

CHAPTER III

EXPERIMENTAL

3.1 General

The infrared spectra were recorded on a Perkin Elmer 1706X Infrared Spectrophotometer.

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Model ACF200 Fourier-Transform NMR Spectrometer using tetramethylsilane (TMS) as an external standard. The chemical shift (δ) reported are given in part per million down field from TMS.

Mass spectra were determined using a Fison model Trio-2000 GC-Mass Spectrometer.

Merck TLC plastic sheets (silica gel 60 F254 precoated) was used for thin layer chromatography. Merck PLC plates (silica gel 60 F254 precoated) was used for preparative layer chromatography Merck silica gel 60 (particle size 0.063-0.200 mm) was used for column chromatography.

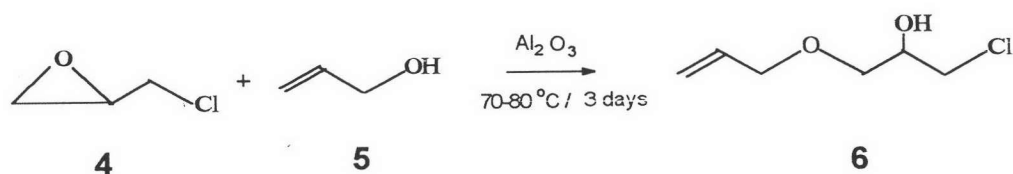
Reagents and raw materials were obtained from various suppliers as shown in Table 3.1.

Table 3.1 Source of chemicals

Materials	Company
Epichlorohydrin	Sigma
Allyl alcohol	Fluka
Bisphenol A	Aldrich
1,6-Hexamethylene diamine	Aldrich
2,5-Dihydroxy-N-(2-hydroxyethyl) benzamide	Aldrich
4,4'-Ethylenedianiline	Aldrich
Methylene chloride	Merck
Chloroform	Aldrich
Methanol	Baker
Ethanol	Baker
Hexane	Baker
Ethyl acetate	Caro Erba
Toluene	Merck
Iodine	Caro Erba
Sodium hydroxide (pellet)	Merck
Sodium chloride	Caro Erba
Sodium sulfate (anhydrous)	Caro Erba
Calcium chloride (anhydrous)	Fluka
Aluminium oxide 90 active	Merck
Magnesium sulfate	Caro Erba

3.2 Experimental Procedure

3.2.1 Preparation of 7-Chloro-6-hydroxy-4-oxa-1-heptene (6)



Epichlorohydrin (**4**) (72.85 g, 0.79 mole) and aluminium oxide 90 active neutral (40.10 g) were placed in a 250 ml three-necked round bottom flask fitted with a reflux condenser and nitrogen inlet tube. Allyl alcohol (**5**) (93.72 g, 1.61 mole) was introduced into a mixture at room temperature. The reaction mixture was left stirring at 70-80 °C for 3 days. The reaction was monitored by thin layer chromatography (TLC) (20% ethyl acetate in hexane as eluent), then the TLC plates were put in iodine chamber. The mixture was cooled to room temperature, filtered, and extracted with dichloromethane. The dichloromethane solution was washed with water, dried (MgSO_4), and concentrated to give a crude material which was partially purified by distillation at reduced pressure to remove mostly epichlorohydrin. The residue containing mostly 7-chloro-6-hydroxy-4-oxa-4-heptene **6** (86.88g) was used in the next experiment (3.2.2) without further purification.

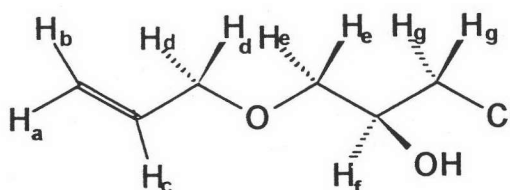
The experiment was repeated with different amount of alumina such as 18.08, 29.65 and 55.04% (% by weight comparing to **4**) (see Table 4.1). The best yield was obtained when 55.04% of alumina was used. A portion of the crude reaction mixture was purified using silica gel column chromatography (10% ethyl acetate in hexane as eluent) to obtained the spectroscopic data of **6** as shown in page 37 and 38.

