Synthesis of Heterocyclic Monomers via Reissert Chemistry

HARRY W. GIBSON, KIMBERLY K. BRUMFIELD, ROGER A. GRISLE,* CHRISTINE K. F. HERMANN†

Department of Chemistry, Virginia Polytechnic Institute & State University, Blacksburg, Virginia 24061-0212

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ABSTRACT: The chemistry of Reissert compounds has been used to synthesize activated difluorotetraketone monomers containing two coupled isoquinolyl moieties, linked at either the 1,1′- or 4,4′-positions. These monomers offer routes to novel families of poly(heteroarylene ether)s. New 4,4′-coupled bis(Reissert compound) **9** containing 4,4′-diketo moieties failed to afford the desired difluorotetraketo monomer upon attempted rearrangement. However, analogous bis(Reissert compound) **19** containing 4,4′-dibenzyl units did so, via aldehyde condensation, hydrolysis of the intermediate ester and oxidation of the four benzylic moieties to keto groups; thus the novel difluorotetraketone monomer **10** was prepared. Novel bis(Reissert compound)s **24**, **28**, and **35** were synthesized from diacid chlorides and 4-(*p*-fluorobenzyl)isoquinoline. Rearrangement of **24** to the diketone **29**, followed by oxidation of the 4-benzyl moieties resulted in difluorotetraketone monomer **30** containing a 1,1′-linked bisisoquinoline. The 1,1′-linked bis(isoquinolylfluorodiketo) monomer **38**, isomeric with **10**, was prepared from 4-(*p*-fluorobenzyl) Reissert compound **36** by condensation with terephthaldehyde, ester hydrolysis to diol **37**, and oxidation. In the course of this effort, a number of new isoquinoline Reissert compounds were synthesized as model systems. © 2010 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 48: 3856–3867, 2010

KEYWORDS: fluoroketone monomer; heteroatom-containing polymers; high performance polymers; isoquinoline; poly(arylene ether); poly(ether ketone)s; reissert compound

INTRODUCTION

Reissert Compounds

Reissert compounds, α-(acylamino)nitriles, are a very interesting class of compounds that were discovered in 1905 by Arnold Reissert.[1] They are formed by the formal addition of an acyl cyanide across a carbon–nitrogen double bond. Various nitrogen heterocycles, such as pyridine, quinoline, benzimidazole, and phenanthridine produce these derivatives.[2] The most studied cases are the isoquinoline Reissert compounds, **1** (Scheme 1).

Several methods have been developed for the preparation of Reissert compounds. These include use of aqueous media (Schotten-Baumann conditions: acid chloride and KCN),[1] single phase nonaqueous media [acid chloride with HCN in benzene[3]; trimethylsilyl cyanide (TMSCN) in methylene chloride or dimethylformamide[4]], and a two phase method (methylene chloride-water, acid chloride, KCN).[5]

Reissert compounds possess an acidic proton alpha to the cyano group that dictates the chemistry of these compounds. It can easily be abstracted to form the anion with a variety of base/solvent combinations.[2] Reissert anions undergo reactions with aldehydes via an intramolecular rearrangement driven by rearomatization to form esters **2**; initially this process was carried out at low temperature in ether-dioxane with phenyllithium as the base,[2,6(a,b)] but subsequently it was found that the process proceeds efficiently and much more conveniently at room temperature using sodium hydride and dimethylformamide (DMF).[6(c,d)] The esters **2** can be hydrolyzed by base to give secondary alcohols **3** (Scheme 1). On the other hand, using 50% sodium hydroxide/acetonitrile for the aldehyde reaction yields a mixture of the ester (**2**) and alcohol (**3**) in many cases.[7] However, it has been shown that the base/solvent combination and the reaction time and temperature dictate which product will be obtained. Shorter reaction times and lower temperatures favor formation of the ester.[8]

Exposure of the anion to an alkyl halide results in formation of the 1-alkyl derivative **4**, which upon basic hydrolysis forms the 1-alkylisoquinoline (**5**) through rearomatization (Scheme 2).[2,9,10] In the absence of an electrophile, an intramolecular rearrangement converts the Reissert anion into ketone **6** via a tricylic aziridine intermediate (Scheme 3).[2,9] Gibson found that the ability of the Reissert compound to undergo rearrangement versus alkylation depends on the nature of the acyl group.[10]

Nitrogen Containing Polymers

Nitrogen-containing polymers are a special class of materials that exhibit very useful features which can be attributed to (1) the basicity of the nitrogen atom(s), (2) hydrogen bonding 7 of N-H moieties, and (3) quaternization. Polyamides,

