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Chemistry of Biphenoxy Radicals

By

Gennaro Barbiero

A thesis submitted to the faculty of Graduate Studies and research in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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This thesis is dedicated to my parents, wife for without their support I would not have complete my Ph.D. and to my two gorgeous baby girls Sabrina and Alyssa.

The following quotation by D. H. R Barton is a perfect indication what wives of chemist must go through and what my wife went through for 5 years.

"What are the characteristics of a great chemist like Koji? Intelligence and dedication. All the great chemists I have known have been totally dedicated to their work. This means that they are working 14 hours or more hours a day for up to seven days a week. This also means that they have to find an unusual kind of wife, who will support a regime where the husband spends most of his time with his mistress (Chemistry). Of course, there will be time occasionally for intimate moments that are needed for the next generation of chemists to be born. Koji and Yasuko have two children."

Derek H.R. Barton, 1992
TetrahedronNews
February 1996

Acknowledgments

I would like to thank my supervisor Prof. Allan S. Hay for giving me the opportunity to work with him, the guidance throughout my Ph.D., and the great research project.

I would also like to thank my colleagues in Room 409 both past and present: Dr. Martino Paventi, Dr. Hu Yang, Dr. Marko Strukelj, Dr. Yifeng Wang, Dr. Ed Elce, Dr. Kwok Pong Chan, Dr. Coromoto Martinez, Dr. W.-Gi. Kim, Dr. Hossein Ghassemi, Dr. Chunping Gao, Yong Ding, Shu Yoshida, Humayan Madal, Linghua Yu, Jin - Wook Shin for their help, friendship, and useful discussions, and Dr. Nadim Saade for mass spectrometry services

I am grateful to General Electric Company and the Natural Science and Engineering Research for financial support.

Chemistry of Bihenoxy Radicals

by Gennaro Barbiero

Abstract

A series of hindered biphenols specifically designed to form stable biphenoxy radicals were prepared by an oxidative coupling reaction of hindered phenols in the presence of CuCl and molecular oxygen in butyronitrile or by reacting the diphenoquinones with HCl gas.

The biphenoxy radicals generated from the oxidation of the original biphenols with an aqueous solution of KOH/$K_3Fe(CN)_6$ or Ag_2O were used as reagents in organic reactions and catalysts in the oxidation of diarylmethanes to corresponding ketones. They were also used in the synthesis of novel ether and acetal monomers through a quantitative radical coupling reaction with monomers containing activated methylene groups. These ether and acetal compounds were readily cleaved under acidic conditions thus providing a new method of cleaving benzylic and t-butyl ethers under mild conditions and for functionalizing activated methylene groups. To simplify the purification steps biphenol **A6.19** was incorporated into the backbone of a poly(aryl ether) chain and used as a polymeric support material.

The quantitative radical coupling reaction and cleavage of the resulting ethers and acetals led to the synthesis of novel carbon - oxygen coupled polymers that could potentially be used as photoresist materials since they are cleaved to low molecular weight organic compounds in the presence of acid.

In part B a new mass spectrometry technique, Matrix Assisted Laser Desorption Ionization-Time of Flight, was examined as a potential tool in determining the absolute molecular weight, sequence distribution, and end groups of low molecular weight polydisperse polymers and cyclic oligomers.

La chimie des radicaux biphénoxy

par Gennaro Barbiero

Sommaire

Une série de biphénol specifiquement designe ont été synthèse par un couplage oxidative des correspondante phénol en présence de CuCl, et l'oxygen dans butyronitrile, ou par une réaction de HCl (gaz) avec les différent diphénoquinone .

Les radicaux biphénoxy obtenu par l'oxidation des correspondant biphénols avec une solution de $KOH/K_3Fe(CN)_6$ ou Ag_2O, ont été utilise comme cataþyst dans l'oxidation du diarylmethane. Dans la synthèse des éthers et acétals, par un couplage radicale que est quantitatif entre une série de monomére que contient le groupement méthylène et les radicaux biphénoxy. Le clivage quantitatif de ces nouvaux produit en précence d'acide nous dont un nouvaux façon de cliver les éthers avec des groupement benzylic et t-butyl, et pour functionalise les groupements méthylène. Pour simlpifier l'étape de purification le biphénol **A6.16** été synthèse et incorpore dans la chaine du polymére , et utilise comme support polymérique.

Les reaction quantitatif du couplage radical and clivage des éther et acétal on conduire á la synthèse des polyméres qui peuvent être utilise comme matériaux electronique (photoresist).

Dans chater B1 un nouvelle technique Matrix Assisted Laser Desorption Ionization - Time of Flight, été examine comme un outil pussiant pour l'analyse des polyemes de bas poids moléculaire et les oligoméres cycliques.

Table of Contents

Part B

List of Figures

List of Tables

GLOSSARY OF ABBREVIATION AND SYMBOLS

Å	Angstrom (1 x 10^{-8} cm)
AgTFA	Silver trifluoroacetate
BCl_3	Boron tribromide
BDE	Bond dissociation energy
DMAc	N,N - dimethyacetamide
DMF	N,N - dimethylformamide
DMSO	Dimethylsulfoxide
DSC	Differential scanning calorimeter
ε	Absorptivity
ESR	Electron spin resonance
HPLC	High pressure liquid chromatography
Ghz	Giga hertz
GPC	Gel permeation chromatography
IR	Infrared
MALDI-TOF-MS	Matrix assisted laser desorption ionization -time of flight -mass spectrometer
mol	mole
mmol	millimole
Mn	Number average molecular weight
mp	Melting point
MS	Mass spectrum
Mw	Average molecular weight
nm	Nanometer
NMP	N-methylpyrrolidinone

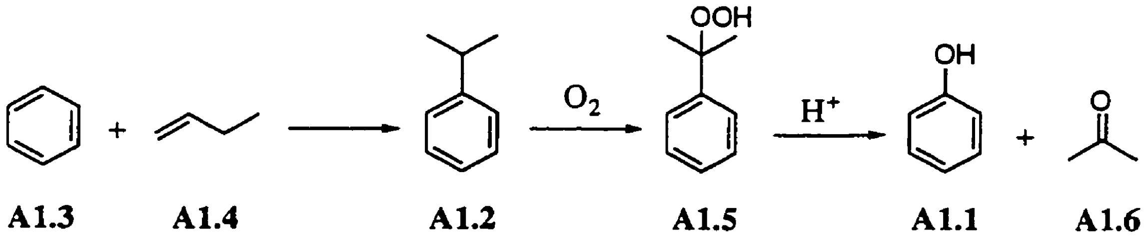
NMR	Nuclear magnetic resonance
T_c	Crystallization temperature
T_g	Glass transition temperature
TGA/DTA	Thermogravimetric / differential thermal analysis
T_m	Crystalline melting temperature
TMEDA	N,N,N,N-tetramethylethylenediamine
TTP	Tritolyl phosphate
UV	Ultraviolet
PEEK®	Poly(ether ether ketone)
PPO®	1,4-Poly (2,6-dimethylphenylene)
λ_{max}	Maximum wavelength
δ	chemical shift
μL	microliter

CHAPTER A1

GENERAL INTRODUCTION

A1.1 History

Phenol **A1.1** was first isolated in 1834 from coal tar. However it wasn't until the early 1940's that the first synthetic procedure for the preparation of **A1.1** was developed, which involved the sulfonation of benzene followed by the hydrolysis of the sulfonate.[1] Currently over 98% of **A1.1** is produced from isopropylbenzene (cumene) **A1.2**. The reaction of benzene **A1.3** with propylene **A1.4** gives **A1.2** which is then oxidized by air over a catalyst to the hydroperoxide **A1.5**. Compound **A1.5** when treated with acid undergoes decomposition to give **A1.1** and acetone **A1.6** as the byproduct (Scheme A1.1). Three main commercial uses of phenol are in the synthesis of phenolic resins, 4,4'-isopropylidenediphenol and caprolactam (see table A1.1).[1]

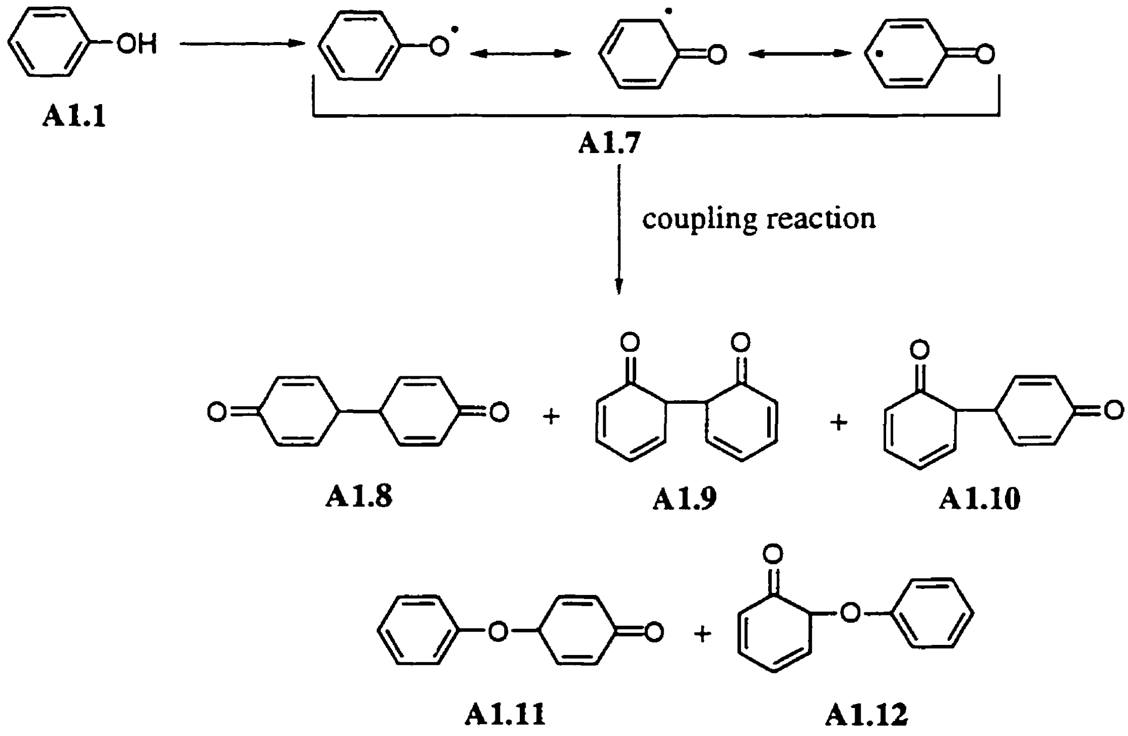


Scheme A1.1

Phenol when oxidized undergoes a series of oxidative coupling reactions (Scheme A1.2) involving a radical intermediate which Pummerer termed phenoxy radical.[2] These radical coupling reactions include the carbon - carbon and carbon - oxygen coupled dimers along with higher molecular weight products since both the ortho and para position are free to be attacked.

Table A1.1 Uses of phenol.

Product	Distribution (%)
Phenolic Resins	43.70
Bisphenol-A	16.50
Caprolactam	13.90
Alkylphenols	4.50
Xylenols and cresols	4.20
Exports	9.10
All others	8.10

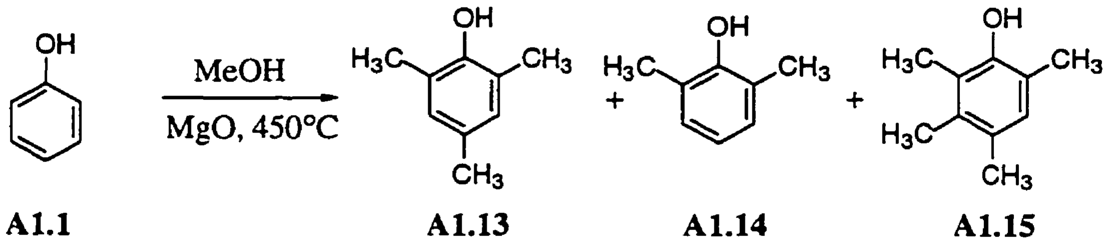


Scheme A1.2

It wasn't until highly substituted phenols were synthesized that stable phenoxy radicals were obtained which have found uses as antioxidants. The bulky groups in the ortho and para position stabilize the radical species by sterically hindering the oxygen radical and extending the delocalization of the unpaired electron. For example by replacing the t-butyl group in the para position of 2,4,6-tri-t-butylphenol with a phenyl group, the stability of the phenoxy group is increased, since the phenyl group enhances the delocalization.[3]

A1.2 Hindered phenols

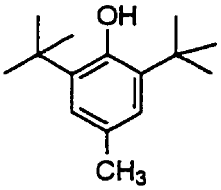
The trialkylated phenols **A1.13-19** are commercially the most widely used hindered phenols. These alkylated phenols are produced industrially by the reaction of readily available olefins with phenol, cresols and xylenols over a catalyst which is generally an ion-exchange resin. If the corresponding olefin is not available, hydrocarbon alcohols or halides can be used instead. Methyl substituted phenols e.g. 2,4,6-trimethylphenol **A1.13** are synthesized from phenol with an excess amount of methanol at 450°C in the gas phase over a magnesium oxide catalyst (Scheme A1.3).[4]

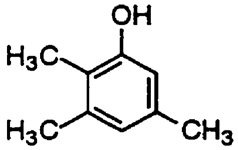


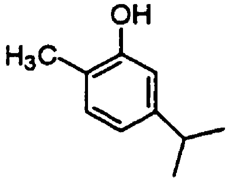
Scheme A1.3

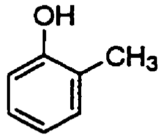
Alkylated phenols are used as antioxidants (e.g. 2,6-di-t-butyl-4-methyl phenol **A1.16**). Other commercial applications are as insecticides (e.g. 2,3,5-trimethylphenol **A1.17**), and as antiseptics (e.g. 5-isopropyl-2-methylphenol **A1.18**), to name a few.[4] The largest volume of alkylated phenol prepared commercially is 2,6-dimethylphenol

A1.14 which is used to manufacture PPO® resin, an intermediate in the synthesis of **A1.19** (2-methylphenol) which is used to make epoxy novolac resins.


A1.16


A1.17


A1.18

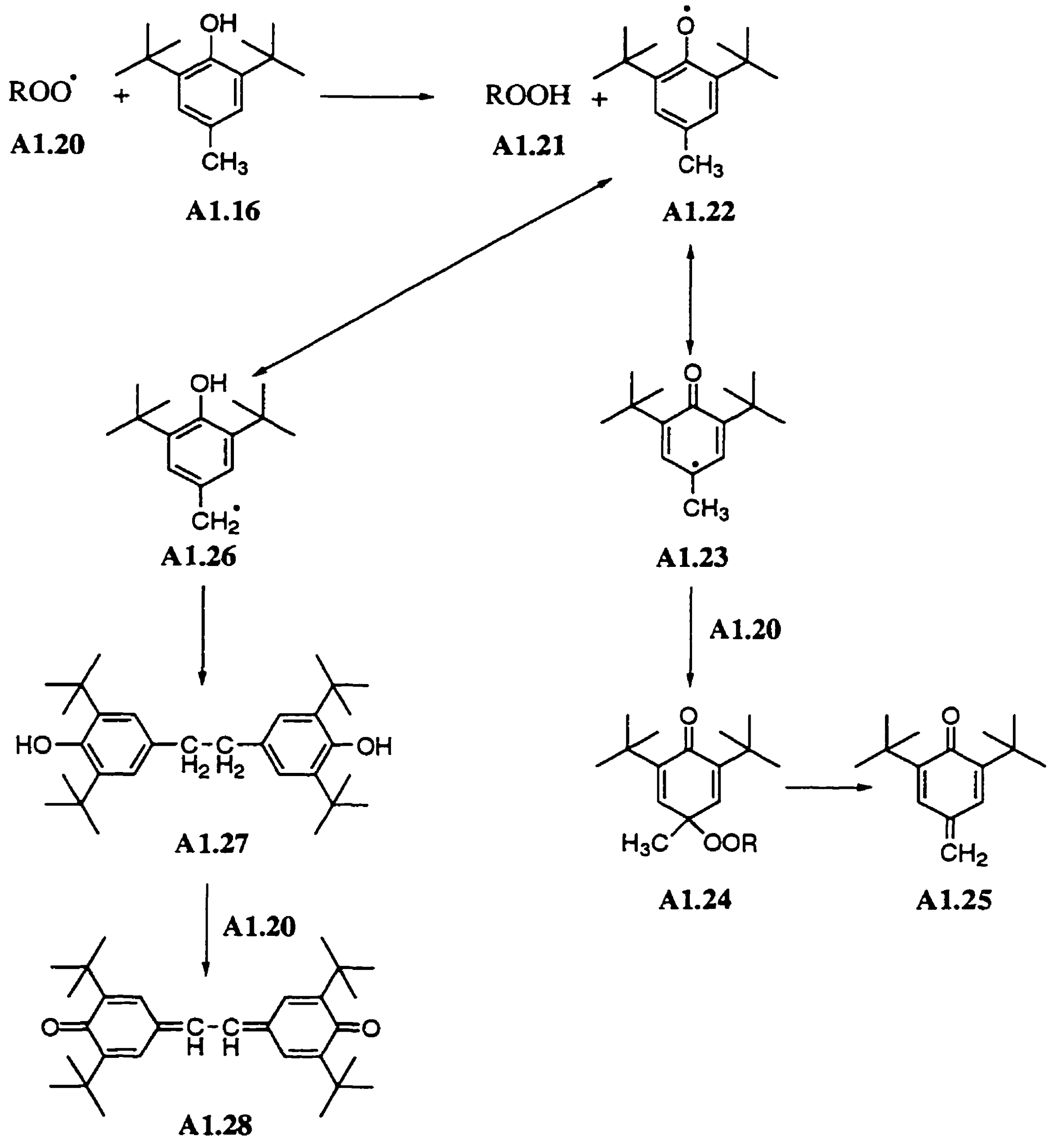

A1.19

A1.3 Antioxidants

An antioxidant is defined as a molecule which suppresses oxidation of a substrate by either oxygen or peroxides. These organic molecules such as **A1.16** are generally easier to oxidize than the substrate. For example **A1.16** is used commercially to inhibit the oxidation of polymers such as polyamides, polystyrene, polyolefins, etc.. The phenoxy radical **A1.22** generated is not as reactive as the peroxy radical **A1.20** and does not participate in the autoxidation chain reaction. Instead the phenoxy radical that is generated reacts with peroxy radicals to form stable quinone products **A1.25,28** (Scheme A1.4)[5]

Antioxidants have also been used in the food industry to preserve the natural flavors and to give foods a longer shelf life. The natural browning that occurs in food is due to the oxidation of phenolic derivatives by polyphenoloxidase and this process is inhibited by **A1.16**. Naturally occurring antioxidants, most of which are flavanoids, have received much attention for prevention of human disease, a recent article by Auoma entitled "Eat, drink and be healthy" states that flavanoinds found in wine are responsible for the prevention of coronary heart disease.[6]

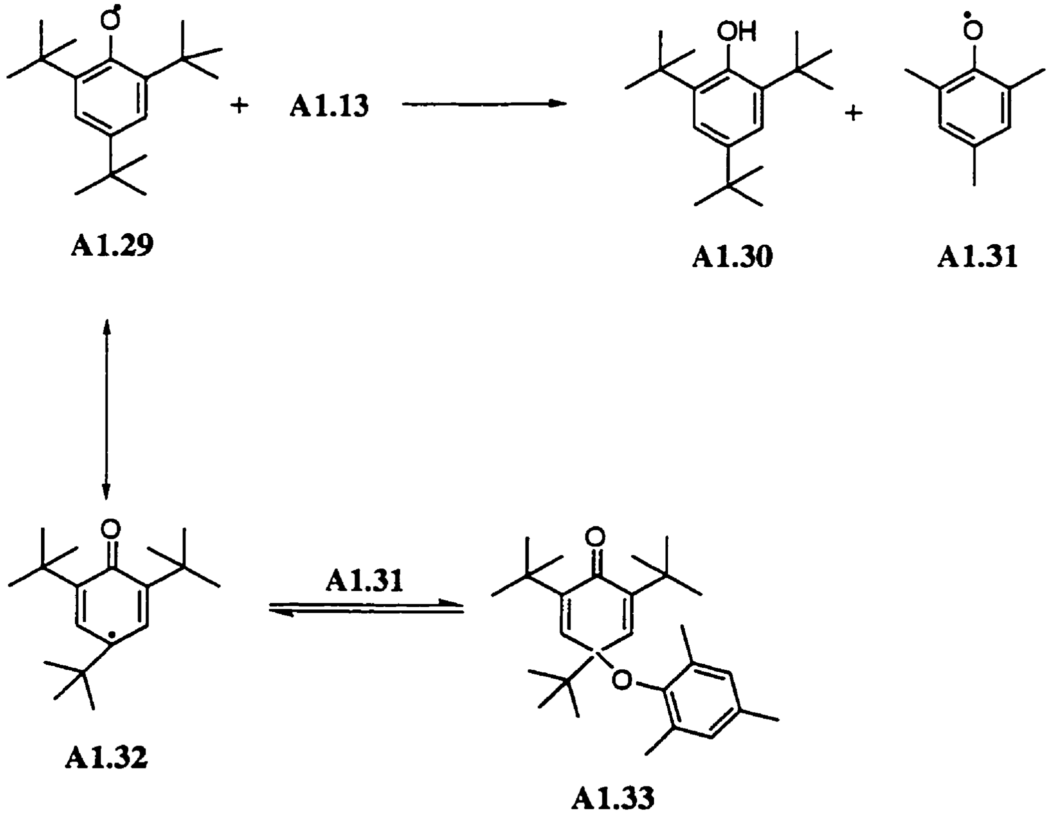
In summary there are many commercial application of hindered phenols. Though the key to their usefulness is their ability to be easily oxidized and form stable phenoxy radicals.



A1.4 Chemistry of Phenoxy Radicals

Phenoxy radicals are generated by abstraction of the phenolic proton followed by a single electron transfer. This can easily be achieved by inorganic oxidizing reagents such as Ag_2O, MnO_2, PdO_2, etc.

The stable hindered phenoxy radicals obtained from trialkylated phenol have been extensively reviewed by Altwicker.[7] He was able to show the broad range of chemistry that can be accomplished with the alkylated phenoxy radicals. Some of the more common reactions are: 1) proton abstraction from a heteroatom (e.g. phenol, thiophenol) with a lower oxidation potential, 2) reaction with aldehydes and ketones, 3) reaction with oximes and 4) reaction with organometallic or metal reagents.



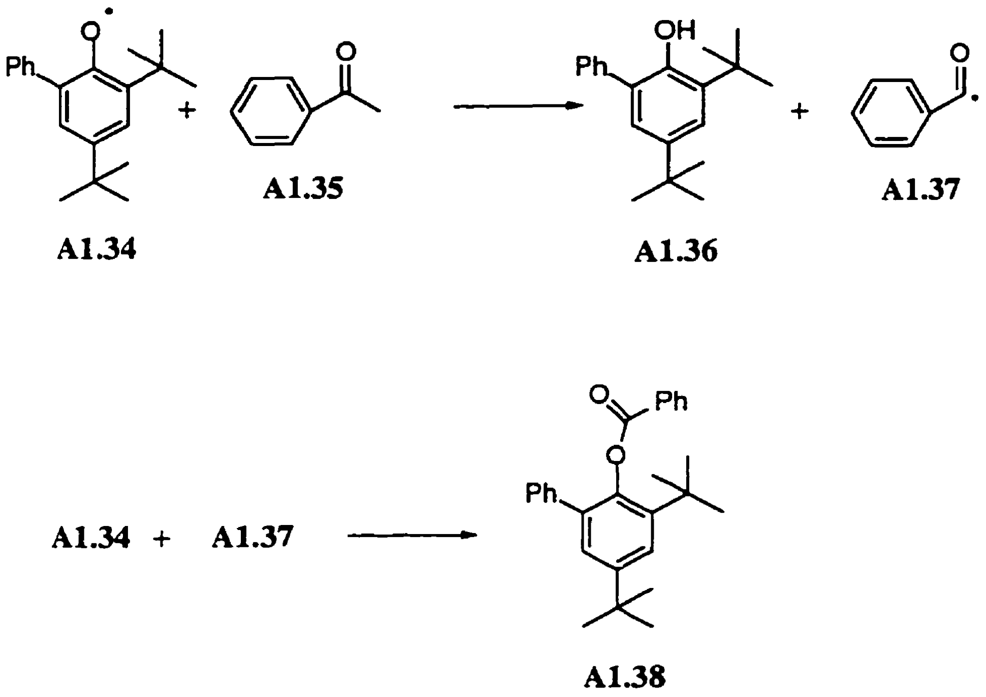
As was mentioned previously phenoxy radicals are formed from the oxidation of phenols. When a phenoxy radical is reacted with a phenol with a lower oxidation potential than the original phenol a new phenoxy radical is formed. A mixed quinol ether may also be obtained. In the reaction of phenoxy radical **A1.29** with **A1.13** one obtains the phenoxy derivative **A1.31**. At the same time **A1.29** can exist as **A1.32** and in this case phenoxy radical **A1.31** attacks the para position generating the quinol ether **A1.33** (Scheme A1.5).[8]

The reaction of 2,4-di-t-butyl-6-phenylphenoxy radical **A1.34** with benzaldehyde **A1.35** involves the abstraction of the aldehyde proton generating the carbonyl radical **A1.37** which couples with **A1.34** to give the ester derivative **A1.38** (Scheme A1.6). Another interesting reaction is the synthesis of the oxygen - substituted oxime **A1.41** from the reaction of **A1.29** with **A1.39** (Scheme A1.7).

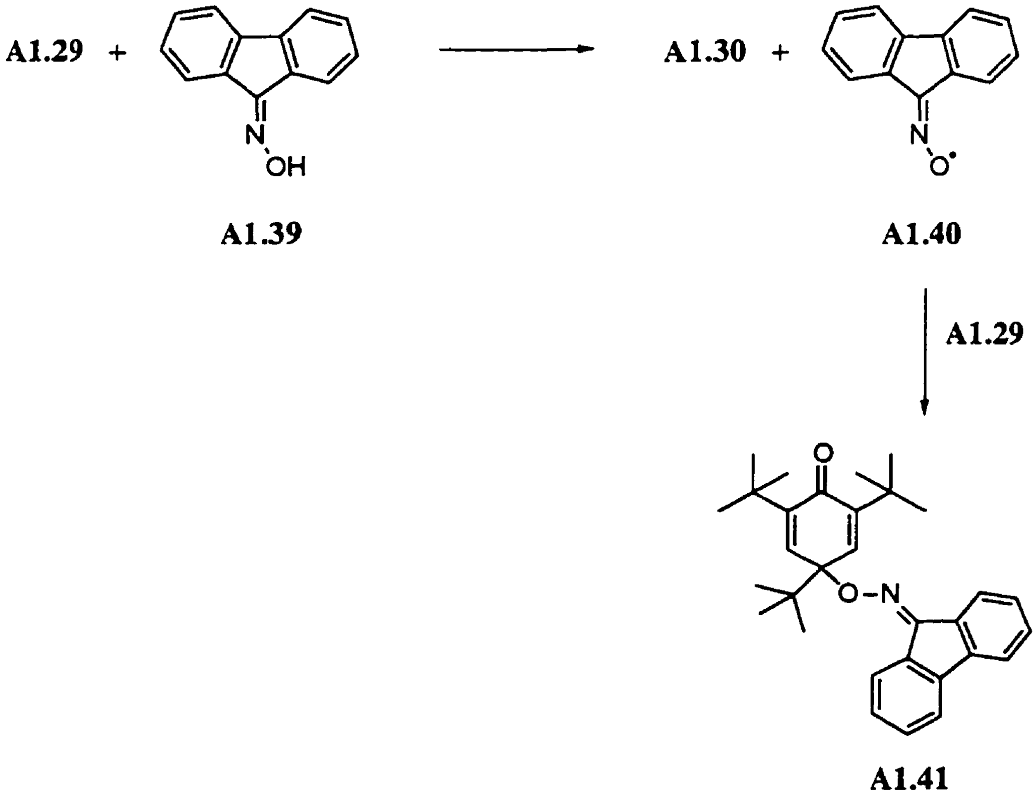
The reaction of phenoxy radicals with organometallics or metals is a good example of an electron transfer reaction. When phenoxy radical **A1.29** reacts with a Grignard reagent **A1.42** an electron transfer reaction occurs generating the phenolate anion **A1.43**, the magnesium salt and a phenyl radical **A1.44** which can undergo a series of reactions. Path A which most probably is the most common reaction path involves the self coupling reaction to the dimer species **A1.45**. The abstraction of a proton from the solvent by the radical compound is another route (path b), generating benzene. An electron transfer reaction with a halide anion to give **A1.8** and the halide radical is yet another route (path c). The radical coupling reaction shown in path d between **A1.29** and **A1.44** results in the formation of ether **A1.46** (Scheme 1.8).[7]

The phenoxy radical chemistry was extended to reaction with diarylmethane compounds (see Chapter A3) with the synthesis of aryl substituted phenols by Dimroth and coworkers.[9-11] These aryl substituted phenols when oxidized were converted to phenoxy radicals that are more stable and have higher oxidation potentials.

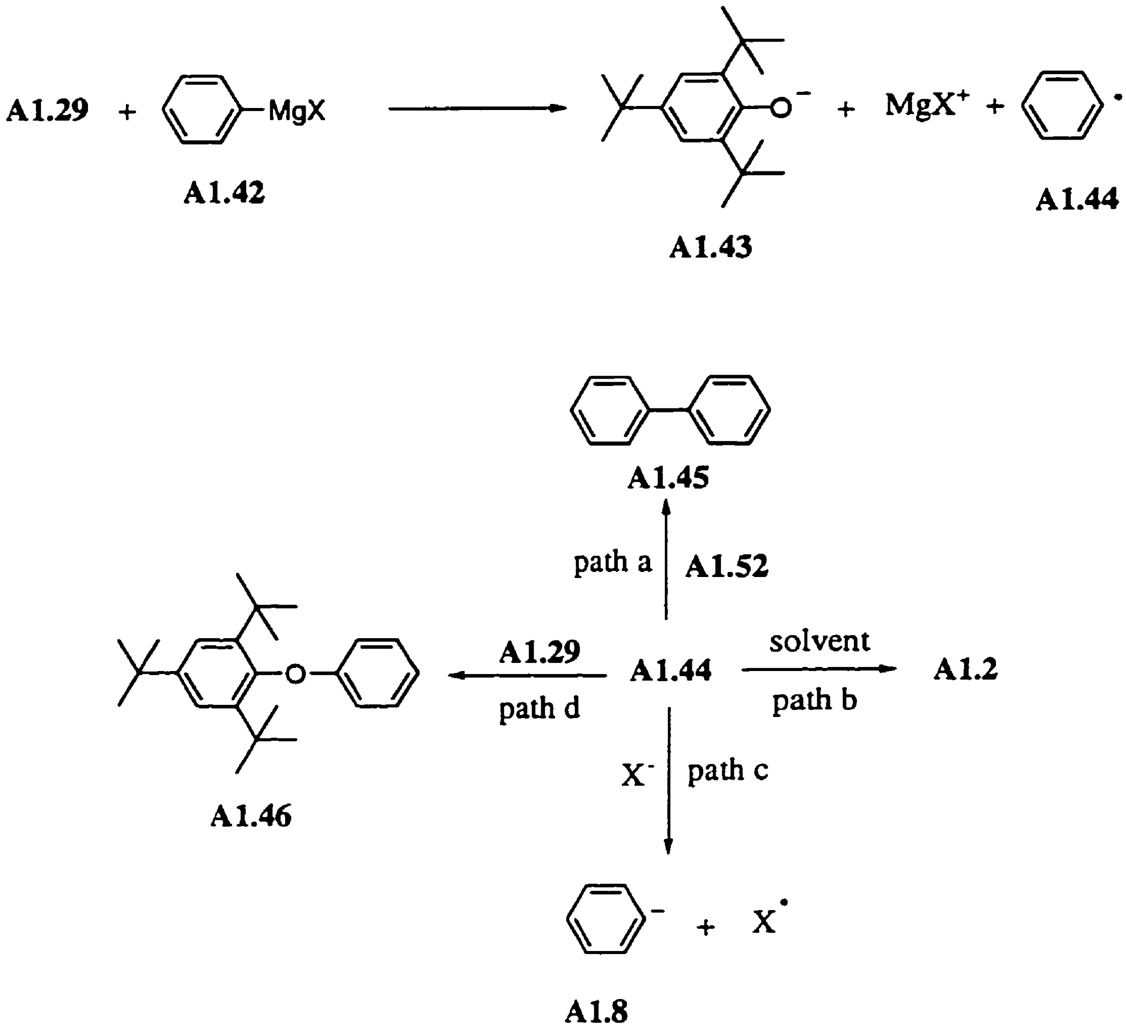
We were interested in exploiting the chemistry of the phenoxy radical with molecules containing activated methylene groups with our novel hindered biphenols. This biphenols should form more reactive and stable phenoxy radicals that have previously been reported.



Scheme A1.6



Scheme A1.7



Scheme A1.8

A1.5 References

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CHAPTER A2

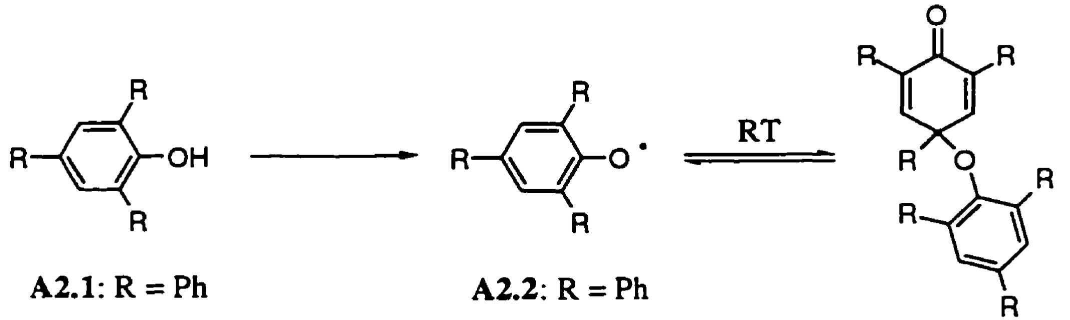
SYNTHESIS AND CHARACTERIZATION OF HINDERED BIPHENOLS AND THEIR BIPHENOXY RADICAL AND QUINONE ANALOGS

A2.1 Introduction

In spite of the immense quantity of work done on hindered phenols, very little effort was directed towards aryl substituted phenols until Dimroth and coworkers in the early 1960's synthesized 2,4,6-triphenylphenol **A2.1** and other aryl substituted phenols.[1-3] These aryl substituted phenols have higher oxidation potentials than the alkyl substituted phenols (e.g. 2,4,6-tri-t-butylphenol **A1.29**),[4] because the phenyl groups are less electron donating than the alkyl groups. These phenyl groups also contribute to resonance delocalization which enhances the stability of the phenoxy radical.

Phenols **A2.1** and **A1.29** are easily oxidized to their corresponding phenoxy radical **A2.2**, and **A1.30**, respectively, using inorganic oxidants such as Ag_2O, MnO_2, PdO_2, or $K_3Fe(CN)_6$.[5] The most effective of these oxidants is $K_3Fe(CN)_6$ which converts the phenol to its corresponding phenoxy radical in quantitative yields.[6,7] The generation of the phenoxy radical is apparent by the appearance of a colored solution, dark red for **A2.2** and blue for **A1.30**. At room temperature these phenoxy radicals are in equilibrium with their quinol ether derivatives **A2.3** and **A2.4** (Figure A2.1).[1,2,5]

Phenoxy radical **A2.2,** when heated in an inert solvent like benzene, dimerizes to form the carbon - oxygen coupled derivative **A2.5** (Scheme A2.1).[2,3] Dimroth *et al* improved the stability of phenoxy radical **A2.2** by substituting t-butyl groups in the para position of the pendant phenyls **A2.6**, therefore eliminating attack at the para position as previously observed with **A2.2.**



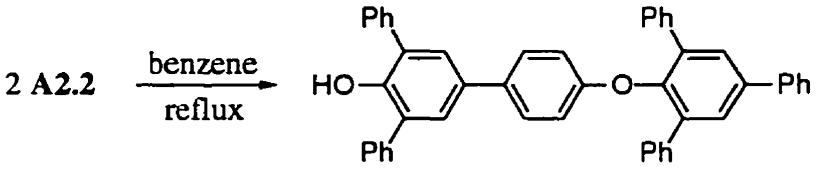
A2.1: R = Ph
A1.29: R = C(CH$_3$)$_3$

A2.2: R = Ph
A1.30: R = C(CH$_3$)$_3$

A2.3: R = Ph
A2.4: R = C(CH$_3$)$_3$

Figure A2.1

At higher temperatures, such as refluxing in 1,2-dichloroethane, a dimer species **A2.7** was obtained.[3] In this case attack occurs at the ortho position of the pendant phenyl (Scheme A2.2).

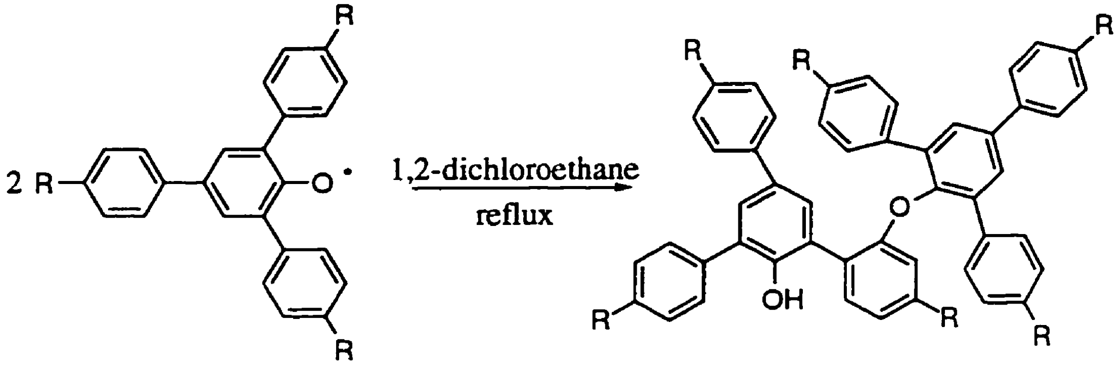


A2.5

Scheme A2.1

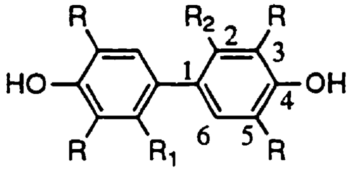
A2.1.1 Goals and Strategies

A series of hindered biphenols **A2.8a-i** (Figure A2.2), which were prepared by an oxidative carbon - carbon coupling reaction of hindered phenols through the para position, were specifically designed so that they would form stable phenoxy radicals. By substituting the meta position of the biphenyl moiety with bulky groups the biphenyl moiety is forced into a nonplanar configuration. This configuration favors the formation of the phenoxy radical, rather than the quinone derivatives which requires a planar configuration (Figure A2.3).[8]



A2.6 $R = C(CH_3)_3$ **A2.7**

Scheme A2.2



A2.8a: R = Ph, $R_1 = R_2$ = Ph

A2.8b: R = Ph, $R_1 = R_2$ = 4-methoxyphenyl

A2.8c: R = Ph, $R_1 = R_2$ = Cl

A2.8d: R = Ph, $R_1 = R_2 = CH_3$

A2.8e: R = Ph, R_1 = H, R_2 = Ph

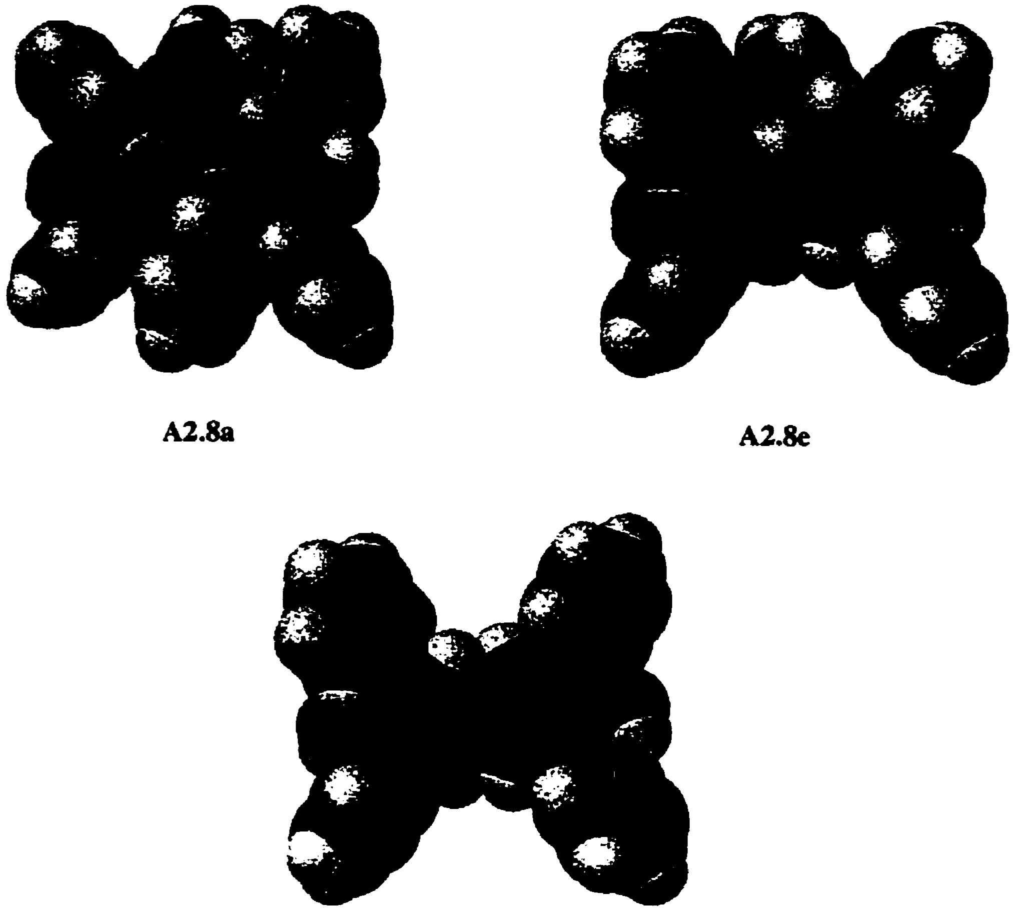
A2.8f: R = Ph, R_1 = H, R_2 = Cl

A2.8g: R = 4-Fluorophenyl, R_1 = H, R_2 = Cl

A2.8h: R = 4-Fluorophenyl, $R_1 = R_2$ = H

A2.8i: R = Ph, $R_1 = R_2$ = H

Figure A2.2



A2.8a

A2.8e

A2.8i

Figure A2.3

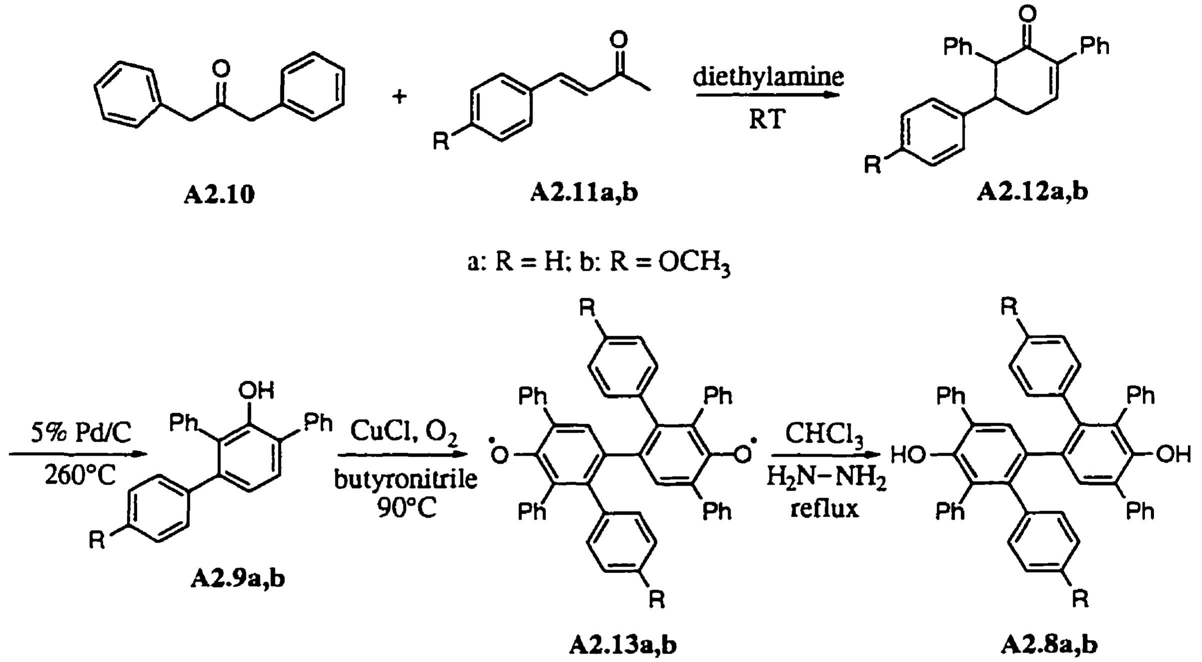
Steric hindrance due to the groups in the meta position also blocks the para position of the biphenyl moiety. This eliminates the possibility of formation of quinol ethers and the carbon - oxygen coupled dimer products.

A2.2 Results and Discussions

A2.2.1 Phenol Synthesis

Phenols **A2.9a,b** were synthesized following the literature procedure.[9,10] A combined Knoevenagel condensation reaction and Michael addition reaction of 1,3-

diphenylacetone **A2.10** with an α,β-unsaturated ketone **A2.11a,b** in diethylamine at room temperature for 45 minutes afforded the cyclohexenone compounds **A2.12a,b** as a mixture of isomers in 90-96% yield. Dehydrogenation of **A2.12a,b** with 5% Pd/C at 260°C yielded phenol **A2.9a,b** in 80-95% yield (Scheme A2.3).

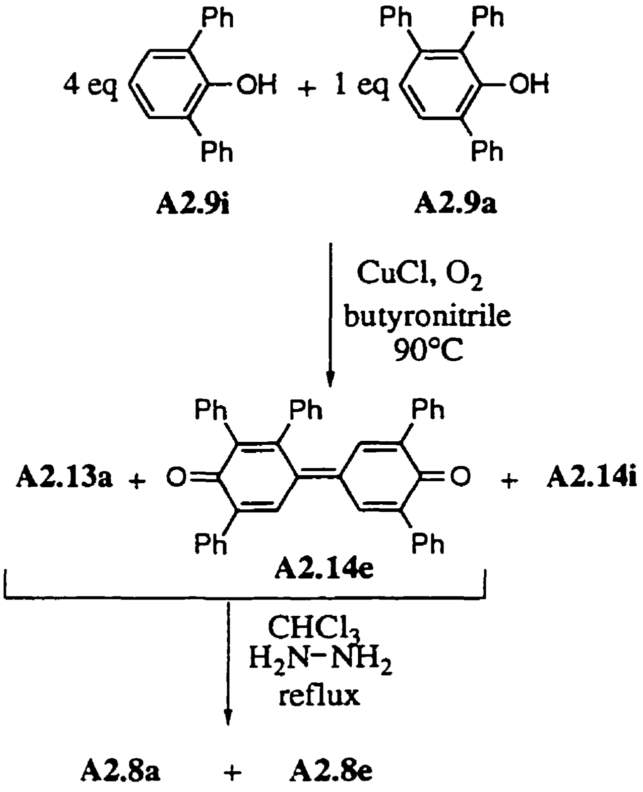


Scheme A2.3

A2.2.2 Biphenol Synthesis

Biphenols **A2.8a,b**[10] & **i** were prepared by an oxidative coupling reaction described by Hay.[11] Phenols **A2.9a,b,i** and CuCl were added to butyronitrile and the solution was heated to 90°C with oxygen bubbling directly into the solution for 6 to 9 hours, depending on the phenol. This afforded either the phenoxy radical **A2.13a,b** or the quinone **A2.14i** (see page 17) which were reduced with hydrazine monohydrate to give the biphenols **A2.8a,b,i** in greater than 60% yield (Scheme A2.3 & A2.5).

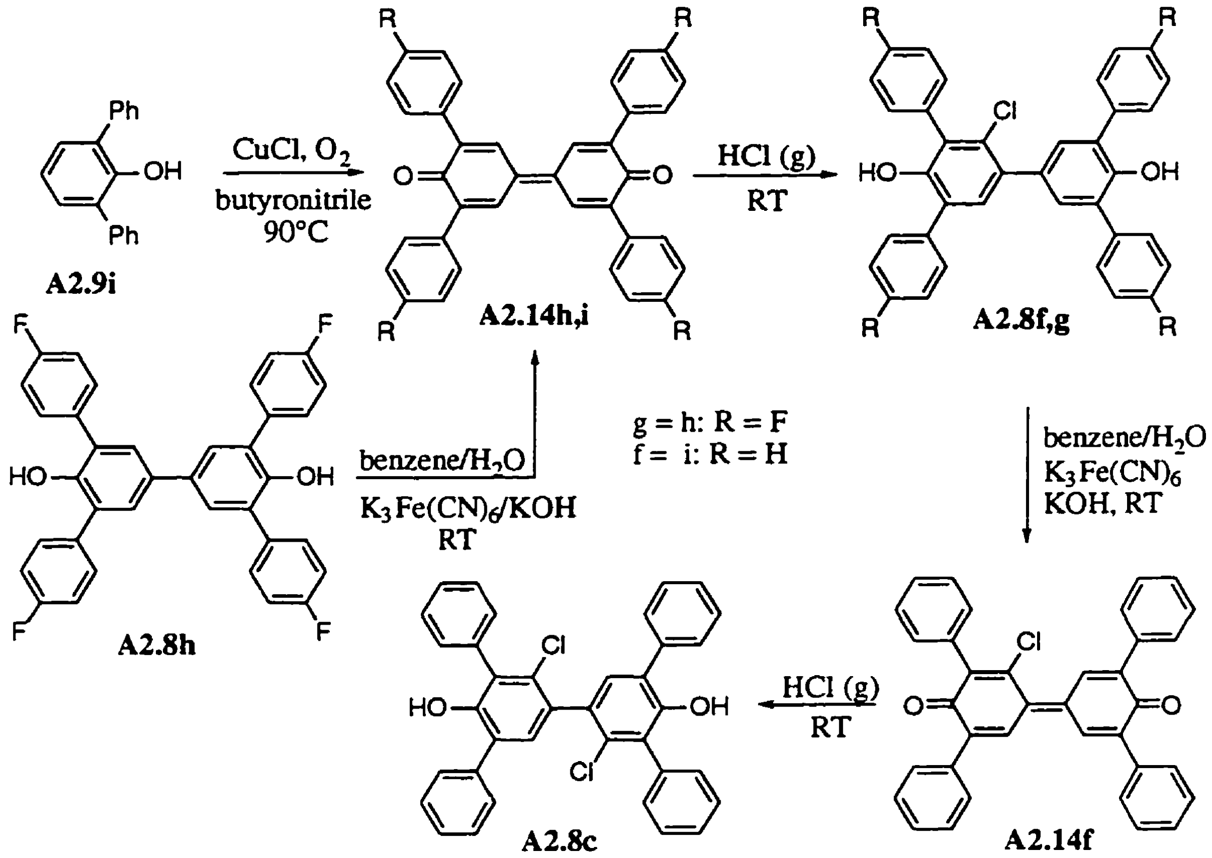
The unsymmetric biphenol **A2.8e** was obtained by reacting phenol **A2.9a** with an excess amount of phenol **A2.9i** under similar conditions as previously mentioned to give 25% of biphenol **A2.8e** and 78% of the quinone **A2.14i** (Scheme A2.4).



Scheme A2.4

The chloro substituted biphenols **A2.8f,g** were prepared in high yields by the procedure described by Becker *et al*[12] which involved bubbling anhydrous HCl gas into a suspension of quinone **A2.14h,i** in a mixture of chloroform and methanol at room temperature for 6-12 hours. The quinone **A2.14h** was generated by oxidizing biphenol **A2.8h** with $K_3Fe(CN)_6$ at room temperature (Scheme A2.5).

Oxidizing biphenol **A2.8f** followed by chlorination by bubbling HCl gas into a suspension of **A2.14f** in chloroform at 50°C afforded **A2.8c** in 92% yield (Scheme A2.5).



Scheme A2.5

A2.2.3 Thermal Properties of the Biphenols

The thermal properties of biphenols **A2.8a-g** were examined by DSC at a stepwise heating rate: 50 to 150°C at 10°C/min , 150 to 200 at 5°C/min and 200 to 340°C at 1°C/min. Biphenols **A2.8b,c,f** all showed one melting point (T_m) in the first and second scan, except for biphenol **A2.8f** where a T_g was obtained in the second scan (Figure A2.4 & A2.5). Two or more melting points were observed for biphenol **A2.8a,e** on the first scan and in the second scan only one T_m and an exothermic peak were obtained. The appearance of the exothermic peak or crystallization peak (T_c) also observed in the second scan of biphenol **A2.8b**, can be explained by either the transformation from the amorphous state to the crystalline state or from one crystalline configuration to a more stable configuration. The thermal properties of the biphenols are listed in table A2.1.

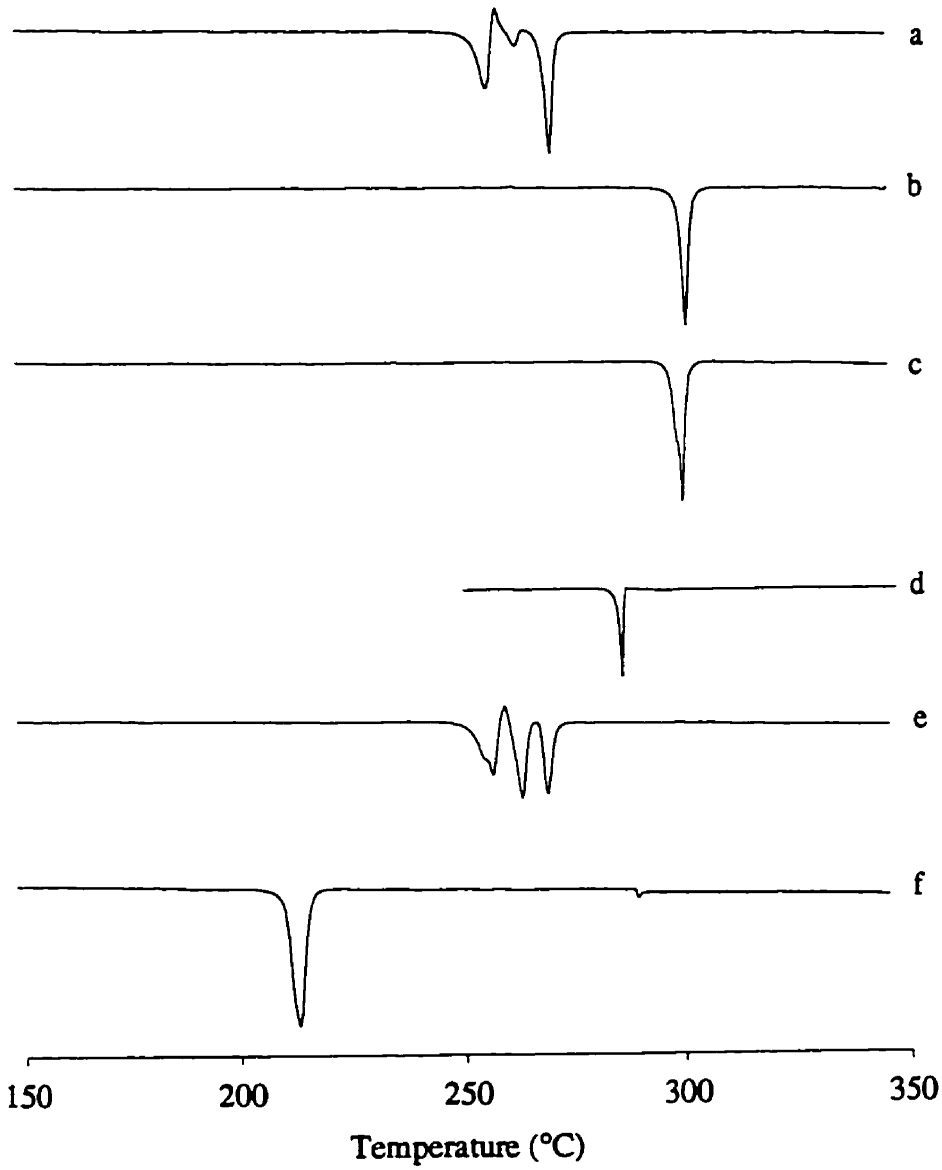


Figure A2.4. DSC traces of biphenols: A) **A2.8a**, b) **A2.8b**, c) **A2.8c**, d) **A2.8d**, e) **A2.8e**, f) **A2.8f** on the first scan.

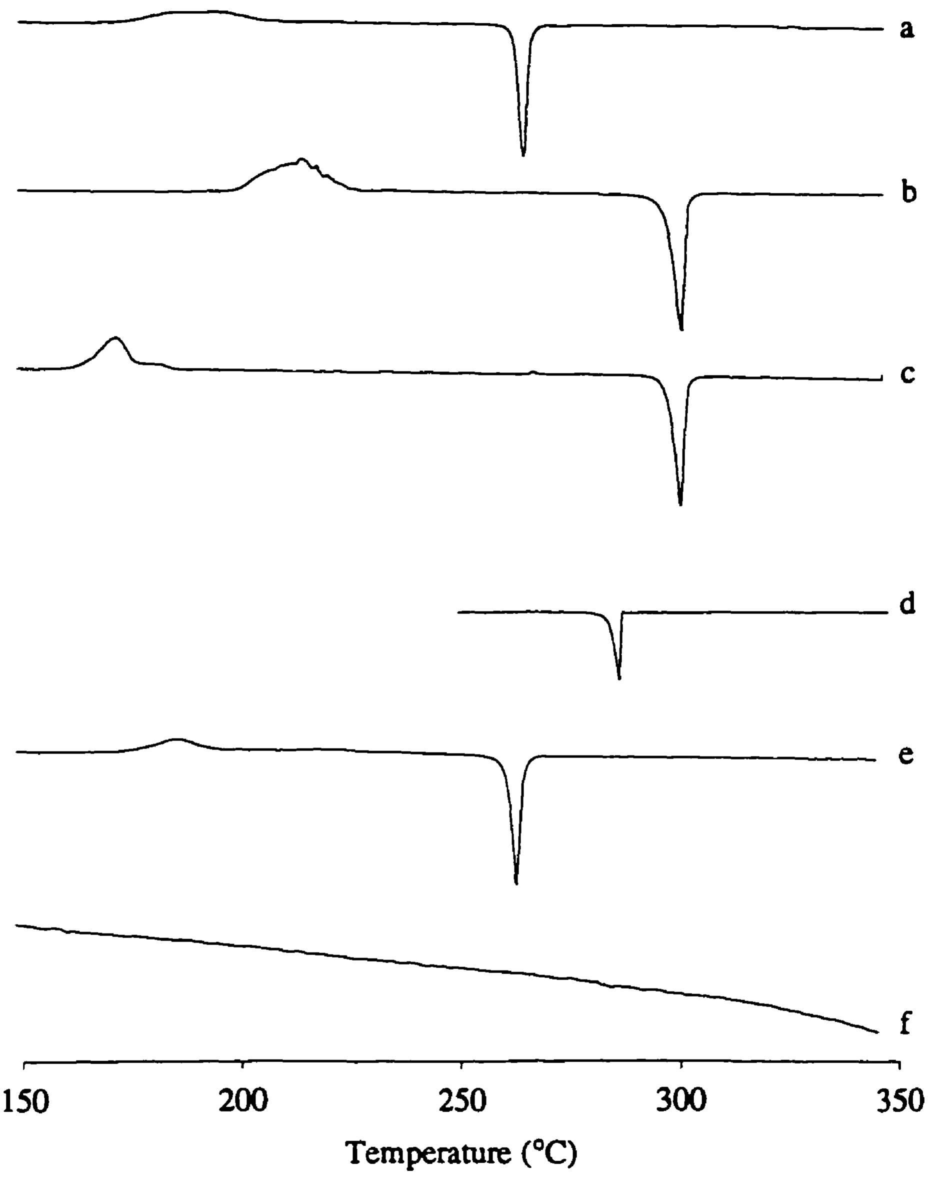


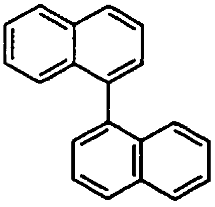
Figure A2.5. DSC traces of biphenols: A) **A2.8a**, b) **A2.8b**, c) **A2.8c**, d) **A2.8d**, e) **A2.8e**, f) **A2.8f** on the second scan.

Table A2.1 Thermal properties of the biphenols.

Entry	1st Heat		2nd Heat		
	T_m (°C)	T_c (°C)	T_m (°C)	T_c (°C)	T_g (°C)
A2.8a	248, 265	--	258	179	--
A2.8b	294	--	292	196	--
A2.8c	294	--	294	177	--
A2.8d	280	--	280	--	--
A2.8e	247, 259, 265	--	256	176	--
A2.8f	207	--	--	--	100
A2.8g[a]	--	--	--	--	--

a) no melting points were observed on the DSC scan, although a melting point of 192-194°C was observed on the Fisher-Johns melting point apparatus.

Organic and inorganic compounds that exhibit two or more melting points brought about by crystallization are quite common. This phenomenon is defined as polymorphism. For example , Badar *et al*[13] have shown that there are at least two crystalline forms for 1,1'-binaphthyl **A2.15**.



A2.15

The trans configuration has a melting point of 157-159°C and is optically active, while the cis configuration is not optically active and has a melting point of 145°C. The trans configuration when heated and cooled recrystallizes to form the more stable cis configuration.

Why certain biphenols exhibit two or more T_m might simply be explained by the method of crystallization and not the structure of the biphenol since all the biphenol monomers are quite similar, and only biphenols **A2.8a,e** exhibit more than one melting point.

A2.2.4 Biphenoxy Radicals

A2.2.4.1 Synthesis

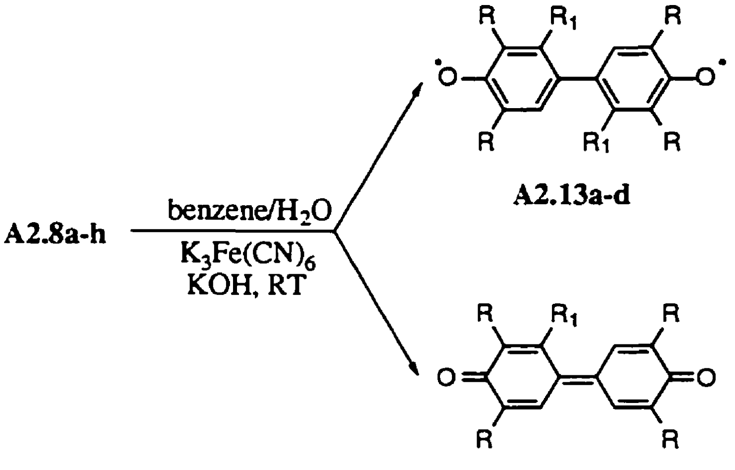
There have been many inorganic reagents used to generate biphenoxy radicals. We limited ourselves to two reagents, Ag_2O and $K_3Fe(CN)_6$, the latter of which was the most efficient and the most practical from the stand point of isolating the biphenoxy radical.

Only biphenols **A2.8a,b** were oxidized using Ag_2O, because the phenoxy radicals were completely soluble in benzene and could be easily separated from excess reagent. Solvents such as carbon tetrachloride and chlorobenzene did not improve the solubility of the other biphenoxy radicals.

Because of the problems of separating the insoluble phenoxy radical from the silver complexes we decided to generate the phenoxy radicals using $K_3Fe(CN)_6$. The biphenols were dissolved in benzene with the addition of a 0.75M aqueous solution of $KOH/K_3Fe(CN)_6$. The organic layer immediately turn dark red in color except for biphenol **A2.8h** which turned black in color. The solution was stirred vigorously at room temperature for 24 hours. Compounds **A2.13a-d** and **A2.14e-h** were isolated in high yields as emerald green crystals except for **A2.14g,h** which gave a brownish red and black powder, respectively (Scheme A2.6). All the oxidized products were dried under high vacuum at room temperature for 6 days.

A2.2.4.2 UV-visible Analysis

Aromatic compounds that are substituted with groups which are in conjugation (e.g. groups with unshared pairs of electron) undergo a bathochromic shift of the aromatic bands. The extent of the shift is dependent on the groups being substituted. In general the order is Ph (highest shift) > OCH_3 > Cl > CH_3 > H.[14] No general pattern was observed for either the biphenols or their corresponding oxidized products, although certain patterns were apparent. Biphenols **A2.8a,b,e** with phenyl substitution in the meta position all showed two Π-Π^* transition bands. The second band at 315 - 318 nm probably corresponds to the Π-Π* transition of the pendant phenyl group at position 2 (Figure A2.2). The bathochromic shift observed when comparing the absorption bands of biphenol **A2.8h** and **A2.8g**, is due to the substitution of a chloro group in the meta position of the biphenyl moiety (Table A2.2).



a: $R = R_1 = Ph$
b: $R = Ph$; R_1 = 4-methoxyphenyl
c: $R = Ph$; $R_1 = Cl$
d: $R = Ph$; $R_1 = CH_3$

e: $R = R_1 = Ph$
f: $R = Ph$; $R_1 = Cl$
g: R = 4-fluorophenyl $R_1 = Cl$

Scheme A2.6

Table A2.2. UV visible absorption bands of the biphenols in chlorobenzene.

Entry	Wavelength λmax (nm)	Molar absorptivity $\varepsilon \times 10^{-4}$ ($M^{-1}cm^{-1}$)
A2.8a	288, 316	2.06, 1.52
A2.8b	290, 317	2.92, 1.93
A2.8c	302	0.89
A2.8d	306	0.63
A2.8e	290, 314	0.98, 1.01
A2.8f	312	0.61
A2.8g	309	0.87
A2.8h	294	1.33

The UV visible spectra of the biphenoxy radicals and the quinones exhibit two bands in the range of 280-290 nm and 490-530 nm which correspond to the Π-Π* and n-Π* transitions, respectively (Table A2.3).

Table A2.3. UV visible absorption bands of the biphenoxy radicals and quinones in chlorobenzene.

Entry	Wavelength	Molar absorptivity
	λmax (nm)	$\varepsilon \times 10^{-4}$ $(M^{-1}cm^{-1})$
A2.13a	288, 502	2.90, 4.37
A2.13b	288, 526	3.74, 4.51
A2.13c	286, 518	1.56, 3.14
A2.13d	288, 502	1.34, 0.82
A2.14e[a]	288, 498	6.97, 4.91
A2.14f[a]	284, 495	1.59, 4.44
A2.14g[a]	286, 502	1.51, 4.59
A2.14h[a]	286,496	2.00, 5.15
A2.14i[a]	318,460	1.77, 2.22

a) the absorptivity values are unreliable values due to solubility problems.

With the oxidized biphenol products, as expected no general pattern was observed since the products can either be in the biphenoxy or quinone form at room temperature. ESR data discussed in the following section clearly identifies which biphenols are converted to their biphenoxy radical analogues. Certain patterns were quite obvious. The methoxy groups contributed to the bathochromic shift of the n-Π* transition band of **A2.13b** to 526 nm compared to **A2.13a** (λmax = 502 nm). Quinones **A2.14f** and **A2.14g** have a similar n-Π* transition band at 495 nm and 496 nm, respectively. It appears that the four fluoro groups at the para position of the pendent phenyls contribute in an equal amount to the wavelength shift as the chloro group in the meta position of the biphenyl moiety. By substituting a chloro group in the meta position of quinone **A2.14g** a shift to lower wavelength was observed for quinone **A2.14h**.

A2.2.4.3 Electron Spin Resonance (ESR) Analysis

Electron spin resonance is a useful technique for the identification of organic and inorganic materials with unpaired electrons such as radical, radical anion and radical cation species.[15]

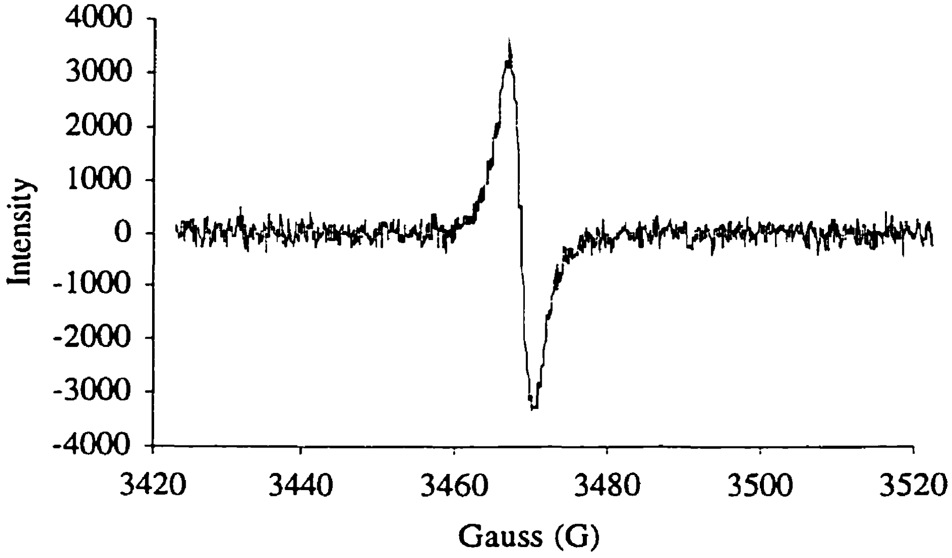


Figure A2.6. ESR spectrum of **A2.13a** in toluene.

The broad singlet obtained from ESR analysis (Figure A2.6) of the oxidized biphenols **A2.8a-d** clearly shows the generation of a radical species. Their *lande g-factor* values listed in table A2.4 were calculated using equation (1),

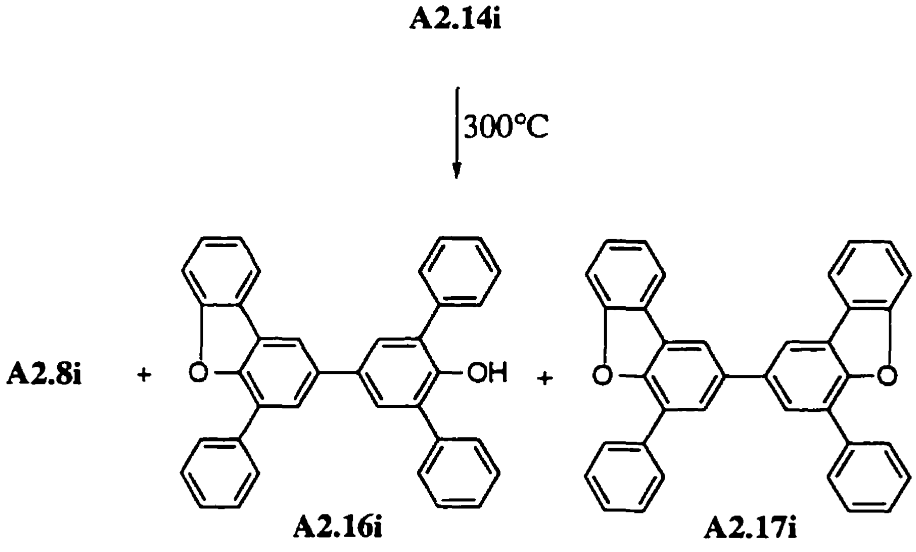
$$h\nu = g\beta H \tag{1}$$

where h (Plancks constant) = $6.626176\text{x}10^{-34}$ J/Hz; ν = applied frequency (Hz); β (applied field) = $9.2741\text{x}10^{-24}$ J/T; H = field value (T); The oxidized biphenols **A2.8e-h** showed no signal, indicating that these products exist as quinone derivatives at room temperature.

Table A2.4. ESR values for the biphenoxy radicals in toluene.

Entry	Lande g-Factor
A2.13a	2.0059
A2.13b	2.0054
A2.13c	2.0062
A2.13d	2.0053

Carbon - oxygen coupled products (see Chapter A3) are still obtained with the quinones **A2.14e,f** at temperatures in the range of 60 to 90°C. This suggests that these quinones including **A2.14g** exist as biphenoxy radicals at higher temperatures. The generation of biphenoxy radicals at higher temperatures has previously been suggested by Hay.[11] He proposed that quinone **A2.14i** must go through a radical intermediate at 300°C in order to obtain the cyclized products **A2.16i and A2.17i**, and biphenol **A2.8i** (Scheme A2.7).



Scheme A2.7

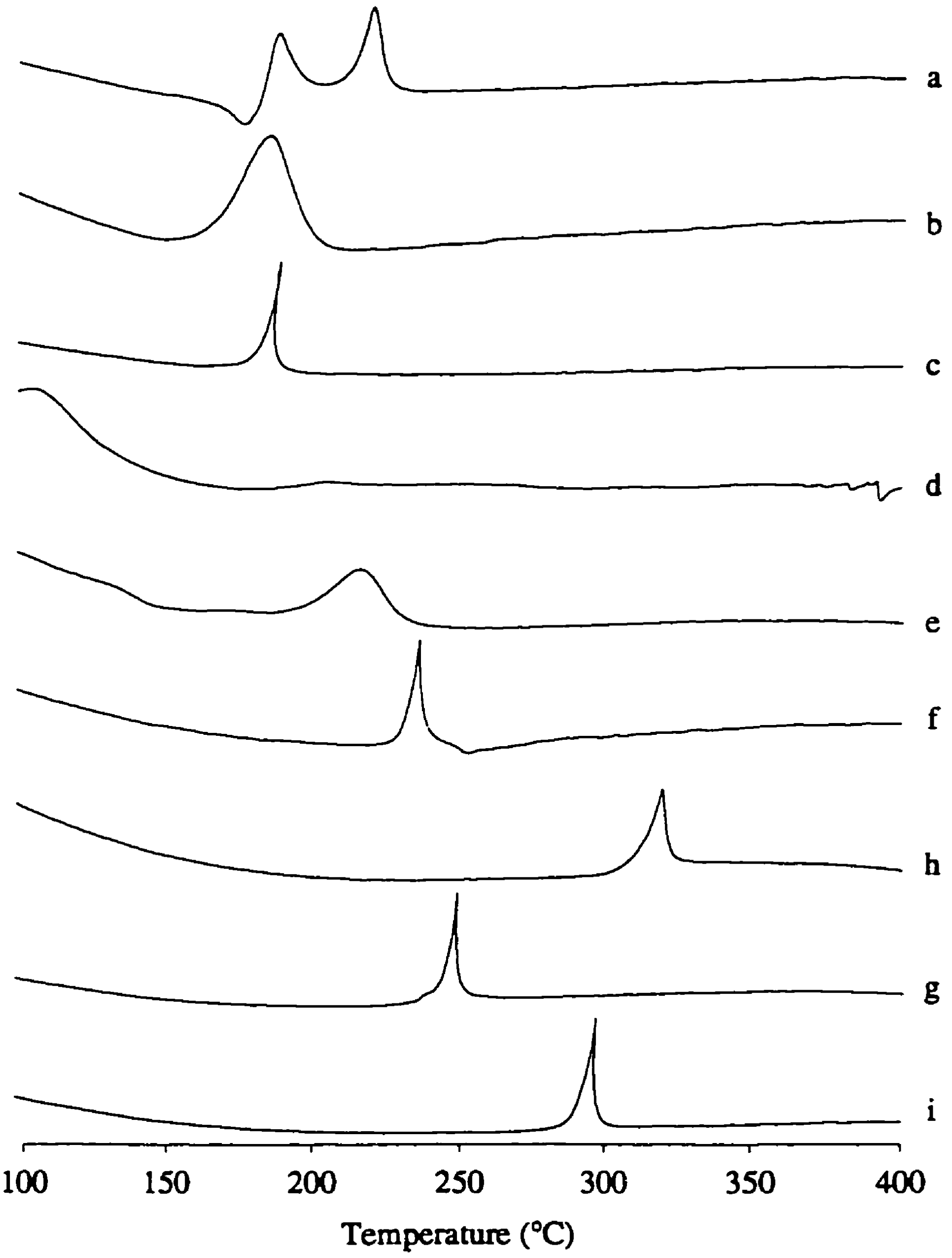


Figure A2.7. DTA traces of the oxidized biphenols: A) **A2.13a**, b) **A2.13b**, c) **A2.13c**, d) **A2.13d**, e) **A2.14e**, f) **A2.14f**, g) **A2.14g** , h) **A2.14h**, i) **A2.14i**.