Spectroscopic data of **6**

IR ν_{\max} (neat)

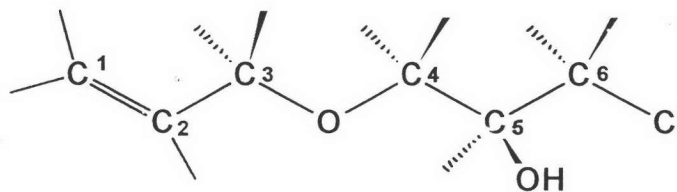
Wave number (cm^{-1})	Bond type
3413	O-H stretching
2910	C-H stretching
2868	C-H stretching
1646	C=C stretching
1120	C-O stretching
1072	C-O stretching
750	C-Cl wagging

$^1\text{H-NMR}$ (d_6 -acetone+ CDCl_3)



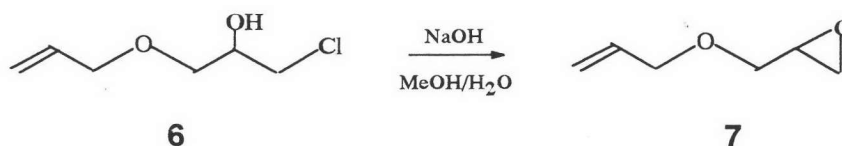
Chemical Shift (δ , ppm)	Multiplicity	Position of proton	number of proton	Coupling constant (Hz)
3.58	dd	e	2	5.5, 12.2
3.66	dd	g	2	5.3, 12.2
3.93-4.09	m	d+f	-	-
5.17-5.32	m	a+b	-	-
5.82-5.96	m	c	-	-

^{13}C -NMR(d_6 -acetone+ CDCl_3)



Chemical Shift (δ , ppm)	Carbon type	Position of carbon
45.9	CH_2	6
70.1	CH	5
70.7	CH_2	3
72.2	CH_2	4
117.1	CH_2	1
134.2	CH	2

3.2.2 Preparation of 6,7-Epoxy-4-oxa-1-heptene (7)



A solution of 7-chloro-6-hydroxy-4-oxa-1-heptene (**6**, the crude product obtained from experiment 3.2.1) (30.48g) in 700 ml of water and 100 ml of methanol was cooled at 0°C then sodium hydroxide (8.27g, 0.2067mole) was added. The reaction mixture was stirred at 0°C for 6 hours. The reaction was monitored by TLC (20% ethyl acetate in hexane as eluent), then the TLC plates were put in iodine chamber. When the spot of **6** disappeared, the reaction was stopped and the crude reaction mixture was extracted with dichloromethane. The organic layer was washed with water, then dried (MgSO₄) and concentrated to obtain the crude product (18.69 g) as colourless liquid.

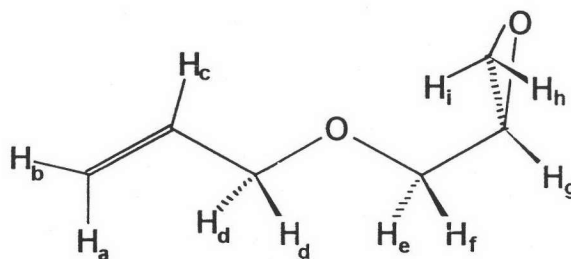
The experiment was repeated with different ratio of water and methanol as shown in Table 4.2. The best yield was obtained when the ratio of water to methanol is 1:3. A portion of the crude reaction mixture was purified using silica gel column chromatography (10% ethyl acetate in hexane as eluent) to obtain the spectroscopic data of **7** as shown in page 40 and 41.

