Synthesis of Polyesters Using an Organic Catalyst and Design of Polyester-based Double Network Gels

有機触媒を用いたポリエステルの合成とポリエステルを基盤としたダブルネットワークゲルの設計

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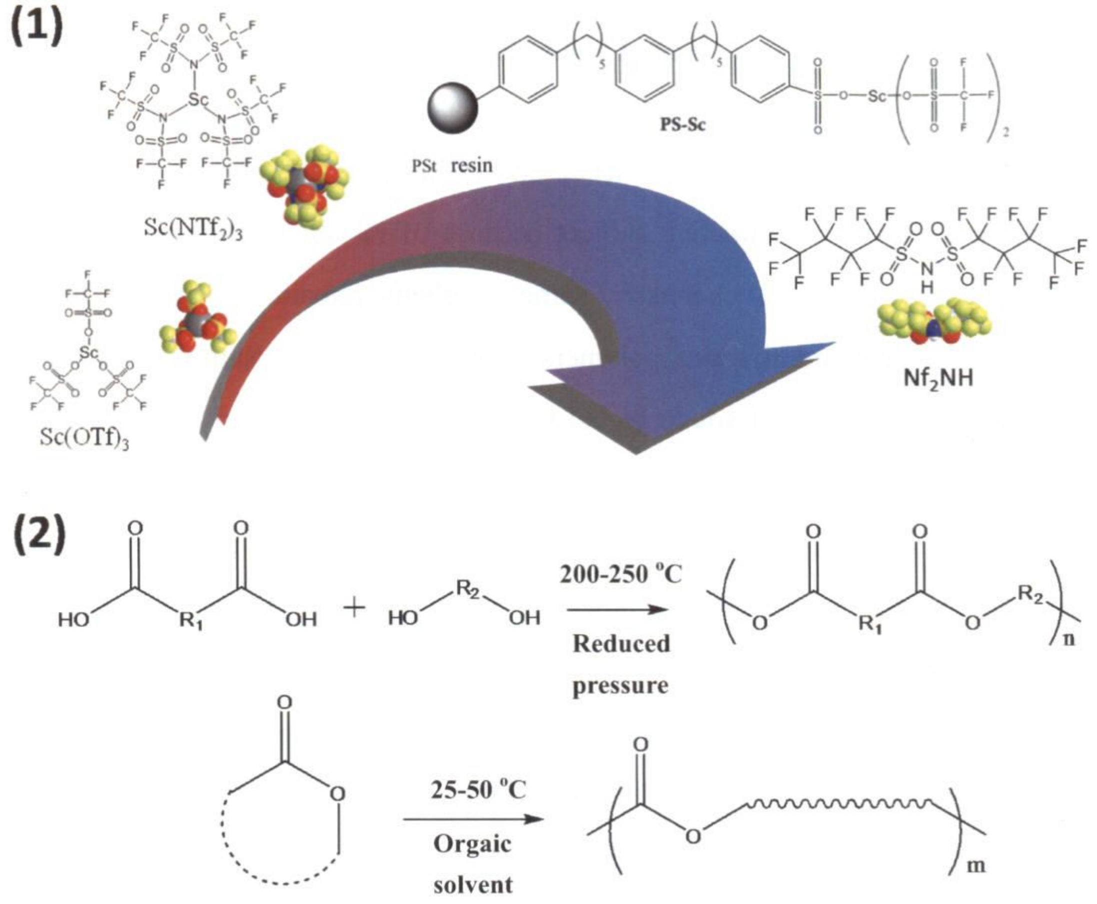
General Introduction

Nowadays, as the development of science and technology, the polymer chemistry has also grown progressively up to an attractive subject because of its ubiquitous applications. However, according to concepts of green chemistry, some problems remain during the production and recycling process of these multifarious polymers. Such as energy consumption of the production releases gas contaminations that leads to global warming. As illustrated in Figure 1, an increase in global temperature causes glaciers to melt and the sea levels to rise. The homeless bear in Figure 1 (a) is sad and helpless. Meanwhile, gas contaminations in Figure 1 (b) also increase the risk of human life. In the last decades, the destructive power of white pollution greatly surpassed many other pollution sources to our world (Figure 1 c). As professor Paul T. Anastas in Yale University said, *Human beings are at the centre of concerns for sustainable developments — they are entitled to a healthy and productive life in harmony with nature.*[1] Our researchers have the responsibility for the conservation of environment and the green chemistry attracts more and more attention.


(a) global warming (b) gas contaminations (c) white pollution

Figure 1. The global warming, gas contaminations, and white pollution in nowadays (the pictures were found from www.google.com).

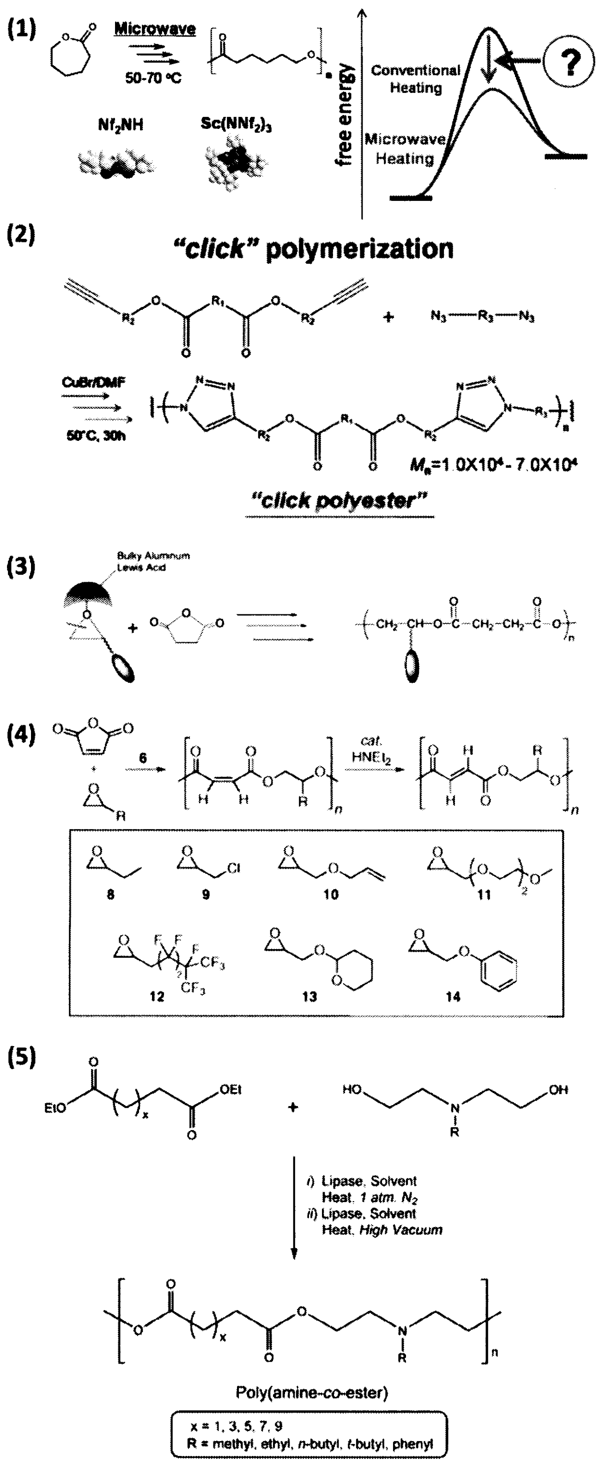
In the field of polymer chemistry, the solutions to these concerns above could be summarized as three points. First of all, ideally, the polymers whose main chains can be degraded are urgently needed. Secondly, the metal-free catalyst should be investigated instead of metal catalyst. Thirdly, the method of the polymerization should be improved, which including reaction temperature, side reaction products, atom economy and so on. In the general introduction, I will introduce the three aspects briefly.



Scheme 1. (1) The development of catalysts in polyester chemistry of our group. (2) The two traditional methods to manufacture aliphatic polyesters. Polycondensation of dicarboxylic acids with diols (Upper) and ring-opening polymerization of cyclic esters (Lower).

The degradable materials, which will replace of traditional plastic, aliphatic polyesters, such as polylactide (PLA), polycaprolactone (PCL), poly(butylene succinate) (PBS), poly(ethylene succinate) (PES), and poly(butylene glutarate) (PBG), are receiving much attention as the important biomaterials[2] because of their biodegradability,[3] biocompatibility,[4] and acceptable mechanical strength.[5] As a result, they are preferred over conventional plastics such as polypropylene and polyethylene in industries related to drug delivery systems,[6] tissue engineering,[7] and commodity materials.[8] One of the key points in synthetic chemistry of aliphatic polyesters is catalyst. Many researchers foucs on the discovering new catalysts. In this decades, metal catalysts were used as efficient catalysts. In our group, the rare-earth elements-based catalyst such as scandium trifluoromethanesulfonate [Sc(OTf)$_3$] and scandium trifluoromethanesulfonimide [Sc(NTf$_2$)$_3$] were first used in polycondensation of dicarboxylic acids with diols[9] and ring-opening polymerization of cyclic esters.[10] Next, in order to simplify the recycle procedure, a polymer-supported catalyst containing Scandium (PS-Sc), which consist of polystyrene (PS) and $Sc(OTf)_3$ were used in ring-opening polymerization of ε-caprolactone.[11] However, these metal-based catalysts are toxic and expensive, and also have metal residue in the products after the polymerization. It is dangerous if these products are used as biomaterials. Thus, we started to investigate an organic catalyst, nonafluorobutanesulfonimide (Nf_2NH).[12] Except for this catalyst, other groups also are interested in organic catalyst (trifluoromethanesulfonimide (Tf_2NH))[13] and enzyme catalyst (Lipase).[14] They are all considered to be environment-friendly.

As we described before, there are many kinds of catalyst, but the aliphatic polyesters have been mostly manufactured via two traditional methods. They are polycondensation of dicarboxylic acids with diols and ring-opening polymerization of cyclic esters. The method of polycondensation requires high reaction temperature (200-250 °C) [see Scheme 1, (2) upper]. Even we published a series papers using rare-earth triflates and trflyimides to decrease the reaction temperature (60-80 °C), the reactions still need highly reduced pressure.[9] Comparing with polycondensation, the ring-opening polymerizations of cyclic esters, such as ε-caprolactone[10,12] and lactide,[13] avoid reduced pressure and can be carried out under mild conditions (25-50 °C) [see Scheme 1, (2) down]. In our group, Yamada investigated the microwave-enhanced polycondensation of dicarboxylic acids with diols and ring-opening polymerization of cyclic esters. In his research, he successfully decreased the reaction energy and improved the reaction speed by microwave-assisted method [Scheme 2 (1)].[15] However, due to the availability of narrow range of monomers, only a few polymeric materials were obtained by this method and organic solvents should be used during the reactions. Thus, many groups have been devoting their time and effort to develop new environment friendly methods for synthesizing aliphatic polyesters. Nagao has reported preparation of click polyesters via well-known click reactions. And in his study, with a high molecular weight in a excellent yield, the triazole ring formation in the polymer structure leads to the improvement of thermal properties and enhancement of the even-odd effect of methylene chain length of the produced click polyesters [Scheme 2 (2)].[16] To avoid energy input and enhance the atom economy, Takasu have already prepared polyesters with carbohydrate unit by ring-opening alternating copolymerization of succinic anhydrides with sugar-substituted epoxides using bulky aluminum Lewis acid as the catalyst [Scheme 2 (3)].[17] Even though the asymmetric epoxidation method opened up the possibility of producing isotactic-rich polyesters with pendant sugar, this system still needed long reaction time (72 h), high reaction temperature (100 °C), and limited architecture based on three-membered cyclic ether (i.e, epoxide). Currently, a million tons of maleic anhydride (MAn) are produced yearly and some of them are converted into unsaturated polyesters. Coates and his coworkers reported the ring-opening copolymerization of maleic anhydride with a variety of epoxides catalyzed by a chromium(III) salen complex, which leads to high M_n and narrow PDI of products. A quantitative isomerization of the *cis*-maleate form to the *trans*-fumarate analogues in the polyester was carried out to synthesize high molecular weight poly(propylene fumarate) [Scheme 2 (4)].[18] Even the MAn is used to synthesize polyesters in polyester chemistry, the itaconic anhydride (IAn), an unsaturated cyclic anhydride prepared from fermentation of biomass resources, still is not widely polymerized via a efficient method due to its unstable double bonds, which can lead to cross-linking during polymerization. Moreover, various kinds of polymers containing amine functional groups were considered to be nonviral carriers for DNA (or gene) delivery. However, few strategies were efficient for preparation of amino-containing polyesters. As I mentioned before, most of catalysts for polycondensation of aliphatic polyesters are metal catalysts or Brϕnsted acids, but these catalysts could be deactivated by amino-containing monomers. Jiang and coworkers synthesized poly(amine-co-esters) via copolymerization of diester with amino-substituted diol using lipase as catalyst. Even though the



Scheme 2. Synthesis of functional polyesters based on green polymer chemistry

enzyme was used as environmentally benign for polyester preparation, the reactions condition was still uneconomical: 80 °C, 1atm nitrogen, 24 h for the first stage oligomerization; 80 °C, 1.6 mmHg vacuum, 72 h for the second stage polymerization [Scheme 2 (5)].[14] After the Michael reactions were discovered by Arthur Michael, following researchers regenerated and improved them, such as Skoloff and Latschinoff, who reported the hetero-Michael addition for the first time.[19] As the Michael additions are stable under air or water environment, high functional group tolerance, a large amount of polymerizable monomers and functional precursors as well as high conversions and favorable reaction rates, they were considered as the most important bond forming strategies for both carbon-carbon and carbon-heteroatom bonds in organic chemistry. Thus, these commonly termed conjugate additions have gained much more attention as strategies of amino-containing polymer synthesis or modification of macromolecular architectures. Daniel G. Anderson and his cooperators used poly(beta-amino ester)s as delivery agents for suicide gene therapy for cancer.[20] To generate degradable poly(beta-amino ester)s, the reaction at high temperamture (95 °C) was performed for 12 h, or at low temperature (60 °C), 2 days was needed. Thus to find a new way, environment-friendly and economical, for synthesis of polyesters is a hot subject so far. To bridge these gaps as I mentioned, I investigated new methods to synthesis of polyesters. In this thesis, I focus on a new organic catalyst, nonafluorobutanesulfonimide (Nf_2NH). In chapter 1, I described a new polymerization of cyclic anhydrides with tetrahydrofuran (THF) under mild conditions to synthesis of polyesters and poly(ester-ether)s. This reactions could be carried out under low temperature and without high pressure. In chapter 2, I chose diols as one of the monomers instead of THF to be copolymerized with cyclic anhydrides.

As we well to know, the linear polyesters could be polymerized via different reactions, however, their mechanical strengths are not high enough for further applications. This barrier has been broken by the historic synthesis of interpenetrating polymer networks (IPNs) by Millar in 1960 [21]. IPNs, combining of two or more polymer networks, are prepared as the strategy that at least one polymer cross-linked in the presence of the other network(s). They can be used for numerous applications due to their strong mechanical strength, excellent thermotolerance, and ideal swelling capacity. Since then, many papers including reviews were published[22]. Recently years, for the continuous development of IPNs, double network (DN) concept was observed in many works. Among these, it has been described that DN gels consisting of two interpenetrating networks can achieve the improved mechanical properties and adjust the balance between rigidity and toughness by control the structures of macromolecules. Gong and her coworkers created a series of modified DN hydrogels,[23] with optimized structures, performed excellent properties. However, these multi-step methods for preparing IPNs or DN gels still have some limitations. First of all, these preparing processes are complicated and time-consuming. The two networks of DN gels were all created by the free radical polymerization, so first network and second network should be created respectively, which takes about 2 days. So, the one-pot strategy was really desired. Secondly, due to the free radical polymerization, limited monomers can be used for the synthesis. Thus the structure of the network was limited. Thirdly, it is difficult to control the molecular weight of the main chain and exactly molar ratio of the networks. Furthermore, the report refer to one-pot method to prepare aliphatic polyester based DN gel is not found until now. Even though some papers referred to polyester based IPNs have been reported, but these methods were time consuming. To find a simple method for Preparation of DN gels at room temperature and without any catalyst is very interesting work. In chapter 3, I combined the Michael reaction with UV-initiated polymerization to synthesize polyesters containing amino group. And I also investigated a new one-pot method to prepare hydrophilic or hydrophobic Double-network gels with high mechanical strengths.

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Chapter 1

Synthesis of Periodic Copolymers via Ring-Opening Copolymerizations of Cyclic Anhydrides with Tetrahydrofuran Using Nonafluorobutanesulfonimide as an Organic Catalyst and Subsequent Transformation to Aliphatic Polyesters

ABSTRACT

To synthesize polyesters and periodic copolymers catalyzed by nonafluorobutanesulfonimide (Nf_2NH), we performed ring-opening copolymerizations of cyclic anhydrides with tetrahydrofuran (THF) at 50-120 °C. At high temperature (100-120 °C), the cyclic anhydrides, such as succinic anhydride (SAn), glutaric anhydride (GAn), phthalic anhydride (PAn), maleic anhydride (MAn), and citraconic anhydride (CAn), copolymerized with THF via ring-opening to produce polyesters (M_n=0.8-6.8×10^3, M_n/M_w=2.03-3.51). Ether units were temporarily formed during this copolymerization and subsequently, the ether units were transformed into esters by chain transfer reaction, thus giving the corresponding polyester. On the other hand, at low temperature (25-50 °C), ring-opening copolymerizations of the cyclic anhydrides with THF produced poly(ester-ether) (M_n=3.4-12.1×10^3, M_w/M_n=1.44-2.10). NMR and MALDI-TOF mass spectra revealed that when toluene (4 M) was used as a solvent, GAn reacted with THF (unit ratio: 1:2) to produce periodic copolymers (M_n=5.9×10^3, M_w/M_n=2.10). We have also performed model reactions to delineate the mechanism by which periodic copolymers containing both ester and ether units were transformed into polyesters by raising the reaction temperature to 120 °C.

1-1. Introduction

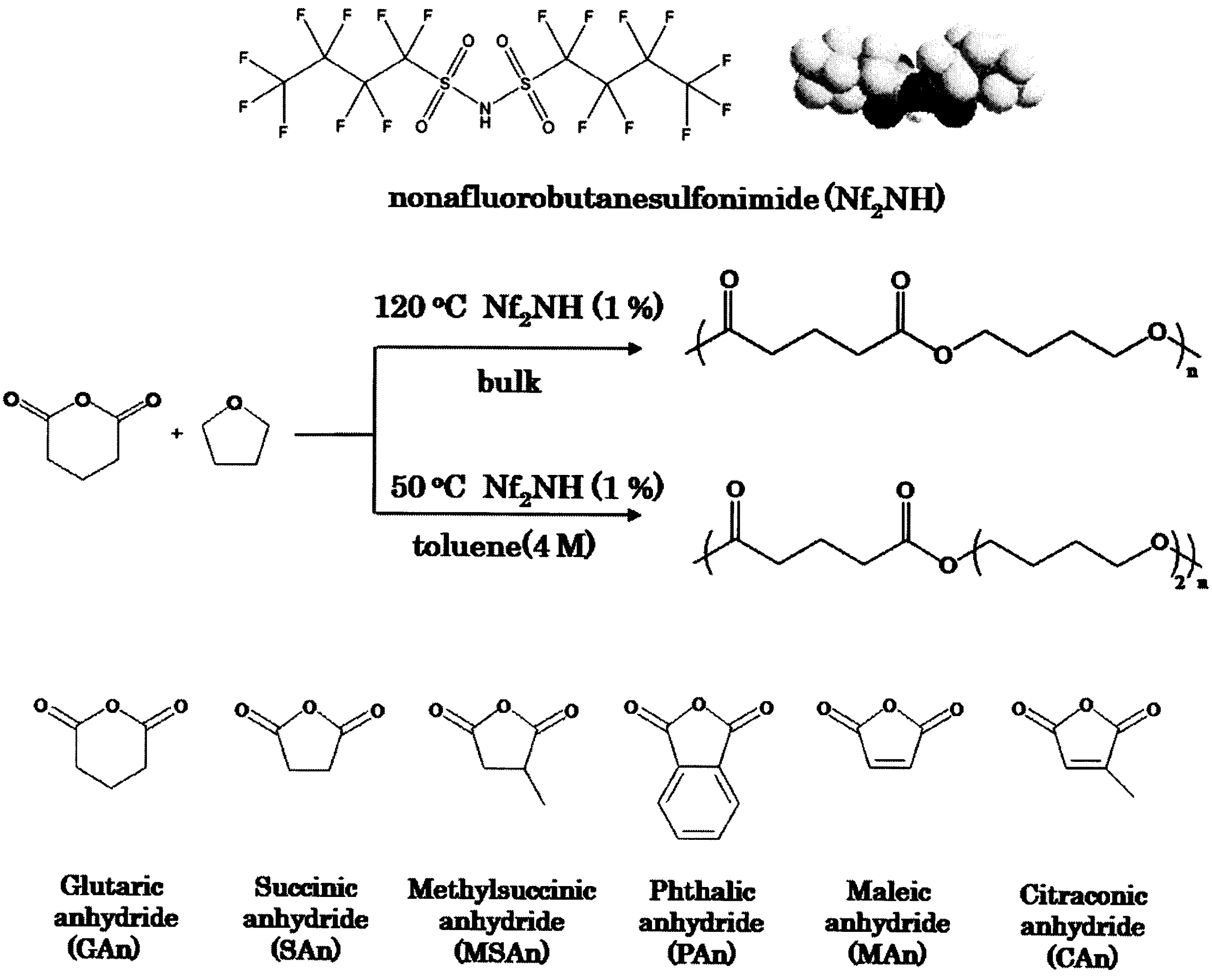
Aliphatic polyesters, such as poly(butylene succinate) (PBS), poly(ethylene succinate) (PES), and poly(butylene glutarate) (PBG), are important biomaterials[1] because of their biodegradability,[2] biocompatibility,[3] and acceptable mechanical strength.[4] As a result, they are preferred over conventional plastics such as polypropylene and polyethylene in industries related to drug delivery systems,[5] tissue engineering,[6] and commodity materials.[7] Currently, aliphatic polyesters are prepared using one of the following two general synthetic approaches. One is the ring-opening polymerization of cyclic esters, such as ε-caprolactone[8] and lactide.[9] Even though this method can be carried out under mild condition, only a few polymeric materials were obtained by this method because of the availability of narrow variety of monomers. The other method is the polycondensation of various diols and dicarboxylic acids;[10] however, because this method requires high reaction temperature (200-250 °C) and highly reduced pressure, synthesizing polyesters using this method is not eco-friendly. Presently, there is a great awareness for green chemistry, which is essential for ensuring earth's sustainability.[11] Thus, many groups have been devoting their time and effort to develop new catalysts and environment friendly polycondensation methods for synthesizing aliphatic polyesters.[12]

As synthesis of polyesters by ring-opening alternating copolymerization of oxiranes with cyclic anhydrides has attracted much attention of researchers,[13-18] new catalyst or method still has the potential to prepare a large variety of copolymers with different backbone structures without severe conditions. We have already prepared polyesters with carbohydrate unit by ring-opening alternating copolymerization of succinic anhydrides with sugar-substituted epoxides using bulky aluminum Lewis acid as the catalyst.[18] Even though the asymmetric epoxidation method opened up the possibility of producing isotactic-rich polyesters with pendant sugar, this system still needed long reaction time (72 h), high reaction temperature (100 °C), and limited architecture based on three-membered cyclic ether (i.e, epoxide). Recently, we have also reported ring-opening polymerization of ε-caprolactone catalyzed by an organic catalyst, nonafluorobutanesulfonimide (Nf_2NH).[19] Compared with trifluorometahnesulfonimide (Tf_2NH) as the catalyst in the polymerizations, Nf_2NH has much higher boiling temperature and is easy to handle under ambient reaction condition.[19]

These results prompted us to study ring-opening copolymerization of tetrahydrofuran (THF) and cyclic anhydrides to give some poly(ester-ether)s or polyesters under economical conditions.

Until now, there are only a report on the synthesis of polyesters by copolymerization of THF and cyclic anhydrides.[20] Since THF is a five-membered cyclic ether and a commercially available useful solvent, use of THF as the monomer in the ring-opening copolymerization reaction should therefore provide an excellent opportunity to prepare polyesters with different structures by chain polymerization technique.

Scheme 1-1. Ring-Opening Copolymerization of Cyclic Anhydride with THF Using Nf_2NH as the Catalyst



Herein we report a series of ring-opening copolymerizations of cyclic anhydrides with THF using Nf_2NH as the catalyst (Scheme 1-1). As it is very important to use a metal-free catalyst from the environmental view point, we have focused on the metal-free catalyst, Nf_2NH, which belongs to the class of super Brϕnsted acids. To the best of our knowledge, this is the first report about copolymerization of cyclic anhydrides with THF to produce poly(alkylene succinate)[20] and formation of periodic copolymers composed of cyclic anhydrides and THF under mild conditions. Although synthesis of sequence-controlled polymer is also important for polymer chemistry, as far as we know, copolymers having periodic sequence are very rare even in vinyl type polymerizations.[21- 23] Therefore, developing any method including ring-opening polymerization for extending the range of monomers for use in the sequence-controlled reaction would be of great interest to polymer chemists.

1-2. Results and Discussion

Ring-Opening Copolymerization of Cyclic Anhydrides with THF at High Temperature

Results of ring-opening copolymerizations of some cyclic anhydrides (M_1) with THF (M_2) at high temperature are summarized in Table 1-1. In runs 1-5, copolymerizaitons of SAn, MSAn, GAn, and PAn with THF were respectively carried out under bulk condition [feed monomer ratio ($[M_1]_0/[M_2]_0$) of 1:1 (Table 1-1)]. Reaction time of run 1 at 100 °C was longer than that of run 2 at 120 °C, because of the lower reaction temperature. It was revealed from runs 2-4 that SAn, GAn, and MSAn could be polymerized to prepare polyesters under high temperature of 120 °C. GAn was also polymerized with the shortest reaction time (8 h), which is ascribed to the greater cyclic strain of its six-membered ring than the cyclic strain of the five-membered rings of SAn (12 h) and MSAn (24 h).[24] Reaction of THF with MSAn (run 3) was more difficult than that with the SAn (run 2) because of the steric hindrance of the methyl group in MSAn. Using PAn as the monomer, the highest molecular weight (M_n=6.8×10^3) polyester was obtained because of the higher thermal stability (run 5 in Table 1-1), indicating that PAn also elicit same trend as previous dicarboxylic anhydrides.

In order to check the effect of methyl group, MAn and CAn were also polymerized (run 6 and 7). Although MAn was copolymerized with THF at 120 °C for 30 h (run 6), CAn hardly underwent copolymerization under same condition (run 7), indicating that the steric hindrance of methyl group hindered the polymerization speed. Runs 1-7 were all carried out under bulk condition; the reaction rate, however, decreased remarkably when the reaction was carried out in solvent (Table 1-1, runs 8 and 9). In runs 8 and 9, solution polycondensations were carried out using toluene and acetonitrile, respectively, as a solvent (see Table 1-1). In acetonitrile (run 9), the proton is bonded by the solvent molecules which lowers its acidity.

To investigate the structure of the products, their ^{1}H-NMR spectra were recorded. In the case of SAn reacting with THF (run 2), the peaks at 3.45-3.49 ppm are assigned to protons from the ether structural units ($-CH_2C\mathit{H_2}OC\mathit{H_2}CH_2-$) and the peaks at 4.01-4.22 ppm are assigned to the protons from the ester structural units ($-CH_2CH_2COOC\mathit{H_2}CH_2-$) (Figure 1-1. a, upper), in which the terminal alcohol was overlapped with the internal ether stretches. Interestingly, in the initial part of this reaction, peaks arising from both of ester and ether units appeared, and as the reaction proceeded, the ether associate peaks decreased (Figure 1-1. a, lower). Finally, the unit ratio of the cyclic anhydride to THF of the polymer chain turned to be almost 1:1, *i.e.*, alternating copolymers, polyesters. Copolymerization of MSAn (run 3) or GAn (run 4) with THF showed similar trend (Figures 1-1. b and c, respectively). At 97% and 88% conversions, the peaks of the ether structural units ($\text{-CH}_2\mathit{CH}_2\text{O}\mathit{CH}_2\text{CH}_2\text{-}$) at 3.45-3.49 ppm disappeared and the peaks at 4.01-4.22 ppm, assigned to the ester structural units were observed, indicating the transformation of the poly(ester-ether) to polyester. Thus, these results suggest that the bulk condition is suitable for the ether to ester transformation and to afford polymers containing alternating sequence.

Table 1-1. Ring-Opening Copolymerization of Cyclic Anhydrides (M_1) with THF (M_2) at High Temperature

run	catalyst[a]	M_1[b]	solvent	temp. (°C)	time (h)	convn.[c] (%)	$[M_1]/[M_2]$[d]	yield (%)	M_n[e] × 10^{-3}	M_w/M_n[e]
1	Nf_2NH (1%)	SAn	bulk	100	42	97	49/51	93	1.9	3.06
2	Nf_2NH (1%)	SAn	bulk	120	12	97	50/50	92	1.8	3.51
3	Nf_2NH (1%)	MSAn	bulk	120	24	88	49/51	84	0.9	2.38
4	Nf_2NH (1%)	GAn	bulk	120	8	96	50/50	90	0.8	2.47
5	Nf_2NH (1%)	PAn	bulk	120	30	98	50/50	87	6.8	2.03
6	Nf_2NH (1%)	MAn	bulk	120	30	75	50/50	75	2.4	2.91
7	Nf_2NH (1%)	CAn	bulk	120	30	trace	-	-	-	-
8	Nf_2NH (1%)	SAn	toluene (4M)[f]	120	24	66	44/56	trace	-	-
9	Nf_2NH (1%)	SAn	CH_3CN (4M)[f]	120	24	0	0	0	-	-

[a] Catalyst [concentration: mol % against cyclic anhydride (M1)].