A2.2.4.4 Thermal Properties of Oxidized Biphenols

Thermal analysis by DTA of the oxidized products all showed an exothermic peak (T_{exo}) in the first scan (Figure A2.7), while no peaks were observed in the second scan. In the case of **A2.13d** no signal was observed. HPLC analysis of the residue showed that a chemical reaction had occurred generating many products. By comparison with authentic samples the original biphenol, and the mono-cyclized and di-cyclized products were identified.

The phenoxy radicals **A2.13a-c** have T_{exo} in the range of 186-189°C. Only **A2.13a** has a second T_{exo} peak at 221°C. The quinones **A2.14e,f,g** have T_{exo}'s in the range of 216 to 249°C, while quinone **A2.14h** and **A2.14i** have T_{exo}'s at 320°C and 297°C, respectively (Table A2.5).

Table A2.5. Thermal properties of the biphenoxy radical and quinone s.

Entry	T_{exo}[a] (°C)
A2.13a	189, 221
A2.13b	186
A2.13c	189
A2.13d	no exothermic peak
A2.14e	230
A2.14f	216
A2.14g	249
A2.14h	320
A2.14i	297

a) T_{exo} values were obtained at maximum peak height.

As expected the biphenoxy radicals have the lowest T_{exo}, because no energy is required to generate the radical species as would be the case for the quinones. The lower T_{exo} observed for quinones **A2.14d,f,g** compared to **A2.14h,i** is due to the presence of the bulky groups in the meta position which twist the biphenyl configuration, thus favoring the formation of the biphenoxy radical. Minimization calculations using the CAChe software have confirmed the twisted geometry of the biphenyl moiety of biphenol **A2.8e-g**.[8] Less

A2.2.4.4 Thermal Properties of Oxidized Biphenols

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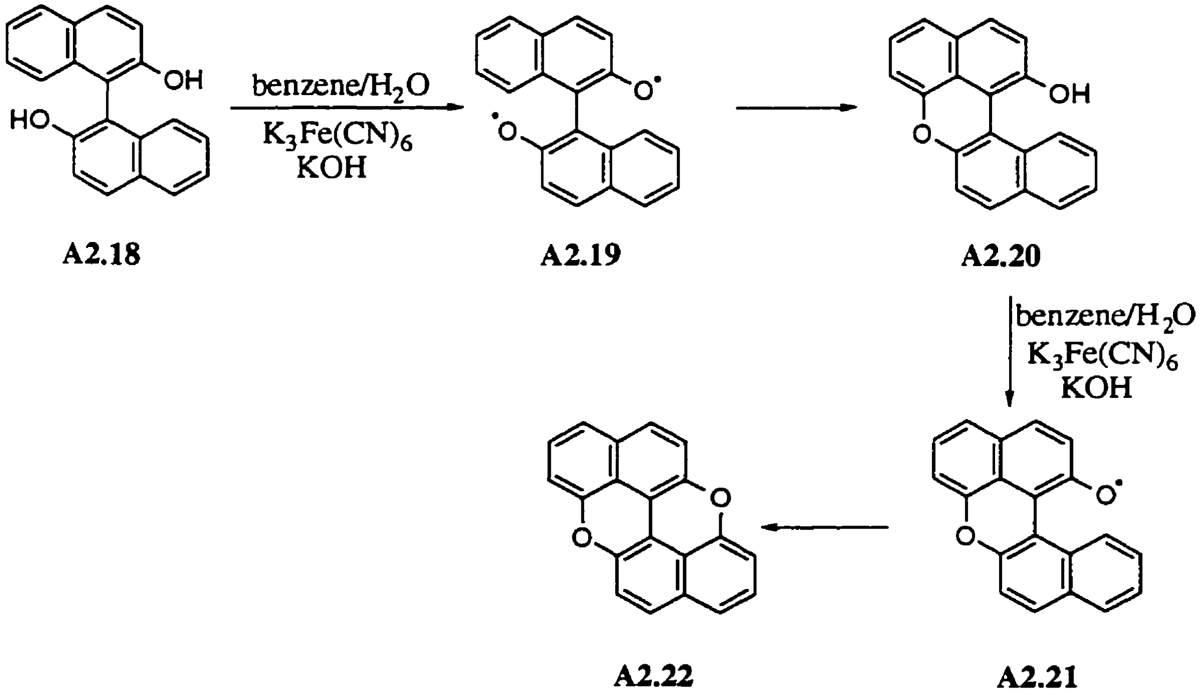
A.2.2.5 Thermolysis of the Oxidized Biphenols

All previous phenoxy radicals suffered from deactivation due to: 1) dimerization either to the quinol ether or to the carbon - oxygen coupled dimer, 2) an intramolecular reaction to form the benzofuran derivative[11]. For example, the oxidized species of 1,1'-binaphthanol **A2.18** when heated converts to **A2.22** (Scheme A2.8),[16] as does quinone **A2.14i** when heated to 300°C (Scheme A2.7).[11]



Scheme A2.8

In our hindered biphenoxy radicals there is enhanced steric hindrance blocking the para position of the biphenol, and the pendant phenyls at the 2 and 3 position can not be planar. We therefore expected to suppress the above side reactions either completely or to a point where these compounds could be used effectively as reagents in chemical reactions.

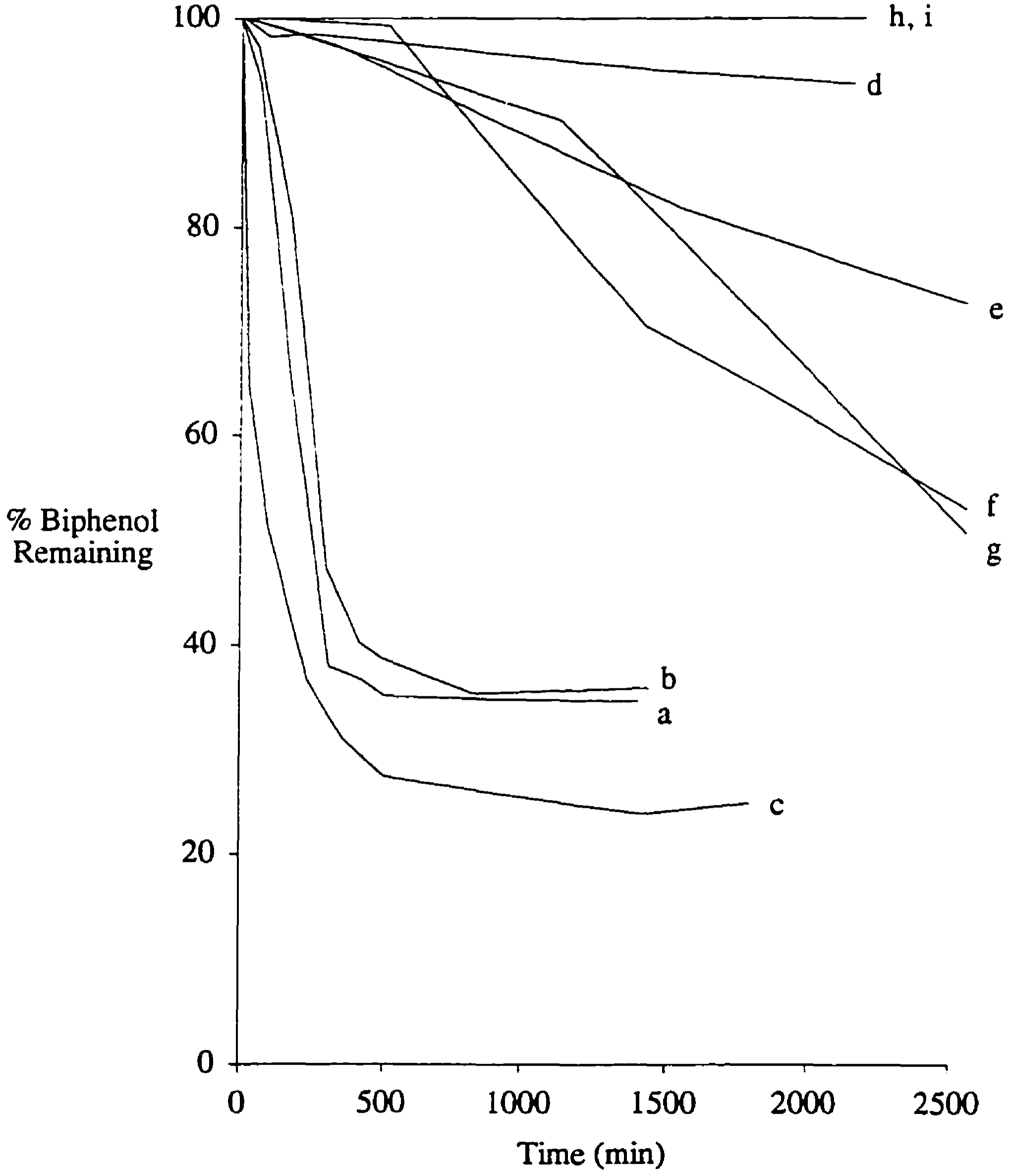
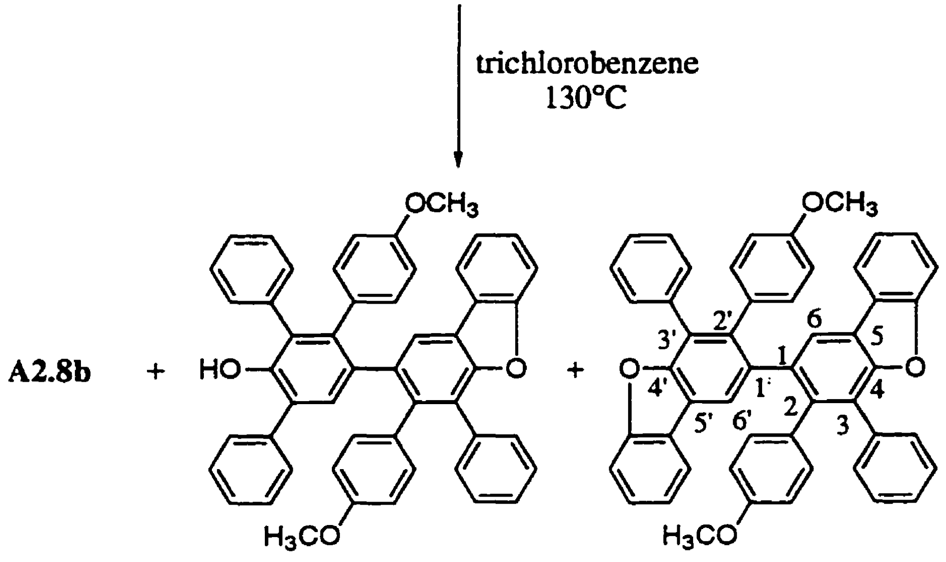


Figure A2.8. Thermal stability of the oxidized biphenols at 130°C: A) **A2.13a**, b) **A2.13b**, c) **A2.13c**, d) **A2.13d**, e) **A2.14e**, f) **A2.14f** , g) **A2.14g**, h) **A2.14h**, i) **A2.14i**.

In order to determine the stability of these oxidized products, they were dissolved in 1,2,6-trichlorobenzene at a concentration of 0.025M and heated to 130°C. The percent disappearance of the biphenol, which was obtained by treating an aliquot solution (5 µl) of the reaction mixture with 1 µl of hydrazine monohydrate was monitored by HPLC (Figure A2.8). The least stable are the biphenoxy radicals **A2.13a-c**, as would have been expected since they have lower T_{exo} values. The most stable oxidized compound, besides **A2.14i**, was **A2.14d**. The electron donating methyl groups in the meta position of compound **A2.13d** might lower the oxidation potential of the biphenoxy radical to a level which disfavors the intramolecular reaction. In general all the mono-substituted compounds were more stable than the di-substituted phenoxy radicals. This is in agreement with the higher T_{exo} observed for these compounds (Table A2.5).

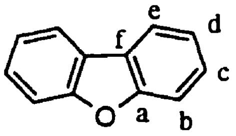
A2.13b



A2.23b **A2.24b**

Scheme A2.9

Three products were isolated from heating the biphenoxy radicals **A2.13b** at 130 °C. The original biphenol **A2.8b**, and the cyclized products **A2.23b** and **A2.24b** were isolated in 24%, 25% and 22% yield, respectively (Scheme A2.9). The ^{1}H NMR doublet at 7.78 ppm and the ^{13}C peak at 111.55 ppm of compounds **A2.23b** and **A2.24b** are characteristic of the proton at position e and the carbon at position b of the dibenzofuran compound **A2.25**.



A2.25

MALDI-TOF -MS analysis (description of this technique is given in Part B) also showed that no higher molecular weight product formed, indicating an intramolecular reaction is occurring and not an intermolecular reaction. Based on HPLC results all the oxidized biphenol compounds behaved similarly. They all cyclized to the dibenzofuran derivatives except for quinones **A2.14h,i** where no reaction occurred.

Our proposed mechanism (Figure A2.9) is an intramolecular attack of the oxygen radical at the ortho position of the pendant phenyl group located at position 5 and 5' (Scheme A2.9), since this phenyl is free to rotate into a planar configuration. The pendent phenyl group at position 3 is not free to rotate because of the steric hindrance from the adjacent phenyl group, confirmed by molecular mechanics calculations for biphenol **A2.8a**. We believe that aromatization of the pendant phenyl group by dehydrogenation occurs by an intermolecular abstraction of the proton at the ortho position by the biphenoxy radical to give the cyclized products.

A.2.3 Conclusions

A series of novel hindered biphenol specifically designed to form radical species were synthesized through an oxidative carbon - carbon coupling reaction of a variety of substituted phenols. These biphenols were oxidized at room temperature using $K_3Fe(CN)_6$

generating either the phenoxy radical or the quinone compound depending on the biphenol.

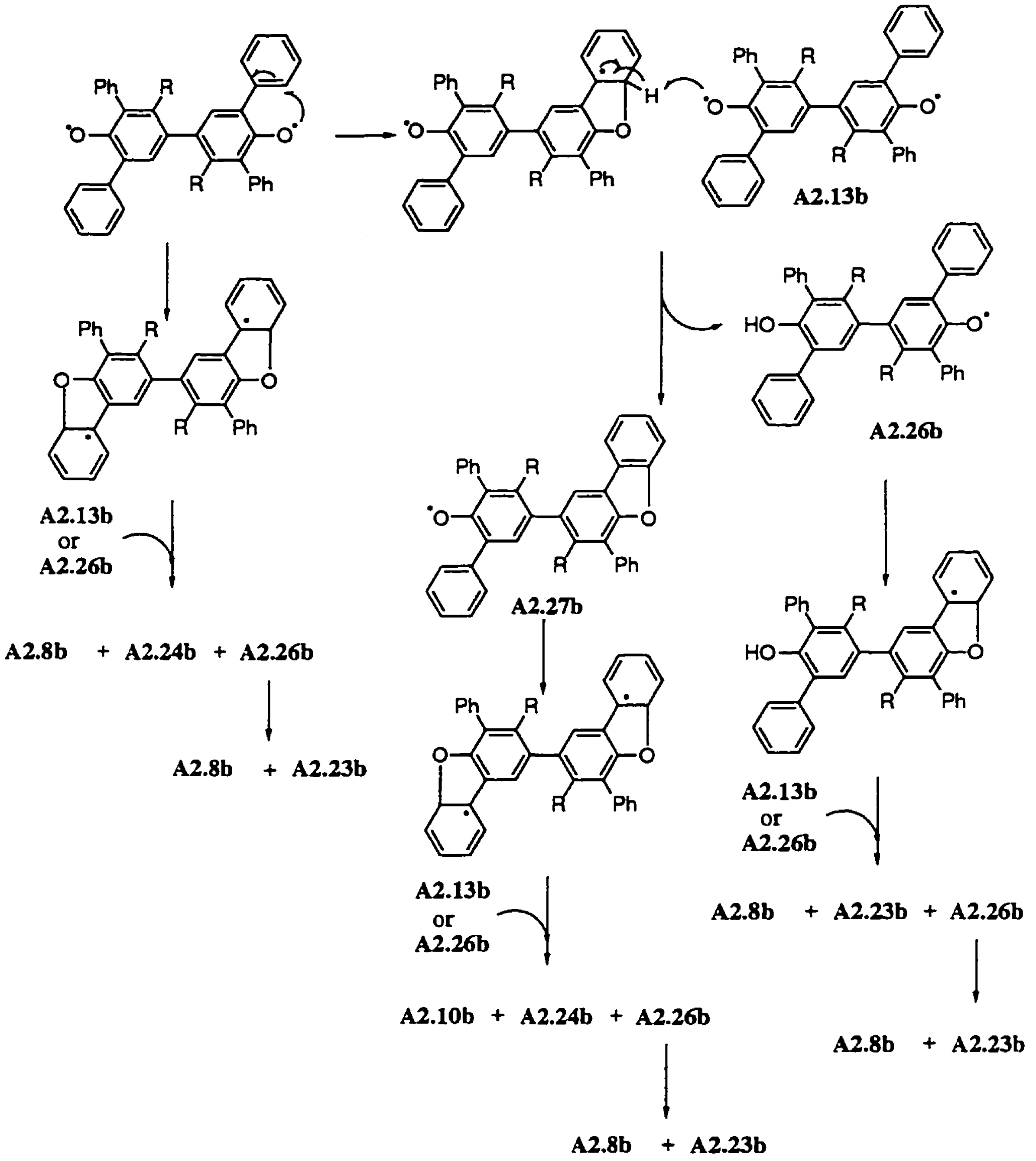


Figure A2.9

The quinones **A2.14e-g** appear to exist in the radical form at higher temperatures (60 to 90°C) based on the intramolecular cyclization reaction and the carbon - oxygen coupled product obtained (see Chapter A3), which does not occur with quinone **A2.14i**.

These oxidized products have shown greater stability than previously synthesized phenoxy radicals by eliminating the possibility of formation of a quinol ether or a carbon - oxygen coupled dimer. The longer lifetimes allow the use of these compounds as reagents in organic reactions, as will be shown in the subsequent chapters.

A2.4 Experimental Section

Materials

Diethylamine, trans-cinnamaldehyde, trans-4-methoxycinnamaldehyde, 1,3-diphenylacetone, 5% palladium on activated carbon, and butyronitrile were purchased from the Aldrich Chemical Co. Copper chloride and reagent grade solvents were obtained from Caledon Laboratories Ltd.. Anhydrous hydrogen chloride gas was purchased from Matheson Gas Products. All the reagents and solvents were used without further purification. Biphenols 2,2'-dimethyl-3,3'-5,5'-tetraphenyl-1,1'-biphenyl-4,4'-diol and 3,3',5,5'-tetra-((4-fluorophenyl)-1,1'-biphenyl-4,4'-diol were prepared in our laboratory by Dr. W.-Gi Kim and Dr. H. Yang, respectively.

Instruments

Elemental analyses were performed by Fine Analysis Laboratories Ltd., Hamilton, Ontario. All ^{1}H and ^{13}C NMR were obtained on a Varian Unity 500 spectrometer. High performance liquid chromatography (HPLC) analyses were carried out on a Milton Roy CM4000 pump equipped with a reverse phase silica column and a UV detector set at 254 nm; methanol was used as the eluent at a flow rate of 1 ml/min. Thermal analyses were obtained on the Seiko 220DSC and 220 TGA/DTA instrument at a heating rate of 20°C/min unless otherwise stated. UV visible analyses were performed on a HP8452A diode array spectrometer. Electron spin resonance spectra (ESR) were recorded on a Bruker ESP 300E spectrometer operating at a microwave frequency of 9.75 GHz. The external reference was 1,1-diphenyl-2-picrylhydrazyl (DPPH) with a *lande g-factor* g = 2.0036. Melting points were also determined on a Fisher-Johns melting point apparatus. Mass spectra were recorded on a Kratos MS25RFA spectrometer. Pure 2,6-diphenylphenol was supplied by the General Electric Company.

Biphenol Synthesis

2,2',3,3',5,5'-Hexaphenyl-1,1'-biphenyl-4,4'-diol **A2.8a**.

The literature procedure for the preparation of biphenol **A2.8a**[9,10] was modified as follows. Trans- cinnamaldehyde (92.80 g; 0.70 mol) and 1,3-diphenylacetone (148.00 g; 0.70 mol) were slowly stirred using a mechanical stirrer at 50°C until all the 1,3-diphenylacetone melted and a homogenous mixture was obtained (approximately 30 minutes). To the cooled solution 50 mL of diethylamine was added. The reaction is exothermic and within 15 to 20 minutes a yellow solid formed. The crude product was recrystallized twice from 95% ethanol to give 203.10 g (89%) of 2,3,6-triphenylcyclohexenone **A2.12a** (mixture of isomers) as white needles. Cyclohexenone **A2.12a** (35.00 g, 0.11 mol) was aromatized to its corresponding phenol by reacting with 5% of palladium on activated carbon (2 g) at 260°C for 25-30 minutes. The hot mixture was poured slowly into ethyl acetate, filtered through celite, the filtrate was evaporated to dryness and the solid residue was stirred overnight in 95% ethanol. The solution was filtered and the crude product was recrystallized from ethyl acetate to give 147.20 g (65%) of **A2.9a** as white flakes: m.p. 162-164°C (lit. m.p. 164°C).[10] Oxygen gas was bubbled into a solution of **A2.9a** (50.00 g, 0.16 mol), CuCl (4.00 g, 0.04 mol) and 500 mL of butyronitrile at 90°C for 8 hours. The dark red solution was filtered and the filtrate was evaporated to dryness. The red residue consisting of a mixture of biphenol and biphenoxy radical was dissolved in 500 mL of chloroform and reduced with 5 mL of hydrazine monohydrate at reflux temperature. The solution become colorless within 6 hours, was filtered and the solvent was evaporated The gummy crude product was treated with methanol and left stirring overnight. The pale yellow product was filtered and recrystallized twice from acetonitrile and then from a chloroform - methanol solution to give 31.71 g (63%) of **A2.8a** as white flakes: T_m 248, 265 °C (lit. T_m 248, 259 °C)[10]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 - 7.36 (m, 10 H), 7.28 - 7.30 (m, 2H), 7.19 - 7.23 (br s, 4H), 7.17 (s, 2H), 7.15 (s, 4H), 7.00 (br s, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.20, 140.48, 139.44, 137.69, 135.79, 133.79, 132.68, 131.25 (broad peak), 129.31, 128.44, 128.17, 127.24, 127.07, 126.88, 126.35, 125.70; Analysis calc'd for $C_{48}H_{34}O_2$: C, 89.69; H, 5.33; found: C, 89.82; H, 5.76.

2,2'-Bis-(4-methoxyphenyl)-3,3',5,5'-tetraphenyl-1,1'-biphenyl-4,4'-diol **A2.8b**.

The title compound was prepared by the method described by Kim.[10] The crude phenol product was dissolved in hot ethyl acetate and filtered. Note that care must be take when filtering to remove the Pd/C residue because the product precipitates out of solution quite rapidly. The product was recrystallized from ethyl acetate to give 49.55 g (83%) of **A2.9b** as white needles: m.p. 171-175°C (lit. m.p. 173-175°C)[10]. Biphenol **A2.8b** obtained from the oxidative coupling reaction was filtered and recrystallized from a solution of chloroform - methanol to give 39.58 g (83%) of **A2.8b** as a white powder: T_m 294°C (lit. m.p. 305-307°C)[10]; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.61 (s, 2H, OH), 7.29 - 7.32 (t, 5H), 7.23 - 7.26 (m, 4H), 7.18 (d, 5H, J = 7.3 Hz), 7.10 (br s, 4H), 6.83 (br d, 5H, J = 6.8 Hz), 6.76 (s, 3H), 6.67 (d, 4H, J = 8.8 Hz), 3.66 (s, 6H, OCH_3); ^{13}C NMR (500 MHz, DMSO-d_6) δ 157.02, 148.81, 140.15, 138.46, 137.46, 133.19, 132.35, 132.22, 131.29, 130.78, 129.18, 127.86, 127.65, 127.36, 126.59, 126.04, 54.90 (OCH_3).

2,2'-Dichloro-3,3',5,5'-tetraphenyl-1,1'-biphenyl-4,4'-diol **A2.8c**.

Biphenol **A2.8f** (21.02 g, 40.10 mmol) was dissolved in 600 mL of benzene at room temperature under an atmosphere of nitrogen. To this solution was added 450 mL of an 0.84 M aqueous solution of $K_3Fe(CN)_6$ and KOH. The solution was stirred for 24 hours. The solid green product was filtered, washed several times with water (3x200 mL), and dried. The organic filtrate was extracted with water (3x100 mL), dried over sodium sulfate, filtered and the filtrate was evaporated to dryness. The isolated products were combined to give 20.20 g (96%) of **A2.14f**. A three neck round bottom flask was charged with **A2.14f** (20.20 g, 38.60 mmol), and 1.3 liter of chloroform. The dark red solution was heated to 50°C and anhydrous HCl gas was bubbled directly into the reaction mixture for 8 hours. The colorless solution that was obtained was evaporated to dryness and the crude product was recrystallized from methylene chloride to give 20.51 g (92%) of **A2.8c** as white flakes: T_m 294°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59-7.61 (d, 4H, J = 7.3 Hz), 7.51-7.54 (m, 4H), 7.41-7.47 (m, 10H), 7.37 (s, 2H), 7.32-7.35 (m, 2H), 5.19 (s, 2H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.05, 136.81, 134.16, 132.48, 132.39, 131.37, 130.75, 130.30, 129.26, 129.21, 128.72, 128.56, 127.93, 127.66, 126.73; MS (EI Direct Inlet at 300 °C) *m/e* 559.94 (M^++2, 72), 558.94 (M^++1, 40), 557.94 (M^+, 100), 279.08 (14); Analysis calc'd for $C_{36}H_{24}Cl_2O_2$: C, 77.28; H, 4.32; found: C, 78.10; H, 4.30.

2,3,3',5,5'-Pentaphenyl-1,1'-biphenyl-4,4'-diol **A2.8e**.

A one liter three-neck round bottom-flask was charged with **A2.8a** (20.6 g, 63.8 mmol), 2,6-diphenylphenol **A2.8i** (63.12 g, 256.30 mmol), CuCl (8.63 g, 87.1 mmol), and 800 mL of butyronitrile. The solution was heated to 90°C and oxygen was bubbled directly into the reaction mixture for 8 hours. The dark red suspension was cooled and filtered to remove 49.11 g (79%) of **A2.14i**. The dark red filtrate solution consisting of a mixture of biphenol and biphenoxy radical was evaporated to dryness, redissolved in 500 mL of chloroform and reduced with 5 mL of hydrazine monohydrate at reflux for 6 hours. The colorless solution was evaporated to dryness to give an oily product which was treated with methanol and left stirring overnight. The crude product which contains approximately 20% of HPBP as the major impurity was recrystallized 6 times with acetonitrile to give 7.9 g (25%) of **A2.8e** as a white powder: T_m 247, 259, 266°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.68 (d, 2H, $J^2 = 6.8$ Hz), 7.53 (s, 1H), 7.44-7.47 (t, 2H), 7.08-7.40 (m, 19H), 7.03 (s, 2H), 6.93-6.95 (m, 2H), 5.28 (s, 1H, OH), 5.23 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.94, 148.49, 140.14, 139.74, 138.61, 138.45, 137.16, 133.29, 132.33, 131.23, 131.17, 130.90, 131.13, 129.41, 129.45, 129.26, 128.17, 127.94, 127.36, 127.18, 126.86, 126.66, 126.19, 125.65; MS (EI Direct Inlet at 350 °C) *m/e* 567.06 (M^++1, 46), 566.07 (M^+); Analysis calc'd for $C_{42}H_{30}O_2$: C, 89.17; H, 5.17; found: C, 89.04; H, 5.38.

2-Chloro-3,3',5,5'-tetraphenyl-1,1'-biphenyl-4,4'-diol **A2.8f**.

Biphenol **A2.8f** was prepared following a literature procedure.[12] A three neck round bottom flask was charged with **A2.8i** (46.23 g, 94 mmol), 310 mL of methanol and 920 mL of chloroform. The solution was stirred at room temperature and anhydrous HCl gas was bubbled into the dark red suspension for 6 hours. A colorless solution was obtained and evaporated to dryness. The crude product was redissolved in chloroform and this organic solution washed and neutralized with a saturated aqueous solution of sodium bicarbonate (3 x 100 mL). The organic layer was dried over $MgSO_4$ and filtered, the filtrate was evaporated to dryness and the pale yellow solid was recrystallized from acetonitrile to give 46.13 g (92 %) of **A2.8f** as white crystals: m.p. 207-210°C (lit. m.p. 208-210°C)[12]; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.55 - 7.63 (dt, 8H), 7.37 - 7.51 (m, 15H), 5.48 (s, 1H, OH), 5.12 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.57, 148.53, 137.25, 136.72, 134.30, 132.70, 132.02, 131.13, 131.03, 130.32, 129.25, 129.13, 129.07, 128.75, 128.72, 128.56, 128.45, 128.24, 128.16, 127.58, 127.55, 126.95; Analysis calc'd for $C_{36}H_{25}ClO_2$: C, 82.35; H, 4.80; found: C, 81.79; H, 5.02.

2-Chloro-3,3',5,5'-tetra-(4-fluorophenyl)-1,1'-biphenyl-4,4'-diol **A2.8g**.

To a vigorously stirring solution of **A2.8h** dissolved in benzene at 60°C was added a 0.75 M aqueous solution of KOH and $K_3Fe(CN)_6$. The organic layer immediately became black in color. The reaction was left stirring at 60°C for 19 hours. The mixture was filtered and the black product was suspended in methylene chloride and washed several times with water until the water layer was clear. The black suspension was filtered, washed with methanol and dried under vacuum at 110°C for 24 hours to give 1.74 g (85%) of **A2.14h** as a black powder. Anhydrous HCl gas was bubbled into a stirring black suspension of **A2.14h** (1.08 g, 1.93 mmol) in 500 mL of chloroform at room temperature. After 8 hours the reaction mixture became transparent indicating the reaction was complete. The solution was evaporated to dryness and the crude product was recrystallized from cyclohexane to give 0.89 g (83%) of **A2.8g** as fine crystals: m.p. 192-194°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 - 7.58 (m, 6H), 7.39 - 7.42 (t, 2H), 7.38 (d, 2H, J = 2 Hz), 7.36 (d, 1H, J = 2 Hz), 7.23 - 7.26 (t, 2H), 7.11 - 7.18 (m, 6H), 5.32 (s, 1H, OH), 5.02 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.89 &161.91 (J_{C-F} = 249 Hz), 163.44 & 161.47 (J_{C-F} = 247 Hz), 163.37 & 161.42 (J_{C-F} = 247 Hz), 149.81, 148.66, 133.06 & 133.03 (J^4_{C-F} = 3.7 Hz), 132.79, 132.60 & 132.58 (J^4_{C-F} = 2.7 Hz), 132.41 & 132.34 (J^3_{C-F} = 8.2 Hz), 132.17, 132.11, 131.44, 131.24, 131.14 & 131.07 (J^3_{C-F} = 8.2 Hz), 130.95 & 130.89 (J^3_{C-F} = 7.3 Hz), 129.97 & 129.94 (J^4_{C-F} = 3.7 Hz), 128.27, 127.58, 127.39, 126.26, 116.59 & 116.42 (J^2_{C-F} = 21.1 Hz), 115.96 & 115.79 (J^2_{C-F} = 21.1 Hz), 115.66 & 115.49 (J^2_{C-F} = 21.1 Hz); MS (EI Direct Inlet at 300C) *m/e* calc'd for $C_{36}H_{21}ClF_4O_2$: 596.1166, found 596.1160; 596.93 (M^++1, 39), 595.93 (M^+, 100), 298.11 (26).

General Procedure for the Synthesis of the Phenoxy Radicals and Quinones.

A 250 mL round bottom flask was charged with **A2.8a** (5.11 g, 7.95 mmol) dissolved in 100 mL of benzene at room temperature under an atmosphere of nitrogen. A 0.75 M aqueous solution of KOH and $K_3Fe(CN)_6$ (75 mL) was added to the reaction mixture and the mixture was stirred at room temperature for 24 hours. The dark red organic layer was washed several times with water until the water layer was clear. The organic layer was dried over sodium sulfate, filtered, and the filtrate was evaporated to dryness. The dark green product was dried at room temperature under reduced pressure for 6 days, to give 4.02 g (79%) of **A2.8a**: T_{exo} 189°C. The oxidized biphenol products were obtained in yields of 79 to 96% yields. The UV visible and thermal properties are listed in tables A2.2 and A2.3.

General Procedure for the Thermolysis Reaction

A solution of phenoxy radical **A2.13b** (0.26 g, 0.38 mmol) in 15 mL of trichlorobenzene was heated at 130 °C under an atmosphere of nitrogen. The reaction was monitored by HPLC and after 24 hours all the phenoxy radical had been converted to three products, the original biphenol **A2.8b**, mono-cyclized compound **A2.23b**, and the di-cyclized compound **A2.24b**. The crude mixture was purified by column chromatography using 20% ethyl acetate in toluene as the eluent. The first fraction **A2.24b** was obtained in 22% yield as white crystals : m.p. 341-344 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, 4H, J = 7.3 Hz), 7.49 - 7.56 (m, 8H), 7.35 - 7.42 (m, 6H), 7.06 (s, 4H), 6.88 - 6.93 (dd, 4H, J = 7.8 & 18.1 Hz), 6.79 (distorted s, 2H), 3.81 (s, 6H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.78, 156.49, 152.30, 136.22, 135.33, 135.03, 131.69, 130.94, 130.30, 128.84, 128.55, 127.66, 126.74, 124.46, 123.45, 122.39, 113.60, 113.37, 111.55, 55.21 (OCH_3); MS (EI Direct Inlet at 370 °C) *m/e* calc'd for $C_{50}H_{34}O_4$: 698.2457, found 698.2423; 699.08 (M^++1, 53), 698.09 (M^+, 100). The second fraction afforded **A2.23b** in 25 % yield as a white powder: m.p. 260-262 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, 2H, J = 7.3 Hz), 7.52 (d, 2H, J = 8.3 Hz), 7.46 - 7.49 (t, 5H), 7.32 - 7.42 (m, 7H), 7.39 (d, 3H, J = 10.5 Hz), 7.17 - 7.20 (distorted t, 2H), 7.01 - 7.05 (m, 4H), 6.89 - 6.92 (m, 2H), 6.44 (br s, 2H), 5.14 (s, 1H, OH), 3.91 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.80, 157.45, 156.43, 152.04, 148.49, 140.41, 137.75, 136.27, 135.82, 135.64, 135.00, 133.73, 132.48, 132.44, 131.86, 131.59, 131.40, 131.07 - 131.17 (br peak), 130.64, 129.38, 128.80, 128.63, 128.46, 128.36, 128.28, 127.54, 127.32, 127.17, 126.61, 126.20, 124.54, 123.42, 123.35, 122.33, 113.75, 113.34, 112.38, 111.51, 55.36 (OCH_3), 54.93 (OCH_3); MS (EI Direct Inlet at 370 °C) *m/e* calc'd for $C_{50}H_{36}O_4$: 700.2613, found 700.2625; 701.15 (M^++1, 54), 700.15 (M^+, 100). The third fraction yielded 24 % of the original biphenol **A2.8b** which was identified by comparison with an authentic sample.

A2.5 References

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CHAPTER A3

SYNTHESIS AND CHARACTERIZATION OF NOVEL CARBON-OXYGEN COUPLED ETHER AND ACETAL COMPOUNDS

A3.1 Introduction

Organic radicals have until recently been considered mainly as intermediates in organic reactions with limited synthetic potential as reagents. These highly reactive species were thought to be non-selective, leading generally to complex products. However free radical reactions, such as bromination of allylic and benzylic compounds with N-bromosuccinimide (NBS) are widely used and very specific. It wasn't until the early 1960s that physical chemists opened the doors to the world of radical chemistry, which led to the explosion in the use of radicals in synthetic reactions in the 1980s. As knowledge of radical chemistry grew, for example, being able to suppress the radical - radical reaction which in turn favors the radical - molecule interaction, these species have come to play a major role in synthetic chemistry.[1-5]

Radical species have been generated by several methods, by oxidizing agents (e.g. Ag_2O, $K_3Fe(CN)_6$) or radical initiators (e.g. AIBN, benzoyl peroxides) to name a few. The most common method used for polymerization reactions is the use of radical initiators. The radical initiators are generated by three methods: 1) thermal, 2) irradiation, and 3) one electron oxidation-reduction process. Peroxides and azo compounds are the most common initiators used these days to initiate radical polymerization (e.g. polystyrene) which consists of three steps: 1) initiation, 2) propagation, and 3) termination (Scheme A3.1).

Besides radical polymerization reactions there are other reactions which involve a radical species, such as free radical substitution, free radical addition, or hydrogen abstraction followed by a radical coupling reaction.

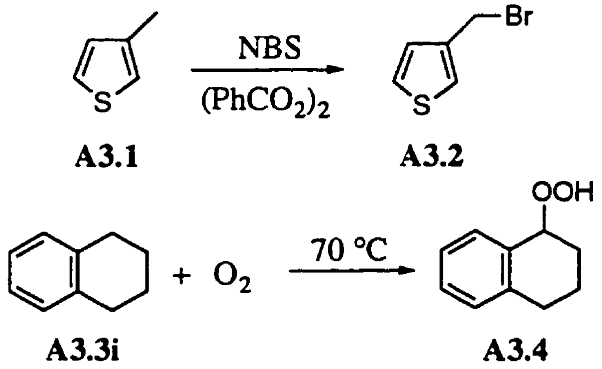
$$\left.\begin{array}{rcl} I{-}I & \longrightarrow & I\bullet \end{array}\right\}\ \text{Initiation}$$

$$\left.\begin{array}{rcl} I\bullet + R{-}R_1 & \longrightarrow & I{-}R + R_1\bullet \\ R_1\bullet + I{-}I & \longrightarrow & R_1{-}I + I\bullet \\ I^\bullet + R{-}R_1 & \longrightarrow & I{-}R + R_1\bullet \\ R_1\bullet + I{-}I & \longrightarrow & R_1{-}I + I\bullet \end{array}\right\}\ \text{Propagation}$$

$$\left.\begin{array}{rcl} 2I\bullet & \longrightarrow & I{-}I \\ 2R_1\bullet & \longrightarrow & R_1{-}R_1 \\ I\bullet + R_1\bullet & \longrightarrow & I{-}R_1 \end{array}\right\}\ \text{Termination}$$

Scheme A3.1

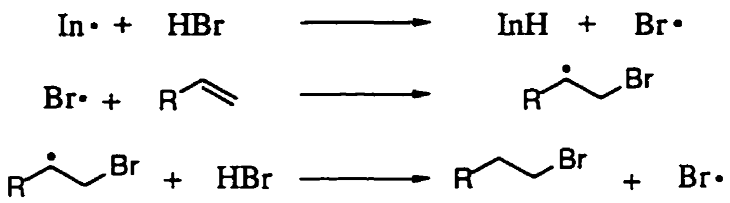
Examples of free radical substitution reactions are the halogenation of hydrocarbons (e.g. 3-methylthiophene **A3.1** to 3-(bromomethyl)thiophene **A3.2**) or the oxidation of tetrahydronaphthalene **A3.3i** with molecular oxygen to give the hydroperoxide **A3.4** (Scheme A3.2).[1]



Scheme A3.2

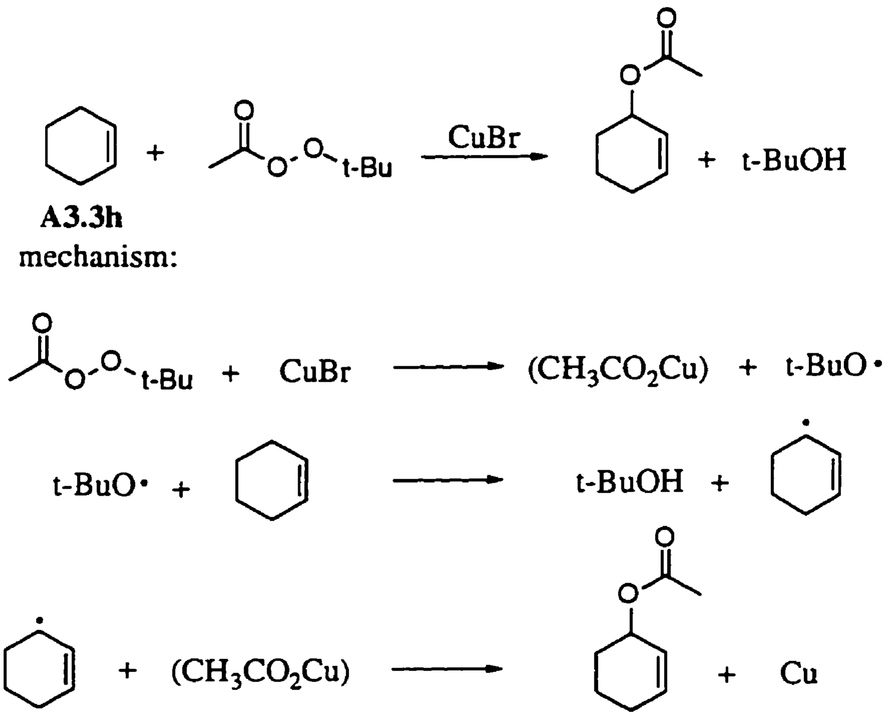
Free radical addition involves the attack of the bromine, carbon, or thiol radical on a double bond (Scheme A3.3).[1]

The most common radical reactions are hydrogen abstraction followed by a radical coupling reaction.



Scheme A3.3

For example, the radical carbon - oxygen coupled product obtained from reacting cyclohexene **A3.3h** with t-buylperoxy ester in the presence of CuBr (Scheme A3.4).[6]



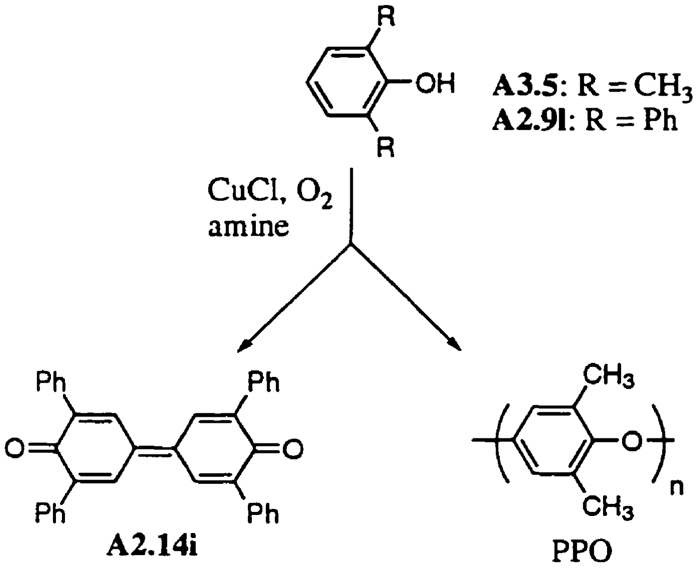
A3.3h

mechanism:

Scheme A3.4

The rate of proton abstraction is tertiary > secondary > primary and these rates are independent of the attacking radical, but are attributed to the strength of the C-H bond (bond dissociation energy BDE).

Phenoxy radicals which have been known for many years (see Chapter A2) react with organic molecules by either abstracting a proton followed by a radical coupling reaction or with another radical species. For example, **A2.14i** was prepared by a radical carbon-carbon coupling reaction of phenol **A2.9i**, while 1,4-poly(2,6-dimethylphenylene) (PPO®) was prepared by a radical carbon - oxygen coupling reaction of phenol **A3.5** in the presence of oxygen and a catalytic amount of CuCl (Scheme A3.5).[7,8]

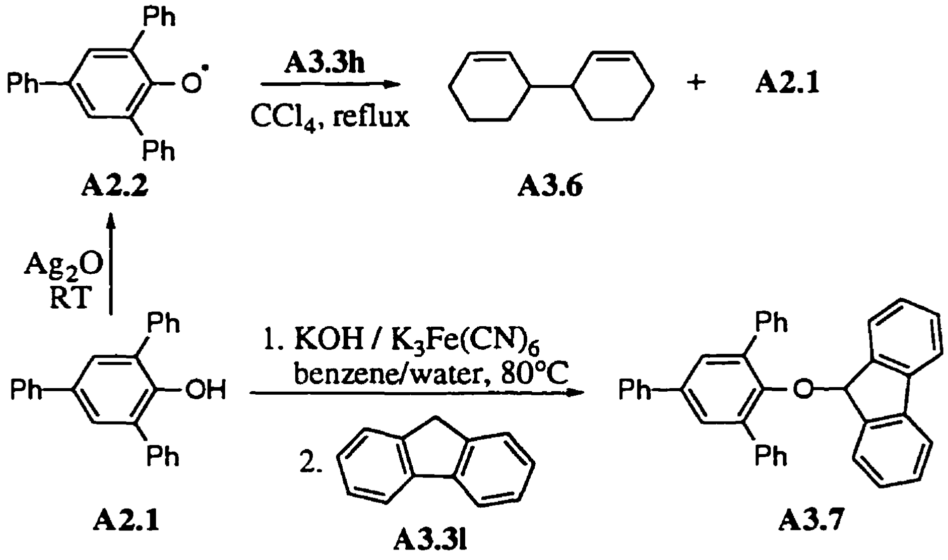


Scheme A3.5

Dimroth and coworker have shown that the pregenerated phenoxy radical **A2.2** reacts with cyclohexene **A3.3h** in refluxing benzene to give the original phenol **A2.1** and the carbon - carbon coupled dimer **A3.6**. When phenol **A2.1** was reacted with fluorene **A3.3l** in a two phase oxidation system only the carbon - oxygen coupled compound **A3.7** was obtained in 80% yield (Scheme A3.6).

A3.1.1 Goals and Strategies

In the present work we were interested in exploring and expanding on the chemistry of the phenoxy radicals described previously. By studying the reaction of the novel hindered biphenoxy radicals **A2.13a-d** and quinones **A2.14e,f** with compounds containing activated methylene groups **A3.3a-q** and **A3.8a-s** (Tables A3.1, A3.2, A3.3) we where able that, besides the carbon - oxygen coupling reaction these radical species can be used in unique methods to: 1) functionalize arylmethanes, 2) protect methylene groups, and 3) deprotect benzylic and t-butyl protecting groups.



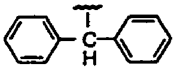
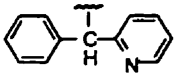
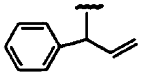
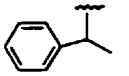
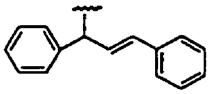
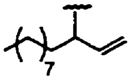
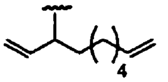
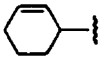
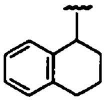
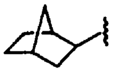
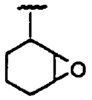
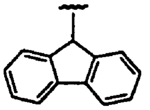
Scheme A3.6

A3.2 Results and Discussions

A3.2.1 Monomer Synthesis

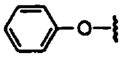
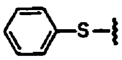
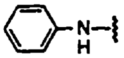
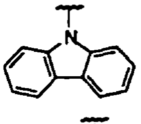
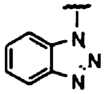
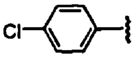
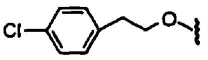
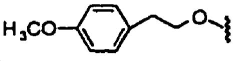
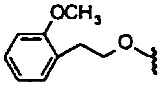
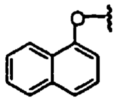
Two methods of synthesizing the carbon - oxygen coupled ether **A3.9a-l** and acetal **A3.10a-p** products were investigated. The first method involved preparing the biphenoxy radical by vigorously stirring a solution of biphenol **A2.8a** with Ag_2O in benzene for 24 hours. The biphenoxy radical was isolated and then reacted with diphenylmethane **A3.3a** at 80°C in benzene under an atmosphere of nitrogen affording four products (Scheme A3.7). The original biphenol **A2.8a**, mono-substituted ether **A3.11**, di-substituted ether **A3.9a**, and **A3.3a**.

Table A3.1. Properties and yields of the ether compounds based on the *in situ* oxidation procedure.

A3.		R	Rxn Time (hrs)	Isolated Yield (%)	m.p. (°C)	Chemical Analysis calc. (found)	
3	9					%C	%H
a	a[a]		3	97	243-245	91.40 (90.77)	5.58 (5.53)
b	b		19	87	252-256	88.49 (88.77)	5.37 (5.73)
c	c[a,b]		5	85	--	--	--
d	d[a]		9	97	245-248	90.32 (90.05)	5.92 (5.94)
e	e		1.5	68	224-228	91.19 (91.25)	5.69 (5.65)
f	f		24	82	114-117	88.65 (88.40)	8.07 (8.19)
g	g		--		150-153	89.23 (89.27)	7.27 (7.25)
h	h[a]		21	90	252-253	89.74 (89.57)	6.28 (6.39)
i	i[c]		--	--	--	--	--
j	j		NR	--	--	--	--
k	k		NR	--	--	--	--
l	l[d]		2	82	284-286	90.78 (90.45)	5.25 (5.13)

a) these compounds were previously made by W.-Gi. Kim.
b) mixture of isomers.
c) mixture of products.
d) monosubstituted ether only.

Table A3.2. Properties and yields of the acetal type compounds based on the *in situ* oxidation procedure.

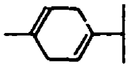
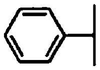
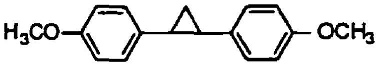
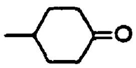
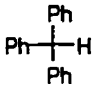
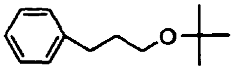
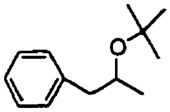
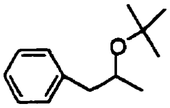
A3.		R	R_1	R_2	Rxn. Time (hrs)	Isolated Yield (%)	m.p. (°C)	Chemical Analysis calc. (found)	
8	10							%C	%H
a	a[a]		Ph	H	5	80	242-243	88.24 (88.13)	5.40 (5.20)
b	b		Ph	H	1.5	79	145-148	85.52 (85.95)	5.24 (5.48)
c	c[b]		Ph	H	NR	--	--	--	--
d	d		Ph	H	2.5	67	200-203	89.55 (89.34)	5.25 (5.20)
e	e		Ph	H	21	20	294-297	84.06 (84.36)	4.96 (5.41)
f	f[a]	CH_3	$(CH_3)_3C$-O-	H	20	80	213-217	85.48 (85.44)	6.93 (7.19)
g	g[c]	$CH_3(CH_2)_9$-CH_2-	$(CH_3)_3C$-O-	H	4	--	--	--	--
h	h	Cholesterol	$(CH_3)_3C$-O-	--	NR	--	--	--	--
i	i	Ph	$(CH_3)_3C$-O-	Ph	NR	--	--	--	--
j	j[a]	Ph	$(CH_3)_3C$-O-	H	3	82	240-243	--	--
k	k[a]		$(CH_3)_3C$-O-	H	2	84		81.14 (80.87)	5.84 (5.60)
l	l		Ph	H	1	85	119-124	88.10 (87.81)	5.88 (6.03)
m	m		Ph	H	17	76	98-104	82.74 (83.02)	5.34 (5.46)
n	n		Ph	H	24	81	110-118	85.53 (85.47)	5.92(6.19)
o	o		Ph	CH_3	24	71	67-74	85.53 (85.90)	5.92(6.22)
p	p		Ph	H	20	82	156-159	88.11 (88.93)	5.30 (5.28)

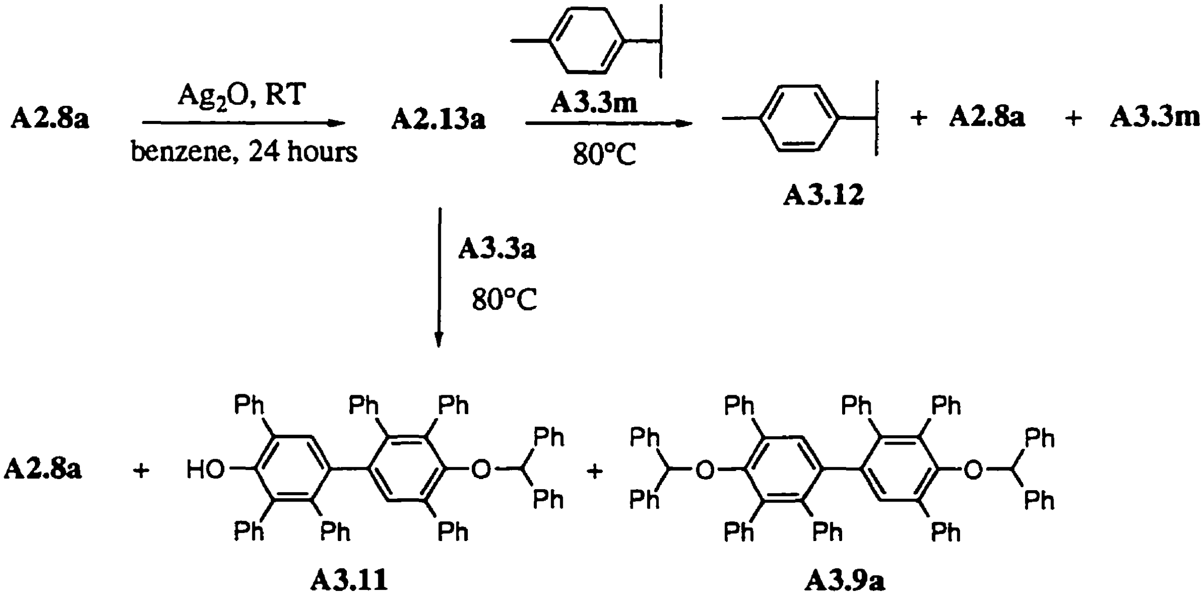
a) previously prepared by W.-Gi. Kim.

b) obtained only benzaldehyde.

c) a mixture of products.

Table A3.3. List of reactants.

Entry	Monomers
A3.3m	
A3.3n	
A3.3o	
A3.3p	
A3.3q	
A3.9q	
A3.9r	
A3.9s	



Scheme A3.7

Depending on the stoichiometry of the reaction the amount of each specific product varied (Table A3.4).

Table A3.4. Yields of products obtained from reacting **A2.13a** and **A3.3a**.

Trail	**A3.3a** (eq)	Products Recovered		
		A2.8a (%)	**A3.11** (%)	**A3.9a** (%)
1	1	21	48	9
2	2	13	72	10

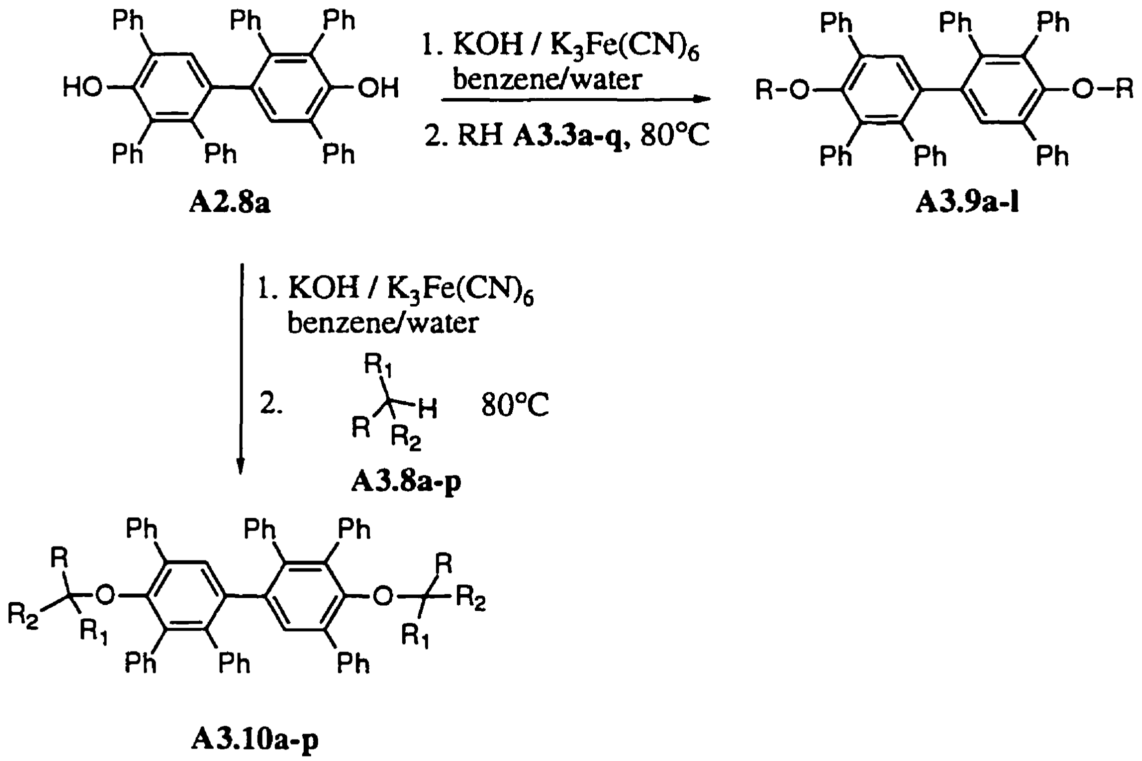
The amount of biphenol does not increase with increasing amount of **A3.3a**, which suggests that the rate limiting step is the abstraction of the proton and not the coupling reaction which is in agreement with the findings of Dimroth and coworkers.[9] The carbon - oxygen coupled compounds are not the only products obtained under these reaction conditions. For example, when γ-terpinene **A3.3m** was reacted with **A2.13a** only aromatization of **A3.3m** to 4-isopropyltoluene **A3.12** occurred. (Scheme A3.7). The aromatization reaction of γ-terpinene was more efficient at 25°C, instead of at 60°C in that a higher yield of **A3.12** was obtained (see table A3.5).

Table A3.5. Yields of products obtained from reacting **A2.8a** and **A3.3m**.

Trail	Rxn Temp. (hrs)	Rxn Time (°C)	Products	
			A2.8a (%)	**A3.12** (%)
1	60	1	80	20
2	25	4	91	57

Therefore, depending on the monomer being reacted only two products formed, either the carbon oxygen coupled ether compound or the aromatization in the cyclic dienes systems. Dimroth and coworkers have shown that when an equimolar amount of phenoxy radical **A2.2** reacts with **A3.3h** the carbon - carbon coupled dimer is exclusively obtained along with the original phenol **A2.1**[10]. Even if cyclohexene was substituted for **A3.3a** the carbon - oxygen compound is still obtained with our biphenoxy radical, suggesting that the biphenoxy radical **A2.13a** is more reactive than **A2.3**.

The second method used was an *in situ* oxidation of the hindered biphenol followed by a coupling reaction with molecules containing activated methylene groups **A3.3a-q** and **A3.8a-s** in the presence of an alkaline $K_3Fe(CN)_6$ solution at 80°C under an atmosphere of nitrogen (Scheme A3.8). The carbon -oxygen coupled products **A3.9a-l** and **A3.10a-p** were obtained in high yields (Table A3.1 and A3.2).



Scheme A3.8

The optimal reaction conditions were obtained by varying the concentration of the alkaline $K_3Fe(CN)_6$ solution (Figure A3.1) and the reaction temperature (Figure A3.2) and were determined to be 0.75M and 80°C, respectively. As expected, as the concentration of the alkaline solution increased so did the rate of reaction until a concentration of 0.75M. At concentrations greater than 0.75M only a slight increase in the reaction rate was observed, see figure A3.1, and the products had an intense yellow color which was difficult to remove. Reaction temperatures greater than 80°C led to the formation of the cyclized products discussed in Chapter A2, which competed with the formation of the carbon -

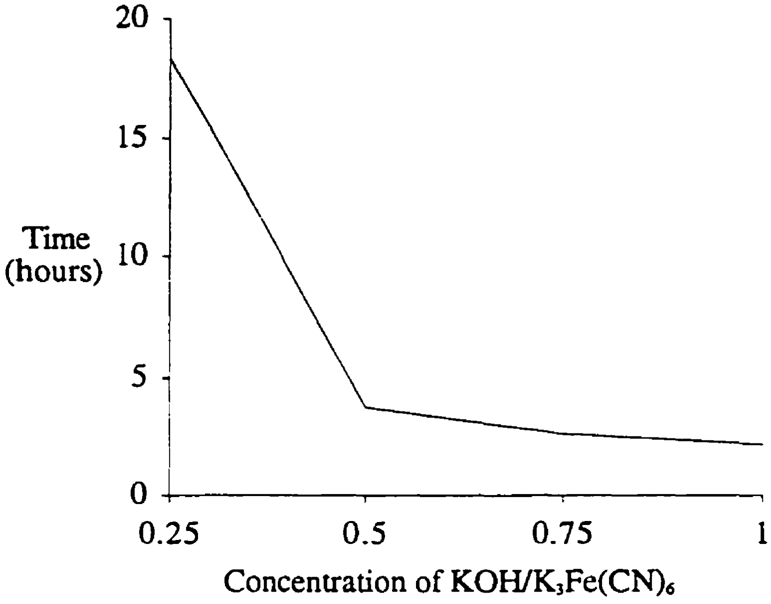


Figure A3.1. The effect of $KOH/K_3Fe(CN)_6$ concentration on the rate of the radical coupling reaction.

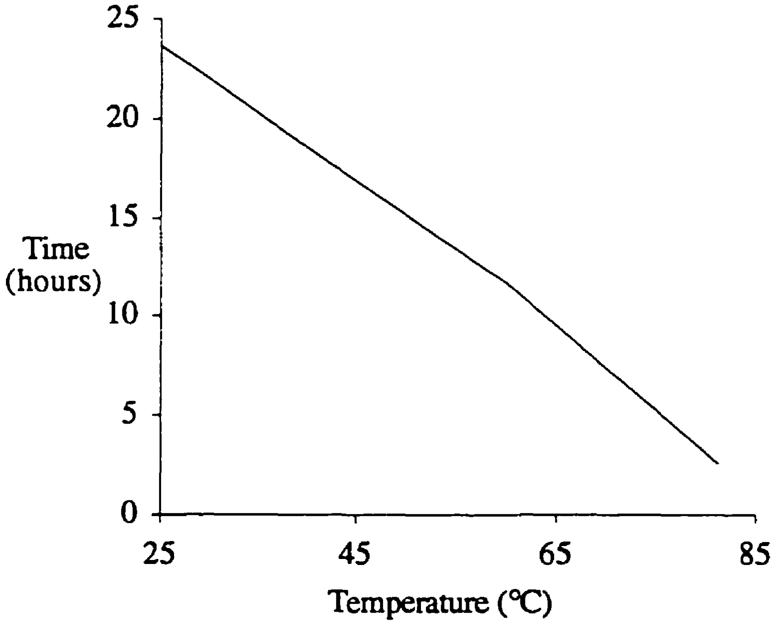
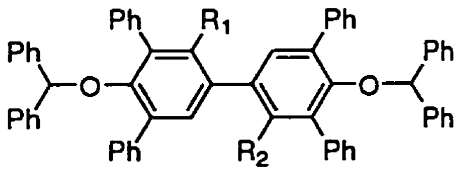


Figure A3.2. Effect of temperature on the radical coupling reaction.

oxygen coupled products thus lowering the yield of the ether or acetal compounds. At temperatures below or at 80°C no cyclized products were observed

The reactivity of a variety of biphenols **A2.8a-f,i** with **A3.3a** at 80°C in a two phase oxidation reaction yielding the ether compounds **A3.13-18** was investigated (Table A3.6).



A3.14-18

Table A3.6 Reactivity of the different biphenols.

Entry	R_1	R_2	Conversion (%)	Rxn Time (min)	Isolated Yield (%)
A3.13	H	H	0	--	--
A3.14	Cl	H	100	110	79
A3.15	Cl	Cl	100	66	80
A3.16	Ph	H	100	134	83
A3.17	CH_3	CH_3	100	111	78
A3.18	4-methoxyphenyl		100	179	74

As expected no reaction occurred with biphenol **A2.8i** because it forms a stable unreactive diphenoquinone at 80°C. As the group in the meta position of the biphenols **A2.8a-f** is changed from an electron withdrawing group to an electron donating group the reactivity of the biphenoxy radical should decrease. This pattern was quite obvious in comparing biphenols **A2.8a-c** in that biphenol **A2.8c** is more reactive than biphenols **A2.8a,b** because of the chloro group which is an electron withdrawing group. The presence of the electron donating methoxy groups in the para position of the meta pendant phenyl should also lower the reactivity of biphenol **A2.8b** compared to **A2.8a,** which is in agreement with the experimental results. Biphenols **A2.8d-f** are not consistent with this hypothesis, since biphenol **A2.8d** was expected to be the least reactive, due to the electron donating methyl groups located at the meta position. Instead **A2.8d** is just as reactive as **A2.8f** and more reactive than **A2.8a,b**. Since the steric hindrance around the oxygen radical is the same for all the biphenols, the difference in reactivity might be explained by the rate of generation of the biphenoxy radical or the solubility of the different radical species. A more detailed study which is beyond the scope of this thesis would be necessary to interpret these results.

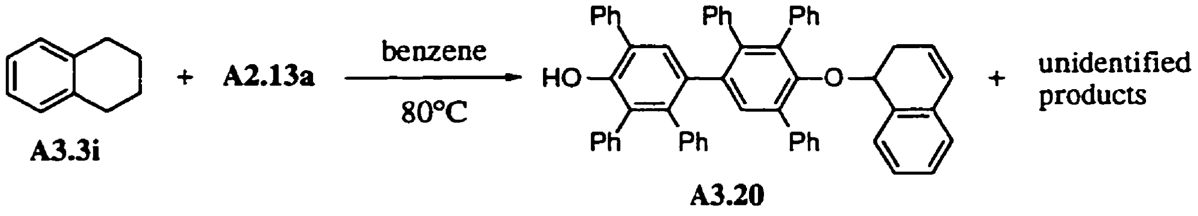
To simplify the characterization of the carbon - oxygen coupled products only biphenol **A2.8a** which was readily available, was used. As with most radical reactions secondary protons were more reactive than primary protons. With these biphenoxy radicals almost no reaction occurred with primary protons, while reactions did occur with tertiary protons (e.g. triphenylmethane **A3.3q** or **A3.3n**), as expected, since their bond dissociation energies (BDE) are generally lower. The formation of ether products was confirmed by HPLC analysis and followed by the disappearance of the intense red color in the reaction mixture. These ethers were never isolated because they readily decompose during the workup. The original biphenol was isolated along with several products that were never identified. Not all tertiary protons are reactive, for example tertiary proton adjacent to an oxygen atom such as **A3.8h,q-s** are not abstracted by the biphenoxy radical. Only with the t-butyl ether of benzhydrol **A3.8i** did a reaction occur, however instead of obtaining the acetal compound we isolated benzophenone **A3.19** in 25% yield along with the starting materials **A2.8a** and **A3.8i**. The increased steric hindrance due to the tertiary butyl groups might reduce accessibility of the tertiary proton, which would explain why no reaction occurs.

Of the molecules **A3.3a-q** and **A3.8a-s** that were reactive the ones with enhanced conjugation around the methylene such as **A3.3e** were more reactive than the less conjugated molecules **A3.3f**. The large difference in reaction times of the various ether and acetal compounds can presumably be attributed to the generation of the methylene radical, which is related to the bond dissociation energy. For example, **A3.3a** (BDE of 81.4 Kcal/mol)[11] reacts within 3 hours while **A3.3d** (BDE of 85.4 Kcal/mol)[11] reacts within 9 hours.

No reactions were observed with **A3.3j,k,o,p** using either synthetic method mentioned previously. Only the original starting materials were identified by HPLC, ^1H NMR and TLC by comparison with authentic samples. We assumed that in compound **A3.3k** the epoxide group adjacent to the methylene, should activate the methylene groups just as the double bond in **A3.3h**, although this was not the case. With compound **A3.3o** we expected the tertiary proton would react with the biphenoxy radical, however it appears that the tertiary proton is too sterically hindered to be abstracted, while the methylene proton in the cyclopropyl group has a high BDE (104 Kcal/mol)[11] making it difficult for the biphenoxy radical to abstract the secondary proton. With compound **A3.8c** no carbon - oxygen coupled product was obtained instead benzaldehyde **A3.23a** was detected by HPLC analysis, indicating that N-phenylbenzylamine **A3.8c** is cleaved during the reaction.

Dehydrogenation, along with the carbon - oxygen coupled products, occurred when tetrahydronaphthalene **A3.3i** was reacted either with the pregenerated radicals or with **A2.8a** in the two phase oxidation reaction. In the reaction with the pregenerated radical three products were isolated, **A2.8a** (11%), and a mixture of products, which are mono substituted ethers based on the presence of a phenolic OH peak at 5.07 ppm in the ^1H NMR spectrum. Only one of the isomers **A3.20** was isolated in 42% yield. In the two phase oxidation reaction a mixture of products was obtained which we were unable to purify and identify (Scheme A3.9).

A pattern similar to that obtained in the formation of the ether compounds was observed in the formation of the acetal compounds **A3.10a-p** (Scheme A3.8). Molecules with secondary protons were the most reactive (Table A3.4). Initially the acetal derivatives were obtained from the reaction of silyl ethers with biphenol **A2.8a** in a two phase oxidation system. These compounds were unstable and difficult to isolate as pure compounds.



Scheme A3.9

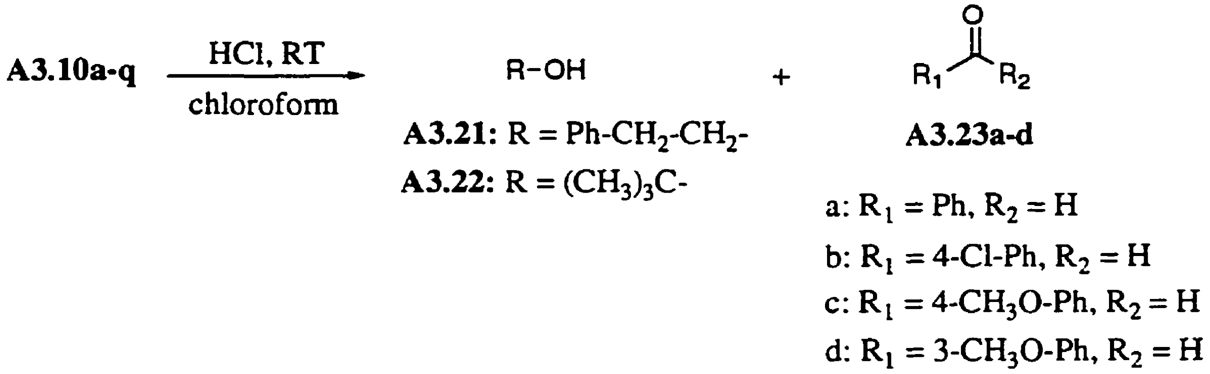
We therefore studied the stable t-butyl and benzylic ethers **A3.8a-s**. The t-butyl ethers were prepared by the method described by A. Alexakis *et al.*[12] Here the appropriate alcohol was reacted with isobutylene gas in either benzene or hexane in the presence of a catalytic amount of Amberlyst A15 at room temperature. The benzylic ethers were prepared by a nucleophilic displacement of a series of benzyl chlorides with phenylethyl alcohol **A3.21** as described by H. H. Freedman et al.[13] The t-butyl and benzylic ethers were obtained in high yields and characterized by ^{1}H NMR and by comparison with authentic samples.[14,15]

As previously mentioned no reactions occurred with molecules **A3.8h,r,s**. With **A3.3q** a mixture of products was obtained. The biphenoxy radical most probably attacks the methylene group adjacent to the phenyl group and oxygen atom. The majority of the acetal compounds were obtained in high yields and are stable during the purification step. They are readily cleaved to their corresponding alcohol and aldehdye derivatives in the presences of mild acids.

A3.2.2 Cleavage of Ether and Acetal Compounds

The carbon - oxygen coupled acetal and ethers compounds were cleaved using a variety of reagents. As expected the acetal compounds were quantitatively cleaved with concentrated HCl in chloroform at room temperature, affording biphenol **A2.8a**, and the corresponding alcohols **A3.21** and **A3.22**, and aldehyde **A3.23a-d** derivatives (Scheme

10) depending on the acetal compound being cleaved (Table A3.7). The benzylic ethers were similar in reactivity and stability to the t-butyl ethers.



Scheme A3.10

Table A3.7. Percent conversion of products obtained from treating the acetal compounds with HCl.

Entry	Cleaved Products				
	A2.8a (%)	Aldehyde (%)		Alcohol (%)	
A3.10j	90	A3.24a	61		--
A3.10k	88	A3.24b	98		--
A3.10l	99	A3.24a	8	A3.23	75
A3.10m	100	A3.24b	48	A3.23	87
A3.10n	93	A3.24c	57	A3.23	91
A3.10o	97	A3.24d	81	A3.23	97

The secondary proton attached to the benzylic group makes these compounds a prime target for cleavage with these hindered biphenoxy radicals. For example **A3.10n** is cleaved to its corresponding aldehyde **A3.23c** (57%) and alcohol **A3.21** (91%) in the presence of HCl (Figure A3.3a,b). Benzylic groups have previously been cleaved by several methods, such as: 1) electrolytic oxidation,[16] 2) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

(DDQ),[15,17-19] and 3) ceric ammonium nitrate (CAN)[20,21] to name a few. These methods are limited to substituted benzyl ethers, for example, DDQ does not cleave off the benzyl

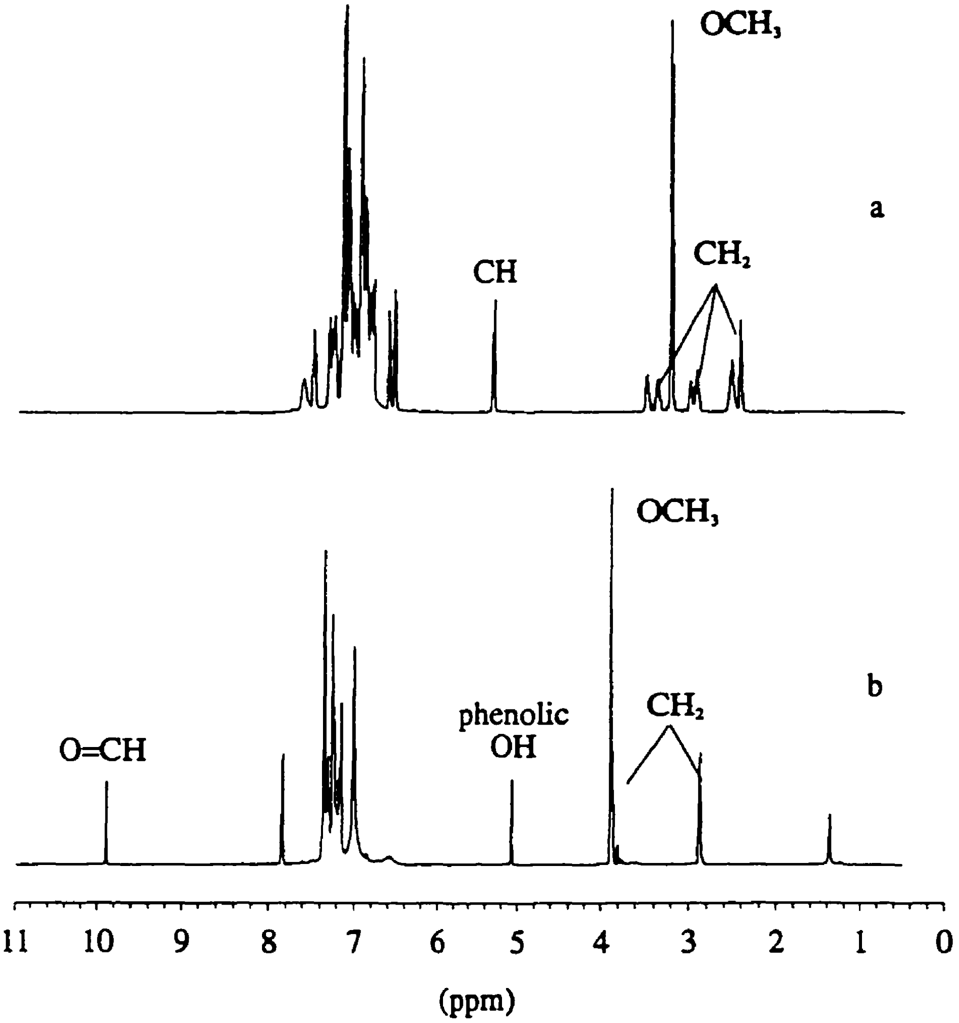
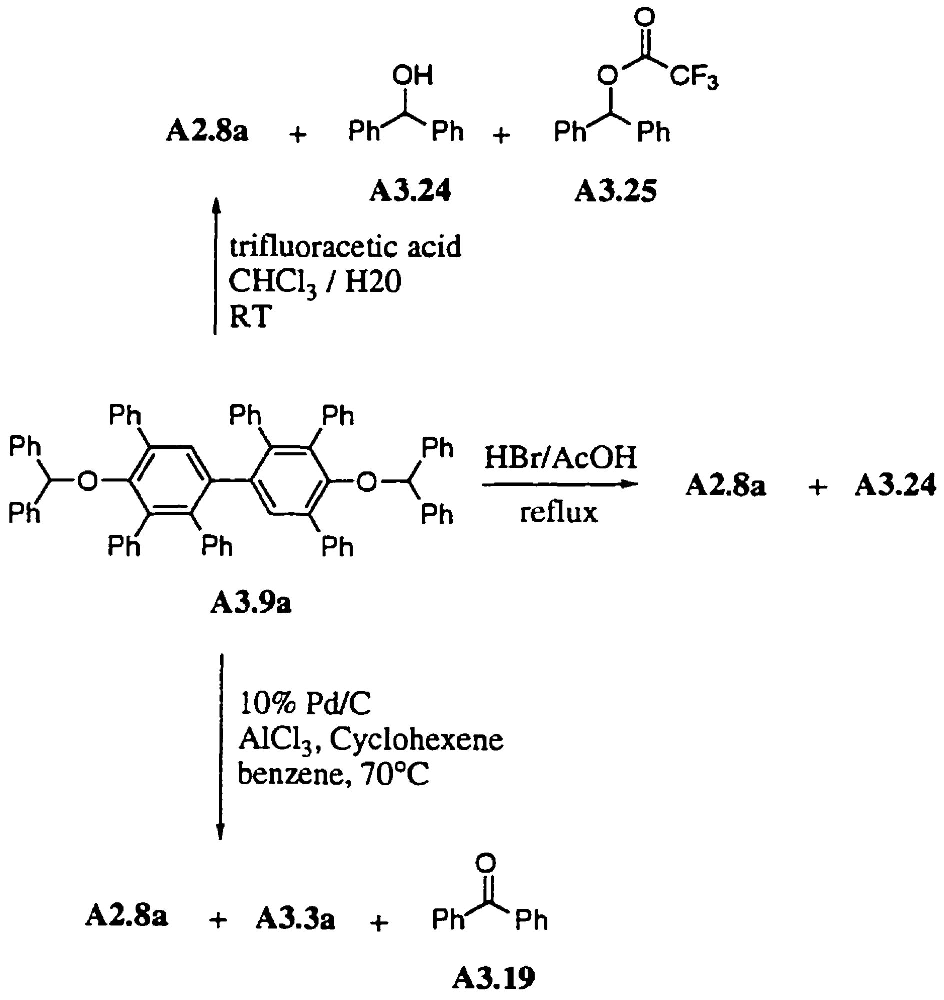


Figure A3.3. ^{1}H NMR spectra of: a) **A3.10n**, b) **A3.10n** after being treated with HCl.

ether group, however it readily cleaves off methoxy substituted benzyl groups. Similar results were obtained in the cleavage of ethers **A3.8n,o** using DDQ[15] and our biphenoxy radical. The advantages of the biphenoxy radical is the greater reactivity towards the cleavage of a benzyl ether or their corresponding substituted derivatives so that one can use the cheaper benzyl chloride as the protecting group. In addition these biphenoxy compounds can easily be incorporated into the backbone of polymer chains thus simplifying the purification step (see Chapter A6).

