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Helix-Sense-Selective Polymerization of 2-(6-Methylpyridyl)diphenylmethyl Methacrylate

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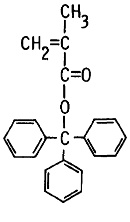
ABSTRACT: 2-(6-Methylpyridyl)diphenylmethyl methacrylate (MPyDMA) was synthesized and polymerized with chiral anionic initiators, organolithium complexes of (2*S*,3*S*)-(+)-1,4-bis(dimethylamino)-2,3-dimethoxybutane (DDB) and (2*S*,3*S*)-(+)-2,3-dimethoxy-1,4-dipiperidinobutane (DPB). The obtained polymer showed a large optical rotation due to prevailing one-handed helical structure. The polymerization of MPyDMA was affected by the addition of a polar compound, piperidine but the extent was less than the polymerization of diphenyl-2-pyridylmethyl methacrylate (D2PyMA). Low-molecular-weight poly(MPyDMA) decreased its optical activity in chloroform. This may be due to a stereomutation with helix–helix transition. Optically active poly(MPyDMA) exhibited lower optical resolving power as a chiral stationary phase for HPLC than poly(D2PyMA).

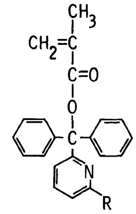
KEY WORDS Optically Active Polymer / Helix-Sense-Selective Polymerization / Anionic Polymerization / 2-(6-Methylpyridyl)diphenylmethyl Methacrylate / Stereomutation of Polymer / Helix–Helix Transition / Optical Resolution / Chiral Stationary Phase /

Triphenylmethyl methacrylate (TrMA) and diphenyl-2-pyridylmethyl methacrylate (D2-PyMA) are the special monomers which give isotactic, helical polymers by anionic polymerization.[1-7] The helical structures of the polymers are stable even in solution because of the bulkiness of the ester groups. Optically active poly(TrMA) and poly(D2PyMA) are known to be useful chiral stationary phases for high-performance liquid chromatography (HPLC), and can resolve many racemic compounds which are difficult to resolve by the other methods.[3,8-11]

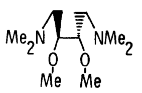
The optical rotatory power of the polymers is dependent on one-handedness of the helix. Pure one-handed helical poly(TrMA) of high optical activity can be obtained by helix-sense-selective polymerization with chiral anionic initiators such as (−)-sparteine-fluorenyllithium (FlLi) and (2*S*, 3*S*)-(+)-1,4-bis(dimethylamino)-2,3-dimethoxybutane (DDB)-*N*,*N*′-diphenylethylenediamine monolithium amide (DPEDA-Li) complexes in toluene at low temperature.[1,2] On the other hand, these chiral initiators are not so useful for the helix-sense-selective polymerization of D2PyMA, giving a mixture of (+)- and (−)-poly(D2-PyMA)s.[3,4] This low selectivity has been ascribed to the existence of polar 2-pyridyl group which can coordinate with Li cation during the polymerization. Poly(D2PyMA) is conformationally less stable compared with poly(TrMA) probably because of the lack of



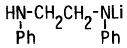
TrMA



D2PyMA, R = H
MPyDMA, R = Me



(+)-DDB



$\underset{Ph}{HN}-CH_2CH_2-\underset{Ph}{NLi}$

DPEDA-Li

one hydrogen at ortho position, and therefore low-molecular-weight polymer exhibited the stereomutation through helix–helix transition in solution.[12]

In order to investigate the role of the 2-pyridyl group, in this study, we synthesized a new monomer 2-(6-methylpyridyl)diphenylmethyl methacrylate (MPyDMA), and investigated its helix-sense-selective polymerization, stability of the helix, and the chiral recognition ability of the polymer.

EXPERIMENTAL

Materials

2-(6-Methylpyridyl)diphenylmethanol was prepared by the reaction of ethyl 6-methylpicolinate with two equiv. of phenylmagnesium bromide in dry ether. The obtained alcohol was recrystallized from methanol: mp 101—102°C (lit.[13] 88—89°C); high-resolution mass spectrum, obsd 275.1307, calcd for $C_{19}H_{17}NO$ 275.1310.

