

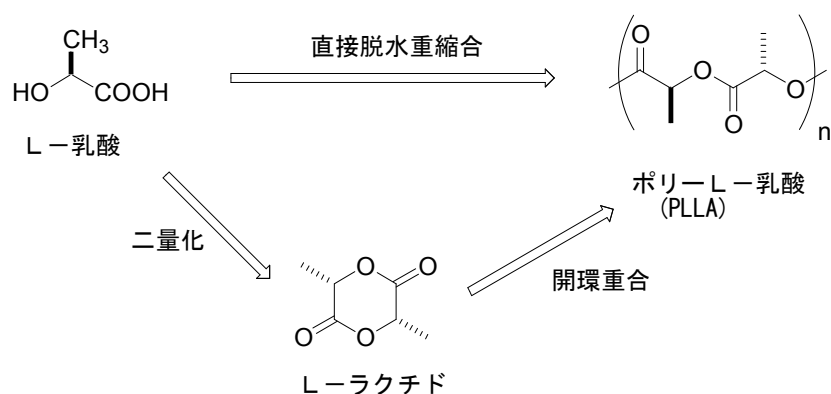
実用的有機酸触媒の開発と応用に関する研究

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現代有機化学においては、優れた機能を持つ化合物の合成と、真に役に立つ実用的な反応の開発が求められている。地域共同研究センターに専任教員として取り組んでいる実用的有機酸触媒の開発とその応用に関する研究成果のなかから、ポリ乳酸合成のための有機酸系触媒の開発研究について報告する。

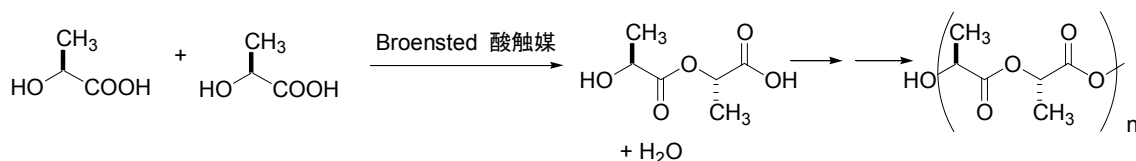
ポリ-L-乳酸に代表されるポリヒドロキシカルボン酸は機械的特性、物理的・化学的性質に優れている上に自然環境下で分解され、最終的には微生物によって水と炭酸ガスになるという生分解性を持っていることから、近年医療用材料や、汎用樹脂代替等、様々な分野で注目されており、今後もその需要が大きく伸びることが期待されている。

ポリ-L-乳酸は乳酸の環状ジエステルモノマーである L-ラクチドの開環重合（ラクチド法）もしくは L-乳酸の直接脱水重縮合によって合成される。ラクチド法の場合、ラクチドの単離により原料が精製され高分子量のポリ-L-乳酸が得られるが、工業的に見て、ラクチドの製造・精製工程の運転面、設備面でのコストが大きくなるので安価な製品を製造するための問題となっている。



一方、L-乳酸の直接脱水重縮合では、用いることができる触媒の種類は豊富とはいえ、さらに活性の高い触媒の開発によるプロセスの簡素化について課題が残されている。

乳酸からのポリ乳酸の生成は、基本的にはエステル化反応であり、触媒存在下共沸脱水により反応を行うことが適当である。そこで、Fischer エステル化反応の触媒を念頭に、有機 Brønsted 酸（オニウム塩）触媒のスクリーニングを行い、新規触媒 TPPT（トリフェニルホスホニウム トリフルオロメタンスルホネート）が、良好な触媒であることを見出した。



本触媒を用いて、分子量 (M_n) 10 万程度のポリ乳酸を直接合成することが出来た。

An Onium Salt Catalyzed Direct Poly-condensation of Lactic Acid

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Poly(lactic acid) (PLLA) has attracted keen attention as one of the promising bio-base polymers. The monomer of PLLA, L-lactic acid, can be produced from corn or other plants, so even after combustion of the wasted PLLA, CO₂ emission can be counted as zero. PLLA is usually produced by the ring-opening polymerization method using Sn^{II} 2-ethylhexanoate as a catalyst.¹ Although the ring-opening polymerization method affords high molecular weight PLLA, this inherently uses purified L,L-lactide (dimer of L-lactic acid) as a starting monomer, which requires steps from readily available L-lactic acid.