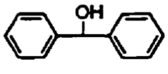
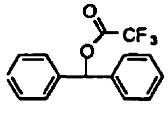
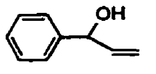
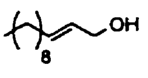
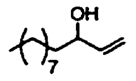
The ethers were found to be more difficult to cleave (Scheme A3.11) than the acetal derivatives. Simple acids had no effect, however stronger acids like trifluoroacetic acid quantitatively cleaved **A3.9a** within 24 hours based on HPLC results. The original biphenol **A2.8a** was recovered in 90% yield. Based on MS and ^{1}H NMR data benzohydrol **A3.24** and the trifluoroacetate derivative **A3.25** (see table A3.8) were identified, though we were never able to isolate these products. Ether **A3.9c** consisted of an isomeric mixture, where attack occurred either at the 1 or 3 position of the allyl group. This compound was cleaved within 5 hours, affording **A2.8a** in 91% yield and the secondary alcohol **A3.26** in 50% yield. The aliphatic ether **A3.9f** was only cleaved to 46% based on a HPLC calibration with the biphenol. The reaction mixture was very messy though we were able to isolate a small amount of the primary and secondary alcohols **A3.27** and **A3.28**, respectively as a mixture in 20% yield. The mixture of aliphatic alcohols was easily identified by ^{13}C NMR. The peak at 64 ppm corresponds to the methylene carbon (-CH=CH-$\underline{C}H_2$-OH) and the peak at 73 ppm corresponds to the methane carbon (-CH_2-$\underline{C}$H(OH)-CH=CH_2) (see table A3.8 for more details).

The cleavage of the ethers with 48% HBr in refluxing acetic acid was also examined. Similar results to the previous method were obtained, in that compounds **A3.9a,e** were quantitatively cleaved while the aliphatic compound **A3.9f** was only cleaved to 90% conversion. In general these cleavage reactions were much faster and in certain cases easier to workup. Ether **A3.9a** was cleaved within 1 hour compared to 24 hours using the previous method, affording **A2.8a** in 79% yield and **A3.24** in 73% yield (Table A3.9). With ethers **A3.9e,f** the reactions were not as clean. The biphenol was easily isolated in 85% and 84% yield, respectively (Table A3.9), along with many minor products which could not be identified. The double bond in these compounds is most probably not stable under these condition and leads to side products which might explain the complex mixture.



Scheme A3.11

Table A3.8. Cleavage of ether compounds with trifluoroacetic acid.

Entry	Rxn Time (hrs)	Conv. (%)	Cleaved Products		Methylene Groups		MS (g/mol)
			A2.8a[c] (%)	Others (%)	^1H (ppm)	^{13}C (ppm)	
A3.9a	4	100	90	 **A3.25**[a]  **A3.26**[a]			184 (C=O) 280(CF_3CO_2)
A3.9c	5	100	91	 **A3.27**[c] 50	4.96 (d)	68.52 (CH)	134
A3.9f	120	50	–	 **A3.28**[b]  **A3.29**[b] 20	4.09 (m)	73.28 (CH) 63.86 (CH_2)	184

a) the diphenylmethane derivatives were characterized only by MS, since the products could not be isolated.
b) isolated yield based on percent conversionof a mixture of isomers, identified by ^1H NMR and MS.
c) isolated yield based on percent conversion.

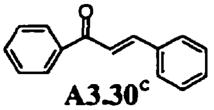
Table A3.9. Cleavage of ether compounds with 48% HBr.

Entry	Rxn Time (min)	Conv. (%)	Cleaved Products		
			A2.8a[a] (%)	Others[a]	
A3.9a	45	100	79	**A3.25**	73%
A3.9e[b]	45	100	85	--	--
A3.9f[b]	60	90	94	--	--

a) isolated yield based on percent conversion.
b) reaction was complex and we were unable to isolate products.

The last cleavage method we looked at was hydrogenation of the ether compounds, which was achieved by the method described by G. A. Olah and coworkers.[22] This involved reacting the ether compound **A3.9a,c-f** with 10% Pd/C, a catalytic amount of $AlCl_3$ and a hydrogen donor such as cyclohexene in benzene at 70°C. Ethers **A3.10a,e** were readily cleaved to **A2.8a** in 92% and 95% yield, respectively, and the original methylene compounds **A3.3a,f** were obtained in 78% and 35% yield, respectively. The ketone derivatives **A3.19** and **A3.29** were also obtained in 7% and 26% yield, respectively (Table A3.10).

Table A3.10. Hydrogenation of the ether compounds.

Entry	Rxn Time (hrs)	Conv. (%)	Cleaved Products		NMR Peaks		MS (g/mol)
			A2.8a^{c} (%)	Others^{b}	^{1}H (ppm)	^{13}C (ppm)	
A3.9a	8	100	92	**A3.3a** 78% **A3.19** 7%	--	--	--
A3.9e^{b}	89	100	95	**A3.3e** 35%  26% **A3.30**^{c}	3.58 (d,CH_2)	39.33 (CH_2) 190.55 (C=O)	194 207
A3.9c^{d}	72	19	--	--	--	--	--
A3.9d^{d}	72	18	--	--	--	--	--
A3.9f^{e}	48	72	--	--	--	--	--

a) isolated yields based on percent conversion.
b) all compounds have been comfirmed by comparison with authetic samples.
c) fully characterized by ^{1}H and ^{13}C NMR.
d) these reactions were very complex.
e) palladium black was used instead of 10% Pd/C.

Even though these reaction were run under an atmosphere of argon oxygen must still be present in order to obtained the oxidized products. More rigorous steps to ensure a completely oxygen free atmosphere should suppress the formation of the oxidized products. With the aliphatic ether **A3.9f** palladium black was used instead of 10% Pd/C, and even under these conditions only 76% conversion to the biphenol based on HPLC analysis, was obtained. Here again the reaction mixture was too complex to isolate any of the products. With compounds **A3.9c,d** less than 20% conversion was observed (Table A3.10). It appears that more vigorous conditions are required to cleave ethers **A3.9c,d,f**.

A3.2.3 Thermal Cleavage of A3.9a

Controlling the architecture of macromolecules has generally been achieved by anionic[23] or cationic[24] polymerization. To expand this "living" polymerization concept to the free radical polymerization process has been a difficult goal. Initially iniferters were used to provide a "living" free radical process. This process involved a sulfur centered radical which reacts reversibly with the growing polymer chain end, controlling the molecular weight. The disadvantage of the system is that the sulfur radical also initiates new polymer chains leading to uncontrolled molecular weights. It wasn't until the pioneer work of M.K. Georges and coworkers[25] that narrow polydisperse polymers (controlled molecular weight polymers) were obtained through a "living" free radical polymerization using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the controller.

The advantage of this method is related to the ability of the nitroxide radical to react with the carbon centered radical in a thermally reversible process. Here the concentration of the carbon centered radical is much lower and the inability of the nitroxide radical to initiate any new chain growth, leads to controlled chain growth. The low molecular weight chains obtained have similar molecular weights and are end capped with TEMPO. When heated at 120°C the carbon - oxygen bond cleaves regenerating the carbon centered radical and the polymerization process proceeds. Since, the oligomer chains are of equal molecular weight the polymers chains that form should also have similar molecular weights which leads to polymers with narrow polydispersities

Hawker *et al* at IBM expanded on this idea by synthesizing monomers end capped with the nitroxide radical and heating these systems at 120°C. Polymers with narrow polydispersities were also obtained.[26,27]

We were interested in exploring this chemistry by substituting TEMPO with the hindered biphenoxy radicals **A2.13a**. The easiest method for evaluating these systems was to determine the optimal temperature require to thermally cleave the ether compounds. Therefore compound **A3.9a** was heated at several different temperatures and the rate of ether disappearance was monitored by HPLC (Figure A3.4). At temperatures of 120°C and 180°C no more that 20% to 25% cleavage of the ether compound was observed after 48 hours, while at 220°C, the ether compound was completely cleaved within 6 hour. The lack of any significant cleavage at 120°C suggests that this system would not be as effective as TEMPO in polymerization reactions.

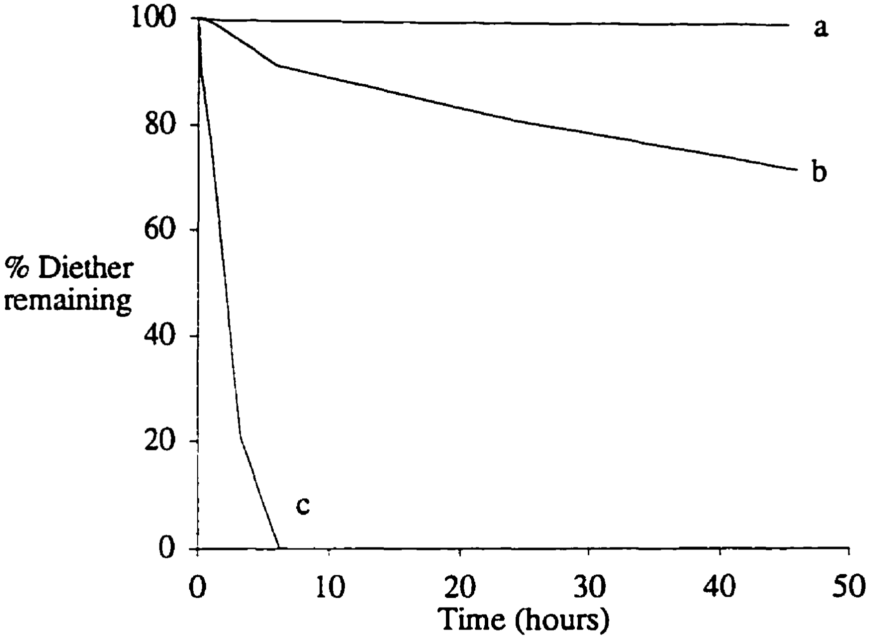


Figure A3.4. Thermal cleavage of the carbon - oxygen bond of **A3.10a** at: a) 120°C, b) 180°C, c) 220°C.

A3.3 Conclusions

In conclusion we have demonstrated an effective radical coupling reaction between hindered biphenoxy radicals and a series of molecules containing methylene groups. The products obtained contain novel ether and acetal groups that can be quantitatively cleaved by a variety of reagents which leads to a new method for functionalizing methylene groups and for deprotecting benzylic and t-butyl ether derivatives .

A3.4 Experimental Section

Materials

Most of the molecules containing activated methylene groups were purchased from the Aldrich Chemical Co. and used without further purification. **A3.3e** was prepared by

Dr. M. Paventi in our laboratory. Hydrobromic acid (48%), aluminum trichloride ($AlCl_3$) and 10% palladium on carbon (Pd/C) were purchased from the Aldrich Chemical Co. and used as recieved. Potassium ferricyanide and potassium hydroxide along with the reagent grade solvents were obtained from Caledon Laboratories Ltd.. All the reagents and solvents were used without further purification.

Instruments

Elemental analyses were performed by Fine Analysis Laboratories Ltd., Hamilton, Ontario. All ^1H and ^{13}C NMR analyses were obtained on a Varian Unity 500 spectrometer. High performance liquid chromatography (HPLC) analyses were carried out on a Milton Roy CM4000 pump equipped with a reverse phase silica column and a UV detector set at 254 nm; methanol was used as the eluent at a flow rate of 1 mL/min. Melting points were determined on a Fisher-Johns melting point apparatus. Mass spectra were recorded on a Kratos MS25RFA spectrometer.

General Procedure for the Carbon - Oxygen Coupling Reaction Using the Pregenerated Phenoxy Radical

The pregenerated phenoxy radical **A2.13a** (0.53 g, .83 mmol) was reacted with **A3.3a** (0.28 g, 1.66 mmol) in refluxing benzene under an atmosphere of nitrogen for 19 hours. Four products were isolated by column chromatography using 3 % ethyl acetate in hexane as the eluent for the reaction mixture. The biphenol **A2.8a** 0.07g (13 %) , **A3.3a** 0.10 g (36 %), the diether **A3.9a** 0.08 g (10 %), and the mono-substituted ether 0.46 g (72%) **A3.11**. All the products except for **A3.11** have been confirmed by comparison with authentic samples: m.p. 200-205°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (br s, 2H), 7.26 - 7.30 (dt, 2H), 7.23 - 7.25 (m, 2H), 7.17 - 7.21 (m, 6H), 7.12 - 7.14 (dd, 3H, J = 1.5 & 7.3 Hz), 7.02 -7.10 (m, 10H), 6.96 - 7.00 (m, 6H), 6.92 (br s, 2H), 6.88 (d, 2H, J = 3 Hz), 6.85 (d, 2H, J = 3 Hz), 6.82 (br s, 2H), 6.66 (d, 2H, J = 7.3 Hz), 6.54 (d, 2H, J = 7.8 Hz), 6.35 (br s, 1H), 5.11 (d, 1H, J = 2.4 Hz, CH), 5.06 (d, 1H, J = 2.9 Hz, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.13, 148.12, 140.52, 140.46, 140.43, 140.38, 139.91, 139.81, 139.14, 137.86, 137.54, 136.11, 135.89, 134.41, 133.65, 133.50, 132.47, 129.41, 129.26, 128.17, 128.09, 127.76, 127.61, 127.50, 127.43, 127.29, 126.99, 126.81, 126.62, 126.38, 125.72, 125.65, 125.57, 83.94 (CH); Analysis calc'd for $C_{61}H_{44}O_2$: C, 90.56; H, 5.48; found: C, 89.65; H, 5.51.

Compound **A3.20**

Isolated by column chromatography using 3% ethyl acetate in hexane as the eluent. The mono-substituted ether **A3.20** was isolated in 42% yield: m.p. > 295°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 - 7.35 (m, 36H), 6.26 (d, 1H), 5.51 - 5.72 (dt, 1H), 5.05 (s, 1H, OH), 3.37 (distorted d, 1H), 0.98 - 1.03 (m, 1H), 0.52 - 0.67 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 75.54, 74.58, 22.55, 22.18, 21.82; Analysis calc'd for $C_{58}H_{42}O_2$: C, 90.36; H, 5.49; found: C, 90.25; H, 5.40.

General Procedure for Carbon - Oxygen Coupling Reactions Using $K_3Fe(CN)_6$

4,4'-Bis-(1,1-diphenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9a**

To a solution of **A2.8a** (0.503 g, 0.783 mmol) in 20 mL of benzene was added a solution of $K_3Fe(CN)_6$ (2.63 g, 8.00 mmol) and KOH (0.455 g, 8.11 mmol) in 15 mL of water. The organic layer immediately turned dark red in color and the mixture was stirred vigorously at room temperature for 2 hours at which point **A3.3a** (0.544 g, 3.23 mmol) was added and the reaction was heated to reflux for 3 hours. The organic layer was washed several times with water (3 X 25 mL), extracted, dried over Na_2SO_4, filtered and the filtrate was evaporated to dryness. The crude product was recrystallized from a methanol - chloroform solution to give 0.740 g (97%) of **A3.9a** as a fine white powder: m.p. 241-243 °C (lit. 243-245°C); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.56 (br, s, 2H), 7.24 (br, s, 2H), 6.94 - 7.12 (m, 32H), 6.82 (br, s, 4H), 6.66 - 6.69 (m, 6H), 6.51 - 6.54 (d, 4H, J = 7.3 Hz), 6.23 (br, s, 2H), 5.16 (s, 2H, CH); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 150.74, 141.18, 141.15, 141.06, 140.67, 139.65, 138.58, 136.63, 135.98, 134.54, 134.16, 132.92, 132.74, 132.46, 132.44, 129.99, 128.32, 128.15, 128.10, 127.94, 127.66, 127.49, 127.24, 126.32, 126.19, 84.49 (CH); Analysis calc'd for $C_{74}H_{54}O_2$: C, 91.14; H, 5.58; found: C, 90.77; H, 5.33.

4,4'-Bis-(1-phenyl-1-(2-pyridine) methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9b**

The reaction was completed within 27 hours. The product was obtained in 87% yield as a light greenish powder after recrystallization from an ethyl acetate - hexanes solution: m.p. 252-256°C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.18 (d, 2H, J = 4.8 Hz), 7.44 - 7.56 (m, 4H), 6.69 - 7.27 (m, 39H), 6.50 - 6.57 (dd, 4H, J = 7.3 & 28.3 Hz), 6.26 (s, 1H), 5.20 (d, 2H, J = 22 Hz, CH); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 85.56 (CH), 85.31 (CH); MS (FAB matrix NBA) *m/e* 977.24 (M^++1, 7), 641.18 (10), 169.11 (88), 168.10 (100); Analysis calc'd for $C_{72}H_{52}N_2O_2$: C, 88.49; H, 5.37; found: C, 88.77; H, 5.73.

4,4'-Bis-(1-methyl-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9d**

The ether compound was obtained in 97% yield after 9 hours. The crude product was recrystallized from a methanol - chloroform solution: m.p. 243-245°C (lit. 245-248°C); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 6.94 - 7.58 (m, 35H), 6.87 (distorted d, 1H), 6.74 (s, 1H), 6.48 (dd, 5H, J = 6.8 & 17.5 Hz), 4.15 (d, 2H, J = 5.9 Hz CH), 0.80 (d, 6H, J = 3.9 Hz, CH$_3$); ^{13}C NMR (125 MHz, CD$_2$Cl$_2$) δ 79.82 (CH), 79.62 (CH), 21.42 (CH$_3$), 20.56 (CH$_3$).

4,4'-Bis-(1-phenyl-(2-phenylpropyl-1-en) methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9e**

The reaction was complete within 1.5 hours. The crude product was purified by reacystallization using a two solvent system (methanol - chloroform) to give 68% yield of **A3.9e** as a white powder: m.p. 224-228°C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.58 (d, 2H, J = 43.5 Hz), 7.39 (s, 1H), 7.20 - 7.27 (dd, 14H), 6.99 - 7.11 (m, 23H), 6.51 - 6.79 (m, 12H), 5.91 (d, 1H J = 15.6 Hz, CH-CH=C$\underline{\text{H}}$-), 5.76 (d, 1H J = 15.6 Hz, CH-CH=C$\underline{\text{H}}$-), 5.35 - 5.48 (m, 2H, CH-C$\underline{\text{H}}$=CH), 4.48 - 4.53 (m, 2H, C$\underline{\text{H}}$-CH=CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 84.72 ($\underline{\text{C}}$H-CH=CH), 84.44 ($\underline{\text{C}}$H-CH=CH); Analysis calc'd for C$_{78}$H$_{58}$O$_2$: C, 91.19; H, 5.69; found: C, 91.25; H, 5.65.

4,4'-Bis-(1-(ethylene)-1-nonyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9f**

The reaction was complete after 24 hours. Purification of the crude product by column chromatography (2 % ethyl acetate in hexanes) resulted in a 85% yield of **A3.9f** as white crystals: m.p. 114-117°C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50 (br d, 2H), 7.01 - 7.31 (m, 21H), 6.99 (d, 4H, J2 = 7.8 Hz), 6.88 - 6.93 (m, 2H), 6.78 (d, 2H, J = 14.4 Hz), 6.7 (br. s, 1H), 4.77 - 4.84 (q, 1H, CH-C$\underline{\text{H}}$=CH$_2$), 4.72 (d, 1H, J = 9.8 Hz, CH-C$\underline{\text{H}}$=CH2), 4.56 - 4.64 (m, 2H, CH-CH=C$\underline{\text{H}}_2$), 4.48 (dd, 1H, J = 1.95, 16.6 Hz, CH-CH=C$\underline{\text{H}}$2), 4.37 (dd, 1H, J = 1.95, 16.6 Hz, CH-CH=C$\underline{\text{H}}_2$), 3.28 - 3.35 (m, 2H, CH), 0.74 - 1.29 (m, 38H); ^{13}C NMR (125 MHz, CD$_2$Cl$_3$) δ 83.74 ($\underline{\text{C}}$H-CH=CH$_2$), 83.09 ($\underline{\text{C}}$H-CH=CH$_2$); Analysis calc'd for C$_{72}$H$_{78}$O$_2$: C, 88.65; H, 8.07; found: C, 88.40; H, 8.19.

4,4'-Bis-(1-(ethylene)-1-(1-pentyl-6-en) methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9g**

The reaction was over in 24 hours and the crude product was purified by column chromatography using 3% ethyl acetate in hexane as the eluent. The pure ether **A3.9g** was recovered in 72% yield as a white powder: m.p. 150 - 153°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 - 7.55 (br d, 2H, J = 39.6 Hz), 7.16 - 7.25 (m, 10H), 7.05 - 7.13 (m, 12H), 6.98 (d, 3H, J = 7.3 Hz), 6.60 (br s, 1H), 5.72 - 5.77 (m, 2H, CH2-C$\underline{H}$=CH$_2$), 4.90 - 4.96 (dd, 4H, J = 17.1, 23.0 Hz, CH$_2$-CH=C$\underline{H}_2$), 4.72 - 4.82 (m, 2H, CH-C$\underline{H}$=CH$_2$), 4.59 - 4.63 (m, 2H, CH-CH=C$\underline{H}_2$), 4.46 - 4.50 (distorted d, 1H, CH-CH=C$\underline{H}_2$), 4.36 (d, 1H, J = 16.1, CH-CH=C$\underline{H}_2$), 3.04 - 3.34 (m, 2H, C$\underline{H}$-CH=CH$_2$), 1.89 - 1.92 (t, 4H), 1.08 - 1.17 (m, 6 H), 0.87 - 0.92 (m, 6H), 0.74 - 0.79 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 83.67 ($\underline{C}$H-CH=CH$_2$), 83.03 ($\underline{C}$H-CH=CH$_2$); Analysis calc'd for $C_{68}H_{66}O_2$: C, 89.23; H, 7.27; found: C, 89.27; H, 7.25.

4,4'-Bis-(cyclohexen-2-en-1-oxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.9h**

Ether **A3.9h** was obtained in 91% yield as white flakes (recrystallized from a methanol -chloroform solution) after 21 hours: m.p. 251-253°C (lit. 252-253°C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17-7.40 (m, 14H), 6.97-7.15 (m, 9H), 6.89-6.95 (m, 9H), 5.50 (dd, 2H, J = 9.2 & 24 Hz), 4.90 (d, 2H, J = 61 Hz), 3.59 (d, 2H, J = 38 Hz, CH), 1.56 (dd, 4H, J = 18 & 46 Hz), 1.17 (d, 2H, J = 73 Hz), 0.70-0.94 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.97, 140.70, 139.95, 139.87, 139.20, 138.24, 136.78, 136.47, 134.64, 134.61, 134.34, 133.86, 133.64, 132.03, 131.82, 131.71, 129.75, 129.66, 127.67, 127.16, 127.04, 126.92, 126.70, 126.66, 126.55, 126.24, 125.87, 125.80, 125.63, 125.60, 125.56, 75.87 (O-CH), 75.72 (CH), 27.73, 24.93, 17.04; Analysis calc'd for $C_{60}H_{50}O_2$: C, 89.74; H, 6.28; found: C, 89.57; H, 6.39.

2,2',3,3',5,5'-Hexaphenyl-1,1'-biphenyl-4-(9-fluorene)-4'-ol **A3.91**

The product came out of solution after 2 hours and was insoluble in common organic solvents. The product was purified by washing the solid several times with water and diethyl ether to remove the starting materials and reagents. The mono-substituted ether was obtained in 82% yield after drying under vacuum for 24 hours at 100°C: m.p. 284-286°C; Analysis calc'd for $C_{74}H_{50}O_2$: C, 90.78; H, 5.23; found: C, 90.45; H, 5.13.

4,4'-Bis-(1,1-diphenyl methoxy)-2-chloro-3,3',5,5'-tetraphenyl-1,1'-biphenyl **A3.14**

The reaction was over in 2 hours. The ether **A3.14** was isolated by column chromatography using 3% ethyl acetate in hexane as the eluent. The pure ether was recovered in 79% yield as a white powder: m.p. 248-250°C (lit. 250-253°C); ^1H NMR (200 MHz, $CDCl_3$) δ 7.24 - 7.52 (m, 22H), 6.92 - 7.06 (t, 11H), 6.66 - 6.75 (t, 10H), 5.29 (d, 2H, J = 7.3 Hz, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.34, 141.00, 140.82, 139.58, 136.52, 136.29, 135.63, 134.82, 132.70, 131.81, 131.52, 130.22, 129.91, 128.61, 128.45, 128.18, 128.04, 127.83, 127.68, 127.60, 127.53, 127.43, 85.24 (CH), 85.11 (CH).

4,4'-Bis-(1,1-diphenyl methoxy)-2,2'-dichloro-3,3',5,5'-tetraphenyl-1,1'-biphenyl **A3.15**

After 7 hours the reaction was complete. The product was recrystallized form a methanol - chloroform solution, affording **A3.15** as a white powder in 65% yield: m.p. 193 - 194°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, 4H, J = 6.8 Hz), 7.24 - 7.35 (m, 18H), 7.04 - 7.07 (distorted t, 4H), 6.98 - 7.01 (t, 8H), 6.70 (d, 8H, J = 7.3 Hz), 5.31 (s, 2H, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.14, 140.15, 140.12, 138.26, 136.12, 135.66, 134.85, 134.21, 132.31, 131.26, 130.98, 129.45, 127.63, 127.34, 127.29, 127.20, 84.50 (CH); Analysis calc'd for $C_{62}H_{44}Cl_2O_2$: C, 83.57; H, 4.98; found: C, 84.13; H, 4.95.

4,4'-Bis-(1,1-diphenyl methoxy)-2, 3,3',5,5'-pentaphenyl-1,1'-biphenyl **A3.16**

The reaction was complete within 3.5 hours, the ether compound **A3.16** was recovered in 83 % yield after purification by column chromatography using 3% ethyl acetate in hexane as the eluent: T_m 225°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (br s, 1H), 7.23 (distorted d, 2H), 6.96 - 7.12 (m, 31H), 6.82 (br s, 4H), 6.69 (br s, 5H), 6.53 (d, 4H, J = 5.9 Hz), 6.24 (br s, 1H), 5.09 (s, 2H, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.95, 140.42, 140.27, 140.15, 139.95, 138.88, 137.75, 135.93, 135.17, 134.06, 133.35, 132.03, 131.72, 129.20, 127.60, 127.40, 127.01, 126.94, 126.88, 126.69, 126.47, 125.57, 125.39, 83.76 (CH); Analysis calc'd for $C_{68}H_{50}O_2$: C, 90.85; H, 5.60; found: C, 90.84; H, 5.60.

4,4'-Bis-(1,1-diphenyl methoxy)-2,2'-dimethyl-3,3',5,5'-tetraphenyl-1,1'-biphenyl **A3.17**

The ether compound **A3.17** was obtained after 2 hours in 78% yield after purification by column chromatography using 3% ethyl acetate in hexane as the eluent.: m.p. 117 - 121°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, 3H, J = 6.8 Hz), 7.21 - 7.31 (m, 11H), 7.12 (s, 1H), 7.08 (s, 1H), 7.02 - 7.06 (t, 3H), 6.96 - 6.98 (q, 6H), 6.71 (d, 6H, J = 7.8 Hz), 5.31 (s, 2H, CH), 1.79 (s, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.50, 140.65, 140.58, 139.24, 138.18, 137.62, 136.44, 134.54, 132.46, 130.84, 130.81, 130.74, 129.33, 127.83, 127.60, 127.51, 127.38, 127.33, 127.29, 127.11, 126.82, 126.74, 126.51, 126.38, 83.92 (CH), 18.14 (CH_3); Analysis calc'd for $C_{64}H_{50}O_2$: C, 90.32; H, 5.92; found: C, 90.43; H, 6.15.

4,4'-Bis-(1,1-diphenylmethoxy)-2,2'-di(4-methoxyphenyl)-3,3',5,5'-tetraphenyl-1,1'-biphenyl **A3.18**

The reaction was complete within 5 hours. The product was isolated by column chromatography using 3% ethyl acetate in hexane as the eluent, affording 74% of **A3.18** as a white powder: m.p. 234 - 236°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (br s, 2H), 7.24 (br s, 2H), 7.13 (br s, 8H), 7.00 - 7.04 (m, 17H), 6.87 (br s, 4H), 6.64 - 6.79 (m, 11H), 6.58 (br s, 4H), 6.32 (br s, 2H), 5.12 (s, 2H, CH), 3.81 (s, 2H, OCH_3); ^{13}C NMR () δ 157.41, 149.90, 140.36, 140.34, 139.85, 139.02, 137.88, 135.98, 135.51, 134.08, 133.20, 132.33, 131.96 - 131.78 (br peak), 129.22, 127.51, 127.35, 127.26, 126.88, 126.82, 126.70, 126.35, 125.45, 83.72 (CH), 55.08 (OCH_3); Analysis calc'd for $C_{76}H_{58}O_4$: C, 88.17; H, 5.65; found: C, 87.95; H, 5.82.

Acetal compounds

4,4'-Bis-(1-phenyl-1-(4-phenylsulfide) methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10b**

The reaction was over in 1.5 hours. The crude product was recrystallized from a chloroform - methanol solution, affording 79% yield of **A3.10b** as a pale yellow fine powder: m.p. 145 - 148°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.20 - 7.40 (m, 56 H), 5.30 - 5.40 (distorted dd, 2H, CH); ^{13}C NMR (125 MHz, CDCl3) δ 90.51 (CH), 90.70 (CH), 91.22 (CH), 91.44 (CH); MS (FAB matrix NBA) *m/e* 1039.47 (M^++1, .3), 929.43 (M^++1 - (C_6H_5S), 4.8); Analysis calc'd for $C_{74}H_{54}O_2S_2$: C, 85.52; H, 5.24; found: C, 85.95; H, 5.48.

4,4'-Bis-(1-(N-carbazole)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10d**

The crude product was purified by column chromatography using 9 % ethyl acetate in hexane as the eluent and recrystallized from a solution of chloroform and methanol. The ether **A3.11d** was obtained in 67% yield as a white powder: m.p. 200-203°C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.91 (d, 1H, J = 7.8 Hz), 7.86 (d, 3H, J = 6.8 Hz), 6.43 - 7.40 (m, 54 H), 6.10 - 6.17 (dt, 1H), 5.62 - 5.68 (dd, 1H, J = 6.8 & 26.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 86.25 (CH), 86.21 (CH), 85.83 (CH), 85.73 (CH); Analysis calc'd for $C_{86}H_{60}N_2O_2$: C, 89.55; H, 5.25; N, 2.43; found: C, 89.34; H, 5.20; N, 2.38.

4,4'-Bis-(1-(1-benzotriazole)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10e**

The mixture of products were separated by column chromatography using chloroform as the eluent. **A3.10e** was isolated as a white powder in 0.190g (20 %), and 0.331 g of an unknown compound which by NMR still appears to be a mixture: m.p. 294 - 297°C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.79 - 7.82 (m, 1H), 6.70 - 7.41 (m, 46H), 6.67 (d, 2H, J = 7.3 hz), 6.20 - 6.27 (m, 1H), 6.14 (d, 1H, J = 8.8 Hz), 6.07 (d, 1H, J = 8.3 Hz); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 89.20 (CH), 88.88 (CH); MS (FAB Matrix NBA) *m/e* 938.27 (M^+-($C_6H_5N_3$), 3.3), 820.25 (2), 653.22 (3.1); Analysis calc'd for $C_{74}H_{52}N_6O_2$: C, 84.06; H, 4.96; found: C, 84.36; H, 5.41.

4,4'-Bis-(1-(2-phenylethyl-1-oxy)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10l**

After 1 hour the acetal compound **A3.10l** was obtained in 85% yield. The product was recrystallized from a methanol - chloroform solution at 5°C: m.p. 119 - 124°C; ^{1}H NMR (500 MHz, benzene-d_6) δ 7.60 (br s, 2H), 7.48 (dd, 2H, J= 7.3 & 14.2 Hz), 7.20 - 7.36 (m, 6H), 6.78 - 7.16 (m, 42H), 5.34 (s, 2H, C$\underline{H}$-O-CH_2-CH_2), 3.45 - 348 (t, 1H, CH-O-C$\underline{H}_2$-CH_2), 3.38 (br s, 1H, CH-O-CH2-C$\underline{H}$2), 2.93 - 3.05 (m, 2H, CH-O-C$\underline{H}_2$-

C$\underline{H}_2$), 2.48 - 2.52 (m, 2H, CH-O-C$\underline{H}_2$-CH$_2$), 2.42 (s, 2H, CH-O-CH$_2$-C$\underline{H}_2$); ^{13}C NMR (125 Mhz, benzene-d$_6$) δ 105.45, 105.41, 105.39, 105.36 ($\underline{C}$H-O-CH$_2$-CH$_2$), 70.07, 70.02, 69.72, 69.64 (CH-O-$\underline{C}$H$_2$-CH$_2$), 36.89, 36.77 (CH-O-CH2-$\underline{C}$H2); Analysis calc'd for $C_{78}H_{62}O_4$: C, 88.10; H, 5.88; found: C, 87.81; H, 6.03.

4,4'-Bis-(1-(2-(4-chlorophenyl)ethyl-1-oxy)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10m**

Compound **A3.10m** was obtained in 76% yield from a solution of methanol and chloroform at 5°C.: m.p. 98 - 104°C; ^{1}H NMR (500 MHz, benzene-d$_6$) δ 7.56 (br s, 2H), 7.38 - 7.43 (t, 2H), 7.18 - 7.33 (m, 4H), 6.68 - 7.14 (m, 38H), 6.59 - 6.63 (d, 4H, J = 16.1 Hz), 5.18 (distorted d, 2H, C$\underline{H}$-O-CH$_2$-CH$_2$), 3.39 - 3.54 (q, 1H, CH-O-C$\underline{H}_2$-CH$_2$), 3.31 - 3.39 (q, 1H, CH-O-CH$_2$-C$\underline{H}_2$), 2.86 - 2.92 (q, 1H, CH-O-CH$_2$-C$\underline{H}_2$), 2.77 - 2.83 (q, 1H, CH-O-C$\underline{H}_2$-CH$_2$), 2.44 - 2.58 (q, 2H, CH-O-C$\underline{H}$2-CH2), 2.35 - 2.43 (s, 2H, CH-O-CH$_2$-C$\underline{H}_2$); Analysis calc'd for $C_{78}H_{60}Cl_2O_2$: C, 82.74; H, 5.34; found: C, 83.02; H, 5.46.

4,4'-Bis-(1-(2-(4-methoxyphenyl)ethyl-1-oxy)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10n**

The acetal compound **A3.10n** was obtained in 81% yield after recrystallization with a solution of methanol and methylene chloride at 5°C: m.p. 110-118°C; ^{1}H NMR (500 MHz, benzene-d$_6$) δ 7.61 (br s, 2H), 7.48 - 7.52 (t, 2H), 7.24 - 7.31 (m, 6H), 6.79 - 7.15 (m, 36H), 6.62 (d, 2H, J = 8.3 Hz), 6.55 (d, 2H, J = 8.3 Hz), 5.33 (d, distorted d, 2H, J = 9.8 Hz, C$\underline{H}$-O-CH$_2$-CH$_2$), 3.46 - 3.52 (q, 1H, CH-O-C$\underline{H}_2$-CH$_2$), 3.37 - 3.41 (q, 1H, CH-O-CH$_2$-C$\underline{H}_2$), 3.22 (d, 6H, J = 12.7 Hz, OCH$_3$), 2.97 - 3.01 (q, 1H, CH-O-CH$_2$-C$\underline{H}_2$), 2.92 - 2.95 (q, 1H, CH-O-C$\underline{H}_2$-CH$_2$), 2.48 - 2.60 (m, 2H, CH-O-C$\underline{H}_2$-CH$_2$), 2.41 - 2.46 (t, 2H, CH-O-CH$_2$-C$\underline{H}_2$); ^{13}C NMR (125 MHz, benzene-d$_6$) δ 105.30

(105.28), 105.17, 105.15 ($\underline{C}H-O-CH_2-CH_2$), 69.83, 69.79, 69.46, 69.42 ($CH-O-\underline{C}H_2-CH_2$), 54.63 ($OCH_3$), 36.90, 36.79 ($CH-O-CH_2-\underline{C}H_2$), ; Analysis calc'd for $C_{80}H_{66}O_6$: C, 85.53; H, 5.92; found: C, 85.47; H, 6.19.

4,4'-Bis-(1-(2-(2-methoxyphenyl)ethyl-1-oxy)-1-phenylmethoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10o**

Compound **A3.10o** was obtained in 71% yield after recrystallization at 5℃ in a solution of methanol and methylene chloride: m.p. 67 - 74°; ^{1}H NMR (500 MHz, benzene-d_6) δ 7.61 (br s, 2H), 7.46 - 7.50 (dd, 2H, J = 7.3 & 14.7 Hz), 7.34 (d, 2H, J = 6.8 Hz), 7.30 (d, 2H, J = 6.8 Hz), 7.23 (br s, 3H), 6.80 - 7.33 (m, 32H), 6.75 (br s, 3H), 6.58 (s, 2H), 6.48 (d, 1H), 6.45 (d, 1H), 5.32 (s, 2H, $C\underline{H}-O-CH_2-CH_2$), 3.45 - 3.48 (m, 1H, $CH-O-C\underline{H}_2-CH_2$), 3.37 - 3.39 (m, 1H, $CH-O-CH_2-C\underline{H}_2$), 3.27 (s, 6H, OCH_3), 2.96 - 3.00 (m, 2H, $CH-O-C\underline{H}_2-C\underline{H}_2$), 2.50 - 2.52 (m, 2H, $CH-O-C\underline{H}_2-CH_2$), 2.40 - 2.46 (m, 2H, $CH-O-CH_2-C\underline{H}_2$); Analysis calc'd for $C_{80}H_{66}O_6$: C, 85.53; H, 5.92; found: C, 85.90; H, 6.22.

4,4'-Bis-(1-(naphthanyl-2-oxy)-1-phenyl methoxy)-2,2',3,3',5,5'-hexaphenyl-1,1'-biphenyl **A3.10p**

The reaction was over in 20 hours and the crude product was purified by column chromatography (2% ethylacetate in hexanes) and recrystallization from a chloroform-methanol solution. **A3.10p** was obtained in 82% yield as transparent crystals: m.p. 156-159°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.71 (m, 2H), 7.58 (t, 2H), 7.48 (d, 3H, J2 = 8.3 Hz), 6.86-7.39 (m, 35H), 6.62-6.72 (m, 9H), 6.46 (br. d, 4H), 6.26 (br s, 1H), 5.73 (q, 2H, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 103.00 (CH), 102.30 (CH); MS (MALDI matrix DHB) *m/e* 1129 (M^++K^+), 963 ((M^+ - $C_{10}H_7O$) + K^+), 731 ((M^+ -

$C_{17}H_{13}O$) + K^+); Analysis calc'd for $C_{82}H_{58}O_4$: C, 88.93; H, 5.28; found: C, 88.11; H, 5.30.

General Procedures for the Cleavage of the Acetal and Ether Compounds

Acetal Cleavage with Concentrated Hydrochloric acid

The acetal compound **A3.10n** (0.30 g, 0.27 mmol) was dissolved in 5 ml of chloroform. To this solution was added 0.2 mL of HCl and 0.2 mL of water and the solution was stirred at room temperature The reaction was monitored by HPLC and within 1 hour the acetal compound was cleaved. The products **A3.23e** and **A3.21** were distilled off as a mixture and the yields of the two compounds were determined based on HPLC calibration curves to be 0.04 g (57%) and 0.06 (91%), respectively. Biphenol **A2.8a** was isolated in 93% (0.16 g) yield. All the compounds were identified by comparison with authentic samples.

Ether Cleavage with Trifluoroacetic Acid

To a solution of ether **A3.9c** in 10 mL of chloroform was added 250 µL of trifluoroacetic acid. The solution was stirred at room temperature 5 hours. The organic layer was washed several times with water and 5% $NaHCO_3$ solution. The organic layer was extracted and evaporated to dryness. TLC showed that there are two compounds which were purified by column chromatography. The biphenol **A2.8a** and the primary alcohol **A3.26** were recovered in 91%(0.35 g) and 50% (0.08g) yield, respectively.

Ether Cleavage with 48% Hydrobromic Acid

A 10 ml flask charged with ether **A3.9a** (0.30g, 0.31 mmol), 5 mL of acetic acid , and 0.5 mL of 48% HBr was heated to reflux. Within 1 hour the ether compound was cleaved, the biphenol **A2.8a** came out of solution and was filtered and recrystallized to give 0.16 g (79%). Benzohydrol **A3.24** was recovered by evaporating the filtrate. The solid was redissolved in methylene chloride and washed several times with water (3x10 mL). The organic layer was evaporated to give 0.08 g (73%) of **A3.24**.

Hydrogenation of the Ether Compounds

A 25 mL flask was charged with **A3.9a** (0.33 g, 0.31 mmol), $AlCl_3$ (5.2 mg, 0.04 mmol), 64.0 mg of 10% Pd/C, 0.29 mL of cyclohexene , and 10 mL of benzene. The reaction was heated to 70°C under an atmosphere of argon for 72 hours. Diphenylmethane **A3.3a** and benzophenone **A3.19** mixture was distilled off at 100-110°C. Total yield of 95.5 mg of which 86.9 mg (73%) was **A3.3a** and 8.6 mg (7%) was **A3.19** based on HPLC calibration curves. Biphenol **A2.8a** was recovered in 92% yield after recrystallization.

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CHAPTER A4

NOVEL CARBON - OXYGEN COUPLED POLYMERS

A4.1 Introduction

The immense advancement in computer technology has placed an increasing demand on the development of new photoresist materials and processes leading to circuits with smaller features and higher resolution.[1-4]

A photoresist is defined as a polymeric material that undergoes a photochemical reaction. There are two types of photoresists. In a positive resist the irradiated region is soluble and washed off during the development step, while in the negative resist the photochemical reaction that occurs on the irradiated area renders the materials insoluble (Figure A4.1).[4] One of the more common positive photoresist materials used is a mixture of novolac resin **A4.1** and a substituted diazonaphthoquinone **A4.2** (the substitutent is generally an aryl sulfonate)[4]. The diazonaphthoquinone compound acts as a dissolution inhibitor rendering the novolac resin insoluble in aqueous base. When a specific area is irradiated **A4.2** is converted to the indene carboxylic acid **A4.3** (Scheme A4.1). **A4.3** is now soluble in base and is therefore not a dissolution inhibitor and the exposed area now becomes soluble in aqueous base. An example of a negative resist is chromated gelatin. This process appears to involve a complex of Cr^{3+} which is generated when irradiated within the polymer resin, such as poly(vinylbutyral and poly (vinyl alcohol).[4] This complex behaves just as a crosslinked polymer.

Current technologies used in the production of microelectronics devices rely on optical photolithography because of cost and convenience. The invention of deep UV photolithography (irradiation at wavelengths below 300 nm) has opened the door for the development of circuits with dimensions of 0.25 μm or lower. New photoresists utilizing

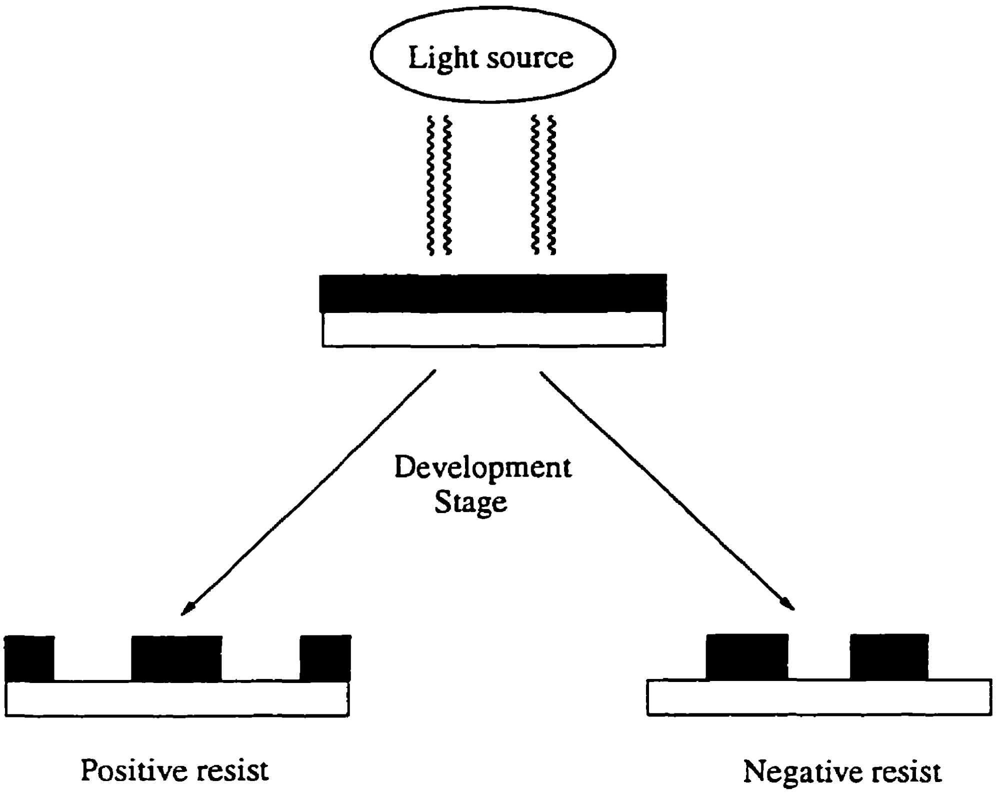
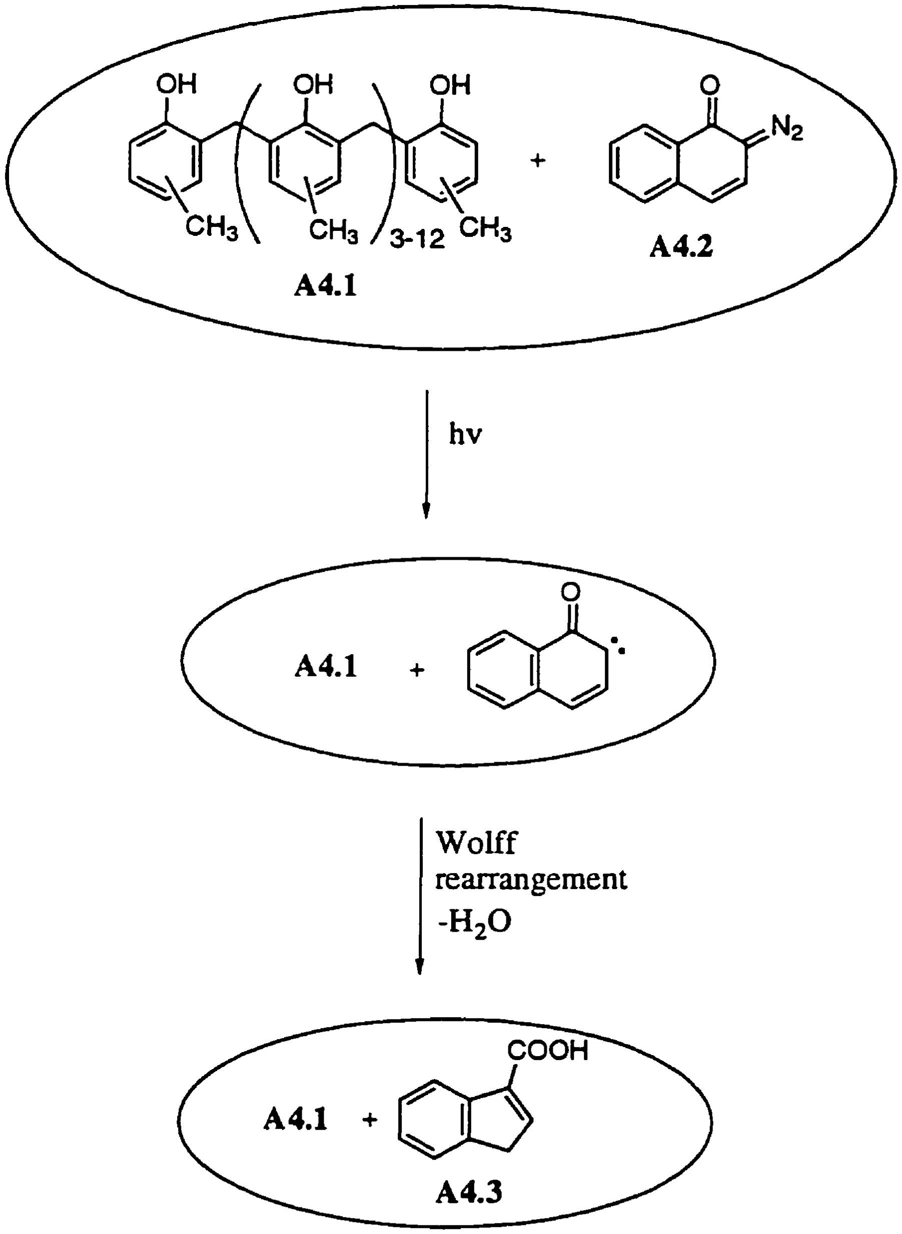


Figure A4.1. Schematic of photoresist process.

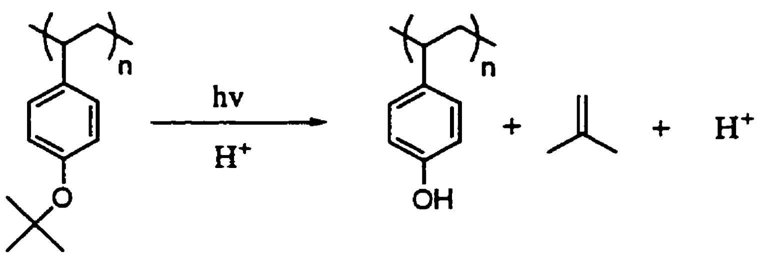
this technique were developed with improved sensitivity and enhanced resolution. Recently the development of photosensitive acid generators which decompose to produce a strong acid when irradiated, such as triphenyl sulfonium hexafluoroantiomy salt, have shown great potential.[5-7] The acid generated either cleaves a functional group or the polymer chain. In the case of poly(4-t-butoxystyrene) the t-butyl group is cleaved to give poly(4-hydroxystyrene) which is now soluble in aqueous base and easily be washed off (Scheme A4.2).[8]

A4.1.1 Goals and Strategies

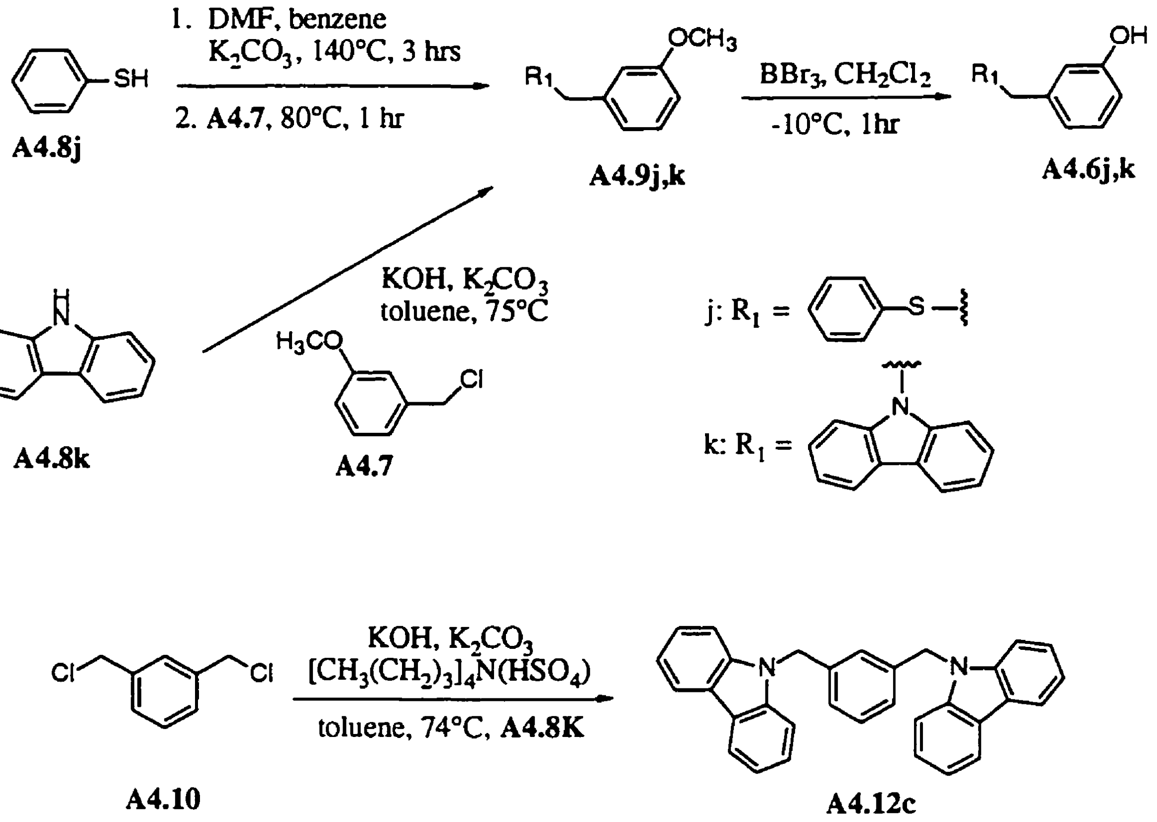
Previously we have shown that the carbon - oxygen coupling reaction between **A2.8a** and activated methylene compounds is quantitative and the corresponding products are cleaved under acidic conditions. In this chapter we describe research exploiting this chemistry by preparing novel carbon - oxygen coupled polymers **A4.4a-g** and **A4.5a-i**, which are potential photoresist candidates in the electronic industry. They should be effectively cleaved to low molecular weight products both thermally and under acidic conditions.



Scheme A4.1



Scheme A4.2



Scheme A4.3

A4.2 Results and Discussions

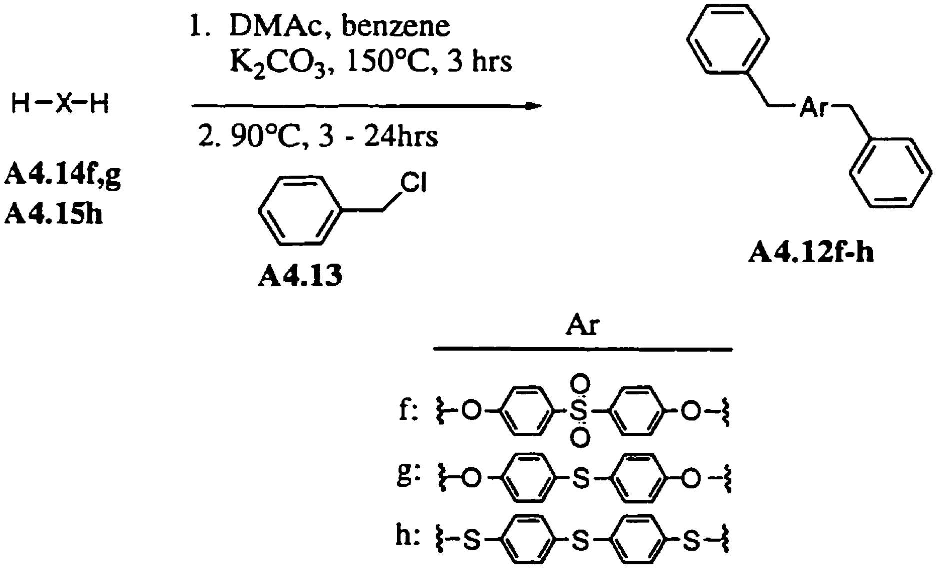
A4.2.1 Monomer Synthesis

The hydroxy compounds **A4.6j,k** were prepared by a nucleophilic displacement of 3-methoxybenzyl chloride **A4.7** with the potassium salt of thiophenol **A4.8j** in DMF at

90°C for 4 hours and with carbazole **A4.8k** by the method described by Dehalow *et al.*[9] Both methoxy derivative **A4.9j,k** were formed in 89% yield. The hydroxy derivatives **A4.6j,k** were obtained in 77% and 44% yield, respectively after cleavage of the methoxy group with boron tribromide in methylene chloride at -10°C (Scheme A4.3).

Compound **A4.12c** was obtained in 49% yield by reacting **A4.8k** with α,α'-dichloro-meta-xylene **A4.10** in the presence of KOH, K_2CO_3 and tetrabutylammonium hydrogen sulfate at 74°C (Scheme A4.3).

The bifunctional methylene monomers **A4.11a-e** and **A4.12a-i** were prepared by several methods (Table A4.1 and A4.2). Method A is a nucleophilic displacement of benzyl chloride **A4.13** with the potassium salts of biphenols **A4.14f,g** and dithiol **A4.15h** prepared at 90°C in DMAc under an atmosphere of nitrogen (Scheme A4.4).



Scheme A4.4

Method B also involves a nucleophilic displacement reaction, in this case a series of activated difluoro monomers **A4.16a-d** were reacted with 4-hydroxydiphenylmethane **A4.17** at 150°C for 6-9 hours. Compounds **A4.11a-d** were obtained in high yields.

Table A4.1. List of methylene monomers and ether polymers.

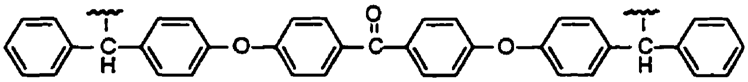
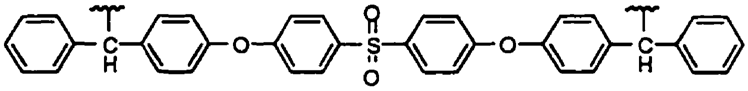
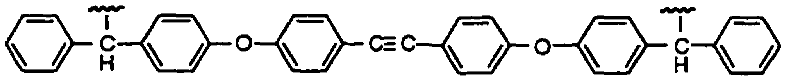
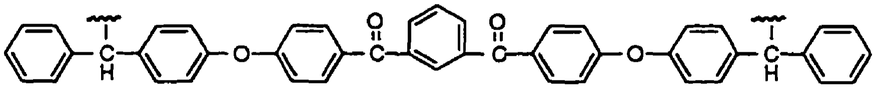
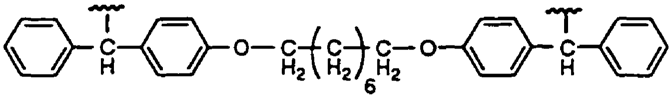
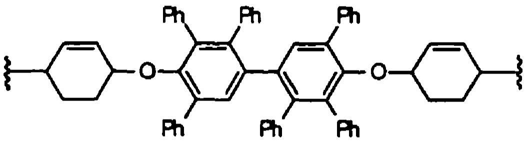
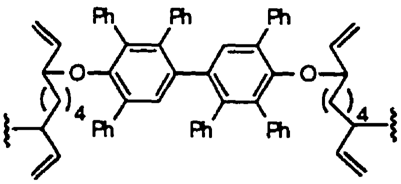
Entry		D
A4.11	A4.4	
a	a	
b	b	
c	c	
d	d	
e	e	
A3.9h	f	
A3.9g	g	

Table A4.2. List of methylene monomers and acetal polymers.

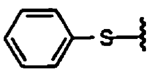
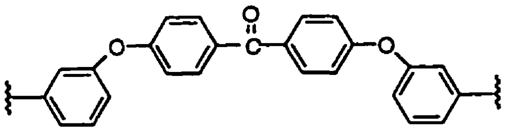
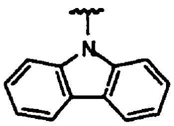
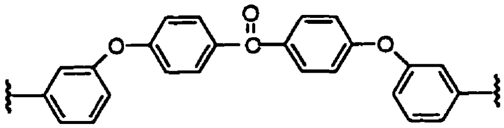
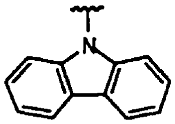
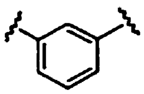
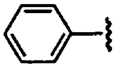
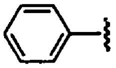
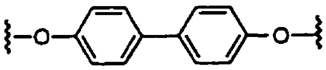
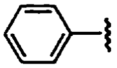
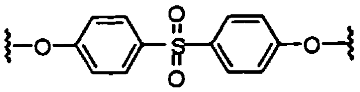
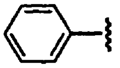
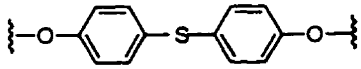
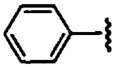
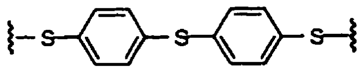
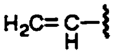
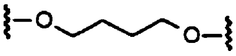
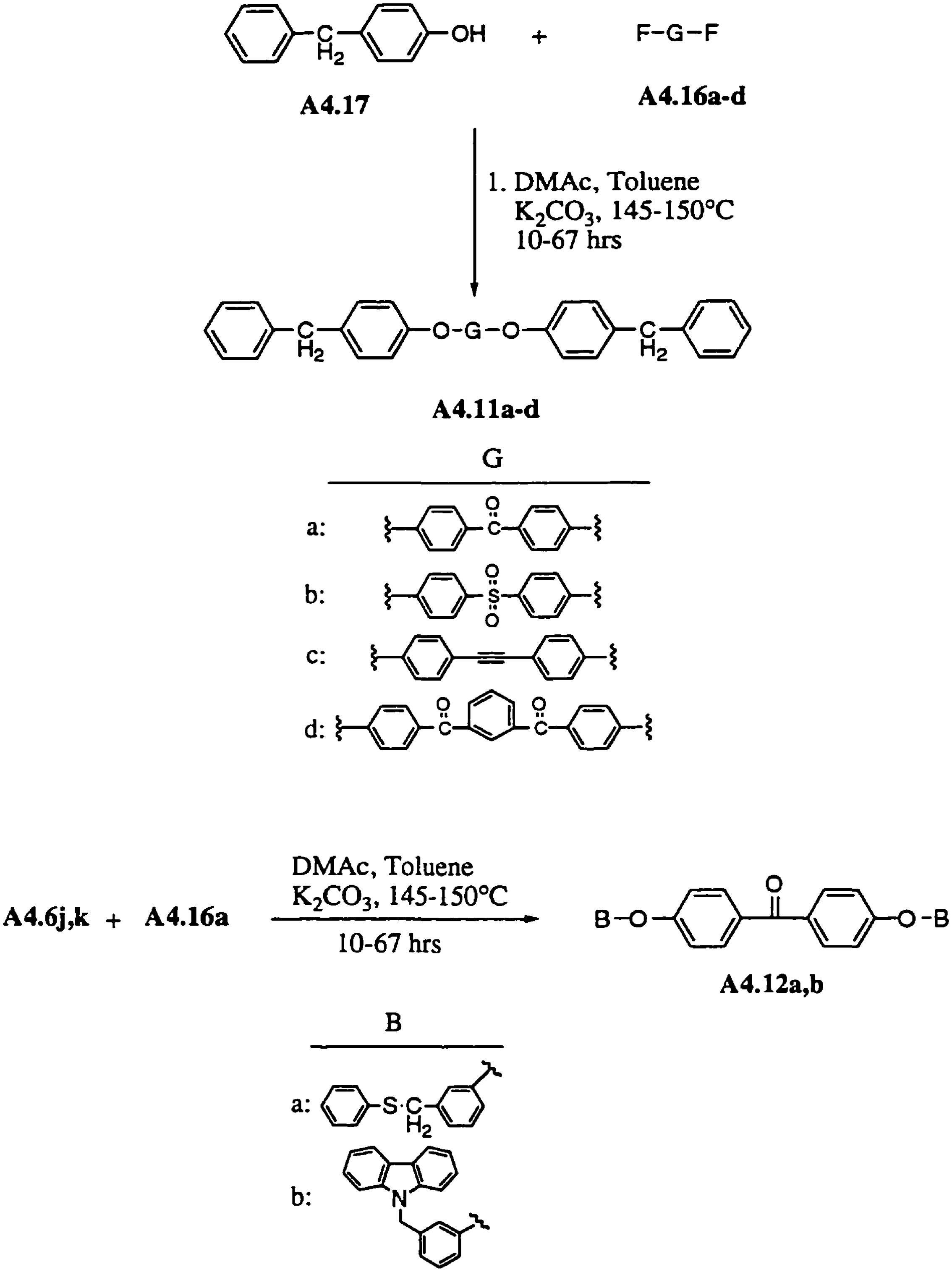
Entry		Y	X
A4.12	A4.5		
a	a		
b	b		
c	c		
d	d		
e	e		
f	f		
g	g		
h	h		
i	i	 $H_2C=\underset{H}{C}-$	

Table A4.3. Yields and NMR Chemical shifts of the methylene containing monomers.

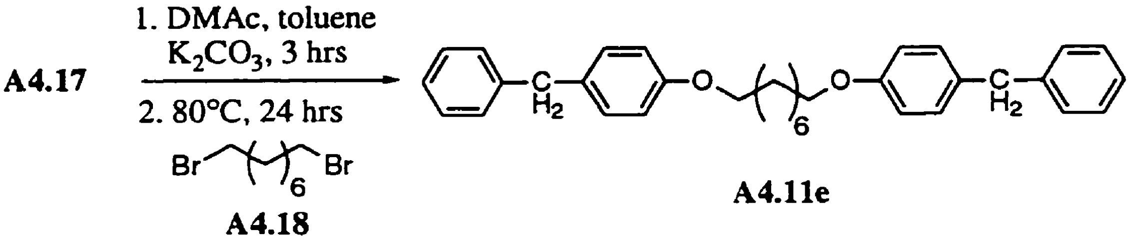
Entry	Isolated Yield (%)	m.p. (°C)	Methylene Group	
			^{1}H (ppm)	^{13}C (ppm)
A4.11a	91	113-115	3.99 (s)	41.23
A4.11b	61	127-129	3.95 (s)	41.55
A4.11c	57	156-159	4.04 (s)	41.60
A4.11d	94	143-155	3.95 (s)	41.55
A4.11e	50	67-69	3.91 (s)	41.00
A4.12a	68	82-85	4.10 (s)	38.86
A4.12b	69	107-110	5.71 (s)	46.12
A4.12c	49	204-107	5.32 (s)	46.30
A4.12f	85	202-206	5.05 (s)	70.30
A4.12g	63	134-136	5.04 (s)	70.12
A4.12h	59	138-140	4.09 (s)	38.84

Monomers **A4.12a,b** obtained in 68% and 69% yield, respectively (Table A4.3), were also prepared using method B, though the hydroxy monomer **A4.17** was replaced by **A4.6j,k**, respectively. The low yield obtained for monomers **A4.12a,b** were due to the difficulty in purification (Scheme A4.5).

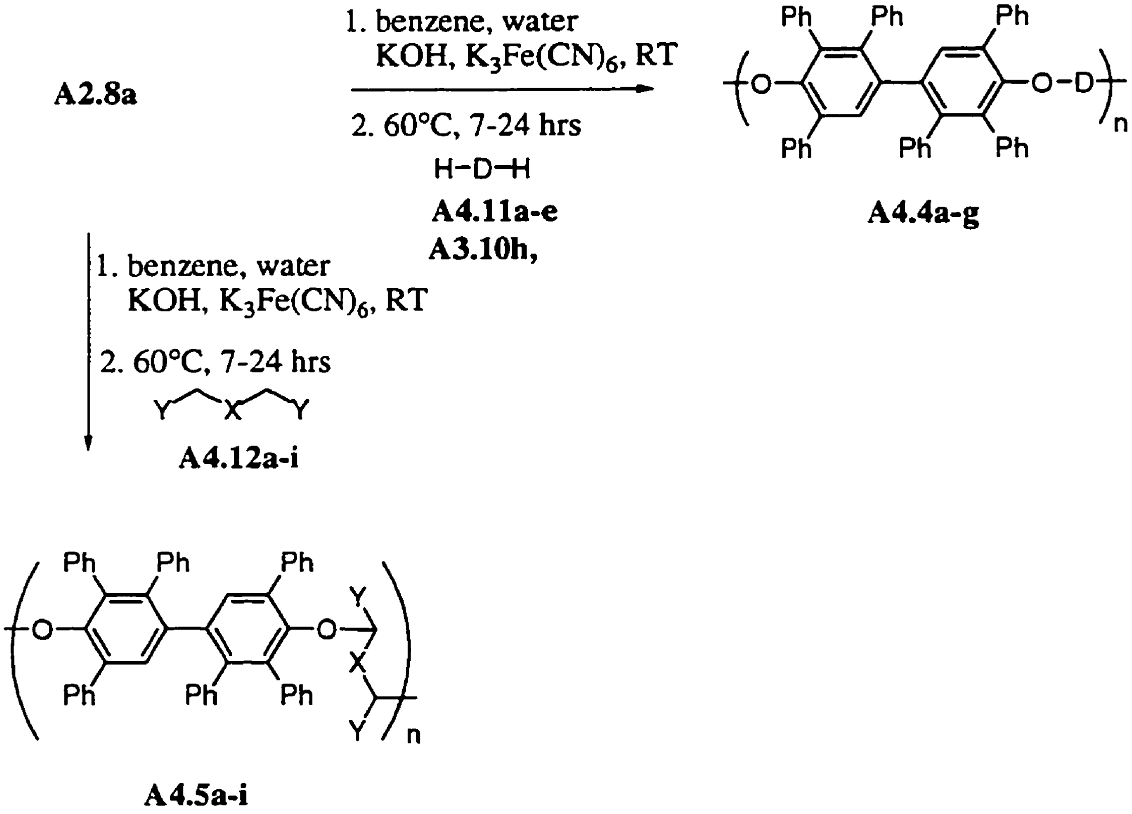
Compound **A4.11e** obtained in 50% yield was prepared by method C, which involved reacting the potassium salt of **A4.17** with 1,8-dibromoctane **A4.18** at 80°C in DMAc for 24 hours (Scheme A4.6). All the yields and physical properties are listed in table A4.3.


OH
+
F−G−F
A4.17
A4.16a-d
1. DMAc, Toluene
K2CO3, 145-150°C
10-67 hrs
O−G−O
A4.11a-d
G
a:
b:
c:
d:
DMAc, Toluene
K2CO3, 145-150°C
10-67 hrs
A4.6j,k + A4.16a
B−O
O−B
A4.12a,b
B
a:
b:
S
N

Scheme A4.5



Scheme A4.6



Scheme A4.7

A4.2.2 Polymer Synthesis and Characterization

The acetal and ether polymers **A4.4a-g** and **A4.5a-i**, respectively (Table A4.1 and A4.2) were prepared by an in situ oxidation of **A2.8a** with an alkaline solution of $K_3Fe(CN)_6$. This was followed by a coupling reaction with monomers **A4.12a-i** and **A4.11a-g**, respectively at 60°C under an atmosphere of argon (Scheme A4.7). The polymers were obtained in high yields (Table A4.4) and are soluble in common organic solvents such as chloroform, NMP, DMAc, etc..

Table A4.4. Physical properties and yields of the acetal and ether polymers[a]

Entry	Solvent	Temp. (°C)	Rxn Time (hrs)	Isolated Yield (%)	T_g (°C)	T_d (°C)	TGA N_2/Air	Mw (g/mol)	Mn (g/mol)	η_{inh} (dL/g)
A4.4a	chlorobenzene	60	24	82	222	312	413 / 423	400 000	38 000	0.82
A4.4b	benzene	60	5	87	225	314	398 / 397	242 000	22 000	0.54
A4.4c	benzene	60	25	86	219	316	403 / 408	114 000	20 000	0.26
A4.4d	benzene	60	21	75	207	317	420 / 421	352 000	32 000	0.66
A4.4e	CCl_4	60	7	91	174	298	356 / 358	53 000	35 000	0.33
A4.4f	CCl_4	60	6	91	228	279	278 / 275	43 000	20 000	0.13
A4.4g[b]	benzene	50	8	--	--	--	--	--	--	--
A4.5a	benzene	60	2	88	168	296	322 / 331	50 000	25 000	0.25
A4.5b	benzene	50	12	83	228	361	387 / 377	52 000	21 000	0.29
A4.5c	benzene	60	23	95	248	364	376 / 380	22 000	8600	0.11
A4.5d	CCl_4	60	21	98	205	301	324 / 313	9600	5600	0.11
A4.5e	CCl_4	60	21	88	226	298	360 / 352	15 000	6400	0.13
A4.5f	phenylether	60	20	96	224	306	379 / 386	22 000	6700	0.11
A4.5g	benzene	50	19	85	195	288	345 / 342	18 000	6000	0.14
A4.5h	CCl_4	60	7	89	195	268	363 / 359	110 000	50 000	0.40
A4.5i	benzene	60	22	86	--	--	--	3000	1700	--

a) all the polymer structures are located in tables A4.1 and A4.2 on pages 84-85.
b) the polymer gelled.

As in the monomer synthesis discussed in Chapter A3 a few variables such as temperature and solvent effects were studied in the polymerization of **A2.8a** with **A4.4a** to determine the optimal conditions. Of the solvents that were examined (Table A4.5) chlorobenzene and dichlorobenzene were the most effective from the standpoint of obtaining high molecular weight polymers with narrow polydispersities. The remaining solvents like anisole and benzonitrile resulted in low molecular weight polymers and when solvents such as benzene, CCl_4, and diphenyl ether were used, polymers with broad molecular weight distributions were obtained (Table A4.5). This is not a general trend, for example, in the synthesis of polymer **A4.4e,f** CCl_4 was the optimal solvent.

We originally thought that a reaction temperature of 80°C was the optimal temperature based on the monomer synthesis (see Chapter A3). This was not the case in the polymerization reactions, polymers with higher inherent viscosities 0.88 dL/g and 0.82 dL/g were obtained at 25°C and 60°C, respectively (Table A4.6). When the temperature was increased from 92°C to 120°C the inherent viscosity of **A4.4a** decreased from 0.38 dL/g to 0.13 dL/g. This suggests that the concentration of end capper, which we believe to be the mono-cyclized dibenzofuran type compound **A2.23b** as shown on page 30, increases with increasing temperature. This would explain why lower molecular weight polymers are obtained at higher temperatures.