The alcohol obtained was treated with thionyl chloride and triethylamine in dry benzene to obtain 2-(6-methylpyridyl)diphenylmethyl chloride. The crude chloride in dry ether was added dropwise to a dispersion of silver methacrylate in dry ether under refluxing in the dark. After separation of silver chloride by filtration, the ether was evaporated to yield a crude product which was recrystallized from ether and hexane; mp 118.5—119.5°C; ^1H NMR ($CDCl_3$): 7.71—7.34 (m, 13H), 6.32 (s, 1H), 5.64 (s, 1H), 2.53 (s, 3H); high-resolution mass spectrum, obsd 343.1559, calcd for $C_{23}H_{21}NO_2$ 343.1572.

The preparation and purification of other materials were described previously.[3,4]

Polymerization

The polymerization was carried out in a glass ampule under dry nitrogen. An initiator solution was prepared at room temperature and added to the monomer solution cooled to -78°C.[3] The reaction was terminated with a small amount of methanol. The polymer was precipitated in a large amount of methanol and separated by centrifugation as quickly as possible.

Poly(MPyDMA) was converted to poly(methacrylic acid) by refluxing in methanol containing a small amount of hydrochloric acid. Poly(methacrylic acid) obtained was treated with diazomethane to convert it to poly(methyl methacrylate). The degree of polymerization (DP) and tacticity of poly(D2PyMA) were estimated by GPC and ^1H NMR analyses of the resulting poly(methyl methacrylate), respectively.

Chiral Stationary Phase

The chiral stationary phase for HPLC was prepared in the manner as reported previously.[3,11] Macroporous silica gel (Merck LiChrospher SI-1000; particle size, 10 μm; pore size, 100 nm) was treated with 3-aminopropyltriethoxysilane. (+)-Poly(MPyDMA) (0.6 g, No. 3 in Table I) was dissolved in chloroform (10 ml) and coated on the silanized silica gel (3.0 g). The stationary phase obtained was packed in a stainless steel tube (25 × 0.46 (i.d.) cm) by slurry method. The plate number of the column for acetone was 3700. Dead time was estimated to be 6.4 min using water as a non-retained compound.

Solvolysis

The solvolysis of MPyDMA was performed in an NMR tube at 35°C.[14] MPyDMA was dissolved in CD_3OD–$CDCl_3$ (1 : 1) ([MPyDMA] = 0.41 mol l^{-1}) and the reaction was monitored by ^1H NMR spectroscopy. The conversion of reaction was determined by the intensity measurement of the olefinic proton signals of MPyDMA and methacrylic acid formed.

Measurement

^{1}H NMR spectra were taken on a JNM-MH-100 (100 MHz) spectrometer. Optical rotation was measured on a JASCO DIP-181 polarimeter in chloroform. Circular dichroism spectra were recorded on a JASCO J-40 CD apparatus equipped with a computerized data processor. Chromatography was conducted on a JASCO TRIROTAR-II chromatograph equipped with UV (UVIDEC-100-III) and polarimetric (DIP-181C) detectors. For optical resolution, methanol (flow rate, 0.5 ml min^{-1}) was used as an eluent at 15°C. The GPC analysis of poly(MPyDMA) was performed on a couple of columns, Shodex GPC K-802.5 (30 cm) and AC-80M (50 cm) with chloroform (1.0 ml min^{-1}) as the eluent.

RESULTS AND DISCUSSION

Table I shows the results of polymerization of MPyDMA with three chiral initiators. All the polymers were optically active. Since the poly(methyl methacrylate) derived from these polymers exhibited very low optical activity ($[\alpha]^{25}_{365} < 5°$), the high optical activity of poly(MPyDMA) is attributed to the prevailing one-handed helical structure similarly to those of poly(TrMA) and poly(D2PyMA). (+)-DDB-DPEDA-Li exhibited high helix-sense-selectivity, giving the polymer of higher optical rotation (*ca.* +1000°). This value is greater than that of poly(D2PyMA) ($[\alpha]^{25}_{365}$ 600—800°).[3] Figure 1 shows the GPC curve of (+)-poly(MPyDMA) (No. 2 in Table I) obtained with (+)-DDB-DPEDA-Li. The GPC was monitored with UV and polarimetric detectors. This reveals that the (+)-poly(MPyDMA) obtained with (+)-DDB consisted of two components as observed for (+)-poly(D2PyMA) obtained with the same initiator[3]: (−)-polymer of high molecular weight

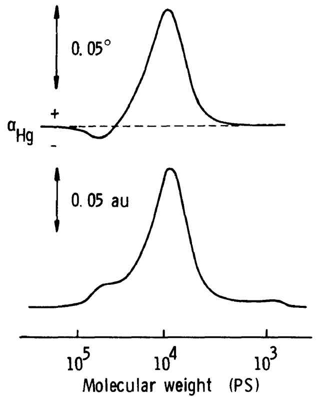


Figure 1. GPC curve of (+)-poly(MPyDMA) (No. 2 in Table I, $[\alpha]^{25}_{365}$ +1001°). Column, Shodex GPC K-802.5 (30 cm)+AC-80M (50 cm); eluent, $CHCl_3$ (1.0 ml min^{-1}).

