

Synthesis and Polymerization of Novel (*S*)-*N*-Maleoyl-L-leucine Propargyl Ester

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(Received May 10, 2006; Accepted September 23, 2006; Published November 2, 2006)

KEY WORDS *N*-Substituted Maleimide / Propargyl Ester / Optically Active Polymer / Anionic Polymerization / Radical Polymerization / Rhodium Catalyst /
[doi:10.1295/polymj.PJ2006029]

N-Substituted maleimides (RMIs) have been known as a kind of important monomers through asymmetric anionic polymerization to provide optically active polymers because of their symmetric characteristic to C_2 -axis and 1,2-disubstituted ethylene circle.^{1,2} In recent years, Oishi *et al.* have investigated systematically the polymerizability of RMIs with various *N*-substituents and chiroptical properties of the polymers and copolymers.^{3–6} Every one of these RMIs has one olefinic group in the maleimide ring which was the only group that could polymerize. This research focuses on the utilization of an ethynyl group as a polymerizable moiety introduced to the *N*-substituent. Such monomers that possess two polymerizable groups of different polymerization reactivities would be able to open a new field for polymer reactions and macromolecular network.⁷ When the anionic and/or radical polymerizations occur on the olefinic groups of RMIs, the poly(RMI)s with pendant ethynyl groups are expected to show chirality induction and thermostable characteristics because of its specific polymer backbone. On the other hand, when the ethynyl groups of RMIs are polymerized, the obtained polyacetylene-type polymers possess the alternation double bonds in the main chain leading to notable functionalities, such as electrical conductivity, paramagnetism, energy migration and transfer, etc. At the same time, a maleimide moiety also acts as dienophile in the Diels-Alder reaction and α,β -unsaturated carbonyl compound in the Michael addition reaction, thus, the polymer with the maleimide moiety might have excellent potential for further polymer design. To the best of our knowledge, there have been no reports on polymerizations of RMI containing ethynyl groups on the *N*-substituent. This paper describes the synthesis and polymerization of novel (*S*)-*N*-maleoyl-L-leucine propargyl ester ((*S*)-PLMI). (*S*)-PLMI

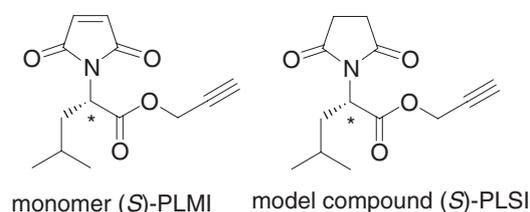


Figure 1. Structures of (*S*)-PLMI and (*S*)-PLSI.

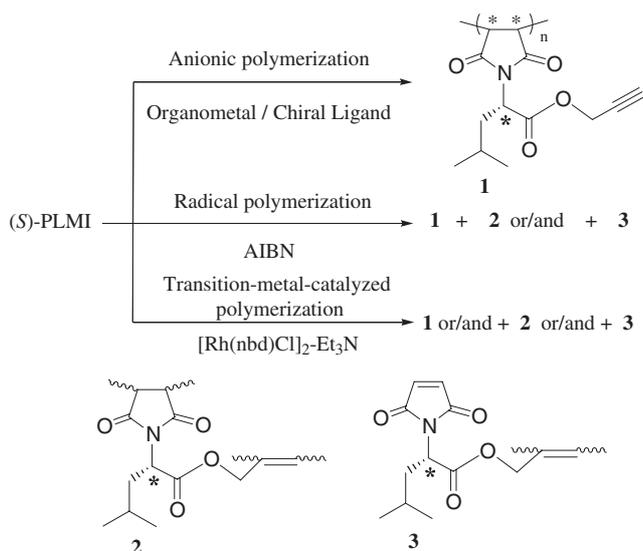
(Figure 1) has an olefinic group of the maleimide moiety and ethynyl group of the propargyl ester moiety simultaneously, and could be selectively polymerized on different reactive groups (olefinic group and/or ethynyl group) with different initiators. The chemoselective polymerization conditions of the monomer were discussed based on the measurements of ¹H NMR and FT-IR spectra respectively.