*Present address: 3M Corporation, 3M Center, Bldg. 230-1D-15, St. Paul, MN 55144-1000.
†Present address: Department of Chemistry and Physics, Box 6949, Radford University, Radford, VA 24142.
Correspondence to: H. W. Gibson (E-mail: hwgibson@vt.edu)
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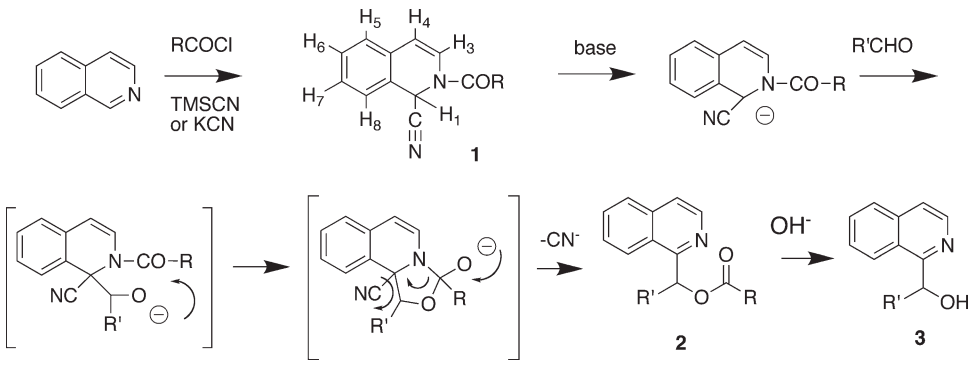


SCHEME 1 Formation of an isoquinoline Reissert compound **1** and reaction of its anion with an aldehyde to produce ester **2** and by hydrolysis alcohol **3**.

such as nylon-6,6 and Kelvar™, possess remarkable strength due to hydrogen bonding between the carbonyl groups and the *N*—H moieties and find applications in fibers and plastics.[11(a)] Aliphatic polyimides also possess valuable mechanical properties combined with dielectric features that make them useful in micro- and opto-electronics.[11(b,c)] Quaternary salt forms are highly polar, ionic polymers that are used as anion exchange resins, coatings, adhesives, ion conductors, and in water treatment and coagulation.[12] Aromatic nitrogen-containing polymers exhibit enhanced thermo-oxidative stability and good mechanical performance.[13] This class includes the (1) polyimides,[11(d)] (2) polyquinoxalines, (3) polyquinolines, (4) polybenzimidazoles, (5) polybenzothiazoles, and (6) polybenzoxazoles. At elevated temperatures, these polymers retain useful mechanical properties for long periods of time.

Poly(ether ketone)s

Poly(ether ketone)s are a class of polymers which have attracted considerable attention as a direct result of their extremely high thermal and chemical stabilities and good mechanical properties.[14] Poly(ether ketone)s are usually crystalline and therefore are resistant to solvent attack, making them ideal for aerospace applications. The only common room temperature solvent known for poly(ether ketone) or poly(ether ether ketone) is concentrated sulfuric acid. Typical poly(ether ketone)s have T_gs ranging from 100 to 200 °C and T_ms ranging from 300 to >400 °C. They exhibit excellent thermo-oxidative stability, withstanding processing temperature as high as 400 °C and can be used at temperatures >200 °C. In addition, they are stiff, tough, resist wear, and possess low flammability.

Bis(isoquinoline Reissert Compound)s from 4,4-Coupled Bis(isoquinolines)

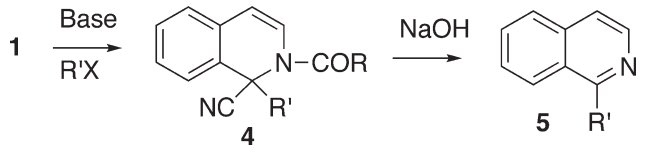
Minter and Re reported a facile synthesis of 4-substituted isoquinolines by reaction of boron-activated enamines derived from isoquinoline with aldehydes.[15] Guilani et al. applied this method to produce a family of novel 4,4′-coupled bis(isoquinoline)s in good yields by reacting isoquinoline with dialdehydes.[16] They also developed a method for the oxidation of the 4-methylene unit of the resultant bis(isoquinoline)s to the corresponding diketones.[16]

Bis(isoquinoline Reissert compound)s Derived from Diacid Chlorides

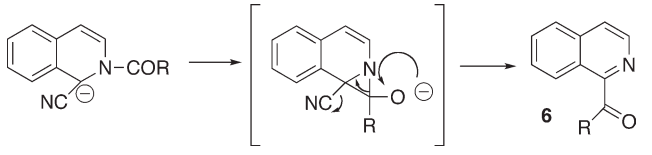
Earlier attempts toward the synthesis of bis(Reissert compound)s using diacid chlorides used the two-phase method, but generally resulted in less than 10% yields, the best yield obtained being 22%.[17] The low yields resulted from the hydrolysis of the diacid chlorides by water prior to the formation of the bis(Reissert compounds).

