Chapter 6

Polymerization and Model Studies of Polyaminonitriles Containing Ether Linkages

6.1 Introduction

As discussed in Chapter 1, poly(arylene ether ketone)s are an important class of high performance engineering thermoplastics which have excellent thermal, mechanical properties and chemical resistivity.[1] However, they are difficult to synthesize. In order to circumvent the solubility problem, high molecular weight, soluble polyaminonitriles (**4.2, 4.4a-b, 4.7a-c**) were successfully synthesized from bis(α–aminonitrile)s **4.1a-b** and activated aromatic dihalides using NaH as base. Hydrolysis of these polyaminonitriles in 70% aqueous acetic acid and HCl produced an entirely new class of polyketones containing no ether linkages and also with alkyl substituents in the polymeric backbone.[2,3] To further explore the scope and limitations of this polymerization, known aromatic polyketones containing ether linkages such as PEKKK[4] can be prepared by this aminonitrile approach and then compared with those made by the conventional nucleophilic and electrophilic approaches. In this chapter, the synthesis and polymerization of bis(α-aminonitrile)s containing ether linkages and model studies will be discussed.

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[1] Staniland, P. A. Poly(ether ketone)s. In *Comprehensive Polymer Science*; Allen, G.; Bevington, J. C., Eds.; Pergamon Press: New York, **1989**; Vol. 5, pp. 484-497.
[2] Pandya, A.; Yang, J.; Gibson, H. W. *Macromolecules* **1994**, 27, 1367.
[3] Yang, J.; Gibson, H. W. *Macromolecules* **1997**, 30, 5629.

6.2 Results and Discussion

6.2.1 Synthesis of Bis(α-aminonitrile)s Containing Ether Linkages

Dialdehyde **6.1a** was synthesized in 99% yield using 10 mol% excess 4-fluorobenzaldehyde, 4,4'-biphenol and K_2CO_3 in toluene and DMAc (Scheme 6.1).[5] Toluene was used as an azeotropic agent to remove the water produced. The ^{1}H NMR spectrum of compound **6.1a** showed an aldehyde proton at 9.94 ppm (Figure 6.1). The COSY spectrum showed two pairs of doublets coupled to each other. The IR spectrum showed strong carbonyl stretches of the aldehyde at 1694 cm^{-1} and C-O-C stretches at 1263 cm^{-1}. Bis(α-aminonitrile) **6.2a** was synthesized using excess of trimethylsilyl cyanide (TMSCN) and morphorline in refluxing methylene chloride (Scheme 6.1).[6] Purification was done by washing with hexane and then hot ethanol to give a light pink solid in 76 % yield. Further purification of this monomer was done by dissolving it in methylene chloride and passage through a short silica gel column, and then recrystallization from EtOAc and CH_2Cl_2 twice to give white crystals (51%). The ^{1}H NMR spectrum of **6.2a** showed three signals in the aliphatic region corresponding to the aminonitrile units and four pairs of doublets in the aromatic region (Figure 6.2). The ^{13}C NMR spectrum also agrees well with the expected structure (Figure 6.3). The FTIR spectrum of **6.2a** showed aliphatic C-H stretches at about 2900 cm^{-1}, nitrile absorbance at 2220 cm^{-1} and C-O-C stretch at 1163 cm^{-1}.

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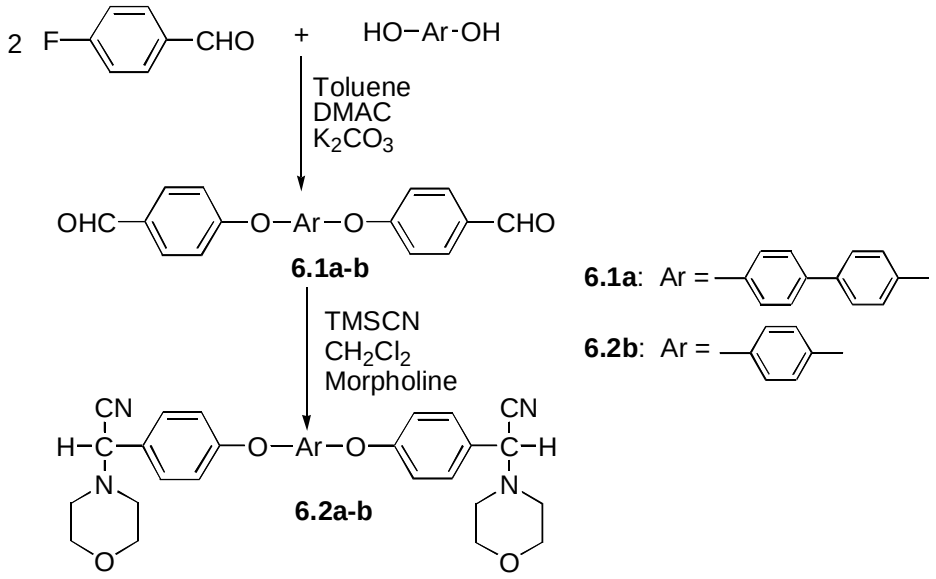
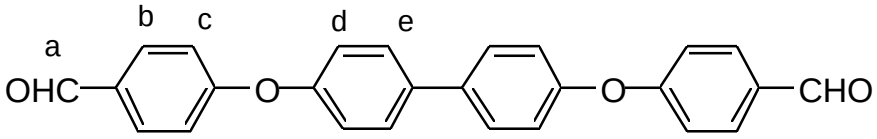
[4] Goodman, I.; McIntyre J. E.; Russell, W. Brit. Patent 971, 227 (**1964**); *Chem. Abstr*. **1964**, 61, 14805b.
[5] Yeager, W. G; Schissel, N. D. *Synthesis* **1991**, 63
[6] Leblanc, J.-P.; Gibson, H. W. *Tetrahedron Lett.* **1992**, 33, 6295.

Scheme 6.1


2 F CHO + HO–Ar-OH
Toluene
DMAC
K_2CO_3
OHC O–Ar–O CHO
6.1a-b
TMSCN
CH_2Cl_2
Morpholine
CN
H–C
N
O
6.2a-b
6.1a: Ar =
6.2b: Ar =



6.1a

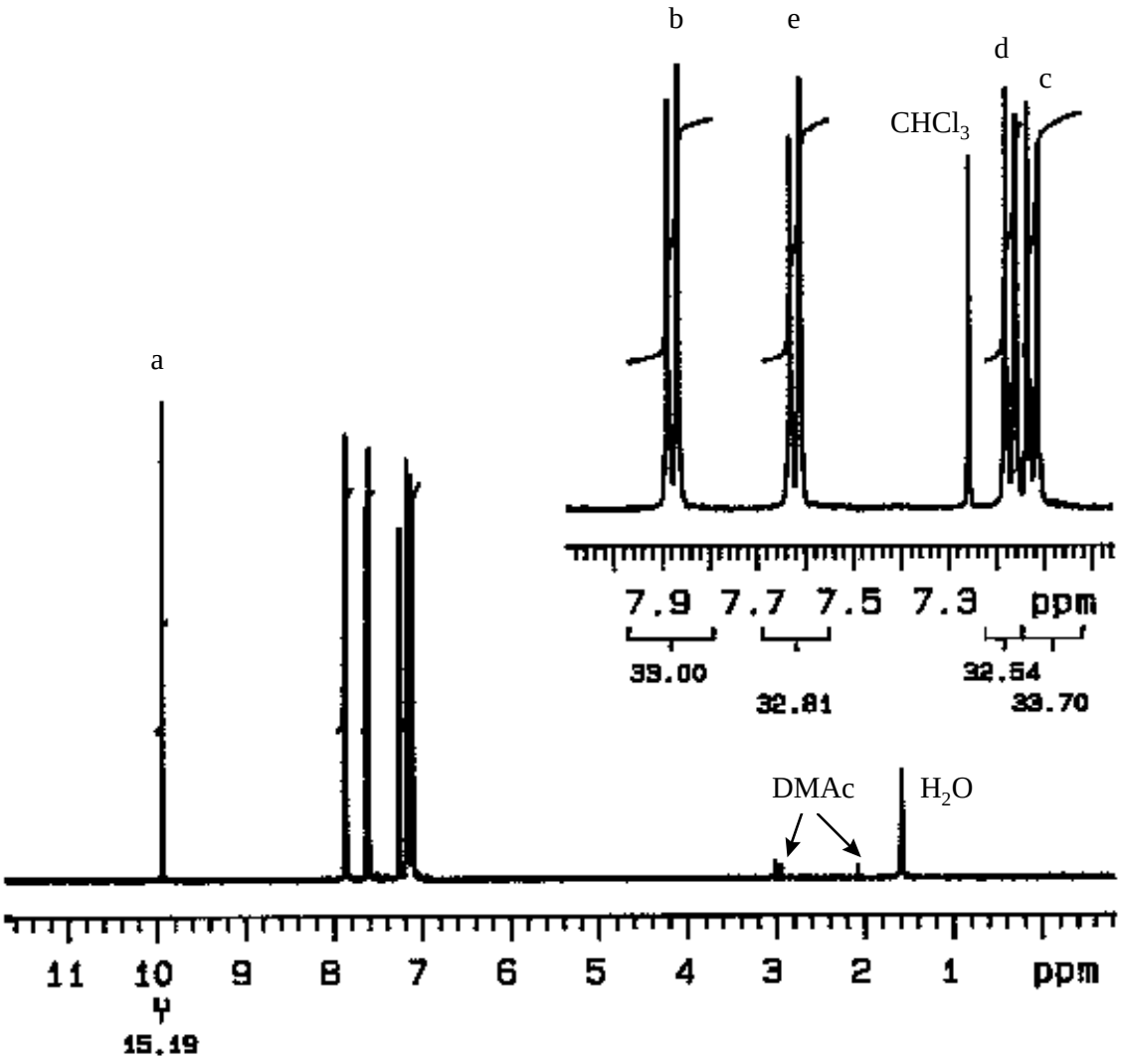


Figure 6.1 400 MHz ^{1}H NMR spectrum of **6.1a** in $CDCl_3$.

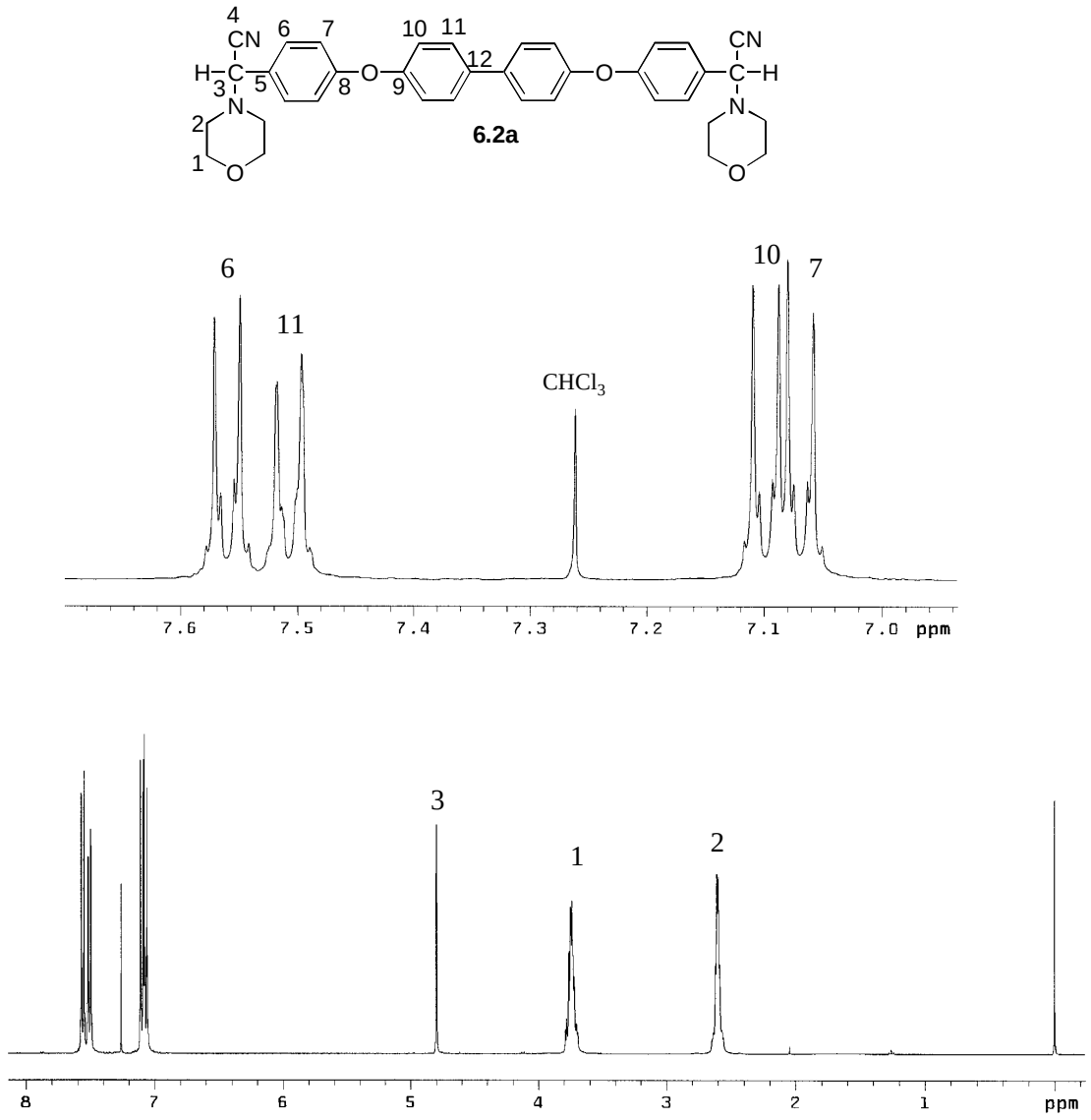


Figure 6.2 400 MHz ^{1}H NMR spectrum of **6.2a** in $CDCl_3$.