EXPERIMENTAL

(*S*)-PLMI (yellow liquid, bp = 160 °C/6.0 × 10⁻¹ mmHg, [α]₄₃₅ = -27.5° (*c* = 1.0, THF)) was synthesized from maleic anhydride, L-leucine, and propargyl alcohol. ¹H NMR (270 MHz, CDCl₃): 6.75 (s, 2H), 4.83–4.77 (dd, 1H, *J* = 4.3, 4.3 Hz), 4.72–4.71 (d, 2H, *J* = 2.3 Hz), 2.50–2.49 (t, 1H, *J* = 2.5 Hz), 2.30–1.84 (m, 2H), 1.53–1.38 (m, 1H), 0.94–0.91 (dd, 6H, *J* = 2.0, 2.0 Hz). ¹³C NMR (δ in ppm from TMS in CDCl₃): 169.9 (N–C=O), 168.9 (C=O), 134.2 (-ethylene), 76.8 ($\equiv\text{C}-\text{CH}_2$), 75.5 ($\equiv\text{CH}$), 53.0 ($\text{CH}_2-\text{C}=\text{O}$), 50.4 (N–CH-), 36.9 (-CH₂), 24.9 (-CH), 23.0 (-CH₃), 20.8 (-CH₃). IR (KBr, cm⁻¹): 3300 (HC \equiv), 3100, 2960, 2110 (C \equiv C), 1750, 1710, 1400, 1250, 840, 700. Anal. (%), Calcd for C₁₃H₁₅NO₄: C, 62.64; H, 6.07; N, 5.62. Found: C, 63.0; H, 6.30; N, 5.83.

Synthesis of model compound (*S*)-*N*-succinoyl-L-leucine propargyl ester ((*S*)-PLSI) was similar to

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Scheme 1.

(*S*)-PLMI (yellow liquid, bp = 175 °C/6.0 × 10⁻¹ mmHg, [α]₄₃₅ = -98.0° (*c* = 1.0, THF)). ¹H NMR (270 MHz, CDCl₃): 4.87–4.81 (dd, 1H, *J* = 4.3, 4.6 Hz), 4.72–4.71 (d, 2H, *J* = 2.3 Hz), 2.77 (s, 4H), 2.50–2.49 (t, 1H, *J* = 2.5 Hz), 2.23–1.86 (m, 2H), 1.51–1.31 (m, 1H), 0.94–0.91 (d, 6H, *J* = 6.6 Hz). ¹³C NMR (δ in ppm from TMS in CDCl₃): 176.5 (N=C=O), 168.4 (–C=O), 76.9 (≡C–CH₂), 75.5 (CH≡), 53.0 (CH₂–C=O), 50.9 (N–CH–), 36.2 (–CH₂), 27.9 (–CH₂), 24.9 (–CH), 22.9 (–CH₃), 21.0 (–CH₃). IR (KBr, cm⁻¹): 3300 (HC≡), 2960, 2110 (C≡C), 1750, 1710, 1400, 1250. Anal. (%), Calcd for C₁₃H₁₇NO₄: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.10; H, 7.12; N, 5.76.

As is shown in Scheme 1, anionic polymerization was carried out according to the published procedures.⁸ Radical polymerization was conducted with 2,2'-azobisisobutyronitrile (AIBN) as an initiator in polymerization solvent (THF or toluene) in a sealed tube at 60 °C for 24 h. The polymerizations using (bicyclo[2,2,1]hepta-2,5-diene) chloro rhodium (I) dimer ([Rh(nbd)Cl]₂) as a catalyst were performed according to the published literature.^{9,10}