The direct polycondensation method has advantages over the ring-opening polymerization, because in addition to the ready availability of the starting monomer, at the initial stage of the polymerization rigorous anhydrous conditions are not essential to ensure high degree of polymerization, which are critical for the latter. Direct polycondensation of lactic acid, however, has been less studied.²⁻⁷ Previous efforts to find catalyst for direct polycondensation were hampered by the low activity of the catalysts and racemization of the resulting polymer. Although tin compounds, such as Sn metal or SnCl₂,² and distannoxene derivative,⁶ were reported to be very reactive for direct polycondensation, other metal catalysts afforded PLLA with low molecular weight,^{4,6,7} and sulfonic acids² requires relatively high catalyst loadings to ensure high molecular weight ($\overline{M}_w \approx 100000$). Combined use of SnCl₂ and *p*-toluenesulfonic acid (*p*-TSA) (1:1) in the melt polycondensation led to PLLA of high molecular weight ($\overline{M}_w \approx 500000$) after solid-state polymerization.⁵

Recently, Tanabe et al. developed pentafluorophenylammonium triflate (PFPAT **1**) and diphenylammonium triflate (DPAT **2**) as Brønsted acid catalysts for condensation of a carboxylic acid and an alcohol to esters.⁸ These acid catalysts are characterized as onium salts of weak base and super acid, and tolerate water generated during condensation. Soon after these, DPAT was reported to be a good catalyst for ring-opening polymerization of lactide or ϵ -caprolactone.¹⁰ We have investigated direct polycondensation of lactic acid using onium salt as a catalyst and found triphenylphosphonium triflate (TPPT)¹⁰ is superior to PFPAT and DPAT in thermal stability and reactivity for synthesis of PLLA and related copolymers. Herein results are summarized.

Table 1 summarizes results of initial survey of several onium salt catalysts. In addition to the conventional catalysts for PLLA synthesis as well as PFPAT and DPAT, triflate salts of representative weak bases were tested for direct polycondensation of aqueous lactic acid in toluene with 1 mol % of catalyst for 24 h with Dean–Stark apparatus. Resulting PLLA was analyzed by gel permeation chromatography (GPC) or ¹H NMR.

Without catalyst, condensation of lactic acid resulted in a formation of oligomer (Entry 10). Among tin compounds tested only SnCl₂ was active for direct condensation to produce PLLA of $\overline{M}_w = 7900$ (Entries 1 and 2). *p*-TSA gave higher \overline{M}_w of 23000. Several onium salt catalysts, **1**, **2**, pyridinium triflate (**3**), *N*-methylimidazolium triflate (**4**), 2,5-dichlorophenylammonium triflate (**5**) and triphenylphosphonium triflate (**6**) showed as high activity as *p*-TSA. These results clearly show onium salts acted as Brønsted acid catalyst with the Fischer esterification mechanism.