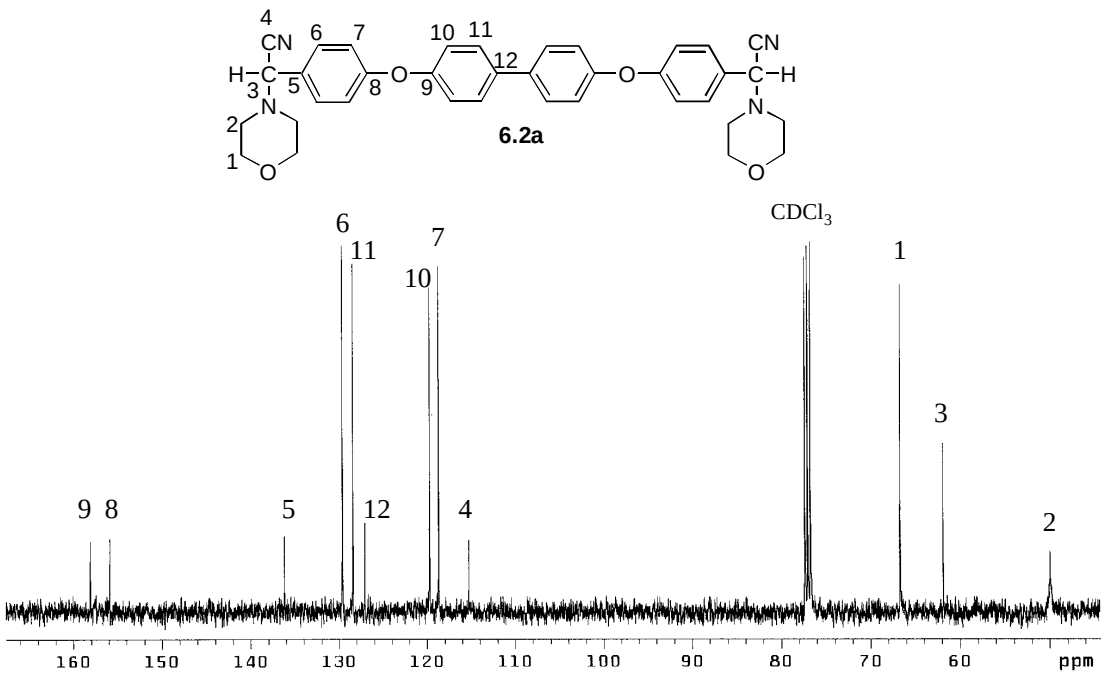


Figure 6.3 100 MHz ^{13}C NMR spectrum of **6.2a** in $CDCl_3$.

Dialdehyde **6.1b** was also synthesized from 4-fluorobenzaldehyde and hydroquinone in 96% yield (Scheme 6.1).[5] The ^{1}H NMR spectrum of **6.1b** showed an upfield aldehyde signal at 9.93 ppm, a singlet at 7.25 ppm and a pair of doublets at 7.17 and 7.93 ppm (Figure 6.4). The FTIR spectrum showed the carbonyl stretches of aldehyde at 1694 cm^{-1} and C-O-C stretches at 1230 cm^{-1}. The corresponding bis(α-aminonitrile) **6.2b** was synthesized using TMSCN and morpholine in 85% yield (Scheme 6.1).[5] The ^{1}H NMR and FTIR spectra of this product agree well with the structure shown.

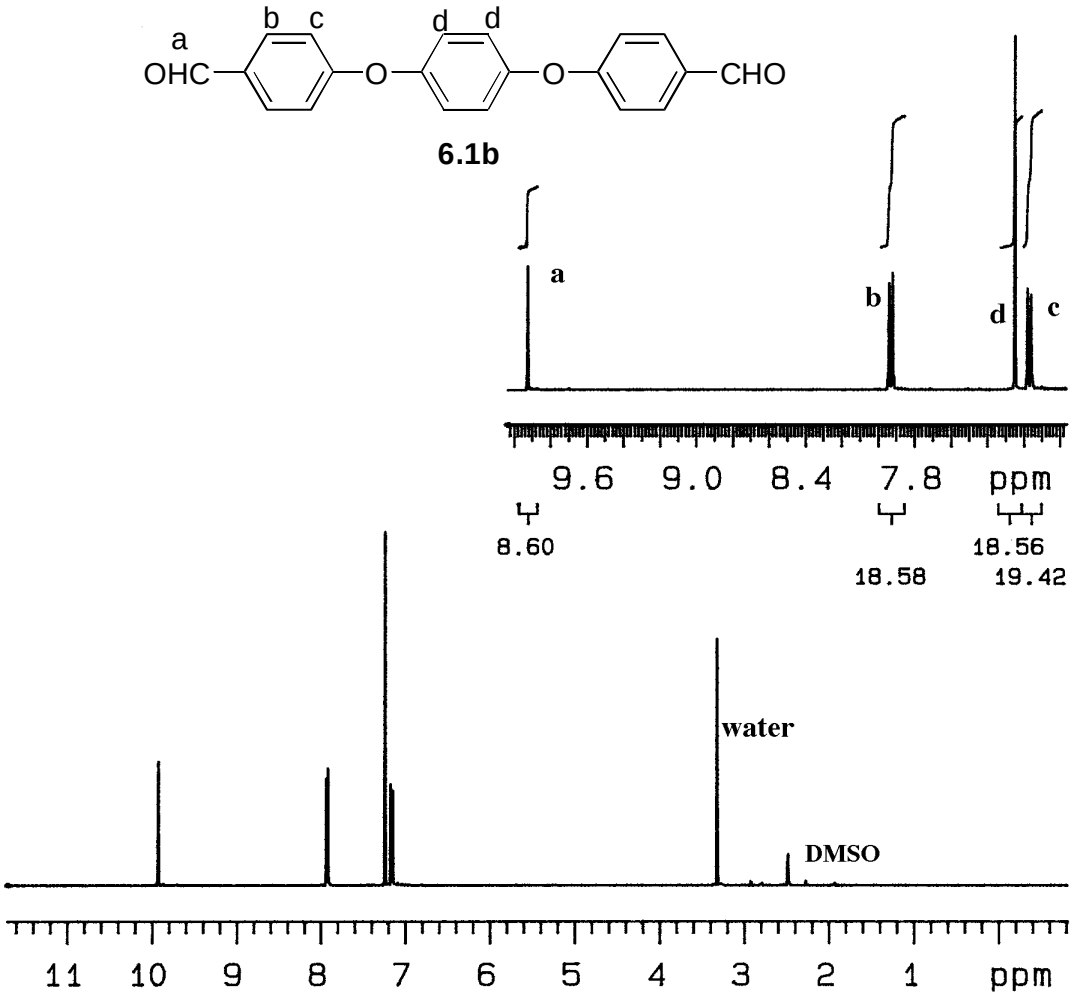
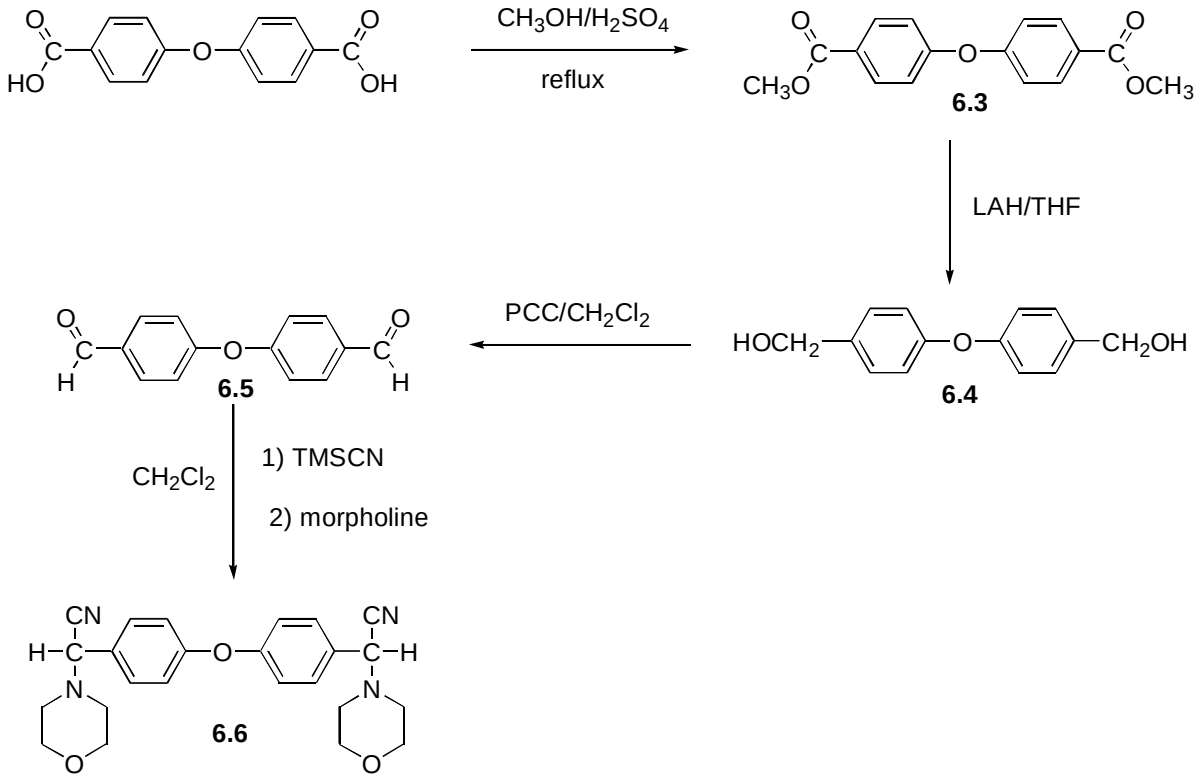


Figure 6.4 400 MHz ^{1}H NMR spectrum of **6.1b** in DMSO-d_6.

Bisaminonitrile **6.6** was synthesized from 4,4'-oxy-bis(benzoic acid) by a four-step synthesis procedure (Scheme 6.2). 4,4'-Oxy-bis(benzoic acid) was converted to the corresponding dimethyl ester **6.3** in 95% yield. Reduction of **6.3** with lithium aluminum hydride (LAH) gave 4,4'-oxy-bis(benzyl alcohol) (**6.4**) in 83% yield. Oxidation of **6.4** with pyridinium chlorochromate (PCC) yielded the corresponding dialdehyde **5.5** in 87% yield. Bis(α-aminonitrile) **6.6** was synthesized in 97% yield by reaction of **6.5** with TMSCN and

morpholine.[5] The monomer was further purified by recrystallization form ethanol three times. The structure of this monomer was further confirmed by ^{1}H and ^{13}C NMR spectra (Figure 6.5 and Figure 6.6) and the FTIR spectrum.

Scheme 6.2



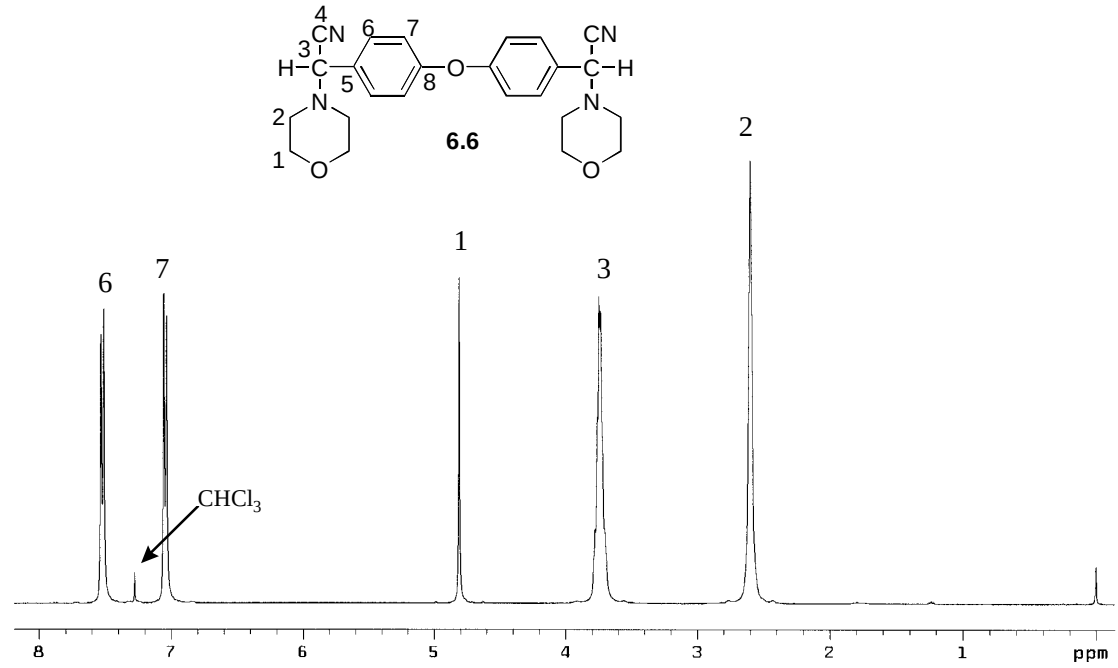


Figure 6.5 400 MHz ^{1}H NMR spectrum of **6.6** in $CDCl_3$.