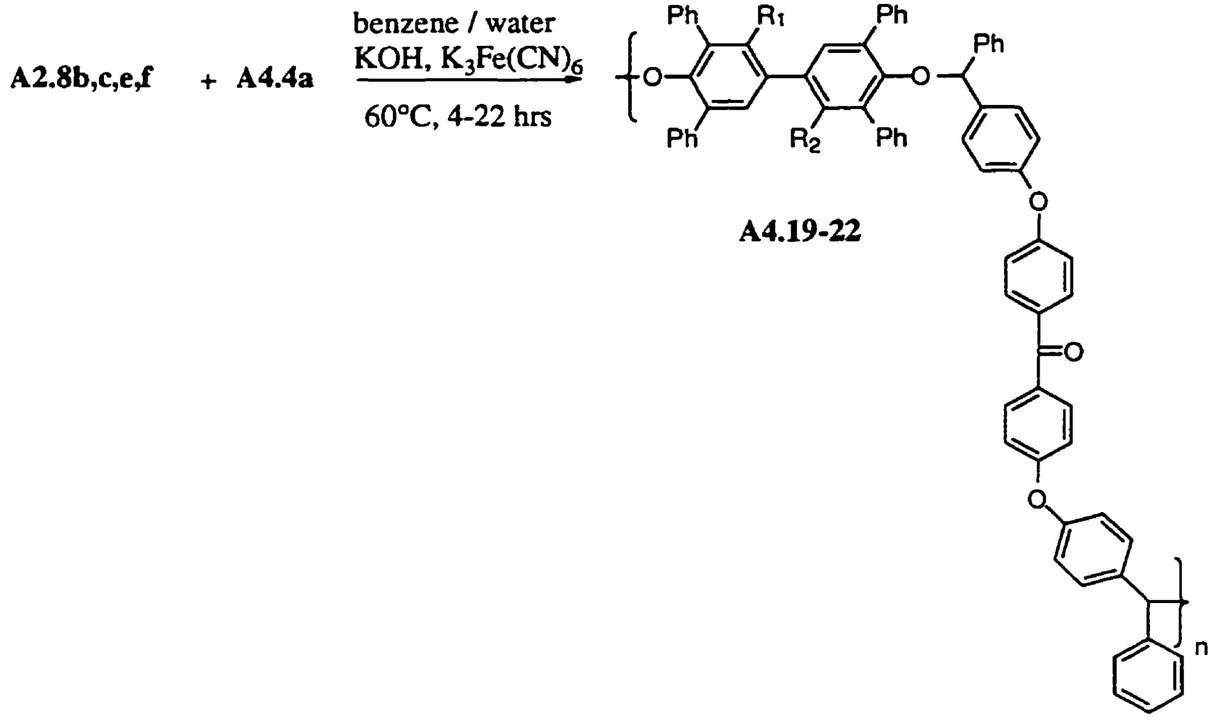
Table A4.5. Solvent effect in the polymerization of **A4.4a**.

Solvent	η_{inh} (dL/g)	Mw (g/mol)	Mn (g/mol)	PD
benzene	0.40	290 000	23 000	12.60
chlorobenzene	0.38	160 000	23 000	7.00
benzonitrile	0.21	100 000	16 000	6.20
dichlorobenzene	0.41	290 000	31 000	9.40
CCl_4	0.37	530 000	25 000	21.20
phenylether	0.61	650 000	38 000	17.10
anisole	0.26	184 000	19 000	9.60

Table A4.6. Temperature effect on the polymerization of **A4.4a** in chlorobenzene.

Rxn. Temp. (°C)	Rxn. Time (hrs)	Isolated Yield (%)	Mw (g/mol)	Mn (g/mol)	η_{inh} (dL/g)
110	24	84	18 000	8000	0.13
92	26	84	160 000	23 000	0.38
60	24	82	400 000	38 000	0.82
25	21	94	420 000	42 000	0.88

The reactivity and the properties of the resulting polymers **A4.19-22** (Scheme A4.8) obtained from different biphenols **A2.8b,c,e,f** were examined.



A4.19-22

Scheme A4.8

We have shown in Chapter A3 that all the biphenols are quantitatively converted to their ether derivatives. We therefore expected to obtain polymers with similar inherent viscosities, except for polymers **A4.4a** and **A4.22** which have inherent viscosity of 0.82 dL/g and 0.23 dL/g, respectively. The remaining polymers **A4.19-21** have similar inherent viscosities in the range of 0.37 dL/g to 0.42 dL/g. The low inherent viscosity obtained for polymer **A4.22** might be due to the presence of trace amounts of an impurity such as **A2.8a**, which would affect the stoichiometry. As we mention in Chapter A2 biphenol **A2.8e** was very difficult to purify, so trace amounts of **A2.8a** could be present.

Even with the increased steric hindrance due to the biphenol moieties in **A2.8a,b** no significant increase in T_g was observed (Table A4.7). The T_g values were in the range of 208°C to 227°C. Their decomposition temperature (T_d) and their 5% weight loss values are quite similar, in the range of 304°C to 318°C and 401°C to 427°C in nitrogen, respectively.

Table A4.7. Physical properties and yields of the ether polymers with different biphenol moieties.[a]

Entry	Solvent	Rxn Time (hrs)	Isolated Yield (%)	T_g (°C)	T_d (°C)	TGA N_2/Air	Mw (g/mol)	Mn (g/mol)	η_{inh} (dL/g)
A4.4a	chlorobenzene	22	82	222	312	413 / 423	400 000	38 000	0.82
A4.19	chlorobenzene	4	96	227	318	427 / 425	130 000	30 000	0.37
A4.20	CCl_4	20	86	221	314	420 / 422	48 000	18 000	0.38
A4.21	benzene	22	70	208	304	401 / 413	290 000	26 000	0.42
A4.22	chlorobenzene	20	94	218	310	405 / 410	36 000	16 000	0.23

a) polymer structures are located in table A4.1 (page 84) and in scheme A4.8 (page 91).

No significant differences in the physical properties were observed by changing the biphenol moiety. The only difference observed was in the reactivity of biphenols **A2.8c** compared to the remaining biphenols. The polymerization was complete within 4 hours with biphenol **A2.8c** while the polymerization reaction with **A2.8a,b,e** required at least 21 hours. These results are in agreement with the results obtained in the synthesis of the ether monomers discussed in Chapter A3, in that **A2.8c** was most the reactive biphenol.

The ether polymers **A4.4a,b,d** exhibit relatively high inherent viscosities and average molecular weights in the range of 0.54 dL/g to 0.82 dL/g and 352 000 g/mol to 400 000 g/mol, respectively. The remaining ether polymers **A4.4c,e,f** have inherent viscosities below 0.33 dL/g. An inherent viscosity of 0.14 dL/g was obtained for polymer **A4.4f**. Similar results were obtained if **A3.9h** was replaced with cyclohexene **A3.3h**. Originally we though the cause for the low molecular weight of some polymers was due to the difficulty in weighing out cyclohexene **A3.3h**. Instead the low viscosity might be due to the formation of a second double bond in the **A3.3h** moiety. The diene species generated would terminate the radical polymerization reaction, since the remaining activated methylene group is hindered and as we have shown in Chapter A3, a diene compound is easily converted to its aromatic counterpart (Figure A4.2).

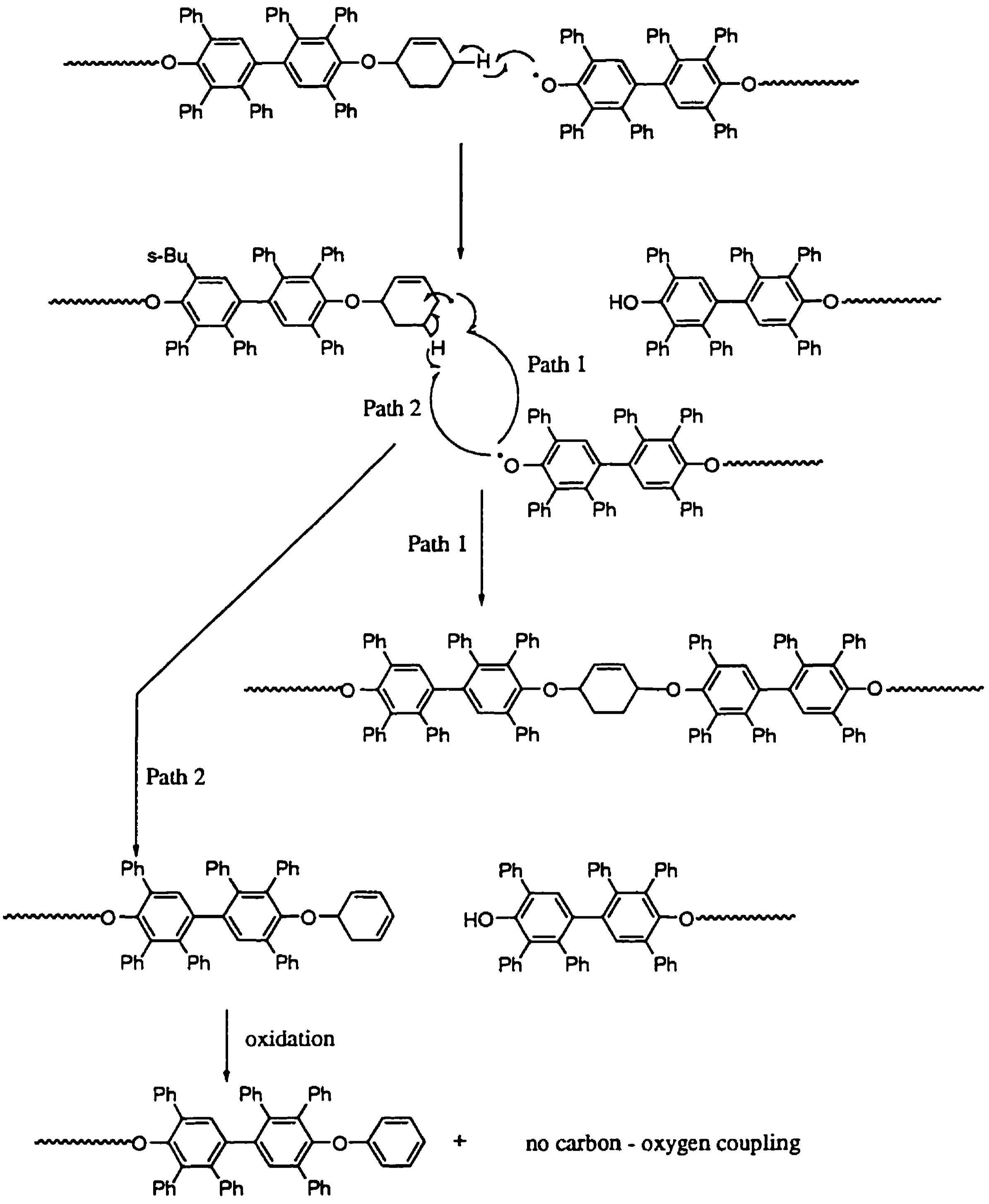


Figure A4.2

With monomer **A3.9f** only gelled materials were obtained after 20 hours. Even by varying the temperature and solvent no high molecular weight polymer was obtained.

Polymers **A4.4a,b,c** formed uniform brittle films and generally had broad molecular weight distributions (Figure A4.3a).

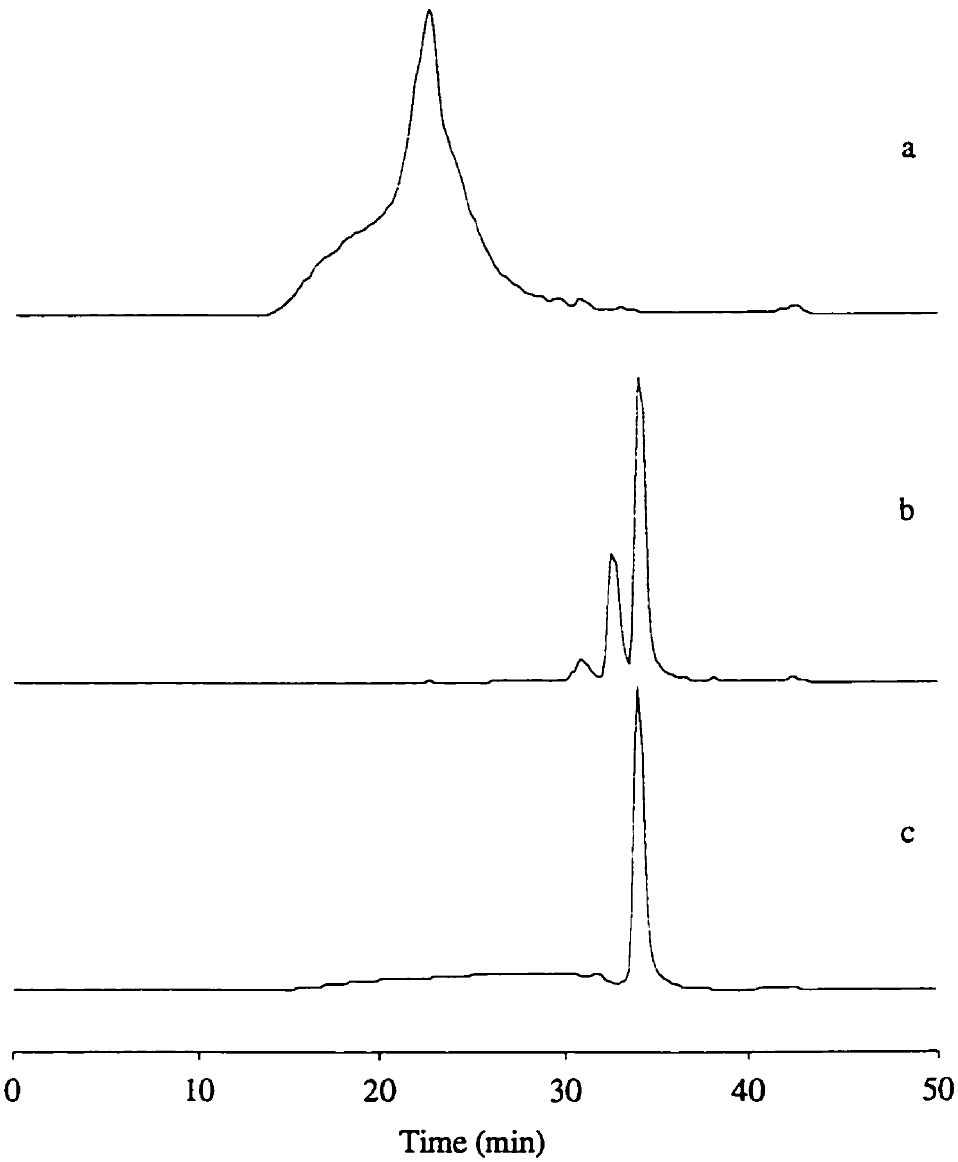


Figure A4.3. GPC trace of polymer **A4.4a**: a) original polymer, b) acid treated, c) thermally treated.

The fact that the polymers form brittle films and have broad molecular distributions suggests that the polymer is either partially crystalline or is branched. No T_m was observed in the DSC trace (Figure A4.4) and the X-ray of the film showed that the polymer **A4.4a** was amorphous. The second possibility would be that the polymer is partially crosslinked. If this were the case attack would have to occur at the tertiary proton.

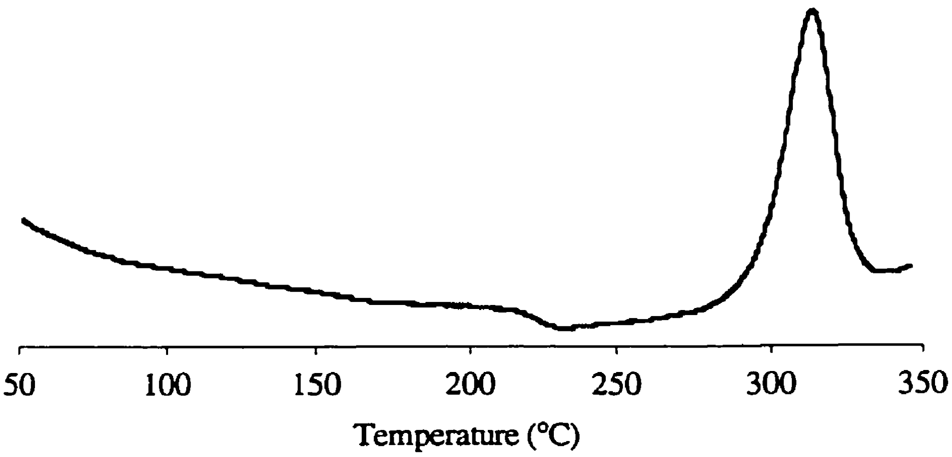
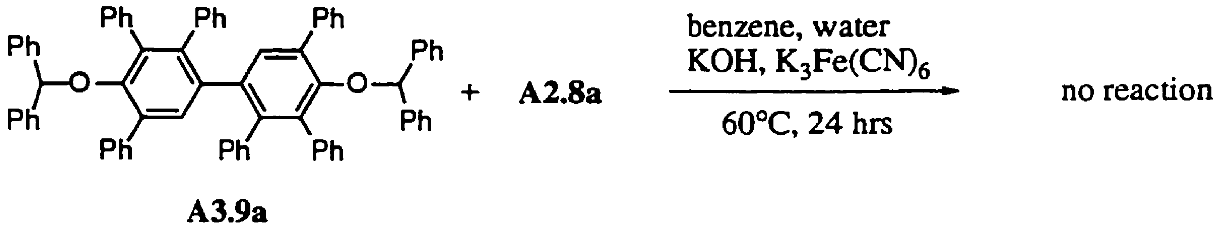


Figure A4.4. DSC trace of polymer **A4.4a**.

We have shown in the previous chapter that essentially no reactions occur with compounds containing hindered tertiary hydrogens. In order to further confirm these results we reacted **A3.9a** with **A2.8a** using similar conditions to the polymerization reactions (Scheme A4.9). After 24 hours no reaction appears to have occurred based on GPC and HPLC results and only the starting materials were identified. Therefore we can most probably rule out that the polymer is crystalline or is crosslinked.



Scheme A4.9

Of the acetal polymers synthesized only polymer **A4.5g** was obtained as a high molecular weight polymer (η_{inh} = 0.40 dL/g). The remaining acetal polymers **A4.5a-f,h** all had inherent viscosities below 0.30 dL/g. In general all the acetal polymers have narrow polydispersities.

As expected these polymers did not form tough, flexible films though they were soluble in common organic solvents. Using the model compounds previously synthesized (Chapter A3) we have shown that quantitative reactions were obtained with **A2.8a** and **A3.8d**. We therefore expected to obtain high molecular weight polymers with monomers **A4.12b,c**. This was not the case with monomer **A4.12c**, a polymer with a molecular weight of 22 000 g/mol and an inherent viscosity of 0.11 dL/g was obtained. The steric hindrance around the methylene group might slow down the rate of the carbon - oxygen reaction, favoring formation of side products such as the mono-cyclization of the biphenoxy radical which would terminate the polymerization reaction. To avoid this problem we synthesized monomer **A4.12b** and in this case we were able to obtain a higher molecular weight polymer (Mw = 52 000 g/mol, η_{inh} = 0.29 dL/g). Therefore it appears that steric hindrance was the problem with monomer **A4.12c**.

Monomer **A4.12h** and **A4.12g** are similar except for the atom adjacent to the methylene group which are sulfur and oxygen, respectively. The polymers obtained from these monomers are quite different. Only with monomer **A4.12h** were we able to obtain high molecular weight polymers (Mw = 110 000 g/mol, η_{inh} = 0.40 dL/g), while the polymerization of **A4.12g** with **A2.8a** led to polymers with low molecular weight and inherent viscosity of 18 000 g/mol and 0.14 dL/g, respectively. Similar results were obtained with monomers **A4.12d-f**. It appears that the oxygen atom adjacent to the methylene group is affecting the reaction. This is clearly seen by the higher ^{1}H and ^{13}C chemical shift of these methylene proton and carbon at approximately 5.04 ppm and 70.30 ppm, respectively compared to the methylene group of **A4.12h** at 4.09 ppm and 38.84

ppm, respectively (Table A4.3). The lower chemical shifts values of the methylene proton and carbon, and the fact that the sulfur atom is more electron donating, suggests that this methylene proton is more readily abstracted. This explains why in the monomer synthesis the reaction was faster and why we obtained higher molecular weights with monomer **A4.12h** compared to **A4.12d-g**.

The acetal polymers appear to be the best candidates for photoresist materials, since they are quantitatively cleaved in the presence of acidic reagents. We were interested in synthesizing polymers with activated methylene monomers, which when cleaved give products that are volatile, so that the development stage would be rendered easier. The allyl ether synthesized by Crivello *et al* [10] fits this criteria, although only low molecular weight polymers were obtained under various reaction conditions.

The T_g values of these polymers are listed in (Table A4.4). Of these polymers **A4.5a** and **A4.4e** have the lowest T_g at 168°C and 174°C, respectively. The kink in the polymer backbone due to the ether linkage in the meta position and the flexible aliphatic chain, respectively contributed to the low T_g values observed. Polymer **A4.5b** which also has a kink in the polymer chain has a T_g of 228°C. The bulkier carbazole group compared to the phenyl group in polymer **A4.5a** and lack of flexibility around the methylene group, contribute to the higher T_g value.

The TGA values at 5% weight loss of the ether and acetal polymers (Table A4.4) were above 380°C in both nitrogen and air. In general a gradual weight loss was observed (Figure A4.5), except in the case of polymer **A4.4f** where two distinct weight loss patterns were observed (Figure A4.6). The first weight loss in the range of 275°C - 325°C was determined to be 10%, which corresponds to the loss of 2 benzene molecules. This could be achieved by the thermal cleavage of the carbon - oxygen bond followed by aromatization of the cyclohexene.

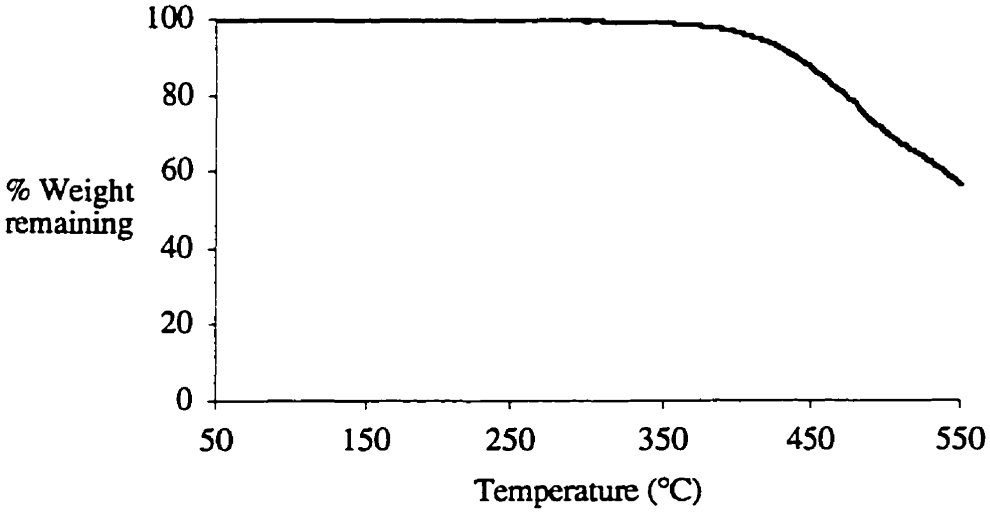


Figure A4.5. TGA trace of polymer **A4.4a**.

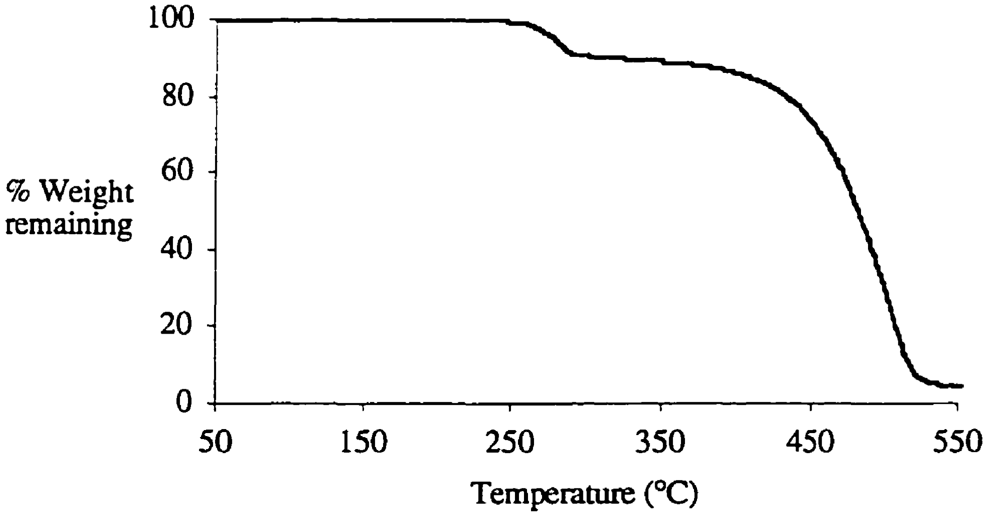


Figure A4.6. TGA trace of polymer **A4.4f**.

A4.2.3 Cleavage of Polymer Chain

As with the monomers prepared in Chapter A3 these polymers were readily cleaved either thermally (Figure A4.3c) or under acidic conditions (Figure A4.3b), except for polymer **A4.4f** which was not cleaved under acid conditions. The fact that these polymers are easily cleaved under acid conditions makes them good candidates for photoresist materials. Preliminary evaluations of polymers **A4.4a,c,f** and **A4.5a** done in Dr Darlings laboratory have shown that the acetal polymer **A4.5a** was the most promising. This is what would have been expected since acetals are easily and quantitatively cleaved under acidic conditions.

In order to evaluate these polymers a solution of the polymer and triphenylsulfonium hexafluoroantimonate salt was spin coated onto a silicon wafer. The resulting thin film was baked at 120°C for a few seconds and specific areas were irradiated with a 450W medium pressure mercury arc and baked at 120°C for 20 seconds. The film was developed with a solution of an equal mixture of methyl acetate and methanol. The irradiated area was completely removed without affecting the non-irradiated area. Of the polymers studied only **A4.5a** gave promising results. The infrared spectra of the non-irradiated (Figure A4.7a), irradiated sections at 30 mJ/cm^2 (Figure A4.7b) and 75 mJ/cm^2 (Figure A4.7c) clearly shows the gradual appearance of a peak at 1650 cm^{-1} corresponding to the carbonyl group of a aldehdye compound and the suppression of the peak at 1047 cm^{-1} which corresponds to an ether linkage. These results clearly indicated that the polymer film in the exposed areas is cleaved.

A4.3 Conclusions

We have synthesized a series of novel ether and acetal polymers by a unique radical carbon - oxygen coupling reaction of hindered biphenols with a variety of methylene containing monomers in a two phase oxidation system. These polymers are quantitatively cleaved upon heating or under acidic conditions to give low molecular weight species. The acetal polymers appear to be the most interesting candidates for evaluation as photoresist materials in the electronics industry.

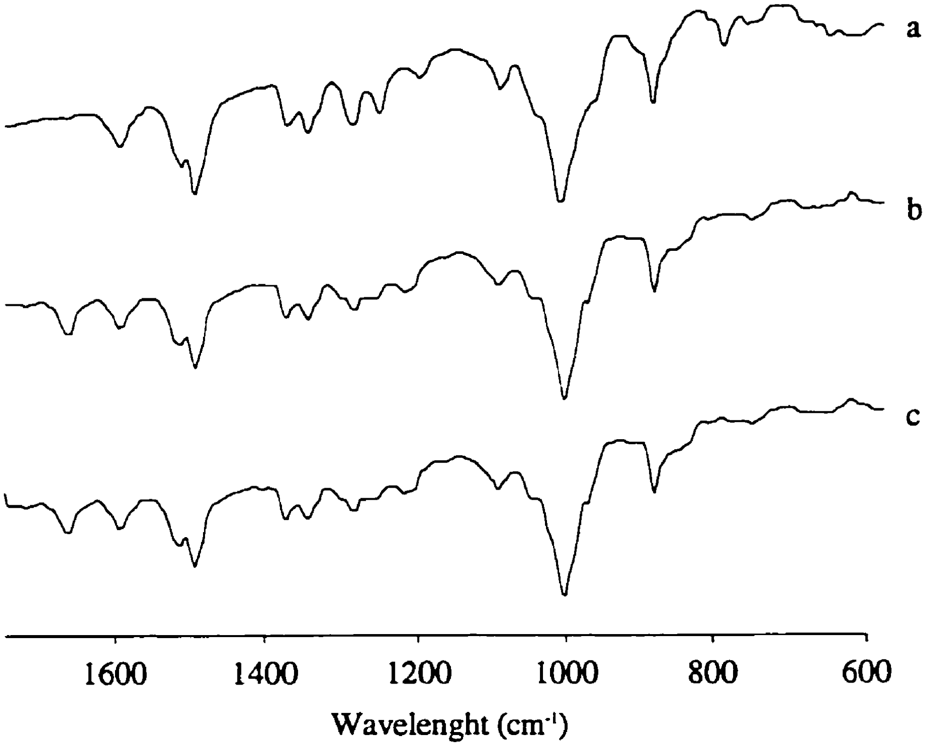


Figure A4.7. Infrared spectra of polymer **A4.5a**: a) non-irradiated region, b) irradiated region at 30 mJ/cm^2, c) irradiated region at 75 mJ/cm^2.

A4.4 Experimental Section

Materials

Benzyl chloride, 3-methoxybenzyl chloride, N,N-dimethylacetamide (DMAc), N,N-dimethylformamide (DMF), 1-methyl-2-pyrrolidinone (NMP), α,α'-(dichloromethylene)-meta-xylene, 4,4'-difluorobenzophenone, bis(4-fluorophenyl)sulfone, thiophenol, carbazole, 1-(4-hydroxyphenyl)-1-phenylmethane, bis(4-hydroxyphenyl)sulfone, bis(4-hydroxyphenyl)sulfide, 4,4'-thiobisbenzenethiol, and tetrabutylammonium hydrogen sulfate were purchased from the Aldrich Chemical Co. and used as received. Reagent grade solvents and potassium hydroxide were obtained from Caledon. Potassium carbonate, sodium sulfate, and sodium bicarbonate were purchased from Omega.

Instruments

Elemental analyses were performed by Fine Analysis Laboratories Ltd., Hamilton, Ontario. All ^{1}H and ^{13}C NMR were obtained on a Varian Unity 500 spectrometer. High performance liquid chromatography (HPLC) analyses were carried out on a Milton Roy CM4000 pump equipped with a reverse phase silica column and a UV detector set at 254 nm; methanol was used as the eluent at a flow rate of 1 mL/min. Thermal analyses were obtained on a Seiko 220DSC and 220 TGA/DTA instrument at a heating rate of 20°C/min unless otherwise stated. Melting points were also determined on a Fisher-Johns melting point apparatus. Mass spectra were recorded on a Kratos MS25RFA spectrometer. GPC analyses were performed on a Waters 510 instrument equipped with a UV detector set at 254 nm and four 5 μm phenogel columns (3 x 500 Å, linear) arranged in series. Chloroform was used as the solvent and all molecular weights are referenced to polystyrene standards.

Monomer Synthesis

1-Methoxy-3-(phenylthiomethyl) benzene **A4.9j**.

The potassium salt of thiophenol generated by dehydrating a solution of thiophenol (20.00 g, 0.18 mol), DMF (100 mL), benzene (40 mL), and K_2CO_3 (15.71 g, 0.11 mol) at 140°C for 3 hours, was reacted with **A4.7** (30.82 g, 0.20 mol) at 80°C for 1 hour. The mixture was poured into water and the product was extracted several times with diethyl ether (3 x 100 mL). The organic layer was separated, dried over $NaSO_4$, filtered, and the filtrate was evaporated to dryness. The oily crude product was purified by distillation to give 37.32 g (89%) of **A4.9j**: b.p. 145-150°C (4 mmHg); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.17 - 7.32 (m, 6H), 6.74 - 6.89 (m, 3H), 4.06 (s, 2H, CH_2), 3.71 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.56, 138.91, 136.30, 129.68, 129.36, 128.74, 126.21, 121.04, 114.08, 112.80, 55.02, 39.40 (CH_2); MS (EI Direct Inlet at 30 °C) *m/e* calc'd for $C_{14}H_{14}OS$: 230.0760, found 230.0764; 229.94 (M^+, 42), 120.99 (100).

N-(3-Methoxyphenylmethyl)carbazole **A4.9k**.

A one liter round bottom flask was charged with carbazole (17.42g, 0.10 mol), ground potassium carbonate (22.11 g, 0.15 mol), ground potassium hydroxide (33.8 g, 0.60 mol) and 500 mL of toluene. The reaction was heated to 75°C under a nitrogen atmosphere and **A4.7** was added. The reaction was complete after 1 hour and the mixture was then filtered and the filtrate was evaporated to dryness. Compound **A4.9k** was obtained in 89% yield (25.51g) as off white needles: m.p. 91-93°C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, 2H), 7.42 (t, 2H), 7.34 (d, 2H), 7.23 (t, 2H), 7.14 (t, 1H), 6.68-6.74 (m, 3H), 5.44 (s, 2H, CH_2), 3.65 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.93, 140.66, 138.86, 129.80, 128.81, 122.99, 120.34, 119.17, 118.64, 112.41, 112.37, 108.85, 55.08, 46.47 (CH_2); MS (EI Direct Inlet at 150 °C) *m/e* calc'd for $C_{20}H_{17}NO$: 287.1310, found 287.1307; 287.03 (M^+, 87), 121.03 (100).

1-Hydroxy-3-(phenylthiomethyl)benzene **A4.6j**.

Boron tribromide (95 mL, 0.10 mol) was added through a syringe over a 20 minute period to a stirring solution of **A4.9j** (10.01 g, 0.04 mol) in 25 mL of methylene chloride cooled to -10 °C under a nitrogen atmosphere. After complete addition the reaction temperature was gradually increased to room temperature. The reaction was complete after 45 minutes and the solution was poured into a cold 10% aqueous solution of $NaHCO_3$ to neutralize the acid. The organic layer was washed several times with water and extracted. This solution was dried over $NaSO_4$, filtered and the filtrate was evaporated to dryness to give 7.22 g (77%) of **A4.6j** as a brownish oil. The oily product solidified after trituration with cyclohexane: m.p. 55-57°C; ^1H NMR (500 MHz, $CDCl_3$) δ 9.42 (s, OH), 7.26-7.33

(m, 4H), 7.17 (d, 1H), 7.06-7.09 (t, 1H), 6.76-6.79 (m, 2H), 6.64 (d, 1H), 4.06 (s, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.42, 139.22, 136.11, 129.69, 129.67, 128.82, 126.34, 121.30, 115.62, 115.22, 38.67 (CH_2); MS (EI Direct Inlet at 70 °C) *m/e* calc'd for $C_{13}H_{12}OS$: 216.0609, found 216.0608; 216.03 (M^+,37), 107.03 (100).

N-(3-Hydroxyphenylmethyl) Carbazole **A4.6k**.

Compound **A4.6k** was recovered in 44% yield as white needles after recrystallization from cyclohexane: m.p. 125-127°; ^1H NMR (200 MHz, $CDCl_3$) δ 8.1 (d, 2H), 7.05-7.45 (m, 7H), 6.75 (d, 1H), 6.61 (d, 1H), 6.40 (s, 1H), 5.39 (s, 2H, CH_2), 4.62 (2, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.84, 140.82, 139.09, 130.05, 125.86, 122.96, 120.37, 119.25, 118.82, 114.39, 113.01, 108.86, 46.20 (CH_2); MS (EI Direct Inlet at 150 °C) *m/e* calc'd for $C_{19}H_{15}NO$: 273.1154, found 273.1152; 272.99 (M^+, 100), 179.99 (10), 166.99 (22), 106.99 (82).

(Phenylene-1,3-dimethyl)-bis-carbazole **A4.12c**.

To a stirring solution of toluene (40 mL), crushed KOH (6.73 g, 0.12 mol), K_2CO_3 (4.47, 0.03 mol), carbazole (3.35 g, 0.02 mol) and tetrabutylammonium hydrogen sulfate (0.69 g, 0.02 mol) was added α,α'-dichloromethyl-m-xylene (1.80 g, 0.01 mol). The solution was reacted for 1.5 hours at 74°C under a nitrogen atmosphere. The reaction mixture was poured into water and filtered. The crude product was recrystallized from a solution of methanol - ethyl acetate, affording **A4.12c** in 49% yield (2.15 g) as white needles: m.p. 204-207°C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, 4H, J = 8.1), 6.90 - 7.36 (m, 16H), 5.32 (s, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.48, 137.76, 129.26, 125.81, 125.49, 124.58, 122.96, 120.35, 119.20, 108.80, 46.30 (CH_2); MS (EI

Direct Inlet at 200 °C) *m/e* calc'd for $C_{32}H_{24}N_2$: 436.1939, found 436.1936; 436.97 (M^++1, 36), 435.96 (M^+, 100), 269.98 (32).

Method A

4-(Phenylmethoxy)-1-[4-(phenylmethoxy)phenylthio]benzene **A4.12g**.

A 250 mL three neck round bottom flask equipped with a Dean-Stark trap was charged with **A4.14f** (20.00 g, 0.09 mol), K_2CO_3 (15.30 g, 0.11 mol), toluene (50 mL) and DMF (100 mL). The reaction mixture was heated to 140°C for 3 hour under a nitrogen atmosphere to ensure complete dehydration. The reaction temperature was reduced to 90°C and benzyl chloride **A4.13** (24.42 g, 0.19 mol) was added to the reaction mixture. After 3 hours the reaction mixture was poured into water and the product that solidified was filtered off. The crude product was recrystallized from acetone yielding 22.80 g (63%) of **A4.12g** as white needles: m.p. 134-136°C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.27-7.41 (m, 14H), 6.89-6.94 (d, 4H), 5.04 (s, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.18, 136.73, 132.71, 128.62, 128.04, 127.67, 127.47, 115.69, 70.12 (CH_2); MS (EI Direct inlet at 200 °C) *m/e* calc'd for $C_{26}H_{22}O_2S$: 398.1344, found 398.1344; 397.90 (M^+, 82), 306.89 (80), 90.97 (100).

Bis-[4-(4-phenylmethoxy)phenylene]sulfone **A4.12f**.

After 22 hours the reaction was complete. The crude product was recrystallized from methanol, affording **A4.12f** in 85% yield as off white prisms: m.p. 202-206°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, 4H, J = 8.8 Hz), 7.35 (d, 6H, J = 4.4 Hz), 7.31 (t, 4H), 6.98 (d, 4H, J = 8.8 Hz), 5.05 (s, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.21, 135.78, 134.12, 129.52, 128.70, 128.32, 127.43, 115.21, 70.30 (CH_2); MS (EI Direct Inlet at 250°C) *m/e* calc'd for $C_{26}H_{22}O_4S$: 430.1239, found 430.1243; 429.92 (M^+, 7.0), 90.98 (100).

Bis-(4-(4-phenylthiomethyl)phenylene)sulfide **A4.12h**.

The reaction was over in 21 hours. Compound **A4.12h** was obtained in 82% yield as yellow crystals after recrystallization from ethyl acetate: m.p. 138-140°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, 8 H, J2 = 7.8 Hz), 7.14-7.24 (m, 12 H), 4.09 (s, 4 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.96, 137.05, 135.66, 131.27, 130.22, 128.76, 128.50, 127.25, 38.34 (CH_2); MS (EI Direct Inlet at 250°C) *m/e* calc'd for $C_{26}H_{22}S_3$: 430.0884, found 430.0880; 431.80 (M^++1, 14), 430.80 (M^+, 23), 429.80 (M^+-1, 76), 338.80 (13), 90.99 (100).

Method B

Bis-[4-(4-(phenylmethyl)phenyleneoxy)phenylene]methanone **A4.11a**.

A three-neck 100 mL round-bottom flask equipped with a condenser and a Dean-Stark trap was charged with **A4.17** (4.24 g, 0.02 mol), 4,4'-difluorobenzophenone **A4.16a** (2.52 g, 0.01 mol), K_2CO_3 (2.08 g, 0.02 mol), 26 mL of DMAc and 10 mL of toluene. The reaction was dehydrated at 140 °C for 3 hours under an atmosphere of nitrogen. The reaction temperature was maintained at 140°C for another 7 hours. The reaction mixture was poured into a 60 % methanol - water solution. The precipitate was filtered, and air dried overnight. The crude product was recrystallized from 95% ethanol to give 5.71 g (91%) of **A4.11a** as prisms: m.p. 113-115°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.77 (d, 4H, J = 8.7 Hz), 7.19-7.31 (m, 14H), 7.0 (d, 8H, J = 8.6 Hz), 3.99 (s, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.25, 161.54, 153.75, 140.86, 137.49, 132.17, 132.07, 130.39, 128.87, 128.53, 126.21, 120.18, 116.94, 41.23 (CH_2); MS (EI Direct Inlet at 370 °C) *m/e* calc'd for $C_{39}H_{30}O_3$: 546.2195, found 546.2189; 545.82 (M^+, 100), 286.88 (45), 166.96 (30).

Sulfonyl-bis(4-(4-phenylmethyl)phenyloxy)benzene **A4.11b.**

The reaction based on HPLC results was over after 18 hours. The gummy residue was extracted with chloroform, and the organic layer was evaporated to dryness to give an off white solid. The crude solid was recrystallized from 95% ethanol, affording **A4.11b** in 61% yield as white flakes: m.p. 127-129°C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.82 (d, 4H, J = 8.1 Hz), 7.14-7.27 (m, 14H), 6.89-6.97 (dd, 8H), 3.95 (s, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.94, 152.09, 139.85, 137.22, 134.53, 129.77, 128.93, 128.15, 127.84, 125.57, 119.76, 116.93, 41.55 (CH_2); MS (EI Direct Inlet at 370 °C) *m/e* 582.12 (M^+, 100), 167.05 (76), 91.03 (24); Analysis calc'd for $C_{38}H_{30}O_4S$: %C, 78.33; %H, 5.19; found: %C, 78.09; %H, 5.12.

Acetylene-Bis-(4-(4-phenylmethyl)phenyloxy)benzene **A4.11c.**

The reaction was complete after 67 hours. The crude product was purified by column chromatography using 20% chloroform in petroleum ether as the eluent. The isolated product was recrystallized from a chloroform-methanol solution to give **A4.11c** in 57% yield as white crystals: m.p. 156-157°C; ^1H NMR (200 MHz, $CDCl_3$) δ 7.54 (d, 4H, J = 8.7 Hz), 7.22-7.38 (m, 14H), 6.99-7.06 (dd, 8H), 4.04 (s, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.66, 153.62, 140.18, 135.96, 132.33, 129.56, 128.21, 127.85, 125.53, 118.95, 117.60, 117.18, 88.16, 41.60 (CH_2); MS (EI Direct Inlet at 370 °C) *m/e* calc'd for $C_{40}H_{30}O_2$: 542.2246, found 542.2241; 542.92 (M^+, 100), 166.98 (17); Analysis calc'd for $C_{40}H_{30}O_2$: %C, 88.52; %H, 5.58; found: %C, 88.38; %H, 5.84.

1,3-Bis-((4-(4-phenylmethyl)-4-phenyloxy)4-phenylcarbonyl) **A4.11d.**

The reaction was complete within 8 hours. The crude product was recrystallized from 95% ethanol. Compound **A4.11d** was obtained in 94% yield as white flakes: m.p.

143-144°C; ^{1}H NMR (200 MHz, CDCl$_3$) δ 8.11 (s, 1H), 7.94 (d, 2H, J = 7.6Hz), 7.79 (d, 4H, J = 8.6), 7.59-7.51 (t, 1H), 7.30-7.16 (m, 14H), 6.98 (d, 8H, J = 8.5), 3.95 (s, 4H, CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 192.88, 161.04, 152.44, 139.92, 137.26, 136.88, 132.14, 131.70, 130.33, 129.97, 129.70, 128.14, 127.81, 127.70, 125.52, 119.69, 116.38, 41.55 (CH^2); MS (EI Direct Inlet at 370 °C) *m/e* 651.03 (M$^+$+1, 52), 650.03 (M$^+$, 100), 287.00 (52), 91.02 (39); Anal. Calcd for $C_{46}H_{34}O_4$: %C, 84.89; %H, 5.27; Found: %C, 84.48; %H, 5.29.

Bis-[4-(3-(phenylthiomethyl)phenyleneoxy)phenylene]methanone **A4.12a**.

The reaction was over within 5 hours. The crude product was purified by column chromatography using toluene as the eluent, affording **A4.12a** in 68% yield as an oily compound which on standing overnight solidified: m.p. 82-85°C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.78 (d, 4H), 7.31 (d, 4H), 7.24 (t, 4H), 7.18 (t, 2H), 7.13 (d, 2H), 7.00 (s, 2H), 6.95 (d, 2H), 4.10 (s, 4H, CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.23, 161.19, 155.60, 140.01, 135.58, 132.25, 132.19, 130.32, 130.05, 128.87, 126.65, 124.99, 120.39, 118.19, 117.18, 38.86 (CH$_2$); MS (EI Direct Inlet at 300 °C) *m/e* calc'd for $C_{39}H_{30}O_3S_2$: 610.1636, found 610.1631; 610.10 (M$^+$, 52), 501.11 (49), 196.09 (59), 110.04 (100).

Bis-[4-(3-((N-phenylmethyl carbazole))phenyleneoxy)phenylene]methanone **A4.12b**.

The reaction was over within 8 hours. Compound **A4.12b** was recovered in 69% yield as a fine white powder after purification by column chromatography using toluene as the eluent: m.p. 107-110°C; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.16 (d, 4H, J = 7.8 Hz), 7.69 (d, 4H, J = 8.8 Hz), 7.63 (d, 4H, J = 8.3 Hz), 7.41 - 7.44 (t, 4H), 7.32 - 7.35 (t, 2H), 7.19-7.22 (t, 4H), 6.97-7.02 (m, 10H), 5.71 (s, 4H, CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 194.03, 160.71, 155.96, 140.37, 139.57, 132.18, 132.03, 130.30, 125.76, 122.94, 122.27, 120.32, 119.22, 118.66, 117.88, 117.13, 108.64, 46.12 (CH_2); MS (EI Direct Inlet at 370 °C) *m/e* calc'd for $C_{51}H_{36}N_2O_3$: 724.2726, found 724.2730; 724.19 (M^+, 8), 472.10 (39), 471.09 (100), 167.04 (21).

Method C

1,8-Bis-[4-(4-phenylmethyl)phenyleneoxy]octane **A4.11e**.

A 100 mL three-neck round-bottom flask equipped with a Dean-Stark trap was charged with **A4.16** (10.14 g, 0.06 mol), DMF 40 mL and 20 mL of toluene used as the azeotropic solvent. The reaction mixture was heated at 140 °C for 3 hours and then reduced to 70°C. 1,8-Dibromooctane **A4.17** was added to the reaction mixture and the reaction was monitored by HPLC. After 23 hours the reaction was complete and the reaction mixture was poured into water. The gummy crude product was dissolved in methylene chloride, dried over $NaSO_4$, filtered, and the filtrate product was absorbed onto silica gel. The crude product was purified by column chromatography using 2% ethyl acetate in hexane as the eluent. To give 6.63 g (50%) of **A4.10e** as white needles: m.p. 67-69°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 - 7.28 (m, 4H), 7.16 - 7.19 (m, 5H), 7.08 (d, 4H, J = 7.1 Hz), 6.81 (d, 5H, J = 7.8 Hz), 3.91 (s, 8H), 1.74 - 1.77 (t, 4H), 1.36 - 1.46 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.48, 141.60, 132.98, 129.79, 128.77, 128.36, 125.9, 114.43, 67.87, 41.00 (CH_2), 29.27, 29.26, 25.97; MS (EI Direct inlet at 100 °C) *m/e* calc'd for $C_{34}H_{38}O_2$: 478.2872, found 479.2879; 478.00 (M^+, 53), 183.97 (100), 90.99 (34.90).

A4.5 References

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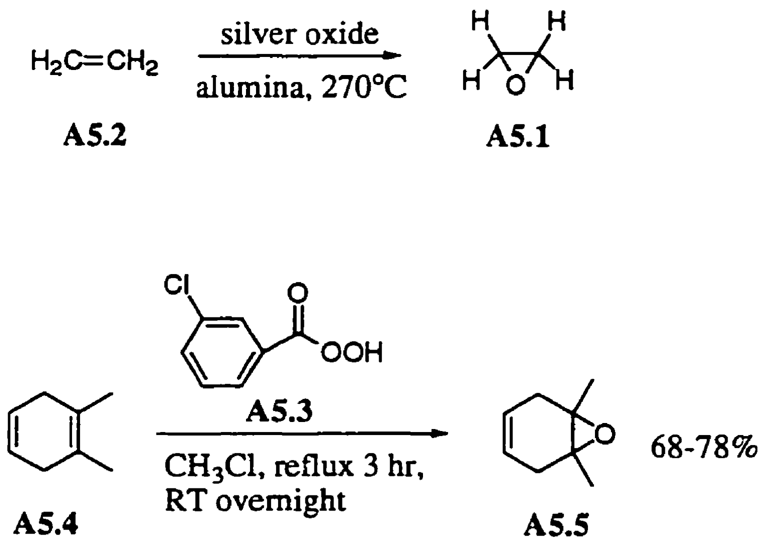
CHAPTER A5

OXIDATION OF ARYLMETHANES

A5.1 Introduction

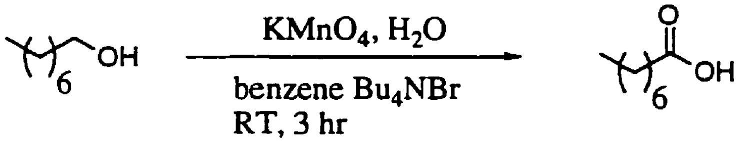
Oxidation of organic compounds which involves increasing the oxygen content in the organic molecule are probably the most frequently encountered reactions by organic chemists. These include: 1) oxidation of alkenes to their epoxide, alcohol or carboxylic acid derivatives, 2) oxidation of alcohols to their aldehyde and ketone derivatives, and 3) oxidation of ketones to their corresponding carboxylic acid.

The industrial production of ethylene oxide **A5.1** involves the epoxidation of ethylene **A5.2** with oxygen in the presence of silver oxide on alumina at 270°C (Scheme A5.1)[1]. More common laboratory procedures involve the use of hydrogen peroxide,[2-5] or meta-chloroperoxybenzoic acid **A5.3**. For example, 1,2-dimethylcyclohexa-1,4-diene **A5.4** is epoxidized to **A5.5** in the presence of **A5.3**[6] (Scheme A5.1).



Scheme A5.1

Alcohols are readily oxidized to aldehydes, ketones , and carboxylic acid depending on the alcohol and oxidizing agent being used. Reagents such as ceric ammonium nitrate, potassium dichromate, DDQ, and MnO_2 convert primary alcohols to aldehydes. Reagents like platinum dioxide and potassium permanganate ($KMnO_4$) convert primary alcohols to their corresponding carboxylic acids.[7,8] For example, octanol **A5.6** is oxidized to octanoic acid **A5.7** in the presence of $KMnO_4$ (Scheme A5.2).[9]



A5.6 **A5.7**

Scheme A5.2

The Kindler modification of the Willgerodt reactions is the most useful procedure for converting ketones to their carboxylic acid derivatives without degradation of the carbon chains.[10-14]

Diarylmethanes have been oxidized to their benzophenone derivatives by molecular oxygen under basic conditions[15] or under phase transfer catalysis conditions.[16-18] The disadvantages of these methods are the harsh experimental conditions (i.e. high pressures or strongly basic media). Other reagents such as potassium permanganate on aluminum oxide[19] require an excess (at least 4 time by weight to **A3.3a**) of $KMnO_4$, while in the presence of N-hydroxynaphthalimide[20] only a 73% conversion to benzophenone was obtained.

A5.1.1 Goals and Strategies

We have previously shown that quantitative carbon - oxygen coupling reactions occur between hindered biphenols **A2.8a-g** and diphenylmethane in the absence of oxygen (see Chapter A3). We now wish to report an efficient and mild catalytic oxidation of arylmethanes **A5.8a-d** and **A3.3a,l** to their benzophenone derivatives **A5.9a-d**,

A3.19 and **A5.10**, respectively and arylmethane moieties incorporated in polymers **A5.11a-g** and cyclic oligomers **A5.12** and **A5.13**. In this reaction the intermediate methylene radical is intercepted by oxygen and oxidation of arylmethanes to their benzophenone derivatives occurs. The advantage of this technique is that the reaction is carried out under mild and neutral conditions.

A5.2 Results and Discussions

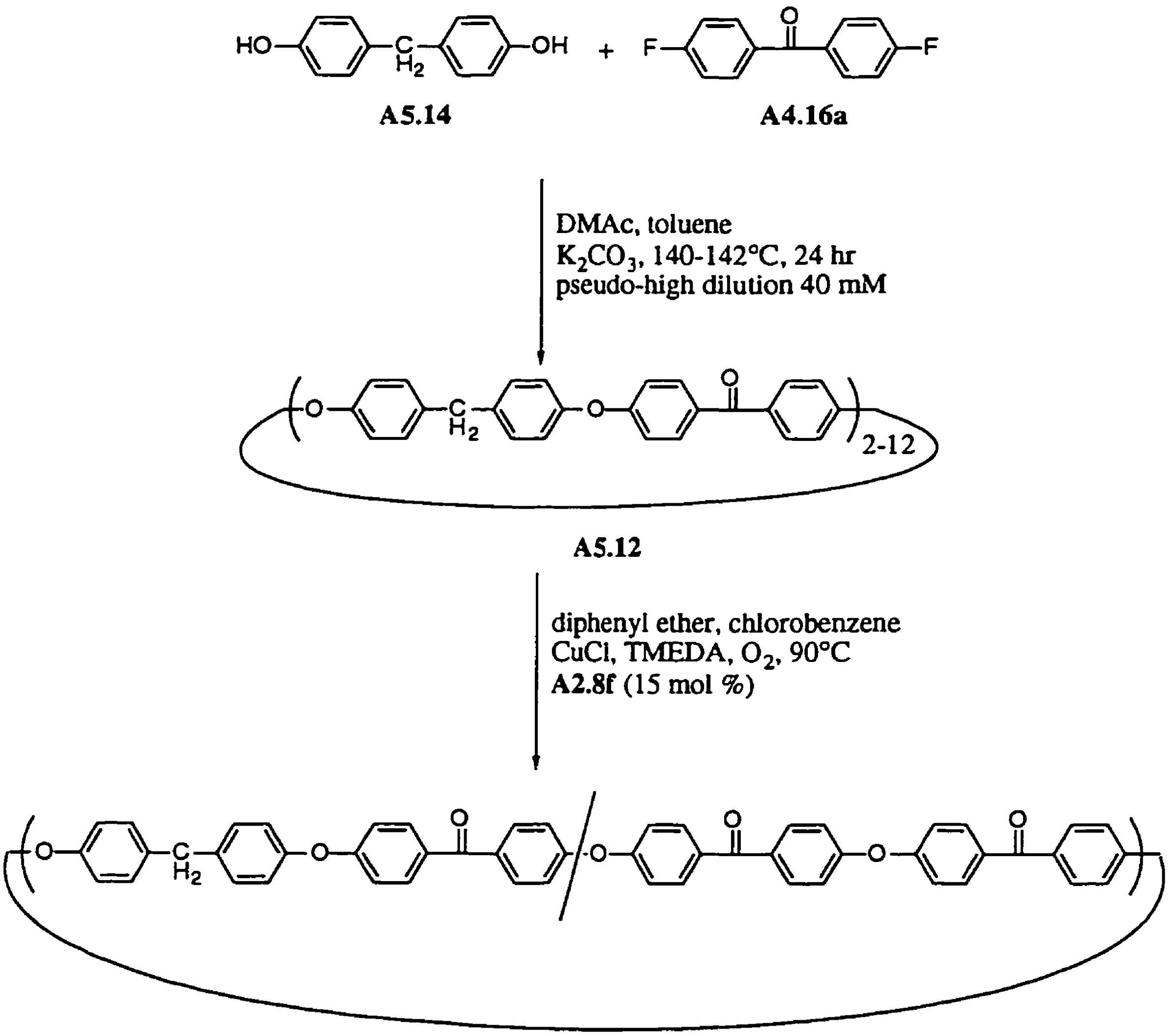
A5.2.1 Monomer Synthesis

A series of substituted diphenylmethanes **A5.8a-d** were synthesized. The chlorinated diphenylmethanes, 4-chlorodiphenylmethane, 4,4'-dichlordiphenylmethane, and 2,4-dichlorodiphenylmethane, were prepared by Friedel-Crafts alkylation of chlorobenzene with chloro substituted benzyl chlorides as described by Halpern and coworkers.[16] With the dichloro substituted compounds two isomers were obtained. For the target molecule **A5.8b** both the 4,4' and 2,4' isomers were obtained in a ratio of 69:39, while for **A5.8c** the 2,2' and 2,4' isomers were obtained in a ratio of 80:20 as determined by proton NMR based on the methylene proton shift. The hydroxy groups of bis(4-hydroxyphenyl)methane which consists of a mixture of isomers 4,4', 2,4', and 2,2' in a ratio of 33:51:16 were methylated with dimethyl sulfate in refluxing ethanol for 24 hours. The methoxy derivative was distilled under reduced pressure to give 70% of **A5.8d** as a mixture of isomers.

A5.2.2 Cyclic Synthesis

Cyclic oligomers **A5.12** and **A5.13** were prepared following the procedure described by Chan *et al.* [21,22] A solution of 4,4'-dihydroxydiphenylmethane **A5.14** and **A4.16a** was added through a syringe over an 8 hour period to a refluxing solution of DMAc, toluene and K_2CO_3. The mixture was heated for a further 8 hours at 140-142°C

(Scheme A5.3). Note that the concentration of the reactants was kept at 40 mM. Cyclic **A5.12** was recovered in 88% yield. Cocyclic **A5.13** obtained in 66% yield was prepared by a similar method. In this case three reactants **A5.14**, **A4.16a** and 4,4'-(hexafluoroisopropylidene)diphenol **A5.15** were added to the reaction mixture (Scheme A5.4, Table A5.1).



A5.14

A4.16a

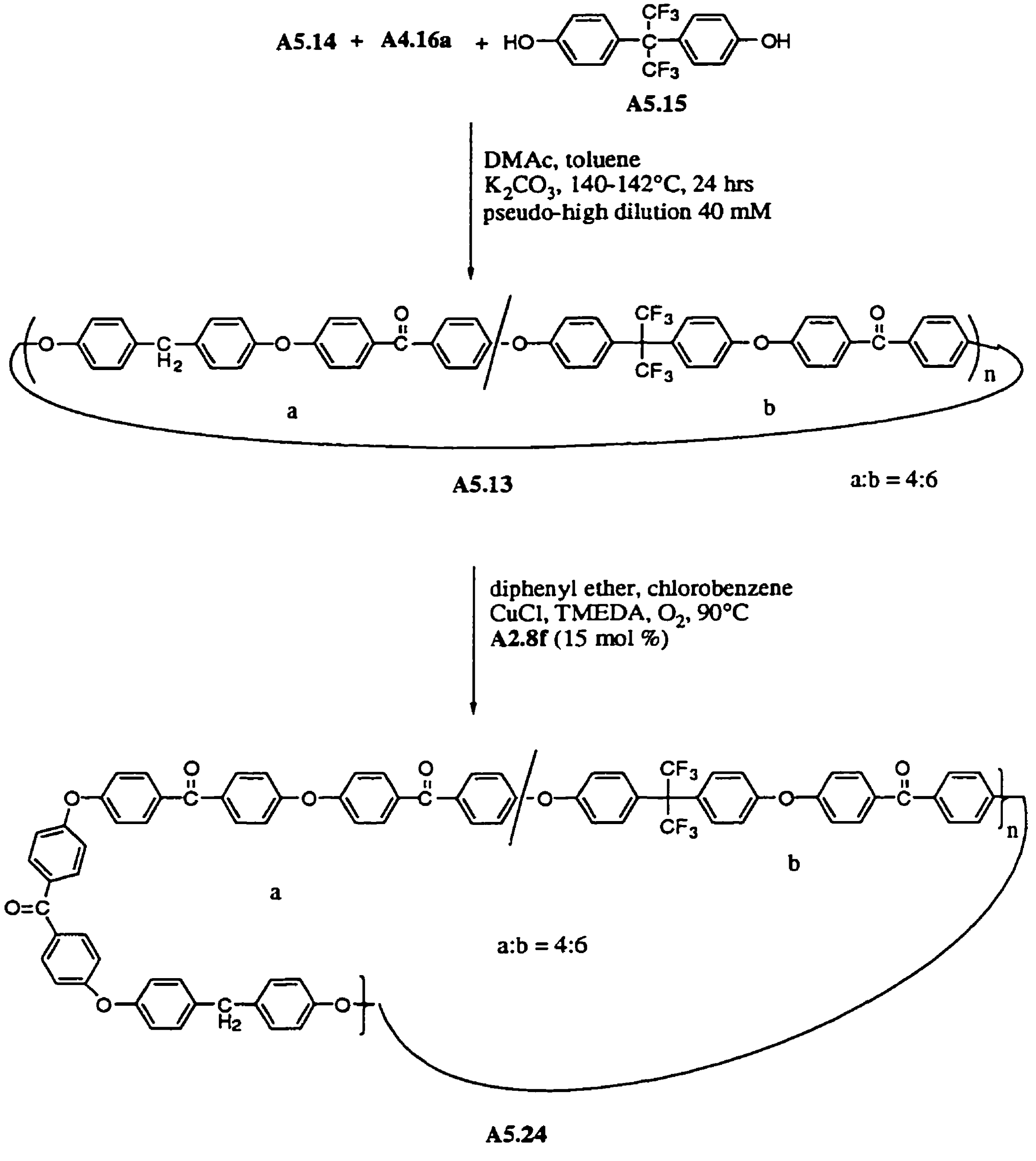
DMAc, toluene
K_2CO_3, 140-142°C, 24 hr
pseudo-high dilution 40 mM

A5.12

diphenyl ether, chlorobenzene
CuCl, TMEDA, O_2, 90°C
A2.8f (15 mol %)

A5.23

Scheme A5.3



Scheme A5.4

Cyclic **A5.12** and **A5.13** have been fully characterized by MALDI-TOF mass spectrometry, oligomers with 12 and 6 repeat units were obtained for cyclics **A5.12** and **A5.13**, respectively (Table A5.2 and A5.3, Figure A5.1).

Table A5.1. Yields and physical properties of the cyclic oligomers and linear copolymers.

Entry	Rxn Time (hrs)	Isolated[a] Yield (%)	T_g (°C)	T_c (°C)	T_m (°C)	5% Weight Loss Nitrogen (°C)	Mw (g/mol)	Mn (g/mol)
A5.12	17	88	--	--	364	494	--	--
A5.13	17	66	159	--	349	503	--	--
A5.11a	10	50	118	--	--	515	6600	4500
A5.11b	10	65	119	--	--	501	5100	3700
A5.11c	21	79	152	--	--	507	19 000	11 700
A5.11d	7	61	148	--	--	512	13 800	8300
A5.11e	6	58	142	--	--	514	10 400	5800
A5.11f	6	66	142	--	--	504	16 200	9300
A5.11g[b]	5	--	107	172	234	495	--	--

a) isolated yield after reverse precipitation.

b) polymer precipitated out of solution during reaction.

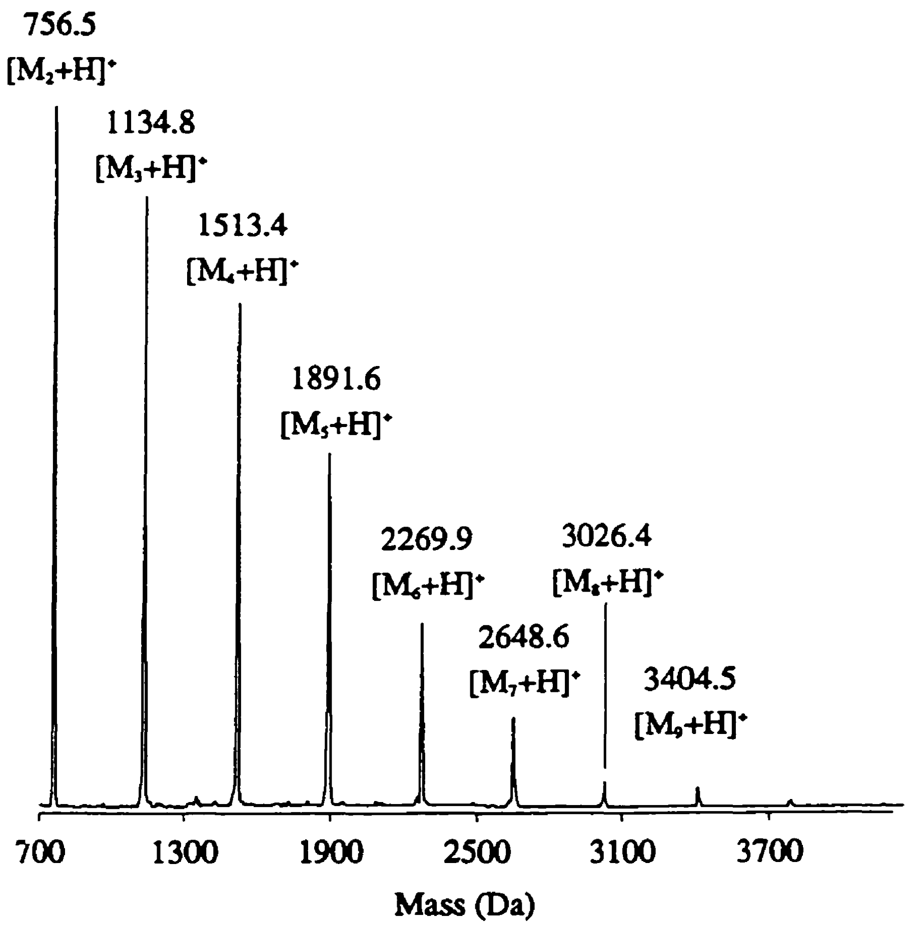


Figure A5.1. MALDI-TOF-MS spectrum of cyclic **A5.12**.

Table A5.2. MALDI-TOF analysis of cyclic **A5.12** and its oxidized products.

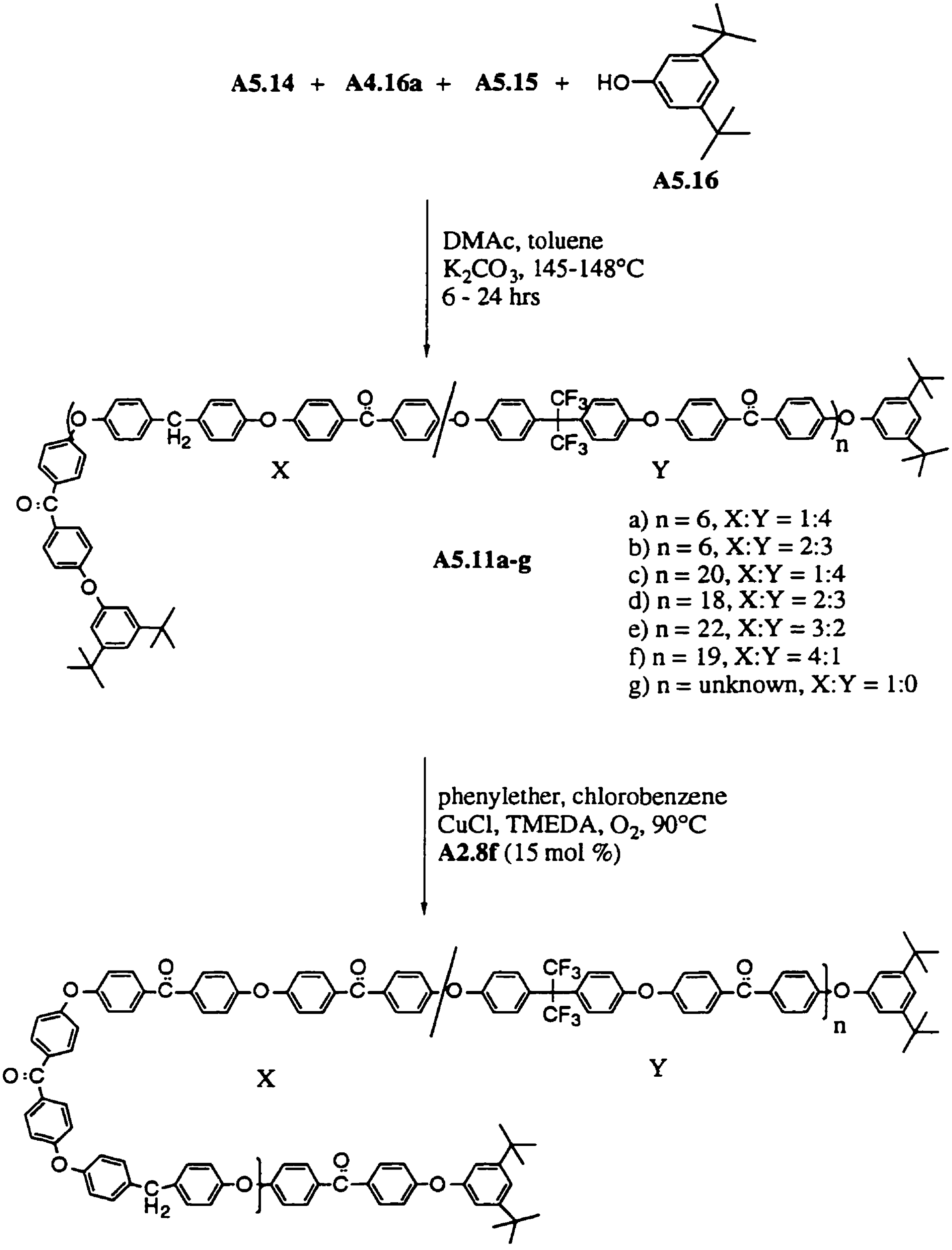
Species (M)	Theoretical Moleculal Weight		Experimental Moleculal Weight	
	Original Cyclic [M+H]+ (g/mol)	Oxidized Cyclic [M+H]+ (g/mol)	Original Cyclic [M+H]+ (g/mol)	Oxidized Cyclic [M+H]+ (g/mol)
2	757.2	–	756.5	756.9
		771.2		769.1
		785.2		–
3	1135.4	–	1134.8	1134.3
		1149.3		1147.6
		1163.3		1162.1
		1177.3		1177.6
4	15.13.5	–	1513.4	1513.7
		1527.5		1525.8
		1541.4		1540.1
		1555.4		1554.7
		1569.4		1569.5
5	1891.6	–	1891.6	1891.9
		1905.6		–
		1919.6		1918.4
		1933.6		1932.7
		1947.5		1947.4
		1961.5		
6	2269.7	–	2269.9	2271.7
		2283.7		–
		2297.7		–
		2311.7		2310.7
		2325.7		2325.3
		2339.6		–
		2353.6		–
7	2647.8		2648.6	–
8	3025.9		3026.4	–
9	3404.1		3404.5	–
10	3782.2		3784.3	–
11	4160.3		4161.2	–
12	4538.4		4538.4	–

Table A5.3. MALDI-TOF analysis of cocyclic **A5.13** and its oxidized products.

		Theoretical MW	Experimental MW				
				Oxidized Cyclic [M+H]$^+$			
Species (M)	Sequence	Original cyclic [M+H]+ (g/mol)	Cyclic [M+H]+ (g/mol)	Original (g/mol)	Mono-oxidized (g/mol)	Di-oxidized (g/mol)	Tri-oxidized (g/mol)
2	A_2B_2	757.2	756.7	756.5	769.2	785.2	--
	ABC	893.2	892.6	892.7	908.7	--	--
	B_2C_2	1029.2	1028.6	1029.2	--	--	--
3	A_3B_3	1135.3	1135.3	1135.4	1149.1	1162.8	1178.1
	A_2B_3C	1271.3	1271.2	1270.1	1284.5	1299.5	--
	AB_3C_2	1407.3	1406.8	1406.5	1421.6	--	--
	B_3C_3	1543.3	1542.7	1543.6	--	--	--
4	A_4B_4	1513.4	1513.7	--	--	--	--
	A_3B_4C	1649.4	1649.6	--	1662.7	1677.5	--
	$A_2B_4C_2$	1785.4	1785.3	1784.7	1799.1	--	--
	AB_4C_3	1921.4	1921.7	1921.7	1935.4	--	--
	B_4C_4	2057.4	2057.3	--	--	--	--
5	A_5B_5	1891.6	1891.4	--	--	--	--
	A_4B_5C	2027.5	2027.8	--	2040.1	2056.9	--
	$A_3B_5C_2$	2163.5	2163.5	2163.2	2177.8	2192.1	--
	$A_2B_5C_3$	2299.5	2300.1	2300	2313.4	--	--
	AB_5C_4	2435.5	2435.3	2435.4	--	--	--
	B_5C_5	2571.5	--	2570	--	--	--
6	A_6B_6	2269.7	--	--	--	--	--
	A_5B_6C	2405.7	--	--	--	--	--
	$A_4B_6C_2$	2541.6	2542.6	--	--	--	--
	$A_3B_6C_3$	2677.6	2678.3	--	2692.8	2706	--
	$A_2B_6C_4$	2813.6	2814.2	--	2827.9	--	--
	AB_6C_5	2949.6	2949.1	--	--	--	--
	B_6C_6	3085.6	--	--	--	--	--

With the dimer species of the cocyclic oligomer one should obtain three peaks with the follow sequence pattern A_2B_2, ABC and B_2C_2. These patterns was observed in the MALDI-TOF analysis of cocyclic **A5.13** (see table A5.3).

Only cocyclic **A5.13** exhibits a T_g on the first scan at 159°C, while both cyclic **A5.12** and **A5.13** have T_m at 364°C and 349°C, respectively. Note that with cocyclic **A5.13** the T_m is not well defined. On the second scan a T_g, T_c and T_m at 138°C, 233°C and 362°C, respectively were obtained for **A5.12** (Table A5.1) indicating the cyclic has undergone ring opening polymerization as has been previously demonstrated in the



a) n = 6, X:Y = 1:4
b) n = 6, X:Y = 2:3
c) n = 20, X:Y = 1:4
d) n = 18, X:Y = 2:3
e) n = 22, X:Y = 3:2
f) n = 19, X:Y = 4:1
g) n = unknown, X:Y = 1:0

A5.25a-g

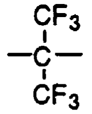
Scheme A5.5

literature with other cyclic oligomers.[21-24] With cocyclic **A5.13** no change in T_g value was observed though the endothermic peak at 349°C disappeared on the second scan.

A5.2.3 Polymer Synthesis

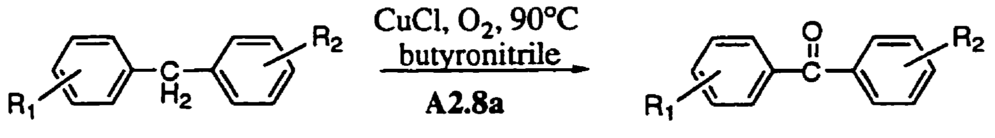
A series of polymers containing **A5.14** in the backbone were prepared through a typical procedure described in the literature.[25] No high molecular weight polymer was obtained by reacting **A5.14** with **A4.16a** since the oligomers prematurely precipitated out of solution. Therefore a series of copolymers **A5.11a-g** end capped with 3,5-di-t-butylphenol **A5.16** (Table A5.4) was prepared by reacting **A5.14** with **A5.15**, **A4.16a** and **A5.16** in DMAc at 145-150°C for 6 to 24 hours (Scheme A5.5). The polymers were obtained in high yields (Table A5.1). Glass transition temperatures in general increase with increasing molecular weight. This phenomenon was clearly observed with polymers **A5.11a,c** which are end capped at 6 and 20 repeat units, respectively. Their T_g values increased from 118°C to 152°C, respectively.

Table A5.4. Copolymers synthesized.

Entry	Number of Repeat Units	Percentage of Dihydroxy Monomer	
		$-CH_2-$	 $-C(CF_3)_2-$
A5.11a	6	20	80
A5.11b	6	40	60
A5.11c	20	20	80
A5.11d	18	40	60
A5.11e	22	60	40
A5.11f	19	80	20
A5.11g	--	100	0

A5.2.4 Oxidation of Arylmethanes

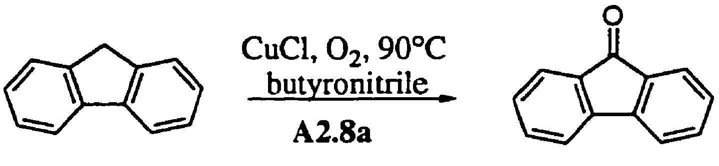
The arylmethanes **A3.3a**, **A5.11a-d**, and **A3.3l** were oxidized in butyronitrile at 90°C with molecular oxygen in the presence of a catalytic amount (10 mol%) of CuCl and



A3.3a
A5.8a-d

A3.19
A5.9a-d

a: $R_1 = Cl$, $R_2 = H$
b: $R_1 = Cl$, $R_2 = Cl$ (mixture of 4,4' and 2,4' isomer)
c: $R_1 = Cl$, $R_2 = Cl$ (mixture of 2,2' and 2,4' isomer)
d: $R_1 = OCH_3$, $R_2 = OCH_3$ (mixture of 4,4', 2,4' and 2,2' isomer)



A3.31

A5.10

Scheme A5.6

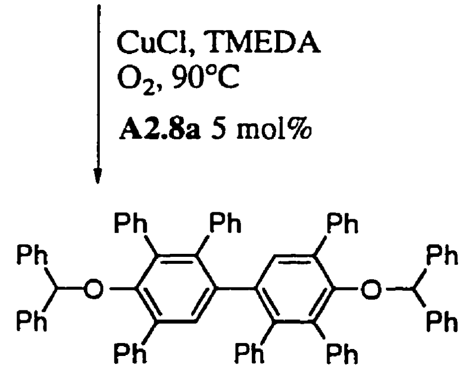
Table A5.5. Oxidation of diarylmethanes.

