

**SYNTHESIS OF AN ACTIVATED DIFLUOROTETRAKETONE MONOMER
VIA REISSERT CHEMISTRY**

by

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MASTER OF SCIENCE

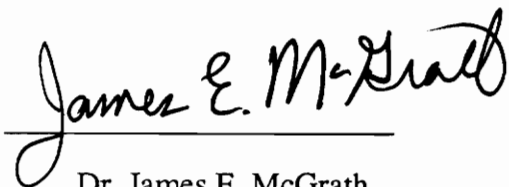
in

Chemistry

APPROVED:



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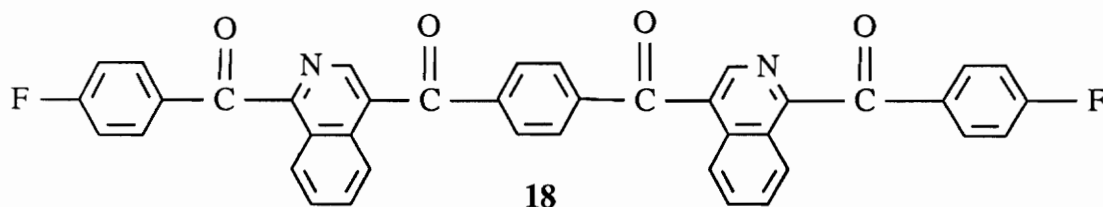
Committee Chairman: Dr. Harry W. Gibson

Chemistry

(ABSTRACT)

The chemistry of Reissert compounds has been utilized to synthesize an activated difluorotetraketone monomer,

1,4-bis{1-[4-(*p*-fluorobenzoyl)isoquinoly]carbonyl}benzene (**18**). Two synthetic routes were explored in an attempt to find an efficient means of preparation. These routes entail preparation via a dibenzylic bis(isoquinoline) and a diketone bis(isoquinoline) system. These compounds were converted to their corresponding Reissert compounds. Reaction of the anion of the dibenzylic Reissert compound with *p*-fluorobenzaldehyde, followed by oxidation of both benzylic sites has produced the novel difluorotetraketone monomer. In addition, rearrangement of the diketone Reissert compound has produced the novel difluorotetraketone monomer. This monomer offers a route to a novel family of poly(heteroarylene ethers).



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To My Parents
and
In Loving Memory Of My Grandfather,
Charlie Holmes

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I. INTRODUCTION

The field of polymer science is rapidly expanding and changing every aspect of day to day living. Once only seen in the production of a few materials, polymers can now be found everywhere from polystyrene cups and plastic bags to silicone heart valves and polyurethane plastic for artificial hearts. Let's face it; we live in a polymer age.

One of the most interesting class of polymers is the heterocyclic polymers. These polymers exhibit excellent thermal stability and mechanical properties and are often used as high performance structure adhesives in aerospace applications. The heterocyclic moiety is usually incorporated into the polymer backbone via a high temperature two-step process. However, heterocyclic rings can also be incorporated into the polymer backbone via the chemistry of Reissert compounds.

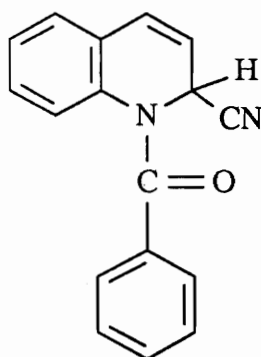
The work described in this thesis utilizes this process to produce an isoquinoline based A-A monomer. This monomer provides potential for a family of novel high performance poly(heteroarylene ether).

II. HISTORICAL BACKGROUND

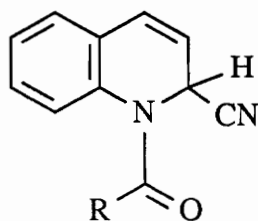
II-1. Reissert Compounds

Reissert compounds [α -(acylamino)nitriles] are a very interesting class of compounds that were discovered in 1905 by Arnold Reissert.¹ Reissert observed that when quinoline reacted with benzoyl chloride in the presence of aqueous potassium cyanide, the reaction yielded a crystalline compound,

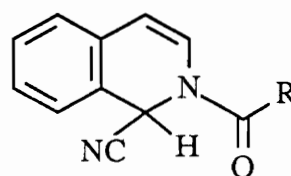
1-benzoyl-1,2-dihydroquinaldonitrile (**1**). Since that time various nitrogen heterocycles, such as pyridine, benzimidazole, and phenanthridine have been shown to produce products analogous to **1** upon reaction with an acid chloride and potassium or hydrogen cyanide. The most studied cases are the quinoline and isoquinoline Reissert compounds, i.e. 1-acyl-1,2-dihydroquinaldonitriles (**2**) and 2-acyl-1,2-dihydroisoquinaldonitriles (**3**).



1



2



3

Reissert compounds are the result of the addition of an acyl cyanide across the carbon-nitrogen double bond of a nitrogen containing heterocycle. First, the nitrogen of the imine is acylated to form the acylimium salt. Then the nucleophile, i.e. cyanide, attacks the carbon of the imine to form the Reissert compound.

Several methods have been developed for the preparation of Reissert compounds. These include preparation via aqueous media, non-aqueous media (single phase), and a methylene chloride-water (two phase) method. The aqueous method, developed by Reissert¹, utilizes conditions similar to those of the Schotten-Baumann procedure to prepare Reissert compounds. The heterocycle is reacted with an acid chloride in an aqueous solution of potassium cyanide. 1-Benzoyl-1,2-dihydroquinolidonitrile (**1**) was originally prepared by this method in quantitative yield. However, the preparation of 2-benzoyl-1,2-dihydroisoquinolidonitrile (**3**, R=C₆H₅) via this method was not effective. The aqueous method has the disadvantage that both starting material and product are insoluble in water. In addition, only unreactive acid chlorides can be employed. Reactive aroyl chlorides and aliphatic acid chlorides tend to hydrolyze.

Since one of the major disadvantages of the aqueous method was hydrolysis of reactive acid chlorides, a non-aqueous method was developed in an attempt to eliminate this problem. This method involves the use of hydrogen cyanide and anhydrous benzene as non-aqueous solvents.³ Due to drawbacks associated with the use of hydrogen cyanide, this non-aqueous method is not a method of choice. However, it has proven to be quite successful in the preparation of Reissert compounds from aliphatic and aromatic acid chlorides.

Another non-aqueous procedure employs trimethylsilyl cyanide (TMSCN) as a cyanide source.⁴ The heterocycle is reacted with an acid chloride in either methylene chloride or dimethylformamide. A catalytic amount of aluminum chloride has proven advantageous.^{5,6} This method, like HCN/benzene, prevents hydrolysis of reactive acid chlorides as well as pseudobase formation where the hydroxide ion attacks instead of the cyanide ion. Reactive aroyl and alkanoyl halides can be employed and in many cases afford quantitative yields. Even though excellent yields are obtained using this method, disadvantages lie in the high cost and toxicity of trimethylsilyl cyanide and length of

reaction time (sometimes several days) necessary for reaction. A more recent non-aqueous procedure uses diethylaluminum cyanide (Et_2AlCN) as a cyanide source.⁷

The most conventional and inexpensive method for the preparation of Reissert compounds was developed in 1961 by Popp and Blount.⁸ This method employs a methylene chloride-water solvent system. The heterocycle is dissolved in methylene chloride and a 3-fold excess of an aqueous solution of potassium cyanide is added. A two-fold excess of the acid chloride is then added over a 2-4 hour period. Even though this method does not give yields comparable to those of the TMSCN method, it is quite inexpensive and starting materials are readily available. Most aroyl halides can be used in this method. However when reactive acid chlorides are used, a competitive hydrolysis occurs, thus producing low yields. A comparison of the methods used in the preparation of Reissert compounds is shown in Table 1.

Table 1. Comparison of Methods of Preparation of Reissert Compounds

<u>Reissert Compound</u>	<u>Yield (%)</u>		
	<u>aq.^a</u>	<u>non-aq.^b</u>	<u>CH₂Cl₂/ H₂O^c</u>
2, R=C ₆ H ₅	87 ⁹	96 (1) ⁹	70 ¹⁰
		42 (3) ⁷	
3, R=C ₆ H ₅	58 ⁹	84 (2) ⁴	58 ¹⁰
2, R=CH ₃	--- ^d	74 (1) ⁹	50 ¹⁰
3, R=CH ₃	---	84 (1) ⁹	87 ¹⁰
3, R=OCH ₂ CH ₃	---	88 (2) ⁴	57 ³⁵
		74 (3) ⁷	
3, R= <i>p</i> -NO ₂ C ₆ H ₄	---	30 (3) ⁷	3 ¹⁰
2, R= <i>p</i> -NO ₂ C ₆ H ₄	---	0 (1) ⁹	3 ¹⁰
2, R= <i>p</i> -CH ₃ OC ₆ H ₄	51 ⁹	88 (1) ⁹	80 ¹⁰

^aaq.: aqueous method

^bnon-aq.: non-aqueous method: (1) HCN/benzene, (2) TMSCN, (3) Et₂AlCN

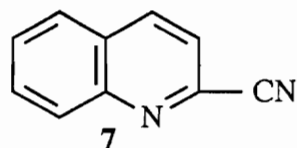
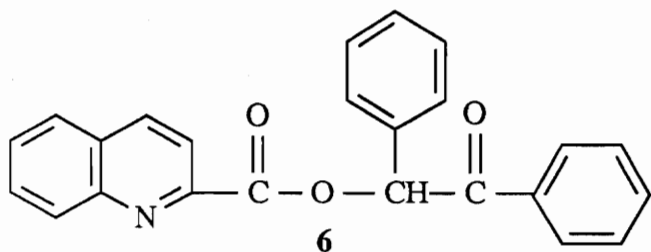
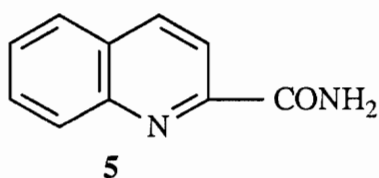
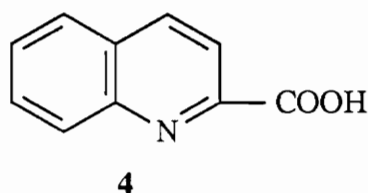
^cCH₂Cl₂/H₂O: methylene chloride-water method

^d---: no yield reported

II-2. Reactions of Reissert Compounds

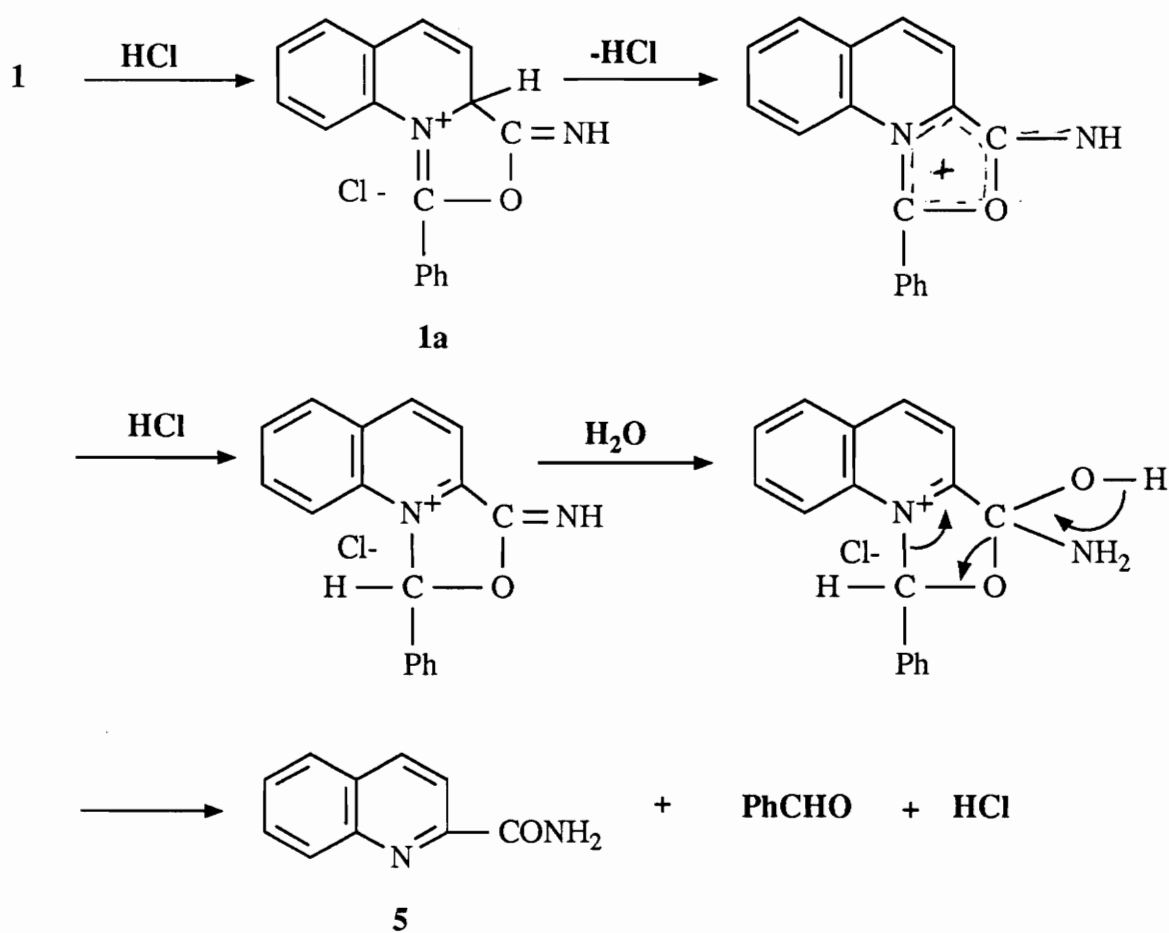
II-2-1. Acid-catalyzed Hydrolysis

In the late 1950's, one of the aspects of Reissert compounds that was attracting considerable interest was their ability to undergo acid-catalyzed hydrolysis to produce aldehydes. It was observed that the acid-catalyzed hydrolysis of 1-benzoyl-1,2-dihydroquinaldonitrile (**1**) resulted in the formation of benzaldehyde, quinaldic acid (**4**), quinaldamide (**5**) and benzoin quinaldate (**6**).¹ Similarly, the acid-catalyzed hydrolysis of 2-benzoyl-1,2-dihydroisoquinaldonitrile (**8**) gave analogous by-products.



The exact details of the mechanism for the formation of aldehydes from Reissert compounds baffled many. Several mechanisms were proposed, but all were based on the assumption that quinaldonitrile (**7**) was the intermediate in the reaction, and that upon hydrolysis it was converted to quinaldic acid (**4**) and quinaldamide (**5**).^{11,12,13} However, this theory could not be proven. After extensive study, Cobb and McEwen proved that quinaldonitrile was not an intermediate in the acid-catalyzed hydrolysis of

1-benzoyl-1,2-dihydroquinaldonitrile (**1**).¹³ They proposed a mechanism (Scheme 1) which involved reaction of **1** with hydrochloric acid to form a five-membered cyclic intermediate **1a**, followed by rearrangement and hydrolysis to yield benzaldehyde and quinaldamide (**5**).¹³ Table 2 lists the hydrolysis of several Reissert compounds to aldehydes.



Scheme 1: Mechanism of Acid Hydrolysis of Quinoline Reissert Compound

Table 2. Hydrolysis of Reissert Compounds to Aldehydes

<u>Heterocycle</u>	<u>Acid Chloride</u>	<u>% Yield of Aldehyde</u>
Quinoline	Benzoyl	98 ³
	<i>p</i> -Chlorobenzoyl	92 ³
	<i>o</i> -Methoxybenzoyl	97 ³
	Acetyl	99* ³
6-Methoxyquinoline	Benzoyl	97 ⁹
Isoquinoline	<i>p</i> -Chlorobenzoyl	50 ⁹
	Butyryl	57* ¹⁰
	Propionyl	75* ⁹

*products isolated as a substituted hydrazone or similar derivatives

II-2-2. Alkylation and Base Hydrolysis

Reissert compounds possess an acidic proton alpha to the cyano group that dictates the chemistry of these compounds. It can easily be abstracted with a variety of base/solvent combinations (sodium/xylene,¹⁴ phenyllithium/ether-dioxane,¹⁴ sodium hydride/dimethylformamide,¹⁵ and 50% sodium hydroxide/acetonitrile catalyzed by triethylbenzylaluminum (TEBA) chloride¹⁶) to form the anion. The anion may be localized as in the case of the isoquinoline Reissert compound or ambident as in the quinoline Reissert compound (Scheme 2). Once formed, the anion can be alkylated by various alkyl halides to produce alkylated derivatives in excellent yields (Table 3).¹⁷ In some cases, however the Reissert compound must be converted to its corresponding anion under mild conditions to obtain moderate yields of the alkylated derivatives.

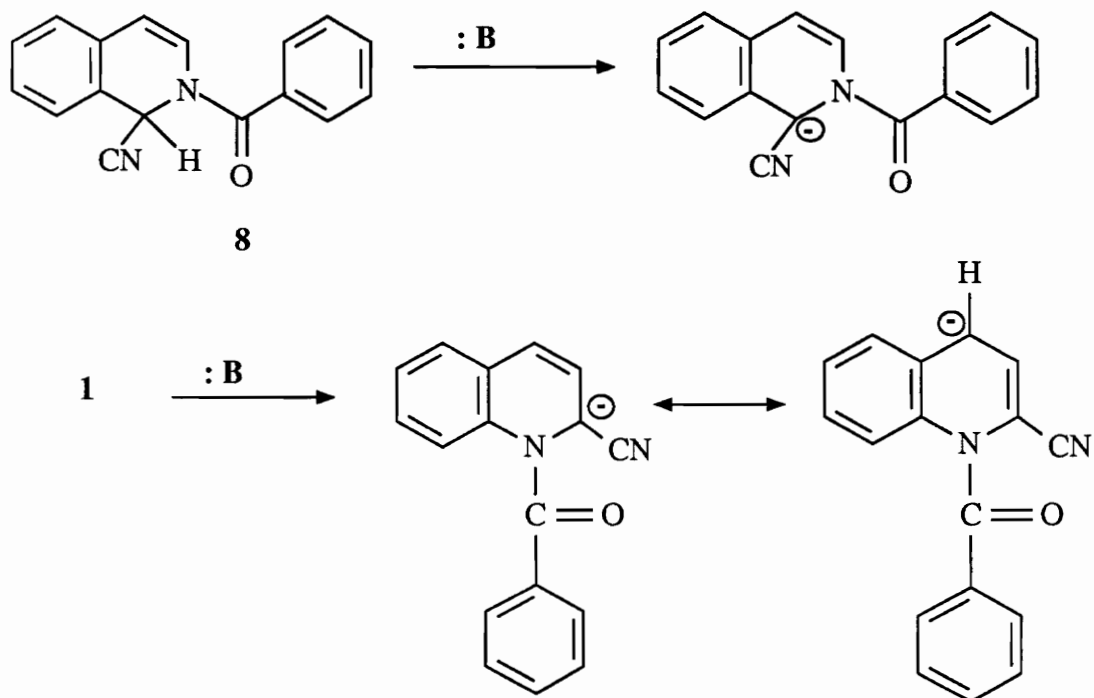
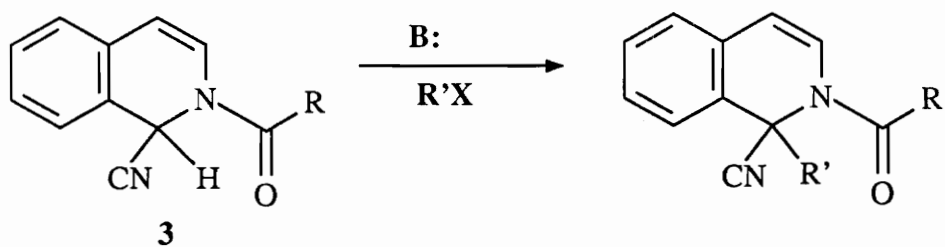