Gibson et al. prepared bis(Reissert compound)s using the single phase TMSCN method in yields ranging from 77 to 100%.[18,19] These bis(Reissert compound)s derived from monoacid chlorides with bisisoquinolines and diacid chlorides with monoisoquinolines constitute a novel class of AA monomers, which along with AB analogs were used in the step-growth syntheses of heterocyclic polymers[20] analogous to the processes used to make small molecules **3** and **4**, that is, through alkylation with dialdehydes or dihaloalkanes. Aliphatic acylaminonitriles, "aliphatic Reissert compounds,"[2(e)] were also used as monomers for preparation of poly(Reissert compound)s.[21] In related work bis(aminonitrile)s were arylated with difluorodiphenyl sulfone to afford novel poly(ketone ketone sulfone)s upon hydrolysis.[22]

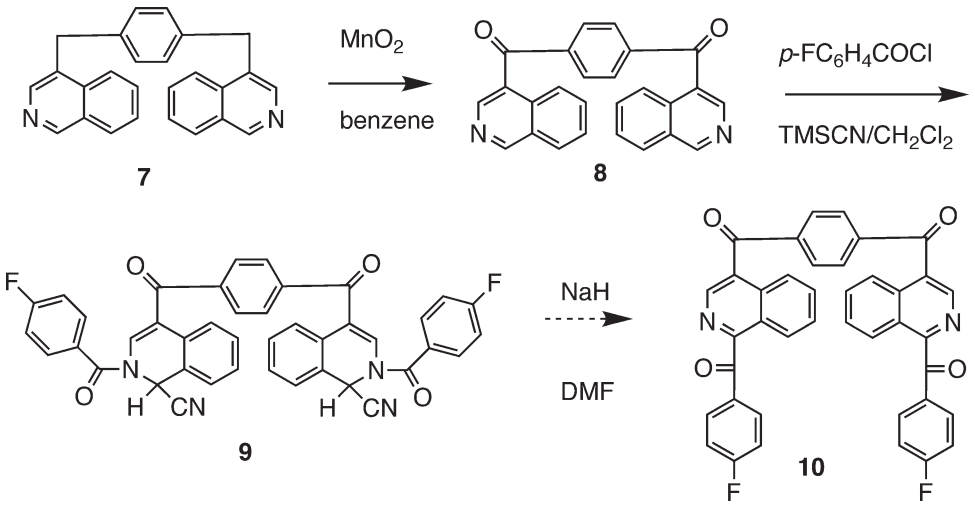
Using Reissert compound chemistry we also reported an isoquinoline functionalized as a monomer for incorporation into poly(arylene ether)s.[18(b)23] The monomer, l,4-bis(*p*-fluorobenzoyl)isoquinoline, was condensed with a number of bisphenols, producing a family of novel poly(1,4-isoquinolinediyl ether ketone)s. These materials were amorphous (T_gs ranging from 180 to 210 °C), in contrast to PEEK, and



SCHEME 2 Alkylation of an isoquinoline Reissert compound **1** and hydrolysis of the resultant **4** to the 1-alkylisoquinoline **5**.



SCHEME 3 Rearrangement of the anion of an isoquinoline Reissert compound **1** to a 1-acylisoquinoline **6**.



SCHEME 4 Conversion of bisisoquinoline **7** to diketo derivative **8** and thence to bis(Reissert compound) **9**, rearrangement of which was anticipated to form difluorotetraketo monomer **10**.

exhibited excellent thermal stability due to the presence of the heterocyclic moiety.

RESULTS AND DISCUSSION

The overall thrust of the research summarized here was to use Reissert chemistry to incorporate isoquinoline moieties into monomers for step-growth polymerizations, specifically activated fluoroketone monomers containing 1,1′- and 4,4′-coupled isoquinolines. Preliminary polymerization results are also reported.

Monomers from 4,4′-Coupled Bisisoquinolines

The primary target of this part of our studies was the tetraketone monomer **10** (Scheme 4). Isoquinoline was reacted with terephthaldehyde in the presence of sodium triethylborohydride to yield the known[16] *p*-bis(4-isoquinolyl)xylene (**7**) in 84% yield.

Tetraketo Monomer from 4,4′-Diketo Bisisoquinoline Reissert Compounds

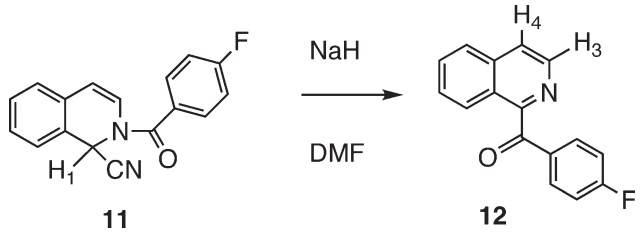
We first considered an approach in which the benzylic moieties of the bisisoquinoline are oxidized before other structural elaboration (Scheme 4). Bisisoquinoline **7**[16] was refluxed with MnO_2/benzene to afford the desired, previously unknown diketo product **8** in 72% yield.

The diketone **8** was reacted with *p*-fluorobenzoyl chloride in the presence of TMSCN and a catalytic amount of $AlCl_3$. The desired product, Reissert compound **9**, was obtained in 89% yield. Initially, there were some reservations regarding this reaction, since TMSCN is known to react with carbonyls to form cyanohydrins.[18(a),24] However, this reaction led to no formation of cyanohydrin or cyanohydrin ester.