Entry	Rxn Time (°C)	Isolated[a] Yield (%)	Percent Conversion[b] -CH₂-	Percent Conversion[b] -CO-	m.p.[c] (°C)
A3.3a[d]	15	95	80	20	–
A3.3a	15	94	14	86	47-48
A5.8a	18	90	18	82	71-72
A5.8b[e]	17	83	16	84	–
A5.8c[f]	27	94	42	58	–
A5.8d[g]	26	90	19	81	–
A3.31	13	86	0	100	81-82

a) mixture of starting material and product.
b) based on HPLC calibration curves of the starting material and/or ketone product.
c) based on isolated fraction.
d) oxidation without HPBP.
e) mixture of 2,4' and 4,4' isomers.
f) mixture of 2,2' and 2,4' isomers.
g) mixture of 2,2', 2,4', 4,4' isomers.

A2.8a (Scheme A5.6). The generation of the ketone derivatives **A3.19**, **A5.9a-d**, and **A5.10** was monitored by HPLC. The percent conversion was in the range of 58 to 100% (Table A5.5). Diphenylmethane in the absence of solvent was oxidized with molecular oxygen and a catalytic amount (5 mol%) of CuCl, TMEDA, and **A2.8a** (Scheme A5.7). Note that in this case a similar percent conversion to **A3.19** was obtained (Table A5.6) and that diphenylmethane was both the reactant and solvent. The oxidized product, benzophenone has a low melting point so it too acts as the solvent for the reaction.

A3.3a



A3.19 +

A3.9a

Scheme A5.7

Table A5.6. The effect of different biphenols on the oxidation of diphenylmethane **A3.3a**.

Trail	Biphenol	Rxn Time (hrs)	Isolated Yield (%)	% Conversion^{b}	
				$-CH_2-$	-CO-
1^{a}	HPBP	30	95^{c}	25	69
2^{a}	ClTPBP	26	93^{c}	22	72
3^{b}	HPBP	26	75	--	75
4^{b}	ClTPBP	24	79	--	79

a) these reactions were done in butyronitrile with 10 mol% of CuCl, and biphenol.
b) these reactions were done in the melt with 5 mol% of CuCl, TMEDA, and biphenol.
c) isolated as a mixture of starting material and product.

A series of variables was examined including the concentration of biphenol, the effect of running the reaction in the melt and the use of different biphenols. When the oxidation was run in butyronitrile the optimal biphenol concentration was 10 mol% (Figure A5.2a), while in the melt the optimal biphenol concentration was 5 mol% (Figure A5.2b).

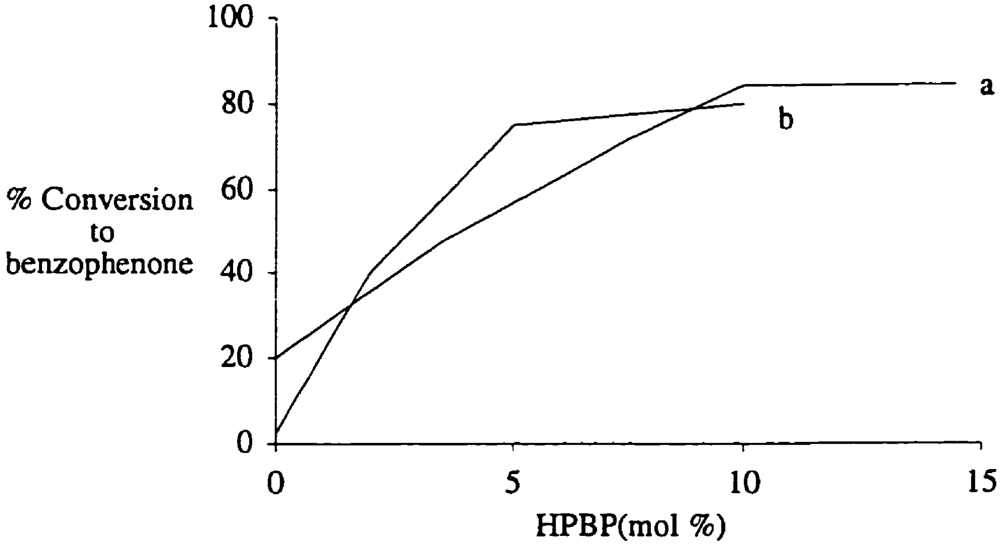


Figure A5.2. Effect of biphenol (HPBP) concentration on the oxidation of diphenylmethane to benzophenone in: a) butyronitrile, b) melt.

The difference in the amount of catalyst used, can simply be explained by the higher concentration of **A3.3a** in the melt reaction which increases the rate of contact and the generation of the methylene radical. The drawback with this method is the competitive deactivation of the biphenoxy radical by the formation of the carbon - oxygen coupled ether compounds discussed in Chapter A3. When the oxidation reactions were run in butyronitrile no carbon - oxygen coupling reaction occurred, instead cyclization of the biphenoxy radical was observed by HPLC. Therefore, each system has its limitation and they are directly correlated to the stability of the biphenoxy radicals. It is worth noting that only 20% conversion to the ketone derivative was obtained when no hindered biphenol or when 3,3'5,5'-tetraphenyl1,1-biphenyl-4,4'-diol **A2.8i** was added to the reaction (Table A5.5). This demonstrates that the hindered biphenols are essential for the oxidation.

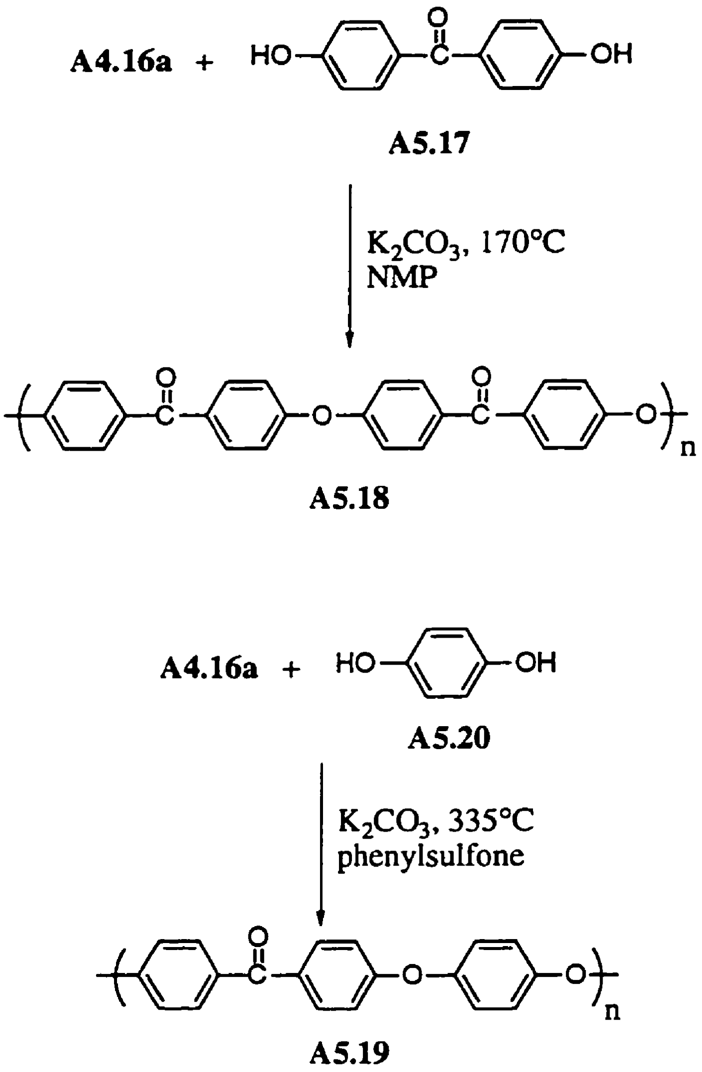
Since the hindered biphenol is the essential component in the oxidation reaction, we were interested in studying the effect of using different biphenols on the oxidation of

A3.3a. We chose biphenols **A2.8a** and **A2.8f** since they are the most readily available and exhibit a large difference in stability (see Chapter A2). Similar results were obtained with both biphenols. This at first was surprising, because **A2.8f** is more reactive and more stable than **A2.8a**. However because of the higher reactivity of biphenol **A2.8f**, side reactions like the carbon - oxygen coupling reaction would be expected to be enhanced, thus deactivating the biphenoxy radical at a faster rate. Therefore, the answer to improving the oxidation reaction is not through the reactivity of the biphenol, but to design a biphenol which would not undergo the carbon - oxygen coupling and the intramolecular reactions without affecting the reactivity of the biphenoxy radical.

The oxidation of a series of substituted biphenols was also examined (Scheme A5.6). In general the addition of electron donating and withdrawing groups in the para position **A5.8b,c,e** had no effect on the percent conversion to their benzophenone derivatives **A5.9b,c** (Table A5.5). For example 4-chlorodiphenylmethane **A5.8b** was converted in 82% yield to its oxidized form compared to **A3.3a** which was converted in 86% yield based on HPLC calibrations. Substitution in the ortho position drastically affects the oxidation of the methylene group (Table A5.5). In the case of dichlorodiphenylmethane **A5.8d** where 80% of the chloro groups are located at the ortho position only 58% conversion to **A5.9d** was observed. The chlorine atoms in the ortho position sterically hinder the methylene protons, reducing the rate of proton abstraction by the biphenoxy radical, which favors the formation of side reactions like the intramolecular cyclization reaction.

In general no higher than 86% conversion to their oxidized compounds were obtained with the diphenylmethane derivatives after 15-28 hours. With fluorene **A3.31** one obtains 100% conversion to 9-fluorenone **A5.10** within 13 hours (Scheme A5.6). This can be in part explained by the lower pK_a value ($pK_a = 23$) compared to **A3.3a** and its derivatives ($pK_a = 31-37$), and the longer reaction times required to oxidize **A3.3a** and

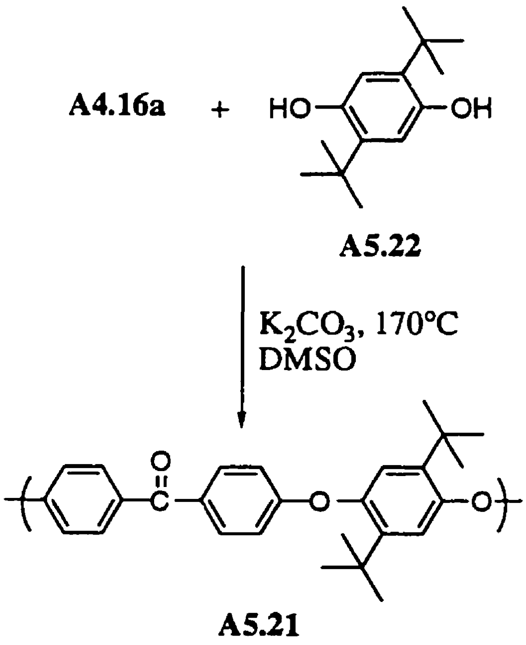
A5.8a-d which enhances the formation of side reactions which destroy the biphenoxy radical.



Scheme A5.8

A5.2.5 Oxidation of Cyclic Oligomers and Linear Copolymers

Poly(aryl ether ketone)s have received considerable commercial interest because these high performance engineering thermoplastics exhibit desirable characteristics such as thermoxidative stability, excellent mechanical properties and resistance to radiation. These polymers were independently synthesized by ICI and Dupont in the early 1960's.[26,27] by Friedel Crafts reaction. The synthesis of poly(aryl ether)s described by Clendinning *et al.*[28] provided an alternative synthesis, which involved reacting **A4.16a** with 4,4'-dihydroxybenzophenone **A5.17** in the presence of potassium carbonate (Scheme A5.8). Due to premature precipitation of oligomers, only low molecular weight polymer **A5.18** was obtained. It wasn't until phenyl sulfone was used as the solvent at temperatures > 300°C[29] that high molecular weight poly(aryl ether ketones) were obtained. In 1977 poly(ether ether ketone) PEEK® **A5.19** was introduced commercially by ICI as prepared by Rose and coworkers[30] by reacting hydroquinone **A5.20** with **A4.16a** in phenyl sulfone at 335°C (Scheme A5.8). In recent years the increasing demand for engineering thermoplastics has led researchers to the development of soluble poly(aryl ether ketone)s which are easier to process than PEEK®. For example, the introduction of t-butyl groups in the ortho position of hydroquinone **A5.20** can suppress crystallization rendering the polymer more soluble (Scheme A5.9).[31]



Scheme A5.9

This polymer **A5.21** in contrast to PEEK® is soluble in common organic solvents and can be processed either in solution or in the melt. The t-butyl groups are then cleaved with trifluoromethane sulfonic acid giving PEEK®. The disadvantage with this system is the additional step (synthesis of monomer **A5.22**) and the subsequent removal of the t-butyl group. With our catalytic oxidation method, the oxidation can occur during the processing step.

A series of cyclic oligomer **A5.12** and **A5.13** and copolymers **A5.11a-g** with repeat units in the range of 6-22 containing diarylmethane moieties were oxidized by the procedure previously discussed. Based on model reactions the optimal conditions were 15 mol % of **A2.8f**, CuCl and TMEDA, in a solution of diphenyl ether and chlorobenzene (5:1) at 70°C.

MALDI-TOF mass spectrometry analysis clearly shows the oxidation of cyclic **A5.12** to its oxidized derivatives **A5.23** (Scheme A5.3) by the appearance of a series of peaks corresponding to the oxidized products (Figure A5.3 and Table A5.3). For example, in the oxidation of the tetramer sequence five peaks were obtained in the MALDI-TOF spectrum (Figure A5.3 insert), corresponding to the original tetramer , the mono, di, tri, and tetra-oxidized cyclic. Similar patterns were obtained with cocyclic **A5.13** (Scheme A5.4, Table A5.4). ^{1}H NMR results indicate that only 67% and 70% of the methylene groups in cyclic **A5.12** and **A5.13**, respectively were oxidized (Table A5.7). In both ^{1}H NMR and MALDI-TOF analysis no peaks corresponding to the carbon - oxygen coupled product was observed, as would have been expected since the oxidation reactions were run at a concentration of 0.17M.

In comparing the GPC trace of cyclic **A5.13** (Figure A5.4a) and its oxidized derivative **A5.24** (Figure A5.4b) an increase in molecular weight along with a increase in T_g was observed with the oxidized cyclic **A5.24**, which possibly indicates that the cyclic has undergone partially ring opening polymerization. Further attempts to clarify these phenomena failed to confirm that these biphenoxy radicals initiated ring opening polymerization.

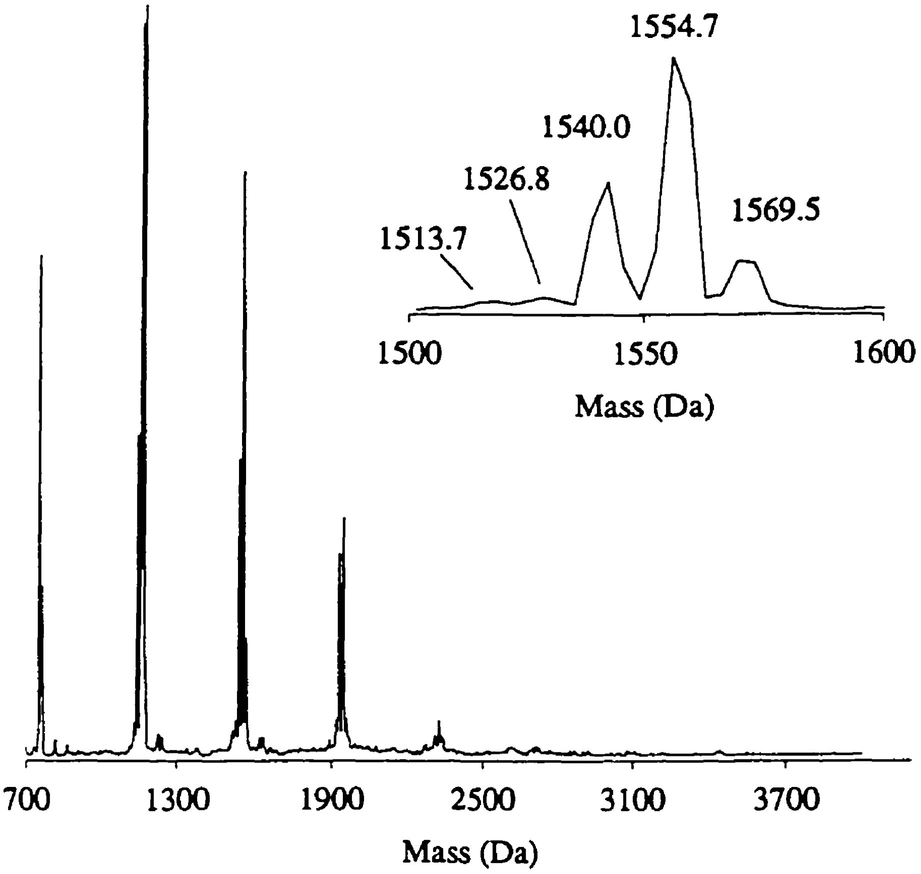


Figure A5.3. MALDI-TOF-MS spectrum of the oxidized cyclic **A5.23.**

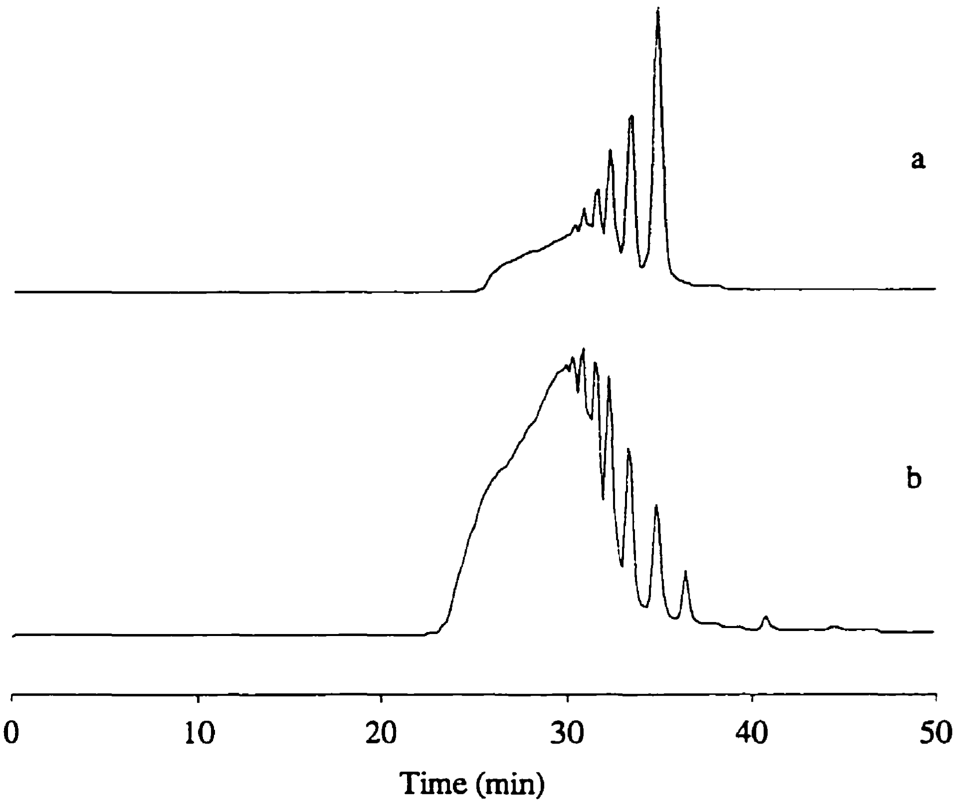


Figure A5.4. GPC trace of cyclic: a) **A5.13**, b) **A5.24**.

Table A5.7 Yields and physical properties of the oxidized products.

Entry	Rxn Time (hrs)	Isolated Yield (%)	T_g (°C)	T_m (°C)	5% Weight Loss Nitrogen (°C)	Mw (g/mol)	Mn (g/mol)	^{1}H NMR % Conv. (%)
A5.23	27	95	180	--	481	3600	1200	67
A5.24	26	60	166	--	501	9000	2600	70
A5.25a	48	58	159	--	508	18 000	7000	100
A5.25b	48	76	173	--	517	33 000	8000	70
A5.25c	48	78	172	--	504	118 000	42 000	99
A5.25d	46	75	170	--	523	41 000	24 000	57
A5.25e[a]	54	90	167	--	510	--	--	--

a) the polymer was insoluble in chloroform.

In the oxidation of the copolymers **A5.11a-g**, the chain length had no effect on the oxidation, since percent conversions of 100% and 99% were obtained for polymer **A5.11a** and **A5.11c**, respectively (Table A5.7). However the percent of monomer **A5.14** in the polymer chain did have an effect since the amount of **A5.14** increased as the percent conversion decreased. In comparing polymers **A5.13c,d,e** containing 20%, 40% and 60% of **A5.14**, respectively the percent conversion decreased from 99% to 57%, respectively (Table A5.7).

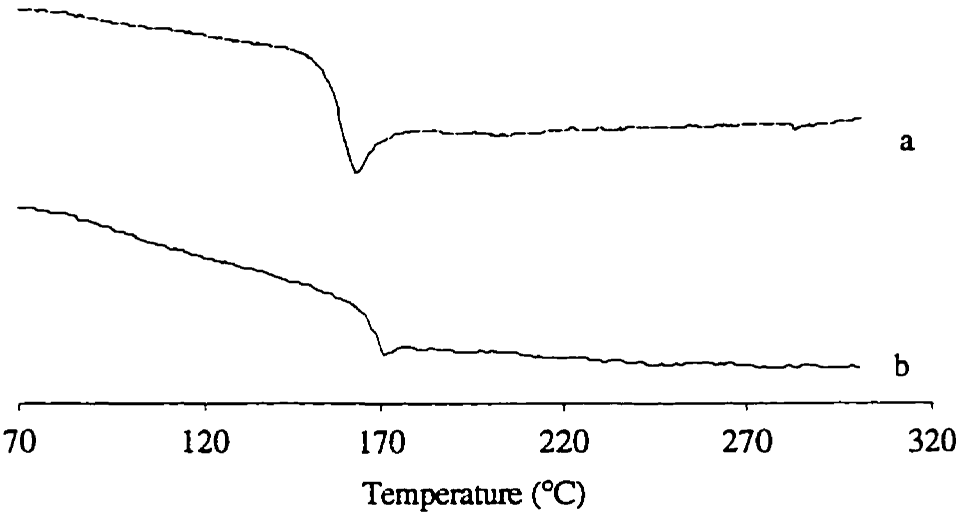


Figure A5.5. DSC trace of copolymer: a) **A5.11c**, b) **A5.25c**.

The T_g values for the oxidized copolymers **A5.25a-g** (Figure A5.5b) were 30 to 50°C higher than for the original polymers **A5.11a-g** (Figure A5.5a). This can be explained by the increased stiffness in polymers **A5.26a-g** due to the higher concentration of the benzophenone moiety in the polymer chain. Similar TGA traces were obtained for copolymer **A5.11c** (Figure A5.6a) and **A5.25c** (Figure A5.6b). The GPC results (Figure A5.7a,b) show that the oxidized copolymers have narrow polydispersities which is a good indication that no crosslinking has occurred and they exhibit higher molecular weights than the original copolymers. This might simply be explained by the behavior of the polymer on the GPC column.

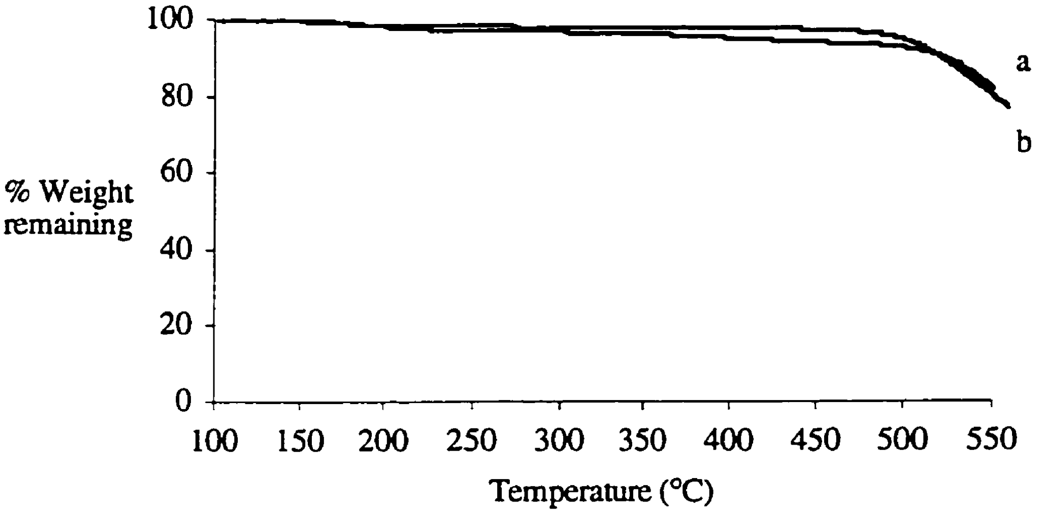


Figure A5.6. TGA trace of copolymer: a) **A5.11c**, b) **A5.25c**.

A5.3 Conclusions

We have demonstrated an efficient catalytic oxidation of diarylmethanes to their ketone derivatives under neutral conditions mediated by biphenols **A2.8a,f**. The para substituted diarylmethanes with either electron donating or withdrawing groups were effectively oxidized however low conversion were obtained with the ortho substituted arylmethanes like 2,2'-dichlorodiphenylmethane.

Oxidation of a series of cyclic oligomers and polymers containing the diphenylmethane moiety in the backbone was not straightforward since the percent conversion decreased as the amount of the diphenylmethane moiety in the chain increased. The catalytic oxidation with hindered biphenols is promising, and once a more stable biphenoxy radical is prepared the methylene groups should be quantitatively oxidized to their ketone derivatives.

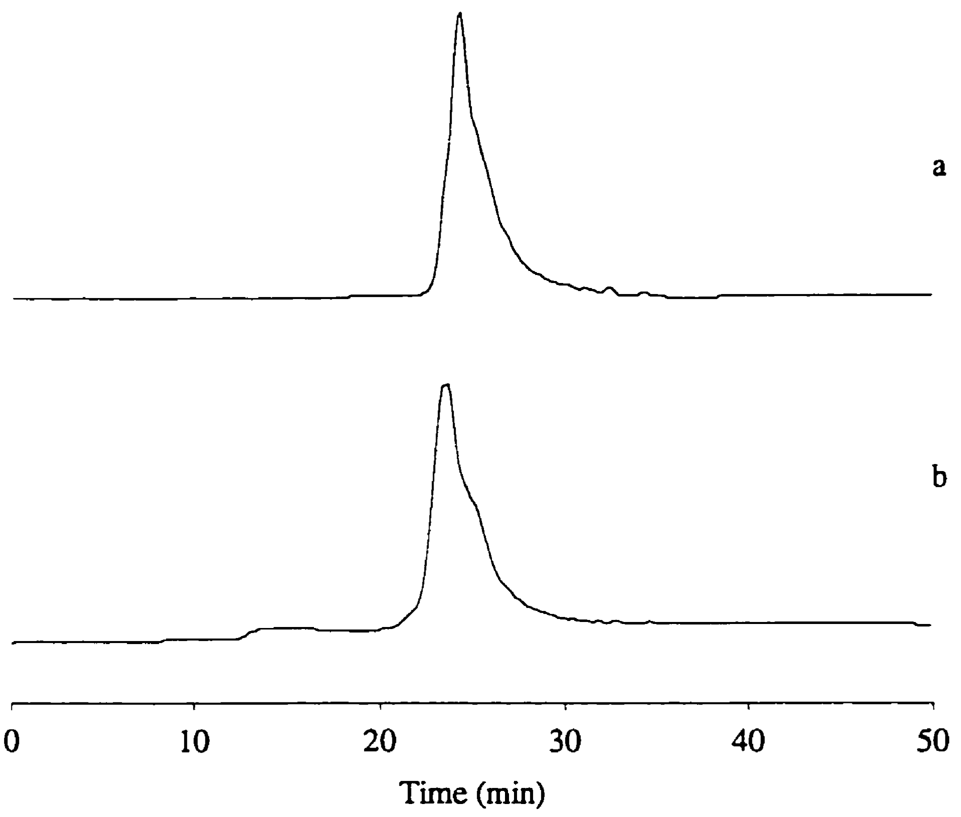


Figure A5.7. GPC trace of copolymer: a) **A5.11c**, b) **A5.25c**.

A5.4 Experimental Section

Materials

Chlorobenzene, 4-chlorobenzyl chloride, 2-chlorobenzylchloride, diphenyl ether, N,N-dimethylacetamide, bis-(4-hydroxyphenyl)methane, butyronitrile, CuCl, N,N,N',N'-tetramethylethylenediamine (TMEDA), diphenylmethane, aluminum trichloride ($AlCl_3$), and fluorene were purchased from the Aldrich Chemical CO. and used as received. Common solvents were obtained from Caledon Ltd.

Instrumentation

All ^1H and ^{13}C NMR were obtained on a Varian Unity 500 spectrometer. High performance liquid chromatography (HPLC) analyses were carried out on a Milton Roy

CM4000 pump equipped with a reverse phase silica column and a UV detector set at 254 nm; methanol was used as the eluent at a flow rate of 1 ml/min. Thermal analyses were obtained on the Seiko 220DSC and 220 TGA/DTA instrument at a heating rate of 20°C/min unless otherwise stated. Melting points were also determined on a Fisher-Johns melting point apparatus. Mass spectra were recorded on a Kratos MS25RFA spectrometer. GPC analyses were performed on a Waters 510 instrument equipped with a UV detector set at 254 nm and four 5 μm phenogel columns (3 x 500 Å, linear) arranged in series. Chloroform was used as the solvent and all molecular weights are referenced to polystyrene standards.

Typical Procedure for the Synthesis of Cyclic Oligomers

A two liter three neck round bottom flask equipped with a mechanical stirrer, condenser, Dean-Stark trap and syringe pump was charged with K_2CO_3 (5.31 g, 38.43 mmol), 1.2 L of DMAc and 100 mL of toluene. The solution was heated to reflux and a solution of **A5.14** (4.81 g, 24.00 mmol) and **A4.16a** (5.24 g, 24.01 mmol) in 50 mL of DMAc was added to the reaction flask using a syringe pump over an 8 hour period. After complete addition the reaction mixture was heated for a further 8 hours at 140 -142°C. The solution was filtered and the filtrate was evaporated to dryness. The crude product was dissolved in a minimum amount of chloroform and precipitated out from methanol. The white product **A5.12** was filtered and dried in a vacuum oven set at 100°C overnight. The cyclic was recovered in 88% (8.01 g) yield. ^1H NMR (500 MHz, CD_2Cl_2) δ 7.76 (br s, 4H), 7.25 (br s, 4H), 7.04 (br s, 8H), 4.01 (br s, 2H, CH_2); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 194.24, 194.22, 161.87, 161.77, 154.33, 154.32, 137.97, 137.81, 132.61, 132.44, 130.77, 120.57, 120.46, 117.31, 40.81 (CH_2), 40.72 (CH_2).

Cocyclic A5.13

A similar procedure as above was used but in this case two dihydroxy monomers were used **A5.14** and **A5.15**. Cyclic **A5.13** was obtained in 66% yield. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.78 (br s, 8H), 7.44 (br s, 5H), 7.25 (br s, 3H), 7.04-7.11 (distorted d, 16H), 4.01 (br s, 2H, CH_2); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 194.16, 162.03, 162.01, 161.87, 160.56, 160.49, 160.34, 160.31, 157.30, 157.18, 157.13, 154.35, 154.33, 154.31, 137.99, 137.94, 137.93, 137.74, 133.69, 133.63, 133.47, 132.77, 132.60, 132.54, 132.47, 132.35, 132.11, 130.77, 129.06, 125.78, 123.49, 123.47, 123.44, 120.60, 120.49, 119.48, 119.33, 119.22, 118.67, 118.58, 118.47, 118.41, 117.81, 117.34, 40.82 (CH_2). Note that these cyclics have been fully characterized by MALDI-TOF-MS see table A5.3 and A5.4.

Typical Procedure for the Synthesis of Copolymers.

A three neck 50 mL round bottom flask equipped with a Dean-Stark trap was charged with **A4.16a** (1.39 g, 6.38 mmol), **A5.14** (0.50 g, 2.50 mmol) **A5.15** (1.26 g, 3.75 mmol), DMAc (12 mL), benzene (6 mL) and K_2CO_3 (1.12 g, 8.12 mmol). The reaction was heated to reflux for 3 hours, and 3,5-di-t-butylphenol **A5.16** (0.08 g, 0.37 mmol) dissolved in 5 mL of DMAc was added to the reaction mixture. The mixture was refluxed for another 2 hours. Benzene was then removed by distillation and the temperature of the reaction mixture was maintained at 140-145°C for a further 17 hours. The product was precipitated from a solution of methanol and water (3:1). Polymer **A5.13c** was recovered in 78% (2.70 g) yield after reprecipitation and being dried under vacuum at 100°C overnight.

General Oxidation Procedures

Method A: Oxidation in Butyronitrile

Oxygen was bubbled directly into a vigorously stirred solution consisting of butyronitrile (15 mL), diphenymethane **A3.3a** (2.00 g, 11.89 mmol), CuCl (0.12 g, 1.19

mmol), biphenol **A2.8a** (0.72 g, 1.12 mmol) at 90°C. After 15 hours the reaction was over, and 2.02 g of a mixture of **A3.3a** and benzophenone **A3.19** was recovered. Based on HPLC calibration curves 0.28 g(14%) of **A3.3a** and 1.77 g (82%) of **A3.19** was obtained.

Method B; Oxidation in the Melt

Oxygen was bubbled into the vigorously stirred solution of **A3.3a** (10.00 g, 59.40 mmol), CuCl (0.30 g, 2.97 mmol), TMEDA (0.34 g, 2.97 mmol), and **A2.8a** (1.91 g, 2.97 mmol) at 90°C for 26 hours. The mixture was dissolved in chloroform and filtered, the filtrate was evaporated to dryness and the residue was distilled under reduced pressure, yielding 8.11 g (75%) of **A3.19**. The remaining solid was purified by column chromatography using 10% ethyl acetate in hexane as the eleuent. The diether **A3.9a** was isolated, in 0.84 g (29%), along with many minor products which we were unable to identify due to difficulties in purifications.

Method C: Oxidation of Cyclic Oligomers and Polymers in Diphenyl Ether and Chlorobenzene

A flask equipped with an oxygen inlet and vibromixer was charged with cyclic **A5.12** (1.66 g, 1.86 mmol), CuCl (0.03 g, 0.31 mmol), **A2.8f** (0.15 g, 0.28 mmol), TMEDA (0.04 g, 0.32 mmol), diphenyl ether (10.15 g) and 2 mL of chlorobenzene. The solution was vigorously stirred at 73°C with oxygen bubbling directly into the reaction mixture. The reaction was stopped after 48 hours, since the red color which indicates the presence of the biphenoxy radical had faded. The mixture was diluted in chloroform and filtered to remove the copper complexes. The filtrate was concentrated and then added to methanol. The precipitate was isolated and washed with methanol using a Soxhlet apparatus for 48 hours to insure complete removal of diphenyl ether.

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CHAPTER A6

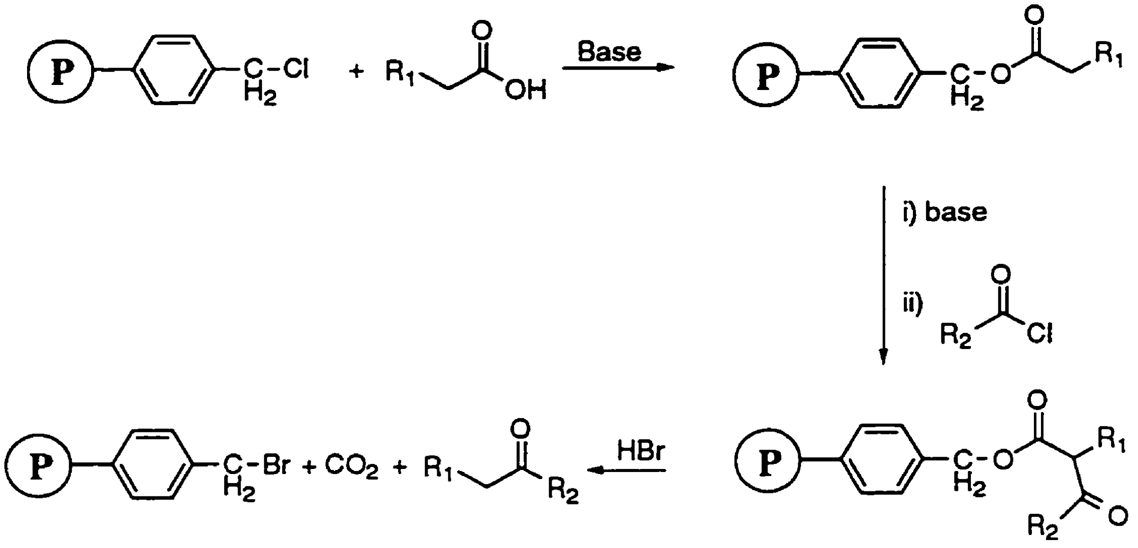
SYNTHESIS AND CHARACTERIZATION OF POLY(ARYL ETHER)S CONTAINING PHENOXY MOIETIES: POLYMER SUPPORTS FOR USE IN ORGANIC REACTIONS.

A6.1 Introduction

A6.1.1 Polymer Supports

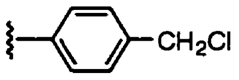
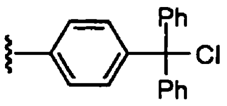
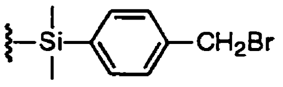
For many years polymer supports have been used with great success in peptide chemistry[1,2] and in other areas of organic chemistry such as acylation of esters, and the Dieckman cyclization reaction to name a few.[1-4] Conventional organic reactions do not always go to completion and a purification step is generally necessary. In most cases this is the most difficult and time consuming part of the process. Improvements have been achieved with the use of a polymer support which reacts with a specific substrate in the mixture. The workup under these conditions is simplified because the polymer, which generally is insoluble in organic solvents, is separated by filtration and washed to remove any impurities. By simply cleaving off the product and removing the polymer by filtration a pure product is obtained without the rigorous purification procedures previously required. A further advantage is that in certain syntheses an excess amount of reactant can be used to either increase the reaction rate and / or push the reaction to completion.

Organic reactions using polymer supports can be categorized into three classes; 1) polymeric carrier, 2) polymeric reagent, and 3) polymeric catalyst. Polymeric carrier type synthesis involves the transformation of a low molecular weight compound covalently bound to a polymer. Chemical promoters (e.g. reagents, catalyst) are added to the reaction mixture converting the attached starting material to the final product while still remaining attached to the polymer. The polymer is then isolated and the product is cleaved off. An example is illustrated in scheme A6.1.[4] Some commonly used polymeric carriers are listed in table A6.1.[3]



Scheme A6.1

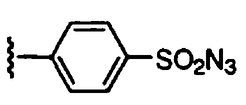
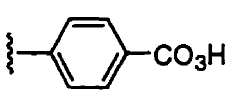
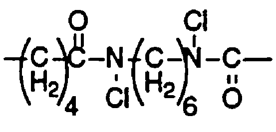
Table A6.1. Examples of polymeric carriers used in organic synthesis.

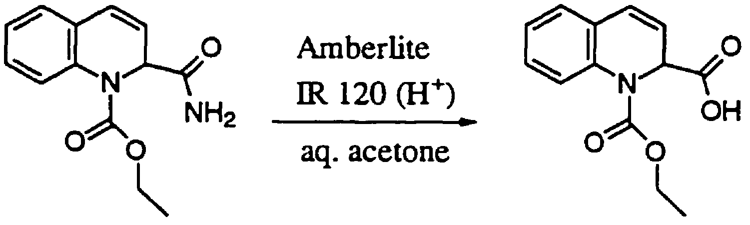
Polymer	Bonding Site	Substrate	Reaction Type
chloromethylated copolystryrene-DVB with high degree of substitution		mixed ester	intramolecular condensation of esters
polyethylene glycol linked to mono-tritylchloride		3' o-acety-deoxy thymide	oligonucleotide synthesis
glass having organic groups (e.g. benzyl bromide) attached to the surface		n-protected amino acid esters	peptide bond formation

DVB = divinylbenzene

The second type is the polymeric reagent synthesis (Table A6.2)[3]. Here the polymer itself reacts with a low molecular weight compound transforming the starting material to the appropriate product. The selective hydrolysis of the amide functionality over the ester functionality using Amberlite IR 120 (H^+) (Scheme A6.2)[4] is a typical example of a polymeric reagent type reaction.

Table A6.2. Examples of polymeric reagents in organic synthesis.

Polymer	Functional Groups	Reaction Type
azide of sulfonated copolystyrene-DVB		diazo transfer reactions with β-ketones
carboxylic group incorporated in copolystyrene-DVB		epoxidation
N-chloropolyamide		oxidation of organic compounds



Scheme A6.2

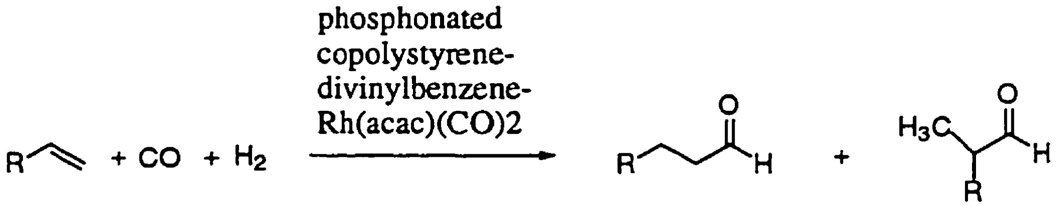
The third class is the polymeric catalyst type synthesis which to some extent is similar to the polymeric reagent type synthesis however these polymers by definition must be recyclable. In this synthesis a conventional catalyst (e.g. $AlCl_3$, Cu(OH)ClPy, $PtCl_3$, $PdCl_2$) is bound to the polymer (Table A6.3)[3] generating the polymeric catalyst which is used to transform low molecular weight organic compounds to their corresponding products (Scheme A6.3).[4]

Polymer supports in order to be effective in their specific roles should have the following properties. 1) The polymer in general should be insoluble in organic solvents, although there are exceptions. For example, similar results were obtained with soluble polymers like functionalized polystyrene (MW 50 000 to 300 000 g/mol). The limitations in the use of these soluble polymers is the loss of material and the time consumed in the workup. 2) The functional groups should be easily accessible and in high concentration. 3) The polymer should be stable to the reaction conditions.

Table A6.3. Examples of polymeric catalysts for organic reactions.

Polymer Type	Catayst Attached	Reactions
phosphonated copolystyrene-DVB bonded to transition metal complexes	$-RhCl(PPh_3)_3$ $-RhCl_3$, $-Rh(acac)(CO)_2$ $-PtCl_2$, $PdCl_2$	hydrogenation hydroformylation
copolystyrene-DVB bound $AlCl_3$	$-AlCl_3$	lewis acid catayzed ether, ester, and acetal formation
polyvinylpyridine-Cu(II) complex	-Cu(OH)ClPy	oxidative polymerization of phenols

PPh_3: triphenylphosphine, acac: 2,4-pentanedione, Py: polyvinylpyridine

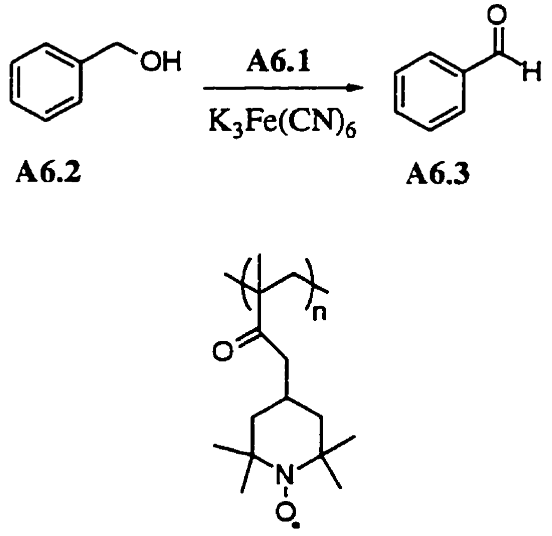


Scheme A6.3

A6.1.2 Redox Polymers

Redox polymers are yet another type of polymeric support because of their ability to oxidize or reduce organic molecules. For example, poly(tempo acrylate) **A6.1** has been used as a polymeric catalyst in the oxidation of benzyl alcohol **A6.2** to benzaldehyde

[5] **A6.3** (Scheme A6.4). These polynitroxides have also been used as stabilizers in polymers and as coatings for electrodes for electrochemical oxidation of amines.[6,7]



A6.1

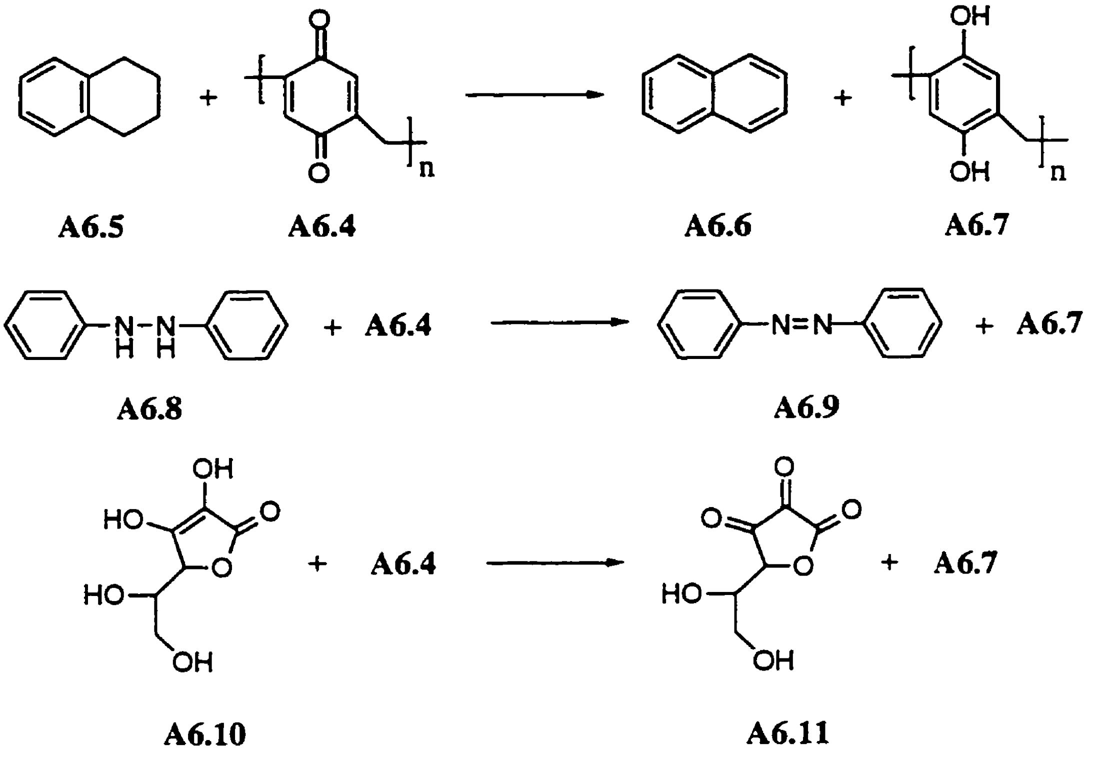
Scheme A6.4

Quinone based polyformaldehydes resins **A6.4** are another class of redox polymers used as oxidizing reagents. Here resin **A6.4** oxidizes 2,3,4,5-tetrahydronaphthalene **A6.5** to naphthalene **A6.6** while the polymer is reduced to its hydroxy derivative **A6.7**. Organic compounds such as hydrazobenzene **A6.8** and ascorbic acid **A6.10** have also efficiently been oxidized to azobenzene **A6.9** and dehydroascorbic acid **A6.11**, respectively, using resin **A6.4** (Scheme A6.5).[8]

In recent years polymers containing phenoxy radicals as pendent groups **A6.12**, **A6.13**, **A6.14** (Figure A6.1) have mainly been designed as magnetic materials.[5,9,10]

A6.1.3 Goals and Strategies

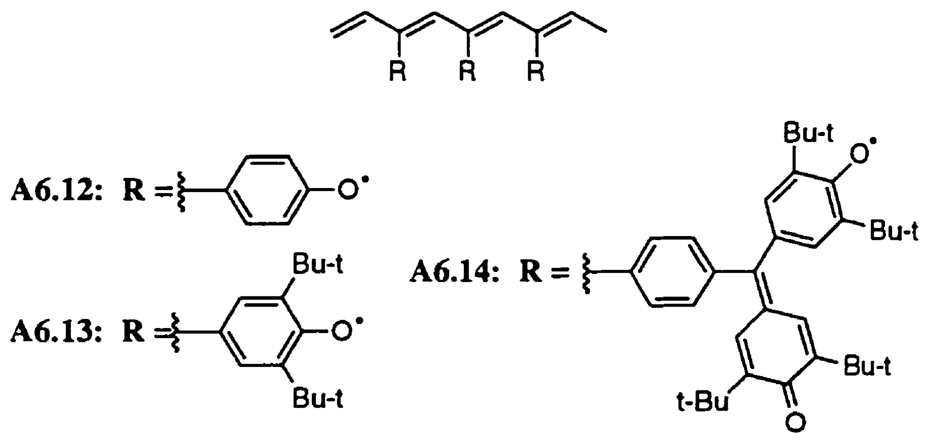
We on the other hand were interested in synthesizing a series of poly(aryl ether)s as potential polymer supports **A6.15,b**, **A6.16,b**, **A6.17,b** containing hindered biphenols


A6.5 A6.4 A6.6 A6.7

A6.8 + A6.4 A6.9 + A6.7

A6.10 + A6.4 A6.11 + A6.7

Scheme A6.5


A6.12: R =

A6.13: R =

A6.14: R =

Figure A6.1

(Figure A6.2), which are easily converted to stable biphenoxy radicals. These polymers could be useful in the oxidative conversion of activated methylene groups such as **A3.3a**, **A3.3e** and **A3.8l** to their alcohol and/or aldehyde counterparts.

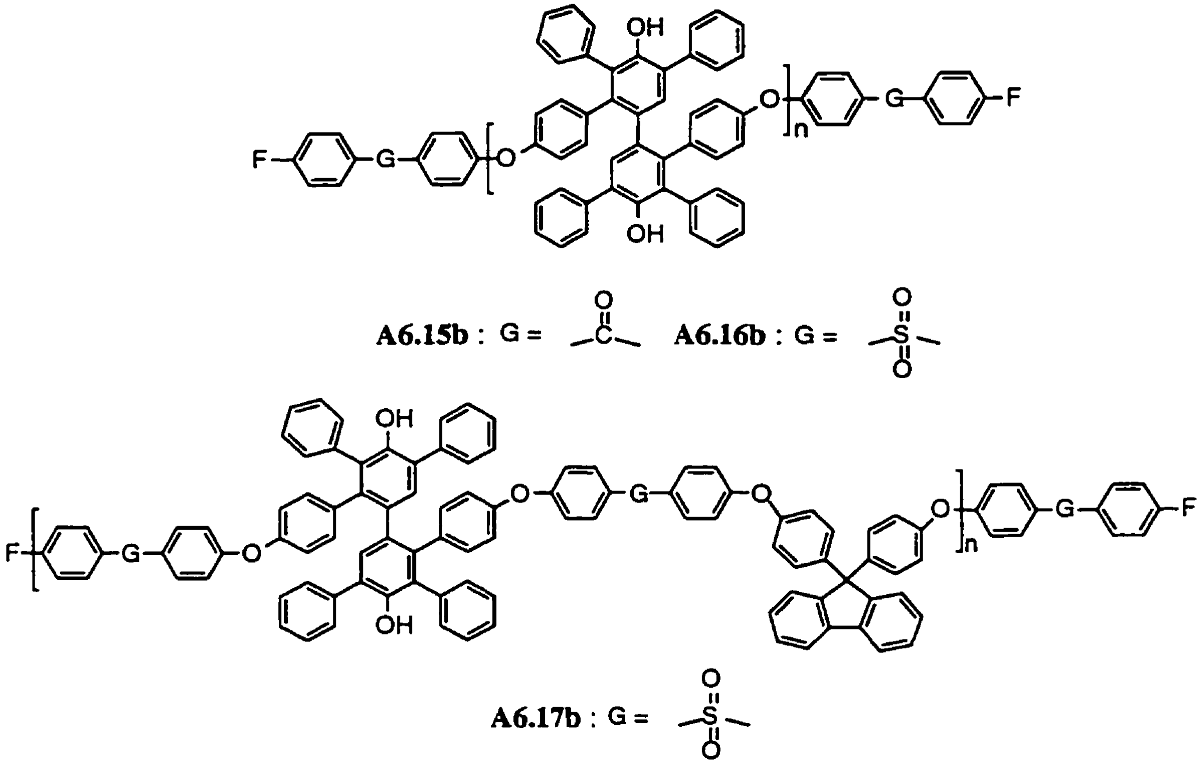
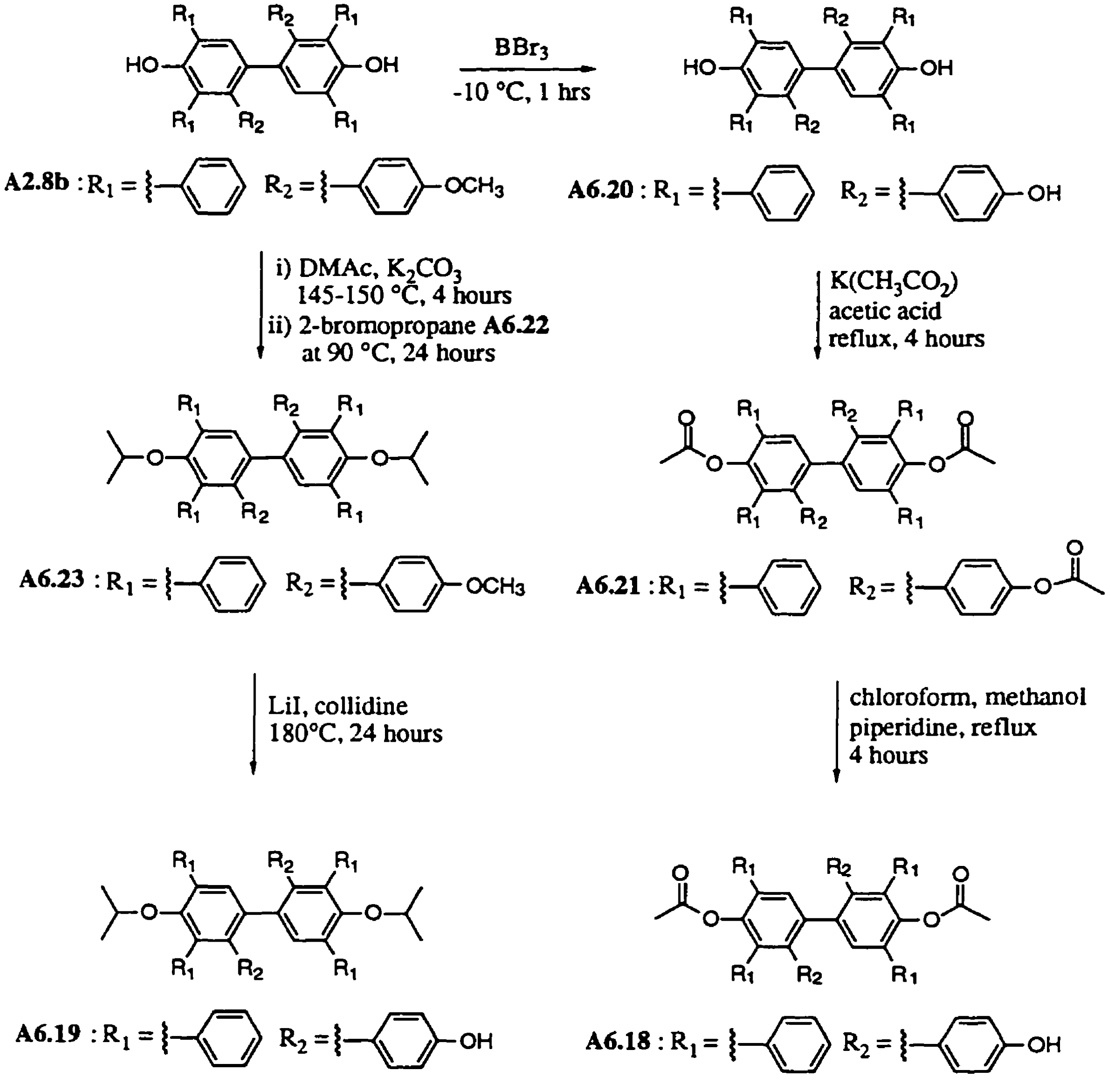


Figure A6.2

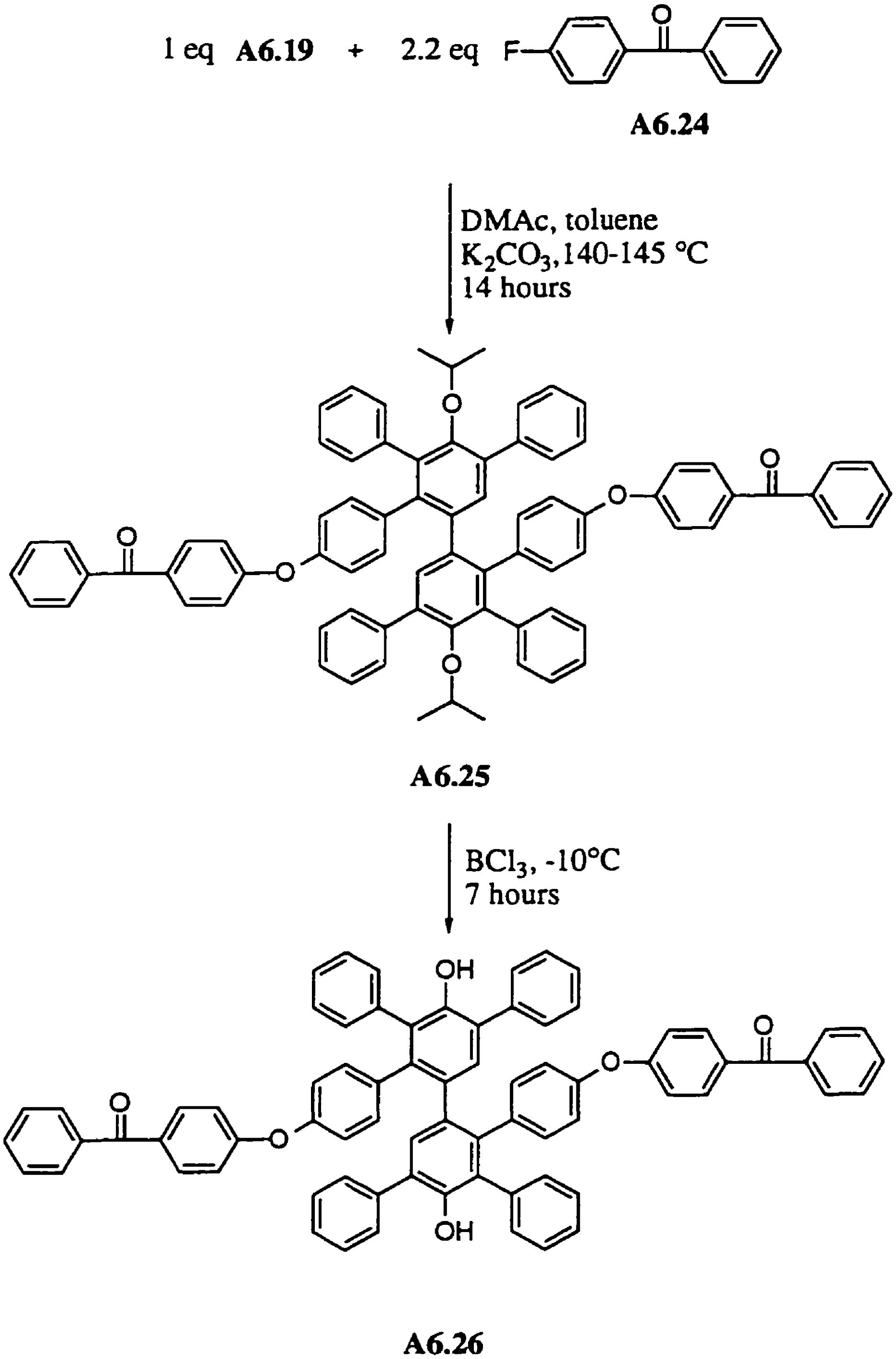
A6.2 Results and Discussions

A6.2.1 Monomer Synthesis

Two new biphenols **A6.18** and **A6.19** were specifically designed for the synthesis of stable redox polymers. Monomer **A6.18** was prepared by the method described by Kim.[11] Deprotection of the methoxy groups with 1M BBr_3 in methylene chloride at -10°C yielded **A6.20** in 90% yield. Treatment with potassium acetate (KOAc) and acetic acid at reflux for 4 hours afforded the tetraacetate monomer **A6.21** in 89% yield. Selective deprotection of the unhindered acetate groups was achieved using piperidine in a mixture of chloroform and methanol at reflux for 4 hours, yielding the diacetate monomer **A6.18** in 94% yield (Scheme A6.6). Biphenol **A6.19** was obtained by reacting the potassium salt of **A2.8b** with 2-bromopropane **A6.22** at 90°C in DMAc for 24 hours affording **A6.23** in 82% yield. This was followed by the selective deprotection of the methoxy groups using lithium iodide in 2,4,6-collidine at 180°C for 24 hours yielding **A6.19** in 58 % yield (Scheme A6.7).



Scheme A6.6


1 eq **A6.19** + 2.2 eq
F
O
A6.24
DMAc, toluene
K_2CO_3, 140-145 °C
14 hours
O
O
O
O
O
O
A6.25
BCl_3, -10°C
7 hours
OH
OH
O
O
O
O
A6.26

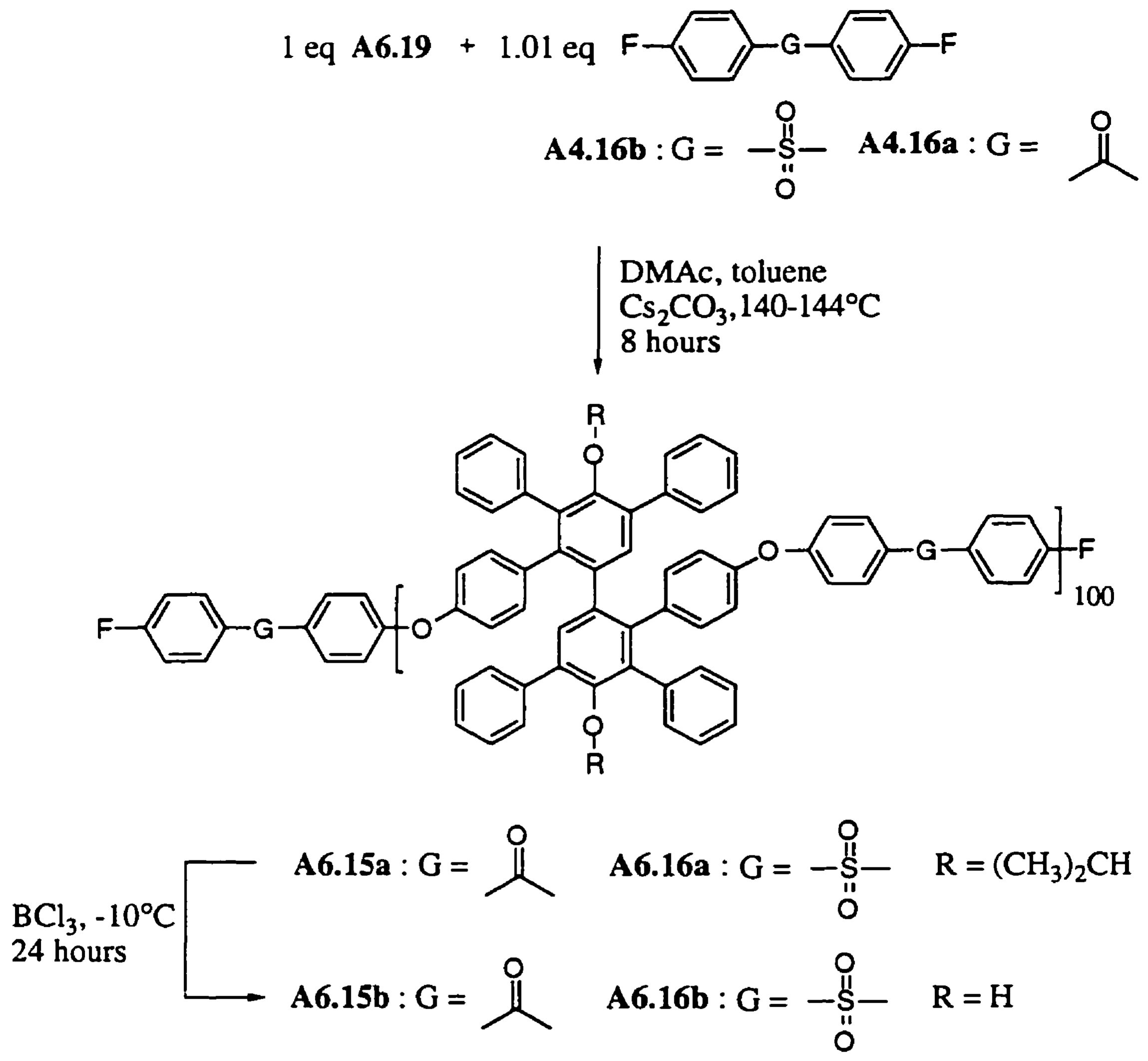
Scheme A6.7

A6.2.2 Polymer Synthesis and Characterization

Preliminary work by W.-Gi Kim[11] on the polymerization of biphenol **A6.18** with a series of activated difluoro monomers yielded only low molecular weight polymers. The possible cleavage of the hindered acetate groups of biphenol **A6.18** under basic condition might explain the low molecular weights obtained by Kim. Theoretically, once the stoichometric balance is altered only low molecular weight materials should be obtained. This would be the case if the acetate groups are cleaved, since now instead of having two reactive hydroxy groups one can have either three or four depending on the extent of the cleavage reaction. In order to determine the stability of biphenol **A6.18** and **A6.19** model reactions were studied by reacting the biphenols with 4-fluorobenzophenone **A6.24** under typical polymerization conditions. All of the reaction were monitored by HPLC and, as we expected, the reaction with biphenol **A6.18** afforded three products clearly indicating that the acetate groups are cleaving during the reaction. On the other hand only one product **A6.25** was isolated in 72% yield (note by HPLC this reaction is quantitative) from the reaction of biphenol **A6.19** and **A6.24** (Scheme A6.7). Using model compound **A6.25** we were also able to show that the isopropyl groups were quantitatively and selectively cleaved with 1M BCl_3 in methylene chloride at -10°C to give **A6.26** in 83% isolated yield.

Initial polymerization of biphenol **A6.19** with bis(4-fluorophenyl)sulfone **A4.16b** or 4,4'-difluorobenzophenone **A4.16a** (Scheme A6.8) using general polymerization procedures described in the literature[12-17] were unsuccessful due to the precipitation of the product during the reaction. Higher temperature and different solvents did not improve the reaction. Only by substituting K_2CO_3 with Cs_2CO_3 were we able to obtain high molecular weight polymers. Since the Cs^+ atom is larger than the K^+ atom the ionic bond of the Cs^+ atom with the biphenol anion is weaker therefore increasing the solubility of the salt in polar solvents and the reactivity of the anion. High molecular weight polymers **A6.15a** and **A6.16a** (Table A6.4, A6.5) were obtained in high yield, 83% and 88%, respectively.

All these polymers were designed to have 100 repeat units by using excess of the difluoro compound.



Scheme A6.8

Proton, ^{31}P[18] and ^{19}F NMR confirm that the polymers are end capped with fluoro groups and have approximately 100 repeat units. Originally these polymers were soluble in common organic solvents, however, when heated in methylene chloride or chloroform they became partially insoluble. Analyses of the insoluble fractions by DSC have shown them to be crystalline, T_m's at 248°C and 268 °C were obtained for polymers **A6.15a** and

A6.16a, respectively. It appears that solvents induce crystallinity in these polymers. The sulfone polymer **A6.16a** was the most difficult to handle because it had a tendency to crystallize more readily and even the soluble fraction became insoluble on standing over time .

Table A6.4. Polymerization reaction conditions.

Entry	Repeat Units (n)	Solvent	Rxn Temp. (°C)	Rxn Time (hour)	Base	Isolated Yield (%)
A6.16a[a]	--	DMAc	145-150	26	K_2CO_3	--
A6.16a	--	DMPU	170-175	22	K_2CO_3	84
A6.16a	100	DMAc	138-142	9	Cs_2CO_3	83
A6.15a	100	DMAc	138-142	9	Cs_2CO_3	88

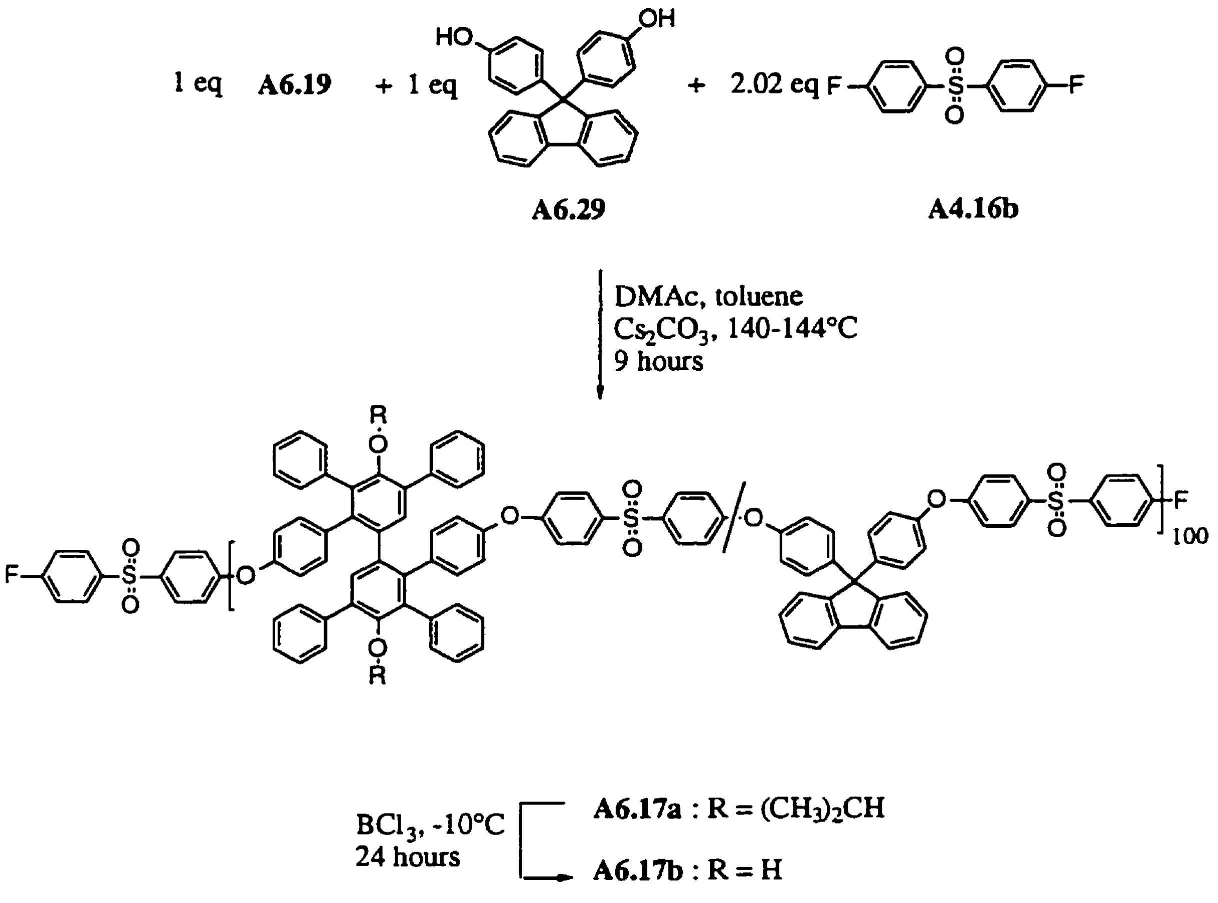
a) precipitated out of solution.

Table A6.5. Physical properties of the isopropyl derivative homopolymers.

Entry	GPC			Thermal Analysis		η_{inh}
	Mw (g/mol)	Mn (g/mol)	PD	T_g (°C)	5% Wt. Loss (°C)	(dL/g)
A6.16a[a]	--	--	--	--	--	--
A6.16a[b]	37 000	8400	4.3	--	--	--
A6.16a[c]	90 000	43 000	2.1	236	402	--
A6.15a	99 000	44 000	2.3	231	411	0.35

a) insoluble product was obtained.
b) low molecular weight fraction.
c) GPC results of soluble fraction only.

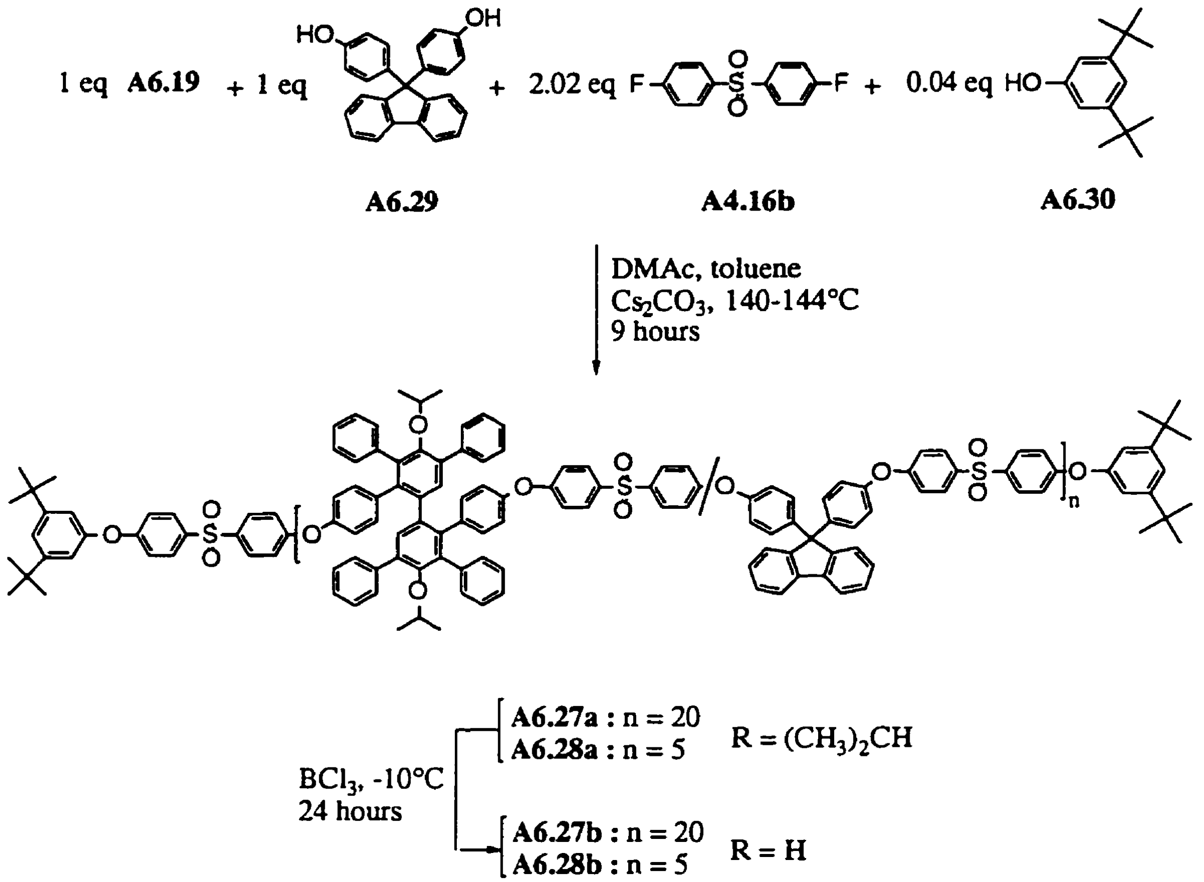
Copolymers **A6.17a**, **A6.27a**, and **A6.28a** (Scheme A6.9,10, Table A6.6, A6.7) were prepared by reacting equivalent molar amounts of biphenol **A6.19** and biphenol **A6.29** with **A4.16b** at 140 to 144 °C in DMAc for 9 hours. Note that polymer **A6.17a** was end capped at 100 repeat units with **A4.16b**, while oligomers **A6.27a** and **A6.28a** (Figure A6.3a) were end capped with 3,5-di-t-butyl-phenol **A6.30** at 20 and 5 repeat units, respectively. All these polymers were soluble in common organic solvents and did not exhibit any changes in solubility when heated in methylene chloride or chloroform as with their homopolymer analogues, due to the random distribution of the monomers found in the copolymers which disfavors crystallization formation.