Table I. Polymerization of MPyDMA with DPEDA-Li in toluene at −78°C[a]

Run	Ligand	[MPyDMA]/[Li]	Time h	Yield %	DP	$[\alpha]^{26}_{365}$
1	(+)-DDB	10	1.7	84	25	+964
2	(+)-DDB	20	5.3	100		+1001
3[b]	(+)-DDB	20	5.0	100	51	+950
4	(+)-DPB	20	2.5	100		−1203
5	(+)-DDEP	20	4.0	82		+552
6	(+)-DDEP	40	12.3	69		+489
7	(+)-DDEP	40	168	100		+426

[a] MPyDMA 0.15 g, toluene 3.0 ml, [Ligand]/[Li] = 1.2.

[b] MPyDMA 1.5 g, toluene 15 ml, tacticity (%) of the polymer I : H : S = 97 : 2 : 1.

and (+)-polymer of low molecular weight. However, the intensity ratio of the chromatogram for (+)- to (−)-poly(MPyDMA) is larger than that for (+)-poly(D2PyMA).[3,4] Figure 2 shows the CD spectrum of (+)-poly(MPyDMA) (No. 3 in Table I). The bands at 250—320 nm are attributed to the absorption of aromatic group and the band around 220 nm carbonyl group. Very weak peaks around 280—310 nm are ascribed to the absorption due to the fragment of the DPEDA-Li attached to α-end of the polymer. The broad positive spectral pattern in the region of 215—275 nm is comparable to that of (+)-poly(D2PyMA).[3] This suggests optically active (+)-poly(MPyDMA) has a helical structure similar to that of (+)-poly(D2PyMA). The chiral ligands, (+)-DPB and (+)-DDEP are more effective for the helix-sense-selective polymerization of D2PyMA than DDB.[3,4] (+)-DPB gave the poly(MPyDMA) of high optical rotation (−1203°). This value is greater than that of poly(D2PyMA) (−1108°) obtained with the same initiator. However, (+)-DDEP did not work well, giving the polymer of rather low optical rotation.

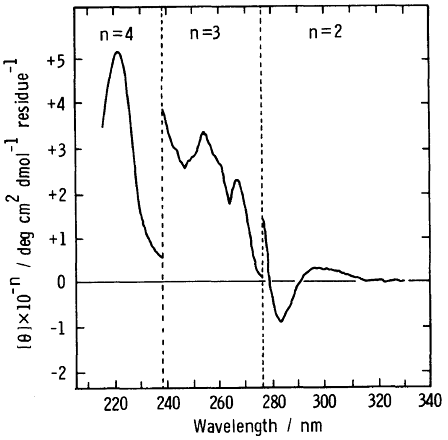
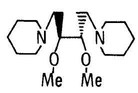
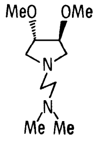


Figure 2. CD spectrum of (+)-poly(MPyDMA) (No. 3 in Table I) in $CHCl_3$.



(+)-DPB



(+)-DDEP

In the previous study,[3] the optical rotation of poly(D2PyMA) was greatly influenced by the unknown factors. This has been attributed to the contamination of a trace amount of a polar impurity. Table II shows the effect of a

Table II. Polymerization of methacrylates with DDB-DPEDA-Li-piperidine in toluene at −78°C[a]

Monomer	(g)	DDB	[piperidine]/[Li]	Time h	Yield %	$[\alpha]^{25}_{365}$	DP	Tacticity/% I	H	S
D2PyMA[b]	1.0	−	0	4	96	−590°[c]	66	95	4	1
D2PyMA[b]	1.0	+	0.01	4	99	+44°[c]	61	94	5	1
D2PyMA[b]	1.0	+	0.1	4	100	−63°[c]	79	85	12	3
TrMA[d]	3.0	−	0	4	100	−1253°[e]	44	>98		
TrMA[d]	1.0	−	0.1	4	100	−1320°[e]	50	>98		
TrMA[d]	1.0	−	1.0	4	100	−814°[e]	45	90	7	3
MPyDMA	1.5	+	0	5	100	+950	51	97	2	1
MPyDMA	0.15	+	0.01	24	97	+864	64	97	2	1
MPyDMA	0.15	+	0.1	24	97	+458	69	95	4	1

[a] [Monomer] = 0.05 g ml^{-1}, [Monomer]/[Li] = 20, [DDB]/[Li] = 1.2.

