Polymer Bulletin 51, 183–190 (2003)
DOI 10.1007/s00289-003-0209-1

Polymer Bulletin

Asymmetric aldol polymerization of bis(triethylsilyl enol ether) and dialdehyde

Shinichi Itsuno (✉) , Hiroshi Watanabe

Department of Materials Science, Toyohashi University of Technology, Tempaku-cho, Toyohashi, 441-8580, Japan
e-mail: itsuno@tutms.tut.ac.jp, Tel & Fax: +81-(0)532-44-6813

Received: 27 June 2003 / Accepted: 20 September 2003

Summary

Mukaiyama aldol reaction smoothly occurred between bis(triethylsilyl enol ether) and dialdehyde in the presence of Lewis acid catalyst to yield polymers that consist of β-hydroxy carbonyl repeating units. When chirally modified Lewis acid catalyst was used, the optically active poly(β-hydroxy ketone)s were obtained by means of the asymmetric aldol polymerization.

Introduction

Mukaiyama aldol reaction is one of the most important C-C bond forming reaction [1]. Various kinds of enol silanes are highly reactive towards aldehyde in the presence of Lewis acid to give aldol adduct in quantitative conversion. The same reaction can be repeated between bis(enol silane) and dialdehyde to give polyaldol, which we term aldol polymerization [2]. We have developed aldol polymerization of bis(silyl ketene acetal) and dialdehyde to afford polymers having unique main chain structure of β-hydroxy ester [3]. A chirally modified Lewis acid catalyst in the Mukaiyama aldol reaction can control the newly created chiral carbons during C-C bond formation [4]. Thus asymmetric polymerization by means of repeated Mukaiyama aldol reaction is a powerful tool for constructing optically active polymers having configurational chiral carbons in their main chain structure [5]. In this paper we prepared new monomers of bis(silyl enol ether)s and dialdehydes having furfural structure. Aldol polymerization of these monomers was performed with both achiral Lewis acid $Yb(OTf)_3$ and chiral oxazaborolidinone derived form (*S*)-tryptophan.

Experimental

*Dialdehyde (**1a**)*

Furfural dimethylacetal **5** (2.8 g, 20 mmol) was dissolved in ether under nitrogen. *n*-BuLi/hexane solution (1.6 M, 12.5 mL, 20 mmol) was added slowly at –78 °C over 30

min. After stirring at –78 °C for 1 h, dichlorodimethylsilane (1.29 g, 10 mmol) was added to the above solution. The reaction mixture was stirred at –78 °C for 1 h, allowed to warm to room temperature, and stirred for 12 h. The reaction mixture was quenched with 2N HCl and extracted with ether. The organic phase was washed with brine and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave the crude product of the dialdehyde. The crude product was purified by column chromatography (hexane/EtOAc 3:1) to give dialdehyde **1a** in 73% yield as a white solid; mp 71-72.5 °C. ^{1}H NMR ($CDCl_3$): δ 9.74 (s, 2H), 7.29 (d, J = 3.6 Hz, 2H), 6.92 (d, J = 3.6 Hz, 2H), 0.69 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 178.4, 163.1, 157.3, 123.9, 120.9, –3.72. IR (KBr): 3104, 2835, 1676, 1262, 815, 758. Anal. Calcd for $C_{12}H_{12}O_4Si$ (248.31): C 58.04, H 4.87. Found C 57.94, H 4.78.

*Dialdehyde (**1b**)*

Yield 75%. Mp 72-74 °C. ^{1}H NMR ($CDCl_3$): δ 9.68 (s, 2H), 7.21 (d, J = 3.6 Hz, 2H), 6.74 (d, J = 3.6 Hz, 2H), 0.73 (s, 4H), 0.31 (s, 12H). ^{13}C NMR ($CDCl_3$): δ 178.2, 167.9, 157.0, 122.3, 121.1, 7.01, –4.02. IR (KBr): 2955, 2893, 1671, 1258, 805, 771. Anal. Calcd for $C_{16}H_{22}O_4Si_2$ (334.51): C 57.45, H 6.63. Found C 57.51, H 6.58.

