

# Synthesis of a Novel Polymethacrylamide Bearing Cyclic Perfluoroalkyl Groups

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**ABSTRACT:** A novel chiral methacrylamide bearing perfluoropyrrolidino groups was synthesized. Perfluoro(2-pyrrolidinopropionyl fluoride), the starting material, was prepared by electrochemical fluorination and resolved into enantiomeric derivatives by preparative high performance liquid chromatography (HPLC) performed with optically active 1-phenethylamine as the diastereomeric counterpart. The polymethacrylamide was obtained by radical polymerization. A clear, colorless, tough film of the polymer was formed by the solution-casting technique, which showed excellent water repulsion with a contact angle of water greater than 100°. Column packings prepared by the coating of silica gels with the optically active polymer showed potential as the chiral stationary phase for HPLC resolving racemic 1,1'-bi-2-naphthol (separation factor = 1.56) with a hexane-isopropanol mixture as the eluent. © 2002 John Wiley & Sons, Inc. *J Appl Polym Sci* 83: 1443–1448, 2002

**Key words:** polymethacrylamide; perfluoroalkyl group; fluoropolymers; column packings; chiral stationary phase; chromatography

## INTRODUCTION

Acrylic and methacrylic polymers that have fluoroalkyl groups, usually polyfluorinated linear alkyl groups, are widely prepared because of their facile monomer synthesis and polymerization.<sup>1–3</sup> Their properties as repellents and optical,<sup>4,5</sup> lithographic,<sup>6</sup> and chromatographic materials<sup>7</sup> have been examined. Therefore, it is of interest to prepare novel fluorinated polymers that carry bulky cyclic perfluoroalkyl groups.

We report here the preparation and polymerization of a methacrylamide that bears the perfluoropyrrolidino group. Perfluoro(2-pyrrolidinopropionyl fluoride), the starting material, is readily prepared by electrochemical fluorination because the nitrogen atom restricts cyclization of the molecule during fluorination.<sup>8,9</sup> It can be re-

solved into enantiomeric derivatives by preparative high performance liquid chromatography (HPLC) performed with optically active 1-phenethylamine as the diastereomeric counterpart.<sup>10</sup> Such enantiomeric fluorinated compounds are useful derivatizing agents for optically active compounds because they give fluorinated diastereomers, in which optical purities can be determined by <sup>19</sup>F-NMR analysis.<sup>10–12</sup> In the preparation of polymethacrylamide, enantiomeric derivatives of perfluoro(2-pyrrolidinopropionyl fluoride) were used to obtain an optically active polymer whose property as the chiral stationary phase for HPLC could be examined.<sup>13,14</sup>

Polymethacrylamide bearing perfluoropyrrolidino groups was obtained by radical polymerization. The polymer film prepared by solution casting showed excellent water repulsion with a contact angle of water greater than 100°. Column packings prepared by the coating of silica gels with the polymer showed potential as the chiral stationary phase for HPLC.

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## EXPERIMENTAL

## Monomer Syntheses

*N*-(1-Phenethyl)perfluoro-2-pyrrolidinopropionamide

Diastereomeric *N*-(1-phenethyl)perfluoro-2-pyrrolidinopropionamides were prepared from perfluoro-2-pyrrolidinopropionyl fluoride and (-)-1-phenethylamine.<sup>10</sup>

<sup>1</sup>H-NMR [(CD<sub>3</sub>)<sub>2</sub>CO]: 9.19 (broad s, 2H), 7.44–7.25 (m, 10 H), 5.27–5.17 (m, 2H), 1.58 (d, 3H,  $J_d = 6.9$  Hz), 1.59 ppm (d, 3H,  $J_d = 7.2$  Hz). <sup>19</sup>F-NMR [(CD<sub>3</sub>)<sub>2</sub>CO]: -74.4 (m, 3F), -74.5 (m, 3F), -86.2 (dm, 2F,  $J_d = 171.4$  Hz), -85.8 (dm, 2F,  $J_d = 172.6$  Hz), -92.7 (dm, 2F,  $J_d = 171.4$  Hz), -93.1 (dm, 2F,  $J_d = 172.6$  Hz), -130.5 (dm, 2F,  $J_d = 246.4$  Hz), -130.3 (dm, 2F,  $J_d = 245.3$  Hz), -135.2 (m, 1F), -135.0 (m, 1F), -136.4 (dm, 2F,  $J_d = 246.4$  Hz), -136.7 ppm (dm, 2F,  $J_d = 245.3$  Hz).

