Available online at www.sciencedirect.com
ScienceDirect
Polymer 48 (2007) 3026–3032
polymer
www.elsevier.com/locate/polymer

# Ring-opening metathesis polymerization of amino acid-functionalized norbornene diester monomers

Sutthira Sutthasupa, Kayo Terada, Fumio Sanda*, Toshio Masuda*

*Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University, Katsura Campus, Kyoto 615-8510, Japan*

Received 12 December 2006; received in revised form 28 March 2007; accepted 11 April 2007
Available online 19 April 2007

**Abstract**

Amino acid-derived novel norbornene diester derivatives, 5-norbornene-*endo*,*endo*-2,3-dicarboxylic acid bis((*S*)-2-*N*-(*tert*-butoxycarbonyl)-aminopropyl) ester (**1a**), 5-norbornene-*exo*,*exo*-2,3-dicarboxylic acid bis((*S*)-2-*N*-(*tert*-butoxycarbonyl)aminopropyl) ester (**1b**), bis(*N*-α-(*tert*-butoxycarbonyl)-L-alanine) 5-norbornene-2,3-*endo*,*endo*-dimethyl ester (**2a**), bis(*N*-α-(*tert*-butoxycarbonyl)-L-alanine) 5-norbornene-2,3-*exo*,*exo*-dimethyl ester (**2b**) were synthesized and polymerized by the Grubbs catalyst, 2nd generation. Ring-opening metathesis polymerization of the monomers satisfactorily proceeded to give the polymers with fairly high molecular weights in good yields. The polymerization rate was not affected by the stereostructure of the monomers, *endo*,*endo*- and *exo*,*exo*-, while largely affected by solvents. The order of polymerization rate was as follows: acetone-$d_6$ > benzene-$d_6$ > DMF-$d_7$ ≈ $CD_2Cl_2$ > $CDCl_3$.

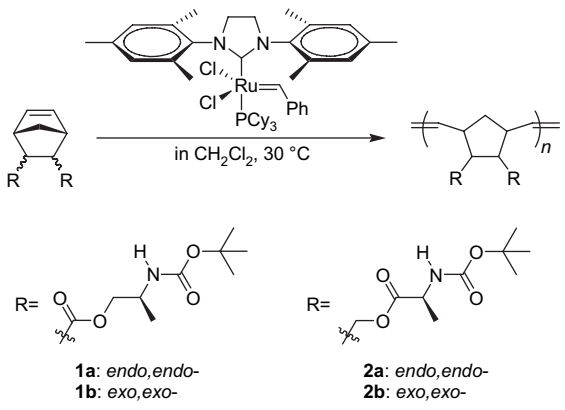

*Keywords:* Amino acid; Norbornene; ROMP

## 1. Introduction

Synthesis of biologically functional polymers has attracted great interest both in academic and industrial fields. Amino acids and peptides are widely used as key components of biopolymers including polymer drugs [1–3]. Structure–activity relationships of biopolymers are dependent upon all aspects of molecular architecture. Ring-opening metathesis polymerization (ROMP) of norbornene derivatives using well-defined transition metal initiators allows a high level of control over many aspects of polymers such as molecular weights, polydispersities, backbone configurations, and tacticities [4–6]. Some ruthenium (Ru) complexes are tolerant toward a wide range of functionalities of biological relevance [7]. They are employed as initiators of ROMP to give polymers functionalized with amino acids and peptides, which are useful for studying the design, synthesis, crystal structure, and self-assembling properties of peptide-mimetic macromolecules. Amino acid-derived norbornene-imide monomers undergo living ROMP to give the corresponding optically active polymers [8]. Grubbs and coworkers have synthesized polymers with peptide pendants, including glycine-arginine-glycine and serine-arginine-asparagine by ROMP of the corresponding norbornene derivatives, and proposed the possibility of their application in cell-adhesive materials. Thus, amino acid-based polymers obtained by ROMP are interesting and promising candidates for biologically useful materials [2,3]. Furthermore, amino acid-derived norbornenes have been polymerized to afford surface-grafted polymer supports as well as block copolymers [9]. We have recently synthesized and examined the ROMP of amino acid-derived novel norbornene *endo*,*endo*-diamide monomers to find that they do not undergo homopolymerization but copolymerization with norbornene [10]. Improvement of molecular design is necessary to achieve homopolymerization of amino acid-based norbornene monomers. The present study deals with the synthesis and ROMP of amino acid- and amino alcohol-derived novel norbornene diester monomers (Scheme 1), along

* Corresponding authors. Tel.: +81 75 383 2589; fax: +81 75 383 2590 (T.M.).
*E-mail addresses:* sanda@adv.polym.kyoto-u.ac.jp (F. Sanda), masuda@adv.polym.kyoto-u.ac.jp (T. Masuda).

0032-3861/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2007.04.014




Scheme 1.

with the effect of stereostructure (*endo*,*endo*- and *exo*,*exo*-) on the polymerization behavior. The solvent effect on the rate of polymerization is also reported.