[b] M2: THF. $[M1]_0$: $[M2]_0$=1:1.

[c] Determined by ^{1}H-NMR measurement in $CDCl_3$ using THF to determine the conversion.

[d] Unit ratio in the copolymer, calculated from ^{1}H-NMR measurement (in $CDCl_3$) using peaks at 4.01-4.22 ppm.

[e] Determined by SEC in chloroform, calibrated using poly(styrene) standards (Before reprecipitation).

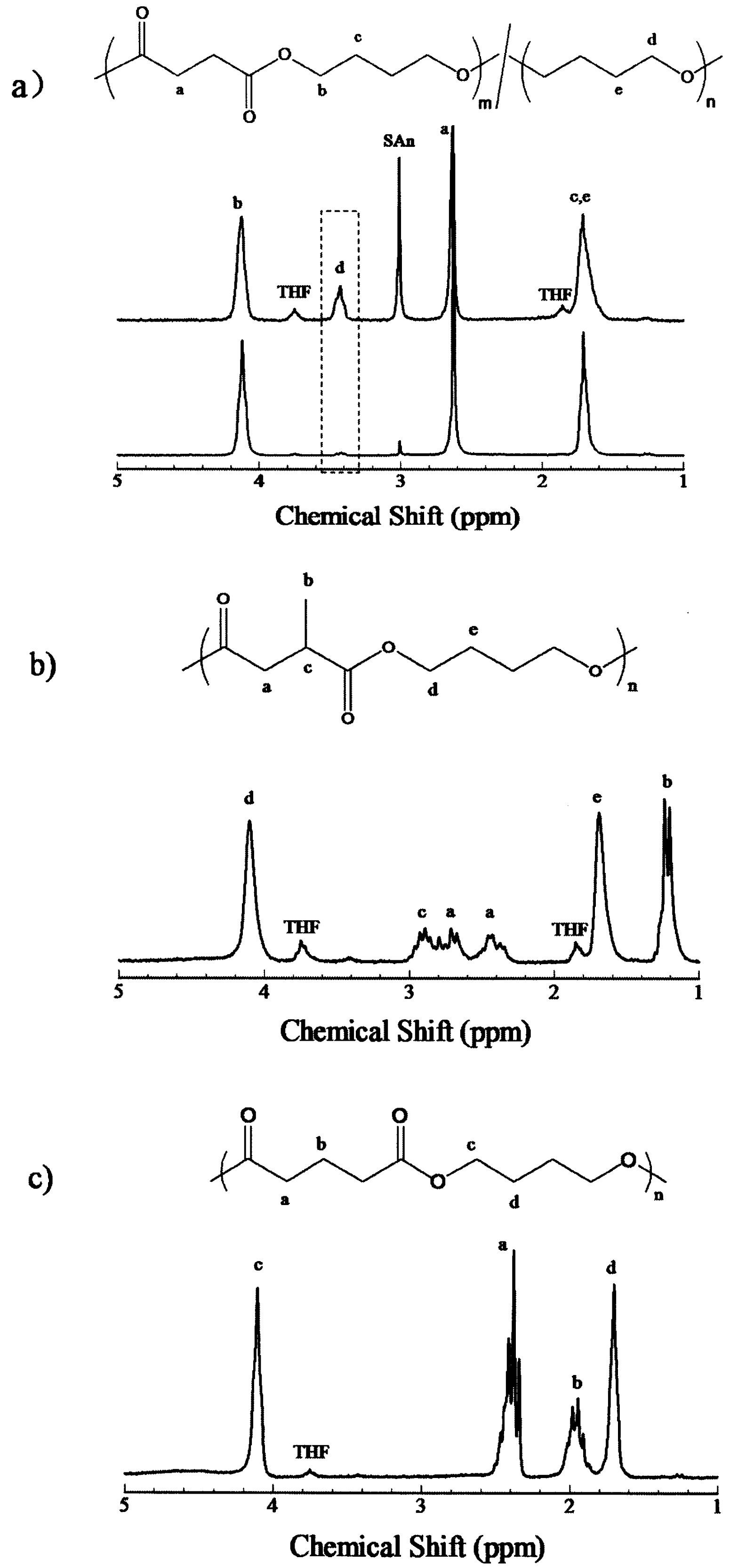


Figure 1-1. ^{1}H-NMR spectra of polyesters prepared by ring-opening copolymerization at high temperature (120 °C). a) Copolymerization of SAn with THF after 4 h (upper spectrum) and 12 h (lower spectrum) (Table 1-1, run 2). b) Copolymerization of MSAn with THF after 24 h (Table 1-1, run 3). c) Copolymerization of GAn with THF after 8 h (Table 1-1, run 4).

MALDI-TOF mass spectra of polymers, synthesized by copolymerization of cyclic anhydrides with THF ($[M_1]_0/[M_2]_0$ was 1:1) under bulk condition, were analyzed to determine the absolute molecular weights and structures of the products (Figure 1-2). Considering the reaction of GAn with THF as an example (Figure 1-2, upper tracing), two sets of peaks appeared in the spectrum, of which the set of repeating peaks at 186 *m/z* correspond to the molecular weight of the repeating unit composed of GAn (114) plus THF (72) unit. When we examined the peak at 1828.1, we found that this peak coincided with the calculated peak [[GAn(114Da)+THF(72Da)] × 9+GAn (114Da)+[Na^+](23Da)+ α-(H-) and ω- (-OH) terminal groups (18 Da)=1829]. This result indicated that both end-units of the polymer are carboxylic acids and the repeating unit was $-M_1M_2-$. The second pattern of peaks, which were offset by 22 *m/z*, were assigned to the polymer product containing two Na^+ (23 Da) ions during the MALDI-TOF mass measurement. The polymer products obtained from the copolymerization of THF with SAn, MSAn, and PAn also showed similar results. ^{1}H-NMR and MALDI-TOF mass apparently revealed that polyesters were produced under bulk condition at 120 °C, although their M_ns were not high ($0.8\text{-}6.8\times10^3$) with broad M_w/M_n (2.03-3.51, Table 1-1). In Table 1-1, the molecular weights are far lower than the theoretical ones, because during the reaction, transformation of ether to ester proceeded, which decrease the molecular weight with broadening of M_w/M_n.

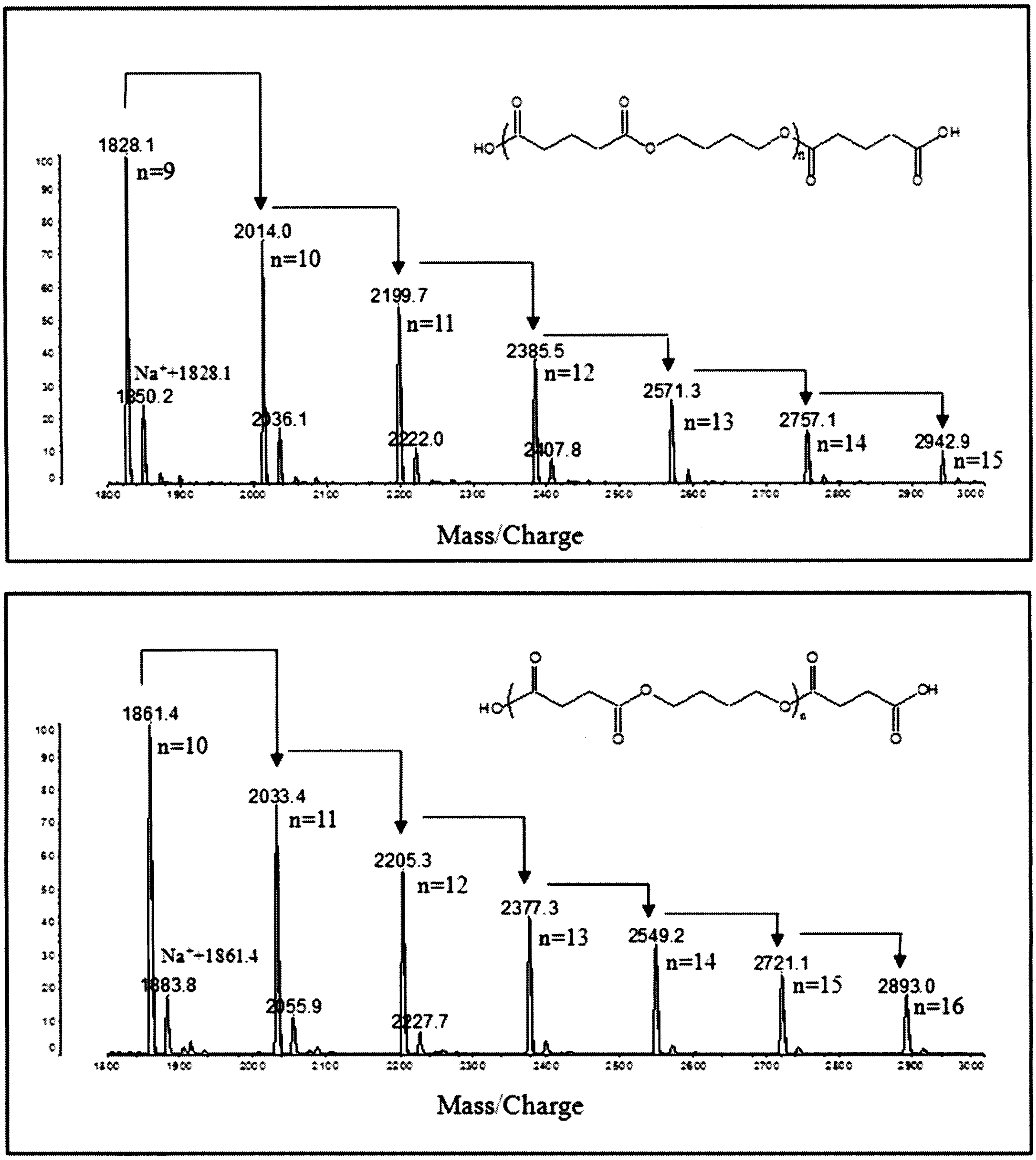


Figure 1-2. MALDI-TOF mass spectra of the polyesters synthesized as a result of ring-opening copolymerizations at high temperature (120 °C) (before reprecipitation). Copolymerization of GAn with THF (1:1) under bulk condition (upper) (Table 1-1, run 4); Copolymerization of SAn with THF (1:1) under bulk condition (lower) (Table 1-1, run 2).

Ring-Opening Copolymerization of Cyclic Anhydrides with THF at Low Temperature

Table 1-2. Ring-Opening Copolymerization of Cyclic Anhydrides (M_1) with THF (M_2) at Low Temperature

run	catalyst (mol%)	M_1[b] ($[M_1]_0$:$[M_2]_0$)	solvent	temp (°C)	time (h)	convn.[c] (%)	$[M_1]/[M_2]$[d] (%)	$M_n \times 10^{-3}$[e]	M_w/M_n[e]
1	Nf_2NH (1%)	SAn (1:1)	bulk	25	48	70	13/87	3.4	1.44
2	Nf_2NH (1%)	SAn (1:1)	bulk	50	24	83	36/64	-	-
					48	97	39/61	7.4	1.85
3	Nf_2NH (1%)	MSAn (1:1)	bulk	50	24	33	36/64	-	-
					144	94	40/60	5.0	1.95
4	Nf_2NH (1%)	PAn (1:1)	bulk	50	24	21	34/66	-	-
					144	90	40/60	2.4	1.85
5	Nf_2NH (1%)	MAn (1:1)	bulk	50	24	9	27/73	-	-
6	Nf_2NH (1%)	CAn (1:1)	bulk	50	24	no polymerization	-	-	-
7	Nf_2NH (1%)	GAn (1:1)	bulk	50	2	99	34/66	5.1	1.87
8	Nf_2NH (0.2%)	GAn (1:1)	bulk	50	24	98	36/64	9.7	1.91
9	Nf_2NH (1%)	SAn (1:2)	bulk	50	48	70	33/67	10.0	1.92
10	Nf_2NH (1%)	MSAn (1:2)	bulk	50	120	71	38/62	4.5	2.10
11	Nf_2NH (1%)	PAn (1:2)	bulk	50	144	86	40/60	2.6	1.83
12	Nf_2NH (1%)	GAn (1:2)	bulk	50	8	96	29/71	12.1	1.97
13	Nf_2NH (1%)	GAn (1:2)	toluene (8M)[f]	50	12	81	30/70	10.4	1.93
14	Nf_2NH (1%)	GAn (1:2)	toluene (4M)[f]	50	72	45	33/67	5.9	2.10
15	Nf_2NH (1%)	GAn (1:2)	dioxane (4M)[f]	50	72	61	32/68	4.7	2.01
16	Nf_2NH (1%)	GAn (1:2)	chloroform (4M)[f]	50	72	53	32/68	3.1	1.90
17	Nf_2NH (1% to THF)	- (0:1)	bulk	50	8	no polymerization	-	-	-

[a] Catalyst ratio: mol% against M_1.

[b] M_2: THF.

[c] Determined by ^{1}H-NMR measurement (in $CDCl_3$) using THF to determine the conversion.

[d] Calculated from ^{1}H-NMR measurement (n $CDCl_3$) using peaks at 4.01-4.22 ppm (assigned to M_1 and M_2 units) and

[e] Determined by SEC in chloroform, calibrated using poly(styrene) standards before reprecipitation.

We next examined the ring-opening copolymerization of cyclic anhydrides (M_1) with THF (M_2) at low temperature of 50 °C. The results are summarized in Table 1-2, the molar ratio in the copolymer ($[M_1]/[M_2]$) was determine by ^{1}H NMR using peaks at 4.01-4.22 ppm (assigned to M_1 and M_2 units) and 3.45-3.49 ppm (assigned to M_2 unit) and the recorded ^{1}H-NMR spectra are shown in Figure 1-3. As expected, copolymers containing both of ether and ester were synthesized. A comparison of the results from runs 1 and 2 (Table 1-2) showed that the THF content in the polymer formed at 25 °C ($[M_1]/[M_2]$=13/87) was more than that in the polymer formed at 50 °C ($[M_1]/[M_2]$=36/64). This result suggested that at 25 °C the propagation rate of THF was faster than that of the cyclic anhydride. Bulk copolymerization of other cyclic anhydrides with THF were also carried out under same conditions (Table 1-2, runs 2-7) and we compared the rate of copolymerization at low temperature. After 24 h, conversion of SAn, MSAn PAn, MAn and CAn with THF respectively were 83%, 33%, 21% , 9% and 0% (runs 2,3,4,5,6). On the other hand, only after 2 h, conversion of the copolymerization of GAn with THF was nearly 99% (run 7). It is ascribed to the greater cyclic strain of its six-membered ring of GAn than the cyclic strain of the five-membered rings of SAn, MSAn, PAn, MAn and CAn.[24] Reaction of THF with MSAn (run 3) was more difficult than that with the SAn (run 2) because of the steric hindrance of the methyl group in MSAn. Because the PAn contains the benzene ring (both of steric and electronic effects), the conversion of PAn (run 4) with THF was lower than that of MSAn. From the ^{13}C-NMR (in $CDCl_3$) chemical shift of carbonyl carbon of SAn (170.7 ppm), MAn (164.6 ppm), and CAn (166.5 and 164.2 ppm), we presumed that the CAn and MAn were also difficult to be copolymerized because of their double bonds which decreased the electrophilicity of cyclic anhydrides. Thus we found the following order of copolymerization rate with THF: GAn>> SAn>MSAn>PAn> MAn > CAn, which did not show any discrepancy in copolymerization at higher temperature described above.

The THF content in the reaction product ($[M_1]/[M_2]$) was also dependent on the cyclic anhydride monomer. If insertion of THF to propagating center consisting of GAn were easier than SAn, MSAn, or PAn , then the molar ratio of THF segments in the copolymer would be more in the case of GAn than in the case of others (SAn, MSAn, or PAn). Consistent with this idea, the higher THF ratio ($[M_1]/[M_2]$ = 34/66) was found in the product obtained from the reaction of GAn with THF (run 7). Although longer reaction time was required when the amount of catalyst was reduced from 1 % (run 7) to 0.2 % (run 8, Table 2), the M_n of the product was however higher (from 5.1×

10^3 to 9.7×10^3) with 98-99% conversions indicating that Nf_2NH acted as initiation species as well as catalyst.

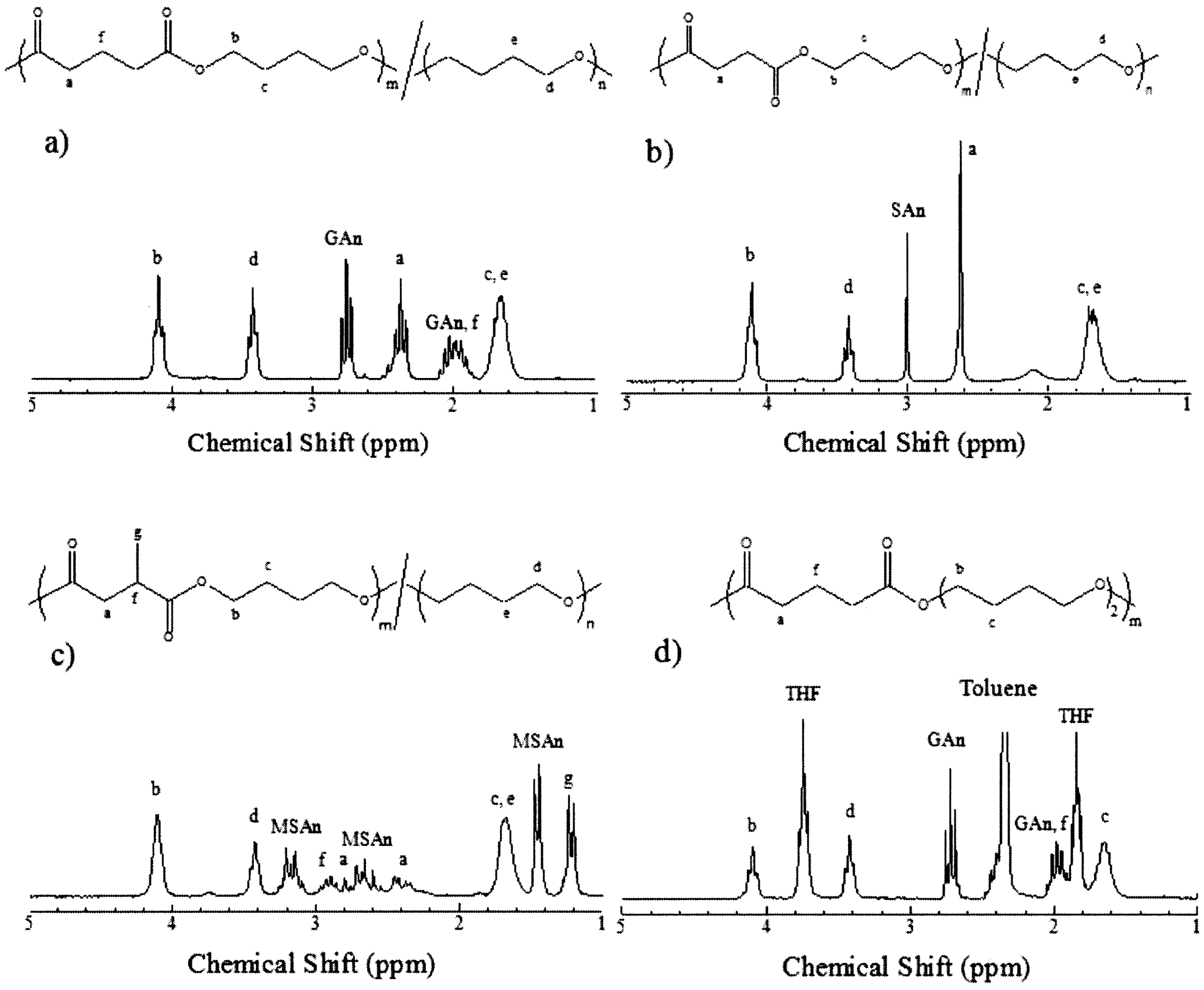
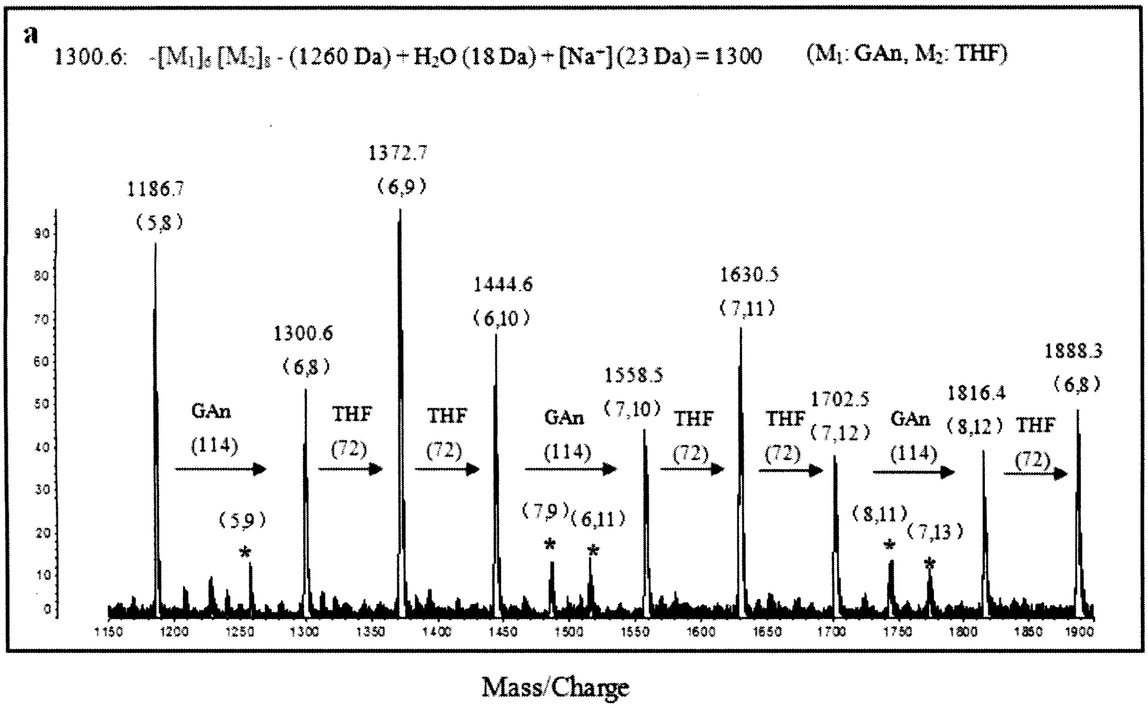


Figure 1-3. ^1H NMR spectra of products from ring-opening copolymerization at low temperature (50 °C). a) Copolymerization of GAn with THF (1:1) after 2 h under bulk condition (Table 1-2, run 7). b) Copolymerization of SAn with THF (1:1) after 48 h under bulk condition (Table 1-2, run 2). c) Copolymerization of MSAn with THF (1:1) after 144 h under bulk condition (Table 1-2, run 3). d) Copolymerization of GAn with THF (1:2) after 72 h using toluene as a solvent (4 M) (Table 1-2, run 14).

From the MALDI-TOF mass spectrum of run 7 (in Table 1-2) shown in Figure 1-4.a, in the products, part of the structure consists of periodic sequence (-$[M_1]$ $[M_2]$ $[M_2]$-). For example, the peak at 1300.6 was ascribed to the structure -$[M_1]_6$ $[M_2]_8$ - (M_1: GAn, M_2: THF; copolymer with M_1: M_2 ratio of 6:8). The peaks marked with (*) represent randomly copolymerized products of GAn and THF. Polymer chains partially propagated according to the sequence -$[M_1]$ $[M_2]$ $[M_2]$- even though the -$[M_1]$ $[M_2]$- repeat units were still present, because the feed monomer ratio ($[M_1]_0$:$[M_2]_0$) was 1:1 and the THF content became low during the propagation. From the crude reaction mixture, cyclic structure and other end groups were not observed in the MALDI-TOF mass spectra.

We also assessed the monomer ratio ($[M_1]_0$:$[M_2]_0$=1:2, runs 9-16) were carried out in order to afford periodic copolymers. However, the results of ^{1}H-NMR (Figure 1-3) and MALDI-TOF mass (Figure 1-4. b) spectra of runs 9-12 suggested that even though the monomer ratio was set to 1:2, periodic polymers were not obtained under the bulk condition. In the MALDI-TOF mass spectrum (Figure 1-4. b), although -($[M_1]$ $[M_2]$ $[M_2]$)$_n$- periodic copolymer associated peaks were found, the peaks marked with (*) represent random copolymerization of GAn and THF. Because GAn was not dissolved in THF during the reaction and the GAn to THF ratio ($[M_1]_0$/$[M_2]_0$) was not maintained at 1:2, the homo sequence of THF was not controlled well. The polymerization was also carried out in solvents, such as in toluene, dioxane, and chloroform, to investigate the effects of solvents on the structure of the products (Table 1-2, runs 13－16). Results of runs 14, 15, and 16 suggested that the conversion was affected by the polarity of solvents and it seems that polar solvents accelerated the copolymerizations.

To investigated how two monomers are consumed and support the periodic copolymerization, the conversion of GAn and THF monomers at different time was examined. We measured the in-situ ^{1}H NMR for three times per one plot and experimental errors were within 1% of conversion (Figure 1-5). As shown in Figures 1-5. a, the initial feed ratio of $[M_1]_0$/$[M_2]_0$ was 1:2, but the conversion of THF was higher than GAn in toluene (8 M), which indicated that in the products unit ratio of GAn and THF was not 1:2. It also can be explained by MALDI-TOF mass spectrum, even though peaks of periodic copolymers could be found which showed –$[M_1]$ $[M_2]$ $[M_2]$– sequence (Figure 1-4. c), the peaks marked with (*) that represent random copolymers were still observed. However, peaks assigned to the random copolymers were much smaller than those observed in Figure 4a and 4b. It proved that this reaction condition is better than those of runs 7 (Figure 1-4. a) and 12 (Figure 1-4. b). When the monomer concentrations were decreased to 4M (Table 1-2, run 14), the reaction rate was slower than the reaction rates in run 13 (8M). In this reaction condition (run 14) both monomers were consumed almost at the same rate in toluene (Figure 1-5. b), thus suggesting that the synthesized copolymer has the $[M_1]$/$[M_2]$ value of 1:2. Then we compared the consumption rates of GAn with THF in different solvents (toluene, dioxane and chloroform), that indicated that the periodic copolymerization in toluene (4M) was better controled than in dioxane (4M) and chloroform (4M). From the ^{1}H-NMR spectrum of copolymerization of GAn with THF ($[M_1]_0/[M_2]_0=1/2$) after 72 h in toluene (4 M) (Figure 1-3. d), we calculated that the molar unit ratio of GAn to THF was also 1:2 and the MALDI-TOF mass spectrum supported the periodic structure (Figure 1-4. d). We found that the peak at 1186.7 consisted of $-[M_1][M_2][M_2][M_1][M_2][M_2][M_1][M_2][M_2][M_1][M_2][M_2][M_1]-$ (1146 Da) + α-(H-) and ω- (-OH) terminal groups (18 Da) + [Na^+] (23 Da), identified with the calculated peak value at 1187 (M_1: GAn, M_2: THF). As shown in Figure 1-4. d, it was clear that the product propagated with the repeat unit $-[M_1][M_2][M_2]-$, and the peaks ascribed to random copolymers were not observed.. When a ~~ $[M_1][M_2](+)$ propagating center was produced, it appeared that THF was selectively inserted to create a ~~ $[M_1][M_2][M_2]$ (+) propagating center, to which cyclic anhydride was then inserted, by which the periodic copolymers could be successfully prepared in the solution polycondensation [in toluene (4M)].