The diastereomers were resolved by preparative HPLC in a silica gel column (Develosile, 60 (15/30); Nomura Chemical, Seto, Japan) with a hexane–isopropanol mixture as the eluent. The second eluted diastereomer [diastereomeric excess (de) > 98% (by <sup>19</sup>F-NMR)], consisting of (+)-perfluoro-2-pyrrolidinopropionic acid and (-)-1-phenethylamine, had a melting point of 124–125°C.

$[\alpha]^{20}$ : -63.40 (c. 1.7, dioxane). <sup>1</sup>H-NMR [(CD<sub>3</sub>)<sub>2</sub>CO]: 9.15 (broad s, 1H), 7.44–7.25 (m, 5H), 5.22 (m, 1H), 1.59 ppm (d, 3H,  $J_d = 7.2$  Hz). <sup>19</sup>F-NMR [(CD<sub>3</sub>)<sub>2</sub>CO]: -74.5 (m, 3F), -85.8 (dm, 2F,  $J_d = 173.9$  Hz), -93.1 (dm, 2F,  $J_d = 173.9$  Hz), -130.3 (dm, 2F,  $J_d = 245.4$  Hz), -135.0 (m, 1F), -136.7 ppm (dm, 2F,  $J_d = 245.4$  Hz).

## Perfluoro-2-pyrrolidinopropionamide

A mixture of optically resolved *N*-(1-phenethyl)perfluoro-2-pyrrolidinopropionamide (13.9 g, 30.1 mmol;  $[\alpha]^{20} = -63.40$ , c. 1.7, dioxane; de > 98%) and concentrated sulfuric acid (20 mL) was stirred at room temperature overnight.<sup>12</sup> Ice water was added to the homogenized mixture, and the oily organic layer obtained was treated several times with ether. The ether solutions were combined, washed with aqueous sodium carbonate, and dried over anhydrous magnesium sulfate. Ether was removed under reduced pressure, giving the amide, which was further purified by recrystallization from a hexane–ethyl acetate mixture (10.6 g, 98% yield).

mp: 114–115°C.  $[\alpha]^{20}$ : +12.1 (c. 1.9, dioxane). IR (KBr): 3430, 3360, 3290, 3205, 1690 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.54 ppm. <sup>19</sup>F-NMR (CDCl<sub>3</sub>): -75.3 (m,

3F), -86.8 (dm, 2F,  $J_d = 177.4$  Hz), -94.1 (dm, 2F,  $J_d = 177.4$  Hz), -130.8 (dm, 2F,  $J_d = 246.9$  Hz), -133.6 (m, 1F), -137.3 ppm (dm, 2F,  $J_d = 246.9$  Hz). Mass spectrometry (MS): 339 [M-F]<sup>+</sup>.

## Perfluoro-2-pyrrolidinopropionitrile

A mixture of perfluoro-2-pyrrolidinopropionamide (10.6 g, 29.6 mmol) and phosphorous pentoxide (16.8 g, 120 mmol) was heated gradually to 260°C.<sup>15,16</sup> Dehydration and simultaneous distillation gave the nitrile as a colorless liquid (7.33 g, 72% yield). It was purified by redistillation.

bp: 84.5–85°C.  $[\alpha]^{20}$ : +3.55 (c. 4.4, CHCl<sub>3</sub>). IR (neat): 2270 cm<sup>-1</sup>. <sup>19</sup>F-NMR (CDCl<sub>3</sub>): -78.2 ppm (m, 3F), -88.7 (dm, 2F,  $J_d = 172.4$  Hz), -90.9 (dm, 2F,  $J_d = 172.4$  Hz), -28.5 (m, 1F) -132.6 (dm, 2F,  $J_d = 240.6$  Hz), -134.0 (dm, 2F,  $J_d = 240.6$  Hz). MS: 321 [M-F]<sup>+</sup>.