## 2. Experimental section

### 2.1. Measurements

$^1$H and $^{13}$C NMR spectra were recorded using tetramethylsilane (TMS) as an internal standard in $CDCl_3$ on a JEOL EX-400 spectrometer. IR spectra were measured on a JASCO FT/IR-4100 spectrophotometer. Melting points (mp) were measured on a Yanaco micro-melting point apparatus. Mass spectra were measured on a JEOL JMS-HX110A mass spectrometer. Elemental analysis was done at the Kyoto University Elemental Analysis Center. The number- and weight-average molecular weights ($M_n$ and $M_w$) of polymers were determined by gel permeation chromatography (GPC) on a JASCO Gulliver system (PU-980, CO-965, RI-930, and UV-1570) equipped with polystyrene gel columns (Shodex columns K804, K805, and J806), using $CHCl_3$ and tetrahydrofuran (THF) as an eluent at a flow rate of 1.0 mL/min, calibrated by polystyrene standards at 40 °C. Specific rotations ($[\alpha]_D$) were measured on a JASCO DIP-1000 digital polarimeter with a sodium lamp as a light source.

### 2.2. Materials

Unless otherwise stated, reagents were purchased and used without purification. $CH_2Cl_2$ used for polymerization was distilled by the standard procedure before use.

### 2.3. Synthesis of 5-norbornene-endo,endo-2,3-dicarboxylic acid bis((S)-2-N-(tert-butoxycarbonyl)aminopropyl) ester (**1a**)

5-Norbornene-*endo*,*endo*-2,3-dicarboxylic anhydride (0.98 g, 6 mmol) and *N*-(*tert*-butoxycarbonyl)-L-alaninol (2.45 g, 14 mmol) were dissolved in $CH_2Cl_2$ (80 mL). 4-Di(methylamino)pyridine (DMAP, 0.34 g, 2.8 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC·HCl, 1.4 g, 7.0 mmol) were added to the solution at 0 °C and the resulting mixture was stirred at room temperature overnight. The mixture was subsequently washed with 1 M HCl, saturated $NaHCO_3$ aq., and water twice. The organic layer was separated and dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by preparative HPLC to obtain **1a** as white solid. Yield 45%. Mp 130 °C. $[\alpha]_D = -28.3°$ ($c$ = 0.1 g/dL in $CHCl_3$, r.t.). IR (KBr): 3380, 2977, 1702, 1529, 1500, 1455, 1392, 1366, 1253, 1198, 1167, 1078, 1031, 977 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.13–1.16 (m, 6H, 2 × CHC$H_3$), 1.44 (s, 18H, (C$H_3$)$_6$), 1.71 (s, 2H, norbornene C$H_2$), 3.19 (d, $J$ = 7.6 Hz, 2H, 2 × C$H$), 3.32 (s, 2H, bridge position), 3.92–4.03 (m, 6H, 2 × C$H$NH, 2 × OC$H_2$), 4.73 (s, 2H, CON$H$), 6.27 (s, 2H, C$H$=C$H$). $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 17.74, 28.34, 46.03, 47.01, 48.00, 48.67, 67.14, 79.31, 135.10, 155.25, 172.71. Anal. Calcd for $C_{25}H_{40}N_2O_8$: C, 60.47; H, 8.12; N, 5.64. Found: C, 59.83; H, 8.12; N, 5.64. HRMS (FAB) $[M + H]^+$ Calcd for $C_{25}H_{41}N_2O_8$: 497.2863. Found: 497.2861.

### 2.4. Synthesis of 5-norbornene-exo,exo-2,3-dicarboxylic acid bis((S)-2-N-(tert-butoxycarbonyl)aminopropyl) ester (**1b**)

The title compound was synthesized from 5-norbornene-*exo*,*exo*-2,3-dicarboxylic anhydride instead of 5-norbornene-*endo*,*endo*-2,3-dicarboxylic anhydride in a manner similar to the synthesis of **1a**. Yield 70%. Mp 104–106 °C. $[\alpha]_D = -20.5°$ ($c$ = 0.1 g/dL in $CHCl_3$, r.t.). IR (KBr): 3380, 2977, 2947, 2882, 1731, 1711, 1647, 1638, 1531, 1516, 1393, 1366, 1284, 1267, 1246, 1194, 1171, 1110, 1061, 997, 872, 732 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.15 (d, $J$ = 6.4 Hz, 6H, 2 × CHC$H_3$), 1.44–1.52 (m, duplicated, 20H, (C$H_3$)$_6$, norbornene C$H_2$), 2.65 (s, 2H, 2 × C$H$), 3.12 (d, $J$ = 8 Hz, 2H, bridge position), 3.93 (4H, 2 × OC$H_2$), 4.10 (s, 2H, C$H$NH), 4.75 (s, 2H, CON$H$), 6.22 (s, 2H, C$H$=C$H$). $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 17.78, 28.39, 44.09, 45.38, 46.85, 48.75, 67.57, 79.43, 137.94, 155.20, 173.41. Anal. Calcd for $C_{25}H_{40}N_2O_8$: C, 60.47; H, 8.12; N, 5.64. Found: C, 60.22; H, 8.05; N, 5.66. HRMS (FAB) $[M + H]^+$ Calcd for $C_{25}H_{41}N_2O_8$: 497.2863. Found: 497.2870.