a
1300.6: -[M₁]₆ [M₂]₈ - (1260 Da) + H₂O (18 Da) + [Na⁺] (23 Da) = 1300 (M₁: GAn, M₂: THF)
1186.7 (5,8)
1372.7 (6,9)
1300.6 (6,8)
1444.6 (6,10)
1558.5 (7,10)
1630.5 (7,11)
1702.5 (7,12)
1816.4 (8,12)
1888.3 (6,8)
(5,9) *
(7,9) *
(6,11) *
(8,11) *
(7,13) *
GAn (114)
THF (72)
THF (72)
GAn (114)
THF (72)
THF (72)
GAn (114)
THF (72)
0
10
20
30
40
50
60
70
80
90
1150
1200
1250
1300
1350
1400
1450
1500
1550
1600
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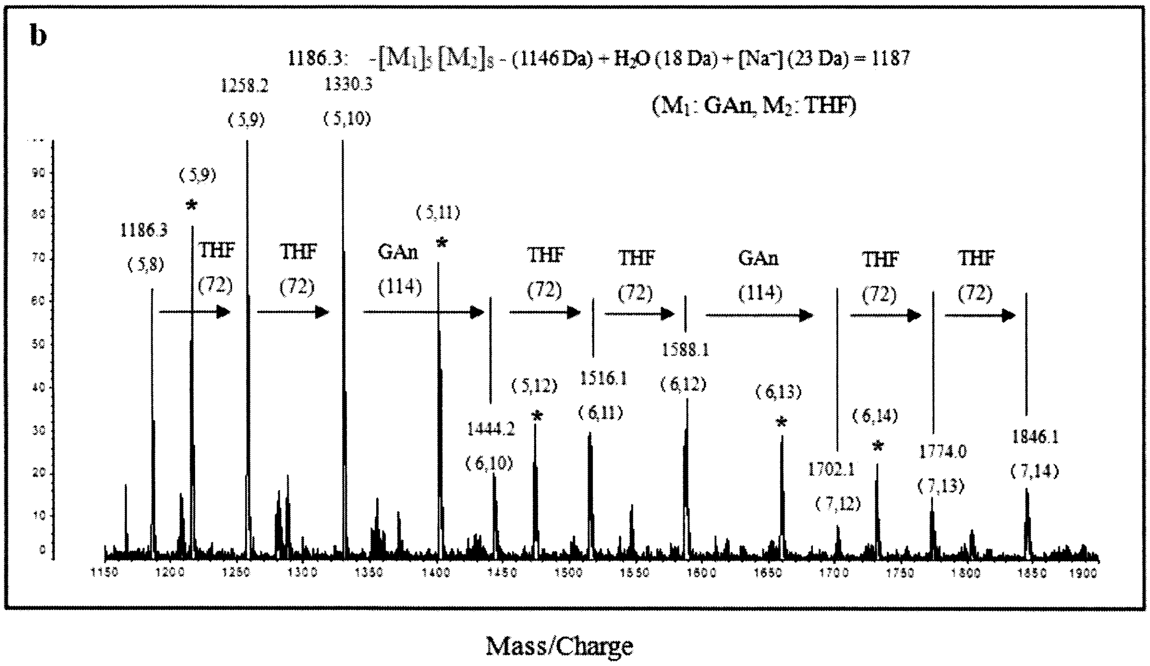
1700
1750
1800
1850
1900
Mass/Charge


b
1186.3: -[M₁]₅ [M₂]₈ - (1146 Da) + H₂O (18 Da) + [Na⁺] (23 Da) = 1187
(M₁: GAn, M₂: THF)
1186.3 (5,8)
1258.2 (5,9)
1330.3 (5,10)
(5,9) *
(5,11) *
1444.2 (6,10)
(5,12) *
1516.1 (6,11)
1588.1 (6,12)
(6,13) *
1702.1 (7,12)
(6,14) *
1774.0 (7,13)
1846.1 (7,14)
THF (72)
THF (72)
GAn (114)
THF (72)
THF (72)
GAn (114)
THF (72)
THF (72)
0
10
20
30
40
50
60
70
80
90
1150
1200
1250
1300
1350
1400
1450
1500
1550
1600
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1800
1850
1900
Mass/Charge

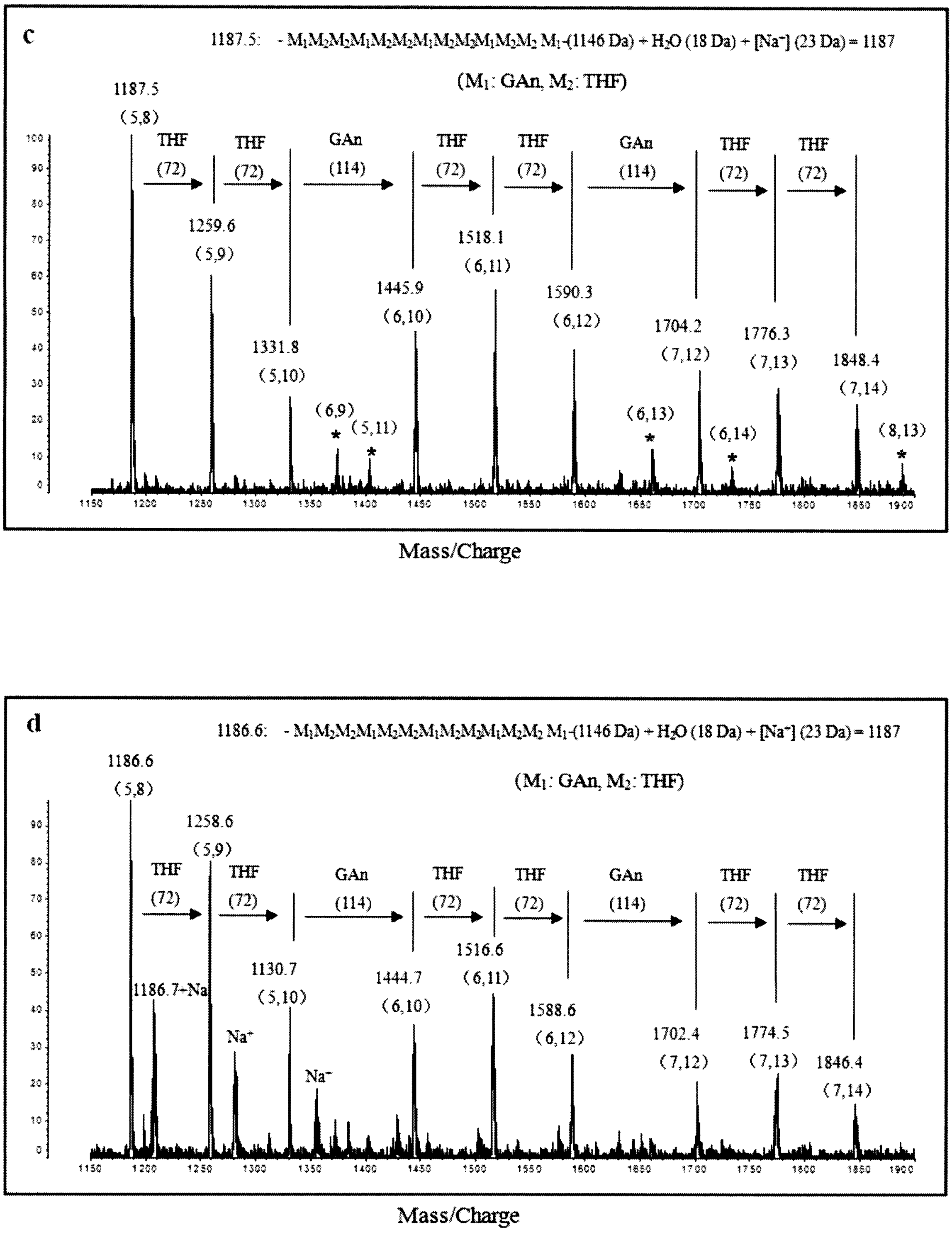


Figure 1-4. MALDI-TOF mass spectra of periodic copolymer obtained via ring-opening copolymerization at low temperature (50 °C). The numbers in parentheses (M_1, M_2) are amount of cyclic anhydride and THF units in the copolymers. a) Copolymerization of GAn with THF (GAn:THF=1:1) under bulk condition (Table 1-2, run 7). b) Copolymerization of GAn with THF (GAn:THF=1:2) under bulk condition (Table 1-2, run 12). c) Copolymerization of GAn with THF (GAn:THF=1:2) using toluene (8M) as the solvent (Table 1-2, run 13). d) Copolymerization of GAn with THF (GAn:THF=1:2) using toluene (4 M) as the solvent (Table 1-2, run 14).

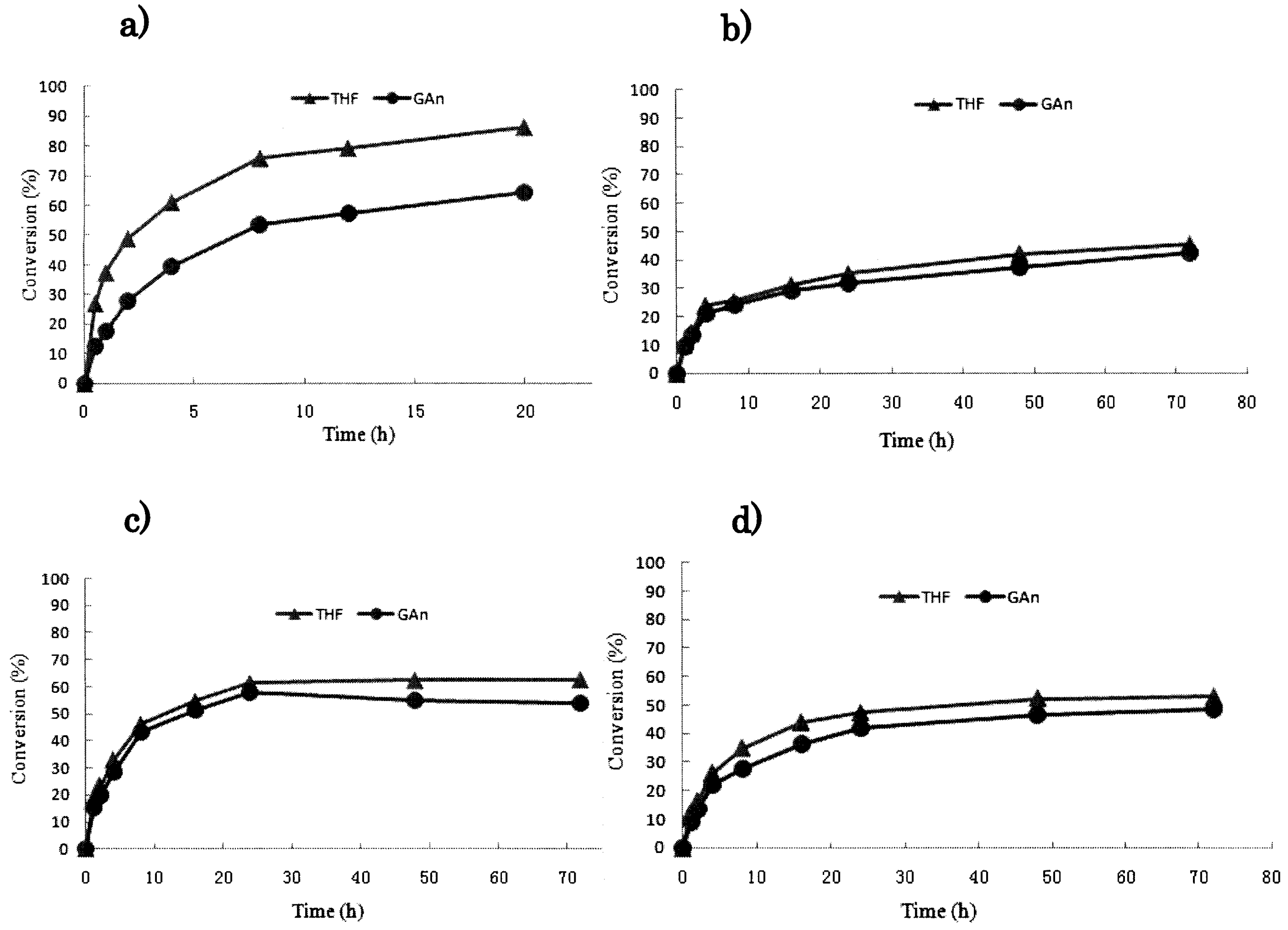
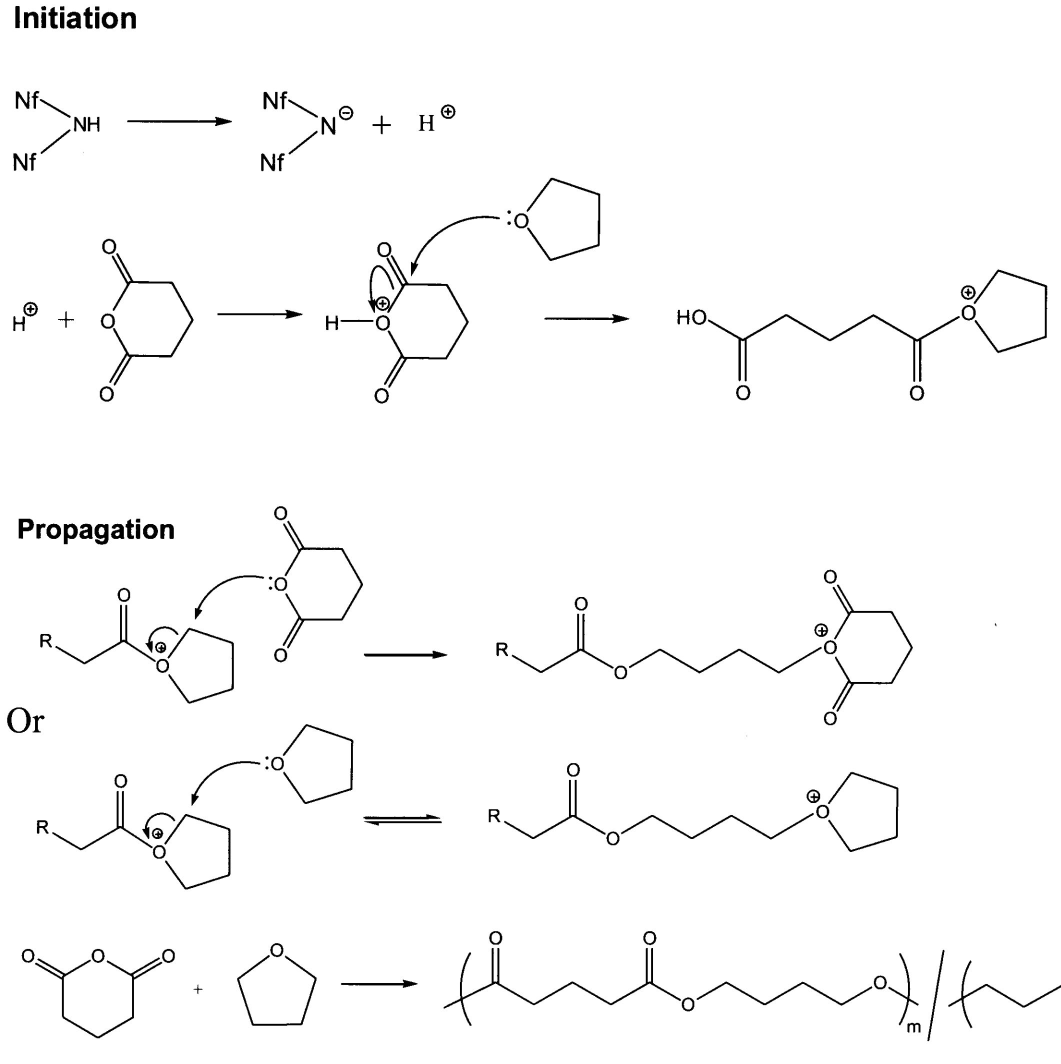


Figure 1-5. Changes of monomer conversions in solution copolymerization of GAn with THF ($[GAn]_0/[THF]_0=1/2$) as calculated from the ^{1}H-NMR spectroscopy (in $CDCl_3$) as the function of time. a) Copolymerization in toluene (8 M) at 50 ^{o}C (Table 1-2, run 13), b) copolymerization in toluene (4 M) at 50 ^{o}C (Table 1-2, run 14), c) copolymerization in dioxane (4 M) at 50 ^{o}C (Table 1-2, run 15), d) copolymerization in chloroform (4 M) at 50 ^{o}C (Table 1-2, run 16).

From the above results, we propose that the copolymerization mechanism consisted of two steps (Scheme 1-2). One step is the initiation and cationic propagation of the reaction and the other step is the transformation reaction at high temperature, in which the THF was easily ring-opened catalyzed by the Brϕnsted acid through cationic reaction.[25] The initiation and propagation of the copolymerization (Scheme 1-2) is induced even at low temperature. We considered that the protons liberated from $HNNf_2$ is, at first, coordinated to the cyclic anhydride to form oxonium ions, because without the cyclic anhydride, polymerization of THF was not initiated by the catalyst (Table 1-2, run 17). In the presence of GAn, the THF was almost consumed (99%) only for 2 h (Table 1-2, run 7). We speculated that the cyclic anhydride not only functioned as a comonomer but also as an initiation species in the copolymerization with THF. Furthermore, in the MALDI-TOF mass spectra, a peak at 226.8 *m/z* was found that was from the $[M_1][M_2]$ and another peak at 340.8 *m/z* was found that belonged to $[M_1][M_2][M_1]$. However, we did not find any peak at 299 *m/z* that could be ascribed to $[M_2][M_1][M_2]$, indicating initiation species are composed of cyclic anhydrides.

Scheme 1-2. Initiation and Propagation of the Ring-Opening Copolymerization of Cyclic Anhydride with THF Using Nf_2NH as the Catalyst



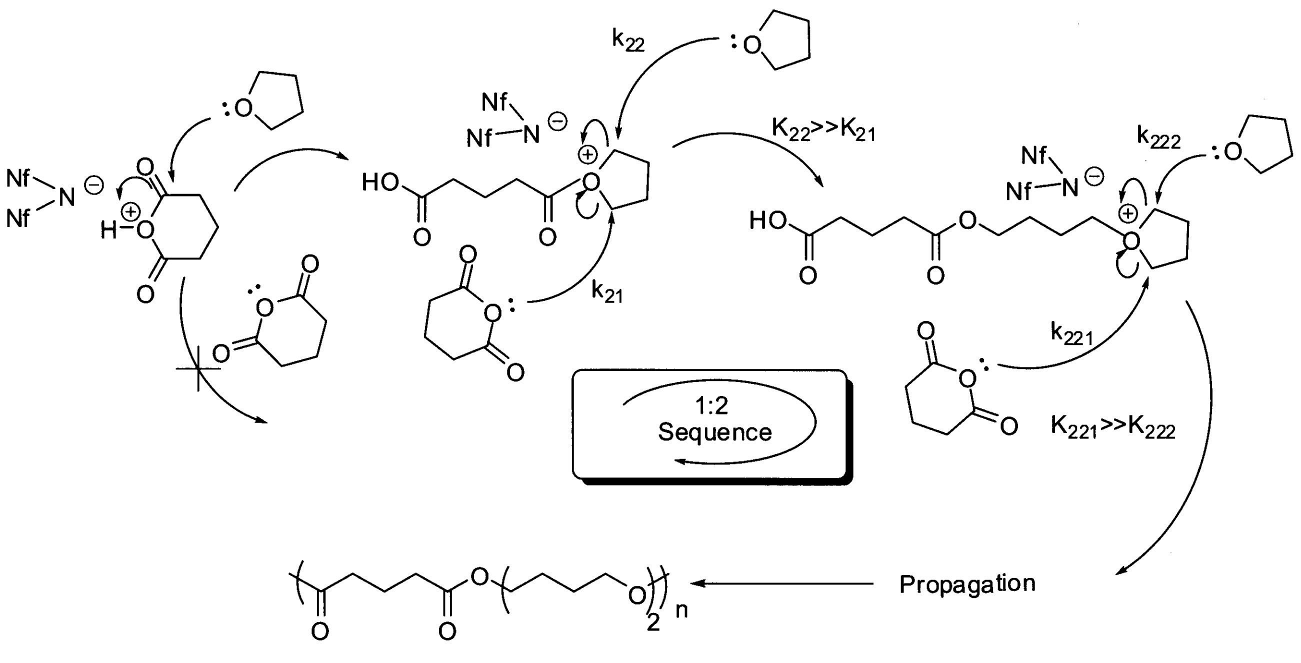
2-1

2-2

2-3

During the propagation, because the cyclic anhydride does not undergo homopolymerization, the oxonium ions of the cyclic anhydride were necessary attacked by THF to form the other oxonium ions, which not only react with cyclic anhydride but also react with THF. Especially, the propagation of THF is an equilibrium reaction of polymerization and depolymerization. The structure of the copolymers depended on the activity of the reactive end groups and the reactivity ratio of the monomers, which was influenced by several factors including the temperature, monomer ratio, monomer structure, and solvents. The following mechanism was used to explain how under certain condition the monomer propagates sequence-selectively and periodic copolymers with sequence of -[M_1] [M_2] [M_2]- are synthesized (Table 1-2, run 14). In Scheme 3, the selective propagation is probably due to the activity of the reactive end group and the reactivity ratio of monomers. At 50 °C, using toluene (4M) as the solvent, after GAn (M_1) is activated by Nf_2NH, THF (M_2) attacks the GAn end group to give ~~[M_1] [M_2] (+). As the reaction rate constant (k) for THF (k_{22}) is higher than that for GAn (k_{21}), because insertion of GAn into a propagating center of –[M_1][M_2](+) seems to be inhibited by steric hindrance of penultimate GAn unit in the presence of bulky counter anion (Nf_2N^-), the hindrance was released after the second THF inserted to –[M_1][M_2](+) to afford –[M_1][M_2][M_2] (+). It seems that this is the mechanism for periodic tendency of [M_1][M_2][M_2] (selective propagation).

Scheme 1-3. Sequence-Controlled Ring-Opening Copolymerization of GAn (M_1) with THF (M_2) in Toluene Using Nf_2NH as a Catalyst at 50 °C.



Mechanism for Transformation of Poly(ester-ethr) to Poly(ester)

As described above, copolymerizations were carried out at low and high temperatures independently, and from the results of these experiments we found that the ether structure was transformed into the ester structure during the reaction at high temperature. Next, to further investigate mechanism of the transformation, a copolymerization was carried out first at low temperature and then the reaction mixture was heated to high temperature. Accordingly, GAn was allowed to react with THF ($[GAn]_0$:$[THF]_0$=1:1) under bulk condition at 50 °C using Nf_2NH (1 mol % to GAn) as the catalyst. After 2 h, the temperature of the reaction mixture was raised to 120 °C. As shown in Figure 6a, the ^{1}H-NMR spectra changed as a function of the reaction time revealed remarkable structural transformation. The ether associated peaks (at 3.45-3.49 ppm) observed at 50 °C decreased after the temperature was raised to 120 °C (dotted line), suggesting that the ether units were transformed into esters. SEC curves (Figure 1-6. b) revealed the changes in the molecular weight of the product during this reaction. At high temperature, the transformation reaction caused a decrease in the ether content and M_n of the products, accompanied with the broadening of M_w/M_n. MALDI-TOF mass spectra of the copolymers obtained from different stage which supported that the structural transformation form poly(ester-ether)s to polyesters.

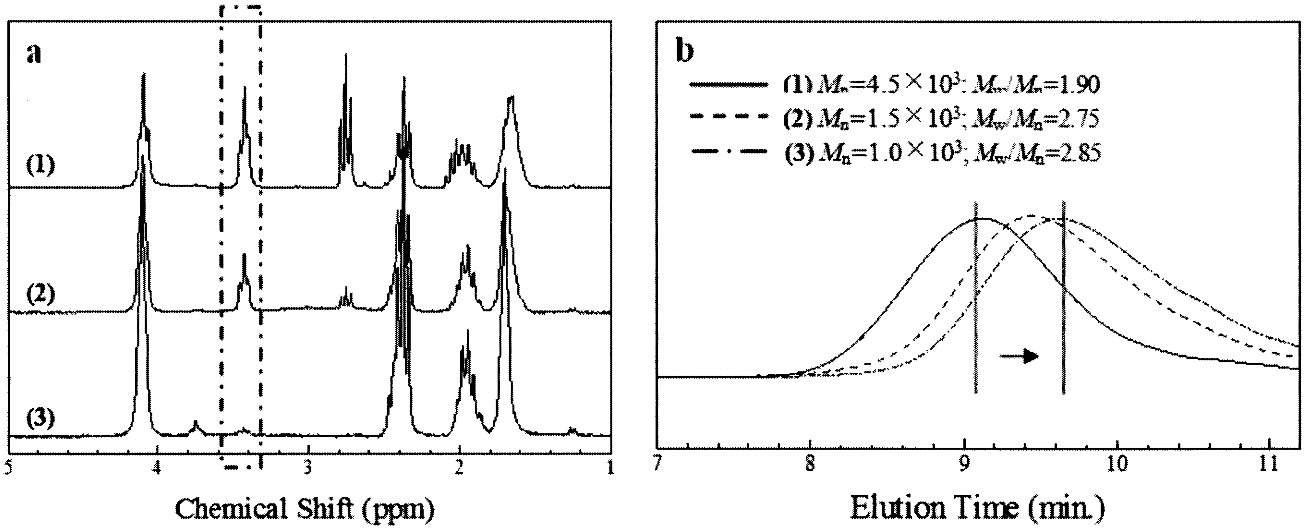
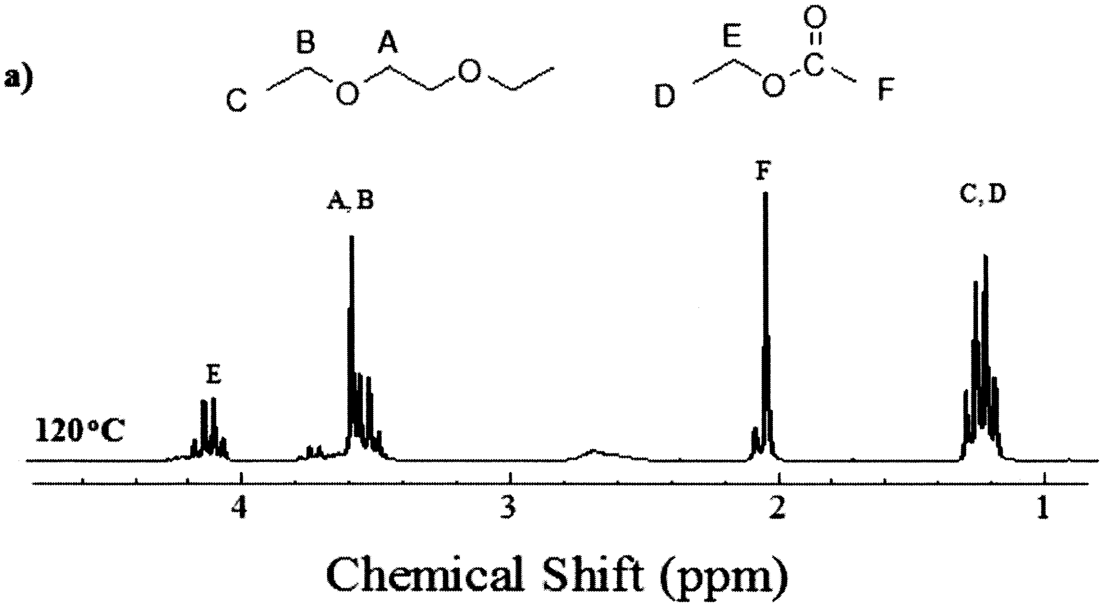


Figure 1-6. a) ^{1}H NMR spectrum at different stages of copolymerization upon shifting the reaction mixture from low temperature to high temperature. ^{1}H NMR charts (from top to bottom) are (1) 50°C, 2 h; (2) 120 °C, 8 h; (3) 120 °C, 24 h. b) SEC curves at different stages of copolymerization. SEC traces (from left to right) are (1) 50 °C, 2 h; (2) 120 °C, 8 h; (3) 120 °C, 24 h.

Model Reaction

At high temperature, a chain transfer reaction proceeds to form polyester. In order to verify the proposed reaction mechanism (Scheme 1-4), several model reactions were carried out. First, a mixture of 1,2-diethoxyethane and ethyl acetate (1:2, mol/mol) was heated at 120 °C for 8 h in the presence of Nf_2NH (1 mol % of ethyl acetate), because 1,2-diethoxyethane contains two ether units.

From the ^{1}H-NMR spectra (Figure 1-7. a), any transesterification of product can not be found. Therefore, nucleophilic attack of the ether to ester moiety is not the main reason for the observed decrease in the ether content. We next examined the reaction between 1,2-diethoxyethane and GAn (1:2, mol/mol). According to our proposed mechanism, two GAn were required to eliminate one ether unit in the presence of Nf_2NH (1 mol % of GAn). The ^{1}H-NMR spectrum of the reaction mixture at 50 °C (Figure 1-7. b, upper) did not show any spectrum changes. On the other hand, the ^{1}H-NMR spectrum of the reaction at 120 °C (Figure 1-7. b, lower tracing) showed that the GAn was completely used up in the reaction. In the spectrum, the peaks A and B (dotted square) decreased and the peaks a and b (solid square) appeared after 8 h, indicating that the ether moiety was transformed into the corresponding ester.