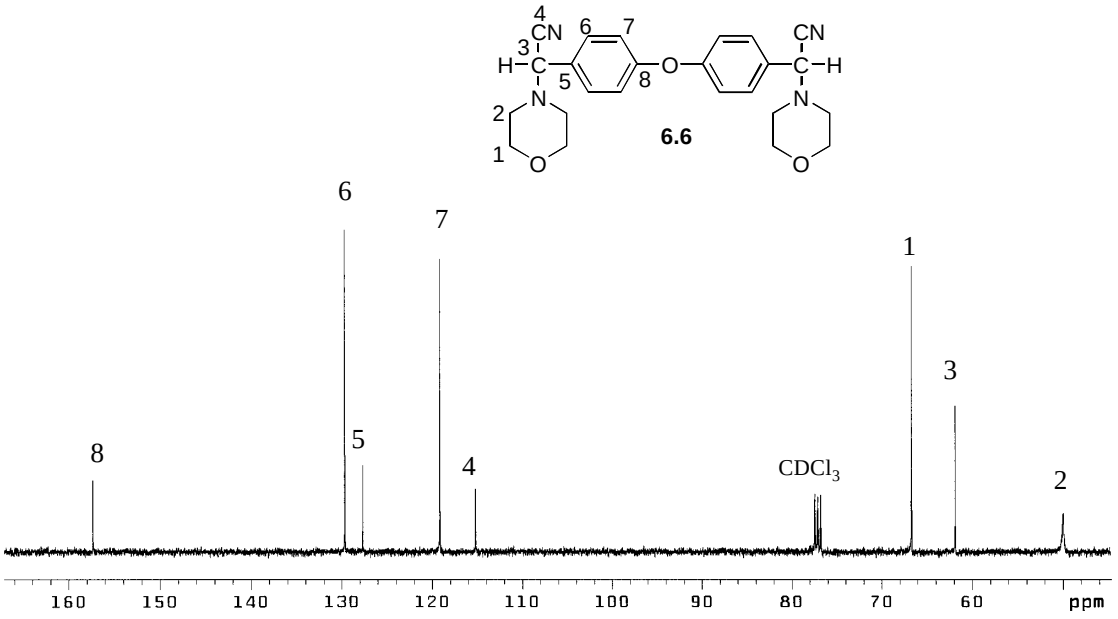
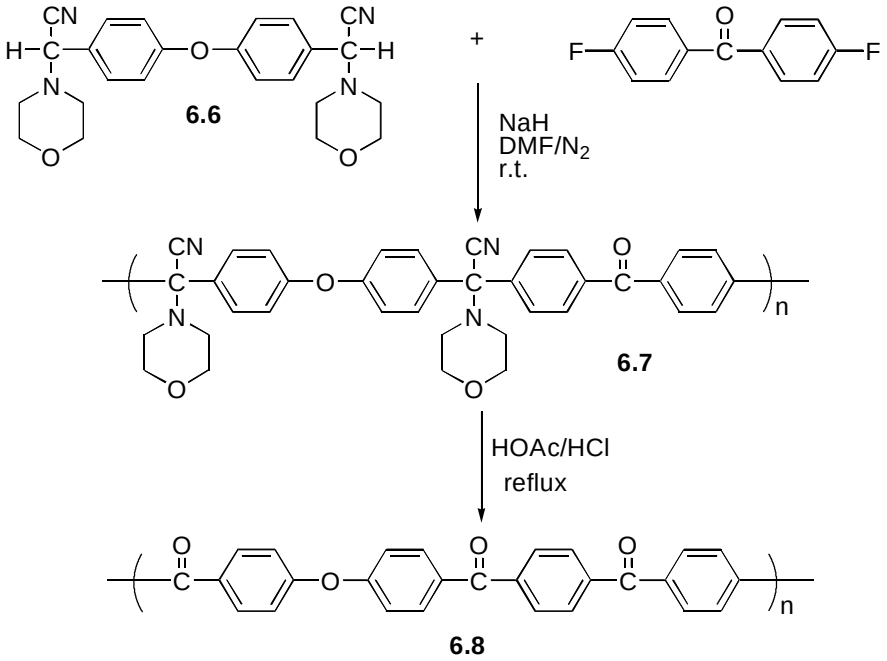


Figure 6.6 100 MHz ^{13}C NMR spectrum of **6.6** in $CDCl_3$.

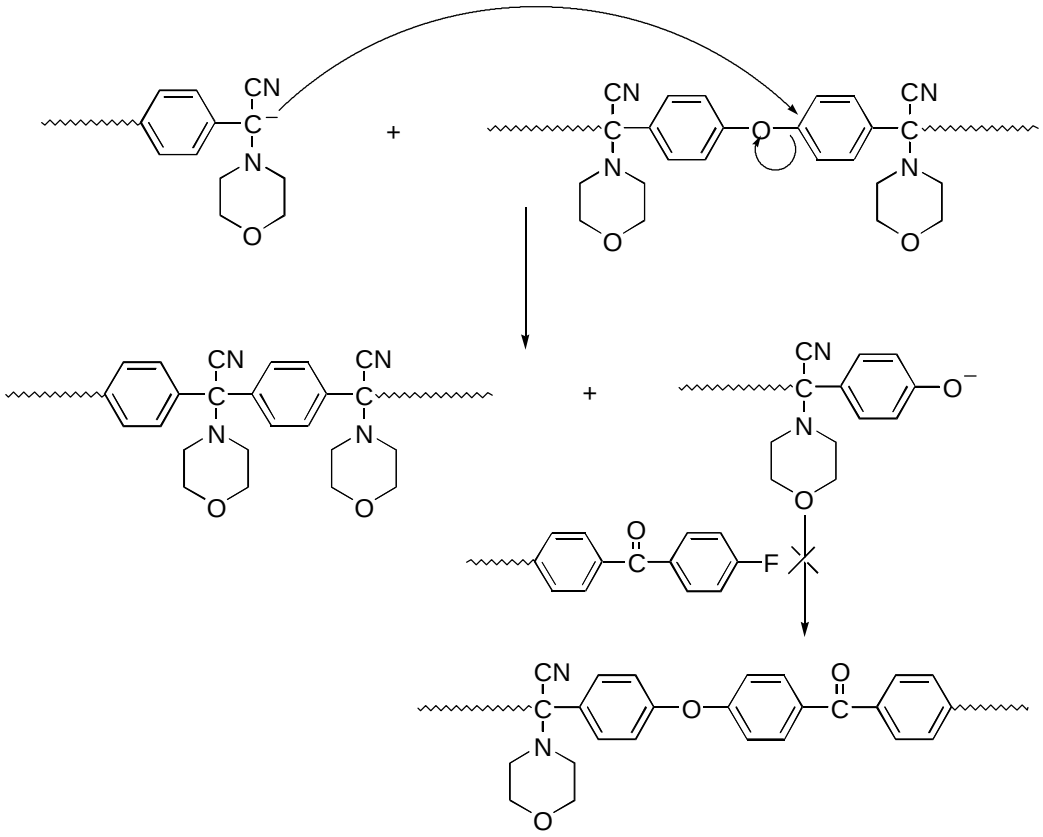
6.2.2 Synthesis of Polyaminonitriles Containing Ether Linkages

To prepare the known aromatic poly(ether ketone) PEKKK, bis(α-aminonitrile) **6.6** was polymerized with 4,4'-difluorobenzophone in DMF at room temperature using NaH as base (Scheme 6.3). After 24 hours reaction time, the color of the solution was still dark brown. However, according to the ^{1}H NMR spectrum of polymer **6.7**, all methine protons at 4.81 ppm were consumed (Figure 6.7). No significant changes were observed after 48 hours reaction time. The color of the solution remained dark brown after one week. The COSY spectrum (Figure 6.8) of polymer **6.7** in the aromatic region showed two pairs of doublets coupled to each other, which agrees with the structure of polymer **6.7**. Several small doublets coupled with each other were also observed. Significant fluoro end group signals were also detected. The FTIR spectrum agreed with the structure of polymer **6.7**. According to the GPC traces (absolute GPC, NMP, 60 °C, Figure 6.9) of polymer **6.7** at different reaction times, there were no significant changes in molecular weights after 24 hours reaction. The molecular weight data are summarized in Table 6.1. A possible explanation for low molecular weight is that the carbanion of the aminonitrile attacked the ether linkage to form a phenoxide anion, which can not further react with the activated fluoro chain end at room temperature (Scheme 6.4). The dark brown color is possibly due to the color of the phenoxide anion. Polymerization of **6.6** with 4,4'-difluorobenzophenone at 0 °C also gave low molecular weight polymer **6.7 (**M_n = 5.21 kg/mol and M_w = 11.5 kg/mol). The ^{1}H NMR spectrum was about the same as that of polymer **6.7** made at room temperature.

Scheme 6.3



Scheme 6.4



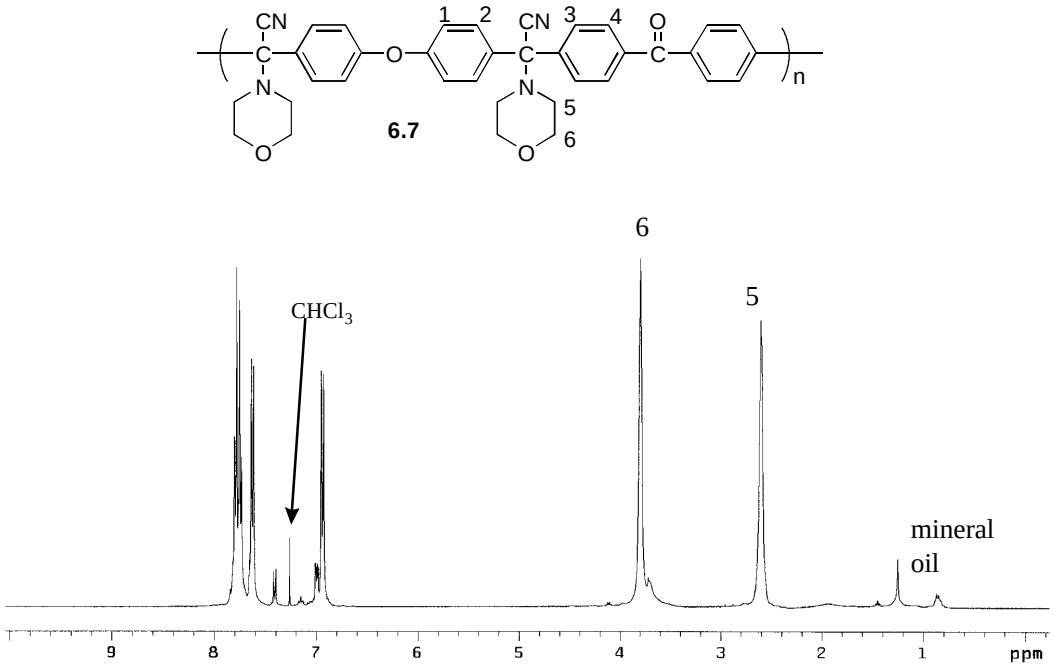


Figure 6.7 400 MHz ^{1}H NMR spectrum of **6.7** in $CDCl_3$.