### 2.5. Synthesis of bis(N-α-(tert-butoxycarbonyl)-L-alanine) 5-norbornene-2,3-endo,endo-dimethyl ester (**2a**)

5-Norbornene-2,3-*endo*,*endo*-dimethanol (0.93 g, 6 mmol) and *N*-(*tert*-butoxycarbonyl)-L-alanine (2.65 g, 14 mmol) were dissolved in $CH_2Cl_2$ (100 mL). DMAP (0.37 g, 3 mmol) and EDC·HCl (2.87 g, 15 mmol) were added to the solution at 0 °C and the resulting mixture was stirred at room temperature overnight. Then, the mixture was subsequently washed with 1 M HCl, saturated $NaHCO_3$ aq., and water twice. The organic layer was separated and dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by preparative HPLC to obtain **2** as colorless solid. Yield 83%. Mp 99–100 °C. $[\alpha]_D = -14.3°$ ($c$ = 0.1 g/dL in $CHCl_3$, r.t.). IR (KBr): 3455, 3297, 2979, 2933, 1739, 1689, 1672, 1542, 1530, 1392, 1379, 1367, 1302, 1281, 1249, 1192, 1165, 1067, 1039, 1025, 973, 789, 759, 731 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.38–1.52 (m, 26H, 2 × (C$H_3$)$_3$, 2 × CHC$H_3$, norbornene

$CH_2$), 2.55 (s, 2H, 2 × $CH$), 2.92 (s, 2H, bridge position), 3.81–3.87 (m, 2H, $CH_2O$), 3.92–3.98 (m, 2H, $CH_2O$), 4.29–4.32 (m, 2H, $CH$NH), 5.06 (d, $J = 6.0$ Hz, 2H, 2 × CON$H$), 6.17 (s, 2H, $CH$=$CH$). $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 18.57, 28.26, 40.47, 45.33, 48.91, 49.17, 65.18, 79.75, 135.37, 155.05, 173.11. Anal. Calcd for $C_{25}H_{40}N_2O_8$: C, 60.47; H, 8.12; N, 5.64. Found: C, 60.21; H, 8.23; N, 5.56. HRMS (FAB) $[M+H]^+$ Calcd for $C_{25}H_{41}N_2O_8$: 497.2863. Found: 497.2863.

### 2.6. Synthesis of bis(N-α-(tert-butoxycarbonyl)-L-alanine) 5-norbornene-2,3-exo,exo-dimethyl ester (**2b**)

The title compound was synthesized from 5-norbornene-2,3-*exo*,*exo*-dimethanol instead of 5-norbornene-2,3-*endo*,*endo*-dimethanol in a manner similar to the synthesis of **2a**. Yield 80%. Mp 79–80 °C. $[\alpha]_D = -16.6°$ ($c = 0.1$ g/dL in $CHCl_3$, r.t.). IR (KBr): 3306, 2979, 2938, 1736, 1691, 1674, 1535, 1474, 1392, 1378, 1367, 1280, 1250, 1192, 1166, 1068, 1043, 966, 857, 790, 760 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.36–1.51 (m, 26H, 2 × ($CH_3$)$_3$, 2 × CHC$H_3$, norbornene C$H_2$), 1.88 (s, 2H, 2 × $CH$), 2.74 (s, 2H, norbornene C$H_2$), 2.92 (s, 2H, bridge position), 4.06–4.12 (m, 2H, $CH$NH), 4.23–4.32 (m, 4H, 2 × C$H_2$O), 5.06 (d, $J = 6.4$ Hz, 2H, CON$H$), 6.18 (s, 2H, 2 × $H$C=C$H$). $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 18.59, 28.29, 39.68, 42.58, 44.64, 49.21, 66.20, 79.80, 135.27, 137.26, 155.08, 173.24. Anal. Calcd for $C_{25}H_{40}N_2O_8$: C, 60.47; H, 8.12; N, 5.64. Found: C, 60.21; H, 8.25; N, 5.53. HRMS (FAB) $[M+H]^+$ Calcd for $C_{25}H_{41}N_2O_8$: 497.2863. Found: 497.2863.

### 2.7. Polymerization

Polymerizations were carried out in a glass tube equipped with a three-way stopcock under nitrogen. A monomer (496 mg, 1 mmol) and Grubbs 2nd generation Ru catalyst (8.5 mg, 0.01 mmol) were dissolved in $CH_2Cl_2$ (0.5 mL) separately. The catalyst solution was added to the monomer solution and the resulting mixture was vigorously stirred. It was kept in a water bath at 30 °C for a set time, during which the colour of the polymerization mixture gradually changed from pink to dark pink. Then, ethyl vinyl ether (0.5 mL) was added to the mixture to quench the reaction, leading to colour change into yellow. The resulting mixture was poured into hexane (250 mL) to precipitate the polymer. It was separated by filtration using a membrane filter (ADVANTEC H100A047A) and dried under reduced pressure. When time–conversion relationship was determined, the polymerization was carried out in an NMR sample tube.

