CHAPTER 2

EXPERIMENTAL

2.1 Chemicals, Apparatus and Instruments

2.1.1 Chemicals

The chemicals used in this research project were as listed in Table 2.1.

Table 2.1 Chemicals used in this research project.

CHEMICAL	USAGE	GRADE	SUPPLIER
1. Acetone*	Solvent	Commercial	BDH Chemicals
2. Ammonium chloride	Adjust pH	99.8%	Scharlau
3. Antimony trioxide	Catalyst	99%	BDH
4. Calcium hydride	Drying agent	≥ 97.0%	Fluka
5. ε-Caprolactone**	Monomer	99%	Acros organics
6. Chloroform	Solvent	AR	Lab Scan
7. Chloroform-d_1	Solvent	≥ 99.8%	Wilmad
8. Dichloromethane*	Solvent	Commercial	BDH Chemicals
9. *N,N'*-Dicyclohexylcarbo-diimide	Reagent	≥ 99.0%	Fluka
10. Diethylamine**	Catalyst Precursor	99.5 %	PS, Panreac
11. 3,4-Dihydro-2*H*-pyran	Reagent	97%	Fluka
12. *N,N'*-Dimethyl formamide**	Solvent	99.8%	CarloErba
13. Ethyl acetate*	Solvent	Commercial	ICI

Table 2.1 Chemicals used in this research project (continued).

CHEMICAL	USAGE	GRADE	SUPPLIER
14. 1-Hexanol	Initiator	GC	Merck
15. Hydrochloric acid	Adjust pH	37%	BDH
16. L(+)-Lactic acid	Monomer Precursor	88%	CarloErba
17. Magnesium sulphate	Drying agent	≥ 98.0%	Fluka
18. Methanol*	Solvent	Commercial	BDH Chemicals
19. Montmorillonite K10	Catalyst	-	Fluka
20. Pentaerythritol	Initiator	Purum, HPLC	Fluka
21. Silica gel 60, GE0030	Stationary phase	-	Scharlau
22. Silica gel 60 PF_{254}	Stationary phase	-	Merck
23. Silicone oil	Heating bath	Commercial	Fluka
24. Stannous octoate**	Catalyst	95%	Sigma
25. Sulfuric acid	Catalyst	96.0%	CarloErba
26. Tetrahydrofuran	Solvent	≥ 99.5%	Merck
27. *p*-Toluene sulfonic acid	Catalyst	98.0%	Sigma

Note * Purified by simple distillation

** Purified by distilled under reduce pressure

2.1.2 Apparatus and Instruments

The main items of apparatus and instruments used were as listed in Table 2.2.

Table 2.2 Apparatus and instruments used in this research project.

APPARATUS AND INSTRUMENTS	COMPANY	MODEL
1. Automatic Viscosity Measuring System	Schott-Geräte	AVS 300
2. Controlled Atmosphere Glove Box	Labconco	50004
3. Differential Scanning Calorimeter (DSC)	Perkin-Elmer	DSC7
4. Gel Permeation Chromatograph (GPC)	Waters	717 Plus
5. High Vacuum Pump	Edwards	Edwards 18
6. Infrared Spectrometer (FT-IR)	Bruker	Tensor 27
7. High Resolution Mass Spectrometer (HR-MS)	Waters	Micromass-Q-Tof-2^{Tm}
8. Mechanical Testing Machine	Lloyd Instruments	LRX+
9. Nuclear Magnetic Resonance Spectrometer (NMR)	Bruker	Avace 400
10. Rotational Rheometer	Malvern	Bohlin Germini HR^{nano}
11. Rotary Evaporator	Büchi	R-200
12. Thermogravimetric Analyzer (TGA)	Perkin-Elmer	TGA7
13. UV-Lamp 254	-	-
14. Vacuum Oven	Eyela	VOS-300SD
15. Weight Balances (2 and 4 positions)	Mettler Toledo	PG802-S and AB204-S

2.2 Monomer Preparation and Purification

The cyclic ester monomers used in this research project were L-lactide (LL) and ε-caprolactone (CL). Since LL is prohibitively expensive to buy (4,320 baht/25g) [60], it was synthesized in our laboratory from its much cheaper than precursor, L-lactic acid. ε-Caprolactone is more readily available and is purchased for use in this research project. The methods of synthesis and purification are described in the following sections 2.2.1 and 2.2.2. The purity of monomers has an important influence on its subsequent polymerizability.

2.2.1 Synthesis of L-Lactide

The synthesis of LL is a two-step reaction involving, firstly the linear polycondensation of L-lactic acid to low molecular weight poly(L-lactic acid) (PLLA) followed, secondly by thermal decomposition of the PLLA to yield LL as the primary decomposition product, as shown in Figure 2.1.

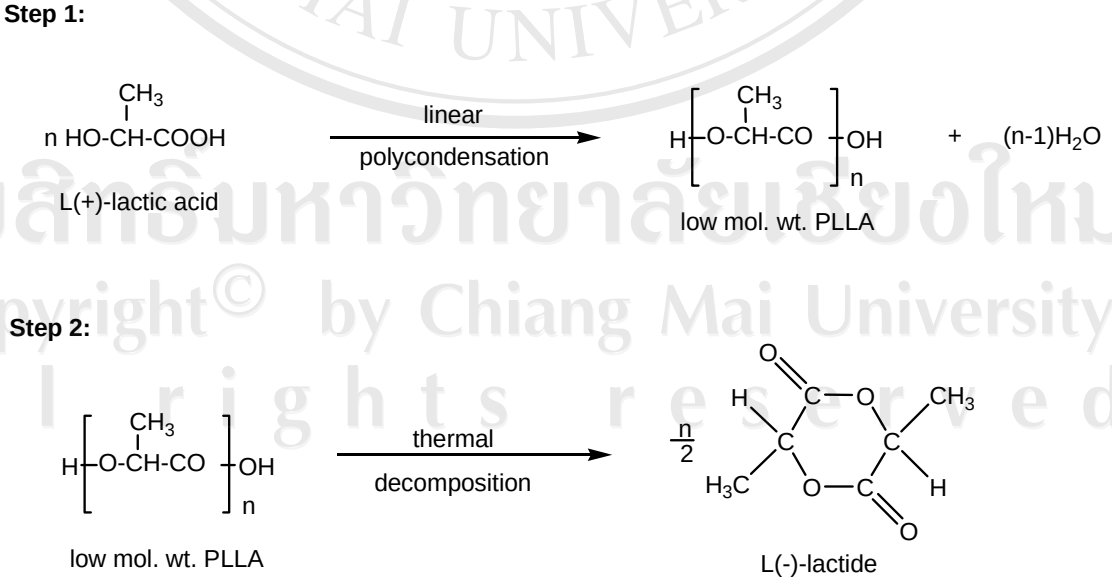


Figure 2.1 Two-step process used for synthesizing LL from L(+)-lactic acid.