Table 6.1 GPC data of polyaminonitrile **6.7** (NMP, 60 °C, 1 mL/min)

reaction time (h)	M_n (kg/mol)	M_w (kg/mol)	M_w/M_n
24	5.22	9.10	1.74
48	5.11	7.81	1.53
168	4.96	7.78	1.57

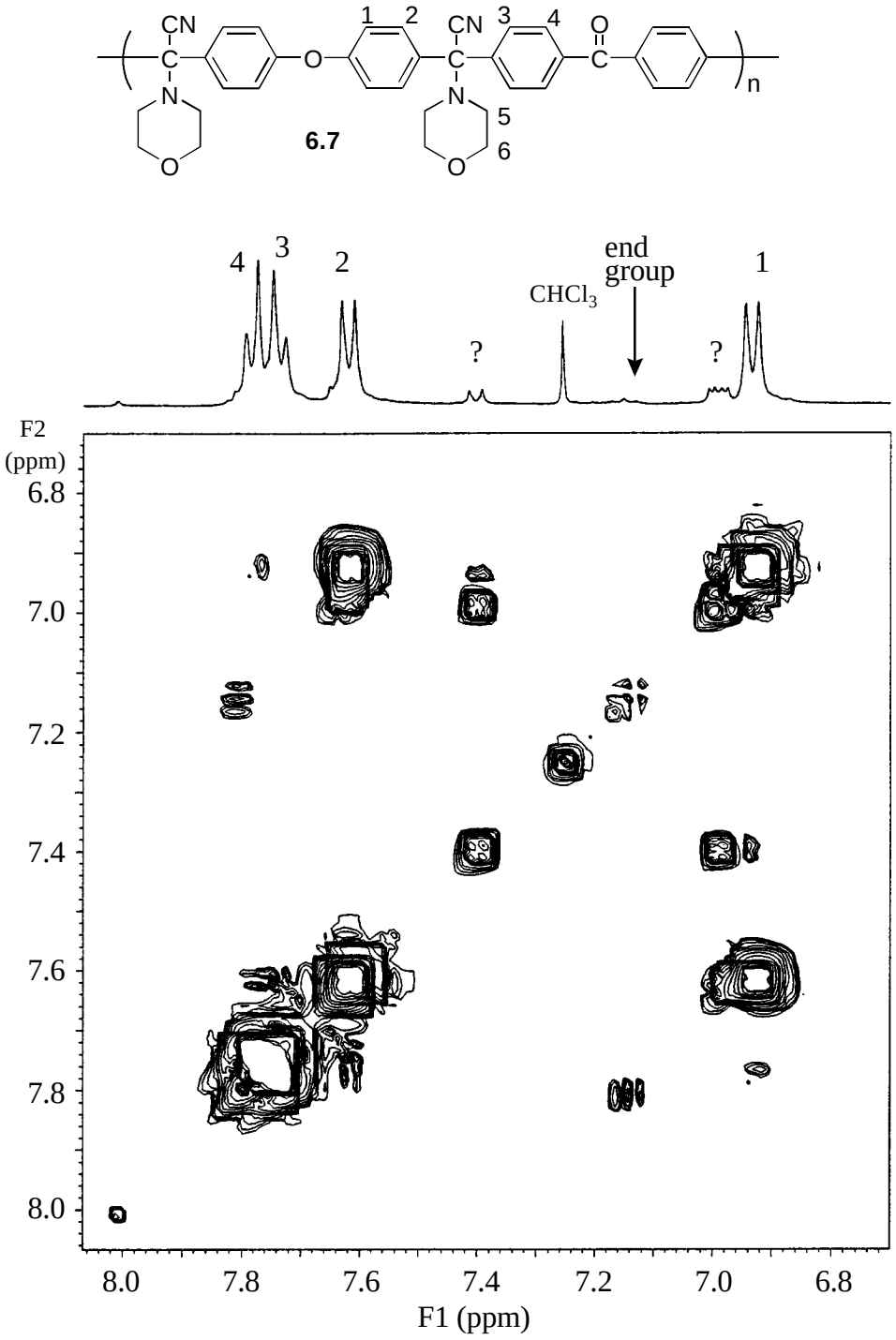


Figure 6.8 400 MHz COSY spectrum of **6.7** in $CDCl_3$ (aromatic region).

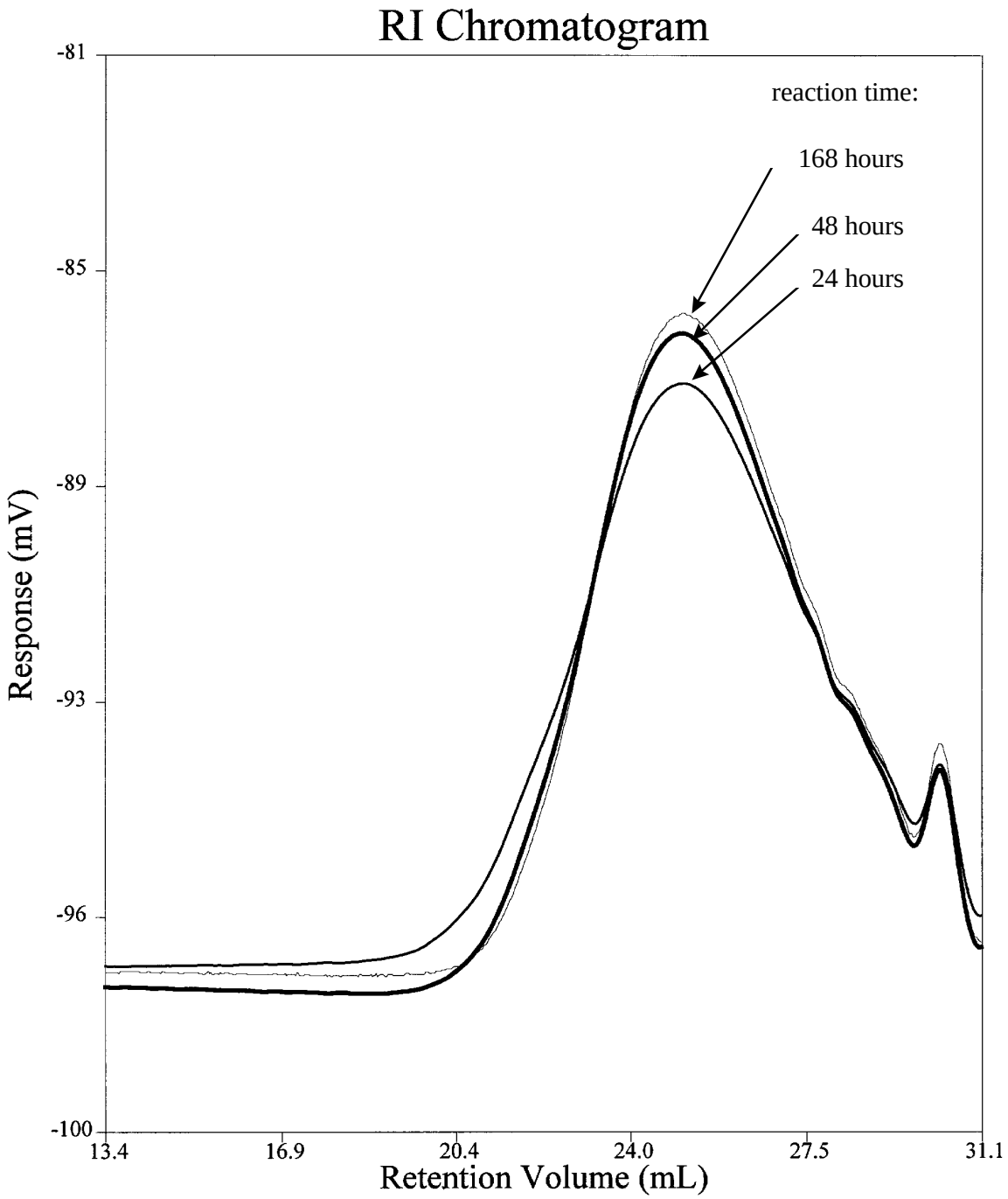
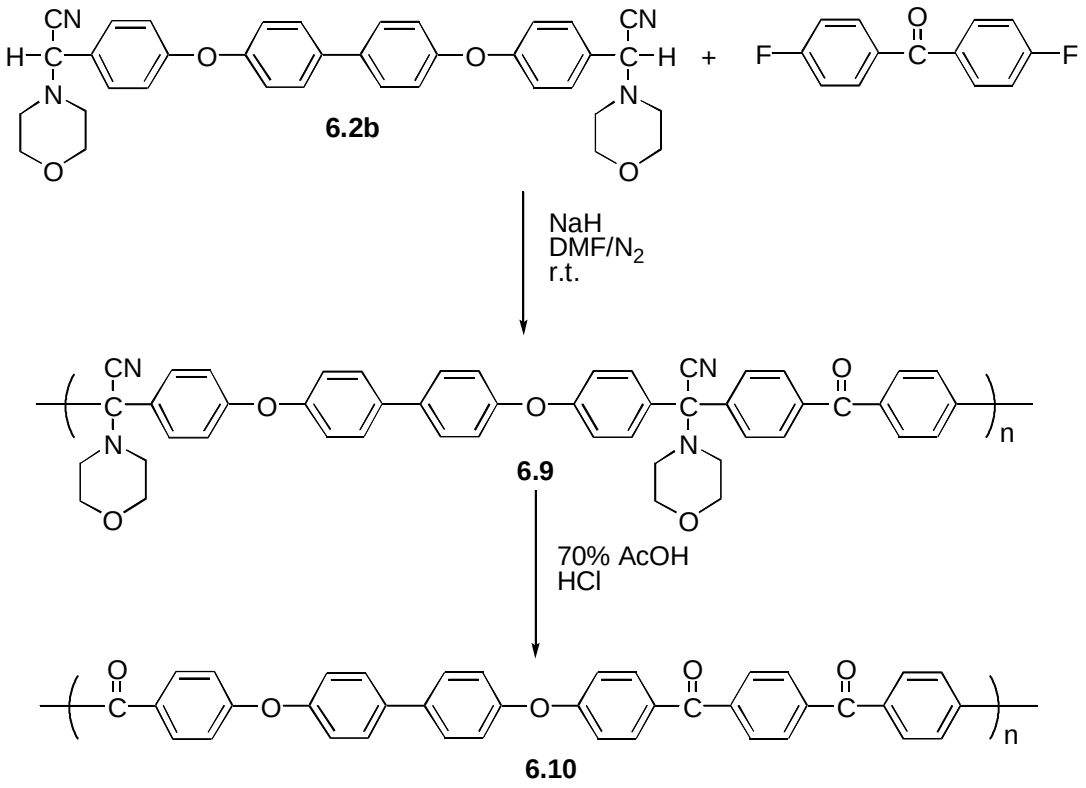


Figure 6.9 GPC traces (RI response) of polymer **6.7** at different reaction times (NMP, 60 °C, 1.0 mL/min).

Bisaminonitrile **6.2a** was also polymerized with 4,4'-difluorobenzophone in DMF at room temperature using NaH as base (Scheme 6.5). After 36 hours reaction, a small portion of solution was withdrawn and precipitated into water and then washed with MeOH. Results similar to those of polymeraminonitrile **6.7** were obtained. The ^{1}H NMR spectrum of polyaminonitrile **6.9** in $CDCl_3$ showed no methine signals of the aminonitrile at 4.79 ppm. However at that time, the color of the solution was still dark brown and the color of the solution was still dark brown after one week.. The COSY spectrum of polyaminonitrile **6.9** in the aromatic region showed three pairs of doublets coupled to each other which agreed with the structure of polymer. It also showed a doublet at 7.42 ppm which is about 20% of one doublet in the polymer backbone according to the integrals (2.88H/13.80H). The FTIR spectrum of polyaminonitrile **6.9** showed the carbonyl stretches at 1656 cm^{-1}, aliphatic C-H stretches at about 2900 cm^{-1}, carbonyl absorbance at 1656 cm^{-1} and C-O-C stretches at 1169 cm^{-1}. GPC analysis (absolute GPC, NMP, 60 °C) indicated an M_n of 5.98 kg/mol and an M_w of 26.9 kg/mol.

Scheme 6.5



6.2.3 Model Studies

All polyaminonitriles containing ether linkages synthesized from bisaminonitriles and activated dihalides are low molecular weight polymers. For both aminonitriles containing ether linkages and activated dihalides containing ether linkages systems, the number average molecular weights are usually less than 10 kg/mol. Significant amount of end-groups can be observed from ^{1}H NMR spectra of these polyaminonitriles. A possible reason for low molecular weight is due to the side reactions. The carbanions of aminonitriles may attack the ether linkages to form more stable phenoxide anions, which can not further react with fluoro chain ends at low temperature. This reaction would cause the termination of the

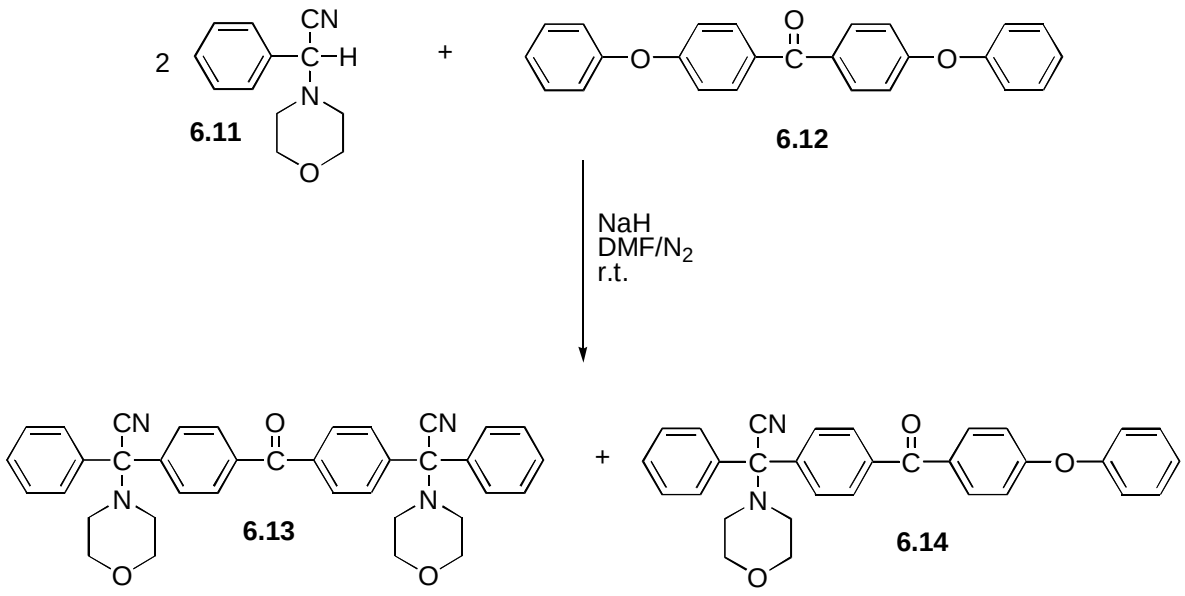
polymerization reaction. To test the stability of ether linkages in the presence of the carbanions of the aminonitriles, several model reactions were performed.