*Diketone (**14**)*

4-Bromoacetophenone dimethylacetal (7.0 g, 28.6 mmol) was dissolved in dry THF (100 mL) under nitrogen. *n*-BuLi/hexane solution (1.6 M, 18.8 mL, 30 mmol) was added slowly at –78 °C over 30 min. After being stirred at –78 °C for 4 h, 1,2-bis(chlorodimethylsilyl)ethane (3.01 g, 14 mmol) was added to the reaction mixture. The reaction mixture was then stirred at –78 °C for additional 1 h, allowed to room temperature and was stirred for 10 h. The reaction mixture was quenched with 1N HCl and stirred at room temperature for 2 h. The reaction mixture was then concentrated under reduced pressure. The aqueous layer was then extracted with EtOAc. Organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by column chromatography to afford a viscous oil (3.75 g, 70%). ^{1}H NMR ($CDCl_3$): δ 7.90 (d, J = 8.2 Hz, 4H), 7.58 (d, J = 8.2 Hz, 4H), 2.60 (s, 6H), 0.64 (s, 4H), 0.27 (s, 12H). ^{13}C NMR ($CDCl_3$): δ 198.7, 146.2, 137.5, 134.1, 127.4, 26.9, 7.84, –3.56. IR (KBr): 2953, 2895, 1677, 1265, 814. Anal. Calcd for $C_{22}H_{30}O_2Si_2$ (382.64): C 69.06, H 7.90. Found: C 68.82, H 7.84.

*Bis(silyl enol ether) monomer (**2b**)*

To a solution of the diketone **14** (1.1 g, 2.87 mmol), Et_3N (0.9 g, 9 mmol) in acetonitrile (5 mL) was added chlorotriethylsilane (1.1 mL, 6.6 mmol) at room temperature. The reaction mixture was heated to 40 °C and acetonitrile (5 mL) solution of NaI (1.0 g, 6.7 mmol) was added. After being stirred at room temperature for 4 h the whole mixture was poured into water and quickly extracted with hexane. The organic layers were combined, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was subjected to chromatography to afford compound **2b** as colorless oil (0.91 g, 52%). ^{1}H NMR ($CDCl_3$): δ 7.61 (d, J = 8.2 Hz, 4H), 7.42 (d, J = 8.2 Hz, 4H), 4.92 (d, J = 1.9 Hz, 2H), 4.43 (d, J = 1.9 Hz, 2H), 1.02 (tr, J = 7.5 Hz, 18H), 0.79 (q, J = 7.5 Hz, 12H), 0.67 (s,

4H), 0.24 (s, 12H). ^{13}C NMR ($CDCl_3$): 156.1, 139.6, 138.2, 133.7, 124.6, 90.6, 8.04, 7.04, 5.19, –3.39. IR (neat): 2962, 1254, 1097, 1024, 751. Anal. Calcd for $C_{34}H_{58}O_2Si_4$ (611.2): C 66.82, H 9.57. Found: C 66.85, H 9.55.

Aldol polymerization with Yb(OTf)$_3$ catalyst

To a solution of $Yb(OTf)_3$ (0.1 mmol) in propionitrile (2 mL) was added a mixture of bis(silyl enol ether) (1 mmol) and dialdehyde (1 mmol) in propionitrile (4 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 5 h. After removal of the solvent under reduced pressure 2N HCl (5 mL) was added to the mixture and stirred at room temperature for 3 h. The reaction mixture was then poured into 300 mL of MeOH/H_2O (2:1) to precipitate the polymeric product. The white precipitate was filtered and dried in vacuo at 40 °C for 8 h.