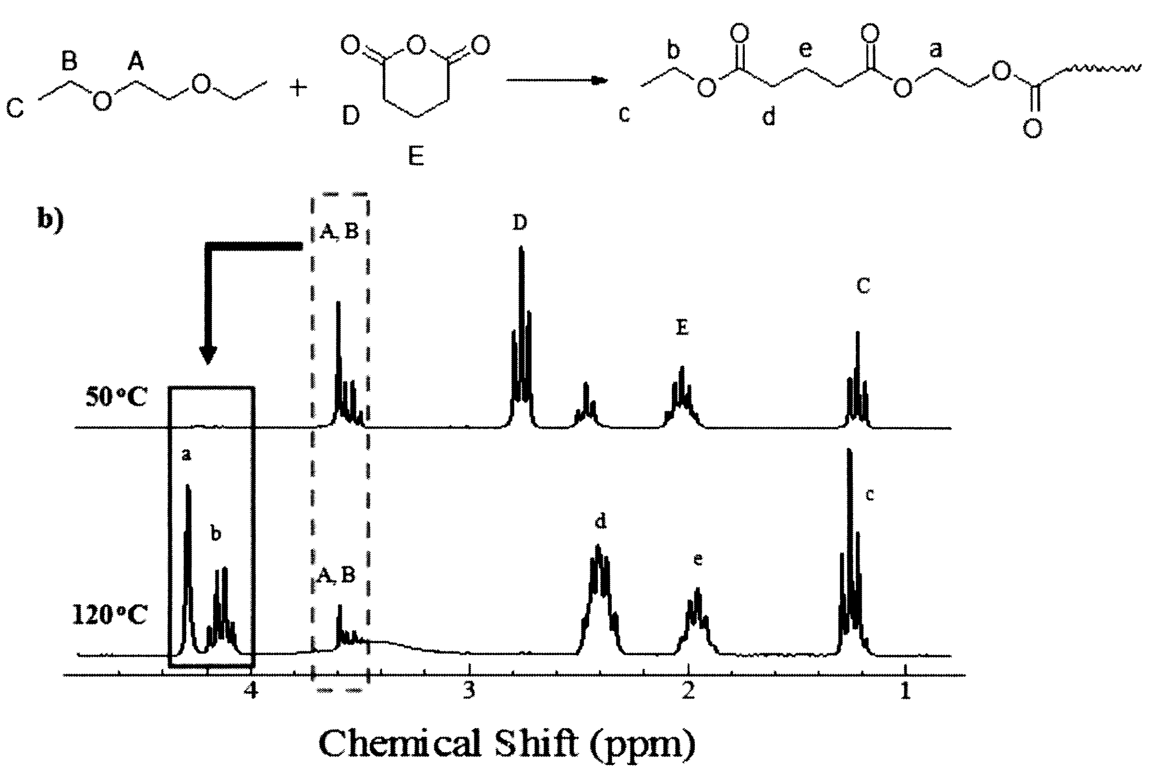
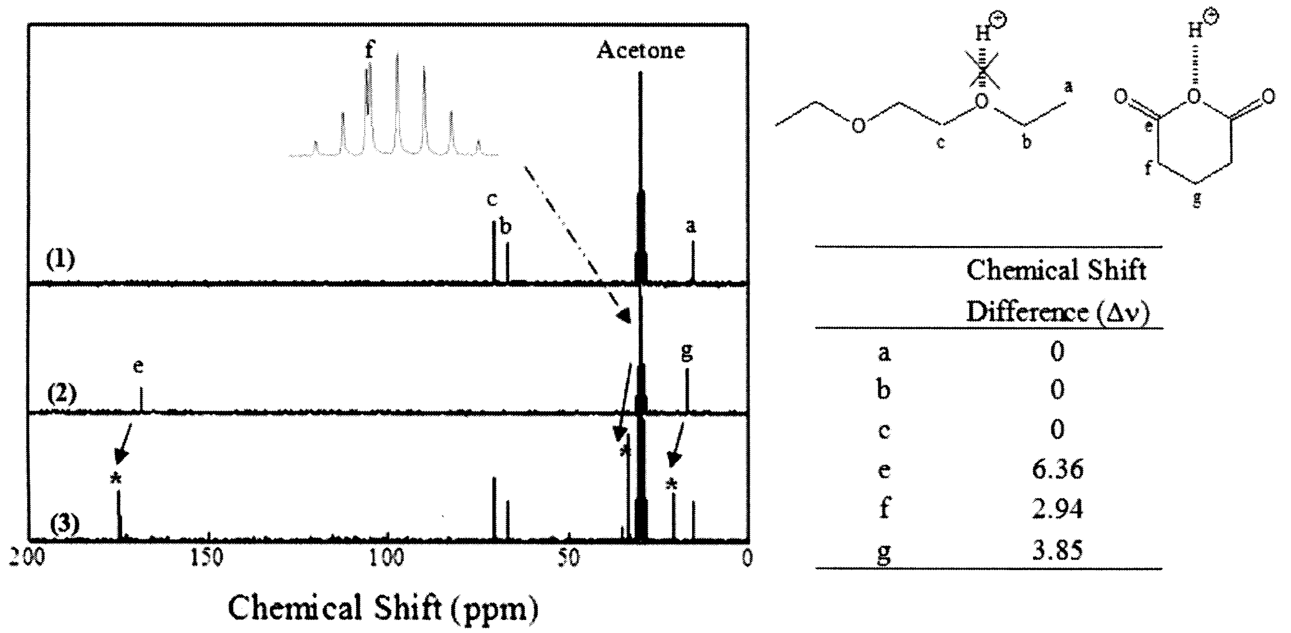


Figure 1-7. Model reaction. a) 1,2-Diethoxyethane: ethyl acetate=1:2, Nf_2NH (1 mol % of ethyl acetate), 120 °C, 8 h. b) upper spectrum: 1,2-Diethoxyethane:GAn=1:2, Nf_2NH (1 mol % of GAn), 50 °C, 8 h; lower spectrum): 1,2-Diethoxyethane: GAn=1:2, Nf_2NH (1 mol % of GAn), 120 °C, 8 h.

In the ether elimination model reaction, the catalyst Nf_2NH provided the proton which may coordinate with GAn or 1,2-diethoxyethane to form the oxonium ions. To determine which is protonated first, GAn or ether segment, we carried out ^{13}C-NMR measurements to examine the interaction between the catalyst and GAn or 1, 2-diethoxyethane. It is obvious from the results shown in Figure 1-8 that after mixing the catalyst, GAn, and 1, 2-diethoxyethane, the peaks of 1,2-diethoxyethane did not shift, but the peaks of GAn shifted to down field, indicating that the catalyst interacts with GAn and form the initiation species as we expected.

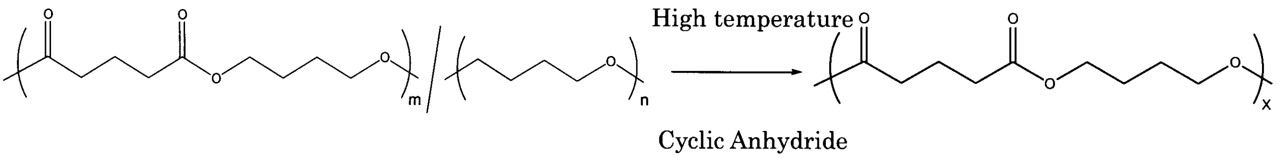


	Chemical Shift Difference (Δv)
a	0
b	0
c	0
e	6.36
f	2.94
g	3.85

Figure 1-8. ^{13}C-NMR spectra for calculating the chemical shift difference (Δv). (1): 1, 2-diethoxyethane; (2): GAn; (3): a mixture of Nf_2NH, GAn, and 1, 2-diethoxyethane (2 : 2 : 1, mol/mol/mol).

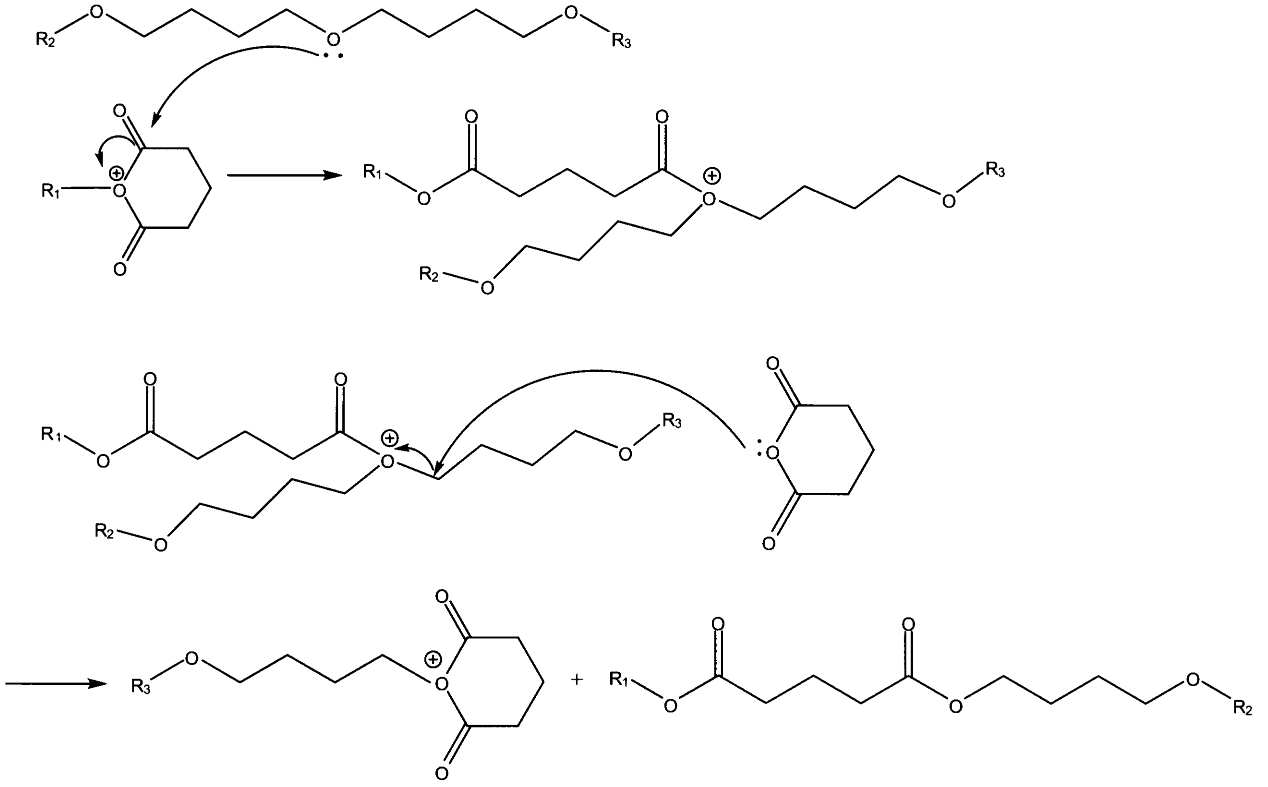
From these model reactions, we conclude that the mechanism for the ether to ester transformation at high temperature is the one shown in Scheme 1-4-1. As shown, at the propagation stage the THF monomers hompolymerized as ether units, and monomers of the cyclic anhydrides remained in the mixture. These results suggested that the mechanism of this chain transfer reaction is via nucleophilic attack of the ether oxygen on the propagating center of the cyclic anhydride, and subsequent insertion of the remaining GAn monomer (Scheme 1-4-3). After the chain transfer reaction, a new oxonium ion of cyclic anhydride was regenerated (Scheme 1-4-4).

Scheme 1-4. Mechanism of the Ring-Opening Copolymerization of Cyclic Anhydride with THF Using Nf_2NH as a Catalyst at High Temperature



4-1

Chain Transfer Reaction



4-2

4-3

4-4

In summary, polyesters were synthesized by copolymerization of cyclic anhydrides with THF at high temperature (100-120 °C) and periodic polyester was obtained when the reaction was carried out at 50 °C using toluene as the solvent. Several model reactions were carried out to prove the proposed chain transfer mechanism. The ester and ether unit containing copolymers were transfromed into polyesters after they were heated to high temperature, and during this transformation process, M_n of the polymers decreased. These fundamental results should provide a new strategy for synthesizing novel polyesters and polyester-based periodic copolymers.

1-3. Experimental section

Materials

Succinic anhydride (SAn), glutaric anhydride (GAn), phthalic anhydride (PAn), maleic anhydride (MAn), and citraconic anhydride (CAn) were purchased from Tokyo Chemical Industry Co., Ltd (Tokyo, Japan). Methylsuccinic anhydride (MSAn) was purchased from Aldrich Co., Ltd. (Milwaukee, WI, USA). Toluene, dioxane, THF, petroleum ether, and acetonitrile were purchased from Nacalai Tesque (Kyoto, Japan), and they were distilled before use. Nf_2NH was purchased from Mitsubishi Materials Electronic Chemicals Co., Ltd. (Akita, Japan), and was dried under reduced pressure before use. 1,2-Diethoxyethane and ethyl acetate were purchased from Nacalai Tesque (Kyoto, Japan).

Measurements

^{1}H-NMR spectra were recorded at 27 °C using a Bruker Analytik DPX200 spectrometer (200 MHz for ^{1}H). ^{13}C-NMR spectra were recorded at 27 °C using a Bruker Analytik DRX600 spectrometer (150 MHz for ^{13}C). Number average molecular weights (M_n) and polydispersity indices (M_w/M_n) of products were determined using a size-exclusion chromatography (SEC) method that was calibrated with polystyrene standards. The chromatographic system included a RI detector (Tosoh RI-8020), a Tosoh DP8020 pump system, and a TSKgel SuperMultiporeHZ-M column. Chromatography was performed using chloroform as the eluent. The flow rate was 0.35 mL/min, and the temperature was maintained at 40 °C. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectra were recorded by using a Kratos PCAxima CFRplus V2.4.0 mass spectrometer, with dithranol as the matrix reagent. NaI was used to generate sodium-cationized ions of the copolymers ($[M+Na]^+$).

Ring-Opening Copolymerization of Cyclic Anhydrides with THF at High Temperature

A typical procedure for copolymerization under bulk condition at high temperature was performed as follows (Table 1, run 2). In a test tube, Nf_2NH (24.7 μmol), SAn (2.47 mmol) were dried first and then mixed. After that THF (2.47 mmol) were added, and then the tube was sealed under reduced pressure. The mixture was stirred at 120 °C for 12 h under nitrogen. The products were first dissolved in $CHCl_3$ and then precipitated using petroleum ether, the precipitated polymers were then dried under reduced pressure (92% yield). Poly(SAn-*co*-THF) (run 2), ^{1}H-NMR ($CDCl_3$, δ , ppm): 4.01-4.22 (br, 4H, $-COOCH_2CH_2CH_2CH_2OOC-$), 2.50-2.69 (br, 4H, $-OOCCH_2CH_2COO-$), 1.61-1.78 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$). Poly(MSAn-*co*-THF) (run 3), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ , ppm): 4.01-4.22 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 2.80-3.02 (m, H, $\mathrm{-OOC}CH\mathrm{(CH_3)CH_2COO-}$), 2.59-2.81, 2.30-2.55 (2m, 2H, $\mathrm{-OOCCH(CH_3)}CH_2\mathrm{COO-}$), 1.61-1.78 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$), 1.07-1.31 (d, 3H, $\mathrm{-OOCCH(}CH_3\mathrm{)CH_2COO-}$). Poly(GAn-*co*-THF) (run 4), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ , ppm): 4.01-4.22 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 2.32-2.50 (m, 4H, $\mathrm{-OOC}CH_2\mathrm{CH_2}CH_2\mathrm{COO-}$), 1.85-2.06 (m, 2H, $\mathrm{-OOCCH_2}CH_2\mathrm{CH_2COO-}$), 1.61-1.78 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$). Poly(PAn-*co*-THF) (run 5), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ , ppm): 7.38-7.59 (2d, 4H, $\mathrm{-OOC}C_6H_4\mathrm{COO-}$), 4.14-4.46 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 1.65-1.94 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$). Poly(MAn-*co*-THF) (run 6), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ , ppm): 6.37-6.52 (2d, 2H, $\mathrm{-OOC}C_2H_2\mathrm{COO-}$), 4.13-4.53 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 1.65-1.94 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$). A typical procedure for copolymerzation in solvent was performed as follows (run 8). In a test tube, $\mathrm{Nf_2NH}$ (24.7 μmol) and GAn (2.47 mmol) were mixed after they were dried, and then toluene (4 M) and THF (2.47 mmol) were added immediately. The recation proceeded at 120 °C for 24 h.

Ring-Opening Copolymerization of Cyclic Anhydrides with THF at Low Temperature

Considering the copolymerization of GAn with THF as an example (run 9, in Table 2), we have synthesized poly(alkylene succinate) through ring-opening copolymerizations using $\mathrm{Nf_2NH}$ as the catalyst at low temperature. First, in a round-bottomed flask $\mathrm{Nf_2NH}$ (24.7 μmol) and GAn (2.47 mmol) were dried first and then mixed and then THF (2.47 mmol) was added. The mixture was stirred at 50 °C for 48 h under nitrogen. After the products were precipitated from $\mathrm{CHCl_3}$ using petroleum ether, the precipitated polymers were dried under reduced pressure (76% yield). Poly(SAn-*co*-THF) (run 2), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ , ppm): 4.01-4.22 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 3.32-3.49 (t, 4H, $\mathrm{-CH_2}CH_2\mathrm{O}CH_2\mathrm{CH_2-}$), 2.50-2.69 (br, 4H, $\mathrm{-OOC}CH_2CH_2\mathrm{COO-}$), 1.61-1.78 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$), 1.50-1.65 (br, 4H, $\mathrm{-CH_2OCH_2}CH_2CH_2\mathrm{CH_2OCH_2-}$). Poly(MSAn-*co*-THF) (run 3), ^{1}H NMR ($\mathrm{CDCl_3}$, δ , ppm): 4.01-4.22 (br, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 3.32-3.49 (br, 4H, $\mathrm{-CH_2}CH_2\mathrm{O}CH_2\mathrm{CH_2-}$), 2.80-3.02 (m, H, $\mathrm{-OOC}CH\mathrm{(CH3)CH_2COO-}$), 2.59-2.81, 2.30-2.55 (2m, 2H, $\mathrm{-OOCCH(CH_3)}CH_2\mathrm{COO-}$), 1.61-1.78 (br, 4H, $\mathrm{-COOCH_2}CH_2CH_2\mathrm{CH_2OOC-}$), 1.50-1.65 (br, 4H, $\mathrm{-CH_2OCH_2}CH_2CH_2\mathrm{CH_2OCH_2-}$), 1.07-1.31 (d, 3H, $\mathrm{-OOCCH(}CH_3\mathrm{)CH_2COO-}$). Poly(GAn-*co*-THF) (run 9), ^{1}H-NMR ($\mathrm{CDCl_3}$, δ, ppm): 4.01-4.22 (t, 4H, $\mathrm{-COO}CH_2\mathrm{CH_2CH_2}CH_2\mathrm{OOC-}$), 3.32-3.49 (t, 4H, $\mathrm{-CH_2}CH_2\mathrm{O}CH_2\mathrm{CH_2-}$), 2.23-2.50 (t, 4H, $\mathrm{-OOC}CH_2\mathrm{CH_2}CH_2\mathrm{COO-}$), 1.85-2.06 (m, 2H,

$-OOCCH_2\mathit{CH_2}CH_2COO-$), 1.61-1.78 (br, 4H, $-COOCH_2\mathit{CH_2CH_2}CH_2OOC-$), 1.50-1.65 (br, 4H, $-CH_2OCH_2\mathit{CH_2CH_2}CH_2OCH_2-$). Poly(PAn-*co*-THF) (run 4), ^{1}H-NMR ($CDCl_3$, δ , ppm): 7.38-7.59 (2d, 4H, $-OOC\mathit{C_6H_4}COO-$), 4.14-4.46 (br, 4H, $-COO\mathit{CH_2}CH_2CH_2\mathit{CH_2}OOC-$), 1.65-1.94 (br, 4H, $-COOCH_2\mathit{CH_2CH_2}CH_2OOC-$), 1.53-1.79 (br, 4H, $-CH_2OCH_2\mathit{CH_2CH_2}CH_2OCH_2-$). Poly(MAn-*co*-THF) (run 6), ^{1}H-NMR ($CDCl_3$, δ , ppm): 6.37-6.52 (2d, 2H, $-OOC\mathit{C_2H_2}COO-$), 4.13-4.53 (br, 4H, $-COO\mathit{CH_2}CH_2CH_2\mathit{CH_2}OOC-$), 1.65-1.94 (br, 4H, $-COOCH_2\mathit{CH_2CH_2}CH_2OOC-$), 1.53-1.79 (br, 4H, $-CH_2OCH_2\mathit{CH_2CH_2}CH_2OCH_2-$). A typical procedure for copolymerzation in solvent was carried out as follows (run 14). In a 10 mL round-bottom flask, Nf_2NH (24.7 μmol) and GAn (2.47 mmol) were mixed and then toluene (4 M) and THF (4.94 mmol) were added. The mixture was stirred at 50 °C for 72h under nitrogen. After the products were precipitated from $CHCl_3$ using petroleum ether, the precipitated polymers were dried under reduced pressure (41% yield).

^{13}C-NMR Spectroscopy of 1,2-Diethoxyethane, GAn, and Nf_2NH Catalyst

1,2-Diethoxyethane (0.08 mmol), GAn (0.16 mmol), and Nf_2NH (0.16 mmol) were dissolved in acetone-d_6 (0.5 mL). NMR spectrum of the mixture was recorded and compared with those of 1,2-diethoxyethane (0.16 mmol) and GAn (0.16 mmol).

Model Reaction.

In a 18×180 mm/mm test tube, GAn (1 mmol) and Nf_2NH (0.05 mmol) were mixed after they were dried, and then 1,2-diethoxyethane (0.5 mmol) was added. The reaction was carried out at 120 °C for 8 h. In a 18×180 mm/mm test tube, ethyl acetate (1 mmol) and Nf_2NH (0.05 mmol) were mixed, and then 1,2-diethoxyethane (0. 5 mmol) was added. The reaction was carried out at 120 °C for 8 h.

Ring-opening Copolymerization of Cyclic Anhydride with THF at Low Temperature and Subsequent Transformation at High Temperature

In a 10 mL round-bottom flask, GAn (2.47 mmol) and Nf_2NH (2.47 μmol) were mixed and THF (2.47 mmol) was added. The mixture was stirred at 50 °C for 2 h and then the temperature was raised and maintained at 120 °C for 24 h under nitrogen.

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Chapter 2

Isomerization-Free Polycondensations of Cyclic Anhydrides with Diols and Preparation of Polyester Gels Containing *cis* or *trans* Carbon Double Bonds via Photo Cross-Linking and Isomerization in the Gels

ABSTRACT

We report herein the polycondensations of unsaturated cyclic anhydrides with diols at moderate temperatures (60–80 °C) using the sublimating organic catalyst, bis(nonafluorobutanesulfonyl)imide (Nf_2NH) to synthesize polyesters containing carbon-carbon double bonds (M_n = 5.3–18.1 kDa, M_w/M_n = 1.7-2.2). We initially synthesized isomerization-free unsaturated polyesters containing alternating maleate or itaconate and 3-methyl-1,5-pentanediol units. To avoid gelation during the polycondensation of itaconic anhydride with diols, addition of a radical inhibitor was essential. Using a polyester that contained maleate units, we converted the maleate units to fumarate units by a diethylamine-catalyzed *cis-trans* isomerization of the maleate double bonds. Additionally, using copolyesters containing maleate and itaconate units, we could selectively photo-crosslink the exo-type double bonds of the itaconate units to afford unsaturated polyester gels. Starting with these gels, we then isomerized the maleate unit *cis* double bonds to *trans* double bonds. The swelling properties of the gels were found to depend on the initial maleate to fumarate unit ratios (degree of isomerization) as well as the maleate to itaconate unit ratios.

2-1. Introduction

Aliphatic polyesters find use in many applications because of their biodegradabilities and biocompatibilities.[1] Unsaturated polyesters are especially interesting classes of polyesters because they can be used as coatings and insulating materials,[2] and in biomedical applications.[3] Currently, a million tons of maleic anhydride (MAn) are produced yearly and some of them are converted into unsaturated polyesters.[4] Itaconic anhydride (IAn), which is an unsaturated cyclic anhydride prepared via fermentation of biomass resources,[5] has been targeted as a starting material for the facile production of unsaturated elastomeric aliphatic polyesters. However, conventional step-growth polymerizations for polyester syntheses, i.e., dehydration polycondensations of diols with dicarboxylic acids,[6] have substantial energy and reaction-time requirements, and often afford polymers of low molecular weights and/or polymers containing undesirable ether linkages formed via side reactions. We have reported on direct dehydration polycondensations of diols and dicarboxylic acids under mild conditions, which were catalyzed by certain rare-earth metals ligated to electron-withdrawing ligands.[7] We could incorporate thermally unstable monomers that contained carbon-carbon double bonds,[8a] bromine,[8a] and hydroxyl,[8b,8c] mercapto,[8d] disulfide[8e] moieties into polyesters synthesized under the aforementioned conditions. To demonstrate the synthesis of unsaturated polyesters containing exo-type carbon-carbon double bonds, we attempted the ring-opening copolymerization of IAn with 1,2-epoxybutane, but during the course of the copolymerization, gelation and conversion of the IAn units to citraconic anhydride (CAn) units occurred.[9] Although Yousaf et al. synthesized photocurable polyesters containing IAn units via thermal polymerization, a high temperature was necessary (>145 °C), and they did not discuss the status of the itaconic double bonds during polycondensation nor demonstrate photo-crosslinking nor thermal crosslinking of the polyesters.[10] Cristobal et al. synthesized a polyester from MAn and 1,3-propylene glycol using *p*-toluenesulfonic acid as the catalyst; however, *cis-trans* isomerization of the MAn double bonds to fumarate (FA) double bonds occurred owing to the high reaction temperatures (188–190 °C).[11] Our survey of the literature indicated that all reported, MAn-based polycondensations performed at high temperatures, produced polyesters containing FA units.[12] To synthesize unsaturated polyesters with well-defined structures, Kricheldorf and colleagues[13] investigated the suitability of low-temperature metal triflate-catalyzed polycondensations of diols and MAn without significant isomerization at 60 °C, but only polyesters of low molecular mass (M_n

<5 kDa) were obtained. Coates and colleagues[4b,14] synthesized polymers containing MAn units by copolymerization of MAn with epoxides and then converted the MAn units to FA units via a diethylamine ($HNEt_2$)-catalyzed *cis-trans* isomerization reaction,[4b] in which they used the metal catalyst, chromium (III) salen complex for the copolymerizations.

Recently we published a preliminary study on the dehydration polycondensation of dicarboxylic acids and diols using the sublimating strong Brϕnsted acid bis(nonafluorobutanesulfonyl)imide (Nf_2NH) as the catalyst,[15] which has also been used in our laboratory for the ring-opening polymerization of ε-caprolactone[16] and copolymerization of cyclic anhydrides with THF.[17]

For the work reported herein, we again focused on Nf_2NH because of its superior catalytic activity for dehydration polycondensations and because it can be used under mild reaction conditions, which should enable isomerization-free synthesis of unsaturated polyesters. We prepared gels from poly[IAn -*alt*-2-methyl-1,5-pentanediol (MPD)]-*co*-poly(MAn-*alt*-MPD) by photo-crosslinking the exo-type double bonds in the IAn units. These gels, which contained the *cis* double bonds in the MAn units were transformed into gels, which contained mostly *trans* double bonds, via in a one pot, $HNEt_2$-catalyzed reaction. The swelling properties of the gels were shown to depend on the initial MAn to FA unit ratios (degree of isomerization) as well as the MAn to IAn ratio. As far as we know, this is the first report of *cis-trans* isomerization of double bonds in unsaturated polyester gels.

2-2. Results and Discussion

Isomerization-Free Ring-Opening Polycondensation of MAn with MPD: Comparison of Catalyst Efficiencies.

Table 2-1. Polycondensation of MAn with MPD using Rare-Earth Metal Triflate, Catalysts, $Sc(NNf_2)_3$, or Nf_2NH as the Catalyst

entry	catalyst[a]	temp.(°C)	time (h)	$M_n{}^b$x10^{-3}	$M_w/M_n{}^b$	yield (%)[c]
1	$Tm(OTf)_3$	80	3	1.8	2.0	92
2	$Nd(OTf)_3$	80	3	1.5	2.2	89
3	$Sm(OTf)_3$	80	3	1.8	2.2	91
4	$Sc(OTf)_3$	80	3	5.3	2.0	87
5	$Sc(NNf_2)_3$	80	3	8.8	2.4	88
6	Nf_2NH	80	3	10.9	2.0	86
7	Nf_2NH	80	8	16.8	2.2	81

[a]0.25 mol% catalyst to monomers. [b]Determined by SEC before purification by precipitation. The column had been calibrated with poly(styrene) standards. Solvent, $CHCl_3$. [c]Yields were calculated after purification.

Polycondensations of MAn with MPD were used to compare the effectiveness of rare-earth metal triflates, $Sc(NNf_2)_3$,[7,13] and Nf_2NH as the catalysts (Table 2-1, runs 1–6; conditions: 80°, 3 h reaction time, 0.25 mol% catalyst/monomers). The M_n values (<2.0 kDa) of the polyesters when $Tm(OTf)_3$, $Nd(OTf)_3$, or $Sm(OTf)_3$ was used as the catalyst were less than that found for the polyester when $Sc(OTf)_3$[7a,7b] was used ($M_n = 5.3$ kDa). $Sc(NNf_2)_3$[7e] was the most effective of the rare-earth metal catalysts ($M_n = 8.8$ kDa), although it produced a polyester with a broader molecular weight distribution ($M_w/M_n = 2.4$). With Nf_2NH as the catalyst (run 6), the M_n value of the polyester was 10.9 kDa, and when the reaction time for these conditions was extended from 3 to 8 h, the M_n value of the polyester increased to 16.8 kDa without substantially broadening the M_w/M_n (run 7). The ^{1}H-NMR spectrum of the polyester prepared in run 7 (Figure 2-1. a) clearly shows that the MAn *cis* double bonds had not been isomerized. The peak at 6.22 ppm was assigned to protons of a *cis* carbon-carbon double bond (*cis* geometry), whereas peaks ascribable to *trans* geometry (at 6.84 ppm) were not observed. The presence of *cis* double bonds was also confirmed by ^{13}C-NMR spectroscopy as a single methine carbon was observed at 128-131 ppm in the spectrum of poly(MAn-*alt*-MPD) (Figure 2-1. b). Taken together, the results identified Nf_2NH as the most effective of the tested catalysts for the isomerization-free polycondensation of MAn with MPD.