A. The Stability of Activated Ether Linkage in the Present of Carbanions

To address the problem of the stability of activated dihalides containing ether linkages, monofunctional model compounds **6.11** and **6.12** were synthesized. Benzalaminonitrile **6.11** was synthesized from benzaldehyde by Strecker synthesis. Compound **6.12** was synthesized from difluorobenzophenone and phenol in toluene and DMAc. To see whether or not the carbanion of aminonitrile can react with activated ether linkages under standard polymerization conditions, 2 equivalents of aminonitrile **6.11** were mixed with one equivalent of compound **6.12** in DMF at room temperature using 2.2 equivalents of NaH as base (Scheme 6.5). After 24 hours, the solution was precipitated into water and the crude product was isolated. The TLC of this crude product in 3:1/hexane:EtOAc showed four spots. Two of them are the starting materials **6.11** and **6.12**. The other possible products are compounds **6.13** and **6.14**. The ^{1}H NMR spectrum of this crude product showed two different signals for the methylene protons of the aminonitrile adjacent to oxygen. The integrals of the methine protons of the aminonitrile units is about 1/8 of the integrals of methylene protons adjacent to nitrogen (NCH_2), which indicates that about half of the methine protons of aminonitrile were consumed. The crude product was also analyzed by reverse phase HPLC (C_{18}) using a gradient solvent system (100% THF:H_2O/55:45 for first 2 minutes, and then decreased from 100% to 20% in a period of 8 minutes; whereas the other solvent THF increased from 0% to 80%). The elution time for the starting materials **6.11** and **6.12** are 57.6 and 170 seconds.

Besides these two starting materials, the HPLC chromatogram of this crude product shows two other peaks at 143 and 154 seconds (Figure 6.10). To prove that compounds **6.13** and **6.14** were formed, flash column chromatography was performed to isolate the products using hexane/ethyl acetate as eluents. According to the ^{1}H NMR spectra and the melting points, the first two fractions isolated were the starting materials **6.11** and **6.12**. The third fraction isolated was compound **6.14** (12%). The Structure of compound **6.14** was confirmed by ^{1}H NMR (Figure 6.11), ^{13}C NMR (Figure 6.12) and COSY (Figure 6.13) spectra. The fourth fraction isolated was compound **6.13** (15%). The ^{1}H NMR (Figure 6.14) and ^{13}C NMR (figure 6.15) spectra agree well with the structures. This experiment confirmed that under these reaction conditions (the same conditions as the polymerization conditions), the carbanions of the aminonitrile attacked the activated ether linkages to form more stable phenoxide anions, which can not further react with activated halides; this causes the termination of the polymerization.

Scheme 6.5


2
CN
C
H
N
O
6.11
+
O
C
O
O
6.12
NaH
DMF/N2
r.t.
CN
C
N
O
O
C
CN
C
N
O
6.13
+
CN
C
N
O
O
C
O
6.14

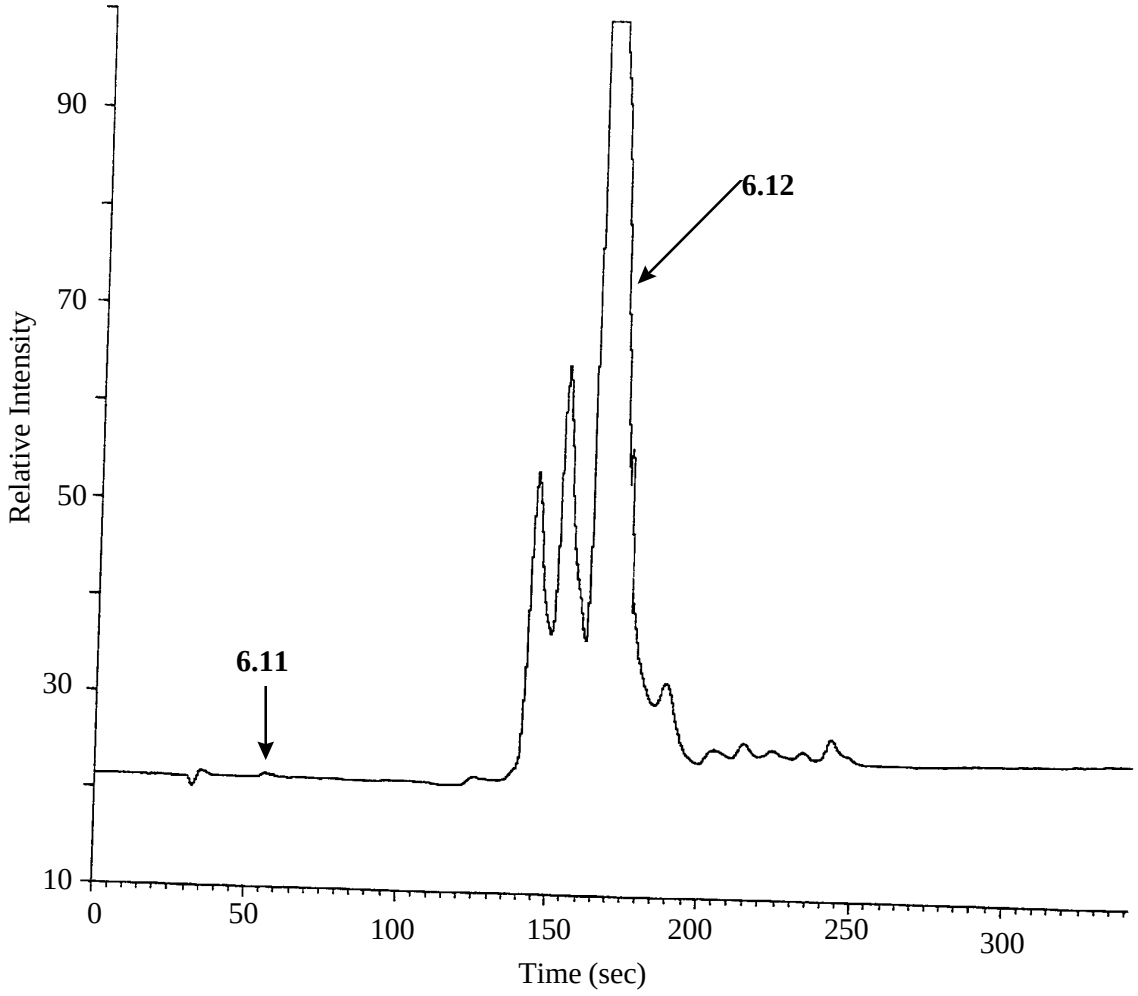


Figure 6.10 Reverse phase HPLC chromatogram of the crude product (C_{18}, THF/water, gradient).

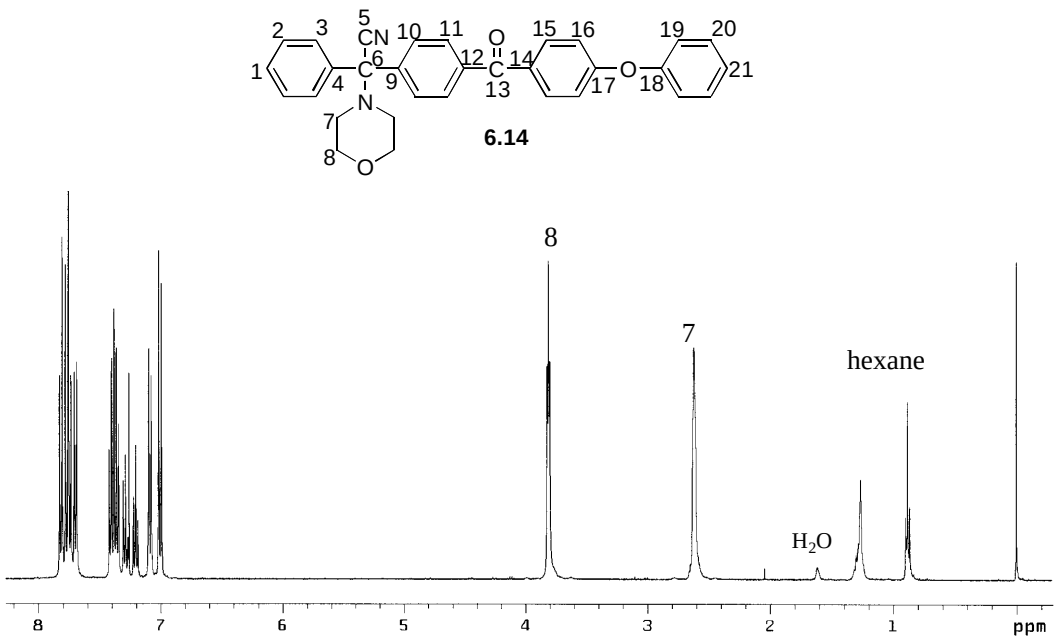


Figure 6.11 400 MHz ^{1}H NMR spectrum of **6.14** in $CDCl_3$.

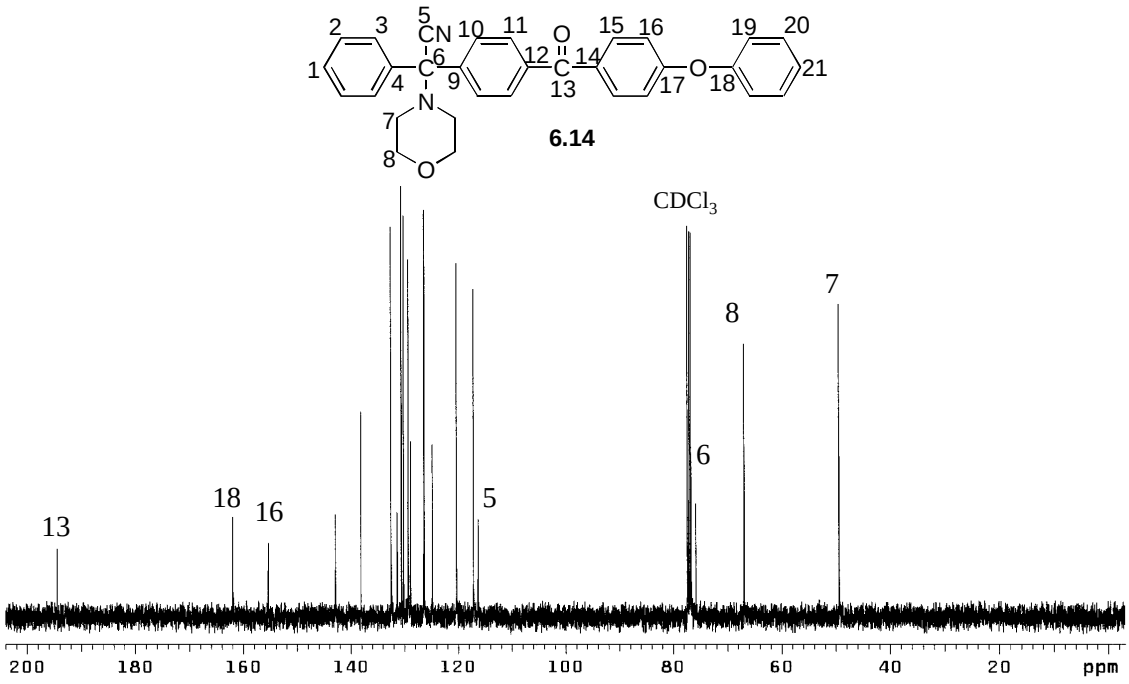


Figure 6.12 100 MHz ^{13}C NMR spectrum of **6.14** in $CDCl_3$.

