Synthesis and polymerization of novel N-substituted maleimides containing an oxazoline group

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Summary

A novel type of maleimide-based monomers, N-[o-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)phenyl]maleimide (DMOPMI), (±)-N-[o-(4-ethyl-4,5-dihydro-1,3-oxazol-2-yl)phenyl]maleimide ((±)-EOPMI), and (R)-N-[o-(4-ethyl-4,5-dihydro-1,3-oxazol-2-yl)phenyl]maleimide ((R)-EOPMI), were synthesized for the first time. Their polymerization behavior was studied briefly by both radical and anionic initiating mechanisms. The results indicated that the addition polymerization takes place mainly in the vinylene group without appreciable side reactions. The polymerization in low polar media tended to increase molecular weights or optical activity of the obtained polymers.

Introduction

There have been a number of reports on synthesis and polymerization of N-substituted maleimide derivatives (RMI) [1-6]. Generally, the polymerization of RMI proceeds via stereoregularity of *trans*-addition giving the polymer of threo-diisotactic and threo-disyndiotactic structures. The polymers of threo-disyndiotactic structure cannot exhibit optical activity because of the equivalence of chiral stereogenic centers (S,S) or (R,R) in the structure of the polymer. Chiroptical properties of poly(RMI) could be attributed to threo-diisotactic structures, which arise from the excess of chiral stereogenic centers (S,S) or (R,R) [7,8]. In the case of chiral RMI monomers bearing α-amino acid residues, (R)-α-methylbenzyl, l-menthyl, and cholesteryl groups [9-12], the chiroptical property of the resultant polymers was ascribed to asymmetric induction of the side chain chromophores. More recently, some chiral initiators have been developed for the asymmetric polymerization of N-substituted maleimides [13-18].

Oxazoline derivatives have gained importance as valuable auxiliary in organic synthesis especially in asymmetric transformations [19-21], however, they were seldom used for making maleimide-based monomers [22]. It is therefore considered of interest to introduce a chiral oxazolinyl group to the maleimide skeleton preparing a new type of monomers. We believe that these compounds should be useful monomers for examining the asymmetric induction effect during polymerization. Furthermore, it is expected that the combination of an optically activity and metal complexation will

impart potentially useful properties to the final materials. As preliminary studies, we synthesized three N-substituted maleimide derivatives from maleic anhydride and 2-(o-aminophenyl)oxazolines. The polymerization was achieved for these oxazoline-containing monomers under the radical or anionic initiating conditions, yielding optically active/non-optically active polymers with the integrity of oxazoline residue.

Experimental

Materials

All chemicals were of reagent grade and used without further purification. 2-Aminoalcohols, isatoic anhydride, and hexamethyldisilane were purchased from Aldrich Chemicals. Other chemicals were purchased from Shanghai Reagent Co. Solvents were purified in the usual manner and dried by refluxing over sodium and distilled prior to use.

Synthesis of monomer (5)

To a stirred solution of 2-(o-aminophenyl)oxazolines (3) (0.05 mol) in ethyl ether (50 ml), Et_2O solution of maleic anhydride (5.88 g, 0.06 mol, 150 mL) was added and allowed to reaction at room temperature for 4 h. The resulted precipitate (4) was filtered and dried (> 90% yield), which was suitable for use in the next step without purification. Both melted $ZnCl_2$ (0.02 mol) and 4 (0.02 mol in 40 ml THF) were placed in a three-necked flask fitted with a thermometer and a Vigreux column. The mixture was heated up to 55~60°C under nitrogen and then into the resulting solution was added dropwise hexamethyldisilane (0.03 mol) in anhydrous THF (10 mL) over a period of 30 min. After stirring at 60°C for a further 1 h, the reaction mixture was cooled and filtered to remove the non-dissoluble matter. The organic solution was dried over anhydrous magnesium sulfate and concentrated using an evaporator. The pure products were obtained by column chromatography on silica gel (70:30 hexane/ethyl acetate eluent) in moderate yield.

Polymerization procedure

The polymerization was carried out using Schlenk techniques in a dry nitrogen atmosphere. The given amount of monomer (1.0 g) was placed in a Schlenk tube, solvent (3~5 ml) and initiator solution (2~5 mole-% of monomer) were successively injected by a syringe with stirring. After a certain time, the reaction mixture was poured into a large amount of methanol and stood for 1~2 h. The precipitated polymer was separated by suction filtration, washed with methanol and then dried. Purification of the product was performed with reprecipitation from a THF-methanol system three times and dried under vaccum at 30°C for 2 days.