*Asymmetric polymerization of **1a** and **2a***

To a solution of chiral oxazaborolidinone catalyst **18** (0.2 mmol) in propionitrile (2 mL) was added a mixture of **1a** (1 mmol, 248 mg) and **2a** (1 mmol, 525 mg) in propionitrile (4 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 4 h. After removal of the solvent under reduced pressure 2N HCl (5 mL) was added to the mixture and stirred at room temperature for 3 h. The reaction mixture was then poured into 300 mL of MeOH/H_2O (2:1) to precipitate the polymeric product **20** ($R_1 = R_2 =$ $SiMe_2$). The white precipitate was filtered and dried in vacuo at 40 °C for 8 h. Yield 81%. $[\alpha]_D$ +25.1 (*c* 1.0 THF). M_n = 15100, M_w/M_n = 1.52. ^{1}H-NMR($CDCl_3$): δ 7.9 (br, 2H), 7.6 (br, 2H), 6.6 (br, 2H), 6.3 (br, 2H), 5.4 (br, 1H), 3.8 (m, 2H), 3.3-3.7(m, 4H), 0.6 (br s, 6H), 0.5 (br s, 6H). IR (KBr, cm^{-1}): 3423, 2955, 2903, 1678, 1255, 808. Anal. Calcd for $(C_{30}H_{32}O_6Si_2)_n$ $(544.74)_n$: C 66.15, H 5.92. Found: C 66.08, H 5.95.

*Preparation of O-acetylmandelate of aldol adduct **22***

O-acetylmandelate **22** was prepared according to the procedure described in the literature [6].

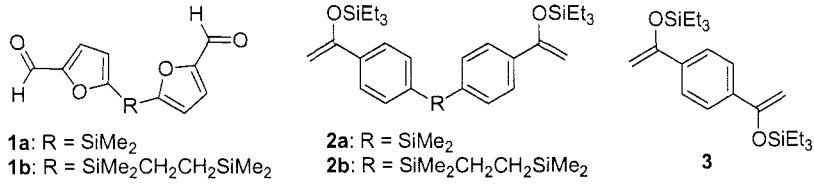
*Preparation of O-acetylmandelate of chiral polymer **23***

To a solution of chiral polymer (100 mg) (*R*)-*O*-acetylmandelic acid (100 mg, 0.5 mmol) and dimethylaminopyridine (10 mg) in CH_2Cl_2 (2 mL) was added a solution of 1,3-dicyclohexylcarbodiimide (100 mg, 0.48 mmol) at –10 °C. After being stirred at room temperature for 12 h precipitated urea was filtered and the solvent was evaporated. The residue was dissolved in CH_2Cl_2 and the remained urea was filtered again and the solvent was evaporated. The solid obtained was dissolved in THF and poured into MeOH/H_2O (1:1) to precipitate the polymer. After filtration the polymer was dried in vacuo at 40 °C for 4 h. The optical purity of the chiral polymer was determined by the ratio of the diastereomeric aromatic protons. **23** ($R_1 = R_2 =$ $SiMe_2$): ^{1}H-NMR ($CDCl_3$): δ 7.9 (*R*,*R*) + 7.7 (*R*,*S*) (4H), 7.6-7.3 (14H), 6.6 (2H), 6.3 (2H), 6.2 (2H), 5.8 (2H), 3.7-3.3 (4H), 2.1 (6H), 0.6-0.2 (12H).

