SYNTHESIS OF NOVEL HETEROCYCLIC DIFLUORO MONOMERS VIA THE CHEMISTRY OF REISSERT COMPOUNDS

by

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(ABSTRACT)

Activated dichloro- and difluoro- monomers are well known for the synthesis of high-performance polymeric materials through the use of aromatic nucleophilic displacement reactions. Here, novel activated difluoro monomers were synthesized using the well established chemistry of Reissert compounds. Difunctional bis(Reissert compound)s were synthesized by the reaction of 4-(p-fluorobenzylisoquinoline) and trimethylsilyl cyanide with the following diacid chlorides: sulfonylbis(p-phenyleneoxy)dibenzoyl chloride, oxybis(benzoyl chloride), and sulfonylbis(benzoyl chloride). These aforementioned compounds were rearranged using NaH/THF to produce the desired diketones. Finally, difluorotetraketone monomers were produced by oxidation of the benzylic methylenes of the diketones. These reactions were evaluated by FTIR and ^{1}HNMR. These new activated heterocyclic difluorotetraketones are precursors to novel heterocyclic poly(ether ketones).

ACKNOWLEDGEMENTS:

The information presented in this thesis would not have been possible were it not for the guidance, understanding, and encouragement of several people. First, I'd like to thank Dr. Harry Gibson for allowing me the opportunity to work and study as a member of his research group for the past 2.5 years. The time spent in Dr Gibson's group allowed me to grow not only educationally, but creatively as well. I also wish to thank Dr. Harold McNair for the support and understanding shown during my last year at Tech. I would like to say thank-you to Dean Martha Johnson and the graduate school for the Particia Harris Roberts fellowship.

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Most of all, I would like to thank my family for standing beside me, and for not losing faith in me. In particular my mom, Laura, who always taught me to set my dreams high, and never give up. I would also like to thank my cousins,

James Grisle and Julian Parker, for being my sounding board throughout this whole ordeal, "may they forever look to the east".

And last, but certainly not least, to my darling wife, Michelle, I would like to say thank-you for the compassion, thoughtfulness, support, understanding, and love shown during the last 3 years. Darling, I couldn't have done it without you.

DEDICATION

This thesis is dedicated to my loving mother, Laura;

my sisters, Cathia, Yvonne, and Natasha;

my wife and loving companion, Michelle;

and finally to the loving memory of my father and brother,

Roger and Derrick Grisle.

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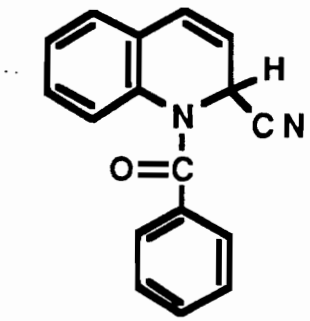
As society prepares to move into the 21st century, there will undoubtly be several challenges awaiting those who have chosen to venture into the realm of polymer science. In today's world, polymers are used in such areas as construction, weapons, clothing, engine components and decoration. Polymers have not only gone to the moon, but are commonly used in the development of human prostheses as well, e.g. the Jarvik-7 heart which was formed from polyurethane. One important class of polymeric materials are heterocyclic polymers. Heterocyclic polymers, especially nitrogen-containing heterocyclic polymers like polyimides, are well-known for their high thermal stabilities and excellent mechanical properties.

Heterocyclic polymers are usually prepared via a two-step process whereby formation of the heterocyclic ring occurs during the polymerization process. However, heterocyclic polymers can also be prepared via aromatic nucleophilic displacement reactions which allows one to preform the heterocylic units prior to polymerization. Here, the synthesis of novel (activated) difluoro-monomers containing isoquinolyl units will be discussed.

II. HISTORICAL SECTION:

1. REISSERT CHEMISTRY:

1-Benzoyl-1,2-dihydroquinaldonitrile (**1**) and 2-benzoyl-1,2-dihydroisoquinaldonitrile (**2**), generally referred to as quinoline and isoquinoline "Reissert compounds," respectively, are members of an interesting class of nitrogen-containing heterocyclic compounds founded in 1905 by their namesake, Arnold Reissert.[1] Reissert found that reacting quinoline and benzoyl chloride in an aqueous solution of sodium hydroxide, analogous to the Schotten-Baumann technique, yielded a crystalline solid, $C_{16}H_{13}NO_2$. When treated with mineral or glacial acetic acid he found cleavage to quinoline and benzoic acid was possible. Based on this information, the structure was tentatively assigned that of **3**. Aldehyde characteristics discovered in later investigations,[2] however, led to its assignment as **4**.



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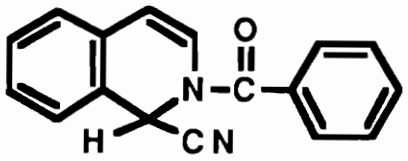

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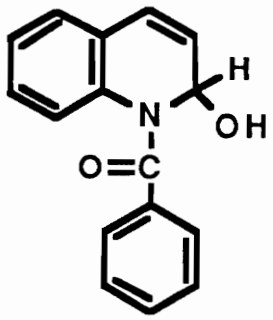

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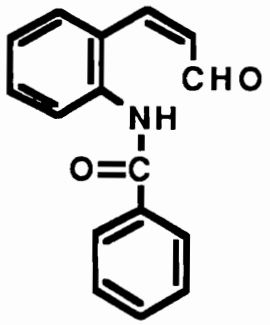

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In a subsequent reaction,[1] quinoline and benzoyl chloride were reacted in aqueous potassium cyanide, yielding yet another crystalline product, $C_{17}H_{12}N_2O$ (**1**). When subjected to acid, it underwent hydrolysis to benzaldehyde and quinaldic acid.

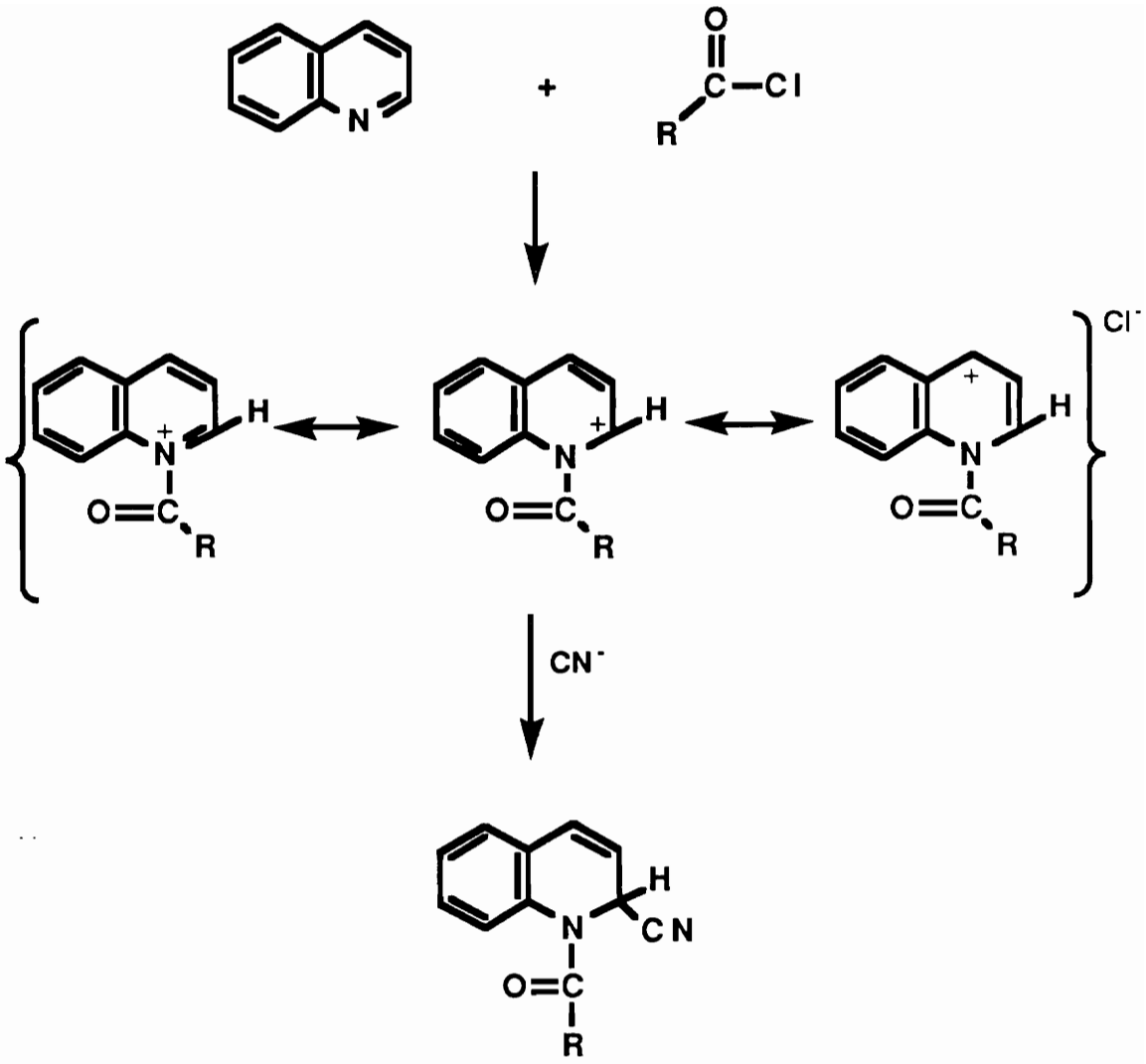
As shown in Scheme 1, formation of these α-acyl-aminonitriles results from addition of an acyl cyanide across the carbon-nitrogen, imine, bond of the parent heterocycle. In the early stages of the reaction, an *N*-acyliminum salt is formed.[3] Once formed, it undergoes nucleophilic attack by the cyanide ion at the 1-position carbon of the heterocyclic ring, thus forming the Reissert compound.

Although Reissert compounds have been reported from such heterocycles as pyridine, benzimidazole, benzoxazoles, and benzothiazoles quinoline and isoquinoline are the most highly studied of all the heterocyclic bases. The main reason is their use as synthetic intermediates in the synthesis of alkaloids. Papaverine (**5**), papaverinol (**6**), and papaveraldine (**7**) are three well-known isoquinoline alkaloids. All three alkaloids can be prepared from 2-benzoyl-6,7-dimethoxy-1,2-dihydroisoquinaldonitrile (**8**). The reader is referred to several interesting articles on the subject by Frank Popp and colleagues.[4-7]

1.1. Preparation of Reissert Compounds:

Reissert compounds may be prepared in one of the following ways:

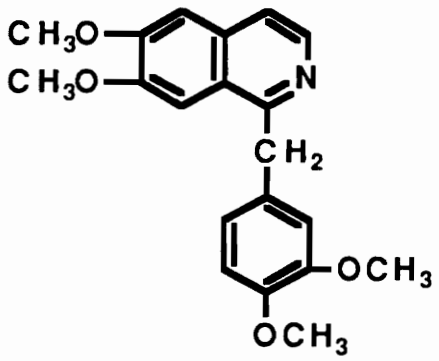
- in an aqueous medium,
- in a two-phase medium,
- in a non-aqueous medium.



Scheme 1: Mechanism of Reissert Compound Formation.

1.1.1. Preparation in an Aqueous Medium:

The aqueous-method, originally employed by Reissert, involves adding 2 moles of an acid chloride, i.e., benzoyl chloride (with vigorous shaking) to a suspension of 1 mole of the heterocycle in an aqueous solution of potassium cyanide. Mechanical stirring has been found to ease the operation of the reaction, but does little to enhance the yields.[8] The use of pure reactants has also proven advantageous in achieving good yields and pure products.[9]



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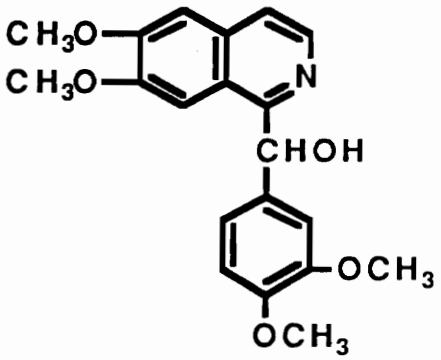

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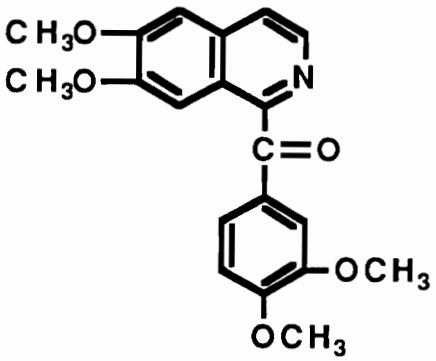

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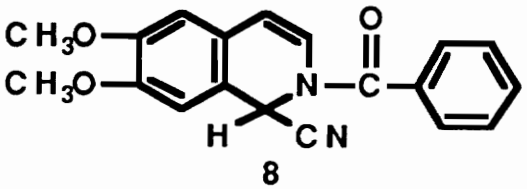

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Because of the aqueous nature of this reaction several limitations are incurred. The biggest limitation is the reactivity of the acid chloride which is of the utmost importance in this reaction since the presence of water could lead to hydrolysis. Hydrolysis limits one to less reactive aroyl chlorides since aliphatic acid chlorides and highly reactive aroyl halides react much too fast with water. Reaction with water can lead to pseudo-base formation.[10] Pseudo bases occur when a hydroxide ion (OH^-) adds, instead of a cyanide ion (CN^-), across the C=N bond of the heterocycle, see structure **3**.

1.1.2. Preparation in a Two-phase Medium:

In 1961, Popp and coworkers enhanced Reissert compound formation with development of the methylene chloride-water (two-phase) system.[11,12,13] In this reaction, one eq. of a heterocycle is dissolved in dichloromethane and three eq. of a metallic cyanide, usually KCN, are dissolved in a minimum amount of water. Vigorous stirring is also employed. Two eq. of an acyl halide (neat or in CH_2Cl_2) are slowly added. Despite the presence of water in this method, Reissert compounds can be prepared in good to moderate yields from a number of acid chlorides. Use of the phase transfer catalyst benzyltrialkyl-ammonium chloride is found to improve yields in some cases.[14,15] Today this method remains the most convenient and cost effective system for Reissert compound synthesis.

1.1.3. Preparation in a Non-Aqueous Medium:

In the methods discussed thus far, the limiting factor has been hydrolysis of the acid halide. Water, as mentioned previously, leads to pseudo-base formation. To eliminate hydrolysis of the acid halide several non-aqueous

methods have been developed. Initially, solvents such as acetonitrile, benzonitrile, ether, dioxane, chloroform, and acetone were used in an effort to synthesize Reissert compounds; however, none led to the desired product.[16] Though anhydrous ether[17] and liquid sulfur dioxide[16] were found to produce Reissert compounds, neither received widespread acceptance. A procedure that did see widespread acceptance prior to 1961 for quinoline Reissert formation was the hydrogen cyanide-benzene method developed by Grosheintz and Fischer.[18] Although a quinolinium-HCN salt supposedly depletes half of the quinoline in the reaction, it has been used to synthesize a variety of quinoline Reissiert compounds, see Table 1. This method has obvious drawbacks in that liquid hydrogen cyanide (highly toxic) and benzene (carcinogen) are used.

Though costly, a procedure that is well revered for Reissert compound synthesis is the single-phase method.[19,20] This method takes advantage of an organic cyanide, trimethylsilyl cyanide, (generally referred to as TMSCN) and methylene chloride to produce what are, in most cases, quantitative yields of the Reissert product. The addition of a catalytic amount of aluminum chloride has proven advantageous to further increase yields.[21,22] This method unlike the two-phase method allows for the use of both aliphatic and reactive aroyl acid halides. In a recent patent,[23] Gibson and coworkers used the single-phase method successfully to synthesize the first benzimidazole bis(Reissert compound).

In a similar method Uff and colleagues[24] using methylene chloride as a solvent and KCN as a cyanide source, successfully synthesized both five- and six-membered ring containing Reissert compounds. Tetrabutylammonium bromide and tris(3,6-dioxaheptyl)amine were employed as catalysts. In a

recent publication, Popp and coworkers reported the synthesis of Reissert compounds utilizing KCN adsorded on Amberlite XAD resins.[25] Since that time they have reported diethylaluminum cyanide in dichloromethane, with or without catalyst, as a means of producing Reissert compounds as well.[26]

A comparison of the aqueous, methylene chloride-water, and non-aqueous methods for quinoline Reissert compound formation can be found in Table 1.

1.2. Effects of Substitution on Reissert Compound Formation:

By now we have already seen how important the reactivity of the acid halide is for Reissert compound formation, but what about substituent effects? Quinoline itself, for example, reacts readily to form Reissert compounds, but what happens if there are substituents on the ring? Do substituents decrease the reactivity of the base? Do they induce steric effects? Popp and colleagues studied such factors for substituted quinoline[27] and isoquinoline[12] Reissert compounds. In the study electron-donating substituents such as 4-hydroxy-, 5-hydroxy-, 6-amino-, and 5,6-benzo- were found to give higher yields of the corresponding Reissert compounds (see Table 2). On the other hand, electron-withdrawing groups such as 3-bromo-, 5-nitro-, 4-chloro- and 7-nitro- yielded opposite effects. According to their findings, by increasing electron density you in turn increase reactivity toward the acid chloride. With formation of a positively charged intermediate, **9**, further stabilization becomes possible if electron-donating substituents are placed at positions 2, 4, 5, and 7 of the ring. Electron-withdrawing groups placed at one of these positions, however, would have the opposite effect. Similar effects were found in isoquinoline; see Table 3.

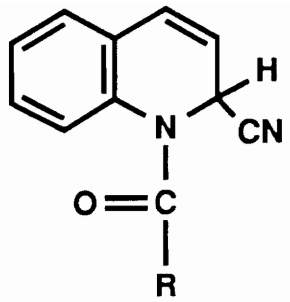


Table 1: Comparison of Three Methods for Reissert Compound Formation.

Compounds		**% Yields**		
heterocycle	**R**	**aqueous[a]**	**methwat[b]**	**nonaque[c]**
Quinoline	C_6H_5	94[1]	70[13]	96(1)[19]
"	"			87(2)[18]
"	"			89(3)[20]
"	"			42(4)[25]
Quinoline	CH_3	**	50[13]	74(1)[13]
"	"			28(4)[25]
Quinoline	*m*-$NO_2C_6H_4$	**	12[13]	trace(1)[10]
Quinoline	*p*-$NO_2C_6H_4$	**	3[13]	0(1)[10]
Quinoline	*p*-ClC_6H_4	26[18]	20[13]	77(1)[18]
Quinoline	PhCH=CH	34[10]	43[13]	91(1)[10]
Quinoline	C_2H_5	**	12[13]	10(1)[10]
Quinoline	*p*-MeO-C_6H_4	51[10]	80[10]	88(1)[10]
Quinoline	n-C_3H_7	**	**	64(1)[10]
Quinoline	i-C_3H_7	**	18[13]	28(1)[10]

(**a**): Aqueous method.

(**b**): Methylene chloride, water, and KCN.

(**c**): Nonaqueous method; (1) anhydrous benzene/HCN, (2) liquid sulfur dioxide, (3) methylene chloride/TMSCN, (4) methylene chloride/ Et_2AlCN.

Typical molar ratio for Heterocycle, Acid chloride, and Cyanide for

Reissert compound formation:

a: 1:2:1

b: 1:2:3

c: (1) = 2:1:1, (3) = 1:1:1, (4) = 1:2:2.

(**): Indicates no reported yield.

Table 2: Substituted Quinoline Reissert Compounds.

The acid halide used is exclusively benzoyl chloride.

	%Yield*	
Heterocycle	**Method A[a]**	**Method B[b]**
3-Acetamidoquinoline	50	15
3-Aminoquinoline	68	0
4-Hydroxyquinoline	98	0
4-Methoxyquinoline	82	-
5-Hydroxyquinoline	99	-
6-Methylquinoline	99	52
3-Bromoquinoline	15	0
4-Chloroquinoline	33	-
5-Nitroquinoline	19	-
6-Nitroquinoline	29	0
7-Nitroquinoline	17	-

(*): Taken from ref. 27.

(**a**): Two-phase method (methylene chloride-water).

(**b**): Aqueous method.

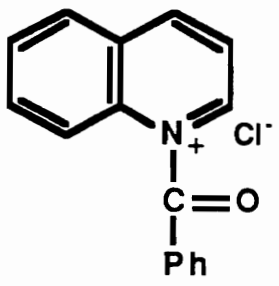
(-): No yield was reported.

Steric effects can play a major role in Reissert compound formation as well. For example, substituents placed at the 2- or 8- position of quinoline prevent formation of such Reissert compounds.[27] Similarly, no product is formed with substituents at position 1- of isoquinoline. For instance, when reacted with benzoyl chloride and KCN, 1-methylisoquinoline, **10**, fails to yield any Reissert product.[12] If the methyl substituent is placed at position 3-, however, Reissert compounds readily form.[28,29] Even more surprising is that though **10** does not form a Reissert compound when reacted with benzoyl chloride and KCN, 2-azafluoranthene, **11**, gives a 23% yield of Reissert product.[12]

1.3. Chemical Reactions of Reissert Compounds:

1.3.1. Acid-catalyzed hydrolysis:

In his original work, Reissert performed an acid-catalyzed hydrolysis of **1** which yielded a quantitative amount of benzaldehyde. Good to fair yields of quinaldic acid, **12**, quinaldamide, **13**, and benzoin quinaldate, **14**, were also obtained.



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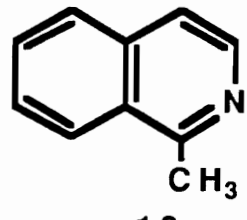

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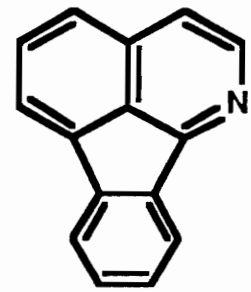

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Table 3: Substituted Isoquinoline Reissert Compounds

The acid halide used is exclusively benzoyl chloride.