In a typical synthesis reaction in this experiment, approximately 1000 g of L-lactic acid were added into a 1000 ml round-bottomed flask which contained about 1.0 g of tin(II) *n*-butoxide ($Sn(OnBu)_2$) as catalyst (0.1% by weight). [61] The flask was then heated at 180-200°C (using heating mantle and vary AC scale 120) in an air condenser connected with short path distillation apparatus as shown in Figure 2.2. Heating and stirring were continued until the water ceased to distill from the reaction flask under atmosphere for about 3 hours. Then, heated at 120-130°C (using heating mantle and vary AC scale 270) before a gentle vacuum (about 4-5 mmHg) was applied to the system for 2 hours to facilitate further removal of water and to increase the polymer molecular weight. The product at this stage was low molecular weight PLLA.

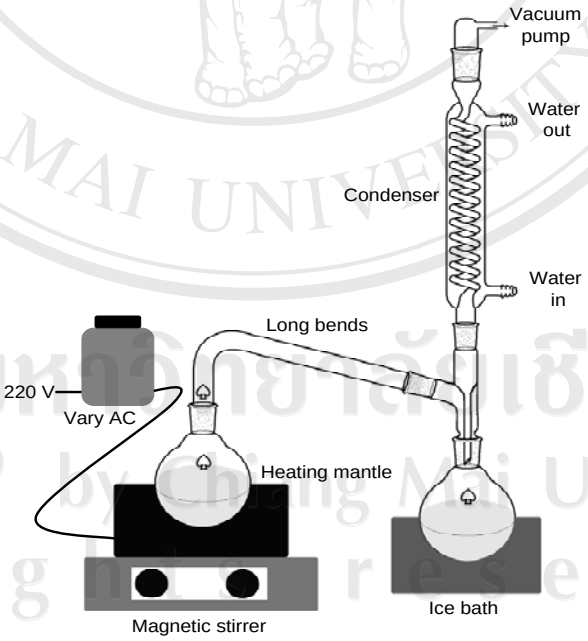


Figure 2.2 The apparatus used in the synthesis of LL. [61]

Finally, for an additional period of about 2 hours, the reaction temperature was heated about 220-240°C (using heating mantle and vary AC scale 270) under reduced pressure of about 4-5 mmHg in order to thermally degrade the low molecular weight PLLA to yield LL as a primary product. Crude LL began to distill out of the flask to a receiving flask as light yellow crystalline solid. This crude product was obtained in approximately 99% yield.

2.2.2 Purification and Purity Analysis of L-Lactide

The crude LL was purified by recrystallisation three times from distilled ethyl acetate. The purified LL was filtered through sintered glass porosity no.4, washed several times with cold ethyl acetate and dried to constant weight at 55°C in a vacuum oven (about 3 mmHg). The purified LL was obtained as a white needle-like solid with approximately 60-70% yield.

Purity analysis by differential scanning calorimetry (DSC) showed that the purified LL had a sharp DSC melting peak from 91 to 92ºC, as shown in Figure 2.3. In order to determine the actual purity of the recrystallized LL by the DSC technique, the instrument's Purity Analysis Software Program was employed [62]. To obtain the best results from purity analysis, a slow scanning rate of 2ºC/min and a small sample size in the range of 1-3 mg were used. From its DSC melting peak, a purity of 99.95% was obtained. These results served to show that the LL synthesized and purified in this work was of a sufficiently high purity (> 99.9%) to produce high molecular weight polymers. Impurities such as moisture, L-lactic acid and L-lactoyl lactate can act either as initiators or chain terminators during ROP leading to a decrease in the molecular weight of the final product.

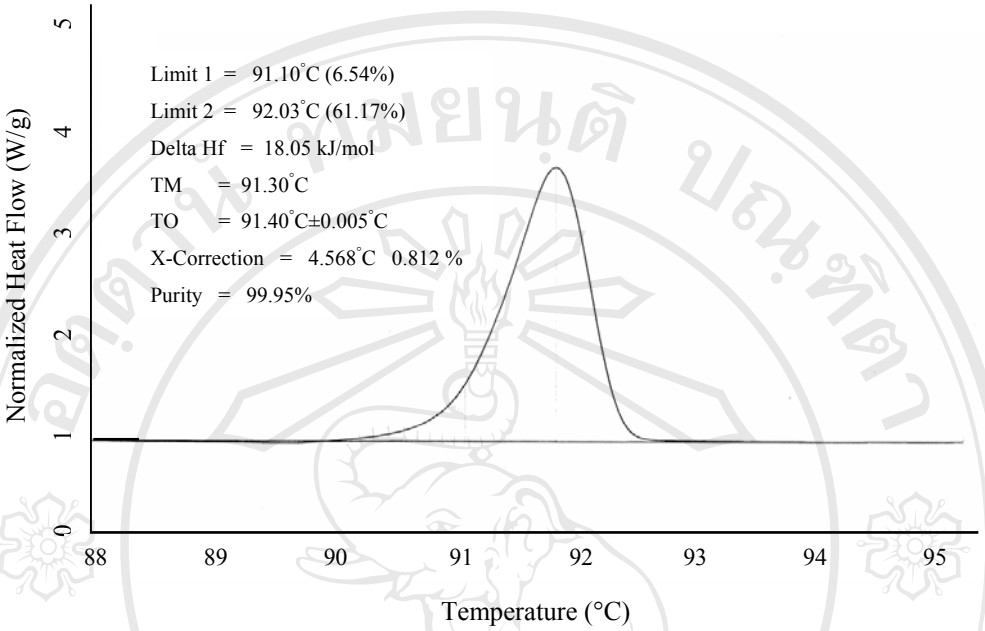


Figure 2.3 DSC melting peak of synthesized LL (after 3rd recrystallisation) (sample size = 2.850 mg, heating rate = 2°C/min).

