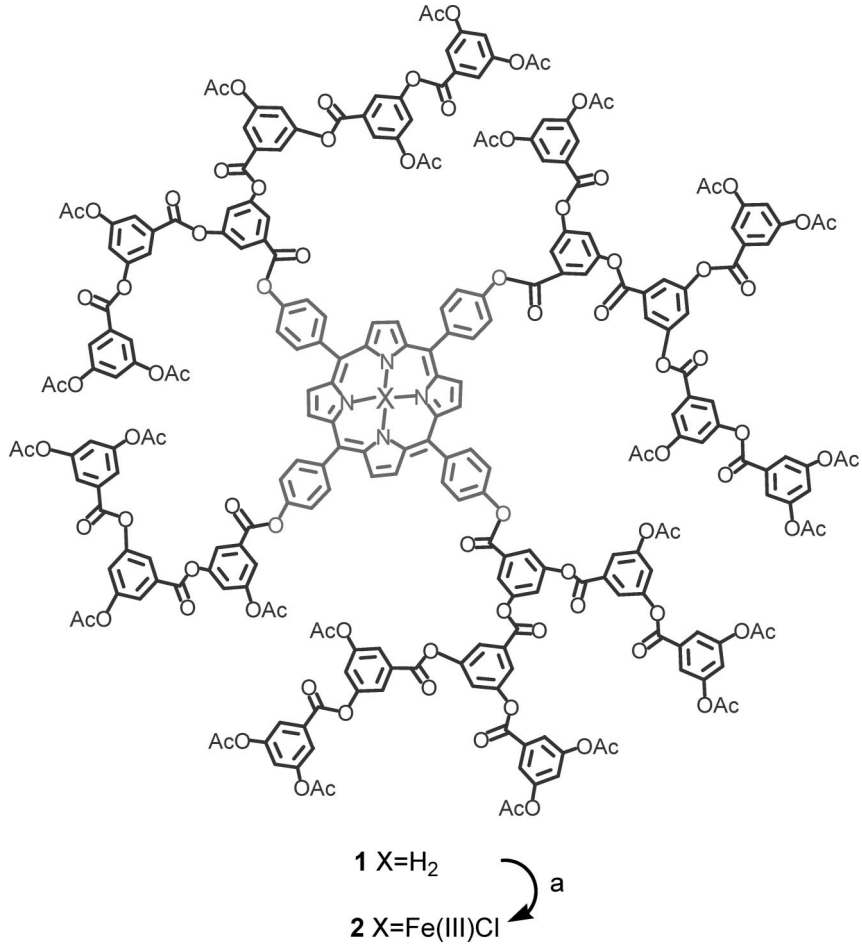
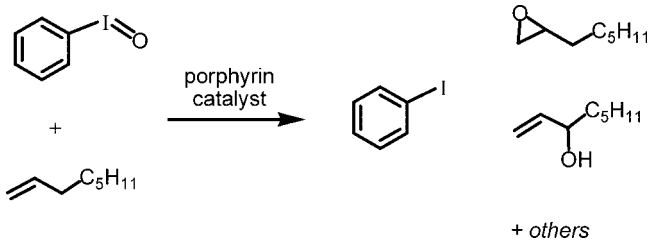
Scheme 1. Metalation of Bulk HBP; (a) $FeCl_2$, 2,6-Lutidine, THF



Scheme 2. Oxidation of 1-Octene



reached around 60% after 30 min and was essentially complete after 4 h.[11] All later reactions were therefore carried out and analyzed after 30 min. This would allow for the simple assessment of any improvement or deterioration in catalytic efficiency with regards to various HBPs.