Spectroscopic data of 7

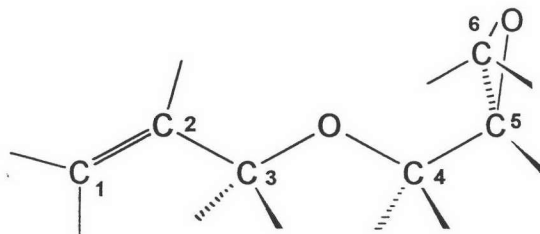
IR ν_{\max} (neat)

Wave number (cm^{-1})	Bond type
3080, 3060	=C-H stretching
2923, 2857	C-H stretching
1648	C=C stretching
1254	C-O-C symmetric stretching
1098	C-O stretching
924	C-O-C asymmetric stretching

$^1\text{H-NMR}$ (CDCl_3)

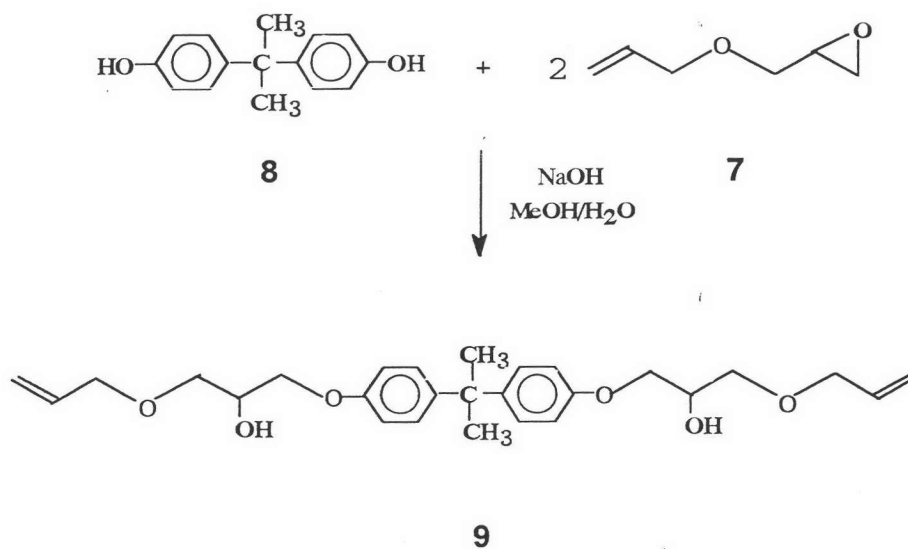


Chemical Shift (δ , ppm)	Multiplicity	position of proton	Number of proton	Coupling constant (Hz)
2.61	dd	h	1	2.7, 5.0
2.79	dd	i	1	4.2, 5.0
3.15-3.18	m	g	1	-
3.40	dd	f	1	5.8, 11.6
3.72	dd	e	1	3.1, 11.6
4.01-4.06	m	d	2	-
5.16-5.32	m	a+b	2	-
5.84	ddt	c	1	4.9, 10.4, 15.5

^{13}C -NMR (CDCl_3)

Chemical Shift (δ , ppm)	Carbon type	Position of carbon
44.1	CH ₂	6
50.6	CH	5
70.6	CH ₂	3
72.1	CH ₂	4
117.1	CH ₂	1
134.3	CH	2

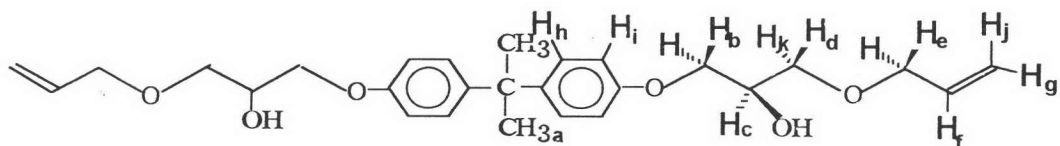
3.2.3 Preparation of 4,4'-Isopropylidenedi(2-hydroxy-4-oxa-6-heptene)phenyl ether (**9**)