RESULTS AND DISCUSSION

The results of asymmetric anionic polymerizations of (*S*)-PLMI using *n*-BuLi or *n*-BuLi/ligand, Et₂Zn/ligand (Figure 2) as initiators are summarized in Table I. When only *n*-BuLi is used as initiator, the yield of methanol-water (7/3; v/v)-insoluble part in toluene (Run 1) was lower than that in THF (Run 2), indicating that polar solvents were efficient to obtain higher yields in the polymerizations of (*S*)-PLMI. But when the polymerizations were performed with organometal/ligand complex, the results were oppo-

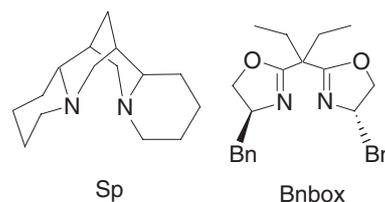

Figure 2. Chiral ligands.

Table I. Anionic polymerizations of (*S*)-PLMI^a with organometal/ligand at 0 °C for 72 h

Run	Initiator ^b	Polym. solv. ^c (mL)	Yield ^d %	<i>M</i> _n ^e × 10 ⁻³	<i>M</i> _w / <i>M</i> _n ^e	[α] ₄₃₅ ^f deg.
1	<i>n</i> -BuLi	Tol.(5)	55.8	2.9	1.6	-112.4
2	<i>n</i> -BuLi	THF(5)	72.0	2.6	1.7	-121.6
3	<i>n</i> -BuLi/Bnbox	Tol.(5)	45.8	3.9	1.5	-171.6
4	<i>n</i> -BuLi/Bnbox	THF(5)	41.8	5.5	1.5	-243.9
5	<i>n</i> -BuLi/Sp	Tol.(5)	79.6	10.8/2.3 ^g	1.2/1.1 ^g	-195.8
6	<i>n</i> -BuLi/Sp	THF(5)	63.6	2.3	1.4	-195.8
7	Et ₂ Zn/Sp	Tol.(5)	60.0	7.4	1.9	-134.4

^aMonomer: 0.5 g. ^b[Organometal]/[monomer] = 0.1. [Organometal]/[ligand] = 1.0/1.2. ^cTHF: tetrahydrofuran, Tol.: toluene. ^dMethanol-H₂O (7/3; v/v)-insoluble part. ^eBy GPC. ^f*c* = 0.1 g/dL, *l* = 10 cm in THF. ^gBimodal chromatogram.

site to those performed with *n*-BuLi. The yields obtained in toluene were higher than that in THF. The number-average molecular weights (*M*_ns) and specific rotations of polymers obtained with organometal/ligand complex as initiators were almost higher than those with only *n*-BuLi. These results confirmed that better asymmetric fields were formed by using the complexes of chiral ligand and organometal in these anionic polymerizations. Most of the polymers have higher specific rotations than model compound, indicating that asymmetric inductions in main chains of these polymers occurred. Compared with ¹H NMR spectra of (*S*)-PLMI (the top spectrum in Figure 3) and poly((*S*)-PLMI) (the middle spectrum in Figure 3) obtained with *n*-BuLi/Sp as initiator in THF (Run 6 in Table I), only the olefinic group in the maleimide ring gave polymerization (a signal at 6.75 ppm assigned to the olefinic proton of monomer disappeared), and ethynyl group was not converted (a signal at 2.50 ppm due to the ethynyl proton was detectable).

In radical polymerizations summarized in Table II, the yield and specific rotation of the polymer obtained in toluene were lower than in THF. The absolute values of specific rotations of polymers were much lower than those obtained by anionic polymerizations (Table I), suggesting that the asymmetric fields formed in the radical polymerization were less than those formed in anionic polymerization. And according to ¹H NMR spectra of polymers, when the poly-

