A Synergic Catalysis of (Salicylaldiminate)$_2$AlEt and (BnO)$_2$AlEt in the Ring-Opening Polymerization of ε-Caprolactone

Running head: Synergic catalysis of L_2AlEt and $(BnO)_2$AlEt

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The aliphatic polyesters obtained via the ring-opening polymerization (ROP) of lactones, such as ε-caprolactone (CL), δ-valerolactone, and lactide, have gained significant attention due to their biodegradability and biocompatibility.[1] Among the various metal catalysts that have been successfully developed for the controlled/living ROP of lactones,[2,3] metal alkoxide complexes bearing designed ancillary ligands play a pivotal role, and a coordinated anionic mechanism has been proposed in many cases. Many of the reports have dealt with well-defined single-site catalysts. On the other hand, the advantages of a mixture of two metal complexes[4,5] or of a bi-/multi-metal complex[6–9] in a system have also been developed, and the number of such studies is rapidly increasing. We previously reported that (salicylaldiminate)$_2$AlEt **1** (L_2AlEt) prepared from $AlEt_3$ and 2 equiv of the substituted salicylaldimine (L–H) in situ (eq 1a) efficiently catalyzed the ROP of CL at ambient temperature in the presence of benzyl alcohol (BnOH) (eq 1b).[10] However, the precise structure of **1**, the active species of the catalyst(s) in the presence of BnOH, and therefore the polymerization mechanism have not been clarified. In this paper, we report the solid-state structure of **1** by X-ray diffraction. We also document that BnOH (1 equiv to complex **1**) selectively reacts with ~0.5 equiv of complex **1** to afford ~1 equiv of free L–H and remaining ~0.5 equiv of complex **1**. The stoichiometric balance suggested the formation 0.5 equiv of $(BnO)_2$AlEt. On the basis of the experiments of the each compound and their combinations, the ROP of CL proceeds via the synergic catalysis of the two Al-complexes, remaining complex **1** (0.50 mol %) as a Lewis acid activator of CL and $(RO)_2$AlEt (0.50 mol %) as a nucleophile, is proposed.

It is often important to determine the stable conformation of the catalyst for elucidation of the reaction mechanism. Although NMR studies of complex **1** suggested that one of the two salicylaldiminate ligands was a bidentate and the other was a monodentate because of the significantly different chemical shifts of the two imine protons (ArC*H*=NAr', 8.02 and 9.14 ppm), but the precise structure of **1** was unclear. We obtained single crystals suitable for X-ray diffraction studies as well as elemental analysis[11] and revealed the monomeric structure of complex **1** (Fig. 1). One of the salicylaldiminate ligands of **1** is bidentate and forms a nearly planar 6-membered ring

(Al1–O1–C3–C4– C9–N1–). Their Al1–O1 and Al1–N1 bond lengths are 1.753(3) and 1.972(4) Å, respectively. These bond lengths are close to the those of reported (salicylaldiminate)$AlMe_2$ complex.[12,13] The other monodentate ligand suggested by ^{1}H NMR studies before[10] is confirmed, and the bond length of Al1–O2 (1.706(3) Å) is significantly shorter than that of the bidentate ligand (Al1–O1, 1.753 Å). The 2,4,6-tri(*t*-butyl)phenyl group of the monodentate ligand is located in the other side of the bidentate one. The coordination of the nitrogen center of the salicylaldiminate is sterically demanding due to the two *t*-Bu groups in the *ortho*-positions of the aniline moiety, and thus only one of the two N atoms can coordinate the Al center. As a result, the coordinatively unsaturated Al center in a distorted tetrahedral structure secure a good coordination site and space for an approaching monomer.