Table 3: Examples of Alkylation of Isoquinoline Reissert Compounds

<u>R</u>	<u>R'</u>	<u>X</u>	<u>Yield(%)</u>	<u>Ref.</u>
C ₆ H ₅	CH ₃	I	98 (b)	18
C ₆ H ₅	CH ₃	I	72 (a)	17
C ₆ H ₅	n-C ₃ H ₇	I	82 (c)	16
C ₆ H ₅	n-C ₃ H ₇	I	99 (b)	18
C ₆ H ₅	n-C ₄ H ₉	I	78 (c)	16
C ₆ H ₅	n-C ₄ H ₉	I	98 (b)	18
C ₆ H ₅	CH ₃	I	80 (a,b)	17
CH ₃	CH ₂ C ₆ H ₅	Cl	83 (b)	19
C ₆ H ₅	CH ₂ C ₆ H ₅	Cl	83 (b)	19
C ₆ H ₅	CH(CH ₃) ₂	Br	83 (b)	19
<i>o</i> -C ₆ H ₄ CH ₃	CH(CH ₃) ₂	Br	73 (b)	19
CH ₃	CH ₂ CH ₃	Br	62 (b)	19

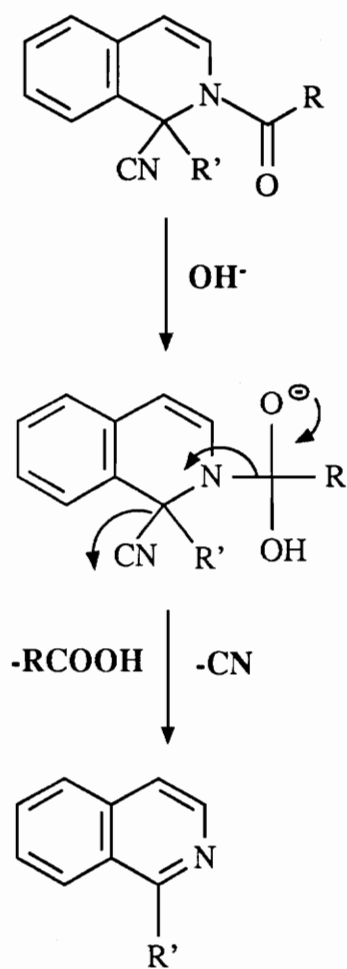
Reaction done in a) PhLi/ether-dioxane; b) NaH/DMF; c) 50% NaOH/CH₃CN, PTC

Basic hydrolysis of the alkylated derivatives with KOH or NaOH, driven by rearomatization, produces the 1-alkylisoquinolines.¹⁴ The formation of 1-alkylisoquinolines via the mechanism depicted in Scheme 3 involves addition of the hydroxide ion to the amide carbonyl, followed by loss of cyanide and benzoic acid. The driving force of the reaction is rearomatization of the heterocyclic ring. This process represents a convenient method of preparing various substituted quinoline and isoquinoline derivatives

II-2-3. Condensation with Aldehydes

Reissert compounds also undergo reactions with aldehydes to form esters which can be hydrolyzed to give secondary alcohols. In many cases, when a Reissert compound is condensed with an aldehyde using 50% sodium hydroxide/acetonitrile a mixture of the ester (**3c**) and alcohol (**3d**) is obtained.²⁰ However, it has been shown that the base/solvent combination, as well as the reaction time, play very important roles in dictating exactly which product will be obtained. Shorter reaction time and lower temperature favor formation of the ester.²¹ If the reaction is carried out in sodium hydride/dimethylformamide, the ester is obtained almost quantitatively.¹⁸ Table 4 shows several examples of the condensation of aldehydes with Reissert compounds.

The condensation of aldehydes with Reissert compounds is believed to occur via an intramolecular rearrangement driven by rearomatization.²² The mechanism depicted in Scheme 4 involves reaction of the aldehyde with the Reissert anion to form an alkoxide (**3a**).²² The alkoxide attacks the amide carbonyl to form a five membered cyclic intermediate (**3b**). The pyridine ring undergoes rearomatization with loss of the cyano group to form the ester. The ester in turn can be hydrolyzed to form the alcohol.



Scheme 3: Mechanism of Hydrolysis of Isoquinoline Reissert Compound and Alkylated Derivatives

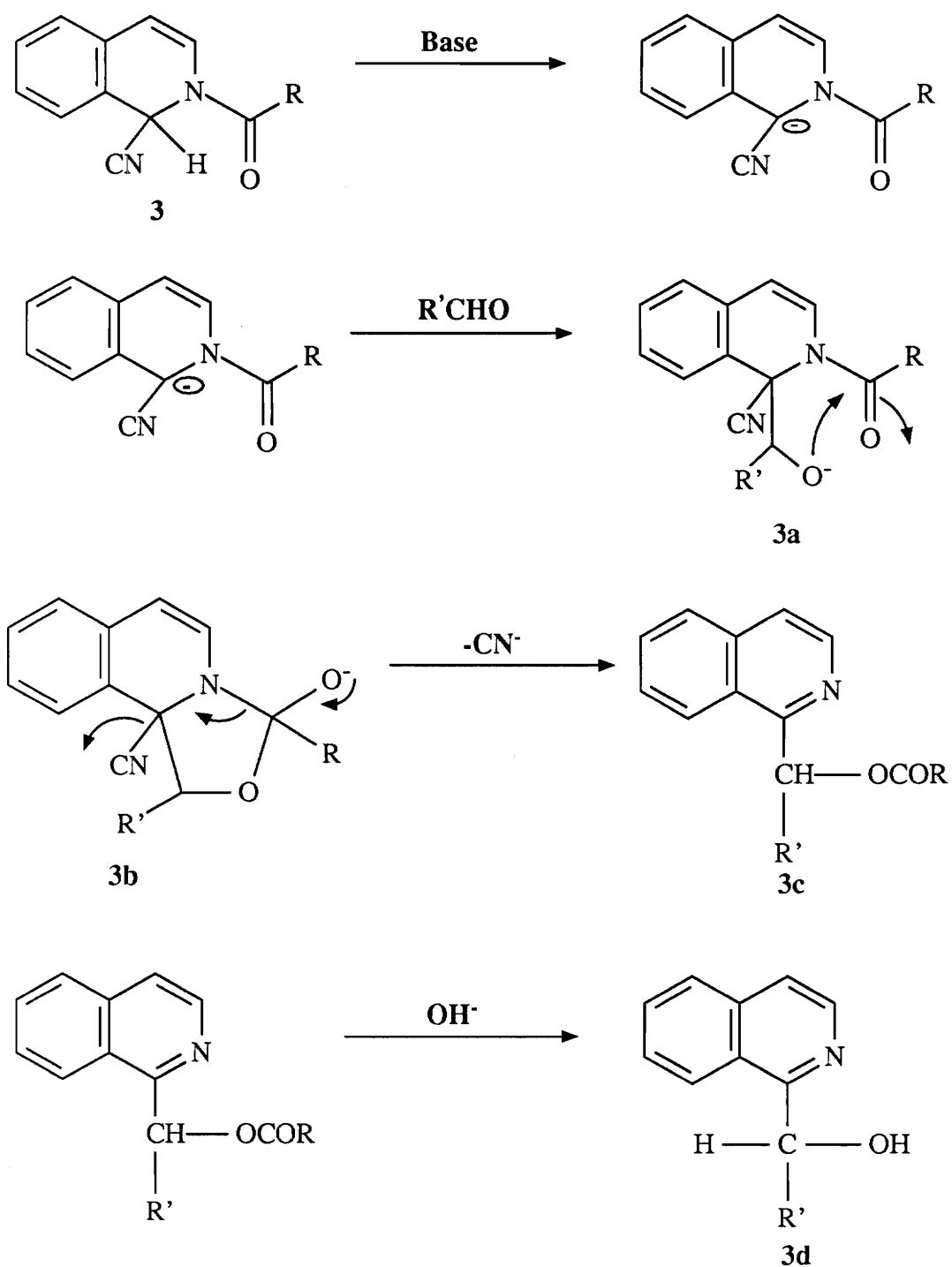
Table 4. Condensation of Reissert Compounds with Aldehydes to Form Esters or Alcohols

Reissert					
<u>Compound</u>	<u>R'</u>	<u>Method</u>	<u>%Ester</u>	<u>%Alcohol</u>	<u>Ref.</u>
1	C ₆ H ₅	a	89	--	22
1	CH ₃ (CH ₂) ₂	a	*	89	22
1	2,6-Cl ₂ C ₆ H ₃	a	82	--	22
8	C ₆ H ₅	b	65	--	18
8	C ₆ H ₅	a	88	--	22
8	CH ₃ (CH ₂) ₂	a	--	75	22
8	<i>p</i> -ClC ₆ H ₄	a	72	--	22
8	2,6-Cl ₂ C ₆ H ₃	a	--	54	22
8	C ₆ H ₅	c	89	93**	20
8	(CH ₃) ₂ CH	c	83	85**	20

Reaction done in a) PhLi/ether-dioxane, b) NaH/DMF, c) 50% NaOH/CH₃CN,

*Isolated as picrate

**Result of hydrolysis of ester in separate reaction

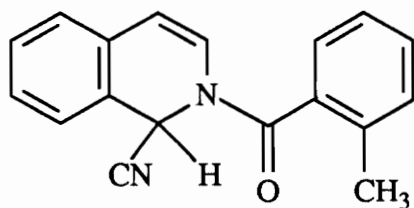


Scheme 4: Condensation of Isoquinoline Reissert Compounds with Aldehydes

II-2-4. Rearrangement

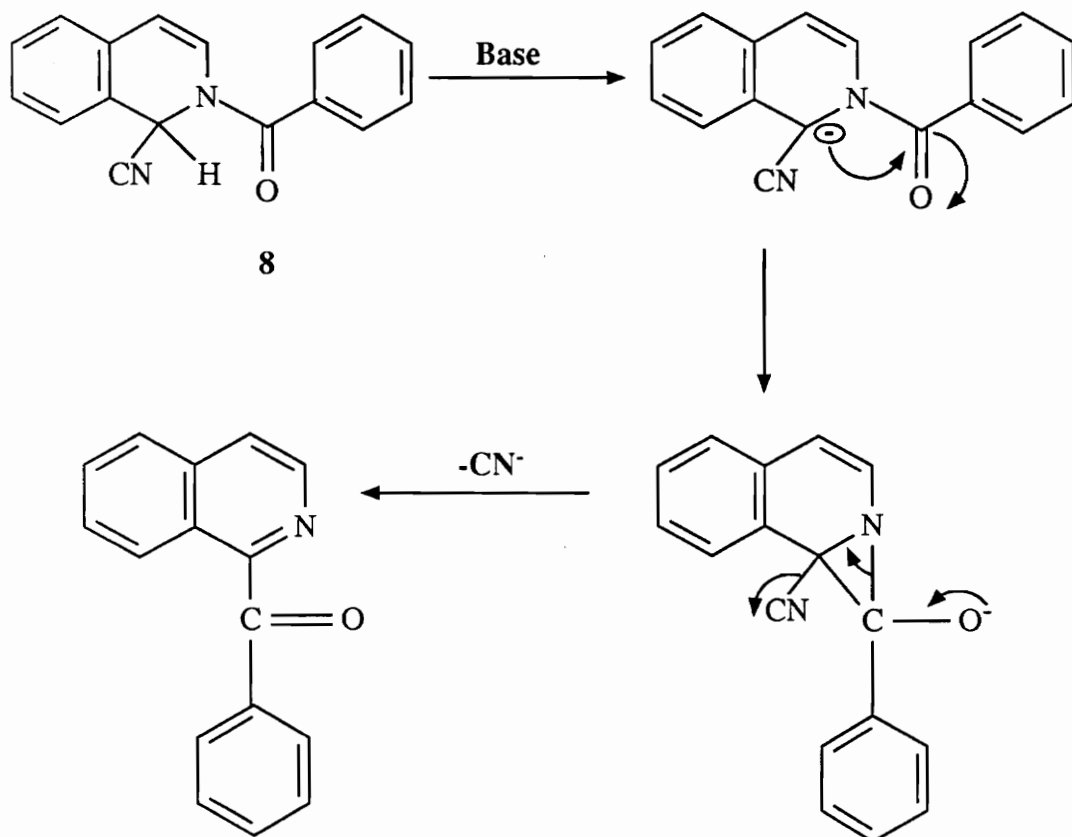
In the absence of an electrophile, an intramolecular rearrangement converts the Reissert anion into a ketone via a tricyclic aziridine intermediate (Scheme 5).¹⁴ Boekelheide and Weinstock observed that when 2-benzoyl-1,2-dihydroisoquinaldonitrile (**8**) was heated in xylene/NaH, a rearrangement occurred yielding 1-benzoylisoquinoline (70%) and loss of a cyanide ion.¹⁷ Rearrangement to the ketone has also been shown to occur using sodium hydride/dimethylformamide.¹⁸

Gibson found that the ability of the Reissert compound to undergo rearrangement depends on the nature of the acyl group.¹⁹ During his investigation, Gibson found that when the benzoyl Reissert compound (**8**) was reacted with NaH/DMF at room temperature rearrangement occurred in less than an hour. However, when the ortho-toluoyl Reissert compound (**9**) was reacted with NaH/DMF, rearrangement did not occur due to the steric effects induced by the presence of the methyl group. Therefore, rearrangement can be decreased or quenched by ortho substitution of the acyl group. However, a decrease or reduction in rearrangement can best be obtained by lowering the reaction temperature to 0°C.² In addition, Gibson found that the presence of a methyl group at the 3-position of the isoquinoline ring or the presence of electron withdrawing groups on the acyl group enhances rearrangement.¹⁹



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In some cases, the presence of an alkyl halide prevents the rearrangement of Reissert compounds. Popp and Wefer found that in the presence of an alkyl halide the benzoyl Reissert failed to undergo rearrangement.¹⁸

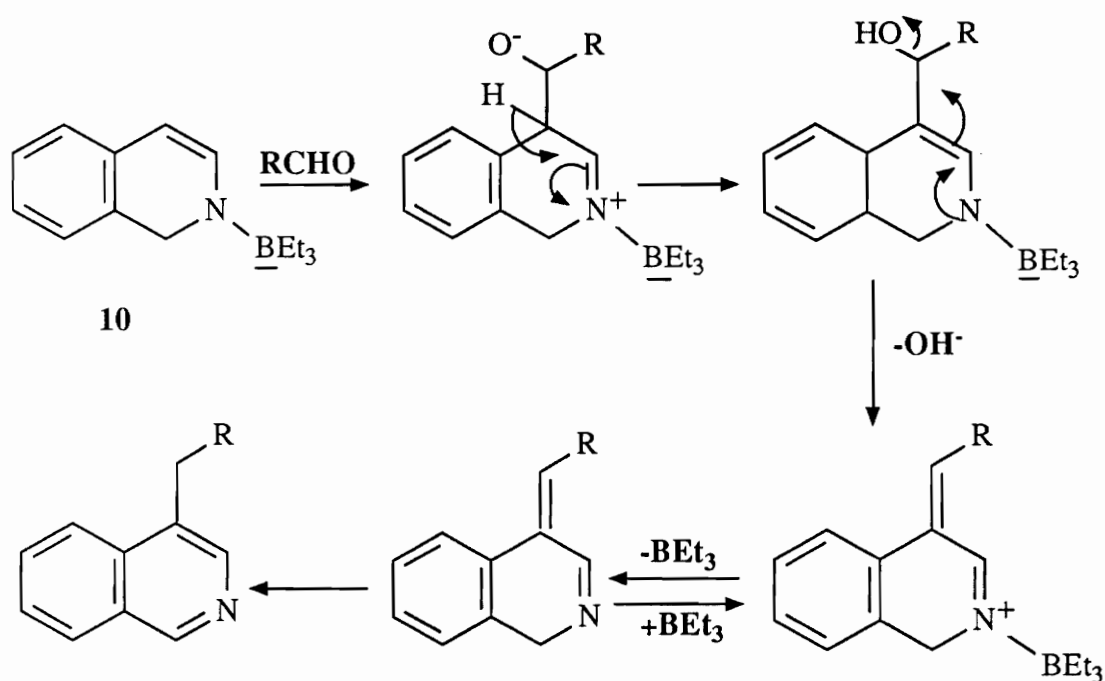


Scheme 5: Rearrangement of Isoquinoline Reissert in the Absence of an Electrophile

II-3. Bis(isoquinoline) Reissert Compounds

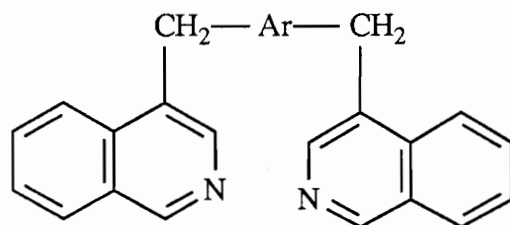
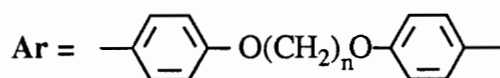
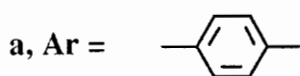
II-3-1. 4-Alkylated Bis(isoquinolines)

Recently, Minter and Re reported a facile synthesis of 4-substituted isoquinolines from reaction of boron-activated enamine (**10**) derived from isoquinoline with aryl aldehydes.²³ Presumably, the overall mechanistic pathway involves electrophilic attack of the aldehyde at the 4-position followed by proton transfer, conjugate loss of hydroxide, and rearomatization (Scheme 6).²³

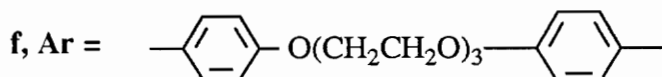
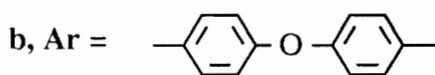


Scheme 6: Reported Mechanism of 4-Alkylation of Isoquinoline

This work has been extended to the synthesis of a variety of 4-substituted isoquinolines, as well as novel 4,4'-coupled bis-isoquinolines. Guilani et al. produced a family of novel 4,4'-coupled bis(isoquinolines) (**11a-f**) in good yield by reacting (**10**) with difunctional aldehydes.²⁴

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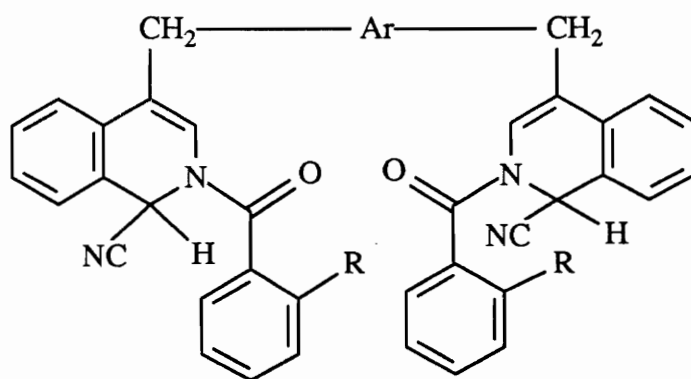
c, n = 4
 d, n = 6
 e, n = 10



They also developed a method for the oxidation of the bis(isoquinolines) to their corresponding diketones.²⁴ Having successfully produced a family of novel 4,4'-coupled bis(isoquinolines), the next step was preparation of the bis(Reissert compounds).

II.3-2. Bis(Reissert compounds) Derived from Monoacid Chlorides:

The bis(Reissert compounds) (**12a-c**) were prepared by reacting the bis(isoquinoline) with a slight excess of the aroyl chloride in the presence of TMSCN (single phase). The reaction produced practically quantitative yields of the diastereomeric compounds.²⁸



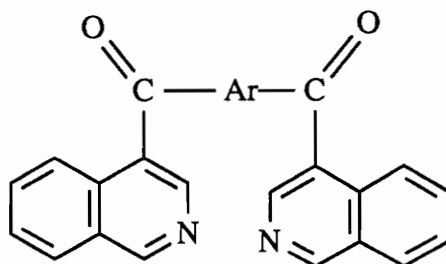
12

a: Ar = *p*-C₆H₄O(CH₂)₁₀OC₆H₅-*p*; R = CH₃

b: Ar = *p*-C₆H₄O(CH₂)₁₀OC₆H₅-*p*; R = H

c: Ar = *p*-C₆H₄; R = H

An attempt was made to form the bis(Reissert compounds) from a diketone (**13**) using the two-phase method. The two-phase method was chosen because it is known that TMSCN reacts with carbonyls to form cyanohydrins.²⁹ However, this method proved unsuccessful. Instead of forming the bis(Reissert compounds), it is believed that diastereomeric mixtures of the bis(cyanohydrin esters) were obtained.²⁸ This finding will become extremely important in the work reported in this thesis.



