



The challenges with low molecular weight catalysts include separation from the product and reuse of the catalyst. These shortcomings have been addressed using fluororous tags,<sup>22–25</sup> magnetically recoverable<sup>26</sup> or ionic liquid based catalysts.<sup>27</sup> Alternatively, the chiral unit can be covalently immobilised on an insoluble carrier matrix.<sup>28</sup> Diarylprolinol catalysts have been made by anchoring to polystyrene via the R-group on the boron atom (Fig. 1),<sup>29</sup> the aryl part,<sup>30–32</sup> via sulfonamides to the nitrogen,<sup>33,34</sup> and to polyethylene.<sup>35</sup> Challenges with such modified or immobilised systems are usually related to the lower activity, and maintaining a high selectivity upon repeated use.

Recently, a new method for preparing polymer linked 4-hydroxy- $\alpha,\alpha$ -diphenyl-L-prolinol catalysts was developed.<sup>36,37</sup> Since this protocol is based on a 'bottom up' approach without any chromatographic purifications, the procedure is well suited for large scale synthesis.<sup>28</sup> In order to investigate the scope of the new and readily obtainable polymethacrylate, **II** (Fig. 1), we herein report its use in the asymmetric borane reduction of ketones.

## 2. Results and discussion

Polymethacrylate **II** was prepared by a suspension co-polymerisation of *O*-(2-methacryloyloxy-ethylsuccinoyl)-*trans*-4-hydroxy- $\alpha,\alpha$ -diphenyl-L-prolinol, methyl methacrylate and ethyleneglycol dimethacrylate (Scheme 1). 2,2'-Azobis(2-methylbutyronitrile) (AMBN) was used as the initiator, polyvinyl alcohol as a suspension stabiliser, while KI inhibits the polymerisation in the aqueous phase.<sup>36</sup> The acrylic polymer was isolated by filtration, and the appearance of the fresh catalyst is shown in Figure 2.

By having a low degree of cross binder, as for **II**, a microporous polymer bead is formed. These are rather compact in dry form with pores of insufficient size to allow for efficient mass transfer. However, when suspended in a suitable solvent, the polymer can swell, allowing for entry of the reagents. Good swelling of the methacrylate polymer, **II**, was observed in THF (Fig. 3) and dichloromethane (not shown). The swelling was complete within 1.5–2 h depending on the bead size.

The use of other solvents, such as 2-methyltetrahydrofuran, acetonitrile, toluene or diethyl ether gave a low degree of swelling and was therefore not suited as the reaction medium. Poor swelling was also seen in MeOH and water.

Since the selectivity in asymmetric reductions often depends on the electronic properties of the substrate ketone,<sup>12,38,39</sup> and the catalyst loading, the initial investigations were performed with 1-(4-bromophenyl)ethanone **1a** as substrate, using 30 mol % cata-

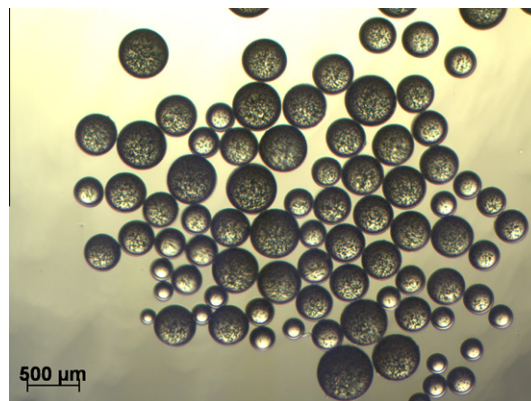
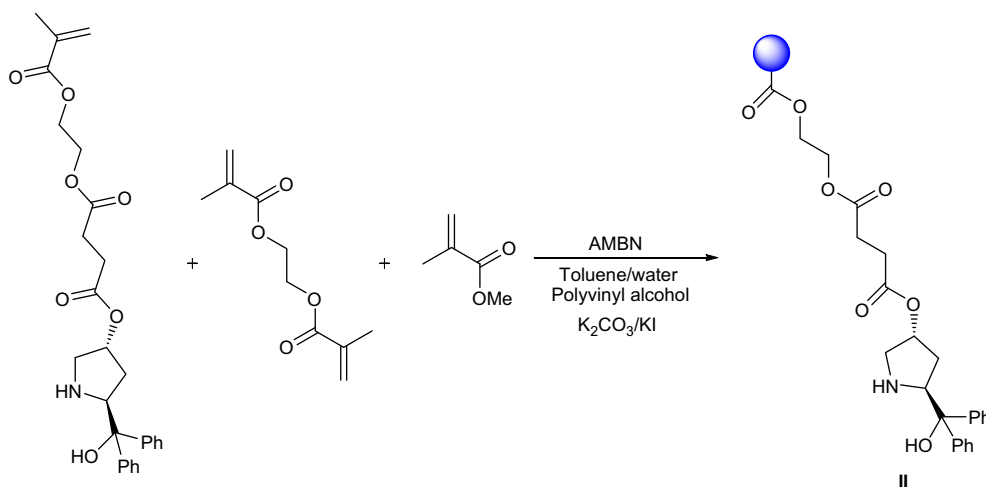


Figure 2. Microscopy image of the methacrylate polymer **II**.

lyst in THF with borane dimethylsulfide complex as the hydride source (Scheme 2).

In contrast to homogenous oxazaborolidine catalysts such as **I**, polymer based catalysis is most conveniently performed using an amino alcohol as the pre-catalyst. Polymer **II** was allowed to react with the borane dimethylsulfide complex for 30 min to produce the active catalyst, prior to the addition of substrate ketone. In refluxing THF, this gave a variable 60–90% ee. Lowering the reaction temperature and portion-wise additions of the ketone and the reducing agent did not improve the situation. By allowing catalyst **II** to stir with dimethylsulfide borane complex in THF overnight, analysis of the reaction mixture by <sup>1</sup>H NMR spectroscopy indicated decomposition of the polymer as the reason for the variable enantioselectivity. Stability testing of **II** as described above revealed that the use of NaBH<sub>4</sub> in combination with BF<sub>3</sub>·diethyletherate also caused decomposition. While the polymer **II** appeared stable to the NaBH<sub>4</sub>/trimethylsilyl chloride system, it failed to give conversion of **1a** to **5a** in test reactions. On the other hand using the *N,N*-diethylaniline borane complex, polymer decomposition was not detected by <sup>1</sup>H NMR, and the product **5a** could be obtained with reproducible ee-values. Further testing using **1a** and the *N,N*-diethylaniline borane complex, revealed that the reduction could be performed at 30 °C and only required one hour for full conversion.

We then investigated how a change in the catalyst loading and substrate concentration affected the selectivity (Table 1). The experiments in entries 1–6 represent a two-level factorial design with catalyst amount and substrate concentration as variables.



Scheme 1. Synthesis of the methacrylate polymer **II**.

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