Although Kirillov and Carpentier et al. reported no reaction between (salicylaldiminate)$AlMe_2$ and 2 equiv of *i*-PrOH in toluene at 70 ˚C for 6 h,[14] complex **1** immediately reacted with 1 equiv of BnOH in C_6D_6-toluene at 25 ˚C. The ^{1}H NMR spectra of the reaction between **1** and BnOH (0–2 equiv) in C_6D_6–toluene at 25 ˚C are shown in Fig. 2, and some of the characteristic peaks (H^a–H^d) are indicated. As the amount of BnOH increased, the integration ratio of (H^b = H^c)/(H^a = H^d) decreased (Fig. 2a–e). By addition of 0.5 equiv of BnOH to complex **1** (Fig. 2a), 33% of **1** consumed on the basis of the ^{1}H NMR analysis, and the formation of free L–H^a was observed (**1**/L–H^a = H^b/H^a ~ 1/1, Fig. 2b). One equiv of BnOH was consumed by 56% of complex **1** (Fig. 2c). In addition to the free L–H^a peaks, new broad peaks appeared around 4.5–6.0 ppm (Fig. 2b–e). From the stoichiometric balance of the reaction, a new compound can be described by $(BnO)_2AlEt$.[15–17] When 2.0 equiv of BnOH was added, the H^b and H^c peaks of complex **1** finally became undetectable (Fig. 2e). Note that all the peaks of ligand L–H and complex **1** in the mixture showed the chemical shifts identical to those of each spectrum of free L–H and complex **1**. It indicates no equilibria between remaining **1** and L–H and also none between $(BnO)_2AlEt$ and L–H on the NMR time scale. Although methylene protons of free benzyl alcohol appeared at 4.7 ppm, those of the aluminum complex appeared around 4.5–6.0 ppm as complex

broad peaks, which are similar to those of $(BnO)_2AlEt$ obtained by the reaction of Et_3Al with 2 equiv of BnOH[15] (Fig. 2f). Some difference might come from the slow formation toward the stable oligo-/polymeric structure of $(BnO)_2AlEt$. Throughout the NMR experiments, no new imine peaks derived from LAl(Et)OBn and L_2AlOBn were detected. These experiments showed that the Et–Al bond, which is often reactive under protic conditions,[18] remained stable,[14] and the bidentate ligand as well as the monodentate one of complex **1** was successively dissociated by the addition of BnOH. The reaction of complex **1** with 1 equiv of BnOH is summarized in Scheme 1. The consumption of complex **1** by BnOH in our NMR experiments (33% by 0.5 equiv BnOH; 56% by 1.0 equiv BnOH) was slightly higher (6–8%) than theoretical consumption (25% by 0.5 equiv BnOH; 50% by 1.0 equiv BnOH), probably due to contamination of H_2O from solvents such as C_6D_6 (5–10 ppm H_2O by Karl Fischer titration).

To elucidate each role of the compounds afforded in the reaction between **1** and BnOH, the experiments in Table 1 were conducted. Complex **1** (0.5 mol %), ligand L–H (1 mol %), and their mixture did not catalyze the ROP of CL at all (entries 1–3). We then examined the ROP of CL using $(BnO)AlEt_2$,[15,16] $(BnO)_2AlEt$,[15,19] and $(BnO)_3Al$,[15,17] respectively (entries 4–6). To compare the initiation efficiencies on the basis of M_n–CL conversion, 1 mol % of benzyloxide was applied in entries 4–6. Each of them slowly polymerized CL, but their efficiencies were much lower than that of eq 1b. In the presence of 0.50 mol % of **1**, $(BnO)AlEt_2$ uncontrollably polymerized CL (entry 7), and the bimodal SEC trace of the polymer was obtained. One of the M_n values was extremely high (M_n = 409,000) after 10 min at 25 ˚C even at a low monomer conversion (27%). Except for entry 7, both entries 8 and 9 were monomodal by SEC analysis. In sharp contrast, the ROP of CL of entry 8 gave a result comparable to that of eq 1b. The initiation efficiency of the benzyloxide group seemed to be high (~80%), and both BnO groups of $(BnO)_2AlEt$ initiated the polymerization. In entry 9, 30–40% of the benzyloxide of $(BnO)_3Al$ were utilized. Trimer and/or tetramer structures of $(BnO)_3Al$ and $(i\text{PrO})_3Al$ are known,[17,20] and the organized rigid and stable structures may have influenced the lower initiation efficiency. Supposing the disproportionation reaction of $(BnO)_2AlEt$

occurs, in other words, supposing both $(BnO)AlEt_2$ and $(BnO)_3Al$ form and work as the major active species in eq 1b, a controlled ROP of CL cannot be achieved judging from the results of entries 7 and 9.