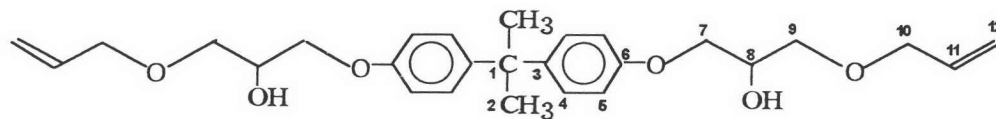
4,4'-Isopropylidenediphenol (bisphenol A, **8**) (0.5471g, 2.40 mmol) was introduced into a solution of sodium hydroxide (0.1906g, 4.76 mmole) in 20 ml methanol and 80 ml of water at 0°C, followed by addition of **7**, the crude product from experiment 3.2.2 (3.08 g). The reaction mixture was heated to reflux for 20 hours. The reaction was monitored by TLC (33% ethyl acetate in hexane as eluent), then the TLC plates were put in iodine chamber. When the spot of **8** disappeared, the reaction was stopped. After cooled to room temperature the mixture were extracted with dichloromethane. The dichloromethane layer was washed with water. Then dried (MgSO₄), and concentrated to obtain the crude product which was chromatographed on a silica gel column using 23% ethyl acetate in hexane as eluent to obtain 4,4'-isopropylidenedi(2-hydroxy-4-oxa-6-heptene)phenoxide **9** (0.7008 g, 64% yield based on **8** and 39.7% overall yield based on **4** from experimental 3.2.1) as colourless liquid.

Spectroscopic data of 9IR ν_{\max} (neat)

Wave number (cm^{-1})	Bond type
3413	O-H stretching
3077, 3037	C-H stretching, aromatic
2967, 2930	C-H stretching, aliphatic
1646	C=C stretching
1609	C=C stretching, aromatic
1582	C=C stretching, aromatic
1462	C=C stretching, aromatic
1250	C-O-C asym. stretching
1041	C-O-C sym. stretching
831	1,4 disubstituted aromatic

$^1\text{H-NMR}$ (CDCl_3)

Chemical Shift (δ , ppm)	Multiplicity	Position of proton	Number of proton	Coupling constant (Hz)
1.63	s	a	3	-
3.57	dd	d	1	5.7, 9.6
3.64	dd	k	1	4.4, 9.6
3.99-4.06	m	b+e	4	-
4.12-4.21	m	c	1	-
5.17-5.35	m	g+j	2	-
5.81-5.98	m	f	1	-
6.82	d	i	2	8.7
7.13	d	h	2	8.7

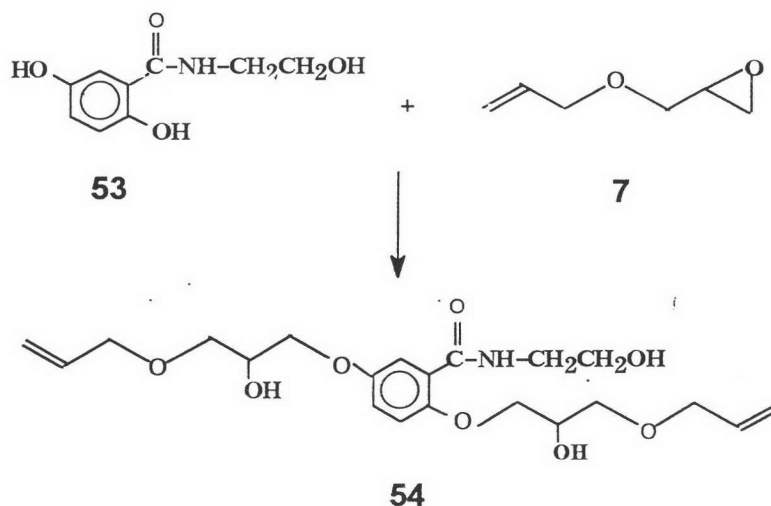
^{13}C -NMR (CDCl_3)

Chemical Shift (δ , ppm)	carbon type	Position of carbon
31.0	CH_3	2
40.1	C	1
68.9	CH_2	10
69.1	CH	8
71.0	CH_2	7
72.3	CH_2	9
113.9	CH	5
117.3	CH_2	12
127.7	CH	4
134.3	CH	11
143.5	C	3
156.4	C	6