Scheme A6.9

Table A6.6. Polymerization reaction conditions for the copolymers.

Entry	Repeat units (n)	Solvent	Rxn Temp. (°C)	Rxn Time (hour)	Base	Isolated Yield (%)
A6.17a	100	DMAc	138-142	8	Cs_2CO_3	82
A6.27a	20	DMAc	138-142	9	Cs_2CO_3	92
A6.28a	5	DMAc	138-142	10	Cs_2CO_3	93



Scheme A6.10

Table A6.7. Physical properties of the isopropyl derivative copolymers.

Entry	GPC			Thermal Analysis		
	Mw (g/mol)	Mn (g/mol)	PD	T_g (°C)	5% Wt. Loss (°C)	ηinh (dL/g)
A6.17a	105 000	64 000	1.6	248	419	0.48
A6.27a[a]	43 000	20 000	2.2	245	415	--
A6.28a[a]	17 000	7200	2.4	226	399	--

a) low molecular weight polymers.

Since polymers **A6.15a**, **A6.17a**, **A6.27a**, and **A6.28a** were easier to handle the remainder of this chapter will deal with these polymers and their corresponding derivatives. Of the higher molecular weight polymers **A6.15a** and **A6.17a** only

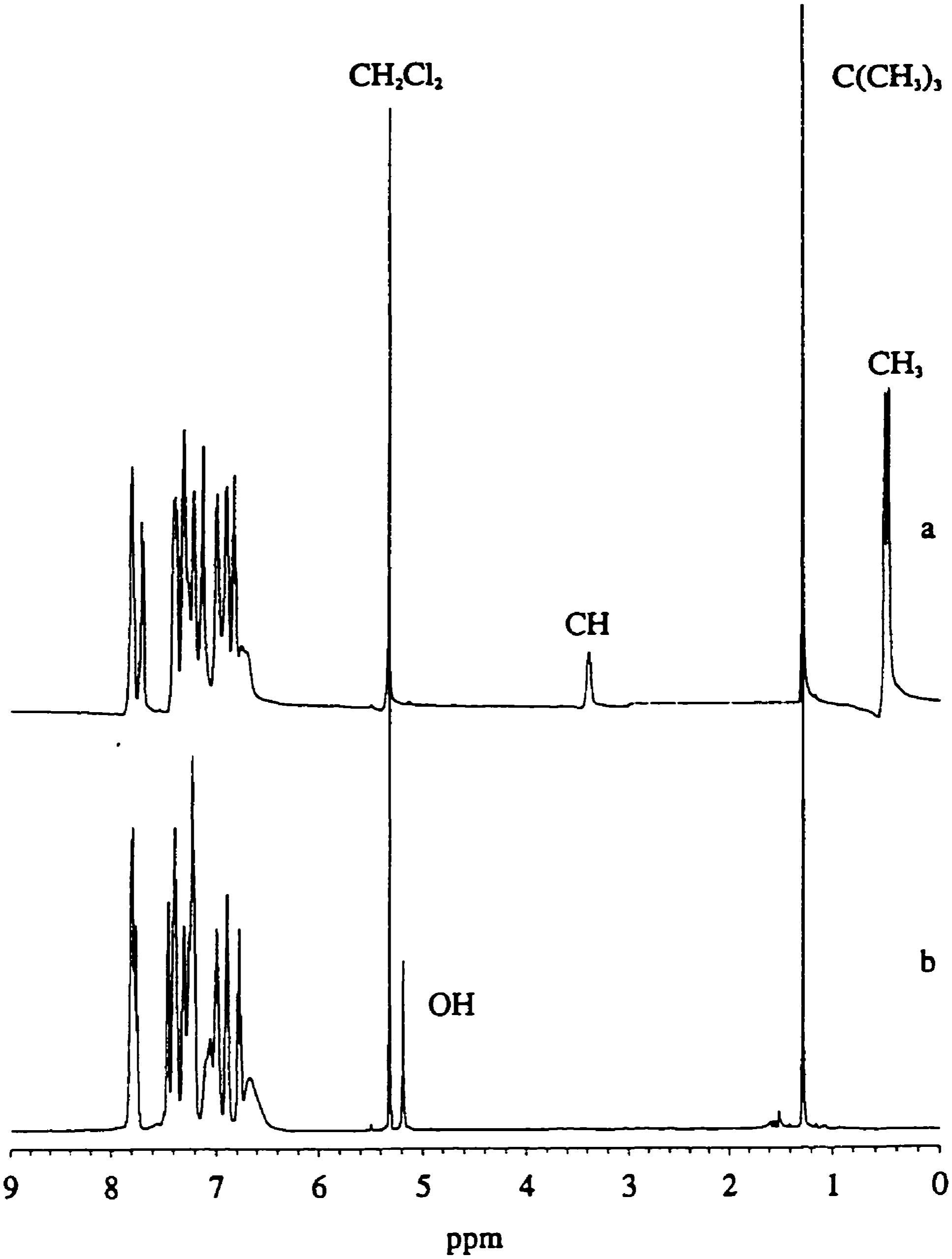


Figure A6.3. ^{1}H NMR spectra of a) polymer **A6.28a**, b) polymer **A6.28b**.

A6.17a formed a clear flexible film. Their inherent viscosities and Mw's are 0.35 dL/g, 0.48 dL/g, and 99000 g/mol, 105 000 g/mol (Figure A6.4b), respectively.

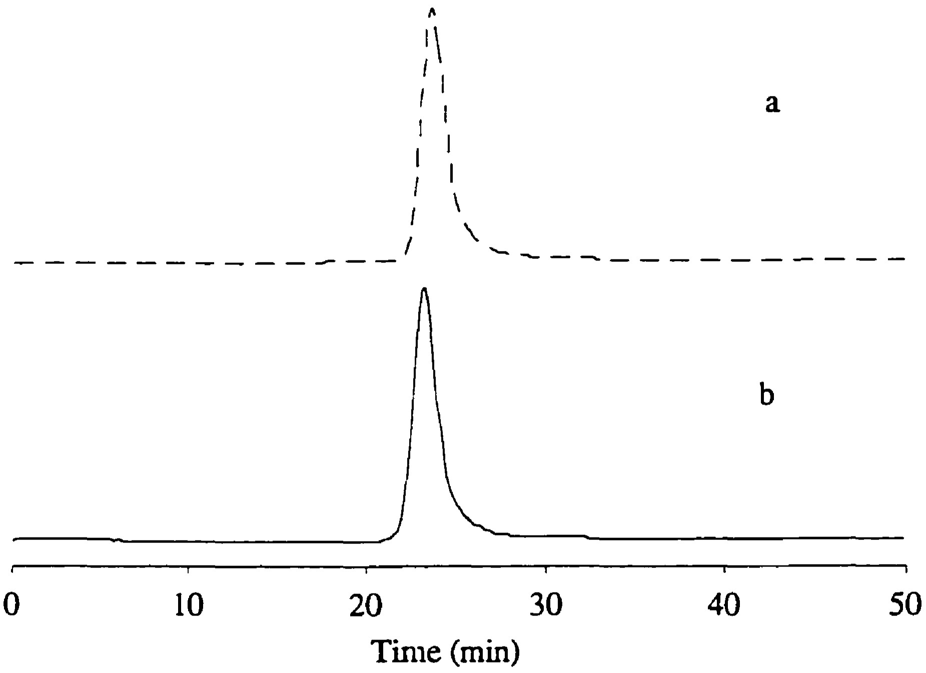


Figure A6.4. GPC curves of: a) polymer **A6.17b**, b) polymer **A6.17a**.

The thermal properties are listed in tables A6.5 and A6.7. Their T_g's are 231°C and 248°C (Figure A6.5b), respectively. The higher T_g observed for copolymer **A6.17a** was expected because the homopolymer of biphenol **A6.29** and difluoro monomer **A4.16b** has a T_g of 280°C[19] which is higher than the T_g of homopolymer **A6.16a** (T_g = 236°C). The theoretical T_g of 252°C (based on Fox's equation)[20], is similar to the experimental T_g of 248°C, which confirms that we have the right copolymer composition.

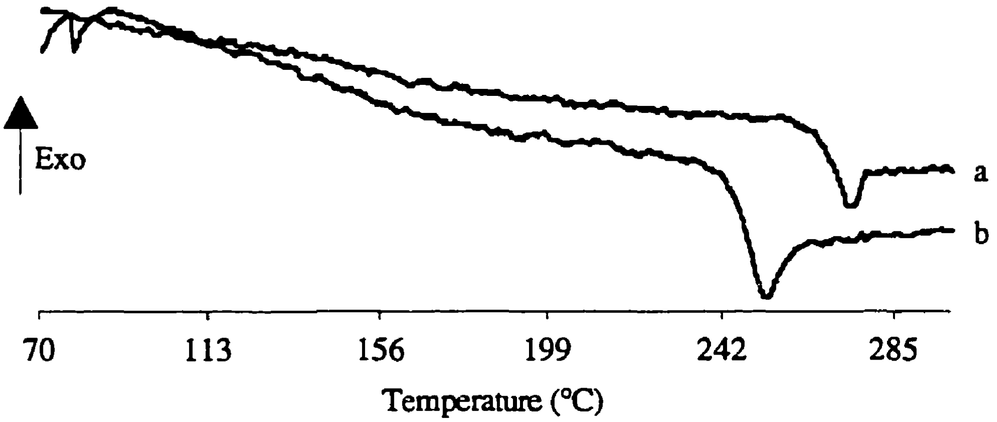


Figure A6.5. DSC traces of: a) polymer **A6.17b**, b) polymer **A6.17a**.

Similar thermal decomposition patterns were observed for polymers **A6.15a** and **A6.17a** (Figure A6.6b). Their 5% weight losses in nitrogen were 411°C and 419°C, respectively (Table A6.5, A6.6).

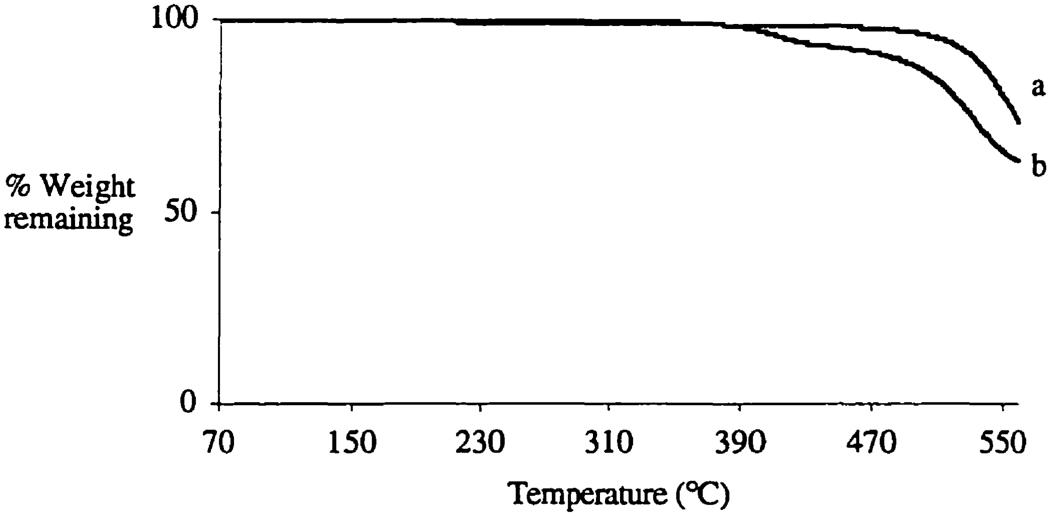


Figure A6.6. TGA traces of: a) polymer **A6.17b**, b) polymer **A6.17a**.

In both TGA curves a sharp weight loss in the range of 360°C to 450°C was observed which corresponds directly to the loss of the isopropyl groups. The percent weight loss for polymers **A6.15a** and **A6.17a** in this range was 9.1 and 5.9, respectively, which when compared to the theoretical values of 8.9 % and 5.6 % are within the 0.5% error limit. This indicates that within instrumental error no cleavage of the isopropyl group occurred during the polymerization reaction.

The next step in the formation of these redox polymers was the cleavage of the isopropyl groups using the method described previously in the synthesis of the model compound **A6.26**. Polymers **A6.15b**, **A6.17b**, **A6.27b**, and **A6.28b** (Figure A6.3b) were obtained in yields of 61% to 87% (Table A6.8). To our surprise both the Mw and inherent viscosity (70 000 g/mol, 73 000 g/mol and 0.29 dL/g, 0.44 dL/g) of polymers **A6.15b**, **A6.17b**, respectively, were lower than their corresponding isopropyl derivative. The decrease in Mw and inherent viscosity cannot be completely explained by the loss of the isopropyl groups which amount to 8516 g/mol and 4208 g/mol for polymer **A6.15b** and **A6.17b**, respectively. Our initial assumptions were that the polymer chains were simultaneously being cleaved under these conditions. This proved not to be the case, since the GPC trace of **A6.17b** (Figure A6.4a) clearly shows a narrower polydispersity and the absence of any low molecular weight fractions. Further, proton NMR data confirmed the quantitative cleavage of the isopropyl groups along with the fact that the same average number of repeat units was obtained for both the hydroxy and isopropyl derivative polymers.

Table A6.8. Yields and physical properties of the hydroxy substituted polymers.

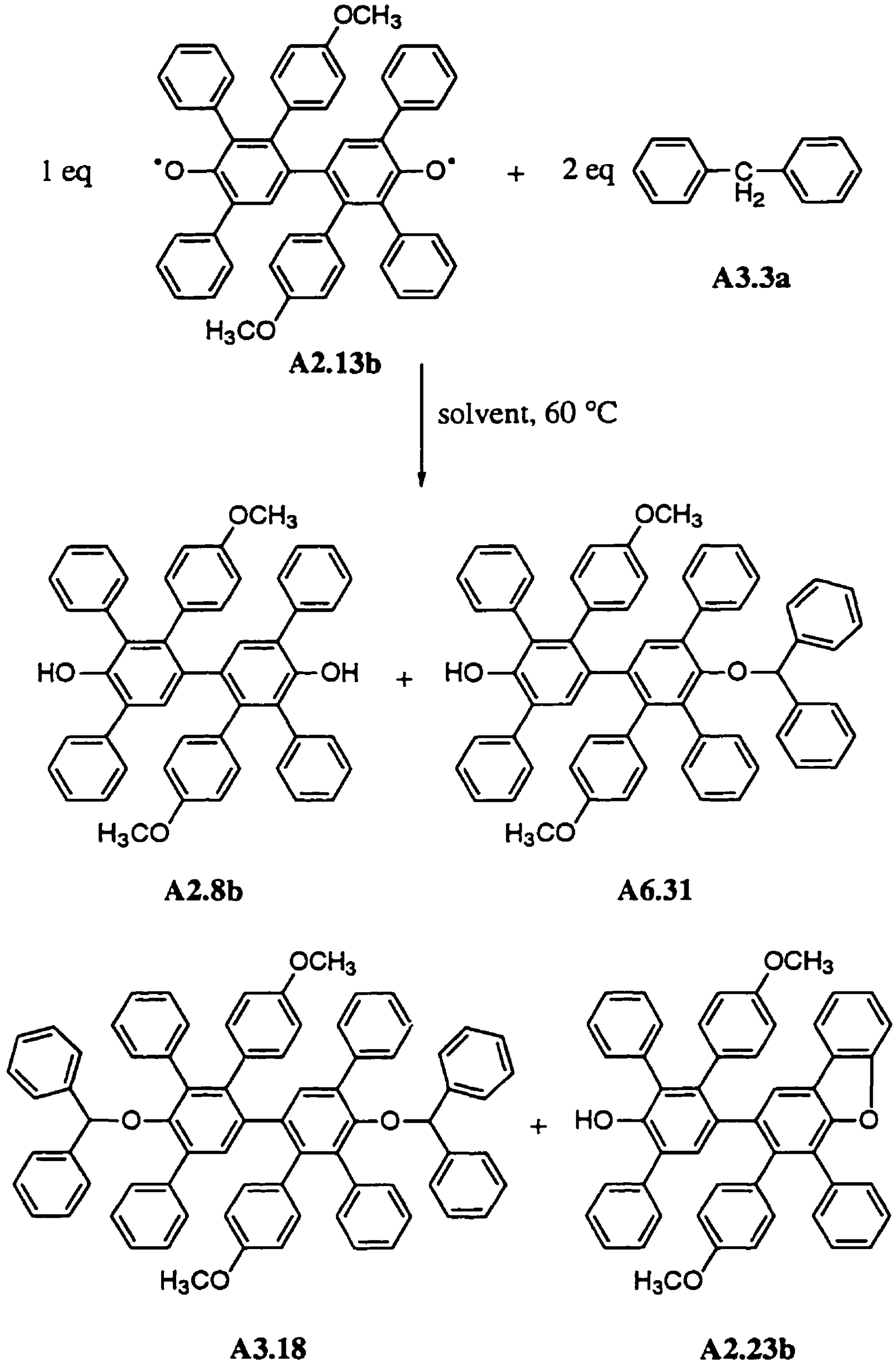
Entry	Repeat Units	Isolated Yield	GPC			Thermal Analysis		ηinh
			Mw	Mn	PD	T_g	5% Wt.Loss	
	(n)	(%)	(g/mol)	(g/mol)		(°C)	(°C)	(dL/g)
A6.15b	100	61	70 000	45 000	1.9	242	524	0.29
A6.17b	100	74	73 000	38 000	1.6	268	517	0.44
A6.27b	20	87	34 000	14 500	2.3	262	515	–
A6.28b	5	84	14 000	5400	2.6	239	500	–

TGA further confirmed the absences of any isopropyl groups because no weight loss was observed in the range of 360 to 450°C. The 5% weight loss of polymers **A6.15b**, **A6.17b** (Figure A6.6a) were 524°C and 517°C, respectively. The lower molecular weight values obtained by GPC and viscosity might simply be explained by the change in polarity and solvent association, respectively, and in the case of polymer **A6.15a** the formation of crystalline phases during the viscosity measurements might increase the viscosity. The T_g of both polymers **A6.15b** and **A6.17b** (Figure A6.5a) increased to 242°C and 268°C, respectively. The higher T_g's observed are attributed to the loss of the bulky isopropyl groups and the presence of hydrogen bonding from the phenolic hydroxy groups.

A6.2.3 Carbon-Oxygen Coupling Reaction

Once the polymer synthesis method was established the generation of the phenoxy radical and the carbon-oxygen coupling reactions were investigated. The phenoxy radical containing polymers were first generated by vigorously stirring a solution of the hydroxy substituted polymer in chlorobenzene with silver oxide (Ag_2O) at room temperature for 48 hours. The appearance of the red color indicates the formation of the radical species. The solution was filtered and two equivalents of diphenylmethane **A3.3a** was added to the filtrate solution. The mixture was then heated at 60°C under an atmosphere of nitrogen. Even after 48 hours no coupling reaction had occurred.

In order to eliminate the effects of solvent and concentration a model reaction using the phenoxy radical **A2.13b** with two equivalents of **A3.3a** (Scheme A6.11) in different solvents and at different concentrations was studied (Table A6.9). The optimal conditions, keeping the solubility of the polymer in mind, was chlorobenzene at a concentration of 0.04 mg/mL. Still all attempts failed to yield any carbon - oxygen coupled products with the polymer radical. Even though the color of the reaction mixture went from dark red to orange, which indicates a reaction has occured. Only the original polymer was recovered



Scheme A6.11

after treating the reaction mixture with hydrazine monohydrate. It appears that proton abstraction by these redox polymers is favored, while the radical coupling reaction between the phenoxy radical and the carbon radical is not, due possibly to steric hindrance or entanglement of the polymer which blocks the reactive sites.

Table A6.9. Product distribution from the model reaction.

Solvent	Concentration	Rxn Time	Percentage of Products			
	(mg/ml)	(hours)	**A2.8b**	**A6.31**	**A3.18**	**A2.23b**
Benzene	0.005	24	84	15	--	0
Chlorobenzene	0.008	46	83	14	1	1
Fluorobenzene	0.006	24	90	8	--	1
Phenylether	0.006	24	78	20	--	1
Benzene	0.04	24	15	75	5	1
Chlorobenzene	0.04	24	24	67	3	1

The UV visible spectrum of the oxidized form of polymer **A6.28b** showed two bands at 288 nm ($\varepsilon = 6.33 \times 10^4$ $M^{-1}cm^{-1}$) and 526 nm ($\varepsilon = 2.69 \times 10^4$ $M^{-1}cm^{-1}$) which correspond to the Π to Π^* and n to Π^* transitions, respectively.

Because of the problems encountered with the pregenerated redox polymers we decided to use a two solvent oxidation system described in the literature.[21] This involved the in situ oxidation of the polymers followed by the carbon-oxygen coupling reaction with a series of activated methylene groups.

Only insoluble products were obtained with the higher molecular weight polymers. Initially we assumed that the phenoxy radical polymer partially crosslinked, although no insoluble materials were obtained when the polymer was subjected to similar reaction conditions used in the carbon - oxygen coupling reactions. It appears that the insoluble products are obtained during the carbon - oxygen coupling reaction. The change in polarity or increased steric hindrance might affect the solubility properties, causing the gel like formation. Another possibility could be the abstraction of the tertiary proton of the methylene compound already attached to the polymer followed by a radical coupling reaction generating a crosslinked material (Figure A6.7). However no carbon - oxygen

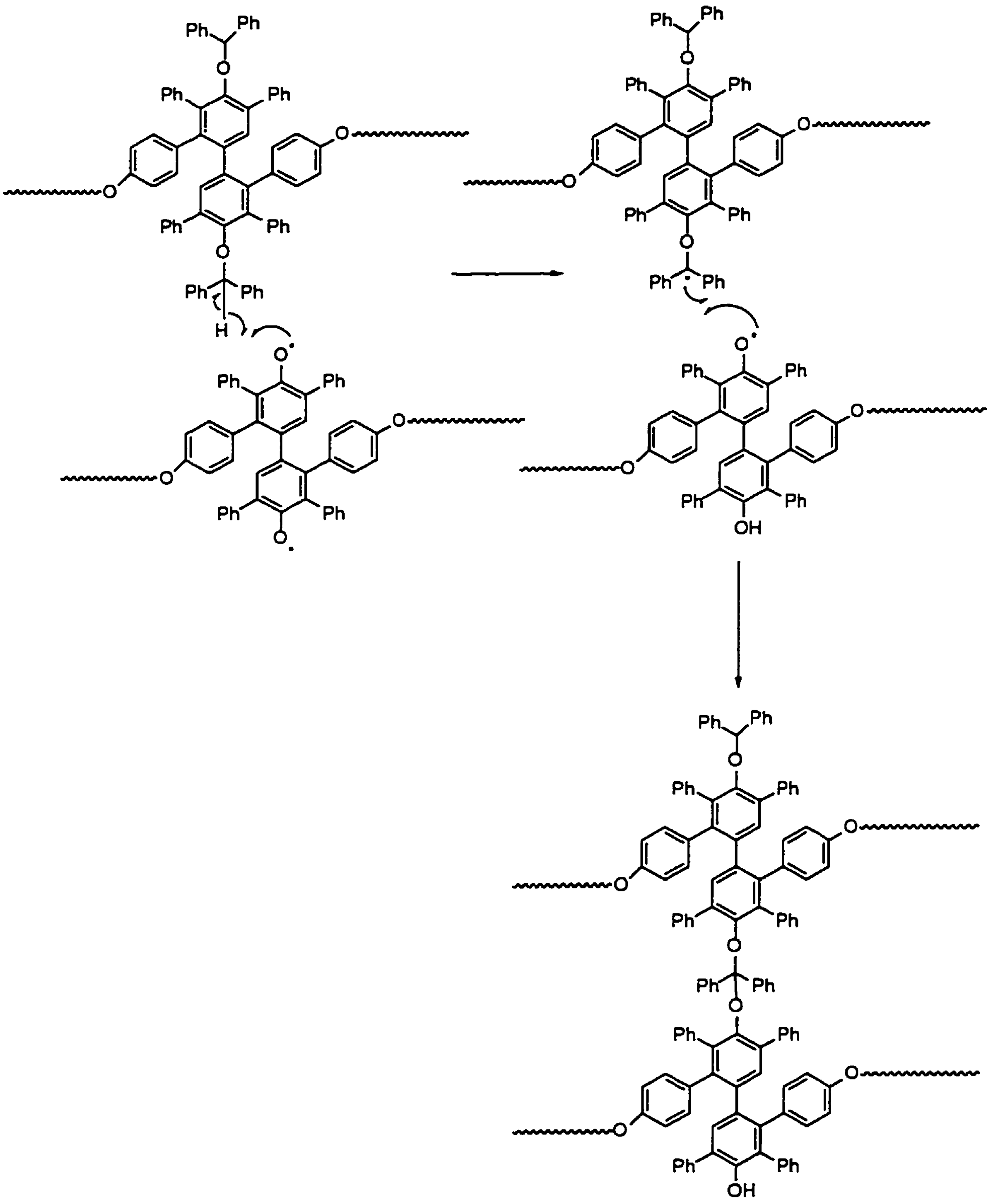
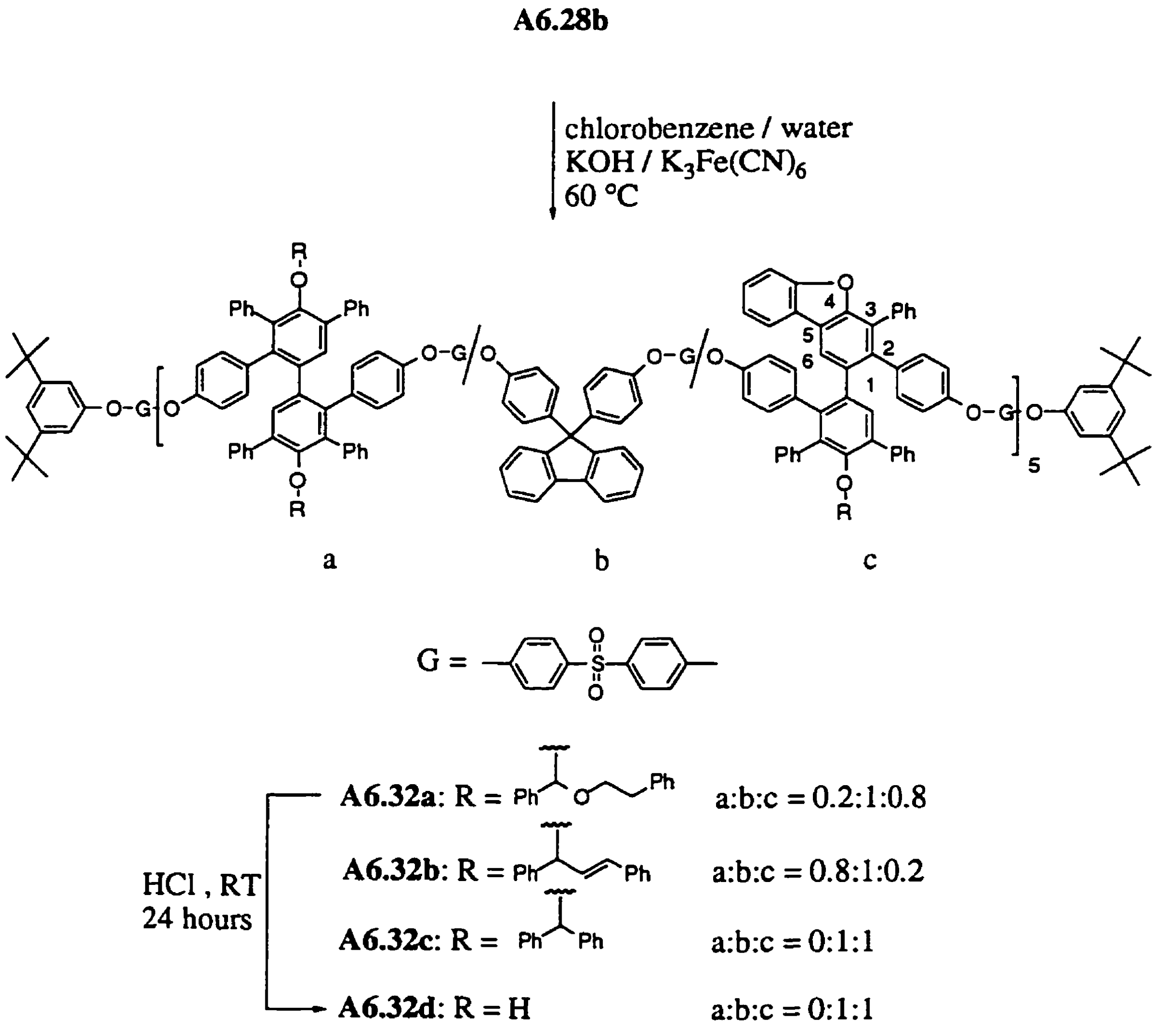


Figure A6.7

coupling reactions were observed between biphenol **A2.8a** and diether derivative **A3.9a** (see Chapter A4 for more details) based on HPLC and GPC results. Approximately 1% of a coupling reaction is required to form a crosslinked product, which is below the error limit of detection of these instruments (approximately 2-4%) so that this assumption is still possible.

When oligomer **A6.28b** was used the corresponding carbon-oxygen coupled products (Scheme A6.12) were obtained in yields ranging from 53% to 79% (Table A6.10).



Scheme A6.12

Table A6.10. Yields and physical properties of the carbon - oxygen coupled polymer.

Entry	Rxn Time	Isolated Yield	Conv.[a]	GPC			Thermal Analysis	
	(hour)	(%)	(%)	Mw (g/mol)	Mn (g/mol)	PD	T_g (°C)	5% Wt. Loss (°C)
A6.32a	18	58	51	127 000	6800	18.7	212	298
A6.32b	17	79	90	24 000	8000	3	212	341
A6.32c	17	53	44	153 000	9000	17.1	184	315

All the carbon - oxygen coupled products were confirmed by proton NMR, and only **A6.32b** was converted in high yield (90%). With polymers **A6.32a** and **A6.32c** the conversions were 60% (Figure A6.8a) and 46%, respectively. The lower reactivity of **A3.3a** and **A3.8l** favors the intramolcular cyclization reaction to the benzofuran derivative discussed in Chapter A2. In general a similar trend was observed for the carbon-oxygen coupled polymers and the isopropyl derivatives. The lower yields obtained for polymer **A6.32a,c** are due to the formation of insoluble product, which was not observed during the synthesis of polymer **A6.32b**. GPC results (Figure A6.9c,e) clearly shows a shift to higher molecular weights and a broader distribution compared to polymer **A6.32b** (Figure A6.9d). The fact that polymers **A6.32a,c** have a higher concentration of the benzofuran moiety which stiffens the polymer might explain the shift to apparent higher molecular weight and the change in solubility properties. Another possibility is that a crosslinked product forms which has been discussed previously. In general the Mw (Figure A6.9a-e) increased and the T_g decreased compared to the hydroxy polymer **A6.28b**.

In order for these polymers to be considered polymeric supports the substrate must be efficiently cleaved off and the polymer must be recyclable. The ^{1}H NMR spectra of polymer **A6.32a** treated with a drop of HCl (Figure A6.8b) clearly shows the cleavage of the acetal group. A phenolic hydroxy group at 5.18 ppm, the aldehyde proton at 10.02 ppm and the methylene protons of phenethyl alcohol at 2.88 and 3.85 ppm were also present after the cleavage reaction.

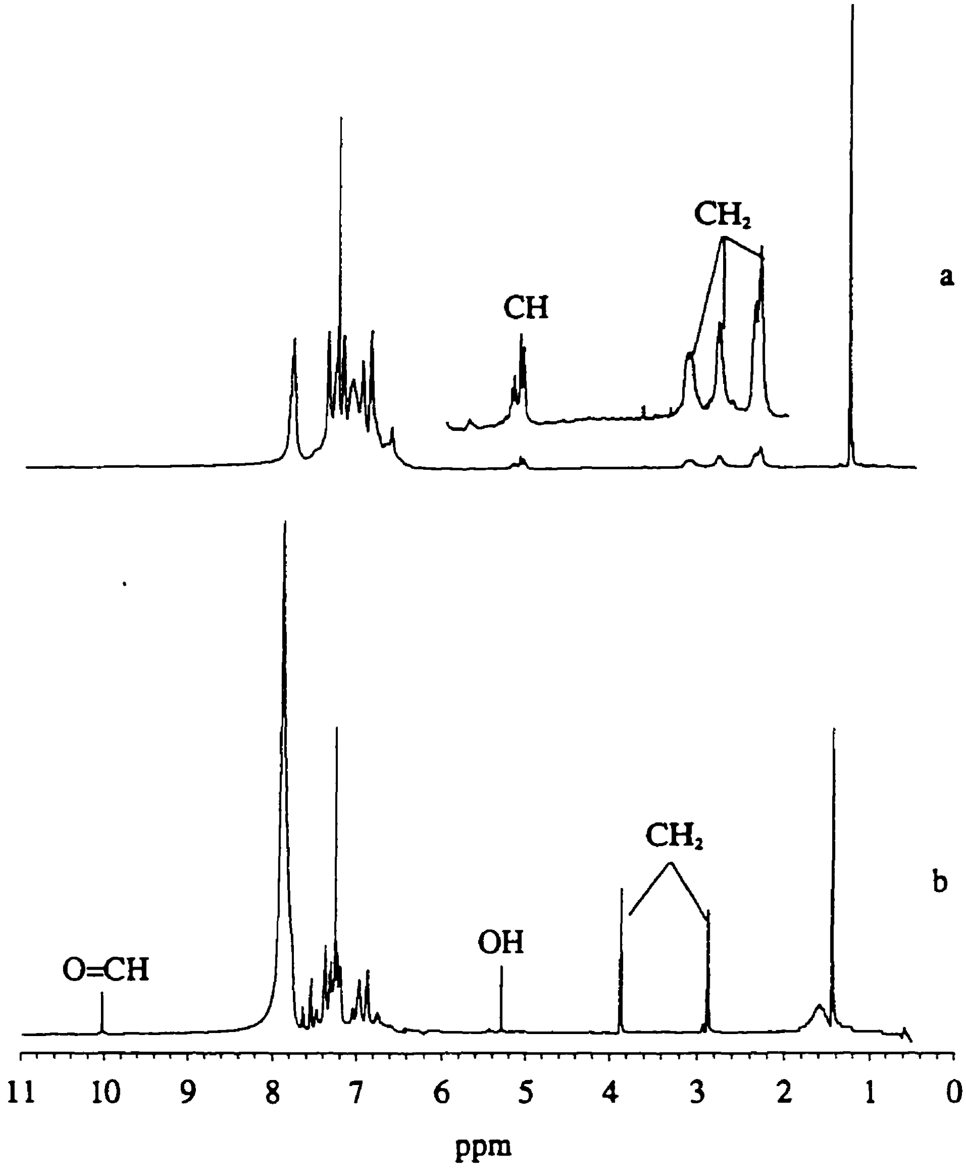


Figure A6.8. ^1H NMR spectra of: a) polymer **A6.32a**, b) polymer **A6.32a** treated with HCl.

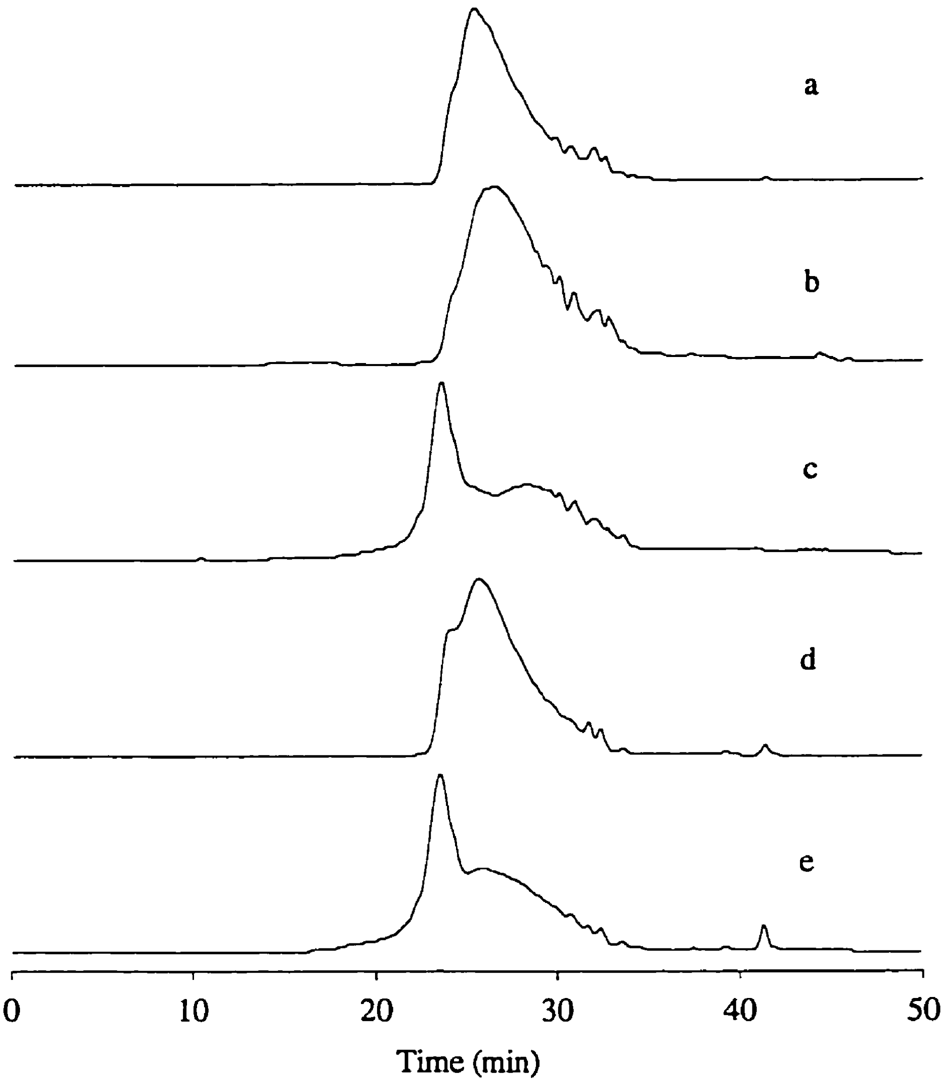


Figure A6.9. GPC traces of: a) polymer **A6.28a**, b) polymer **A6.28b**, c) polymer **A6.32a**, d) polymer **A6.32b**, e) polymer **A6.32c**.

Polymer **A6.32a** was dissolved in chloroform, treated with concentrated HCl and stirred at room temperature for 24 hours. This regenerated the hydroxy polymer **A6.32d** which was recovered in 84% yield. Proton NMR of the cleaved polymer **A6.32d** confirmed that a side product, probably the cyclization product, occurred because only 57% of the phenolic groups remain on the polymer chain. The regenerated polymer was once again oxidized and coupled with **A3.81** using the method previously described. The carbon-oxygen coupled polymer was obtained in 33% yield. In this reaction a lower yield compared to the original polymer was obtained, because more of the polymer came out of solution. In the second reaction approximately 50% of the phenoxy radical is converted to the benzofuran moiety compared to 40% in the original polymer, which might give a polymer with lower solubility properties.

Theoretically, since we are using the same monomer **A3.81**, the reaction rate should have been the same and one would have expected only 36 % conversion based on previous results and not the 50% conversion we obtained based on ^{1}H NMR results. In the regenerated polymer we believe that approximately 50% of the hindered biphenol moiety has been converted to the benzofuran derivative. Studies on the model reactions tend to favor this assumption.[11] The benzofuran derivative forces the phenyl group in the 5 position to be planar to the biphenyl moiety. In this case the phenyl group is more electron donating because it is planar and conjugated with the biphenyl moiety, than in the original polymer. Lowering the oxidation potential to a level where the rate of abstraction of the methylene proton (D°_{298} = 76 - 93 kcal/mol)[12] is faster than the abstraction of an aromatic proton (D°_{298} = 111 kcal/mol)[12] favors the carbon - oxygen coupling reaction.

Even with the problems of low yields which have also been observed with soluble polystyrene,[4] and the formation of cyclized byproducts which have been discussed in Chapter A2, these polymers have potential to be excellent polymeric supports in the oxidation conversion of methylene group to their alcohol and/or aldehyde derivatives.

A6.3 Conclusions

By incorporating stable phenoxy radical into a polymer backbone we were able to mimic the chemistry previously established with the bisphenoxy radicals and thus simplify the purification step by eliminating the use of column chromatography.

Of the polymers studied only the low molecular weight polymers gave promising results. Preliminary results have shown that with reactive methylene groups such as in monomer **A3.8e** the reaction does go to completion and that these polymers are recyclable as was shown with polymer **A6.32a**. These polymers are quite promising as polymeric supports.

A6.4 Experimental Section

Materials

Solvents N,N-dimethylacetamide (DMAc), 1-methyl-2-pyrrolidinone (NMP), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU) were purchased from Aldrich Chemical Co. and dried over 4Å molecular sieves for 24 hours before use. Chloroform, methanol, chlorobenzene , methylene chloride were purchased from Caledon and used as received. Reagents 2-bromopropane, 1M BBr_3 in methylene chloride, 1M BCl_3 in methylene chloride, cesium carbonate, 2,4,6-collidine, and lithium iodide were purchased from Aldrich Chemical company and used as received. Bis-(4-fluorophenyl)sulfone was purchased from Aldrich Chemical Co. and recrystallized from toluene. 4,4'-Difluorobenzophenone was purchased from Maybridge Chemical Co., 9,9-bis(4-hydroxyphenyl)fluorene was purchased from Kennedy & Klim Inc., and potassium carbonate was purchased from Omega and all were used as received.

Instrumentation

Elemental analyses were performed by Fine Analysis Laboratories Ltd., Hamilton, Ontario. All ^{1}H and ^{13}C NMR were obtained on aVarian Unity 500 spectrometer. GPC analyses were performed on a Waters 510 instrument equipped with a UV detector set a 254 nm and four 5 μm phenogel columns (3 x 500Å, linear) arranged in series. All molecular weights are referenced to polystyrene standards. Thermal analyses were carried out using Seiko 220DSC and 220 TGA/DTA instrument at a heating rate of 20°C under a nitrogen atmosphere. UV visible analysis were preformed on a HP8452A diode array spectrometer. Inherent viscosity data were from chloroform solution with a concentration of 0.5 dL/g in a calibrated Ubbelohde viscometer at 25°C.

Monomer Synthesis

2,2'-Di-(4-methoxyphenyl)-3,3',5,5'-tetraphenyl-1,1'-biphenyl-4,4'-di-(1,1-(dimethyl)methyleneoxy) **A6.23.**

A three neck 500 mL round bottom flask equipped with a condenser and Dean-Stark trap was charged with **A2.8b** (40.00 g, 56.96 mmol), K_2CO_3 (19.81 g, 143.33 mmol), 200 mL of DMAc, and 100 mL of benzene. The solution was refluxed for 17 hours under an atmosphere of nitrogen. Benzene was then removed from the reaction flask and the oil bath temperature was lowered to 90°C. 2-Bromopropane (57.23 g, 465.25 mmol) was added dropwise over 40 minutes and after 24 hours the reaction was complete. The solution was poured into water and the crude precipitate was dried and recrystallized from DMSO to give 36.5 g (82%) of **A6.23** as tannish crystals: m.p. 265-269°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.393 (br s, 1H), 7.18 - 7.31 (m, 13H), 7.02 - 7.12 (m, 4H), 6.92 (br s, 4H), 6.79 (d, 4H, J^2 = 8.8 Hz), 6.60 (br s, 4H), 3.71 (s, 6H, OCH_3), 3.35 (q, 2H, CH), 0.46 - 0.54 (dd, 12H, J= 5.8 & 30.8 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.55, 151.34, 140.17, 139.45, 138.46, 136.51, 135.90, 134.24, 133.56, 132.40, 131.62, 129.64, 127.57, 126.99, 126.50, 125.73, 112.49, 74.60 (CH), 55.16 (OCH_3), 21.73 (CH_3), 21.43 (CH_3); MS (FAB Matrix: NBA) *m/e* 787.23 (M^+, 3), 745.19 (M^+ - (C_3H_7), 2), 702.11 (M^+ - (C_6H_{14}), 4); Analysis calc'd for $C_{56}H_{50}O_4$: C, 85.46; H, 6.40; found: C, 85.63; H, 6.54.

2,2'-Di-(4-hydroxyphenyl)-3,3',5,5'-tetraphenyl-1,1'-biphenyl-4,4'-di-(1,1-(dimethyl)methyleneoxy) **A6.19.**

A 500 mL three neck round bottom flask was charged with **A6.23** (25.02 g, 31.79 mmol), lithium iodide (89.16 g, 666.16 mmol), and 175 mL of 2,4,6-collidine. The solution was refluxed for 24 hours, cooled to room temperature and poured into a 5% aqueous solution of HCl. The crude product was filtered dried and recrystillized from DMSO, to give 13.80 g (58%) of **A6.19** as white crystals: m.p. >295°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 - 7.30 (m, 20H), 6.93 (br s, 2H), 6.67 (br s, 4H), 6.48 (br s, 4H), 4.48 (s, 2H, OH), 3.34-3.36 (q, 2H, CH), 0.47-0.53 (dd, 12H, J = 4.9 & 24.4 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.08, 151.31, 140.31, 139.50, 138.55, 136.54, 134.03, 133.61, 131.91, 131.80, 129.64, 127.64, 126.89, 126.46, 125.60, 113.92, 74.65 (CH), 21.72 (CH_3), 21.55 (CH_3); MS (EI Direct Inlet at 370 °C) *m/e* 758.27 (M^+, 62), 716.25 (M^+ - (C_3H_7), 14), 674.19 (M^+ - (C_6H_{14}), 100); Analysis calc'd for $C_{54}H_{46}O_4$: C, 85.46; H, 6.11; found: C, 85.99; H, 6.31.

Model Compound **A6.24**

In a 25 mL flask a solution of **A6.19** (0.78 g, 1.03 mmol), 4-fluorobenzophenone (0.42 g, 2.10 mmol), 8 mL of DMAc and 4 mL of benzene was azeotroped at reflux under an atmosphere of nitrogen for 3 hours. Benzene was then removed and the reaction temperature was maintained at 145-150°C for another 12 hours. The solution was poured into water and the precipitated was filtered, dried and recrystallized from a solution of methanol and chloroform. There was obtained 0.83g (72%) of **A6.24** as a fine white powder: m.p. 273-276°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 - 7.75 (dd, 8H, J = 7.8 &11.7 Hz), 7.56 - 7.59 (t, 2H), 7.45 - 7.48 (t, 4H), 7.43 (d, 4H, J^2 = 7.8 Hz), 7.32 - 7.35 (t, 4H), 7.24 - 7.27 (t, 3H), 7.21 (s, 5H), 7.18 (br s, 5H), 6.99 (br s, 3H), 6.85 (d, 5H, J^2 = 8.8 Hz), 6.73 (br s, 5H), 3.37-3.42 (q, 2H, CH), 0.48-0.55 (dd, 12H, J = 6.3 & 27.8, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 1395.26, 161.74, 153.04, 151.56, 139.60, 138.94, 137.90, 137.79, 136.67, 136.34, 135.65, 134.43, 133.33, 132.25, 131.64, 131.62, 131.48, 129.59, 129.35, 128.08, 127.75, 126.94, 126.78, 125.93, 118.81, 116.50, 74.82 (CH), 21.59 (CH_3), 21.43 (CH_3); MS (MALDI-TOF-MS) *m/e* 1078.2 (M^+ - C_3H_7, 2), 1036.0 (M^+ - C_6H_{14}, 100).

Model Compound **A6.25**.

Boron trichloride (2.20 ml, 2.20 mmol) was added through a syringe to a stirring solution of **A6.24** (0.30 g, 0.27 mmol) in 10 mL of methylene chloride cooled at -10 °C under an atmosphere of nitrogen. The reaction mixture was stirred at -10C for 20-25 minutes and for another 7 hours at room temperature. The mixture was poured in to a 10% aqueous solution of $NaHCO_3$. The white solid was filtered, redissolved in methylene chloride and filtered through celite. The filtrate was evaporated to dryness and the white solid was recrystallized from a solution of methanol and chloroform. There was obtained 0.23 g (83%) of **A6.25** as a white powder.: m.p. > 300 °C; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.76 (dd, 8H, J = 7.3 Hz), 7.47-7.58 (dt, 10H), 7.39-7.42 (t, 4H), 7.32-7.34 (distorted d, 5H), 7.20-7.24 (m, 7H), 7.05-7.10 (br d, 5H), 6.80 (d, 5H, J^2 = 8.8 Hz), 6.66-6.76 (br s, 4H), 6.64-6.65 (br s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 195.41, 162.18, 153.75, 149.02, 140.18, 138.41, 138.10, 136.59, 136.14, 134.01, 133.63, 133.61, 133.59, 133.56, 133.53, 133.18, 132.64, 132.43, 132.13, 131.60, 130.02, 129.64, 128.98, 128.94, 128.76, 128.61, 127.82, 127.67, 127.13, 119.35, 117.00; MS (MALDI-TOF-MS) *m/e* 1036.2 (M^+, 100).

Polymer Synthesis

Synthesis of Copolymer A6.17a.

A 25 mL three neck round bottom flask equipped with a condenser, Dean-Stark trap, and nitrogen inlet was charged with biphenol **A6.19** (0.54g, 0.71 mmol), **A4.16b** (0.36 g, 1.42 mmol), biphenol **A6.29** (0.21 g, 0.72 mmol), Cs_2CO_3 (0.65 g, 2.0

mmol), 4.5 mL of DMAc and 3 mL of toluene. The reaction mixture was dehydrated for 3 hours at 135-138 °C. The reaction temperature was then increased to 142-144 °C and left for another 6 hours. The mixture was diluted by 30 % with DMAc and precipitated out in a solution of methanol-water-acetic acid (300 mL/100 mL/1mL) ayield of 0.90 g (82 %) of polymer **A6.17a** was obtained after being dried at 110°C under vacuum for 24 hours.

General Procedures

Synthesis of Homopolymers End Capped with Activated Difluoro Monomers

A 25 mL three neck round bottom flask equipped with a condenser, Dean-Stark trap, and nitrogen inlet was charged with biphenol **A6.19** (1.20g, 1.59 mmol), **A4.16a** (0.35 g, 1.60 mmol), Cs_2CO_3 (0.85 g, 2.61 mmol), 6 mL of DMAc and 4 mL of toluene. The reaction mixture was dehydrated for 3 hours at 135-138°C. The reaction temperature was then increased to 142-144°C and left for another 5 hours. The mixture was diluted by 30% with DMAc and precipitated out in a solution of methanol-water-acetic acid (300 mL/100 mL/1mL). The polymer was dried at 110°C under vacuum for 24 hours.

Synthesis of Copolymers End Capped with 3,5-Di-t-butylphenol

A 25 mL three neck round bottom flask equipped with a condenser, Dean-Stark trap, and nitrogen inlet was charged with biphenol **A6.19** (0.52g, 0.69 mmol), **A4.16b** (0.39 g, 1.55 mmol), biphenol **A6.29**, 3,5-di-t-butylphenol **A6.30** (0.06 g, 0.28 mmol), Cs_2CO_3 (0.80 g, 2.46 mmol), 5 mL of DMAc and 3 mL of toluene. The reaction mixture was dehydrated for 3 hours at 135-138°C. The reaction temperature was then increased to 142-144°C and left for another 7 hours. The mixture was diluted by 30% with DMAc and precipitated out in a solution of methanol-water-acetic acid (300 mL/100 mL/1mL), to give 1 g (93%) of polymer **A6.28a**: ^1H NMR (500 MHz, CD_2Cl_2) δ 7.80 (br s, 37H), 7.69 - 7.73 (distorted t, 18H), 7.18 - 7.40 (m,124H), 7.12 (br s, 31H), 6.97 - 7.00 (br d, 37H), 6.89 -6.94 (br d, 36H), 6.81 - 6.84 (distorted t, 26H), 6.70 - 6.78 (br s, 15H), 3.38 - 3.40 (q, 10H, CH), 1.29 (s, 36H, t-butyl methyl groups), 0.47 - 0.53 (dd, 60H, isopropyl methyl groups).

Cleavage of the Isopropyl Groups

In a 50 mL round bottom flask boron trichloride 1M solution in methylene chloride (7.00 mL, 7.00 mmol) was added slowly with a syringe over a 20 minute period to a solution of 10 mL of methylene chloride and polymer **A6.28a** (1.00 g, 0.65 mmol) at -10°C. After complete addition the reaction mixture was left stirring at room temperature under an atmosphere of nitrogen for another 24 hours. The solution was poured into a 10% aqueous solution of $NaHCO_3$. The polymer that precipitated was redissolved in chloroform and precipitated out from methanol. There was obtained 0.79 g (84%) of **A6.28b**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.74 - 7.82 (m, 54H), 7.45 (d, 19H), 7.34 - 7.39 (br d, 41H), 7.21 - 7.30 (m, 84H), 6.98 - 7.12 (m, 54H), 6.90 (br s, 25H), 6.75 - 6.79 (t, 22H), 6.58 - 6.70 (br s, 25H), 5.19 (s, 10H, OH), 1.29 (s, 36H, t-butyl methyl groups).

Carbon-Oxygen Coupled Reactions

To a solution of polymer **A6.28b** (0.25 g, 0.17 mmol) in 10 mL of chlorobenzene was added a 0.77 M aqueous solution of KOH and $K_3Fe(CN)_6$ under an atmosphere of nitrogen. The two phase mixture was stirred at room temperature for 20 minutes generating the phenoxy radical which is easily detected by the appearance of the dark red color. Excess **A3.81** (0.21 g, 1.00 mmol) was added to the mixture and than heated to 60°C for 18 hours, yielding 0.18 g (58%) of polymer **A6.32a**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.76 - 7.84 (m, 54H), 7.38 (br s, 57H), 7.28 (s, 28H), 6.93 - 7.14 (m, 116H), 6.86 (s, 56H), 6.60 - 6.71 (br s, 28H), 5.05 - 5.21 (dd, 6H, CH), 3.08 - 3.21 (br s, 6H,

CH_2), 2.74 - 2.85 (br s, 6H, CH_2), 2.30 - 2.43 (br d, 12H, CH_2), 1.29 (s, 36H, t-butyl methyl groups).

Polymer **A6.32b**

Yield 0.24 g (79%) of **A6.32b:**^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.76 - 7.82 (m, 54H), 7.65 - 7.71 (m, 4H), 7.39 (s, 49H), 7.26 - 7.34 (m, 49H), 7.20 (s, 44H), 6.74 - 7.14 (m, 182H), 6.62 - 6.65 (br s, 31H), 5.89 - 5.94 (m, 4H CH=CH), 5.58 - 5.75 (m, 5H, CH=CH), 5.32 - 5.49 (m, 9H, CH=CH), 4.52 - 4.63 (m, 9H, CH-O), 1.29 (s, 36H, t-butyl methyl groups).

Polymer **A6.32c**

Yield 0.08 g (53%) of **A6.32c:**^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.78 - 7.85 (m, 54H), 7.38 (s, 35 H), 7.28 - 7.30 (distorted d, 20H), 7.19 (s, 50H), 7.15 (s, 10H), 6.81 - 7.08 (m, 136H), 6.68 (s, 35H), 6.54 - 6.59 (br t, 15H), 6.41 (s, 9H), 5.15 (s, 5H, CH), 1.29 (s, 36H, t-butyl methyl groups).

Cleavage of the Carbon-Oxygen Bond

In a 25 mL round bottom flask polymer **A6.32a** (0.06 g, 0.03 mmol) was dissolved in 10 mL of chloroform and 0.5 mL of HCl was added. The solution was stirred for 24 hours at room temperature. There was obtained 0.04 g (83%) of polymer **A6.32d**.

A6.5 References

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PART B

CHAPTER 1

ANALYSIS OF HIGH MOLECULAR WEIGHT POLYDISPERSE POLYMERS AND CYCLIC OLIGOMERS BY MATRIX ASSISTED LASER DESORPTION IONIZATION - TIME OF FLIGHT - MASS SPECTROMETRY

B1.1 Introduction

What is mass spectrometry? It is a microanalytical technique which gives the accurate molecular weights and a fragmentation pattern specific to individual low molecular weight compounds. In all cases an energetic force is applied to the sample exploding the sample into many ionized fragments (Figure B1.1).[1]

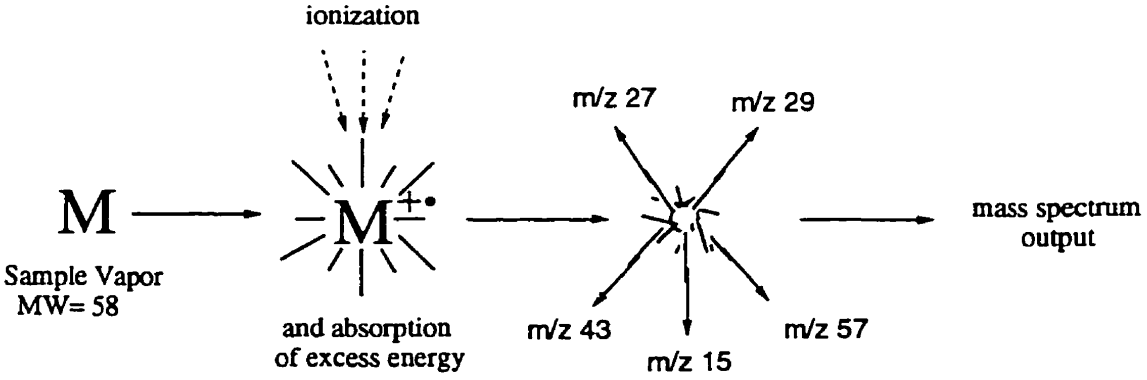


Figure B1.1. A general concept of mass spectrometry analysis.

Why use the technique of mass spectrometry for the analysis of higher molecular weight organic materials (e.g. proteins, polystyrene (PS), etc.)? Besides the obvious, which is the determination of the exact molecular weight of each polymeric chain, they are 1) sequence distribution of copolymer mixtures, and 2) end group analysis.

In the world of polymer chemistry the techniques previously and currently available for the determination of polymer molecular weights are gel permeation chromatography (GPC), light scattering, nuclear magnetic resonance (NMR) and solution viscosity (η)

which give only the average molecular weight of the polymer and not a detailed description of the polymer composition.

For many years mass spectrometry methods like electron impact (EI), chemical ionization (CI) and fast atomic bombardment (FAB) to name a few have been extremely useful in the analysis of small organic molecules. When it comes to the analysis of higher molecular weight compounds these methods are of little use because in general proteins and polymers are non-volatile, leading to fragmentation instead of ionization of an intact polymer sequence.

New methods of ionization have been developed in the early 1970's using short - pulse lasers (typically 1-100 ns) like CO_2 lasers and ultraviolet lasers. These were considered soft ionization techniques which supplied sufficient energy to ionize the polymer, and at the same time reduce the fragmentation. Their molecular weight limitation were approximately 1000 Daltons (Da) for biopolymers and 9000 Da for synthetic polymers.[2] It wasn't until the late 1980's that two relatively new methods of mass spectrometry were developed, electrospray,[3] and MALDI-TOF-MS[2,4] which have shown great promise in the analysis of higher molecular weight biopolymers (up to approx. 150 000 Da). A description of both methods follows, although the results presented in this chapter will deal exclusively with the MALDI-TOF-MS technique.

In general both techniques are quite similar in that they efficiently ionize high molecular weight compounds, however in other ways they are quite different. Their differences lie in the mass range, mass accuracy, and mass sensitivity (see Table B1.1)[5] attainable but most importantly in the sample preparation procedure.

The method of electrospray mass spectrometry has been extensively applied to biological molecules because it is a soft ionization which gives low levels of detection. This technique requires that the analyte be dissolved in a volatile organic solvent such as methanol, tetrahydrofuran, and in a few cases methylene chloride. A mixture of chloroform and methanol has been used with limited success. A dilute solution of the

Table B1.1. Brief summary of the properties of both mass spectrometry techniques.

Property	Electrospray MS (ESMS)	MALDI-TOF-MS
Mass range	50 to 150 KDa	upto 300 kDa
Mass accurancy	1 in 20000	1 in 10000
Mass resolution	1 in 1000	1 in 400
Interference by Salts	yes	no
Analyse complex mixtures	no	yes
Couple to HPLC	yes	no

analyte is injected into a chamber where an electrical potential difference (approx. 2-4 kV)[6] ionizes the solutions and disperses the liquid into charged droplets. The solvent slowly evaporates upon heat transfer resulting in the accumulation of surface charge. When the electric field reaches a threshold level (up to 10^9 V/cm) the analyte ions are absorbed into the mass spectrometer. The advantage of this method is the ease in attaching a high performance liquid chromatography Instrument (HPLC) directly to the electrospray instrument so that fractions of high molecular weight biopolymers can be continuously injected (Figure B1.2).[6]

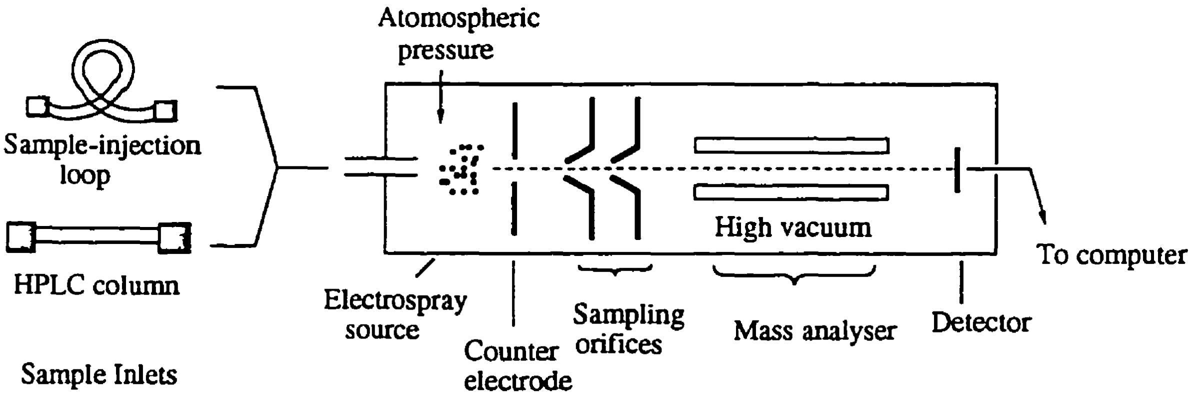
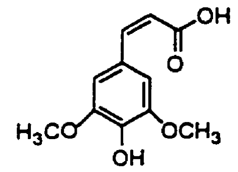
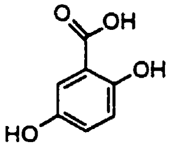
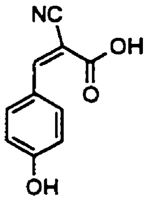
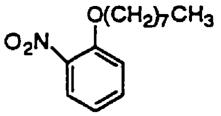
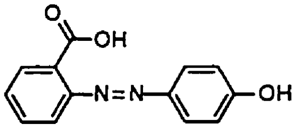
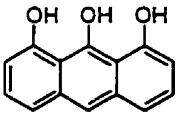
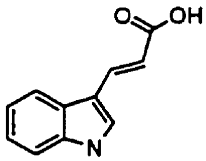
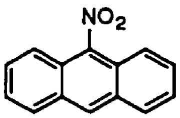


Figure B1.2. A schematic of the electrospray instrument.

This method has had limited success in the analysis of synthetic polymers[7] due mainly to solubility problems and salt contamination which tend to complicate the mass spectrometry spectrum.

Table B1.2. A summary of commonly used matrices and their applications.

Entry	Compound	Abbrv.	Application
B1.1		SA	peptide,protein,lipids polar polymers
B1.2		DHBA	peptide, protein, oligosaccharide, polar polymers
B1.3		CHCA	peptide, protein, polar polymer
B1.4		NPOE	nonpolar polymer
B1.5		HABA	peptide, protein, polar and nonpolar polymers
B1.6		dithranol	nonpolar polymer
B1.7		IAA	nonpolar polymer
B1.8		9-NO2-Anthr	non polar polymer

In the MALDI-TOF-MS technique the analyte is mixed with a matrix solution. The matrix is a low molecular weight ultraviolet absorbing organic compound such as 1,8,9-

anthracenetriol **B1.6**, 2,5 - dihydroxybenzoic acid **B1.2**, 2-(4-hydroxyphenylazo)benzoic acid **B1.5**, and 3,5-dimethoxy - 4-hydroxycinnamic acid **B1.1** (Table B1.2).

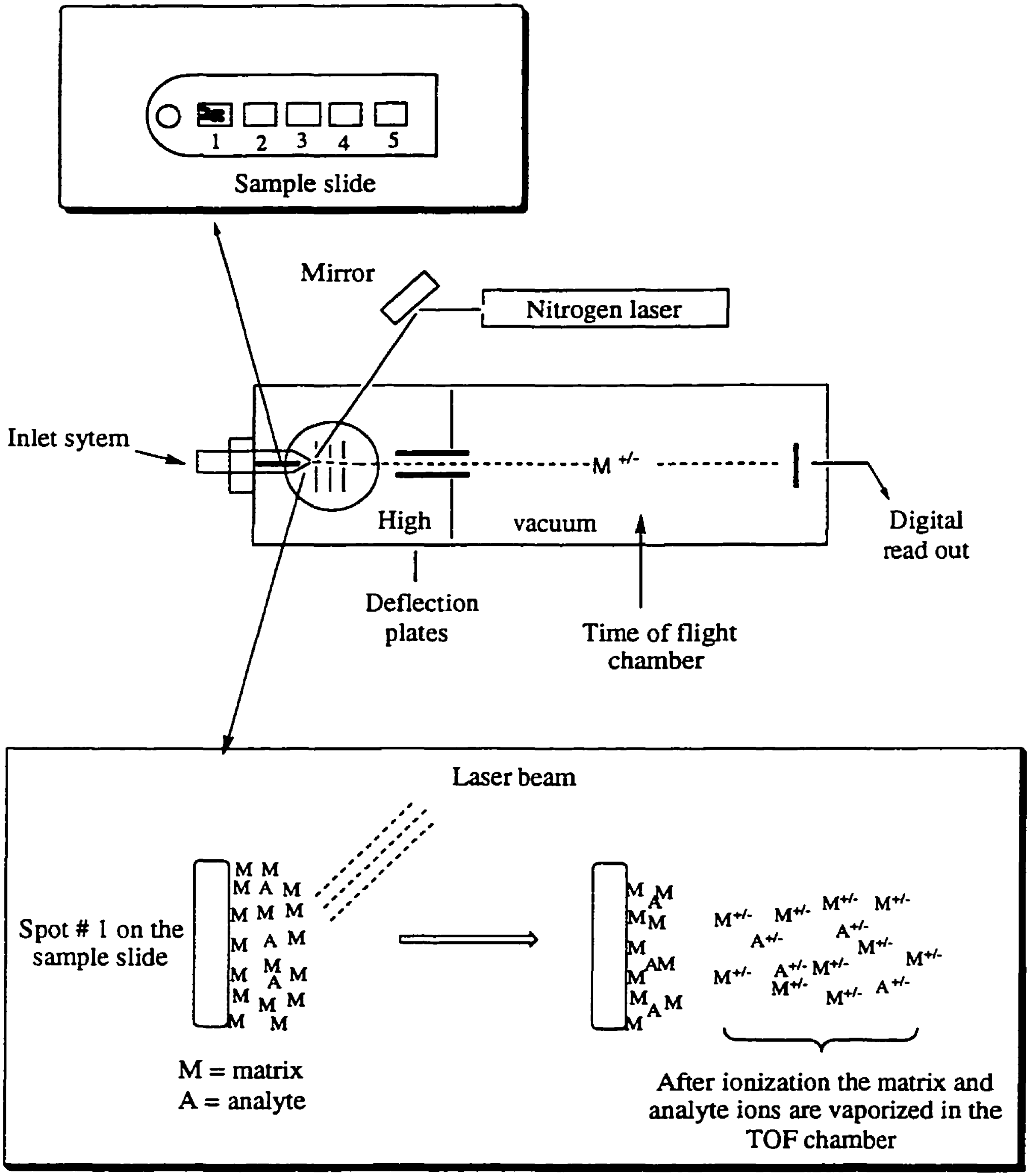


Figure B1.3. Schematic of the MALDI-TOF-MS instrument.

A pipette tip of this solution is applied to a sample slide (Figure B1.3) and left to air dry. The slide is placed in the mass spectrometer and a laser pulse ionizes the sample causing the matrix and the analyte which is embedded in the matrix is vaporize into the time of flight chamber (Figure B1.3). The time from the point of ionization to detection is proportional to the mass.

The choice of matrix and sample preparation are the key to this technique. It is believed that the matrix serves three purposes: 1) absorbs the energy of the laser beam preventing fragmentation of the analyte, 2) electron transfer to the sample, and 3) isolation of the analyte molecules from each other. The complete role of the matrix is not completely understood, although there are certain criteria that have to be met. First, the matrix must have a ultraviolet absorbance at the wavelength the laser beam is set at. In our case we are using a nitrogen laser set at a wavelength of 337 nm. Second, the matrix must ionize efficiently (i.e. low laser power and have a strong signal). These characteristics can easily be determined by simply analyzing the matrices by MALDI-TOF-MS.

Even after all these criteria are met it is still difficult to predict which matrix will be miscible with the analyte. It is extremely important that the matrix and analyte form a homogenous mixture. This is where sample preparation becomes a factor, choosing the right matrix and sample preparation procedure is still a matter of trial and error. A series of commonly used matrices and their application to specific classes of compounds are listed in table B1.2. The disadvantage of this technique is that the analyses are not quantitative and the shot to shot signal reproducibility is poor.

As in most mass spectrometers the mass/charge ratio (m/z) where m = mass and z = number of electrostatic units on an ion determines the velocity of the analyte ions. In the time of flight (TOF) spectrometer an electric potential accelerates a packet of ions at a fixed electric velocity which is proportional to $(m_i/z_i)^{-1/2}$ where $(m_i/z_i)^{-1/2}$ is the mass to charge ratio of a particular ion species.[2] The pack of ion species then pass through a field free region were they separate into different groups based on the velocity of the ions. The time required from ionization to the point of arrival to the detector is proportional to $(m_i/z_i)^{+1/2}$ which can be used to calculate the mass of each ion.

To date there are two configurations used for the TOF mass spectrometer, the linear and reflectron mode. Superficially the difference lies in the length of the time of flight chamber which increases from 0.91m for the linear mode to 2.73 m for the reflectron mode (Figure B1.4a & B1.4b).[2] In the resulting spectra the linear mode shows significant differences in the mass resolution and mass accuracy to the reflectron mode. Mass resolution (m/Δm) is defined by the mass of the ion signal (m) divided by the width of the ion signal at 50% peak height (Δm).[2]

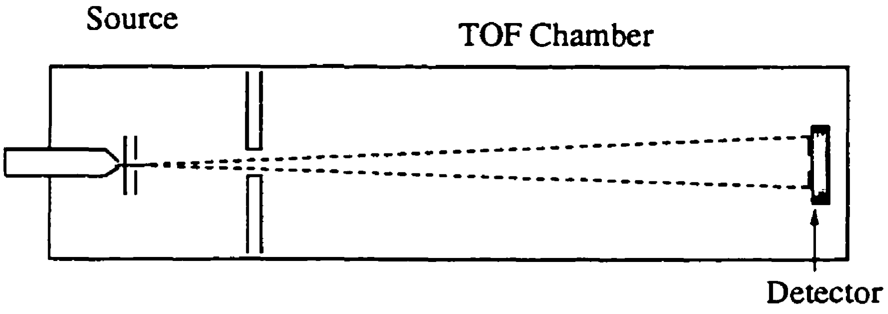


Figure B1.4a. Schematic of the time of flight mass spectrometer in the linear mode.

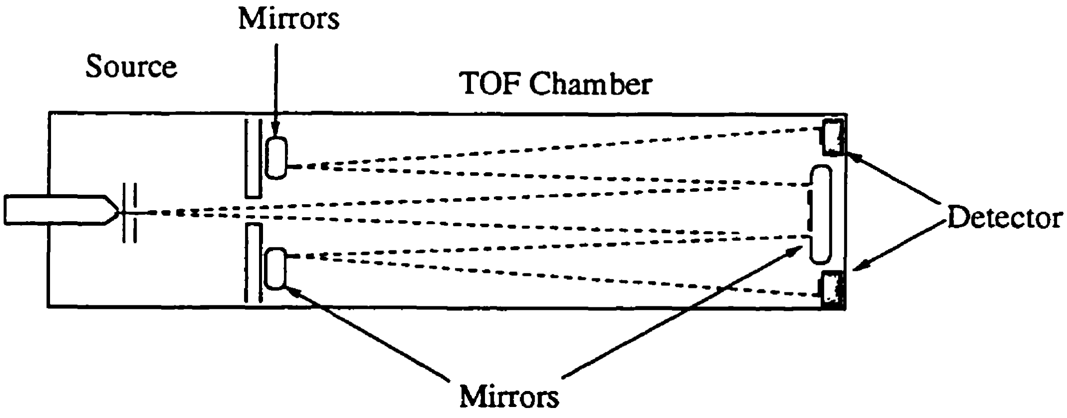


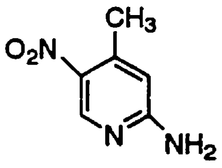
Figure B1.4b. Schematic of the time of flight mass spectrometer in the reflectron mode.

Mass accuracy is defined by the measure of the percent error in assigning a mass to an ion signal. As a pack of ions with different velocities travels a longer distance theoretically better separation of the individual ions will occur. This results in a narrower peak signal which increases the mass resolution and improves the mass accuracy.

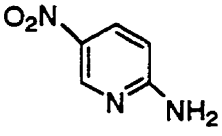
There are also many factors that can effect the appearance of the mass spectrometry spectrum. They are 1) choice of matrix, 2) salt contamination, 3) matrix adducts, and 4) multiply charged species.

MALDI-TOF-MS spectra of biological compounds are quite simple in appearance. Figure B1.5[8], is the MS spectrum of an equimolar mixture of cyctochromo c (Cy, 12 327 Da), egg white lysozyme (Ly, 14 305 Da), horse heart myoglobin (My, 16 951 Da) and soybean trypsin inhibitor (TI, 20 100 Da). Here the choice of matrix changes the appearance of the spectrum. When a basic matrix like 2-amino-4-methyl-5-nitropyridine **B1.9** is used (Figure B1.5a) only cyctochromo c gives an intense broad peak while the signals for Ly, My, and TI are weak. If the matrix is changed to sinapinic acid **B1.1** (Figure B1.5b) a completely different spectrum is obtained. In this spectrum all the compounds Cy, Ly, My,TI are equally ionized and at the same time have a narrower peak width. The latter spectrum gives a true representation of the sample mixture while the former spectrum is misleading. This is a good example which illustrates that choosing the right matrix is extremely important.

Matrices themselves can form adducts with the parent peaks and it is still a matter of trial and error in determining which matrix will or will not form an adduct with a certain analyte. The addition of excess salts in general eliminates this problem.