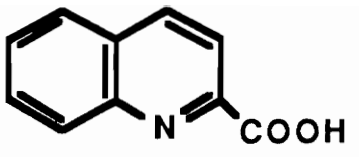
	% Yield*	
Heterocycle	**Method A[a]**	**Method B[b]**
4-Aminoisoquinoline	20	-
4-Bromoisoquinoline	38	0
5-Hydroxyisoquinoline	68	-
5-Nitroisoquinoline	10	0
8-Nitroisoquinoline	9	-
3-Methyl-5-cyanoisoquinoline	45	-
3-Methyl-5-nitroisoquinoline	83	-
3-Methyl-8-nitroisoquinoline	28	-
5-Carbomethoxyisoquinoline	29	-

(*): Taken from ref. 12

(**a**): Methylene chloride-water method.

(**b**): Aqueous method.

(-): No yield was reported.



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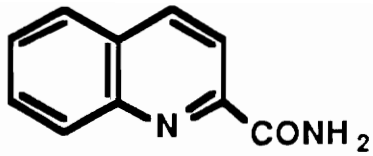

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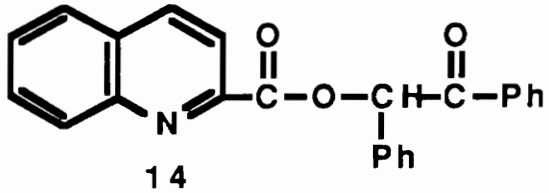

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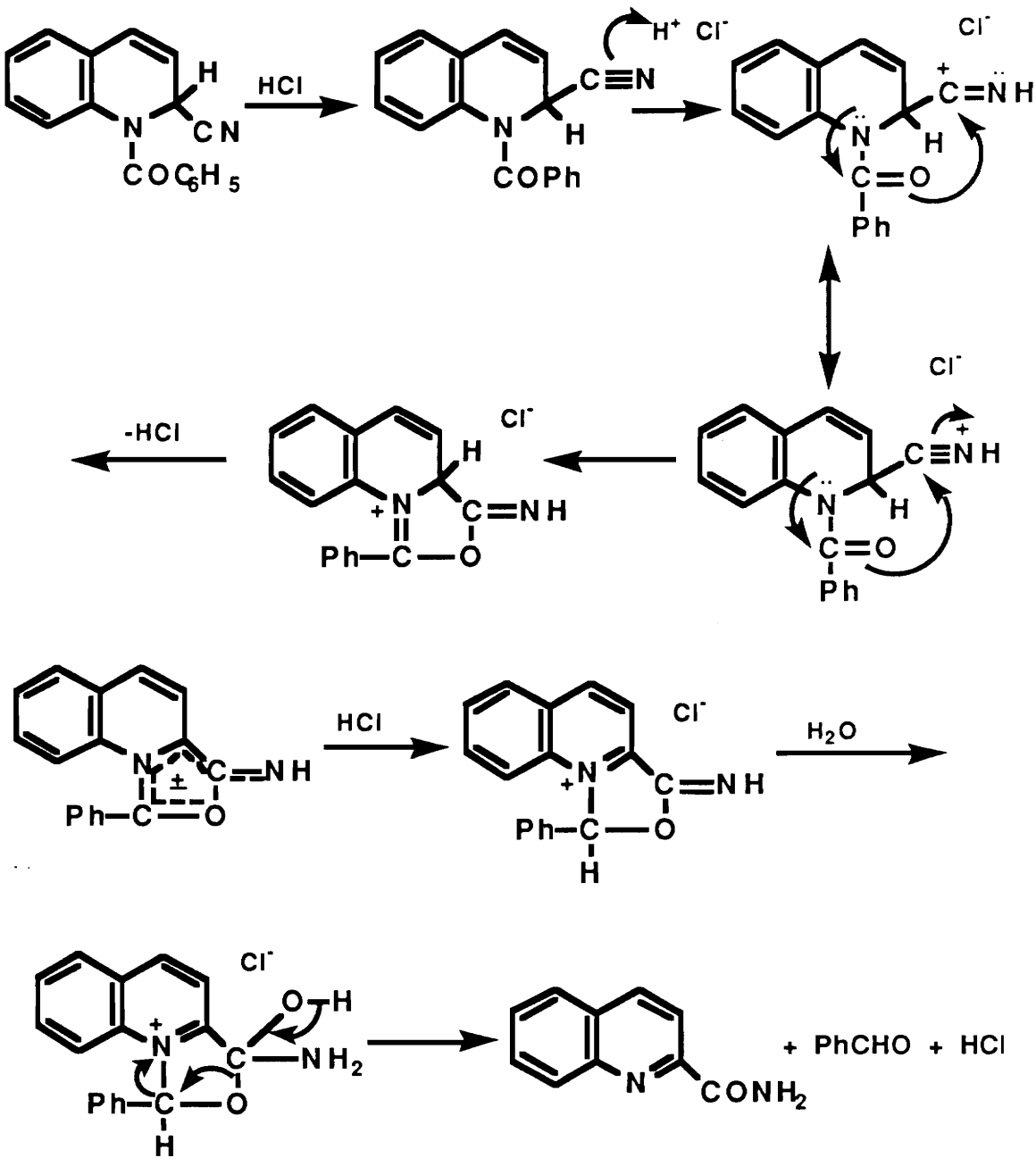
The isoquinoline Reissert compound, **2**, also undergoes acid-catalyzed hydrolysis.[1] The hydrolysis of **2** has been shown to generate a small amount of 2-(1-isoquinolyl)-4,5-diphenyloxazole.[30] Hydrolysis takes place via the mechanism shown in Scheme 2.[31,10,32] As seen in the scheme, the first step is formation of a cyclic intermediate that with isomerization yields the second intermediate. According to McEwen, isomerization is attributed to the stable meso-ionic intermediate formed therein.[31,10,32] Following the addition of water, and collapse of the intermediate, benzaldehyde and quinaldamide are formed. Further hydrolysis of quinaldamide yields quinaldic acid, **13**. Benzoin quinaldate, **14**, results from addition to the meso-ionic intermediate, **I**, by the conjugate acid of benzaldehyde yielding complex **II**. Then, following an intramolecular rearrangement[31,10,32] **III** is formed. Further hydrolysis of **III** yields **14** as the overall product. The imino-ether hydrochloride, **III**, has been found to undergo cyclization to a hydroxydihydrooxazole intermediate, **IV**, that following acid-catalyzed dehydration yields 2-(2-quinolyl)-4,5-diphenyloxazole, **V**.[10,32]

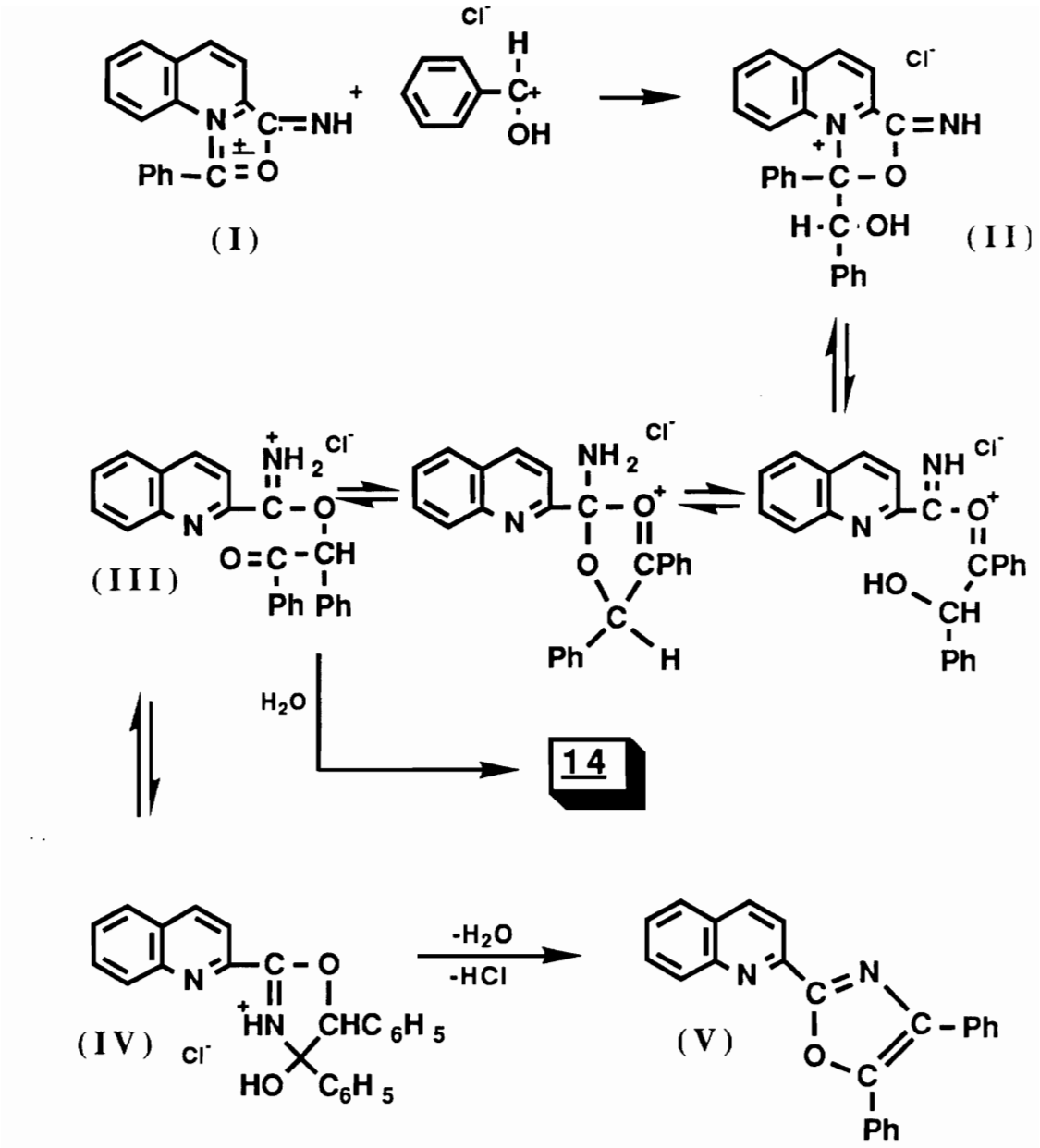
As seen above, the acid-catalyzed hydrolysis of Reissert compounds offers a practical alternative for synthesizing aldehydes from acid chlorides.

Table 4: Aldehydes from the Acid Hydrolysis of Reissert Compounds.

Heterocycle	Acid Chloride	Yield	Ref.
Quinoline	*p*-Fluorobenzoyl	97	13
"	Isobutyryl	98	10
"	*p*-Methoxybenzoyl	96	13
"	1-Naphthoyl	99	13
"	*m*-Nitrobenzoyl	97	13
Isoquinoline	*p*-Chlorobenzoyl	92	13
"	*p*-Methoxybenzoyl	90	13
"	2-Naphthoyl	90	13
"	*m*-Nitrobenzoyl	92	13
"	Propionyl	75	13
Phenanthridine	*p*-Methoxybenzoyl	99	13
"	Benzoyl	97	10
"	Cinnamoyl	97	10



Scheme 2: Mechanism for the Formation of Aldehydes from Reissert Compounds.



Scheme 2: (continued).

Generally, the hydrolysis of such compounds produces good yields of the corresponding aldehyde under mild conditions, see Table 4.

1.3.2. Alkylation of Reissert Compounds:

In Reissert compounds the proton alpha to the cyano group is quite acidic due to the electron-withdrawing nature of the nitrile moiety. Because of this acidity abstraction of the α-proton can be easily performed with a variety of base/solvent combinations. In 1950, Boekelheide and colleagues[33,34] found that treatment of **1** with Na° in refluxing xylene readily produced its corresponding anion. Later research conducted by the Boekelheide group revealed that phenyllithium/ether-dioxane also deprotonated Reissert compounds.[35] In this reaction however, as pointed out by Uff and Kershaw,[36] the strength of the PhLi used can not be accurately known without titration. Also, the intense red color of the anion prevents one from telling when the reaction has ceased. Solubility and steric problems exist in this reaction as well. The major concern, however, is the formation of side products arising from the use of PhLi. To control such side reactions ambient temperatures are usually employed.[35]

Another base/solvent combination used for anion formation is NaOH/ acetonitrile.[37,38] Trialkylbenzylammonium chlorides are most often used as catalysts. One of the most convenient methods for anion formation, however, is NaH/DMF. Reported in 1967 by Popp and Wefer,[39] this method conveniently generates Reissert anions at room temperature. Unlike the PhLi method, the molarity of the NaH is known prior to the reaction and the liberation of hydrogen gas can be used as a means of monitoring the reaction.

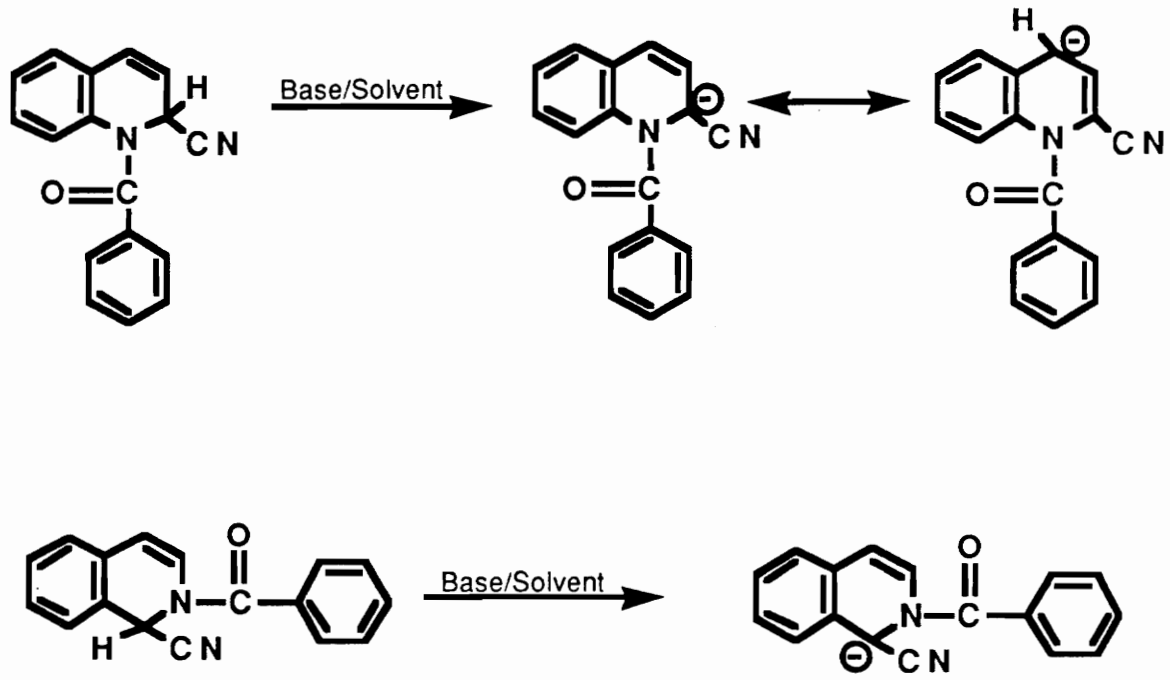
As seen in Scheme 3, when the isoquinoline Reissert compound **2** is

deprotonated its anion is localized (except for the cyano group), but in the quinoline Reissert, **1**, the anion is ambident due to the alternate resonance form. Once the isoquinoline anion has been generated, it can be condensed with a variety of alkyl or aromatic halides. And, since the condensation of isoquinoline Reissert compounds with alkyl or aromatic halides takes place exclusively at position 1- of the ring, yields are usually quanitative. For example, if *p*-nitrofluorobenzene is reacted with the anion of **2** in NaH/DMF it gives a quanitative yield of the 1-substituted product. Similarly, near quanitative yields of 1-benzylisoquinoline can also be produced from the same combination. In quinoline, however, the second resonance form can lead to formation of two possible products e.g., alkylation at positions 2- or 4- of the ring.[35,61]

1.3.3. Condensation of Reissert Anions with Aldehydes:

Reissert anions are known to undergo reaction with aldehydes to form esters.[40,41,43] The first step in this reaction is formation of an alkoxide resulting from nucleophilic addition of the Reissert anion to the carbonyl of the aldehyde. Once formed, the intermediate reacts intramolecularly with the amide carbonyl to produce what is eventually an ester. The driving force for this reaction, as seen in Scheme 4, is rearomatization of the six-membered ring.

Using NaH/DMF, Popp and Wefer obtained ester products in good yields.[39] Phenyllithium also serves as a suitable base for ester formation as demonstrated by Walters and coworkers.[41] Sodium hydroxide/acetonitrile has also been found to produce esters in good yields, but alcohol products are produced here as well.[42] By varying the reaction time, however, one can preferrentially isolate either the alcohol or the ester product.[42]



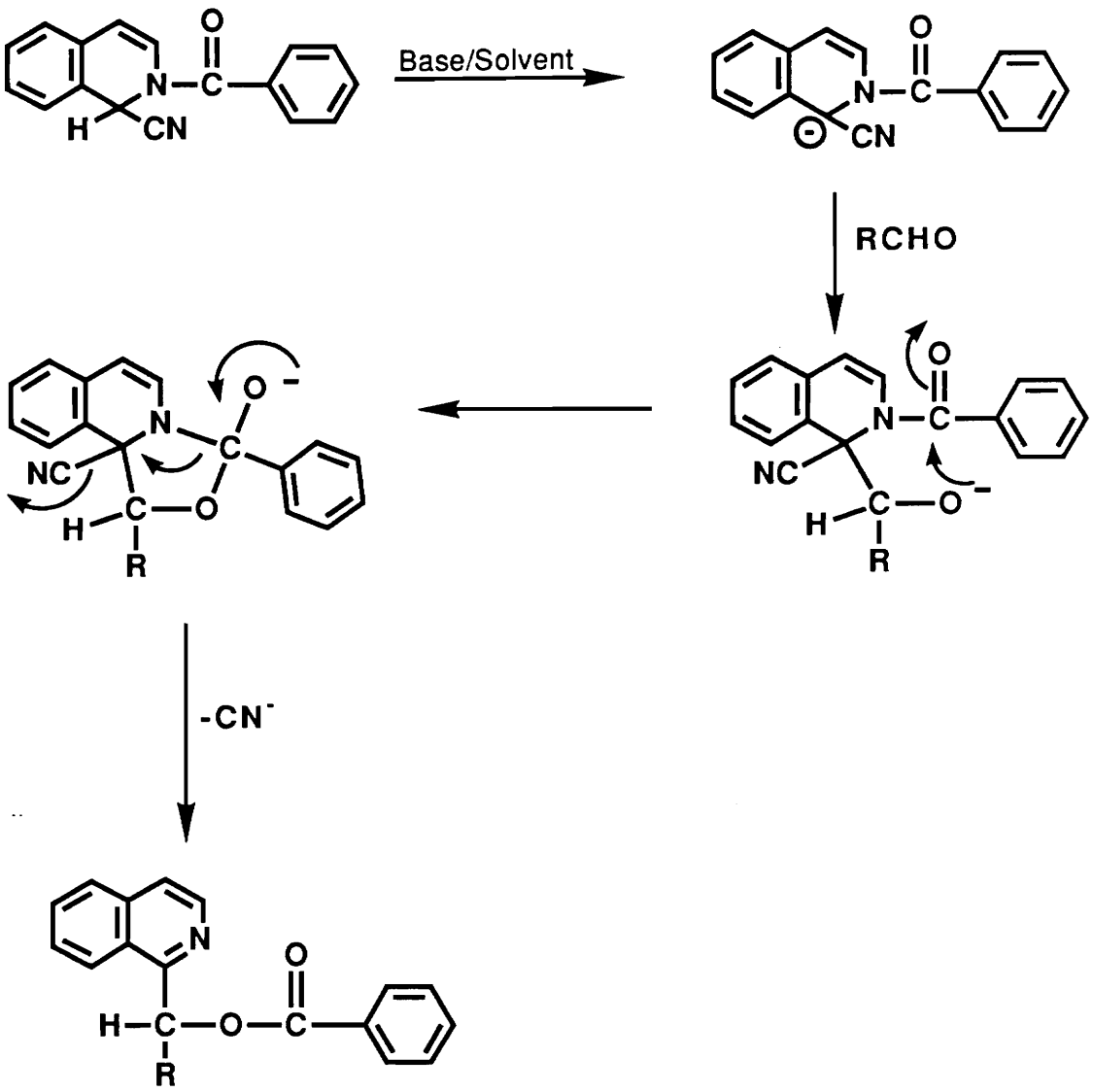
Scheme 3: Formation of Quinoline and Isoquinoline Anions.

The anion of **2** can be reacted with a variety of aldehydes[43] or ketones[42] to produce several different types of ester products. For example, Popp and Watts found that esters could be produced from the reaction of **2** with 1-substituted-4-piperidones in either NaH/DMF or 50% NaOH-acetonitrile.[44] They also found that tertiary alcohols could be readily produced upon hydrolysis. Although 4-piperidones gave good yields, some ketones like, acetylferrocene, flavanone, *p*-methoxyacetophenone, tropinone, adamantyl-methyl ketone, and 3-acetylindole yielded no product at all.

1.3.4. Reissert Compound Rearrangement:

We have just seen how easy it is to condense a Reissert anion with an electrophile to form esters, but what happens when there's no electrophile present in the reaction? In the absence of an electrophile, Reissert compounds undergo rearrangement to form ketones via formation of an aziridinyl type intermediate.[45] As outlined in Scheme 5, formation of this tricyclic aziridine intermediate results from intramolecular nucleophilic attack of the carbanionic center on the carbonyl moiety.[10] The driving force, again, is rearomatization of the six-membered ring. Several different methods including Na° in refluxing xylene[35] and NaH/DMF[39] have been used in the rearrangement process.

