Asymmetric Free Radical Polymerization and Copolymerization of *N*-(Triphenylmethyl)methacrylamide Derivatives

N-(トリフェニルメチル)メタクリルアミド誘導体の
不斉ラジカル重合および共重合

A.K.M. Fakhrul Azam

2007

Dedicated to my loving

parents, Md. Moslem Ali Khamaru

and Mrs. Sufia Khatun

brother, A.K.M. Kamrul Ramzan

my wife, Shirin Akther

and

to all my friends

for their continuous encouragement

this thesis is a token of gratitude and affection

Asymmetric Free Radical Polymerization and Copolymerization of *N*-(Triphenylmethyl)methacrylamide Derivatives

(Table of Contents)

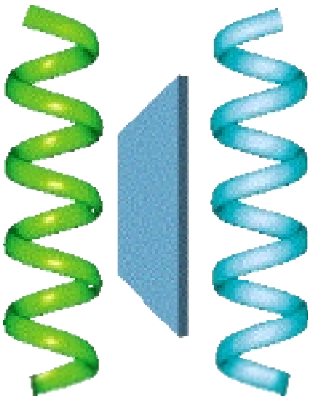
General Introduction

Nature has developed a multitude of biomacromolecules tailored to deal with complicated tasks such as information storage, support of tissue, transport, and the performance of localized chemical transformations. Although a large number of researchers in the fields of chemistry and polymer science have been, and still are, pursuing the same goals using synthetic systems, nucleic acids and proteins still outclass man-made materials. Thus a number of scientists over the past decades turn their eyes to nature to design and synthesize increasingly precise nanoscopic and even mesoscopic helical structures using polymeric materials. The smallest building blocks, such as the amino acids, can contain information in the form of chirality, hydrogen-bonding capacity, steric demands, electrostatic properties, hydrophilic or hydrophobic character, or metal ion binding capability.

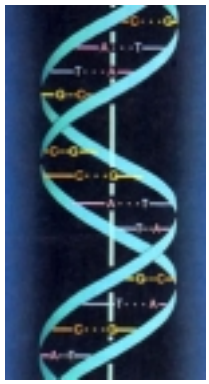
Supramolecular chemistry since its early days has been inspired by biological assembly methods and has already delivered a large number of architectures of macromolecular size based on these secondary interactions.[1,2] Usually higher order structure of a polymer, such as helical structure, significantly influences their physical and chemical properties. A number of naturally occurring macromolecules such as proteins, nucleic acids and polysaccharides are optically active and take a helical structure, which is closely related to their characteristic functions, such as chiral recognition toward racemic compounds, liquid crystal formation, and catalytic activity.[3-7] Therefore, design and synthesis of the helical polymers are not only one of the most interesting and important fields of fundamental studies for understanding the

relationship between the structure and properties of the polymers, but also one of the most challenging goals to control higher order structure and development of novel functional polymers based on the stereospecific introduction of many functional groups into a polymer main chain.

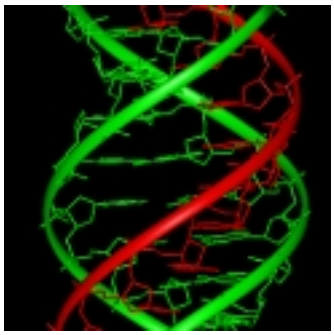
Helical Structures



Left-handed helix **Right-handed helix**

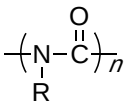


DNA double-helix

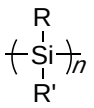


DNA triple-helix

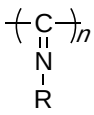
Although a helical conformation is found for stereoregular synthetic polymers in a solid state, it often disappears in solution because of fast conformational dynamics.



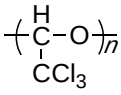
Polyisocyanate



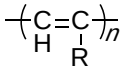
Polysilane



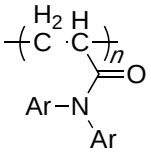
Polyisocyanide



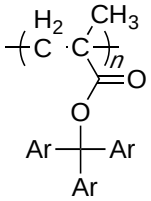
Polychloral



Polyacetylene



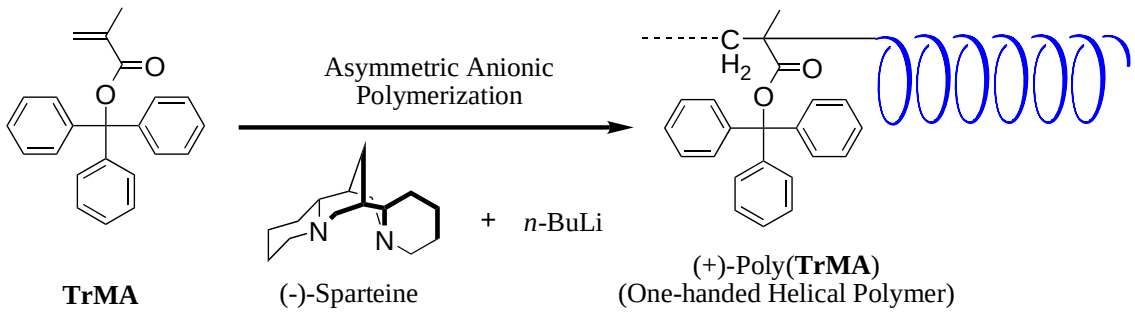
Poly(*N*,*N*-diarylacrylamide)



Poly(triarylmethyl methacrylate)

However, there are several classes of polymers, such as polyisocyanates,[8,9] polysilanes,[10] polyisocyanides,[11] polychloral,[12] polyacetylenes,[13] poly(*N*,*N*-diarylacrylamide)s,[14] and poly(triarylmethyl methacrylate)s,[15] which can maintain the helical conformation even in solution.

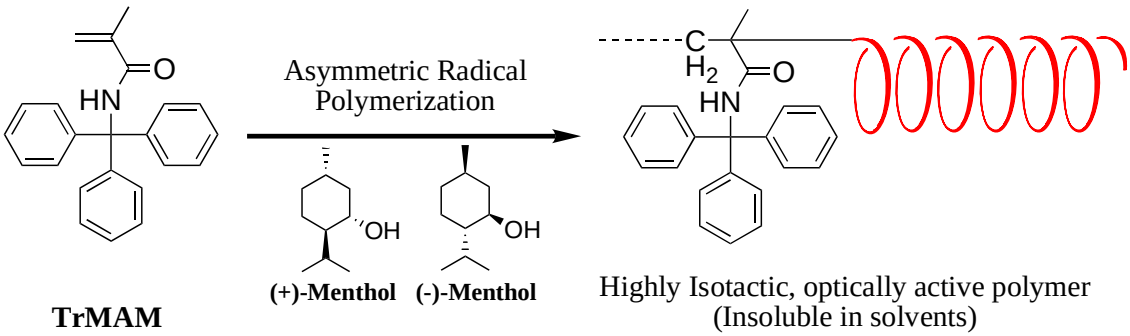
Optically active poly(triphenylmethyl methacrylate)s with predominantly one-handed screw sense can be prepared by asymmetric anionic polymerization (helix-sense-selective polymerization) using optically active anionic initiators. Triphenylmethyl methacrylate (TrMA) is the first example of a vinyl monomer that directly affords a highly optically active isotactic polymer arising from the one-handed helicity produced through the polymerization procedure with chiral anionic initiators. This has been explained on the basis of the helical conformation of the growing polymer chain which forces the monomer to add in an isotactic manner to the chain end, due to the steric repulsion between bulky trityl groups on the side chain. The one-handed helical poly(TrMA) is known to show remarkable chiral recognition ability to various types of racemic compounds, and has been successfully used as a chiral stationary phase for high-performance liquid chromatography (HPLC) to resolve a wide range of enantiomers.[16]



TrMA (-)-Sparteine (+)-Poly(**TrMA**)
(One-handed Helical Polymer)

The chiral stationary phase prepared from poly(TrMA) can resolve many racemic compounds including hydrocarbons, esters, amides, alcohols, and so on, most of which are difficult to resolve by other methods. As the eluent, a polar solvent like methanol is more effective rather than a nonpolar solvent like hexane. However, when methanol is used as the eluent, the ester groups of poly(TrMA) are slowly solvolyzed, which causes the decrease of the column efficiency.[16(f)] Therefore, it is highly desirable to prepare the helical polymer, which is durable against the solvolysis by alcohol and can be used as a chiral stationary phase for an HPLC column.

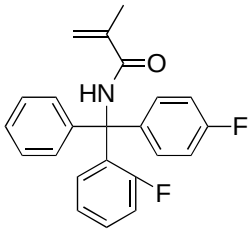
The radical polymerization of methacrylates with a bulky side group, such as TrMA[17] and 1-phenyldibenzosuberyl methacrylate (PDBSMA),[18] also proceeds in an isotactic-specific manner due to the steric repulsion among the bulky side groups. The helix-sense-selective polymerization of PDBSMA through free radical mechanism gives rise to an optically active, helical polymer having an excessive one-handed helicity from an achiral monomer.[18] Recently, Okamoto et al. reported that the radical polymerization of *N*-(triphenylmethyl)methacrylamide (TrMAM) in the presence of (+)- and (-)-menthol proceeds in good yields to afford highly isotactic, optically active polymer.[19] These polymers were insoluble in common organic solvents but highly durable against the solvolysis by alcohols.



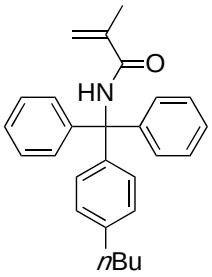
TrMAM **(+)-Menthol** **(-)-Menthol**

Highly Isotactic, optically active polymer
(Insoluble in solvents)

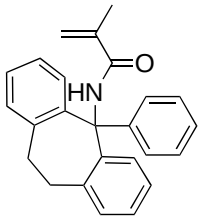
This result encouraged the author to design, synthesize and polymerize several new derivatives of TrMAM, such as *N*-[(±)-(2-fluorophenyl)(4-fluorophenyl)-(phenyl)methyl]methacrylamide (2F4FPhMAM), *N*-[(4-butyl)triphenylmethyl]methacrylamide (BuTrMAM), *N*-(1-Phenyldibenzosuberyl)methacrylamide (PDBSMAM),



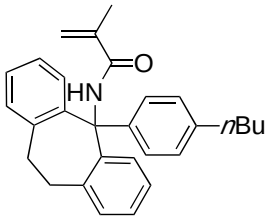
(±)-2F4FPhMAM



BuTrMAM



PDBSMAM



BuPDBSMAM

and *N*-[(4-butylphenyl)dibenzosuberyl]methacrylamide (BuPDBSMAM), to obtain one-handed helical polymers that can be used as a chiral stationary phase for HPLC.

Thus, the author studied the following four themes.

1. Helix-Sense-Selective Free Radical Polymerization of *N*-(Triphenylmethyl)-methacrylamide Derivatives.

2. Helicity Induction in *N*-[(4-Butyl)triphenylmethyl)]methacrylamide Sequence *via* Radical Copolymerization with Chiral Monomers.

3. Asymmetric Radical Polymerization and Copolymerization of *N*-(1-Phenyldibenzosuberyl)methacrylamide and Its Derivative Leading to Optically Active Helical Polymers.

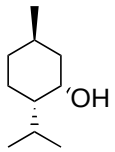
4. Chiral Adsorption with the Optically Active Helical Polymers.

Each theme is described in the following four chapters.

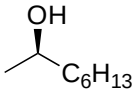
Chapter 1 mainly deals with the polymerization of *N*-[(±)-(2-fluorophenyl)(4-fluorophenyl)(phenyl)methyl]methacrylamide (2F4FPhMAM) and *N*-[(4-butyl)triphenylmethyl]methacrylamide (BuTrMAM) in the presence of (+)- and (-)-menthol as the chiral additive at different temperatures. The obtained polymers, poly(2F4FPhMAM) and poly(BuTrMAM), were optically active. Poly(2F4FPhMAM) was not soluble in common organic solvents and no enantiomer selection was observed in the polymerization of racemic 2F4FPhMAM in the presence of the optically active additive (+)- and (-)-menthols. The circular dichroism spectra of the polymers in a solid state (in liquid paraffin) is similar to that of the optically active poly[*N*-(triphenylmethyl)methacrylamide] (poly(TrMAM)) with a prevailing one-handed helicity, suggesting that the present polymers also have a prevailing one-handed helicity. Poly(BuTrMAM) is soluble in THF and chloroform. The optical activity of the polymers obtained in the presence of (+)- or (-)-menthol was gradually decreased with an increase in polymerization temperature. Thus, the polymerization of BuTrMAM at 0 °C in (+)-menthol produced the polymer having higher specific rotation ($[\alpha]_D$ = -9.7) than those at 20 °C ($[\alpha]_D$ = -7.0) and at 60 °C (($[\alpha]_D$ = -3.1). The CD spectra of the polymers obtained in the presence of (+)- and (-)-menthols were the mirror images of each other. The tacticity of the polymers was estimated from the ^{1}H NMR spectrum of poly(methacrylamide) derived in D_2SO_4. The ^{1}H NMR showed only one methyl peak due to the isotactic (mm) sequence at 1.05 ppm and two sets of doublet due to the methylene group at 1.60 and 1.95 ppm, indicating that the polymers were almost 100% isotactic.

Other chiral alcohols and acids, such as (+)-neomenthol (**1**), (*R*)-(-)-2-octanol (**2**), (*R*)-(-)-2-heptanol (**3**), (*S*)-(-)-3-hydroxytetrahydrofurane (**4**), and (*R*)-(+)-tetrahydrofuran-2-carboxylic acid (**5**), were also used as the optically active additives or

solvents for the polymerization of BuTrMAM to enhance the optical activity or the one-handedness of the PBuTrMAM. However, compared with menthol, these compounds did not enhance the optical activity, probably one-handedness of the polymers.



1



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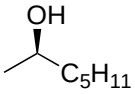

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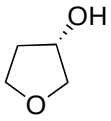

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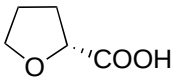

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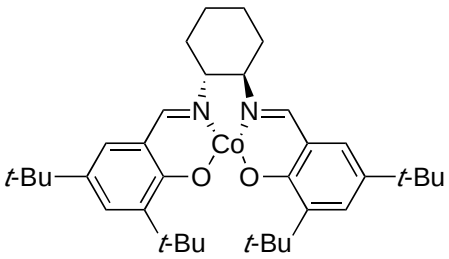

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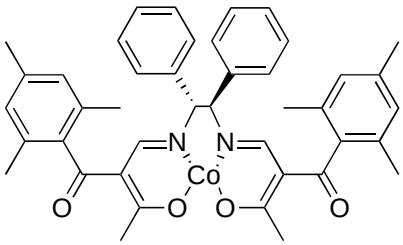
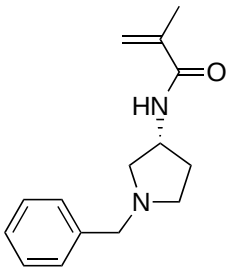


7

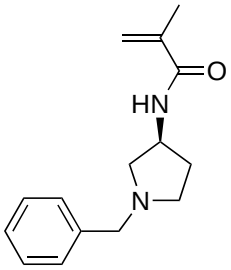
Chiral cobalt complexes have been successfully used for the asymmetric radical polymerization of TrMA derivatives. The radical polymerization of PDBSMA in the presence of *N*,*N*'-bis(3,5-di-*tert*-butylsalicylidene)-(1*R*,2*R*)-1,2-cyclohexane-diaminato-cobalt(II) (**6**) and *N*,*N*'-bis{2-(2,4,6-tri-methylbenzoyl)-3-oxobutylidene}-(1*S*,2*S*)-1,2-diphenylethylenediaminatocobalt(II) (**7**) effectively induces a single-handed helicity.[20] These Co complexes were also used as chiral additives for the polymerization of BuTrMAM. However, the complexes functioned as the polymerization inhibitors. The optically inactive polymer was obtained in low yields only using the complex of **6**.

Chapter 2 describes the radical copolymerization of BuTrMAM with optically

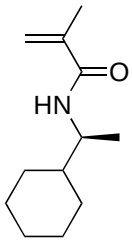
active monomers, such as *N*-((*R*)-(+)-1-benzylpyrrolidin-3-yl)methacrylamide ((+)-BPMAM), *N*-((*S*)-(-)-1-benzylpyrrolidin-3-yl)methacrylamide ((-)-BPMAM), *N*-((*S*)-(+)-1-cyclohexylethyl)methacrylamide ((+)-CHEMAM), *N*-((*R*)-(-)-1-cyclohexyl-ethyl)methacrylamide ((-)-CHEMAM), *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide ((+)-NEMAM), *N*-[(*S*)-(-)-1-(1-naphthyl)ethyl]methacrylamide ((-)-NEMAM), *N*-((1*R*,2*S*)-(+)-2-hydroxy-1,2-diphenylethyl)methacrylamide (HDMAM), and (*S*)-(-)-diphenyl(1-methylpyrrolidine-2yl)methyl methacrylate ((-)-DMPMA).



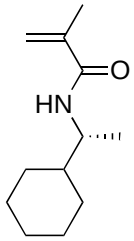
(+)-BPMAM



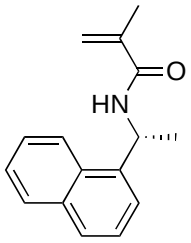
(-)-BPMAM



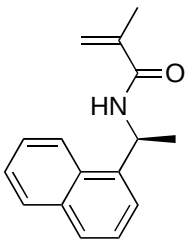
(+)-CHEMAM



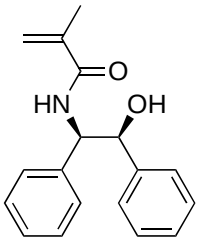
(-)-CHEMAM



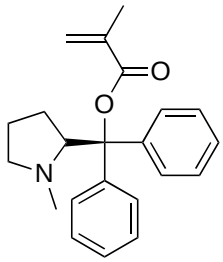
(+)-NEMAM



(-)-NEMAM



(+)-HDMAM

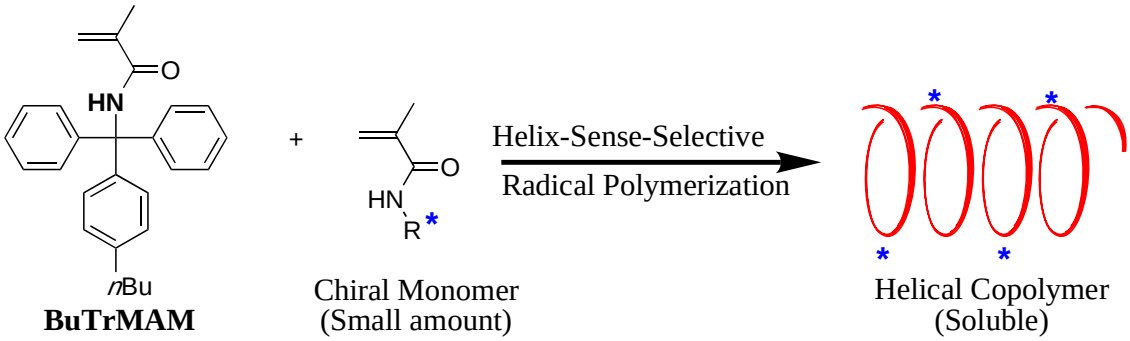


(-)-DMPMA

The optical activity of the obtained copolymers significantly depended on the monomer contents. When the chiral monomer content was low in the copolymers, the chiral monomeric units were effective in inducing an excess of the one-handed helix consisting of BuTrMAM monomeric sequences.

In the radical copolymerization of BuTrMAM with (-)-CHEMAM, the optical

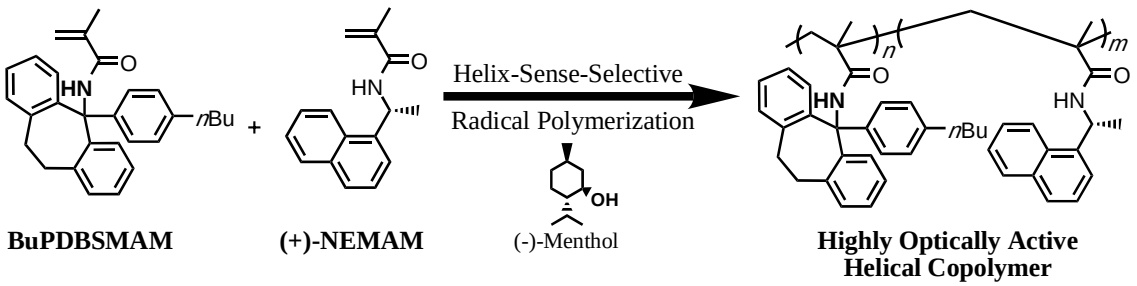
rotation of the copolymers increased up to 4% chiral monomer content in the copolymer, and further addition of the chiral monomer resulted in gradual increase of the optical rotation in negative direction. When the content of the chiral monomer was low, the copolymers exhibited the optical rotation opposite to that of the feed CHEMAM. BuTrMAM sequences may form a prevailing one-handed helical chain. Similar results were observed in the copolymerization of BuTrMAM with optically active (+)- or (-)-BPMAMs.



In the copolymerization of BuTrMAM with (-)-NEMAM at 60 °C, the optical rotations of copolymers also gradually increased with an increase in the chiral monomer contents up to 20% and further increase of the chiral monomer resulted in the increase of the optical rotation in opposite direction and finally arrived at the optical rotation of the homopolymer of (-)-NEMAM, which was opposite to that of the monomer. The decrease in the polymerization temperature more significantly increased the optical rotation of the copolymer. Thus, the helicity induction by the chiral monomer may be more effective when the polymerization temperature is lower. It was most effectively attained using *N*-[1-(1-naphthyl)ethyl]methacrylamide at low temperature.

Chapter 3 describes the synthesis and polymerization of *N*-(1-phenyldibenzosuberyl)methacrylamide (PDBSMAM) and its derivative *N*-[(4-butylphenyl)dibenzosuberyl]methacrylamide (BuPDBSMAM). Optically active polymers were obtained by the asymmetric radical polymerization of PDBSMAM and BuPDBSMAM in the presence of (+)- and (-)-menthols at different temperatures. The tacticity of the polymers was estimated to be nearly 100% isotactic from the ^{1}H NMR spectra of poly(methacrylamide)s (poly(MAM)) derived in D_2SO_4. Poly(PDBSMAM) was not soluble in the common organic solvents, and its circular dichroism spectrum in a solid state was similar to that of the optically active poly(1-phenyldibenzosuberyl methacrylate) (poly(PDBSMA)) with a prevailing one-handed helicity, indicating that the poly(PDBSMAM) also has a similar helicity.