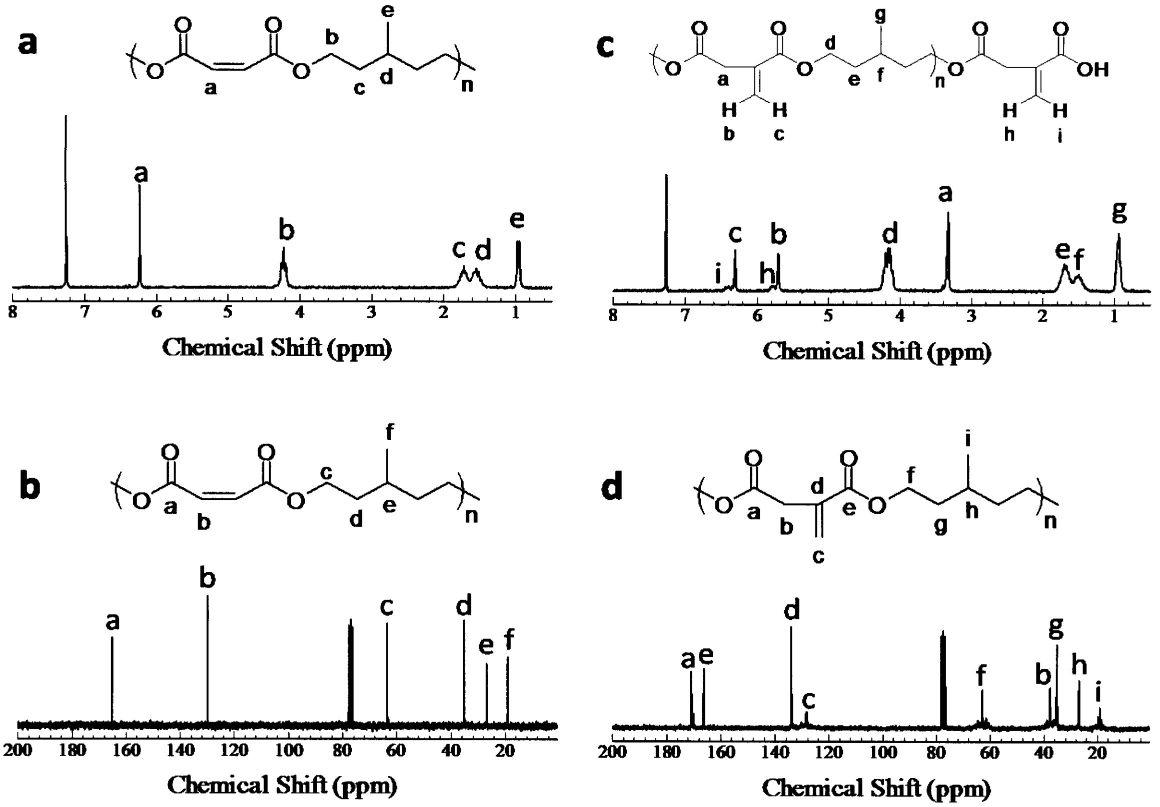
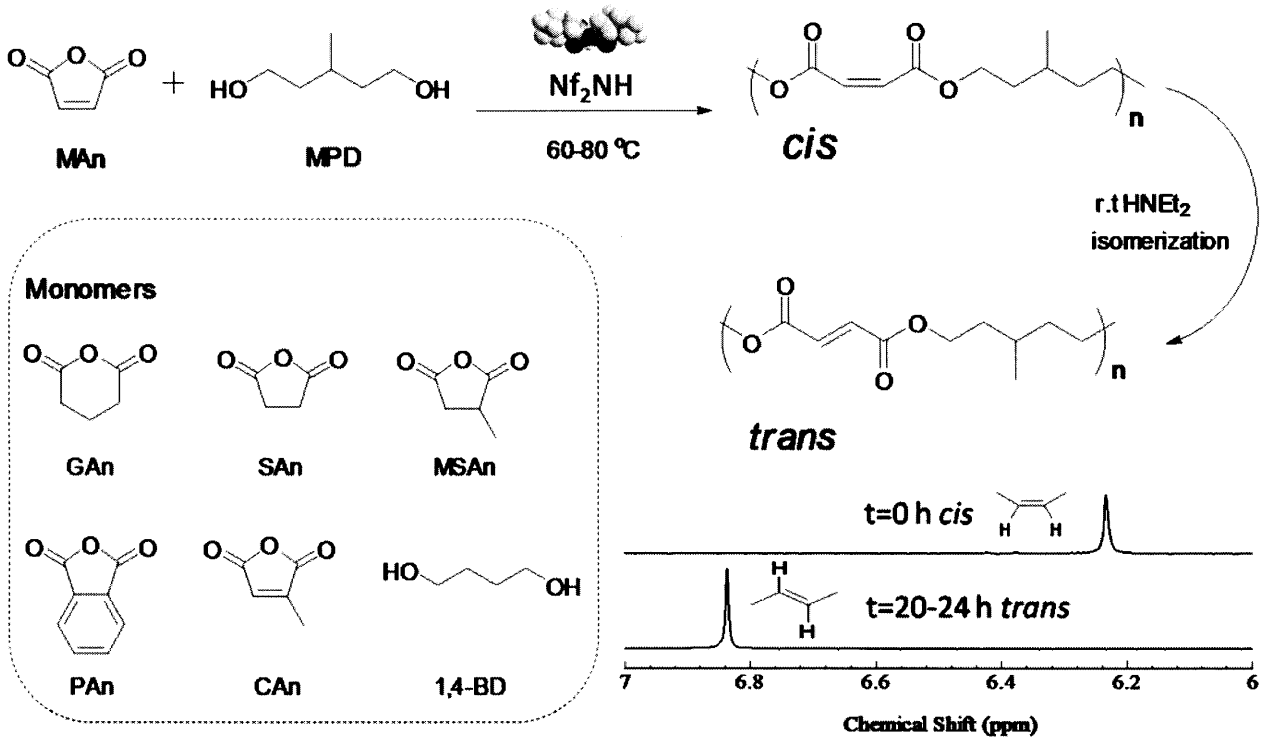


Figure 2-1. ^{1}H-NMR spectra of (a) poly(MAn-*alt*-MPD) and (c) poly(IAn-*alt*-MPD) and ^{13}C-NMR spectra of (b) poly(MAn-*alt*-MPD) and (d) poly(IAn-*alt*-MPD).

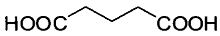
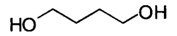
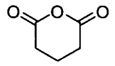
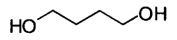
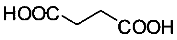
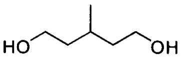
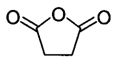
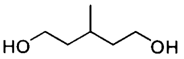
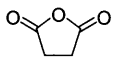
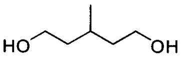
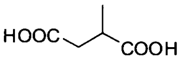
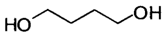
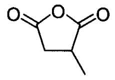
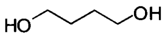
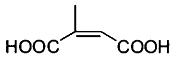
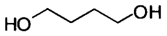
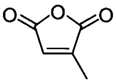
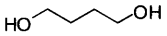
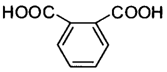
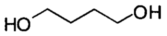
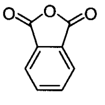
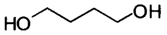
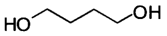
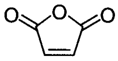
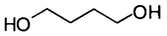
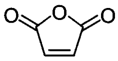
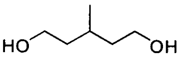
Because we could polymerize MAn and MPD in an isomerization-free manner, we next assessed the ability to convert poly(MAn-*alt*-MPD) to poly(FA-*alt*-MPD), i.e., controlled *cis-trans* isomerization of the MAn unit double bonds. Coates and colleagues reported the $HNEt_2$-catalyzed *cis-trans* isomerization of MA polyester units.[4b] Using their procedure, we converted poly(MAn-*alt*-MPD) in toluene (Table 2-1, entry 7) to poly(FA-*alt*-MPD) using 1% (v/v) $HNEt_2$ as the catalyst (at r.t. for 20-24 h). In the ^{1}H-NMR spectrum of poly(MAn-*alt*-MPD) (the starting material; Scheme 2-1, bottom right, top spectrum), the signal at 6.22 ppm assigned to *cis* double bond geometry had completely disappeared by the end of the reaction, and a new signal was present at 6.84 ppm (Scheme 2-1, bottom right, bottom spectrum) indicative of a *trans* geometry. The M_n values for the polyester before and after the isomerization were very similar (before isomerization, 16.8 kDa, $M_w/M_n = 2.2$; after isomerization, $M_n = 15.1$ kDa, $M_w/M_n = 2.3$). Full assignment of the

^{1}H-NMR of the product identified it as an unsaturated polyester with all *trans* double bonds, i.e., poly(FA-*alt*-MPD).



Scheme 2-1. Scheme of polycondensation of MAn with MPD. Expanded ^{1}H-NMR spectra of poly(FA-*alt*-MPD) (bottom) prepared from poly(MAn-*alt*-MPD) by HNEt$_2$-catalyzed *cis-trans* double bond isomerization in chloroform. At the bottom left are shown other monomers used in this work.

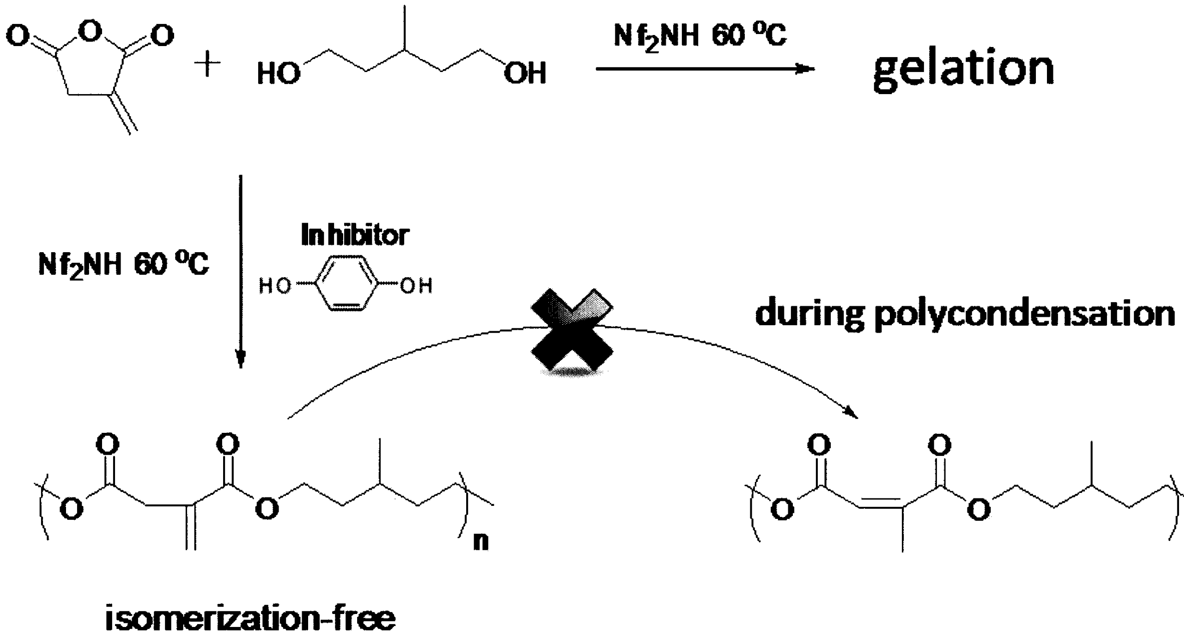
Table 2-2. Polycondensation of Dicaboxylic Acids or Cyclic Anhydrides with Diols Catalyzed by Nf_2NH

entry	Nf_2NH[a]	monomer[b]		temp	time	yield[c]	M_n[d]	M_w/M_n[d]	T_g[e]	T_m[f]
	(mol%)	M_1	M_2	(°C)	(h)	(%)	$\times 10^{-3}$		(°C)	(°C)
1	0.25			80	3	88	10.9	1.8		
2	0.25			80	3	86	14.4	1.8	-60	35
3	0.25			80	3	91	6.2	2.0		
4	0.25			80	3	87	15.4	1.8	-44	none
5	0.5			60	6	85	15.9	2.0		
6	0.25			80	3	93	5.5	1.8		
7	0.25			80	3	89	7.4	1.7	-40	27
8	0.5			60	24	81	7.2	1.9		
9	0.5			60	24	72	18.1	2.0	-36	27
10	0.5			80		No polymerization				
11	0.5			80	6	82	3.1	1.8	3	none
12	0.25			80	3	88	4.9	1.9		
13	0.25			80	3	84	8.4	1.8	-27	31
14	0.25			80	3	See table 1, entry 6			-29	25

[a] Mol% catalyst to monomers. [b] M_1 are dicarboxylic acids or cyclic anhydrides. M_2 are diols. [c] Yields were calculated after purification by reprecipitation. [c] Yields were calculated after purification. [d] Determined by SEC before purification. The column had been calibrated with poly(styrene) standards. Solvent, $CHCl_3$. [e] Determined by DSC (heating rate: 10°C/min, 2nd run). [f] Determined by DSC (heating rate: 10°C/min, 1st run)

Next, we investigated the Nf_2NH-catalyzed polycondensations of the dicaboxylic acids (GA, SA, MSA, CA, PA, MA) or other the cyclic anhydrides (GAn, SAn, MSAn, CAn, or PAn) with MPD or 1,4-BD at 80 or 60 °C (Table 2-2). To avoid the gelation, certain polycondensations were performed at the lower temperature (Table 2-2, entries 8 and 9). For runs 3 and 4, we used MPD as the co-monomer to decrease the melting point of the product polyester. All ring-opening polycondensations employing the cyclic anhydrides occurred more rapidly than did the polycondensations of their corresponding dicarboxylic acids. Polyesters of greater molecular weights (M_n = 3.1–18.1 kDa) were prepared. When polycondensation of SAn with MPD was carried out at 60 °C for 3 h with 0.5 mol% catalyst, a polyester with an M_n value of 15.9 kDa was obtained (Table 2-2, entry 5). Previously a polycondensation of CA with 1,4-BD had been carried out at 60 °C, for 50 h, with 1 mol% $Sc(OTf)_3$ to obtain a polyester with an M_n value of 14.1 kDa.[7b] However, the Nf_2NH-catalyzed polycondensation of CAn with 1,4-BD at 60 °C for 24 h with 0.5 mol% Nf_2NH (Table 2-2, entry 9) produced a polymer with an M_n value of 18.1 kDa (M_w/M_n = 2.0), indicating that Nf_2NH is a more effective catalyst than is $Sc(OTf)_3$.[7b] Polycondensation of PA with 1,4-BD did not proceed at 80 °C (Table 2-2, entry 10) because 1,4-BD was not miscible in solid PA at 80 °C. In support of this conclusion, when PAn was used instead a homogenous state was observed and a polyester was produced at 80 °C (entry 11), which is probably a consequence of the lower melting temperature of PAn compared with that of PA.

Scheme 2-2. Isomerization-Free Nf_2NH-Catalyzed Polycondensation of IAn and MPD with Hydroquinone as the Radical Inhibitor.



As described above, bulk isomerization-free polycondensation of IAn with diols was difficult to be accomplished, because gelation occurred and the IAn units partially isomerized to CAn units during the synthesis. To control the IAn content (Scheme 2-2), we investigated the ternary polycondensation of MPD with IAn and a second cyclic anhydride using Nf_2NH (1 mol% to monomers) as the catalyst at 60 °C (Table 2-3). Gelation was observed after 2 h for the polycondensation of IAn with MPD (Table 2-3, entry 1). Even when we used MAn as a co-monomer (initial monomer ratio $[IAn]_0$:$[MAn]_0$:$[MPD]_0$ of 1:8:9) to decrease the IAn content, gelation still occurred within 8 h (Table 2-3, entry 2). To inhibit gelation, 1, 0.5, or 0.1 mol% (to total monomers) of hydroquinone, a radical inhibitor, was added into reaction mixtures (runs 3–5, respectively, Table 2-3). In all three runs, polymerization occurred without gelation; therefore, 0.1 mol% hydroquinone was sufficient to inhibit radical-induced cross-linking. Remarkable differences among the molecular weights of the polymers prepared in runs 3–5 were not found (see Table 2-3 for the M_n values). In the ^{1}H-NMR spectrum of the run 5 (Table 2-3) sample, peaks at 6.22 and at 5.63 ppm could be assigned to the double bond hydrogens in the IAn units; whereas, signals associated with CA units were not present. Therefore, when a radical inhibitor was present during the polycondensation of IAn, isomerization of the IAn double bond did not occur.

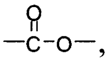
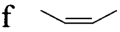
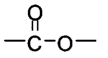
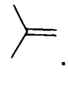
Table 2-3. Preparation of Copolymers via Nf_2NH-Catalyzed Polycondensation of Cyclic Anhydrides and Diols with Hydroquinone as the Radical Inhibitor

entry	diols	cyclic anhydride ($[M1]_0$:$[M2]_0$)[a]	catalyst[b] (mol %)	inhibitor[c] (mol %)	temp. (°C)	time (h)	yield[d] (%)	M_n[e] × 10^{-3}	M_w/M_n[e]
1	MPD	IAn	1	0	60	< 2	gelation	-	-
2	MPD	IAn:MAn (1:8)	1	0	60	< 8	gelation	3.1[f]	1.7[f]
3	MPD	IAn	1	1	60	24	92	1.5	2.0
4	MPD	IAn	1	0.5	60	24	85	1.4	1.9
5	MPD	IAn	1	0.1	60	24	88	1.6	1.8
6	MPD	IAn:MAn (1:2)	1	0.1	60	12	84	3.4	1.8
7	MPD	IAn:MAn (1:4)	1	0.1	60	12	87	5.6	1.7
8	MPD	IAn:MAn (1:8)	1	0.1	60	12	82	8.1	1.8
9	MPD	IAn:SAn (1:4)	1	0.1	60	12	84	5.0	1.9
10	MPD	IAn:PAn (1:4)	1	0.1	60	12	83	5.2	1.8

[a]The initial M_1 to M_2 ratio (mol/mol). [b]Catalyst ratio (mol% to total moles of monomers). [c]Radical inhibitor ratio (mol% to total moles of monomers). [d]Yields were calculated after purification by reprecipitation. [e] Determined by SEC. The column had been calibrated with poly(styrene) standards. Solvent, $CHCl_3$. [f]Determined for the $CHCl_3$-soluble polyester fraction.

To expand the range of synthesized polyesters, different initial ratios of MAn and IAn were used. As the initial IAn to MAn ratio ($[\mathrm{IAn}]_0/[\mathrm{MAn}]_0$) decreased from 1:2 to 1:8 (Table 2-3, entries 6–8,), the molecular weights of the products increased from 3.4 to 8.1 kDa. Polyesters containing IAn and SAn or PAn were also synthesized (Table 2-3, runs 9, 10), with M_n values of 5.0 kDa and 5.2 kDa, and M_w/M_n of 1.8 and 1.9, respectively.

Preparation of Polyester Gels Containing MAn and IAn Units Prepared by Photo-Crosslinking the Exo-Type Double Bonds in the IAn Units with or without Subsequent *cis-trans* Isomerization of MA-Unit Double Bonds.

To demonstrate that the exo-type double bonds of IAn units could be selectively photo-crosslinked to produce gels, we first prepared, under the same conditions, poly(IAn-*alt*-MPD) and poly(MAn-*alt*-MPD), with the latter serving as a control. The two of polyesters had similar molecular weights [oligo(MAn-*alt*-MPD): M_n = 1.8x10^3, M_w/M_n = 2.0; oligo(IAn-*alt*-MPD): M_n = 1.6 x10^3, M_w/M_n = 1.8 (Table 2-3, entry 5)]. After individually dissolving each polymer in toluene (1 g/mL), the photo-initiator Irgacure (1 wt%) was added, and the samples were UV light-irradiated for 30 min at r. t. FT-IR spectra of the samples before and after irradiation were recorded. The peak at 1728 cm^{-1} in the poly(MAn-*alt*-MPD) spectrum (Figure 2-2. a, left panel) was ascribed to the stretching mode of the carbonyl ester group  $-\overset{\overset{O}{\|}}{C}-O-$, and the peak at 1643 cm^{-1} to the *cis* double bond stretching mode or MAn double bond of . The peak at 1735 cm^{-1} in the poly(IAn-*alt*-MPD) spectrum (Figure 2-2. b, left panel) was assigned to the  $-\overset{\overset{O}{\|}}{C}-O-$ and the peak at 1638 cm^{-1} was assigned to the double bonds of IAn units . The changes in the numbers of *cis* and *trans* before and after irradiation were calculated using Lambert-Beer's law, $A = \varepsilon[c]l$, where A is the absorbance at the selected wavenumber, ε is the molar extinction coefficient at the selected wavenumber, [c] is the concentration of the double bond in the polyester or polyester gel, and l is the thickness of the sample.

For the poly(IAn-*alt*-MPD) spectrum (Figure 2-2. b), the absorbance of the peak at 1735 cm^{-1} was unchanged by irradiation, but the peak at 1638 cm^{-1} had decreased in intensity after irradiation. To quantitatively assess the degree of crosslinking, the absorbance values for the peaks of the double bonds were normalized to those of the carbonyl stretchings. For poly(MAn-*alt*-MPD), the absorbance ratio $\left(\frac{A_{1643}}{A_{1728}}\right)$ was 0.14 constant before and after irradiation of the sample. Conversely, the absorbance ratio $(\frac{A_{1638}}{A_{1735}})$ for poly(IAn-*alt*-MPD) before irradiation was 0.18, whereas the value was 0.10 after irradiation, which indicated that the number of IAn units had decreased. Additionally, the ^{1}H-NMR spectrum of poly(MAn-*alt*-MDP) was unchanged by irradiation, which showed that *cis-trans* isomerization had not occurred (Figure 2-2. a, right panel).

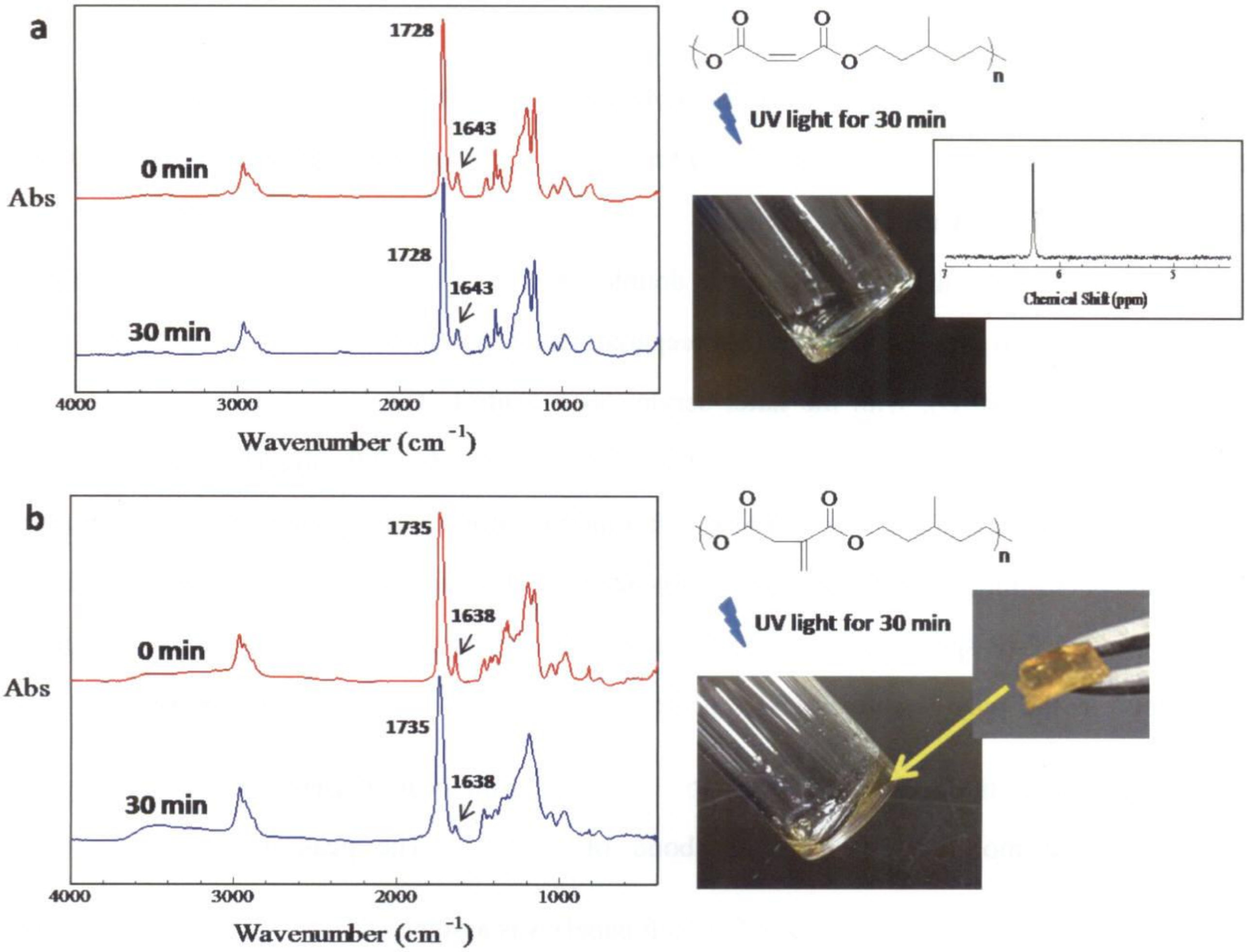


Figure 2-2. FT-IR spectra (left panel) and photos accompanied with expanded ^{1}H NMR spectra (right panel) of (a) poly(IAn-*alt*-MPD) and (b) poly(MAn-*alt*-MPD) before and after photo irradiation.

Table 2-4. Photocured polyesters containing MA and IA units

entry	photo-cross linking[a]			isomerization[b]	
	parent polyester	gel yield	*cis*-gels		*trans*-gels
1	Table 3, entry 6	67 %	*cis*-gel **1**	$HNEt_2$ (24 h)	*trans*-gel **1**
2	Table 3, entry 7	71 %	*cis*-gel **2**	$HNEt_2$ (24 h)	*trans*-gel **2**
3	Table 3, entry 8	65 %	*cis*-gel **3**	$HNEt_2$ (24 h)	*trans*-gel **3**

[a]Prepared via UV light irradiation (250–400 nm) for 30 min. [b]To convert the *cis*-gels to *trans*-gels, the gels were immersed in $CHCl_3$, 1% (v/v) $HNEt_2$.

Finally, copolymers containing different IAn to MAn ratios (Table 2-3, entries 6, 7, and 8) were selected to prepare polyester gels and to examine the effects of the IAn to MAn ratios on the physical properties of the gels. Each copolymer was individually dissolved in toluene (1 g/mL). The polyester with an initial IAn to MAn ratio ($[IAn]_0 : [MAn]_0$) of 1:8 (Table 2-3, entry 8) was less amenable to crosslinking that were those of entries 6 and 7 ($[IAn]_0$:$[MAn]_0$ = 1:2 and 1:4, respectively). Thus, 1, 2, and 4, wt% of Irgacure 184 was added into the samples of runs 6, 7, and 8, respectively. The polyesters from these runs, were irradiated with UV light (240–400 nm) for 30 min to produce *cis* gels (Figure 2-3, top; Table 4). The degree of crosslinking, which was controlled by the initial ratio of IAn to MAn ($[IAn]_0$:$[MAn]_0$), affected the mechanical properties of the *cis* gels: *cis* gel **1** was brittle and *cis* gel **3** was more elastic than was *cis* gel **2**. Using the *cis* gels in toluene, we then prepared *trans* gels by $HNEt_2$-catalyzed isomerization of the *cis* double bonds (Table 2-4). FT-IR spectra were recorded to ascertain that *cis*-*trans* isomerization of the double bonds had occurred (Figure 2-3). After isomerization, the peaks at 1377–1408 cm^{-1} (circled in red) ascribed to *cis* double bonds had disappeared, and peaks at 1261–1298 cm^{-1} (circled in blue) assigned to *trans* double bonds had appeared, and we could not find signals at 815 cm^{-1} indicating the presence of *cis* double bonds. The results indicated that *cis*-*trans* isomerization of the MAn double bonds had occurred quantitatively even in the *cis* gel.

The degree to which the gels could swell in toluene, acetone, and DMF was evaluated using the ratio of the weights (Ws/W_0) of the gel in their swollen (Ws) and dry (W_0) states (Figure 2-4). The solvents were chosen to sample different polar environments, i.e., the relative polarities of toluene, acetone, and DMF are 0.10, 0.36, and 0.39, respectively.[19] As shown by the Ws/W_0 values (Figure 2-4), as the initial, relative amount of MAn increased, the swelling ratio increased, as a consequence of a decrease in the crosslinking density. Comparing the Ws/W_0 values of the *cis* gels with the *trans* gels for the toluene system, the latter are larger than the former. Conversely, for the acetone and DMF systems, the values of W_s/W_0 for the *trans* gels are smaller than are those of the *cis* gels. A reported solubility data in acetone (29.7 °C) of the model compounds, i.e., fumaric acid (1.97 g/solvent 100g)[20] and malic acid (26.3 g/solvent 100g) [20] also coincided with the swelling property of the polyester gels. Because the polarity of a *cis* carbon- carbon double bond is greater than that of a *trans* double bond. Actually, in acetone, the solubility test was as follows: poly(MAn-*alt*-MPD) (1330 mg/mL); and poly(FA-*alt*-MPD) (870 mg/mL). We conclude, therefore, that *cis-trans* isomerization of carbon double bonds and the choice of solvent can be used to control how much a gel swells. To the best of our knowledge, this is the first to report on *cis-trans* isomerization of double bonds in polyester gels and on their swelling properties.