13

II.3-3. Bis(Reissert compounds) Derived from Diacid Chlorides

Earlier attempts toward the synthesis of difunctional Reissert compounds had been made via the two-phase method, but generally resulted in less than 10% yields, the best yield obtained being 22%.^{25,26} The low yields resulted from the hydrolysis of the diacid chlorides by water ($\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$) prior to the formation of the bis(Reissert compounds).

Gibson et al. attempted the synthesis of difunctional Reissert compounds from isoquinoline, quinoline, benzoxazole, and benzothiazole utilizing the single phase method and obtained the desired compounds as diastereomeric mixtures in yields ranging from 77 to 100%.²⁷

These bis(Reissert compounds) derived from mono and di-acid chlorides constitute a novel class of AA monomers (two acidic alpha protons) capable of undergoing step-growth polymerization. These monomers were further used in the synthesis of heterocyclic polymers.³⁰

III. NITROGEN-CONTAINING POLYMERS

Nitrogen-containing polymers are a special class of materials. These polymers exhibit very useful features which can be attributed to (1) basicity of the nitrogen atom(s), (2) hydrogen bonding of N-H moiety, and (3) quaternization. The presence of the nitrogen atom(s) imparts basicity to the resultant polymer and has been known to be useful in catalysis and interaction with acidic media and surfaces. Polyamides, such as nylon-6,6 and KelvarTM, show remarkable strength due to hydrogen bonding between the carbonyl groups and the N-H moieties. A large percentage of these polymers find usage in fabric application. Quaternary salt forms of some polymers can be used to create highly polar, ionic, water soluble polymers. These polymers can be used as anion exchange resins, coatings, adhesives, in water treatment and coagulation.

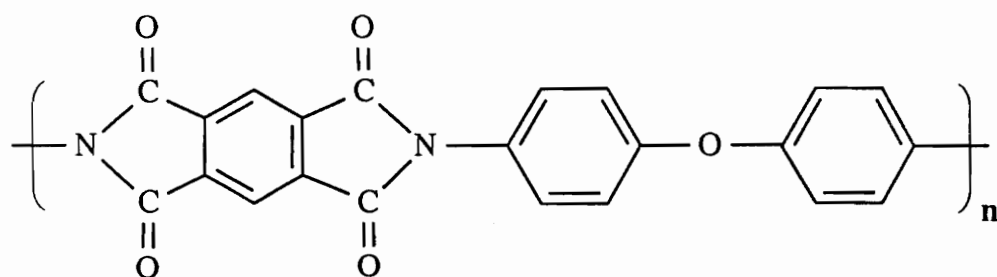
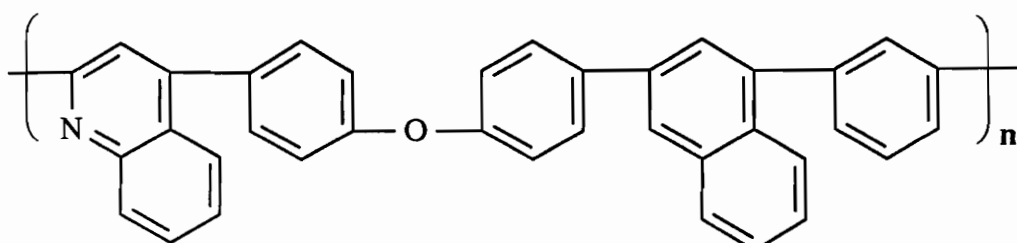
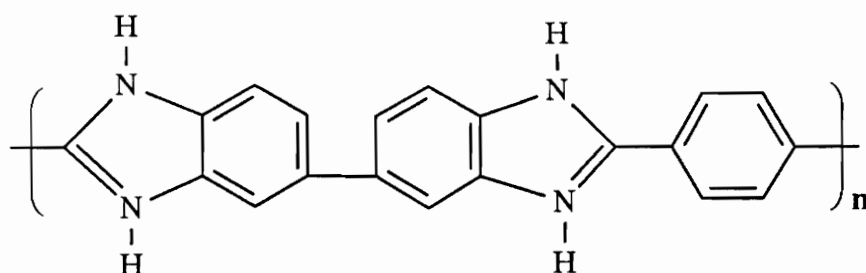
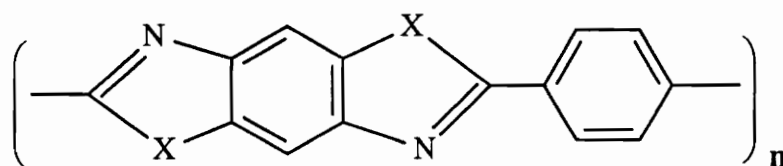
The aromatic nitrogen-containing polymers impart enhanced thermo-oxidative stability. This class includes the (1) polyimides, (2) polyquinoxalines, (3) polyquinolines, (4) polybenzimidazoles, (5) polybenzothiazoles, and (6) polybenzoxazoles. At elevated temperatures, these polymers retain useful properties for long periods of time. Polyimides, a well known class of polymers, exhibit high strength and excellent heat resistance. Aromatic polyimides are usually synthesized by reacting dianhydrides with diamines in a polar solvent (N,N-dimethylacetamide, DMAC). Most commercially available polyimides, such as Kapton (Scheme 7), H-film, or Vespel, are synthesized by reacting *p,p'*-diaminodiphenylether with pyromellitic anhydride. These polyimides possess excellent stability ranging from 250-300°C, sometimes higher, and widespread industrial use.³¹ Kapton, for example, has excellent mechanical properties which makes it ideal for use in aerospace and electronic substrate and material packaging applications.³² LARC-TPI, a polyimide, shows excellent high temperature adhesive properties and is often used to bond Kapton to itself and other substrates, eg., copper

foil.³²

Another example of thermally stable heterocyclic polymers is polyquinolines (Scheme 7). Polyquinolines are prepared by reacting a bis(*o*-aminoketone)s with aromatic diacetyl and di(phenylacetyl) monomers at 130°C in a 3:1 mixture of *m*-cresol and polyphosphoric acid. The resulting polyquinolines exhibit various degrees of crystallinity depending on chemical structure and thermal history.³² The glass transition temperatures of polyquinolines are directly related to the extent of phenyl substitution present. Bulky substitution prevents molecular motion, thus causing an increase in T_g.³² Polyquinolines are mainly utilized in adhesives applications.

Polybenzimidazoles (PBIs), shown in Scheme 7, are synthesized by melt condensation of aromatic bis(*o*-diamines) with diphenyl esters of aromatic dicarboxylic acids.³² Aromatic bis(*o*-anilinoamino) compounds and aromatic dicarboxylic derivatives have been used to prepared phenyl substituted PBIs.³³ However, the resulting PBIs are more thermoplastic with a much lower T_g than unsubstituted PBIs. The PBI shown in Scheme 7 has very good mechanical properties and stability (300°C and greater). Compared to polyimides and polyimides, it is more hydrolytically stable. PBIs have found usage as fiber, films, and low to medium density foams.³² But, a major disadvantage is the high cost associated with their preparation.

Polybenzothiazoles (PBTs) and polybenzoxazoles (PBOs) (Scheme 7) are lyotropic liquid crystalline polymers referred to as rigid rodlike polymers. Both exhibit extremely high modulus properties, especially PBT, because of their high degree of molecular orientation along the axis and their well-defined two dimensional structure. They possess relatively high thermooxidative stability which makes them ideal as high temperature reinforcements, eg., fibers and ribbons.³²

Kapton, polyimide, $T_g=327^\circ\text{C}^{34}$ Polyquinoline, $T_g=268^\circ\text{C}$ Polybenzimidazole, $T_g=430^\circ\text{C}$ 

X= S, Polybenzothiazole, liquid crystalline

X= O, Polybenzoxazole, liquid crystalline

Scheme 7: Heat Resistant N-Heterocyclic Polymers³²

IV. POLY(ETHER KETONE)S

Poly(ether ketone)s are a class of polymers which are attracting considerable attention. This increase in interest is a direct result of their extremely high thermal and chemical stabilities, exceptional stability against irradiation and good mechanical properties. Poly(ether ketone)s are usually crystalline and therefore are resistant to solvent attack. The only common room temperature solvent known for poly(ether ketone) or poly(ether ether ketone) is concentrated sulfuric acid.

Although crystallinity greatly enhances the properties of these polymers, it along with melting points above 300°C, make their synthesis very difficult. The presence of crystallinity prevents the polymer from remaining in solution, thus making it difficult to obtain high molecular weights. However, these problems can be overcome by carrying out the synthesis at very high temperatures³⁶ or in strongly acidic media.^{37,38}

Various combinations of reactant(s) and process conditions have been attempted to synthesize poly(ether ketone)s. The first attempt to produce PEK used aluminium chloride in dichloromethane to self condense *p*-phenoxybenzoyl chloride at room temperature (Friedel-Crafts acylation).³⁹ The resulting polymer had a reduced viscosity of 0.57 dl/g but was too low in molecular weight to give any useful mechanical properties.

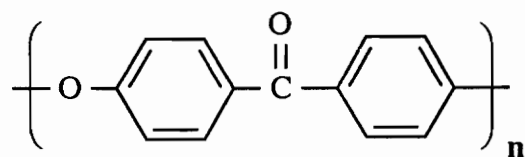
Poly(ether ketone)s were also attempted via a mixed HF/BF₃ solvent/catalyst combination.^{37,40} This led to the first high molecular weight poly(ether ketone). *p*-Phenoxybenzoyl chloride was polymerized to give a 97% yield of PEK with an inherent viscosity of 2.76, T_g=163°C and T_m=361°C.

Now, the most commonly used method of producing poly(ether ketone)s is via nucleophilic aromatic substitution.³⁸ Although originally developed for the production of polysulfones, Imperial Chemical Industries (ICI) adapted this process to the

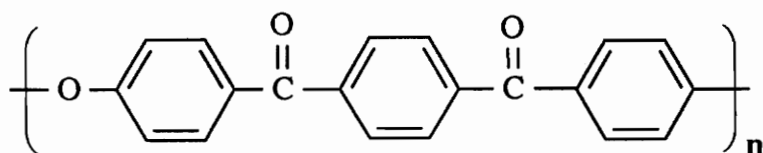
production of poly(ether ketone)s. The overall mechanism involves attack of a phenate, resulting from the reaction of a phenol with a base, upon an activated halide in the presence of a dipolar aprotic solvent to produce polysulfones or poly(ether ketone)s.

The crystalline poly(ether ketone)s possess very useful properties which make them ideal for use in aerospace applications. They exhibit excellent thermo-oxidative stability, withstanding processing temperature as high as 400°C and can be utilized at temperature > 200°C without undergoing oxidation or loss of properties. In addition, they are stiff, tough, resist wear, and possess low flammability.

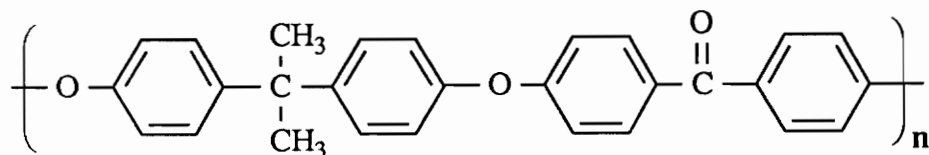
Typical poly(ether ketone)s have T_g 's ranging from 100°C-200°C and T_m 's ranging from 300°C->400°C. Several examples are given in Scheme 8.



$T_g = 154^\circ\text{C}$, $T_m = 367^\circ\text{C}$



$T_g = 165^\circ\text{C}$, $T_m = 391^\circ\text{C}$



$T_g = 155^\circ\text{C}$, amorphous

Scheme 8: Examples of Poly(ether ketone)s³⁸

V. MOTIVATION FOR CURRENT RESEARCH

Poly(ether ketone)s are rapidly finding widespread industrial usage. This can be attributed to their extremely high thermal and chemical stabilities, good mechanical properties, solvent resistance and moderate T_g 's (100°C-200°C). These desirable properties have prompted research into the synthesis of isoquinoline based monomers for incorporation into poly(arylene ether)s via Reissert chemistry. It is hoped that the forementioned properties exhibited by poly(ether ketone)s along with those exhibited by nitrogen-containing polymers will result in poly(ether ketone)s with properties better than or similar to the poly(ether ketone)s currently being used.

Recently, a synthetic route to an isoquinoline nucleus functionalized as a monomer for incorporation into poly(arylene ethers) was reported.⁴¹ The monomer, 1,4-bis(*p*-fluorobenzoyl)isoquinoline, contained the heterocycle preformed prior to polymerization. The activated difluorodiketone monomer was condensed with a number of bisphenols producing a family of novel poly(1,4-isoquinolinediyl ether ketones). These materials were amorphous, in contrast to PEEK, and exhibited excellent thermal stability (T_g 's ranging from 180°C to 210°C) due to the presence of the heterocyclic moiety. Now this work is being extended into the investigation of an activated difluorotetraketone, 1,4-bis{1-[4-*p*-(fluorobenzoyl)isoquinoly]carbonyl}benzene, derived from a 4,4'-coupled bis-isoquinoline system.

VI. RESULTS AND DISCUSSION

The main thrust of this work was dedicated to the synthesis of a difluorotetraketone monomer, 1,4-bis{1-[4-*p*-(fluorobenzoyl)isoquinoly]carbonyl}benzene. Two synthetic routes were explored to find an efficient route for the preparation of this monomer. Attempts were made to synthesize the monomer via a dibenzylic bis(isoquinoline) and a diketone bis(isoquinoline) system which are discussed below.

VI-1. Synthesis of Novel Difluorotetraketone via Dibenzylic Bis(isoquinoline)

The first step in the synthesis of the tetraketone monomer (**18**) was preparation of α,α' -bis(4-isoquinolyl)-*p*-xylene (**14**) (Scheme 9). Isoquinoline was reacted with terephthalaldehyde in the presence of sodium triethylborohydride to yield the 4-alkylated bis-isoquinoline compound **14** in an 84% yield compared to a reported yield of 74%.⁴² After recrystallization from ethanol/water, a pure product was obtained with a melting point of 190.4-190.7°C compared to a reported melting point of 186.5-187.5°C.⁴²

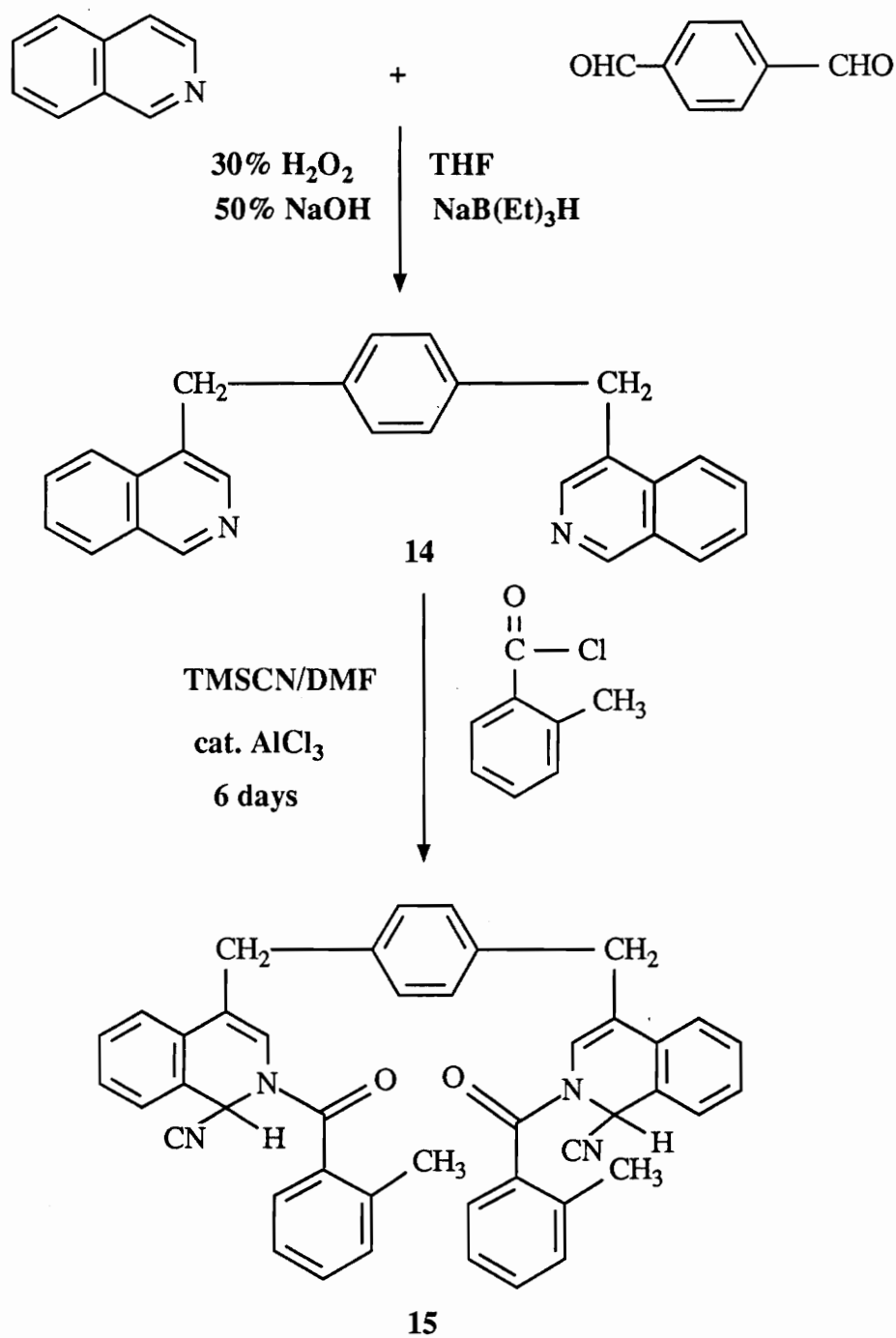
The next step in the synthesis of the tetraketone monomer **18** was preparation of the bis(Reissert compound) (**15**) via the single phase method using TMS-CN as cyanide source (Scheme 9). Bis-isoquinoline was reacted with ortho-toluoyl chloride and trimethylsilyl cyanide in the presence of a catalytic amount of aluminum chloride. The reaction was first attempted in CH₂Cl₂. However, the bis-isoquinoline would not go into solution, thereby, hindering the reaction from going to completion. Therefore, the reaction was attempted again using DMF as a solvent. Unfortunately, solubility still remained a problem. When heat was applied to the solution, the bis-isoquinoline went into solution. However, as soon as the solution cooled to room temperature, the solid precipitated out of solution. This reaction proceeded at room temperature leading to the desired crude product **15** in a 93% yield. The ¹H NMR spectrum (Figure 1) of the crude

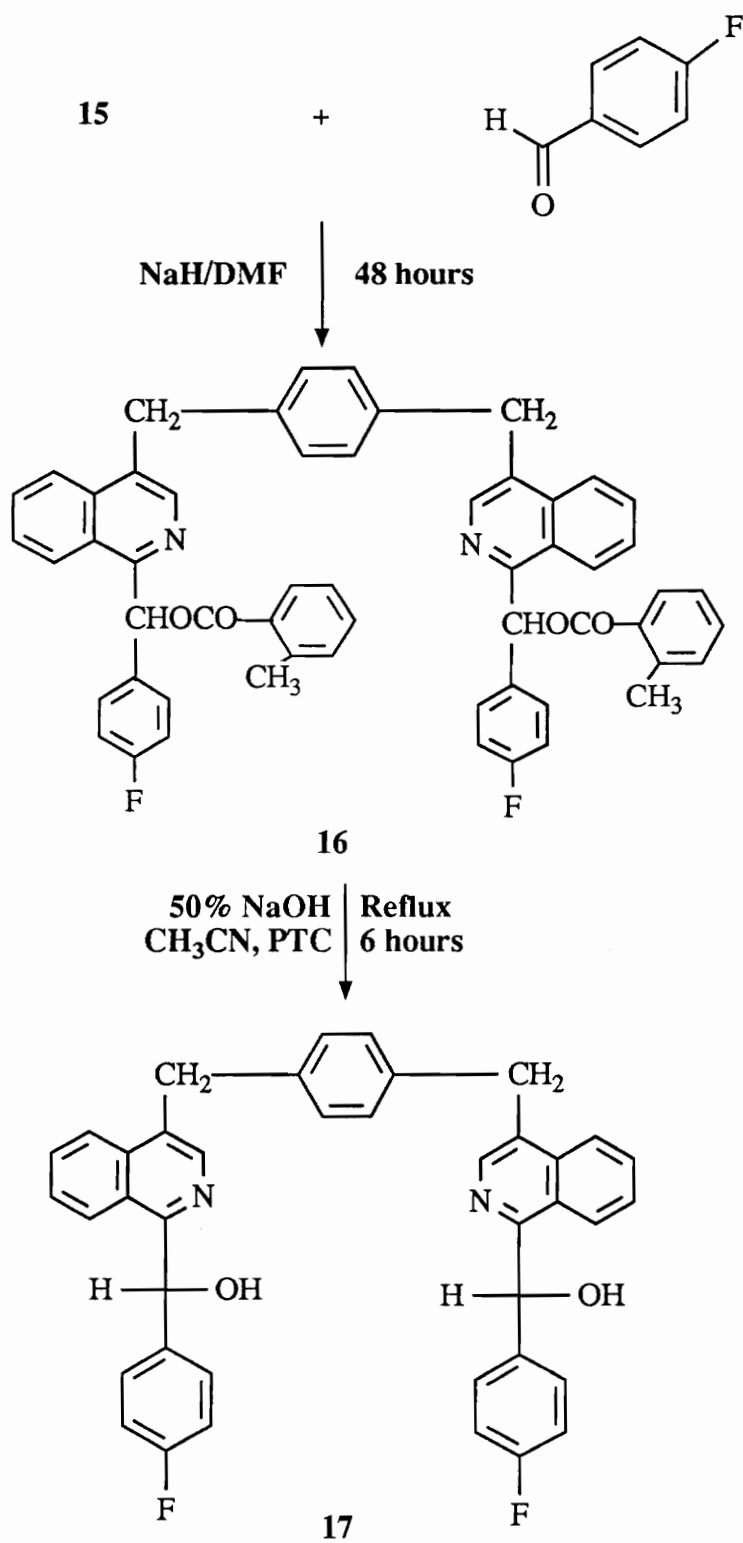
product showed an AB pattern at 3.60 ppm corresponding to the diastereotopic methylene protons and a singlet at 2.27 ppm corresponding to the methyl protons. Due to the rigidity of this compound, a desirable solvent from which to recrystallize was hard to find. TLC of the crude product showed two spots corresponding to the diastereomers present. After recrystallization from chloroform/hexanes, a pure product was obtained with a melting point of 220.5-221.5°C. It should be noted that the synthesis of the ortho-toluoyl Reissert compound was chosen because it has been shown that ortho substitution on the acyl group eliminates rearrangement.