1*H*,1*H*-Perfluoro-2-pyrrolidinopropylamine

Perfluoro-2-pyrrolidinopropylamine (3.40 g, 10.0 mmol) in ether (6 mL) was added dropwise to a suspension of lithium aluminum hydride (0.80 g, 21 mmol) in ether (18 mL) at -10°C under an argon atmosphere. After additional stirring at room temperature overnight, water (0.8 mL), 15 wt % aqueous sodium hydroxide (0.8 mL), and water (2.4 mL) were added successively to the stirred, cooled reaction mixture under an argon atmosphere. Precipitates were removed by filtration, after which the filtrate was dried with anhydrous magnesium sulfate. After removal of the ether under reduced pressure, the amine was obtained by distillation (1.64 g, 48% yield).

bp: 61°C at 57 Torr.  $[\alpha]^{20}$ : -0.35 (c. 9.4, dioxane). IR (neat): 3430, 3350, 2970, 2880, 1640 cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.42 ppm (d, CH<sub>2</sub>,  $J = 20.9$  Hz), 1.36 (broad s, NH<sub>2</sub>). <sup>19</sup>F-NMR (CDCl<sub>3</sub>): -80.4 ppm (m, 3F), -84.7 (dm, 2F,  $J_d = 177.4$  Hz), -92.5 (dm, 2F,  $J_d = 177.4$  Hz), -131.4 (dm, 2F,  $J_d = 249.3$  Hz), -134.2 (dm, 2F,  $J_d = 249.3$  Hz), -158.9 (m, 1F). MS: 325 [M-F]<sup>+</sup>.

*N*-(1*H*,1*H*-Perfluoro-2-pyrrolidinopropyl)methacrylamide (RfMA)

Methacryloyl chloride (1.60 g, 15.3 mmol) in ether (5 mL) was added dropwise at 0°C under an argon atmosphere to an ether solution (15 mL) of 1*H*,1*H*-perfluoro-2-pyrrolidinopropylamine (4.05 g, 11.8 mmol), excess triethylamine (1.8 g, 18 mmol), and a trace of 2,6-di-*tert*-butyl-*p*-cresol. The resulting mixture was stirred at room tem-

perature, washed with water, and concentrated by evaporation of the ether. Distillation of the residue over ferric chloride(III) under reduced pressure gave RfMA (4.10 g, 84% yield).

bp: 51.5–53°C at 0.08 Torr.  $[\alpha]^{20}$ : +2.37 (c. 4.8, dioxane). IR (neat): 3320, 1680, 1640  $\text{cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 5.98 ppm (broad s, NH), 5.71 (m, CH=), 5.44 (m, CH=), 3.80–4.50 (m,  $\text{NCH}_2$ ), 1.98 (m,  $\text{CH}_3$ ).  $^{19}\text{F-NMR}$  ( $\text{CDCl}_3$ ): -80.5 ppm (m, 3F), -84.7 (dm, 2F,  $J_d = 176.1$  Hz), -92.5 (dm, 2F,  $J_d = 176.1$  Hz), -131.2 (dm, 2F,  $J_d = 249.3$  Hz), -134.5 (dm, 2F,  $J_d = 249.3$  Hz), -157.2 (m, 1F). MS: 412  $[\text{M}]^+$ .

### Polymerization

RfMA (1.20 g, 2.91 mmol) in tetrahydrofuran (THF; 0.6 mL) and  $\text{CCl}_2\text{FCClF}_2$  (0.6 mL) was polymerized *in vacuo* at 60°C for 24 h in a glass ampule with 2,2'-azobisisobutyronitrile (AIBN; 2.23 mg, 0.0136 mmol) and hexanethiol (9.61 mg, 0.0813 mmol). The poly(RfMA) that formed was precipitated in methanol and purified by reprecipitation (0.78 g, 65% yield).