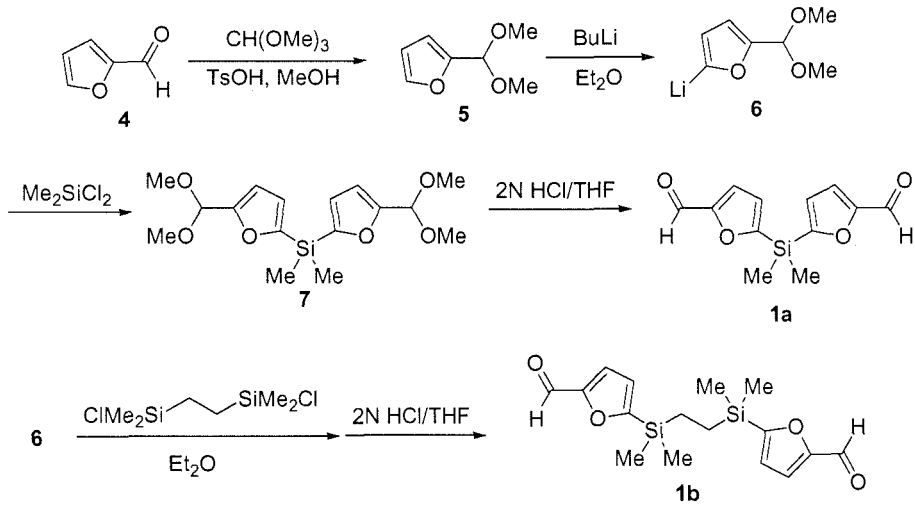
Results and Discussion

Preparation of monomers

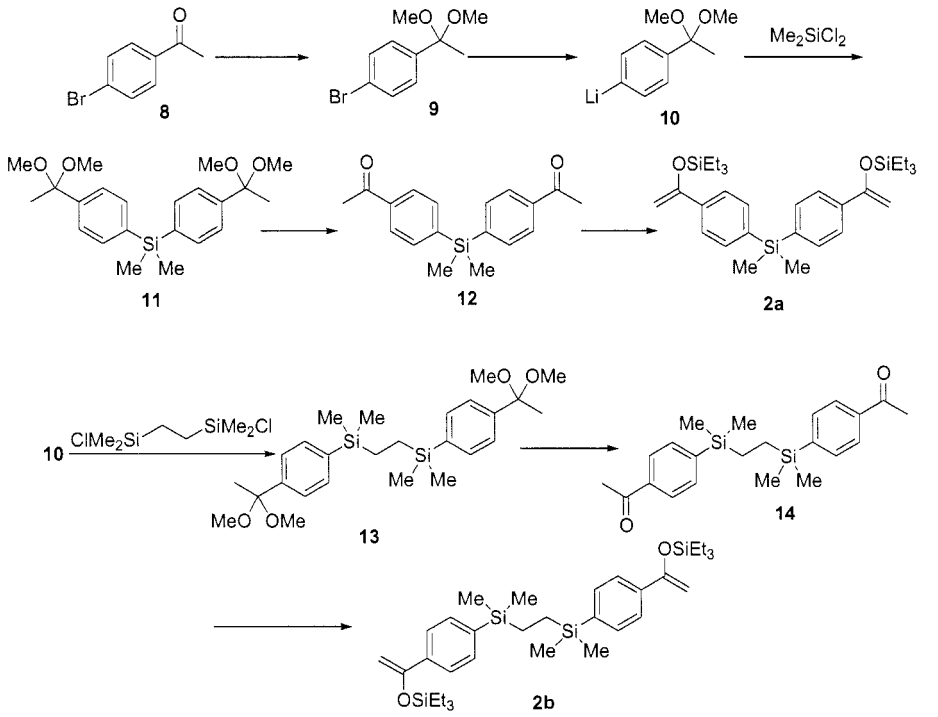
We have prepared dialdehydes (**1**) and bis(silyl enol ether)s (**2**, **3**) as monomers for asymmetric aldol polymerization. Chiral polymers can be synthesized by means of repeated asymmetric aldol reaction between these monomers. Dialdehydes **1** were prepared by coupling of 2-lithiated furfural dimethylacetal and chlorosilanes (Scheme 2). We have also prepared bis(silyl enol ether) monomers **2** (Scheme 3). Protected bromoacetophenone **9** was lithiated and coupled with 0.5 equiv of dichlorodimethylsilane to form bisacetal **11**. Deprotection of the acetal followed by silyl enol ether formation gave bis(triethylsilyl enol ether) **2a**. Another monomer **2b** was prepared from 1,2-bis(chlorodimethylsilyl)ethane. These monomers are stable enough to be purified by usual silica gel chromatography.