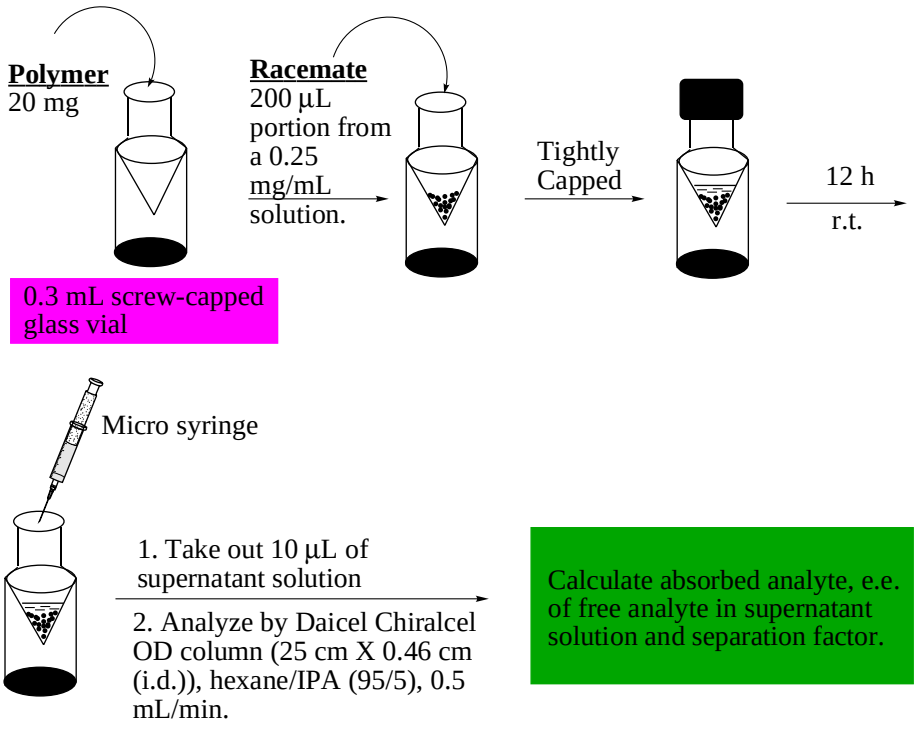
Poly(BuPDBSMAM) was optically active and soluble in chloroform. Its optical activity was much higher than that of the poly(BuTrMAM), suggesting that one-handed helicity may be more efficiently induced on the poly(BuPDBSMAM). The copolymerization of BuPDBSMAM with a small amount of optically active *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide [(+)-NEMAM], particularly in the presence of (-)-menthol, produced a polymer with a high optical activity. The prevailing helicity may also be efficiently induced.



BuPDBSMAM **(+)-NEMAM** (-)-Menthol **Highly Optically Active Helical Copolymer**

Chapter 4 deals with the chiral adsorption experiments of the optically active polymers obtained by the asymmetric polymerization and copolymerization of the bulky methacrylamides described in chapter 2 and 3. The chiral recognition ability of the optically active poly(BuTrMAM-*co*-NEMAM) (BuTrMAM/NEMAM = 96/4 at 0 °C), poly(PDBSMAM) (in the presence of (+)- or (-)-menthol at 60 °C) and poly(BuPDBSMAM-*co*-(+)-NEMAM) (BuPDBSMAM/(+)-NEMAM = 96/4 at 0 °C in (-)-menthol) was evaluated by the chiral adsorption method[21] using *trans*-stilbene oxide and Tröger's base as the racemates. Each racemate was adsorbed by ca. 30~50% on the optically active polymers in methanol and hexane (see below). The enantiomeric excess (e.e.) of the free solutes in a supernatant solution was estimated by HPLC using a chiral column and found to be very low. The enantioselectivity of these polymers was very low compared to that of the one-handed helical poly(TrMA).

Chiral Adsorption Experiment Method



The conclusions drawn in this thesis are summarized as follows:

Chapter 1. The asymmetric radical polymerization of (±)-2F4FPhMAM and BuTrMAM in the presence of (+)- and (-)-menthol produced the polymers with a prevailing one-handed helicity and nearly 100% isotacticity. The optical activity and the CD adsorption of these polymers are ascribed to an excess right or left-handed helical conformation. As the BuTrMAM is much stronger toward hydrolysis the obtained polymer must be more stable when used as a chiral stationary phase for HPLC with polar alcoholic solvents.

Chapter 2. The copolymerization of BuTrMAM with a small amount of optically active monomer in toluene produced the optically active helical copolymers. The CD patterns of the copolymers containing low contents of the chiral monomers resemble that of the helical BuTrMAM homopolymer obtained in the presence of (+)- and (-)-menthol, suggesting that the optically active monomeric units can induce a single-handed helical conformation of the BuTrMAM sequence via copolymerization. The helical induction by chiral (-)-NEMAM was more effective at low temperature, and the obtained copolymer exhibited a higher optical activity than that of the homopolymer of BuTrMAM obtained in optically active menthol.

Chapter 3. The free radical polymerization of PDBSMAM and BuPDBSMAM using chiral additives produced optically active polymers with a CD adsorption based on an excess right- or left-handed helical conformation. All the polymers were nearly 100% isotactic. The copolymer of BuPDBSMAM with optically active (+)-NEMAM in the presence of (-)-menthol produced a helical polymer with a high optical activity, which was much higher than that of the other polymethacrylamides having bulky side groups, such as poly(TrMAM), poly(BuTrMAM), and

poly(DBuTrMAM).

Chapter 4. All the optically active helical polymers obtained by the asymmetric radical polymerization and copolymerization of TrMAM derivatives show low chiral recognition ability compared to poly(TrMA). The propeller structure of bulky methacrylamides may not be suitable for high chiral recognition.

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Chapter 1

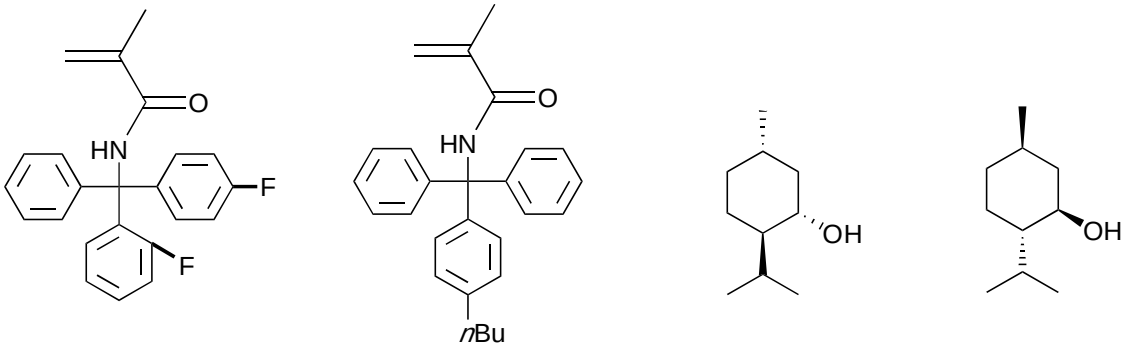
Helix-Sense-Selective Free Radical Polymerization of *N*-(Triphenylmethyl)methacrylamide Derivatives

1-1. Introduction

Optically active polymers, especially helical polymers, play an important role in the field of polymer science as they have a wide variety of potential applications based on a chiral structure, such as chiral recognition toward racemic compounds and liquid crystal formation.[1-8] Many stereoregular polymers are known to have a helical conformation in a solid state, which may be maintained even in solution if side chains are very bulky. The optical activity of these polymers is mainly based on a single-handed helical conformation of the main chain which is maintained by steric repulsion between the bulky side groups. Recently, it was found that Lewis acids such as rare earth metal triflates significantly increase the isotactic specificity during the radical polymerization of acrylamide and methacrylamide derivatives.[9-12] The radical polymerization of methacrylates with a bulky side group, such as triphenylmethyl methacrylate (TrMA)[13] and 1-phenyldibenzosuberyl methacrylate (PDBSMA),[14] proceeds in an isotactic-specific manner due to the steric repulsion among the bulky side groups. The helix-sense-selective polymerization of PDBSMA through free radical mechanism gives rise to an optically active, helical polymer having an excessive single-handed helicity from a achiral monomer.[14] Recently, this asymmetric radical polymerization was extended to the polymerization of bulky methacrylamides, *N*-

(triphenylmethyl)methacrylamide (TrMAM) and its derivative, *N*-[(4,4'-dibutyl)triphenylmethyl]methacrylamide (DBuTrMAM).[15] The polymers (poly(DBuTrMAM)s) prepared by the polymerization of DBuTrMAM in (+)- and (-)-menthol were optically active, and their optical rotation was opposite to that of menthol. This suggests that the optical rotation may not due to the incorporation of menthol residue in the polymer. The CD intensity of the poly(DBuTrMAM) was lower than that of the anionically polymerized one-handed helical poly(TrMA) with a specific rotation of $[\alpha]_D$ +350°, indicating that the one-handedness of the poly(DBuTrMAM)s may not be high.

In this chapter, the asymmetric radical polymerization of two monomers, 2F4FPhMAM and BuTrMAM, is discussed. Chiral 2F4FPhMAM was synthesized to investigate the possibilities of the enantiomer selective polymerization of the racemic monomer under chiral condition. To investigate the helix-sense-selective polymerization, BuTrMAM was copolymerized with a small amount of optically active 2F4FPhMAM. Radical polymerization of BuTrMAM was also carried out in the presence of (+)- and (-)-menthol (Scheme 1-1). The polymer (poly(2F4FPhMAM)) prepared from 2F4FPhMAM was not soluble in common organic solvents but poly(BuTrMAM) was



2F4FPhMAM **BuTrMAM** **(+)-Menthol** **(-)-Menthol**

Scheme 1-1.

soluble in chloroform and THF. The optically active poly(BuTrMAM) exhibited a low chiral recognition. The chiroptical properties of these polymers were also studied in details.

1-2. Experimental Section

Materials. All the reagents used for synthesis of monomers were bought from Aldrich, Kishida, and Kanto Kagaku, and were used without further purification. 2,2'-Azobisisobutyronitrile (AIBN; Kishida; purity >99%) was purified by recrystallization from methanol. The chiral additives, (+)-neomenthol (TCI; >96%), (*R*)-(-)-2-octanol (TCI; >98%), (*R*)-(-)-2-heptanol (Aldrich; >98%), (*S*)-3-hydroxytetrahydrofurane (TCI; >98%), and (*R*)-(+)-tetrahydrofuran-2-carboxylic acid (TCI; >98%), were used after being distilled from CaH_2 under a reduced pressure. Dry solvents, THF and toluene (Kanto Kagaku), and the chiral solvents (additives), (-)- and (+)-menthols (Kishida; >99%), were used for polymerization without further purification.

(±)-2F4FPhMAM Synthesis. The author has synthesized this monomer by three steps reaction. Firstly, synthesis of the corresponding alcohol, then the amination of the alcohol, and finally, synthesis of the monomer from the obtained amine.

Synthesis of Alcohol. Phenyl magnesium bromide in diethyl ether was prepared by a conventional method from bromobenzene (43.6 mL, 0.41 mol) and Mg turnings (10.2 g, 0.42 mol). A solution of 2,4'-difluorobenzophenone (65 g, 0.298 mol) in dry ether (200 mL) was added dropwise to the Grignard reagent, and the reaction was continued for 6 h at room temperature. Then, 400 mL of 3 N aq. HCl was slowly added to the reaction mixture. The aq. solution was neutralized by 4 N aq. NaOH and aq. NH_4Cl. The product was extracted with ether and dried over $MgSO_4$. After the

evaporation of the solvent, the obtained alcohol was recrystallized twice from hexane. Yield: 74.4 g (84%), mp 59-60 °C.

Synthesis of Amine from Alcohol. Phosphorus tribromide (5.12 mL, 0.028 mol) was added dropwise to the alcohol (25 g, 0.084 mol) dissolved in diethyl ether (150 mL) at 0 °C. The reaction was continued for 4 h and the solution in a flask turned to brownish color. Then, liquid ammonia was added to the reaction mixture at -78 °C.[16] The organic phase was separated, dried ($MgSO_4$), and evaporated under a reduced pressure. The obtained compound was recrystallized in hexane. Yield: 21.5 g (86.4%), mp 51-52 °C.

Synthesis of (±)-2F4FPhMAM from the Amine. Triethylamine (12.3 mL, 0.088 mol) was added to a chloroform solution of the amine (13 g, 0.044 mol) in a flask. The solution was cooled in an ice water bath and methacryloyl chloride (5 mL, 0.048 mol) was added dropwise to the flask. The reaction was continued for 2 h at 0 °C and then for 24 h at room temperature, and finally the mixture was refluxed for 1 h. The reaction mixture was washed with saturated aq. $NaHCO_3$ (200 mL) three times and two times with distilled water. The organic phase was separated and dried with $MgSO_4$. After the evaporation of the solvent, the product was recrystallized with hexane and chloroform. Yield: 13.5 g (76%), mp 95 °C. ^{1}H NMR ($CDCl_3$): δ 1.97(s, 3H, allyl CH_3), 5.36 (s, 1H, vinyl), 5.72 (s, 1H, vinyl), 6.95 (s, 1H, -NH), 7.01-7.29 (m, 13H, aromatic) ppm. Elemental analysis. Found: C, 76.01%; H, 5.27%; N, 3.74%. Calculated for $C_{23}H_{19}F_2NO$: C, 76.02%; H, 5.27%; N, 3.85%.

BuTrMAM Synthesis. (4-Butyltriphenyl)methanol was synthesized by the Grignard reaction of benzophenone with 4-butylphenylmagnesium bromide in ether. The obtained liquid alcohol was purified by column chromatography (20 g, 75%). From

this alcohol, (4-butyltriphenylmethyl)amine was synthesized with liquid ammonia.[16] The obtained liquid amine was purified by column chromatography (7.3 g, 49%). Finally BuTrMAM was synthesized by the reaction of (4-butyltriphenylmethyl)amine and methacryloyl chloride in the presence of triethylamine in chloroform in the same way as the synthesis of 2F4FPhMAM. Yield: 8.5 g, (95%). ^{1}H NMR ($CDCl_3$): δ 0.92 (m, 3H, *n*-butyl CH_3), 1.36 (m, 2H, *n*-butyl CH_2), 1.56 (m, 2H, *n*-butyl CH_2), 1.97(s, 3H, allyl CH_3), 2.58 (t, 2H, *n*-butyl CH_2), 5.34 (s, 1H, vinyl), 5.7 (s, 1H, vinyl), 6.96 (s, 1H, -NH), 7.09-7.31 (m, 14H, aromatic) ppm. Elemental analysis. Found: C, 84.53%; H, 7.45%; N, 3.66%. Calculated for $C_{27}H_{29}NO$: C, 84.55%; H, 7.62%; N, 3.65%.

Polymerization Procedure. The radical polymerization was carried out under dry nitrogen in a glass tube equipped with a three-way stopcock using AIBN as an initiator at 60 °C. The polymerization using AIBN at -20 ~ 40 °C was initiated by the irradiation of UV light (400-W high-pressure mercury lamp). Liquid materials were transferred to the glass tube using syringes and the solid monomer using a funnel having a nitrogen gas inlet tube. As BuTrMAM is very reactive, it was preserved as a hexane solution. The BuTrMAM solution was placed in the glass tube and then hexane was evaporated under a reduced pressure at low temperature (0 °C) and a solvent of polymerization was added in it. The solution was maintained at the prescribed temperature for 24 h. The polymerization was terminated by cooling the reaction mixture at -78 °C. The reaction mixture was dissolved in chloroform (5 mL), and the solution was poured into a large amount of methanol. The precipitated polymers were isolated using a centrifuge, washed several times with methanol to remove the unreacted monomer and the chiral additives, and dried at 60 °C for 10 h. The absence of menthol in the obtained polymers was confirmed by measuring the IR spectra in the solid state and the ^{1}H NMR of the polymer in D_2SO_4.

CD Measurements in a Solid State. The insoluble polymers were dispersed in liquid paraffin by grinding in a mortar, and imposed between quartz plates.[15] Polymer concentrations and the UV intensities of the samples were almost the same for all cases.

Solvolysis of BuTrMAM. The solvolysis reaction of BuTrMAM was carried out in a mixture of $CD_3OD/CDCl_3$ (1/1, v/v) at 35 °C in an NMR tube (Wilmad 507-PP).[17] BuTrMAM (0.15 g, 0.4 mmol) was dissolved in the solvent (1 mL), the tube was placed in a water bath at 35 °C, and reaction was monitored by ^{1}H NMR spectroscopy at 35 °C.

Measurements. The ^{1}H NMR spectra were recorded on a Varian Gemini 2000 spectrometer (400 MHz for ^{1}H). The number average molecular weight (M_n) and polydispersity (M_w/M_n) of the obtained polymers were determined by size-exclusion chromatography (SEC) calibrated using standard polystyrenes on a JASCO PU-980 pump equipped with a JASCO RI-930 detector using TSKgel GMH_{HR}-H and $G3000_{HR}$ columns connected in series (eluent THF; temperature 40 °C). The optical rotation was measured in either THF or chloroform at room temperature with a JASCO P-1030 polarimeter. The circular dichroism (CD) spectra were measured with a JASCO J-720L spectrometer.

Resolution of 2F4FPhMAM. The resolution of racemic 2F4FPhMAM was examined using several commercially available chiral HPLC columns, such as CHIRALCEL OD, CHIRALPAK AD, CHIRALCEL OJ, and many other home-made polysaccaride-based chiral columns. Enantiomers were partially resolved (enantiomeric excess 80%), but enantiomeric pure isomers were not obtained.

1-3. Results and Discussion

It is already reported that some methacrylates having bulky side groups afford the prevailing one-handed helical polymers by anionic polymerization using optically active initiators, and even by the radical process in the presence of optically active additives such as menthol and menthanethiol.[14] The formation of the prevailing one-handed helical polymers by the radical process has been ascribed to the fact that the chain transfer rates of the growing radicals with a right- or left-handed helicity to an optically active transfer agent can be different, and the helical growing polymer with a large transfer constant has a lower chance to propagate to the high molecular weight polymer compared with the opposite helical polymer with a lower transfer constant.

Radical Polymerization of 2F4FPhMAM

The results of radical polymerization of 2F4FPhMAM are summarized in Table 1-1. Although the radical polymerization of 2F4FPhMAM afforded the polymer

Table 1-1. Radical Polymerization of 2F4FPhMAM[a]

Run	Temp. (°C)	Initiator	Solvent	Yield[b] (%)
1	60	AIBN	THF	92
2	60	AIBN	Toluene	90
3	60	AIBN	Toluene/(+)-Menthol (5/2)	99
4	60	AIBN	Toluene/(-)-Menthol (5/2)	99
5	0	AIBN/UV	Toluene/(+)-Menthol (5/2)	75
6	0	AIBN/UV	Toluene/(-)-Menthol (5/2)	70

[a]Initiator = AIBN (0.02 M), time = 24 h, $[M]_0$ = 0.5 mol / L. [b]Methanol-insoluble part.

in good yields (Table 1-1), the anionic polymerization of this monomer using *n*-BuLi in toluene at -78 °C did not proceed and no polymer was obtained. Usually, acrylamides and methacrylamides with an amide proton cannot be polymerized by the typical anionic process with alkyl lithiums and Grignard reagents.[18]

The radically obtained polymers were insoluble in organic solvents as well as poly(TrMAM).[15] These polymers were dissolved in strong acids, such as concentrated sulfuric acid, accompanying with the cleavage of the bulky side derivative of trityl group to produce polymethacrylamide. The tacticity of the obtained polymers was directly determined from the ^{1}H NMR spectra of the polymethacrylamide derived from the original polymers in D_2SO_4.[15,19] The ^{1}H NMR spectra indicated that the obtained

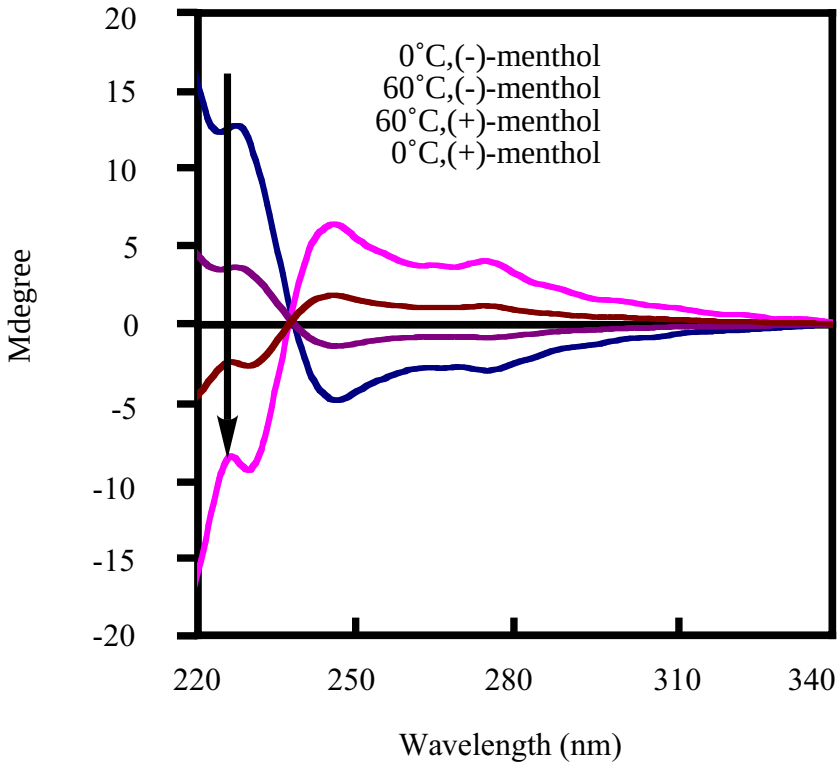


Figure 1-1. CD spectra of poly(2F4FPhMAM) in paraffin (run 3 to 6 in Table 1-1) at r.t.

polymers were nearly 100% isotactic similar to poly(TrMAM).[15] The polymer may be an equimolar mixture of left- and right-handed helices.

Optically active polymers were obtained in the polymerization of racemic 2F4FPhMAM in the presence of chiral additive (+)- and (-)-menthol but no enantiomer selection was observed in this process. As poly(2F4FPhMAM)s were insoluble in organic solvents, the CD spectra of these polymers could not be measured in solution, but were able to obtaine for the polymer particles dispersed in liquid paraffin (Nujol) (Figure 1-1).[20] The spectral pattern was similar to that of poly(TrMAM) obtained in menthol,[15] and the CD intensity was higher for the polymers prepared at 0 °C. These results support the formation of the prevailing one-handed helical poly(2F4FPhMAM) in menthol.

When BuTrMAM was copolymerized with a small amount of optically active 2F4FPhMAM, the obtained copolymer showed the chiroptical properties, which are expected only from the contribution of 2F4FPhMAM, suggesting that no helix-sense-selective polymerization proceeded.