Having successfully prepared the Reissert compound, the next step was preparation of the ester (**16**) (Scheme 10). The Reissert compound **15** was reacted with *p*-fluorobenzaldehyde in the presence of NaH/DMF. The reaction afforded an 83% yield of the crude product **16**. The crude product was purified by column chromatography yielding 50% of a light yellow solid. The desired product was recrystallized from ethyl acetate/hexanes yielding a white solid with a melting point of 145.6-146.7°C. The ¹H NMR spectrum showed a singlet at 4.35 ppm corresponding to the methylenes instead of an AB pattern as seen in the Reissert compound. The ester was then refluxed in 50% sodium hydroxide and acetonitrile in the presence of a small amount of benzyltrimethylammonium chloride (phase transfer catalyst) to yield the alcohol (**17**) in a 79% yield compared to a reported yield of 13.1% (isolated) (Scheme 10).⁴³ Complete hydrolysis of the ester was confirmed by FTIR spectrum which showed a hydroxyl at 3363.9 cm⁻¹ and no ester carbonyl peak. The ¹H NMR spectrum of the product showed a broad signal at 6.15 ppm corresponding to the hydroxy protons and a singlet at 6.29 ppm corresponding to the methine protons.

The alcohol **17** can be obtained directly by reacting the Reissert compound with *p*-fluorobenzaldehyde. In this case, the Reissert compound **15** was reacted with *p*-fluorobenzaldehyde in the presence of 50% sodium hydroxide, acetonitrile, and a small

amount of benzyltrimethylammonium chloride. The reaction afforded a crude yield of 94%. The FTIR spectrum of the crude product showed an ester carbonyl at 1715.6 cm^{-1} and no hydroxyl group, signifying incomplete reaction. Using the hydrolysis method reported by Gibson and Bailey,⁴⁴ the desired product was obtained in a 73% yield compared to a reported yield of 13.1% (isolated).⁴³ The melting point of the crude product was found to be $171\text{-}173^{\circ}\text{C}$ compared to a reported melting point of $174.2\text{-}175.5^{\circ}\text{C}$.⁴³ The ^1H NMR spectrum showed the presence of the hydroxyl protons at 6.15 ppm and the methine protons at 6.28 ppm.

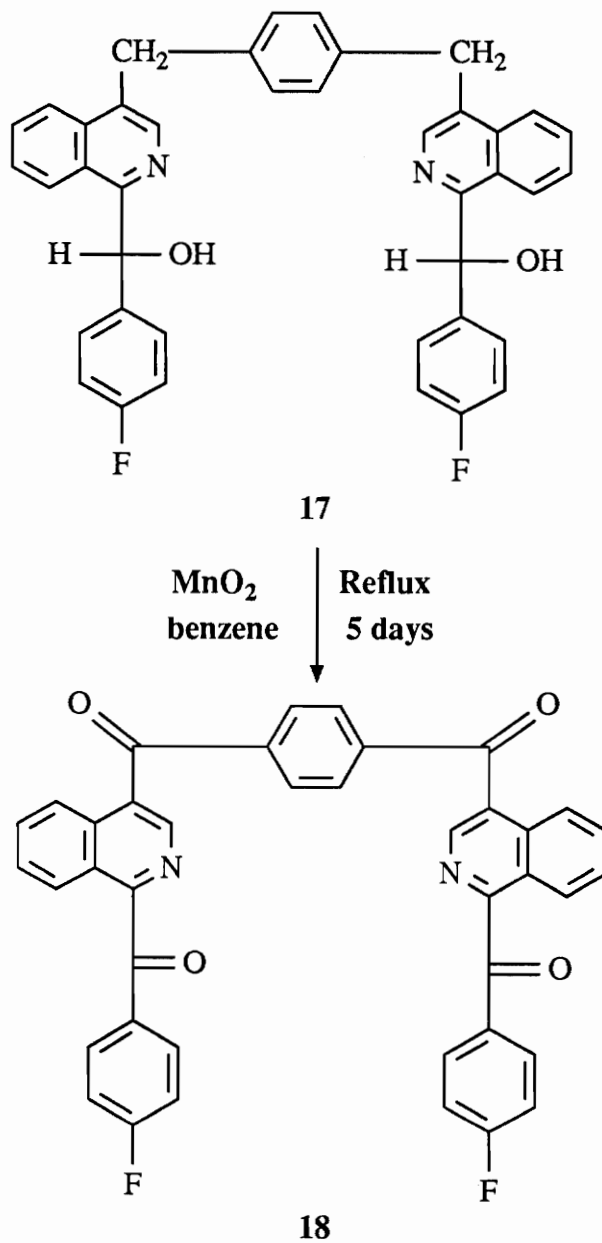
Scheme 9: Synthesis of *o*-Toluoyl Reissert Compound



Scheme 10: Synthesis of Bis-Alcohol

The final step in the synthesis of the tetraketone monomer was oxidation of the methylene and hydroxyl moieties of **17** to ketone moieties (Scheme 11). The alcohol **17** was refluxed in MnO_2 /benzene for five days. The tetraketone **18** was obtained in a 34% yield. When the MnO_2 at the end of the reaction was Soxhlet extracted for five days, the yield improved to 44% compared to a reported yield of 60.6%.⁴³ The melting point of the crude product was found to be 210-214°C compared to a reported melting point of 224.5-226.2°C.⁴³ The purification of this monomer proved to be extremely tedious and difficult. Recrystallizations were attempted using various solvents, such as toluene, xylene, and ethyl acetate/hexane, but all proved unsuccessful. TLC of the crude product showed four spots. Therefore, column chromatography was attempted on 0.27g of the crude product using 30/70 ethyl acetate/hexanes; however, only 0.01g (3%) of the desired product was obtained. The ^1H NMR spectrum (Figure 2) corresponded to the desired product and the FTIR spectrum (Figure 3) showed the presence of carbonyl groups at 1723.0 cm^{-1} and 1664 cm^{-1} . The extremely low yield of the desired product is a result of the elution of spots one and two together possibly suggesting the presence of two products similar in nature or structure. The reaction was repeated and this theory was latter confirmed when the spots were removed directly from the TLC plate and analyzed. The ^1H NMR and FTIR spectra of spots one and two were identical. The FTIR showed the presence of a hydroxyl group in both cases. The product (3 mg/ml) was also examined by HPLC which showed four peaks, the first two in great abundance. The product was eluted at a flow rate of 2.0 ml/min at a lambda max of 330. The first two peaks were collected and analyzed by ^1H NMR and FTIR. The results were the same as those obtained from the TLC plate. Therefore, the purification problems present are resulting from the presence of two isomers. Further investigation into the oxidation reaction will definitely have to be done. It seems as if the number of sites to be oxidized has some bearing on the extent of the reaction since simpler systems have been shown to

work so well.



Scheme 11: Synthesis of Tetraketone Monomer via Dibenzylc Bis(isoquinoline)

VI-2. Synthesis of Tetraketone Monomer via Diketone-Bis(isoquinoline)

The reaction sequence leading to the tetraketone monomer depicted above has proven feasible; however, this route has several major drawbacks, among them purification difficulties, low yields, and long synthesis time. The last step (Scheme 11) involves oxidation of the methylene and alcohol moieties to ketone moieties using MnO_2 . A majority of the monomer remains adhered to the MnO_2 , thus producing extremely low yields. Therefore, another approach was attempted in which the oxidation occurs in the first step. It was hoped that this approach would not only allow the low yield to be obtained in the first step, thus increasing the amount of tetraketone obtained in the final step, but would also reduce the synthesis time and hopefully purification problems.

The first step in the preparation of the tetraketone **18** was oxidation of the methylene moieties of α,α' -bis(4-isoquinolyl)-*p*-xylene (**14**) to ketone moieties (Scheme 12). The bis-isoquinoline **14** was placed in the presence of MnO_2 /benzene and allowed to reflux. The desired product (**19**) was obtained in a 72% yield after the MnO_2 at the end of the reaction was Soxhlet extracted with chloroform for five days. The crude product **19** was recrystallized from toluene/hexanes, yielding a melting point of 248.2-249.2°C. The FTIR spectrum of the product showed the appearance of a carbonyl at 1644.5 cm^{-1} . The ^1H NMR spectrum of the resulting product showed the disappearance of the methylene signal at 4.33 ppm.

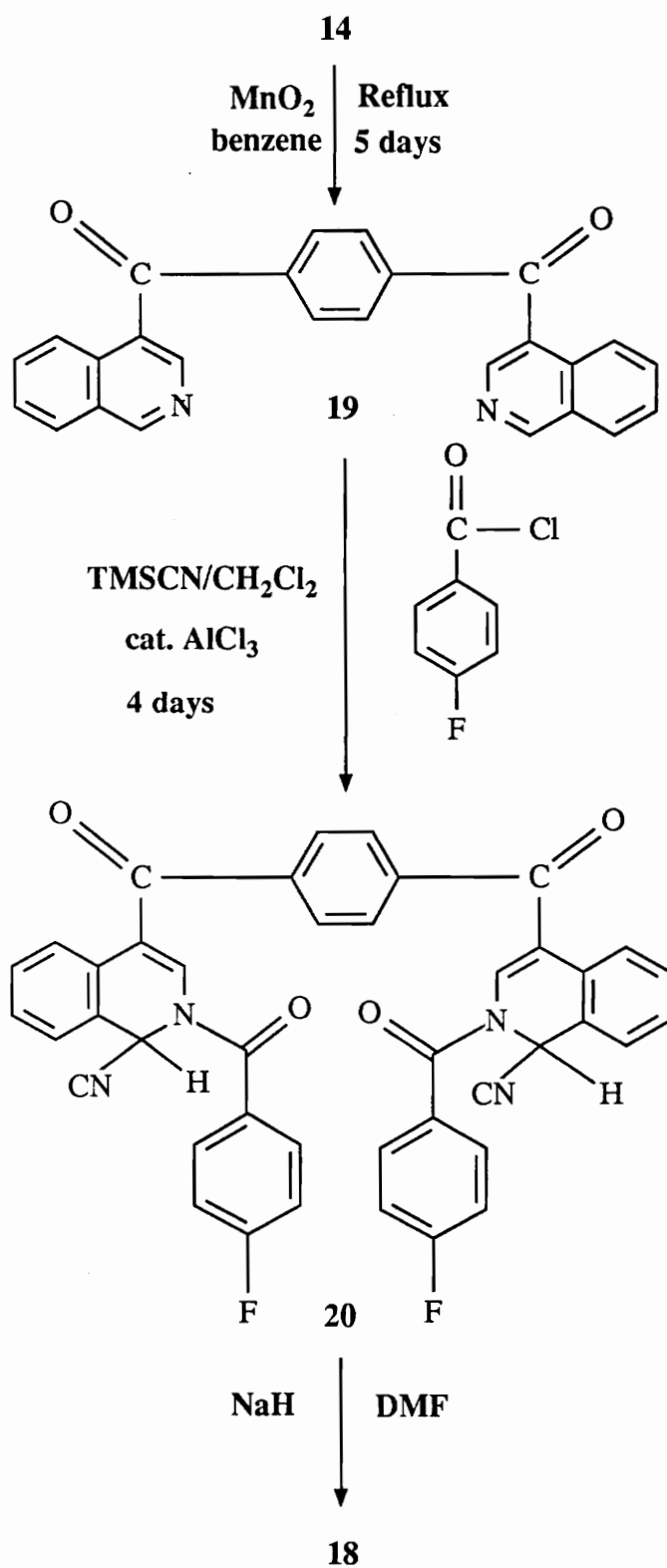
The next step in the synthesis of the tetraketone **18** was preparation of the tetraketone-bis(Reissert compound) (**20**). The diketone **19** was reacted with *p*-fluorobenzoyl chloride in the presence of TMSCN and a catalytic amount of AlCl_3 . The desired product was obtained in an 89% yield. FTIR spectrum (Figure 4) of the product showed a carbonyl group at 1677.2 cm^{-1} and 1651.1 cm^{-1} . Recrystallization from

chloroform/hexanes yielded a pure product with a melting point of 249.0-249.5°C. Initially, there were some reservations regarding this reaction. Rasco attempted to synthesize a Reissert compound from a diketone utilizing the two phase method since TMSCN is known to react with carbonyls to form cyanohydrins.^{28,29} The reaction afforded the cyanohydrin ester instead of the desired product. The reaction depicted in Scheme 12 showed no formation of cyanohydrins.

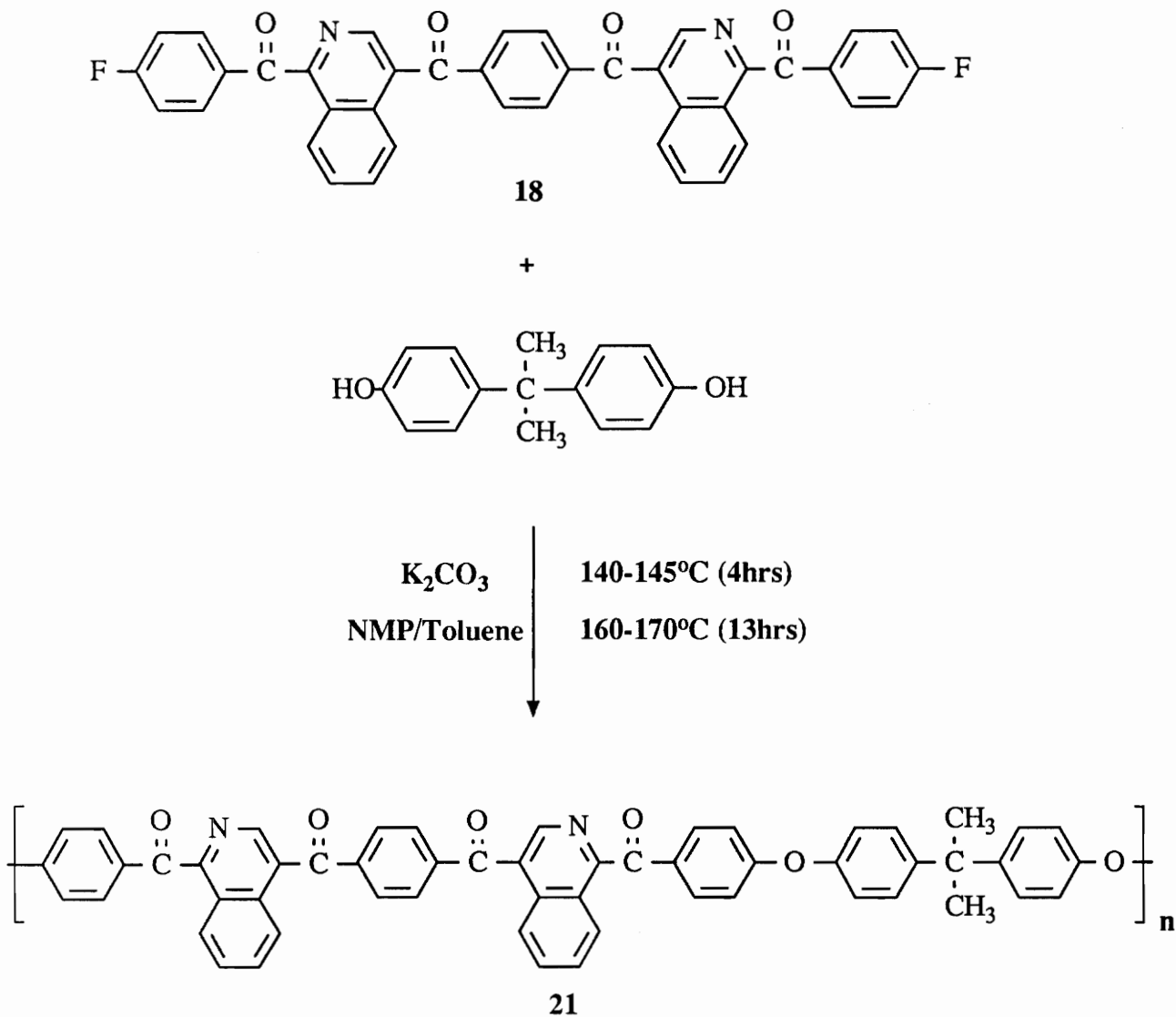
The final step in the synthesis of the tetraketone monomer was rearrangement of the diketone bis(Reissert compound) **20**. The diketone bis(Reissert compound) **20** was reacted with NaH in the presence of DMF at room temperature. Upon addition of NaH, the anion formed instantly producing a black solution. The reaction was allowed to proceed for 48 hours to ensure complete rearrangement of the Reissert compound. The reaction afforded dark yellow solid. However, it was observed that when the solid was dissolved in CDCl₃, some black particles remained insoluble. Initially, it was suspected that the anion was forming so rapidly that it had a chance to attack the carbonyl of the acyl group before the rearrangement was complete or when rearrangement occurred some type of side product was occurring possibly resulting from the attack of the carbonyl by sodium hydride. Therefore, the rearrangement was attempted again but at 0°C to slow down formation of the anion. The reaction was allowed to proceed for 36 hours and produced a gold solid in a 69% yield. The black particles were also present when the solid was dissolved in CDCl₃. The exact origin and reason behind the formation of the black particles are unknown. Therefore, the analogous mono system was examined in an attempt to optimize the reaction.

In the meantime, the polymerization of the tetraketone monomer (**18**) (obtained from Christine Hermann) with bisphenol A was attempted using NMP/toluene as a solvent/azeotroping agent and potassium carbonate as base (Scheme 13). The reaction

mixture was precipitated into methanol, yielding 74% of crude tan polymer (**21**). ^1H NMR spectrum (Figure 5) of the polymer corresponded to the structure. The resulting polymer was found to have an intrinsic viscosity of 0.16 dl/g at 25°C in chloroform and was found to be stable up to 454°C in air by TGA (Figure 6). GPC (using polystyrene standards) showed an $M_n=4800$ and $M_w=7800$. DSC (Figure 7) showed a $T_g=180^\circ\text{C}$ and no T_m . The viscosity and molecular weight of this polymer are low due to impurities in the tetraketone monomer.