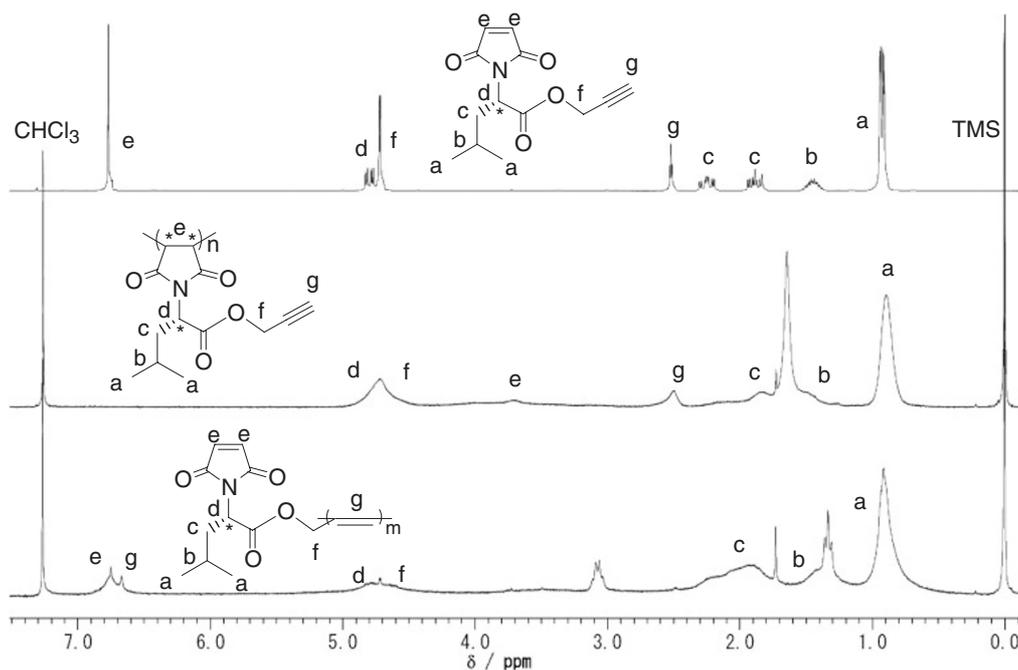


Figure 3. ^1H NMR spectra (270 MHz, CDCl_3) of (*S*)-PLMI (the top spectrum) and poly((*S*)-PLMI)s obtained with *n*-BuLi/Sp in THF (the middle spectrum) and $[\text{Rh}(\text{nbd})\text{Cl}]_2\text{-Et}_3\text{N}$ in THF (the bottom spectrum).

Table II. Radical polymerizations of (*S*)-PLMI^a at 60 °C

Run	Initiator ^b	Polym. solv. ^c (mL)	Polym. time (h)	Yield ^d (%)	M_n^e $\times 10^{-3}$	M_w/M_n^e	$[\alpha]_{435}^f$ deg.
1	AIBN	Tol.(2)	24	33.0	6.9/2.0 ^g	1.3/1.2 ^g	-69.0
2	AIBN	THF(2)	24	59.2	2.2	1.4	-90.7

^aMonomer: 0.5 g. ^b[Initiator]/[monomer] = 0.1. ^cTHF: tetrahydrofuran, Tol.: toluene. ^dMethanol-H₂O (7/3; v/v)-insoluble part. ^eBy GPC. ^f $c = 0.1$ g/dL, $l = 10$ cm, in THF. ^gBimodal chromatogram.

merization was carried out in toluene (Run 1 in Table II), both an olefinic and an ethynyl group partly reacted (conversion of olefinic group was 85% and conversion of ethynyl group was 37%). The structure of the polymer obtained was a mixture of **1**, **2**, and **3** as is shown in Scheme 1. In THF (Run 2 in Table II), the olefinic group entirely polymerized, while the ethynyl group partly reacted, mixture of **1** and **2** was obtained. Although both the vinyl and the ethynyl groups were consumed, we did not think the products contained cross-linked gel because the obtained poly((*S*)-PLMI)s were soluble in common organic solvents, such as THF, CHCl_3 and so on.