2F4FPhMAM was not solvolyzed at all in methanol/chloroform (1/1, v/v) at 35 °C even after 10 days, whereas the half-life of TrMA under the same conditions is only 15 min.[21] This indicates that 2F4FPhMAM is much stronger towards hydrolysis and the obtained polymer must be more stable compared with poly(TrMA) when used as a chiral stationary phase in HPLC with polar alcoholic solvents.

Radical Polymerization of BuTrMAM

The results of the radical polymerization of BuTrMAM are shown in Table 1-2. Although poly(TrMAM) is not soluble in common organic solvents, poly(BuTrMAM) is soluble in chloroform and THF because of the *n*-butyl group in one

of the phenyl group of bulky trityl side chain. The tacticity of the obtained polymer was estimated by the same method as that for poly(2F4FPhMAM).[15,19]

Table 1-2. Radical Polymerization of BuTrMAM[a]

Run	Temp. (°C)	Solvent	Yield[b] (%)	M_n[c] × 10^{-4}	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	60	Toluene	65	2.6	5.2	-	-
2	60	THF	71	1.5	2.1	-	-
3	-20/UV	(+)-Menthol	30	6.1	6.2	-9.4	-28.2
4	-20/UV	(-)-Menthol	27	9.6	5.4	+9.5	+28.9
5	0/UV	(+)-Menthol	81	30.0	5.3	-9.7	-29.3
6	0/UV	(-)-Menthol	79	29.4	5.3	+9.8	+29.4
7	20/UV	(+)-Menthol	88	6.4	9.7	-7.0	-21.7
8	20/UV	(-)-Menthol	91	8.2	9.8	+6.8	+21.8
9	60	(+)-Menthol	90	5.2	3.6	-3.1	-8.8
10	60	(-)-Menthol	84	4.2	3.0	+2.9	+8.6

[a]Initiator = AIBN (0.02 M), time = 24 h, $[M]_0$ = 0.5 mol / L. [b]Methanol-insoluble part. [c]Determined by SEC in $CHCl_3$ (polystyrene standard) at 40 °C. [d]In $CHCl_3$ at r.t.

When poly(BuTrMAM)s (run 1 and 2 in Table 1-2) were dissolved in D_2SO_4, the ^1H NMR in Figure 1-2 shows only one methyl peak due to the isotactic (mm) sequence at 1.05 ppm and two sets of doublet due to the methylene group at 1.60 and 1.95 ppm, indicating that the poly(BuTrMAM)s are highly isotactic. The two ^1H NMR spectra are almost identical to each other, which indicates the absence of solvent effect on the polymer tacticity.

The polymerization in an optically active medium may helix-sense-selectively proceed because the propagation rates of right- and left-handed helical polymer radicals might be different due to the existence of a chiral substance. The chain transfer to the chiral medium may also be responsible for the helix-sense-selection as described before. Table 1-2 shows the results of the radical polymerization of BuTrMAM in (+)- and (-)-menthols. The poly(BuTrMAM)s prepared in (+)- and (-)-menthol were optically active, and their optical rotation was opposite to that of menthol. This suggests that the optical rotation may be not due to the incorporation of the

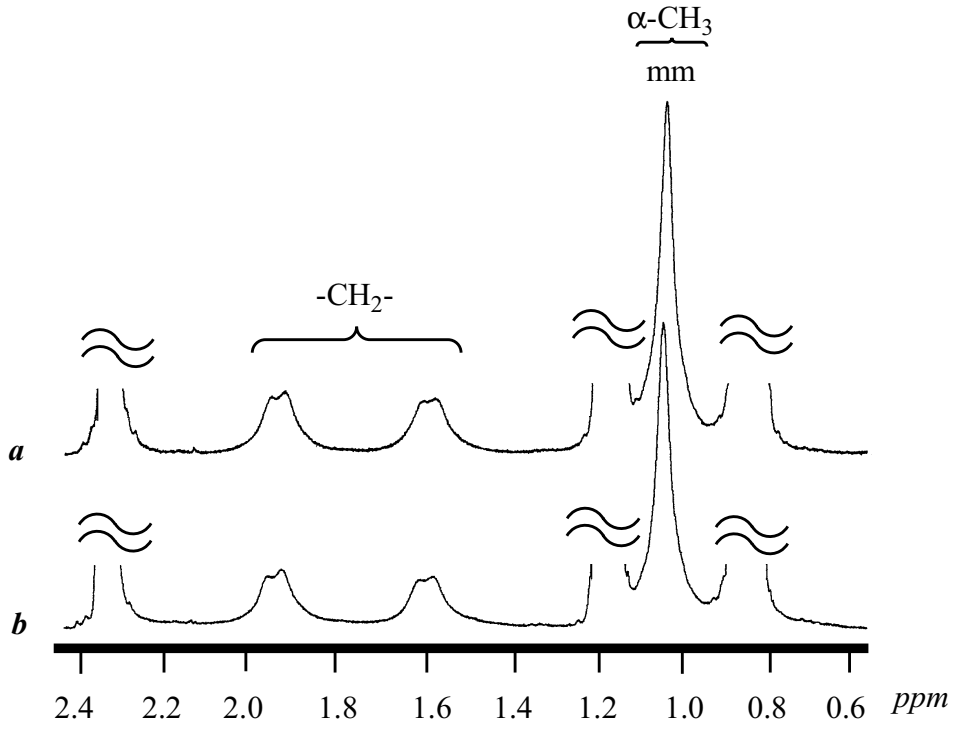


Figure 1-2. 400 MHz ^{1}H NMR spectra of PMAM (A, derived from PBuTrMAM (run 1 in Table 1-2); B, derived from PBuTrMAM (run 2 in Table 1-2)) (at 60 °C in D_2SO_4). The peaks (0.85, 1.2, 2.35 ppm) are due to the butyl protons on the triphenylmethyl residue of the by-product during sulphuric acid-induced decomposition.

menthol residue in the polymer. The polymerization at 0 °C produced the polymers having a larger specific rotation than that at 20 °C. The optical activity gradually decreased with an increase of the polymerization temperature.

The CD spectral pattern of poly(BuTrMAM)s is similar to that of the poly(DBuTrMAM) obtained in the same menthol (Figure 1-3).[15] The CD intensity of the polymer also decreased with an increase in the polymerization temperature. These results support the formation of the prevailing one-handed helical poly(BuTrMAM) in

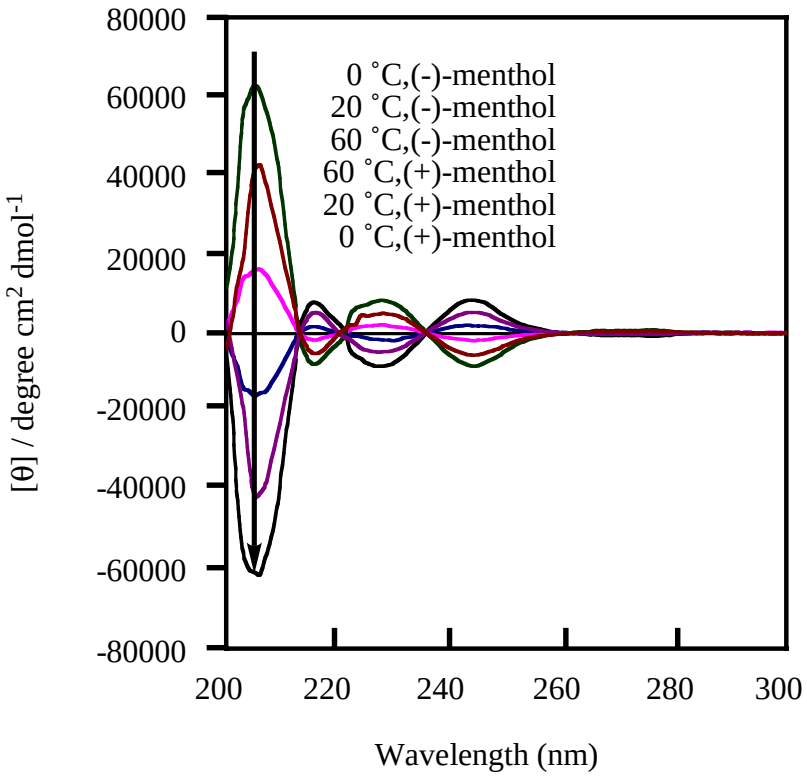


Figure 1-3. CD spectra of the poly(BuTrMAM)s in THF (Table 1-2) at r.t.

menthol. In Figure 1-3, split-type CD peaks were observed at 205, 215, 225 and 245 nm, and their pattern is different from that of the highly one-handed helical poly(TrMA) that

has the CD peaks at 208 and 232 nm.[22] Furthermore, the CD patterns of poly(TrMA)[22] and poly(1-phenyldibenzosuberyl methacrylate)[14] are similar to each other but those are different from that of the poly(*N*-triphenylmethylmethacrylamide).[15] Moreover, the crystal structure of the trityl group of TrMA[23] is different from that of TrMAM.[24] Thus, the author believes that the propeller structures of the trityl groups in the bulky polymethacrylates are likely different from that of the bulky polymethacrylamides. The CD intensity around 205 nm and optical rotation of the helical poly(BuTrMAM)s were lower than those of the one-handed helical poly(TrMA)s. This indicates that the one-handedness of the poly(BuTrMAM)s may not be high, and the propeller structure of the trityl group in poly(BuTrMAM) may not effectively contribute to the optical activity and CD intensity.

Table 1-3. Radical Polymerization of BuTrMAM in Different Concentration of (+)-Menthol in Hexane[a]

Run	Temp. (°C)	Menthol/Hexane (v/v)	Yield[b] (%)	M_n[c] $\times 10^{-4}$	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	0/UV	1/0	81	30.0	5.3	-9.7	-29.3
2	0/UV	2/1	72	3.7	3.5	-7.4	-22.3
3	0/UV	1/1	67	4.9	3.6	-7.3	-22.1
4	0/UV	1/2	65	6.2	4.7	-7.1	-21.3
5	0/UV	1/3	65	4.1	4.6	-6.9	-20.8

[a]Initiator = AIBN (0.02 M), time = 24 h, $[M]_0$ = 0.5 mol / L. [b]Methanol-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In $CHCl_3$ at r.t.

The molecular weights of the polymers obtained in menthols were higher than that prepared in THF (Table 1-2), probably because of the lower chain transfer constant

of menthols. The molecular weight of the polymer obtained at 0 °C was higher than that of 60 °C. The chain transfer may more frequently occur at 60 °C. The polymer yield became very low at -20 °C. Menthol was easily solidified at this temperature and the polymerization system become heterogeneous.

The polymerization of BuTrMAM was also carried out using different amounts of (+)-menthol in hexane (Table 1-3). The polymer exhibited the highest CD intensity when the solvent was pure (+)-menthol (Figure 1-4). The CD intensities of these polymers were proportional to their optical rotation (Figure 1-5), and the optical activity decreased with a decrease of (+)-menthol concentration in the polymerization system.

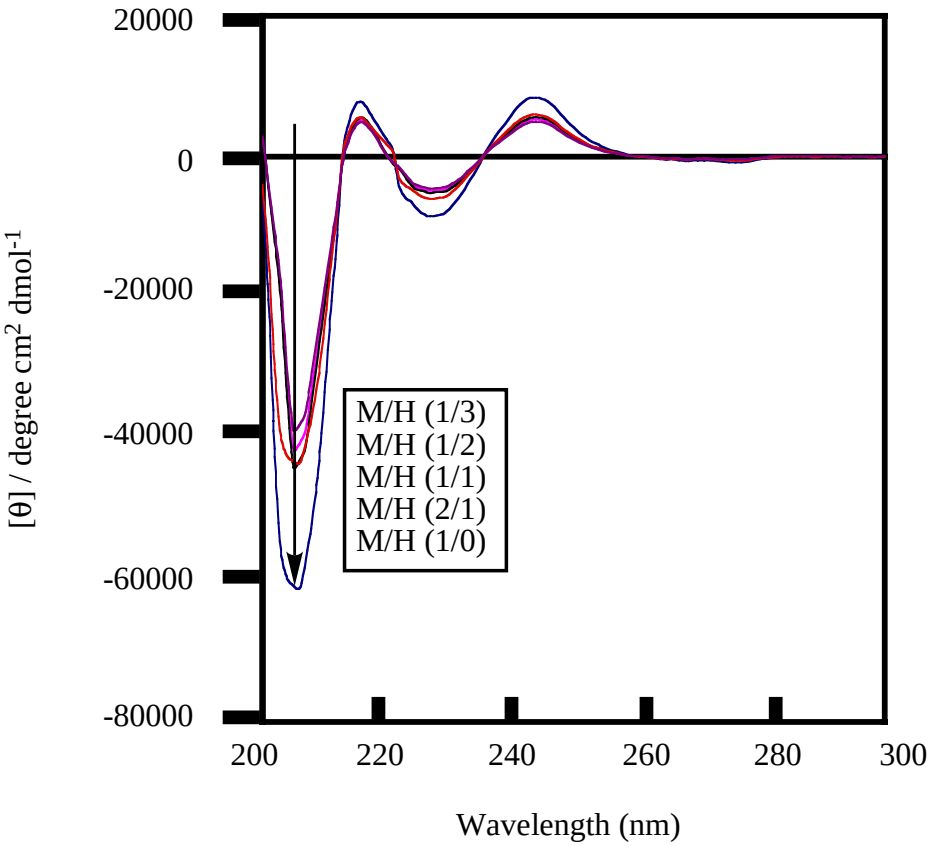


Figure 1-4. CD spectra of the poly(BuTrMAM)s (polymerized in presence of different amount of (+)-menthol in hexane) in THF (Table 1-3) at r.t.

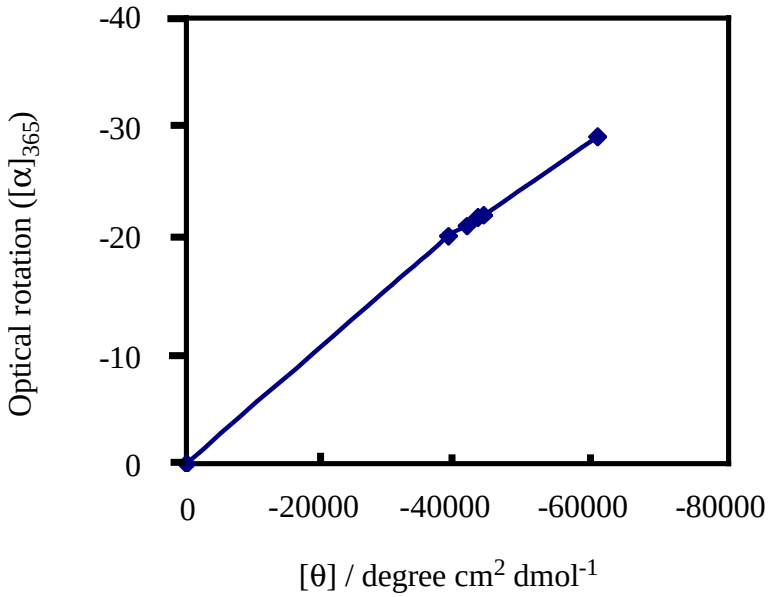


Figure 1-5. Plot of CD intensity at 205 nm (Figure 1-4) *vs* optical rotation of the poly(BuTrMAM)s (polymerized in presence of different amount of (+)-menthol in hexane) (Table 1-3).

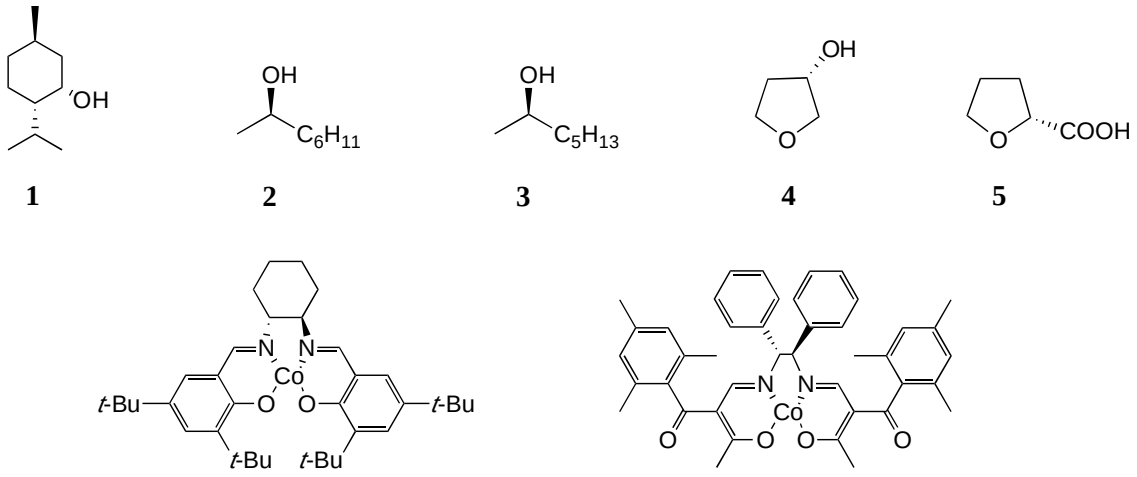
Radical Polymerization of BuTrMAM in the Presence of Optically Active Additives

Other chiral alcohols and acid, such as (+)-neomenthol (**1**), (*R*)-(-)-2-octanol (**2**), (*R*)-(-)-2-heptanol (**3**), (*S*)-3-hydroxytetrahydrofurane (**4**), and (*R*)-(+)-tetrahydrofuran-2-carboxylic acid (**5**) (Scheme 1-2), were also used as the optically active additives or solvents for the polymerization of BuTrMAM to enhance the optical activity or the one-handedness of the poly(BuTrMAM) (Table 1-4). However, compared with menthol, these compounds did not enhance the optical activity and probably one-handedness of the polymers. When pure (+)-neomenthol (**1**) was used as the solvent (run 6, Table 1-4), the optical activity of the obtained polymer was higher than that of the polymer obtained in (+)-neomenthol/hexane (1/1, v/v) (run 1, Table 1-4). But the effect is reverse when (*R*)-(-)-2-octanol (**2**) was used as a solvent (run 2 and 7, Table 1-4). In this case the optical activity decreased when the concentration of (*R*)-(-)-2-octanol

Table 1-4. Radical Polymerization of BuTrMAM in a Mixture of Chiral Additive and Hexane[a]

Run	Temp. (°C)	Chiral additive/Hexane (v/v)	Yield[b] (%)	M_n[c] × 10^{-4}	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	0/UV	**1**(1/1)	79	6.3	5.84	-2.8	-9.1
2	0/UV	**2**(1/1)	91	9.1	4.58	+1.8	+5.4
3	0/UV	**3**(1/1)	89	6.7	4.50	+1.1	+3.3
4	0/UV	**4**(1/1)	90	11.8	4.68	-	-
5	0/UV	**5**(1/1)	69	1.3	3.04	+0.8	+2.1
6	0/UV	**1**(1/0)	76	24.7	4.45	-5.8	-16.8
7	0/UV	**2**(1/0)	89	17.9	4.33	+1.0	+3.1

[a]Initiator = AIBN (0.02 M), time = 24 h, $[M]_0$ = 0.5 mol / L. [b]Methanol-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In $CHCl_3$ at r.t.



Scheme 1-2.

increased in the polymerization solvent. The CD pattern of these polymers resembles with the polymers obtained in the presence of (+)- and (-)-menthol (Figure 1-6), which

supports the formation of one-handed helical poly(BuTrMAM). The CD intensities of these polymers are low, which is probably due to the lower one-handedness of the polymers.

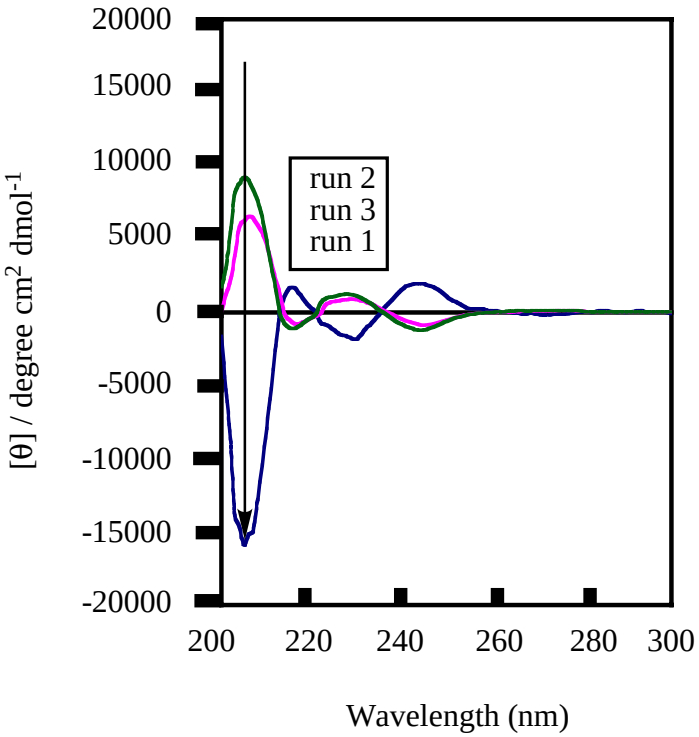


Figure 1-6. CD spectra of the poly(BuTrMAM)s (polymerized in presence of different chiral additives) in THF (Table 1-4) at r.t.

Chiral cobalt complexes have been successfully used for the asymmetric radical polymerization of TrMA derivatives. The radical polymerization of PDBSMA in the presence of *N*,*N*'-bis(3,5-di-*tert*-butylsalicylidene)-(1*R*,2*R*)-1,2-cyclohexane-diaminatocobalt(II) (**6**) and *N*,*N*'-bis{2-(2,4,6-tri-methylbenzoyl)-3-oxobutylidene}-(1*S*,2*S*)-1,2-diphenylethylenediaminatocobalt(II) (**7**) effectively induces a single-handed helicity.[25] These Co complexes were also used as chiral additives for the polymerization

of BuTrMAM (Table 1-5). However, the complexes functioned as the polymerization inhibitors. The optically inactive polymer was obtained in low yields only using complex **6**.

Table 1-5. Radical Polymerization of BuTrMAM in the Presence of Optically Active Cobalt Complex[a]

Run	Temp. (°C)	Solvent (v/v)[e]	Cobalt Complex (conc./M)	Yield[b] (%)	M_n[c] × 10^{-4}	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	60	50/50(py/ch)	**6**(0.010)	28	8.1	2.17	-	-
2	60	50/50(py/ch)	**6**(0.020)	26	3.0	1.29	-	-
3	60	50/50(py/ch)	**6**(0.030)	21	10.3	2.29	-	-
4	60	15/85(py/ch)	**7**(0.020)	-[f]	-	-	-	-
5	60	50/50(py/tol)	**7**(0.014)	-[f]	-	-	-	-
6	60	50/50(py/ch)	**7**(0.007)	-[f]	-	-	-	-

[a]Initiator = AIBN (0.03 M), time = 24 h, $[M]_0$ = 0.5 mol / L. [b]Methanol-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In $CHCl_3$ at r.t. [e]py = Pyridine, ch = Chloroform, tol = Toluene. [f]Not polymerized.