In particular, we were interested in determining whether a "dendritic" effect and/or any site isolation properties occurred with HBPs. In order to achieve this aim, we needed to obtain a series of HBPs with different molecular weights and ideally, relatively low polydispersities.[12] There are two possible ways this can be achieved; first we could synthesize a series of dendrimers using the core to monomer ratio as a method to control molecular weight.[13] Alternatively, we could take the polymer previously used to evaluate catalytic activity (i.e., HBP **2**, Scheme 1) and fractionate it using preparative size exclusion chromatography. This is a more efficient method as it requires just one synthetic step. As such, the bulk HBP **2** was fractionated by preparative size exclusion chromatography using SX-1 Biobeads with DCM as eluent. After separation and reprecipitation, three different number-average molecular weight HBPs were obtained. These had M_n values of 5400, 10 000, and 16 000 as determined by analytical GPC (see Table 1).[14] Core incorporation of each fraction was confirmed using UV and mass spectrometry (as previously reported).[6] The three HBP samples spanned a reasonable molecular weight range and have been given the terms HBPFe-*small*, HBPFe-*medium*, and HBPFe-*large* (for the HBPs with M_n 5400, 10 000, and 16 000, respectively). Knowing the molecular weights of the core, the average monomer and the final polymer (estimated from GPC) enabled us to estimate the number of repeat units as 25, 50,

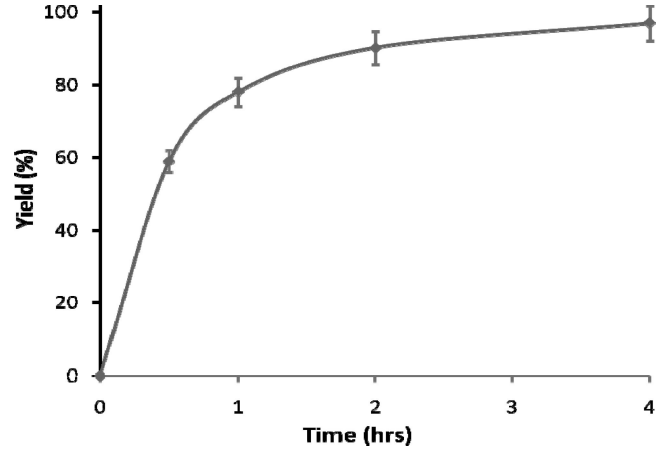


Figure 1. Reaction profile for the porphyrin catalyzed epoxidation of 1-octene (as determined from the GC analysis of the iodobenzene byproduct; see Scheme 2).

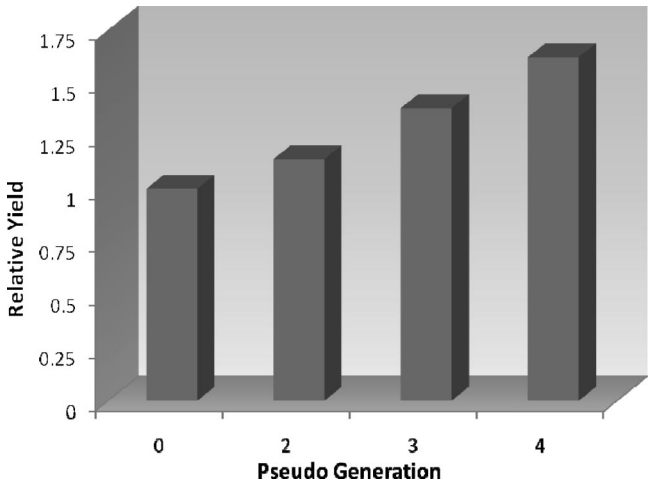


Figure 2. Relative yield of the epoxidation product produced using the pseudo-generation HBP catalysts. The G0 catalyst is the core molecule Fe−tetra(acetoxyphenyl)porphyrin.