2.2.3 Purification of ε-Caprolactone by Vacuum Distillation

Commercial CL (Acros Organics, assay 99%) was purified by vacuum distillation as shown in Figure 2.4, the constant boiling fraction from 72°C/0.8 torr (cf. boiling point = 80°C/0.75 torr [63]) pressure being collected. Pure ε-caprolactone was obtained as a clear colorless liquid at room temperature and was stored over molecular sieves 4 Å in a refrigerator in a tightly sealed container until required for use in polymerization.

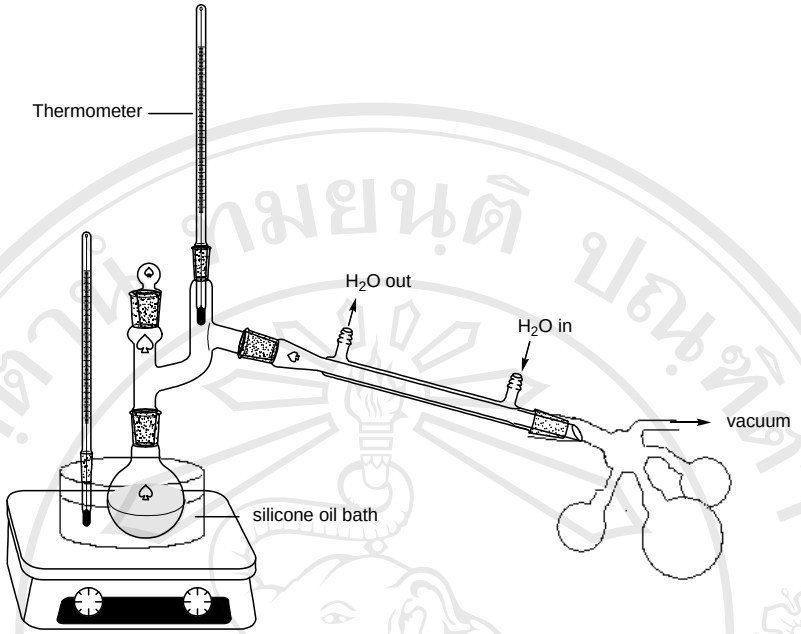


Figure 2.4 Vacuum distillation apparatus used for the purification of ε-caprolactone.

2.3 Catalyst and Initiator Purification

Because trace amounts of water and other impurities could be presented in the catalyst and various initiators used in this research project, they required further purification. Since moisture can have a serious effect on the polymer molecular weight obtained. In general, the method used was followed from references with appropriate drying agent employed.

2.3.1 Stannous Octoate

Commercial stannous octoate, $SnOct_2$ typically 95% pure as received, commonly contains 2-ethylhexanoic acid and water as impurities. $SnOct_2$ used in this research project was purified by bulb-to-bulb vacuum distillations. The first is the

distillation under vacuum at room temperature for removing residual water, and then distilled under vacuum at 120-126°C/15 torr for removing 2-ethyl hexanoic acid (cf. 2-ethyl hexanoic acid boiling point = 140°C/23 torr [64]). Purified $SnOct_2$ remaining in the heating flask was obtained as a colorless viscous liquid and was stored in vacuum desiccator.

2.3.2 1-Hexanol

1-Hexanol, monofunctional hydroxyl initiator used for the preparation of linear polymers was purified by vacuum distillation. The distilled 1-hexanol was collected as the constant boiling fraction at 47ºC/4.0 torr (cf. boiling point = 156ºC/1.0 torr [64]) and then stored over molecular sieves 4 Å in vacuum desiccator.

2.3.3 Pentaerythritol

Pentaerythritol, PTOL multifunctional initiator was dried to constant weight in a vacuum oven at 120ºC to remove any residual moisture traces. It was stored in a vacuum desiccator at room temperature. The melting peak of purified PTOL from DSC is 252-260ºC.

2.4 Characterization Methods

In this research project, the monomer, initiators, catalyst and polymer products obtained were characterized by the following combination of instrumental methods.

2.4.1 Fourier Transform Infrared Spectroscopy (FT-IR)

Fourier transform infrared (FT-IR) spectroscopy is the most extensively used method for the analysis of functional groups. In this research project, FT-IR was used, mainly for the structural characterization of the catalyst. A Bruker Fourier transform Infrared Spectrometer was used for the recording of FT-IR spectra with the range 400-4000 cm^{-1}. The samples were prepared in the form of neat liquid on a sodium chloride plate.

2.4.2 High Resolution Mass Spectroscopy (HR-MS)

In this research project, high resolution mass spectroscopy (HR-MS) was used for the structural identification of star-core macroinitiator. The samples were analyzed on micromass Q-Tof-2^{Tm} (Waters) spectrometer**.** The GC was equipped with a 19091S-433 capillary column. Nitrogen was used as carrier gas. The samples were analyzed utilizing the following temperature program of the column: the temperature was allowed to rise from 100 to 250ºC at a heating rate of 10ºC min^{-1} and then held at 250ºC for 25 minutes.

2.4.3 Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) spectroscopy was used to analyze the chemical structures and number-average molecular weight ($\overline{M}_n$) and microstructure of the polymer formed in this research project. For NMR measurement, the samples were dissolved in deuterated-chloroform ($CDCl_3$) in 5 mm NMR tubes. The sample concentration was about 5% by weight. Chemical shifts

were relative to tetramethylsilane (TMS) (internal standard at $\delta = 0$ ppm). Both ^{1}H-NMR and ^{13}C-NMR spectra were obtained from MestRe-C data processing software and recorded on a Bruker Avace spectrometer working at 400 MHz ^{1}H and 100 MHz ^{13}C respectively.