Mass Spectrum

m/e	% relative intensity
456 [M ⁺]	51
441	100
327	29
213	46
135	35
41	34

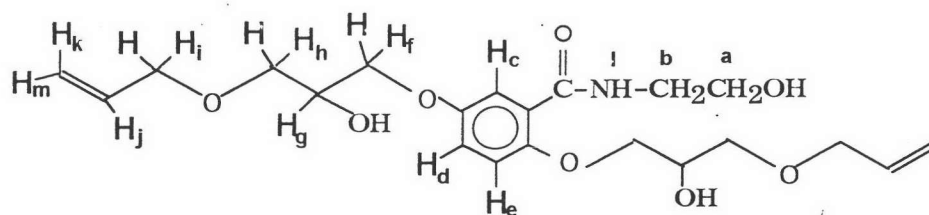
3.2.4 Preparation of 2,5-Di(2-hydroxy-4-oxa-6-hepteoxy)-N-(2-hydroxyethyl)benzamide (**54**)



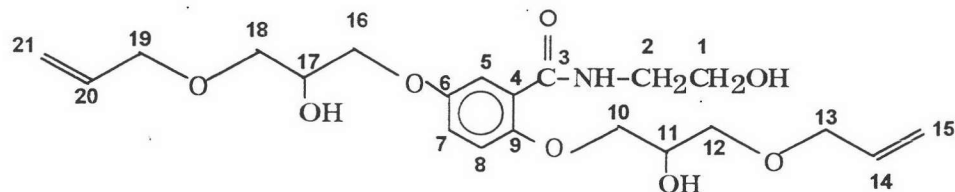
Employing the procedure described in the experiment 3.2.3 using **7**, the crude product from experiment 3.2.2 (2.8320 g) and 2,5-dihydroxy-N-(2-hydroxyethyl)benzamide **53** (0.6375 g 3.2329 mmole) as starting material. The reaction mixture was heated to reflux for 10 hours. The reaction mixture was heated to reflux for 20 hours. The reaction was monitored by TLC (10% methanol in dichloromethane as eluent), then the TLC plates were put in iodine chamber. When the spot of **53** disappear, the reaction was stopped. After cooled to room temperature the mixture were extracted with dichloromethane. The dichloromethane layer was washed with water, then dried (MgSO_4), and concentrate to obtain the crude product which was chromatographic separation on a silica gel column (1-10% methanol in dichloromethane as eluent) to afford 2,5-Di(2-hydroxy-4-oxa-6-hepteoxy)-N-(2-hydroxyethyl) benzamide **54** (0.5936 g, 43.20% yield based on **53**, and 26.8% overall yield based on **4** from experiment 3.2.1) as yellow liquid.

Spectroscopic data of 54IR ν_{\max} (neat)

Wave number (cm^{-1})	Bond type
3383	O-H stretching
3101	C-H stretching, aromatic
2900	C-H stretching, aliphatic
1724	C=O stretching
1644	C=C stretching
1455	C=C stretching, aromatic
1275	C-N asymmetric stretching
1195	C-O-C symmetric stretching
1095	C-O-C symmetric stretching
812	1,2,4-trisubstitution

$^1\text{H-NMR}$ (CDCl_3)

Chemical Shift (δ , ppm)	Multiplicity	Position of proton	Number of proton	Coupling constant (Hz)
3.59	m	b+h	6	-
3.79	t	a	2	4.6
4.02-4.05	m	i+f	8	-
4.15-4.20	m	g	2	-
5.16-5.32	m	k+m	4	-
5.82-5.90	m	j	2	-
6.86	d	e	1	8.9
6.98	dd	d	1	3.1, 8.9
7.68	d	c	1	3.1
8.60-8.68	m	l	1	-