### 2.8. Spectroscopic data of the polymers

Poly(**1a**) (run 1 in Table 1). IR (KBr): 3395, 2977, 2934, 1719, 1655, 1520, 1458, 1392, 1366, 1319, 1244, 1167, 1064, 981, 869 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.14–1.16 (m, 6H, 2 × CHC$H_3$), 1.44 (s, 18H, ($CH_3$)$_6$), 1.90 (m, 2H, norbornene C$H_2$), 3.19 (d, $J = 7.6$ Hz, 2H, 2 × $CH$), 3.32 (s, 2H, bridge position), 3.92–4.03 (m, 6H, 2 × $CH$NH, 2 × OC$H_2$), 4.73 (s, 2H, CON$H$), 5.23–5.58 (m, 2H, 2 × –C$H$=). Poly(**1b**) (run 2 in Table 1). IR (KBr): 3390, 2978, 1713, 1655, 1520, 1457, 1392, 1366, 1247, 1168, 1064, 853, 780 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.16–1.25 (m, 6H, 2 × CHC$H_3$), 1.44–1.52 (m, duplicated, 20H, ($CH_3$)$_6$, norbornene C$H_2$), 2.65–3.10 (m, 2H, 2 × $CH$), 3.37–3.49 (m, 2H, bridge position), 3.92–4.04 (m, duplicated, 6H, 2 × OC$H_2$, 2 × $CH$NH), 4.72 (s, 2H, CON$H$), 5.25–5.46 (m, 2H, 2 × –C$H$=). Poly(**2a**) (run 4 in Table 1). IR (KBr): 3380, 2979, 1718, 1637, 1520, 1457, 1393, 1367, 1252, 1159, 1069, 1023, 972, 858, 776, 759 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.39–1.59 (m, duplicated, 26H, 2 × ($CH_3$)$_3$, 2 × CHC$H_3$, norbornene C$H_2$), 2.08–2.51 (m, 2H, 2 × $CH$), 2.78–3.08 (m, 2H, bridge position), 4.16–4.26 (m, duplicated, 6H, C$H_2$O, C$H_2$O, 2 × $CH$NH), 5.02 (s, 2H, CON$H$), 5.31–5.38 (m, 2H, 2 × –C$H$=). Poly(**2b**) (run 6 in Table 1). IR (KBr): 3382, 2980, 1718, 1654, 1509, 1457, 1393, 1367, 1307, 1250, 1163, 1067, 1024, 971, 856, 785, 757 cm$^{-1}$. $^1$H NMR (400 Hz, $CDCl_3$): $\delta$ 1.38–1.59 (m, duplicated, 26H, 2 × ($CH_3$)$_3$, 2 × CHC$H_3$, norbornene C$H_2$), 1.91–2.13 (m, 2H, 2 × $CH$), 2.31–2.63 (m, 2H, bridge position), 4.17–4.26 (m, duplicated, 6H, C$H_2$O, C$H_2$O, 2 × $CH$NH), 5.03 (s, 2H, CON$H$), 5.25–5.34 (m, 2H, 2 × –C$H$=).

Table 1
Polymerization of **1a**–**2b**[a]

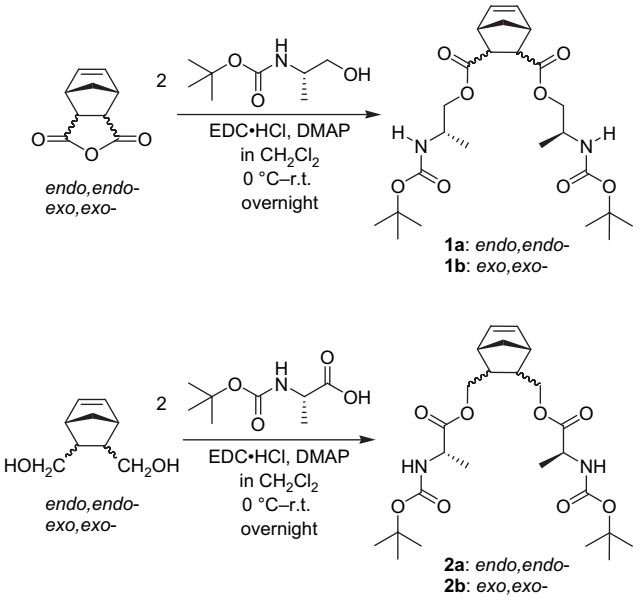
| Run | Monomer | Time (h) | Polymer | | | |
|---|---|---|---|---|---|---|
| | | | Yield[b] (%) | $M_n$[c] | $M_w/M_n$[c] | *cis* Content[d] (%) |
| 1 | **1a** | 1 | 43 | 15 500 | 1.6 | 46 |
| 2 | **1b** | 1 | 36 | 15 400 | 1.6 | 60 |
| 3 | **1b** | 2 | 98 | 16 000 | 1.9 | 58 |
| 4 | **2a** | 0.5 | 97 | 223 500 | 2.0 | 51 |
| 5 | **2a** | 1 | 85 | 210 000 | 2.0 | 49 |
| 6 | **2b** | 1 | 93 | 261 000 | 3.1 | 43 |

[a] Conditions: Grubbs 2nd generation Ru catalyst, $[M]_0/[Ru] = 100$, $[M]_0 = 1.0$ M in $CH_2Cl_2$, 30 °C, 1 h.
[b] Hexane-insoluble part.
[c] Determined by GPC.
[d] Determined by $^1$H NMR.

## 3. Results and discussion

### 3.1. Monomer synthesis

Monomers **1a** and **1b** were synthesized by the reaction of 5-norbornene-*endo*,*endo*-2,3-dicarboxylic anhydride and the *exo*,*exo*-counterpart with 1 equiv of Boc-L-alaninol, followed by the condensation of the formed half esters with another 1 equiv of Boc-L-alaninol in 45 and 70% yields, respectively (Scheme 2). EDC·HCl was employed as a condensation agent, because the urea derivative can be easily removed from the reaction mixture by washing with water [9]. Monomers **2a** and **2b** were synthesized by the condensation of 5-norbornene-2,3-*endo*,*endo*-dimethanol and the *exo*,*exo*-counterpart with 2 equiv of Boc-L-alanine in 83 and 80% yields, respectively (Scheme 2). The structures of the monomers were confirmed




Scheme 2.