2.4.4 Gel Permeation Chromatography (GPC)

Molecular weight ($\overline{M}_n$, $\overline{M}_w$ and $\overline{M}_v$) and polydispersities ($\overline{M}_w/\overline{M}_n$) were determined by gel permeation chromatography (GPC). The Waters associated system equipped with a Waters 717 plus autosampler injector, a Waters 515 HPLC solvent pump with styragel HR 4E, 5E column (pore size; 5 μm) connected a Waters 2414 Refractive Index and Viscotex 270 Dual detectors at 40ºC and a TriSEC Version 3.00 as data processing software was used. Narrow polydispersities polystyrene standards were used for calibration, range 1,100-186,000 g mol^{-1}. Tetrahydrofuran (THF) was used as the eluent at the flow rate of 1 ml min^{-1}. The samples were dissolved in THF at a concentration of 3-5% (w/v).

2.4.5 Differential Scanning Calorimetry (DSC)

The purities, temperature transitions (T_g, T_c and T_m) and morphology (% crystallinity) were investigated by differential scanning calorimetry (DSC). DSC measurement was made on a Perkin-Elmer DSC7 instrument with Pyris software. Pure indium and tin were used as reference material to calibrate the temperature. The thermal properties measurements were run from 0ºC to 200ºC at a heating rate of

10ºC min^{-1}. The samples with a typical mass of 3-5 mg were encapsulated in sealed aluminium pans and were heated and cooled under nitrogen atmosphere.

2.4.6 Thermogravimetric Analysis (TGA)

Thermogravimetry (TG) was used as a method for the investigation of the thermal stability and decomposition profile of a polymer. TG analysis was carried out on a Perkin-Elmer Pyris instrument with a TGA7 model. Nitrogen gas was used as the purge gas at pressure of 30 Ibs in^{-2} for the sample zone and 50 Ibs in^{-2} for the balance zone. The heating rate used was 20ºC min^{-1} and the sample was heat from 50ºC to 600ºC with initial sample weights in the range of 5-10 mg. Data was recorded as a thermogram of % weight versus temperature.

2.4.7 Dilute-Solution Viscometry

The intrinsic viscosity, [η] and viscosity average molecular weight ($\overline{M}_v$) of the polymers were determined from dilute solution viscometry. The viscosities were measured at concentration of 0-1.0% (m/v) in solvent with Schott-Geräte Ubbelohde type viscometer (type No. 532 00, capillary No. 0_c) in conjunction with Schott-Geräte AVS300 Automatic Viscosity Measuring System. The results were plotted between reduced and inherent viscosity versus concentration and the viscosity-average molecular weight were calculated from intrinsic viscosity and constant as the Mark-Houwink Sakurada Equation.

2.4.8 Mechanical Tensile Testing

The mechanical tests perform on Lloyds LRX+ Universal Mechanical Testing Machine were used for determining the mechanical properties such as tensile strength, % elongation at break, and Young's modulus. Thin film samples were prepared by a simple solvent casting method. The polymer was dissolved in ethyl acetate to form solutions with concentrations of 20% (w/v). The solution was spread over a glass mold (10 cm × 15 cm). The solvent was evaporated slowly in air at room temperature over three days and the obtained films were further dried under vacuum at room temperature for 48 hours. Each film was cut into 1.0 cm widths and 15.0 cm lengths and kept in a vacuum desiccator until use. The test conditions were followed as ASTM D882-91 with a sample grips, load cell of 100 N (preload = 0.1 N) at a crosshead speed of 10 mm min^{-1}. The tests were required at least five samples from each polymer at 23±2ºC and 50±5% relative humidity.

2.4.9 Melt Rheology Measurements

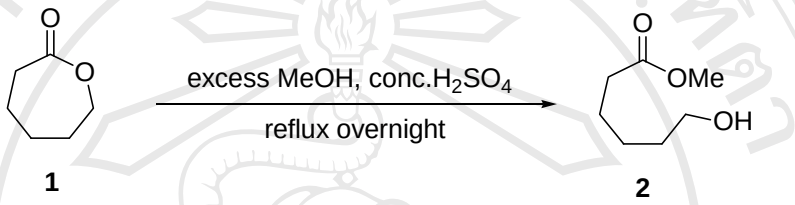
Rheology is defined as the science of the deformation and flow of matter. In an ideal viscous liquid, the energy of deformation is dissipated in the form of heat and cannot be recovered just by releasing the external forces; whereas, in an ideal solid, the deformation is fully recovered when the stresses are released. Due to the dependence of rheology on the structure and the basic inherent chemistry of the polymers, rheological data can be used effectively to control material parameters like molecular weight, molecular weight distribution, branching, crosslinking and so forth so that the right choice of the polymer to be processed can be made under a given set of processing conditions.

Measurements on PCL homopolymer in this study were performed using Bohlin Gemini HR^{nano} Rotational Rheometer, Malvern as shown in Figure 2.5. The diameter of the plates was 25 mm and the gap between the plates was set to 0.5 mm. The rheological behaviors of all samples were analyzed by shear rate range of 0.01 to 100 (1/s) under isothermal condition at 80ºC. The zero shear rate viscosity, [η_0] measurements were preformed by measuring viscosity as a function of shear rate.

Figure 2.5 Bohlin Gemini HR^{nano} Rotational Rheometer apparatus; (a) parallel plate geometry and (b) the gap between the plates.

2.5 Synthesis of Pentaerythritol tetrakis(6'-hydroxyhexanoate) Star-Core Macroinitiator

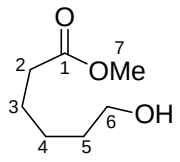
2.5.1 Synthesis of Methyl 6-hydroxyhexanoate (2)



1 **2**

A mixture of *ε*-caprolactone (**1**) (20.00 g, 0.1752 mol) and conc. sulfuric acid (10 ml) in anhydrous methanol (1600 ml) was heated to reflux overnight. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate solution at 0°C and the crude mixture was extracted several times with CH_2Cl_2. The combined organic extracts were washed with H_2O, dried over $MgSO_4$, filtered, and evaporated to dryness.