Properties of Poly(BuTrMAM)s

BuTrMAM gave highly isotactic polymers by the radical polymerization. The isotactic specificity is ascribed to the helical structure of the growing chain.[26] Poly(BuTrMAM)s have a stable helical structure. No change in CD was obtained after heating the polymer solution at 60 °C for 10h. The CD intensity and pattern were also not changed when measured in different temperatures. In case of the polymer with a stable helical structure, the polymer may be separated into (+)- and (-)-fractions with

opposite helicity. This was examined by the HPLC using several chiral stationary phases, but no separation has so far attained.

The optically active poly(BuTrMAM)s obtained with (+)- and (-)-menthol at 0 °C were coated on silica gel to be used as chiral packing materials in an HPLC column (25 cm x 0.2 cm (i.d.)). The chiral recognition ability of the optically active poly(BuTrMAM) was very low. The low chiral recognition ability of poly(BuTrMAM) might be due to the lack of the propeller structure and also the low one-handedness of the polymers. As mentioned before, the propeller structure of the poly(BuTrMAM) may not clearly exist in the polymer. Since the propeller structure is chiral, the absence of this structure may result in a decrease in the chiral recognition ability of the helical polymer.

The one-handed helical poly(TrMA) exhibits a high chiral recognition ability for many racemates,[27] but the polymer was easily solvolysed by alcohols and acids used as the mobile phase in HPLC.[21] On the other hand, BuTrMAM was very stable against the solvolysis under the same conditions, and therefore, the polymer would be very valuable as a chiral stationary phase for HPLC column, if it could show a high chiral recognition.

1-4. Summery

The helix-sense-selective radical polymerization of *N*-(triphenylmethayl)methacrylamide derivatives, 2F4FPhMAM and BuTrMAM, were carried out. All the polymers were nearly 100% isotactic. The free radical polymerization of 2F4FPhMAM and BuTrMAM using chiral additives gave the polymers with the optical activity and CD adsorption based on an excess right- or left-handed helical conformation. The CD intensity and optical rotation of poly(BuTrMAM) were lower than those of one-handed helical poly(TrMA). This indicates that the one-

handedness of the poly(BuTrMAM)s may not be high. As the BuTrMAM is much stronger toward hydrolysis, the obtained polymer must be more stable when used as a chiral stationary phase for HPLC with polar alcoholic solvents.

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Chapter 2

Helicity Induction in *N*-[(4-Butyl)triphenylmethyl]methacrylamide Sequence via Radical Copolymerization with Chiral Monomers

2-1. Introduction

The synthesis of helical polymers is an important field in macromolecular science as they are used in a wide variety of potential applications based on the chiral structure.[1-6] Helical structures are often found in naturally occurring macromolecules, which show characteristic features based on the structure. Although a helical conformation is also found for stereoregular synthetic polymers in a solid state, it often disappears in solution because of fast conformational dynamics. However, there are several classes of polymers that can maintain the helical conformation even in solution.[7]

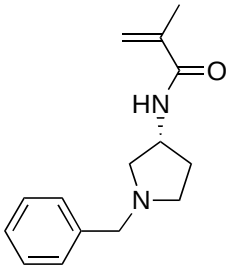
Triphenylmethyl methacrylate (TrMA) produces a highly isotactic, optically active polymer through the asymmetric anionic polymerization using the complexes of organolithium compounds and chiral ligands.[7-9] The optical activity of poly(TrMA) is mainly based on a one-handed helical conformation of the main chain, which is maintained by steric repulsion between the bulky side groups. The direction of the helix is controlled by the chirality of the ligands of the initiator complexes. Optically active phenyl-2-pyridyl-o-tolylmethyl methacrylate (PPyoTMA),[10-11] a TrMA analogue with a chiral ester group, also produces an optically active helical polymer by anionic polymerization.[12] However, during this polymerization, the helix sense is controlled by

the chirality of the ester group rather than by that of the initiator. The radical copolymerization of PPyoTMA with TrMA also produced optically active, isotactic polymers, in which the PPyoTMA residues effectively induced an excess of a one-handed helix consisting of TrMA monomeric sequences.[13]

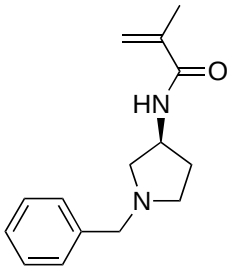
Lewis acids, such as rare earth metal triflates, significantly increase the isotactic specificity during the radical polymerization of acrylamide and methacrylamide derivatives.[14-18] However, these polymerization systems have been unsuccessful in producing optically active polymers. On the other hand, the radical polymerization of bulky methacrylamides, *N*-(triphenylmethyl)methacrylamide (TrMAM) and its derivatives, *N*-[(4,4'-dibutyl)triphenylmethyl]methacrylamide (DBuTrMAM),[19] and *N*-[(4-butyl)triphenylmethyl]methacrylamide (BuTrMAM),[20] in the presence of (+)- and (-)-menthol afforded highly isotactic and optically active polymers. The optical rotation and CD intensities of these polymers were lower than that of the anionically obtained one-handed helical poly(TrMA), indicating that the one-handedness of the poly(methacrylamide)s may not be very high. Copolymers prepared from achiral and chiral vinyl monomers sometimes show disproportionately high optical activities.[21] Thus, higher one-handed helical sequences of the bulky methacrylamides may be formed through the copolymerization with a chiral methacrylamide.

In this Chapter, the author describes the radical copolymerization of BuTrMAM with six optically active methacrylamides, i.e., *N*-((*R*)-(+)-1-benzylpyrrolidin-3-yl)methacrylamide ((+)-BPMAM), *N*-((*S*)-(-)-1-benzylpyrrolidin-3-yl)methacrylamide ((-)-BPMAM), *N*-((*S*)-(+)-1-cyclohexylethyl)methacrylamide ((+)-CHEMAM), *N*-((*R*)-(-)-1-cyclohexylethyl)methacrylamide ((-)-CHEMAM), *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide ((+)-NEMAM), *N*-[(*S*)-(-)-1-(1-naphthyl)ethyl]-methacrylamide ((-)-NEMAM), *N*-((1*R*,2*S*)-(+)-2-hydroxy-1,2-diphenylethyl)-methacrylamide (HDMAM), and (*S*)-(-)-diphenyl(1-methylpyrrolidine-2yl)methyl methacrylate ((-)-DMPMA) (Scheme 2-1). The optical activities of the obtained

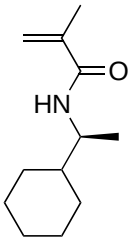
copolymers were significantly different from those expected from the chiral monomer contents, indicating that the prevailing one-handed helical sequences of BuTrMAM monomeric units may be induced by the chiral monomer. The CD data of the copolymers also supported this hypothesis.



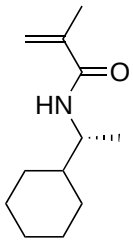
(+)-BPMAM



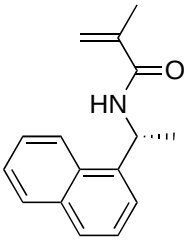
(-)-BPMAM



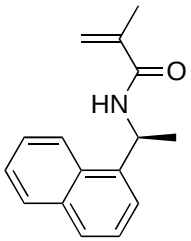
(+)-CHEMAM



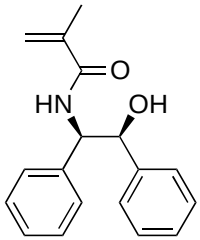
(-)-CHEMAM



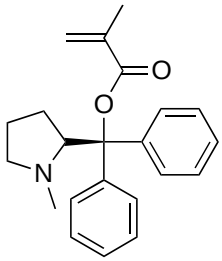
(+)-NEMAM



(-)-NEMAM



(+)-HDMAM



(-)-DMPMA

Scheme 2-1

2-2. Experimental Section

Materials. Methacryloyl chloride was distilled before use. Triethylamine was dried over KOH and distilled. Anhydrous solvents, including dichloromethane, chloroform, tetrahydrofuran (THF), methanol, and toluene were purchased from Kanto Chemical, and used as received. 2,2'-Azobisisobutylonitrile (AIBN) was recrystallized from methanol. Chiral amines, (*R*)-(-)-1-cyclohexylethylamine (Aldrich; >98%), (*S*)-

(+)-1-cyclohexylethylamine (Aldrich; >98%), (*R*)-(+)-1-(1-naphthyl)ethylamine (Aldrich; >99%), (*S*)-(-)-1-(1-naphthyl)ethylamine (Aldrich; >99%), (*R*)-(-)-1-benzyl-3-aminopyrrolidine (Aldrich; >95%), (*S*)-(+)-1-benzyl-3-aminopyrrolidine (Aldrich; >97%), were used as commercially obtained.

Monomer Synthesis. BuTrMAM was synthesized by the previously reported procedure.[20] Optically active monomers were prepared by the reaction of the corresponding amines and methacryloyl chloride in the presence of triethylamine in chloroform according to the previously reported procedure.[22] (+)-BPMAM and (-)-BPMAM are new monomers to the best of our knowledge.

***N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide ((+)-NEMAM).** Yield 70%. Mp: 112.1-112.8 °C. (Mp: 112 °C[23]) $[\alpha]_D^{25}$ +40.9°. $[\alpha]_{365}^{25}$ +221.3°.

***N*-[(*S*)-(-)-1-(1-naphthyl)ethyl]methacrylamide ((-)-NEMAM).** Yield 73%. Mp: 112.4-112.9 °C. $[\alpha]_D^{25}$ -41.1°. $[\alpha]_{365}^{25}$ -222.4°.

***N*-((*S*)-(+)-1-cyclohexylethyl)methacrylamide ((+)-CHEMAM).** Yield 56%. Mp: 93.4-93.8 °C. $[\alpha]_D^{25}$ +16.0°. $[\alpha]_{365}^{25}$ +40.1°.

***N*-((*R*)-(-)-1-cyclohexylethyl)methacrylamide ((-)-CHEMAM).** Yield 61%. Mp: 93.1-93.6 °C. (Mp: 92 °C[23]) $[\alpha]_D^{25}$ -16.1°. $[\alpha]_{365}^{25}$ -40.3°.

***N*-((*S*)-(-)-1-benzylpyrrolidin-3-yl)methacrylamide ((-)-BPMAM).** Yield: 80%. Mp: 77.7-78.6 °C. $[\alpha]_D^{25}$ -14.1°. $[\alpha]_{365}^{25}$ -48.1°. ^{1}H NMR ($CDCl_3$): δ 1.65 (m, 1H, pyrrolidine), 1.94(s, 3H, allyl CH_3), 2.31 (m, 2H, pyrrolidine), 2.60 (m, 2H, pyrrolidine), 2.87 (m, 1H, pyrrolidine), 3.61 (s, 2H, benzylene CH_2), 4.50 (m, 1H, pyrrolidine -CH

(CH-NH)), 5.3 (s, 1H, vinyl), 5.65 (s, 1H, vinyl), 6.15 (s, 1H, -NH), 7.25-7.35 (m, 5H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.82, 140.25, 138.84, 128.93, 128.48, 127.26, 119.46, 60.99, 60.33, 52.94, 49.09, 32.88, 19.02; Elemental analysis; Found: C, 73.75%; H, 8.17%; N, 11.28%. Calcd for $C_{15}H_{20}N_2O$: C, 73.74%; H, 8.25%; N, 11.47%.

***N*-((*R*)-(+)-1-benzylpyrrolidin-3-yl)methacrylamide ((+)-BPMAM).** Yield: 72%. Mp: 77.5-78.5 °C. $[\alpha]_D^{25}$ +14.2°. $[\alpha]_{365}^{25}$ +48.3°. ^{1}H NMR ($CDCl_3$): δ 1.65 (m, 1H, pyrrolidine), 1.94(s, 3H, allyl CH_3), 2.31 (m, 2H, pyrrolidine), 2.60 (m, 2H, pyrrolidine), 2.87 (m, 1H, pyrrolidine), 3.61 (s, 2H, benzylene CH_2), 4.50 (m, 1H, pyrrolidine -CH (CH-NH)), 5.3 (s, 1H, vinyl), 5.65 (s, 1H, vinyl), 6.15 (s, 1H, -NH), 7.25-7.35 (m, 5H, aromatic) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.82, 140.25, 138.84, 128.93, 128.48, 127.26, 119.46, 60.99, 60.33, 52.94, 49.09, 32.88, 19.02; Elemental analysis; Found: C, 73.74%; H, 8.23%; N, 11.38%. Calcd for $C_{15}H_{20}N_2O$: C, 73.74%; H, 8.25%; N, 11.47%.

Polymerization Procedure. The radical polymerization was carried out under dry nitrogen in a glass tube equipped with a three-way stopcock using AIBN as an initiator at 60 °C. The polymerization using AIBN at 0 °C was initiated by the irradiation of UV light (400-W high-pressure mercury lamp). Liquid materials were transferred to the glass tube using syringes and the solid monomer using a funnel having a nitrogen gas inlet tube. As neat BuTrMAM is very reactive, it was preserved as a hexane solution. The BuTrMAM (0.1 g, 0.26 mmol) in hexane solution was placed in the glass tube and then hexane was evaporated under a reduced pressure at low temperature (0 °C) and a polymerization solvent (0.52 mL) was added in it. The chiral monomers were added in the polymerization system according to the molar ratio with BuTrMAM. The solution was maintained at prescribed temperature for 24 h. The polymerization was terminated by cooling the reaction mixture at -78 °C. The reaction mixture was dissolved in chloroform (5 mL), and was poured into a large amount of

methanol. The precipitated polymers were isolated using a centrifuge, washed several times with methanol to remove the unreacted monomers, and dried at 60 °C for 10 h.

Measurements. The ^{1}H NMR spectra were recorded on a Varian Gemini 2000 spectrometer (400 MHz for ^{1}H). The number average molecular weight (M_n) and polydispersity (M_w/M_n) of the obtained polymers were determined by size-exclusion chromatography (SEC) calibrated using standard polystyrenes on a JASCO PU-980 pump equipped with a JASCO RI-930 detector using TSKgel GMH_{HR}-H and $G3000_{HR}$ columns connected in series (eluent THF; temperature 40 °C). The optical rotation was measured in either THF or chloroform at 25 °C temperature with a JASCO P-1030 polarimeter. The circular dichroism (CD) spectra were measured with a JASCO J-720L spectrometer.

2-3. Results and Discussion

Radical Copolymerization of BuTrMAM with (+)- or (-)-BPMAM

As the isotactic BuTrMAM chain produced by radical polymerization can form a helical comformation,[20] the copolymerization of BuTrMAM and (-)-BPMAM was carried out to obtain a copolymer with a high one-handed helicity induced by the optically active monomer. These results are shown in Table 2-1. All the copolymers were soluble in THF and chloroform. The copolymer compositions were very close to the corresponding feed monomer composition, suggesting that the copolymerization mostly proceeded in a random manner. When a small amount of (-)-BPMAM (runs 1 to 5, Table 2-1) was copolymerized with BuTrMAM, dextrorotatory (positive) polymers were obtained. The sign of the rotation is opposite that of the homopolymer and copolymers with the higher (-)-BPMAM contents. This suggests that the rotation of the polymer may be based on helical conformation of the main chain. The CD pattern of the

obtained copolymers having a small amount of chiral BPMAM (Figure 2-1) is similar to that of the helical BuTrMAM homopolymers obtained in the presence of (+)- and (-)-menthol.[21] This result also supports the one-handed helical conformation of the

Table 2-1. Radical Copolymerization of BuTrMAM with (-)-BPMAM in Toluene[a]

Run	BuTrMAM/ (-)-BPMAM (mol/mol)	Temp. (°C)	Yield[b]	(-)-BPMAM in copolymer[f] (mol%)	M_n[d] $\times 10^{-4}$	M_w/M_n[d]	$[\alpha]_D$[e] (deg)	$[\alpha]_{365}$[e] (deg)
1	99/1	60	85	1.0	4.31	29.12	+2.3	+6.5
2	98/2	60	83	2.0	3.86	16.15	+2.9	+7.8
3	97/3	60	81	2.6	3.43	12.95	+4.2	+12.3
4	96/4	60	80	3.4	3.15	9.30	+0.6	+1.8
5	95/5	60	82	4.5	2.71	9.08	+0.4	+1.1
6	90/10	60	73	10.1	1.98	5.06	-1.5	-4.5
7	80/20	60	67	21.1	1.66	3.29	-3.9	-11.8
8	70/30	60	63	31.2	1.43	2.54	-6.8	-19.7
9	60/40	60	58[c]	40.3	1.37	1.95	-11.2	-33.7
10	50/50	60	53[c]	51.0	1.08	1.64	-16.9	-51.6
11	98/2	0/UV	70	1.9	4.13	11.51	+2.8	+7.6
12	97/3	0/UV	67	2.5	3.95	10.23	+4.1	+12.1
13	100/0[g]	60	66	-	0.42	1.98	-19.7	-61.9

[a]Initiator = AIBN (0.02 M), time = 24 h, $[BuTrMAM]_0 + [BPMAM]_0 = 0.5$ mol / L. [b]MeOH-insoluble part. [c]Hexane insoluble part. [d]Determined by SEC in THF (PMMA standard) at 40 °C. [e]In THF at 25 °C, conc. = 5 mg / mL, cell length = 2 cm. [f]Calculated by ^{1}H NMR. [g]Homopolymerization of (-)-BPMAM.

BuTrMAM sequence in the copolymer. The CD intensities of the copolymers are much lower than that of the BuTrMAM homopolymers obtained in the presence of (+)- and (-)-menthol. This indicates that the helicity induction by the BPMAMs is not very high. The optical activities of the copolymers obtained at 0 and 60 °C were similar, indicating that the polymerization temperature cannot significantly influence the helicity induction.

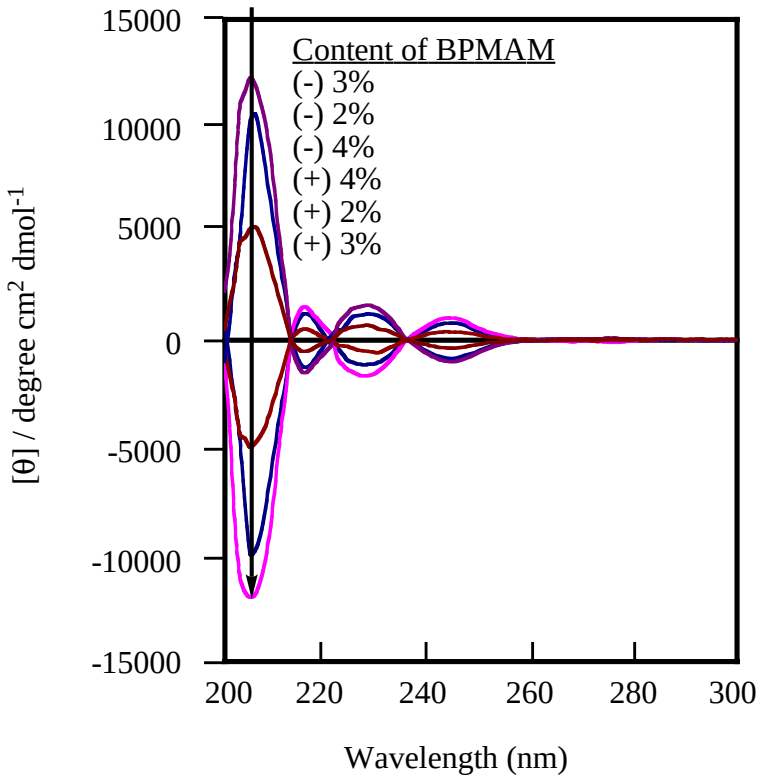


Figure 2-1. CD spectra of the copolymers of BuTrMAM with (+)- and (-)-BPMAM (2% to 4%) (THF, r.t.).

The optical activity and CD intensity of the copolymers were the highest for the copolymerization system using 3% (-)-BPMAM (Figure 2-1). When the amount of the feed (-)-BPMAM in the copolymerization system is very low (1~3%), the obtained polymer may contain high molecular weight BuTrMAM homopolymer and also

copolymer of low molecular weight, which will result in broad molecular weight distribution. Once (-)-BPMAM is incorporated into a BuTrMAM sequence, the polymerization may be retarded giving a low molecular weight copolymer, because homopolymerization of (-)-BPMAM gives a very low molecular weight polymer. The molecular weights of the copolymers were in between the range of the two homopolymers. When (-)-BPMAM content exceeded 10%, the optical rotation of the copolymers became levorotatory or negative. The optical activity of these copolymers may be mainly due to the chiral side group of the (-)-BPMAM units because the optical rotation of the (-)-BPMAM homopolymer (run 13, Table 2-1) is negative. Before the

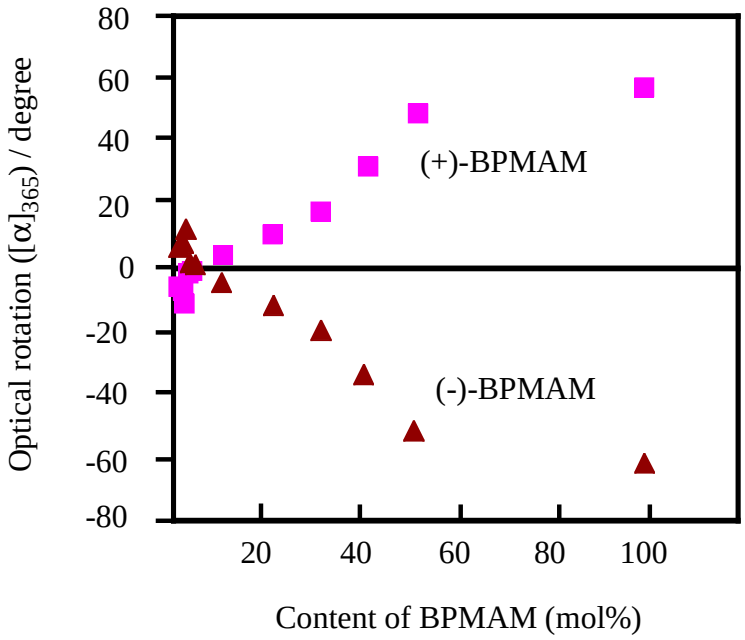


Figure 2-2. Plot of optical rotation *vs* the content of BPMAM in the copolymers.

formation of the helical structure of the BuTrMAM sequences, the BuTrMAM units neighboring a (-)-BPMAM residue seem to contribute exhibiting the negative rotation,

because the 1:1 copolymer (run 10, Table 2-1) has a specific rotation rather similar to that of the (-)-BPMAM homopolymer (run 13, Table 2-1). However, as the BuTrMAM sequence gets longer, it starts to form a helical structure with a positive rotation, and its contribution will become a maximum at about 3% of the (-)-BPMAM content, because the induced helical structure may not be maintained for a very long sequence.