[b] Data from ref 3.

[c] In $CHCl_3$–2,2,2-trifluoroethanol (9 : 1).

[d] The DP and tacticity are estimated after excluding the oligomer (*ca.* 10%).

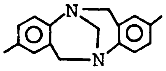
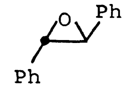
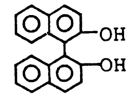
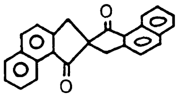
[e] In tetrahydrofuran.

polar additive, piperidine, on the polymerization of the methacrylates. Addition of piperidine to the initiator solution of (+)-DDB-DPEDA-Li resulted in a decrease of optical rotation and isotacticity of the polymers. In the polymerization of D2PyMA, the addition of even 1 mol% of piperidine to Li cation resulted in the formation of the almost optically inactive polymer, and the addition of 10 mol% of piperidine brought about the lowering of isotacticity of poly(D2PyMA). The polymerization of TrMA was much less affected by piperidine, and the addition of 10 mol% did not change the optical activity and isotacticity of the polymer obtained. The influence of piperidine on the polymerization of MPyDMA was between those for D2PyMA and TrMA. Therefore, the polymerization of MPyDMA was more easily reproduced than that of D2PyMA. The introduction of 6-methyl group may reduce the coordination ability of 2-pyridyl group due to steric hindrance. This may result in improvement of the reproducibility of the polymerization.

The solvolysis of MPyDMA in CD_3OD–$CDCl_3$ was measured by ^1H NMR spectroscopy. First-order rate constant of the solvolysis was determined to be $k_1 = 0.055\,h^{-1}$ which was obtained from the equation, $d[MPyDMA]/dt = k_1[MPyDMA]$, assuming that $[CD_3OD]$ is constant. The half-life period of this reaction was 756 min. The rate constant is about one fiftieth that of TrMA and about two times that of D2PyMA.[11] This suggests that poly(MPyDMA) may show similar resistance to poly(D2PyMA) in the solvolysis by methanol.

The low-molecular-weight poly(MPyDMA) gradually decreased its optical activity in solution. The optical rotation (+964°) of poly(MPyDMA) (No. 1 in Table I) decreased to +251° for 4 h in $CHCl_3$ at 60°C. The original polymer and polymer after change of optical activity showed the almost same GPC curves. The latter may still have a helical conformation. Low-molecular-weight poly(MPyDMA) probably undergoes the helix-helix transition (stereomutation) similarly to poly(D2PyMA).[12] In the case of poly(D2PyMA), the polymer with a low optical activity was separated into (+)- and (−)-fractions by HPLC using optically active poly(TrMA) bonded to silica gel[15] as the chiral stationary phase. However, in the case of poly(MPyDMA) such a separation could not be attained. The existence of the 6-methyl group appears to prevent the effective chiral interaction between poly(TrMA) and poly(MPyDMA).

Table III. Optical resolution of racemates on (+)-poly(MPyDMA)

Racemate	k_1'[a]	α[b]	R_s[c]
	0.36 (+)	1.24	0.65
	0.46 (−)	1.23	0.61
	0.63	1	0
	1.98 (−)	1.67	1.58

[a] Capacity factor and optical rotatory power of first eluted enantiomer.
[b] Separation factor.
[c] Resolution factor.

Table III shows the results of optical resolution of four racemic compounds by (+)-poly(MPyDMA). The chiral recognition ability of the poly(MPyDMA) was lower than that of poly(D2PyMA).[11] Optically active poly(tris(*m*-tolyl)methyl methacrylate) also exhibited lower chiral recognition ability than poly(TrMA).[10] Again, the existence of a methyl group may prevent interaction between the chiral propellers of triarylmethyl groups of the polymers and racemates. This interaction probably is most important to attain effective chiral recognition.

The introduction of a methyl group at the 6-position of the pyridyl group of D2PyMA leads to more steady formation of the polymer with higher one-handed helicity in comparison with D2PyMA itself. However, the polymer showed lower optical resolving power than poly(D2PyMA), probably because of steric hindrance.

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