Scheme 1. Monomers for asymmetric aldol polymerization



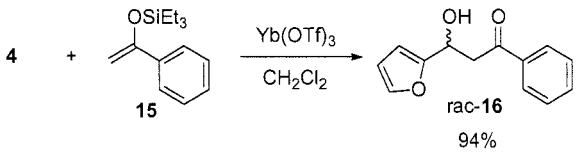
Scheme 2. Preparation of dialdehyde monomer **1**



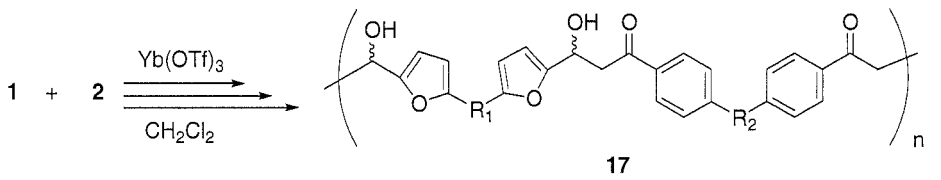
Scheme 3. Preparation of bis(silyl enol ether) monomer **2**

Aldol polymerization of dialdehyde and bis(silyl enol ether)

Mukaiyama aldol reaction of furfural **4** and triethylsilylenol ether **15** was performed using achiral Lewis acid catalyst. We found that $Yb(OTf)_3$ was efficient catalyst for the reaction to give the corresponding aldol adduct **16** in high yield (Scheme 4). Quantitative reaction system without any side product can be applied to polymer synthesis. Repetition of such reaction between bifunctional monomers efficiently affords polymers. First, we used $Yb(OTf)_3$ for aldol polymerization of dialdehyde and bis(silyl enol ether). When 10 mol % of $Yb(OTf)_3$ was added to the CH_2Cl_2 solution of **1** and **2**, aldol reaction was repeated to give the polymer **17** which has unique main chain structure of β-hydroxy ketone (Scheme 5). Polymers isolated by precipitation in $MeOH/H_2O$ showed the molecular weights in the range of 5800 to 13400 (Table 1).



Scheme 4. Mukaiyama aldol reaction of furfural and triethylsilyl enol ether



Scheme 5. Aldol polymerization of bisfurfural and bis(silyl enol ether)

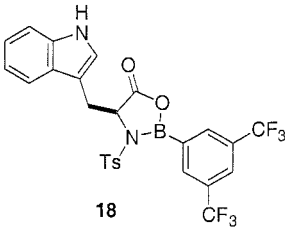
Table 1 Aldol polymerization of dialdehyde and bis(silyl enol ether) in the presence of $Yb(OT)_3$

Entry	Monomer		Polymer yield (%)[a]	M_n[b]	M_w/M_n[b]
1	**1a**	**2a**	79	8600	1.32
2	**1a**	**2b**	89	11400	2.08
3	**1a**	**3**	77	7400	1.20
4	**1b**	**2a**	85	13400	1.28
5[c]	**1b**	**2a**	30	8500	1.29
6	**1b**	**2b**	87	7300	1.64
7	**1b**	**3**	73	5800	1.15