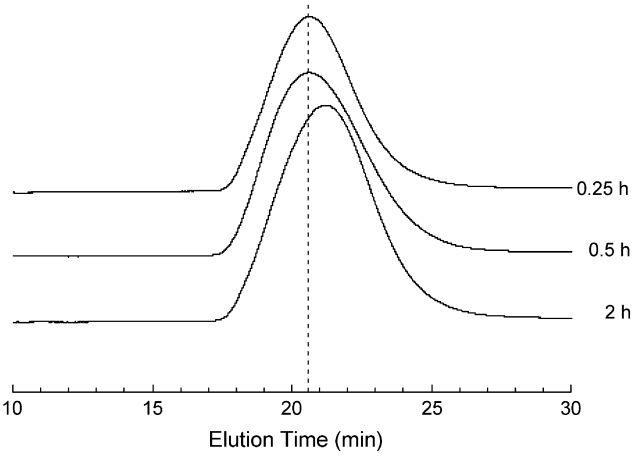



Fig. 1. GPC traces of poly(**2a**) isolated 0.25, 0.5, and 2 h after initiation of polymerization. Conditions: Grubbs 2nd generation Ru catalyst, $[M]_0/[Ru] = 100$, $[M]_0 = 1.0$ M in $CH_2Cl_2$, 30 °C. $M_n$ (PDI) after 0.25 h: 281 000 (1.6), 0.5 h: 223 500 (2.0), 2 h: 166 000 (2.2).

by IR, $^1$H, and $^{13}$C NMR spectroscopies, besides elemental analysis and mass spectrometry.

### 3.2. Polymerization

ROMP of novel diester monomers **1a**–**2b** were carried out in $CH_2Cl_2$ at 30 °C. The Grubbs 2nd generation Ru catalyst was used as an initiator because of its high functional group tolerance [7,11]. As shown in Table 1, all the monomers satisfactorily underwent polymerization to produce the polymers with molecular weights ranging from 15 500 to 261 000 in 43–98% yields. The polymerization mixtures of **2a** and **2b** became viscous soon after the polymerization was initiated, while those of **1a** and **1b** did not. The molecular weights of the formed poly(**2a**) and poly(**2b**) were one-order higher than those of poly(**1a**) and poly(**1b**), which agreed with the viscosity increase during polymerization. The polydispersity indices (PDIs) of the polymers ranged from 1.6 to 3.1. It seems that the relatively large PDIs are due to fast propagation compared with initiation [11b,12]. Additionally, backbiting possibly caused broadening of the PDIs, because the yield and molecular weight of the polymer decreased by extending the polymerization time from 0.5 to 1 h as shown in runs 4 and 5 in Table 1. The presence of backbiting reaction is also suggested from runs 2 and 3 in Table 1; the polymer yield increased with time, while the $M_n$ did not increase so much, and the PDI increased. The GPC traces of poly(**2a**) isolated 0.25–2 h after initiation of polymerization confirm the backbiting reaction as shown in Fig. 1. Namely, the $M_n$ of the polymer decreased from 281 000 to 166 000 and PDI increased from 1.6 to 2.2.

It has been reported that *exo*,*exo*-2,3-disubstituted 5-norbornene monomers are more reactive than the *endo*,*endo*-counterparts [12,13]. In the present study, no clear difference of polymerizability between the stereoisomers was observed under the conditions in Table 1. It should be noted that a norbornene *endo*,*endo*-diamide monomer substituted with $-CONHCH(CH_3)COCH_3$ at the 2,3-positions, an analogous monomer of **1a**, does not undergo ROMP at all [10]. We can say that the ester groups at the 2,3-positions of norbornene are much more favorable than amide groups from the view point of ROMP activity. It is likely that the N–H moiety hinders the coordination of the double bond to the Ru center of the catalyst, resulting in no polymerizability in the case of the diamide monomer.

The structures of the polymers were determined by IR and $^1$H NMR spectroscopies. All the absorption peaks and signals reasonably supported the proceeding of ROMP of the norbornene moiety, keeping the amino acid and amino alcohol moieties intact. The *cis*/*trans* ratio at the double bond in the polymer main chain was determined by the integration ratio of $^1$H NMR signals around 5.1 and 5.3 ppm assignable to *cis* and *trans* protons, respectively. The polymers exhibited IR absorption peaks based on N–H and C=O around 3380 and 1718 $cm^{-1}$, respectively, all of which were broad compared to those of the corresponding monomers. The *cis* contents of the double bond in the polymer main chain ranged from 43 to 60%.

Tables 2 and 3 summarize the effect of monomer/initiator ratio on the polymerization of **1a** and **2a**. In the polymerization of **1a** (Table 2), decreasing the initiator ratio resulted in decreasing the polymer yield, keeping the molecular weight almost constant. It is considered that the increase of $[M]_0/[Ru]$ decreases the initiation rate of the initiator. A complex equilibrium seems to exist, but the detail is not clear. Meanwhile, in the polymerization of **2a** (Table 3), decreasing the initiator ratio resulted in increasing the $M_n$, producing the polymer quantitatively in every case. These results confirm the higher reactivity of **2a** than that of **1a**, as indicated in Table 1. Judging from the aforementioned result, it is considered that the polymerizability of the monomers depends on the substituent and stereostructure.