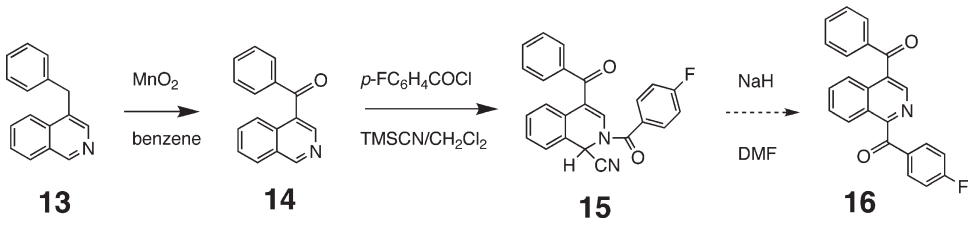
In the case of an *N*-(*p*-fluorobenzoyl) Reissert compound such as **9**, the anion might displace the activated fluoride of the *N*-acyl moiety, causing polymerization instead of rearrangement. This led to the investigation of the rearrangement of a model compound. 2-(*p*-Fluorobenzoyl)-1,2-dihydroisoquinaldonitrile (**11**)[25] was reacted with NaH/DMF to obtain the rearranged product **12** in 90% yield. Its ^{1}H NMR spectrum demonstrated complete loss of the H_1 proton and a shift of H_3 and H_4 protons downfield into the aromatic region, confirming that rearrangement instead of displacement of the fluoride occurred (Scheme 5).

With elimination of this possible side reaction, the final step in the synthesis of the tetraketone monomer **10** was rearrangement of the diketo bis(Reissert compound) **9** by reaction with NaH in DMF at room temperature (Scheme 4). The reaction afforded a black solid, of which less than 50% was soluble in $CDCl_3$; some black particles remained insoluble. Therefore, the rearrangement was attempted at 0 °C, but again the $CDCl_3$ insoluble black particles, more than 1/2 the sample, were also present. No well defined product was isolated, although it did appear from ^{1}H NMR that the desired product **10** was produced. In an attempt to optimize the reaction, model systems were examined.

The first model system investigated was one in which there was a carbonyl moiety at the 4-position (Scheme 6). 4-Benzylisoquinoline (**13**)[15] was refluxed in MnO_2/benzene, giving 4-benzoylisoquinoline (**14**). The ketone **14** was reacted with *p*-fluorobenzoyl chloride in the presence of TMSCN and a catalytic amount of $AlCl_3$. The new Reissert compound **15** was obtained in 94% yield. Attempted rearrangement of Reissert compound **15** to the corresponding new diketone **16** with NaH in DMF yielded only 33% of a crude product, whose TLC indicated the presence of seven spots, none presenting itself in great abundance. The ^{1}H NMR spectrum was complicated, confirming a mixture of products. When the solid was dissolved in $CDCl_3$, insoluble black particles were noticed as was the case of the rearrangement product of



SCHEME 5 Rearrangement of Reissert compound **11** to ketone **12**.



SCHEME 6 Preparation of Reissert compound **15** and its rearrangement to ketone **16**.

bis(Reissert compound) **9**. It was suspected that the formation of this side product(s) was occurring due to an electron transfer process brought about by the 4-carbonyl moiety.

This hypothesis led to the investigation of the rearrangement of 2-(*p*-fluorobenzoyl)-4-benzyl-1,2-dihydroisoquinaldonitrile (**17**). If an electron transfer process involving the carbonyl moiety was indeed occurring, then the benzylic analog might rearrange smoothly. 4-Benzylisoquinoline (**13**)[15] was reacted with *p*-fluorobenzoyl chloride via the two phase method using KCN as a cyanide source; new Reissert compound **17** was obtained in 83% yield (Scheme 7). Reissert compound **17** was then reacted with NaH in DMF, affording 79% of rearrangement product **18**.

The rearrangement of **17** resulted in the desired product and no black particles were observed; therefore, we concluded that the presence of the carbonyl group at the 4-position results in the formation of side products, possibly via an electron transfer process.

Tetraketo Monomer from 4,4′-Dibenzylic Bisisoquinoline Reissert Compounds

Therefore, to avoid this problem, the second approach to the target difluorotetraketone monomer **10** involved maintaining the benzylic moieties at the 4-position of the isoquinoline unit until later in the synthetic sequence and using the aldehyde condensation (Scheme 1) as a means of introducing the *p*-fluorobenzoyl moiety at the 1-position of the isoquinoline nuclei (Scheme 8). Bisisoquinoline **7**[16] was reacted with *o*-toluyl chloride and TMSCN with a catalytic amount of $AlCl_3$ at room temperature, leading to the desired new Reissert compound **19** in 93% yield. The *o*-toluyl Reissert compound was chosen because this substitution on the acyl group essentially eliminates base catalyzed rearrangement to the ketone.[10]

Reissert compound **19** was reacted with *p*-fluorobenzaldehyde using NaH/DMF, affording an 83% yield of new diester **20**. The diester **20** was refluxed in 50% sodium hydroxide and acetonitrile in the presence of a small amount of benzyltrimethylammonium chloride (phase transfer catalyst) to yield the diol **21** in 79% yield. Complete hydrolysis of the diester was confirmed by the FTIR spectrum. Reaction of Reissert compound **19** with *p*-flurobenzaldehyde in 50% NaOH/MeCN also produced diol **21** directly in 73% yield.