Scheme 12: Synthesis of Tetraketone Monomer via Diketone Bis(isoquinoline)



Scheme 13: Polymerization of Tetraketone Monomer with Bisphenol A

VI-3. Synthesis of 4-benzoyl-1-(p-fluorobenzoyl)isoquinoline (Model Study #1)

In an attempt to optimize the rearrangement of the tetraketone bis(Reissert compound) **20**, two model systems were investigated. The first model system investigated was one in which there was a carbonyl at the 4-position and the other was

one in which there were benzylic protons at the 4-position.

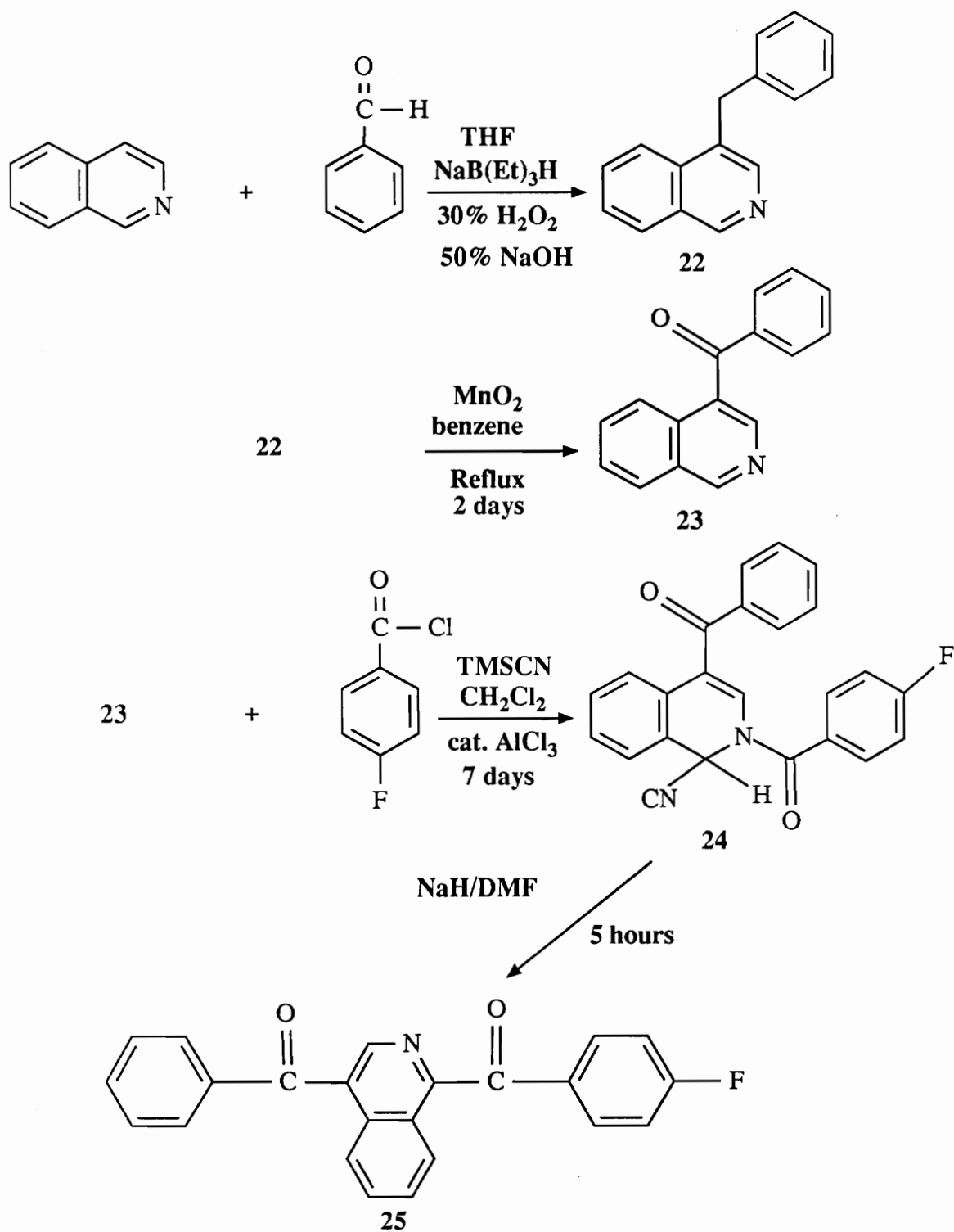
The first step in the synthesis of the model compound (**25**) was preparation of 4-benzylisoquinoline (**22**) (Scheme 14). Isoquinoline was reacted with benzaldehyde in the presence of sodium triethylborohydride to yield the 4-benzylisoquinoline **22** in a >100% crude yield compared to a reported yield of 65%.²³ The crude melting point was found to be 81-88°C compared to a reported melting point of 117.5-118.5°C.²³

4-Benzylisoquinoline **22** was then refluxed in MnO₂/benzene for two days giving the ketone (**23**). After the MnO₂ was Soxhlet extracted for four days, the reaction afforded 66% of a viscous yellow oil **23**. The oil was triturated with ethanol and a white solid was isolated. ¹H NMR of the white solid did not show indication of the desired product nor the starting material. An attempt was made to recrystallized the resulting product from ethyl acetate/hexanes however, the precipitate obtained proved only to be impurities. This procedure was performed several times to remove as much of the impurities as possible. The crude product was finally recrystallized from toluene/hexanes and afforded a pure product with a melting point of 77.4-78.7°C. ¹H NMR spectroscopy of the oil showed the disappearance of the singlet at 4.36 ppm corresponding to the methylene protons. FTIR spectroscopy showed the appearance of a carbonyl at 1657.6 cm⁻¹.

The next step was preparation of the Reissert compound. The ketone **23** was reacted with *p*-fluorobenzoyl chloride in the presence of TMSCN and a catalytic amount of AlCl₃. The desired product (**24**) was obtained in an 94% yield. The product was recrystallized from toluene/hexanes and afforded a pure product with a melting point of 170.4-171.7°C.

The final step was rearrangement of the Reissert compound to the diketone. The Reissert compound **24** was reacted with NaH in DMF. Upon addition of NaH the anion did not form instantly. Within minutes the mixture started changing from yellow to dark

brown. The reaction was allowed to proceed for five hours, yielding 33% of a crude product (**25**). TLC of the crude product showed the present of seven spots none presenting itself in great abundance. ^1H NMR of the crude product showed a mass of complicated splitting. When an attempt was made to dissolve the product in CDCl_3 , insoluble black particles were noticed as was the case of the bis system **20**. It was suspected that the formation of this side product was occurring due to an electron transfer process. Therefore, this hypothesis led to the investigation of the rearrangement of 2-(*p*-fluorobenzoyl)-4-benzyl-1,2-dihydroisoquinaldonitrile (**26**). If an electron transfer process was indeed occurring then the abstraction of a benzylic proton to form a radical species might be observed.



Scheme 14: Synthesis of 4-Benzoyl-1-(p-fluorobenzoyl)isoquinoline

VI-4. Synthesis of 1-(*p*-fluorobenzoyl)-4-benzylisoquinoline (Model Study #2)

Finally, the model system where there were benzylic protons at the 4-position instead of a carbonyl oxygen was investigated. This was done to establish the effect (if any) of the presence of the carbonyl group on the rearrangement. Therefore, 4-benzylisoquinoline was reacted with *p*-fluorobenzoyl chloride via the two phase method using KCN as a cyanide source (Scheme 15). The Reissert compound (**26**) was obtained in an 83% yield as a viscous brown oil. The oil was purified by column chromatography and 23% of white crystals were obtained. The desired product was recrystallized from hexanes/ethyl acetate giving a melting point of 148.3-149.3°C.

The Reissert compound **26** was then reacted with NaH in DMF. The yellow solution gradually turned green over a 24 hour time period. After 48 hours, the reaction mixture had turned black. The reaction was allowed to proceed for two days, at the end of which time the reaction mixture had turned a deep red. The reaction afforded 79% of crude product (**27**). The crude product was purified by column chromatography yielding 28% of a viscous yellow oil. The oil was recrystallized once from ethyl acetate/hexanes yielding a melting point of 135-136.3°C. Mass spectroscopy of the pure product showed an intense peak at 340 corresponding to the (M-1) peak due to fragmentation (loss of H⁺) probably resulting from loss of a benzylic proton. The molecular ion peak (M⁺) was found to be at 341. This was confirmed by calculating the relative intensities of the (M+1) and (M+2) peaks.

This reaction also yielded a second product in a 4% yield. Unlike the desired product, the ¹H NMR showed the presence of the methylene protons but loss of the H₃ proton. The exact product obtained is unknown, however, a plausible mechanism has been suggested which would explain the loss of the H₃ proton. This mechanism involves rearrangement of the acyl group to the 3-position (See Appendix). This product has been

submitted for mass spectroscopy and will be further examined.

The rearrangement of **26** resulted in the desired product and no black particles were observed, therefore it can be concluded that the presence of the carbonyl group at the 4-position is resulting in the formation of some type of side product possibly via an electron transfer process

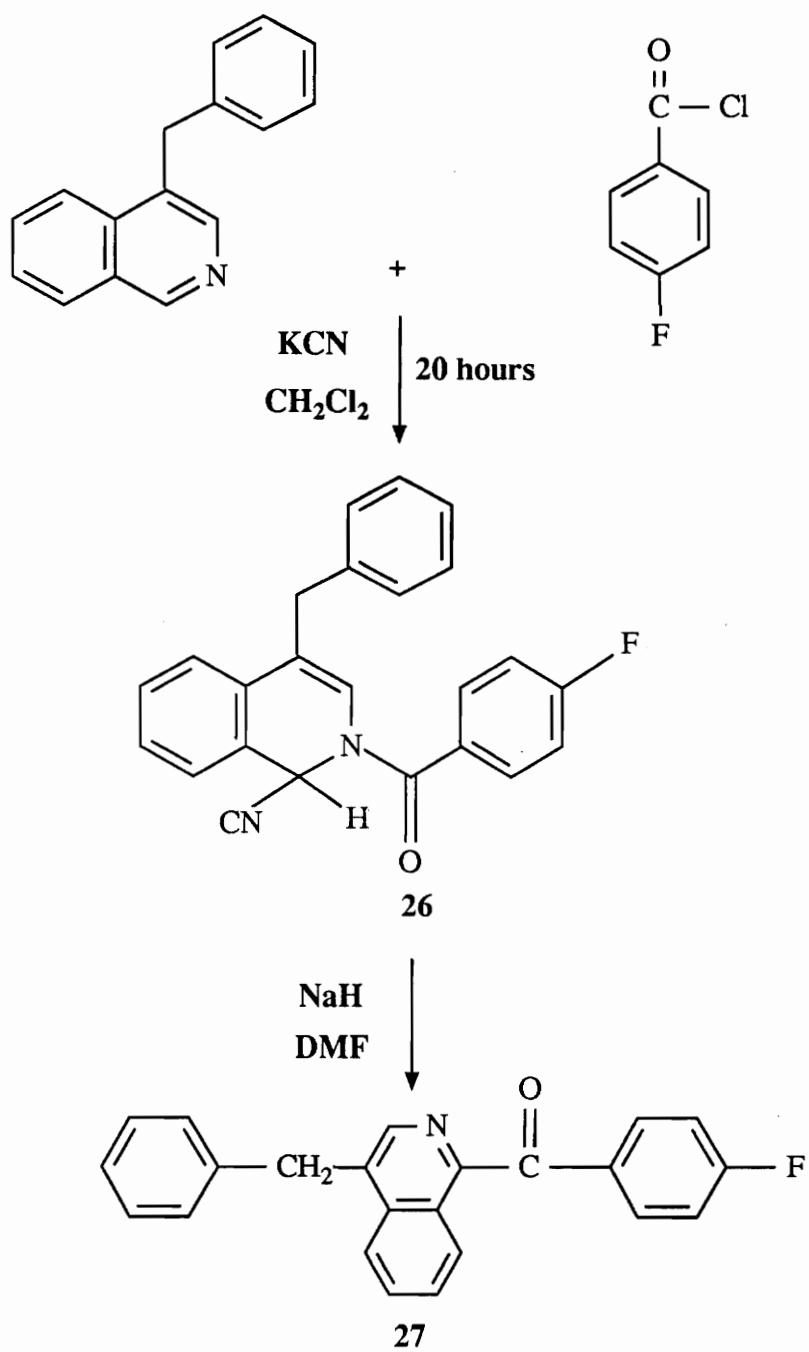
VI-5. Rearrangement of 2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinaldonitrile

In the case of a fluoro Reissert compound the anion might be displaced by the activated fluoride, causing polymerization instead of rearrangement to occur. This led to the investigation of the rearrangement of

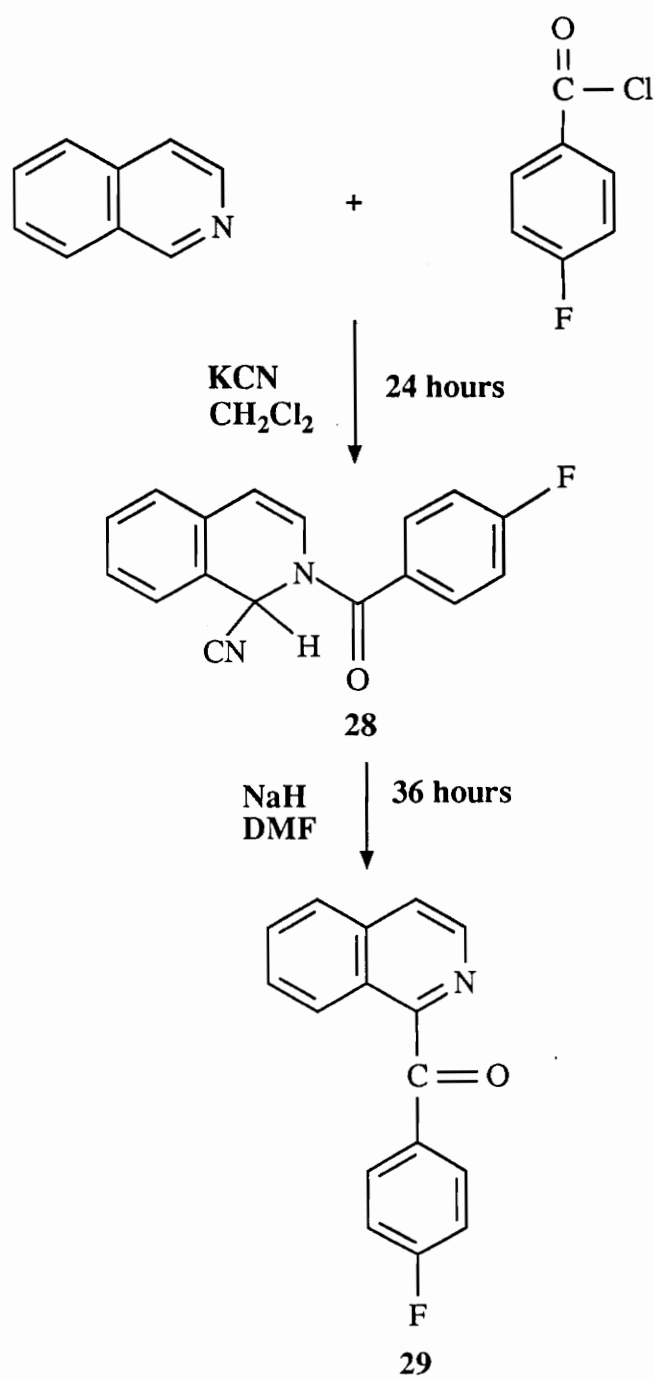
2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinaldonitrile (**28**) (Scheme 16). If the anion is displaced by the fluorine, the ¹H NMR spectrum (Figure 8) would show a slight chemical shift of the H₁, H₃, and H₄ protons.

2-(*p*-Fluorobenzoyl)-1,2-dihydroisoquinaldonitrile (**28**) was prepared via the two phase method. The desired product **28** was obtained in a 43% yield compared to a reported yield of 37%.¹⁰ After recrystallization from ethanol, a pure product was obtained with a melting point of 177-178°C, compared to a reported melting point of 178-179°C.¹⁰

2-(*p*-Fluorobenzoyl)-1,2-dihydroisoquinaldonitrile (**28**) then was reacted with NaH/DMF to obtain the rearranged product. The reaction was allowed to proceed for 36 hours to ensure complete rearrangement. The desired product **29** was obtained in a 90% yield as a brown oil. The crude product was purified by column chromatography and recrystallized from ethyl acetate/hexanes giving yellow crystals with a melting point of 91.0-92.2°C. ¹H NMR spectrum (Figure 9) showed complete loss of the H₁ proton and a shift of H₃ and H₄ protons upfield, confirming that rearrangement instead of displacement of the anion occurred.



Scheme 15: Synthesis of 1-(p-Fluorobenzoyl)-4-benzylisoquinoline



Scheme 16: Rearrangement of 2-(*p*-Fluorobenzoyl)-1,2-dihydroisoquinaldonitrile

VII. CONCLUSIONS AND FUTURE WORK

Bis(Reissert compound)s (**15**) and (**20**) were synthesized in good yield via a dibenzylic bis(isoquinoline) and a diketone bis(isoquinoline) system, respectively via the single phase method.

A novel difluorotetraketone monomer for high temperature polymers was prepared utilizing the chemistry of Reissert compounds and the enamine reaction reported by Minter and Re. Incorporation of the heterocyclic moiety into this monomer has produced a thermally stable polymer. This poly(ether ketone) hopefully will similar or better adhesive properties that the PEK adhesives currently being used.

In the model studies conducted, Reissert compounds (**24**) and (**26**) were synthesized in good yield. Investigation of their rearrangement indicated that the presence of a carbonyl at the 4-position results in the formation of a side product possibly via electron transfer.

Rearrangement of (**28**) resulted in the preparation of (**29**) rather than displacement of the anion causing polymerization to occur.

Future work entails conducting a HPLC prep scale separation of the isomers present in the tetraketone monomer, finding a efficient means of separation of a large scale of the monomer and finding another method of oxidation. If oxidation can be achieved by another route, this might eliminate the formation of isomers, as well as purification problems. Also, silylating the ketones prior to purification may be an alternative to the purification problem.

Once the tetraketone has been obtained it should be polymerized with various diphenols, eg. biphenol or hydroquinone. The mechanical properties of the resulting polymers should be investigated and see how they compare with the currently used PEK. In addition, the synthesis of a diketone dibenzylic compound along with its

polymerization with various diphenols will be attempted.

Also, the model system with a carbonyl at the 4-position should be thoroughly examined and exactly what is occurring should be determined. This could lead to a new route for the synthesis of the tetraketone monomer.

VIII. EXPERIMENTAL SECTION

General

Dichloromethane was used as received. N,N-dimethylformamide (DMF) and 1-methyl-2-pyrrolidinone (NMP) were distilled from calcium hydride and tetrahydrofuran (THF) from sodium/benzophenone prior to use. All yields are for crude products unless otherwise stated. Melting points were determined in a Mel-temp II melting point apparatus and are corrected. All proton NMR spectra were done in CDCl₃ and recorded on a Bruker 270 MHz instrument using trimethylsilane as an internal standard. FTIR spectra were recorded on a Nicolet MX-1 with KBr pellets or solutions on salt plates. Thermogravimetric analysis was performed on a Perkin-Elmer 7700 Thermal Analysis System, interfaced to an IBM PS2 computer. Differential Scanning Calorimetry was performed on a DuPont 2100 Dual-Sample interfaced to an IBM PS2 computer at 10°C/min. Gel Permeation Chromatograms (GPC) were run using a Waters 150-C equipped with an RI detector; this instrument provides absolute molecular weights, polydispersity index and Mark-Houwink constants. GPC (absolute) was done in THF using polystyrene standards. Intrinsic viscosity was measured in a Fisher Unelohde Scientific Viscometer 7300. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

α,α'-Bis(4-isoquinolyl)-p-xylene, (14). Isoquinoline, (10.33 g, 0.080 mole), was dissolved in 150 ml of dry THF. Sodium triethylborohydride was added gradually in four portions of 20 ml of 1.0 molar solution (80 ml, 0.80 mole). The reddish-brown solution was allowed to stir at room temperature for 30 minutes under nitrogen, after which terephthaldehyde, 5.10 g (0.038 mole), was added in one portion. The reaction was cooled to 0°C and 160 ml 0.5N NaOH were added. Ten minutes later, 80 ml of 30%

H₂O₂ were added gradually. Stirring was continued for 20 hours, at the end of which time the precipitate was collected and dried. Yield: 11.50 g (84%). Reported yield: 74%.⁴² After two recrystallizations from ethanol/water, the pure product was obtained, m.p. 190.4-190.7°C. Reported m.p. 186.5-187.5°C.⁴² ¹H NMR (CDCl₃): s, 4.33 ppm, 4H, methylene protons; s, 7.10 ppm, 4H, phenyl; m, 7.5-8.0 ppm, 8H, isoq. H_{5,8}; s, 8.38 ppm, 2H, isoq. H₃; s, 9.15 ppm, 2H, isoq. H₁.