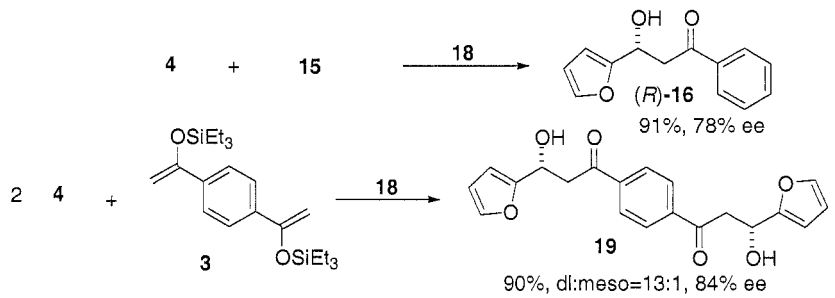
[a] isolated yield of the polymer precipitated in $MeOH/H_2O$; [b] values measured by SEC, calibrated with polystyrene standards; [c] $Sc(OTf)_3$ was used in stead of $Yb(OTf)_3$

Asymmetric aldol reaction of furfural and silyl enol ether

Chiral oxazaborolidinones are known to be effective catalyst for Mukaiyama aldol reaction [7]. We have tested the asymmetric reaction between furfural and triethylsilyl enol ether using the chiral oxazaborolidinone **18** originally developed by Yamamoto [7]. The reaction smoothly occurred to give the corresponding aldol adduct **16** with 78% ee (Scheme 6). Bis(silyl enol ether) **3** also reacted with 2 equiv of furfural under the same reaction condition to yield **19**. High reactivity of furfural and silyl enol ether using **18** prompted us to apply the reaction to asymmetric polymerization.



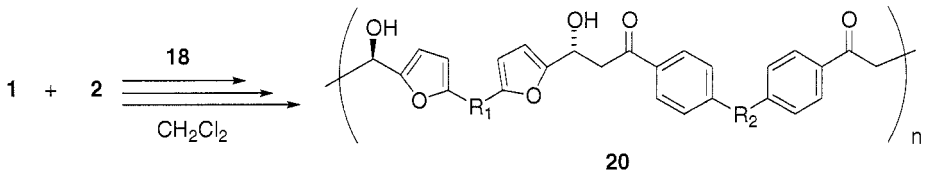
Chiral oxazaborolidinone catalyst



Scheme 6. Asymmetric aldol reaction of furfural and **7**

Asymmetric aldol polymerization

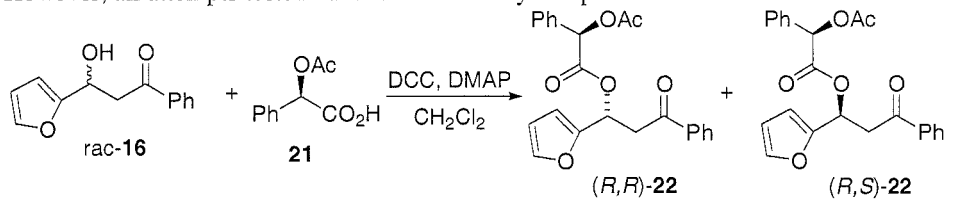
When chiral oxazaborolidinone catalyst **18** was added to a dichloromethane solution of dialdehyde **1a** and its equimolar amount of bis(silyl enol ether) **2a**, aldol reaction occurred between monomers to give the polymer of M_n=15100. The produced polymer showed optical activity based on the main chain configurational chirality. Molar rotation values are shown in Table 2.



20

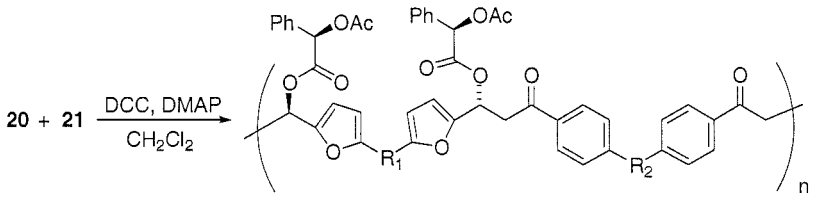
Scheme 7. Asymmetric aldol polymerization of **1** and **2**

In order to estimate the optical purity of the obtained chiral polymer we have tried polymer degradation reaction in terms of the cleavage of main chain Si-C bonds. However, all attempts tested have failed and only complex mixture was obtained.