The mechanistic rationale is illustrated in Scheme 2. $(RO)_2AlEt$ and complex **1** coexist as documented in Fig. 2, and CL is activated by the coordination of Lewis acid **1**. In the ^{13}C NMR spectra (150 MHz), the carbonyl carbon (C=O) of free CL appeared at 174.5 ppm (C_6D_6), and it was highfield shifted (172.8 ppm, C_6D_6–toluene) by the addition of complex **1** (1.3 equiv to CL). Although $(RO)_2AlEt$ (RO = BnO/oligo- or polymeric alkoxide) by itself slowly polymerized CL,[19] it becomes an excellent nucleophile when CL is appropriately activated. After the ring-opening of CL, another CL coordinated by complex **1** is repeatedly attacked by $RO^-/R'O^-$ from the Al center. A similar synergic mechanism in the highly efficient ROPs of δ-valerolactone and β-butyrolactone was originally reported by Aida and Inoue, who called it the Lewis acid-assisted polymerization using bulky Lewis acids and porphyrin–AlOMe.[4] The ROP of CL via this mechanism is rather rare to the best of our knowledge.

In conclusions, the single crystal X-ray diffraction of **1** shows that one of the ligands of **1** is bidentate and the other monodentate. BnOH (1 equiv to complex **1**) is consumed by ~0.5 equiv of **1**, and the bidentate ligand of **1** as well as the monodentate one is successively dissociated to afford free ligand L–H (~1 equiv) and $(BnO)_2AlEt$ (~0.5 equiv). Although complex **1** does not polymerize CL at all and $(BnO)_2AlEt$ does but rather slowly, the coexistent combination of those two complexes is found to be highly efficient in the ROP of CL. Remaining complex **1** (~0.5 equiv) coordinates CL, and $(BnO)_2AlEt$ acts as an excellent nucleophile toward the CL activated by complex **1**. Since Lewis acidity and nucleophilicity of two metal complexes can independently be designed and tuned, it may be achievable that the development of more efficient synergic catalysis than single-site one in which Lewis acidity and nucleophilicity of the metal center are inevitably correlated. Further studies of such synergic catalysis are now in progress in our laboratory.

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References

1 Jérôme C, Lecomte P. Recent advances in the synthesis of aliphatic polyesters by ring-opening polymerization. Adv Drug Delivery Rev. 2008;60:1056–1076.

2 Tong R. New chemistry in functional aliphatic polyesters. Ind Eng Chem Res. 2017;56:4207–4219.

3 Dove AP. Controlled ring-opening polymerisation of cyclic esters: polymer blocks in self-assembled nanostructures. Chem Commun. 2008:6446‑6470.

4 Aida T, Inoue S. Metalloporphyrins as initiators for living and immortal polymerizations. Acc Chem Res. 1996;29:39–48.

5 Takeuchi D, Watanabe Y, Aida T, Inoue S. Lewis acid-promoted anionic polymerization of a monomer with high cationic polymerizability. Synthesis of narrow molecular weight distribution polyoxetane and polyoxetane-poly(methyl methacrylate) block copolymer with aluminum porphyrin initiators. Macromolecules. 1995;28:651–652.

6 Tang L, Wasserman EP, Neithamer DR, Krystosek RD, Cheng Y, Price PC, He Y, Emge TJ. Highly active catalysts for the ring-opening polymerization of ethylene oxide and propylene oxide based on products of alkylaluminum compounds with bulky tetraphenol ligands. Macromolecules. 2008;41:7306–7315.

7 McInnis JP, Delferro M, Marks TJ. Multinuclear group 4 catalysis: olefin polymerization pathways modified by strong metal–metal cooperative effects. Acc Chem Res. 2014;47:2545–2557.