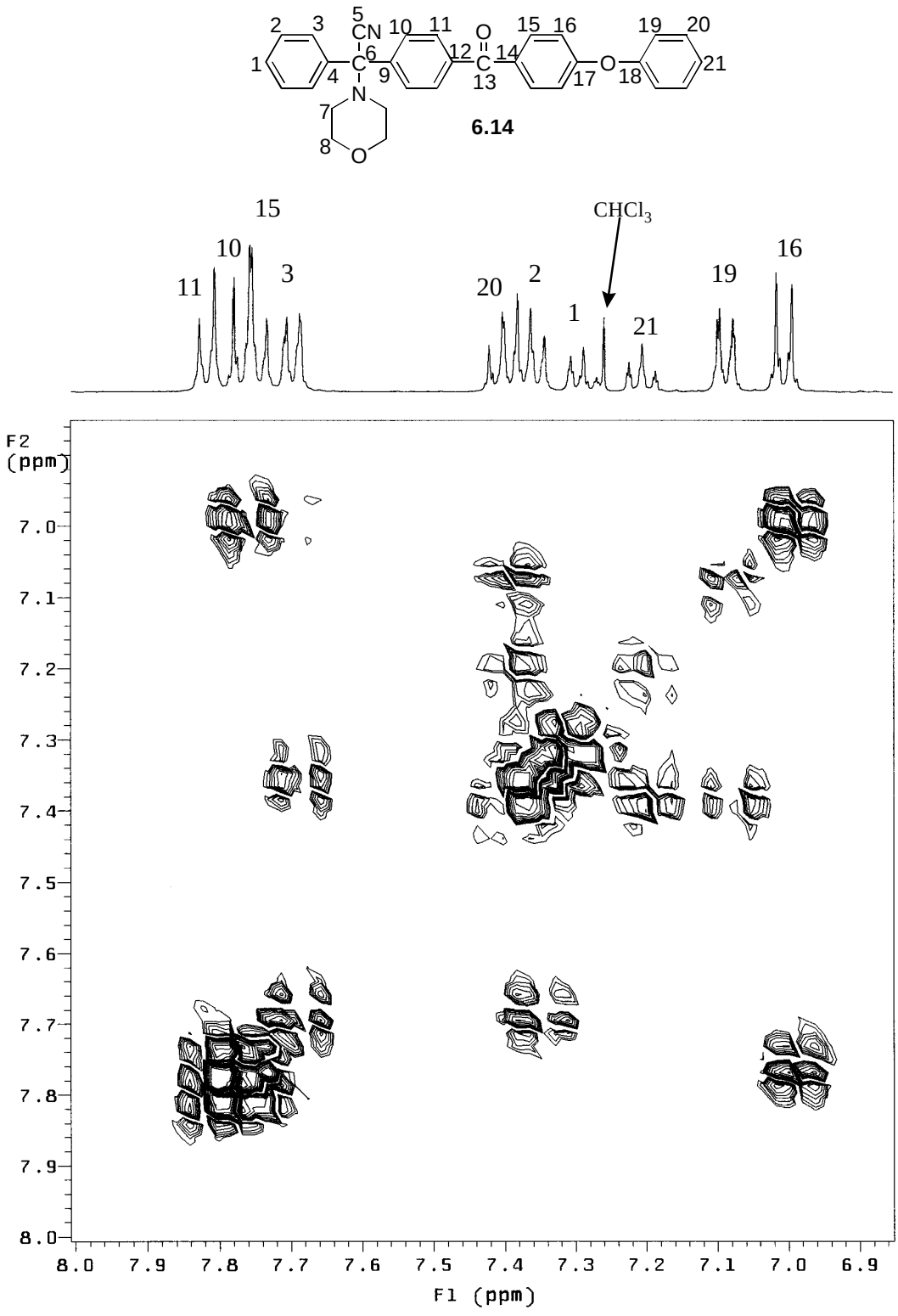


Figure 6.13 400 MHz COSY spectrum of **6.14** in $CDCl_3$ (aromatic region).

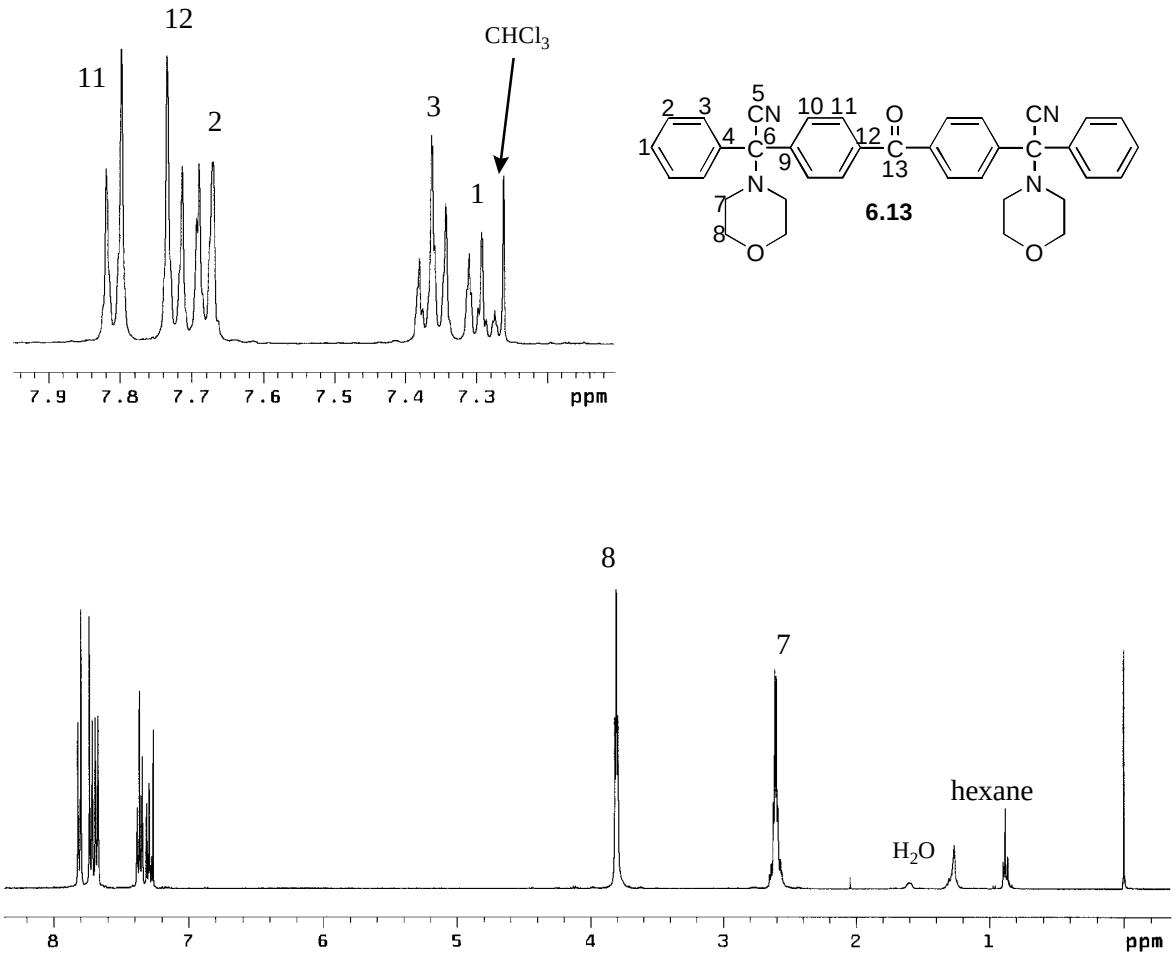


Figure 6.14 400 MHz ^{1}H NMR spectrum of **6.13** in $CDCl_3$.

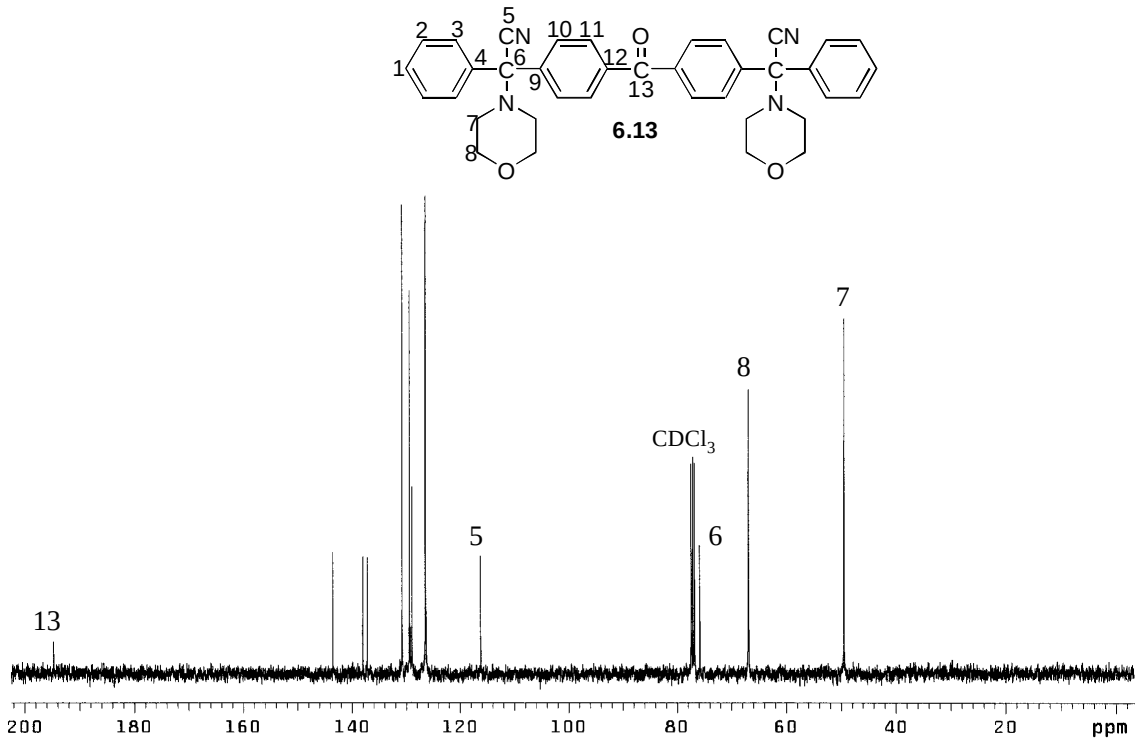


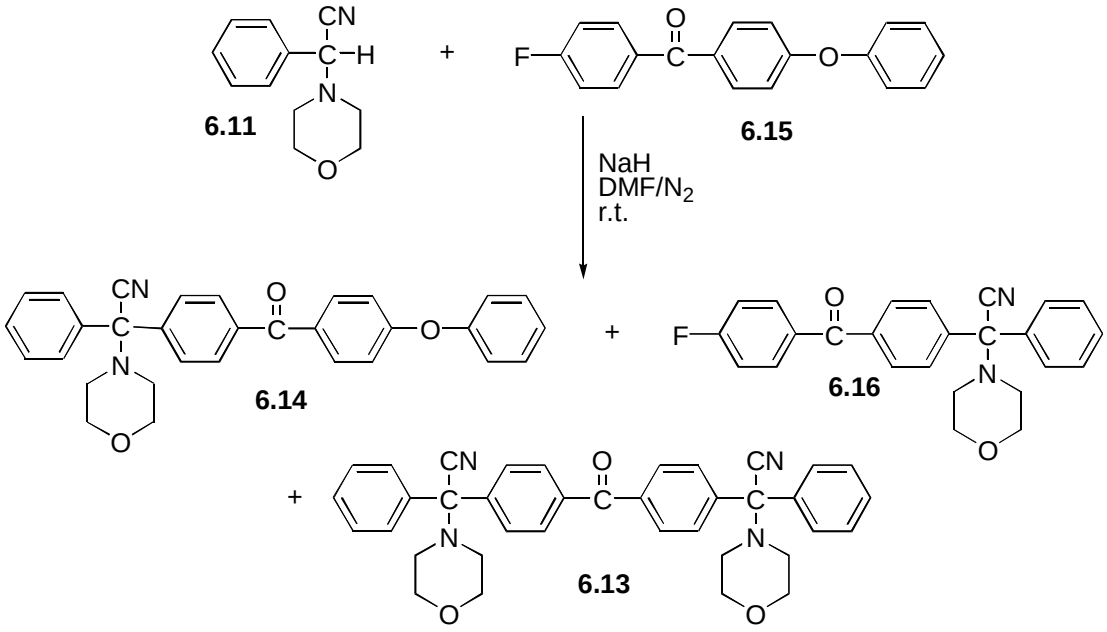
Figure 6.15 100 MHz ^{13}C NMR spectrum of **6.13** in $CDCl_3$.

B. Competing Reactions of Carbanion with Activated Halide and Ether Linkage

Model compound **6.15** is a good example to test the competing reactions of the activated halides and activated ether linkages with the anions of the aminonitriles. If the reaction rates of these two different reactions are comparable, compound **6.13** or compound **6.16** will form as well as the normally expected product **6.14**. Benzalaminonitrile **6.11** was reacted with compound **6.15** (1:1 mole ratio) in DMF at room temperature using 1.1 equivalents of NaH as base (Scheme 6.6). After 24 hours, the solution was precipitated into water and the product was isolated. The TLC of this crude product in 3:1/hexane:EtOAc showed only one spot. The ^{1}H NMR spectrum of the product agreed well with the structure

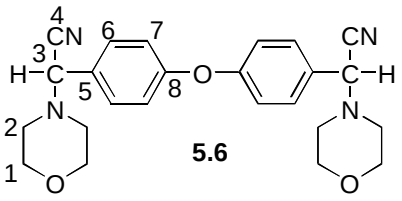
of compound **6.14**. Only a trace amount of methine proton of the aminonitrile unit was observed. Most of the aminonitrile reacted with the activated fluoro group. This experiment confirmed that the reaction between the carbanion of the aminonitrile and the activated halide is much faster than the reaction between the carbanion of the aminonitrile with activated ether linkages. However, for condensation polymerization, even small amounts of side reaction can result in low molecular weight polymers. As fluoro groups are consumed, the relative rates become such that the large numbers of ether linkages undergo reaction with the carbanions. This reduces the molecular weight in two ways: 1) consumption of one of the monomers and disrupting the stoichiometry and 2) cleavage of already existing polymer molecules.

Scheme 6.6



C. Stability of an Aminonitrile with Ether linkage in DMF and NaH

To test the stability of aminonitriles containing ether linkages in the presence of carbanions of aminonitriles, bisaminonitrile **6.6** was dissolved in DMF together with 2.2 equivalents of NaH at room temperature. The mixture was stirred for 24 hours and then precipitated into water. If the ether linkages are stable under these conditions, only bisaminonitrile **6.6** should be recoved. The ^{1}H NMR spectrum of the precipitate showed a small doublet at 7.43 ppm that accounted for about 30% of the two doublets of the starting aminonitrile (Figure 6.16). The doublet appears at almost the same position as that of polyaminonitrile **6.7** (Figure 6.7). The low molecular weight of polyaminonitrile **6.7** could be due to the instability of the aminonitrile **6.6** in the presence of NaH.



