Asymmetric Aldol Polymerization of Bis(trimethylsilylketene thioacetal) and Dialdehyde

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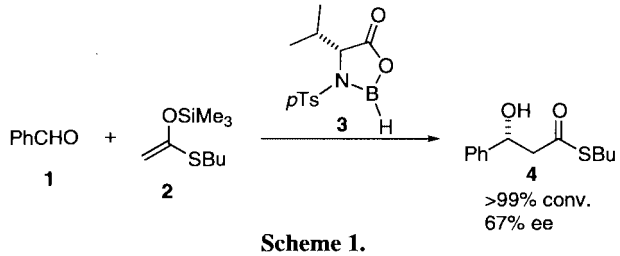
Asymmetric repetitive Mukaiyama aldol reaction between bis(trimethylsilylketene thioacetal) and dialdehydes proceeded in the presence of chiral oxazaborolidinone to afford optically active poly(β-hydroxy thioester)s. Degree of asymmetric induction during polymerization was evaluated both by a model reaction and chiral HPLC analysis of degradation products of the chiral polymers.

The synthesis of optically active polymers by means of asymmetric synthesis polymerization has attracted a considerable amount of attention.[1] Although number of researches on enantioselective transformations including C–C bond forming reactions have been extensively studied,[2–4] these reactions have not been utilized for asymmetric synthesis polymerization reaction. If these reactions can be repeated between the molecules bearing functional groups suitable for asymmetric C–C bond formation, it would be efficient method to obtain optically active polymers having main-chain configurational chirality. Such approach to chiral polymer synthesis is one of the most important method of asymmetric synthesis polymerization.[5] Recently, we have reported a new polymerization based on Mukaiyama aldol reaction.[9,10] Although asymmetric version of the aldol polymerization of bis(triethylsilyl enol ether) and dialdehyde was also examined, the product was only oligomer with low optical activity.[10] A number of enantioselective aldol additions have been reported to construct chiral β-hydroxy carbonyl structure,[11] in which thioketene acetals have been often used due to their high reactivity and stereoselectivity.[12,13] We have prepared bis(silylketene thioacetal) **5** as a novel monomer for the asymmetric aldol polymerization. In this paper, we report the demonstration of the asymmetric polyaddition between **5** and dialdehyde using chiral oxazaborolidinone catalyst **3**.

Silylketene thioacetal is an important substrate in the Mukaiyama aldol reaction and is known to be a highly active nucleophile.[13] In the presence of chiral Lewis acid catalyst silylketene thioacetal reacts smoothly with aldehyde to give optically active β-hydroxy thioester.[14] Thus, bis(trimethylsilylketene thioacetal) **5** should be one of the most promising monomer structure for the asymmetric aldol polymerization. Monomers for polyaddition reaction always require their high purity to obtain polymers. The monomer **5** was readily prepared from the corresponding bisthioacetate and is stable enough to be purified by distillation. Dialdehydes (**6**, **7**) were also readily prepared and used for the asymmetric polymerization with **5**.

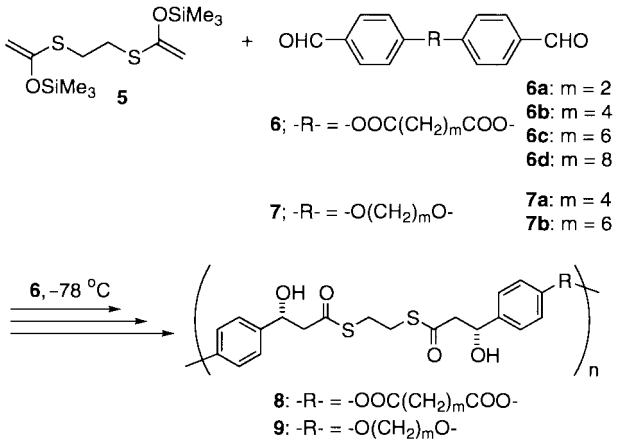
In order to succeed the asymmetric aldol polymerization, the reaction should proceed quantitatively with no side reaction. Chiral oxazaborolidinone complexes developed by Kiyooka are among the various catalysts for aldol addition.[15] These complexes are readily obtained in optically pure form from simple α-amino acid and showed high efficiency in enantioselective aldol reactions.[15,16] Thus chiral catalyst of choice for the asymmetric aldol polymerization in this study is *N*-tosyloxazaborolidinone **3** derived from (*R*)-valine.