Table 1. Catalyst screening for the direct poly-condensation

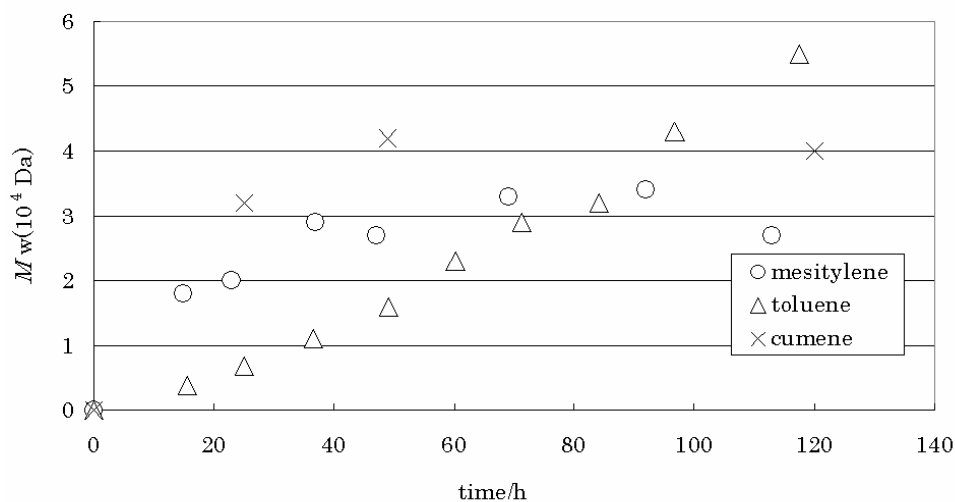
catalyst	1 mol%		0.1 mol%	
	\overline{M}_w^a	PDI ^b	\overline{M}_w^a	PDI ^b
1 SnCl ₂	7900	1.4	360*	---
2 Sn 2-ethylhexanoate	180*	---		
3 <i>p</i> -TSA	23000	1.6	4000	1.7
4 PFPAT (1)	33000	1.6	31000	1.5
5 DPAT (2)	17000	1.5	6800	1.8
6 Py ⁺ H ⁻ OTf (3)	13000	1.3	900*	---
7 Me-imid ⁺ H ⁻ OTf (4)	8700	1.2	810*	
8 Cl ₂ C ₆ H ₃ N ⁺ H ₃ ⁻ OTf (5)	69000	1.4	17000	1.4
9 Ph ₃ P ⁺ H ⁻ OTf (6)	16000	1.3	48000	1.7
10 no	360*	---		

^a \overline{M}_w by GPC with polystyrene standards. * By ¹H NMR. ^bPDI = $\overline{M}_w / \overline{M}_n$

Under reduced catalyst loadings (0.1 mol %, toluene, reflux 22.5 h), SnCl₂, **3** and **4** afforded oligomers, presumably due to their weaker acidity. Although *p*-TSA was active for polycondensation, \overline{M}_w of the resulting PLLA was significantly lowered compared to that obtained by the use of 1 mol % catalyst. This should be attributed to esterification of the sulfonic acid itself to deactivate the catalyst during condensation reaction. Also **2** and **5** afforded PLLA of lower molecular weight.

Naturally, the reaction proceeded depending on the reaction time. With **3** (0.1 mol %), the \overline{M}_w of the resulting PLLA increased linearly in cumene and ethylbenzene, with higher \overline{M}_w in higher temperature. Contrary to this, with **6** (0.1 mol %) linearity was retained in toluene (≈120 h), but in cumene or mesitylene the polymerization terminated after 20–40h (Figure 1), when the reaction turned badly colored.

This should be attributed to the decomposition of the catalyst. Thermogravimetric analysis (TGA) measurements of the onium salts are summarized in Figure 2. The order of thermal stability of the salts was **4** > **3** > **6** > **2** > **5** > **1**. From the viewpoint of thermal stability and reactivity, TPPT **6** was found to be a catalyst of choice.

