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Aldol polymerization as a novel polyaddition based on Mukaiyama aldol reaction and its application to the synthesis of optically active polymer

Kenichi Komura, Shinichi Itsuno* and Koichi Ito

Department of Materials Science, Toyohashi University of Technology, Toyohashi, 441-8580 Japan.
E-mail: itsuno@tutms.tut.ac.jp

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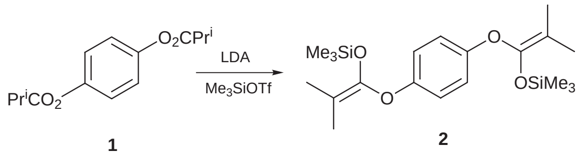
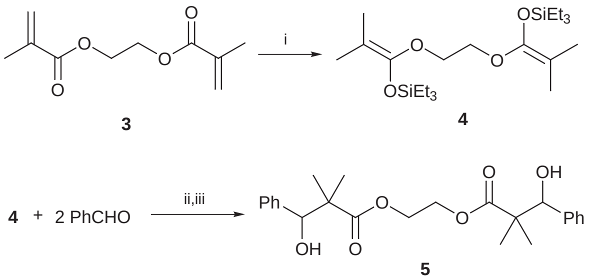
Repetitive Mukaiyama aldol reaction between bis(silyl ketene acetal) and dialdehyde proceeded in the presence of Lewis acid to afford poly(hydroxy ester).

The Mukaiyama aldol reaction is one of the most powerful tools for the construction of new C–C bonds in organic synthesis.[1–4] In spite of high reactivity and the subtle possibilities of side reactions in a number of aldol reactions under controlled reaction conditions, polymer synthesis utilizing this excellent reaction has not been studied extensively. Aldol-GTP (Aldol - Group Transfer Polymerization)[5,6] is the only exception, which is based on repetitive aldol reaction. Monomers for the aldol-GTP are however limited to trialkylsilyl vinyl ethers,[7,8] which give silylated poly(vinyl alcohol)s. In the Mukaiyama aldol reaction, Lewis acid activates or catalyses the reactions of silyl enolates or silyl ketene acetals with carbonyl compounds to give β-hydroxycarbonyl derivatives in excellent yield. If the same reaction occurs with the combination of bis(silyl enol ether)s and dialdehyde, this would be one of the most suitable ways for the preparation of poly(β-hydroxycarbonyl)s in a polyaddition manner. We found that bis(silyl ketene acetal)s reacted with dialdehydes in the presence of Lewis acid to afford poly(hydroxy ester)s. Here we report a polyaddition between bis(silyl ketene acetal) and dialdehyde, which we propose to term ‘aldol polymerization’. Asymmetric aldol reactions have also been studied extensively.[9] Several efficient chiral catalysts were designed for the aldol reaction. Thus, it should be possible to prepare optically active polymers if a chiral catalyst is employed in the aldol polymerization. Asymmetric aldol polymerization was also examined.