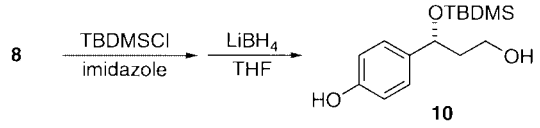
Scheme 1.

In the first place, as a model reaction of the asymmetric aldol polymerization, we attempted enantioselective aldol reaction of benzaldehyde **1** with trimethylsilylketene thioacetal **2** in the presence of **3**. As shown in Scheme 1, quantitative conversion was attained with enantioselectivity of 67%. This result encouraged us to apply monomers **5**, **6** and **7** to the asymmetric polymerization (Scheme 2). Without catalyst no reaction occurred between **5** and **6**. Oxazaborolidinone **3** could initiate the polymerization even at –78 °C. For example, asymmetric aldol polymerization of **5** and **6a** in THF took place smoothly at –78 °C for 2 h to give polymer **8a**. Optical rotation measurement of **8a** showed optical activity of $[\Phi]_{405}$+332 (Table 1). Gel permeation chromatography analysis of **8a** relative to polystyrene standards gave an average M_n of 4300 with molecular weight distribution of 1.55. Polymerizations of **6b**, **6c**, and **6d** with **5** were also performed in THF to afford optically active polymers **8b**, **8c**, and **8d**, respectively. Dialdehyde **7** reacted with **5** to give the corresponding chiral polymer **9** with somewhat lower optical rotation values and molecular weights. In all cases monomers were consumed completely. The polymers were isolated by precipitation from MeOH/2M HCl. This process was found to be the most suitable to remove the catalyst completely. The chiral polymers obtained as white powder were completely soluble in THF, DMF and DMSO, and insoluble in chloroform, methanol, and water. ^{1}H NMR spectra of the polymeric products revealed their desired structure illustrated in Scheme 2.

The asymmetric polymerization should proceed in a manner similar to the model reaction. However, it is quite difficult to know the degree of asymmetric induction and the optical purity of chiral polymers by their direct analysis. In order to obtain more precise information on the optical purity of the chiral polymers, we have degraded the polymer main-chain of **8** to mono protected triol **10** (Scheme 3). Results of chiral HPLC analysis of the degradation products **10** show the optical purities of the polymers, which were summarized in Table 1.



Scheme 2.



Scheme 3.

Table 1. Asymmetric aldol polymerization of **5** and dialdehyde using catalyst **3** in THF at –78 °C

Dialdehyde	Polymer	Yield[a] /%	M_n[b]	M_w/M_n[b]	$[\Phi]_{405}$[c]	% ee[d]
6a	**8a**	74	4300	1.55	+332	64
6b	**8b**	77	4800	1.65	+348	61
6c	**8c**	90	5700	2.00	+355	51
6d	**8d**	36	2100	1.40	+208	60
7a	**9a**	70	2500	1.49	+258	
7b	**9b**	63	2700	2.33	+176	

[a]Isolated yield of the polymer. [b]Determined by GPC calibrated by linear polystyrene standards. [c]Measured in THF, *c* 1.0. [d]% ee of the degraded product **10**, determined by chiral HPLC analysis using Daisel Chiralcel OD (hexane:2-propanol=9:1).

In summary, we have developed a new asymmetric synthesis polymerization based on Mukaiyama aldol addition. Bis(silylthioketene acetal) **5** as a novel monomer for the asymmetric aldol polymerization was readily prepared, which is stable enough to be isolated in pure form. Oxazaborolidinone catalyst **3** was effective for the asymmetric aldol polymerization of **5** and dialdehydes. Degree of asymmetric induction and optical purity of the polymers were evaluated both by model reaction and chiral HPLC analysis of their degradation product.

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