$[\alpha]^{20}$ : -16.4 (c. 5.0,  $\text{CCl}_2\text{FCClF}_2$ ).  $^1\text{H-NMR}$  (1/1 THF- $d_6$ / $\text{CCl}_2\text{FCClF}_2$ ): 0.90 [t,  $\text{CH}_3(\text{CH}_2)_5\text{S}$ ,  $J = 6.75$  Hz], 1.25–1.40 [m,  $\text{CH}_3(\text{CH}_2)_4\text{CH}_2\text{S}$ ], 1.45–1.60 (m,  $\text{C}_5\text{H}_{11}\text{CH}_2\text{S}$ ), 0.60–1.60 (m,  $\text{CH}_3$ ), 1.60–3.20 (m,  $\text{CH}_2$ ), 3.40–5.00 (m,  $\text{NCH}_2$ ), 6.30–7.60 ppm (m, NH).

### Preparation of the Chiral Stationary Phase for HPLC

Macroporous, spherical silica gels (Merck LiChrospher Si 1000, Whitehouse Station, NJ; mean particle size = 10  $\mu\text{m}$ , mean pore diameter = 100 nm, specific surface area = 20  $\text{m}^2/\text{g}$ ) were silane-coupled with dimethoxydiphenylsilane before the absorption of poly(RfMA). The silica gel particles (10.0 g) were dispersed in toluene (250 mL), and traces of water were removed by azeotropic distillation of the toluene. Dimethoxydiphenylsilane (5 mL) was added to the residue (ca. 25 mL), and the mixture was refluxed for 12 h under an argon atmosphere. Particles collected by filtration and dried *in vacuo* at 60°C for 2 days gave silane-coupled gels (10.9 g).

The gels (2.4 g) were allowed to absorb poly(RfMA) (0.60 g) in  $\text{CCl}_2\text{FCClF}_2$  (10 mL). After evaporation of the solvent at room temperature, the residue was dried *in vacuo* overnight.

The modified silica gels obtained were packed in a stainless steel column [25  $\times$  0.46 (inner di-

ameter) cm] by the slurry method at 300  $\text{kgf}/\text{cm}^2$  with hexane as the packing fluid. The theoretical plate number of the column for benzene was 1200 at a flow rate of 1.0 mL/min in hexane.

### Instruments

Diastereomeric amides were resolved on a Shimadzu LC-8A preparative liquid chromatograph equipped with a silica gel column [Develosile (60 (15/30); Nomura Chemical, Seto, Japan)]. IR spectra were obtained with a Shimadzu FTIR-8600PC spectrophotometer (Kyoto, Japan). Mass spectra were taken with a Shimadzu QP-5000 instrument at 70 eV.  $^1\text{H-NMR}$  (300.0 MHz) and  $^{19}\text{F-NMR}$  (282.2 MHz) measurements were recorded on a Varian Unity Inova-300 (Palo Alto, CA), the chemical shifts being defined as  $\delta$  values relative to TMS and  $\text{CFCl}_3$ , respectively. Specific optical rotations were measured with a Jasco DIP-370 (Tokyo, Japan) with 589-nm light at 20°C. Gel permeation chromatography (GPC) was performed with a Tosoh HLC-802A (Tokyo, Japan; Tosoh GMH6 columns with THF as an eluent). Thermal decomposition temperatures of polymers were measured with a Seiko I&E TG20 thermogravimeter (Chiba, Japan). The contact angles of water droplets to polymer film surfaces were measured with a Erma G-1 goniometer (Tokyo, Japan).

Liquid chromatography with the column we prepared was accomplished on a Jasco PU-980 pump and a Tosoh UV-8000 detector.

