



A high enantioselective Proline-based helical polymer catalyst for aldol type reaction

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INTRODUCTION

The induction of chirality still a very intricate and exciting research area being the organocatalysis one of the most recent focus of investigation. Helical chirality is present on nature. Inspired on this asymmetric concept, some synthetic helical compounds, especially polymers have been applied for asymmetric synthesis¹, enantiomeric separations² and studies related to the properties of liquid crystalline compounds³. The preferential helicity of a polymer can be induced by the nature of the pendant molecular residue. Many applications have been found for this kind of molecules.

Recently we have proposed the synthesis of helical polymers for catalytic application since the recovery of a polymer from the reaction media can be easier than a smaller parent compound. In addition, we wonder if the helicity could play some role on the chirality induction. In this way, we designed and synthesized a proline-based helical polymer and subjected it to aldol reaction.

RESULTS AND DISCUSSION

In figure 1 is presented a proline-based polymer-catalyzed (**Poly-1**) aldol reaction model between cyclohexanone and *p*-nitrobenzaldehyde.

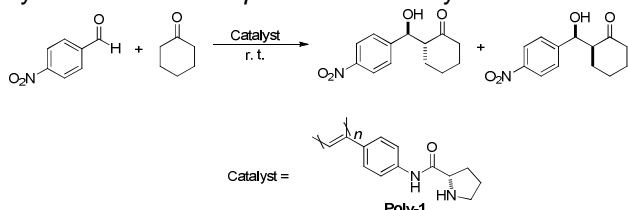


Figure 1. helical polymer catalyzed aldol reaction

In 2011 Fu reported⁴ a proline catalyzed aldol reaction using the same starting materials under similar reaction condition and the achieving Using similar reaction condition giving the product in 72% isolated yield and 68%(58%) *anti*(*syn*) enantiomeric excess respectively. The **Poly-1** catalyst allows the isolation of the same product in 78% yield and an enantiomeric excess of 91(53) *anti*(*syn*) respectively.

In order to optimize the reaction conditions we carried out other experiments and the results are presented in Table 1. As can be seen, best results were achieved by using 20 mol% of both, the catalyst and AcOH as additive. Similar good yields and e.e. were also achieved by using higher amount of the catalyst without additive.

Table 1 – Reaction condition optimization

entry	Cat. (mol%)	Addit. ¹	t (h)	η (%)	<i>anti:syn</i> ²	e.e. <i>anti</i> (<i>syn</i>) ²
1	10	-	72	81	75:25	60 (50)
2	5	-	72	60	80:20	53 (40)
3	10	-	72	78	85:15	69 (50)
4	10	AcOH	48	85	80:20	73 (60)
5	20	-	48	77	88:12	78 (50)
6	20	AcOH	24	78	75:25	91 (53)
7	30	-	24	75	86:14	92 (43)

¹ the same stoichiometry of the catalyst

² analyzed by HPLC

CONCLUSION

CD analysis of the polymer confirms the presence of a preferential helical orientation. If the enantiomeric excess were a result resultant only from the proline stereocenter on the transition state, no significant improvement of the e.e. would be observed. Albeit not yet elucidate the role of the helicity on the observed e.e., the results corroborate such proposition. The recovery of the catalyst for reuse is possible and other substrates are under investigation for the same transformation.

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