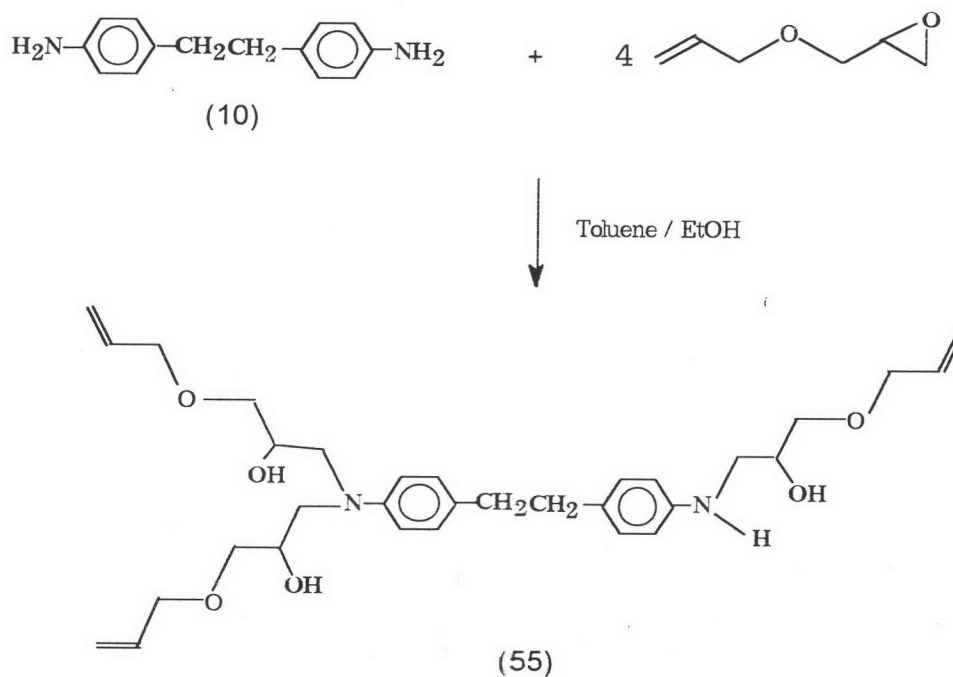
^{13}C -NMR (CDCl_3)

Chemical Shift (δ , ppm)	Carbon type	Position of carbon
42.4	CH_2	2
61.6	CH_2	1
68.8, 69.0	CH	11, 17
69.8, 70.8	CH_2	13, 19
70.9, 71.6	CH_2	10, 16
72.3, 72.4	CH_2	12, 18
114.4	CH	5
116.5	CH	8
117.4, 117.6	CH_2	15, 21
119.5	CH	7
122.4	C	4
134.1, 134.3	CH	14, 20
151.2	C	9
153.0	C	6
165.6	C	3

Mass Spectrum

m/e	% Relative intensity
425 [M ⁺]	15
354	82
293	54
179	43
136	58
115	31
62	44
57	30
41	100
32	77

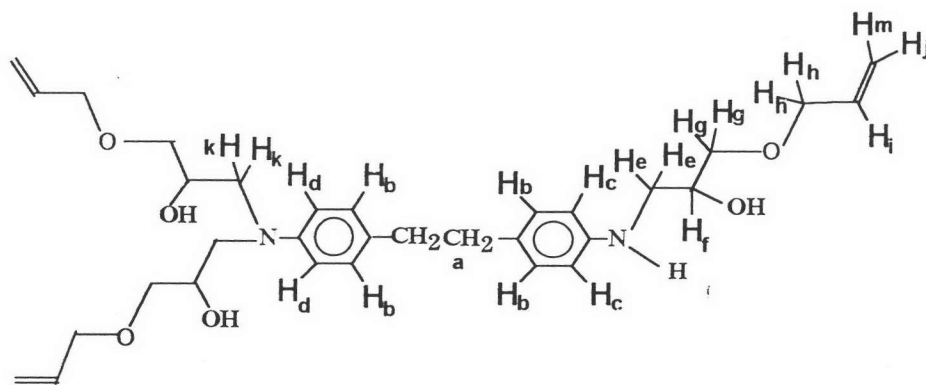
3.2.5) Preparation of N,N,N'-Tris(-2-hydroxy-4-oxa-6-heptenyl)ethylenedianiline (**55**)