Table 2
Polymerization of **1a** at various monomer/initiator ratios[a]

| $[M]_0/[Ru]$ | Polymer | | | |
|---|---|---|---|---|
| | Yield[b] (%) | $M_n$[c] | $M_w/M_n$[c] | *cis* Content[d] (%) |
| 20 | 83 | 14 000 | 1.4 | 50 |
| 50 | 87 | 16 000 | 1.5 | 46 |
| 100 | 54 | 19 000 | 1.4 | 43 |
| 150 | 21 | 14 000 | 1.6 | –[e] |
| 200 | 17 | 13 000 | 1.4 | 44 |

[a] Conditions: Grubbs 2nd generation Ru catalyst, $[M]_0 = 0.21$ M in $CH_2Cl_2$, 30 °C, 1 h.
[b] Hexane-insoluble part.
[c] Determined by GPC.
[d] Determined by $^1$H NMR.
[e] Not determined.

Table 3
Polymerization of **2a** at various monomer/initiator ratios[a]

| $[M]_0/[Ru]$ | Polymer | | | |
|---|---|---|---|---|
| | Yield[b] (%) | $M_n$[c] (%) | $M_w/M_n$[c] | *cis* Content[d] (%) |
| 20 | 98 | 213 000 | 1.74 | 46 |
| 50 | 98 | 236 000 | 1.98 | 47 |
| 100 | 99 | 301 600 | 1.87 | 47 |
| 150 | 98 | 367 000 | 2.01 | 48 |
| 200 | 98 | 562 000 | 1.92 | 48 |

[a] Conditions: Grubbs 2nd generation Ru catalyst, $[M]_0 = 0.21$ M in $CH_2Cl_2$, 30 °C, 1 h.
[b] Hexane-insoluble part.
[c] Determined by GPC.
[d] Determined by $^1$H NMR.

### 3.3. Rate of polymerization monitored by $^1$H NMR spectroscopy

Further, we directly monitored the monomer conversion of a polymerization mixture by $^1$H NMR spectroscopy to determine the rate of polymerization. The conversion was calculated from the integration ratio between the signals at 6.2 ppm corresponding to the olefinic protons of the monomer and those at 5.1–5.3 ppm of the polymer. Fig. 2 shows the curves of time–conversion of monomers **1a** and **1b** in $CD_2Cl_2$. A half amount of monomer **1a** converted into a polymer in 17 min and the polymerization was completed in 40 min. Monomer **1b** also converted quantitatively in 40 min. Fig. 3 depicts the kinetic plot based on the first-order equation of the polymerization of **1a** and **1b**. In the early stage of the polymerization, the polymerization rates of the two monomers were almost equal, indicating that the stereostructure, *endo*,*endo*- and *exo*,*exo*-, hardly affected the polymerizability.

Fig. 4 confirms that monomers **2a** and **2b** are highly polymerizable compared to **1a** and **1b**. Both **2a** and **2b** completely polymerized in less than 4 min. These results supported the aforementioned discussion on the polymerization of **1a**–**2b** summarized in Table 1. The *exo*,*exo*-monomer **2b** polymerized faster than *endo*,*endo*-monomer **2a**, presumably because the *exo*,*exo*-substituents at the 2,3-positions cause less steric hindrance to the polymerization than the *endo*,*endo*-ones [12].

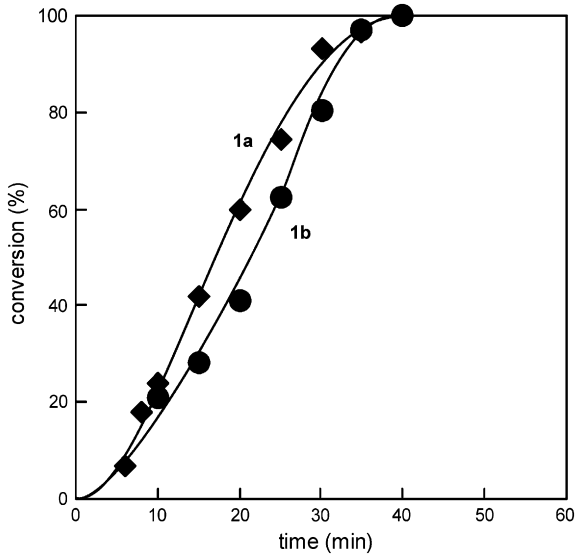



Fig. 2. Relationships between monomer conversion and time in the polymerization of **1a** and **1b** in $CD_2Cl_2$. Conditions: $[M]_0 = 0.105$ M, $[M]_0/[$Grubbs 2nd generation Ru catalyst$] = 20$, at 30 °C.

Solvents commonly affect the rate of polymerization including ROMP [14,15]. In the present study, we carried out the polymerization of **1a** in various solvents to examine the solvent effect on the polymerization rate. As depicted in Figs. 5 and 6, the polymerization rate was in the order of acetone-$d_6$ > benzene-$d_6$ > DMF-$d_7$ ≈ $CD_2Cl_2$ > $CDCl_3$. Table 4 summarizes the kinetic data depicted in the figures, along with the data of monomers **1b**–**2b** taken in $CDCl_3$. The slow polymerization rate in $CDCl_3$ compared to that in benzene has also been reported in ROMP of a diester-functionalized norbornene monomer [16]. Considering the order of dielectric constants of the solvents, i.e., DMF (38) > acetone (21) > $CH_2Cl_2$ (9.1) > $CHCl_3$ (4.8) > benzene (2.3), it