Rearrangement can be promoted or retarded by placing substituents on either the heterocycle or the acyl moiety. Gibson found that when a methyl substituent was placed at position-3 of **2** it decreased the stability of the resulting anion.[46] The decreased stability in turn increased the possibility for rearrangement. Gibson also found that ortho-substitution on the aryl moiety of aromatics acid halides actually retarded rearrangement of the resultant Reissert



Scheme 4: Aldehyde Condensation of Reissert Anion.

anion. Lowering the reaction temperature to 0°C can also retard rearrangement.[47] As will be shown later in this dissertation, rearrangement can be a very useful tool for the synthesis of novel *N*-heterocyclic monomers.

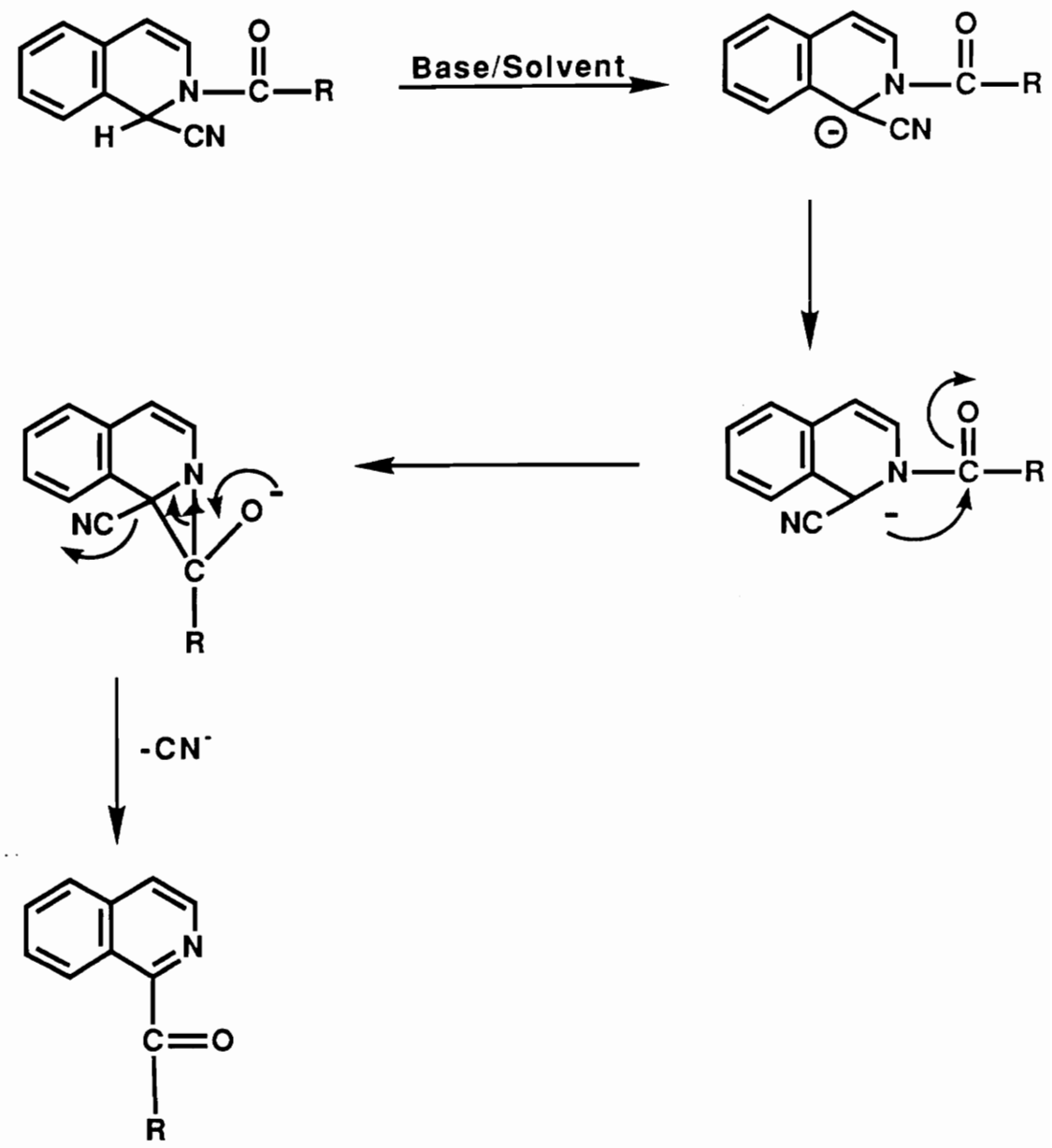
1.4. Formation of Bis(Reissert Compounds):

1.4.1. 4-Substituted Isoquinolines:

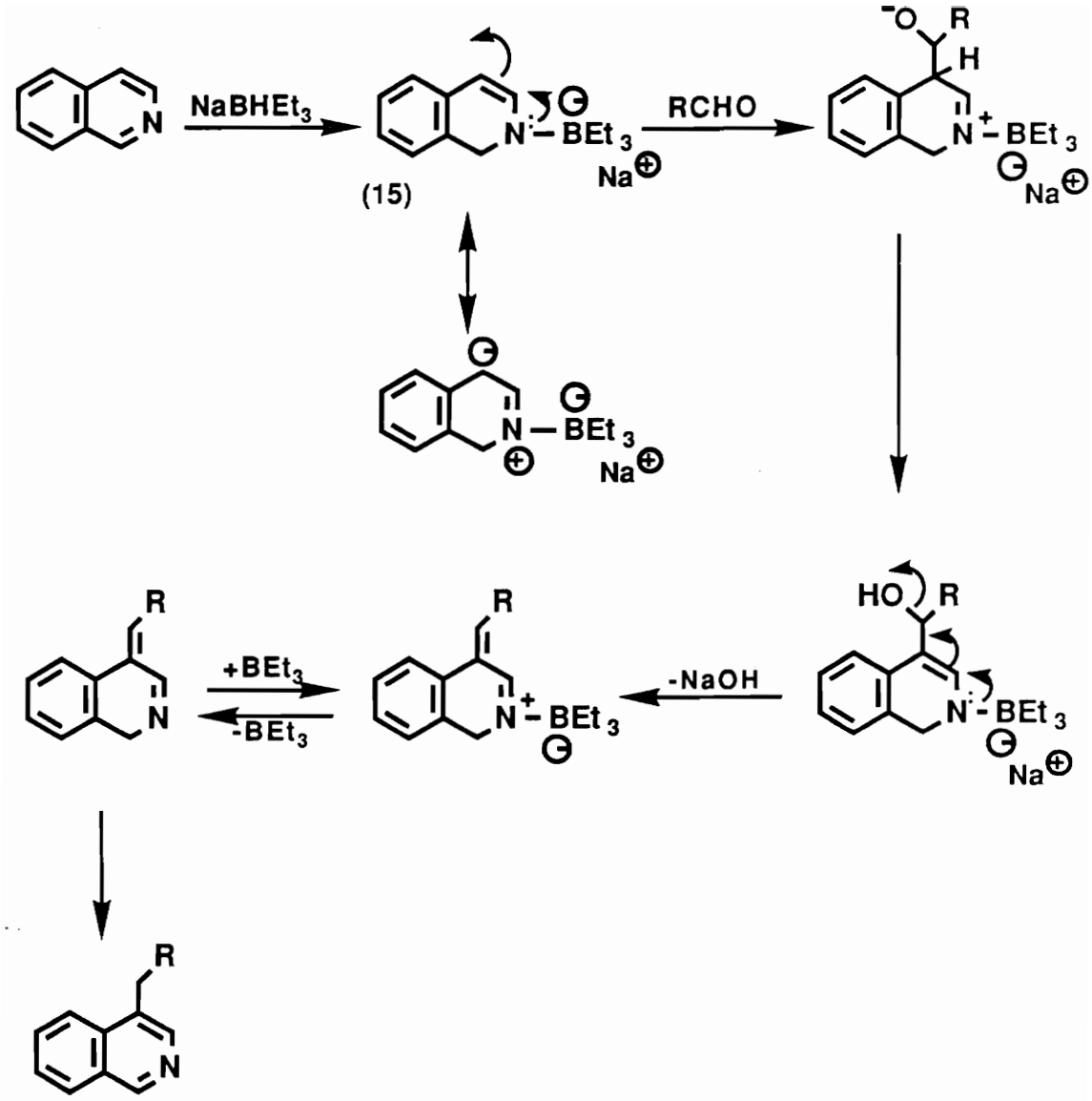
In 1988, D. E. Minter and M. A. Re developed an eneamine reaction that allowed for the formation of 4-substituted isoquinoline compounds.[48] The mechanism, shown in Scheme 6, involves electrophilic attack of the aldehyde at carbon-4, followed by proton transfer, conjugate loss of hydroxide, and rearomatization of the six-membered ring.[48] The eneamine, **15**, forms instantaneously at room temperature and has been duly confirmed by ^{11}B n.m.r.[48] The base used for formation of **15** is sodium triethylborohydride, $NaBHEt_3$. Introduction of this mechanistic pathway allows one to synthesize isoquinoline precursors that when reacted with an appropriate acid halide and cyanide source leads to 4-substituted Reissert compounds.

1.4.2. Bis-Isoquinoline Route:

Using an extension of the Minter and Re reaction described above, Gibson and colleagues have developed an efficient pathway for the synthesis of bis-isoquinolines.[49] In the synthesis, two eq. of the eneamine, **15**, are reacted with one eq. of a dielectrophile, usually an aromatic dialdehyde, to produce the bis-isoquinoline product. The bis-isoquinolines produced are readily oxidized to the corresponding benzylic diketones using manganese dioxide/benzene.[49] The bis-isoquinolines were confirmed by ir and n.m.r. A representative compound is shown by **16**. As seen in Table 5, good yields of these compound

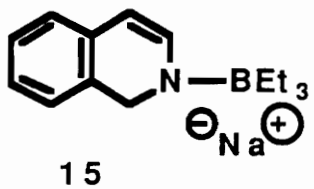


Scheme 5: Rearrangement of Isoquinoline Reissert Compounds.



Scheme 6: Mechanism for 4-Alkylation of Isoquinolines.

were produced.



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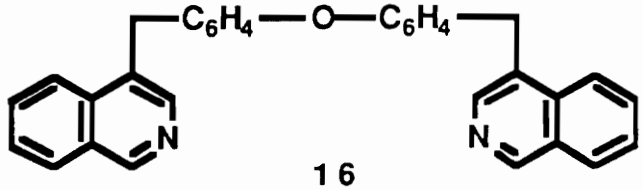

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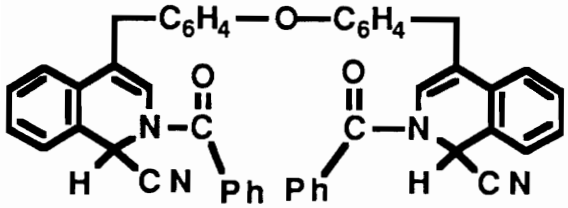
Following the formation of **16**, the bis-Reissert compound **17** was formed by reacting one eq. of **16** with two eq. of benzoyl chloride (or other acid halides) and excess TMSCN. The bis-Reissert compounds were isolated as a mixture of distereomers in yields as high as 100%.[50,51] These compounds contain two acidic alpha protons which for polymerization purposes makes them suitable as AA-monomers.[62]



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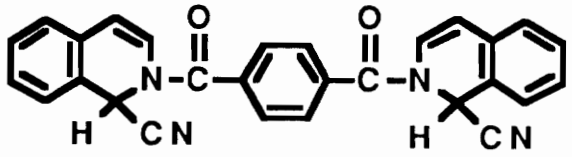

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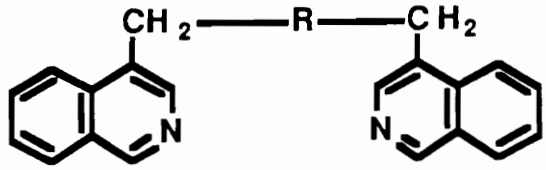
Table 5: Bis-Isoquinolines from Dialdehydes.



R	Yield
p-C_6H_4	74%[49]
p-$C_6H_4O(CH_2)_{10}OC_6H_4$-*p*	76%[49]
p-$C_6H_4O(CH_2)_6OC_6H_4$-*p*	87%[47]
p-$C_6H_4O(CH_2)_4OC_6H_4$-*p*	90%[47]
p-$C_6H_4OC_6H_4$-*p*	88%[47]

1.4.3. Diacid Chloride Route:

The second well known route for bis-Reissert compound formation is the diacid chloride route. The diacid chloride route involves formation of bis-Reissert compounds via reaction of one eq. of a diacid halide with two eq. of a heterocycle and a cyanide source. Such compounds were first synthesized by Popp and colleagues[13,52] via the two-phase method. This route generally gives only trace to low amounts of the bis-Reissert compounds. Hydrolysis of the intermediate mono(acid-chloride)-mono(Reissert compound) could be one reason for the low yields.[50] Introduction of the single phase method, however, increased the yields as demonstrated by Gibson and coworkers[50,51] who were the first group to report bis-Reissert compounds with this method.

Using this method, Gibson and his group were able to synthesize bis-Reissert compounds with yields ranging from 77% to quantitative.[51]

Compounds were synthesized using not only quinoline and isoquinoline, but benzothiazoles and benzoxazoles as well. A representative compound is shown by **18**. Like their bis-isoquinoline counterparts, these bis-Reissert compounds were isolated as diastereomeric mixtures. Since these compounds also contain two acidic protons, they can be further reacted in an appropriate base/solvent combination to give dianions. Using NaH/DMF, Gibson and coworkers prepared and condensed these dianions with dielectrophiles, e.g., dialdehyes, to produce polyesters.[50,51]

2. HIGH-PERFORMANCE POLYMERS:

High performance polymers have been well-known in the literature since the late 1950's. During the '50's primary interest in such polymers stemmed from their increased usage in the aircraft, weapons, and electronics industries. Since that time, however, many different types of high-performance polymers have been synthesized with a wide range of properties and applications.

2.1. Introduction to Step-growth Polymerizations:

A step-growth polymerization can be viewed as a process whereby a polymer chain grows step-wise by reactions occuring between any two molecular species, i. e., monomer + monomer = dimer; dimer + monomer = trimer; dimer + dimer = tetramer; etc. In this process the molecular weight of the polymer increases at a relatively slow rate. The above process will continue, however, until high molecular polymer is produced. In order to attain high molecular weight via this process *seven crucial rules* must be adhered too.

i). Must have at least difunctional starting materials, e.g., *f=2*: Difunctionality is attainable two ways 1) by having monomers that contain the

same two polymerizable end-groups, AA-, 2) with monomers containing two different functional groups, AB-. Mono-functionality in such polymerizations can lead to the formation of low molecular weight oligomers, or endcapping.

ii). Highly pure monomers: The purity of the starting materials should be on the order of 99.9%. This rule, like all the rest, is crucial since impurties can upset the stoichiometry and decrease molecular weights.

iii). Exact stoichiometry: The molecular ratio of the starting monomers should be *exactly* 1.000 to 1.000. Why? Because the degree of polymerization, $\mathbf{X_n}$, is related via the equation, $\mathbf{X_n = (1 + r)/(1 + r - 2rp)}$ to the stoichiometric imbalance ratio, **r**. If one deviates from this molar ratio, then $\mathbf{X_n}$ will decrease drastically, thus affecting molecular weight.

iv). High extent of conversion: The reaction must proceed to >98% conversion to obtain high molecular weight. Why? According to the Carothers equation, if **r** in the above equation is equal to **1** then the equation can be rewritten as $\mathbf{X_n = 1/1-p}$. We also know from the Carothers equation that to obtain high molecular weight polymer $\mathbf{p \geq 0.98}$, i.e., $\mathbf{X_n = 50}$.

v). Side reactions must be kept at a minimum: Any side reactions taking place during this process could lead to a decrease in both $\mathbf{X_n}$ and **p** which in turn decrease molecular weight.

vi). Mutual accessibility of reactants: For the reaction to proceed to high conversion functional groups must be readily accessible to one another, i.e., stay in the same phase. It should be kept in mind that this is a stepwise process whereby different species (or oligomers) connect to form a continuous chain.

vii). Must chose the appropriate temperature and solvent combination for the reaction to yield high molecular weight polymer.

2.2. Heat-Resistance:

What attributes or qualities must a polymer possess to be heat-resistant? According to a well-known author,[53] a potential heat-resistant material must be able retain its useful properties (usually mechanical properties) for a stated period of time under defined conditions such as pressure, mechanical loading, radiation, or chemical influences at temperatures ranging from cryogenic (low/sub-ambient temperatures) to ≥500°C. As one might expect from elevated temperatures, deformation and degradation changes in the material are a major concern. Therefore, two key considerations must be addressed: (1) reversible changes in the material, and (2) irreversible changes. The first phenomena is usually a function of the polymer's T_g, i.e., if a polymer is placed under load at or near its T_g, it can suffer deformation changes without actual changes in its chemical structure. In the latter case, however, any changes that do occur usually result in alteration of the polymer structure, usually bond breaking.

In synthesizing new heat-resistant materials, there are several factors one must keep in mind: T_g, molecular weight, molecular weight distribution, crystallinity, etc., but perhaps the single most important factor is primary bond strength. The bond dissociation energy of the polymers is of the utmost importance if the material is to have a high-temperature application. Carbon-carbon single bonds for example, have bond dissociation energies of ~350 kJ/mole.[53] In a carbon-carbon double bond however, the bond dissociation energy increases sharply to ~610 kJ/mole. If placed in an aromatic compound, the carbon-carbon double bond's dissociation energy increases by 164-287 kJ/mole, which is quite substantial when compared to aliphatic or non-aromatic compounds. The phenomena described above is due to the aromatic compounds' ability to stabilize via resonance.[53] This characteristic makes

aromatic and heterocyclic ring containing polymers ideal for high temperature usage.

Another criterion for heat-resistancy is strong secondary or van der Waals bonding forces. These forces provide increased strength and thermal stability in the material. They can also mean increased T_g as well. Most high temperature polymers contain polar groups like C=O and SO_2 because such groups have strong intermolecular interactions. Some heat-resistant polymeric materials do, however, contain ether linkages.

Another very important factor to consider when synthesizing heat resistant polymers is molecular weight. It is well-known that if two polymeric materials are synthesized simultaneously and one attains a higher molecular weight than the other, then this material should have better mechanical properties. Let's look at T_g for example! The T_g of a polymer is a function of its molecular weight; therefore in the example above the higher molecular weight material should possess a higher T_g. For high temperature applications high molecular weight is a requirement. Why? Because the higher the molecular weight, the more chain entanglements within the polymer. What do chain entanglements have to do with polymer longevity? Simply this, a polymer is more able to retain its structural features during chain cleavage if there's a high degree of chain entanglements within the material. *The more chains one has to break in order to free himself, the longer it will take to do so.*

2.2.1. Nitrogen-Containing Heterocyclic Polymers:

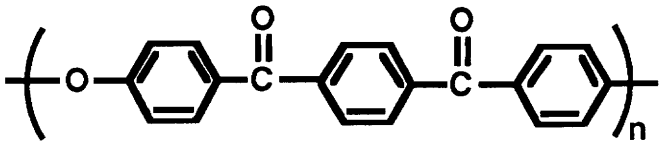
N-heterocyclic polymers are an important class of polymeric materials receiving considerable attention in the electronic and aerospace industries due

in part to the presence of the C-N bond. Nitrogen-containing polymers are well known for their thermal stability and mechanical strength, especially when they contain H-bonding. The presence of the nitrogen atom can influence such characteristics as interchain bonding, adhesion (due to the basicity of the nitrogen), and mechanical strength (because of the C-N bond). Another important characteristic is their ability for quarternization which increases water solubility and coagulation in such polymers.

Perhaps the most well known all the N-heterocyclic polymers are the polyimides. Polyimides possess excellent mechanical and thermal properties such as high T_g's, heat and solvent resistancy, and high overall strength. In general, polyimides are insoluble in non-degrading solvents and decompose before melting. Polyimides are usually synthesized via a two-step process.[54] The first stage is formation of a soluble polyamic acid usually carried out in a polar aprotic solvent like NMP, DMAc, DMF, or DMSO at temperatures from 25°-70°C.[54] In the initial stage of the reaction the polyamic acid is fusible and can be molded into any desired shape. The second stage of the reaction is imidization (or dehydrocyclization) of the polyamic acid at temperatures ranging from 150°-300°C, thus forming the insoluble, infusible polyimide.

Other heat-resistant *N*-heterocyclic polymers include polyquinoxalines (PQ's), polyquinolines, polybenzimidazoles (PBI's), polybenzoxazoles and polybenzothiazoles, Scheme 7. In the polymers listed above, the heterocycle is usually formed during the polymerization process. However, Connell and Hergenrother at NASA, have developed a process for polyimidazoles (PI)[55] and polyphenylquinoxalines (PPQ's)[56] in which the heterocyclic moiety is pre-formed prior to polymerization. In the polyimidazole the heterocycle is formed by reaction of a bisphenol imidazole monomer with an activated (aromatic)

difluoro compound. This synthetic route enables one to design the polymer for a specific application by way of the monomer. The reaction is an aromatic nucleophilic displacement reaction that uses potassium carbonate/DMAc with toluene as an azeotroping agent. As will be shown later, this process has a significant bearing on the research presented in this thesis.