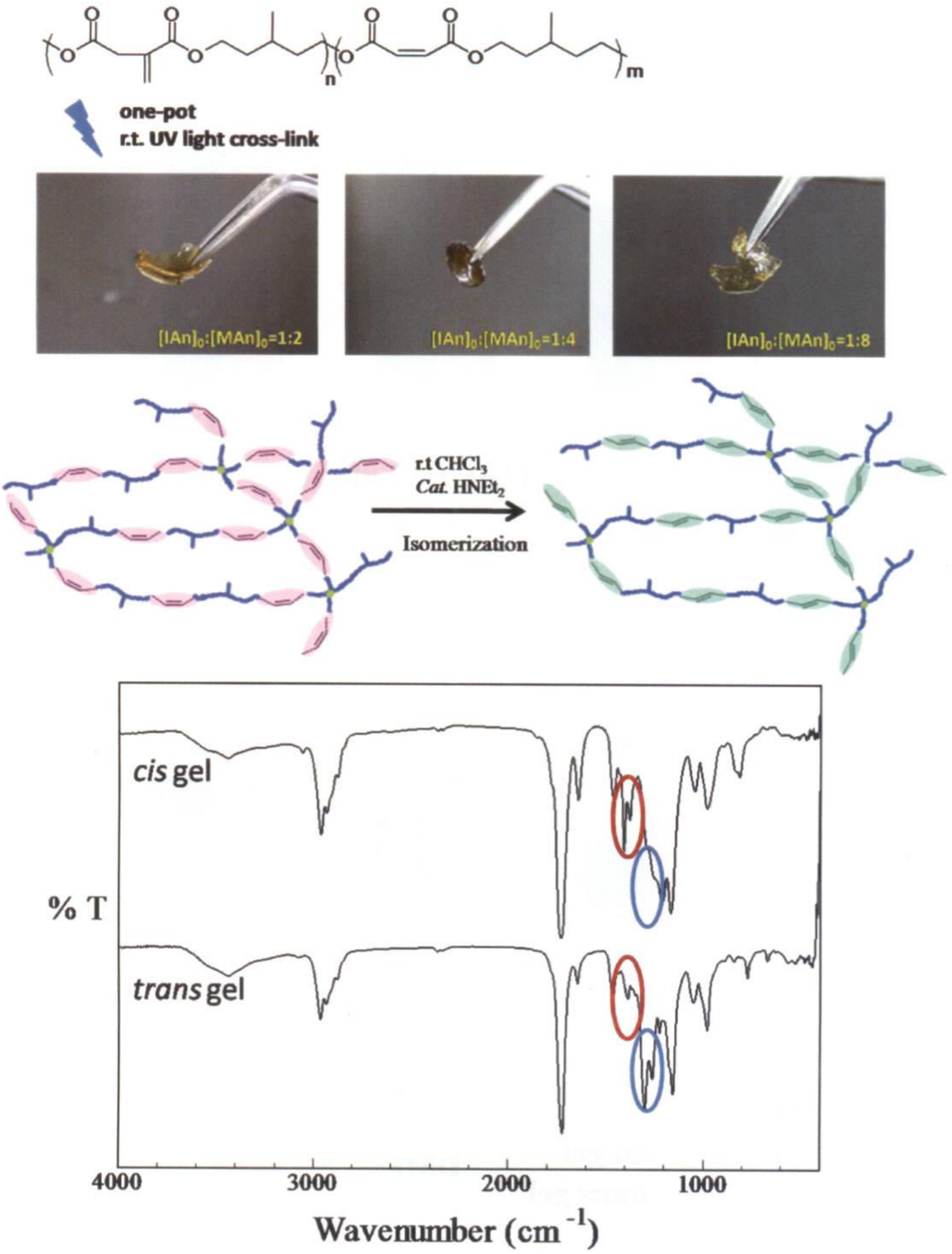


Figure 2-3. Photo-crosslinking of unsaturated polyesters and transformation of a *cis* gel to a *trans* gel ($[IAn]_0:[MAn]_0=1:4$).

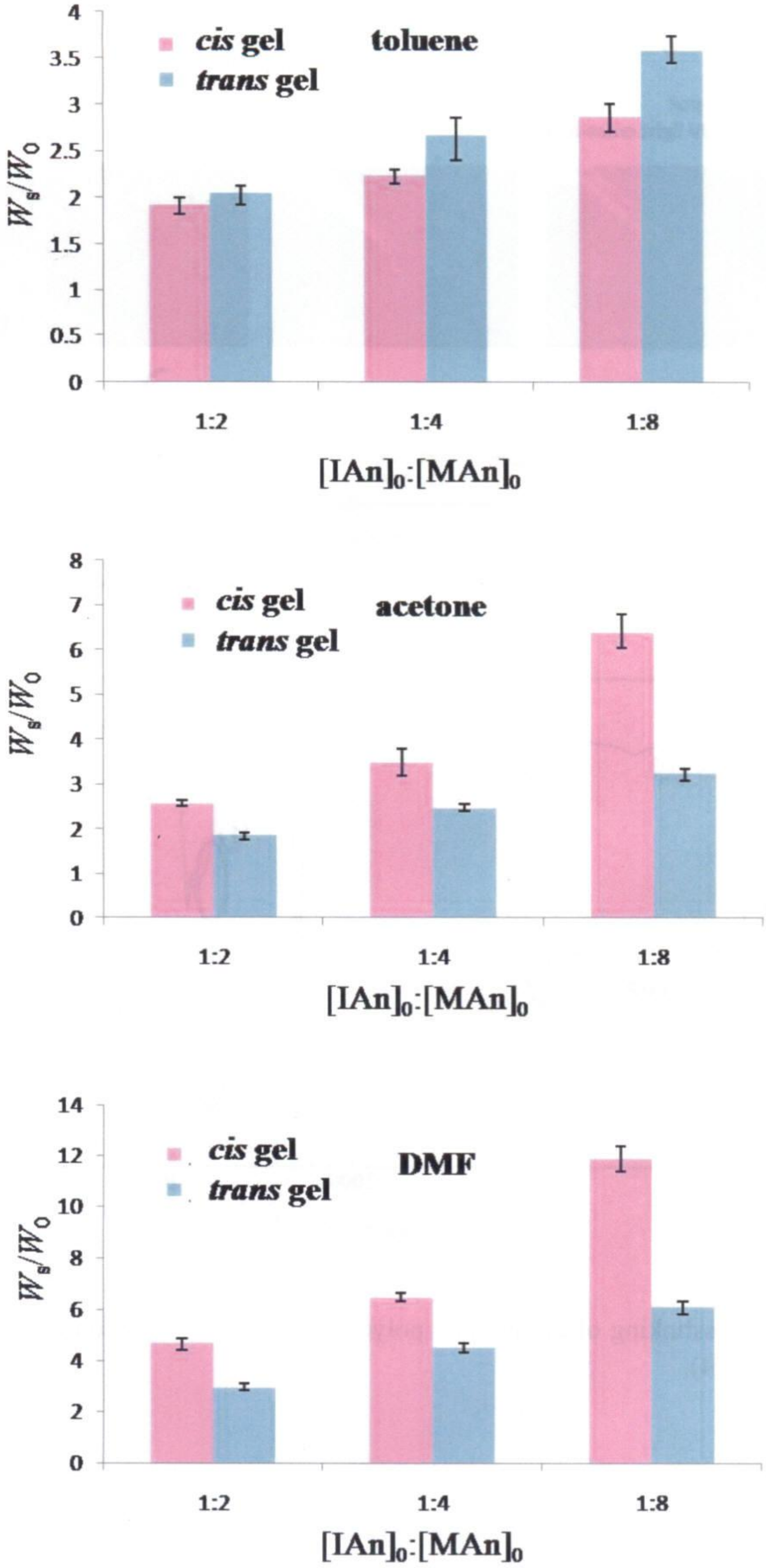


Figure 2-4. Swelling property of unsaturated polyester gels in some organic solvents.

In summary, Nf_2NH-catalyzed polycondensations of cyclic anhydrides and diols provided unsaturated polyesters with $M_n > 10.0 \times 10^3$, in shorter periods of time, and at lower reaction temperatures than did polycondensation of Nf_2NH-catalyzed dicarboxylic acids and diols. We prepared polyesters/copolyesters from a variety of anhydrides. The copolyesters with exo-type double bonds ascribed to IAn units were photo-crosslinked to afford unsaturated *cis* polyester gels. The *trans* Gels were prepared via $HNEt_2$-catalyzed isomerization of the double bonds in the *cis* gels. The swelling properties of these gels were found to be dependent on the geometries of their double bonds. Our discoveries should find use in drug-release systems and other biomedical applications.

2-3. Experimental section

Materials.

Succinic anhydride (SAn), succinic acid (SA), glutaric anhydride (GAn), glutaric acid (GA), phthalic anhydride (PAn), phthalic acid (PA), MAn, maleic acid (MA), itaconic anhydride (IAn), itaconic acid (IA), citraconic anhydirde (CAn), and citraconic acid (CA), were purchased from Tokyo Chemical Industry Co., Ltd (Tokyo, Japan). Methylsuccinic anhydride (MSAn) and methylsuccinic acid (MSA) and were purchased from Aldrich Co., Ltd. (Milwaukee, WI, USA). Hexane, methanol, acetone, dimethylformamide (DMF), toluene, and chloroform were purchased from Nacalai Tesque (Kyoto, Japan) and were distilled before use. Thulium-trifluoromethanesulfonate [Tm(OTf)$_3$] and samarium-trifluoromethanesulfonate [Sm(OTf)$_3$] were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). Neodymium-trifuloromethanesulfonate [Nd(OTf)$_3$] was purchased from Aldrich Co., Ltd. (Milwaukee, WI, USA). Nf$_2$NH was purchased from Mitsubishi Materials Electronic Chemicals Co., Ltd. (Akita, Japan), and dried under reduced pressure before use. HNEt$_2$, MPD, and 1,4-butanediol (1,4-BD) were purchased from Nacalai Tesque (Kyoto, Japan). 1-Hydroxycyclohexyl phenyl ketone (Irgacure 184) was purchased from Tokyo Chemical Industry Co., Ltd (Tokyo, Japan). Sc(NNf$_2$)$_3$ was prepared according to a literature report.[7e]

Measurements.

^{1}H-NMR spectra were recorded at 27 °C using a Bruker DPX200 spectrometer (200 MHz). Chemical shifts were referenced to tetramethylsilane ($\delta = 0$). The number average molecular weight (M_n) and polydispersity index (M_w/M_n) of each polymer were determined using a size exclusion chromatography (SEC) system that included a Tosoh DP8020 pump system, an RI (Tosoh RI-8020) detector, and a Tosoh TSK-GEL SUPERMULTIPOREHZ-M column calibrated with polystyrene standards. The eluent was CHCl$_3$; the flow rate was 0.35 mL/min; and the temperature was 40 °C. Differential scanning calorimetry (DSC), using a DSC6220S calorimeter (Seiko Instruments Inc., Chiba, Japan), was investigated from -80 to 80 °C, with the temperature increased or decreased at a rate of 10 °C/min. The instrument was calibrated using indium and tin samples. For all experimental samples, a complete temperature heating cycle from -80 to 80 °C and back to -80 °C was obtained. Each sample weighted between 6 and 10 mg and was placed into an aluminum pan that was covered with a lid within the calorimeter. The glass transition temperature (T_g) was taken as the inflection point of the corresponding heat capacity jump of theDSC trace. The melting temperature (T_m) was defined as the minimum point of the endothermic trough. FT-IR spectra were recorded in KBr disks using a JASCO FT/IR-430 spectrometer.

Ring-Opening Polycondensation of Cyclic Anhydrides with Diols.

A typical procedure (Table 2-1, entry 6) for bulk copolymerization at a relatively low temperature was performed as follows. Nf_2NH (11.68 mg, 0.02 mmol), MAn (392 mg, 4.00 mmol), and MPD (473 mg, 4.00 mmol) were mixed and then stirred at 80 °C until a homogeneous state was observed. The pressure was gradually decreased to 0.3–3 mmHg for 3 h. For purification, the products were dissolved in $CHCl_3$ and reprecipitated with hexane several times, and dried under reduced pressure (86% yield).

Isomerization of poly(MAn-*alt*-MPD) to poly(FA-*alt*-MPD).

To prepare poly(FA-*alt*-MPD) from poly(MAn-*alt*-MPD), the latter was dissolved in $CDCl_3$ to which 1% (v/v) $HNEt_2$ was added. The mixture was stirred at r. t. for 20-24 h while monitored by ^{1}H-NMR spectroscopy. After isomerization was complete, volatiles were removed by vacuum evaporation. The polyester, dissolved in $CHCl_3$, was consecutively precipitated with hexane and methanol.

Preparation of Polyester Gels Containing MAn and IAn Units Prepared by Photo-Crosslinking of the Exo-Type Double Bonds in the IAn Units Followed by *cis-trans* Isomerization of the MA Double Bonds.

A typical procedure (Table 2-4, entry 1) was performed as follows. Irgacure 184 (1% wt/wt monomers) was mixed with poly(IAn-*alt*-MPD)-*co*-poly(MAn-*alt*-MPD). Then, toluene (1 g/mL) was added. After the polyester was dissolved in the toluene, the sample was irradiated with UV light (250–400 nm) from a Toshiba H-400p high-pressure mercury lamp (400 W) for 30 min for gelation. Then the gel was immersed in $CHCl_3$ containing 1% (v/v) $HNEt_2$ to allow for *cis-trans* isomerization of the MA double bonds (at r. t. for 24 h).

2-4. References and Notes

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Chapter 3

Facile Synthesis of Unsaturated Polyester-Based Double-Network Gels via Selective Cross-Linking of Michael Addition and UV-Initiated Polymerization

ABSTRACT

The Michael addition and UV-initiated radical polymerization were used to build a one-pot method for synthesis of polyester-based double-network (DN) gels by catalyst-free selective cross-linking at room temperature. The unsaturated copolyesters containing itaconate and maleate units were prepared via polycondensation under mild conditions using an organic catalyst. Then a DN gel was synthesized by two-steps. After dissolved polyester, methyl methacrylate and UV-initiator in toluene, diamine was added into the mixture. The first gel was prepared by the catalyst-free selective cross-linking of maleate double bonds with diamine at room temperature. Subsequently, the first gel was irradiated under UV-light for 3 h. The obtained hydrophobic polyester/PMMA DN gel containing amino group with high mechanical strength showed shape recovery property. To expand the application of this method, a poly(ester-*co*-ether)/PAM DN hydrogel was synthesized. This hydrogel with amino group, containing 70 wt% water, can be used as biomaterial or commodity.

3-1. Introduction

Aliphatic polyesters, especially unsaturated polyesters, are now familiar world-wide because of their biodegradability and biocompatibility. [1] They can be used in many fields, such as coating and insulating materials[2], biomedical applications[3] and lightweight fiber-reinforced composites for automotive parts[4]. We already published a series of papers about the synthesis of polyesters using rare-earth catalysts[5] or Brønsted acids[6] under mild conditions. However, how to enhance the mechanical strength of the polyesters in order to suit for further applications is also still remained subject. This barrier has been broken by the historic synthesis of interpenetrating polymer networks (IPNs) by Millar in 1960[7]. IPNs, combining of two or more polymer networks, are prepared as the strategy that at least one polymer cross-linked in the presence of the other network(s). They can be used for numerous applications due to their strong mechanical strength, excellent thermotolerance, and ideal swelling capacity. Since then, many papers including reviews were published[8]. Recent years, for the continuous development of IPNs, double network (DN) concept was observed in many works, such as polyethyleneoxide/polyacrylic acid DN gels[9] and hydraluronan/poly(N,N-dimethylacrylamide) DN hydrogels.[10] Among these, it has been described that DN gels consisting of two interpenetrating networks can achieve the improved mechanical properties and adjust the balance between rigidity and toughness by control the structures of macromolecules. Gong and her coworkers created a series of modified DN hydrogels,[11] with optimized structures, performed excellent properties. However, these multi-step methods for preparing IPNs or DN gels still have some challenges and limitations. First of all, these preparing processes are complicated and time-consuming. The two networks of DN gels were all created by the free radical polymerization, so first network and second network should be created respectively, which takes about 2 days. So, the one-pot strategy was really desired. Secondly, due to the free radical polymerization, limited monomers can be used for the synthesis. Thus the structure of the network was limited. Agar/polyacrylamide DN hydrogels[12] was reported as a one-pot method to prepare DN gel, however, they used only agar as a fisrt network, which can not change the main chain structure for different applications. Thirdly, it is difficult to control the molecular weight of the main chain and exactly molar ratio of the networks. Furthermore, the report refers to one-pot method to prepare aliphatic polyester based DN gel is not found until now. Even though some papers referred to polyester based IPNs have been reported, but these methods were time consuming. As we know, there are many methods can lead to cross-linking, however, most of them need using catalyst or high temperature. To find a simple method for cross-linking of polyester at room temperature and without any catalyst is very interesting work. To bridge these gaps, a new method should be explored.

As originally defined by Arthur Michael, and the the first report of hetero-Michael addition reactions has been published by Skoloff and Latschinoff,[13] the Michael and Michael hetero-Michael addition reactions were considered as the most important bond forming strategies for both carbon-carbon and carbon-heteroatom bonds in organic chemistry.[14] Particularly, the Michael additions' great strength lie in mild reaction conditions (stable under air or water environment), high functional group tolerance, a large amount of polymerizable monomers and functional precursors as well as high conversions and favorable reaction rates. Thus, these commonly termed conjugate additions have gained much more attention as strategies of amino-containing polymer synthesis or modification of macromolecular architectures.[15] However, the Michael additions of amines with different kinds of unsaturated polyesters were not investigated carefully until now.

Herein, we used the Michael addition and UV-initiated polymerization to build a smart, diversified and one-pot method for synthesis of new polyester based DN gels by catalyst-free selective cross-linking at room temperature. Coates and colleagues converted the maleate polyester to fumarate polester via a diethylamine ($HNEt_2$)-catalyzed *cis-trans* isomerization reaction.[16] And we also used this method to proceed the isomeization in polyester gels.[6d] We continued to investigate the isomerization speed of maleate units to fumarate units in different polarity sovents. When the primary amines were used to react with maleate polyester at room temperature without catalyst, the Michael addition of amines with maleate double bonds proceed rapidly and at the same time, partial maleate double bonds transformed to fumarate double bonds. This kind of polymers containing amine functional groups were considered to be nonviral carriers for DNA (or gene) delivery.[17] Interestingly, the Micheal reactions of fumarate double bonds or itaconate double bonds with primary amines were difficult at room temperature and isomerization of these two double bonds was not observed. Next, we investigated the UV cross-link of unsaturated polyester by MMA with UV initiator. The itaconate polyester was cross-linked by MMA, however, the fumarate polyester and maleate polyester both can not. These results provide the potential to prepare of DN gels by one-pot selective cross-linking. First step, after the poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)], MMA, UV initiator were mixed with toluene, 1,2-ethanediamine was added into the mixture. The gel was prepared at room temperature in 5 min. Second step, the gel was cured by UV light for 3 h to make

MMA polymerized and cross-link with itaconate double bonds. Compare with the single gel (poly(MAn-co-MPD) cross-linked by $H_2NCH_2CH_2NH_2$), the polyester/PMMA DN gel containing amino group performance high mechanical property. To expand the range of this method, we also prepared poly(ester-*co*-ether)/PAM DN hydrogel by cross-linking of poly(IAn-MAn-TEG), acrylamide (AM) and 1,4-butanediamine. This hydrogel, containing 70 wt% water, can be used as biomaterial or commodity.

3-2. Results and Discussion

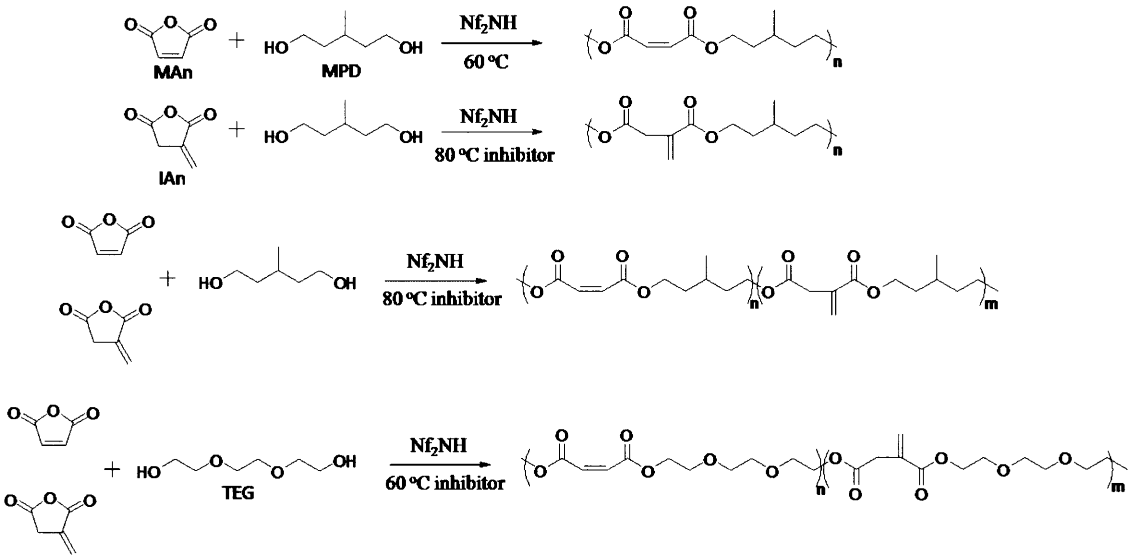
Synthesis of unsaturated polyesters and poly(ester-*co*-ether) under mild conditions

We have already published the paper about synthesis of unsaturated polyesters and copolyesters containing maleate and itaconate carbon-carbon double bonds using Nf_2NH as catalyst via ring-opening polycondensation of cyclic anhydrides with diols. Herein, firstly, we also used this method to prepare poly(IAn-*alt*-MPD), poly(MAn-*alt*-MPD), Poly poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)]s and poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)] under mild conditions for the further applications (See Scheme 3-1 and Table 3-1).

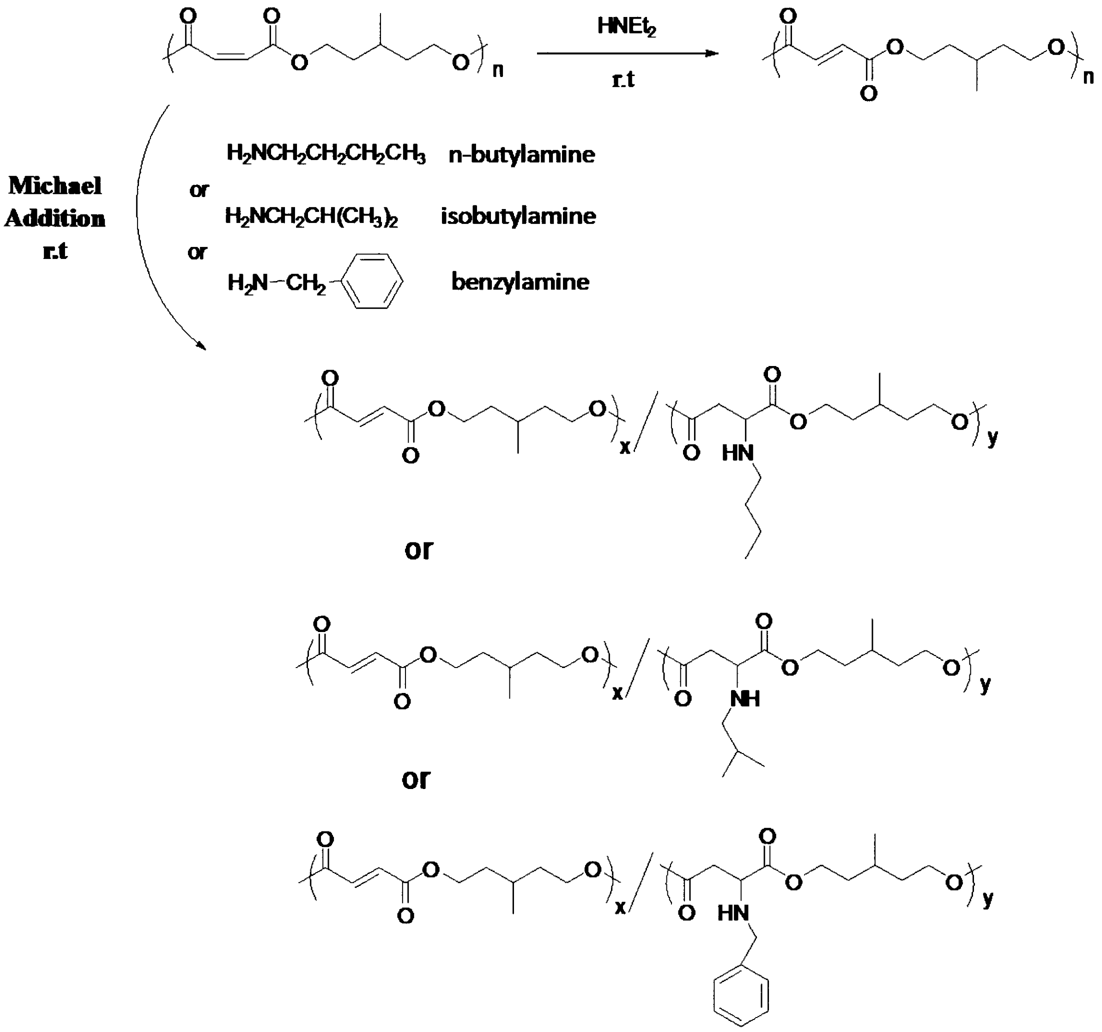
Table 3-1. Preparation of copolymers via Nf_2NH-catalyzed polycondensation of cyclic anhydeides and diols with hydroquinone as the radical inhibitor

entry^a	cyclic anhydride ($[M_1]_0$:$[M_2]_0$)	diol	catalyst^b (mol %)	inhibitor^c (mol %)	temp (°C)	yield^d (%)	$M_n^e \times 10^{-3}$	M_w/M_n^e
1	MAn	MPD	0.25	-	60	82	12.8	2.3
2	IAn	MPD	1	0.1	80	81	3.0	2.4
3	IAn:MAn (1:4)	MPD	1	0.1	80	79	10.1	2.3
4	IAn:MAn (1:8)	MPD	1	0.1	80	81	13.0	2.3
5	IAn:MAn (1:6)	TEG	1	0.1	60	83	4.7	1.9

^{a}All of the polycondensations were carried out for 12 h. In entries 2-5, the time of homogeneous period cost 10-12 h. ^{b}Catalyst ratio (mol % to total monomers). ^{c}Radical inhibitor ratio (mol % to total monomers). ^{d}Yields were calculated after purification by reprecepitation. ^{e}Determined by SEC. The column had been calibrated with poly(styrene).



Scheme 3-1. Ring-opening polycondensation of unsaturated cyclic anhydrides with diols under mild conditions to prepare unsaturated polyesters or copolyesters.



Scheme 3-2. *Cis-trans* isomerization of carbon-carbon double bonds by secondary amine and Michael addition of primary amines with poly(MAn-*alt*-MPD)

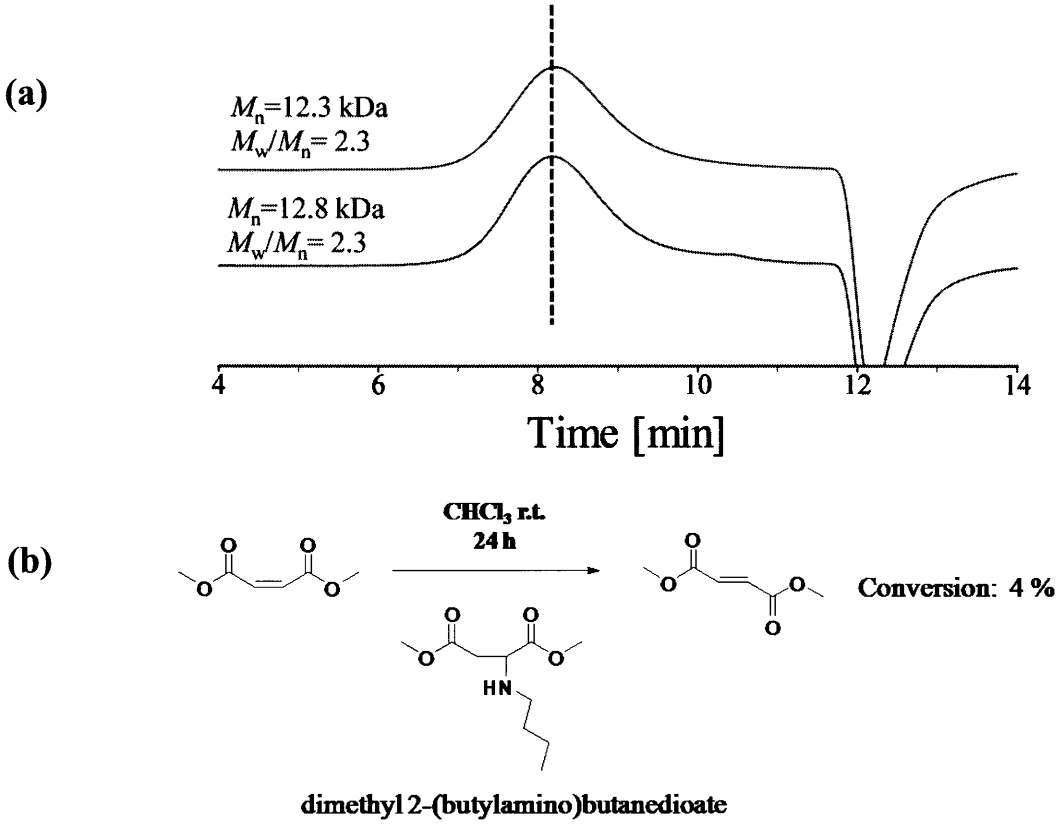
Isomerization of poly(MAn-*alt*-MPD) in different organic solvents

W. Coates reported the isomerization of maleate polyester units to fumarate polyester units using $HNEt_2$ as catalyst in $CHCl_3$. To synthesize high molecular weight fumarate polyester, we also reported isomerization-free polycondensation of MAn and MPD, and then carried out $HNEt_2$-catalyzed *cis-trans* isomerization of maleate polyester units in $CHCl_3$ in a previous report. Herein we continued to investigate the effect of polarity of different solvents on the isomrization ratio. DMF, 1,4-dioxane, $CHCl_3$, THF, toluene were selected as solvents, and carried out $HNEt_2$-catalyzed *cis-trans* isomerization of maleate polyester units in these solvents respectivity. From the Table 3-2, as the polarity of the solvents increased, the reaction speed also increased. When we used DMF as solvent, the isomerization was completed within 12 h, and it was considered as best solvent for isomerization comparing with other solvents (Table 3-2). As shown by ^1H NMR spectroscopy, after reaction with diethylamine (1 v % to solvent) in DMF, the sigal at 6.20-6.22 ppm of the *cis*-alkene was completely changed to 6.82-6.84 ppm of the *trans*-alkene. The M_n kept consistently during the isomerization (before isomerization, M_n = 12.8 kDa, M_w/M_n=2.3; after isomerization, M_n = 12.3 kDa, M_w/M_n=2.3, Scheme 3-3 (a)). The mechanism of this reaction was reported in previous organic chemistry papers and we favor the mechanism shown in Scheme 3-4, a..