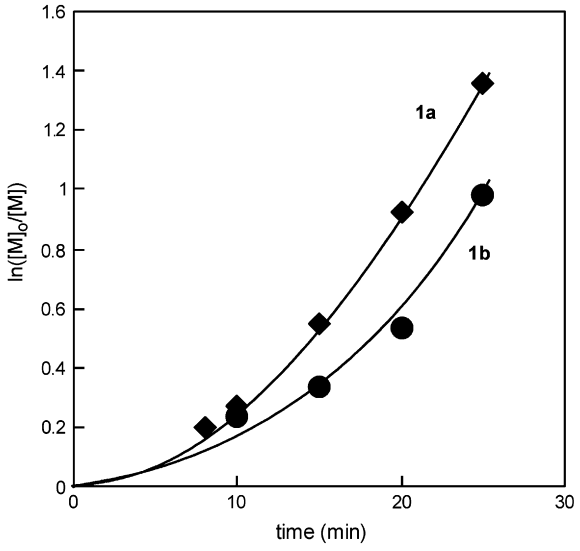



Fig. 3. Relationships between $\ln([M]_0/[M])$ and time in the polymerization of **1a** and **1b** in $CD_2Cl_2$. Conditions: $[M]_0 = 0.105$ M, $[M]_0/[$Grubbs 2nd generation Ru catalyst$] = 20$, at 30 °C.

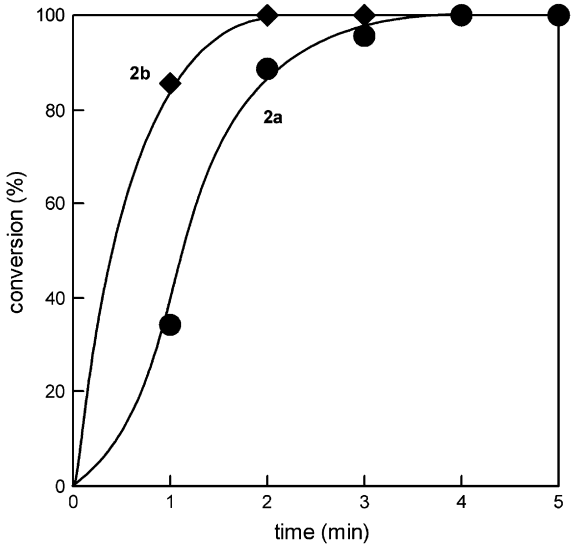



Fig. 4. Relationships between monomer conversion and time in the polymerization of **2a** and **2b** in $CDCl_3$. Conditions: $[M]_0 = 0.105$ M, $[M]_0$/[Grubbs 2nd generation Ru catalyst] = 20, at 30 °C.

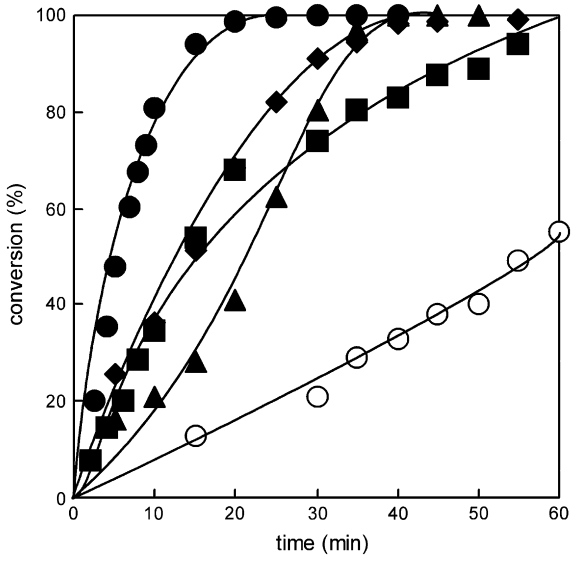



Fig. 5. Relationships between monomer conversion and time in the polymerization of **1a** in acetone-$d_6$ (●), benzene-$d_6$ (◆), DMF-$d_7$ (■), $CD_2Cl_2$ (▲), and $CDCl_3$ (○). Conditions: $[M]_0 = 0.105$ M, $[M]_0$/[Grubbs 2nd generation Ru catalyst] = 20, at 30 °C.

is not easy to explain the order of polymerization rate simply from the polarity of the solvents. It has been reported that solvent nature significantly affects the initiation rates of ROMP catalyzed with Ru complexes; initiation becomes faster upon employing a polar solvent [17]. We assume that the monomer conformation as well as competition of coordination between the ligand and solvent molecules to Ru center affects the polymerization rate, because the monomers have ester and carbamate moieties, both of which should largely interact with acetone and DMF molecules containing carbonyl group. Consequently, it seems that the solvent effect in the present study is rather complicated. Anyhow, it is apparent that the

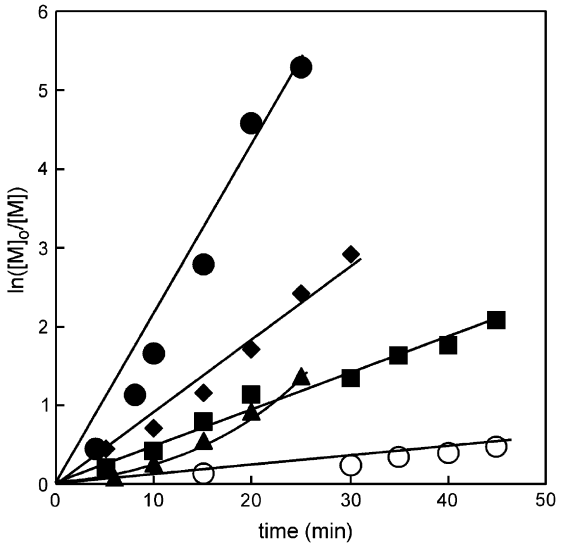



Fig. 6. Relationships between $\ln([M]_0/[M])$ and time in the polymerization of **1a** in acetone-$d_6$ (●), benzene-$d_6$ (◆), DMF-$d_7$ (■), $CD_2Cl_2$ (▲), and $CDCl_3$ (○). Conditions: $[M]_0 = 0.105$ M, $[M]_0$/[Grubbs 2nd generation Ru catalyst] = 20, at 30 °C.