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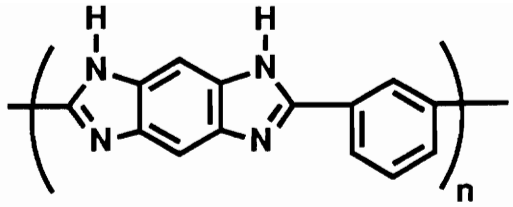
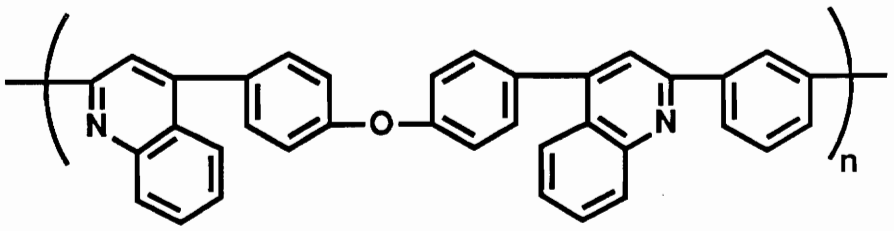
2.2.2. Poly(Ether Ketones):

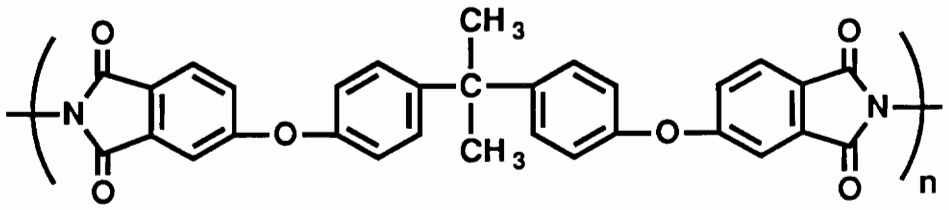
Poly(ether ketones) are another important class of polymers possessing high thermal stability and excellent mechanical properties, e.g., **19**. The name poly(ether ketones), often referred to as PEK's, stems from the fact that these polymers are linked by ether and carbonyl groups. Because these polymers possess arylene units along their backbone they may be referred to as poly(arylene ether ketones), PAEK's, as well. Morphologically, these materials are usually semi-crystalline with T_m's near 300°C.[57] Since they are highly crystalline, they're usually tough and resistant to solvents, abrasion, and fatigue. They also possess low flammability, so when burned they give off only low levels of smoke and toxic gases. One of the key features of this class of polymers is their crystallinity which gives them excellent solvent resistancy. In some cases (i.e., PEK and PEEK) the resulting polymer is not soluble in traditional organic solvents so concentrated H_2SO_4 must be employed to dissolve the material.[57] Although crystallinity and high melting temperatures give these polymer a unique set of characteristics among thermoplastics, it can



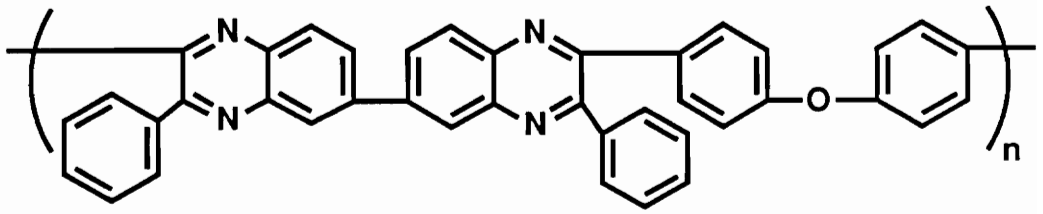
polybenzimidazole *(PBI)* Tg = 430°C



polyquinoline Tg = 268°C



polyetherimide, GE*(Ultem 1000)* Tg = 220°C



polyphenylquinoxaline *(PPQ)* Tg = 290°C

Scheme 7: Nitrogen-Containing Heterocyclic Polymers.[53]

make processing painstakingly difficult. The processing temperature for some of these polymers can reach upwards of 400°C.[57]

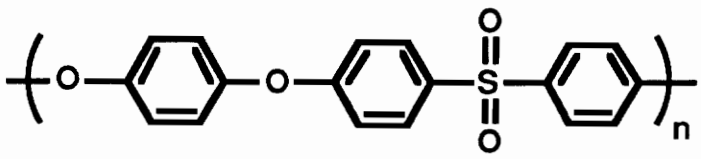
In a recent study, Gibson and Guilani reported the synthesis of a novel difluorodiketone monomer, 1,4-bis(p-fluorobenzoyl)isoquinoline, and its subsequent polymerizations with several biphenols.[58] Introduction of this monomer led to the development of a new and novel family of poly(1,4-isoquinolinediyl ether ketone)s. These polymers were amorphous and exhibited high T_g's with excellent thermooxidative stabilities. They yielded thermal data similar to that of Udel(GE), Victrex(ICI), PEEK(ICI), and Ultem 1000(GE). The aforementioned thermoplastics have T_g's ranging from 190°C (Udel) to 220°C (Victrex & Ultem 1000), while the isoquinoline containing polymers reported showed T_g's of 181°C (isoquinoline monomer + Bis-A) to 209°C (isoquinoline monomer + biphenol), and with only a 10% weight loss at 500°C (in air) for the latter case.

2.2.3. Poly(Sulfones):

Poly(sulfones), in particular poly(arylene ether sulfones), **20**, are well known in the literature for their high thermal stability, chemical inertness, and flame retardancy. Polysulfones are typically amorphous; however, some do possess crystallinity, e.g., poly(ether sulfones), with melting temperatures as high as 300°-360°C.[59,60] In the case of poly(ether ketone sulfones), the melting temperature supposedly increases as the molar ratio of crystallizable ether-ketone units *vs.* amorphous ether-sulfone units increases.[59] The presence of a flexible ether unit in poly(arylene ether sulfones) has been shown to lower the T_g and melt viscosity of these polymers which in turn enhances their thermoplasticity and processability.[59] As mentioned previously,

polysulfones are well known among thermoplastics for their high distortion-temperatures, electrical performance, flame retardancy, and overall thermal stability. Since the majority of these materials are amorphous, solvents like paint stripper, hydraulic fluids or kerosene can cause softening or perhaps cracking in these materials. Although in the case of poly(ether ketone sulfones), the crystallinity contained therein can help to prevent such occurrences.

The properties of poly(ether sulfones) and poly(ether ketones) are very important to our research since the polymers proposed in this thesis are expected to show similar or perhaps better properties than the poly(arylene ethers) currently being used.



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III. OBJECTIVE OF RESEARCH:

The study described in the *Historical Section* by Gibson and colleagues has prompted further research into this area as detailed in the present work. The present work was undertaken with a view to study the mechanical effects of substituting *two* isoquinolinediyl units into the backbone of polymers to create yet a new family of novel high temperature thermoplastics. Incorporation of the isoquinolinediyl units will be performed exclusively via the monomer, utilizing Reissert chemistry. Once synthesized these AA-monomers will possess fluorine polymerizable end groups and spacer units such as sulfones, ketones, and ethers. The presence of these groups should enhance solubility and flexibility in the polymers proposed. The poly(arylene ethers) will be synthesized via a condensation polymerization utilizing an aromatic nucleophilic displacement technique.[47] These polymers should exhibit excellent thermal and mechanical properties. Since the polymers proposed will contain a (basic) nitrogen adhesive properties are expected as well.

IV. RESULTS AND DISCUSSIONS:

As mentioned in the *Objective,* the main thrust of this research was to use Reissert chemistry to incorporate isoquinolinediyl units into the backbone of different monomers. Once synthesized, these monomers would then be used to prepare a new family of high-temperature thermoplastics using step-growth polymerization techniques.

In the work presented in this thesis, the diacid chloride route was used exclusively to synthesize all bis(Reissert compound)s. These bis(Reissert compounds) were in turn rearranged, and finally oxidized to produce a new family of nitrogen containing monomers.

1.1 A Study of the Rearrangement of Reissert compounds:

In the absence of an electrophile Reissert compounds are known to undergo rearrangement to form ketones. This rearrangement occurs via formation of a tricyclic aziridine intermediate.[45] And, since rearrangement was one of the major reactions in our synthetic scheme for new monomeric materials we first decided to take a closer look at the rearrangement process.

To better understand this process, first the rearrangement of a simple mono-Reissert compound was performed. The Reissert compound chosen was 1-benzoyl-1,2-dihydroisoquinaldonitrile, **2**. The thought process here was to rearrange the compound and then use NMR to follow the rearrangement over time, so that in future reactions we would have a means of determining the extent of reaction.

First, the benzoyl Reissert compound, **2**, was synthesized via the two-phase method ($KCN/H_2O/CH_2Cl_2$). The crude yield of **2** was 93%. Following

two recrystallizations in EtOH, the isolated yield of **2** was 64%. The melting point of the pure product was 125°-126°C (lit.[13] mp, 126°-127°C).

Having synthesized the simple Reissert compound, **2**, it was dissolved in DMF followed by the addition of 1.2 equivalents of NaH. After adding the hydride, 1 ml aliquots were taken via syringe at 10, 20, 40, 60, 90, 120, 150, and 225 minute time intervals. These samples were then quenched by pouring them into water to allow for precipitation. After precipitation, ^{1}HNMR spectra were taken of the 10 and 225 minute samples in $CDCl_3$.

When the 10 minute sample was analyzed, it was evident that the compound had already begun to rearrange as indicated by the substantial reduction in the H_1 peak at 6.55 δ, and the appearance of two downfield doublets at 8.25 and 8.62 δ, respectively. These doublets were expected since formation of the ketone caused the H_3 proton on the isoquinoline ring to split the H_4 proton. The 225 minute sample, however, showed no trace of H_1 but did show two very distinct downfield doublets at 8.25 (H_4) and 8.62 δ (H_3), signaling completion of the rearrangement. Proton n.m.r. spectra were also taken of the remaining 6 samples and as expected they too showed similar results.

The model rearrangement proved that the process can be easily evaluated by ^{1}H-NMR. It also showed us that rearrangement is virtually instantaneous. The next task was to see how the rearrangement was affected by substituting at the 4-position of isoquinoline. This reaction was done much later, however, so it will be discussed in a subsequent section of this thesis.

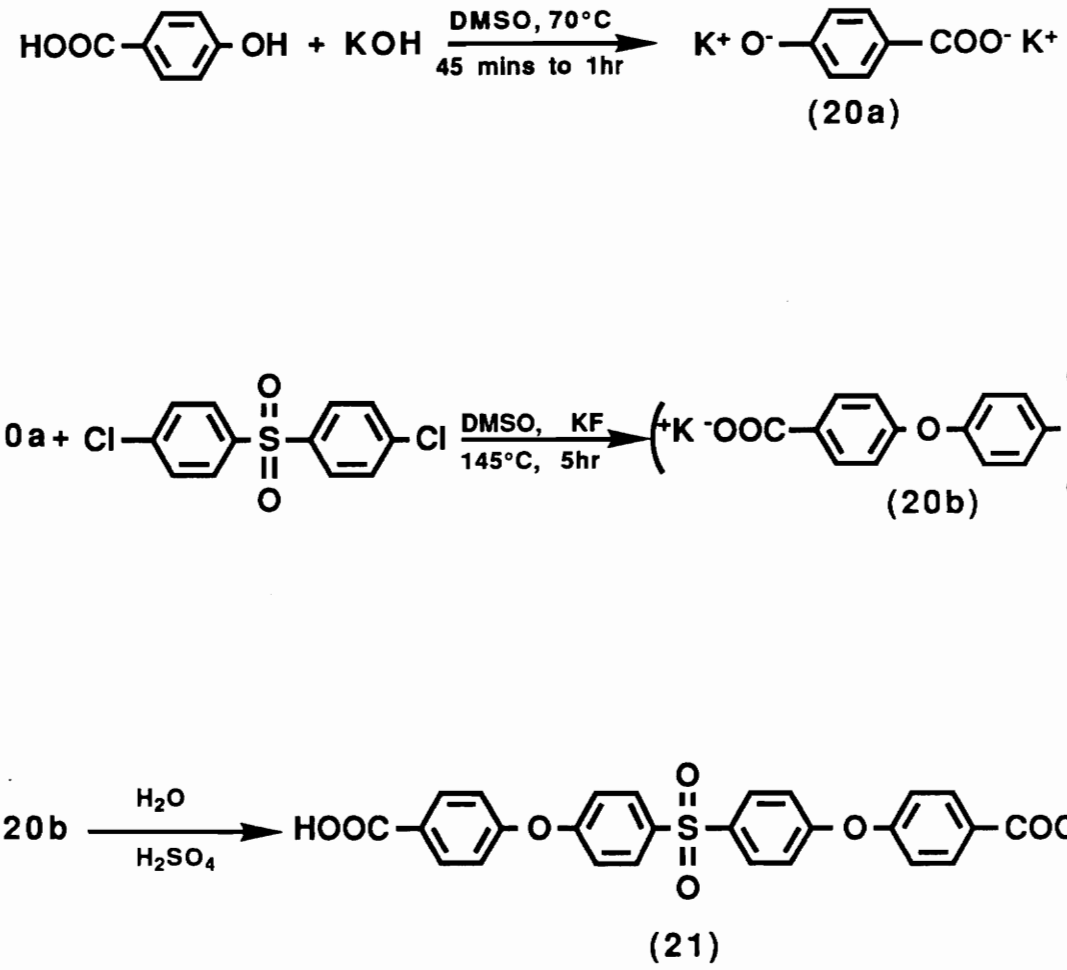
2.1 Synthesis of Sulfonylbis(p-Phenyleneoxy)-Bis(Reissert):

As stated in my *Introduction to Step-growth Polymerizations*, the first criteria for step-growth polymers is difunctionality of the starting materials.

Therefore, the first step in our quest for new AA-monomers was to chose an appropriate acid chloride for bis(Reissert compound) synthesis. Once synthesized, these difunctional Reissert compounds would serve as potential precursors for new AA-monomers. Until now, most of the monomers prepared via the diacid chloride route were made with either terephthaloyl or isophthaloyl chloride. Though both are commercially available, we were looking for an acid chloride with groups like ether oxygens, sulfonyls, or carbonyls since such groups are known to add flexibility. Therefore, any monomers or polymers possessing these groups should have excellent solubility.

With this thought in mind, I began the project by working on the synthesis of a sulfone-containing dicarboxyclic acid using a modified route reported by Idage *et al.*[63] (Scheme 8). The synthesis involved reacting 4-hydroxybenzoic acid and KOH in dry DMSO which yielded a dipotassium salt. Once formed the salt was reacted *in situ* with dichlorodiphenylsulfone. After 5 hours the reaction was quenched and finally acidified with concentrated sulfuric acid (until pH 2). The diacid, **21**, precipitated as a white fluffy solid which was filtered, and washed with water to remove any residual acid. Following several days of air drying, the compound was finally placed in a vacuum oven. The crude yield of **21** was 72%. The melting point of the *crude* product was 270°-273°C (lit.[63] mp, 306°-308°C). The reported recrystallization solvent was dioxane, but after several days at room temperature (and in the refrigerator) this solvent failed to yield any crystals.

^{1}HNMR spectroscopy attempted in $CDCl_3$ proved futile as the compound was totally insoluble in this deuteriated medium. FTIR spectroscopy of the crude compound (KBr pellet) showed an acid peak at 3200-2561 cm^{-1} and



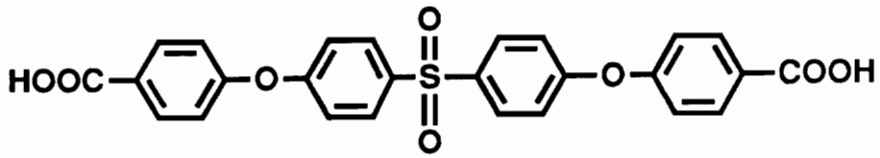
Scheme 8: Synthesis of SulfonylBis(p-Phenyleneoxy)Dibenzoic Acid.

C-O-C sym. and asym. stretches at 1250 and 1109 cm^{-1}, respectively. The carbonyl peak was found at 1684 cm^{-1}. Sulfone asym. and sym stretches were also detected at 1327 and 1163 cm^{-1}.

Next, **21** was converted to the methyl ester. The methyl groups were used as a tag in NMR to confirm the number of protons in the compound, (PNMR #1, Appendix). The dimethyl ester, **22**, was prepared by refluxing **21** in concentrated sulfuric acid and methanol for 24 hrs, Scheme 9. Following two successive recrystallizations in EtOAc/hexane, the isolated yield of the ester was 55%. The melting point of the recrystallized product was 136°-139°C.

As expected, the NMR spectroscopy of the compound showed a sharp singlet at 3.82 δ in the aliphatic region for the methoxy protons. The aliphatic and aromatic protons were then integrated, and a proton ratio calculated. The singlet for the methyl protons equated to 6 protons, and the aromatic region ~ 18 protons. A quick look at the structure of the compound revealed that the actual ratio was 6 to 16, but the NMR ratio did include a chloroform peak. With this information, we felt confident that the compound was indeed difunctional, so it was converted to the dibenzoyl chloride.

The diacid chloride, **23**, was prepared by refluxing the diacid in thionyl chloride, Scheme 10. After two hours, a few drops of DMF were added to catalyze the reaction, and heating was continued for an additional 4 hrs. At the end of the reaction, the excess thionyl chloride was removed via reduced pressure distillation. Recrystallization of the compound in toluene yielded off-white crystals melting at 179°-184°C (lit.[63] 184°-189°C). The isolated yield of the compound after two recrystallizations was 50%. The proton-n.m.r. spectrum taken in $CDCl_3$ agreed exactly with the structure of **23**. The structure of **23** was further confirmed via FTIR spectrocopy, which showed complete loss of the acid



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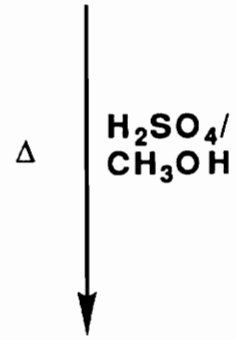
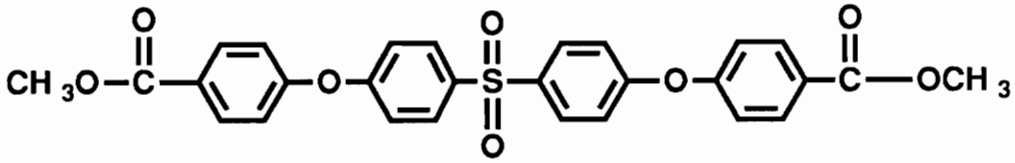




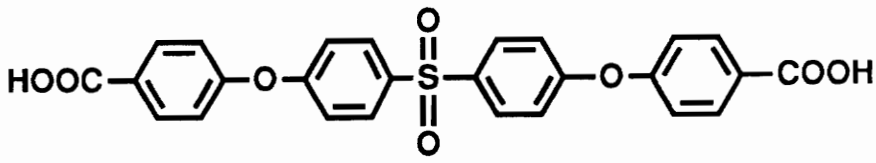
22

Scheme 9: Conversion of Dicarboxyclic Acid to Dimethyl Ester.

bands at 3200-2561 cm^{-1} and 930 cm^{-1}, and the appearance of C-Cl bending vibrations at 885 cm^{-1}. The carbonyl peak remained at 1735 cm^{-1} as it did in the acid product.

Having synthesized and characterized the difunctional acid chloride, **23**, the next task was to find a suitable fluorine containing isoquinoline heterocycle. After reviewing the literature, it was found that Guilani *et al.*[47] had prepared such a compound using the method reported by Minter and Re. The synthesis involved reacting an eneamine with an electrophile in the presence of THF to form a 4-substituted isoquinoline derviative; see *Historical*. The electrophile used in the synthesis was 4-fluorobenzaldehyde. Kimberly Brumfield had prepared this compound previously so a few grams of *(pure)* 4-(p-fluorobenzyl)isoquinoline, **24**, were obtained from her.