The alcohol **21** was refluxed in MnO_2/benzene for 12 h. The desired tetraketone **10** was isolated in 61% yield and confirmed by IR, NMR, and elemental analysis.

1,1′-Bisisoquinoline Monomers via Diacid Chloride-Based Reissert Compounds

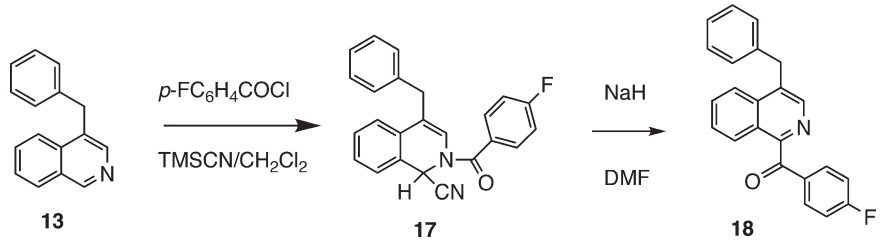
One way to obtain difunctional Reissert compounds is through the use of diacid chlorides to form a bis(Reissert compound) from a simple isoquinoline. We reported a number of such bis(Reissert compound) monomers previously.[18,19] One problem associated with some of the monomers prepared earlier was their rigidity. Recall that one of the requirements for step-growth polymerizations is accessible reacting groups. The more flexible the monomer, the more accessible the reacting groups because of better solubility of the product polymer. Therefore, one goal of this work was to synthesize flexible diacid chlorides from which flexible bis(Reissert compound) monomers could be made. Aromatic acids were chosen to maintain good thermal stability. In line with the overall objectives of this particular portion of the project, we used this approach to prepare activated difluoro monomers containing 1,1′-coupled isoquinolines resulting from rearrangement of the new bis(Reissert compound)s.

Oxybis(benzoyl) Bis(Reissert Compound)

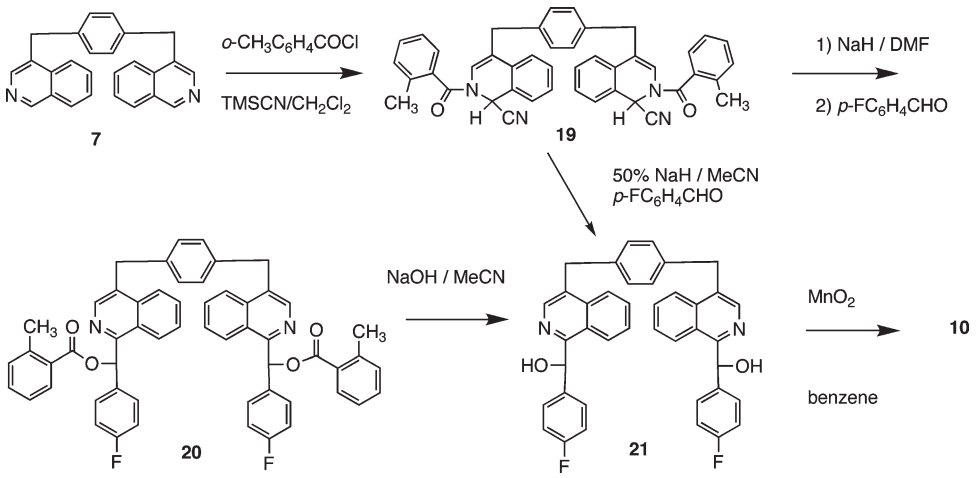
4,4′-Oxybis(benzoyl chloride) (**22**) was reacted with 4-(*p*-fluorobenzyl)isoquinoline (**23**) via the single phase method ($TMSCN/CH_2Cl_2$) producing new bis(Reissert compound) **24** in 67–70% yield (Scheme 9).

Sulfonylbis(benzoyl) Bis(Reissert Compound)

Commercially available 4,4′-sulfonylbis(methyl benzoate) (**25**) was converted to the corresponding known dibenzoic acid **26** by hydrolysis in 96% yield. The dibenzoic acid was then converted to the diacid chloride **27** using thionyl chloride. 4-(*p*-Fluorobenzyl)isoquinoline (**23**),[23] dibenzoyl



SCHEME 7 Preparation of Reissert compound **17** and successful rearrangement to ketone **18**.



SCHEME 8 Conversion of bisisoquinoline **7** to bis(Reissert compound) **19**, its condensation with *p*-flurobenzaldehyde to produce diester **20**, which was hydrolyzed to diol **21**, and oxidation of the latter to tetraketo monomer **10**.

chloride **27** and TMSCN were reacted in the preparation of the new bisReissert compound **28**, affording a 53–58% yield (Scheme 10).