α,α'-Bis[1-cyano-2-(*o*-toluoyl)-1,2-dihydroisoquinolin-4-yl]-*p*-xylene, (15).

Bis-isoquinoline **14**, (8.00 g, 0.0222 mole), was dissolved in 150 ml of DMF, after which 7.55 g (0.0488 mole) of *o*-toluoyl chloride were added. After 30 min of stirring, 4.84 g (0.0433 mole) of TMSCN were added, along with a catalytic amount of AlCl₃. The reaction was stoppered and stirred for five days. The solution was poured into water and filtered. Yield: 13.43 g (93%). After three recrystallizations from chloroform/hexanes, the pure product was obtained, m. p. 220.5-221.5°C. FTIR (KBr): 1672 cm⁻¹ (C=O). ¹H NMR (CDCl₃): s, 2.27 ppm, 6H, methyl protons; AB pattern, 3.60 ppm, 4H, methylene protons; s, 6.11 ppm, 1H, H₃; s, 6.76 ppm, 1H, H₁; m, 7.04-7.32 ppm, 22H, aromatic protons. Elemental analysis, found (calcd. for C₄₄H₃₄N₄O₂): C: 81.19 (81.21), H: 5.33 (5.27), N: 8.56 (8.61).

α,α'-Bis[4-{1-(*α*-toluoyloxy-*p*-fluorobenzyl)isoquinolyl}]-*p*-xylene, (16). To a

stirring solution of 8.00 g (0.012 mole) of the Reissert compound **15** and *p*-fluorobenzaldehyde in 150 ml of DMF, NaH (0.026 mole, 1.06 g of 60% dispersion in oil) was added at 25°C. The reaction mixture was stirred for two days, poured into water, and filtered. Yield: 8.38 g (83%). 0.62 g of the crude product was purified by column chromatography (silica gel, 50:50 hexanes/ethyl acetate) to afford 0.32 g (50%) of the desired product. The product was recrystallized once from ethyl acetate/hexanes,

m. p. 145.6-146.7°C. FTIR(KBR): 1714 cm^{-1} (C=O). ^1H NMR (CDCl_3): s, 2.58 ppm, 6H, methyl; s, 4.31 ppm, 4H, methylenes; s, 7.09 ppm, 4H, phenyl protons; s, 7.77 ppm, 2H, methine; s, 8.35 ppm, 2H, H_3 ; m, 6.99-8.32 ppm, 24H, remaining aromatic protons. Elemental analysis, Found (calcd. for $\text{C}_{56}\text{H}_{42}\text{N}_2\text{O}_4\text{F}_2 \cdot 1/5 \text{C}_4\text{H}_8\text{O}_2$): C: 78.72 (79.09), H: 4.88 (5.09), N: 3.23 (3.24) (note: calculated values were determined on the bases of 1/5 of a mole of ethyl acetate per mole being present).

α,α' -Bis[4-{1- α -hydroxy-*p*-fluorobenzyl}isoquinolyl]-*p*-xylene, (17). 10.00 g (0.0154 mole) of bis-isoquinoline Reissert compound **15**, 4.21 g (0.0339 mole) of *p*-fluorobenzaldehyde, and 1.07 g of benzyltrimethylammonium chloride were dissolved in 113 ml of acetonitrile. After 30 min of stirring, 14 ml of 50% NaOH were added. The reaction was allowed to stir for six hours with gradual heating in an oil bath to reflux the acetonitrile. After six hours of reflux, the reaction was diluted with 1L of water. The product was extracted with CHCl_3 and washed 3x with water. Yield: 8.84 g (94%). The FTIR spectrum of the crude product showed an ester carbonyl at 1715.6 cm^{-1} and no hydroxyl group, signifying incomplete reaction. The crude product was dissolved in 200 ml ethanol, 100 ml H_2O , and 40 g (0.71 mole) of KOH were added.⁴⁴ After refluxing overnight, the product was isolated by precipitation into water. Yield: 6.45 g (73%). Reported yield: 13.1% (isolated).⁴³ The crude product was found to have a melting point of 171-173°C. Reported m. p.: 174.2-175.5°C.⁴³ FTIR(KBr): 3378 cm^{-1} (OH). ^1H NMR (CDCl_3): s, 4.37 ppm, 4H, methylene protons; br, 6.21 ppm, 2H, hydroxyl protons; br, 6.32 ppm, 2H, methine protons; t, 6.96 ppm, 4H, ortho to fluorine; s, 7.14 ppm, 4H, phenyl; t, 7.29 ppm, 4H, meta to fluorine; t, 7.46 ppm, 2H, H_6 ; t, 7.60 ppm, 2H, H_7 ; m, 7.92, 4H, H_5 and H_8 ; s, 8.37 ppm, 2H, H_3 .

1,4-Bis[1-{4-(fluorobenzoyl)isoquinoly}carbonyl]benzene, (18). For 5.00 g (0.0082 mole) of alcohol **17**, 180 ml benzene, and 60 g manganese dioxide were used. The benzene/water azeotrope was collected via a Dean-Stark trap. The reaction was allowed to reflux for five days. At the end of the reaction, the oxides were filtered through Celite, and the Celite was washed with chloroform. The MnO₂ was Soxhlet extracted for five days with CHCl₃. The filtrates were dried over MgSO₄. The solvent was removed giving a crude yellow product. Yield: 2.30 g (44%). Reported yield: 60.6%.⁴³ 0.27 g of the crude product was purified by column chromatography (silica gel, 30:70 ethyl acetate/hexanes) to afford 0.01 g (3%) of pure product. The crude product was found to have a melting point of 210-214°C. Reported melting point: 228.2-230.2°C. FTIR(KBR): 1664.1 cm⁻¹, 1598.7 cm⁻¹ (C=O). ¹H NMR (CDCl₃): t, 7.18 ppm, 4H, ortho to fluorine; t, 7.72 ppm, 2H, H₆; t, 7.84 ppm, 2H, H₇; m, 8.03 ppm, 8H, phenyl and meta to fluorine; m, 8.24 ppm, 4H, H₅ and H₈; s, 8.71 ppm, 2H, H₃.

α,α'-Bis(4-isoquinolyl)carbonyl-*p*-xylene, (19). For 7.00 g (0.019 mole) of bis-isoquinoline **14**, 210 ml of benzene, and 70 g of manganese dioxide were used. The benzene/water azeotrope was collected via a Dean-Stark trap. The reaction was allowed to reflux for two days. At the end of the reaction, the oxides were filtered through Celite and the Celite was washed with chloroform. The MnO₂ was Soxhlet extracted for five days with CHCl₃. The collected filtrates were combined and dried over MgSO₄. The solvent was removed yielding a gold solid. Yield: 4.72 g (72%). The crude product was recrystallized three times from toluene/hexanes, m. p. 248.2-249.2°C. FTIR(KBr): 1664.5 cm⁻¹ (C=O). ¹H NMR (CDCl₃): m, 7.70-7.85 ppm, 4H, H₆ and H₇; s, 8.00 ppm, 4H, phenyl; d, 8.10 ppm, 2H, H₈; d, 8.25 ppm, 2H, H₅; s, 8.69 ppm, 2H, H₃; s, 9.42 ppm, 2H, H₁. Mass spect. (EI+): 388 (M+). Elemental analysis, found (calcd. for C₂₆H₁₆N₂O₂·1/3 C₈H₈): C: 80.77 (81.17), H: 4.47 (4.50), N: 6.68 (6.69) (note:

calculated values were determined on the bases of 1/3 of a mole of toluene per mole being present).

1,4-Bis[4-{1-cyano-2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinolinyl}carbonyl]benzene, (20). 4.00 g (0.0111 mole) of diketone bis-isoquinoline **19** were dissolved in 200 ml of CHCl₂, after which 3.87 g (0.0244mole) of *p*-fluorobenzoyl chloride were added. After 30 min of stirring, 2.42 g (0.0244 mole) of TMSCN were added, along with a catalytic amount of AlCl₃. The reaction was stoppered and stirred for four days. The solution was poured into water and filtered. Yield: 7.62 g (89%). 1.28 g of the crude product was purified by column chromatography (silica gel, 40:60 hexanes/ethyl acetate) to afford 0.39 g (30%) of the desired product. The crude product was recrystallized from chloroform/hexanes, m. p. 249.0-249.5°C. FTIR(KBr): 1677.2 cm⁻¹, 1651.1 cm⁻¹ (C=O). ¹H NMR (CDCl₃): s, 6.47 ppm, 2H, H₁; m, 7.16-7.18 ppm, 8H, ortho to fluorine and H₅ and H₈; s, 7.26 ppm, 4H, phenyl; m, 7.68-7.78 ppm, 8H, H₆ and H₇; s, 7.82, 1H, H₃. Mass spect. (EI): 686 (M+). Elemental analysis, found (calcd. for C₄₂H₂₄N₄O₄F₂): C: 73.20 (73.46), H: 3.65 (3.52), N: 8.16 (8.09).

1,4-Bis{1-[4-*p*-(fluorobenzoyl)isoquinoly]carbonyl}benzene, (18). To a stirring solution of 0.50 g of the diketone Reissert compound **20** in 20 ml of DMF, NaH (0.07 g, 0.0015 mole) was added at 0°C. The reaction mixture was stirred for two days at 0°C, poured unto ice, filtered, and dried. Yield: 0.30 (68%). FTIR(KBr): 1670.4 cm⁻¹ (broad peak). ¹H NMR spectrum was complicated due to side products resulting from the presence of the carbonyl group.

Polymerization of 1,4-Bis{1-[4-*p*-(fluorobenzoyl)isoquinoly]carbonyl}benzene with Bisphenol A to form (21). 1.0000 g (0.00157 mole) of the tetraketone **18** and 0.3584 g

(0.00157 mole) of bisphenol A were dissolved in 9 ml of NMP freshly distilled from CaH. Then, 0.2604 g (0.00157 mole) of anhydrous K_2CO_3 and 4 ml of toluene were added. The mixture was heated in an oil bath under N_2 and kept at 140-145°C for 4 hours. The temperature was then raised to 160-170°C and maintained for 13 hours. The reaction mixture was cooled, diluted with $CHCl_3$, filtered, acidified with acetic acid, and precipitated into methanol to yield 0.95 g (74%) of crude tan polymer. Intrinsic viscosity of the polymer in chloroform was determined to be 0.16 dl/g at 25°C. GPC of the polymer in THF showed $M_n=4800$ and $M_w=7800$. The polymer was found to be stable up to 454°C in air. DSC showed a $T_g=180^\circ C$ and no T_m . FTIR(KBr): 1664.1 cm^{-1} (C=O), 1592.2 cm^{-1} , 1500.6 cm^{-1} (C=C), 1245.4 cm^{-1} (C-O-C). 1H NMR ($CDCl_3$): s, 1.70 ppm, 6H, methyl; m, 6.90-7.09 ppm, 8H, ortho to oxygen; m, 7.2-7.28 ppm, 6H, ortho to carbonyl; t, t, 7.68 ppm, 7.80 ppm, 2H each, isoquinolyl H_6 and H_7 ; d, 7.92 ppm, 2H, isoquinolyl H_5 ; s, 8.04 ppm, 4H, ortho to isopropylidene; d, 8.15 ppm, 2H, isoquinolyl H_8 ; s, 8.70 ppm, 2H, isoquinolyl H_3 .

4-Benzylisoquinoline, (22). Isoquinoline, (10.00 g, 0.077 mole), of was dissolved in 150 ml of dry THF. Sodium triethylborohydride was added gradually in three portions 30 ml, 30 ml, 17 ml of a 1.0 molar solution (80 ml, 0.080 mole). The brown solution was allowed to stir at room temperature for 30 min under nitrogen, after which 12.20 g (0.115 mole) of benzaldehyde was added. The solution turned black and faded to a yellow color over two hours. The reaction was cooled to 0°C and 154 ml of 0.5N NaOH were added followed by the gradual addition of 77 ml of 30% H_2O_2 . Stirring was continued rapidly for 17 hours, after which it was poured into a separatory funnel containing 50 ml of H_2O . The product was extracted with CH_2Cl_2 (3x 75 ml), dried over Na_2SO_4 and concentrated. Yield: >100%. Reported yield: 65%. The crude product was found to have a melting point of 81-88°C. Reported m.p.: 117.5-118.5°C.²³

$^1\text{H NMR}$ (CDCl_3): s, 4.36 ppm, 2H, methylene protons; m, 7.13-7.28 ppm, 5H, phenyl; t, 7.54 ppm, 1H, H_7 ; t, 7.61 ppm, 1H, H_6 ; d, 7.89 ppm, 1H, H_5 ; d, 7.95 ppm, 1H, H_8 ; s, 8.41 ppm, 1H, H_3 ; s, 9.17 ppm, 1H, H_1 .

4-Benzoylisoquinoline, (23). For 5.00 g (0.0228 mole) of crude 4-benzylisoquinoline **22**, 150 ml of benzene, and 50 g of manganese dioxide were used. The benzene/water azeotrope was collected via a Dean-Stark trap. The reaction was allowed to reflux for two days. At the end of the reaction, the oxides were filtered through Celite and the Celite was washed with chloroform. The MnO_2 was Soxhlet extracted for four days with CHCl_3 . The collected filtrates were combined and dried over MgSO_4 . The solvent was removed producing a viscous yellow oil. Yield: 3.54 g (66%). The yellow oil was triturated with ethanol and further recrystallized three times from ethyl acetate/hexanes (note: ethyl acetate/hexanes precipitated the impurities present). The resulting product was then recrystallized twice from toluene/hexanes. The melting point of the pure product was found to be 77.4-78.7°C. FTIR(KBr): 1657.6 cm^{-1} (C=O). $^1\text{H NMR}$ (CDCl_3): m, 7.48-7.53 ppm, 2H, meta to carbonyl; m, 7.62-7.81 ppm, 3H, $\text{H}_{6,7}$ and para to carbonyl; m, 7.87-7.91 ppm, 2H, ortho to carbonyl; d,d, 8.09 ppm, 8.17 ppm, 1H each, H_5 and H_8 ; s, 8.65 ppm, 1H, H_3 ; s, 9.41 ppm, 1H, H_1 . Elemental analysis, found (calcd. for $\text{C}_{16}\text{H}_{11}\text{NO}$): C: 82.37 (82.38), H: 4.81 (4.75), N: 5.93 (6.00).

2-(*p*-fluorobenzoyl)-4-benzoyl-1,2-dihydroisoquinolidonitrile, (24). Ketone **23**, (1.00 g, 0.0043 mole), was dissolved in 20 ml of CH_2Cl_2 , after which 0.745 g (0.0047 mole) of *p*-fluorobenzoyl chloride was added. After 30 min of stirring, 0.466 g (0.0047 mole) of TMSCN was added along with a catalytic amount of AlCl_3 . The reaction was stoppered and stirred for seven days. The solution was poured into 500 ml of water, stirred

overnight and filtered. Yield: 1.40 g (85%). After three recrystallizations from toluene/hexanes, the pure product was obtained, m. p. 170.4-171.7°C. ^1H NMR (CDCl_3): s, 8.49 ppm, 1H, H_1 ; d, 7.13 ppm, 1H, H_5 ; m, 7.38-7.46 ppm, 5H, phenyl; d, 7.54 ppm, 1H, H_8 ; m, 7.64-7.80 ppm, 6H, remaining aromatic protons. Elemental analysis, found (calcd. for $\text{C}_{24}\text{H}_{15}\text{N}_2\text{O}_2\text{F}$): C: 75.38 (75.38), H: 3.96 (3.95), N: 7.33 (7.33).

4-Benzoyl-1-(*p*-fluorobenzoyl)isoquinoline, (25). To a stirring solution of 0.50 g (0.0013 mole) of the Reissert compound **24** in 20 ml DMF, NaH (0.07 g, 0.0016 mole) was added at 25°C. The reaction mixture was stoppered for one day, poured unto ice, filtered and dried. Yield: 0.15 g (33%). ^1H NMR spectrum complicated due to side products resulting from the presence of the carbonyl group.

2-(*p*-Fluorobenzoyl)-4-benzyl-1,2-dihydroisoquinaldonitrile, (26).

4-Benzylisoquinoline **22**, (5.00 g, 0.0228 mole) was dissolved in 50 ml of CH_2Cl_2 . Then, 4.45 g (0.0684 mole) of KCN dissolved in 11 ml of water were added to the CH_2Cl_2 solution. The resulting mixture was stirred for 15 min prior to the dropwise addition of 7.23 g (0.0456 mole) of *p*-fluorobenzoyl chloride over two hours. The reaction was stirred for 20 hours, after which 100 ml water were added. The layers were separated. The organic layer was washed with water 3x, 10% HCl 3x, H_2O 3x, 10% NaHCO_3 3x, and water 3x. The solution was dried over NaSO_4 for one day and concentrated. Yield: 6.96 (83%). 2.00 g of the crude product were purified by column chromatography (silica gel, 90:10 hexanes/ethyl acetate) to afford 0.46g (23%) of product, which were recrystallized from hexanes/ethyl acetate to give a pure product, m. p. 148.3-149.3°C. FTIR (KBr): 1664.1 cm^{-1} (C=O). ^1H NMR (CDCl_3): AB pattern, 3.82 ppm, 2H, methylene protons; s, 6.37 ppm, 1H, H_3 ; s, 6.52 ppm, 1H, H_1 ; m,

7.08-7.63 ppm, 11, H, aromatic protons; m, 8.09-8.15 ppm, 2H, alpha to oxygen.

Elemental analysis, found (calcd. for $C_{24}H_{17}N_2OF$): C: 77.99 (78.25), H: 4.71 (4.65), N: 7.53 (7.60).

1-(*p*-Fluorobenzoyl)-4-benzyisoquinoline, (27). To a stirring solution of 0.63 g of the 4-benzyisoquinoline Reissert compound **26** in 40 ml of DMF, NaH (0.0020 mole, 0.08 g of 60% dispersion in oil) was added at 25°C. The reaction was stirred for 2 days, poured unto ice, and filtered. Yield: 0.46 g (79%). 0.46 g of the crude product was purified by column chromatography (silica gel, 60:40 hexanes/ethyl acetate) to afford 0.13 g (28%) of a yellow solid. The solid was recrystallized once from ethyl acetate/hexanes, m. p. 135-136.3°C. FTIR(KBr): 1723.0 cm^{-1} (C=O). 1H NMR ($CDCl_3$): s, 4.47 ppm, 2H, methylene; m, 7.07-7.42 ppm, 7H, ortho to fluorine and phenyl protons; m, 7.76-7.79 ppm, 2H, meta to fluorine; m, 8.03-8.39 ppm, 4H, $H_{5,8}$; s, 8.53 ppm, 1H, H_3 . Mass spect. (EI): 341 (M^+), 340 (M^+-H).