**Figure 1.** Molecular weight vs. reaction time:

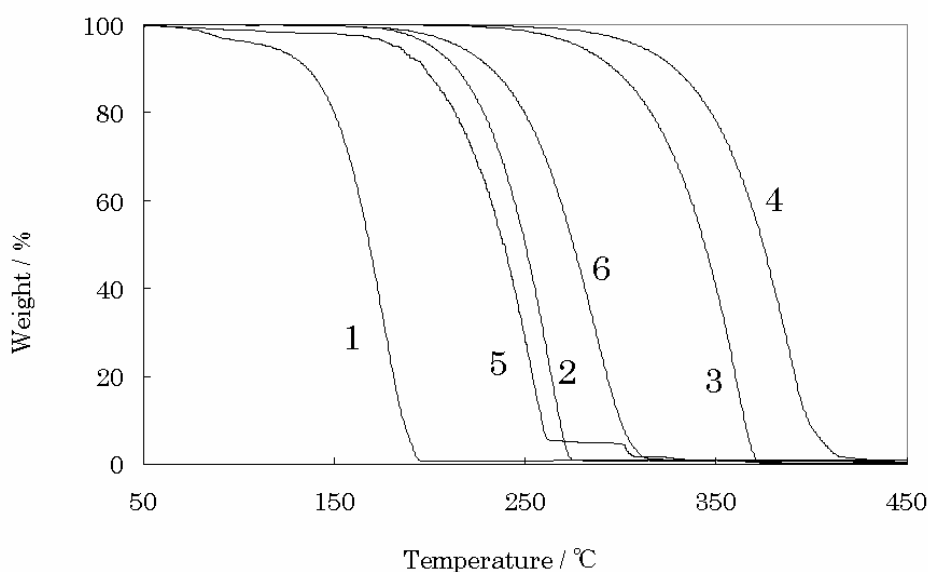


Figure 2. Thermogravimetric analysis of onium salts.

With 0.1 mol % of **6**, \overline{M}_w of the resulting PLLA reached to 83000 after 72 reflux in xylene.¹¹ Higher catalyst loadings (0.5 mol %) accelerated the condensation and \overline{M}_w of 160000 was attained after 72 h. At higher reaction temperature (in cumene), **6** gradually decomposed after 24 h, and PLLA of \overline{M}_w =69000 was obtained using 0.5 mol % of **6**. (Table 2)

In order to improve the physical properties of PLLA, introduction of aromatic substituents in the polymer chain have been examined.^{12,13} For this purpose, the conventional ring-opening polymerization methodology requires preparation of cyclic dimer of lactic acid and the corresponding α -hydroxyacids, such as phenyllactic acid, and can not utilize other hydroxyacids than α -hydroxyacids. Without such limitations, several co-polymers of lactic acid and hydroxyacids with an aromatic ring were synthesized using TPPT as a catalyst (Table 3).

Table 2. Direct polycondensation of L-lactic acid with TPPT catalyst^a

TPPT loadings	solvent	time	\overline{M}_w (GPC)	PDI
0.1 mol %	xylene	24 h	18000	1.6
		72 h	83000	1.7
0.5 mol %	xylene	24 h	35000	1.5
		72 h	160000	1.6
0.1 mol %	cumene	24 h	30000	1.5
		72 h	21000	1.5
0.5 mol %	cumene	24 h	69000	1.4

^a Aliquot was taken and analyzed at the indicated time

Although the molecular weight was moderate or low, a variety of hydroxyacids, including phenol compounds, were introduced in the polymer. It should be noted that the composition of the co-polymer was almost the same as used for the poly condensation.

Table 3. Synthesis of co-polymers by direct polycondensation

HA ^a	LA:HA loadings	TPPT loadings	Yield (%)	\overline{M}_w (GPC)	PDI	LA:HA found
7	95:5	0.5	71	7000	1.6	94:6
	90:10	1	65	2900	1.7	86:14
8	95:5	0.5	75	6800	1.6	95:5
	90:10	1	70	7100	1.5	95:5
9	95:5	0.5	70	8300	1.6	95:5
	90:10	0.5	67	6200	1.7	91:9
10	90:10	1	45	1700	1.9	91:9
	70:30	1	41	1100	1.5	72:28

^aHA: **7** *p*-Hydroxybenzoic acid, **8** *m*-Hydroxybenzoic acid, **9** *p*-Hydroxymethylbenzoic acid, **10** Phenyllactic acid. In conclusion we have introduced new onium salt catalyst, TPPT, as a thermally more stable catalyst useful for direct polycondensation of lactic acid and related hydroxyacids to polyesters. Further studies on the application of this catalyst for synthesis of various bio-base polymers are in progress in our laboratories.

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