## RESULTS AND DISCUSSION

The monomer was synthesized according to Scheme 1. Diastereomeric *N*-(1-phenethyl)perfluoro-2-pyrrolidinopropionamides prepared from perfluoro-2-pyrrolidinopropionyl fluoride and (-)-1-phenethylamine were resolved by preparative HPLC in a silica gel column with a hexane-isopropanol mixture as the eluent. The second eluted diastereomer (de > 98% by  $^{19}\text{F-NMR}$ ), consisting of (+)-perfluoro-2-pyrrolidinopropionic acid and (-)-1-phenethylamine, was used in the following reaction. The resolved amide was converted to the primary amine, which reacted with methacryloyl chloride to give the optically active monomer.

Radical polymerization of the fluoroalkylated methacrylamide, RfMA, was done *in vacuo* at 60°C in THF and  $\text{CCl}_2\text{FCClF}_2$  with AIBN as the initiator and hexanethiol as the chain-transfer





Table I Polymerization of Methacrylamide Bearing the Perfluoropyrrolidino Group (RfMA)<sup>a</sup>

Feed					Polymer					
RfMA (g)	MMA (g)	C <sub>6</sub> H <sub>13</sub> SH (mol %)	AIBN (mol %)	THF/CCl <sub>2</sub> FCClF <sub>2</sub> (mL)	Time (h)	Yield <sup>b</sup> (g)	RfMA (mol %)	M <sub>n</sub>	θ <sup>c</sup> (degrees)	T <sub>d</sub> <sup>d</sup> (°C)
1.20	—	2.8	0.47	0.6/0.6	24	0.78	—	3.3 × 10 <sup>4,e</sup>	103	305
1.50	—	—	2.00	1.0/1.0	8	1.15	—	insoluble	—	—
0.80 (1.9 mmol)	0.20 (2.0 mmol)	3.0	0.45	0.6/0.6	48	0.65	63 <sup>e</sup>	1.4 × 10 <sup>4,f</sup>	101	282
0.80 (1.9 mmol)	0.58 (5.8 mmol)	—	2.00	1.4/—	3	0.45	insoluble	—	—	294

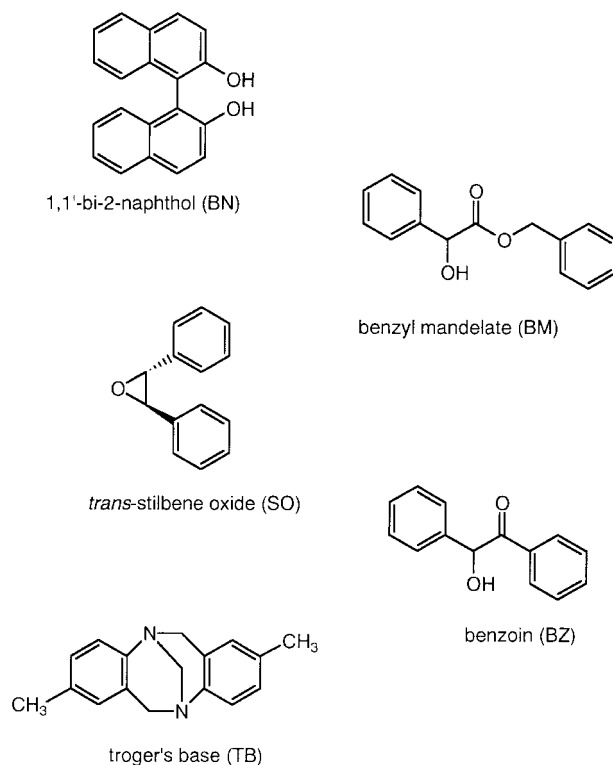
<sup>a</sup> *In vacuo* at 60°C.<sup>b</sup> Methanol-insoluble part.<sup>c</sup> Contact angle of the water droplet to the polymer film.<sup>d</sup> 10% weight loss temperature in air.<sup>e</sup> Determined by <sup>1</sup>H-NMR.<sup>f</sup> Determined by GPC correlated to standard polystyrenes for the THF-soluble part.

Figure 1 Racemate structures.

be the main adsorbing force, the reason BZ and BM were not resolved may be that methylene spacers existed between the chiral centers and amide groups in the polymer.