Table 3-2. *Cis-trans* isomerization of maleate polyester units in different solvents at room temperature and the change of the M_n before and after isomerization in DMF for 12 h.

entry[a]	Solvent	Time	conversion
1	DMF	12	100
2	1,4-dioxane	12	73
3	$CHCl_3$	12	66
4	THF	12	64
5	Toluene	12	46

[a] All the entries was catalyzed by 1 % (v/v) $HNEt_2$ (0.2 mol/mol to maleate carbon-carbon bond units)



Scheme 3-3. (a) SEC spectra of maleate polyester (down) and fumarate polyester after isomerization in DMF for 12 h (upper). (b) Model reaction for the proposed mechanism of the isomerization of maleate double bonds by produced secondary amine.

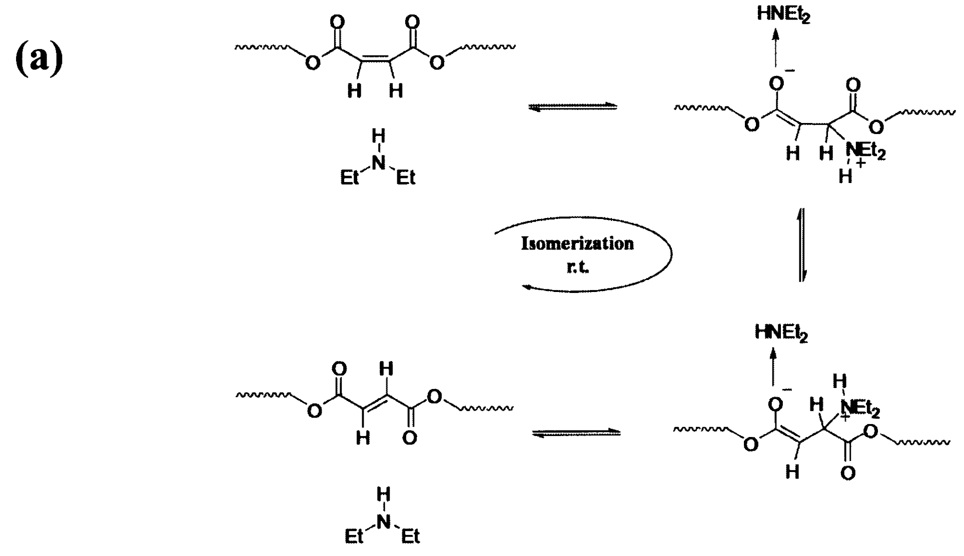
Preparation of poly(amino-ester) by catalyst-free Michael addition of carbon-carbon double bonds with primary amine at room temperature

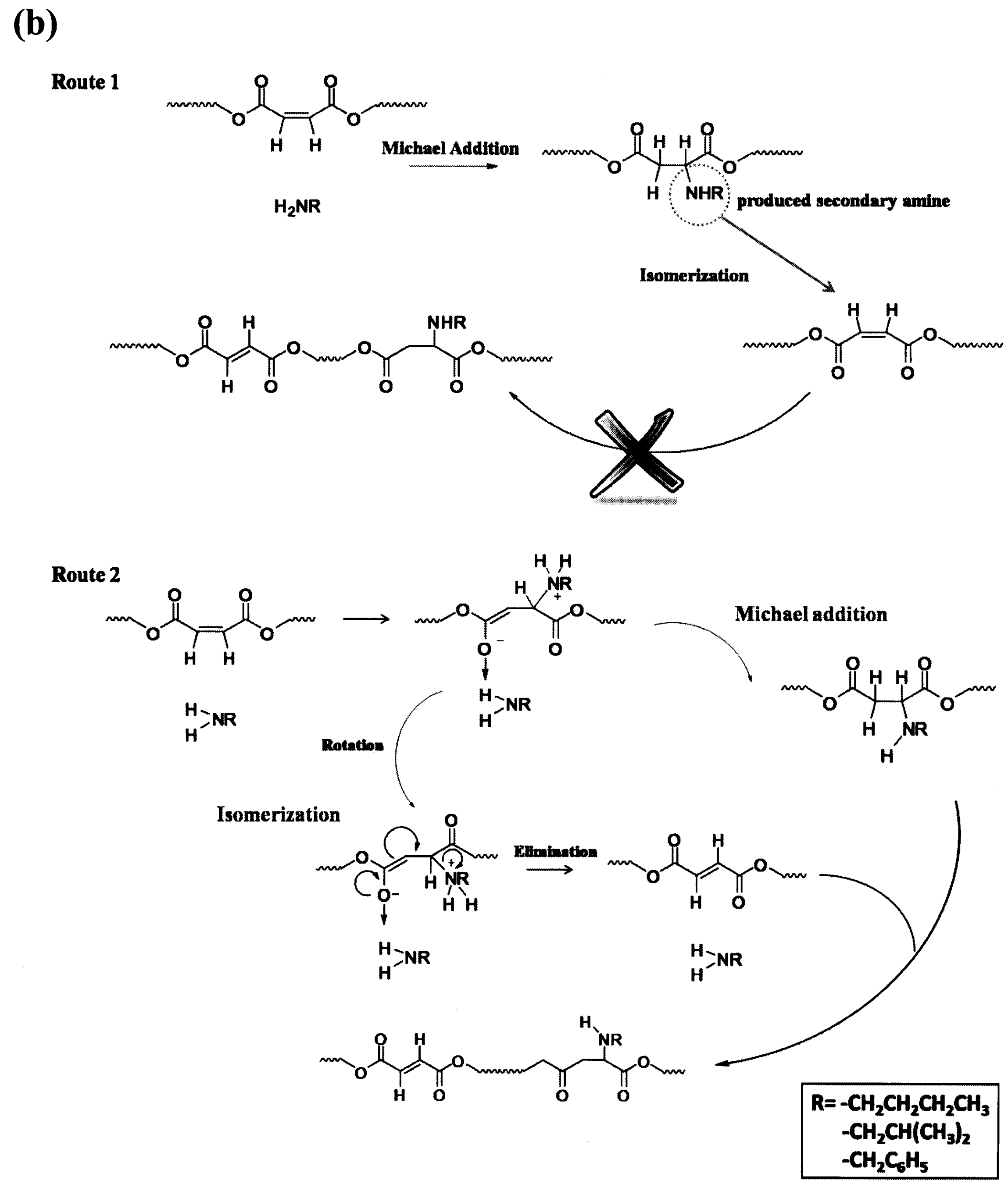
Table 3-3. Catalyst-free Michael addition of maleate polyesters with different kinds of primary amines at room temperature

entry	solvent[a]	polyester	amine[b]	time (min)	convn.[c] (%)	Mich:Isom:Unreact[c] (%:%:%)
1	$CHCl_3$	Fumarate	*n*-butylamine	20	0	0:0:100
2	$CHCl_3$	Itaconate	*n*-butylamine	20	0	0:0:100
3	$CHCl_3$	Maleate	*n*-butylamine	20	56	27:29:44
4	1,4-dioxane	Maleate	*n*-butylamine	20	87	44:43:13
5	THF	Maleate	*n*-butylamine	20	82	48:34:18
6	Toluene	Maleate	*n*-butylamine	20	76	58:18:24
7	DMF	Maleate	*n*-butylamine	5	93	54:39:7
				15	100	60:40:0
8	DMF	Maleate	Isobutylamine	20	98	49:49:2
				30	100	52:48:0
9	DMF	Maleate	Benzylamine	20	75	43:32:25
				50	100	51:49:0

[a] Solvent concentration: 0.15 g/mL, polymer weight/solvent volume). [b]The feed ratio is about 1:1 (maleate unit : amine, mol:mol). [c]The ration of conversion was calculated by ^1H NMR spectra and the conversion included both of Michael addition part and isomerization part.

With maleate polyester, fumarate polyester and itaconate polyester in hand, the reactions of unsaturated polyester with primary amines, such as *n*-butylamine, isobutylamine and benzylamine without any catalyst at room temperature were investigated (Table 3-3). Entries 3-7 in Table 3-3 demonstrated the reactions of the maleate polyester with *n*-butylamine, isobutylamine or benzylamine in DMF, 1,4-dioxane, $CHCl_3$, THF and toluene respectively. The ^1H-NMR spectra of these reactions disclosed that part of the maleate double bonds reacted with amines through the Michael reaction to afford poly(amino ester)s and simultaneously, part of the maleate double bonds were isomerized to fumarate double bonds. The ratios of Michael addition part to isomerization part were calculated from ^1H-NMR spectra. From entries 3-7, we could easily find that in DMF, the isomerizations and Michael additions were faster than in other solvents. In toluene, because of the low speed of isomerization as Table 1 disclosed, the Michael reaction part was more than isomerization part comparing with in other solvents. It conformed to the results of isomerization reactions catalyzed by $HNEt_2$ in Table 2. Entries 1 and 2 indicated that different from maleate polyester, the fumarate and itaconate polyesters did not react with n-butylamine within 20 min at room temperature. We inferred two of reaction routs for this phenomenon (Scheme 3-4, b). **Route 1**: after the secondary amine group was created by Michael addition of maleate double bonds with primary amine, the secondary amine group catalyzed isomerization of maleate double bonds to fumarate double bonds. We did a model reaction shown in Scheme S2 (b). Dimethyl 2-(butylamino)butanedioate was used as catalyst for ismerization of dimethyl maleate in $CHCl_3$ under same condition of entry 5, Table 3. After 24 h, the isomerization conversion was only 4% (The result of ^1H NMR spectrum was showed in Figure S12) comparing with the entry 5, 29% by n-butylamine (reaction time was 20 min). It was showed that the isomerization of *cis* double bonds by the created secondary amine in **route 1** was difficult for the possible reason of steric effect. So we favor the **route 2** as the possible procedure of the isomerization. In **route 2**, two reactions proceed. One is Michael addition, which creates polyester units containing amino-group. And at the same time, the isomerization and elimination reactions proceed, that prepare *trans* double bonds units in the products.





Scheme 3-4. Mechanism of isomerization of maleate double bonds to fumarate double bonds (a). Mechanism of reaction of primary amine with maleate polyester (b).

Preparation of polyester/PMMA double-network gels by one-pot method via selective Michael addition and UV cross-linking at room temperature

The primary amines can be reacted with carbon-carbon double bonds via Michael reaction without initiator or catalyst at room temperature. And the reactions are stable under air or water environment. Due to these advantages, we considered to use 1,2-ethanediamine as a cross-linker to prepare polyester gel under room temperature without any catalyst or initiator. Poly(MAn-*alt*-MPD), poly(FA-*alt*-MPD) and poly(IAn-*alt*-MPD) were chosed as unsaturated polyesters for cross-linking by 1,2-ethanediamine. As the reactions showed in Figure 3-1, after 5 min, the maleate polyester (***Cis* P1**) was quickly cross-linked by 1,2-ethanediamine, however, the fumarate polyester (***Trans* P2**) and itaconate polyester (**P3**) could not that because of the selective Michael addition among the different double bonds as we described before. The maleate polyester before and after reprecipitation were both cross-linked by this method, which indicated the residual catalyst in the polymer did not effect on the gelation. Next, we used DMF, 1,4-dioxane, THF and toluene as solvents respectively and the results were shown in Table 3-4. The cross-linking in DMF was faster than in other solvents, that might because the high polarity solvent accelerate Michael addition. In $CHCl_3$, the gelation was the slowest and in toluene, gelation is faster than in 1,4-dioxane, THF and $CHCl_3$. Within the same time, in DMF and toluene, the Michael addition was faster than in 1,4-dioxane and THF. In $CHCl_3$, the reaction was the lowest. The FT IR tests of the linear polymer and single gel were all carried out and were showed in Figure 3-2. The *cis* double bonds were transformed to *trans* double bonds during the Michael cross-linking. The peaks at 1377-1408 cm^{-1} ascribed to *cis* double bonds and the peaks at 1261-1298 cm^{-1} assigned to *trans* double bonds.

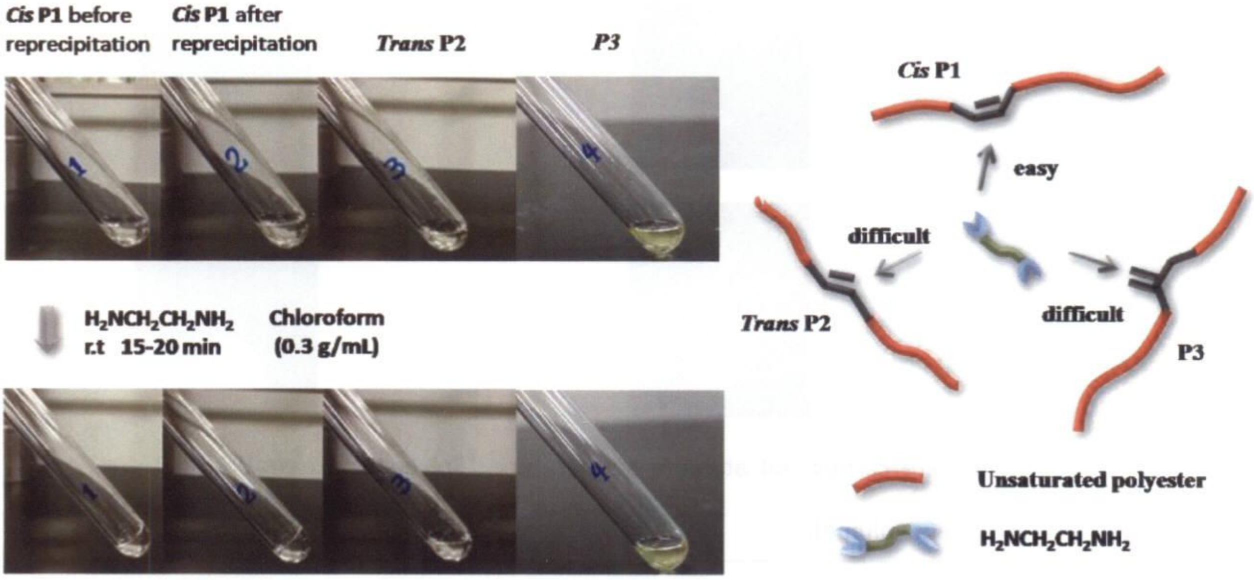
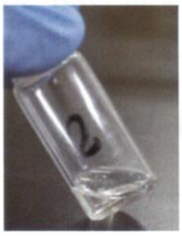
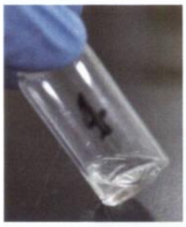
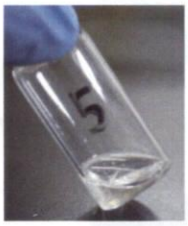


Figure 3-1. Selective cross-linking of different unsaturated polyesters with ethylenediamine.

Table 3-4. Catalyst-free cross-linking of maleate polyester with 1,2-ethanediamine in different solvents at room temperature.

entry[a]	solvent[b]	before cross-link	time (min)	after cross-link
1	DMF		< 2	
2	1,4-dioxane		< 5	
3	$CHCl_3$		< 20	
4	THF		< 5	
5	Toluene		< 5	

[a] All the reactions were carried out at room temperature. [b] Solvent concentration: 0.3 g/mL, polymer weight/solvent volume).

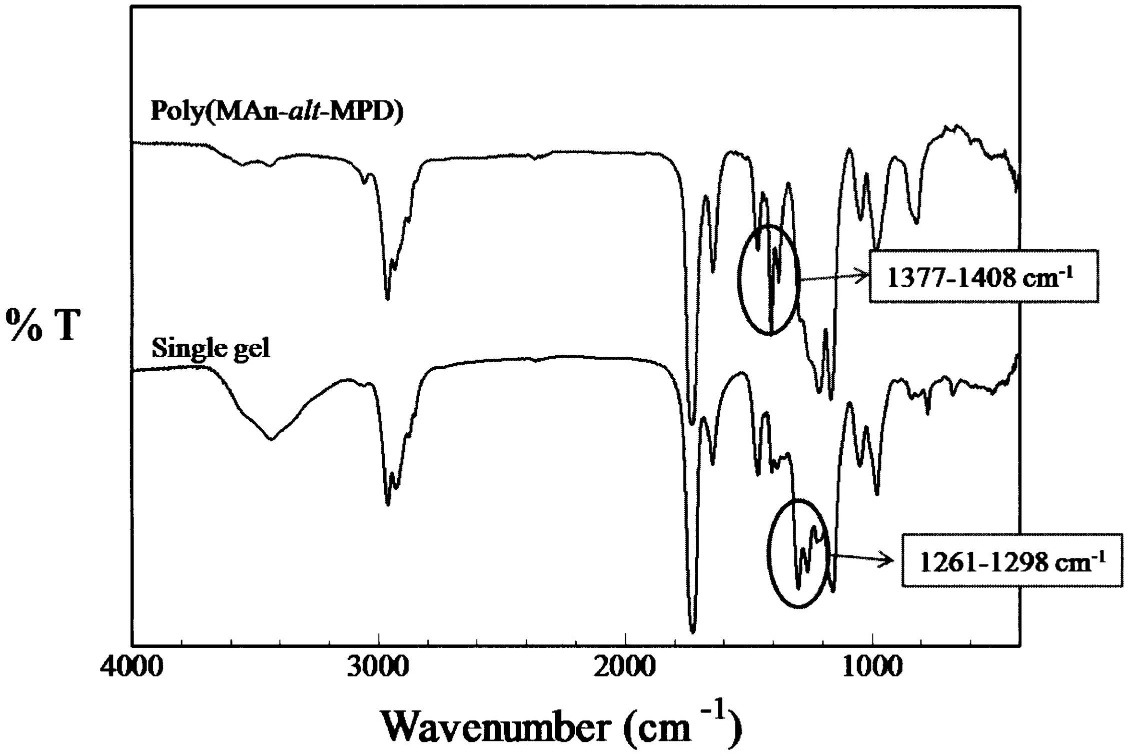


Figure 3-2. FT IR spectra of poly(MAn-*alt*-MPD) before (up) and after (down) cross-linked by 1,2-ethanediamine. The peaks at 1377-1408 cm^{-1} ascribed to *cis* double bonds and the peaks at 1261-1298 cm^{-1} assigned to *trans* double bonds

With the selective Michael cross-linking in hand, we next to investigate the different of UV cross-linking among three kinds of carbon-carbon double bonds: Poly(MAn-*alt*-MPD), poly(FA-*alt*-MPD) and poly(IAn-*alt*-MPD). As we reported in a previous paper,[6d] the maleate polyester was easier cross-linked by UV initiator under UV light (250-400 nm). Herein, we used the different unsaturated polyesters with MMA and photoinitiator Irgacure to carry out the irrigation respectively under 250-400 nm UV light (Figure 3-3). After 30 min, the poly(IAn-*alt*-MPD) was cross-linked by the free radical polymerized MMA, however the samples of poly(MAn-*alt*-MPD) and poly(FA-*alt*-MPD) were dissolved in $CHCl_3$ after 30 min. It is revealed that the selective UV cross-linking by the free radical polymerized MMA proceeded. The poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)] with different unit ratio (IAn:MAn=1:4, IAn:MAn=1:8) also be irrigated in UV light with MMA and Irgacure, and after 1.5 h, both of the polyesters cross-linked.

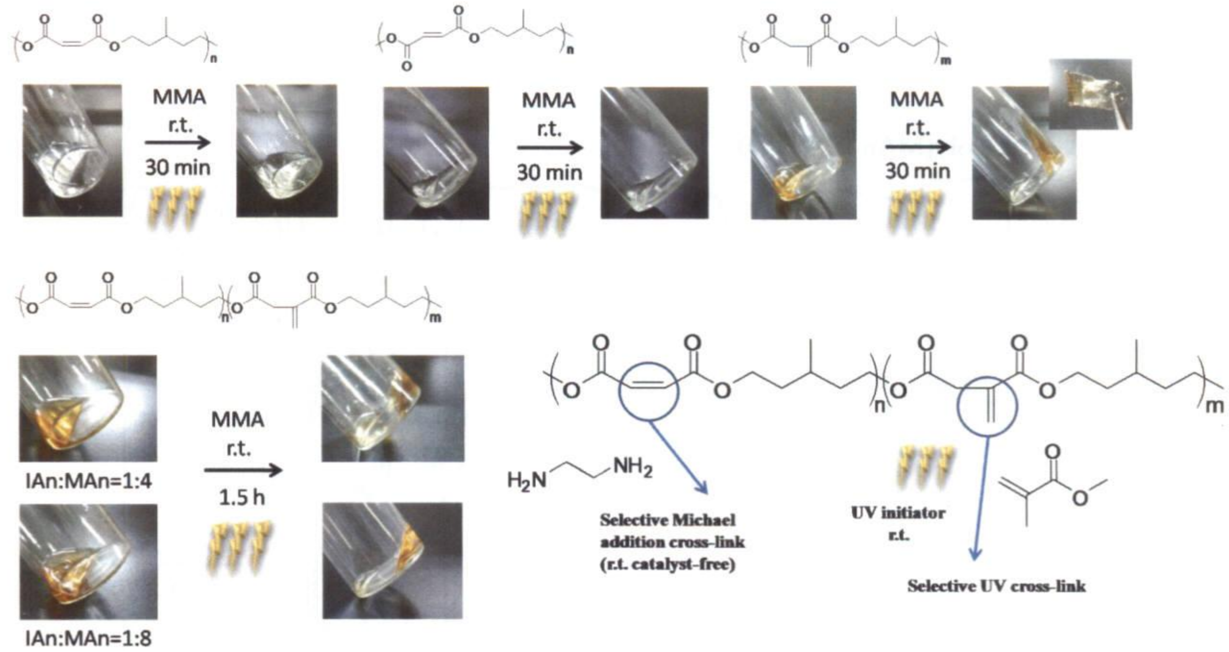


Figure 3-3. Selective cross-linking of different double bonds with MMA under UV light and exhibition of a strategy for preparation of DN gel.

At room temperature, 1,2-ethanediamine was difficult to react with MMA. From the results we got, a new one-pot selective cross-linking design to prepare a double-network gel (DN gel) came forth (Figure 3-3 and Figure 3-4 (a)): poly(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD), MMA, photoinitiator Irgacure were mixed in toluene. After the mixture completely dissolved, an appropriate amount of 1,2-ethanediamine was added into the mixture, oscillated. The first gel would be created after 5 min, then it was irradiated under 250-400 nm UV light for 3 h. The chemical structure of DN gel was shown in Figure 3-4 (c). The first network was synthesized from selective cross-linking of 1,2-ethanediamine with maleate double bonds at room temperature without catalyst. After that, free radical polymerized PMMA was synthesized by irradiation of UV light and interpenetrated in the first network and cross-linked with itaconate double bonds. The polyester/PMMA double-network gel could be prepared [Figure 3-4,(b), (1)]. The DN gel exhibited excellent mechanical property. The DN gel was tough and withstanding high-level deformations of bending [Figure 3-4, (b), (2)] and contorting [Figure 3-4, (b), (3)]. Particularly, once remove the deformation force, the DN gel recovered to the initial shape gradually, indicating shape-recovery property [Figure 3-4, (b), (3)]. Furthermore, the DN gel could be made as different shape easily due to the one-pot method, for example, bear head shape (Figure 3-4, (b), (4)). From the FT IR test of the DN gel Showed in Figure 3-5, we can find the peaks at 1261-1298 cm^{-1} assigned to *trans* double bonds. It indicated that the

DN gel still contained carbon to carbon double bonds inside, which can be used for the further modification.

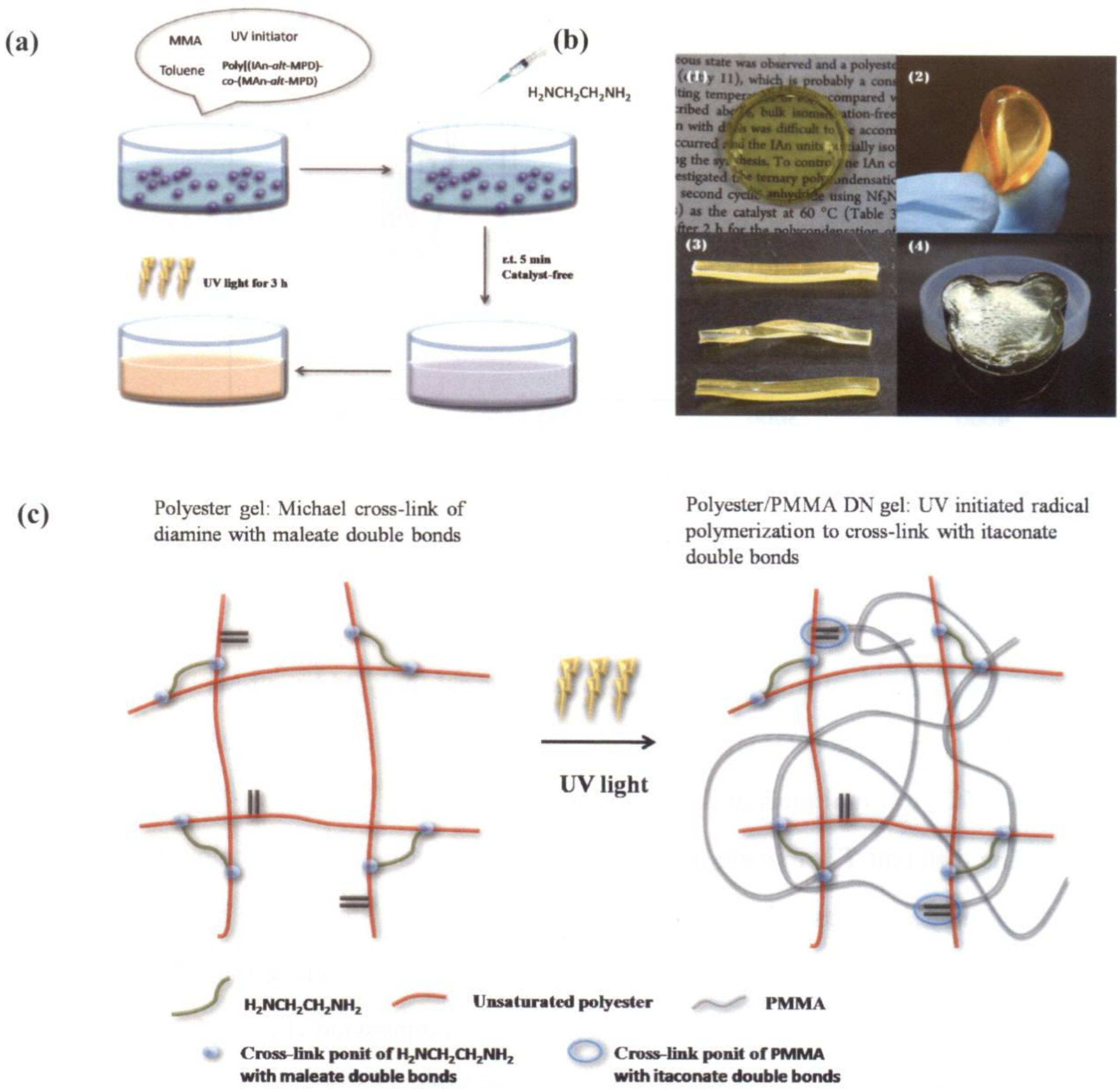


Figure 3-4. (a) The procedure of preparing of DN gel via Michael cross-linking and UV-initiated cross-linking. (b) The pictures of prepared DN gels. (c) The exhibition of chemical structure of DN gel.

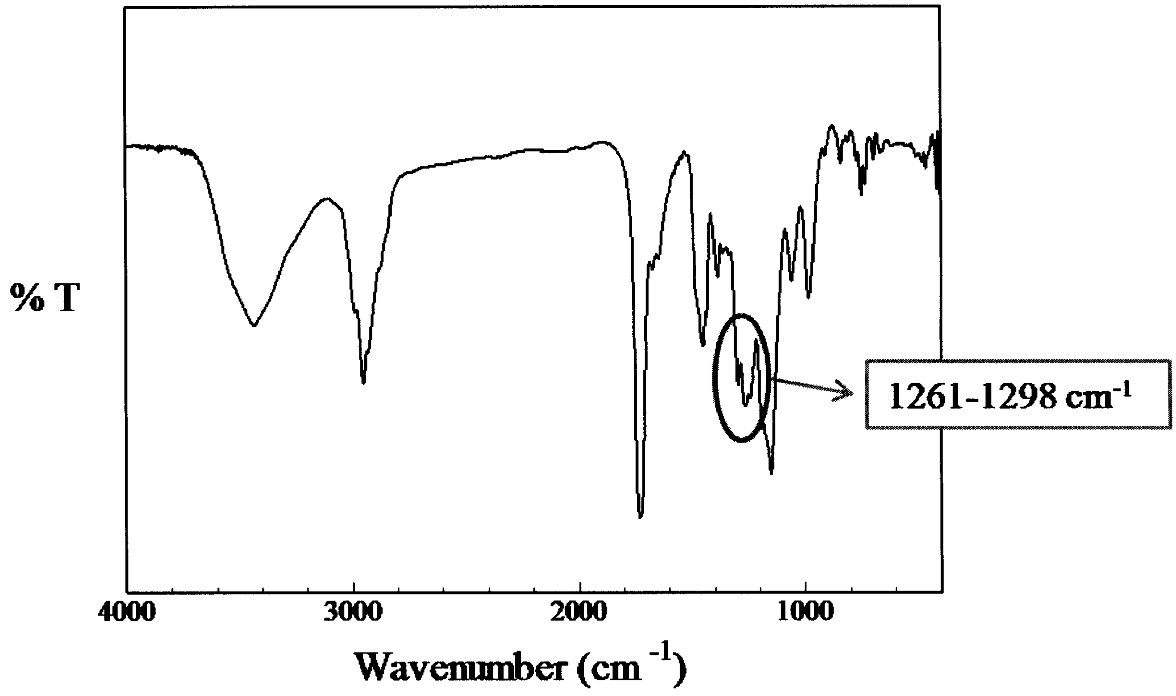


Figure 3-5. FT IR spectrum of polyester-based DN gel (Containing *trans* carbon-carbon double bonds).