Di- and Retra-Ketones from Oxybisbenzoyl(Reissert Compound) 27

Oxygen linked bis(Reissert compound) **24** was subjected to treatment with NaH in DMF at room temperature. From NMR it was quite clear that the reaction had not worked as the AB-pattern for the benzylic methylene protons was still present along with the upfield signals for H_1 and H_3; upon rearrangement with attendant aromatization the benzylic methylene protons become equivalent and the signals for H_1 and H_3 move downfield into the aromatic region. Therefore, the rearrangement of **24** was repeated using THF/NaH at reflux. The reaction was continuously monitored by proton NMR. After 2 days, the compound had completely rearranged, producing diketone **29** in 86–100% yield (Scheme 11).

The final step was oxidation of the remaining 4-benzylic methylenes using MnO_2/benzene[16] to produce the new difluorotetraketone monomer **30** in 57% yield.

Sulfonylbisbenzoyl Diketone from Bis(Reissert Compound) 28

The diketone **31** was similarly synthesized via rearrangement of bis(Reissert compound) **28**, which was dissolved in THF, treated with 2.2 eq. of NaH and refluxed for 2 days under nitrogen. The yield of diketone **31** was 76% (Scheme 12). Oxidation to the tetraketone has not been executed, but is expected to proceed without difficulty.

*Sulfonylbis(*p*-phenyleneoxy) Bis(Reissert Compound) 35*

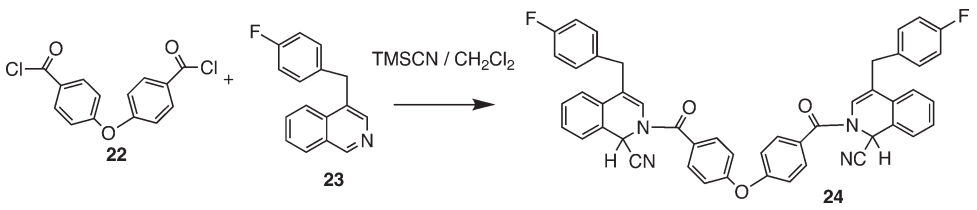
The synthesis of a novel sulfone-containing dicarboxyclic acid used a modification of a route reported by Idage et al.,[26] which involved reacting the dipotassium salt of 4-hydroxybenzoic acid with dichlorodiphenylsulfone, producing the diacid **33** (72%, Scheme 13), which was partially converted to the methyl ester for characterization. The diacid chloride **34** was prepared by refluxing the diacid in thionyl chloride. The bis(Reissert compound) **35** was prepared in 62% yield from diacid chloride **34** and 4-(*p*-fluorobenzyl)isoquinoline (**23**)[23] using the single-phase method (Scheme 13).

1,1′-Bisisoquinolines via Dialdehyde Condensation of Reissert Compounds

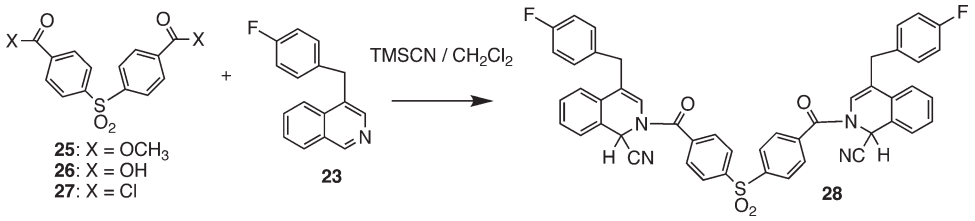
Another protocol for coupling isoquinoline nuclei at the 1-position is the reaction of isoquinoline Reissert compounds with dialdehydes, producing diester analogs of monoester **2** (Scheme 1). Here, this was verified by reaction of the new 4-(*p*-fluorobenzyl)isoquinoline Reissert compound **36**, which was prepared from isoquinoline **23** by the TMSCN method in quantitative yield (Scheme 14). Reissert compound **36** was condensed with terephthaldehyde using 50% NaOH, followed by subsequent basic hydrolysis of the intermediate diester, to afford the 1,1′-linked bisisoquinoline diol **37** in 70% yield. Treatment of diol **37** with MnO_2 in refluxing benzene produced the tetraketo difluoro monomer **38** (in 45% yield without exhaustive extraction of the metal oxide).