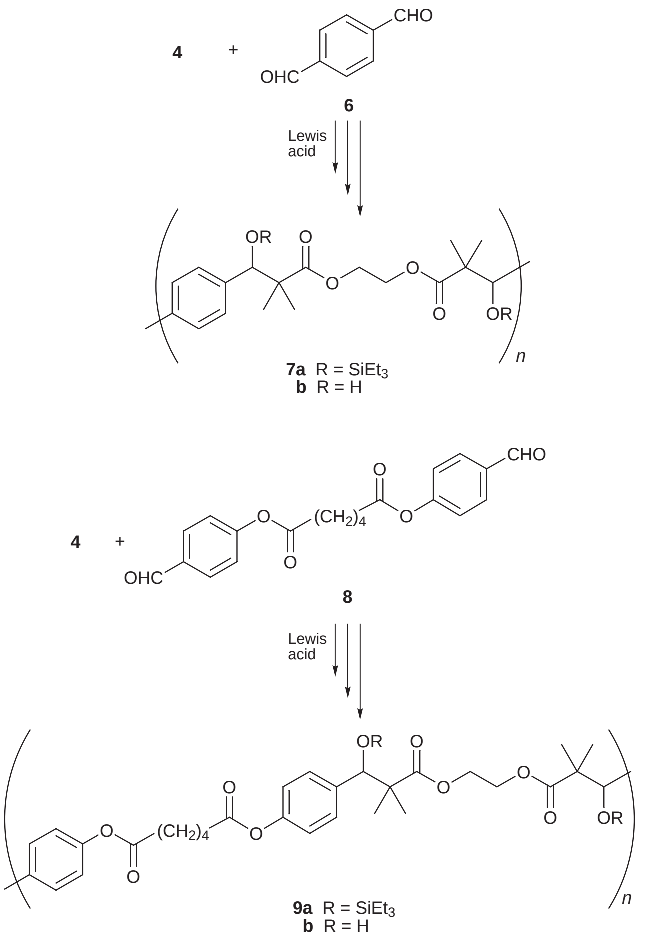
In the first place, we attempted to prepare bis(trimethylsilylketene acetal) **2** as a monomer for aldol polymerization using LDA/Me_3SiOTf (Scheme 1).[10] However the monomer **2** was contaminated with a small amount of the monoketene acetal after distillation of the product, since trimethylsilylketene acetal is susceptible to hydrolysis. Monomers for polyaddition reactions always require high purity in order to obtain high molecular weight polymers. In stead of trimethylsilylketene acetal, the preparation of triethylsilyl derivatives **4** was then examined. In the literature it was reported that aldol reaction of triethylsilylketene acetals with aldehyde smoothly occurred to afford the aldol products in high yield.[11,12] We found that the hydrosilylation method shown in Scheme 2 was suitable for the preparation of **4**. Hydrosilylation of bismethacrylate **3** with triethylsilane in the presence of a rhodium catalyst afforded **4** in good yield.[13,14] More importantly, the higher stability of the triethylsilylketene acetal made it possible to use normal silica gel column chromatography for its purification. It is also possible to purify this monomer by simple distillation. As a model reaction of polyaddition, the monomer **4** was allowed to react with 2 equiv. of benzaldehyde in the presence of $TiCl_4$. Aldol reaction between **4** and benzaldehyde occurred smoothly at −78 °C to give the corresponding aldol in good isolated yield. This result encouraged us to apply the reaction to the polymer synthesis. Terephthalaldehyde **6** was chosen as the comonomer in this polymerization (Scheme 3). Results for the aldol polymerization are shown in Table 1. Since aldol reactions of silylketene acetal with aldehyde using $TiCl_4$ were reported to give excellent yields at −78 °C,[15] the polymerization was carried out at this temperature. Without Lewis acid, no reaction was detected between **4** and **6**. When neat $TiCl_4$ was added to the monomer solution in CH_2Cl_2, resulting in a heterogeneous system, the reaction afforded a polymer insoluble in common organic solvents (run 1). Addition of a 1.0 M CH_2Cl_2 solution of $TiCl_4$ to the mixture of **4** and **6** at −78 °C initiated the aldol polymerization to give the desired aldol polymer which was isolated after precipitation into MeOH–H_2O (7:3). During isolation of the polymer **7a**, a small number of the triethylsilyl ether groups in the polymer were converted to hydroxy groups (**7b**). Although this polymeric silyl ether is quite resistant towards dilute hydrochloric acid, the use of TBAF in THF led to the complete cleavage of the Si–O bonds to give poly(hydroxy ester) **7b**. The structure of the obtained polymer **7** was supported by spectroscopic analyses. The molecular weight of **7** was measured by GPC (THF as an eluent) using polystyrene calibration curves. The use of $ZnBr_2$ as Lewis acid resulted in a high yield of the polymer at room temperature (run 3). Mukaiyama aldol reaction is normally activated by stoichiometric amounts of Lewis acid, whereas catalytic activity of rare earth metal triflates has recently been reported in the same reaction.[16,17] We have found that catalytic amount of triflates such as $Yb(OTf)_3$ and $Sc(OTf)_3$ were effective for the aldol polymerization to give the polymer. In the case of $Sc(OTf)_3$, the temperature should be kept below 0 °C during its addition into the monomer solution (run 6), otherwise insoluble polymer was yielded as the main product (run 5). As another novel dialdehyde monomer for the aldol polymerization, we prepared **8**, which has somewhat better solubility than **6**. As can be seen in the polymerization of **4** with **6**, addition of a 1.0 M CH_2Cl_2



Scheme 1



Scheme 2 *Reagents and conditions*: i, Et_3SiH, $(Ph_3P)_3RhCl$, $CHCl_3$, 60 °C, 1 min, 80%; ii, $TiCl_4$, CH_2Cl_2, −78 °C, 4 h, 80%; iii, TBAF, THF, room temp., 94%.