Table 4
Kinetic data of ROMP of monomers **1a**–**2b**[a]

| Monomer | Solvent | $t_{1/2}$[b] (min) | $k_{observed} \times 10^{-3}$[c] ($s^{-1}$) |
|---|---|---|---|
| **1a** | Acetone-$d_6$ | 5 | 3.3 |
| **1a** | Benzene-$d_6$ | 15 | 1.5 |
| **1a** | DMF-$d_7$ | 14 | 0.8 |
| **1a** | $CD_2Cl_2$ | 17 | 0.7 |
| **1a** | $CDCl_3$ | 57 | 0.2 |
| **1b** | $CDCl_3$ | 47.5 | 0.2 |
| **2a** | $CDCl_3$ | 1.5 | 16.7 |
| **2b** | $CDCl_3$ | 0.5 | 32.3 |

[a] Conditions: Grubbs 2nd generation Ru catalyst, $[M]_0/[Ru]_0 = 20$, $[M]_0 = 0.105$ M, 30 °C.
[b] Time for 50% monomer conversion.
[c] Observed first-order rate constant of polymerization.

polymerization proceeded very fast in acetone. Acetone presumably enhances the initiation efficiency and slows down the backbiting reaction as reported in ROMP of ester-functionalized norbornene monomers [18].

## 4. Conclusions

We have demonstrated the synthesis and ROMP of amino acid- and amino alcohol-based novel norbornene monomers **1a**–**2b** with *exo*,*exo*- and *endo*,*endo*-structures using the Grubbs 2nd generation Ru catalyst. All the monomers successfully underwent homopolymerization to give the polymers with moderate molecular weights in good yields. The monomer reactivity dramatically increased compared to the amino acid-based diamide analogous monomers showing poor homopolymerizability [9]. No apparent difference in polymerizability was observed with respect to stereostructure. Monomers **2a** and **2b** gave the polymers with much higher molecular weights

than did **1a** and **1b** and the polymerization rates of the former two monomers were much faster than those of the latter two monomers. The polymerization rate was significantly affected by solvents. The observed polymerization rate of **1a** in acetone-$d_6$ was one-order higher than that in $CDCl_3$.

## References


[1] Biagini SCG, Coles MP, Gibson VC, Giles MR, Marshall EL, North M. Polymer 1998;39:1007–14.

[2] Maynard HD, Okada SY, Grubbs RH. Macromolecules 2000;33: 6239–48.

[3] Maynard HD, Okada SY, Grubbs RH. J Am Chem Soc 2001;123:1275–9.

[4] (a) Grubbs RH, Tumas W. Science 1989;243:907–15;
(b) Schrock RR. Acc Chem Res 1990;23:158–65.

[5] Bazan GC, Schrock RR, Khosravi E, Feast WJ, Gibson VC, O'Regan MB, et al. J Am Chem Soc 1990;112:8378–87.

[6] Feast WJ, Gibson VC, Marshall EL. J Chem Soc Chem Commun 1992; 1157–8.

[7] Kiessling LL, Owen RM. In: Grubbs RH, editor. Handbook of metathesis, vol. 3. Weinheim: Wiley-VCH; 2003 [chapter 3.6].

[8] (a) Biagini SCG, Bush M, Gibson VC. Tetrahedron 1995;5:7247–62;
(b) Biagini SCG, Davies RG, Gibson VC, Giles MR, Marshall EL, North M. Polymer 2001;42:6669–71;
(c) Coles MP, Gibson VC, Mazzariol L, North M, Teasdale WG, Williams CM, et al. J Chem Soc Chem Commun 1994;2505–6.

[9] Buchmeiser MR, Sinner F, Mupa M, Wurst K. Macromolecules 2000;33: 32–9.

[10] Sutthasupa S, Terada K, Sanda F, Masuda T. J Polym Sci Part A Polym Chem 2006;44:5337–43.

[11] (a) Scholl M, Ding S, Lee CW, Grubbs RH. Org Lett 1999;1:953–6;
(b) Choi TH, Grubbs RH. Angew Chem Int Ed 2003;42:1743–6;
(c) Romero PE, Piers WE, Mcdonald R. Angew Chem Int Ed 2004;43: 6161–5.

[12] Kanaoka S, Grubbs RH. Macromolecules 1995;28:4707–13.

[13] Rule JD, Moore JS. Macromolecules 2002;35:7878–82.

[14] Cazalis C, Herogeuz V, Fontanille M. Macromol Chem Phys 2000;201: 869–76.

[15] Klavetter FL, Grubbs RH. J Am Chem Soc 1988;110:7807–13.

[16] Sandra D, Wolfgang S, Slugovc C, Stelzer F. J Mol Catal A Chem 2003; 200:11–9.

[17] Sanford MS, Love JA, Grubbs RH. J Am Chem Soc 2001;123:6543–54.

[18] Slugvoc C, Demel S, Riegler S, Hobisch J, Stelzer F. J Mol Catal A Chem 2004;213:107–13.