Preliminary Polymerization of Tetraketone Monomer 10

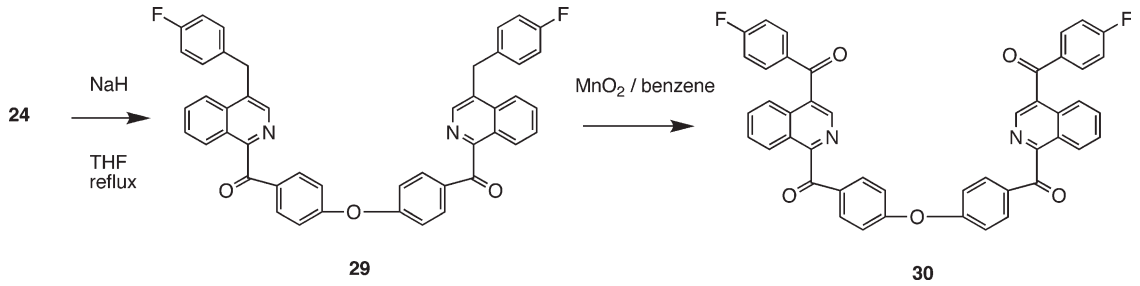
In a preliminary experiment, the tetraketone monomer **10** was reacted with bisphenol-A using NMP/toluene as a solvent/azeotroping agent and potassium carbonate as base (Scheme 15). The reaction mixture was precipitated into methanol, yielding polymer **39**, which possessed an intrinsic viscosity of 0.16 dL/g (25 °C, $CHCl_3$) and was stable up to 454 °C in air by TGA. GPC (polystyrene standards) indicated



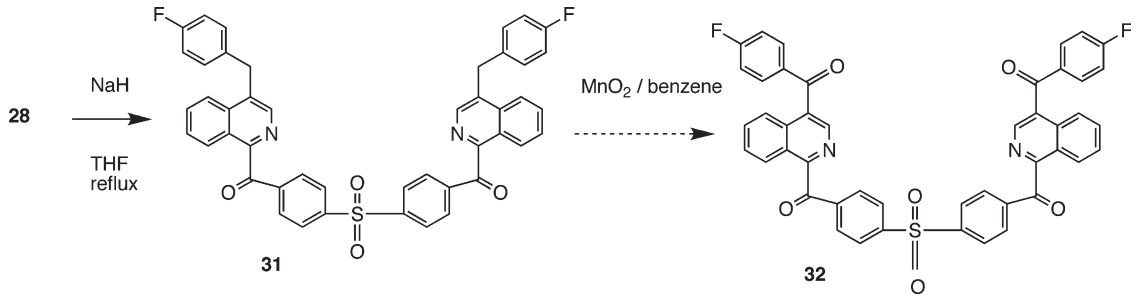
SCHEME 9 Synthesis of bis(Reissert compound) **24**.



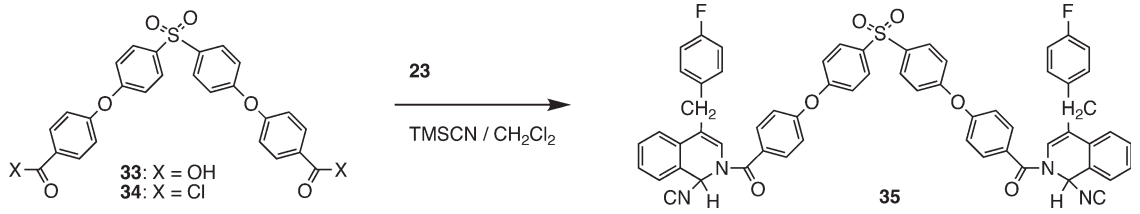
SCHEME 10 Synthesis of bis-(Reissert compound) **28**.



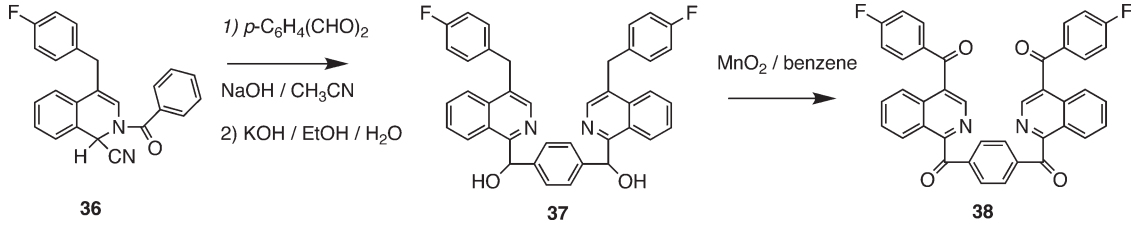
SCHEME 11 Rearrangement of bis(Reissert compound) **24** to diketone **29** and oxidation of the latter to tetraketone **30**.



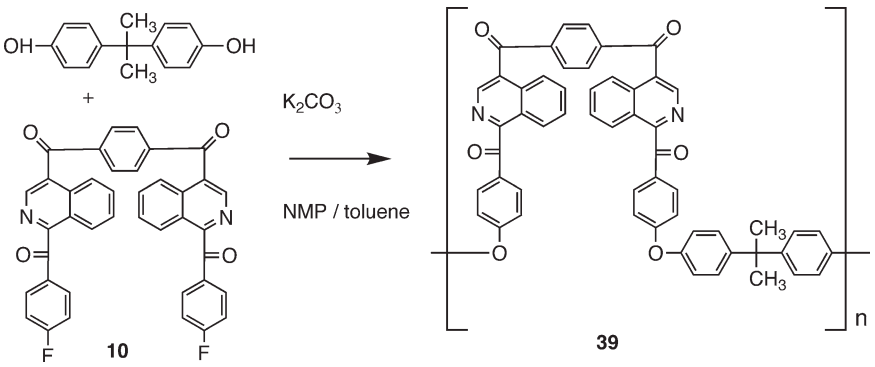
SCHEME 12 Rearrangement of bis(Reissert compound) **28** to diketone **31** and proposed oxidation of the latter to tetraketone **32**.