2-(*p*-Fluorobenzoyl)-1,2-dihydroisoquinolidonitrile, (28). 1.00 g (0.0077 mole) of isoquinoline was dissolved in 10 ml of CH_2Cl_2 . Then, 1.50 g (0.0231 mole) KCN dissolved in 4 ml of water were added to the CH_2Cl_2 solution. The resulting mixture was stirred for 15 min prior to the dropwise addition of 2.44 g (0.0154 mole) of *p*-fluorobenzoyl chloride over 2 hours. The reaction was stirred overnight, after which 100 ml of water was added. The layers were separated. The organic layer was washed with water 3x, 10% HCl 3x, water 3x, 10% $NaHCO_3$ 3x, and water 3x. The final solution was dried over Na_2SO_4 for one day and the solvent was removed. Yield: 0.92 g (43%). Reported yield: 37%.¹⁰ The crude product was recrystallized once from ethanol giving white needles, m. p. 177-178°C.¹⁰ Reported m. p.: 178-179°C.¹⁰ FTIR(KBr): 1664.1 cm^{-1} (C=O). 1H NMR ($CDCl_3$): d, 6.10 ppm, 1H, H_4 ; s, 6.52, 1H, H_1 ; d, 6.61

ppm, 1H, H₃; m, 7.13-7.67 ppm, 8H, aromatic protons.

1-(*p*-fluorobenzoyl)isoquinoline, 29. To a stirring solution of 1.00 g of 2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinolaldehyde **28** in 40 ml of DMF, NaH (0.0043 mole, 0.17 g of 60% dispersion in oil) was added at 25°C. The reaction mixture was stirred for 36 hours, poured onto ice, and extracted with CH₂Cl₂. Yield: 1.63 g (90%) (viscous brown oil). 0.67 g of a yellow solid (obtained after first column) was purified by column chromatography (silica gel, 60:40 hexanes/ethyl acetate) to afford 0.51 g (76%) of product which was recrystallized two times from ethyl acetate/hexanes to give a pure product, m. p. 91.0-92.2°C. FTIR (KBr): 1664.1 cm⁻¹ (C=O). ¹H NMR (CDCl₃): m, 7.12-7.18 ppm, 2H, ortho to fluorine; m, 7.61-8.04 ppm, 6H, remaining aromatic protons; d, d, 8.22 ppm, 8.59 ppm, 1H each, H₄ and H₃. Elemental analysis, found (calcd. for C₁₆H₁₀NOF): C: 76.38 (76.49), H: 4.00 (4.01), N: 5.53 (5.57).

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APPENDIX

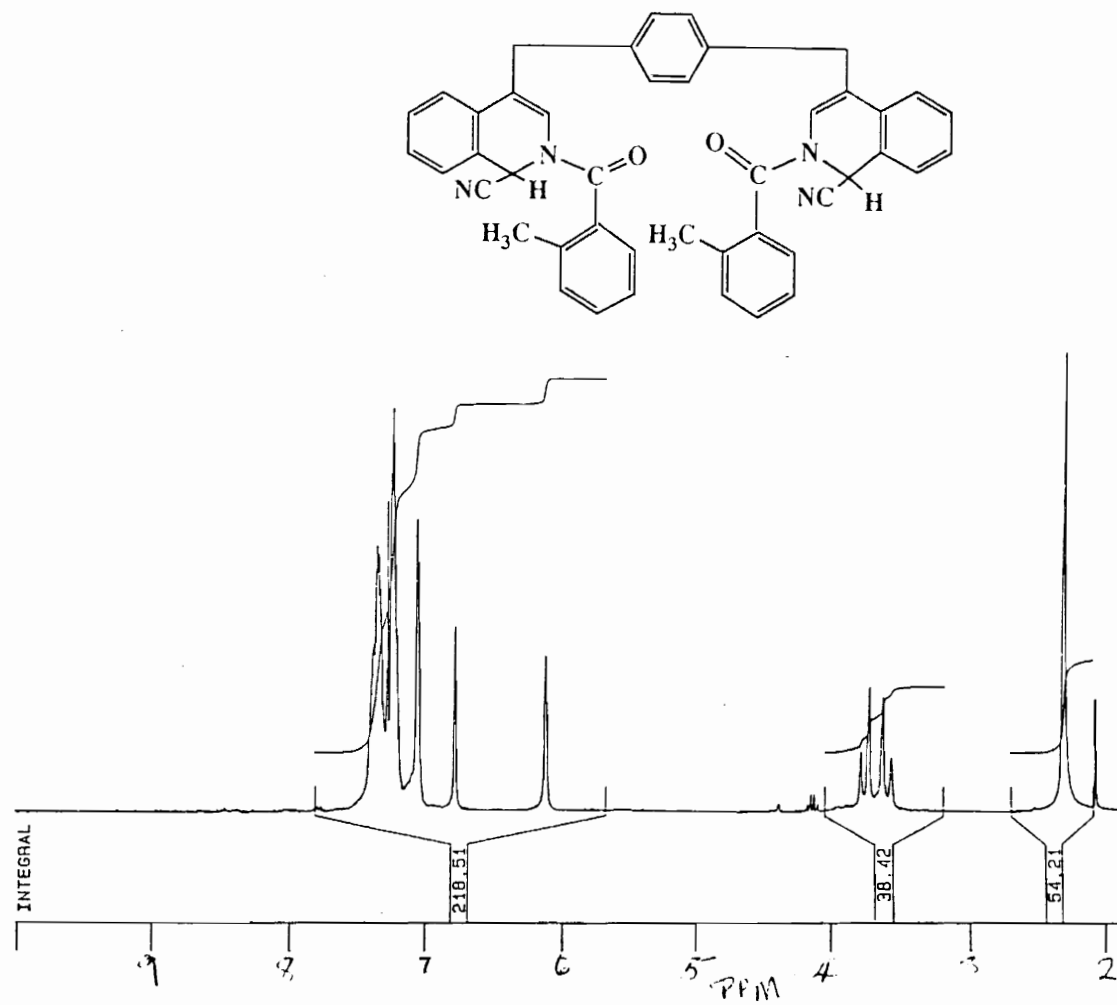


Figure 1: ¹H NMR spectrum of *o*-Toluoyl Reissert Compound (15) in CDCl₃.

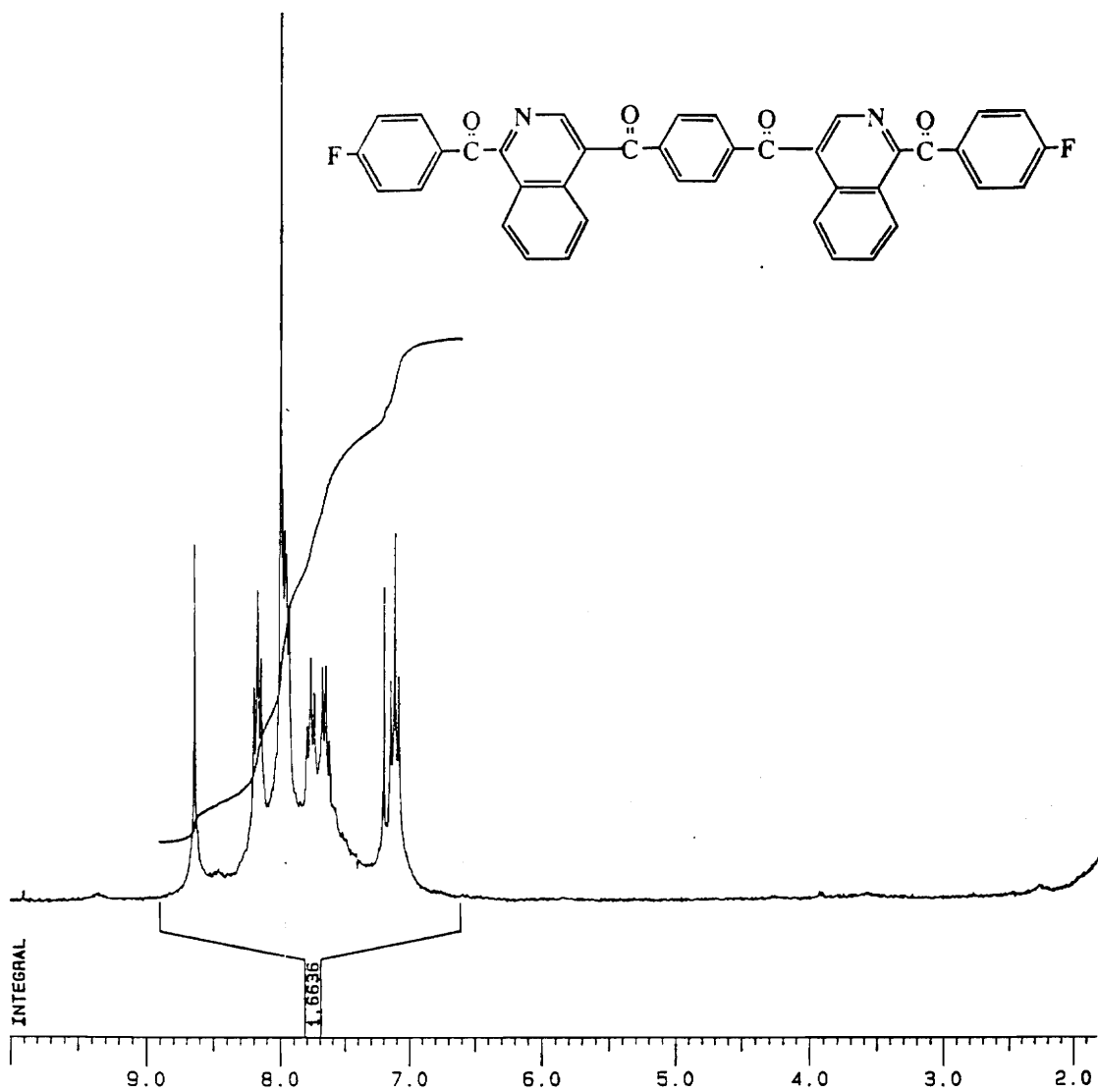


Figure 2: ^1H NMR spectrum of Tetrakertone Monomer (18) in CDCl_3 .

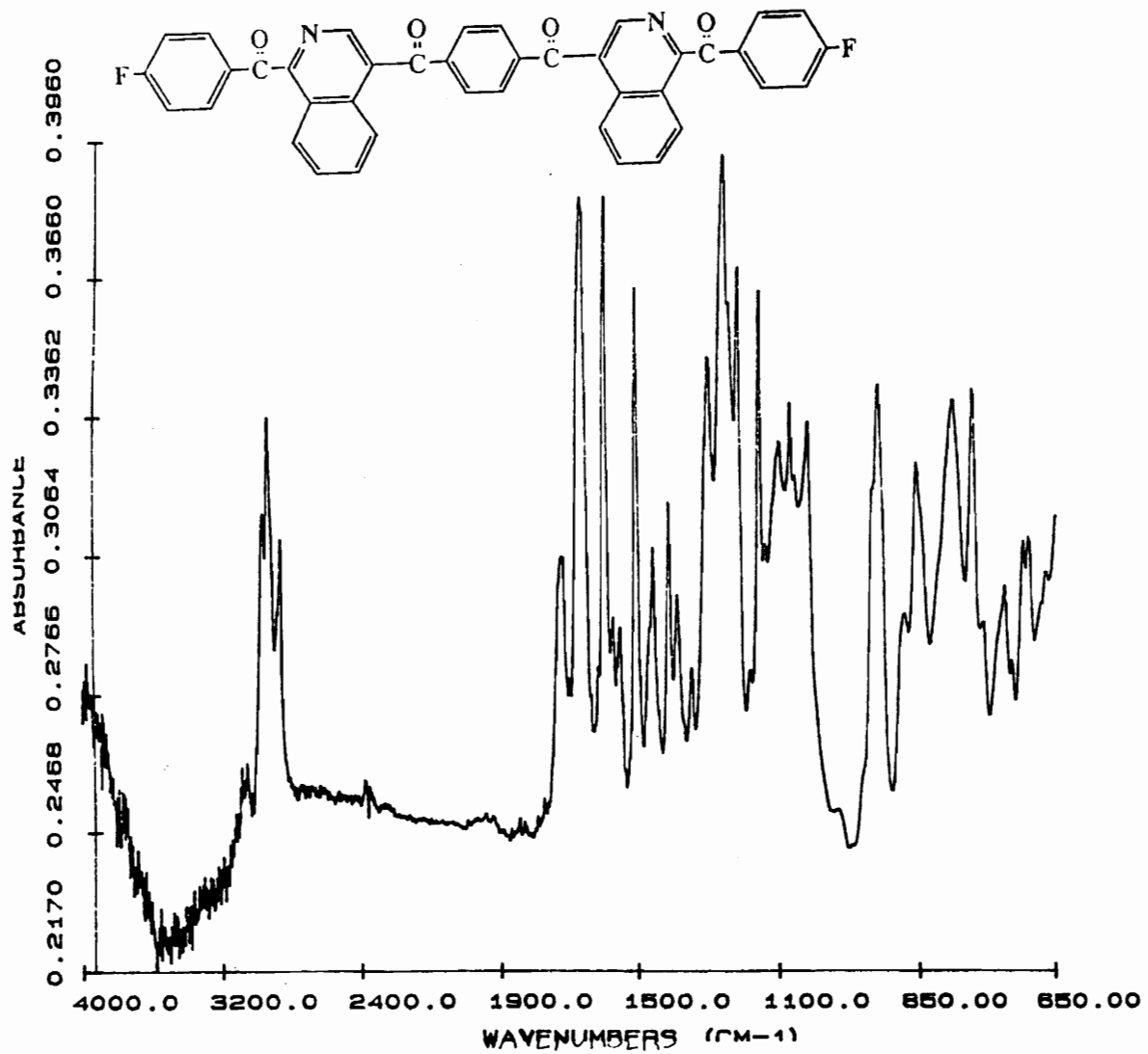


Figure 3: FTIR spectrum of Tetraketone Monomer (18) in CDCl₃.

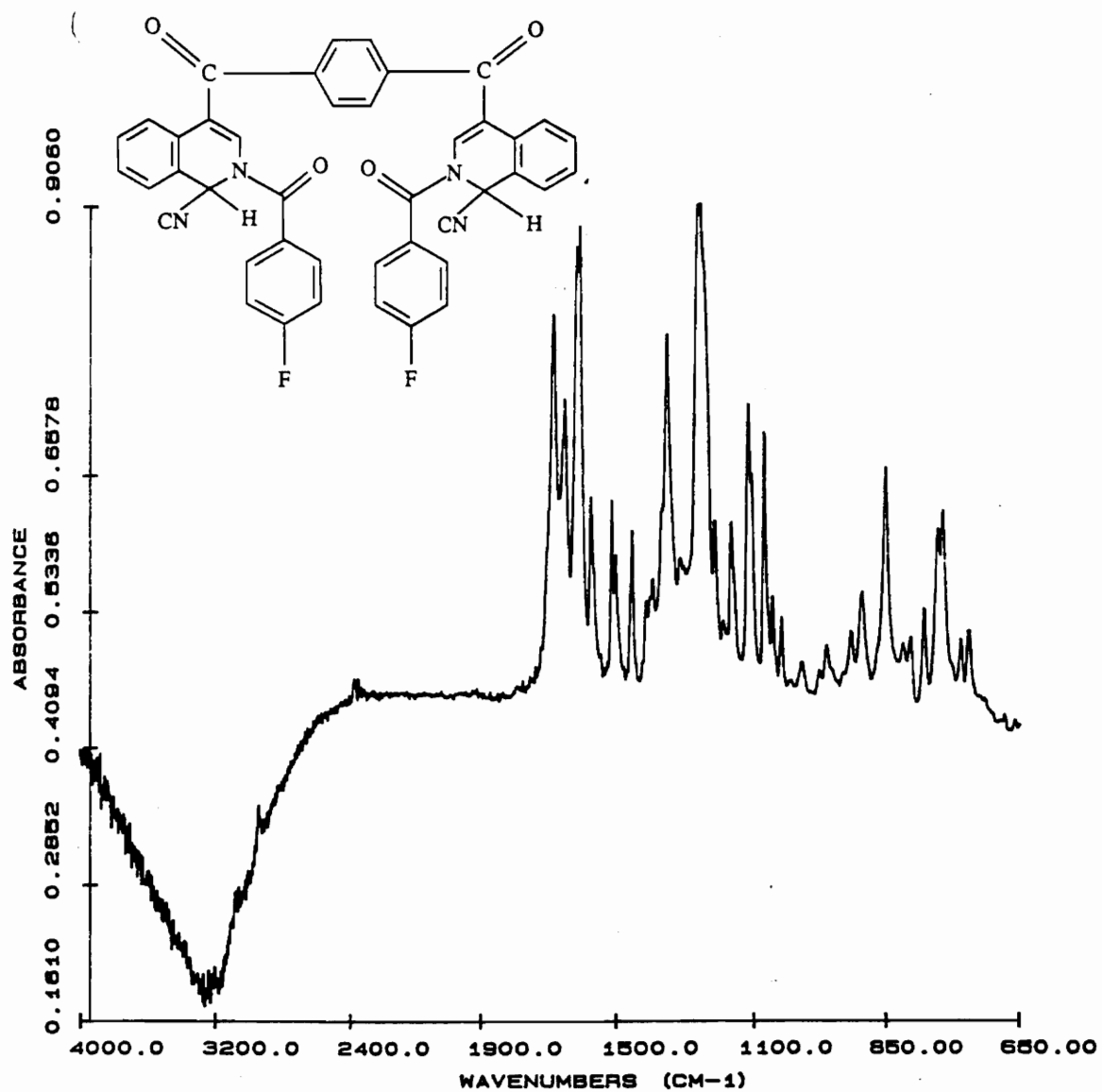


Figure 4: FTIR spectrum of Diketone Bis(isoquinoline) Reissert Compound (20) in CDCl₃.

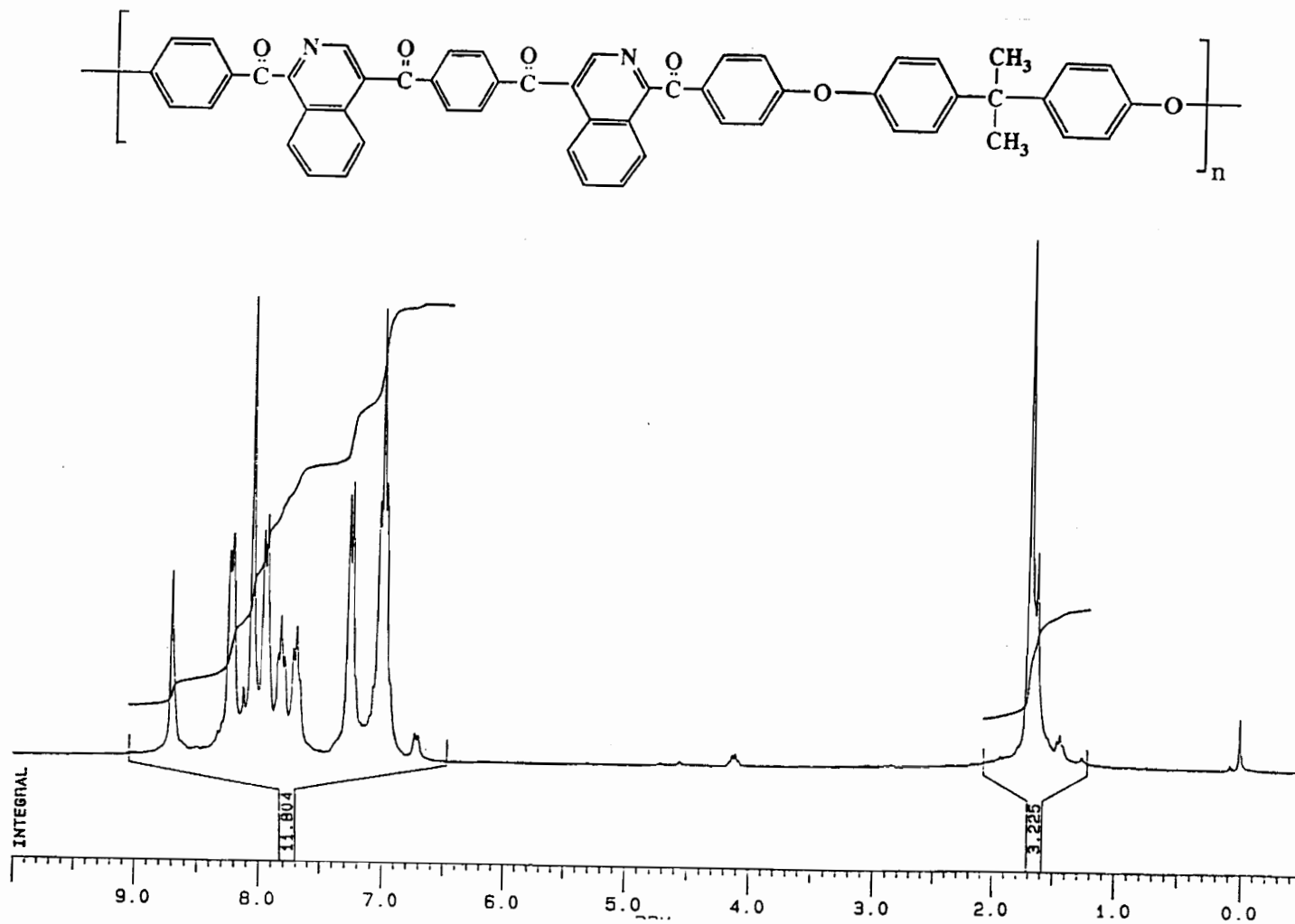


Figure 5: ¹H NMR spectrum of Polymerization of Tetraketone Monomer with Bisphenol A (21) in CDCl₃.