Characterization

^{1}H NMR spectra were recorded on a Bruker Avance AMX-500 NMR instrument in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. A Bruker Vector 22 Fourier Transform Infrared (FT-IR) spectrometer was applied for recording spectra in KBr

pellets or films. Elemental analysis was performed on a Parloerba EA1110. The molecular weight and polydispersity of polymers were determined by gel permeation chromatography (GPC) using a Waters 208 GPC apparatus (THF as eluent at a flow rate of 1.0 ml/min). The GPC chromatogram was calibrated against standard polystyrene samples. Specific optical rotation ($[\alpha]^{25}_D$) in THF was measured at 25°C with a Jasco DIP-140.

Results and discussion

Scheme 1 shows the synthetic route for oxazoline-containing N-phenylmaleimides (**5**). 2-(*o*-Aminophenyl)oxazoline (**3**), as an intermediate, was synthesized from isatoic anhydride and different 2-aminoalcohols according to the reported method [23, 24]. In general, N-substituted maleimides can be prepared by the reaction of maleic anhydride with primary amines, followed by the cyclodehydration of the resulting N-substituted maleamic acid. Usually, sodium acetate and acetic anhydride were used to carry out the imidization. However, in the case of synthesizing oxazoline substituted N-phenylmaleimides by this general method the purification turned out to be problematic so that the yield was very low. To improve this synthesis, some modification was made based on the literature procedure [25, 26]. The present method, in which melted $ZnCl_2$ and hexamethyldisilane (HMDS) were used in the imidization step, could give higher yields. The results are summarized in Table 1. The desired compounds have been structurally confirmed by FT-IR, ^{1}H NMR, and elemental analysis. As expected, the reaction between maleic anhydride with (R)-2-(4-ethyl-4,5-dihydro-1,3-oxazol-2-yl)aniline (**3c**) yielded optically active product (R)-EOPMI (**5c**).
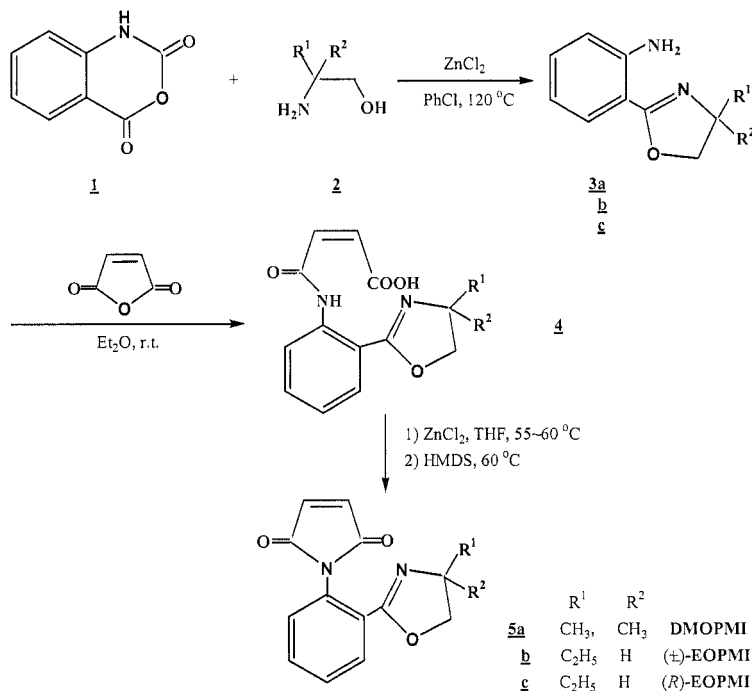
Scheme 1. Synthetic route for monomers (**5a-b**)

Table 1. The results on synthesis of oxazoline-substituted N-phenylmaleimides

Product	Yield (%)	Mp (°C)	E.A., % Found (Calcd.)[a]	^{1}H NMR (CDCl$_3$, ppm)[b]	$[\alpha]_D$[c] /deg.
5a	52	111-113	C 66.65 (66.40) H 5.22 (5.26) N 10.36 (10.32)	1.24 (s,CH$_3$), 3.96 (s, CH$_2$), 6.83 (s, =CH), 7.30 (d, ArH), 7.48-7.59 (m, ArH), 8.02 (d, ArH)	—
5b	55	87-89	C 66.75 (66.40) H 5.32 (5.26) N 10.34 (10.32)	0.92 (t,CH$_3$), 1.53 (m, CH$_2$), 3.86 (t, CH), 4.09 (m, -OCH$_2$), 4.31 (t, -OCH$_2$), 6.82 (s, =CH), 7.29 (d, ArH), 7.47-7.59 (t, ArH), 8.02 (d, ArH)	—
5c	50	—[d]	C 66.55 (66.40) H 5.27 (5.26) N 10.33 (10.32)	0.90 (s, CH$_3$), 1.51 (m, CH$_2$), 3.86 (t, CH), 4.08 (m, -OCH$_2$), 4.49 (t, -OCH$_2$), 6.82 (s, =CH), 7.29 (d, ArH), 7.48-7.58 (t, ArH), 8.02 (d, ArH)	(+)-68.4