B1.9



B1.10

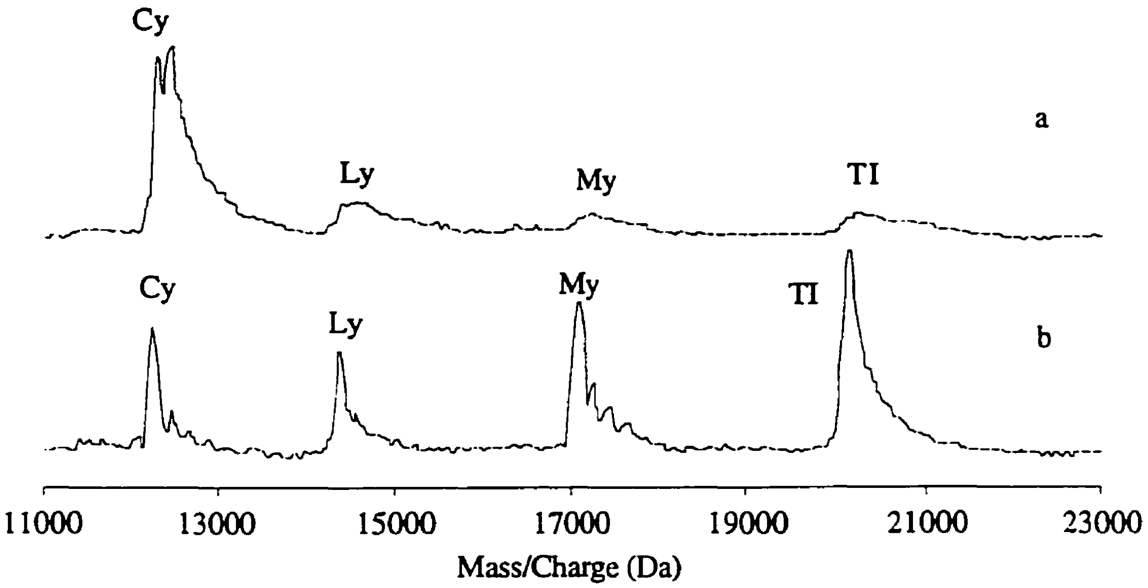


Figure B1.5 MALDI-TOF-MS spectra of an equimolar mixture of cyctochromo c (Cy), egg white lysozyme (Ly), horse heart myoglobin (My), and soybean trypsin inhibitor (TI) using: a) matrix **B1.9**, b) matrix **B1.1**.

Salt contamination tends to make the MS spectrum much more complicated (Figure B1.6).[8]

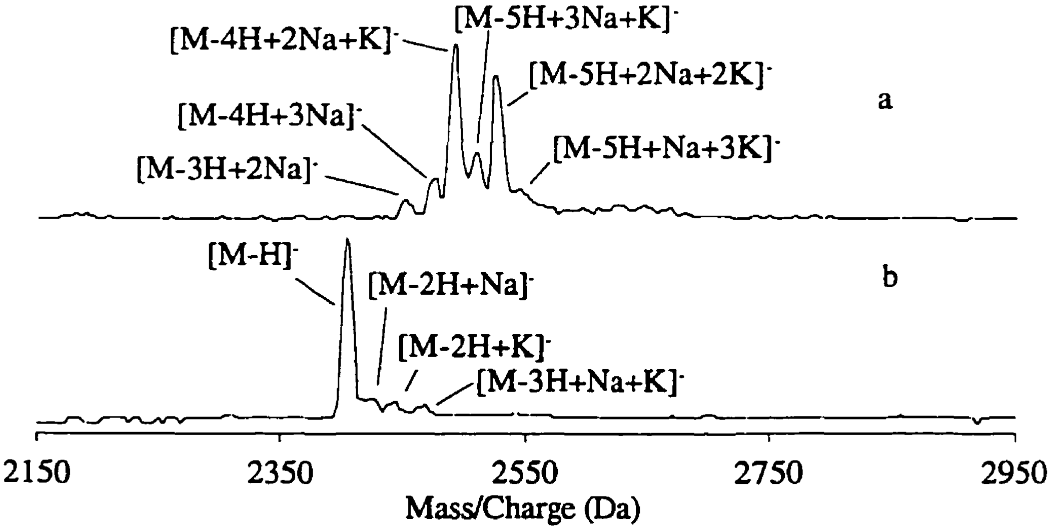
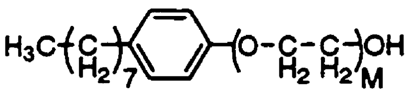


Figure B1.6. MALDI-TOF-MS of octamer SspI using matrix **B1.10**: a) original sample, b) sample after treatment with a cation exchange resin.

The MALDI-TOF-MS of octamer SspI, d(AAATATTT) in 2-amino-5-nitropyridine **B.10** consists of six peaks dominated by the presence of the sodium and potassium adduct peaks (Figure B1.6a). If the sample and matrix are passed through an ion exchange column and analyzed the mass spectrometry spectrum is simplified (Figure B1.6b) and the predominant peak is the parent ion minus a proton. Note that in this case MS analysis was done in the negative mode and the ion species have a negative charge. If the analysis was done in the positive mode then a proton would be added to the parent peak giving a positive charge.



B1.11

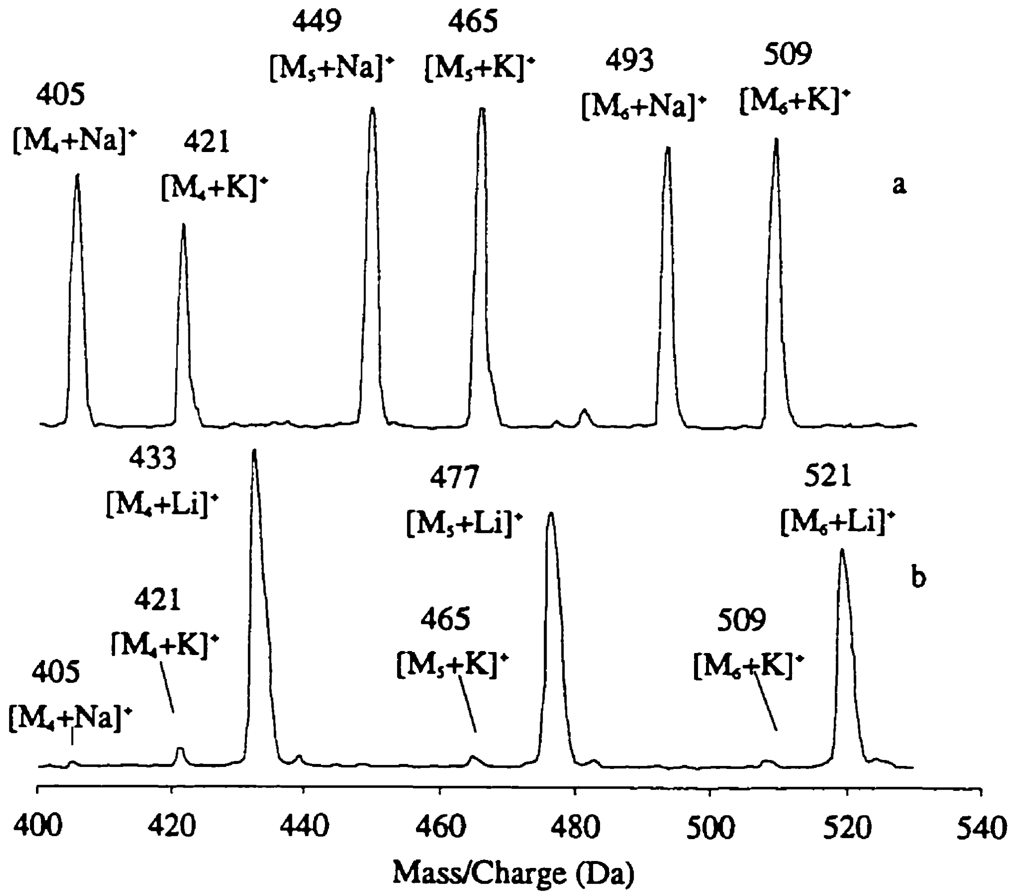


Figure B1.7. MALDI-TOF-MS spectra of **B1.11** using DHBA: a) original sample, b) addition of LiBr.

The presence of salts does not always complicate the MS spectra. If an excess amount of one specific salt is added the spectrum is often simplified (Figure B1.7a,b)[9] by cationization of the analyte which facilitates the ionization. The analysis of poly(ethylene glycol) **B1.11** using **B1.2** as the matrix is a good example. In figure B1.7a only the matrix is added to the analyte and a series of peaks containing either the sodium or potassium adduct are dominant at 405, 449, 493 Da , etc., and 421, 465, 509 Da, etc. respectively. With the addition of LiCl to the mixture a cleaner spectrum is obtained. The lithium cation (Li^+) is smaller than Na^+ and K^+ cations and more readily solvated, therefore, it is a more efficient cationizing agent resulting in the suppression of the Na^+ and/or K^+ adducts (Figure B1.7b). The dominant ion peaks now correspond to the lithium adduct ($[M+ Li]^+$).

In all the MALDI-TOF-MS spectra previously shown only the singly charged species were observed. The analyte can either be positively or negatively charged depending on the parameters of the instrument. If the mass spectrometer is set in the positive mode the analyte carries a positive charge either by the addition of a proton ($[M+H]^+$)which is believed to be transferred from the matrix or by the addition of cations ($[M+Li]^+$). On the other hand, if the mass spectrometer is set in the negative mode the analyte carries a negative charge either by the removal of a proton ($[M-H]^-$) or a combination of the addition of a cation and the removal of two protons ($[M-2H+Li]^-$). The appearance of multiple charges is quite common in this technique and tends to complicate the MS spectra (Figure B1.8)[2]. There are many possible combination of either singly or a multiply charged ion species. In figure B1.8 the following combinations were observed ($[M+H]^+$), ($[2M+H]^+$), ($[M+2H]^{2+}$), ($[3M+H]^{2+}$), ($[M+3H]^{3+}$), ($[2M+3H]^{3+}$) in the analysis of a monoclonal antibody found in mice. The cause of these multiple charges can be due to many factors such as the matrix and possibly even the sample itself. It is therefore impossible to predict the appearance of these multiple charged species and one must be aware of these possibilities when analyzing MALDI-TOF-MS spectra.

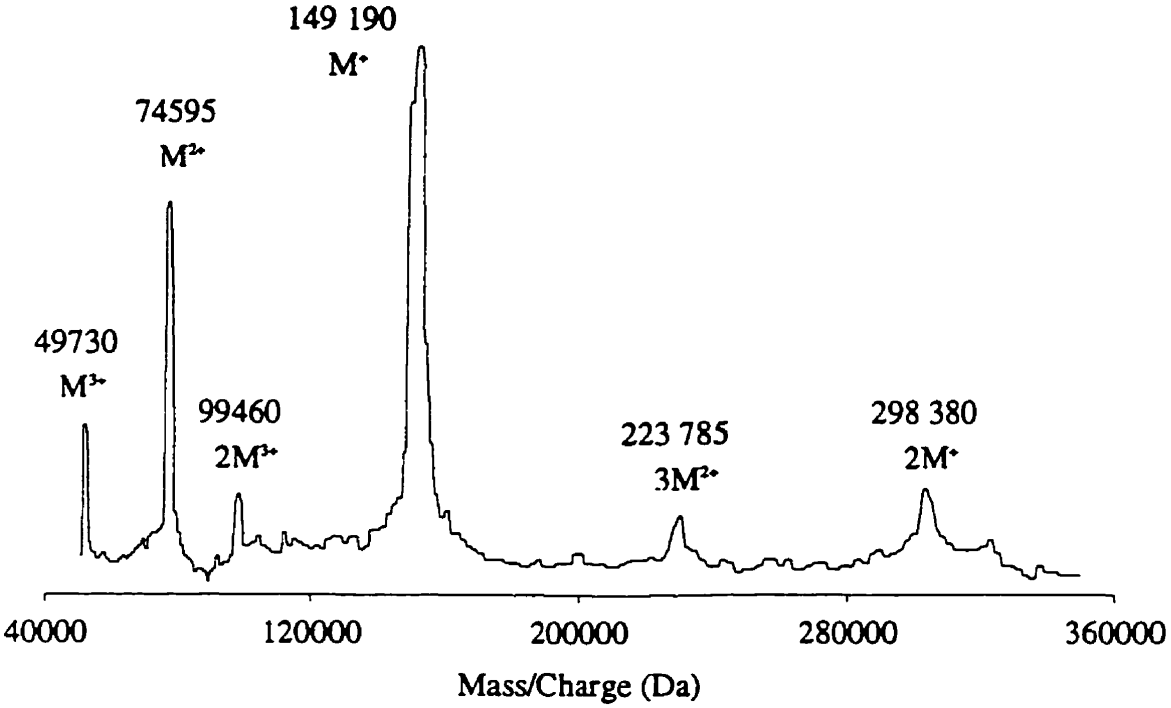


Figure B1.8. Laser desorption ionization mass spectrometry spectrum of monoclonal antibody from a mouse.

The analysis of synthetic polymers by MALDI-TOF-MS has received great attention in the last few years. Most of the work has been on the characterization of monodisperse polymers like polystyrene (PS)[10-13], poly(methyl methylacrylate) (PMMA)[11,12], and poly(ethylene glycol) (PEG)[14,15].

In general the characterization of the previously mentioned polymers has been quite successful. In the case of PS, molecular weights up to 80 000 Da were observed. On the other hand the analysis of polydisperse systems remains as a major challenge. In polydisperse systems, in contrast to monodisperse systems, the ion current is spread over many species with different molecular weights thus drastically lowering the sensitivity. The systems that have been analyzed, for example polycarbonate **B1.12** (approx. MW= 19 000 g/mol), do not show a true representation of the polymer distribution (Figure B1.9).[16]

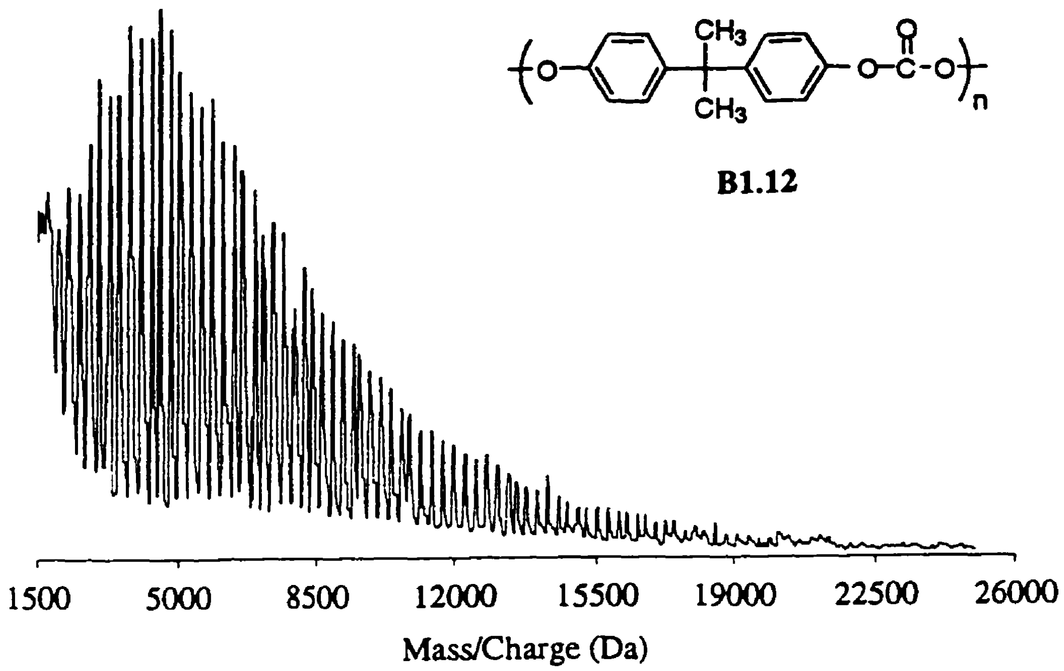


Figure B1.9. MALDI-TOF-MS spectrum of polycarbonate **B1.12** (Mw = 20 000 g/mol) using HABA.

This MALDI-TOF-MS spectrum illustrates that the more intense signals are below 10 000 Da, meaning either that the low molecular weight oligomers are ionizing more efficiently or that the oligomers have multiple charges. However analysis of this spectrum indicates that it is not a true representation of the polymer. Theoretically, the more intense peaks should lie around 19 000 Da and a gaussian distribution from this point to higher and lower molecular weights should be observed. A simulated MALDI-TOF-MS spectrum of the theoretical distribution pattern for polycarbonate with an average molecular weight of 19000 g/mol is shown in figure B1.10.

B1.1.1 Goals and Strategies

Our goals were to screen a series of organic compounds as possible matrices and to develop new sample preparation procedures for the analysis of oligomers **B1.13**, cyclic oligomers **B1.14-16** and polydisperse high performance amorphous polymers **B1.17** using the MALDI-TOF-MS technique. Our principal objective was the evaluation of this technique for the characterization of these polydisperse polymers and cyclic oligomers.

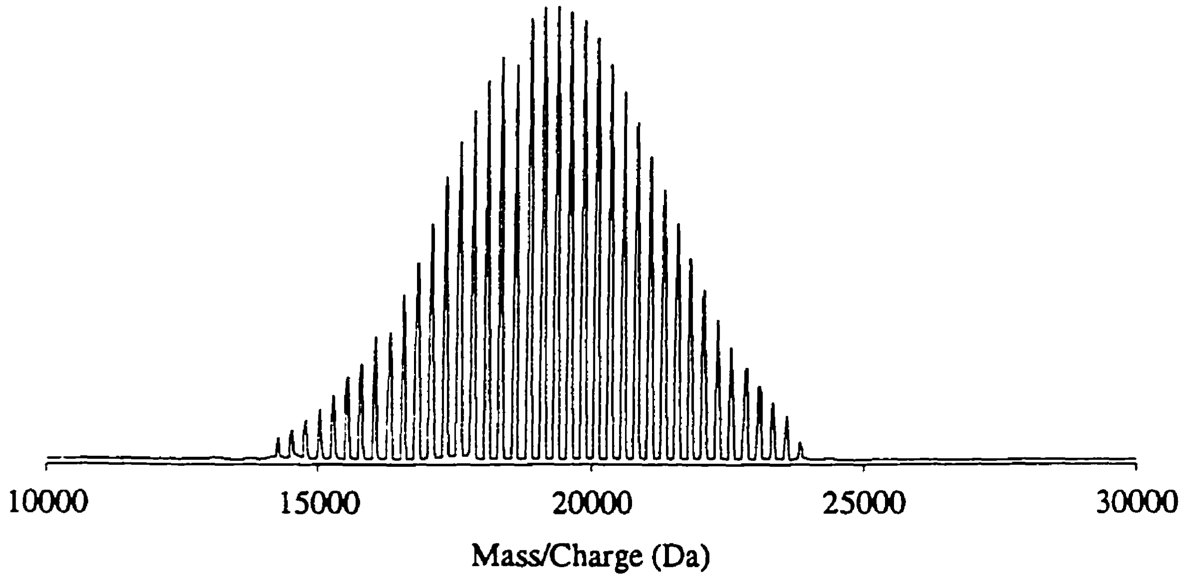
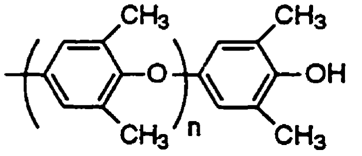
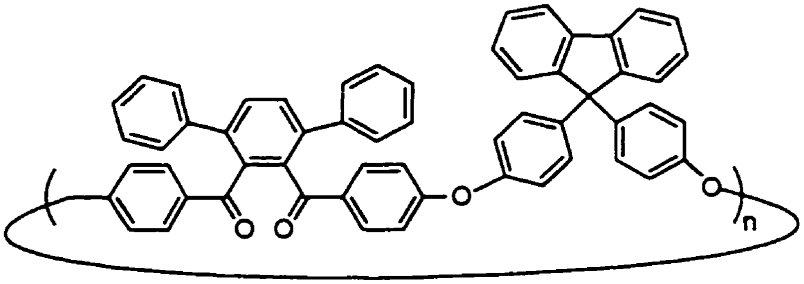


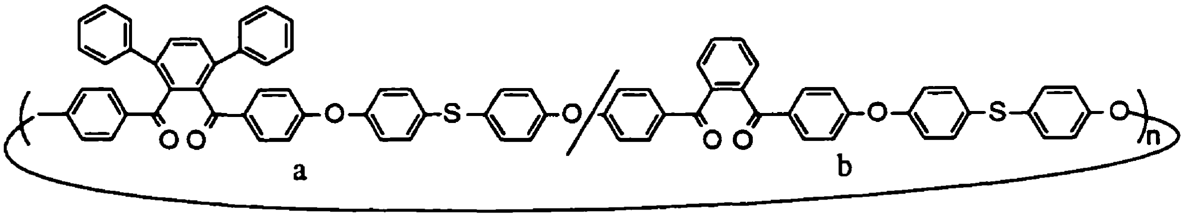
Figure B1.10. A simulated MALDI-TOF-MS spectrum of **B1.12** (Mw = 19 000 g/mol).



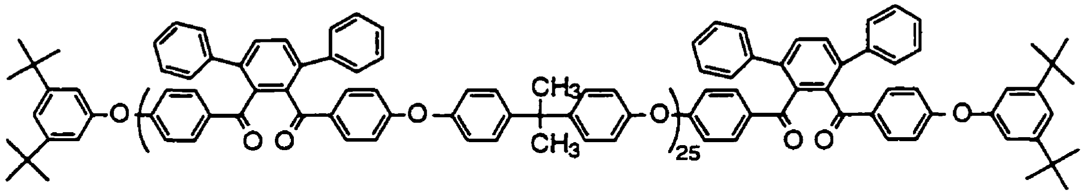
B1.13



B1.14



B1.15 = (a:b = 1:1)
B1.16 = (a:b = 3:1)



B1.17

B1.2 Results and Discussions

B1.2.1 Matrices

The common matrices currently being used (Table B1.2) have had moderate success in the analysis by MALDI-TOF-MS of synthetic polymers. Our first objective was to screen a series of organic monomers and intermediates that were either purchased or prepared in our laboratory as potential matrices (Table B1.3). Many of these compounds would be expected to be more miscible with our systems than the commonly used matrices.

Table B1.3. A list of potential matrices.

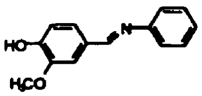
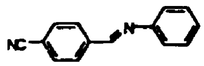
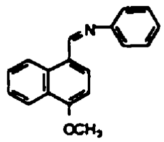
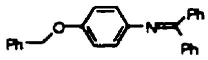
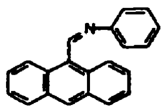
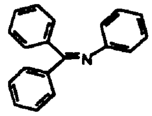
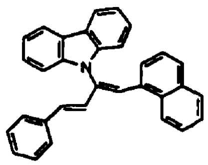
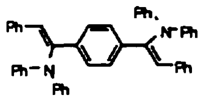
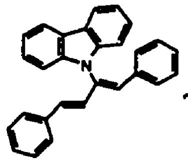
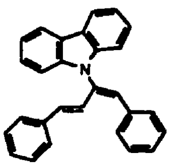
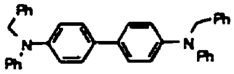
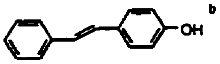
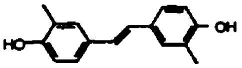
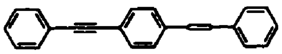
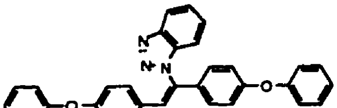
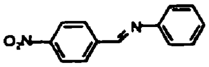
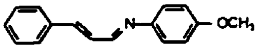
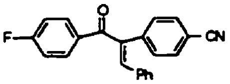
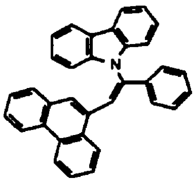
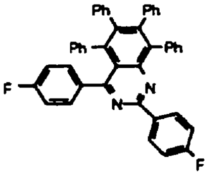
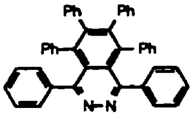
Entry	Monomers^a		Abbrev	Ionization (mV)	Parent Peak (M)^c (Da)
B1.18		227.26 g/mol	---	6	228.3
B1.19		206.20 g/mol	---	---	NS
B1.20		261.30 g/mol	---	---	NS
B1.21		363.45 g/mol	---	0	364.2
B1.22		281.00 g/mol	---	14	282.3
B1.23		257.30 g/mol	---	---	NS
B1.24		421.50 g/mol	---	49	422.1
B1.25		616.80 g/mol	---	---	NS
B1.26	 Trans	371.17 g/mol	ECarbDO	81	372.2
B1.27	 Cis	371.17 g/mol	ZCarbDO	311	372.2

Table B1.3 continued.

B1.28	 516.68 g/mol		105	517.5
B1.29	 196.25 g/mol	HS	539	197
B1.30	 212.15 g/mol	DHS	432	212.9
B1.31	 240.12 g/mol	DMDHS	254	240.2
B1.32	 280.37 g/mol	TPEE	956	281
B1.33	 481.18 g/mol	---	7	453 $(M-N_2)$
B1.34	 226.20 g/mol	---	---	NS
B1.35	 237.30 g/mol	---	---	NS
B1.36	 328.30 g/mol	---	---	NS
B1.37	 455.56 g/mol	CarbSD	549	446.5
B1.38	 622.22 g/mol	---	---	NS
B1.39	 586.24 g/mol	---	---	NS

a) all these compounds were synthesized in our laboratory.
b) compounds purchased from Lancaster chemical company.
c) M = parent molecular weight plus a proton ($[M+H]^+$).

To test the compounds we simply ionized the individual compounds with no added matrix by MALDI-TOF-MS. The compounds with the highest parent peak ionization potential were considered as matrices. They are compounds **B1.27**, **B1.29**, **B1.30**, **B1.31**, **B1.32**, **B1.37**. Of these only **B1.30**, **B1.31**, and **B1.32** have been shown to be good matrices for the cyclic oligomers. For the polymeric systems no improvements were observed using these matrices and in most cases worse results were obtained. These results however, illustrate that the MALDI-TOF instrument can be readily used to obtain low resolution mass spectra for compounds that absorb in the 337 nm region and the instrument is now used routinely in our laboratory for this purpose. Impurities in the sample can also be identified. This is just another indication that choosing the appropriate matrix is still an art and is based principally on trial and error.

B1.2.2 Characterization of Cyclic Oligomers

All the cyclic oligomers were synthesized by Dr. Yifeng Wang using the procedure described by Chan [17]. The analysis of cyclic **B1.14** and its fractions **B1.14.1** to **B1.14.5** has shed light on the composition of the cyclic oligomer mixture and has provided information on the limitations of this technique.

A series of matrices were used in the analysis of cyclic **B1.14**. A typical spectrum is shown in figure B1.11a. The Mn values for each experiment were calculated using the polymer program supplied with the Kratos Kompact MALDI III software and are listed in table B1.4. The relatively large differences seen in Mn values can be explained by the effect of the matrix and/or cationizing agent. This can be due to better miscibility, electron transfer and/or more efficient formation of the cation species either by the matrix or cationizing agent. The higher Mn values can be explained by the fact that under certain conditions the higher molecular weight fraction ionizes easier. Whatever the case the optimal conditions determined for cyclic **B1.14** are the use of dithranol and LiBr in a ratio of 1:20:1. Is this a true representation of the composition of cyclic oligomers **B1.14**? It is difficult to say because, as previously mentioned, simple changes in sample preparations tend to have dramatic effects on the resulting mass spectrometry spectrum. One can conclude that this is a reasonable representation of the composition of the cyclic mixture

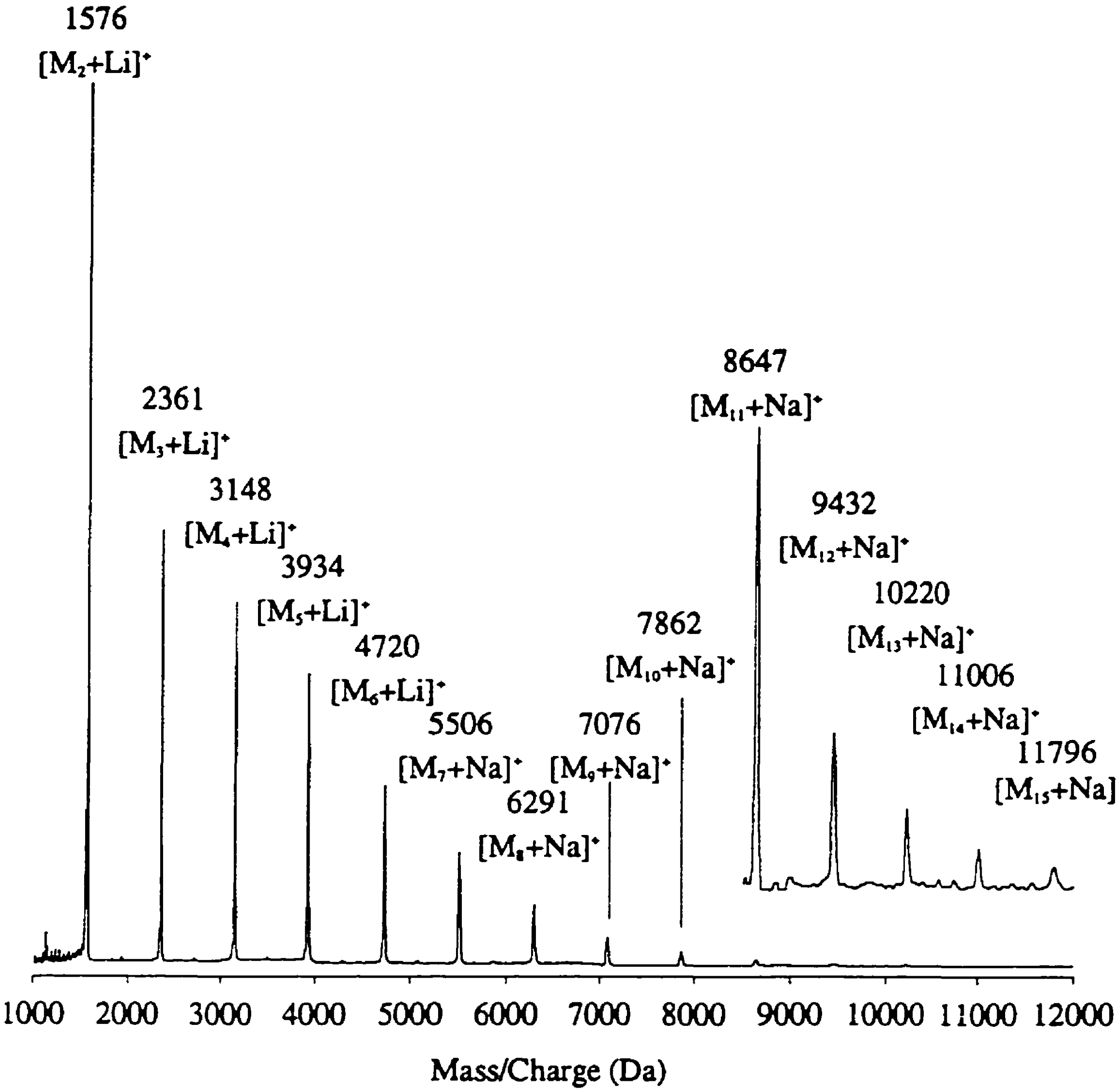


Figure B1.11a. MALDI-TOF-MS in the positive reflectron mode of **B1.14** using dithranol and LiBr (1:20:1).

and the results obtained using this technique give the exact molecular weight of each cyclic oligomer as well as the identification of any impurities or side reactions.

The Mn values obtained by GPC (Figure B1.11b) and MALDI-TOF-MS were 1866 g/mol and 2386 Da (this is an average Mn value based on the results in table B1.4), respectively.

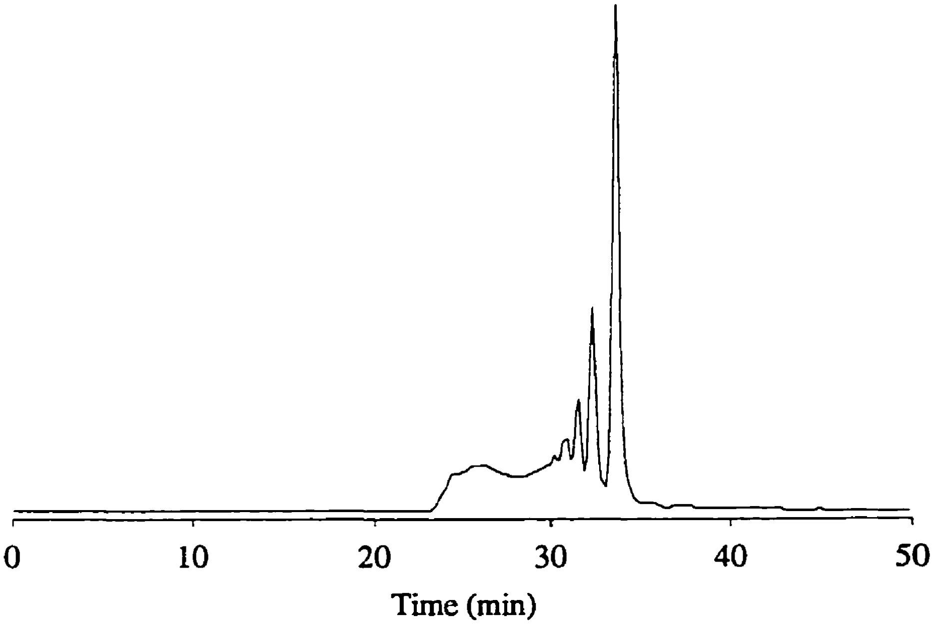
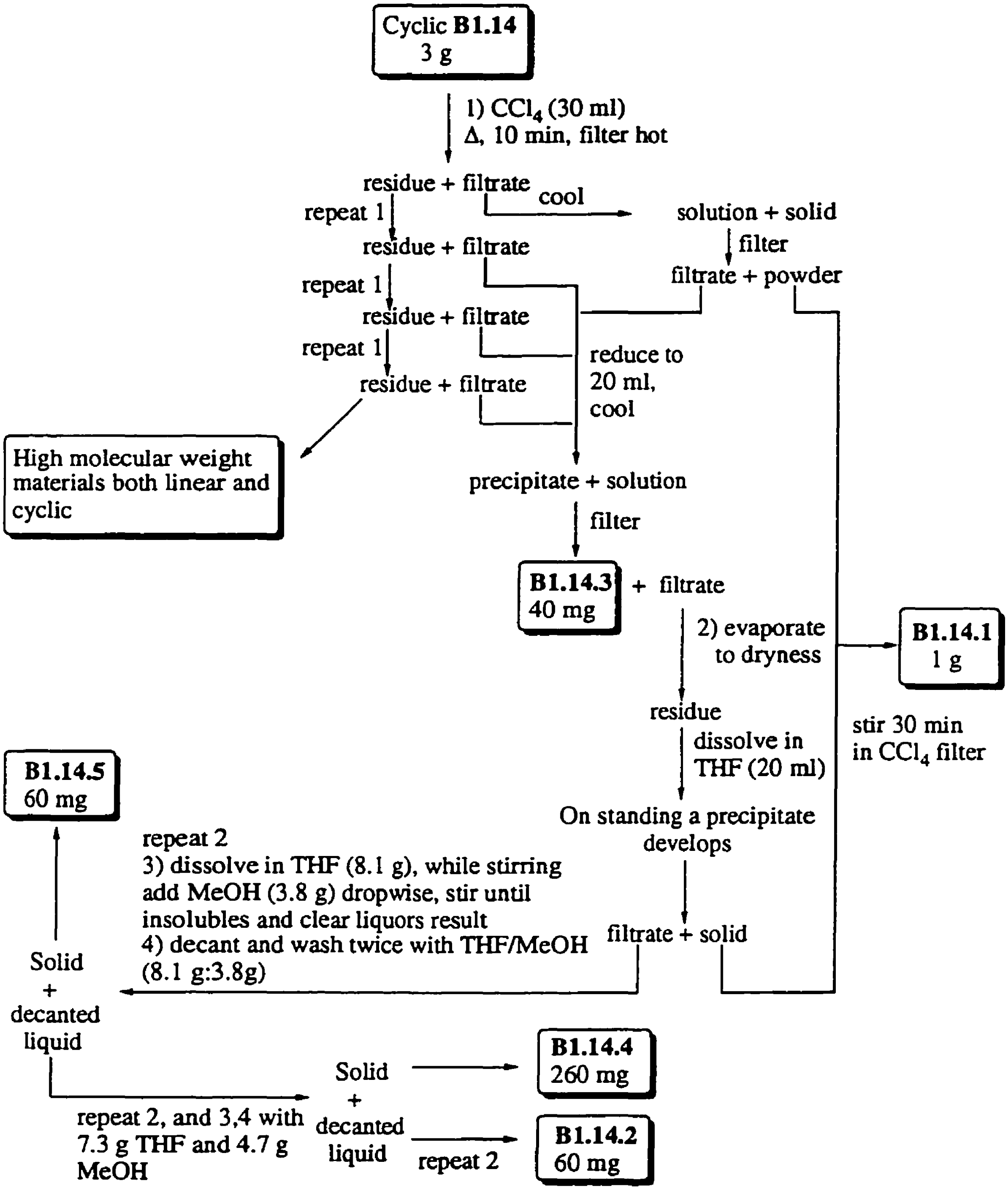


Figure B1.11b. GPC trace of cyclic **B1.14**.

Table B1.4. Comparison of Mn values of cyclic **B1.14** using different matrices.

Matrix	Cationizing agent	Acid	Ratio (Analyte:Matrix:Salt:Acid)	Mn (Da)
B1.6			1:20:0:0	1450
B1.6	AgTFA	Oxalic Acid	1:20:1:1	2654
B1.6	LiBr	---	1:20:1:0	3042
B1.29	---	---	1:20:0:0	1610
B1.29	AGTFA	---	1:20:1:0	2212
B1.30	---	---	1:20:0:0	2550
B1.30	AGTFA	---	1:20:1:0	2954
B1.5	---	---	1:20:0:0	2613

The method by which GPC and MALDI-TOF-MS detect and assign molecular weights can explain to some extent the difference in Mn values, although this pattern is consistent with literature results.[18,19] Peak detection by GPC is based on the UV absorbance at 254 nm. Therefore all the different cyclic fractions in the mixture absorb equally and the peak area is directly proportional to the amount of each cyclic fraction in the mixture. Detection by MALDI-TOF-MS is based on the degree of ionization.



Scheme B1.1

This method of detection is not as reliable based on the results we have obtained for cyclic oligomers **B1.14**. The higher molecular weight oligomers are not ionized as efficiently as the lower molecular weights. This results in an inaccurate representation of the cyclic mixture which in turn affects the Mn value. The other factor is the method of calibration; both techniques use an external calibration. In GPC the mass values are based on the flow rate of the polystyrene standard through the column. Therefore, if the analyte absorbs and desorbs at a different rate than PS the flow rate changes and an inaccurate mass value (Mn) is obtained. The mass values obtained from the MALDI-TOF-MS technique are based on the velocities of the individual mass ion and are independent of the structural properties of the analyte and theoretically speaking are more accurate values. The problem lies in the ionization of the cyclic mixture as previously mentioned. Therefore, the Mn values obtained by both techniques are average values and the difference in values we believe is due the method of calibration.

Table B1.5. Mn values obtained from GPC and MALDI-TOF-MS for a series of cyclic **B1.14** fractions.

Entry	MALDI-TOF-MS		GPC
	Linear (Da)	Reflectron (Da)	(g/mol)
B1.14	2137	3042	1866
B1.14.1	1804	1396	1358
B1.14.2	2724	2928	1443
B1.14.3	2975	3626	2113
B1.14.4	3198	3910	2751
B1.14.5	3364	4354	2863

We further tested the usefulness and limitations of this technique by analyzing a series of fraction obtained through an elaborate extraction procedure of cyclic oligomers **B1.14** (Scheme B1.1) developed by Dr. M. Paventi in our laboratory. A similar trend was observed for all the fractions in that the Mn values obtained (Table B1.5) by GPC are much lower than the MALDI-TOF-MS values and that a similar increase in Mn values for the different fractions was observed by both techniques.

In comparing the MALDI-TOF-MS spectra (Figure B1.12-16) and the GPC spectra (Figure B1.17a-e) of the cyclic fractions, MALDI-TOF-MS provides much more detail of the components found in the cyclic.

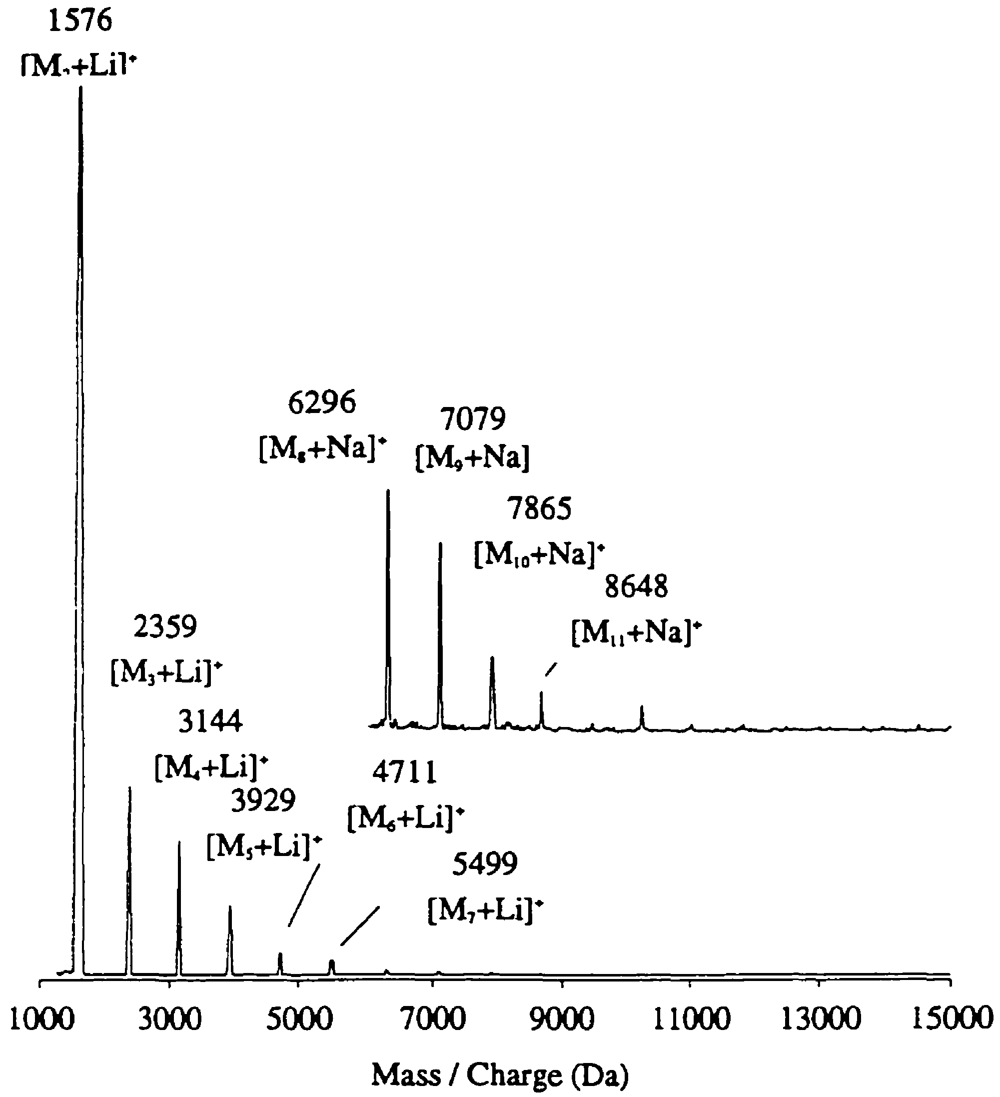


Figure B.12. MALDI-TOF-MS spectrum in the positive reflectron mode of cyclic fraction **B1.14.1** using dithranol and LiBr (1:20:1).

For example, in the analysis of fraction **B1.14.3** (Figure B1.14) besides the signal peaks corresponding to the cyclic oligomers minor signal peaks appear which have been identified as linear oligomers **B1.40**. Without the MALDI-TOF-MS technique we would not have been able to identify these linear oligomers which are not seen by using GPC (Figure B1.17e) or NMR.

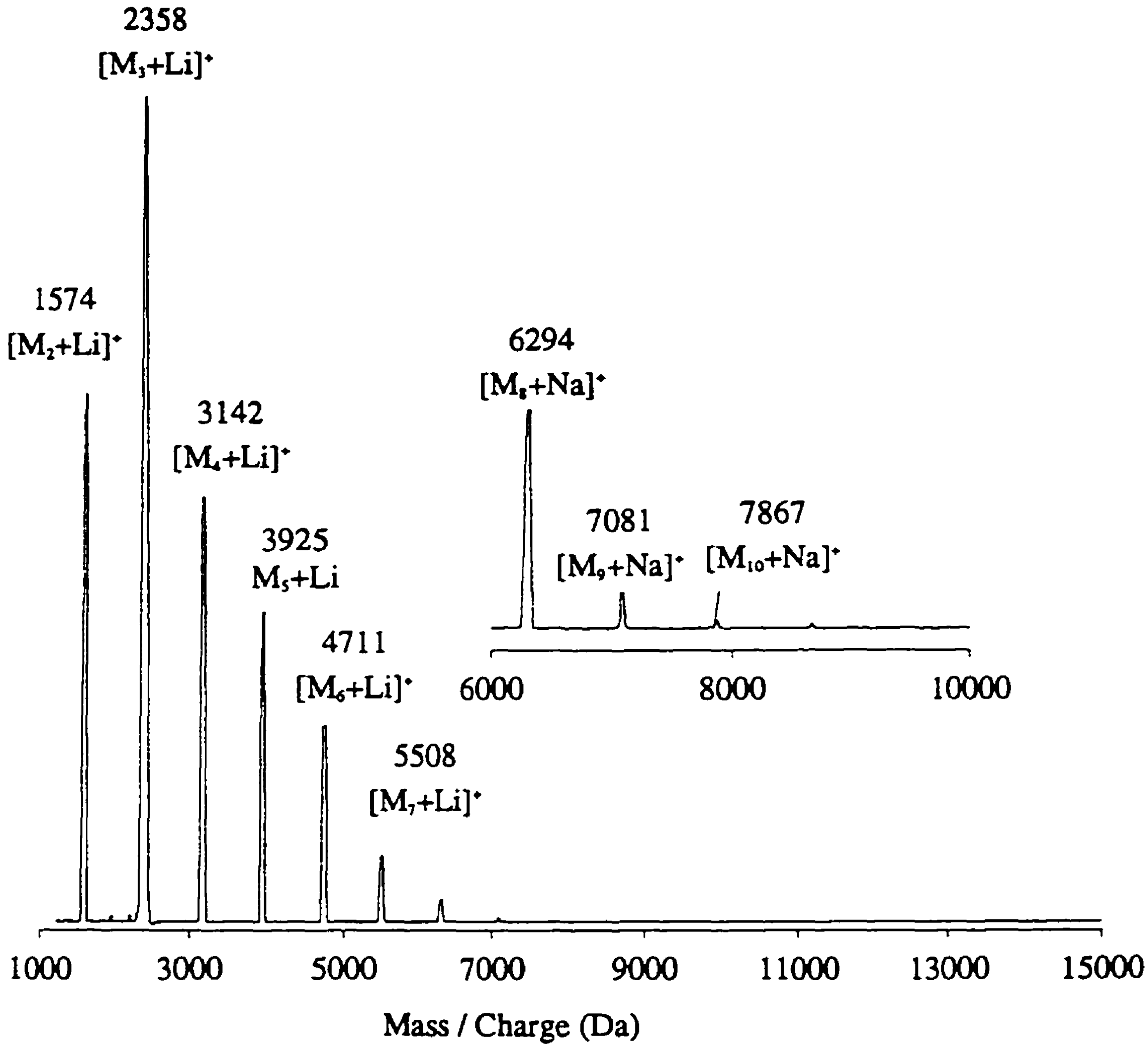


Figure B1.13. MALDI-TOF-MS spectrum in the positive reflectron mode of cyclic fraction **B1.14.2** using dithranol and LiBr (1:20:1).

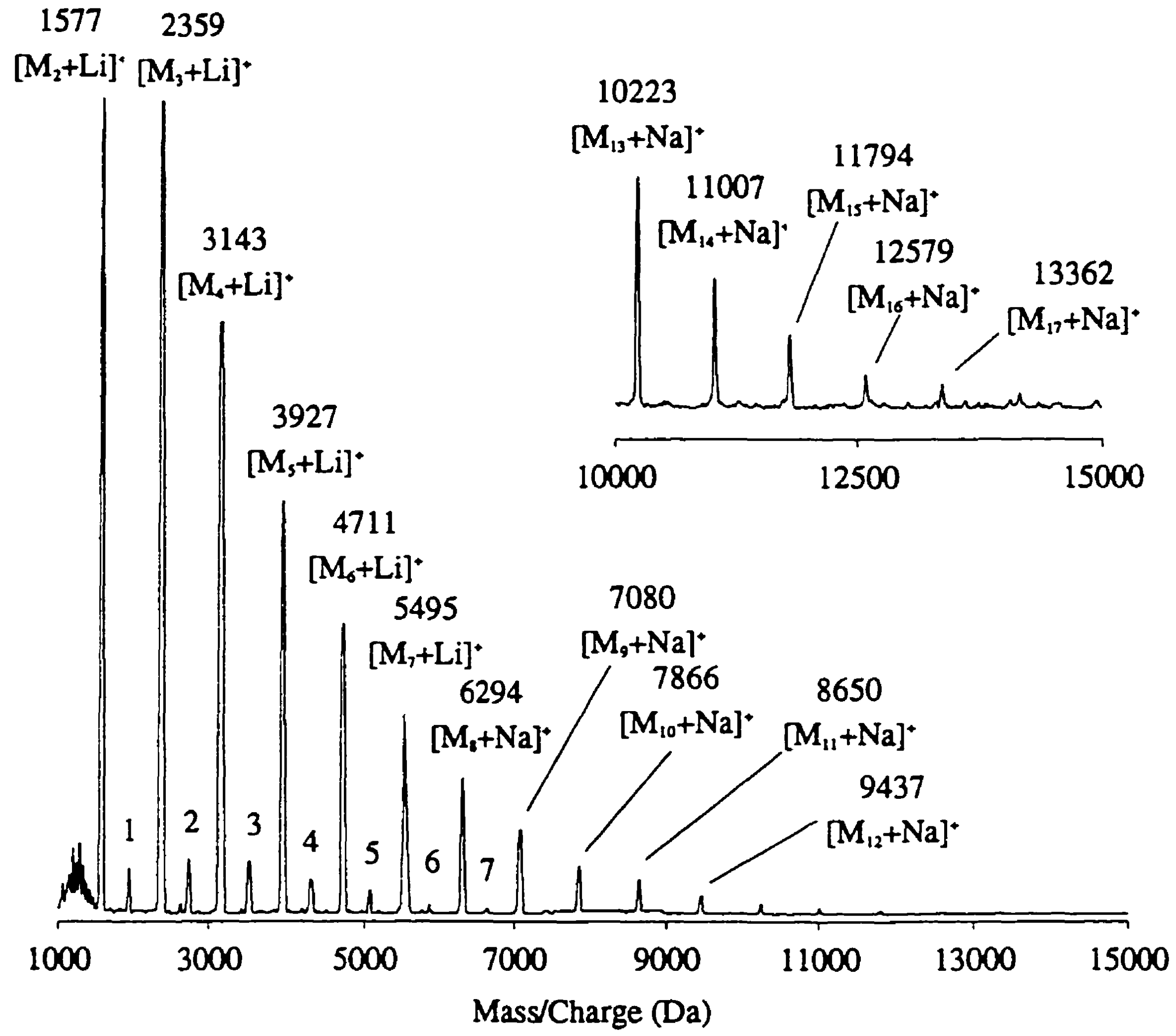
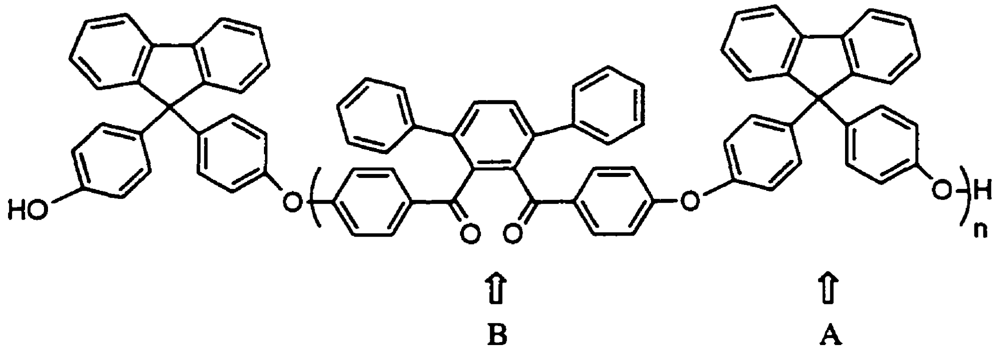


Figure B1.14. MALDI-TOF-MS spectrum in the positive reflectron mode of cyclic fraction **B1.14.3** using dithranol and LiBr (1:20:).



B1.40

Table B1.6. Peak listing for the linear oligomers **B1.40** found in the cyclic mixture **B1.14**.

Peak	Sequence	Mass (Da)
1	[(AB)$_2$A+Li]$^+$	1925
2	[(AB)$_3$A+Li]$^+$	2709
3	[(AB)$_4$A+Li]$^+$	3493
4	[(AB)$_5$A+Li]$^+$	4279
5	[(AB)$_6$A+Li]$^+$	5060
6	[(AB)$_7$A+Li]$^+$	5841
7	[(AB)$_8$A+Li]$^+$	6622

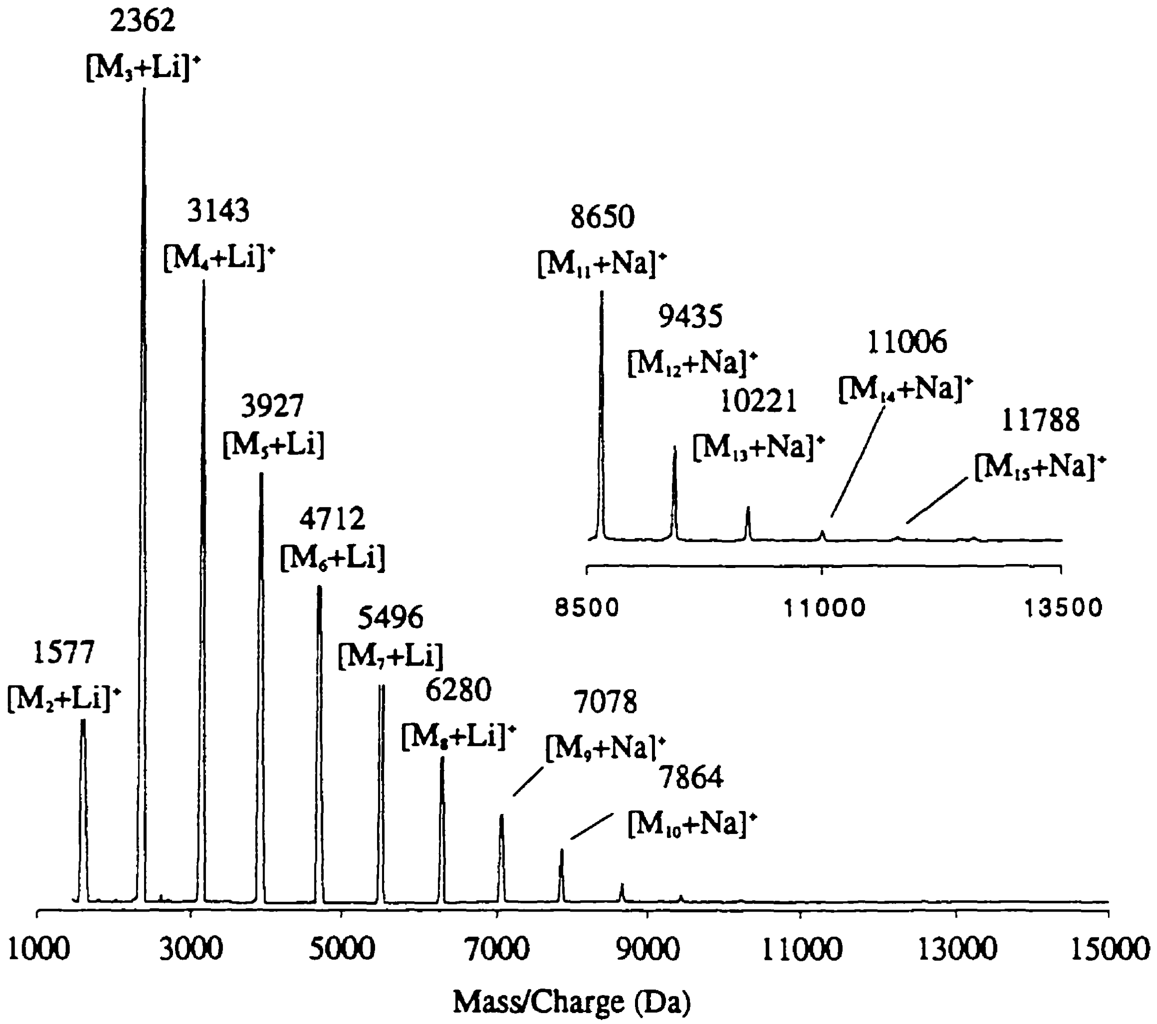


Figure B1.15. MALDI-TOF-MS spectrum in the positive reflectron mode of cyclic fraction **B1.14.4** using dithranol and LiBr (1;20:1).

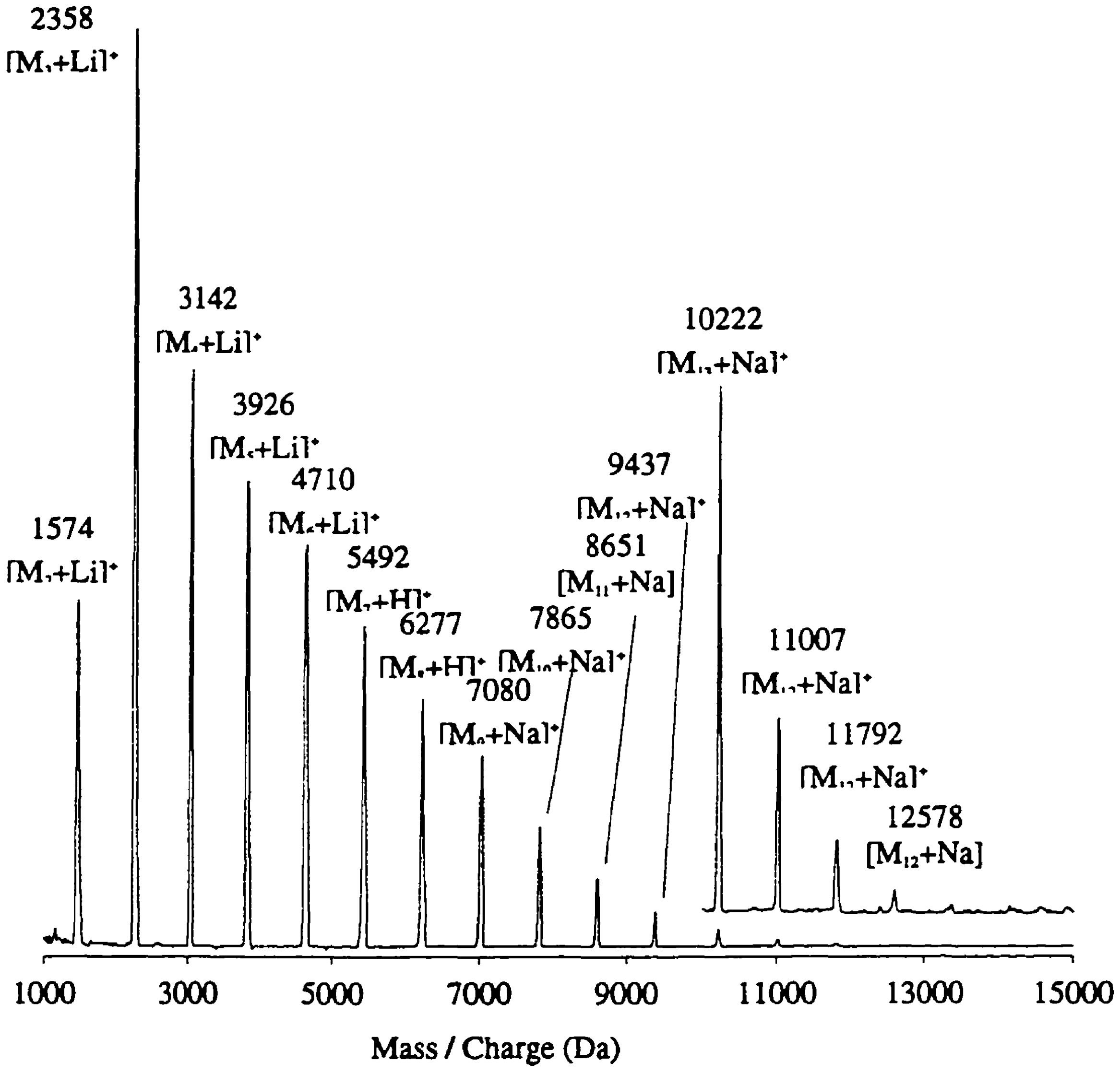


Figure B1.16. MALDI-TOF-MS spectrum in the positive reflectron mode of cyclic fraction **B1.14.5** using dithranol and LiBr (1:20:1).

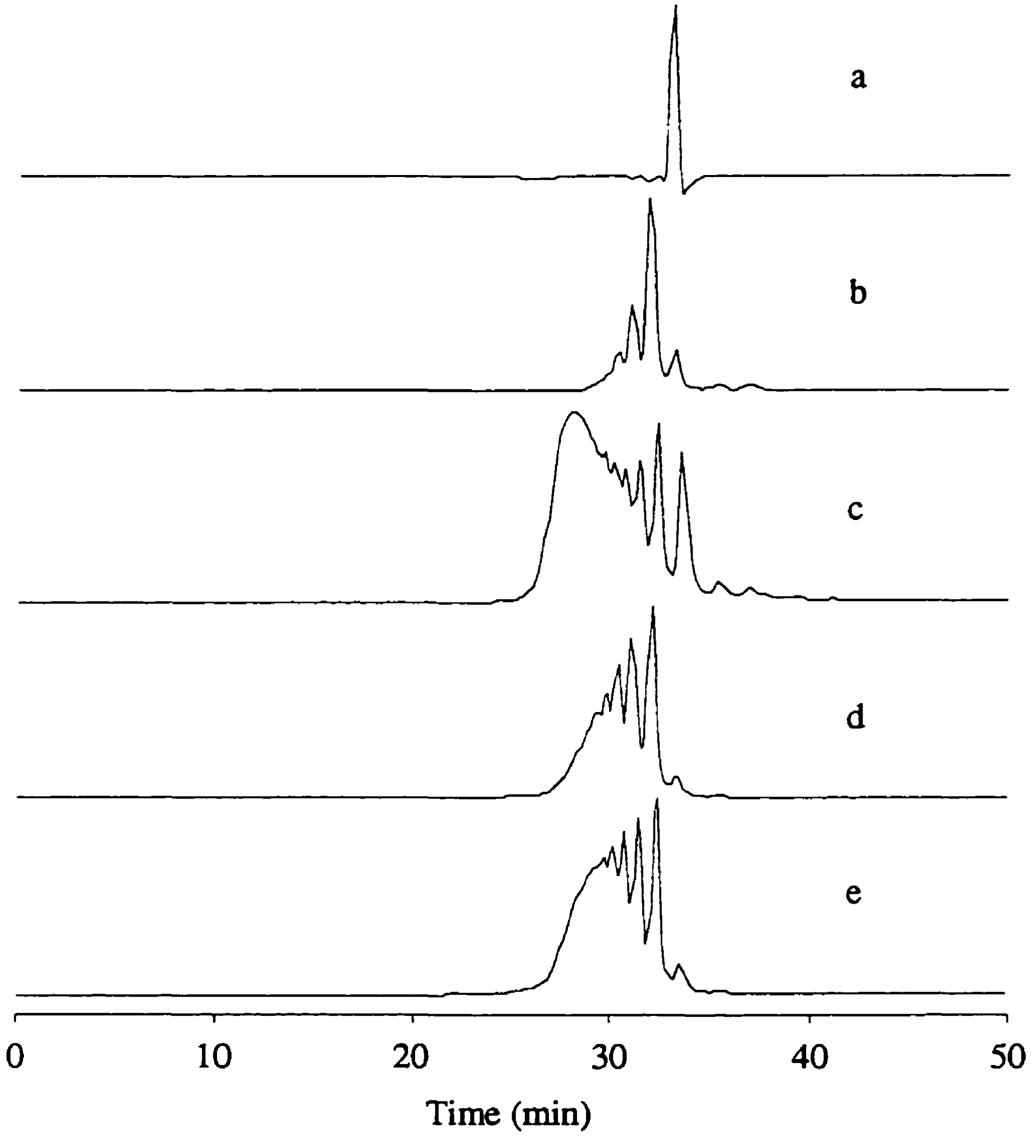


Figure B1.17. GPC spectra of cyclic fractions, a) **B1.14.1**, b) **B1.14.2**, c) **B1.14.3**, d) **B1.14.4**, e) **B14.5**.

In the analysis of these fractions we have also been able to show that the presence of lower molecular weight cyclics affects the ionization of the higher fractions (see figure

B1.12 &16). In the latter spectrum the higher molecular weight sequences ionize more efficiently.

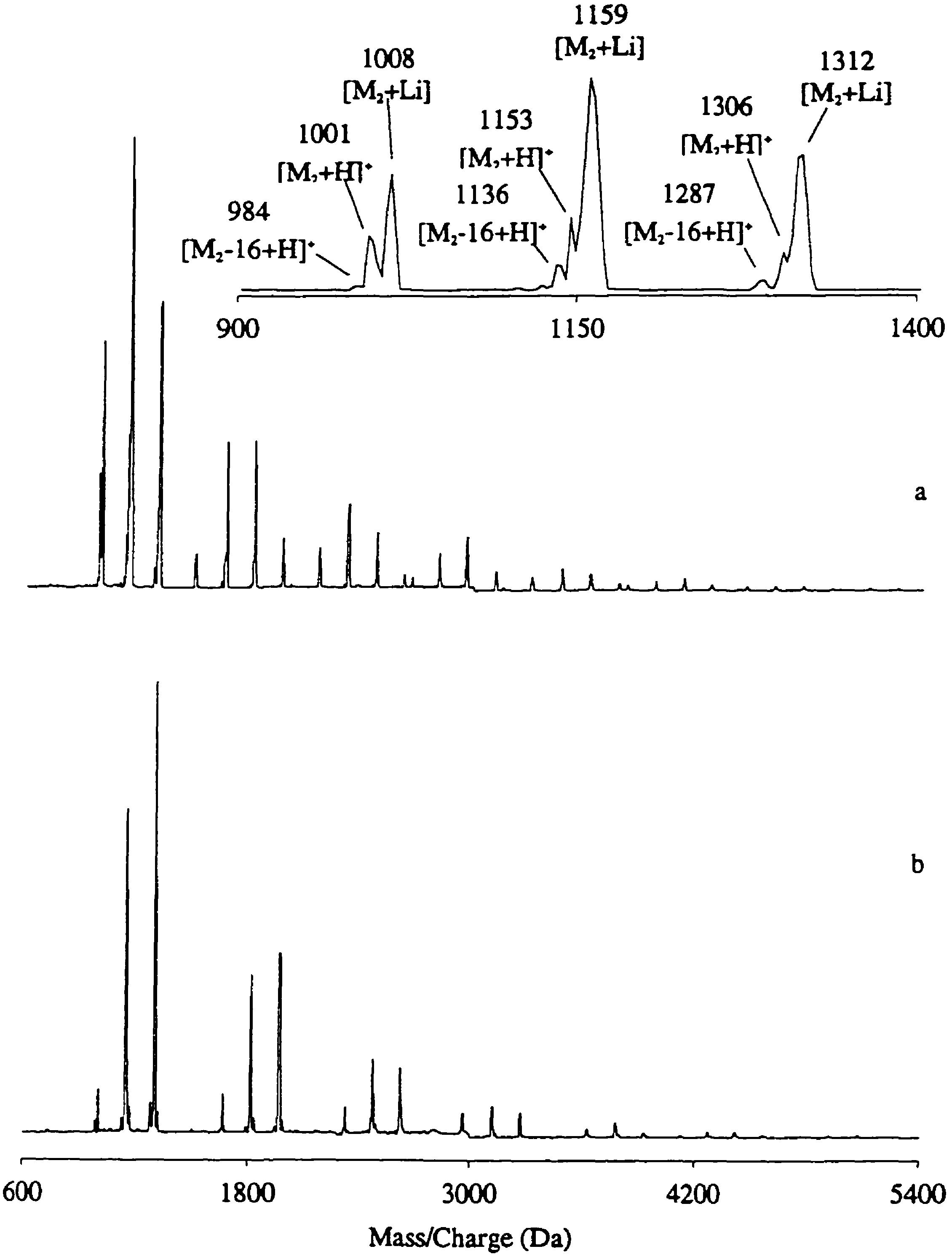
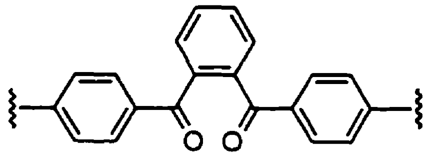
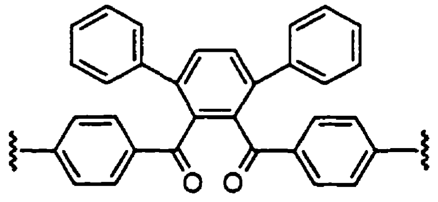


Figure B1.18. MALDI-TOF-MS spectrum in the positive reflectron mode of cocyclic, a) **B1.15** and b) **B1.16** using dithranol and LiBr (1:20:1).

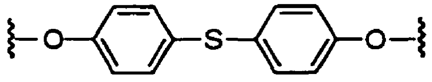
We were also interested in using this technique to analysis the sequence distribution pattern and the percentage of each monomer found in the cocyclic **B1.15** and **B1.16**. Our objective was to determine if the values obtained by MALDI-TOF-MS are similar to theoretical values. The MALDI-TOF-MS spectra of cocyclic **B1.15** and **B1.16** were obtained using dithranol and LiBr in a ratio of 1:20:1 (Figure B1.18a,b). The sequence patterns obtained are similar to the statistical predicted pattern (Table B1.7,8). We were also able to calculate the percentage of monomer **B1.41A** and **B1.41C** based on the peak area of the individual peaks associated with the dimer species; they are A_2B_2, AB_2C, B_2C_2 (Table B1.9,10). The values obtained are similar to the theoretical values, indicating that this technique, at least in the lower molecular weight range, can be used to determine the accurate percent of each monomer found in the cocyclic oligomer.



B1.41A



B1.41C



B1.41B

In the analysis of these cyclic oligomers we have shown the limitations and usefulness of this technique. There is still one aspect we have not considered that is the calibration of the instruments. Proteins are commonly used as standards although the disadvantage of these materials is their stability. Generally their life spans are from 4-6 months when kept refrigerated. We have found the cyclics can be used for the calibration of the lower molecular weight region. The advantage of these systems is that they are extremely stable and ionize as efficiently as the protein materials both in the linear and reflectron mode. Currently we are using cyclic oligomers **B1.14** as a calibration standard on our instrument.

Table B1.7. Peak listing for cyclic oligomers **B1.15**.

Mass (Da)	Peak identification	Sequence^a	Theoretical Mass (g/mol)	Error (%)
984	$[M_2-17+H]^+$	A_2B_2	985	0.10
1001	$[M_2+H]^+$	A_2B_2	1001	0.00
1008	$[M_2+Li]^+$	A_2B_2	1007	0.10
1023	$[M_2+Na]^+$	A_2B_2	1023	0.00
1136	$[M_2-17+H]^+$	$A_1B_2C_1$	1137	0.09
1153	$[M_2+H]^+$	$A_1B_2C_1$	1153	0.00
1160	$[M_2+Li]^+$	$A_1B_2C_1$	1159	0.09
1176	$[M_2+Na]^+$	$A_1B_2C_1$	1175	0.09
1287	$[M_2-17+H]^+$	B_2C_2	1289	0.16
1306	$[M_2+H]^+$	B_2C_2	1305	0.08
1312	$[M_2+Li]^+$	B_2C_2	1311	0.08
1328	$[M_2+Na]^+$	B_2C_2	1327	0.08
1508	$[M_3+Li]^+$	A_3B_3	1507	0.07
1661	$[M_3+Li]^+$	$A_2B_3C_1$	1659	0.12
1790	$[M_3-15+H]^+$	$A_1B_3C_2$	1789	0.06
1813	$[M_3+Li]^+$	$A_1B_3C_2$	1811	0.11
1829	$[M_3+Na]^+$	$A_1B_3C_2$	1827	0.11
1942	$[M_3-15+H]^+$	B_3C_3	1941	0.05
1965	$[M_3+Li]^+$	B_3C_3	1963	0.10
1981	$[M_3+Na]^+$	B_3C_3	1980	0.05
2162	$[M_4+Li]^+$	$A_3B_4C_1$	2159	0.14
2314	$[M_4+Li]^+$	$A_2B_4C_2$	2312	0.09
2330	$[M_4+Na]^+$	$A_2B_4C_2$	2328	0.09
2442	$[M_4-17+H]^+$	$A_1B_4C_3$	2441	0.04
2466	$[M_4+Li]^+$	$A_1B_4C_3$	2464	0.08
2483	$[M_4+Na]^+$	$A_1B_4C_3$	2480	0.12
2618	$[M_4+Li]^+$	B_4C_4	2616	0.08
2968	$[M_5+Li]^+$	$A_2B_5C_3$	2964	0.13
3120	$[M_5+Li]^+$	$A_1B_5C_4$	3116	0.13
3621	$[M_6+H]^+$	$A_2B_6C_4$	3616	0.14
3772	$[M_6+Li]^+$	$A_1B_6C_5$	3768	0.11
4120	$[M_7+Li]^+$	$A_3B_7C_4$	4116	0.10
4274	$[M_7+Li]^+$	$A_2B_7C_5$	4268	0.14
4427	$[M_7+Li]^+$	$A_1B_7C_6$	4420	0.16
4926	$[M_8+Li]^+$	$A_2B_8C_6$	4920	0.12
5078	$[M_8+Li]^+$	$A_1B_8C_7$	5072	0.12

Table B1.8. Peak listing of cyclic **B1.16**.

Mass (Da)	Peak Identification	Sequence[a]	Theoretical Mass (g/mol)	Error (%)
984	$[M_2\text{-}17+H]^+$	A_2B_2	985	0.10
1001	$[M_2+H]^+$	A_2B_2	1001	0.00
1008	$[M_2+Li]^+$	A_2B_2	1007	0.10
1023	$[M_2+Na]^+$	A_2B_2	1023	0.00
1136	$[M_2\text{-}17+H]^+$	$A_1B_2C_1$	1137	0.09
1153	$[M_2+H]^+$	$A_1B_2C_1$	1153	0.00
1160	$[M_2+Li]^+$	$A_1B_2C_1$	1159	0.09
1287	$[M_2\text{-}17+H]^+$	B_2C_2	1289	0.16
1306	$[M_2+H]^+$	B_2C_2	1305	0.08
1312	$[M_2+Li]^+$	B_2C_2	1311	0.08
1501	$[M_3+H]^+$	A_3B_3	1501	0.00
1508	$[M_3+Li]^+$	A_3B_3	1507	0.07
1636	$[M_{3\text{-}16}+H]^+$	$A_2B_3C_1$	1637	0.06
1660	$[M_3+Li]^+$	$A_2B_3C_1$	1659	0.06
1788	$[M_3\text{-}15+H]^+$	$A_1B_3C_2$	1789	0.06
1812	$[M_3+Li]^+$	$A_1B_3C_2$	1811	0.06
1965	$[M_3+Li]^+$	B_3C_3	1963	0.10
2161	$[M_3+Na]^+$	$A_3B_4C_1$	2159	0.09
2313	$[M_4+Li]^+$	$A_2B_4C_2$	2312	0.04
2465	$[M_4+Li]^+$	$A_1B_4C_3$	2464	0.04
2618	$[M_4+Li]^+$	B_4C_4	2616	0.08
2814	$[M_4+Li]^+$	$A_3B_5C_2$	2812	0.07
2967	$[M_5+Li]^+$	$A_2B_5C_3$	2964	0.10
3119	$[M_5+Li]^+$	$A_1B_5C_4$	3116	0.10
3315	$[M_6+Li]^+$	$A_4B_6C_2$	3312	0.09
3620	$[M_6+H]^+$	$A_2B_6C_4$	3616	0.11
3773	$[M_6+Li]^+$	$A_1B_6C_5$	3768	0.13
3968	$[M_7+Li]^+$	$A_4B_7C_3$	3964	0.10
4122	$[M_7+Li]^+$	$A_3B_7C_4$	4116	0.15
4274	$[M_7+Li]^+$	$A_2B_7C_5$	4268	0.14
4425	$[M_7+Li]^+$	$A_1B_7C_6$	4420	0.11
4470	$[M_8+Li]^+$	$A_5B_8C_3$	4464	0.13
4622	$[M_8+Li]^+$	$A_4B_8C_4$	4616	0.13
4774	$[M_8+Li]^+$	$A_3B_8C_5$	4768	0.13
4927	$[M_8+Li]^+$	$A_2B_8C_6$	4920	0.14
4970	$[M_9+H]^+$	$A_6B_9C_3$	4964	0.12
5123	$[M_9+Li]^+$	$A_5B_9C_4$	5116	0.14

Table B1.9. Percent distribution of the different sequences of the dimer species by MALDI-TOF-MS.