The bis(Reissert compound), **25**, was prepared using the single-phase method, see Scheme 11. The single phase method was chosen because of previous work done by our group.[47] After 4 days the reaction was quenched and the standard work-up procedure performed; see *Experimental*. Following drying over sodium sulfate and solvent removal, the crude yield of **25** was 60%. Recrystallization was attempted in EtOAc/hexane but no precipitate was found after 2 days at room temperature so the flask was transferred to a refrigerator for an additional 2 days, but again no product formation was noted. The EtOAc/hexane was removed and toluene substituted, but again to no avail. TLC's in both 50:50 and 60:40 EtOAc/hexane showed two spots. The product spot, however, showed the best separation in the 60:40 case. Chromatography was then performed using silica gel and 60:40 EtOAc/hexane. The compound eluted from the column as an off-white solid. The isolated yield of **25** after chromatography was 62%. TLC showed sonly one spot. The ^{1}HNMR spectrum



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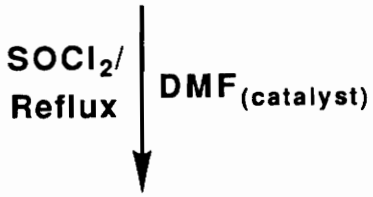
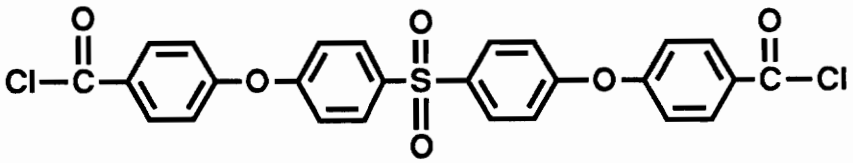




23

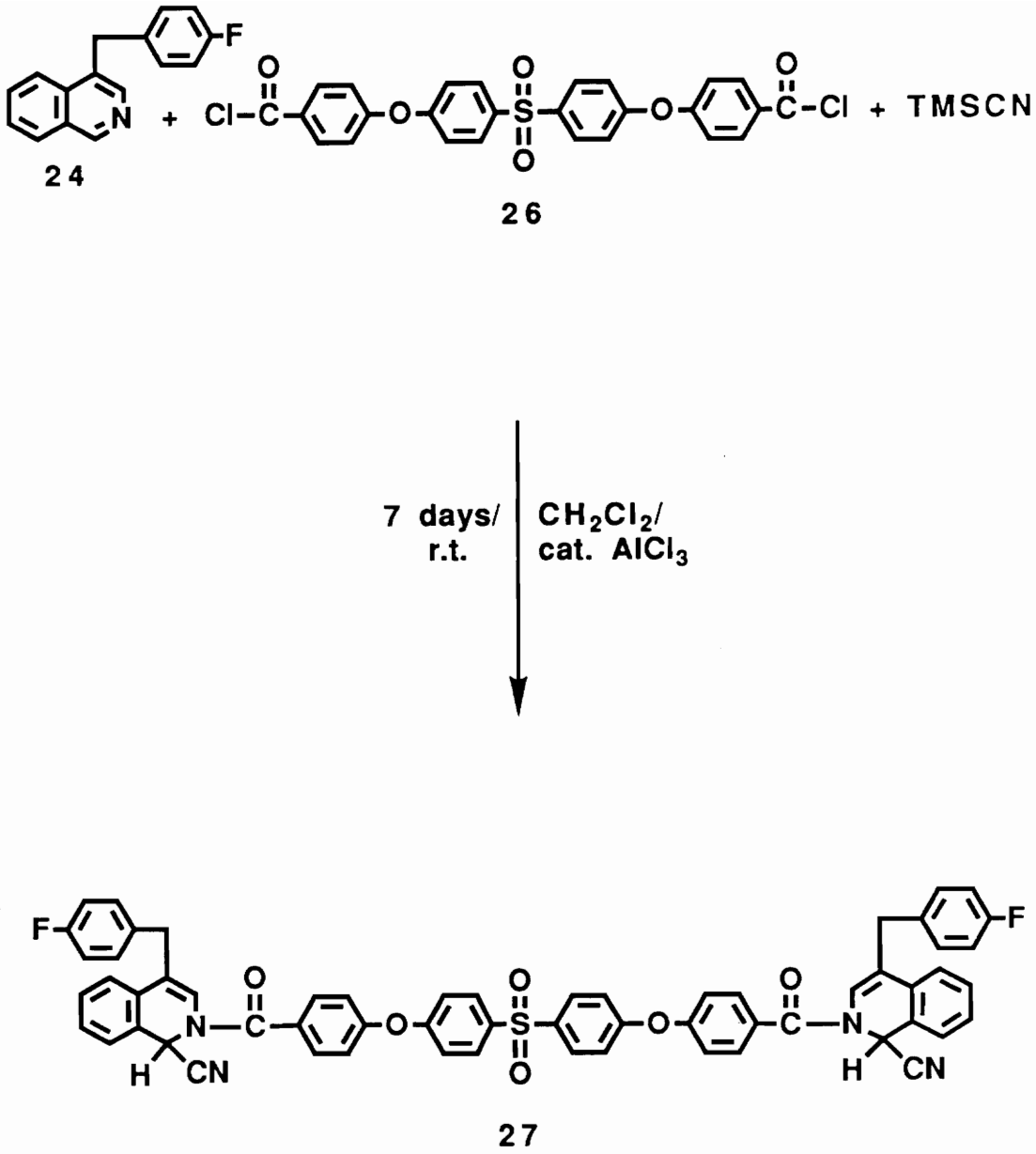
Scheme 10: Synthesis of SulfonylBis(p-Phenyleneoxy)Dibenzoyl Chloride.

of the product showed: AB-pattern, 3.83 δ, 4H, methylene protons; s,s, 6.37 δ, 6.52 δ, 2H,2H, isoquinolyl H_1, H_3; t, 6.94 δ, protons ortho to fluorine; m, 7.03 - 7.37 δ, 26H, Ar-H (isoquinolyl & phenyl) protons; d, 7.60 δ, 2H, isoquinolyl H_5; d, 7.95 δ, 2H, isoquinolyl H_8.

In the process of drying the compound, it was accidently decomposed in the vacuum oven when the temperature exceeded 210°C therefore a second synthesis was warranted. In the second synthesis, the crude yield recorded was only 19%. To purify the compound, initially EtOH/hexane and EtOAc/hexane were used but neither showed crystallization. The compound was then dissolved in chloroform and precipitated into hexane. The melting point of the precipitated product was 151°-156°C.

The large difference in yields is believed to be from a side reaction since a larger amount of precipitate was recovered at the end of the reaction. The spectral data of the precipitate did not agree with any of the starting materials. TLC of the precipitate showed only one spot but the nature of the side product is yet to be determined.

PNMR is extremely useful in the bis-Reissert case since formation of the compound can be monitored by, 1) the appearance of singlets for H_1 and H_3, 2) the appearance of an AB-pattern for the diastereotopic benzylic methylenes at the 4-position of isoquinoline. In the starting material the benzylic methylenes of **24** are seen as a singlet at 4.34 δ. The H_1 and H_3 protons are also seen as singlets at 9.18 δ and 8.39 δ , respectively. One might also think that FTIR could be used to identify the cyano group at C_1 of isoquinoline, but in Reissert compounds it does not show a strong absorption in IR. According to the literature, the oxygen atom of the carbonyl appears to have some interaction with the cyano group, thus causing the lack of a strong absorption in IR.[10]



Scheme 11: Synthesis of SulfonylBis(p-Phenyleneoxy)Dibenzoyl-Bis(Reissert Compound).

2.2. Synthesis of Oxybis(benzoyl)-Bis(Reissert Compound):

Having successfully synthesized the sulfonyl-bis(Reissert compound), **25**, attention was then focused on synthesizing an oxygen linked bis-Reissert. To synthesize this compound an appropriate acid chloride, again, would have to be synthesized. The diacid chloride chosen was 4,4'-oxybis-(benzoyl chloride), **26**. The dicarboxyclic acid compound was received as a gift from Amoco, and was not further purified before use. The synthetic method used was $SOCl_2$/reflux. Following successful synthesis of **26**, more of the isoquinoline heterocycle, **24**, was synthesized. A large scale (40 g) was used to create a surplus of the compound.

With both of the above starting materials synthesized, the next step was to prepare the bis-Reissert, again, via the single phase method, Scheme 12. The reaction was done using **24** and **26**. After work-up and drying, the crude yield of **27** was 67%. TLC of the compound showed two spots which after comparison were determined to be the product and starting material. The compound was then recrystallized using EtOH/hexane (and a small amount of toluene). After four recrystallizations a light-yellow solid was obtained with a melting point of 156.3°-160.5°C. The NMR spectrum of the compound after recrystallization agreed exactly with the proposed structure, (PNMR#2, Appendix). Before elemental analysis of the compound was performed the synthesis was repeated on a much large scale, which afforded a 70% yield. The elemental analysis of the compound was satisfactory.

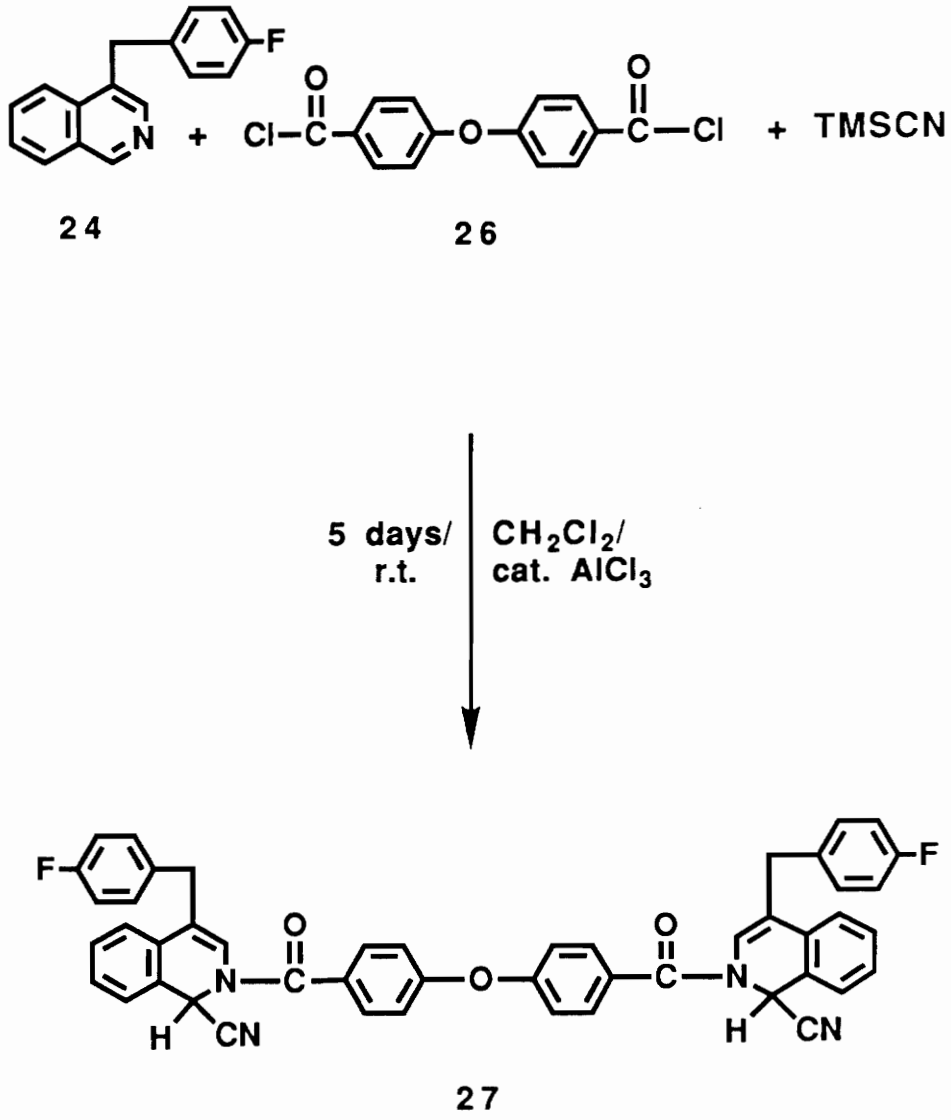
2.3. Rearrangement Study of 4-Substituted Reissert Compound:

As mentioned earlier, rearrangement of 4-substituted Reissert compounds

would have to be further studied before an actual synthesis was performed on a bis-system. The biggest difference between this rearrangement and the previous one is the 4-substitution of isoquinoline. To study the rearrangement a compound of similar nature was chosen. The compound, **28**, was synthesized via the single phase method from benzoyl chloride and 4-(p-fluorobenzyl)isoquinoline, **24**, and was obtained (pure) from Kim Brumfield. The base/solvent combination used for the rearrangement was again NaH/DMF. The reaction was done at room temperature with 1.2 equivalents of NaH. After 3 days the reaction was quenched with water, which caused the compound to precipitate as an orange solid. The compound was then dissolved in dichloromethane and washed with water to remove residual DMF. Following drying of the compound over magnesium sulfate the solvent was removed, and finally the compound was vacuum dried. The yield in this case was monitored by NMR, which showed complete loss of the AB-pattern at 3.80 δ and the appearance of a sharp singlet at 4.34 δ. Complete loss of the H_1 proton at 6.40 δ and the downfield shift of H_3 to 6.60 δ further confirmed the rearrangement. The reaction was repeated with 1.1 equivalents of NaH to see what effect a shorter reaction time would have on the yields. After 4 hrs and identical work-up, proton-n.m.r., again, showed quantitative conversion to the ketone, **29**, see Scheme 13.

2.4. Syntheses of Di- and tetraketone of Oxybis(Reissert), 27

Having performed the above experiment, the next step was to prepare the tetraketone monomer. The first hurtle was to rearrange one of the bis-Reissert compounds discussed previously. The compound chosen was the

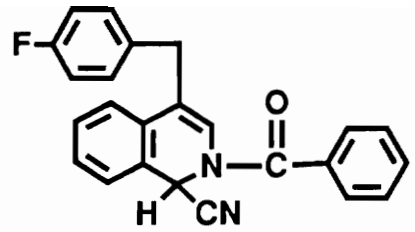


Scheme 12: Synthesis of 4,4'-Oxybis(benzoyl)-Bis(Reissert Compound).

oxygen linked compound, **27**, see Scheme 14. The reaction was done as close to that of the model as possible, and since this was our first trial the reaction was performed on a small scale.

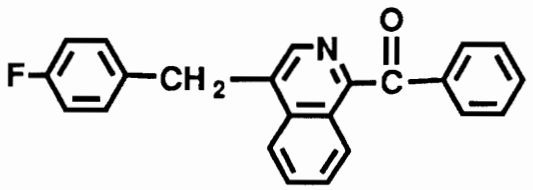
2.2 eq. of NaH were used. With the addition of the hydride, the solution changed from orange to light brown with what appeared to be white particles suspended in the flask. The reaction was allowed to stir for 4 hrs, after which it was quenched by pouring it onto crushed ice. The compound precipitated as an off-white solid with the addition of NaCl (wash w/H_2O to remove). After drying the compound at ~90°C overnight, an NMR was taken. From NMR it was quite clear that the reaction had not worked as the AB-pattern for the benzylic methylenes was still present, along with the singlets for H_1 and H_3. What we had expected to see was complete loss of the benzylic methylenes and H_1, and the downfield shift of H_3. Since the reaction did not proceed as planned another model study was preformed, but this time with a different solvent so that heat could be applied.

Tetrahydrofuran was the solvent chosen since at the end of the reaction it can be easily removed with water. We were unsure whether the bis-Reissert compounds would rearrange directly at room temperature, so the reaction was done at 60°C. The reaction time was 4 hrs. After four hours, the reaction was quenched by pouring the entire contents into dichloromethane. The dichloromethane was then placed in a separatory funnel and washed with water. Next, the compound was dried over magnesium sulfate overnight. After solvent removal and vacuum drying, a proton-n.m.r. spectrum was taken. Again, NMR showed complete loss of H_1 at 6.40 δ and the AB-pattern at 3.80 δ, and the downfield shift of H_3 to 6.60 δ. The mono-Reissert compound seemed to rearrange easily in both THF and DMF, but the true test was the bis-system.



28

Temp. | Base/ Solvent



29

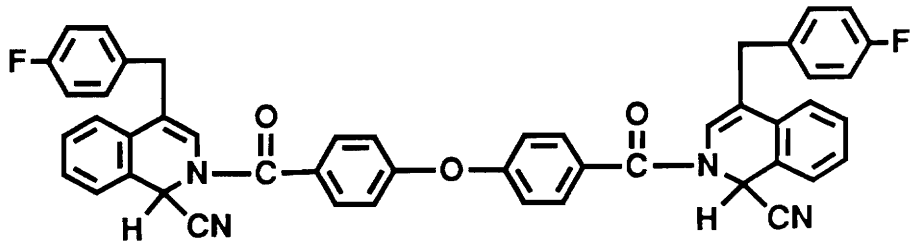
BASE	SOLVENT	TIME	TEMP	YIELD
NaH, 1.2 eq.	DMF	3 days	r. t.	Quantitative
NaH, 1.1 eq.	DMF	4 hrs.	r. t.	Quantitative

Scheme 13: Model Rearrangement of 4-Substituted Reissert Compound.

The rearrangement of **27**, reaction was repeated using THF/NaH. This time, however, the reaction was continuously monitored by proton-n.m.r. to assure the reaction would not be quenched too soon. The reaction was brought to 60°C for three hours, after which an n.m.r. spectrum was taken. The PNMR spectrum showed that the compound had indeed begun to rearrange so the reaction was allowed to continue. At the end of 24 hrs, an n.m.r. spectrum was again taken. The second n.m.r. spectrum showed that the rearrangement was proceeding as planned. After two days, the reaction was quenched by pouring the contents into CH_2Cl_2 repeatedly washing with water to remove THF and any residual hydride. After drying over magnesium sulfate the solvent was removed via rotorary evaporation. The compound was then dried under vacuum for 24 hrs. A PNMR spectrum was then taken and revealed that the compound had completely rearranged, as no trace of the H_1 protons of the AB-pattern remained, (PNMR #3 and FTIR #1, Appendix).

With the above reaction complete, two large scale syntheses were performed. In the first synthesis 12.16 g of **27** were converted to the diketone, **30**, in an 86% (9.74 g) crude yield. The second synthesis was done with 20.27 g of **27**; the crude yield after work-up was 19.35 g (~100%). The melting point of the diketone was 115.2°-117°C. The elemental analysis of the compound was off slightly due to solvated ethyl acetate.

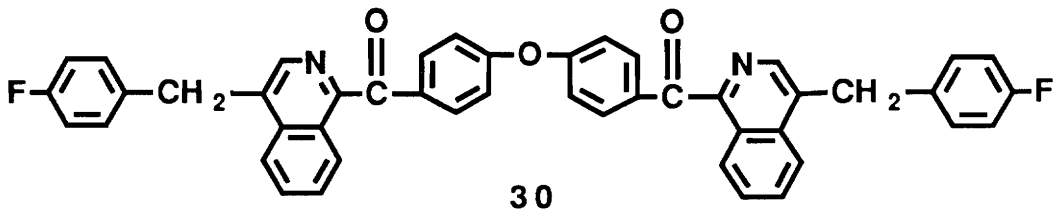
Having successful prepared **30**, the final step was oxidation of the benzylic methylenes to produce the difluorotetraketone monomer, **31**; see Scheme 15. Guilani et al.[58] had previously shown MnO_2/benzene to be a fairly efficient method for the oxidation; therefore, the reaction was carried out using this procedure. The crude yield of **31** after work-up was 39%. However, as reported by Guilani, a Sohxlet extractor was used to remove residual compound



27

Temp/
Time

Base/
Solvent



30

CMPD	BASE	SOLVENT	TIME	TEMP	YIELD
27	NaH	DMF	4 hrs	r. t.	no reaction
28	***NaH***	***THF***	***4 hrs***	***60°C***	***~100%***
27	NaH	THF	2 days	60°C	86%
27	NaH	THF	2 days	60°C	~100%

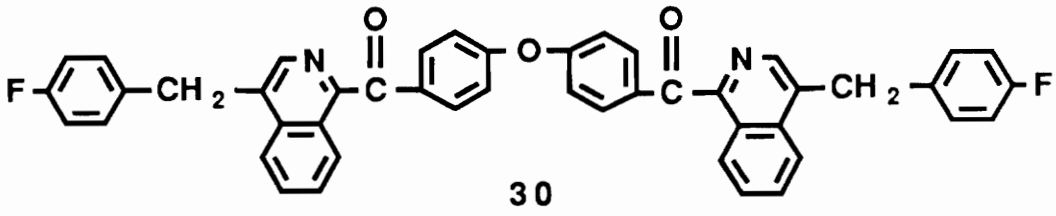
Scheme 14: Rearrangement of OxyBis(Benzoyl)-Bis(Reissert Compound).

the MnO_2. The combined yield after Sohxlet extraction was 57%. Recrystallization from ethanol/hexane afforded an analytically pure sample with a melting point of 176.8°-178.5°C. The PNMR spectrum of the compound showed complete loss of the benzylic methylenes seen previously at 4.45 δ, (PNMR #4, Appendix). The FTIR spectrum also showed a loss of all aliphatic bands. Although there are two different types of ketones in **31**, only one carbonyl absorption was detected at 1662 cm^{-1}, (FTIR #2, Appendix). According to Guilani,[47] the separation of the two ketone bands is apparently less than the resolution of the instrument.

3.1 Synthesis of Sulfonylbis(benzoyl)-Bis(Reissert Compound):

Having successful synthesized both the sulfonylbis(p-phenyleneoxy)-bis(Reissert), **25** and the oxybis(benzoyl)-bis(Reissert compound), **27**, the next task was to synthesize a bis-Reissert compound containing a sulfonyl linkage like **25** but without the presence of the ether oxygens. To synthesize this type of sulfonyl containing compound, first a commercially available diester was obtained from Aldrich. The compound, 4,4'-sulfonylbis(methyl benzoate), **32a**, was converted to the corresponding dibenzoic acid, **32**, using KOH/ethanol/ reflux. The crude yield of the acid after work-up and drying was 96%. The melting point of the acid was >400°C. FTIR spectroscopy of the compound showed: -COOH band at 3200-2500 cm^{-1} and the C=O absorption was detected at 1690 cm^{-1}. Sulfonyl stretches were detected at 1284 and 1160 cm^{-1}, (FTIR #3, Appendix).

The dibenzoic acid was then converted to the diacid chloride, **33**, using thionyl chloride at reflux. After two recrystallizations with toluene a melting point



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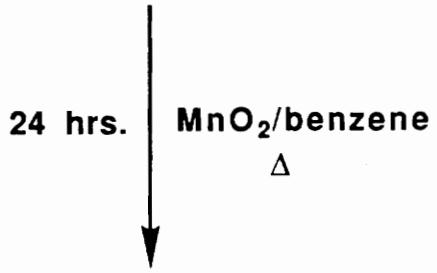
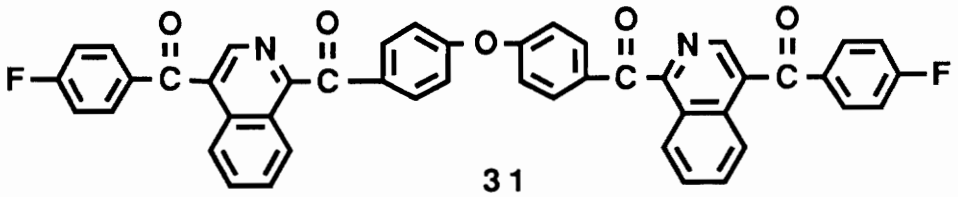




31

Scheme 15: Synthesis of the Oxybis(benzoyl)-Difluorotetraketone.