[a] Elemental analysis was performed on a Parloerba EA1110; [b] ^{1}H NMR spectra were recorded on a Bruker Avance AMX-500 NMR instrument with TMS as internal standard; [c] D-Line specific rotations were measured with a Jasco DIP-140 (Japan Spectroscopic Co.), 1.0 g/dl, EtOH, 25°C; [d] No measurement for the matter was sticky solid at room temperature.

Table 2. Polymerization of oxazoline-substituted N-phenylmaleimides [a]

No.	Monomer	Initiator	Temp (°C)	Solvent[b]	Yield[c] (%)	M_w[d] (10^3)	M_w/M_n[d]	$[\alpha]^{25}_D$[e] /deg.
1	**5a**	AIBN	60	THF	67.2	1.34	1.09	–
2	**5a**	AIBN	60	Tol.	90.0	2.70	1.24	
3	**5a**	n-BuLi	0	THF	65.5	3.62	1.50	–
4	**5a**	n-BuLi	0	THF-Tol. (2:1)	96.3	9.93	1.79	–
5	**5b**	AIBN	60	THF	85.4	1.38	1.08	–
6	**5b**	n-BuLi	0	THF	79.3	1.47	1.26	–
7	**5c**	AIBN	60	THF	34.0	2.19	1.43	(+)-34.0
8	**5c**	n-BuLi	0	THF	76.5	1.30	1.21	(+)-11.8
9	**5c**	n-BuLi	0	THF-Tol. (2:1)	47.2	1.26	1.08	(+)-33.8

[a] Initiator: 5 mole-%; solvent 5 mL. Monomer: 1.0 g, reaction time 24 h. [b] Tol.:toluene; [c] Insoluble in CH$_3$OH; [d] By GPC; [e] c = 1.0 g/dL, THF, l = 10 cm

To examine the polymerization reactivity of these monomers, both radical and anionic polymerizations were performed with AIBN or n-BuLi as an initiator. Table 2 shows the polymerization results under different reaction conditions. All the polymerizations proceeded homogeneously throughout except in toluene at 0°C. In comparison with runs 1-4 in Table 2, the yield and molecular weight of polymers prepared in toluene or

THF-toluene were higher than those obtained in THF regardless of initiating systems, which suggests that solvents with low polarity seemed to favor the polymerization. However, such a tendency was not observed in the case of **5c** (runs 8 and 9) and this chiral monomer exhibited lower polymerization reactivity than other monomers, but the reason for this has not been clarified.

In all cases the polymers obtained as white or yellowish powders and exhibited relatively low molecular weights ($M_w = 1.3-9.9\times10^3$). The M_w of the polymer varied depending on reaction conditions, which means that accidental quenching of initiator or growing anion could take place. The accidental quenching may result from some side reactions such as an attack of the propagating species on the carbonyl group. This observation was similar to that in the polymerizabilities of reported other N-substituted maleimides [15].

It is also noteworthy that the specific optical rotation of poly(R-EOPMI) obtained by n-BuLi in THF-toluene (2:1) was high as compared with those prepared in THF, although they had nearly same molecular weights (runs 8 and 9 in Table 2). If the optically activity was attributed to only an optically active oxazolinyl group, the polymer prepared in THF-toluene should possess more perfect threo-diisotactic structure than those via anionic or radical polymerization in THF. This assumption may be reasonable because asymmetric anionic polymerizations are usually carried out in nonpolar solvents at low temperature [18]. Certainly, the specific rotation of resulting poly(R-EOPMI)s was relatively low probably due to the weaker asymmetric induction since the chiral carbon is far from the maleimide ring.