The crude product was purified by flash column chromatography on silica gel using EtOAc : hexane = 1 : 9 as eluent to give hydroxyl ester **2**, *methyl 6-hydroxyhexanoate* in 79% yield (20.22 g) and 100% conversion from the starting material.



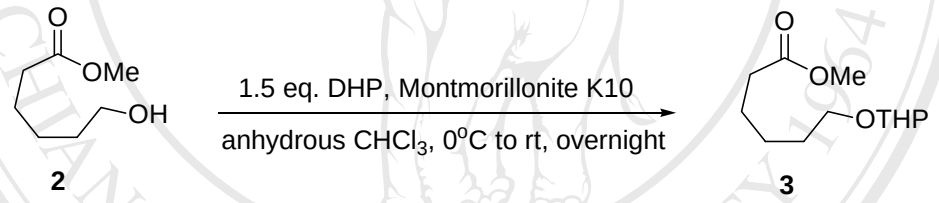
2

Table 2.3 Data of compound **2**.

Physical property	
Colorless oil	
IR spectroscopy (evaporated thin film)	
Frequency (v, cm^{-1})	Type of vibrations
3403	O-H stretching of hydroxyl
2937, 2865	CH_2, CH_3 stretching
1732	C=O stretching of ester
1436, 1356	CH_2, CH_3 bending
1182	C-O stretching of ester
1051	O-H bending of hydroxyl
NMR spectroscopy	
^{1}H NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.41	2H, *m*, CH_2-4
1.60	2H, *m*, CH_2-3
1.67	2H, *m*, CH_2-5
2.34	2H, *t* (J = 7.4 Hz), CH_2-2
3.66	2H, *t* (J = 6.6 Hz), CH_2-6
3.68	3H, *s*, $COOCH_3$-7
^{13}C NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
24.58	CH_2-4
25.24	CH_2-3

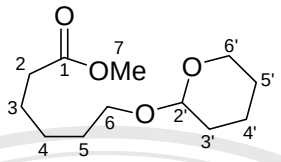
^{13}C NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Chemical shift (δ, ppm)
32.25	CH_2-5
33.94	CH_2-2
51.49	CH_3-7
62.58	CH_2-6
174.19	C_q-1

2.5.2 Synthesis of Methyl 6-(tetrahydro-2*H*-pyran-2-yloxy)hexanoate (3)



Montmorillonite K10 was added into a solution of **2** (20.00 g, 0.1369 mol), in anhydrous chloroform (500 ml) followed by 3,4-dihydro-2*H*-pyran (DHP) (17.27 g, 0.2054 mol) at 0°C over 15 min. The reaction mixture was stirred at room temperature overnight and then passed through Celite 545, washed with CH_2Cl_2. The organic phase was evaporated to dryness.

The crude product was purified by flash column chromatography on silica gel using EtOAc : hexane = 1 : 9 as eluent to give the protected hydroxyl ester **3**, *methyl 6-(tetrahydro-2H-pyran-2-yloxy)hexanoate* in 92% yield (22.68 g) and 72% conversion from starting material.



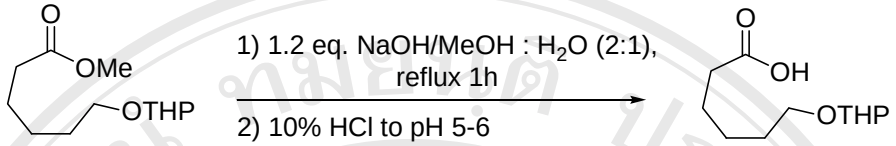
3

Table 2.4 Data of compound **3**.

Physical property	
Colorless oil	
IR spectroscopy (evaporated thin film)	
Frequency (ν, cm^{-1})	Type of vibrations
2945, 2871	CH_2, CH_3 stretching
1735	C=O stretching of ester
1445, 1356	CH_2, CH_3 bending
1167	C-O stretching of ester
1074, 1035	C-O stretching of ether
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.36-1.48	2H, *m*, CH_2-4
1.48-1.91	10H, *m*, CH_2-3, 5, 3', 4', 5'
2.34	2H, *t* (J = 7.47 Hz), CH_2-2
3.41	1H, *dt* (J = 9.61, 6.53 Hz), CH_2-6'
3.76	1H, *dt* (J = 9.61, 6.73 Hz), CH_2-6'
3.52, 3.88	2H, *m*, CH_2-6
3.69	3H, *s*, $COOCH_3$-7

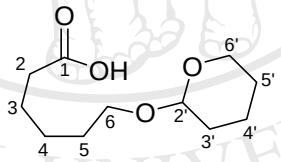
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Chemical shift (δ, ppm)
4.59	1H, *dd* (J = 2.74 Hz), CH-2'
^{13}C-NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
19.67, 25.84, 29.38	CH_2-3', 4', 5'
24.78	CH_2-4
25.46	CH_2-3
30.74	CH_2-5
34.02	CH_2-2
51.47	CH_3-7
62.37	CH_2-6
67.32	CH_2-6'
98.88	CH-2'
174.19	C_q-1
Mass spectroscopy (HR-MS)	
Molecular weight	m/z
Calc. for $C_{12}H_{22}O_4$	231.1596 $(M + H)^+$
Lock mass of $C_9H_{10}N_4O_2S_2$	293.0143 $(M + Na)^+$
Calc. for $C_{12}H_{22}O_4Na$	253.1416 $(M + Na)^+$
Found for $C_{12}H_{22}O_4Na$	253.1416 $(M + Na)^+$

2.5.3 Synthesis of 6-(Tetrahydro-2*H*-pyran-2-yloxy)hexanoic acid (4)



3 **4**

A solution of NaOH (3.13 g, 0.0782 mol) in H_2O (150 ml) was added to a solution of **3** (15.00 g, 0.0652 mol) in MeOH (300 ml) and heated to reflux for 1 h. The mixture was acidified with 10% HCL (pH 5-6) followed by extraction several times with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated to dryness to give the ether acid **4**, *6-(tetrahydro-2H-pyran-2-yloxy)hexanoic acid* in 75% yield (10.56 g) and 100% conversion from the starting material.