5.6

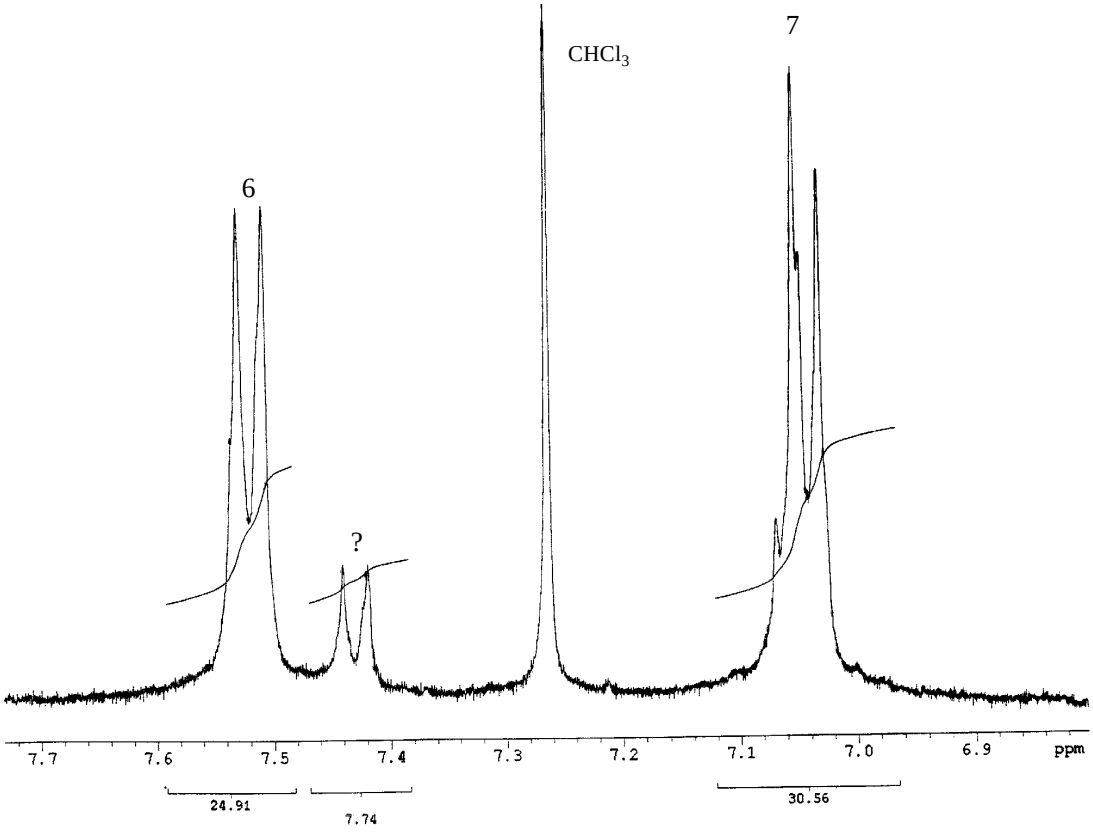


Figure 6.16 400 MHz ^{1}H NMR spectrum of the crude product of **6.6** + NaH in $CDCl_3$.

6.3 Conclusions

For the synthesis of polyaminonitriles containing ether linkages in the polymeric backbone, only low to medium molecular weight polymers were obtained. The model studies proved that the carbanions of the aminonitriles can react with ether linkages to form more

stable phenoxide anions, which can not further react with the activated fluoro sites; this causes the termination of the polymerization. However, the reaction between the activated fluoro sites and the carbanions of the aminonitriles is much faster than the reaction of the ether linkages with the anions of the aminonitriles. As the molecular weight of the polyaminonitriles increases, the concentration of the activated fluoro chain ends decreases, and the side reactions between carbanionic polymer chain ends and the ether linkages become significant.

6.4 Experimental Section

Materials and Instrumentation

Unless specified otherwise, anhydrous, reagent grade materials and solvents were used as received from chemical suppliers. 4,4'-Difluorobenzophenone was recrystallized from ethanol three times. Monomers were dried in a vacuum oven for 24 hours prior to use.

All melting points were determined on a MEL-TEMP 2 melting point apparatus. The melting points are corrected. The ^{1}H NMR spectra were obtained on a Varian Unity-400 NMR spectrometer operating at 399.95 MHz, with tetramethylsilane ($\delta = 0$) as internal standard. All ^{1}H COSY (COrrelated SpectroscopY) spectra were obtained using a 16-step phase cycle. The spectral window was centered. A 90° pulse (177.5 μs) was used for both dimensions (F_1 and F_2); 128 increments of 512 point FID's (acquisition time 247 ms) with 16 scans were accumulated. Zerofilling, multiplication by sine window function, Fourier transformation and symmetrization were applied. The ^{13}C NMR spectra were obtained on a Varian Unity 400 spectrometer operating at 100.60 MHz. Spectra were proton-decoupled and recorded in deuteriochloroform ($\delta = 76.9$) as solvent and internal standard. FTIR spectra were recorded

on a Nicolet MX-1 with KBr pellets. GPC analyses were done with a Waters 150C ALC/GPC system with permagel 10^2-10^6 Angstrom polystyrene-divinylbenzene columns. This instrument was equipped with a Viscotek 100 differential viscometer and differential refractive index detectors. The viscometric data plus differential refractive index data yielded absolute molecular weights by application of the universal hydrodynamic volume calibration concept.

Synthesis of Dialdehyde 6.1a[5]

Into a flame dried 250 mL round bottom flask equipped with Dean-Stark trap and N_2 inlet, 4,4'-biphenol (3.724 g, 20.00 mmol) was dissolved in 35 mL of DMAC and 10 mL of toluene. K_2CO_3 (2.76 g, 20.0 mmol) was then added. The mixture was then refluxed at 140 °C for 4 hours to remove water. 4-Fluorobenzaldehyde (5.46 g, 44.0 mmol) was then added. The temperature was then raised to 160 °C by removing toluene and reflux was continued at this temperature for 12 hours. The mixture was quenched into 800 mL of water; 7.78 g (99%) of pale yellow crystals were collected by suction filtration, mp 168-171°C (in slow heating, it was oxidized to carboxylic acid, lit.[5] mp: 150-151 °C). ^{1}H NMR ($CDCl_3$): δ 7.12 (d, *J* = 8.8 Hz, 2 H), 7.17(d, *J* = 8.8 Hz, 2 H), 7.62 (d, *J* = 8.8 Hz, 2 H), 7.88 (d, *J* = 8.8 Hz, 2 H), 9.94 (s, 1 H). FTIR (KBr): 1694 (carbonyl), 1597 (phenyl), 1263 (C-O-C), 1496, 1152, 837, 822, cm^{-1}.

Synthesis of Dialdehyde 6.1b[5]

Procedural details were the same as those of **6.1a**. The yield was 6.08 g (96%). It was dissolved in hot CH_2Cl_2 with depdecolorizing charcoal to remove the colored impurities. The melting point was 162.8-164.5 °C (lit.[5] mp: 157-158 °C). ^{1}H NMR (DMSO-d_6): δ 7.17 (d, *J* = 8.8 Hz, 2 H), 7.25 (s, 1 H), 7.93 (d, *J* = 8.8 Hz, 2 H), 9.93 (s, 1 H). FTIR (KBr): 1695, 1684 (carbonyl), 1600, 1579 (phenyl), 1230 (C-O-C), 1491, 1155, 874, cm^{-1}.

Synthesis of Bisaminonitrile 6.2a

Anhydrous methylene chloride was dried over P_2O_5 for 12 hours and then distilled. To a 100 mL round bottom flask equipped with nitrogen inlet and a stirring bar, the dialdehyde **6.1a** (3.94 g, 10.0 mmol) and 30 mL methylene chloride were added. Trimethylsilyl cyanide (TMSCN, 2.98 g, 30.0 mmol) and morpholine (2.61 g, 30.3 mmol) were added to the flask. The solution was refluxed for 24 hours. It was allowed to cool to room temperature and then extracted with three portions of water (15 mL). The methylene chloride was removed on a rotary evaporator to give a gummy oil. It was redissolved in 20 mL of methylene chloride and 2.61 g of morpholine. The solution was refluxed for 12 hours. Upon removing methylene chloride, a light brown oil was obtained. It was washed with hexane to give light brown crystals. It was washed with hot ethanol to give a light pink solid, 4.46 g (76%), mp: 192.0-195.7 °C. This product was then passed through a short silica gel column using methylene chloride as solvent and then recrystallized from methlene chloride and ethyl acetate twice to give white crystals, 2.99 g, (51%), mp 193.5-194.7 °C. ^{1}H NMR ($CDCl_3$): δ 7.59 (d, *J* = 8.8 Hz, 2 H), 7.51(d, *J* = 8.4 Hz, 2 H), 7.10 (d, *J* = 8.8 Hz, 2 H), 7.07 (d, *J* = 8.4 Hz, 2 H), 4.79

(s, 1 H), 3.73-3.75 (m, OCH_2, 4 H), 2.58-2.61 (m, NCH_2, 4 H), ppm. ^{13}C NMR ($CDCl_3$): δ 158.06 (C), 155.87 (C), 136.15 (C), 129.55 (CH), 128.35 (CH), 127.04 (C), 119.64 (CH), 118.64 (CH), 115.20 (CN), 66.64 (OCH_2), 61.84 (CH), 49.91 (NCH_2), ppm. FTIR (KBr): 2800-3000 (C-H stretches), 2220 (nitrile), 1597 (phenyl), 1244 (C-O-C), 1163 (C-O-C), 865, cm^{-1}.

Synthesis of Bisaminonitrile 6.2b

The procedural details were the same as those of diaminonitrile **6.2a**. Bisaldehyde **6.1b** (8.35 g, 26.24 mmol), methylene chloride (60 mL), trimethylsilyl cyanide (TMSCN, 7.82 g, 78.72 mmol) and morpholine (6.85 g, 78.72 mmol) were used. The yield was 11.39 g (85%), mp: 176.1-178.3 °C. ^1H NMR ($CDCl_3$): δ 7.49 (d, *J* = 8.8 Hz, 2 H), 7.03(s, 4 H), 7.01 (d, *J* = 8.8 Hz, 2 H), 4.80 (s, 1 H), 3.67-3.79 (m, OCH_2, 4 H), 2.54-2.66 (m, NCH_2, 4 H), ppm. ^{13}C NMR ($CDCl_3$): δ 158.49 (C), 152.36 (C), 129.61 (CH), 126.75 (C), 121.04 (CH), 118.15 (CH), 115.20 (CN), 66.63 (OCH_2), 61.81 (CH), 49.91 (NCH_2), ppm. FTIR (KBr): 2800-3000 (C-H stretches), 2223 (nitrile), 1601 (phenyl), 1248 (C-O-C), 1164 (C-O-C), 868, cm^{-1}.

4,4'-Oxy-bis(methyl benzoate) 6.3

To a 1L round bottom flask was added 4,4'-oxy-bis(benzoic acid) (51.65 g, 0.2000 mol) and methanol (650 mL). Concentrated sulfuric acid (20 mL) was slowly added to the reaction flask with stirring. The mixture was heated at reflux for 24 hours. The white shiny flakes were filtered and washed with distilled water to remove sulfuric acid and methanol,

54.39 g (95%), mp: 158.5-160.0 °C (lit.[7] mp: 154-155 °C). ^{1}H NMR ($CDCl_3$): δ 8.05 (d, *J* = 8.8 Hz, 2 H), 7.06 (d, *J* = 8.8 Hz, 2 H), 4.92 (s, 3 H), ppm. ^{13}C NMR ($CDCl_3$): δ 166.40 (C=O), 160.17 (C=O), 131.86 (CH), 125.75 (C), 118.65 (CH), 52.13 (CH_3), ppm.

4,4'-Oxy-bis(benzyl alcohol) 6.4

To a 1 L three neck flask were added compound **6.3** (42.94 g, 150.0 mmol) and dry THF (500 mL). A solution of LAH in THF (100 mL, 225.0 mmol) was added dropwise to the reaction flask. The stirring was continued for 24 hours. Ethyl acetate (150 mL) was then added to the flask and the mixture was precipitated into water. HCl was added with stirring until the solution was slightly acidic. The solution was then transferred to a separatory funnel and the ethyl acetate layer was separated. The aqueous layer was washed with ethyl acetate (2 × 50 mL) twice. The solvent was removed by rotary evaporation to give the product **6.4**, 28.7 g (83%), mp: 137-139.5 °C (lit.[8] mp: 135.5-136 °C). ^{1}H NMR (DMSO-d_6): δ 7.34 (d, *J* = 8.6 Hz, 2 H), 6.93 (d, *J* = 8.6 Hz, 2 H), 5.17 (s, OH, 1 H), 2.01 (S, CH_2, 2 H), ppm.