When (+)-BPMAM was used in the copolymerization system, the copolymers showed an optical activity almost exactly opposite to that of the copolymers with (-)-BPMAM (Figure 2-2). The optical activity of the copolymers was not significantly changed by the polymerization solvents, such as THF and toluene.

Radical Copolymerization of BuTrMAM with (+)- or (-)-CHEMAM

The results of the radical copolymerizations of BuTrMAM with (+)- or (-)-CHEMAM in toluene at 60 °C are summarized in Table 2-2. The copolymer compositions were similar, particularly for low CHEMAM contents, to the feed monomer contents. During the radical copolymerization of BuTrMAM with (-)-CHEMAM, the optical rotation of the copolymers increased up to ca. 4% (-)-CHEMAM content in the copolymer, and the further addition of this monomer resulted in a gradual increase in the optical rotation in the negative direction (Figure 2-3) and a gradual decrease in the molecular weight (Table 2-2). When the content of the chiral monomer was low, the copolymer exhibited an optical rotation opposite to that of the feed (-)-CHEMAM, suggesting that BuTrMAM sequence may form a prevailing one-handed helical chain. The CD patterns also support this suggestion (Figure 2-4). When the chiral monomer content was low, the CD spectra of the copolymers resemble that of the optically active BuTrMAM (3% to 5%) homopolymer obtained in menthol, although the CD intensities of the copolymers are lower. These results are similar to those for the previous copolymers consisting of (-)-BPMAM.

Table 2-2. Radical Copolymerization of BuTrMAM with (+)- and (-)-CHEMAM in Toluene at 60 °C[a]

Run	BuTrMAM/ CHEMAM (mol/mol)	Yield[b]	CHEMAM in copolymer[f] (mol%)	M_n[c] $\times 10^{-4}$	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	97/3(+)	100	3.0	9.6	5.1	-3.8	-11.5
2	96/4(+)	98	4.0	8.5	6.3	-4.1	-12.5
3	95/5(+)	98	5.0	8.1	9.0	-2.8	-8.3
4	94/6(+)	94	6.0	4.6	5.9	-2.6	-7.7
5	97/3(-)	97	3.0	9.4	5.3	+4.0	+12.1
6	96/4(-)	97	4.0	8.6	6.5	+4.9	+14.8
7	95/5(-)	98	5.0	8.1	7.9	+2.9	+9.0
8	94/6(-)	94	6.0	4.9	12.7	+2.5	+7.8
9	90/10(-)	95	7.8	5.0	9.1	+1.9	+5.7
10	80/20(-)	99	20.0	4.5	3.1	+0.6	+1.7
11	70/30(-)	98	28.7	3.7	2.7	-0.7	-2.2
12	60/40(-)	97	38.6	2.2	1.7	-5.1	-15.3
13	50/50(-)	79	43.2	1.7	1.6	-8.5	-25.5
14[e]	100/0(-)[g]	61	-	1.6	1.3	-18.8	-57.1

[a]Initiator = AIBN (0.02 M), time = 24 h, $[BuTrMAM]_0 + [CHEMAM]_0 = 0.5$ mol / L. [b]MeOH-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In THF at 25 °C, conc. = 5 mg / mL, cell length = 2 cm. [e][M] = 1.0 M. [f]Calculated by ^{1}H NMR. [g]Homopolymerization of (-)-CHEMAM.

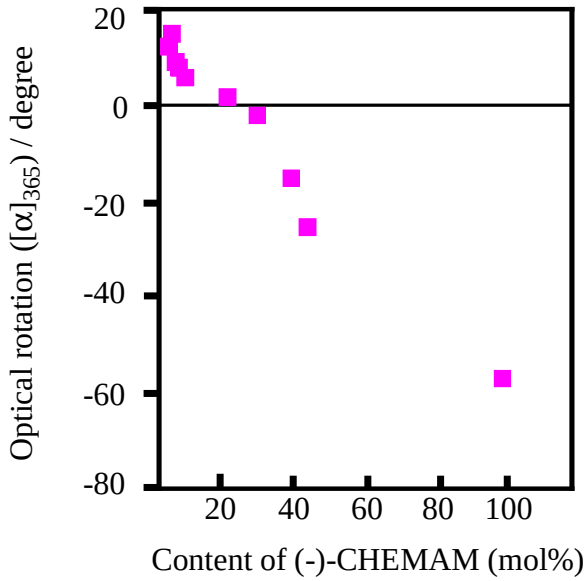


Figure 2-3. Plot of optical rotation *vs* the content of (-)-CHEMAM in the copolymers (Table 2-2).

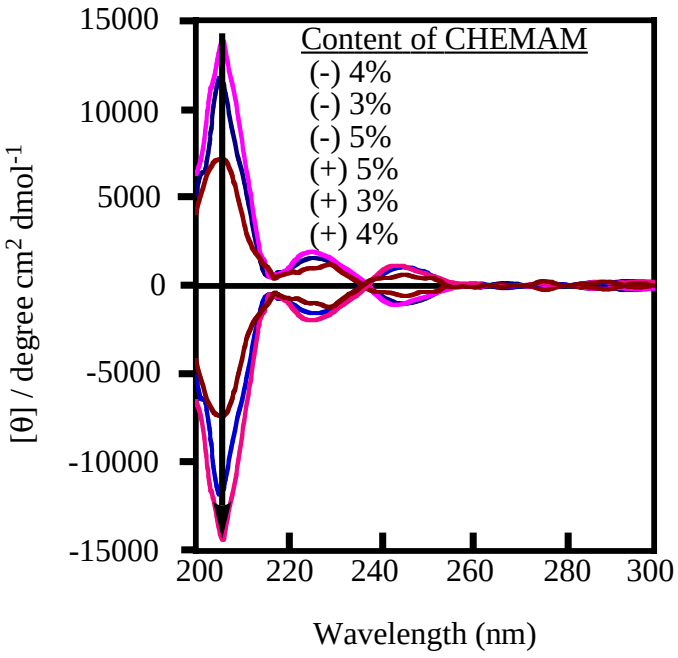


Figure 2-4. CD spectra of the copolymers of BuTrMAM with (+)- and (-)-CHEMAM (THF, r.t.).

For the copolymerization of BuTrMAM with (+)- or (-)-CHEMAM, the optical activity of the copolymers was not noticeably influenced by the polymerization temperature as well as in the previous polymerization system.

Radical Copolymerization of BuTrMAM with (+)- or (-)-NEMAM

The results of radical copolymerizations of BuTrMAM with (+)-NEMAM in toluene at 60 °C are shown in Table 2-3. The optical rotation of the copolymers

Table 2-3. Radical Copolymerization of BuTrMAM with (+)-NEMAM in Toluene[a]

Run	BuTrMAM/ (+)-NEMAM (mol/mol)	Temp. (°C)	Yield[b]	(+)-NEMAM in copolymer[e] (mol%)	M_n[c] $\times 10^{-4}$	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	99/1	60	84	1.0	5.46	4.16	+5.1	+18.7
2	98/2	60	81	2.0	3.31	6.33	+6.6	+26.8
3	97/3	60	80	3.0	2.94	6.70	+8.8	+36.0
4	96/4	60	79	4.0	2.33	6.70	+13.4	+50.3
5	90/10	60	72	10.5	4.23	2.10	+15.5	+59.6
6	80/20	60	85	21.0	1.32	4.84	+29.2	+113.8
7	70/30	60	86	31.2	1.29	3.50	+26.3	+101.2
8	60/40	60	80	41.3	1.12	2.90	+12.5	+47.5
9	50/50	60	76	52.0	1.02	2.52	+0.4	+1.4
10	100/0[f]	60	74	-	1.01	2.35	-24.0	-43.2

[a]Initiator = AIBN (0.02 M), time = 24 h, $[BuTrMAM]_0 + [NEMAM]_0$ = 0.5 mol / L. [b]MeOH-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In THF at 25 °C, conc. = 5 mg / mL, cell length = 2 cm. [e]Calculated by ^{1}H NMR. [f]Homopolymerization of (+)-NEMAM.

gradually increased with an increase in the chiral monomer content up to 20%, and a further increase of the chiral monomer resulted in an increase in the optical rotation in the opposite direction and finally arrived at the optical rotation of the (+)-NEMAM homopolymer, which was opposite that of the monomer. The CD spectra due to the helical structure of the BuTrMAM sequences were clearly observed when the (+)-NEMAM content in the copolymers was low (Figure 2-5). In the copolymers, the BuTrMAM units neighboring (+)-NEMAM seem to contribute to the positive rotation as well as the helical structure of the BuTrMAM sequences induced by (+)-NEMAM. Due to these synergy effects and probably higher helical induction, the copolymer appears to exhibit higher optical activities.

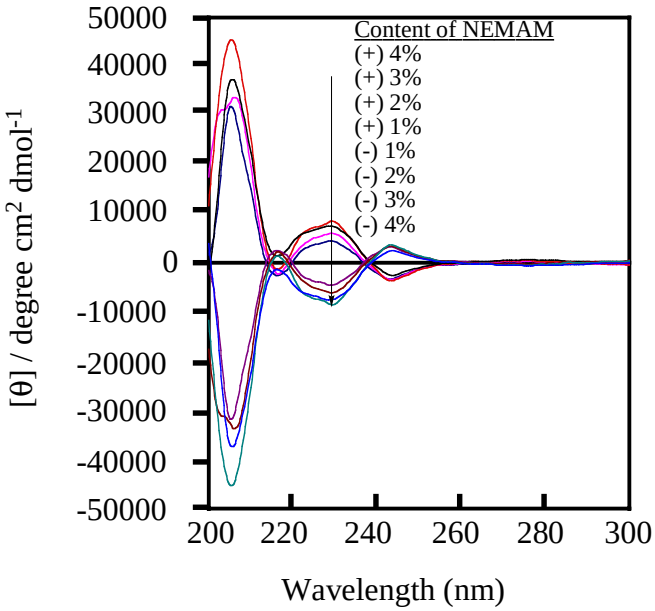


Figure 2-5. CD spectra of the copolymers of BuTrMAM with (+)- and (-)-NEMAM (1% to 4%) obtained at 60 °C in toluene (THF, r.t.).

The optical activities of the copolymers of BuTrMAM with (+)- and (-)-NEMAM are opposite of each other as expected.

Temperature Dependence of Helical Induction in Poly(BuTrMAM-*co*-NEMAM)

Although no significant change in the optical activity was observed for the copolymers of BuTrMAM with the optically active BPMAM and CHEMAM obtained at different temperatures, the copolymer of BuTrMAM with the optically active (-)-NEMAM obtained at 0 °C exhibited a higher optical activity than the copolymer prepared at 60 °C (Table 2-4). The temperature more significantly influenced the optical

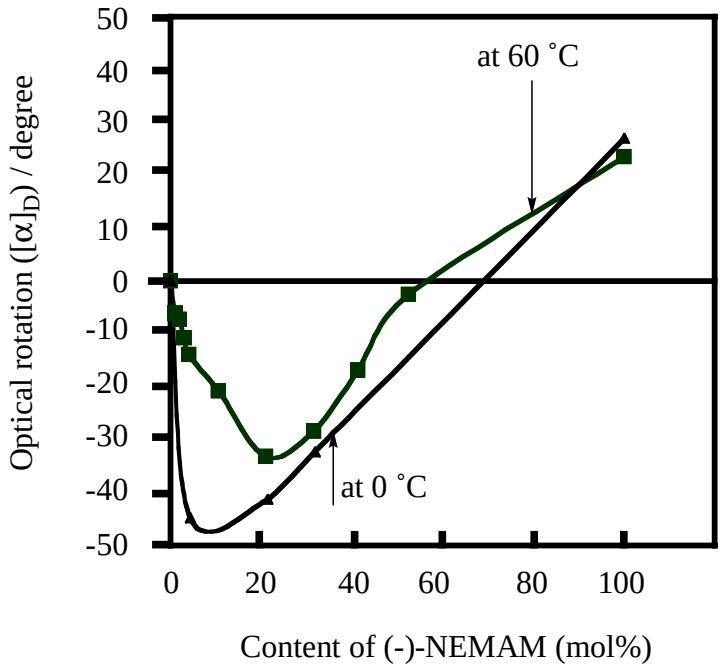


Figure 2-6. Plots of (-)-NEMAM content vs optical rotation ($[\alpha]_D$) of poly[BuTrMAM-*co*-NEMAM]s obtained at 0 and 60 °C (Table 2-3 and Table 2-4).

activity when the (-)-NEMAM content was low (Figure 2-6). The CD pattern of the copolymer (run 1, Table 2-4) containing 4.3% of the chiral monomer residue resembles that of the homopolymer (run 9) of BuTrMAM obtained in the presence of (+)-menthol (Figure 2-7), and its intensity is greater than that of the homopolymer. The helicity induction by the optically active NEMAM seems to be more effectively attained when the polymerization temperature is low.

Table 2-4. Radical Copolymerization of BuTrMAM with (-)-NEMAM at 0 an 60 °C in Toluene[a]

Run	BuTrMAM/ (-)-NEMAM (mol/mol)	Temp. (°C)	Yield[b]	(-)-NEMAM in copolymer[e] (mol%)	M_n[c] $\times 10^{-4}$	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	96/4	0/UV	59	4.3	2.53	3.08	-44.8	-169.3
2	96/4	60	78	4.0	3.02	5.20	-13.9	-49.3
3	80/20	0/UV	34	21.4	1.26	2.59	-41.2	-156.0
4	80/20	60	76	21.0	1.62	4.04	-33.2	-127.7
5	70/30	0/UV	25	31.8	1.21	2.56	-32.3	-148.7
6	70/30	60	82	31.5	1.32	3.61	-28.4	-107.8
7	0/100[f]	0/UV	17	-	1.11	1.98	+27.3	+53.5
8	0/100[f]	60	76	-	1.13	2.04	+23.5	+42.8
9	100/0[g]	0/UV	81	-	30.01	5.30	-9.7	-29.3

[a]Initiator = AIBN (0.02 M), time = 24 h, $[BuTrMAM]_0 + [NEMAM]_0 = 0.5$ mol / L. [b]MeOH-insoluble part. [c]Determined by SEC in THF (PMMA standard) at 40 °C. [d]In THF at 25 °C, conc. = 5 mg / mL, cell length = 2 cm. [e]Calculated by ^{1}H NMR. [f]Homopolymerization of (+)-NEMAM. [g]Homopolymerization of BuTrMAM in (+)-menthol (0.45g).

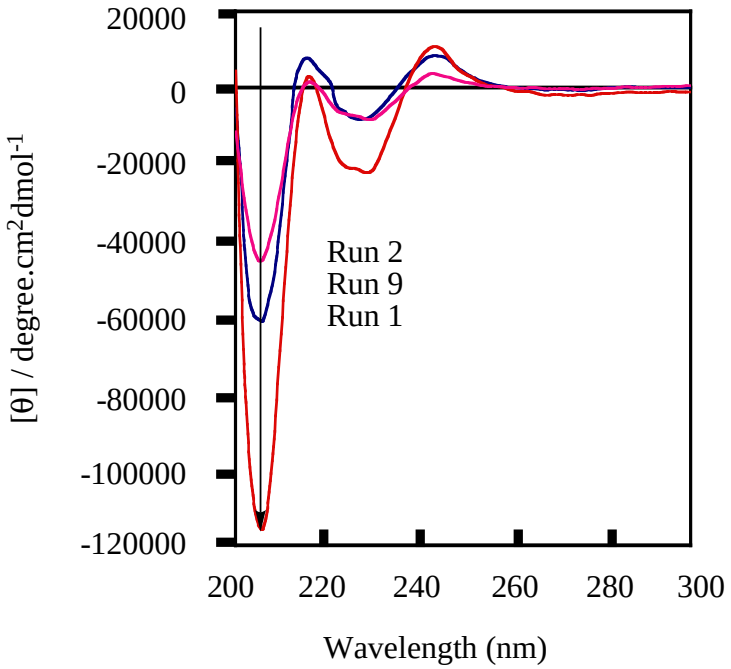


Figure 2-7. CD spectra of copolymers with lower content of (-)-NEMAM (4%) and the homopolymer of BuTrMAM (Table 2-4) (THF, r.t.).

2-4. Summery

The helix-sense-selective radical copolymerization was examined using BuTrMAM as a helix forming unit and three optically active monomers, BPMAM, CHEMAM, and NEMAM, as the helix inducing unit. The CD patterns of the copolymers containing low contents of the chiral monomers resemble that of the helical homopolymer of BuTrMAM obtained in the presence of (+)- and (-)-menthol, suggesting that the optically active monomeric units can induce a one-handed helical conformation of the BuTrMAM sequence via copolymerization. The helical induction by the chiral (-)-NEMAM was very effective at low temperature, and the obtained copolymer exhibits a higher optical activity than that of the homopolymer of BuTrMAM obtained in the optically active menthol.

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Chapter 3

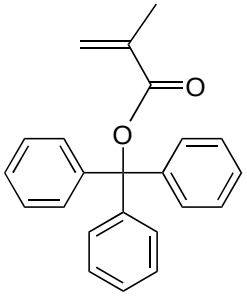
Asymmetric Radical Polymerization and Copolymerization of *N*-(1-Phenyldibenzosuberyl)methacrylamide and Its Derivative Leading to Optically Active Helical Polymers

3-1. Introduction

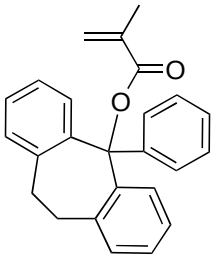
Naturally occurring polymers, such as proteins, nucleic acids, and polysaccharides, are optically active and have a helical conformation, which plays an important role for the polymers to exhibit their potential functions, such as chiral recognition toward racemic compounds, liquid crystal formation, and catalytic activity.[1-7]

The radical polymerization of the methacrylates with a bulky side group, such as triphenylmethyl methacrylate (TrMA)[8] and 1-phenyldibenzosuberyl methacrylate (PDBSMA),[9] proceeds in an isotactic-specific manner due to the steric repulsion among the bulky side groups (Scheme 3-1). The helix-sense-selective polymerization of PDBSMA by a free radical process under chiral conditions gives rise to an optically active, helical polymer having a prevailing one-handed helicity.[9] The one-handedness of poly(PDBSMA) was higher than that of poly(TrMA) obtained under the same chiral conditions,[10] indicating that the 1-phenyldibenzosuberyl group is more suitable for obtaining a helical polymer than the triphenylmethyl group. During the radical polymerization of acrylamide and methacrylamide derivatives, Lewis acids, such as rare earth metal triflates, significantly increase the isotactic contents of the polymers.[11-15]

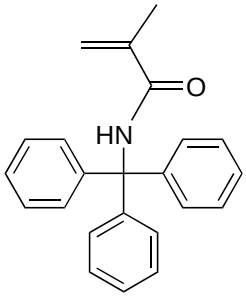
However, these polymerization systems with Lewis acids have so far been unsuccessful in producing optically active polymers. On the other hand, it was found that the radical polymerization of bulky methacrylamides, *N*-(triphenylmethyl)methacrylamide (TrMAM) and its derivatives, *N*-[(4,4'-dibutyl)triphenylmethyl]methacrylamide



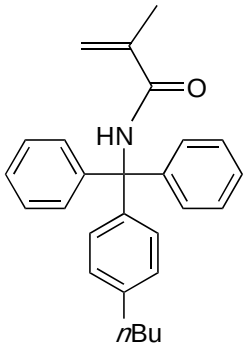
TrMA



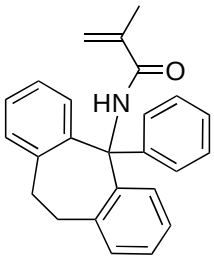
PDBSMA



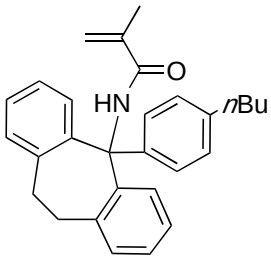
TrMAM



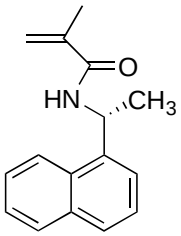
BuTrMAM



PDBSMAM



BuPDBSMAM



(+)-NEMAM

Scheme 3-1

(DBuTrMAM),[16] and *N*-[(4-butyl)triphenylmethyl]methacrylamide (BuTrMAM)[17] in the presence of the (+)- and (-)-menthols afforded highly isotactic and optically active polymers. The optical rotation and CD intensities of these polymers were lower than that of the anionically obtained one-handed helical poly(TrMA). In the radical

copolymerization of BuTrMAM with a small amount of a chiral monomer at a low temperature, the obtained copolymer exhibits a higher optical activity than the BuTrMAM homopolymer obtained in the optically active menthol.[18]

In this chapter, based on the results from the polymerization of the bulky methacrylates, the asymmetric radical polymerization and copolymerization of *N*-(1-phenyldibenzosuberyl)methacrylamide (PDBSMAM) and *N*-[(4-Butylphenyl)dibenzo-suberyl]methacrylamide (BuPDBSMAM) is discussed. PDBSMAM was synthesized and polymerized using a radical initiator under chiral conditions to obtain the polymer with a higher one-handed helical structure. BuPDBSMAM was synthesized to enhance the solubility of the polymer. The copolymerization of these monomers with optically active *N*-[(*R*)-(+)-1-(1-naphthyl)ethyl]methacrylamide] ((+)-NEMAM) was also carried out in the presence of chiral additives. The PDBSMAM homopolymers and copolymers with a small amount of (+)-NEMAM were not soluble in the common organic solvents, but the homopolymers and copolymers prepared from BuPDBSMAM were soluble in chloroform and THF. The chiroptical properties of all the polymers were studied in detail.

3-2. Experimental Section

Materials. All the reagents used for the synthesis of monomers were obtained from Aldrich, Kishida, and Kanto Kagaku, and were used without further purification. Triethylamine was dried over KOH and distilled. 2,2'-Azobisisobutyronitrile (AIBN; Kishida; purity >99%) was purified by recrystallization from methanol. The chiral additives, (+)-neomenthol (TCI; >96%), was used after being distilled from CaH_2 under a reduced pressure and (+)-isomenthol (TCI; >96%) was used without further purification. Anhydrous solvents, THF, chloroform, pyridine, and toluene (Kanto Kagaku), and the chiral solvents (additives), (+)- and (-)-menthols (Kishida; >99%),

were used as received.