4

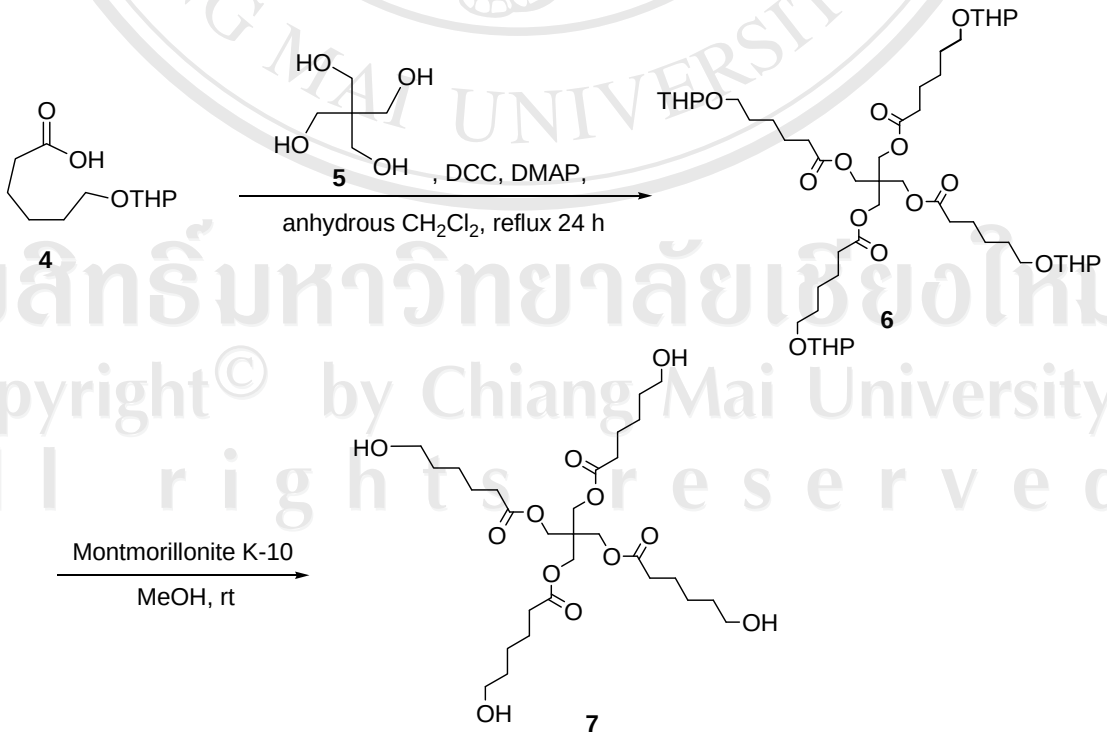
Table 2.5 Data of compound **4**.

Physical property	
Colorless oil	
IR spectroscopy (evaporated thin film)	
Frequency (ν, cm^{-1})	Type of vibrations
3698-2319	O-H stretching of hydroxyl
2949, 2875	CH_2 stretching

IR spectroscopy (evaporated thin film)	
Frequency (ν, cm^{-1})	Type of vibrations
1711	C=O stretching of carboxylic acid
1450	CH_2 bending
1370	C-O stretching and O-H deformation of carboxylic acid
1065, 1029	C-O stretching of ether
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.39-1.92	12H, *m*, CH_2-3, 4, 5, 3', 4', 5'
2.39	2H, *t* (J = 7.4 Hz), CH_2-2
3.41	1H, *dt* (J = 9.6, 6.5 Hz), CH_2-6'$_{ax}$
3.76	1H, *dt* (J = 9.6, 6.7 Hz), CH_2-6'$_{eq}$
3.52, 3.88	2H, *m*, CH_2-6
4.60	1H, *m*, CH-2'
^{13}C-NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
19.61, 25.74, 29.34	CH_2-3', 4', 5'
24.49	CH_2-4
25.43	CH_2-3
30.70	CH_2-5
33.87	CH_2-2
62.33	CH_2-6

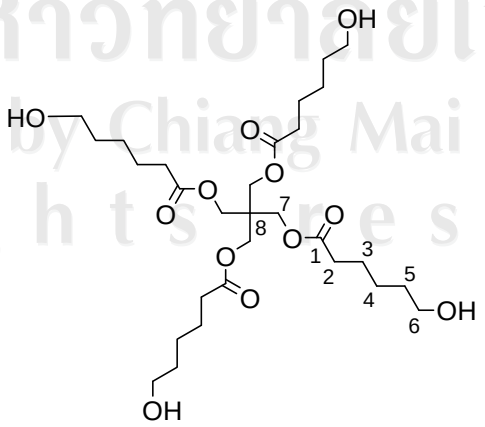
^{13}C-NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
67.27	CH_2-6'
98.85	CH-2'
179.22	C_q-1
Mass spectroscopy (HR-MS)	
Molecular weight	m/z
Calc. for $C_{11}H_{20}O_4$	217.1440 $(M + H)^+$
Lock mass of $C_9H_{10}N_4O_2S_2$	293.0143 $(M + Na)^+$
Calc. for $C_{11}H_{20}O_4Na$	239.1259 $(M + Na)^+$
Found for $C_{11}H_{20}O_4Na$	239.1259 $(M + Na)^+$

2.5.4 Synthesis of Pentaerythritol tetrakis(6'-hydroxyhexanoate) (7)



To a 250 ml, three necks, round-bottomed flask equipped with a magnetic stirred with a septum cap and nitrogen inlet was added anhydrous CH_2Cl_2 (100 ml) and dry compound **4** (6.98 g, 0.0323 mol). The mixture was cooled down to 0ºC followed by addition of 4-dimethylaminopyridine (DMAP) (5.83 g, 0.0477 mol) and pentaerythritol (PTOL) (1.00 g, 0.0073 mol in *N,N*-dimethylformamide (DMF)). After stirring at 0ºC for few min, then *N,N'*-dicyclohexylcarbodiimide (DCC) (9.85 g, 0.0477 mol in anhydrous CH_2Cl_2) was added. The reaction mixture was heated to reflux for 24 h. The crude product was filtrated, washed with CH_2Cl_2 and evaporated to dryness.