4,4'-Oxy-bisbenzaldehyde 6.5

To a 500 mL round bottom flask were added compound **6.4** (23.23 g, 100.0 mmol), methylene chloride (300 mL) and pyridinium chlorochromate (49.58 g, 230.0 mmol). The mixture was stirred under nitrogen for 2.5 hours. The brown solid was filtered and the filtrate was passed through a short silica gel column. The solvent was removed by rotary evaporation

[7] Nakaazawa, J. H. *Chem. Pharm. Bull.* **1968**, 16, 2503.
[8] Kuzmichev, O. V. *J. Org. Chem. USSR (Engl. Transl.)* **1968**, 4, 445.

to give the product **6.5**, which was washed with hexane. The yield was 19.68 g (87%), mp: 60.1-62.0 °C (lit.[9] mp: 55-57 °C). ^{1}H NMR (DMSO-d_6): δ 10.0 (s, 1 H, aldehyde), 7.95 (d, *J* = 8.2 Hz, 2 H), 7.11 (d, *J* = 8.2 Hz, 2 H), ppm.

Bis(α-aminonitrile) 6.6

The procedural details were the same as those of bisaminonitrile **6.1a**. Dialdehyde **5.5** (11.31 g, 50.00 mmol), methylene chloride (75 mL), trimethylsilyl cyanide (TMSCN, 14.90 g, 150.0 mmol) and morpholine (13.05 g, 150 mmol) were used. The yield was 22.30 g (97%), mp: 180.1-181.5 °C. ^{1}H NMR ($CDCl_3$): δ 7.52 (d, *J* = 8.2 Hz, 2 H), 7.04 (d, *J* = 8.2 Hz, 2 H), 4.81 (s, 1 H), 3.64-3.81 (m, OCH_2, 4 H), 2.53-2.65 (m, NCH_2, 4 H), ppm. ^{13}C NMR ($CDCl_3$): δ 157.34 (C), 129.67 (CH), 127.67 (CH), 119.14 (CH), 115.19 (CN), 66.67 (CH), 61.84 (OCH_2), 49.97 (NCH_2), ppm. FTIR (KBr): 2800-3000 (C-H stretches), 2222 (nitrile), 1598 (phenyl), 1245 (C-O-C), 1166 (C-O-C), 867, cm^{-1}.

Synthesis of Polyaminonitrile 6.7 from Bis(α–aminonitrile) 6.6

Into a 100 mL flame dried flask equipped with a nitrogen inlet and a magnetic stirrer, anhydrous DMF (15 mL) and NaH (0.293 g, 7.33 mmol, 60% in mineral oil) were added. the mixture was stirred for 10 minutes. Bis(α–aminonitrile) **6.6** (1.3950 g, 3.3333 mmol) and difluorobenzophenone (0.7273 g, 3.3333 mmol) were then added to the flask. Vigorous

[9] Baratov, N. U.; Milgrom, E. G.; Vinogradova, V. I.; Roshkes, Y. V.; Yunusov, M. S. *Chem. Nat. Compd. (Engl. Transl.)* **1993,** 29, 748.

bubbling and an immediate color change to dark brown were observed. After 24 hours, a small aliquot was withdrawn from the flask and precipitated into water. After 48 hours, another small aliquot was withdrawn from the flask and precipitated into water. The stirring was continued at room temperature for 120 hours. The color of the solution remained dark brown. The mixture was then precipitated into 300 mL distilled H_2O and the white precipitate was filtered and washed with MeOH. ^{1}H NMR ($CDCl_3$): δ 2.52-2.71 (m, NCH_2, 4 H), 3.64-3.83 (m, OCH_2, 4 H), 6.90-6.96 (d, 2 H), 6.98-7.20 (m, 0.45 H), 7.41 (d, 0.28 H), 7.60-7.65 (d, 2 H), 7.72-7.76 (d, 2 H), 7.76-7.82 (d, 2 H), ppm (all signals are broad). ^{13}C NMR ($CDCl_3$): δ 194.73 (C=O), 156.87 (C), 143.54 (C), 137.22 (C), 133.16 (C), 130.80 (CH), 129.34 (C), 128.04 (CH), 126.37 (CH), 119.52 (CH), 116.12 (CN), 66.83 (C), 49.43 (OCH_2), 31.57 (NCH_2), ppm. FTIR (KBr): 2800-3000 (C-H stretches), 1660 (carbonyl), 1605 (phenyl), 1250 (C-O-C) 1169 (C-O-C), cm^{-1}.

Synthesis of Polyaminonitrile 6.9 from Bis(α-aminonitrile) 6.1a

The procedural details were the same as those of polyaminonitrile **6.7**. Anhydrous DMF (15 mL), NaH (0.2106 g, 5.260 mmol, 60% in mineral oil), bis(α–aminonitrile) **6.1a** (1.4040 g, 2.3931 mmol) and 4,4'-difluorobenzophenone (0.5222 g, 2.3931 mmol) were used. Vigorous bubbling and an immediate color change to dark brown were observed. After 36 hours, a small aliquot was withdrawn from the flask and precipitated into water. The white precipitate was filtered and washed with methanol. The stirring was continued at room temperature for 120 hours. The color of the solution remained dark brown. The mixture was then precipitated into 300 mL distilled H_2O and the white precipitate was filtered and washed

with MeOH. ^{1}H NMR ($CDCl_3$): δ 2.54-2.68 (m, NCH_2, 4 H), 3.67-3.88 (m, OCH_2, 4 H), 6.94-7.21 (d, 2 H), 7.21-7.09 (d, 2 H), 7.40-7.44 (d, 0.42 H), 7.49-7.56 (d, 2 H), 7.58-7.66 (d, 2 h), 7.72-7.78 (d, 2 H), 7.78-7.84 (d, 2 H), ppm (all signals are broad). FTIR (KBr): 2800-3000 (C-H stretches), 1656 (carbonyl), 1597 (phenyl), 1230 (C-O-C) 1169 (C-O-C), cm^{-1}.

α-(*N*-Morpholino)benzyl Cyanide (6.11)[2]

To a solution of $NaHSO_3$ (20.81 g, 200.0 mmol) in 300 mL of water was added benzaldehyde (44.17 g, 200.0 mmol), and the mixture was stirred for 2 hours until homogeneous. Morpholine (17.42 g, 200.0 mmol) was then added to the solution and the stirring was continued for 2 hours. Finally, sodium cyanide (98.02 g, 200.0 mmol) was added and the mixture was stirred overnight (8 hours); the product precipitated out of the solution. The yield was 38.83 g (96%). It was recrystallized from hexane and ethyl acetate to give white shiny platelets, mp: 68.1-69.3 °C (lit.[10] mp: 68-70 °C). ^{1}H NMR ($CDCl_3$): δ 2.60 (m, 4 H, CH_2N), 3.77 (m, 4 H, CH_2O), 4.81 (s, 1 H, CH), 7.36-7.44 (m, 3 H, ArH), 7.52-7.56 (m, 2 H, ArH), ppm.

4,4'-Diphenoxybenzophenone (6.12)

To a 100 mL three neck round bottom flask, equipped with magnetic stirrer, Dean-Stark trap and N_2 inlet, were added phenol (2.964 g, 31.50 mmol), potassium carbonate (4.353 g, 31.50 mmol) DMAc (50 mL) and toluene (15 mL). The mixture was heated at

reflux for 2 hours to remove the side product H_2O. 4,4'-Difluorobenzophenone (3.273 g, 15.00 mmol) was then added to the reaction flask and the mixture was refluxed at 135 °C for 4 hours. The temperature was then raised to 150 °C by removing toluene from the Dean-Stark trap. The mixture was refluxed for another 12 hours and then allowed to cool to room temperature. The solid residue was removed by suction filtration and the filtrate was precipitated into 400 mL of water. The white precipitate was filtered and washed with water. The yield was 5.39 g (98%). It was recrystallized from ethanol to give white shiny flakes, mp: 146.0-147.1 °C (lit.[11] mp: 146-147 °C). ^{1}H NMR ($CDCl_3$): δ 7.80 (d, *J* = 8.8 Hz, 4 H), 7.40(m, 4 H), 7.21 (m, 2 H), 7.10 (m, 4 H), 7.03 (d, *J* = 8.8 Hz, 4 H), ppm. ^{13}C NMR ($CDCl_3$): δ 194.20 (C=O), 161.37 (C), 155.80 (C), 132.21 (CH), 124.51 (CH), 120.09 (CH), 117.13 (CH), ppm.

Reaction of Aminonitrile 6.11 and Diphenoxybenzophenone (6.12) in the presence of Base

Into a 100 mL flame dried flask equipped with a nitrogen inlet and a magnetic stirrer, anhydrous DMF (25 mL) and NaH (0.44 g, 11.0 mmol, 60% in mineral oil) were added. The mixture was stirred for 10 minutes. Compound **6.11** (2.023 g, 10.00mmol) and compound **6.12** (1.823 g, 5.000 mmol) were then added to the flask. Vigorous bubbling and an immediate color change to dark brown were observed. After 24 hours, the solution was precipitated into water and the white solid precipitate was filtered and dried. The TLC of this

[10] Takahashi, K.; Matsuzaki, M.; Ogura, K.; Iida, H. *J. Org. Chem.* **1983**, 48, 1909.
[11] Fuson, L. T. *J. Am. Chem. Soc.* **1959**, 81, 4858.

precipitate in 3:1/hexane:EtOAc showed four spots. Two of them were the starting materials **6.11** and **6.12**. Flash column chromatography (silica gel) using 3:1/hexane:EtOAc as eluent gave four fractions. The first fraction was compound **6.12** and the second fraction was compound **6.11**. The ^{1}H NMR spectra and the melting points of these two compounds were the same as those of the starting materials. The third fraction was identified as compound **6.14**, 0.29 g, (12%), mp: 112.6-114.2 °C. ^{1}H NMR ($CDCl_3$): δ 7.82 (d, *J* = 8.2 Hz, 4 H), 7.77 (d, *J* = 8.2 Hz, 4 H), 7.74 (d, *J* = 8.2 Hz, 4 H), 7.70 (m, 2 H), 7.40 (m, 2 H), 7.36 (m, 2 H), 7.29 (m, 1 H), 7.21 (m, 1 H), 7.09 (m, 2 H), 7.00 (d, *J* = 8.2 Hz, 4 H), 3.77-3.85 (m, OCH_2, 4 H), 2.56-2.66 (m, NCH_2, 4 H), ppm. ^{13}C NMR ($CDCl_3$): δ 194.48 (C=O), 161.95 (C), 155.36 (C), 142.90 (C), 138.11 (C), 132.47 (CH), 131.31 (C), 130.52 (CH), 130.11 (CH), 129.28 (CH), 128.83 (C), 126.38 (CH), 126.31 (CH), 124.74 (CH), 120.27 (CH), 117.13 (CH), 116.30 (CN), 75.81 (C), 66.90 (OCH_2), 49.43 (NCH_2), ppm. FTIR (KBr): 2800-3000 (C-H stretches), 2228 (nitrile), 1663 (carbonyl), 1604 (phenyl), 1116 (C-O-C), 756, cm^{-1}. The fourth fraction was identified as compound **6.13**, 0.44 g, (15%), mp: 89.1-124.2 °C (lit.[2] mp: 88-122 °C, diastereomeric). ^{1}H NMR ($CDCl_3$): δ 7.81 (d, *J* = 8.2 Hz, 4 H), 7.73(d, *J* = 8.2 Hz, 4 H), 7.68 (m, 4 H), 7.36 (m, 4 H), 7.29 (m, 2 H), 3.80 (t, *J* = 8.2 Hz, OCH_2, 8 H), 2.53-2.67 (m, NCH_2, 8 H), ppm. ^{13}C NMR ($CDCl_3$): δ 194.72 (C=O), 143.53 (C), 137.98 (C), 137.18 (C), 130.72 (CH), 129.31 (CH), 128.89 (CH), 126.41 (CH), 126.35 (CH), 116.20 (CN), 75.79 (C), 66.87 (OCH_2), 49.43 (NCH_2), ppm. FTIR (KBr) 2800-3000 (C-H stretches), 2226 (nitrile), 1662 (carbonyl), 1606 (phenyl), 1117 (C-O-C), 755, cm^{-1}.

Competing Reaction between Activated Halides and Ether Linkages, 6.11 + 6.15

The procedural details were the same as those of compound **6.11** and **6.12**. Compound **6.11** (1.0113 g, 5.000 mmol), compound **6.15** (1.4616 g, 5.000 mmol) and NaH (0.220 g, 5.50 mmol, 60% in mineral oil) were used. The crude yield was 2.34 g (97%), mp 62.0-114 °C. The TLC of the product in 3:1/hexane:EtOAc showed only one spot. ^{1}H NMR ($CDCl_3$) and ^{13}C NMR spectra were the same as compound **6.14** obtained from compound **6.11** and compound **6.12**.

Stability of Aminonitrile 6.6 in DMF and NaH

The procedural details are the same as above. Compound **6.6** (0.500 g, 1.20 mmol) and NaH (0.105 g, 2.63 mmol, 60% in mineral oil) were used. It was stirred at room temperature for 24 hours and then precipitated into water. ^{1}H NMR ($CDCl_3$): δ 2.52-2.74 (m, NCH_2, 3.7 H), 3.63-3.85 (m, OCH_2, 5.2 H), 4.81 (s, CH, 1 H), 7.02-7.08 (m, 1.86 H), 7.43 (d, 0.48 H), 7.49-7.55 (d, 1.56 H), ppm.