Monomer Synthesis

PDBSMAM. 5-Phenyldibenzosuberyl-5-ol was synthesized by the Grignard reaction of 5-dibenzosuberone (7.5 g, 36 mmol) with phenylmagnesium bromide in THF. The obtained alcohol was purified by recrystallization from hexane (7.4 g, 72%). From this alcohol (7.0 g, 24 mmol), 5-phenyldibenzosuberyl-5-amine was synthesized with liquid ammonia.[19] The obtained amine was purified by recrystallization in a mixture of hexane and diethyl ether (5/1, vol/vol) (4.5 g, 66%). PDBSMAM was synthesized by the reaction of 5-phenyldibenzosuberyl-5-amine (4.0 g, 14 mmol) and methacryloyl chloride (1.53 mL, 14.7 mmol) in the presence of triethylamine in chloroform.[17] The obtained monomer was purified by recrystallization in diethyl ether (3.5 g, 70%). mp 165.2~166.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 2.02 (s, 3H, allyl CH_3), 2.89 (m, 4H, suberyl CH_2), 5.41 (s, 1H, vinyl-H), 5.78 (s, 1H, vinyl-H), 6.62 (s, 1H, -NH), 6.91-7.58 (m, 13H, aromatic-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, δ): 167.1, 148.0, 141.2, 141.2, 140.2, 131.0, 128.8, 128.6, 129.0, 127.7, 127.6, 126.0, 119.5, 70.8, 35.0, 19.4. Anal. Calcd. (%) for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.96. Found: C, 84.91; H, 6.52; N, 3.98.

BuPDBSMAM. 5-(4-Butylphenyl)dibenzosuberyl-5-ol was synthesized by the Grignard reaction of 5-dibenzosuberone (25 g, 120 mmol) with 4-butylphenylmagnesium bromide in THF. The obtained liquid alcohol was purified by column chromatography (35.3 g, 86%). From this alcohol (35 g, 102 mmol), 5-(4-butylphenyl)dibenzosuberyl-5-amine was synthesized with liquid ammonia.[19] The obtained liquid amine was purified by column chromatography (18.0 g, 52%). BuPDBSMAM was synthesized by the reaction of 5-(4-butylphenyl)dibenzosuberyl-5-amine (10.3 g, 30 mmol) and methacryloyl chloride (3.1 mL, 32 mmol) in the presence

of triethylamine in chloroform.[17] Obtained monomer was purified by column chromatography (10.2 g, 83%). mp 121.3~122.5 °C. ^{1}H NMR ($CDCl_3$, 400 MHz δ): 0.89 (m, 3H, *n*-butyl CH_3), 1.32 (m, 2H, *n*-butyl CH_2), 1.52 (m, 2H, *n*-butyl CH_2), 2.02 (s, 3H, allyl CH_3), 2.52 (t, 2H, *n*-butyl CH_2), 2.89 (m, 4H, suberyl CH_2), 5.40 (s, 1H, vinyl-H), 5.76 (s, 1H, vinyl-H), 6.61 (s, 1H, -NH), 6.80-7.56 (m, 12H, aromatic-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, δ): 167.1, 145.3, 142.3, 141.2, 141.18, 140.3, 130.9, 128.8, 128.6, 127.8, 127.4, 125.9, 119.4, 70.6, 35.4, 35.0, 33.7, 22.8, 19.3, 14.3. Anal. Calcd (%) for $C_{29}H_{31}NO$: C, 85.05; H, 7.63; N, 3.42. Found: C, 85.01; H, 7.65; N, 3.43.

Polymerization. The radical polymerization was carried out under dry nitrogen in a glass tube equipped with a three-way stopcock using AIBN as an initiator at 60 °C. The polymerization using AIBN at 0 ~ 30 °C was initiated by the irradiation of UV light (400-W high-pressure mercury lamp). Liquid materials were transferred to the glass tube using syringes and the solid monomer using a funnel having a nitrogen gas inlet tube. PDBSMAM (0.10 g, 0.28 mmol) or BuPDBSMAM (0.10 g, 0.24 mmol) was placed in a glass tube and a polymerization solvent (0.50 mL) was added in it. For the copolymerization systems, calculated amount of BuTrMAM or (+)-NEMAM was added to the suberyl monomer solution. The polymerization solution was maintained at the prescribed temperature for 24 h. The polymerization was terminated by cooling the reaction mixture at -78 °C. The reaction mixture was dissolved in chloroform (5 mL), and the solution was poured into a large amount of methanol. The precipitated polymers were isolated using a centrifuge, washed several times with methanol to remove the unreacted monomer and the chiral additives, and dried at 60 °C for 10 h.

CD Measurements in a Solid State. The insoluble polymers (5 mg) were dispersed in liquid paraffin (3 drops) by grinding in a mortar, and imposed between quartz plates.[16] The polymer concentrations and the UV intensities of the samples were

almost the same for all cases.

Solvolysis of PDBSMAM and BuPDBSMAM. The solvolysis reaction of PDBSMAM and BuPDBSMAM was carried out in a mixture of $CD_3OD/CDCl_3$ (1/1, v/v) at 35 °C in an NMR tube (Wilmad 507-PP).[20] PDBSMAM (0.15 g, 0.42 mmol) or BuPDBSMAM (0.15 g, 0.37 mmol) was dissolved in the solvent (1 mL), the tube was placed in a water bath at 35 °C, and the reaction was monitored by ^{1}H NMR spectroscopy at 35 °C.

Measurements. The NMR spectra were recorded on a Varian Gemini 2000 spectrometer (400 MHz for ^{1}H and 75 MHz for ^{13}C). The number average molecular weight (M_n) and polydispersity (M_w/M_n) of the obtained polymers were determined by size-exclusion chromatography (SEC) calibrated using standard PMMA on a JASCO PU-980 pump equipped with a JASCO RI-930 detector using two Shodex KF-606M columns connected in series (eluent THF or chloroform; temperature 40 °C). The optical rotation was measured in either THF or chloroform at room temperature with a JASCO P-1030 polarimeter. The circular dichroism (CD) spectra were measured with a JASCO J-720L spectrometer.

3-3. Results and Discussion

Polymerization of PDBSMAM

1-Phenyldibenzosuberyl methacylate (PDBSMA) affords a prevailing one-handed helical polymer by the radical process in the presence of optically active additives such as menthol and menthanethiol.[9] The formation of the prevailing one-handed helical polymers by radical process has been ascribed to the fact that the chain-transfer rates of the growing radicals with a right- or left-handed helicity to an optically

active transfer agent can be different, and the helical growing polymer with a large transfer constant has a lower chance to propagate to the high molecular weight polymer compared with the opposite helical polymer with a lower transfer constant.

When the radical polymerization of PDBSMAM was carried out at 60 °C, the polymers were obtained in good yields (runs 1-4 in Table 3-1), but at 0 °C the monomer slowly precipitated and the polymerization did not sufficiently proceed (runs 5 and 6 in Table 3-1). All the polymers were insoluble in organic solvents as well as poly(TrMAM).[16] The tacticity of the obtained polymers was directly determined from the ^{1}H NMR spectra of the polymethacrylamides (poly(MAM)s) derived from the original polymers in D_2SO_4.[16]

Table 3-1. Radical Polymerization of PDBSMAM[a]

Run	Temp. (°C)	Solvent	Yield[b] (%)
1	60	Toluene	53
2	60	THF	70
3	60	(+)-Menthol	61
4	60	(-)-Menthol	65
5	0/UV	(+)-Menthol	17
6	0/UV	(-)-Menthol	18

[a]$[AIBN]_0$ = 0.02 M; $[PDBSMAM]_0$ = 0.5 mol / L; time = 24 h. [b]Methanol-insoluble part.

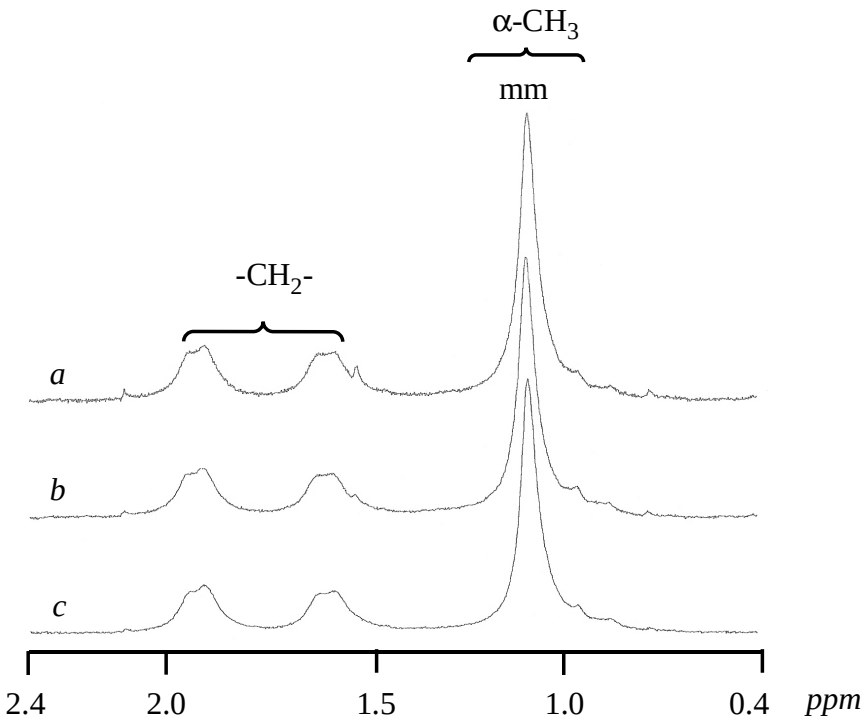
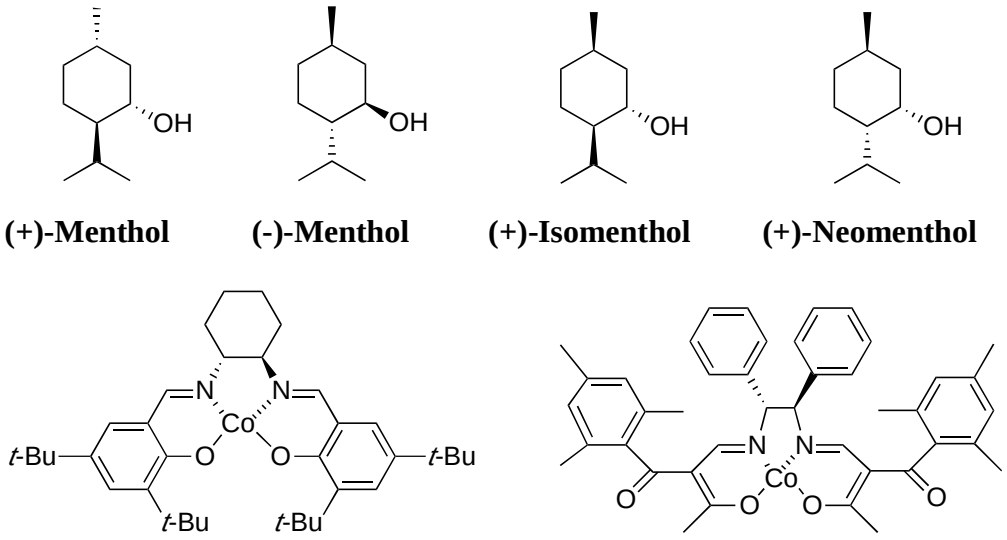


Figure 3-1. 400 MHz ^{1}H NMR spectra of poly(MAM)s derived from poly(PDBSMAM)s in Table 3-1 (*a*; in toluene at 60 °C, *b*; in THF at 60 °C, *c*; in (+)-menthol at 60 °C) (D_2SO_4, 60 °C).

When the poly(PDBSMAM)s (runs 1-3 in Table 3-1) were dissolved in D_2SO_4, the ^{1}H NMR spectra showed only one clear methyl peak due to the isotactic (mm) sequence at 1.1 ppm and two sets of doublets due to the methylene group at 1.65 and 1.95 ppm (Figure 3-1), indicating that the poly(PDBSMAM)s are highly isotactically similar to poly(TrMAM).[16] These three ^{1}H NMR spectra are almost identical to each other, indicating that the polymerization solvents only slightly affect the polymer tacticity.

The poly(PDBSMAM)s obtained in the presence of the (+)- and (-)-menthols (Scheme 3-2) were insoluble in organic solvents, and the CD spectra of the optically active polymers could not be measured in solution. However, the spectra were obtained for the polymer particles dispersed in liquid paraffin (Nujol) (Figure 3-2).[21] The spectral

pattern of these CD spectra in a solid state was similar to that of the THF-soluble poly(PDBSMA)s obtained in menthol,[9] which supports the formation of the prevailing one-handed helical poly(PDBSMAM) in menthol.



(+)-Menthol **(-)-Menthol** **(+)-Isomenthol** **(+)-Neomenthol**

1 **2**

Scheme 3-2

PDBSMAM was not solvolyzed at all in methanol/chloroform (1/1, v/v) at 35 °C even after 15 days, whereas the half-life of TrMA under the same conditions is only 15 min.[22] This indicates that PDBSMAM is much stronger towards hydrolysis and the obtained polymer must be a more stable compared with poly(TrMA) when used as a chiral stationary phase in HPLC with polar alcoholic solvents.

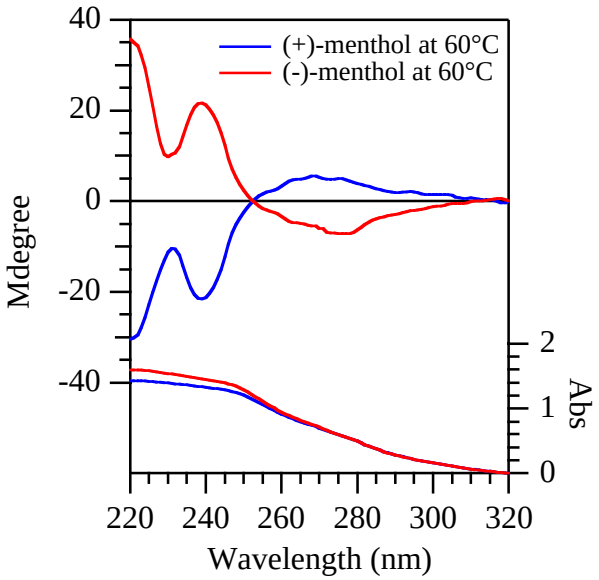


Figure 3-2. UV (lower) and CD (upper) spectra of poly(PDBSMAM)s (runs 3 and 4 in Table 3-1) (dispersed in liquid paraffin, r.t.).

Copolymerization of PDBSMAM and BuTrMAM

As the isotactic PDBSMAM and BuTrMAM[17] chains produced by radical polymerization can form a helical conformation, the copolymerization of these two monomers was carried out in the presence of chiral additives to obtain soluble copolymers with a high one-handed helicity (Table 3-2). All the copolymers were almost 100% isotactic (Figure 3-3).

When the copolymerization was carried out at 60 °C, the copolymer was obtained in good yields and the copolymer compositions were very close to the corresponding feed monomer compositions (runs 6-9 in Table 3-2). However, at 0 °C PDBSMAM slowly precipitated and polymer yield became low. Therefore, the obtained copolymers had slightly higher BuTrMAM content than the feed monomer (runs 2-5 in Table 3-2). Only the copolymer obtained from the copolymerization of PDBSMAM with BuTrMAM (50/50, mol/mol) was soluble in chloroform, while other copolymers in Table 3-2 were not soluble in the common organic solvents. The UV and the CD spectra

(Figure 3-4) of the insoluble copolymers measured by dispersing them in liquid paraffin (Nujol)[21] changed depending on the feed monomer contents.

Table 3-2. Radical Copolymerization of PDBSMAM and BuTrMAM in (-)-Menthol[a]

Run	PDBSMAM/BuTrMAM (mol/mol)	Temp. (°C)	Yield[b] (%)	PDBSMAM/ BuTrMAM in copolymer[c] (mol%)
1	100/0	0/UV	18	-
2	80/20	0/UV	34	66/34
3	70/30	0/UV	47	56/44
4	60/40	0/UV	51	49/51
5	50/50	0/UV	57	37/63
6	80/20	60	80	79/21
7	70/30	60	81	69/31
8	60/40	60	84	59/41
9	50/50	60	90	48/52

[a]$[AIBN]_0$ = 0.02 M; $[PDBSMAM]_0$+$[BuTrMAM]_0$ = 0.5 mol / L; time = 24 h. [b]Methanol-insoluble part. [c]Calculated by ^{1}H NMR.

The solubility of the copolymers increased with an increase in the BuTrMAM content in the copolymers but the CD intensity gradually decreased with an increase in the BuTrMAM content in the copolymer. The contribution of the BuTrMAM units to the CD intensity may be lower than that of the PDBSMAM units in the copolymers.

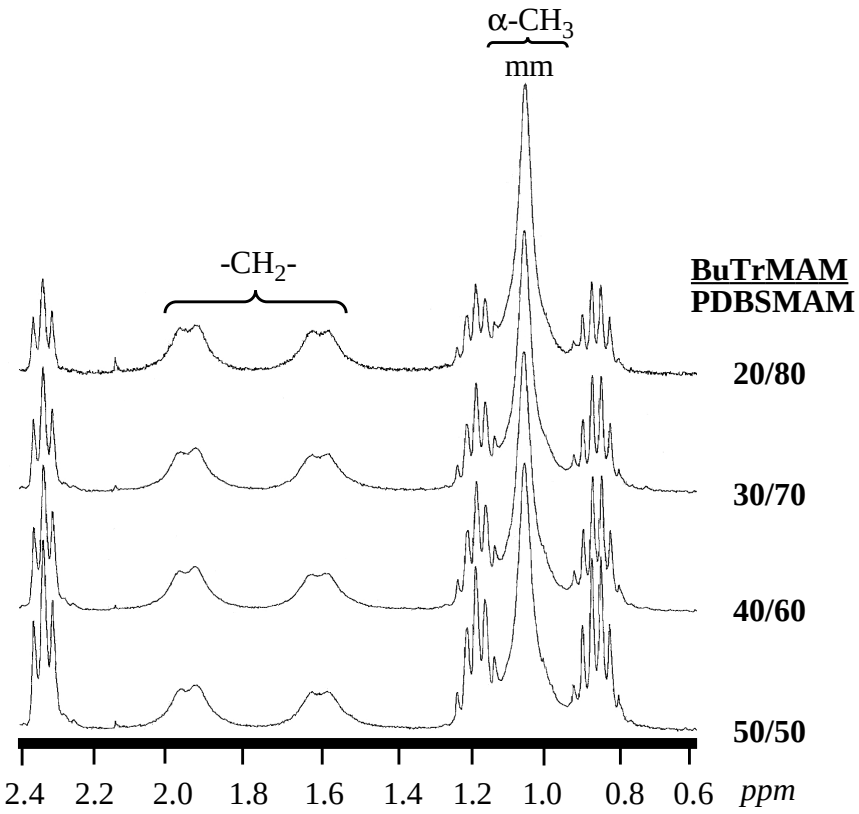


Figure 3-3. ^{1}H NMR spectra of the copolymers of PDBSMAM and BuTrMAM (polymerized at 60 °C, Table 3-2) in D_2SO_4 at 60 °C. The peaks (0.85, 1.25, 2.35 ppm) are due to the butyl protons of the product yielded by the dissolution in D_2SO_4.

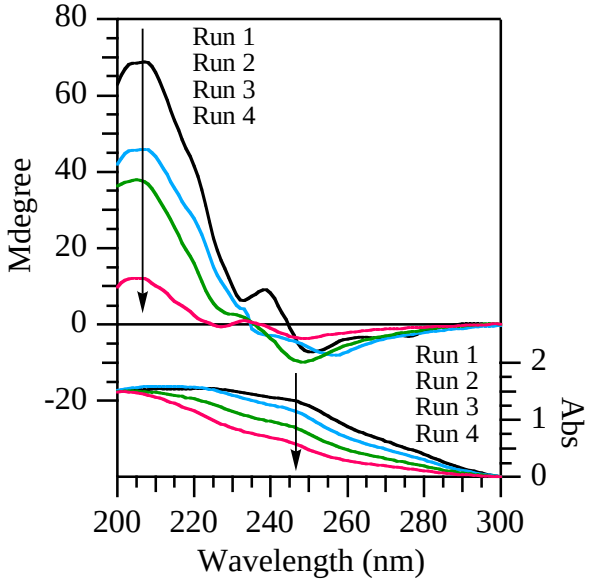


Figure 3-4. UV (lower) and CD (upper) spectra of poly(PDBSMAM) and poly(PDBSMAM-*co*-BuTrMAM)s (Table 3-2) (dispersed in liquid paraffin, r.t.).

Polymerization of BuPDBSMAM

The results of the radical polymerizations of BuPDBSMAM in toluene, THF, and optically active solvents are summarized in Table 3-3. Although poly(PDBSMAM) was insoluble in the common organic solvents, poly(BuPDBSMAM) was soluble in chloroform and partially soluble in THF due to the *n*-butyl group on the phenyl group of the side chain. The tacticity of the obtained polymers was estimated by the same method used for poly(PDBSMAM), and found to be almost 100% isotactic.[16]

Table 3-3. Radical Polymerization of BuPDBSMAM[a]

Run	Temp. (°C)	Solvent	Yield[b] (%)	$M_n \times 10^{-4}$ [c]	M_w/M_n [c]	$[\alpha]_D$ [d] (deg)	$[\alpha]_{365}$ [d] (deg)
1	60	Toluene	86	9.5	6.2	-	-
2	60	THF	87	7.4	5.4	-	-
3	60	(+)-Menthol	86	8.4	11.8	-29.1	-107.0
4	60	(-)-Menthol	88	7.9	12.7	+29.2	+117.4
5	30/UV	(+)-Menthol	83	9.4	14.6	-57.1	-173.0
6	30/UV	(-)-Menthol	84	8.1	18.7	+56.5	+170.1
7	0/UV	(+)-Menthol	79	-	-	-	-
8	0/UV	(-)-Menthol	81	-	-	-	-
9	30/UV	(+)-Isomenthol	81	-	-	-	-
10	30/UV	(+)-Neomenthol	80	9.8	16.7	-36.8	-97.4
11	60	(+)-Isomenthol	75	7.9	12.6	-22.5	-65.7
12	60	(+)-Neomenthol	74	8.0	12.1	-20.2	-57.3

[a]$[AIBN]_0$ = 0.02 M; $[BuPDBSMAM]_0$ = 0.5 mol / L; time = 24 h. [b]MeOH-insoluble part. [c]Determined by SEC in $CHCl_3$ (PMMA standard) at 40 °C. [d]In $CHCl_3$ at 25 °C; *c* = 5 mg / mL; cell length = 2 cm.