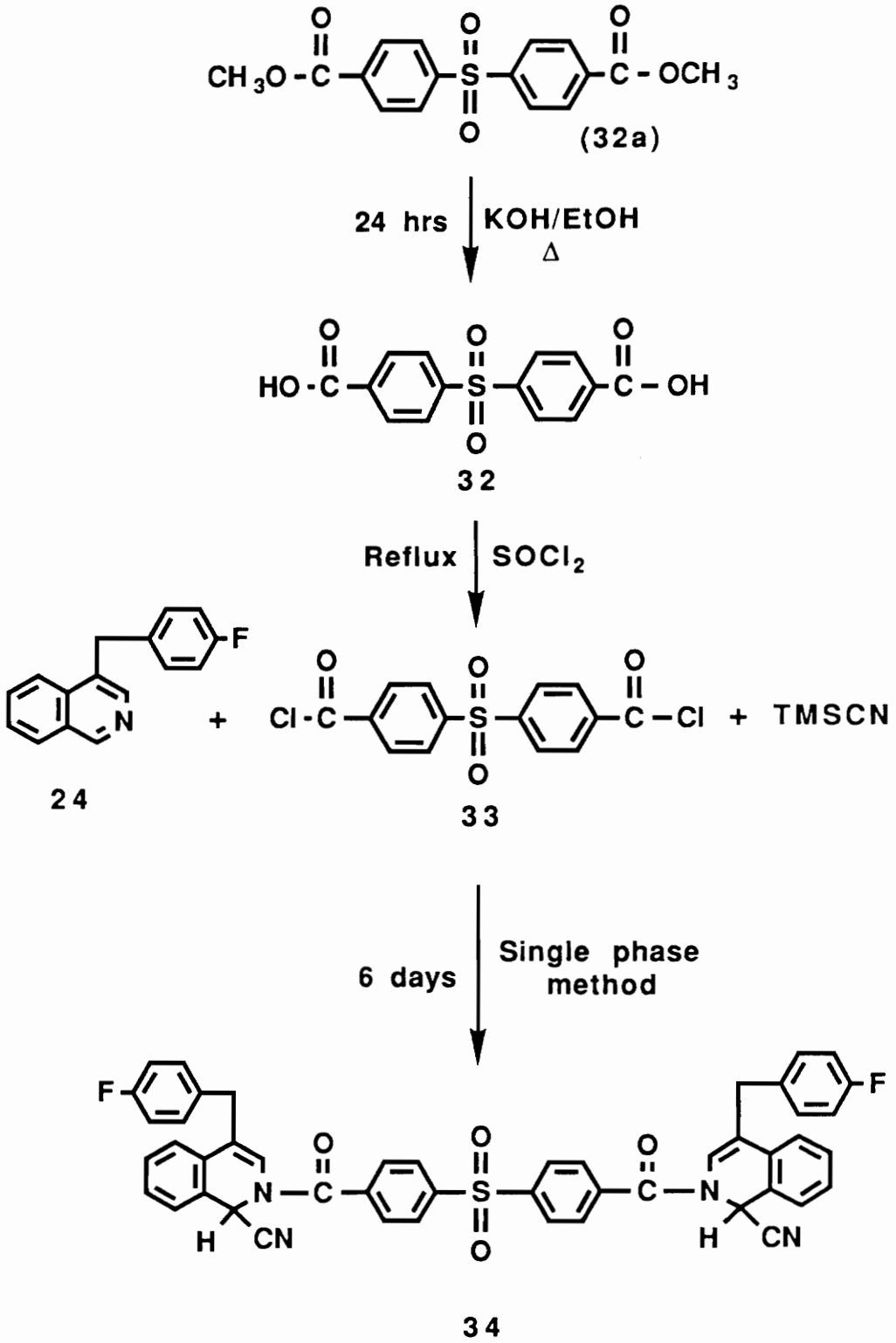
of 159°-160°C was obtained. The isolated yield after purification was 93%. FTIR spectroscopy of the compound showed complete loss of the carboxyclic acid band at 3200 cm^{-1}.

The next step was preparation of the bis-Reissert compound, **34**; see Scheme 16. In the synthesis 2.05 eq. of **24** and 2.10 eq. of TMSCN were reacted with 1.0 eq. of the dibenzoyl chloride, **33**. The reaction was continued for 6 days. Following the standard work-up procedure, the crude yield of **34** was 53%. Recrystallizations from EtOAc/hexane yielded an elementally pure product with a melting point of 165.8°-166.7°C. The proton-n.m.r. spectrum of the pure product showed the typical Reissert compound spectrum, with the peaks of interest being the AB-pattern at 3.76 δ for the benzylic methylenes and singlets for the H_1 and H_3 at 6.22 and 6.56 δ, respectively, (PNMR #5, Appendix). The compound gave a satisfactory elemental analysis.

The reaction was repeated on a 13 gram scale which produced 58% yield of the desired product. The compound was confirmed on the basis of its n.m.r. spectrum and melting point.

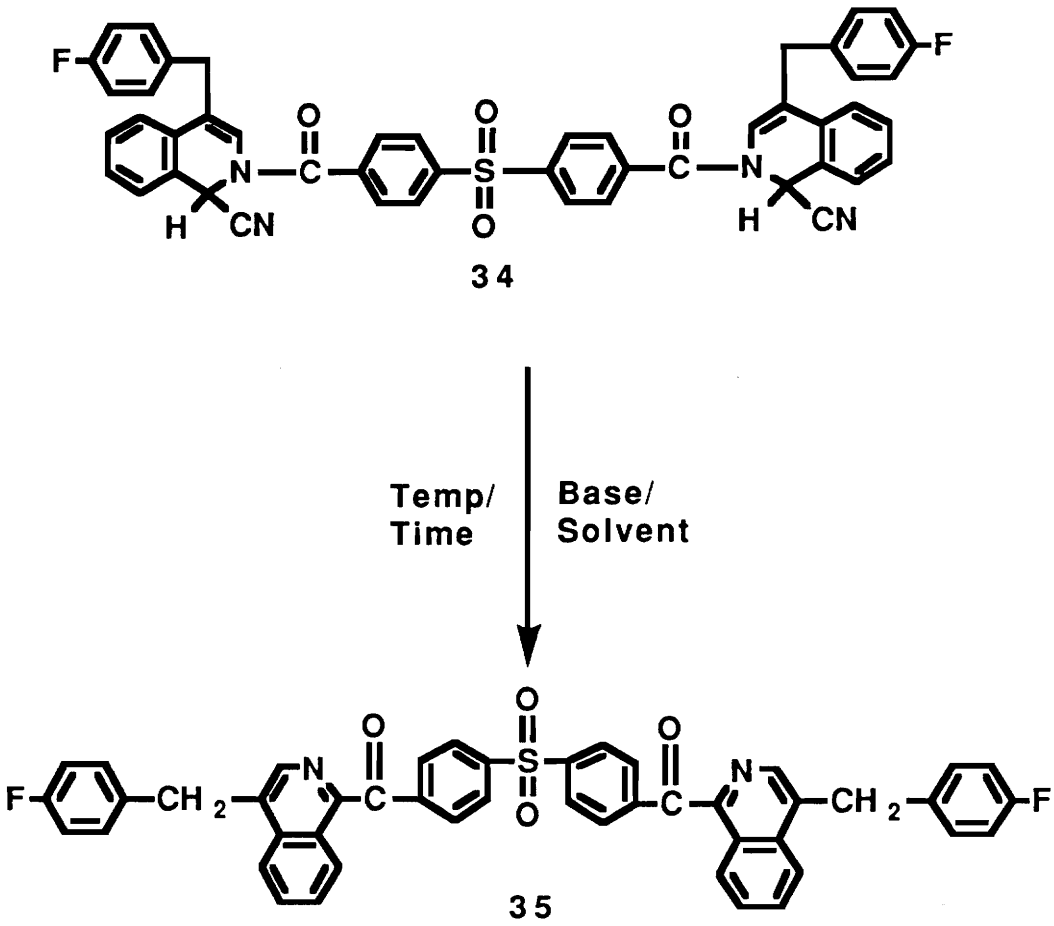
3.1 Synthesis of the Sulfonyl-diketone:

With the synthesis of the sulfonylbis(Reissert compound), **34**, complete the next step was to synthesize the diketone, **35**, via rearrangement of **34**. The rearrangement was done using the procedure mentioned previously for the synthesis of the oxybis(benzoyl)-diketone. In the synthesis, **34** was dissolved in THF and treated with 2.2 eq. of NaH. The reaction was refluxed for two days under nitrogen, after which the reaction was quenched and the standard work-up procedure performed; see *Experimental*. The crude yield of the diketone



Scheme 16: Synthesis of Sulfonylbis(benzoyl)-Bis(Reissert Compound).

after work-up was 76%. The compound was then reprecipitated three times using chloroform/hexane to remove any mineral oil or other impurities. TLC of the compound (after precipitation) in 65:35 EtOAc/hexane showed multiple spots so the compound was passed through a silica gel column. An NMR spectrum of the chromatographed sample showed a trace of the starting material so another precipitation was performed. The proton-nmr spectrum of the precipitated compound again showed a small trace of impurities so the compound was then recrystallized. After two recrystallization from EtOAc/hexane(w/small amount of toulene), an analytically pure product having a melting point of 153.7°-155.2°C was obtained. The elemental analysis of the compound was off slightly due to the presence of toluene.



Scheme 17: RAR of SulfonylBis(Benzoyl)-Bis(Reissert Compound).

V. SUMMARY AND FUTURE WORK:

In conclusion, it has been shown that bis(Reissert compound)s containing flexible spacer units can indeed by prepared in good to moderate yields using the diacid chloride route and the eneamine reaction of Minter and Re.[48] It has been demonstrated that the rearrangement of these compounds to diketones can be easily accomplished using NaH/THF. Yields for the rearrangement ranged as high as 86%. This reaction has a definite advantage over NaH/DMF in that the THF is more easily removed at the end of the reaction.

A novel (activated) difluorotetraketone monomer has also been prepared using MnO_2/benzene. This monomer is easily purified via recrystallization from ethanol/hexane. Activation of this monomer has produced a monomer that is indeed suitable for polymerization via nucleophilic displacement. This monomer is unique in that it contains two isoquinolyl groups within the monomer which are known to impart thermal stability.

Future research in this area should definitely included the following: 1) polymerization the difluorotetraketone monomer with different diphenols, 2) conversion of the two sulfonyl compounds to difluoro monomers and finally polymers, 3) testing of these systems for adhesive characteristics, and finally 4) devise a more efficient method for the oxidation of the benzylic methylenes. A small amount of work was done on the latter process but the results were inconclusive.

It is strongly believed that the diacid chloride route can be used to tailor bis(Reissert compounds) for a variety of different AA-monomer systems. One system in particular is the phosphine oxide system used by Dr. McGrath's group. Experimentally, phosphine oxides are well-known for their flame

retardency and thermal stability. It would be interesting to see what type of mechanical properties the phosphine oxide system would have when used in conjunction with the bis-isoquinoline system.

Extension of the 4-alkylation reaction should also be explored, as this could possibly give rise to different function groups for polymerization.

VI. EXPERIMENTAL DATA:

All melting points were determined with a Mel Temp II capillary melting point apparatus and are corrected unless otherwise indicated. NMR spectra were taken at 270 MHz on a Bruker 270 spectrometer interfaced to an Aspect 2000 Hewlett Packard 7550A graphics printer. The solvents used were $CDCl_3$ and DMSO-d_6 with tetramethylsilane (TMS) as the internal standard. IR spectra were determined using KBr pellets or thin films cast from dichloromethane. The instrument used was a Nicolet MX-1 FTIR spectrophotometer interfaced to a Hewlett Packard Color Pro plotter. In all NMR peak assignments the following abbreviations were used; **s** (singlet), **d** (doublet), **m** (multiplet), **t** (triplet), **Ar-H** (aromatic hydrogen). All elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia. Mass spectroscopy was performed by the Midwest Center for Mass Spectroscopy, Lincoln, Nebraska. All reported compounds were characterized by their melting points. Dichloromethane was obtained from Fisher Scientific and dried over molecular sieve before using. DMF (N,N-dimethylformamide) was obtained from Aldrich Chemicals and used without further purification. THF (tetrahydrofuran) was purified from sodium/benzophenone prior to use. Sodium hydride was used as 60% dispersion in mineral oil, and was obtained from Aldrich Chemicals. DMSO (N,N-dimethyl sulfoxide) was obtained from Aldrich and was distilled with calcium carbonate prior to use. All other solvent were used as received from the vendor.

1-Benzoyl-1,2-dihydroisoquinaldonitrile, 2:

In a 3-neck RB-flask (fitted with a mechanical stirrer, nitrogen inlet, and addition funnel) were dissolved 32.57 g (0.498 moles) of KCN in 70 ml of water with stirring. To this solution were added 21.50 g (0.166 moles) of isoquinoline and 134 ml of dichloromethane, again, with moderate stirring. Next, 38.54 ml (0.332 moles) of benzoyl chloride were added dropwise over a 2 hr. period. Vigorous stirring was used to properly mix the two phases. After the addition of the acid chloride, the reaction was continued for an additional 3 hours. At the end of the reaction the solution was a reddish-brown color. The reaction was quenched into 250 ml of distilled water, and stirred slowly for 2 hours. Next the organic phase was washed in a separatory funnel according to the following sequence: 3 x water, 3 x 10% HCl, 3 x $NaHCO_3$, 3 x water and finally dried over sodium sulfate. Following removal of the solvent and vacuum drying, the crude yield was 40.20 g (93%). Isolated yield after recrystalliztion in EtOH was 25.55 g (64%), m.p. 125°C-126°C [lit.[13] m.p., 124°-126°C]. The protons of interest in the NMR spectrum were the isoquinolyl H_1, (s, 6.60 δ, 1H); isoquinolyl H_3, (d, 6.65 δ, 1H); and isoquinolyl H_4, (d, 1H, 6.10 δ).

Rearrangement of Isoquinoline Reissert Compound, (Scheme 5):

In a 3-neck 50 ml RB-flask (fitted with a nitrogen inlet) were dissolved 2.0 g (0.0077 moles) of **2** in 20 ml of (dry) DMF. To this stirred solution were added 0.34 g (0.014 moles) of NaH (60% dispersion in mineral oil) in one portion. The reaction was allowed to stir at room temperature for 4 hr, during which time 1 ml aliquots were taken (via syringe) at 10, 20, 40, 60, 90, 120, 150 and 225

minute time intervals. The samples were quenched with water, and washed several times to remove any residual DMF. The PNMR spectrum (*10 and 225* min. samples) showed complete loss of the H_1 proton @ 6.55 δ, and the appearance of two new doublets @ 8.25 and 8.62 δ, respectively (assigned as H_4 and H_3).

4,4'-[Sulfonylbis(p-Phenyleneoxy)]dibenzoic acid, 21:

To a three-neck 250 ml RB-flask, equipped with reflux condenser, thermowell, nitrogen gas inlet tube, and stirring apparatus were charged 11.05 g (0.08 moles) of 4-hydroxybenzoic acid, 8.98 g (0.16 moles) of KOH, and 75 ml of DMSO. The reaction was heated to 70°C for 45 minutes, with the water of neutralization removed via vacuum distillation. To the resulting dipotassium salt were added 11.49 g (0.04 moles) of 4,4'-dichlorodiphenylsulfone, 2.0 g of KF and 50 ml of dry DMSO. The mixture was then heated to 145°C for 5 hrs. After cooling, the reaction mixture was quenched into 1 liter of acetone and stirred for 1 hour at 50°C. The dipotassium salt was filtered and washed repeatedly with acetone. The product was then dissolved in water and treated with activated charcoal, after which it was acidified with sulfuric acid (at pH 2). The crude yield after drying was 12.94 g (72%). The crude m.p. was 270°-273°C, [lit.[63] m.p. 306°-308°C]. The FTIR spectrum of the product showed an acid peak at 3200 - 2561 cm^{-1} and C-O-C sym. and asym. stretches at 1250 and 1109 cm^{-1}. The carbonyl absorption was found at 1684 cm^{-1}. Sulfonyl stretches were detected at 1327 and 1163 cm^{-1}.

Dimethyl-4,4'-[Sulfonylbis(p-Phenyleneoxy)]dibenzoate, 22:

In a 100 ml RB-flask were mixed 6.67 g (0.013 moles) of **21** and 10 ml of sulfuric acid (conc.) in 50 ml of methanol. The solution was brought to reflux and allowed to react for 24hrs. The reaction was allowed to cool to room temperature before quenching with CH_2Cl_2. The solution was then washed with water X 3, 10% $NaHCO_3$ X 2 and water X 1, and finally dried over sodium sulfate. After two recrystallizations from EtOAc/hexane, the isolated yield of **22** was 3.76 g (55%). The melting point of the purified product was 136°-139°C. The NMR spectrum of the purified product showed: s, 3.83 δ, 6H, methoxy protons; t, 7.0 δ, 4H, protons beta to sulfonyl; d, 7.42 δ, 4H, protons alpha to carbonyl; t, 7.65 δ, 4H, beta to carbonyl; d, 8.0 δ, 4H, alpha to sulfonyl.

4,4'-[Sulfonylbis(p-Phenyleneoxy)]dibenzoyl chloride, 23:

In a 100 ml flask fitted with a condenser and a guard tube were mixed 12.00 g (0.0245 moles) of 4,4'-[sulfonylbis(p-phenyleneoxy)]dibenzoic acid and 18.09 ml (0.245 moles) of $SOCl_2$. The mixture was heated at reflux for 2 hrs., after which 3-4 drops of DMF were added. The heating was continued for another 2 hrs and then left overnight at room temperature. The excess thionyl chloride was distilled off under reduced pressure. The crude product was recrystallized from toluene in 6.46 g (50%) isolated yield. The melting point was 179°-184°C [lit. m.p.[63] 184°-189°C]. The FTIR spectrum of the product showed: C=O stretch @1735 cm^{-1}; C-O-C asym. and sym. stretch @ 1250 and 1104 cm^{-1} respectively; C-Cl bending @ 885 cm^{-1}, and the loss of the carboxyclic acid bands @ 3200 - 2561 cm^{-1}. The ^{1}HNMR spectrum showed: d, 7.10 δ, 2H, beta

to sulfone; d, 7.20 δ, 2H, beta to carbonyl; d, 8.05 δ, 2H, alpha to carbonyl; d, 8.15 δ, 2H alpha to sulfone.

4-(p-Fluorobenzyl)isoquinoline, 24:[47]

29.00 g (0.224 moles) of isoquinoline were dissolved in 160 ml of THF (freshly distilled form Na°/benzophone). Sodium triethylborohydride was added as a 1.0 M solution in five parts of total volume 233 ml (0.233 moles). The reaction was then cooled and stirred under nitrogen for 30 minutes, after which 28.24 g (0.235 moles) of p-fluorobenzaldehyde were added. The reaction was continued for 4 hours. At the end of the reaction, the solution was reddish in color. The reaction was cooled via ice bath, quenched with 466 ml 0.5 N NaOH, followed by the careful addition of 233 ml 30% H_2O_2. The quenched reaction was allowed to stir for 24 hours prior to extraction with chloroform. The extract was then washed with water 4 x and dried over sodium sulfate. The solvent was removed via rotovap, crude yield 42.5 g (80%) [as confirmed by PNMR]. Melting point of the recrystallized product (petroluem ether) was 64.2°-66.3°C (lit.[47] mp 66°-67°C).

N,N'-[Sulfonylbis(p-phenyleneoxy)]-Bis{4,4'-(p-fluorobenzyl)-1,2-dihydroisoquinaldonitrile}, 25:

To a 250 ml flask were added 3.87 g (0.0163 mole) of **24** and 4.00 g (0.0076 mole) of 4,4'-[sulfonylbis(p-phenyleneoxy)dibenzoyl chloride (SPCl) in 75 ml of dry CH_2Cl_2 (dried over molecular sieve) under a nitrogen blanket. After 15 minutes, 2.23 ml (0.0167 mole) of TMSCN were added via syringe

along with a cat. amount of $AlCl_3$. After 4 days the reaction was quenched into water. The organic layer was then washed 3 x H_20, 2 x 5% NaOH, 1 x 10% $NaHCO_3$, 3 x 10% HCl, and 3 x H_2O, and finally dried over Na_2SO_4. Removal of solvent afforded 4.48 g (60%) of a yellow solid. Column chromatography was performed on 2.66 g of the crude using silica gel and 60:40 ethyl acetate/hexane. The isolated yield of product after chromatography was 1.66 g (62%). The ^{1}HNMR spectrum of the product showed: AB-pattern, 3.83 δ, 4H, methylene protons; s,s, 6.37, 6.52, 2H, 2H, isoquinolyl H_1, H_3; t, 6.94 δ, protons ortho to fluorine; m, 7.03 - 7.37 δ, 26H, Ar-H protons; d, 7.60 δ, 2H, isoquinolyl H_5; d, 7.95 δ, 2H, isoquinolyl H_8.

The synthesis was repeated on a small scale which produced a 1.81 g (19%) crude yield. The compound was dissolved in chloroform and precipitated into to hexane three times. Column chromatography (65:35; EtOAc/hexane) was preformed on the compound, but yield an unpure product as shown by TLC. Two further recrystallizations from EtOAc/hexane yielded a pure product with a melting point of 151°-156°C Elemental analysis of the compound calculated for $C_{60}H_{40}N_4O_6SF_2 \cdot C_4H_8O_2$ showed calc'd (found): %C, 71.76 (71.62); %H, 4.52 (4.12); %N, 5.23 (5.21). (Note: calculated values were determined on the basis of 1 mole of ethyl acetate per mole being present). Mass spectrometry: $C_{60}H_{40}N_4O_6SF_2$, M = 982.26; found (FAB in 3-nitrobenzyl alcohol): m/z 983.26, $(M+H)^+$; 982.26, M^+; 956, $(M-CN)^+$; 719, $(M-C_{17}H_{12}N_2F)^+$; 665, $(M-CN-C_{17}H_{12}N_2F)^+$.

4,4'-Oxybis(benzoyl chloride), 26:

In a 500 ml RB-flask (equipped with a reflux condenser and Drierite tube) were

reacted 30.00 g (0.116 moles) of 4,4'-oxybis(benzoic acid), and 85.00 ml of (1.19 moles) of $SOCl_2$. The solution was allowed to reflux for two hours, after which a few drops of DMF were added as a catalyst. Refluxing was continued for an additional 22 hrs. The excess thionyl chloride was removed via reduced pressure distillation. After drying and recrystallization (toluene), the isolated yield of product was 30.14 g (88%). Melting point 87.4°-88.6°C (lit.[47] m.p., 82°-83°C). FTIR showed carbonyl absorptions at 1750 and 1710 cm^{-1}.