8 Tsai C-Y, Cheng F-Y, Lu K-Y, Wu J-T, Huang B-H, Chen W-A, Lin C-C, Ko B-T. Dinuclear and trinuclear nickel complexes as effective catalysts for alternating copolymerization on carbon dioxide and cyclohexene oxide. Inorg Chem. 2016;55:7843–7851.

9 Meléndez DO, Castro-Osma JA, Lara-Sánchez A, Rojas RS, Otero A. Ring-opening polymerization and copolymerization of cyclic esters catalyzed by amidinate aluminum complexes. J Polym Sci Part A Polym Chem. 2017;55:2397–2407.

10 Nomura N, Aoyama T, Ishii R, Kondo T. Salicylaldimine–aluminum complexes for the facile and efficient ring-opening polymerization of ε-caprolactone. Macromolecules. 2005;38:5363–5366.

11 CCDC 724752 contains the supplementary crystallographic data. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif or by emailing data_request@ccdc.cam.ac.uk. Anal. calcd for $C_{56}H_{81}AlN_2O_2$: C, 79.95; H, 9.71; N, 3.33. Found: C, 80.12; H, 10.07; N, 3.30.

12 Fuoco T, Pappalardo, D. Aluminum alkyl complexes bearing salicylaldiminato ligands: versatile initiators in the ring-opening polymerization of cyclic esters. Catalysts. 2017:7;64.

13 Iwasa N, Liu J, Nomura K. Notable effect of imino substituent for the efficient ring-opening polymerization of ε-caprolactone initiated by Al complexes containing phenoxy-imine ligand of type, $Me_2Al(L)$ [L: O-2-^{t}Bu-6-(RN=CH)C_6H_3; R: 2,6-^{i}Pr$_2$C$_6$H$_3$, ^{t}Bu, adamantyl, C_6F_5]. Catal Commun. 2008;9:1148–1152.

14 Normand M, Kirillov E, Roisnel T, Carpentier J-F. Meerwein–Ponndorf–Verley-type reduction processes in aluminum and indium isopropoxide complexes of imino-phenolate ligands. Organometallics. 2012;31:5511–5519.

15 Mole T & Jeffery EA. in *Organoaluminium Compounds* ch. 8, 205–228 (Elsevier, 1972). In contrast to $(R'O)AlR_2$[16] and $(R'O)_3Al$,[17] the structural studies of $(R'O)_2AlR$ on the simplistic compound such as $(MeO)_2AlMe$ have not been successfully reported probably due to their unorganized oligo-/polymeric structures. Therefore, the complex is described by $(BnO)_2AlEt$ on the basis of the stoichiometric balance such as RMgX under the Schlenk equilibrium.

16 Kunicki A, Ziemkowska W. Studies on the reaction of triethylaluminium with methyl alcohol. Bull Pol Acad Sci Chem. 1985;33:199–208.

17 Pauls J, Neumüller B. Lithium- und caesium-alkoxometallate. Z Anorg Allg Chem. 2001;627:2127–2132.

18 Dzugan SJ, Goedken VL. Factors affecting Al–C bond reactivity of tetradentate Schiff-base organoaluminum complexes. Inorg Chem. 1986;25:2858–2864.

19 Akatsuka M, Aida T, Inoue S. Alcohol/methylaluminum diphenolate systems as novel, versatile initiators for synthesis of narrow molecular weight distribution polyester and polycarbonate. Macromolecules 1995;28:1320–1322.

20 Duda A, Penczek S. On the difference of reactivities of various aggregated forms of aluminium triisopropoxide in initiating ring-opening polymerizations. Macromol Rapid Commun. 1995;16:67–76.