Scheme 3

solution of $TiCl_4$ to the mixture of **4** and **8** at −78 °C also yielded the desired aldol polymer **9a**. A catalytic amount of $Yb(OTf)_3$ or $Sc(OTf)_3$ as a Lewis acid catalyst also made it possible to synthesize the aldol polymer **9** having high molecular weight (runs 9 and 10). The structure of **9a** was confirmed by NMR and IR analysis.

The use of chiral Lewis acids for enantioselective aldol reactions has recently received great attention.[9] One of the efficient chiral catalyst for the asymmetric Mukaiyama aldol reaction is chiral *N*-sulfonyloxazaborolidinone **10** reported by Kiyooka.[18,19] For example, benzaldehyde activated with chiral Lewis acid **10** reacted with silylketene acetal to afford the corresponding *R*-aldol product in high yield with high enantiopurity (up to 94% ee).[19] We applied this chiral catalyst for the aldol polymerization of **4** with **8**. The asymmetric polymerization was performed at −78 °C, since undesired reduction of the ester group with the hydride of **10** might take place after aldol reaction at higher temperature, which destroys the polymer main chain. Although relatively low molecular weight polymer was obtained at −78 °C, the produced polymer showed optical activity.[20] To the best of our knowledge, this is the first example of the synthesis of optically active polymer from prochiral monomer using repetitive asymmetric aldol reaction.

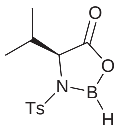


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Table 1 Aldol polymerization of bis(silyl ketene acetal) **4** with dialdehyde in CH_2Cl_2

Run	Dialdehyde	Lewis acid (equiv.)	T/°C	t/h	Yield (%)[a]	M_n[b]	M_w/M_n[b]
1	**6**	$TiCl_4$[c] (2.0)	−78	4	86	—[d]	—[d]
2	**6**	$TiCl_4$[e] (2.0)	−78	4	21	1500	1.60
3	**6**	$ZnBr_2$ (2.0)	20	48	84	2800	2.21
4	**6**	$Yb(OTf)_3$ (0.2)	20	72	17	2200	1.60
5	**6**	$Sc(OTf)_3$ (0.1)	20	72	21	—[d]	—[d]
6	**6**	$Sc(OTf)_3$ (0.1)	−5 to 20	72	40	3800	3.89
7	**8**	$TiCl_4$[e] (2.0)	−78	4	29	2700	3.27
8	**8**	$ZnBr_2$ (2.0)	20	48	47	1800	3.41
9	**8**	$Yb(OTf)_3$ (0.2)	20	72	15	11300	7.32
10	**8**	$Sc(OTf)_3$ (0.1)	−5 to 20	72	50	55700	2.38
11	**8**	**10** (1.0)	−78	4	62	1900	2.38

[a] Isolated yield after purification by reprecipitation. [b] Obtained by GPC calibrated by polystyrene standards using THF as an eluent. [c] Neat reagent was used. [d] Insoluble in common organic solvents. [e] 1.0 M solution in CH_2Cl_2.

In summary, we have found that Mukaiyama aldol reaction could be successfully utilized for the polyaddition of bis(silylketene acetal)s with dialdehydes. Polymers having a unique main chain structure consisting of poly(hydroxy ester)s were prepared readily by this polymerization. Catalytic amounts of rare earth metal triflates such as $Yb(OTf)_3$ and $Sc(OTf)_3$ are effective for the polyaddition to give polymers with high molecular weights. It is also possible to prepare optically active polymers using chirally-modified Lewis acid catalyst.

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