N,N'-[4,4'-Oxybis(benzoyl)]-Bis{(α,α'-p-fluorobenzyl)-1,2-dihydroiso-quinaldonitrile}, 27:

In a 250 ml RB-flask were dissolved 6.55 g (0.0276 moles) of p-fluorobenzylisoquinoline, **24**, and 3.01 g (0.0105 moles) of **26** in 75 ml of (dry) CH_2Cl_2. This solution was allowed to stir under nitrogen for 20 minutes before 3.01 ml (0.0226 moles) of TMSCN were added via syringe; followed by a cat. amount of $AlCl_3$. Stirring was continued for 7 days, after which the reaction was quenched with 150 ml of water. Following two hours of stirring in water, the organic phase was washed in a separatory funnel 3 x water, 3 x 10% HCl, 3 x 10% $NaHCO_3$, 3 x 5% NaOH. After drying over sodium sulfate for 24 hrs., the solvent was removed via rotorary evaporation and the compound dried under vacuum. The crude yield of **27** was 5.42 g (67%). Four recrystallizations via EtOH/hexane (small amount of toluene) afforded a light yellow powder melting at 156.3°-160.5.°C. The PNMR spectrum of the product showed: AB-pattern, 3.80 δ, 4H, methylene protons; s, s, 6.43, 6.53 δ, 2H, 2H, isoquinolyl H_1, H_3; t, 6.96 δ, 4H, protons ortho to fluorine; d, 7.05 δ, 4H, protons ortho to oxygen; m, 7.18 - 7.39 δ, 12H, Ar-H protons; d, 7.63 δ, 4H, protons ortho to carbonyl.

Results of elemental analysis for $C_{48}H_{32}N_4O_3F_2$, calc'd (found): %C, 76.79 (76.29); %H, 4.30 (4.35); %N, 7.46 (7.26).

The above reaction was repeated on a larger scale using 22.30 g (0.094 moles) of **24**, 13.20 g (0.046 moles) of **26**, and 12.93 ml (0.097 moles) of TMSCN. The reaction was allowed to stir under nitrogen for 5 days. After identical work-up , 24.25 g (70%) of crude product were obtained. TLC [(65:35), EtOAc/ hexane] and PNMR were used to confirm the compound.

Synthesis of N-Benzoyl-4-(p-fluorobenzyl)-1,2-dihydroisoquinaldonitrile, 28:[47]

23.73 g (0.08 moles) of **24** (crude) were dissolved in 120 ml of CH_2Cl_2. Then, 15.63 g (0.24 mole) KCN, dissolved in 40 ml of water, were added to the dichloromethane solution. The mixture was then stirred for 15 minutes prior to the dropwise addtion of 22.49 g (0.16 mole) of benzoyl chloride over 2 hours. The reaction was stirred for 7 hours, after which 100 ml of water were added. The organic layer was then washed in a separatory funnel 3 x water, 3 x 5% NaOH, 1 x 10% $NaHCO_3$, 3 x 10% HCl, and 3 x water. The solution was then dried over sodium sulfate for 24 hrs. Removal of solvent afforded 23.45 g (80%) of the crude compound. Four recrystallizations from ethanol afforded a pure product melting at 164.3° - 165.1°C (lit.[58] mp, 163° - 164°C). Obtained from Kimberly Brumfield.

Synthesis of Mono-ketone, 29, via rearrangement:

0.59 g (1.60 mmoles) of **28** were obtained from Kimberly Brumfield. The

compound was dissolved in 25 ml of freshly distilled THF (distilled over Na°/benzophenone). To this stirred solution were *carefully* added 0.07 g (2.90 mmoles) 1.2 eq. of NaH (60% dispersion in mineral oil) in one portion. With the addition of the hydride, the solution became dark purple. The solution was reacted under nitrogen for 3 days. Following the three days of reaction time, the solution was quenched with 120 ml of water. Next, the compound was dissolved in dichloromethane and washed with water to remove residual DMF. The compound was finally dried over magnesium sulfate for 24 hrs. After solvent removal and drying, NMR spectroscopy showed complete loss the AB-pattern @ 3.80 δ and the H_1 proton @ 6.40 δ. The methylenes were seen as a singlet @ 4.34 δ and H_3 as a singlet @ 6.60 δ.

The reaction was repeated using 0.5 g (1.6 mmoles) of **28** and 1.1 eq. of NaH. The reaction time was 4 hours. The yield after identical work-up was quanitative. PNMR showed appearance of singlets for methylenes and H_3, and the loss of the AB-pattern and H_1 proton.

Synthesis of Oxybis(benzoyl)-diketone, 30:

To a clean dry 500 ml RB-flask were dissolved 12.16 g (0.0162 mole) of **27** in 170 ml of freshly distilled THF. Once dissolved, 1.42 g (0.0593 moles) [2.2 eq.] of NaH (60% dispersion in mineral oil) were added in one portion. The reaction was then heated to 60°C under nitrogen and allowed to proceed for 2 days. The reaction was quenched with dichloromethane and then washed with water in a separatory funnel. The compound was then dried over magnesium sulfate for 24 hrs. Removal of solvent afforded 9.74 g (86%) of the crude product. After reprecipitation of the compound in chloroform/hexane and two

recrystallizations in EtOAc/hexane a melting point 115.2°-117°C was obtained. PNMR of the compound showed: s, 4.44 δ, 4H, benzylic methylenes; t, 6.98 δ, 4H, protons ortho to fluorine; m, 7.07 - 7.21 δ, 8H, protons ortho to oxygen & the benzylic methylens; t, t, 7.61, 7.72 δ, 2H, 2H, isoquinolyl H_6 and H_7; m, 7.98 - 8.09 δ, 6H, protons ortho to carbonyl and H_5; d, 8.26 δ, 2H, isoquinolyl H_8; s, 8.45 δ, 2H, isoquinolyl H_3. FTIR showed C=O, 1664.1 cm^{-1}; C=C, C=N, 1598.7 - 1507.1 cm^{-1}; C-O-C, 1238.9 cm^{-1}. Elemental analysis for $C_{46}H_{30}N_2O_3F_2 \cdot 1/3\ C_4H_8O_2$ calc'd (found): %C, 78.23 (78.06); %H, 4.52 (4.45); %N, 3.86 (4.19). (Note: calculated values were determined on the bases of 1/3 mole of ethyl acetate per mole being present). Mass spectrometry: $C_{46}H_{30}N_2O_3F_2$, M = 696.22; found (FAB in 3-nitrobenzyl alcohol): m/z 697.23, $(M+H)^+$; 236.0, $C_{16}H_{11}NF^+$.

Synthesis of Difluorotetraketone monomer, 31:

In a clean dry 500 ml RB-flask were added 9.00 g (0.013 moles) of **30** and 90.00 g (1.03 moles) of MnO_2 in 300 ml of benzene. The benzene/water azeotrope was collected via a Dean-Stark trap. The solution was then heated to reflux via oil bath for 24hrs. At the end of the reaction the MnO_2/benzene solution was filtered through a Celite. The Celite bed was then washed with $CHCl_3$, and finally with (hot) EtOAc. The solutions were combined and then dried over $MgSO_4$. The crude yield of **31** was 5.03 g (54%). An analytically pure sample melting at 176.8°-178.5°C was obtained after four recrystallizations from EtOH/hexane. The PNMR of the pure product showed: m, 7.14 - 7.23 δ, 8H, protons ortho to fluorine and benzylic methylenes; t, t, 7.69, 7.79 δ, 2H, 2H, isoquinolyl H_6 and H_7; m, 7.94 - 8.11 δ, 8H, protons ortho carbonyl and

oxygen; d, d, 8.10, 8.24 δ, 2H, 2H, isoquinolyl H_5 and H_8; s, 8.65 δ, 2H, isoquinolyl H_3. FTIR of the pure showed: C=O stretch, (strong) 1662 cm^{-1}; C-O-C stretches, 1251 and 1151 cm^{-1}. Elemental analysis for $C_{46}H_{26}N_2O_5F_2.1/2C_2H_5OH$, calc'd (found): %C, 75.49 (75.30); %H, 3.91 (3.74), %N, 3.75(3.83); %F, 5.08(4.57). (Note: calculated values were determined on the basis of 1/2 mole ethanol per mole being present).

Synthesis of 4,4'-Sulfonylbis(benzoic acid), 32:

In a 500 ml RB-flask were added 40.12 g (0.120 moles) of dimethyl-4,4'-sulfonylbis(benozate) [obtained from Aldrich] and 19.64 g (0.350 moles) of KOH in 300 ml of (absolute) ethanol. The solution was heated to reflux and allowed to react overnight. At the end of the reaction, the dipotassium salt was filtered, and finally dissolved in water. The salts were acidified by adding conc. sulfuric acid dropwise until pH 2. The compound was then filtered and washed with water to remove residual acid. The crude yield of acid after drying was 35.16 g (96%). The compound did not melt even at 400°C. FTIR of the product showed: COOH band, 3200 - 2500 cm^{-1}; carbonyl absorption band, (strong) 1690 cm^{-1}; sulfonyl stretches, 1284 and 1160 cm^{-1}.

Synthesis of 4,4'-Sulfonylbis(benzoyl chloride), 33:

In a 250 ml RB-flask were mixed 34.16 g (0.1115 moles) of **32** and 84.03 ml (1.115 moles) of thionyl chloride (Aldrich). The solution was allowed to reflux for 2 hours, after which a 2-3 drops of DMF were added as a catalyst. Refluxing was then continued for an additional 22 hrs. At the end of the reaction the

excess thionyl chloride was removed via reduced pressure distillation. Recrystallization of the compound in toluene gave a white fluffy solid with a melting point of 159°-160°C. The isolated yield of after purification was 35.52 g (93%). The FTIR spectrum showed complete loss of the carboxyclic acid band at 3200 cm^{-1}.

Synthesis of N,N'-[4,4'-Sulfonylbis(benzoyl)]-Bis{(α,α'-p-fluoro-benzyl)-1,2-dihydroisoquinaldonitrile}, 34:

In a 250 ml RB-flask were added 3.63 g (0.0153 moles) of **24** and 2.51 g (0.0073 moles) of **33** in 75 ml of (dry) CH_2Cl_2. After approximately 20 minutes 2.10 ml of TMSCN were added via syringe, followed by a cat. amount of $AlCl_3$. The reaction was stirred, under nitrogen, for 6 days. The reaction was then quenched with 300 ml of water and stirred for 2 hours. The organic layer was washed 3 x water, 3 x 5% NaOH, 3 x 10% $NaHCO_3$, 3 x 10% HCl, and 3 x water. The final solution was dried over sodium sulfate for a day. Solvent removal and drying affored 3.08 g (53%) crude yield. After three recrystallizations from EtOAc/hexane, a yellow solid melting at 165.8°-166.7°C was obtained. The NMR spectrum of the pure product showed: AB-pattern, 3.82 δ, 4H, benzylic methylenes; s, s, 6.22, 6.56 δ, 2H, 2H, isoquinolyl H_1 and H_3; t, 6.92 δ, 4H, protons ortho to fluorine; m, 7.16 - 7.38 δ, 16H, Ar-H protons; d, 7.72 δ, 2H, isoquinolyl H_5; d, 8.03 δ, 2H, isoquinolyl H_8. FTIR a showed C=O, 1670 cm^{-1}, C≡≡C, C≡≡N, 1598 - 1507 cm^{-1}; -SO_2-, 1395, 1330 cm^{-1}. Elemental analysis for $C_{48}H_{32}N_4O_4SF_2$, calc'd (found): %C, 72.17 (71.93); %H, 4.04 (4.09); %N, 7.01 (6.94).

The reaction was repeated on a larger scale using 18.51 g (0.078 moles) of **24**, 13.04 g (0.038 moles) of **33**, and 10.67 ml (0.080 moles) of TMSCN. The crude yield of the reaction was 17.70 g (58%).

Synthesis of Sulfonyl-diketone, 35:

In a 500 ml RB-flask were mixed 14.14 g (0.0177 moles) of **34** in 200 ml of freshly distilled THF. 1.56 g (0.0649 moles) of NaH (60% dispersion in light mineral oil) were added. The reaction was then heated at 60°C under nitrogen for 2 days. At the end of the reaction the THF was poured into dichloromethane and washed repeatedly with water. The compound was then dried over $MgSO_4$ for one day. The crude yield after solvent removal and drying was 9.69 g (76%). The compound was then reprecipitated using chloroform/hexane, but multiple spots were seen on TLC. The compound was then passed through a silicia gel column using a (65:35A) EtOAc/hexane. After three additional reprecipitation from chloroform/hexane and two recrystallizations from EtOAc/hexane, a melting point of 153.7°-155.2°C was obtained. PNMR of the compound showed s, 4.45 δ, 4H, benzylic methylenes; t, 6.99 δ, 4H, protons ortho to fluorine; 7.17 δ, 4H, Ar-H; t, t, 7.66, 7.75 δ, 2H, 2H, isoquinolyl H_5, H_8; m, 8.01 - 8.09 δ, 12H, Ar-H protons; s, 8.42 δ, 2H, isoquinolyl H_3. Mass spectrometry: $C_{46}H_{30}N_2O_4SF_2$, M = 744.19; found (FAB in 3-nitrobenzyl alcohol); m/z 745.196, $(M+H)^+$; 634, $(M-CH_3C_6H_4F)^+$; 526, $(M-2\ CH_2C_6H_4F)^+$; isotopic peaks were present in theoretical intensities.

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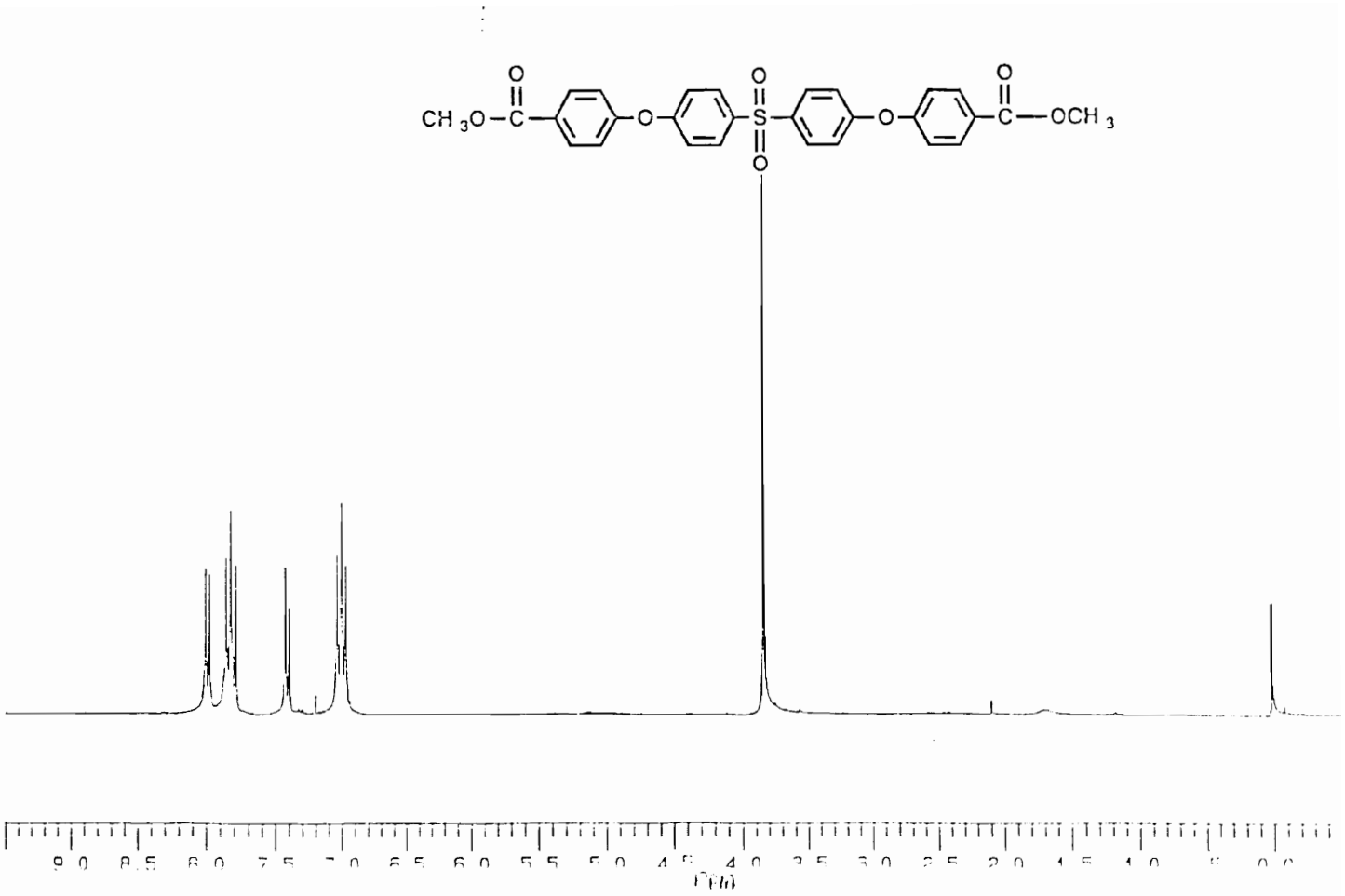
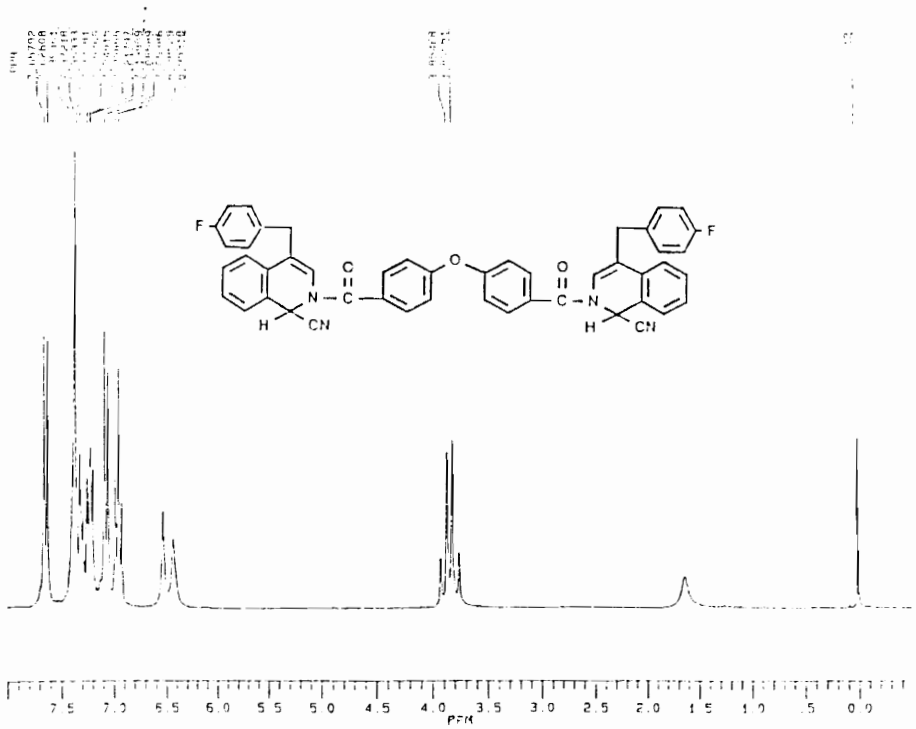
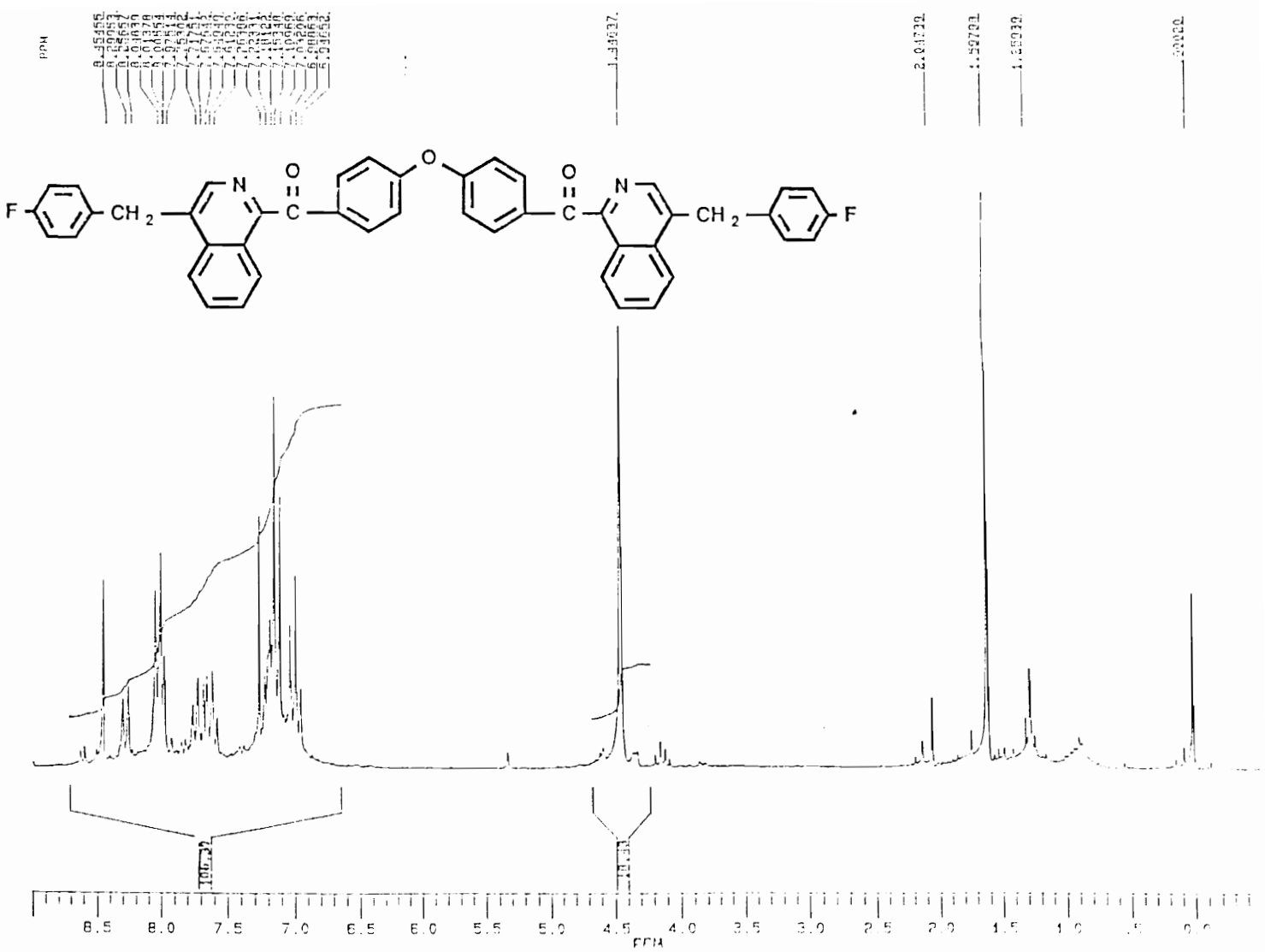
VIII. APPENDIX:



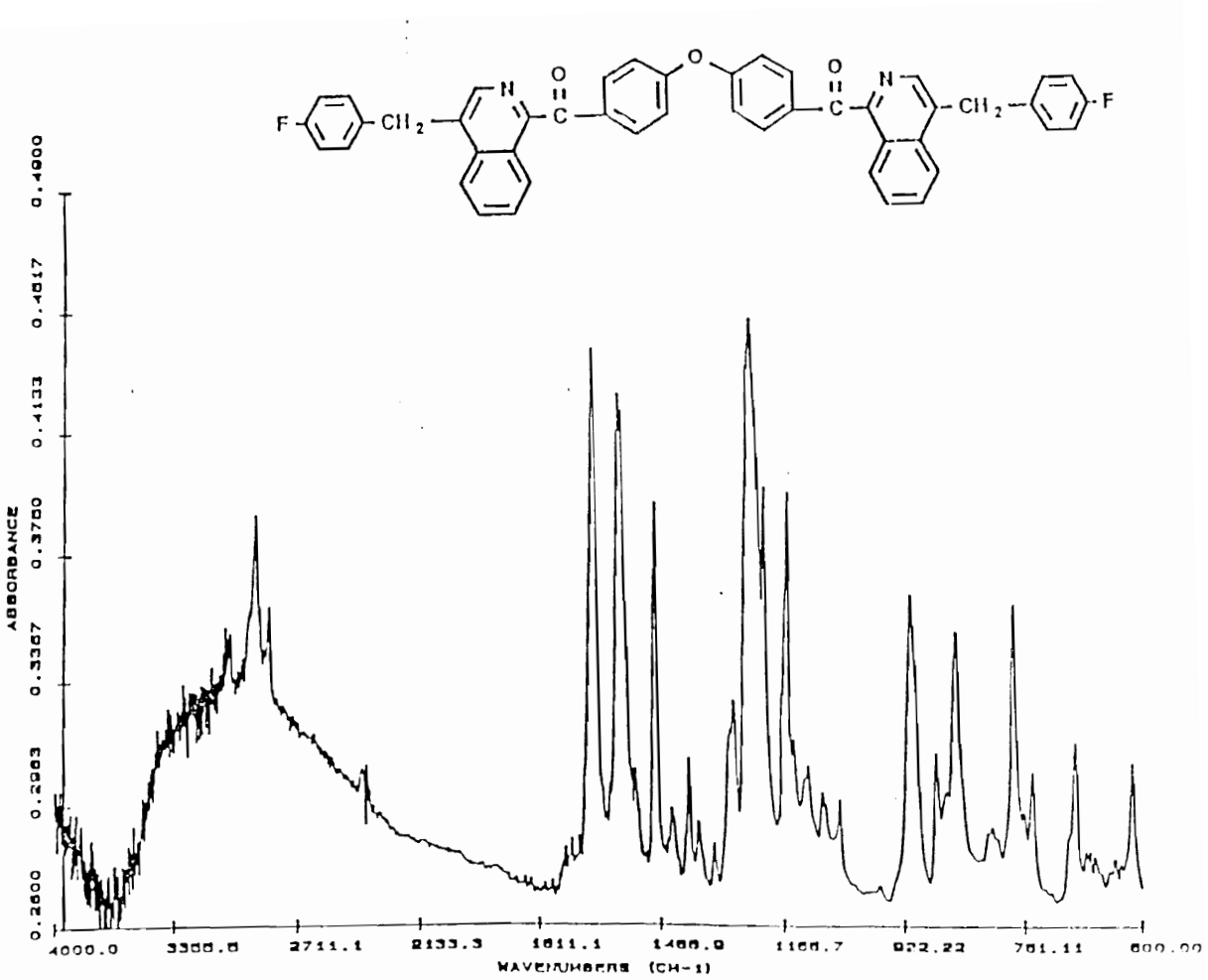
PNMR # 1: Dimethyl-4,4'-sulfonylbis(p-phenyleneoxy)dibenzoate, **22:**



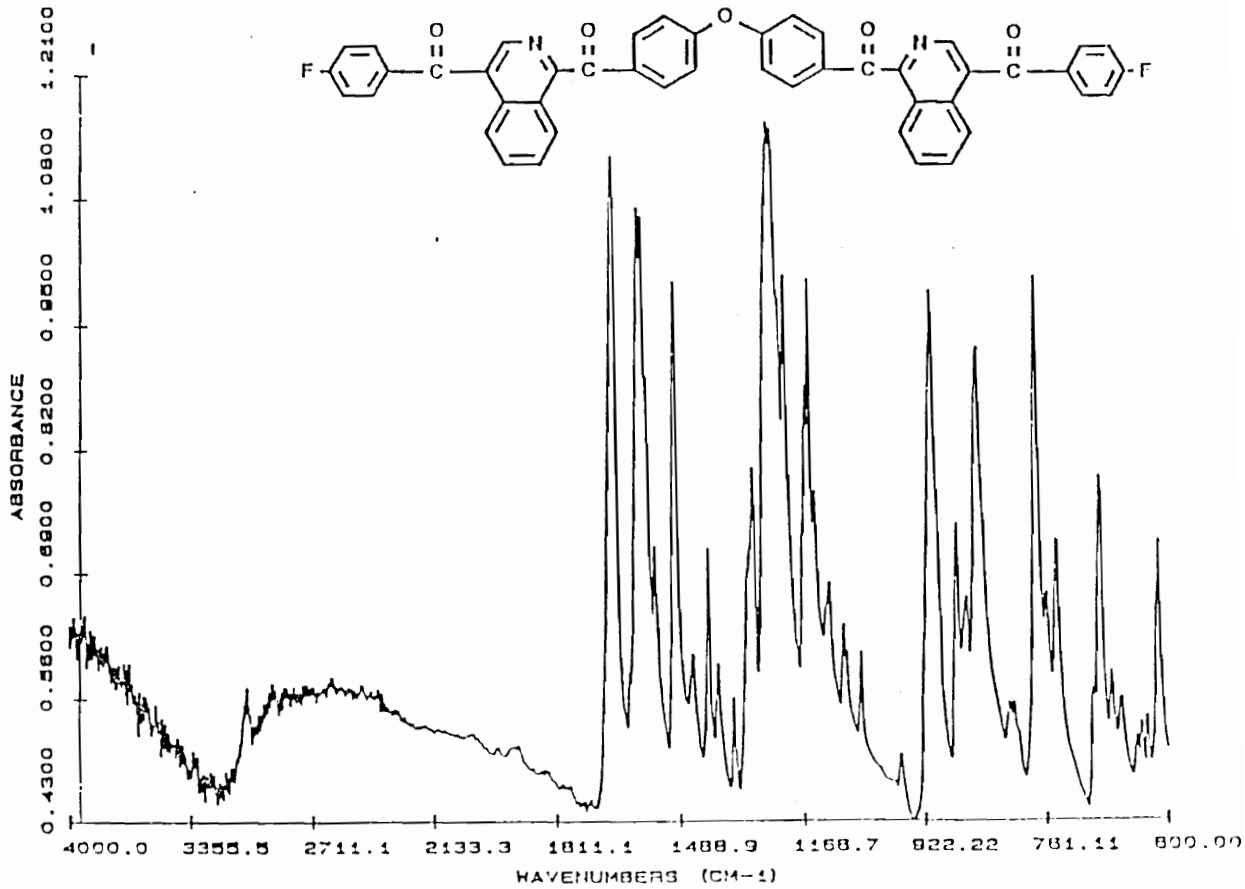
PNMR #2: N,N'-[4,4'-Oxybis(benzoyl)]-bis{(α,α'-p-fluorobenzyl)-1,2-dihydroisoquinaldonitrile, **27:**



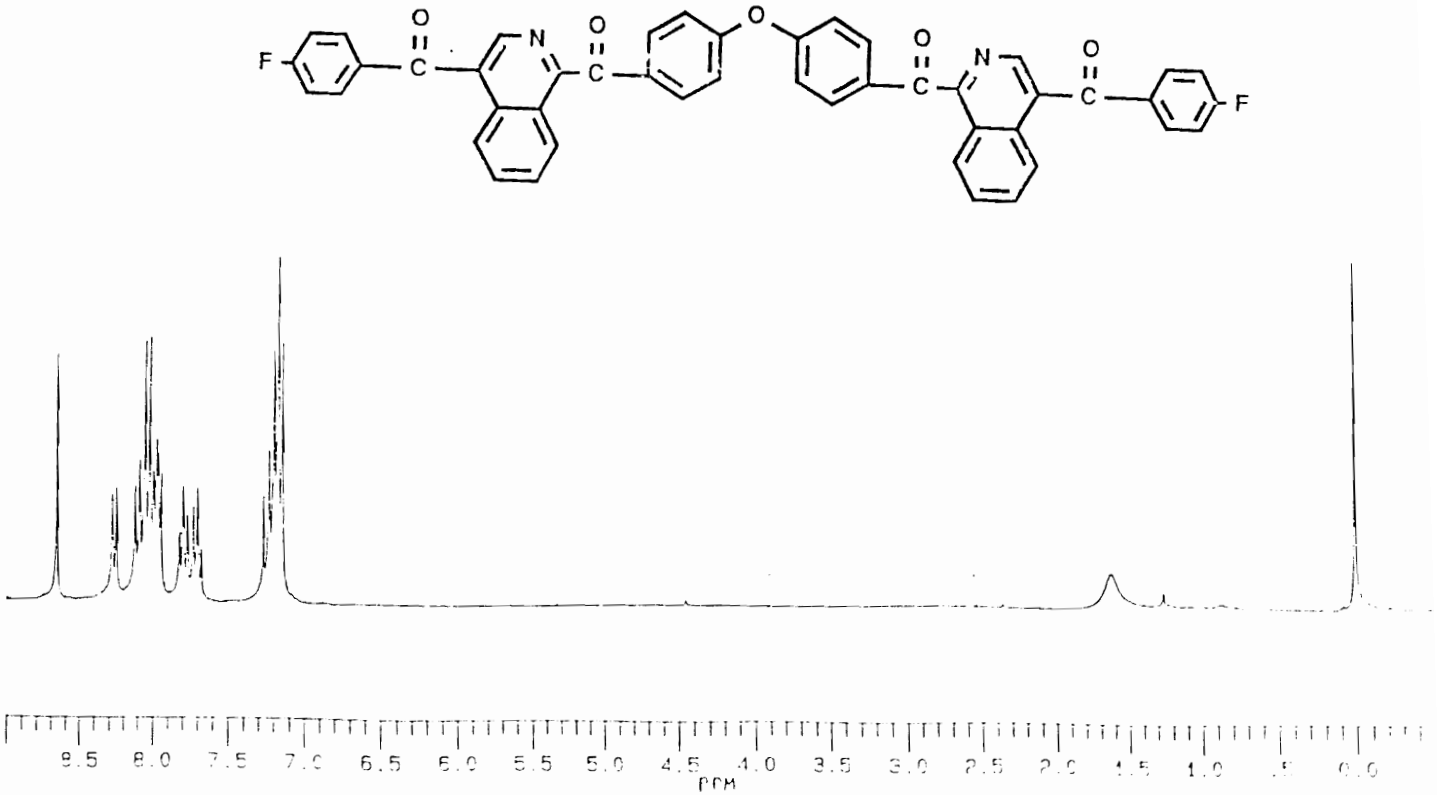
PNMR #3: N,N'-[4,4'-Oxybis(benzoyl)]-bis{(α,α'-p-fluorobenzyl)-isoquinolyl}, **30:**



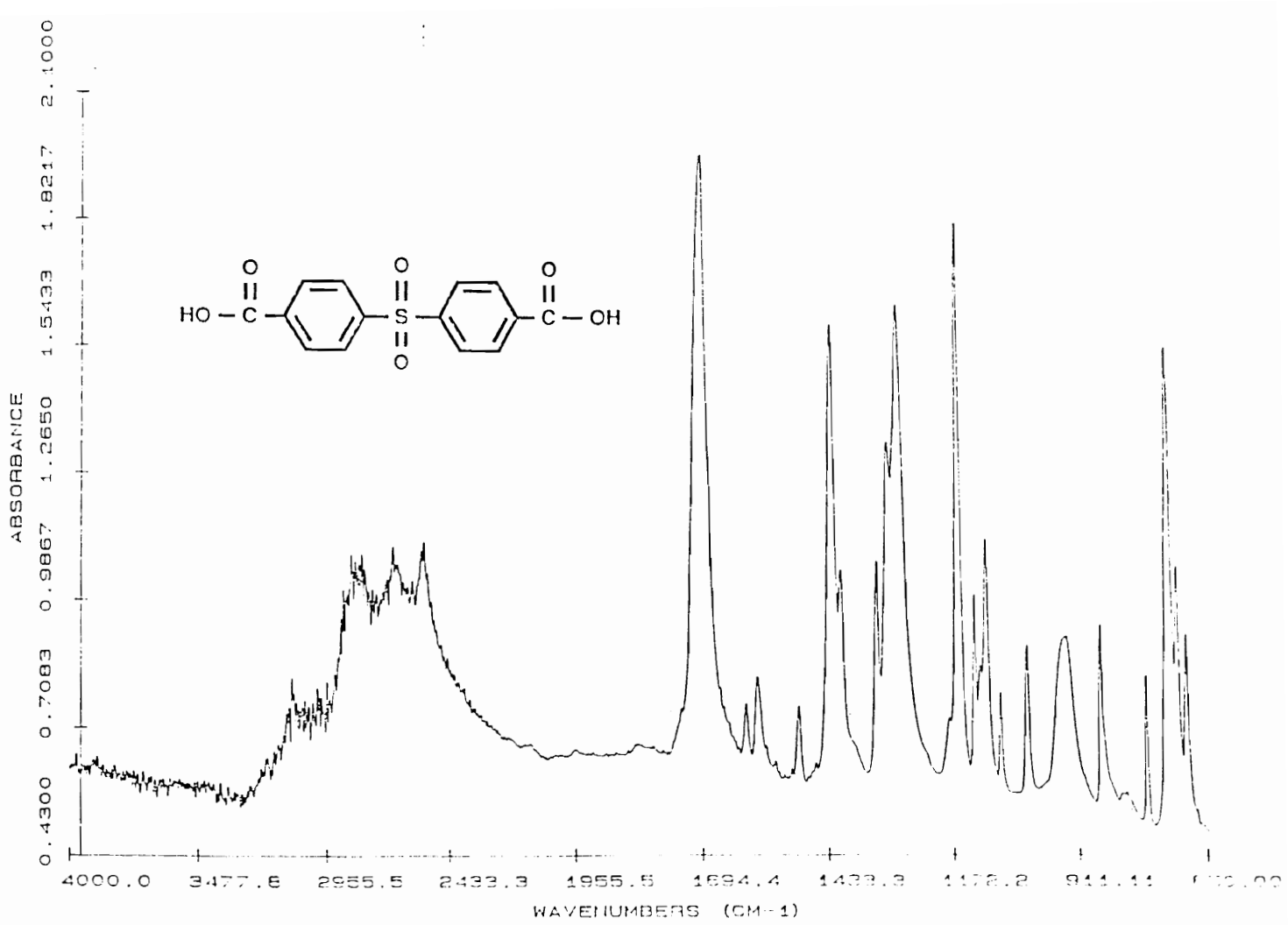
FTIR #1: N,N'-[4,4'-Oxybis(benzoyl)]-bis{(α,α'-p-fluorobenzyl)-isoquinolyl}, **30:**



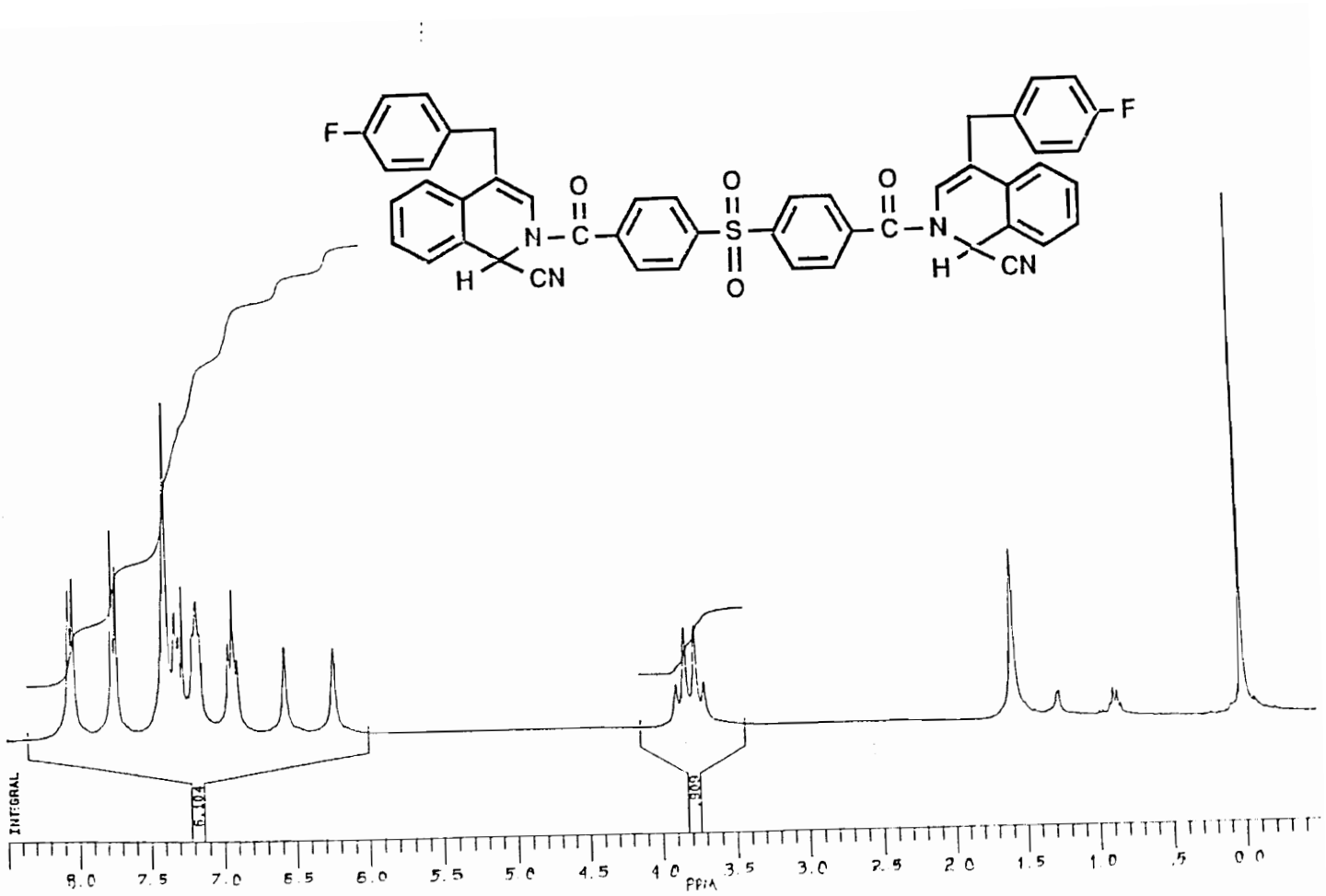
FTIR #2: N,N'-[4,4'-Oxybis(benzoyl)]-bis{(α,α'-p-fluorobenzoyl)-isoquinoline}, **31:**



PNMR #4: N,N'-[4,4'-Oxybis(benzoyl)]-bis{(α,α'-p-fluorobenzoyl)-isoquinoline}, **31:**



FTIR #3: 4,4'-Sulfonylbis(benzoic acid), **32:**



PNMR #5: N,N'-[4,4'-Sulfonylbis(benzoyl)]-bis{(α,α'-p-fluorobenzyl)-1,2-dihydroisoquinaldonitrile, **27:**

IX. VITA:

Roger Anthony Grisle was born on January 25, 1965, in Newton, MS to Laura Lee and the late Roger Lee Grisle. Following his high school graduation in May of 1983, he enrolled in the engineering program at Alcorn State University. In August of 1986, he changed his major from engineering to chemistry and later received a Bachelor of Science degree in May of 1988. The Fall of 1988 found him enrolled in the graduate chemistry program at Virginia Tech. One year later, the author married his sweetheart of four years Ms. Michelle Bradford. Then following a brief stint in physical chemistry, he entered Dr. Harry Gibson's synthetic polymer group. The author is currently a candidate for the degree of Master of Science in Chemistry at Virginia Tech. Upon completion of this degree the author and his lovely wife (Michelle) will reside in St. Paul, MN where the author is employed at 3M Masking and Packaging.