Table 1 Role of complex **1,** L–H, and/or $(BnO)_nAlEt_{3-n}$[a]

entry	complex **1**, mol %	$(BnO)_nAlEt_{3-n}$,[b] (mol %)	conv. of CL,[c] %	M_n x 10^{-3} (M_w/M_n)[d]
1	0.5	NA[e]	0	NM[f]
2[g]	0	NA[e]	0	NM[f]
3[g]	0.5	NA[e]	0	NM[f]
4	0	n = 1 (1.0)	20	NM[f]
5	0	n = 2 (0.50)	8	NM[f]
6	0	n = 3 (0.33)	6	NM[f]
7	0.5	n = 1 (0.25)	27	39.0 (6.0)[h]
8	0.5	n = 2 (0.50)	91	28.7 (1.1_9)[i]
9	0.5	n = 3 (0.25)	85	83.7 (1.4_2)

[a] Polymerization conditions: complex **1** prepared in situ, 0.010 mmol (Entries 1, 3, and 7–9); $BnOAlEt_2$, 0.020 mmol (Entry 4) or 0.005 mmol (Entry 7); $(BnO)_2AlEt$, 0.010 mmol (Entries 5 and 8); $(BnO)_3Al$, 0.007 mmol (Entry 6) or 0.005 mmol (Entry 9); CL, 0.220 mL (2.00 mmol); toluene, 2.0 mL; temp., 25 ˚C; time, 10 min. [b] Each complex was prepared according to the ref 15. [c] The conversion of CL was determined by 300 MHz ^{1}H NMR. [d] M_n and M_w/M_n were determined by SEC (polystyrene standards, $CHCl_3$, 40 ˚C). [e] Not added. [f] Not measured. [g] The salicylaldimine ligand (L–H, 0.020 mmol, 1 mol %) was added. [h] The SEC trace was bimodal, and each peak respectively showed M_n = 409,000 ($M_w/M_n = 1.2_3$) and 19,000 ($M_w/M_n = 1.1_8$). [i] The expected M_n in this entry was 23,300. $M_{n(SEC)} = M_{n(theo)}/0.45$ (correlation factor for PSt standards, THF). $M_{n(theo)}$ = 108.14 (BnOH) + 114.14 (CL) x 91 (CL conv. %)/1 (BnOH, mol %) ~ 10,500. Since the correlation factor in $CHCl_3$ that we used for SEC analysis has not been known, we applied the value of THF (0.45) for convenience. The calculated efficiency of BnOH was ~80% (23,300/28,700 = 0.81).

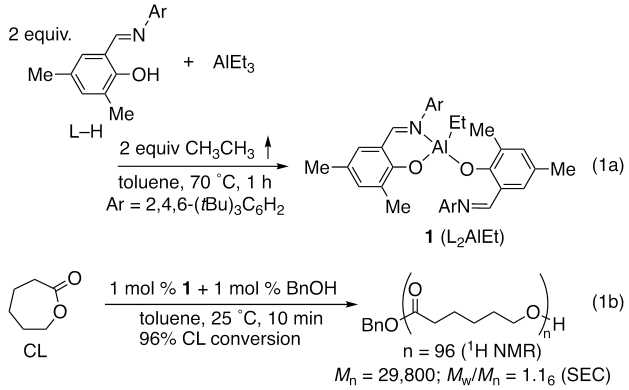
Figure Legends

Fig. 1 Crystal structure of complex **1**. Thermal ellipsoids are drawn at 30% probability level and H atoms are omitted for clarity

Fig. 2 400 MHz ^{1}H NMR spectra of reaction between complex **1** with BnOH (C_6D_6–toluene)

Scheme 1 Reaction of complex **1** with 1 equiv of BnOH

Scheme 2 Mechanistic rationale of synergic catalysis


2 equiv.
Ar
N
Me
OH
+ AlEt3
Me
L–H
2 equiv CH3CH3
toluene, 70 °C, 1 h
Ar = 2,4,6-(tBu)3C6H2
Et
Al
O
ArN
1 (L2AlEt)
(1a)
1 mol % 1 + 1 mol % BnOH
toluene, 25 °C, 10 min
96% CL conversion
CL
BnO
H
n = 96 (1H NMR)
Mn = 29,800; Mw/Mn = 1.16 (SEC)
(1b)