The poly(BuPDBSMAM)s prepared in (+)- and (-)-menthols were optically active, and their optical rotation was opposite to that of menthol. This suggests that the optical rotation may not be due to the incorporation of the menthol residue in the polymer. The polymerization in an optically active medium may helix-sense-selectively proceed because the chain-transfer rates of the right- and left-handed helical polymer radicals to a chiral reagent can be different, as observed for the polymerization of the bulky methacrylates.[9]

When the polymerization was carried out at 0 °C, the obtained polymer became insoluble in the common organic solvents. The molecular weight of the polymers may be higher, and this can be the reason for the lower solubility. The polymers obtained at 30 °C showed a larger specific rotation than those at 60 °C. Two chiral alcohols, (+)-isomenthol and (+)-neomenthol, were also used as the chiral additives/solvents, but the effect of menthol is clearer in producing the one-handed helical poly(BuPDBSMAM)s than these alcohols. The optical rotation of the obtained poly(BuPDBSMAM) is almost 10 times higher than that of poly(BuTrMAM).[17] For the one-handed helical methacrylate polymers, poly(PDBSMA) shows a 10~20% higher optical activity than poly(TrMA).[10,23] In case of the methacrylamide polymers obtained in this study, poly(BuPDBSMAM) had a much higher optical activity than poly(BuTrMAM). Besides the effect of the 1-phenyldibenzosuberyl group on the optical activity, the one-handedness of the poly(BuPDBSMAM) may also be much higher than that of poly(BuTrMAM).

As these polymers are soluble only in chloroform, their CD spectra were measured up to 220 nm in chloroform at room temperature. In this solvent, the most intense peak around 206 nm could not be measured (Figure 3-5). There was no change in the CD spectrum after heating the polymer solution at 60 °C for 10 h. The CD intensity and pattern were also unchanged when measured at different temperatures. These results suggest that the poly(BuPDBSMAM)s have a stable helical structure. The

CD pattern of poly(BuPDBSMAM) is different from those of poly(TrMA)[24] and poly(PDBSMA).[9] The propeller structures of the bulky polymethacrylamides[17] in solution are likely different from those of the trityl groups in the poly(triarylmethyl methacrylate)s.

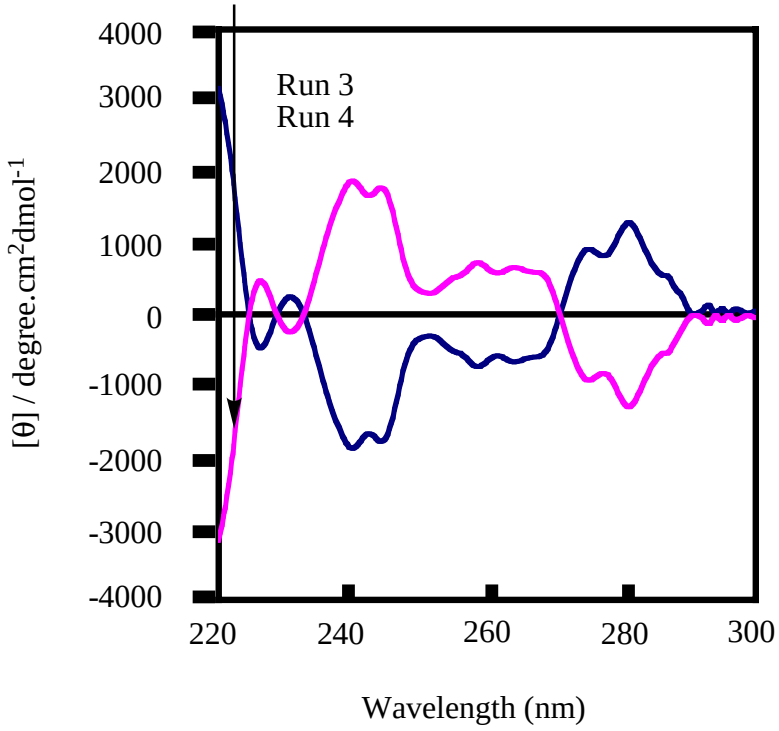


Figure 3-5. CD spectra of optically active poly(BuPDBSMAM)s (runs 3 and 4 in Table 3-3) ($CHCl_3$, r.t., path length = 0.1 mm).

The polymerization at 0 °C resulted in only a slight decrease in the polymer yield. However, no polymer was produced at -20 °C in the presence of menthol because menthol was solidified at this temperature and the polymerization system became heterogeneous.

Polymerization of BuPDBSMAM in the Presence of Optically Active Cobalt Complexes

The helix-sense-selective free radical polymerization of PDBSMA in the presence of *N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-(1*R*,2*R*)-1,2-cyclohexanediaminato-cobalt(II) (**1**)[25] and *N,N'*-bis{2-(2,4,6-tri-methylbenzoyl)-3-oxobutylidene}-(1*S*,2*S*)-1,2-diphenylethylenediaminatocobalt(II) (**2**)[26] effectively produces a highly optically active polymer with a high one-handed helicity (Scheme 3-2). These Co complexes were also used as the chiral additives for the polymerization of TrMAM[27] and BuTrMAM.[17] However, the complexes functioned as polymerization inhibitors. The complexes were also examined

for the polymerization of BuPDBSMAM (Table 3-4). The polymers with low optical activities were obtained in low yields, indicating that complexes **1** and **2** did not effectively function as chiral additives.

Table 3-4. Radical Polymerization of BuPDBSMAM in the Presence of Optically Active Cobalt Complex[a]

Run	Temp. (°C)	Cobalt Complex (*c*/M)	Yield[b] (%)	M_n[c] × 10^{-4}	M_w/M_n[c]	$[\alpha]_D$[d] (deg)	$[\alpha]_{365}$[d] (deg)
1	60	**1** (0.035)	27	0.8	5.1	+4.9	+14.6
2	60	**1** (0.015)	69	1.6	5.3	+3.4	+10.9
3	60	**2** (0.035)	7	0.7	2.2	-11.5	-40.5
4	60	**2** (0.015)	9	1.1	2.9	-20.2	-60.5

[a]$[AIBN]_0$ = 0.02 M; $[BuPDBSMAM]_0$ = 0.5 mol / L; time = 24 h. [b]MeOH-insoluble part.
[c]Determined by SEC in $CHCl_3$ (PMMA standard) at 40 °C. [d]In $CHCl_3$ at 25 °C; *c* = 5 mg / mL; cell length = 2 cm.

Copolymerization of BuPDBSMAM with (+)-NEMAM in Different Solvents

The copolymers prepared from achiral and chiral vinyl monomers sometimes show disproportionately high optical activities.[28] Recently, it is reported that the radical copolymerization of BuTrMAM with a small amount of chiral NEMAM gave the optically active polymers, whose optical activity was opposite to that of the NEMAM residue, indicating that the chiral NEMAM effectively induced an excess of a one-handed helix consisting of BuTrMAM sequences.[18] As the isotactic BuPDBSMAM chain produced by radical polymerization can also form a helical conformation, the copolymerization of BuPDBSMAM with (+)-NEMAM was carried out in different solvents to obtain a copolymer with a high one-handed helicity induced by the optically active monomer (Table 3-5). All the obtained copolymers were soluble in THF and chloroform. The copolymer compositions were very close to the corresponding feed monomer compositions, suggesting that the copolymerization mostly proceeded in a random manner. When the copolymerization was carried out in toluene, the optical rotation of the copolymers increased with an increase in the chiral monomer content up to 4%. A further increase of the chiral monomer resulted in a decrease in the optical rotation and finally arrived at the negative optical rotation of the (+)-NEMAM homopolymer, which is opposite to that of the monomer (Figure 3-6).

Before the formation of the helical structure of the BuPDBSMAM sequence, the BuPDBSMAM units neighboring a (+)-NEMAM residue seem to contribute to the exhibited positive rotation, because the 1:1 copolymer (run 10 in Table 3-5) was almost optically inactive by cancelling the negative rotation due to the (+)-NEMAM residues. As the BuPDBSMAM sequence gets longer, it starts to form a helical structure with a positive rotation, and the contribution becomes a maximum at the 4% (+)-NEMAM content, because the induced helical structure may not be maintained for a very long sequence.

Table 3-5. Radical Copolymerization of BuPDBSMAM with (+)-NEMAM in Different Solvents[a]

Run	BuPDBSMAM /(+)-NEMAM (mol/mol)	Temp. (°C)	Solvent	Yield[b]	(+)-NEMAM in copolymer[c] (mol%)	M_n[d] $\times 10^{-4}$	M_w/M_n[d]	$[\alpha]_D$[e] (deg)	$[\alpha]_{365}$[e] (deg)
1	99/1	60	Toluene	84	**1.0**	5.2	5.1	+61.9	+217.7
2	98/2	60	Toluene	83	2.0	3.6	4.7	+80.1	+281.5
3	97/3	60	Toluene	81	3.0	3.3	5.9	+88.7	+312.8
4	96/4	60	Toluene	80	4.0	3.7	4.7	+92.6	+326.8
5	95/5	60	Toluene	78	5.1	3.5	5.2	+87.3	+304.5
6	90/10	60	Toluene	76	10.7	3.3	4.1	+75.8	+279.2
7	80/20	60	Toluene	73	21.3	3.1	3.5	+50.7	+182.0
8	70/30	60	Toluene	75	31.1	2.6	3.7	+26.3	+97.2
9	60/40	60	Toluene	68	41.6	2.3	3.2	+6.7	+27.3
10	50/50	60	Toluene	71	52.3	1.8	2.9	+1.1	+4.9
11	0/100[f]	60	Toluene	74	-	1.0	2.4	-24.0	-43.2
12	96/4	0/UV	Toluene	74	4.0	2.5	3.3	+158.2	+567.0
13	96/4	60	(+)-Menthol	77	4.0	3.9	4.7	+73.4	+258.7
14	96/4	60	(-)-Menthol	78	4.0	3.2	5.5	+102.5	+360.0
15	96/4	0/UV	(+)-Menthol	75	4.0	6.4	5.4	+129.3	+459.9
16	96/4	0/UV	(-)-Menthol	71	4.0	5.5	5.3	+169.4	+600.3

[a]$[AIBN]_0$ = 0.02 M; $[BuPDBSMAM]_0 + [NEMAM]_0$ = 0.5 mol / L; time = 24 h. [b]MeOH-insoluble part. [c]Calculated by ^{1}H NMR. [d]Determined by SEC in $CHCl_3$ (PMMA standard) at 40 °C. [e]In $CHCl_3$ at 25 °C; *c* = 5 mg / mL; cell length = 2 cm. [f]Homopolymerization of (+)-NEMAM.

The temperature dependence of the helicity induction in these copolymerizations are similar to that of the copolymerization of BuTrMAM with (+)-

NEMAM[18] and the copolymers of BuPDBSMAM and (+)-NEMAM obtained at 0 °C exhibited a higher optical activity than the copolymer prepared at 60 °C (runs 4 and 12 in Table 3-5).

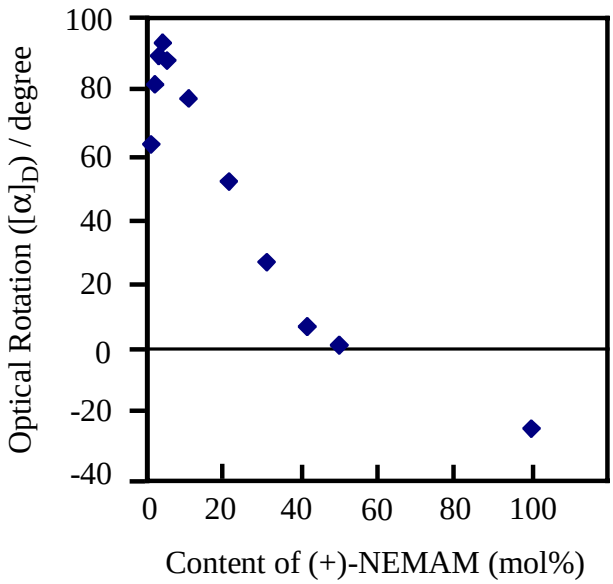


Figure 3-6. Plot of optical rotation *vs* the content of (+)-NEMAM in the poly(BuPDBSMAM-*co*-(+)-NEMAM)s obtained at 60 °C in toluene (Table 3-5).

The radical copolymerization of BuPDBSMAM with (+)-NEMAM was also carried out in (+)- and (-)-menthols. One of menthols is expected to enhance the helicity induction by (+)-NEMAM. As shown in Table 3-3, (-)-menthol produced a helical polymer exhibiting a positive optical rotation. Therefore, when the copolymerization of BuPDBSMAM with (+)-NEMAM is carried out in (-)-menthol, the copolymers are expected to exhibit a higher optical activity (runs 14 and 16 in Table 3-5) than the copolymers obtained in toluene. The experimental data support this expectation. As the copolymer obtained in (-)-menthol exhibits a higher optical activity (Table 3-5) and CD intensity (Figure 3-7) than that in toluene, the helicity induction by the (+)-NEMAM

seems to be more effectively attained when the polymerization solvent is (-)-menthol. The (+)-menthol showed the opposite effect as described in Table 3-5 (runs 13 and 15). All the copolymers were not chemically decomposed in alcoholic solvents and had a stable helical conformation as well as poly(PDBSMAM).

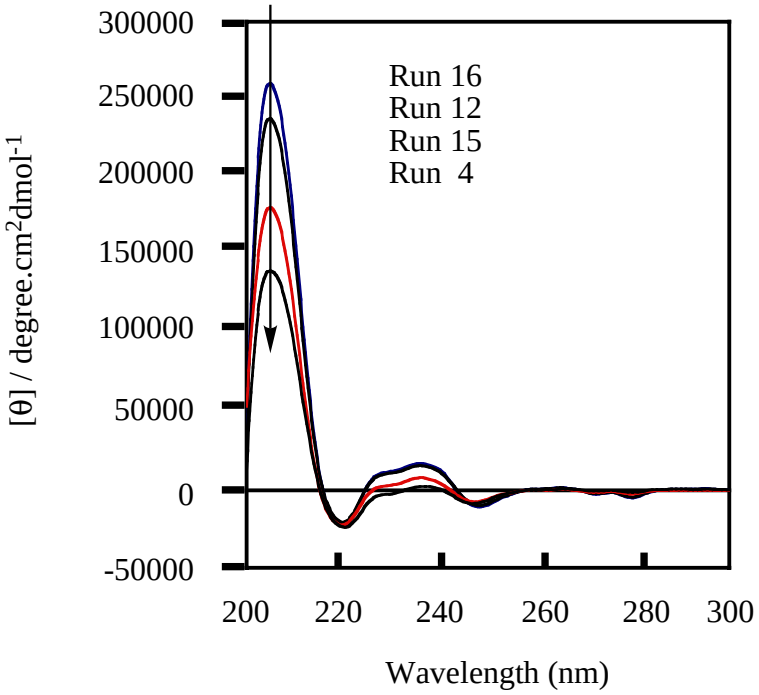


Figure 3-7. CD spectra of optically active poly(BuPDBSMAM-*co*-(+)-NEMAM)s (Table 3-5) (THF, r.t., path length = 0.1 mm).

3-4. Summery

The helix-sense-selective radical polymerizations of PDBSMAM and its derivative BuPDBSMAM were carried out. All the polymers were nearly 100% isotactic. The free radical polymerization of PDBSMAM and BuPDBSMAM using chiral additives produced optically active polymers with a CD adsorption based on an

excess right- or left-handed helical conformation. The copolymerization of BuPDBSMAM with optically active (+)-NEMAM in the presence of (-)-menthol produced a helical polymer with a high optical activity. Its optical activity was much higher than those of the other bulky polymethacrylamides, such as poly(TrMAM), poly(BuTrMAM), and poly(DBuTrMAM).

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Chapter 4

Chiral Adsorption with the Optically Active Helical Polymers

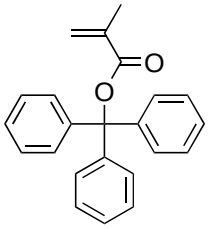
4-1. Introduction

Synthesis of optically active polymers is an important field in macromolecular science and have potential applications in chiral recognition based on a chiral structure.[1-12] This ability of chiral polymers has been utilized in various forms of catalytic and separation chemistry. One of the most practical and widely accepted applications of chiral polymers is the use as chiral stationary phase (CSP) for high-performance liquid chromatography (HPLC) for the separation of racemic compounds. Various CSP's have been developed so far and some of them are commercialized as very useful materials for chiral separation in many fields including synthetic and medicinal chemistry. Although HPLC was once considered to be a useful method only for analytical separation, preparative scale resolution has also become practically valuable.

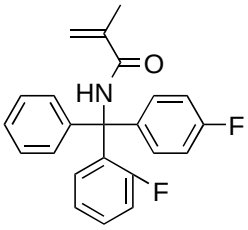
Many kinds of chiral polymers have been used as CSPs, such as biopolymers, polymers prepared by modification of naturally occurring polymers like polysaccharides, and fully synthetic polymers. Some optically active linear polymers are known to show chiral recognition ability. Among them, one-handed helical poly(methacrylate)s[13] and poly(methacrylamide)s[13] bearing chiral side groups are especially effective as CSP for HPLC and some of them are commercialized.

In 1979, Okamoto and coworkers reported that the anionic polymerization of

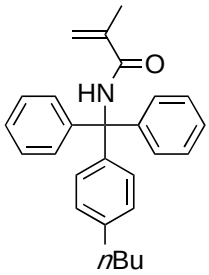
TrMA using a complex of *n*-BuLi with (-)-sparteine (Sp) at low temperature produces a highly isotactic polymer showing high optical activity and circular dichroism (CD) absorptions.[14-20] The one-handed helical poly(TrMA) shows remarkable chiral recognition ability to various types of racemic compounds, and has been successfully used as a chiral stationary phase for high-performance liquid chromatography (HPLC) to resolve a wide range of enantiomers.[21] However, when methanol is used as the eluent, the ester groups of poly(TrMA) are slowly solvolized, which causes the decrease of the column efficiency.[21(f)] Therefore, it is highly desirable to prepare the helical polymer, which is durable against the solvolysis by alcohol and can be used as a chiral stationary



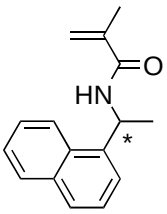
TrMA



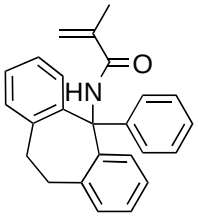
(±)-2F4FPhMAM



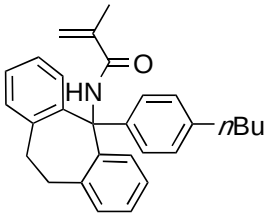
BuTrMAM



NEMAM



PDBSMAM



BuPDBSMAM

Scheme 4-1

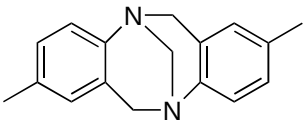
phase for HPLC column. In the polymerization of *N*-[(±)-(2-fluorophenyl)(4-fluorophenyl)(phenyl)methyl]methacrylamide (2F4FPhMAM), *N*-[(4-butyl)triphenyl-

methyl]methacrylamide (BuTrMAM), *N*-(1-Phenyldibenzosuberyl)methacrylamide (PDBSMAM), and *N*-[(4-butylphenyl)dibenzosuberyl]methacrylamide (BuPDBSMAM) (Scheme 4-1) in the presence of (+)- and (-)-menthol afforded the polymers with one-handed helicity and a high durability against alcoholic solvents.[22] The copolymeization of BuTrMAM or BuPDBSMAM with a small amount of (+)- or (-)-*N*-[1-(1-naphthyl)ethyl]methacrylamide (NEMAM) also afforded the polymers with a high optical activity.[22(b),(c)]

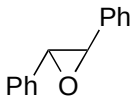
In this chapter, the author describes the chiral adsorption experiments of some optically active helical polymers homopolymers and copolymers to determine their chiral recognition ability.

4-2. Experimental Section

Materials. Anhydrous solvents, including hexane, methanol, and isooctane were purchased from Kanto Chemical, and used as received. Tröger's base (Aldrich; >99%) and *trans*-Stilbene (Aldrich; >98%) oxide used as commercially obtained.



Tröger base



trans-Stilbene oxide

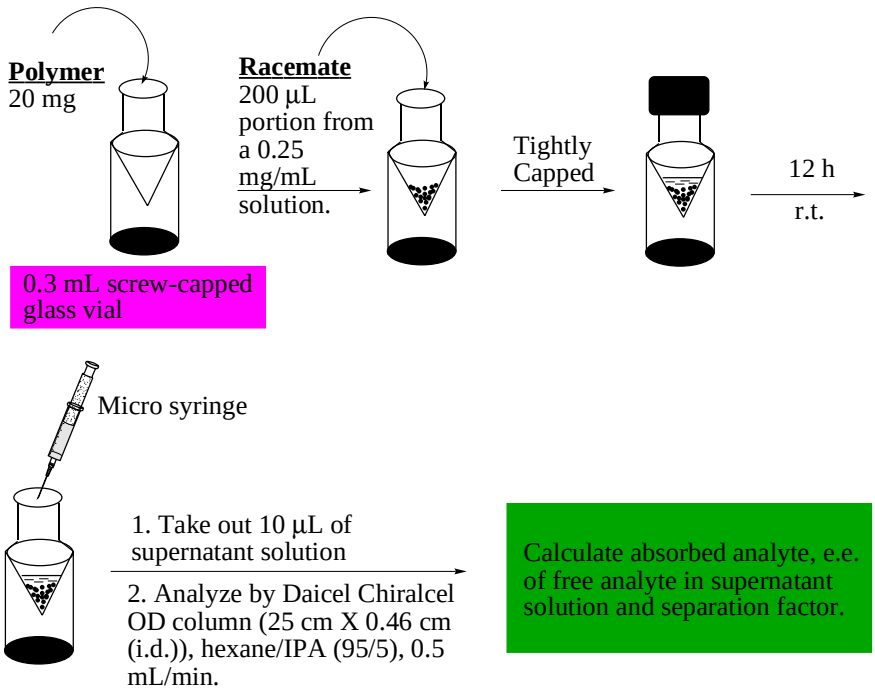
Scheme 4-2

Polymers Used in Chiral Adsorption Experiment. Copolymers of BuTrMAM with (+)- or (-)-NEMAM (BuTrMAM/NEMAM (96/4, mol/mol), initiator = AIBN (0.02

M), time = 24 h, $[BuTrMAM]_0$ + $[NEMAM]_0$ = 0.5 mol/L, at 0 °C in toluene), homopolymers of PDBSMAM (in (+)- or (-)-menthol/toluene (3/1, v/v) at 60 °C), and copolymer of BuPDBSMAM with (+)-NEMAM (BuPDBSMAM/NEMAM (96/4, mol/mol), initiator = AIBN (0.02 M), time = 24 h, $[BuPDBSMAM]_0$ + $[NEMAM]_0$ = 0.5 mol/L, in (-)-menthol at 0 °C) were used for the chiral adsorption experiment.