The crude product **6**, *pentaerytritol (6-(tetrahydro-2H-pyran-2-yloxy)hexanoate))* and montmorillonite K10 (as a catalyst) in MeOH (100 ml) were stirred at room temperature for 7 h, then filtrated through celite 545 and evaporated to dryness. The crude product was purified by flash column chromatography on silica gel using acetone : EtOAc : hexane = 1 : 1 : 8 as eluent to give the star-core macroinitiator **7**, *pentaerythritol tetrakis(6'-hydroxyhexanoate)* in 43% yield (1.87 g), and 100% conversion from the starting material.



7

Table 2.6 Data of compound **7**.

Physical property	
Colorless oil	
IR spectroscopy (evaporated thin film)	
Frequency (v, cm^{-1})	Type of vibrations
3381	O-H stretching of hydroxyl
2946, 2871	CH_2 stretching
1747	C=O stretching of ester
1407	CH_2 bending
1153	C-O stretching of ester
1065	O-H bending of hydroxyl
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.38	8H, *m*, CH_2-4
1.55	8H, *m*, CH_2-3
1.64	8H, *m*, CH_2-5
2.35	8H, *m*, CH_2-2
3.61	8H, *t* (J = 6.3 Hz), CH_2-6
4.10	8H, *s*, CH_2-7
^{13}C-NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
24.55	CH_2-4
25.17	CH_2-3
32.09	CH_2-5

^{13}C-NMR (100 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of carbons
34.05	CH_2-2
43.56	C_q-8
62.21	CH_2-6
77.00	CH_2-7
173.30	C_q-1
Mass spectroscopy (HR-MS)	
Molecular weight	m/z
Calc. for $C_{29}H_{52}O_{12}$	593.3537 $(M + H)^+$
Lock mass of $C_{33}H_{40}N_2O_9$	609.2812 $(M + H)^+$
Calc. for $C_{29}H_{52}O_{12}Na$	615.3356 $(M + Na)^+$
Found for $C_{29}H_{52}O_{12}Na$	615.3356 $(M + Na)^+$

2.6 Polymer Synthesis and Purification

All ring-opening polymerization (ROP) were carried out in bulk at 120°C in a round-bottomed flask with ground-glass joints with a magnetic stirring bar. All glassware was dried in a vacuum oven at 120ºC for 12 hours.

The catalyst, initiators and monomers were weight and added to the reaction flask under nitrogen in a controlled-atmosphere glove box at room temperature. After removing the flask from the glove box, it was immersed in a silicone oil bath at a constant temperature and for given period of time as shown in Figure 2.6 (a). At the end of the polymerization period, the flask was rapidly cooled at room temperature. The polymers were purified by dissolving in chloroform then re-precipitating in iced-

cold *n*-hexane for low molecular weight polymers and in methanol for high molecular weight polymers as shown in Figure 2.6 (b). Then, the purified homopolymer products were dried in a vacuum oven until constant weight.

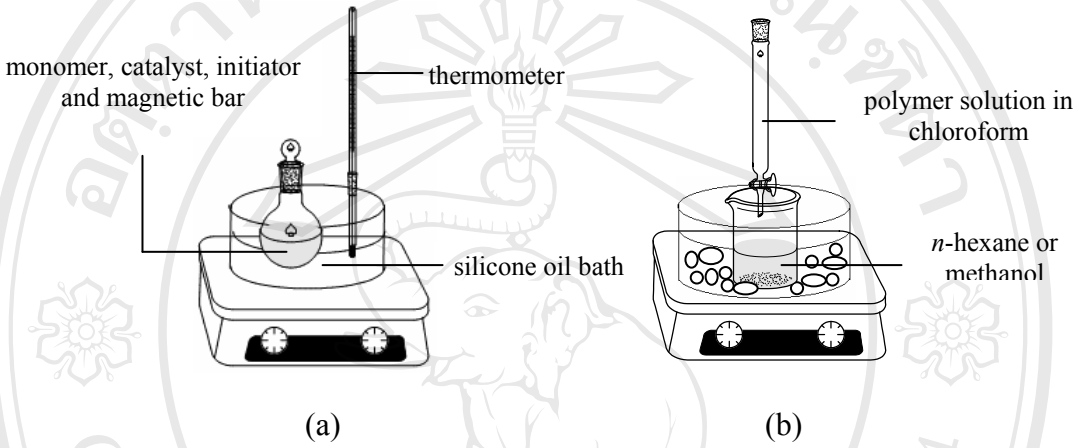


Figure 2.6 Apparatus used in (a) the ring-opening bulk polymerization and (b) polymer purification by re-precipitation from solution.

2.6.1 Synthesis of Low Molecular Weight Poly(*ε*-caprolactone), PCL Model Compounds with Different Molecular Architectures

Linear and star-shaped low molecular weight PCLs were synthesized by ROP at 120°C for 48 hours using 0.1 mole% $SnOct_2$ as a catalyst and 4 mole% 1-hexanol, PTOL and pentaerythritol tetrakis(6'-hydroxyhexanoate) as initiators. The conditions used in the polymerization are shown in Table 2.7. The polymers were purified by dissolving in chloroform then re-precipitating in iced-cold *n*-hexane and drying in a vacuum oven at room temperature until constant weight.

Table 2.7 Polymerization conditions of low molecular weight PCLs with different molecular architectures synthesis at 120°C for 48 hours.

Homopolymer	Initiator	Monomer feed CL (g)	$SnOct_2$: Initiator 0.1 : 4 mole% (g)
PCL_1-hexanol	1-hexanol	2.0062	0.0077 : 0.0710
PCL_PTOL	PTOL	2.0073	0.0087 : 0.0940
PCL_macroinitiator	macroinitiator	2.0100	0.0079 : 0.4989

2.6.2 Synthesis of High Molecular Weight Poly(*ε*-caprolactone), PCL with Different Molecular Architectures

Linear and star-shaped high molecular weight PCLs were synthesized by ROP at 120ºC for 72 hours using 0.1 mole% $SnOct_2$ as a catalyst and 0.05 and 0.005 mole% mono- and multifunctional alcohol (1-hexanol, PTOL and pentaerythritol tetrakis(6'-hydroxyhexanoate)) as initiators respectively. The conditions used in the polymerization are shown in Tables 2.8 and 2.9.