Because (*S*)-PLMI has an ethynyl group, the authors chose $[\text{Rh}(\text{nbd})\text{Cl}]_2$ as catalyst to investigate the polymerizability of the two reactive groups. Table III shows the polymerization results of (*S*)-PLMI using $[\text{Rh}(\text{nbd})\text{Cl}]_2\text{-Et}_3\text{N}$ as catalyst. Yields and specific rotations of polymers were strongly influenced by polymerization solvents. The FT-IR spec-

Table III. Polymerizations of (*S*)-PLMI^a catalyzed with $[\text{Rh}(\text{nbd})\text{Cl}]_2\text{-Et}_3\text{N}^b$ at 30 °C for 24 h

Run	Polym. solv. ^d (mL)	Yield ^e (%)	M_n^f $\times 10^{-3}$	M_w/M_n^f	$[\alpha]_{435}^g$ deg.
1	Tol.(5)	9.3	—	—	—
2 ^c	THF(7)	28.8	1.8	1.5	-8.7
3	DMF(3)	19.2	1.7	1.5	-252.9
4	DMSO(3)	77.8	3.0/1.1 ⁱ	1.2/1.1 ⁱ	-158.6 ^h

^aMonomer: 0.5 g. ^b[Monomer]/[catalyst] = 100, $[\text{Et}_3\text{N}]/[\text{catalyst}] = 100$. ^c[Monomer]/[catalyst] = 50, $[\text{Et}_3\text{N}]/[\text{catalyst}] = 100$. ^dTol.: toluene. ^ediethyl ether-insoluble part. ^fBy GPC. ^g $c = 0.1$ g/dL, $l = 1$ cm, in THF. ^h $c = 0.1$ g/dL, $l = 10$ cm, in THF. ⁱBimodal chromatogram.

trum of the polymer (Run 2 in Table III) exhibited no absorption bands around 2110 and 3300 cm^{-1} due to the stretching vibrations of $\text{C}\equiv\text{C}$ and $\text{C}\equiv\text{C-H}$ bonds, respectively. In the ^1H NMR spectrum (the bottom spectrum in Figure 3), the distinct signal for the maleimide groups was confirmed around 6.75 ppm, while the signal (2.50 ppm) ascribed to the methane proton of the propargyl group almost disappeared. At the same time, a new signal assignable to the olefinic protons in the main chains was observed at 6.67 ppm, indicating the cis-transoidal structure of the polyacetylene-type main chain.¹¹ These spectral results confirmed that the ethynyl group was entirely polymerized to provide the structure **3**. According to the ^1H NMR and FT-IR spectra of other polymers, polymerization occurred on different reactive groups in different polymerization solvents.

Further studies on the details of the polymerization are in progress.

REFERENCES

1. Y. Okamoto, T. Nakano, H. Kobayashi, and K. Hatada, *Polym. Bull.*, **25**, 5 (1991).
2. T. Oishi, Y. Zhang, T. Fukushima, and K. Onimura, *Polym. J.*, **37**, 453 (2005).
3. T. Oishi, H. Yamasaki, and M. Fujimoto, *Polym. J.*, **23**, 795 (1991).
4. K. Onimura, H. Tsutsumi, and T. Oishi, *Macromolecules*, **31**, 5971 (1998).
5. Y. Isobe, K. Onimura, H. Tsutsumi, and T. Oishi, *Macromolecules*, **34**, 7617 (2001).
6. Y. Isobe, K. Onimura, H. Tsutsumi, and T. Oishi, *Polym. J.*, **34**, 18 (2002).
7. T. Hagiwara, I. Suzuki, K. Takeuchi, H. Hamana, and T. Narita, *Macromolecules*, **24**, 6856 (1991).
8. K. Onimura, H. Tsutsumi, and T. Oishi, *Chem. Lett.*, **27**, 791 (1998).
9. S. M. A. Karim, R. Nomura, and T. Masuda, *J. Polym. Sci., Part A: Polym. Chem.*, **40**, 2458 (2002).
10. E. A. Rahim, F. Sanda, and T. Masuda, *J. Polym. Sci., Part A: Polym. Chem.*, **44**, 810 (2006).
11. T. Masuda, in "Catalysis in Precision Polymerization," S. Kobayashi, Ed., Wiley, Chichester, 1997, chap. 2.4, p 67.