Chiral Adsorption Experiment Method. A finely ground polymer (20 mg) was placed in a 0.3-mL screw-capped glass vial. A solution of a racemic compound (Scheme 4-2) in methanol, hexane or isooctane (200 μL, conc. = 0.25 gL^{-1}) was added to the polymer. The mixture was allowed to stand for 12 h in a tightly capped container. The e.e. of the analyte in the sample solution was analyzed using the supernatant solution (10 μL) by an HPLC system equipped with a JASCO UV-970 UV detector, a JASCO OR-990 polarimeter, and a Daicel Chiralcel OD column (25 cm x 0.46 cm (i.d.)).

Chiral Adsorption Experiment Method



The separation factor (α) was determined by the following equation where the superscripts 'f' and 'ads' denote the free (in solution part) and adsorbed (on the polymer), respectively:[23]

$$\alpha = \frac{(\text{major antipode}^{f}\ (\%))/(\text{minor antipode}^{f}\ (\%))}{(\text{major antipode}^{ads}\ (\%))/(\text{minor antipode}^{ads}\ (\%))} = \frac{(\text{major antipode}^{f}\ (\%))/(\text{minor antipode}^{f}\ (\%))}{(50 - \text{major antipode}^{f}\ (\%))/(50 - \text{minor antipode}^{f}\ (\%))}$$

where,

$\text{major antipode}^{f}\ (\%) = (100 - \text{adsorption yield}\ (\%)) \times (100 + |\text{e.e.}^{f}|)/2 \times 1/100$

$\text{minor antipode}^{f}\ (\%) = (100 - \text{adsorption yield}\ (\%)) \times (100 - |\text{e.e.}^{f}|)/2 \times 1/100$

4-3. Results and Discussion

Chiral Recognition by Optically Active Poly(BuTrMAM-*co*-NEMAM)

The chiral recognition ability of the optically active poly(BuTrMAM-*co*-NEMAM) obtained by the copolymerization of BuTrMAM with (+)- and (-)-NEMAM (96/4, mol/mol) at 0 °C was evaluated by the chiral adsorption method[22] using *trans*-Stilbene oxide and Tröger base as the racemates (Table 4-1). Each racemate was adsorbed by ca. 30 ~ 50 % on the optically active poly(BuTrMAM-*co*-NEMAM) in methanol, hexane, and isooctane. The enantiomeric excess (e.e.) of the free solutes in a supernatant solution was estimated by HPLC using a chiral column. Although the e.e. was very low, the excess enantiomers were reversed depending on the chirality of the copolymers. This suggests that the data are sufficiently reliable.

The low enantioselectivity of the poly(BuTrMAM-*co*-NEMAM)s compared to that of the one-handed helical poly(TrMA) may be due to the existence of the butyl group. It is known that the existence of a methyl group on the helical diphenyl-2-pyridylmethyl methacrylate polymers reduces the chiral recognition ability of the

polymer.[24] The low one-handedness or the lack of a propeller structure of the trityl group in the copolymers may also cause this lower enantioselectivity.

Table 4-1. Chiral Recognition ability of the copolymers [BuTrMAM (96%) with (+)- or (-)-NEMAM (4%) at 0 °C] at r.t.[a]

Polymer (Monomer) (Additive)	Solvent	Racemate (Analyte)	Adsorbed Analyte[b] (%)	E.E. of Free Analyte in Supernatant[b] Solution (%)	Separation Factor (α)[c]
Copolymer (BuTrMAM/ (-)-NEMAM) (96/4)	MeOH	Stilbene oxide	38	(-) 2.7	1.14
	MeOH	Tröger base	45	(+) 2.1	1.10
	Hexane	Stilbene oxide	34	(-) 1.7	1.11
	Hexane	Tröger base	41	(+) 1.6	1.09
	Isooctane	Stilbene oxide	51	(-) 1.3	1.06
	Isooctane	Tröger base	46	(+) 1.6	1.08
Copolymer (BuTrMAM/ (+)-NEMAM) (96/4)	MeOH	Stilbene oxide	37	(+) 1.9	1.11
	MeOH	Tröger base	49	(-) 2.9	1.15
	Hexane	Stilbene oxide	48	(+) 2.2	1.10
	Hexane	Tröger base	32	(-) 1.1	1.07
	Isooctane	Stilbene oxide	50	(+) 1.2	1.08
	Isooctane	Tröger base	42	(-) 1.0	1.06

[a]Copolymer = 20 mg; racemic analyte 0.05 mg (200 μl portion from a 0.25 mg/mL solution in methanol or hexane or isooctane). [b]Determined by HPLC analysis of supernatant solution using a Chiralcel OD column; hexane/IPA (95/5); flow rate = 0.5 mL/min. [c]Calculated according to $\alpha = (F_{minor}(\%)/F_{major}(\%))/(A_{major}(\%)/A_{minor}(\%))$.

Chiral Recognition by Optically Active Poly(PDBSMAM)s Poly[BuPDBSMAM-*co*-(+)-NEMAM]

Table 4-2. Chiral Recognition by Optically Active Poly(PDBSMAM)s[a] and Poly[BuPDBSMAM-*co*-(+)-NEMAM][b] at r.t.[c]

Polymer (Monomer) (Additive)	Solvent	Racemate (Analyte)	Adsorbed Analyte[d] (%)	E.E. of Free Analyte in Supernatant[d] Solution (%)	Separation Factor (α)[e]
Homopolymer[a]	MeOH	Stilbene oxide	40	(+) 0.3	1.02
(PDBSMAM)	MeOH	Tröger base	54	(-) 1.0	1.07
((+)-Menthol)	Hexane	Stilbene oxide	29	(+) 0.1	1.00
	Hexane	Tröger base	52	(-) 0.3	1.03
Homopolymer[a]	MeOH	Stilbene oxide	37	(-) 0.1	1.01
(PDBSMAM)	MeOH	Tröger base	49	(+) 1.5	1.12
((-)-Menthol)	Hexane	Stilbene oxide	34	(-) 0.4	1.02
	Hexane	Tröger base	45	(+) 0.2	1.01
Copolymer[b]	MeOH	Stilbene oxide	30	(-) 1.1	1.09
(BuPDBSMAM/	MeOH	Tröger base	34	(+) 2.2	1.15
(+)-NEMAM)	Hexane	Stilbene oxide	24	(+) 2.1	1.16
((-)-Menthol)	Hexane	Tröger base	22	(-) 1.3	1.12

[a] Obtained in a mixture of (+)- or (–)-menthol/toluene = 3/1 (v/v) at 60 °C. [b]BuPDBSMAM/(+)-NEMAM = 96/4 (mol/mol) in (-)-menthol at 0 °C. [c]Polymer = 20 mg; racemic analyte 0.05 mg (200 μl portion from a 0.25 mg/mL solution in methanol or hexane). [d]Determined by HPLC analysis of supernatant solution using a Chiralcel OD column; hexane/IPA (95/5); flow rate = 0.5 mL/min. [e]Calculated according to $\alpha = (F_{minor}(\%)/F_{major}(\%))/(A_{major}(\%)/A_{minor}(\%))$.

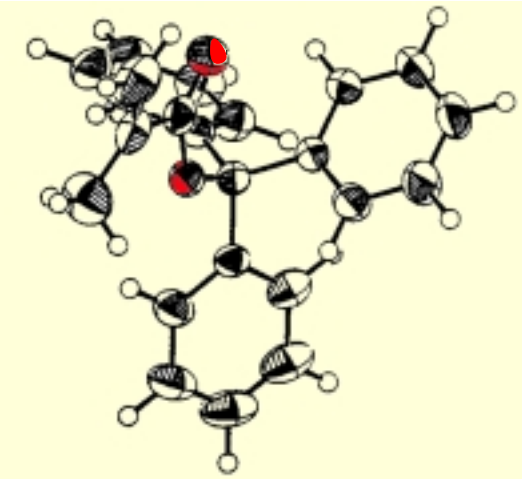
The chiral recognition ability of the optically active poly(PDBSMAM)s was evaluated by the chiral adsorption method[20] using *trans*-stilbene oxide and Tröger base as the racemates (Table 4-2). Each racemate was adsorbed by ca. 30 ~ 50 % on the optically active poly(PDBSMAM) in methanol and hexane. Although the e.e. was very low, the excess enantiomers were reversed depending on the chirality of the polymers. This suggests that the data are sufficiently reliable. The enantioselectivity of the poly(PDBSMAM)s is very low compared to that of the one-handed helical poly(TrMA) and poly(PDBSMA).[23] The propeller structure of the copolymer may not be suitable for high chiral recognitions.

The copolymer obtained from the radical copolymerization of BuPDBSMAM with (+)-NEMAM in the presence of (-)-menthol exhibited high optical activity and the CD intensity. The chiral adsorption experiment of the this highly optically active copolymer [BuPDBSMAM-*co*-(+)-NEMAM] was also carried out. The copolymer exhibited a lower chiral recognition than poly(TrMA),[23] although this chiral recognition seems to be higher than that by the poly(PDBSMAM) shown in Table 4-2, probably due to the higher one-handedness of the polymer.

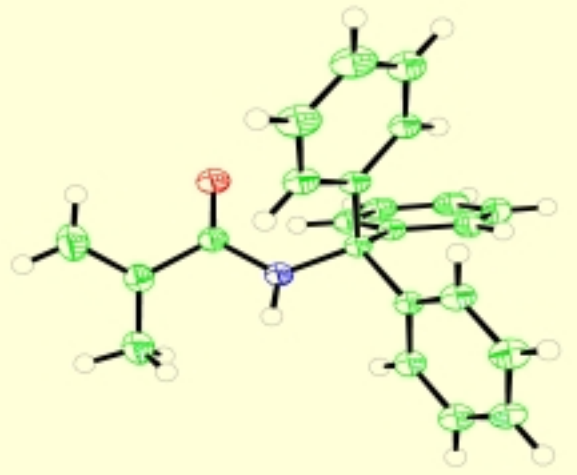
4-4. Structure of Monomers

The chiral recognition ability of the bulky poly(methacrylate)s[23] are much higher than that of bulky poly(methacrylamide)s.[22(b),(c)] The propeller structure of the bulky methacrylamides may not be suitable for high chiral recognition. This hypothesis became much clear when the crystal structures and the computer simulated structures of the bulky methacrylates and methacrylamides were compared.

X-ray Crystallographic Structures



TrMA



TrMAM

Comparison of the Structures of Monomers

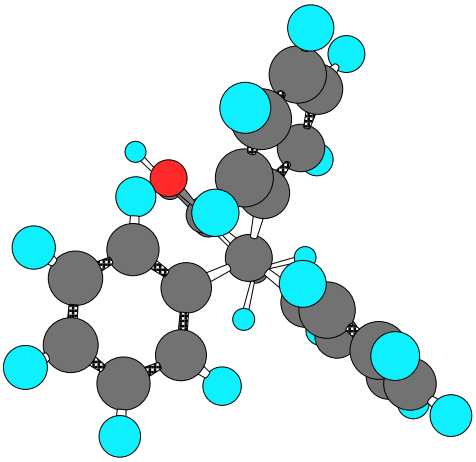
The computer simulated structures of the bulky methacrylates and methacrylamides were compared from three different angles as follows.

1. From Trityl Side of the Monomer
2. From Vinyl Side of the Monomer

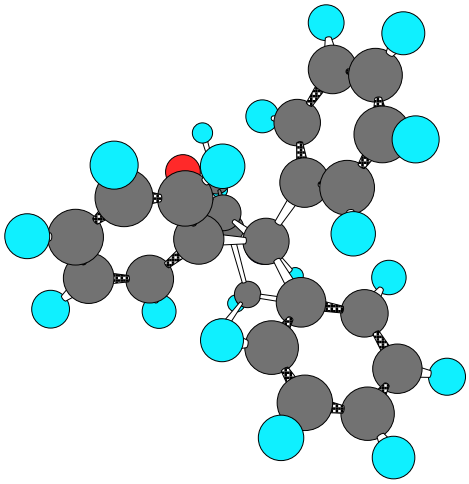
3. From One Side of the Monomer

The comparison of the structures of methacrylates and methacrylamides bearing trityl group and the suberyl group in the bulky side chain are as follows.

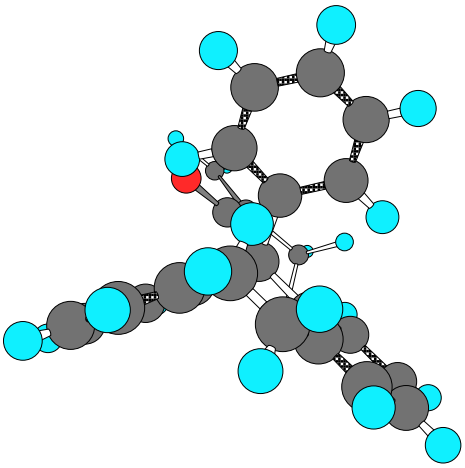
1. From Trityl Side of the Monomer



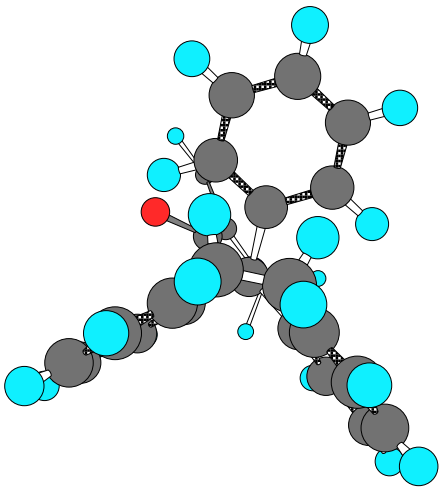
TrMA



TrMAM

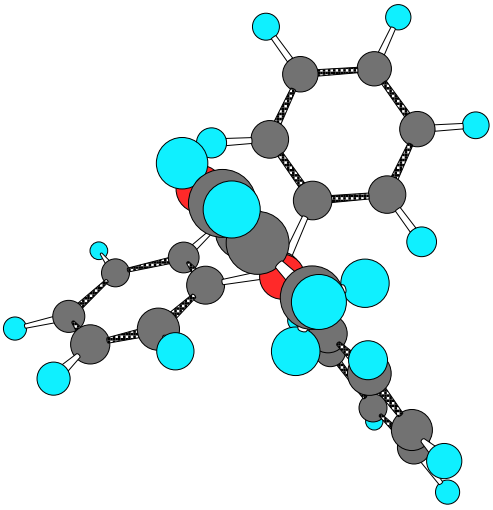


PDBSMA

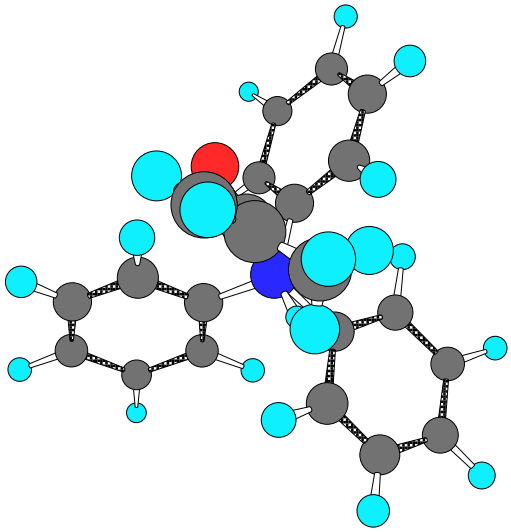


PDBSMAM

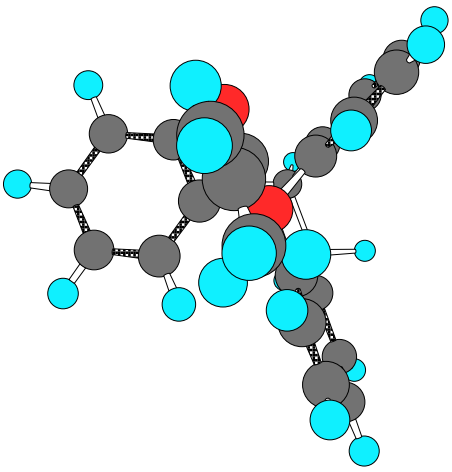
2. From Vinyl Side of the Monomer



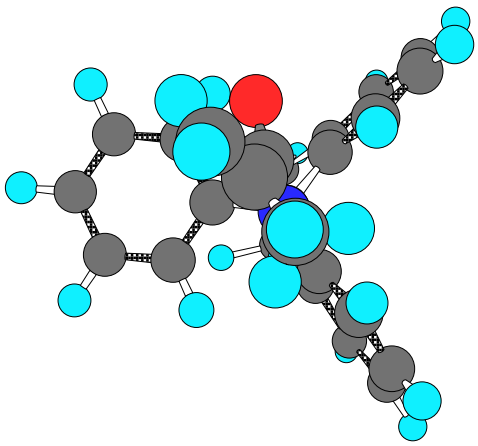
TrMA



TrMAM

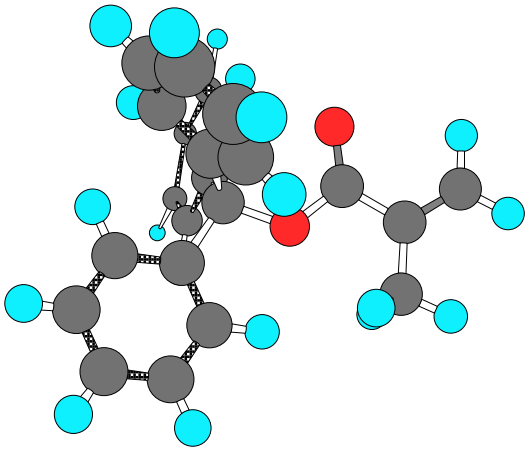


PDBSMA

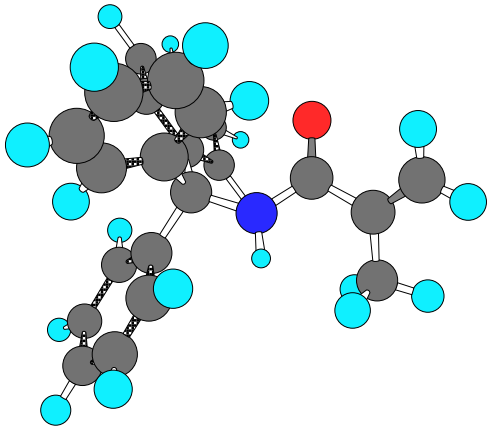


PDBSMAM

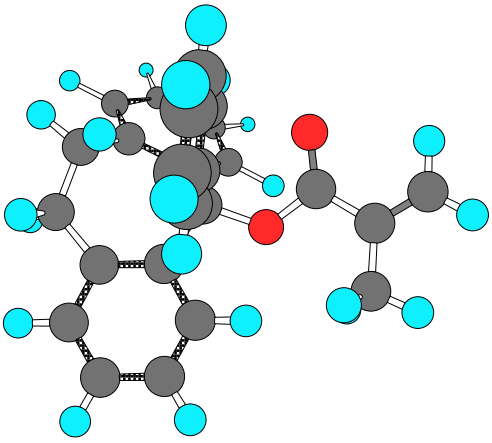
3. From One Side of the Monomer



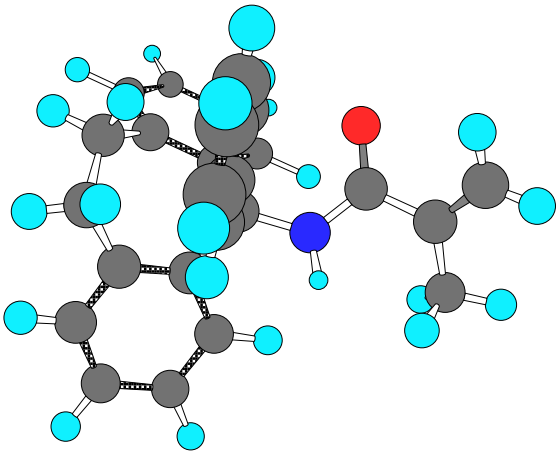
TrMA



TrMAM



PDBSMA



PDBSMAM

Although the side bulky groups for TrMA and TrMAM are the same trityl group, the propeller structures of these two trityl groups are different from each other. The propeller structure of the bulky methacrylamide (TrMAM) may not be suitable for high chiral recognition.[25]

On the other hand, the propeller structure of the 1-phenyldibenzosuberyl groups for PDBSMA and PDBSMAM are similar to each other. The methylene bridge between two phenyl groups in the bulky side group may restrict the free rotation of the phenyl groups and thus the propeller structure of the bulky side groups of PDBSMA and PDBSMAM were similar. The chiral recognition ability of the poly(PDBSMA)s were not high[23] and similar results were also observed for the poly(PDBSMAM)s.[22(c)]

4-5. Summery

The chiral recognition ability of poly(PDBSMAM)s, poly[BuTrMAM-*co*-NEMAM]s, and poly[BuPDBSMAM-*co*-(+)-NEMAM] were evaluated by the absorption method. These polymers showed much lower recognition compared to that of the one-handed helical poly(TrMA). The propeller structures of the bulky methacrylamides may not be suitable for high chiral recognition.

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List of Publications

[Papers]

(1) “Helix-Sense-Selective Free Radical Polymerization of *N*-(Triphenylmethyl)methacrylamide Derivatives”
A.K.M. Fakhrul Azam, Masami Kamigaito, and Yoshio Okamoto
Polym. J., **38**, 1035-1042 (2006).

(2) “Helicity Induction in *N*-[(4-Butyl)triphenylmethyl)]methacrylamide Sequence *via* Radical Copolymerization with Chiral Monomers”
A.K.M. Fakhrul Azam, Masami Kamigaito, Masashi Tsuji, and Yoshio Okamoto
Polym. J., **38**, 1173-1181 (2006).

(3) “Asymmetric Radical Polymerization and Copolymerization of *N*-(1-Phenyldibenzosuberyl)methacrylamide and Its Derivative Leading to Optically Active Helical Polymers”
A.K.M. Fakhrul Azam, Masami Kamigaito, and Yoshio Okamoto
J. Polym. Sci., Part A: Polym. Chem., in press.

[Other Related Papers]

(1) “Helix-Sense-Selective Radical Polymerization of Methacrylamides”
Yoshio Okamoto, Masami Kamigaito, Yukata Isobe, and A.K.M. Fakhrul Azam
Polym. Mater. Sci. Eng., **91**, 320 (2004).

(2) “Helix-Sense-Selective Anionic Polymerization of Bulky Methacrylamide Using Organozincate Having Sugar Residue”
Masashi Tsuji, A.K.M. Fakhrul Azam, Masami Kamigaito, and Yoshio Okamoto
in preparation.

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