Table 2.8 Polymerization conditions for high molecular weight PCLs with different molecular architectures synthesis at 120°C for 72 hours (10 g).

Homopolymer	Initiator	Monomer feed CL (g)	$SnOct_2$: Initiator 0.1 : 0.05 mole% (g)
PCL_1-hexanol	1-hexanol	10.0183	0.0871 : 0.0019
PCL_PTOL	PTOL	10.0443	0.0981 : 0.0021
PCL_macroinitiator	macroinitiator	10.0851	0.0899 : 0.0069

Table 2.9 Polymerization conditions for high molecular weight PCLs with different molecular architectures synthesis at 120ºC for 72 hours (25 g).

Homopolymer	Initiator	Monomer feed CL (g)	$SnOct_2$: Initiator 0.1 : 0.005 mole% (g)
PCL_1-hexanol	1-hexanol	25.0112	0.1391 : 0.0019
PCL_PTOL	PTOL	25.0283	0.1434 : 0.0028
PCL_macroinitiator	macroinitiator	25.0098	0.1429 : 0.0114

The polymers were purified by dissolving in chloroform then re-precipitating in iced-cold methanol and drying in a vacuum oven at room temperature until constant weight.

2.6.3 Synthesis of High Molecular Weight Poly(L-lactide), PLL with Different Molecular Architectures

Linear and star-shaped high molecular weight PLLs were synthesized by ROP at 120ºC for 48 hours using 1 mole% and for 72 hours using 0.005 mole% mono- and multifunctional alcohol (1-hexanol, PTOL and pentaerythritol tetrakis(6'-hydroxyhexanoate)) as initiators respectively and 0.1 mole% $SnOct_2$ as a catalyst. The conditions used in the polymerization are shown in Tables 2.10-2.11. The polymers were purified by dissolving in chloroform then re-precipitating in iced-cold methanol and drying in a vacuum oven at 55ºC until constant weight.

Table 2.10 Polymerization conditions for low molecular weight PLLs with different molecular architectures synthesis at 120ºC for 48 hours (10 g).

Homopolymer	Initiator	Monomer feed LL (g)	$SnOct_2$: Initiator 0.1 : 1 mole% (g)
PLL_1-hexanol	1-hexanol	10.0686	0.0289 : 0.9674
PLL_PTOL	PTOL	10.0916	0.0293 : 0.9696
PLL_macroinitiator	macroinitiator	10.4113	0.0304 : 1.0004

Table 2.11 Polymerization conditions for high molecular weight PLLs with different molecular architectures synthesis at 120ºC for 72 hours (25 g).

Homopolymer	Initiator	Monomer feed LL (g)	$SnOct_2$: Initiator 0.1 : 0.005 mole% (g)
PLL_1-hexanol	1-hexanol	25.0019	0.1221 : 0.0020
PLL_PTOL	PTOL	25.0103	0.1184 : 0.0025
PLL_macroinitiator	macroinitiator	25.0202	0.1199 : 0.0085

2.7 *In Vitro* Hydrolytic Biodegradation Studies

In vitro experiments were conducted in order to evaluate the potential biodegradability of the high molecular weight PCL and PLL homopolymer with different molecular architectures (PCL_1-hexanol, PCL_PTOL, PCL_macro, PLL_1-hexanol, PLL_PTOL and PLL_macro)

2.7.1 Preparation of Phosphate Buffer Saline (PBS)

The preparation phosphate buffer saline (PBS) followed European Pharmacopoeia [65]. A 0.2 M PBS solution of pH 7.40 was prepared from anhydrous disodium hydrogen orthophosphate (Na_2HPO_4) 2.38 g, potassium dihydrogen phosphate (KH_2PO_4) 0.19 g and sodium chloride (NaCl) 8.00 g dissolved in 1000 ml deionized water. The pH of the solution, which was almost 7.40, was adjusted to exactly 7.40±0.01 with 1 M sodium hydroxide (NaOH).

2.7.2 Preparation of Polymer Samples and Glassware

The PCL and PLL films with different molecular architecture were prepared by solvent casting method using chloroform as solvent (2.4g/30 ml) in mold (12×15 cm^2) and then the solvent allowed to evaporate for 48 hours and further dried under vacuum at room temperature for 48 hours. The films were cut by puncture into circular discs with a diameter 10 mm and thickness 0.15 mm. A total of 216 samples (6 sets) were dried in vacuum oven at 40°C (Figure 2.7) to constant weight and their weight accurately recorded (±0.0001 g). The experiments were divided into 6 sets.

Set 1: PCL_1-hexanol	36	bottles
Set 2: PCL_PTOL	36	bottles
Set 3: PCL_macroinitiator	36	bottles
Set 4: PLL_1-hexanol	36	bottles
Set 5: PLL_PTOL	36	bottles
Set 6: PLL_macroinitiator	36	bottles

All glassware items were sterilized before use by stream autoclaving at 120ºC for 90 minutes. The dried film was then immersed individually in a 50 ml screw-top glass bottles, each containing 10 ml of PBS. The bottles were then immediately placed in an incubator, thermostatically controlled at 37±1ºC, for the *in vitro* hydriolytic biodegradation experiments (zero time). The experiments lasted for a total of 20 weeks.

Figure 2.7 Incubator for *in vitro* hydrolytic degradation studies.

2.7.3 Sampling Procedure

At time intervals (0, 1, 2, 3, 5, 7, 9, 11, 13, 15, 17 and 20 weeks), the bottles were removed from the incubator and samples filtered off by sintered glass (porosity no.3), washed carefully with deionized water and dried to constant weight in vacuum oven at room temperature. Their weights were accurately recorded. Various properties of the samples were then tested, *e.g.* % weight loss, % weight retention and DSC. The pH of the medium was also re-measured since the hydrolytic mechanism of polyester biodegradation is well-known to be pH-dependent.