To compare the mechanical strength, the single network gel [poly(MAn-*alt*-MPD) cross-linked by 1,2-ethanediamine], polyester/PMMA double-network gels with different MMA ratio (double bonds units:MMA=1:2, 1:3. mol:mol) or different double bonds ratio (IAn:MAn=1:4, 1:8. mol:mol) were prepared. The different T_g of single gel and DN gels were tested by DSC calorimeter (Figure 3-6 (1)). The T_g of Single gel was -23.3 °C. However the T_g of DN gels could not be detected due to the special double network structures. The compression properties of single gel and DN gels were shown in Figure 3-6 (2). The **single gel** was easily broke by compression (Figure 3-6 (3)), and its fraction strain and elastic modulus were about 30 % and 4.98 MPa. The **DN gel 1**, polyester/PMMA DN gel (double bonds units:MMA=1:2, mol:mol; $[IAn]_0$:$[MAn]_0$=1:8, mol:mol) exhibited higher mechanical property, however, we could find the marked change in the diagram after the fraction strain of 36% and elastic modulus of 21.3 MPa. It illuminated a wide range of destruction during the compression. After we increased the cross-linking density of the DN gel, for example, changing the $[IAn]_0$:$[MAn]_0$ from 1:8 to 1:4 (mol:mol) (**DN gel 2**), the destruction of **DN gel 2** during the compression was not obvious. From the diagram, we can only find a small change point (compression strain of 42%, compression stress of 33.4 MPa), which due to the small destruction in the DN gel. This indicated that the **DN gel 2** exhibited higher mechanical strength than **DN gel 1**. In order to prepare strong DN gel, we increased the ratio of MMA (compare with **DN gel 2**, the double bonds units:MMA was increased from 1:2 to 1:3, mol:mol) (**DN gel 3,** Figure 3-6 (2)). The **DN gel 3** exhibited the excellent mechanical property. Even with the compression stress of 41.8 MPa, the **DN gel 3** still exhibited a smooth curve in the diagram, and the compression strain was about 51%. Interestingly, at the early stage, the compression strain of **DN gel 3** increased faster than **DN gel 1** and **DN gel 2**. However, at the late stage, it increased slowest among the three DN gels. That might because of higher PMMA ratio of the second network, the **DN gel 3** have the highest interspace between the polymer chain in the gel. At the early stage, the gel could be easily compressed. However, at late stage, due to the high containing of PMMA and high cross-linking density ($[IAn]_0:[MAn]_0=1:4$, mol:mol), the **DN gel 3** is showed the highest mechanical strength. After interspace reduced, it becomes much harder than other gels, so its compression strain was difficult to be changed. From Figure 3-6 (4), the pictures before compression and after compression of **DN gel 3** were shown. After moving the compression force, the shape of DN gel was seriously changed. However, after 12 h, the DN gel recovered more than 99%. The DN gel also displayed much better tensile properties than single gel (Figure 3-7). From these results we can concluded that by the one-pot method, the polyester-based DN gel with excellent mechanical property could be obtained. And we believe, a wide range of DN gels can be synthesized using this method by changing the structure of first network or changing the monomer species of the second network.

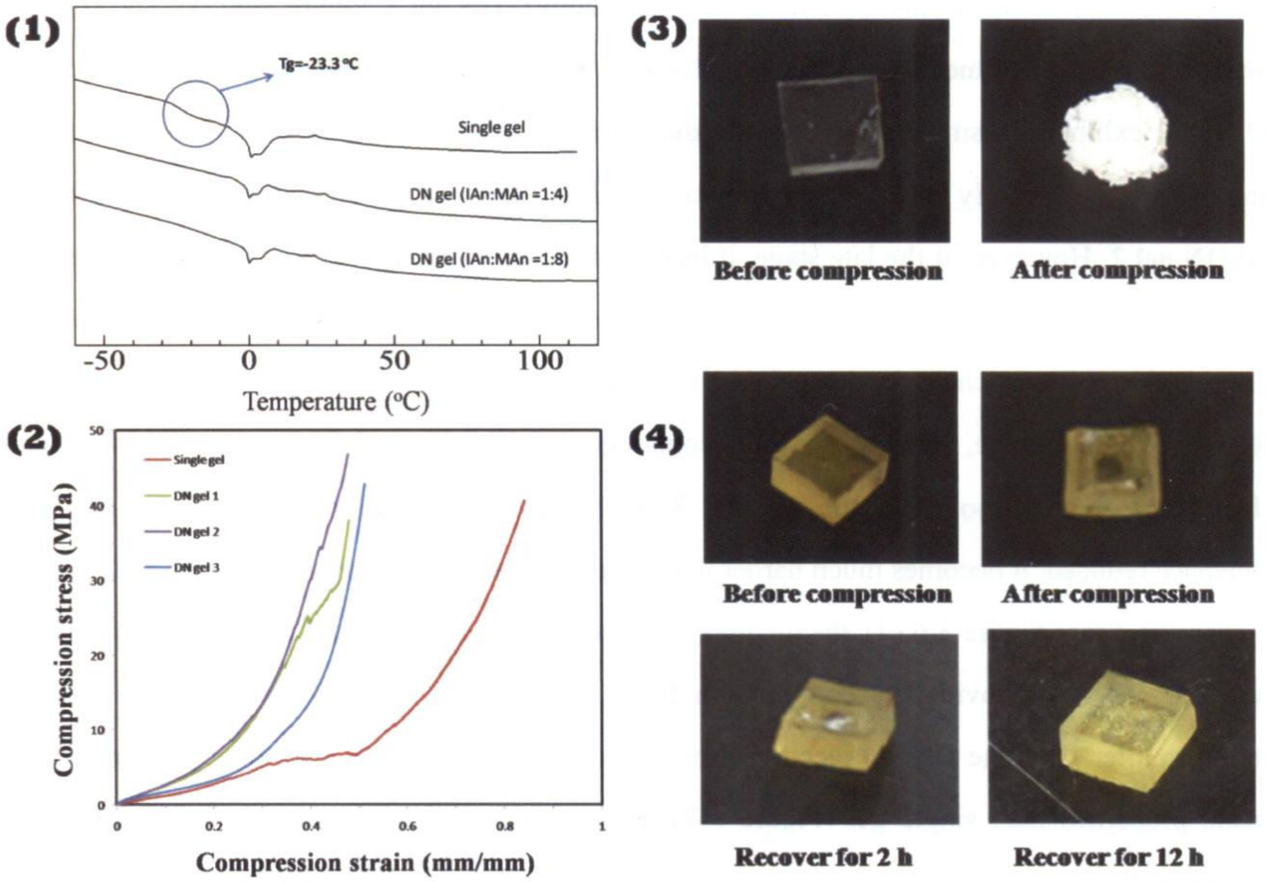


Figure 3-6. (1) DSC test of single gel and DN gels. (2) Compression properties of single gel and DN gels (DN gel 1: polyester/PMMA DN gel (double bonds units:MMA=1:2, mol:mol; $[IAn]_0$:$[MAn]_0$=1:8, mol:mol); DN gel 2: polyester/PMMA DN gel [double bonds units:MMA=1:2, mol:mol; $[IAn]_0$:$[MAn]_0$=1:4, mol:mol); DN gel 3: polyester/PMMA DN gel (double bonds units:MMA=1:3, mol:mol; $[IAn]_0$:$[MAn]_0$=1:8, mol:mol)]. (3) The pictures of before and after compression of single gel. (4) The pictures of before and after compression of DN gel 3, and recovery for 2 h and 12 h.

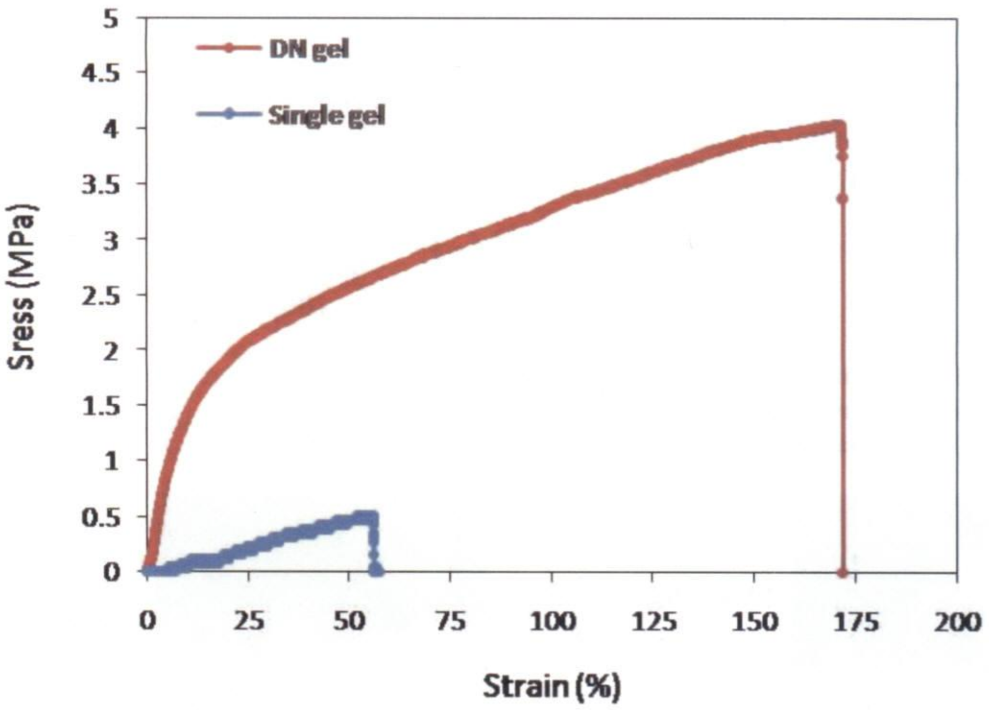


Figure 3-7. Tensile strengths of DN gel (double bonds units:MMA=1:2, mol:mol; $[IAn]_0$:$[MAn]_0$=1:8, mol:mol) and single gel.

Preparation of poly(ester-*co*-ether)/PAM double-network hydrogel

As we described a new way to prepare aliphatic polyester based DN gel, how to expand the method to create other new style gels would be an interesting subject. Before, we prepared the hydrophobic polyester/PMMA DN gel, and herein, we prepared a new DN hydrogel using poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)] (IAn:MAn:TEG=1:6:7, mol:mol:mol) as based unsaturated polyester. We used TEG instead of MPD for the hydrophilic property of ether structure. And the cross-linker we used was 1,4-diaminobutane, because the chain length of TEG was lager than MPD, that might increase the distance of intermolecular or intramolecular maleate double bonds. 1,2-ethanediamine was not long enough to cross-linked the polyesters. The AM was chosed as the monomer to create second network for its high water solubility. The poly(ester-*co*-ether)/PAM DN hydrogel was prepared by the same method as described before. poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)], AM (double bond unit in polyester : AM=1:2, mol/mol), and photoinitiator were dissolved in THF. The first network was created by 1,4-diaminobutane within 10 min, and after through UV light irrigation for 3 h, the hydrogel was created (Figure 3-8). The hydrogel was immersed into water for 1 day and the water containing was up to 70 wt%. This DN hydrogel which contained amino group could be widely used in fields of release systems and tissue engineering.

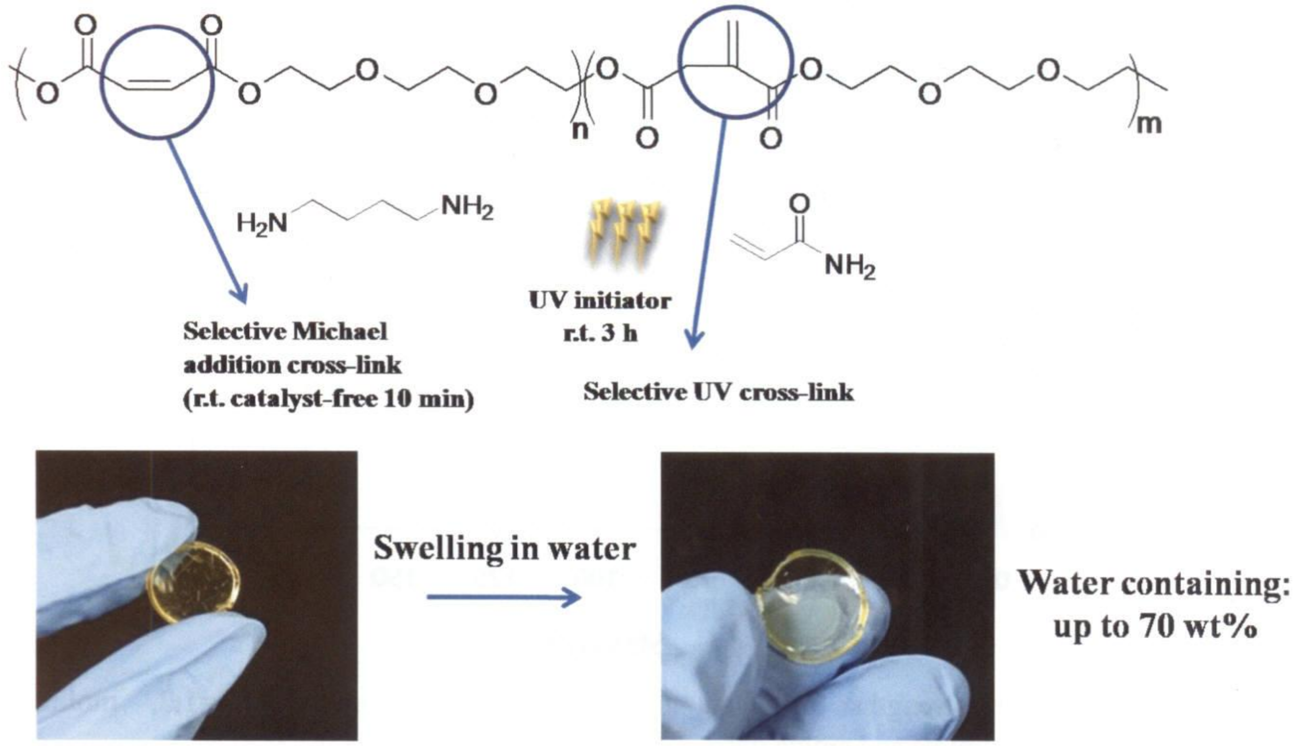


Figure 3-8. The strategy of the preparation of DN hydrogel and the picture of the hydrogel before or after swelling in water.

In this paper, we first investigated the isomerization speed of maleate units to fumarate units in different polarity solvents. The isomerization in DMF was the most efficient. After isomerization, the molecular weight and PDI of the polymer did not change. When the primary amines were used to react with maleate polyester at room temperature without catalyst, the Michael addition of amines with maleate double bonds proceed rapidly and at the same time, partial maleate double bonds transformed to fumarate double bonds. Interestingly, the Micheal reactions of fumarate double bonds or itaconate double bonds with primary amines were difficult at room temperature and isomerization of these two double bonds was not observed. Next, we investigated the UV cross-link of unsaturated polyester by MMA with UV initiator. The itaconate polyester was cross-linked by MMA, however, the fumarate polyester and maleate polyester both was not. These results provide the potential to prepare of DN gels by one-pot selective cross-linking. First step, after the poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)], MMA, UV initiator were mixed with toluene, $H_2NCH_2CH_2NH_2$ was added into the mixture. The gel was prepared at room temperature in 5 min. Second step, the gel was cured by UV light for 3 h to make MMA polymerized and cross-link with itaconate double bonds. The polyester/PMMA DN gel performed high mechanical property. To expand the application of this method, we also prepared poly(ester-*co*-ether)/PAM DN hydrogel by cross-linking of poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)], AM and 1,4-butanediamine. This hydrogel, containing 70 wt% water, can be used as biomaterial or commodity. We believe this new strategy with the advantages of one-pot, low temperature, simple procedure, structural diversity and stability under air or water environment, will be widely applied in various fields.

3-3. Experimental section

Materials

Maleic anhydride (MAn), dimethyl maleate, itaconic anhydride (IAn) were purchased from Tokyo Chemical Industry Co., Ltd (Tokyo, Japan). 1,4-Dioxane, tetrahydrofuran (THF), dimethylformamide (DMF), toluene and chloroform were purchased from Nacalai Tesque (Kyoto, Japan), and they were distilled before use. Bios(nonafluorobutanesulfonyl)imide (Nf_2NH) was purchased from Mitsubishi Materials Electronic Chemicals Co., Ltd. (Akita, Japan), and was dried under reduced pressure before use. 3-Methyl-1,5-pentanediol (MPD), 2-[2-(2-Hydroxyethoxy)ethoxy]ethanol (TEG), methyl methacrylate (MMA) and acrylamide (AM) were purchased from Nacalai Tesque (Kyoto, Japan). 1-Hydroxycycloohexyl phenyl ketone (Irgacure 184) was purchased from Tokyo Chemical Industry Co., Ltd (Tokyo, Japan). Diethylamin, 1,2-ethanediamine, 1,4-butanediamine, *n*-butylamine, isobutylamine and benzylamine were purchased from Nacalai Tesque (Kyoto, Japan).

Measurements

^{1}H-NMR spectra were recorded at 27 °C using a Bruker Analytik DPX200 spectrometer (200 MHz for ^{1}H). ^{13}C-NMR spectra were recorded at 27 °C using a Bruker Analytik DRX600 spectrometer (150 MHz for ^{13}C). Number average molecular weights (M_n) and polydispersity indices (M_w/M_n) of products were determined using a size-exclusion chromatography (SEC) method that was calibrated with polystyrene standards. The chromatographic system included a RI detector (Tosoh RI-8020), a Tosoh DP8020 pump system, and a TSKgel SuperMultiporeHZ-M column. Chromatography was performed using chloroform as the eluent. The flow rate was 0.35 mL/min, and the temperature was maintained at 40 °C. FT-IR spectra were recorded in KBr disks using a JASCO FT/IR-430 spectrometer. Differential scanning calorimetry (DSC), using a DSC6220S calorimeter (Seiko Instruments Inc., Chiba, Japan), was investigated from -80 to 120 °C, with the temperature increased or decreased at a rate of 10 °C/min. The instrument was calibrated using indium and tin samples. For all experimental samples, a complete temperature heating cycle from -80 to 120 °C and back to -80 °C was obtained. Each sample weighted between 6 and 10 mg and was placed into an aluminum pan that was covered with a lid within the calorimeter. The glass transition temperature (T_g) was taken as the inflection point of the corresponding heat capacity jump of the DSC trace. The compression properties and tensile strengths of products were investigated by a universal testing machine (SHIMADZU, AGS-G). Cubical samples with a height of ~3 mm and a length of ~10 mm were used for compression test. The compression rate was 0.1 mm/min. For tensile strength tests, the gel samples were cut into stripe shape with a gauge length of ~15 mm, a width of ~5 mm and a thickness of ~1 mm. The loading rate was 0.1 mm/min for single gel and 1 mm/min for DN gels.

Preparation of unsaturated polyesters

A typical procedure for copolymerization under bulk condition at low temperature was performed as follows (Table 1, entry 1). Nf_2NH (23.36 mg, 0.04 mmol), MAn (784.00 mg, 8.00 mmol), and MPD (945.44 mg, 8.00 mmol) were mixed. This mixture was stirred at 60 °C for 1 h. The pressure and temperature were gradually decreased to 0.3-3 mmHg at 60 °C for 12 h. The products were first dissolved in $CHCl_3$ and then precipitated using hexane. The precipitated polymers were then dried under reduced pressure (82 % yield).

Isomerization of poly(MPD-*alt*-Maleic acid) to poly(MPD-*alt*-Fumaric acid)

To investigate one-pot isomerization, polyester mixture after the polymerization was dissolved in DMF, Dioxane, $CHCl_3$, THF, toluene respectively, and then 1 % (v/v) $HNEt_2$ (0.2 mol/mol to maleate carbon-carbon bond units) was added. The mixtures were stirred at room temperature for 12 h and the progress was checked by ^1H NMR spectroscopy respectively. After the end of the transformation, all volatiles were removed under vacuum. The polyester was dissolved into chloroform and precipitated into hexane and methanol respectively.

Reactions of poly(MAn-*alt*-MPD) with primary amines in different solvents at room temperature without catalyst

The poly(MAn-*alt*-MPD) was dissolved by DMF, Dioxane, $CHCl_3$, THF and toluene respectively (Solvent concentration: 0.15 g/mL, polymer weight/solvent volume). One of the primary amines (n-butylamine, isobutylamine and benzylamine), which feed ratio is about 1:1 (maleate unit : amine, mol:mol), was added into the mixture. After the reaction finished, the product was dissolved into chloroform and precipitated into hexane and methanol respectively.

Preparation of single gel via cross-linking of poly(MAn-*alt*-MPD) with 1,2-ethanediamine in different solvents at room temperature without catalyst

The poly(MAn-*alt*-MPD) was dissolved by DMF, Dioxane, $CHCl_3$, THF and toluene respectively (solvent concentration: 0.3 g/mL, polymer weight/solvent volume). The 1,2-ethanediamine, in which feed ratio is about 0.25 (diamine/maleate unit, mol/mol), was added into the mixture at room temperature. The gel was prepared after the certain time.

Preparation of poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)]/PMMA double-network gels by one-pot method

The poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)] with unit ratio of IAn:MAn:MPD=1:4:5 (mol:mol:mol) was dissolved with MMA (double bond unit in polyester:MMA=1:2, mol:mol) and photoinitiator Irgacure (4 wt % to polyester and MMA) into toluene [concentration: 0.3 g/mL, polyester weight/(toluene volume+MMA volume)]. Then 1,2-ethanediamine (feed ratio is about 0.25, diamine/maleate unit, mol/mol) was added into the mixture at room temperature. The first network was prepared after the 5 min, and then put the gel under 250-400 nm UV light for 3 h. The DN gel was prepared. As the same procedure, the DN gel with unit ratio of IAn:MAn:MPD=1:8:9 (double bond unit in polyester:MMA=1:2) and the DN gel with unit ratio of IAn:MAn:MPD=1:8:9 (double bond unit in polyester:MMA=1:3) were prepared under same condition.

Preparation of poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)]/PAM double-network hydrogel by one-pot method and investigation of swelling property in water

The poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)] with unit ratio of IAn:MAn:TEG=1:4:5 (mol:mol:mol) was dissolved with AM (double bond unit in polyester:AM=1:2, mol:mol) and photoinitiator Irgacure (4 wt % to polyester and AM) into THF (concentration: 0.3 g/mL, polyester weight/(THF volume+AM volume)). Then 1,4-butanediamine (feed ratio is about 0.25, diamine/maleate unit, mol/mol) was added into the mixture at room temperature. The first network was prepared after the 5 min, and then put the gel under 250-400 nm UV light for 3 h. The DN hydrogel was prepared. After that the DN hydrogel was put in water for 1 day. The swelling test in water was carried out. The weight of dried DN hydrogel was 84.67 mg, and after immersed in water for at least 1 day, the weight of DN hydrogel with water inside was 289.53 mg. The containing water was calculated as 70 wt%.

Model reaction

Dimethyl 2-(butylamino)butanedioate was synthesized by Michael addition of dimethyl maleate (0.40 mmol) with *n*-butylamine (0.40 mmol) at room temperature without catalyst. The product obtained with conversion of more than 98%.

Dimethyl 2-(butylamino)butanedioate was mixed with dimethyl maleate with feed feed ratio of 1:1 (mol/mol). $CHCl_3$ was used as solvent [0.3 g/mL, dimethyl maleate weight/($CHCl_3$ volume+ dimethyl 2-(butylamino)butanedioate volume)]. The reaction was carried out for 24 h at room temperature. The isomerization ratio was calculated by ^{1}H NMR test. And the conversion was 4 %.

3-4. References and Notes

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Conclusions

This thesis focused on the synthesis of polyesters or poly(ester-ether)s under mild conditions using organic catalyst and design of double network gel to improve the mechanical strength.

Chapter 1. Synthesis of Periodic Copolymers via Ring-Opening Copolymerizations of Cyclic Anhydrides with Tetrahydrofuran Using Nonafluorobutanesulfonimide as an Organic Catalyst and Subsequent Transformation to Aliphatic Polyesters

In this chaper, polyesters were synthesized by copolymerization of cyclic anhydrides with THF at high temperature (100-120 °C) and periodic polyester was obtained when the reaction was carried out at 50 °C using toluene as the solvent. Several model reactions were carried out to prove the proposed chain transfer mechanism. The ester and ether unit containing copolymers were transfromed into polyesters after they were heated to high temperature, and during this transformation process, M_n of the polymers decreased. These fundamental results should provide a new strategy for synthesizing novel polyesters and polyester-based periodic copolymers.

Chapter 2. Isomerization-Free Polycondensations of Cyclic Anhydrides with Diols and Preparation of Polyester Gels Containing *cis* or *trans* Carbon Double Bonds via Photo Cross-Linking and Isomerization in the Gels

In this chapter, Nf_2NH-catalyzed polycondensations of cyclic anhydrides and diols provided unsaturated polyesters with $M_n > 10.0 \times 10^3$, in shorter periods of time, and at lower reaction temperatures than did polycondensation of Nf_2NH-catalyzed dicarboxylic acids and diols. We prepared polyesters/copolyesters from a variou of cyclic anhydrides. The copolyesters with exo-type double bonds ascribed to IAn units were photo-crosslinked to afford unsaturated *cis* polyester gels. *trans* Gels were prepared via $HNEt_2$-catalyzed isomerization of the double bonds in the *cis* gels. The swelling properties of these gels were found to be dependent on the geometries of their double bonds. Our discoveries should find use in drug-release systems and other biomedical applications.

Chapter 3. Facile Synthesis of Unsaturated Polyester-Based Double-Network Gels via Selective Cross-Linking of Michael Addition and UV-Initiated Polymerization

In this chapter, we first investigated the isomerization speed of maleate units to fumarate units in different polarity sovents. The isomerization in DMF was the most efficient. After isomerization, the molecular weight and PDI of the polymer did not change. When the primary amines were used to react with maleate polyester at room temperature without catalyst, the Michael addition of amines with maleate double bonds proceeded rapidly and at the same time, partial maleate double bonds transformed to fumarate double bonds. Interestingly, the Micheal reactions of fumarate double bonds or itaconate double bonds with primary amines were difficult at room temperature and isomerization of these two double bonds was not observed. Next, we investigated the UV cross-link of unsaturated polyester by MMA with UV initiator. The itaconate polyester was cross-linked by MMA, however, the fumarate polyester and maleate polyester both was not. These results provide the potential to prepare of DN gels by one-pot selective cross-linking. First step, after the poly[(IAn-*alt*-MPD)-*co*-(MAn-*alt*-MPD)], MMA, UV initiator were mixed with toluene, $H_2NCH_2CH_2NH_2$ was added into the mixture. The gel was prepared at room temperature in 5 min. Second step, the gel was cured by UV light for 3 h to make MMA polymerized and cross-link with itaconate double bonds. The polyester/PMMA DN gel performed high mechanical property. To expand the application of this method, we also prepared poly(ester-*co*-ether)/PAM DN hydrogel by cross-linking of poly[(IAn-*alt*-TEG)-*co*-(MAn-*alt*-TEG)], AM and 1,4-butanediamine. This hydrogel, containing 70 wt% of water, can be used as biomaterial or commodity. We believe this new strategy with advantages of one-pot, low temperature, simple procedure, structural variation and stability under air or water environment, will be widely applied in various fields.

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List of Publications

1. **Tang, T.**; Oshimura, M.; Takasu, A.; Shinji, Y.; Yang, X, P.; Cai, Q. Synthesis of Periodic Copolymers via Ring-Opening Copolymerizations of Cyclic Anhydrides with Tetrahydrofuran Using Nonafluorobutanesulfonimide as an Organic Catalyst and Subsequent Transformation to Aliphatic Polyesters. J. Polym. Sci, Part A: Polym. Chem. 2012. 50, 3171-3183.

2. Moyori, T.; **Tang, T.**; Takasu, A. Dehydration Polycondensation of Dicarboxylic Acids and Diols Using Sublimating Strong Brønsted Acids. Biomacromolecules. 2012, 13(5), 1240-1243.

3. **Tang, T.**; Takasu, A. Isomerization-Free Polycondensations of Cyclic Anhydrides with Diols and Preparation of Polyester Gels Containing *Cis* or *Tans* Carbon Double Bonds via Photo-Cross-linking and Isomerization in the Gels. Macromolecules. 2013, Tang, T.; Moyori, T.; Takasu, A. Macromolecules 2013, 46, 5464-5472.

4. **Tang, T.**; Takasu, A. Facile Synthesis of Unsaturated Polyester-Based Double-Network Gels via Selective Cross-Linking of Michael Addition and UV-Initiated Polymerization. (to be submitted)

List of Other Publications

1. Ohimura, M.; **Tang, T.**; Takasu, A. Ring-opening polymerization of ε-caprolactone using perfluoroalkanesulfonates and perfluoroalkanesulfonimides as organic catalysts. J. Polym. Sci. Par A: Polym. Chem. 2011, 49, 1210-1218.

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