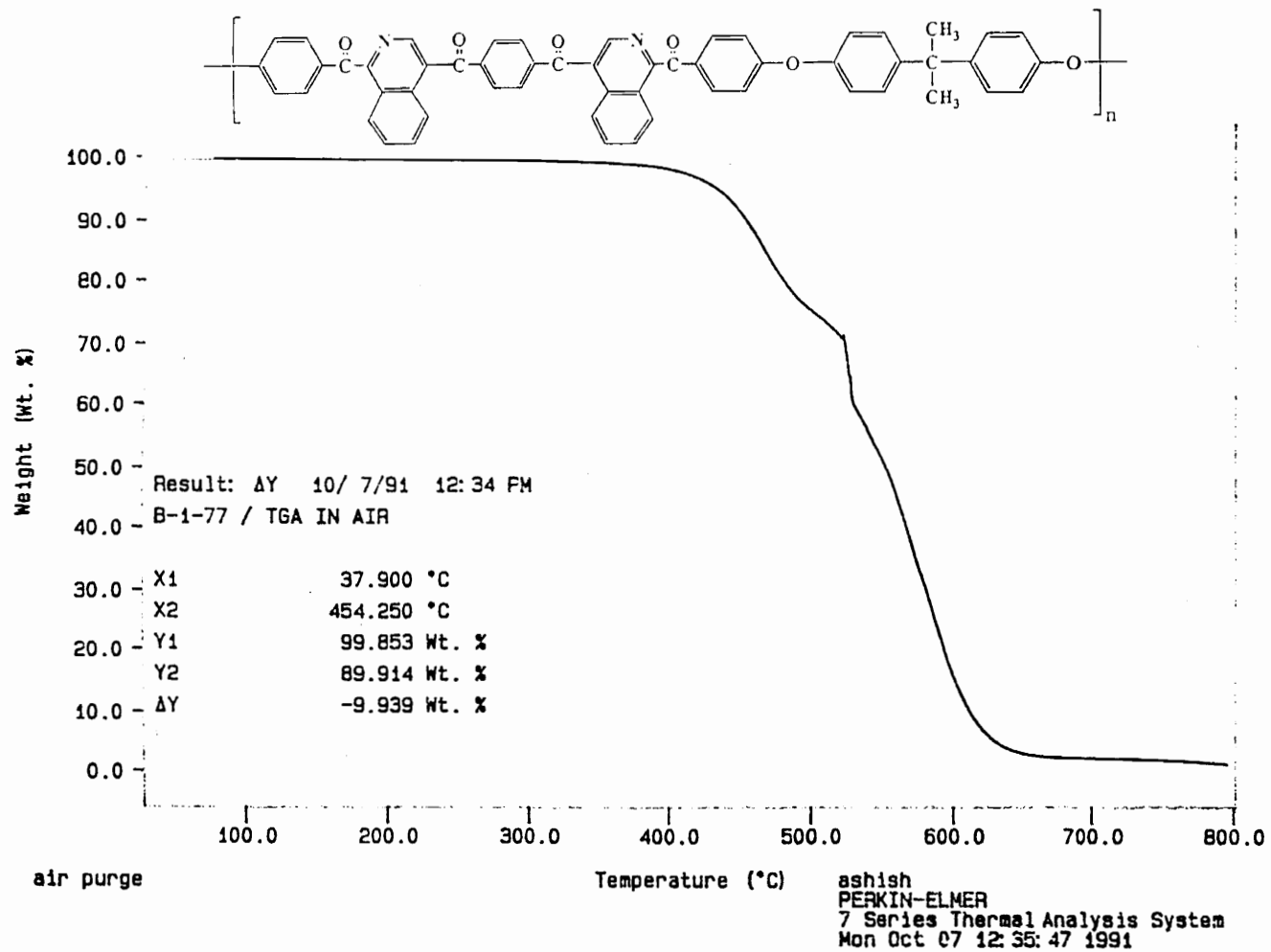


Figure 6: TGA of (21) in air.

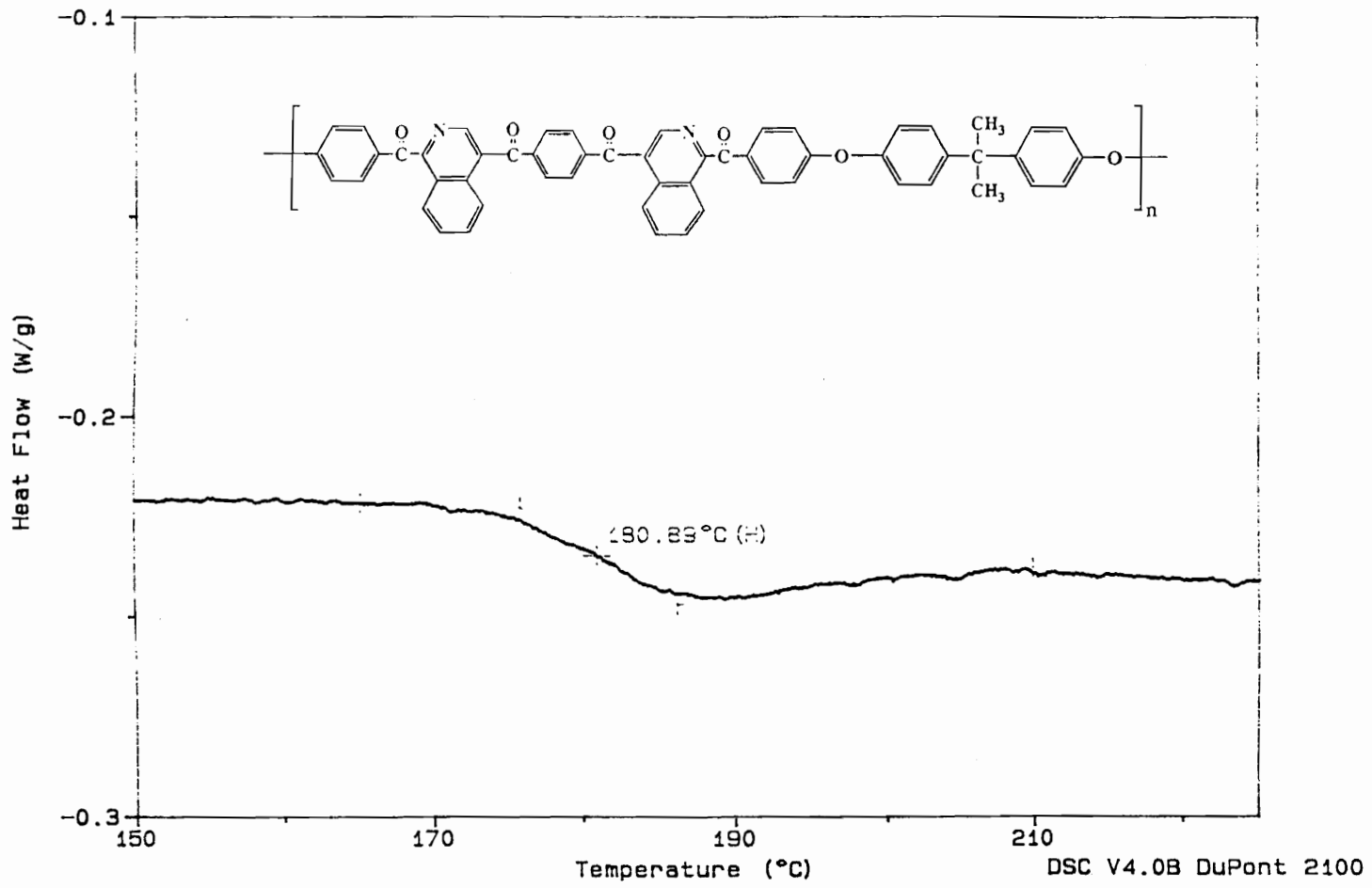


Figure 7: DSC of (21), second heat after cooling at 10°C/min.

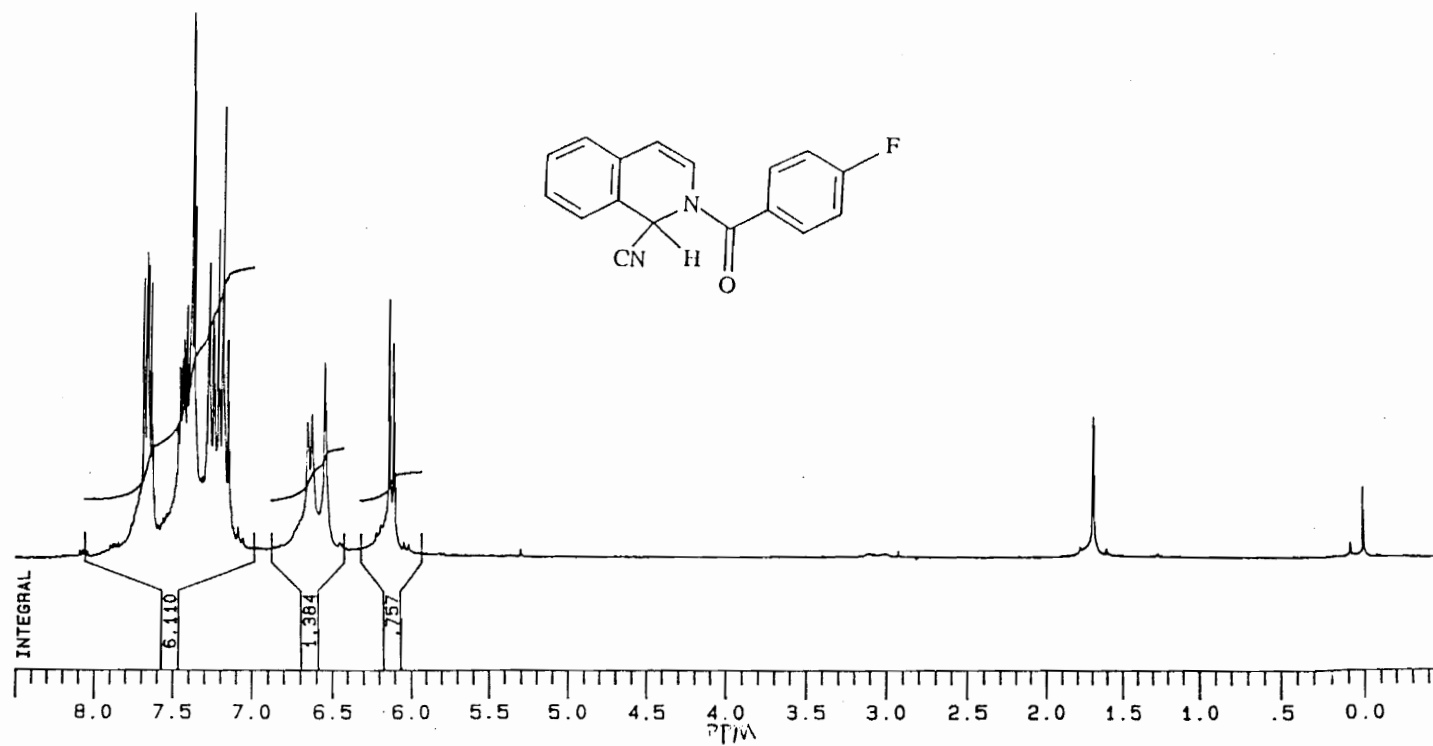


Figure 8: ^1H NMR spectrum of (28) in CDCl_3 .

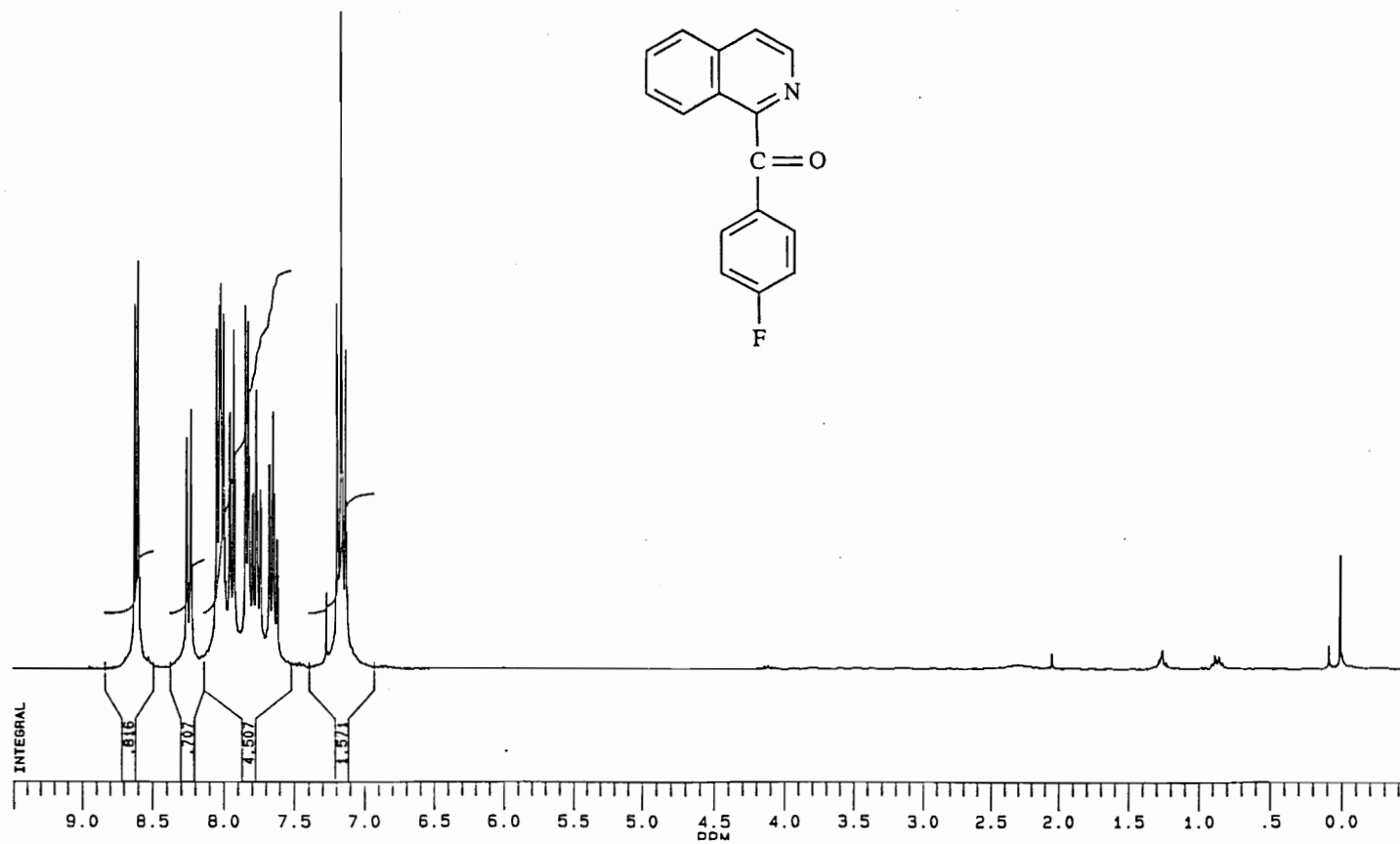
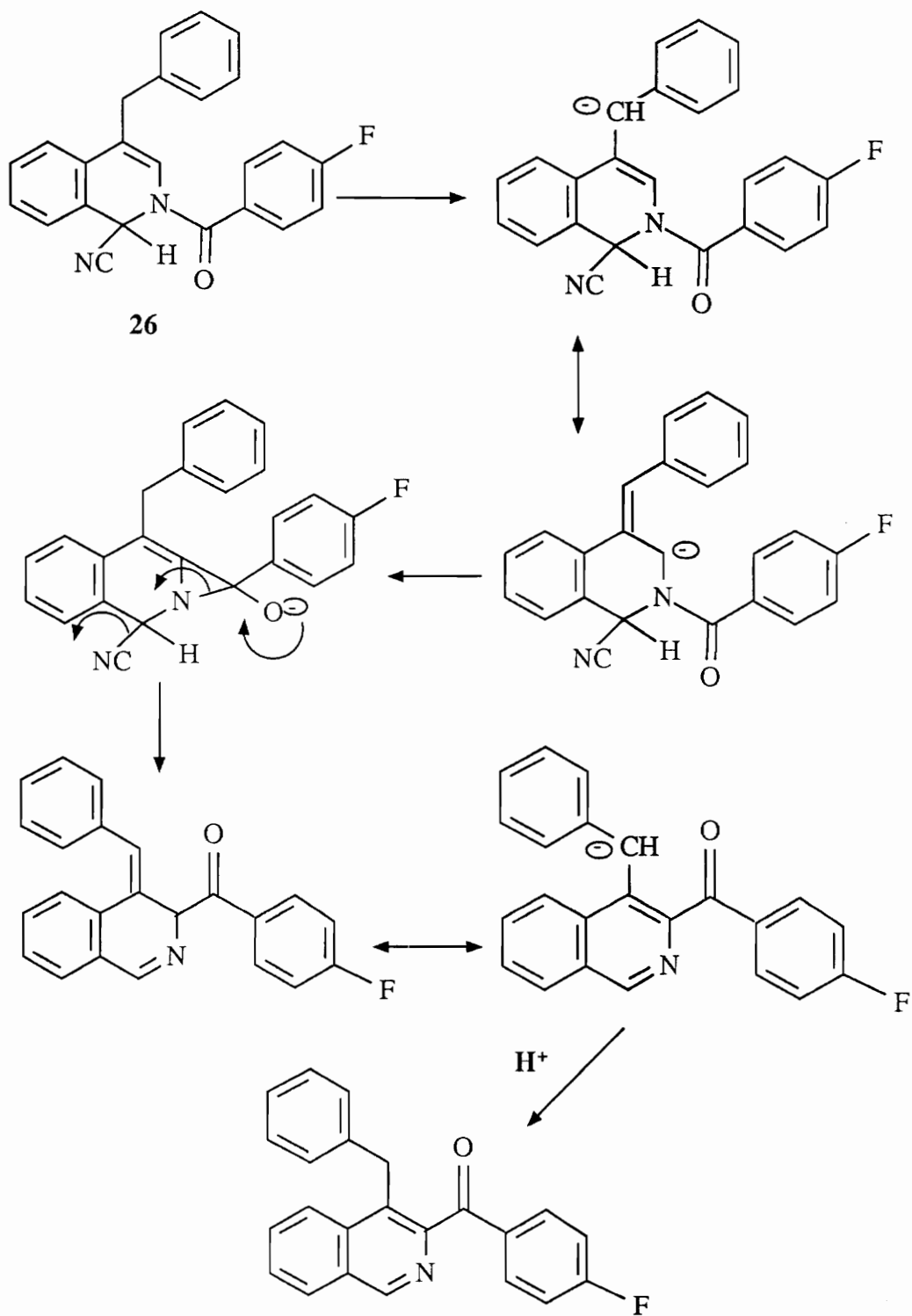


Figure 9: ^1H NMR spectrum of (29) in CDCl_3 .



Proposed Mechanism of Alternate Rearrangement of (**26**)

XI. VITA

Kimberly Kenyaratta Brumfield was born July 14, 1967 to Barbara and Joseph Brumfield. In 1985, she attended Alcorn State University where she received a Bachelor of Science in Chemistry in 1989. Immediately after her undergraduate studies, she chose to pursue a graduate degree in chemistry at Virginia Tech under the direction of Dr. H. W. Gibson.

A handwritten signature in black ink that reads "Kimberly A. Brumfield". The signature is written in a cursive style with a long horizontal flourish underneath.