The best resolution for BN was achieved with 2.0 vol % isopropanol in hexane as the eluent, which gave a separation factor  $\alpha$  of 1.56 (Fig. 2).

Spherical porous beads of heptadecafluorodecyl acrylate polymer are prepared and used as column packings.<sup>7</sup> This stationary phase is highly efficient for separating fluorinated compounds in reverse-phase liquid chromatography, which is indicative of a specific fluorine-fluorine interaction between the stationary phase and solutes.

The column we prepared appreciably retained the fluorinated compounds, such as hexafluorobenzene (retention time = 6.56 min), trifluoromethylbenzene (retention time = 5.65 min), and *p*-bis(trifluoromethyl)benzene (retention time = 7.32 min), in comparison with benzene (retention time = 5.17 min) and toluene (retention time = 5.22 min), with 50 vol % acetonitrile in water as the eluent (flow rate = 0.50 mL/min).

The highly fluorinated racemic compounds 4-(perfluoro-2-pyrrolidinopropionyloxy)phenol and 4'-(perfluoro-2-pyrrolidinopropionyloxy)-4-biphenol, however, were not resolved by the column

**Table II Chromatographic Resolution of Racemates by the Chiral Polymethacrylamide-Absorbed Column**

Racemates	$t_1$ (min)	$t_2$ (min)	$k_1$	$k_2$	$\alpha$
SO	10.43	—	0.03	—	1
TB	14.79	—	0.45	—	1
BN	17.23	19.23	0.70	0.89	1.28
BZ	20.46	—	1.01	—	1
BM	20.94	—	1.06	—	1

At 25°C; eluent = 0.5 vol % isopropanol in hexane; flow rate = 0.25 mL/min; dead time ( $t_0$ ) = 10.17 min;  $k_1 = (t_1 - t_0)/t_0$ ,  $k_2 = (t_2 - t_0)/t_0$ ;  $\alpha = k_2/k_1$ .

with either a hexane–isopropanol mixture or an acetonitrile–water mixture as the eluent. In the reverse-phase system, BN also was not resolved. Nonpolar interaction between the stationary phase and racemic compounds appears to be ineffective as the adsorbing force for chiral recognition in this column.

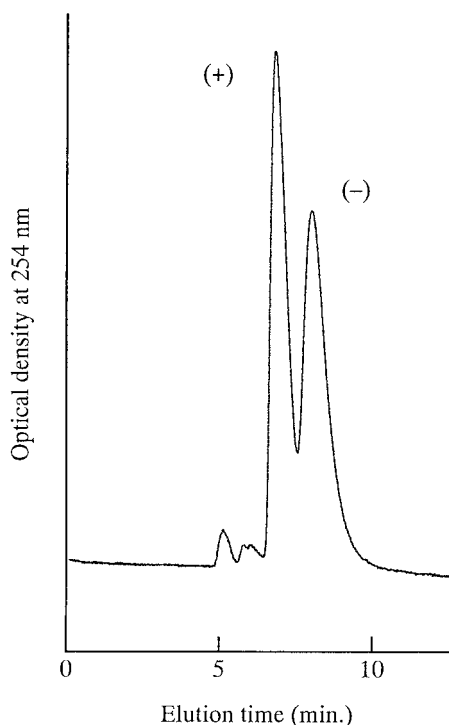
## CONCLUSIONS

A novel chiral methacrylamide bearing perfluoropyrrolidino groups was synthesized. Its ho-

mopolymer and copolymer with MMA were obtained by radical polymerization. Clear, colorless, tough films of these polymers were formed by the solution-casting technique. Large contact angles of water to the film surfaces were observed. The homopolymer shows potential use as a chiral stationary phase in liquid chromatography.

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**Figure 2** Chromatographic resolution of BN (eluent = 2.0 vol % isopropanol in hexane; flow rate = 0.50 mL/min; temperature = 25°C;  $t_0$  = 4.99 min;  $t_1$  = 6.75 min;  $t_2$  = 7.74 min;  $\alpha$  = 1.56).