Scheme 8. Chiral derivatization with enantiopure (*R*)-*O*-acetylmandelic acid

On the other hand, when racemic mixture of the model aldol product was modified with (*R*)-*O*-acetylmandelic acid (**21**), peaks of ^{1}H NMR spectra are clearly split in its aromatic region. Then we have modified the chiral polymer with **21**. After the chiral derivatization with **21**, we could recognize the peaks (7.9 and 7.7 ppm) corresponding to (*R*,*R*) and (*R*,*S*) configuration respectively in ^{1}H NMR spectra. By using ^{1}H NMR data of the *O*-acetylmandelated polymer **23** we determined the optical purity of the chiral polymers. From the ^{1}H NMR data *R*/*S* ratio of main chain stereogenic centers in the chiral polymers was determined and shown in Table 2. These results indicate that asymmetric aldol polymerization of bis(silyl enol ether) and dialdehyde occurred in stereoselective manner to give optically active polymer.



23

Scheme 9. Preparation of (*R*)-*O*-acetylmandelate of chiral polymer

Table 2. Asymmetric aldol polymerization

Entry	Monomer		Polymer yield (%)[a]	M_n[b]	M_w/M_n[b]	$[\alpha]_D$[c]	$[\Phi]_{546}$[c]	R:S[d]
1	**1a**	**2a**	81	15100	1.52	+25.1	+176.4	86:14
2	**1a**	**2b**	84	10100	1.53	+18.2	+159.0	85:15
3	**1a**	**3**	87	5400	1.34	+108.1	+371.5	88:12
4	**1b**	**2a**	87	15300	1.80	+19.0	+156.3	83:17
5	**1b**	**2b**	91	14600	1.63	+25.1	+220.9	85:15
6	**1b**	**3**	78	7400	1.61	+131.2	+730.1	85:15

[a] isolated yield of the polymer precipitated in MeOH/H_2O; [b] values measured by SEC, calibrated with polystyrene standards; [c] *c* 1.0, THF; [d] determined by ^{1}H NMR

In conclusion, we have prepared bis(triethylsilyl enol ether)s **2** and dialdehydes **1** as monomers for aldol polymerization. $Yb(OTf)_3$ was found to be an efficient catalyst for the aldol polymerization. Chiral oxazaborolidinone **18** also catalyzed the same polymerization to afford the optically active polymers having main chain configurational chirality. We have determined the optical purity of the chiral polymers by means of ^{1}H NMR measurement after the chiral derivatization with enantiopure *O*-acetylmandelic acid.

Acknowledgements: This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. Financial supports by Amano Institute of Technology and the Naito Research Grant are also gratefully acknowledged.

References

1. Mukaiyama T (1977) Angew Chem Int Ed Engl 16: 817; Mukaiyama T, Kobayashi S (1994) ibid 46: 1.
2. Komura K, Itsuno S, Ito K (1999) Chem Commun 35.
3. Komura K, Itsuno S (2001) Chem Lett 730; Komura K, Itsuno S (2002) J Macromol Chem Phys 203: 931.
4. Mukaiyama T (1996) Aldrichimica Acta 29: 59.
5. Reviews on asymmetric polymerzation: Coates GW, Polymerization Reactions in Comprehensive Asymmetric Catalysis, Vol III, Jacobsen EN, Pfaltz A, Yamamoto H, Eds, Springer, Berlin 1999, 1329; Okamoto Y, Nakano T (1994) Chem Rev 94: 349; Wulff G, Zweering U (1999) Chem Eur J 5: 1898; Nozaki K (2001) Kobunshi Ronbunshu 58: 375.
6. Simchen G, West W (1977) 247.
7. Ishihara K, Kondo S, Yamamoto Y (1999) Synlett 1283; Ishihara K, Kondo S, Yamamoto Y (2000) J Org Chem 65:9125.