Sequence	Cyclic **B1.15**		Cyclic **B1.16**	
	Peak Area	Peak Percentage	Peak Area	Peak Percentage
A_2B_2	9.1	5.2	46.5	23.1
AB_2C	67.8	38.3	100.0	49.8
B_2C_2	100.0	56.5	54.4	27.1

Table B1.10. Comparison of the theoretical percentage of the diketone monomer **B1.41A,C** with the experimental values.

Cyclic	Monomer **B1.41A**		Monomer **B1.41C**	
	Theoretical (%)	Experimental (%)	Theoretical (%)	Experimental (%)
B1.15	50	48	50	52
B1.16	25	24	75	76

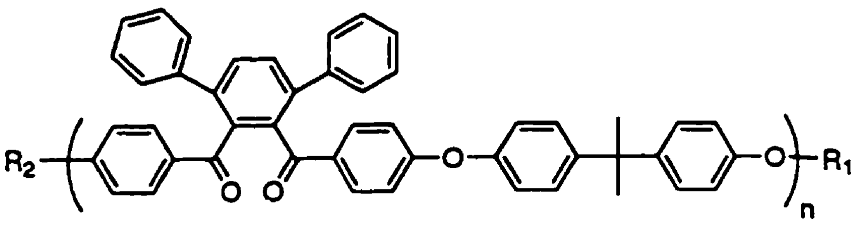
B1.2.3 Polymer Analysis

The analysis of polymer **B1.13** and **B1.17** by MALDI-TOF-MS provided to be more of a challenge than the cyclic oligomers. The reason might lie in the fact that the cyclic oligomers are semi-crystalline and have a narrower polydispersity. In addition chain entanglements would be expected to be less of a problem in the cyclics.

As we previously mentioned synthetic polymers have been identified up to 80 000 Da and most of these polymers were monodisperse samples. We on the other hand were interested in the analysis of polydisperse poly(aryl ether) systems. Our first task was to develop the sample preparation procedure and to choose the appropriate matrix which would effectively separate the different polymer fractions. A series of sample preparation procedures were examined. They were: 1) premixing, 2) melt, 3) film formation, 4) addition of plasticizer, 5) addition of PS, 6) addition of strong acid and/or a cationizing reagent, and 7) mixtures of matrices. Only sample preparation methods 1, 4, 5, and 6 have been effective in the analysis of polymers.

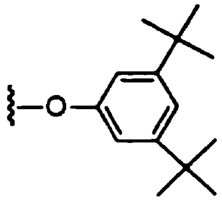
Since MALDI-TOF-MS analysis of cyclic oligomers was successful, we decided to analysis linear polymer **B1.17** which is end capped at 25 repeat units and contains a diketone moiety similar to the cyclic oligomers. The optimal conditions found for analysis were the use of HABA and LiBr in a ratio of 1:20:1. One interesting aspect was that as the amount of matrix increased in the mixture only the lower molecular weight fractions were observed. This is just another indication of how the MALDI-TOF-MS spectra are affected by changes in sample preparation. The signal peaks that were obtained from the mass spectrometry spectrum (Figure B1.19) have a mass range of 4015 to 16132 Da corresponding to approximately 6 to 24 repeat units and to polymer fractions with end groups of HO/F and HO/ 3,5-di-tert-butyl phenol. Proton NMR confirmed that the majority of polymer chains are end capped at both ends with 3,5-di-tert-butylphenol. Therefore the MALDI-TOF-MS spectrum obtained for this polymer only represents a very small fraction of the polymer mixture. Signal peaks with molecular weights corresponding to polymer chains end capped at both ends and having a molecular weight range of 15000 to 35000 Da should have been observed.

The analysis of the higher molecular weight polymers was unsuccessful. Ding [20] have shown that the lower molecular weight oligomers with similar diketone moieties can be characterized up to 10000 Da by MALDI-TOF-MS. The problem lies in the ionization of the higher molecular weight fraction either due to interference from the lower molecular weight fractions or the difficulty for the matrix to isolate the higher molecular weight chains from each other. Whatever the reason the analysis of polymer **B1.17** has clearly shown that high molecular weight polydisperse polymers of this type cannot be directly analyzed by MALDI-TOF-MS. This has been confirmed by G. Monntaudo *et al* [21]who have shown that by separating the polydisperse polymer into fractions of different molecular weights MALDI-TOF-MS characterization of the higher molecular weights was possible. By combining the results of the different fractions a more accurate mass spectrometry spectrum was obtained. With this in mind we decided to



B1.42

P1: R_1 = OH; R_2 = F   P2: R_1 = OH; R_2 =



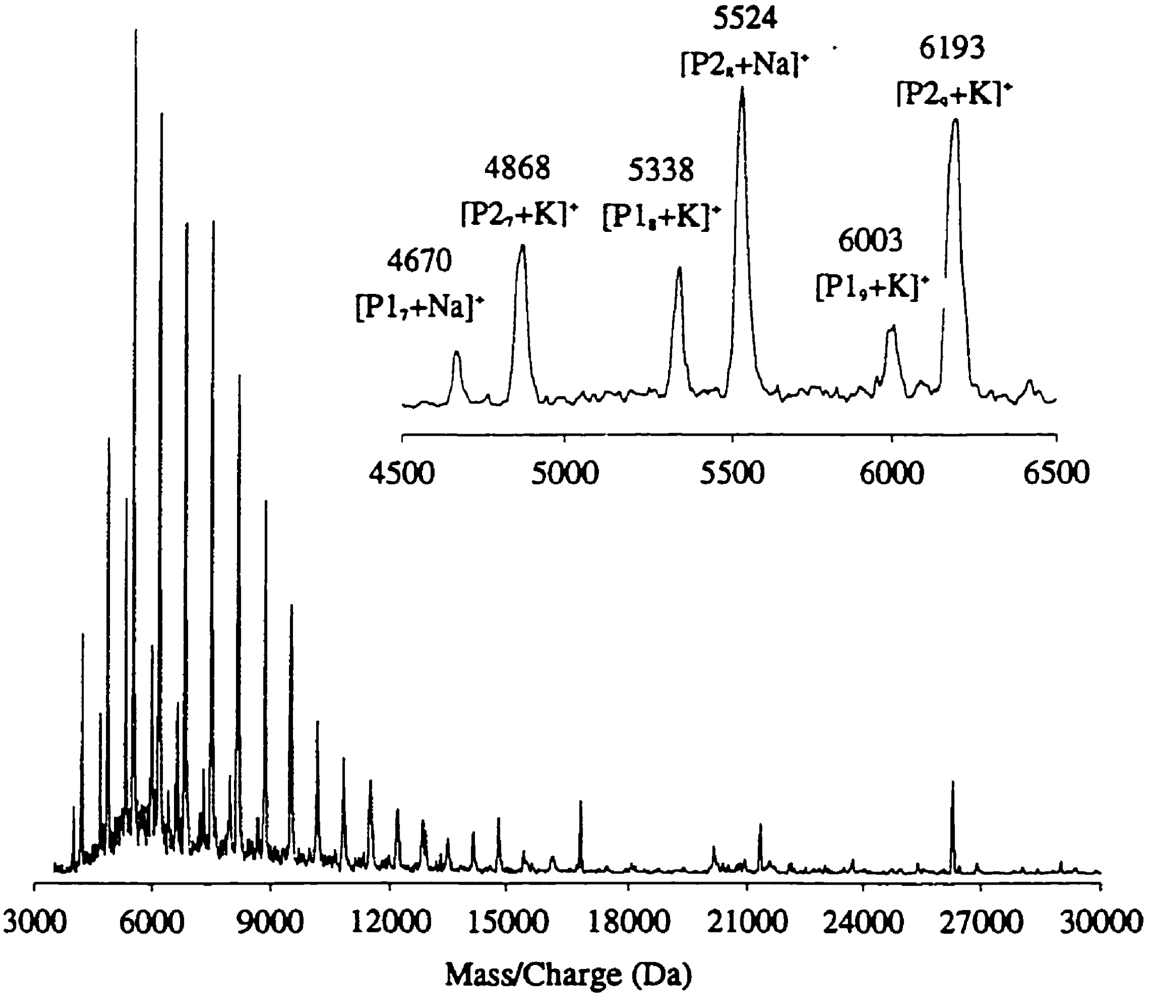


Figure B1.19. MALDI-TO-MS spectrum in the positive reflectron mode of polymer **B1.17** using HABA and LiBr.

Table B1.11. Mass listing of polymer **B1.17**.

Repeat Units	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error %
6	4008	$[P1_{6}+K]^{+}$	4016	0.20
6	4198	$[P2_{6}+K]^{+}$	4202	0.10
7	4670	$[P1_{7}+Na]^{+}$	4662	0.17
7	4867	$[P2_{7}+K]^{+}$	4865	0.04
8	5338	$[P1_{8}+K]^{+}$	5341	0.06
8	5524	$[P2_{8}+K]^{+}$	5528	0.07
9	6003	$[P1_{9}+K]^{+}$	6004	0.02
9	6193	$[P2_{8}+K]^{+}$	6190	0.05
10	6660	$[P1_{10}+K]^{+}$	6667	0.10
10	6853	$[P2_{10}+K]^{+}$	6853	0.00
11	7515	$[P2_{11}+K]^{+}$	7516	0.01
11	7972	$[P3_{11}+K]^{+}$	7970	0.03
12	8181	$[P2_{12}+K]^{+}$	8179	0.02
13	8655	$[P1_{13}+K]^{+}$	8655	0.00
13	8844	$[P2_{13}+K]^{+}$	8841	0.03
14	9510	$[P2_{14}+K]^{+}$	9504	0.06
15	9979	$[P1_{15}+K]^{+}$	9981	0.02
15	10168	$[P2_{15}+K]^{+}$	10167	0.01
16	10838	$[P2_{16}+K]^{+}$	10830	0.07
17	11502	$[P2_{17}+K]^{+}$	11492	0.09
18	12173	$[P2_{18}+K]^{+}$	12155	0.15
19	12835	$[P2_{19}+K]^{+}$	12818	0.13
20	13484	$[P2_{20}+K]^{+}$	13481	0.02
21	14145	$[P2_{21}+K]^{+}$	14144	0.01
22	14810	$[P2_{22}+K]^{+}$	14806	0.03
23	15477	$[P2_{23}+K]^{+}$	15469	0.05
24	16157	$[P2_{24}+K]^{+}$	16132	0.15

characterize a low molecular weight PPO oligomer and see if we could determine the molecular weight limitations of this instrument.

B1.2.3.1 Characterization of PPO Oligomers

Two series of PPO oligomers with intrinsic viscosities of 0.19 and 0.25 were characterized by ^{31}P, using the procedure described in the literature[22], GPC and MALDI-TOF-MS. Their Mn values were compared and used to evaluate the MALDI-TOF-MS technique.

The PPO oligomers were analyzed using several different matrices at various concentrations. It is beyond the scope of this thesis to discuss all the experimental conditions used in the analysis of these oligomers. Only a few selected examples will be discussed which gives a general view of the usefulness and limitation of this technique.

A series of matrices (Table B1.2) and comatrices (Table B1.12) were used at different ratios (analyte to matrix) ranging from 1:1 to 1:100000. Only dithranol with the addition of oxalic acid, AgTFA, TPP, and PS worked effectively (see figures B1.20 through B1.27). The corresponding mass values are listed in tables B1.13-20 and their Mn values are listed in table B1.21. The difference in Mn values can again be attributed to the different sample preparation procedures.[23]

Table B1.12. A list of the matrix mixtures used in the analysis of PPO oligomers.

Matices	Ratio
dithranol / HABA / oxalic acid	(3:3:1)
dithranol / DHSt / oxalic acid	(3:3:1)
dithranol / HSt / oxalic acid	(3:3:1)
dithranol / NPOE / oxalic acid	(3:3:1)
dithranol / 9-NO_2-Anthr / oxalic acid	(3:3:1)
dithranol / 9-NO_2-Anthr / NPOE / oxalic acid	(3:3:3:1)
dithranol / 9-NO_2-Anthr / HABA / Oxalic acid	(3:3:3:1)

PPO and polystyrene are known to be completely miscible in all proportions. In the analysis of a PPO/PS mixture using conditions 5, 6, and 7 listed in table B1.21 (Figure B1.24 to B1.26) an interesting phenomenon occurred. When oxalic acid was added to the mixture of PPO, dithranol and PS4075 only the signal peaks corresponding to PPO were observed. By replacing oxalic acid with AgTFA only the peaks corresponding to PS were observed. Initially we believed that oxalic acid and AgTFA selectively cationized one analyte over the other.

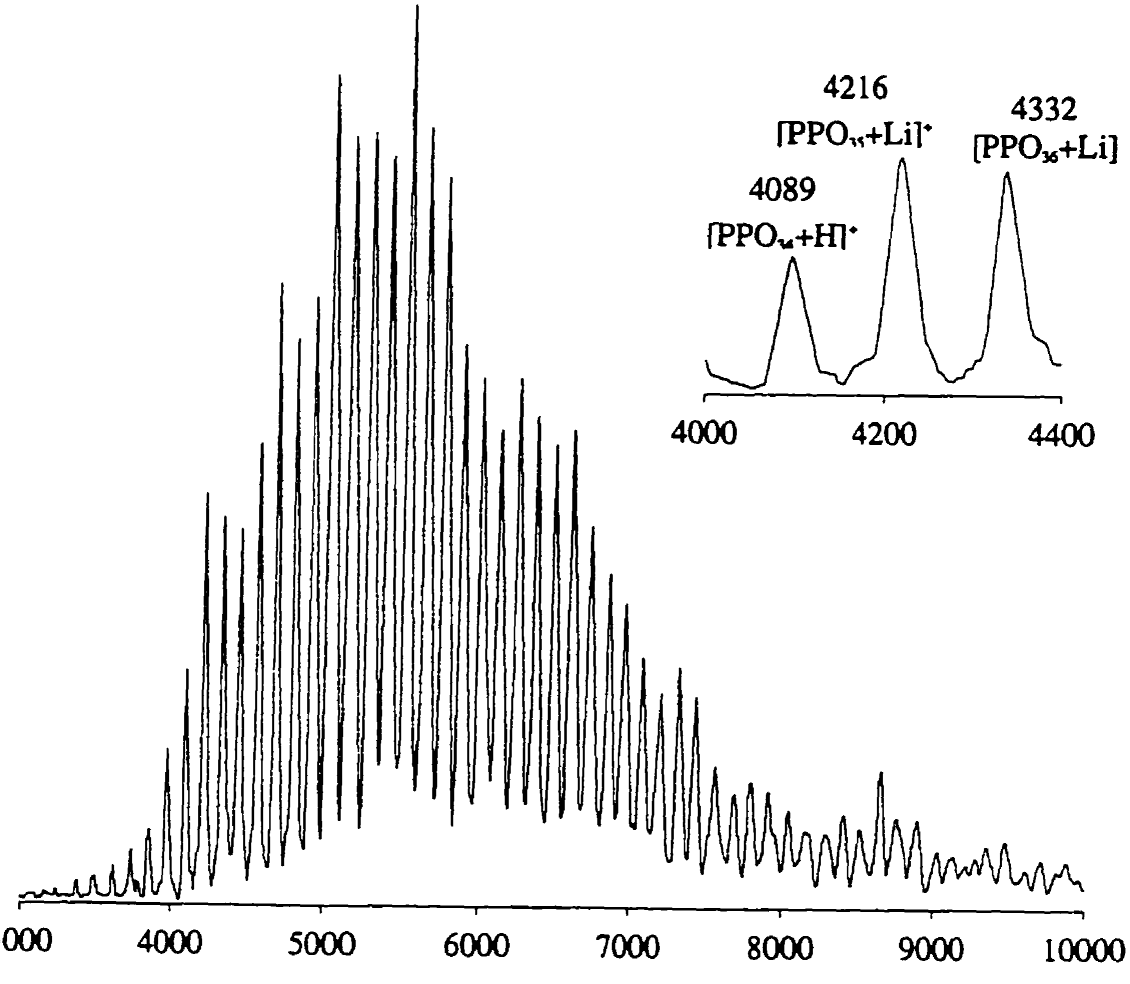


Figure B1.20. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η= 0.19) using dithranol and oxalic acid (1:23:1).

Table B1.13. Mass listing for figure B1.20.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
33	$[PPO_{33}+Li]^+$	3971	3973	0.05
34	$[PPO_{34}+H]^+$	4089	4088	0.02
35	$[PPO_{35}+Li]^+$	4216	4214	0.05
36	$[PPO_{36}+Li]^+$	4332	4334	0.05
37	$[PPO_{37}+H]^+$	4449	4449	0.00
38	$[PPO_{38}+H]^+$	4570	4569	0.02
39	$[PPO_{39}+H]^+$	4690	4688	0.04
40	$[PPO_{40}+H]^+$	4810	4809	0.02
41	$[PPO_{40}+H]^+$	4930	4929	0.02
42	$[PPO_{42}+H]^+$	5048	5049	0.02
43	$[PPO_{43}+H]^+$	5171	5170	0.02
44	$[PPO_{44}+H]^+$	5291	5290	0.02
45	$[PPO_{45}+H]^+$	5412	5410	0.04
46	$[PPO_{46}+H]^+$	5528	5530	0.04
47	$[PPO_{47}+H]^+$	5650	5650	0.00
48	$[PPO_{48}+H]^+$	5769	5770	0.02
49	$[PPO_{49}+Li]^+$	5893	5896	0.05
50	$[PPO_{50}+H]^+$	6012	6011	0.02
51	$[PPO_{51}+H]^+$	6128	6131	0.05
52	$[PPO_{52}+H]^+$	6253	6251	0.03
53	$[PPO_{53}+H]^+$	6372	6371	0.02
54	$[PPO_{54}+H]^+$	6491	6491	0.00
55	$[PPO_{55}+H]^+$	6608	6611	0.05
56	$[PPO_{56}+H]^+$	6731	6732	0.01
57	$[PPO_{57}+H]^+$	6849	6852	0.04
58	$[PPO_{58}+H]^+$	6969	6972	0.04
59	$[PPO_{59}+H]^+$	7088	7092	0.06
60	$[PPO_{60}+H]^+$	7208	7212	0.06
61	$[PPO_{61}+H]^+$	7329	7332	0.04
62	$[PPO_{62}+H]^+$	7445	7452	0.09
63	$[PPO_{63}+H]^+$	7571	7572	0.01
64	$[PPO_{64}+H]^+$	7693	7693	0.00
65	$[PPO_{65}+H]^+$	7805	7813	0.10

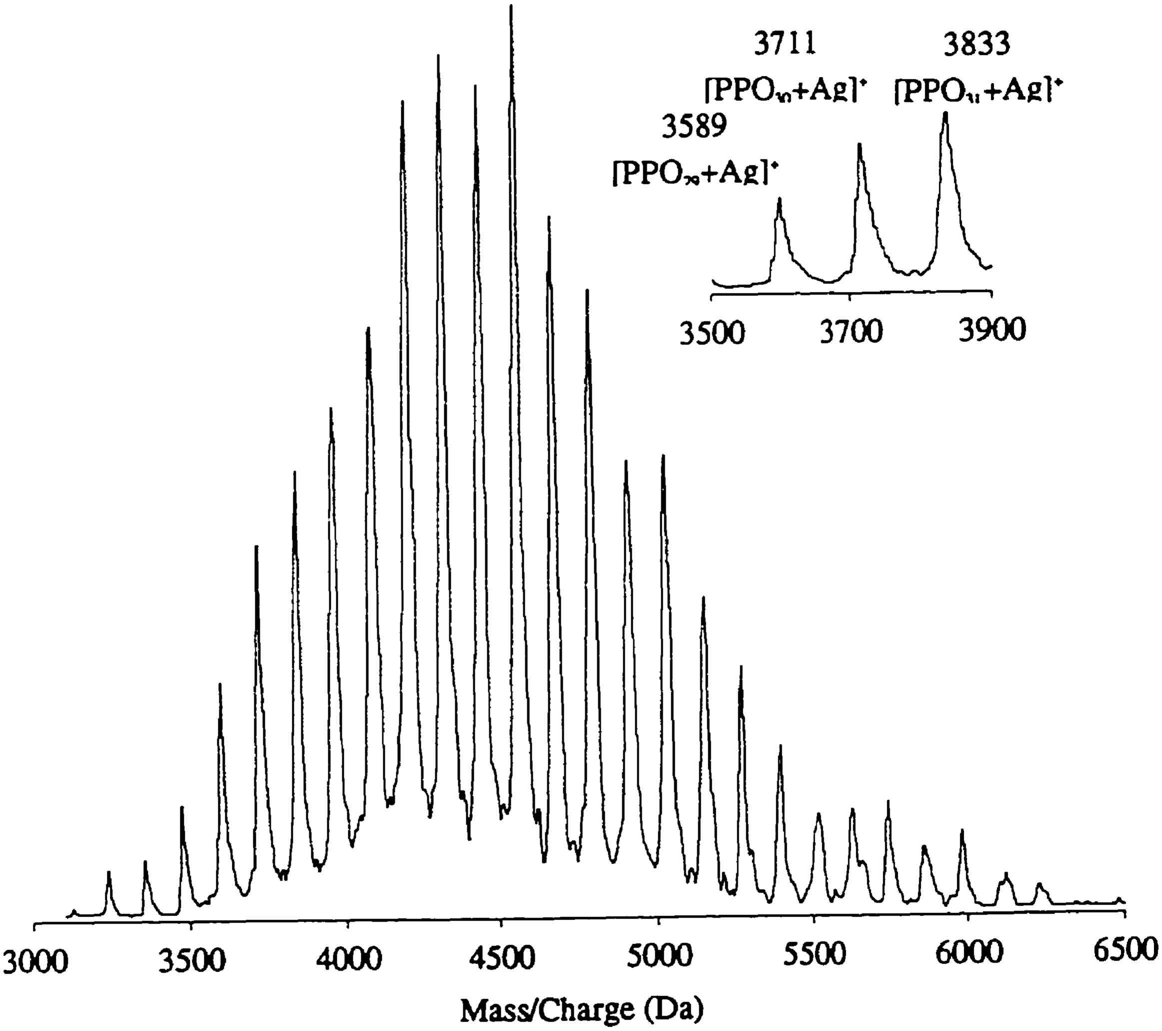


Figure B1.21. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.19) using dithranol and AgTFA (1:23:0.1).

Table B1.14. Mass listing for figure B1.21.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
26	$[PPO_{26}+Ag]^+$	3234	3234	0.00
27	$[PPO_{27}+H]^+$	3350	3354	0.12
28	$[PPO_{28}+Li]^+$	3469	3474	0.14
29	$[PPO_{29}+Li]^+$	3589	3594	0.14
30	$[PPO_{30}+H]^+$	3711	3714	0.08
31	$[PPO_{31}+H]^+$	3833	3835	0.05
32	$[PPO_{32}+H]^+$	3950	3955	0.13
33	$[PPO_{33}+H]^+$	4072	4075	0.07
34	$[PPO_{34}+H]^+$	4192	4195	0.07
35	$[PPO_{35}+H]^+$	4314	4315	0.02
36	$[PPO_{36}+H]^+$	4433	4435	0.05
37	$[PPO_{37}+H]^+$	4552	4556	0.09
38	$[PPO_{38}+H]^+$	4671	4676	0.11
39	$[PPO_{39}+H]^+$	4792	4796	0.08
40	$[PPO_{40}+H]^+$	4910	4916	0.12
41	$[PPO_{41}+H]^+$	5030	5036	0.12
42	$[PPO_{42}+Li]^+$	5154	5156	0.04
43	$[PPO_{43}+H]^+$	5270	5276	0.11
44	$[PPO_{44}+H]^+$	5394	5396	0.04
45	$[PPO_{45}+H]^-$	5521	5517	0.07
46	$[PPO_{46}+H]^+$	5632	5637	0.09
47	$[PPO_{47}+H]^+$	5750	5767	0.29
48	$[PPO_{48}+H]^+$	5865	5877	0.20
49	$[PPO_{49}+H]^+$	5987	5997	0.17
50	$[PPO_{50}+H]^+$	6127	6117	0.16

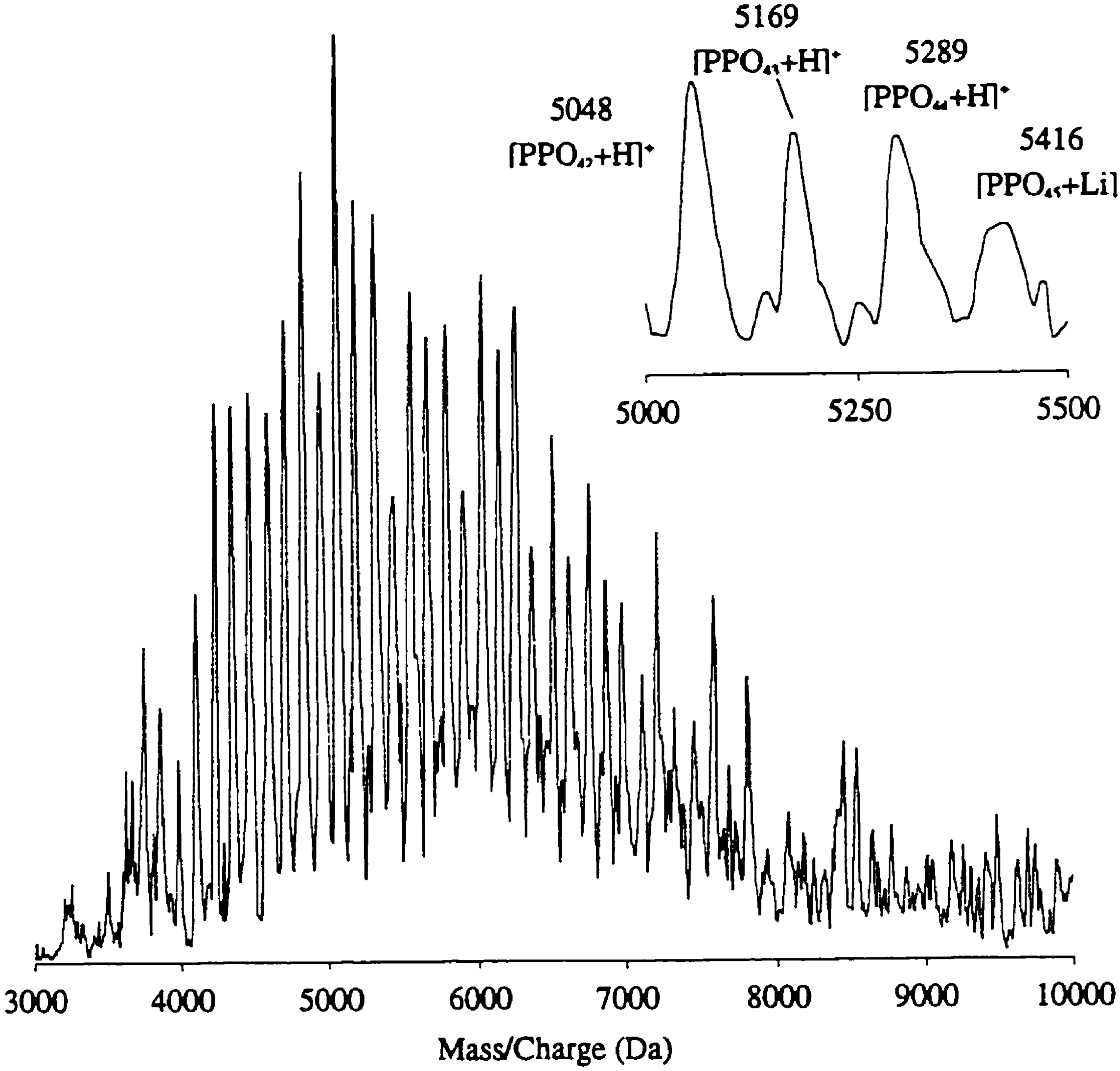


Figure B1.22. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.19) using dithranol, oxalic acid and TTP (1:23:1:1).

Table B1.15. Mass listing for figure B1.22.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
30	$[PPO_{30}+H]^+$	3608	3608	0.00
30	$[PPO_{30}+Na]^+$	3628	3630	0.06
30	$[PPO_{30}+K]^+$	3652	3646	0.16
31	$[PPO_{31}+Li]^+$	3741	3734	0.19
32	$[PPO_{32}+H]^+$	3848	3848	0.00
32	$[PPO_{32}+Na]^+$	3871	3870	0.03
33	$[PPO_{33}+H]^+$	3965	3968	0.08
34	$[PPO_{34}+H]^+$	4090	4088	0.05
35	$[PPO_{35}+Li]^+$	4220	4214	0.14
36	$[PPO_{36}+H]^+$	4330	4328	0.05
37	$[PPO_{37}+H]^+$	4450	4449	0.02
38	$[PPO_{38}+H]^+$	4571	4569	0.04
39	$[PPO_{39}+H]^+$	4692	4689	0.06
40	$[PPO_{40}+Li]^+$	4815	4815	0.00
41	$[PPO_{41}+Li]^+$	4933	4935	0.04
42	$[PPO_{42}+H]^+$	5048	5049	0.02
43	$[PPO_{43}+H]^+$	5169	5170	0.02
44	$[PPO_{44}+H]^+$	5289	5290	0.02
45	$[PPO_{51}+Li]^+$	5416	5416	0.00
46	$[PPO_{46}+Li]^+$	5537	5536	0.02
47	$[PPO_{47}+Li]^+$	5655	5656	0.02
48	$[PPO_{48}+Li]^+$	5784	5776	0.14
49	$[PPO_{49}+H]^+$	5888	5890	0.03
50	$[PPO_{50}+Li]^+$	6016	6016	0.00
51	$[PPO_{51}+Li]^+$	6138	6137	0.02
52	$[PPO_{52}+H]^+$	6252	6251	0.02
53	$[PPO_{53}+H]^+$	6357	6371	0.22
54	$[PPO_{54}+Li]^+$	6496	6497	0.02
55	$[PPO_{55}+H]^+$	6611	6611	0.00
56	$[PPO_{56}+Na]^+$	6751	6753	0.03
57	$[PPO_{57}+Li]^+$	6863	6858	0.07
58	$[PPO_{58}+H]^+$	6970	6972	0.03
59	$[PPO_{59}+Na]^+$	7110	7114	0.06
60	$[PPO_{60}+H]^+$	7212	7212	0.00
61	$[PPO_{61}+H]^+$	7321	7332	0.15
62	$[PPO_{62}+H]^+$	7448	7452	0.05
63	$[PPO_{63}+H]^+$	7802	7812	0.13
64	$[PPO_{64}+Na]^+$	8441	8436	0.06

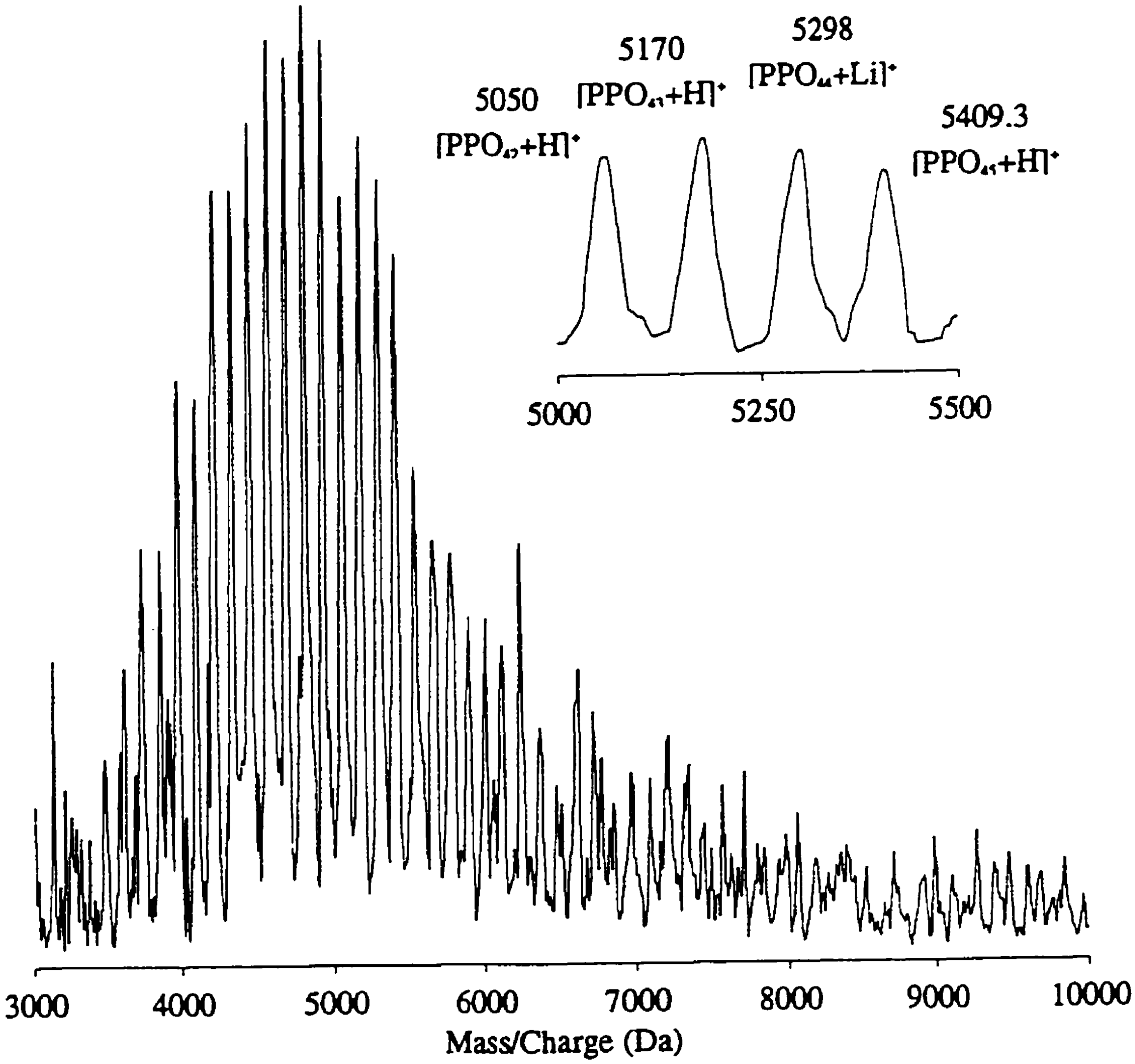


Figure B1.23. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.19) using dithranol, AgTFA, and TTP (1:20:1:2).

Table B1.16. Mass listing for figure B1.23.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
25	$[PPO_{25}+H]^+$	3008	3007	0.03
26	$[PPO_{26}+H]^+$	3126	3127	0.03
26	$[PPO_{26}+Ag]^+$	3238	3234	0.12
27	$[PPO_{27}+Li]^+$	3253	3253	0.00
27	$[PPO_{27}+Na]^+$	3277	3269	0.24
28	$[PPO_{28}+H]^+$	3365	3367	0.06
29	$[PPO_{29}+H]^+$	3481	3487	0.17
30	$[PPO_{30}+H]^+$	3605	3608	0.08
30	$[PPO_{30}+K]^+$	3658	3646	0.33
31	$[PPO_{31}+H]^+$	3727	3728	0.03
32	$[PPO_{32}+Li]^+$	3852	3854	0.05
33	$[PPO_{33}+H]^+$	3970	3968	0.05
34	$[PPO_{34}+H]^+$	4088	4088	0.00
35	$[PPO_{35}+H]^+$	4209	4208	0.02
36	$[PPO_{36}+H]^+$	4330	4328	0.05
37	$[PPO_{37}+H]^+$	4450	4449	0.02
38	$[PPO_{38}+Li]^+$	4574	4575	0.02
39	$[PPO_{39}+H]^+$	4691	4689	0.04
40	$[PPO_{40}+H]^+$	4810	4809	0.02
41	$[PPO_{41}+H]^+$	4928	4929	0.02
42	$[PPO_{42}+H]^+$	5050	5049	0.02
43	$[PPO_{43}+H]^+$	5170	5170	0.00
44	$[PPO_{44}+Li]^+$	5297	5296	0.02
45	$[PPO_{51}+H]^+$	5409	5410	0.02
46	$[PPO_{46}+Li]^+$	5534	5536	0.04
47	$[PPO_{47}+H]^+$	5648	5650	0.04
48	$[PPO_{48}+H]^+$	5772	5770	0.03
49	$[PPO_{49}+Li]^+$	5898	5896	0.03
50	$[PPO_{50}+H]^+$	6008	6010	0.03
51	$[PPO_{51}+H]^+$	6124	6131	0.11
52	$[PPO_{52}+H]^+$	6247	6251	0.06
53	$[PPO_{53}+Li]^+$	6382	6377	0.08
54	$[PPO_{54}+Na]^+$	6519	6514	0.08
55	$[PPO_{55}+Na]^+$	6628	6633	0.08
56	$[PPO_{56}+H]^+$	6730	6732	0.03
56	$[PPO_{56}+Ag]^+$	6836	6838	0.03
57	$[PPO_{57}+Li]^+$	6865	6858	0.10
58	$[PPO_{58}+H]^+$	6974	6972	0.03
59	$[PPO_{59}+H]^+$	7091	7092	0.01
60	$[PPO_{60}+H]^+$	7208	7212	0.06

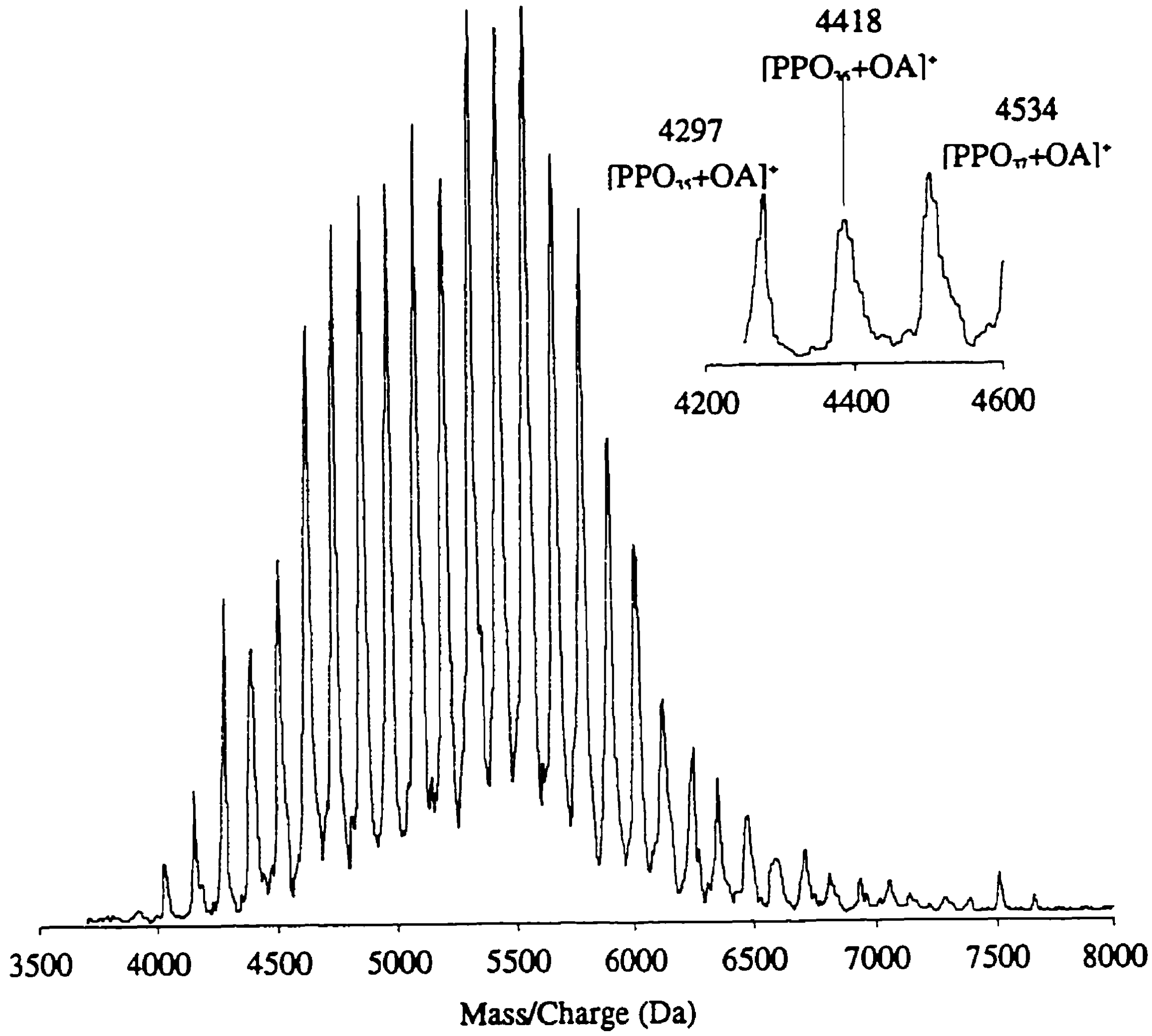


Figure B1.24. MALDI-TOF-MS spectrum in the positive linear mode of PPO ($\eta = 0.19$) using dithranol, oxalic acid and PS 4075 (1:50:1:1).

Table B1.17. Mass listing for figure B1.24.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
32	$[PPO_{32}+OA]^+$	3933	3937	0.10
33	$[PPO_{33}+OA]^+$	4058	4057	0.02
34	$[PPO_{34}+OA]^+$	4188	4177	0.26
35	$[PPO_{35}+OA]^+$	4297	4297	0.00
36	$[PPO_{36}+OA]^+$	4414	4417	0.07
37	$[PPO_{37}+OA]^+$	4534	4538	0.09
38	$[PPO_{38}+OA]^+$	4651	4658	0.15
39	$[PPO_{39}+OA]^+$	4773	4778	0.10
40	$[PPO_{40}+OA]^+$	4891	4898	0.14
41	$[PPO_{40}+OA]^+$	5007	5018	0.22
42	$[PPO_{42}+OA]^+$	5129	5138	0.18
43	$[PPO_{43}+OA]^+$	5250	5259	0.17
44	$[PPO_{44}+OA]^+$	5365	5379	0.26
45	$[PPO_{45}+OA]^+$	5482	5499	0.31
46	$[PPO_{46}+OA]^+$	5604	5619	0.27
47	$[PPO_{47}+OA]^+$	5724	5739	0.26
48	$[PPO_{48}+OA]^+$	5841	5859	0.31
49	$[PPO_{49}+OA]^+$	5959	5979	0.33
50	$[PPO_{50}+OA]^+$	6076	6100	0.39
51	$[PPO_{51}+OA]^+$	6208	6220	0.19
52	$[PPO_{52}+OA]^+$	6311	6340	0.46
53	$[PPO_{53}+OA]^+$	6440	6460	0.31
54	$[PPO_{54}+OA]^+$	6558	6580	0.33
55	$[PPO_{55}+OA]^+$	6681	6700	0.28
56	$[PPO_{56}+OA]^+$	6798	6820	0.32
57	$[PPO_{57}+OA]^+$	6918	6941	0.33
58	$[PPO_{58}+OA]^+$	7038	7061	0.33
59	$[PPO_{59}+OA]^+$	7158	7181	0.32
60	$[PPO_{60}+OA]^+$	7276	7301	0.34
61	$[PPO_{61}+OA]^+$	7400	7421	0.28

OA: represents oxalic acid.

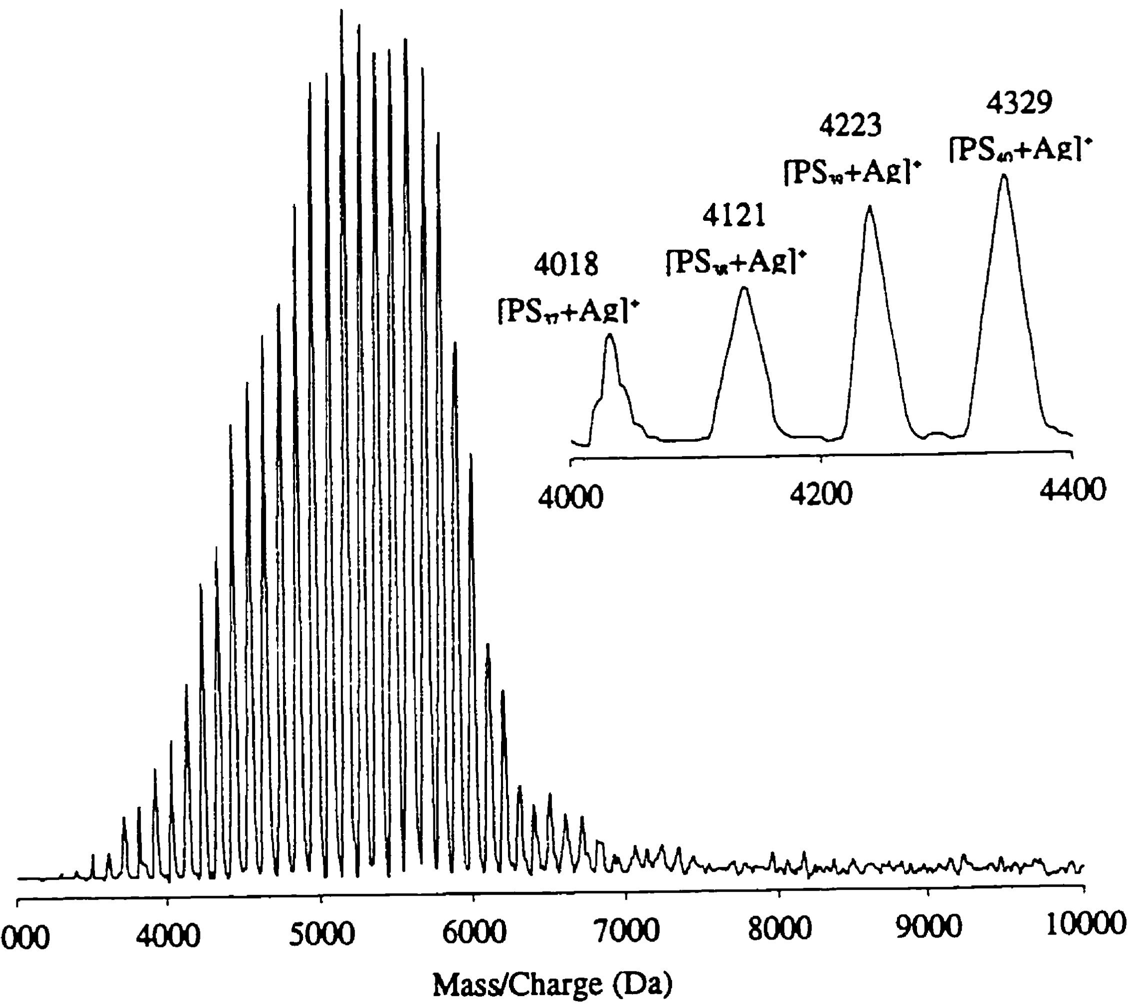


Figure B1.25. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.19) using dithranol, AgTFA, and PS 4075 (1:50:0.2:1).

Table B1.18. Mass listing for figure B1.25.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
32	$[PS_{32}+Ag]^+$	3497	3493	0.12
33	$[PS_{33}+Ag]^+$	3600	3597	0.09
34	$[PS_{34}+Ag]^+$	3708	3701	0.19
35	$[PS_{35}+Ag]^+$	3808	3805	0.08
36	$[PS_{36}+Ag]^+$	3912	3909	0.08
37	$[PS_{37}+Ag]^+$	4018	4013	0.13
38	$[PS_{38}+Ag]^+$	4121	4117	0.10
39	$[PS_{39}+Ag]^+$	4223	4221	0.05
40	$[PS_{40}+Ag]^+$	4329	4325	0.10
41	$[PS_{41}+Ag]^+$	4433	4429	0.09
42	$[PS_{42}+Ag]^+$	4538	4533	0.11
43	$[PS_{43}+Ag]^+$	4642	4637	0.11
44	$[PS_{44}+Ag]^+$	4746	4741	0.11
45	$[PS_{45}+Ag]^+$	4850	4845	0.11
46	$[PS_{46}+Ag]^+$	4954	4949	0.10
47	$[PS_{47}+Ag]^+$	5060	5053	0.14
48	$[PS_{48}+Ag]^+$	5163	5157	0.12
49	$[PS_{49}+Ag]^+$	5266	5261	0.10
50	$[PS_{50}+Ag]^+$	5374	5365	0.17
51	$[PS_{51}+Ag]^+$	5475	5469	0.11
52	$[PS_{52}+Ag]^+$	5580	5573	0.13
53	$[PS_{53}+Ag]^+$	5683	5677	0.11
54	$[PS_{54}+Ag]^+$	5788	5781	0.12
55	$[PS_{55}+Ag]^+$	5891	5885	0.10
56	$[PS_{56}+Ag]^+$	5998	5989	0.15
57	$[PS_{57}+Ag]^+$	6102	6093	0.15
58	$[PS_{58}+Ag]^+$	6204	6197	0.12
59	$[PS_{59}+Ag]^+$	6309	6301	0.13
60	$[PS_{60}+Ag]^+$	6410	6405	0.08
61	$[PS_{61}+Ag]^+$	6511	6509	0.03
62	$[PS_{62}+Ag]^+$	6618	6613	0.08
63	$[PS_{63}+Ag]^+$	6724	6717	0.11
64	$[PS_{64}+Ag]^+$	6825	6821	0.06

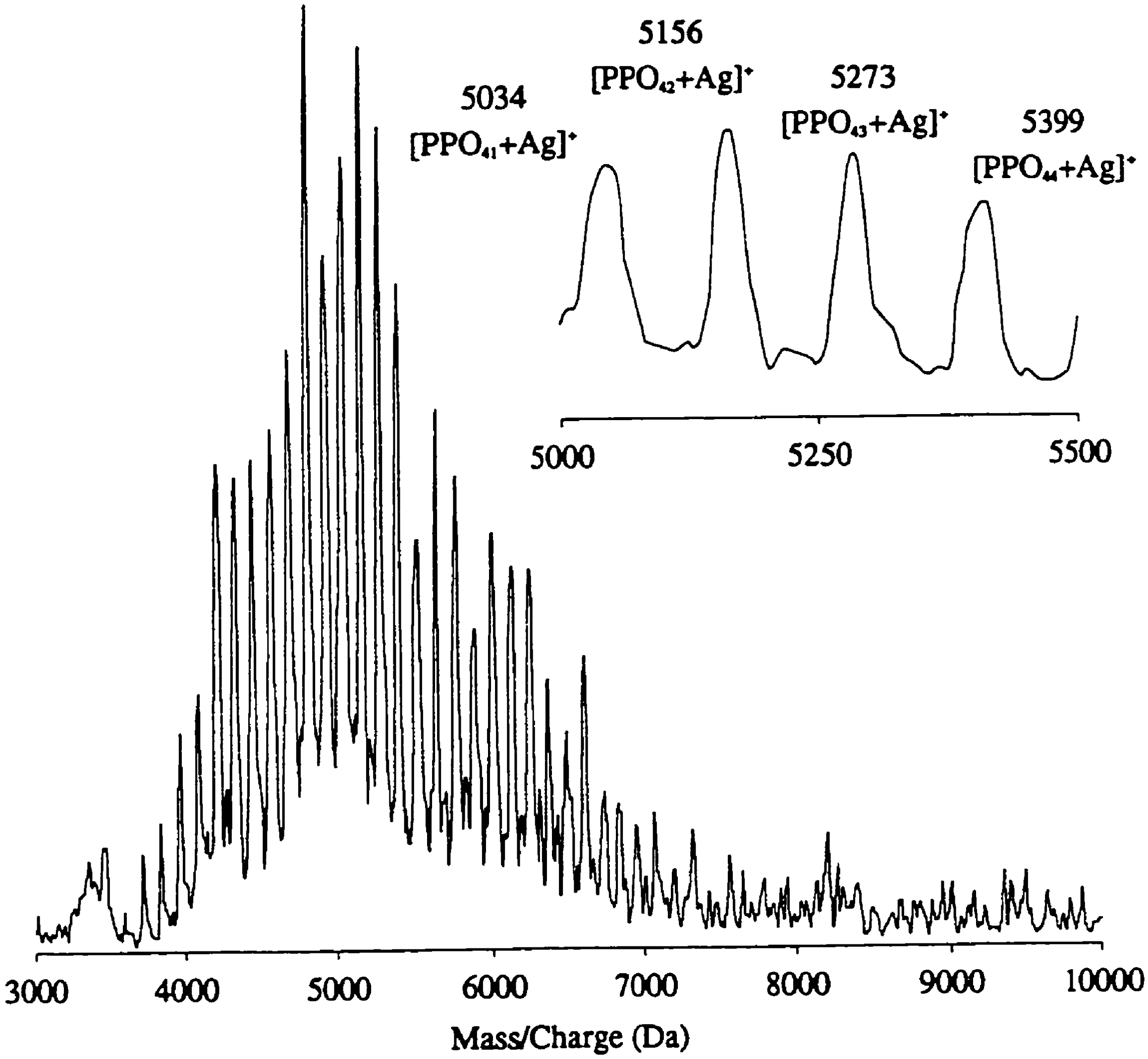


Figure B1.26. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.19) using dithranol, AgTFA, and PS 16700 (1:50:0.2:1).

Table B1.19. Mass listing for figure B1.26.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
30	$[PPO_{30}+Ag]^+$	3712	3714	0.05
31	$[PPO_{31}+Ag]^+$	3834	3834	0.00
32	$[PPO_{32}+Ag]^+$	3960	3954	0.15
33	$[PPO_{33}+Ag]^+$	4086	4075	0.27
34	$[PPO_{34}+Ag]^+$	4200	4195	0.12
35	$[PPO_{35}+Li]^+$	4221	4214	0.17
35	$[PPO_{35}+Ag]^+$	4317	4315	0.05
36	$[PPO_{36}+Ag]^+$	4436	4435	0.02
37	$[PPO_{37}+Ag]^+$	4559	4555	0.09
38	$[PPO_{38}+Ag]^+$	4676	4675	0.02
39	$[PPO_{39}+Ag]^+$	4797	4796	0.02
40	$[PPO_{40}+Ag]^+$	4915	4915	0.00
41	$[PPO_{41}+Ag]^+$	5034	5036	0.04
42	$[PPO_{42}+Ag]^+$	5156	5156	0.00
43	$[PPO_{43}+Ag]^+$	5273	5276	0.06
44	$[PPO_{44}+Ag]^+$	5399	5396	0.06
45	$[PPO_{45}+Ag]^+$	5521	5517	0.07
46	$[PPO_{46}+Ag]^+$	5636	5637	0.02
47	$[PPO_{47}+Ag]^+$	5758	5757	0.02
48	$[PPO_{48}+Ag]^+$	5881	5877	0.07
49	$[PPO_{49}+Ag]^+$	5999	5997	0.03
50	$[PPO_{50}+Ag]^+$	6122	6117	0.08
51	$[PPO_{51}+Ag]^+$	6238	6238	0.00
52	$[PPO_{52}+Ag]^+$	6352	6358	0.09
53	$[PPO_{53}+Ag]^+$	6475	6478	0.05
54	$[PPO_{54}+Ag]^+$	6592	6598	0.09
56	$[PPO_{56}+Ag]^+$	6824	6838	0.20
57	$[PPO_{57}+Ag]^+$	6949	6958	0.13
59	$[PPO_{59}+Ag]^+$	7202	7199	0.04
60	$[PPO_{60}+Ag]^+$	7321	7319	0.03
62	$[PPO_{62}+Ag]^+$	7565	7559	0.08

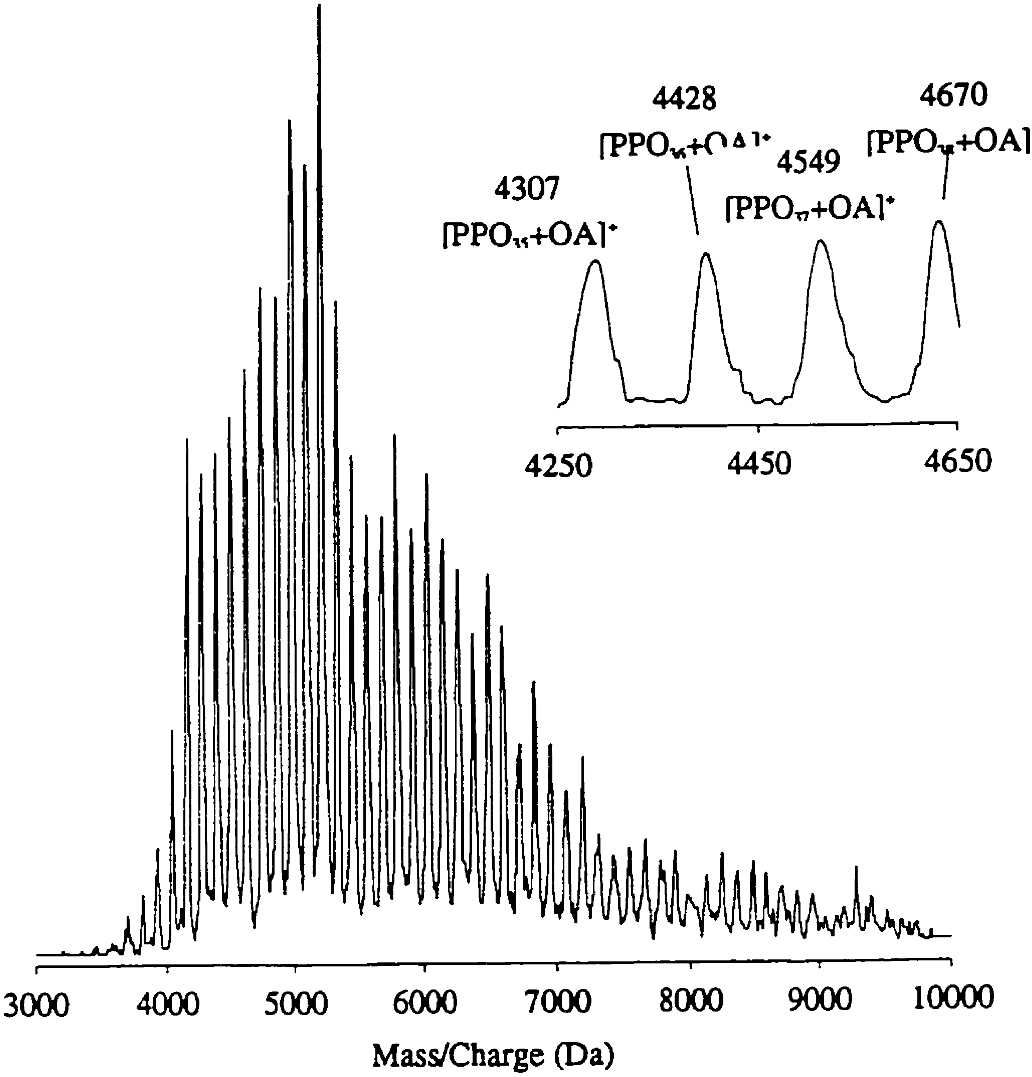


Figure B1.27. MALDI-TOF-MS spectrum in the positive linear mode of PPO (η = 0.25) using dithranol and oxalic acid (1:23:1).

Table B1.20. Mass listing for figure B1.27.

Repeat Unit	Peak Identification	Mass (Da)	Theoretical Mass (g/mol)	Error (%)
30	$[PPO_{30}+OA]^+$	3702	3697	0.14
31	$[PPO_{31}+OA]^+$	3823	3817	0.16
32	$[PPO_{32}+OA]^+$	3944	3937	0.18
33	$[PPO_{33}+OA]^+$	4065	4057	0.20
34	$[PPO_{34}+OA]^+$	4186	4177	0.22
35	$[PPO_{35}+OA]^+$	4307	4297	0.23
36	$[PPO_{36}+OA]^+$	4428	4417	0.25
37	$[PPO_{37}+OA]^+$	4549	4538	0.24
38	$[PPO_{38}+OA]^+$	4670	4658	0.26
39	$[PPO_{39}+OA]^+$	4791	4778	0.27
40	$[PPO_{40}+OA]^+$	4912	4898	0.29
41	$[PPO_{40}+OA]^+$	5033	5018	0.30
42	$[PPO_{42}+OA]^+$	5154	5138	0.31
43	$[PPO_{43}+OA]^+$	5250	5259	0.17
44	$[PPO_{44}+OA]^+$	5372	5379	0.13
45	$[PPO_{45}+OA]^+$	5493	5499	0.11
46	$[PPO_{46}+OA]^+$	5616	5619	0.05
47	$[PPO_{47}+OA]^+$	5735	5739	0.07
48	$[PPO_{48}+OA]^+$	5845	5859	0.24
49	$[PPO_{49}+OA]^+$	5966	5979	0.22
50	$[PPO_{50}+OA]^+$	6087	6100	0.21
51	$[PPO_{51}+OA]^+$	6208	6220	0.19
52	$[PPO_{52}+OA]^+$	6329	6340	0.17
53	$[PPO_{53}+OA]^+$	6450	6460	0.15
54	$[PPO_{54}+OA]^+$	6571	6580	0.14
55	$[PPO_{55}+OA]^+$	6692	6700	0.12
56	$[PPO_{56}+OA]^+$	6813	6820	0.10
57	$[PPO_{57}+OA]^+$	6934	6941	0.10
58	$[PPO_{58}+OA]^+$	7055	7061	0.08
59	$[PPO_{59}+OA]^+$	7176	7181	0.07
60	$[PPO_{60}+OA]^+$	7297	7301	0.05
61	$[PPO_{61}+OA]^+$	7418	7421	0.04
61	$[PPO_{61}+OA]^+$	7539	7421	1.59
62	$[PPO_{62}+OA]^+$	7660	7662	0.03

Table B1.21. Mn values obtained from MALDI-TOF-MS data.

Trail	Matrix	Salt	Acid	TPP	PS (Mw)	Ratio[a]	Mn (Da)
1	dithranol		oxalic			(1:23:1)	5142
2	dithranol		oxalic	yes		(1:23:1:1)	4688
3	dithranol	AgTFA		yes		(1:23:1:2)	4578
4	dithranol	AgTFA				(1:23:0.1)	4395
5	dithranol	AgTFA			4075	(1:50:0.2:1)	4648[b]
6	dithranol		oxalic		4075	(1:50:1:1)	5129
7	dithranol	AgTFA			16700	(1:50:0.2:1)	4954
Average							4814

This assumption appears to be true in the case of oxalic acid because no MALDI-TOF-MS spectrum of PS4075 was obtained under these conditions. However in the case of AgTFA a MALDI-TOF-MS spectra (Figure B1.21,26) of PPO was obtained using dithranol and AgTFA and in a mixture of PS 16700, AgTFA. Even though AgTFA tends to enhance the ionization of PS over PPO as previously seen. This is just another example of how the low molecular weight oligomers ionize more efficiently than the higher molecular weight oligomers. Possible explanations are: 1) PS has a lower ionization potential than PPO, 2) AgTFA has a higher tendency to for charged complexes with PS than PPO, and/or 3) in the presence of AgTFA PS is more effectively solvated than PPO.

The Mn values obtained from GPC and ^{31}P are 8600 g/mol and 5000 g/mol respectively. The average Mn values obtained by ^{31}P NMR and MALDI-TOF-MS (4800 Da) are quite similar indicating that a certain extent we are observing a true representation of the mixture by MALDI-TOF-MS, while the GPC value is quite different (Table B1.22). This again can be explained by the fact that the Mn values obtained by ^{31}P and MALDI-TOF-MS techniques are not influenced by the difference in structural properties of the analyte and standard while GPC is.

Table B1.22. Number average molecular weight of the different PPO oligomers.

η (dL/g)	GPC (g/mol)	31P (g/mol)	MALDI-TOF-MS (Da)
0.19	8600	5000	4800
0.25	10000	8100	5400

A reasonably accurate representation of PPO (η = 0.19) was obtained. Therefore we were interested to see if we could obtain MALDI-TOF-MS spectrum of the higher molecular weight PPO oligomers (η = 0.25) see figure B1.27. The Mn values obtained by GPC, ^{31}P, and MALDI-TOF-MS are 10000 g/mol, 8100 g/mol and 5400 Da, respectively (Table B1.22). The large difference in Mn values between the three methods and the relatively similar Mn values obtained by MALDI-TOF-MS for both PPO oligomers (η = 0.19 and η = 0.25) further emphasize the difficulty in identification of the high molecular weight fractions. We have also been able to determine the upper mass limit of detection by this technique, which is in the range of 5000 to 7000 Da for the polydisperse PPO oligomers we were investigating.

B1.3 Conclusions

The MALDI-TOF-MS technique has had a major impact in the characterization of cyclic oligomers. This includes the identification of the different cyclic oligomers as well as the percentage for the different monomers in cocyclics and the distribution pattern of each cocyclic oligomer. It has also been shown that by characterizing the different fractions obtained from cyclic oligomers **B1.14** a more complete analysis of the cyclic mixture is obtained.

This technique on the other hand was not effective in the analysis of higher molecular weight polydisperse linear polymers. In all the cases studied no true representation of the polymer mixture was observed because in general the higher molecular weight fraction does not ionize. This is clearly shown in the MALDI-TOF-MS spectra of PPO ($\eta = 0.19$) and PPO ($\eta = 0.25$) (Figure B1.20,27) where in both cases the spectrum window and Mn values are similar. Alternative analyses by ^{31}P and GPC demonstrated that these two PPO oligomer have quite different Mn values.

This technique has been shown to be very useful in the identification of end groups, side reactions, etc. It should be kept in mind that some of these impurities represent a very small fraction of the polymer composition. In the case of polymer **B1.17** we obtained signals for oligomers that only account for approximately 5% of the polymer composition.

However, even with these limitations this technique in combination with GPC, HPLC, ^{31}P, and NMR gives the chemist a better understanding of the composition of the linear polymers being studied.

B1.4 Experimental Section

Materials

The matrices and cationizing agents such as lithium bromide (LiBr) and silver trifluoroactate (AgTFA) were purchased from Aldrich Chemical Co. unless otherwise specified. The solvents tetrahydrofuran, methylene chloride, acetone and chloroform were of HPLC grade and obtained from Caledon. The derivatized reagent 1,3,2-dioxaphospholanyl chloride was purchased from Fluka Chemical Co. The cyclic oligomers were synthesized in our laboratory by Dr. Yifeng Wang using the procedure described by K.P Chan and A.S. Hay[24] and the corresponding linear polymer was synthesized in by Dr. R. Singh[25]. PPO samples were supplied by the General Electric Company. All reagents and compounds were used as received.

Instrumentation

Mass spectrometry data was obtained on a Kratos Kompact MALDI III instrument equipped with a time of flight spectrometer which can be operated either in the linear or reflectron mode with flight paths of 0.91 m or 2.73 m respectively. The laser used is a nitrogen laser set at a wavelength of 337 nm with a pulse length of 3 ns. The extraction voltage on this instrument is either 5 of 25 kV. Normally all MALDI-TOF-MS spectra were obtained from an accumulation of 100 laser shots for the cyclic oligomer and 300 laser shots for the polymer set at an extraction voltage of 25 kV. All ^{31}P analyses were obtained on a Varian Unity 500 MHz spectrometer. GPC analyses were performed on a Waters 510 instrument equipped with a UV detector set at 254 nm and four 5 µm phenogel columns (3 x 500 Å, linear) arranged in series. Chloroform was used as the solvent and all molecular weights are referenced to polystyrene standards.

Sample Preparation

A series of sample preparation procedures were undertaken in order to determine the optimal conditions for the analysis of high performance materials. They are:

1) Premixing

The analyte and matrix solutions are mixed together in a solvent and approximately 0.5 to 1 ul of the solution is added to the sample slide and left to air dry.

2) Melt

A solution of analyte containing a total amount of 1 mg was added to a mixture of m-terphenyl (100 mg) and matrix (100 mg) and preheated to 100 °C. Heating was continued for another 10 - 15 min. The mixture was then applied to a preheated sample slide using a pipette (an unknown quantity was added) and the slide was left to cool down to room temperature.

3) Film Formation

In this procedure the goal was form a clear film on the sample slide. This was achieved by dissolving the analyte and matrix in tetrachloroethane and applying approximately 0.5 to 1 ul of the solution to the sample slide. The slide was baked in an oven at 90 °C for two hours.

4) Addition of plasticizer

A similar procedure to sample preparation 1 with the exception that tritolylphosphate (TTP) is added to the solution in quantities of 20 to 200 % by weight of the analyte.

5) Mixture with Polystyrene (PS 4075 and PS 16700)

A similar procedure to sample preparation 1 with the exception that an equal amount by weight of PS to analyte is added to the original solution.

6) Addition of Strong acid and/or cationizing agent

A similar procedure to sample preparation 1, although in this case either a strong acid or cationizing agent or a combination of both are added to the mixture in quantities of 20 % to 100 % by weight of the analyte.

7) Mixture of matrices

A similar procedure to sample preparation 1, have instead of using one matrix a combination of two or more matrices are used in different quantities.

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Contributions to Knowledge

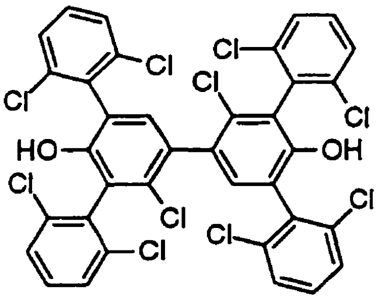
Phenoxy radicals have been extensively studied, though the stability of these phenoxy radicals limits their use in organic reactions. One of the contributions of this research was to develop stable biphenoxy radicals which can be used as reagents in organic reactions. This was accomplished by synthesizing a series of hindered biphenols with bulky groups in the meta position of the biphenyl moiety.

These biphenoxy radicals quantitatively couple with a variety of molecules containing activated methylene groups resulting in novel ether and acetal monomers that are cleaved under acidic condition. It is these reactions that make the biphenoxy radicals interesting reagents in the protection of methylene groups, and in the quantitative deprotection of benzylic, substituted benzylic and t-butyl groups, which the currently used reagent DDQ cannot accomplish. In all the reactions the biphenol is completely recovered, though column chromatography was necessary to purify the mixture. To simplify the purification step poly(aryl ether)s containing the biphenoxy moiety incorporated in the backbone were prepared and successfully used as polymeric supports. The fact that the coupling and cleavage reaction were quantitative led to the synthesis of carbon - oxygen coupled polymers that have shown potential as photoresist materials.

In general harsh experimental conditions have been used in the oxidation of diphenylmethane to benzophenone. With our hindered biphenols, only a catalytic amount of biphenol is required and the reactions are performed under mild conditions, CuCl, oxygen, butyronitrile at 90°C for a few hours. Conversions of 80% or greater are obtained with diphenylmethane and its substituted derivatives. This chemistry was applied to the oxidation of cyclic oligomers and polymers containing diphenylmethane moieties. Conversions in the range of 70 % to 100 % were obtained without degradation of the cyclic oligomers or polymer chains.

The low percent conversions obtained in the oxidation are due to the consumption of the biphenoxy radical by either an intramolecular cyclization reaction to the dibenzofuran compound also observed in the radical coupling reaction, or by a carbon - oxygen coupling reaction to the ether compound. Initially we believe that deactivating the pendent phenyl group by substituting the phenyl ring with an electron withdrawing group one should suppress the intramolecular cyclization reaction. This was not the case, since quinones **A2.14g** (the pendent groups are 4-fluorophenyl) and **A2.14f** (the pendent groups are phenyl) cyclized at approximately the same rate (see Chapter A2).

A possible solution in preventing the intramolecular reaction from occurring is by the synthesis of biphenols where the ortho position of the pendent phenyls at position 3 and 5 are blocked, for example with a chloro group **1**. This serves two purposes; 1) it further forces the pendent phenyl at position 3 into a nonplanar configuration which would reduce accessibility of the reactive site, 2) the large chloro groups should block the ortho position preventing attack of the oxygen radical.



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With the development of a more stable biphenoxy radical, this catalytic oxidation method should lead to a simpler synthesis of PEEK®, a commercially important high performance polymer.

In the final chapter B1 the new technique of Matrix Assisted Laser Desorption Ionization - Time of Flight - Mass Spectrometry (MALDI - TOF - MS) was used in the characterization of polydisperse polymers and cyclic oligomers. Low molecular weight polydisperse PPO® resins were correctly identified up to 5000 Da using a series of new matrices and sample preparation techniques. The cyclic oligomers were identified up to 15000 Da. We were also able to correctly determine the percentage content of each of the monomers in the cocyclics based on the peak intensity of the individual cyclic oligomers.

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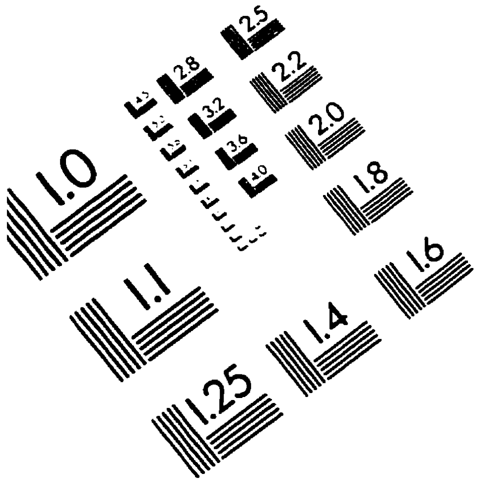

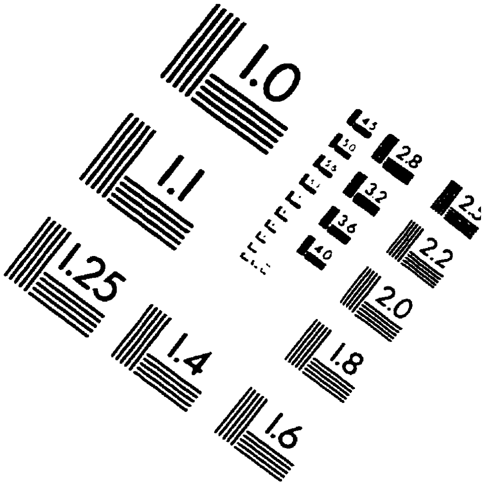

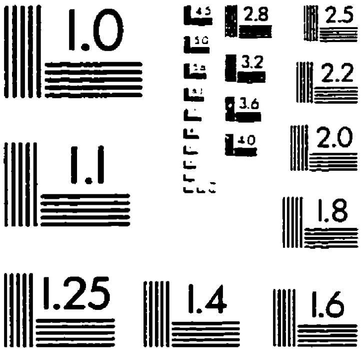

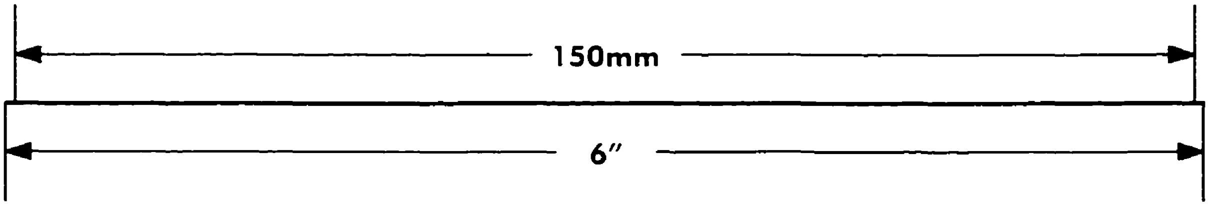

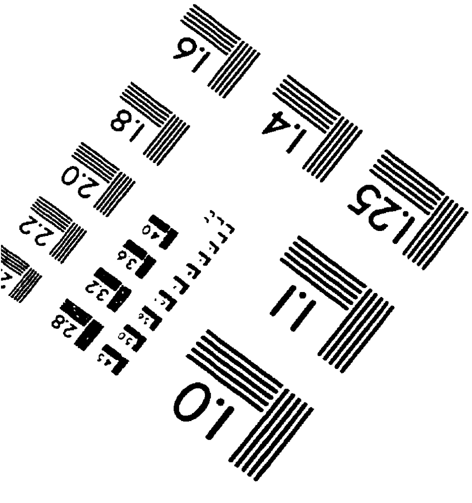

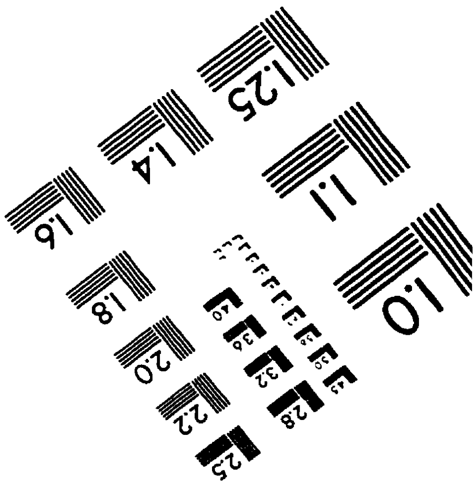

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