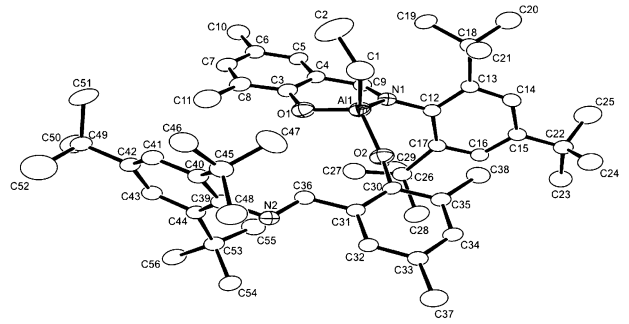


Fig. 1

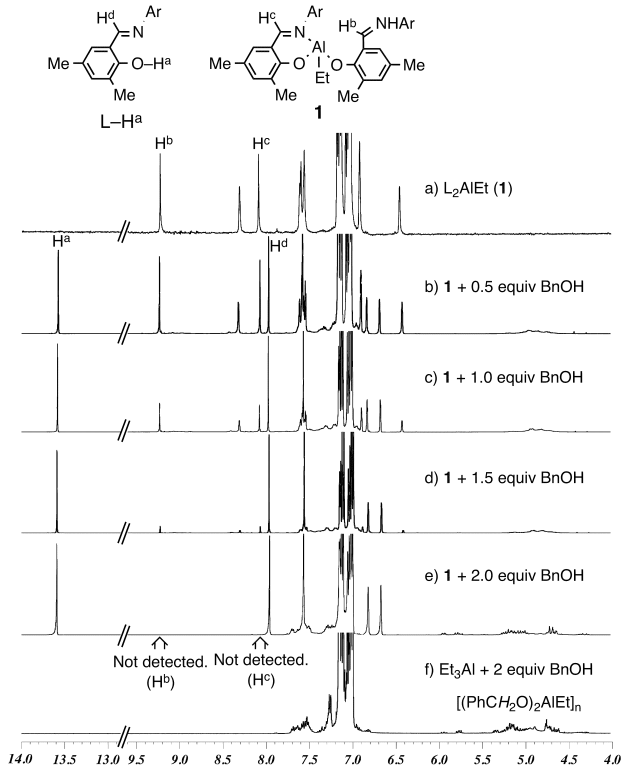
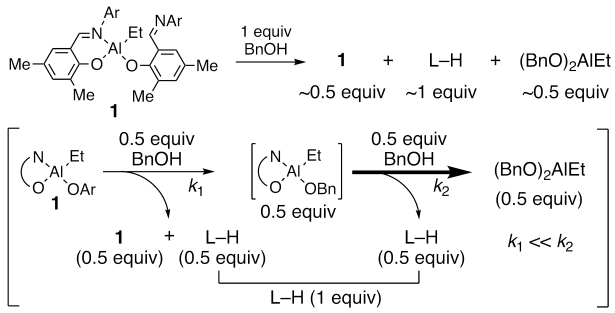
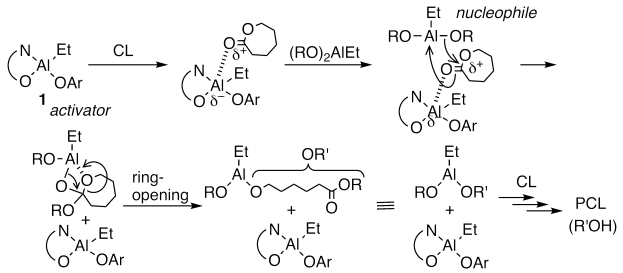

Hd
Ar
N
Me
O–Ha
Me
L–Ha
Hc
Ar
N
Al
O
Et
Me
Me
1
Hb
NHAr
Me
Hb
Hc
a) L2AlEt (1)
Ha
Hd
b) 1 + 0.5 equiv BnOH
c) 1 + 1.0 equiv BnOH
d) 1 + 1.5 equiv BnOH
e) 1 + 2.0 equiv BnOH
Not detected. (Hb)
Not detected. (Hc)
f) Et3Al + 2 equiv BnOH
[(PhCH2O)2AlEt]n
14.0 13.5 13.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0

Fig. 2



Scheme 1



Scheme 2

Graphic Abstract