Figure 1 shows FT-IR spectra of monomer EOPMI (**5b**) together with its polymers obtained with AIBN and n-BuLi, respectively. It can be seen that spectra for the two polymers were almost identical in terms of their absorption position and fashions, which suggests that both polymers have almost similar structures. Comparing with the spectrum of monomer, the absorptions at 1645 (C=N), 1056 (C-O-C), and 952 cm^{-1} from oxazoline skeleton retained in the spectra for polymers. The characteristic absorption band of C=C linkage at 826 cm^{-1} from imide ring nearly disappeared in the polymer's spectra. On the other hand, no olefinic proton resonance was evident in the ^{1}H NMR spectra for the polymers as shown in Figure 2. The methine signals of main chain merged with that of oxazoline ring to form a broad band from 3 to 5 ppm. These results indicate that the addition polymerization mainly took place in the C=C double bond of the maleimide ring. Additionally, a reported investigation may provide further supports for the above conclusion, in which it was demonstrated that cationic catalysts can bring about a ring-opening polymerization for 2-substituted 2-oxazolines while no polymers produced with anionic catalysts such as potassium methylate and n-butyl lithium [27].

As described in the experimental part, the polymer was separated by addition of a large excess of methanol to the reaction medium. The evaporation of the filtrate gave a small amount of residue mainly containing monomer. These polymer samples were soluble in ordinary solvent such as THF, dioxane, chloroform, and acetone. Typical GPC traces are presented in Figure 3. The polymers prepared by different initiators have a narrower polydispersity. However, the GPC curve of the anionically polymerized product exhibited a bimodal pattern with a shoulder peak, which may correspond to oligomers. It seems that the chain transfer tendency or some side reactions were comparatively strong in the case of anionic polymerizations for the
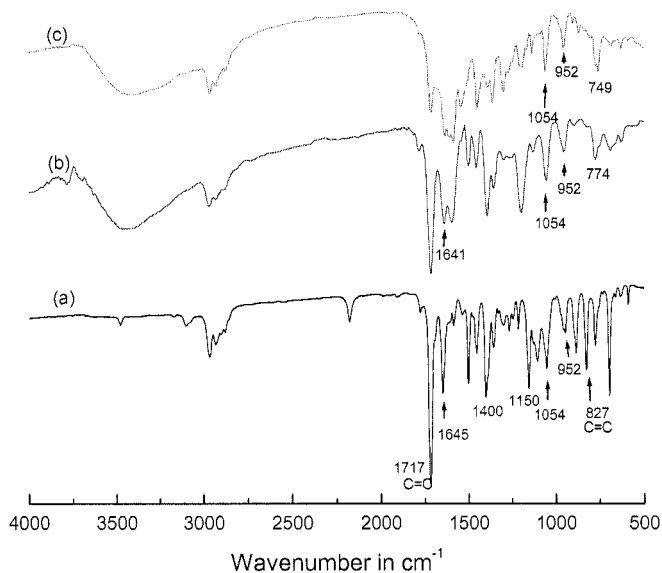
monomers.

Figure 1. FT-IR spectra of monomer (±)-EOPMI (a) and its polymers obtained with (b) AIBN and (c) n-BuLi in THF, respectively.
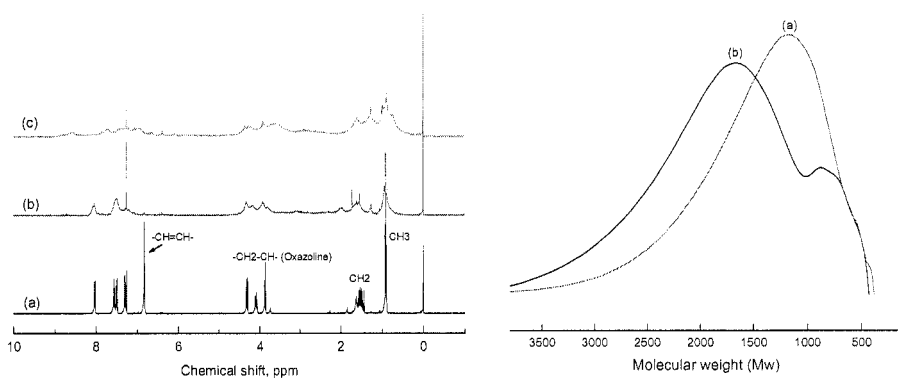

Figure 2. ^{1}H NMR of monomer (±)-EOPMI (a) and its polymers obtained with (b) AIBN and (c) n-BuLi, respectively.

Figure 3. GPC curves for the poly(EOPMI)s obtained with (a) AIBN and (b) n-BuLi in THF (see: runs 5 and 6 in Table 2)

Conclusions

A novel type of maleimide-based monomers with an oxazoline residue was successfully synthesized. Preliminary studies indicated that an ordinary addition polymerization took place in the vinylene group in spite of a radical or anionic

mechanism yielding polymers with the integrity of oxazoline skeleton. It is feasible to use solvents with low polarity for obtaining polymers of higher molecular weight or of higher specific optical rotation. Further investigations on both chiroptical property and chelation to metal ions of the polymers are in progress.

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