Table 1. Molecular Weight and Terminal Group Data for the HBPs

Fe-cored HBP	M_n	PD	number of repeat units	pseudo-generation[a]
TAPPFe-*core*	900	1.0	4	0
HBPFe-*small*	5400	1.9	25	2
HBPFe-*medium*	10000	2.3	50	3
HBPFe-*large*	16000	2.5	85	4

[a] Rounded to the nearest integer.

and 85 for the small, medium, and large HBPs, respectively. Taking these numbers and treating the fractionated HBPs as idealized dendrimers, they approximate to the second, third, and fourth "pseudo"-generation dendrimers, respectively. As the size of the HBPs increase (i.e., as the molecular weight increases), the local environment around the catalytic porphyrin core will also change. This change should have an effect on the catalytic activity. For example, if the environment around the porphyrin is more amenable to the requirements of the catalytic reaction (i.e., polarity effects), then an increase in yield/efficiency will be expected—a so-called *positive dendritic effect*.[15] On the other hand, as the HBPs get larger, the central porphyrin core will become more isolated and sterically hindered. If this is the case, then the yield/efficiency will drop as molecular weight increases—a *negative dendritic effect*. A third possible outcome is a combination of both effects, where an initial increase in yield/efficiency is observed, due to an improved local environment, followed by a decrease in yield due to sterics. Finally, if sterics or local environment effects play no part, then no change in yield/efficiency will be observed as the HBPs get larger. To probe these possibilities, the activity of the fractionated HBPs was investigated using the same reaction conditions as previously described for the bulk hyperbranched polymer **2**.[16] The activity of the Fe(III) tetraacetoxyphenylporphyrin core (TAPPFe) was also assessed for comparison (generation 0).

The results are shown graphically in Figure 2. In all cases the product yield was greater than that obtained using the core molecule (i.e., the TAPPFe-*core* or "pseudo"-generation zero molecule). In addition, as the molecular weight increases, the yield/efficiency also increased. This reached a maximum for the largest polymer tested (HBP-*large* or "pseudo-genertation 4 molecule), where a 60% increase in yield/efficiency was observed. In fact, the yield recorded for the largest HBP was almost quantitative, reaching 96% after 30 min (compared to just 60% for the simple porphyrin catalyst: TAPPFe-*core*) This increase in yield/efficiency occurs despite an increase in monomer density/steric hindrance around the core. Furthermore, the rate of increase per generation shows an ~20% increase in efficiency as we move from one generation to the next.

Therefore, it appears that as the HBPs become larger, the environment around the catalytic cores gradually becomes better suited to substrate binding and catalysis. Any negative effects due to steric hindrance are minor. This is in contrast to most of the published data on core functionalized dendrimers, where a tailing off in efficiency (i.e., binding/catalysis) occurs at much lower molecular weight (and lower generation). This is due to the constrained structure and environment of the more densely branched and larger dendrimers, which are more compact and densely branched relative to the open and flexible structure of a HBP (particularly at the core). It is interesting to note that catalytic efficiency continued to increase even when the largest HBP was tested (HBPFe-*large*, M_n 16 000/M_w 40 000). As such, core-functionalized HBPs may offer some advantage over dendrimers when it comes to *simple* catalysis. Specifically, the lower branching density and more open structure of a HBP may allow it to provide a reasonably balanced and controlled microenvironment for catalysis to occur (i.e., a balance between sterics and polarity). However, the lack of a significant steric effect probably represents a disadvantage when it comes to catalysis or certain other applications that demand selectivity. For example, the porphyrin cored dendrimers developed by Suslick, which had the ability to select substrates based on their size and shape.[17] Nevertheless, the simplicity of synthesis and catalytic ability of core functionalized HBPs means they have the potential to be exploited as useful and efficient catalyst. The ability these and other core functionalized HBPs to catalyze other reactions in various solvents is currently under investigation in our group.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) It is important to appreciate that the molecular weights obtained by GPC are not absolute. As is common for most dendritic molecules (i.e., dendrimers and HBPs), molecular weights are quoted relative to linear polymeric standards (polystyrene in our case). Linear polymers possess a larger hydrodynamic radii for a given moleculer weight (relative to globular dendritic macromolecules). When used as calibrants this results in an *underestimation* when calculating the molecular weight ofdendritic molecules. For example see: Twyman, L. J.; Beezer, A. E.; Mitchell, J. C. *J. Chem. Soc. Perkin Trans. I*. **1994**, *14*, 407 (and references within).
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