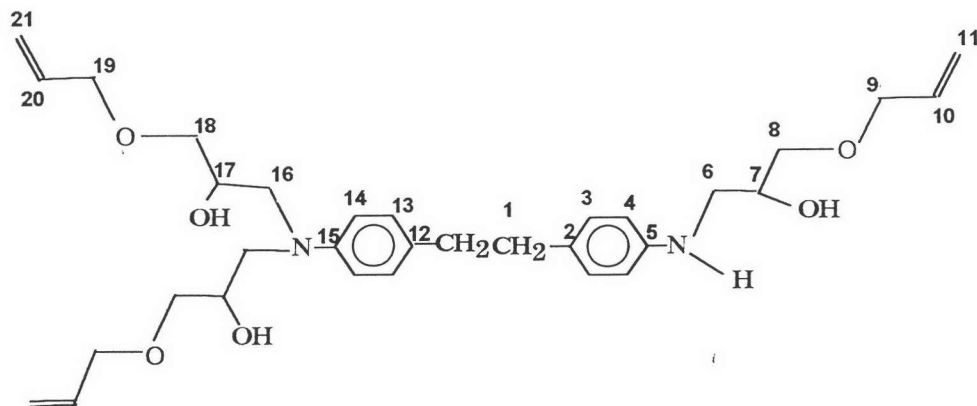
The crude product from experiment 3.2.2, **7** (4.0133g) was introduced into a mixture of 4,4'-ethylenedianiline (**10**) (0.5735 g, 2.70 mmole) in a mixture of ethanol (1.0 ml) and toluene (1.0 ml) at room temperature. The reaction mixture was left stirring at 100 °C for 24 hours. The reaction was monitored by TLC (10% methanol in dichloromethane as eluent), then the TLC plates were put in iodine chamber. When the spot of **10** disappeared, the reaction was stopped. After cooled to room temperature the mixture were evaporated and concentrated to obtain a crude material which was chromatographed on a silica gel column 1-10% methanol in dichloromethane as eluent to obtain N,N,N',-tris(2-hydroxy-4-oxa-6-heptenyl)ethylenedianiline (1.0130 g, 70.65 % overall yield based on **10**, and 43.8% yield based on **4** from experiment 3.2.1) as dark-brown liquid.

Spectroscopic data of 55IR ν_{\max} (neat)

Absorption (cm^{-1})	Bond Type
3420	O-H stretching
3358	N-H stretching
3012	C-H stretching, aromatic
2920	C-H stretching, aliphatic
1648	C=C stretching
1615	C=C stretching, aromatic
1519	C=C stretching, aromatic
1454	C=C stretching, aromatic
1356	C-N stretching
1222	C-O-C asymmetric stretching
1101	C-O-C symmetric stretching
818	<i>p</i> -substituted aromatic

$^1\text{H-NMR}$ (CHCl_3)

Chemical Shift (δ , ppm)	Multiplicity	Position of protons	number of proton	coupling constant (Hz)
2.76	s	a	4	-
3.06-3.18	m	e	2	-
3.38-3.52	m	k+g	10	-
4.00	m	h+f	9	-
5.17-5.33	m	j+m	6	-
5.84-5.98	m	i	3	-
6.62	d	c	2	8.0
6.75	d	b	2	8.1
7.05	d	d	4	6.5

^{13}C -NMR (CHCl_3)

Chemical shift (δ , ppm)	Carbon type	Position of carbon
37.1	CH_2	1
55.6	CH_2	6
57.7	CH_2	16
68.4, 68.7	CH_2	7, 17
72.0, 72.1	CH	9, 19
72.2, 72.3	CH_2	8, 18
112.3	CH	14
113.7	CH	4
117.1, 117.2	CH_2	11, 21
129.0	CH	13
129.1	CH	3
130.2	C	12
130.9	C	2
134.4, 134.5	CH	10, 20
146.0	C	5
147.0	C	15