SCHEME 13 Synthesis of bis(Reissert compound) **35**.



SCHEME 14 Condensation of bis(Reissert compound) **36** with terephthaldehyde to produce a diester, which was hydrolyzed to diol **37**, and oxidation of the latter to tetraketo monomer **38**, an isomer of tetraketo monomer **10**.



SCHEME 15 Polymerization of activated difluorotetraketo monomer **10** with bis(phenol-A) to form poly(heteroarylene ether ketone) **39**.

M_n = 4.9 kDa and M_w = 7.8 kDa. DSC revealed T_g = 180 °C and no T_m. The viscosity and molecular weight of this polymer can no doubt be improved by optimization of the reaction conditions.

CONCLUSIONS

New bis(Reissert compound)s **9** and **19** were synthesized from 4,4′-bisisoquinolines in good yields. The former Reissert compound based on the 4,4′-diketo system failed to afford the desired difluorotetraketo monomer upon attempted rearrangement. However, the latter Reissert compound based on the 4,4′-dibenzyl structure did ultimately do so, via aldehyde condensation, hydrolysis of the intermediate ester and oxidation of four benzylic moieties to keto groups. In the way the novel 4,4′-linked bisisoquinolyl difluorotetraketone monomer **10** was prepared. In the course of this effort new model Reissert compounds **11**, **15,** and **17** were synthesized; investigation of their rearrangements indicated that the presence of a carbonyl at the 4-position results in the formation of a side product, possibly via electron transfer, that is detrimental.

Novel bis(Reissert compound)s **24**, **28**, and **35** were synthesized from diacid chlorides and 4-(*p*-fluorobenzyl)isoquinoline. Rearrangement of **24** to the diketone, followed by oxidation of the 4-benzyl moieties resulted in 1,1′-linked bisisoquinolyl difluorotetraketone **30**. Rearrangement of the model *N*-(*p*-fluorobenzoyl) Reissert compound **11** rather than displacement of the fluoride, that is, polymerization, takes place upon treatment with NaH/DMF.

4-(*p*-Fluorobenzyl) Reissert compound **36** was condensed with terephthaldehyde and the resultant ester hydrolyzed to form diol **37**, which in turn was oxidized to the 1,1′-linked bisisoquinolyl difluorotetraketo monomer **38**, which is an isomer of **10**.

EXPERIMENTAL

General

Dichloromethane was obtained from Fisher Scientific and dried over molecular sieves before use. *N*,*N*-dimethylformamide (DMF) and *l*-methyl-2-pyrrolidinone (NMP) were distilled from calcium hydride and tetrahydrofuran (THF) from sodium/benzophenone prior to use. DMSO (*N*,*N*-dimethylsulfoxide) was obtained from Aldrich and was distilled with calcium carbonate prior to use. Sodium hydride was used as a 60% dispersion in mineral oil as obtained from Aldrich Chemicals. All other solvents were used as received from the vendor. Melting points were determined in a Mel-temp II melting point apparatus and are corrected. All proton NMR spectra were recorded on a Bruker 270 MHz instrument using tetramethylsilane as an internal standard; the following abbreviations are used: s (singlet), d (doublet), m (multiplet), t (triplet), ArH (aromatic hydrogen). FTIR spectra were recorded on a Nicolet MX-I with KBr pellets or films on salt plates. Thermogravimetric analysis was done on a Perkin–Elmer 7700 Thermal Analysis System. Differential scanning calorimetry was performed on a DuPont 2100 Dual-Sample at 10 °C/min. Gel permeation chromatography (GPC) was carried out in THF using a Waters 150-C equipped with RI and viscometric detectors; this instrument provided absolute molecular weights, polydispersity index, and Mark-Houwink constants. Mass spectrometry was performed by the Midwest Center for Mass Spectroscopy, Lincoln, Nebraska, with the exception of the ms of compound **18**, which was acquired on an in-house Agilent 6220 Accurate Mass TOF LC/MS Spectrometer. Intrinsic viscosities were measured in a Fisher Ubelohde Scientic Viscometer 7300. Elemental analyses were performed by Atlantic Microlab (Norcoss, GA).

α,α′-Bis(4-isoquinolyl)-*p*-xylene (7)

Isoquinoline (10.33 g, 80 mmol) was dissolved in 150 mL of dry THF. Sodium triethylborohydride was added gradually in four portions of 20 mL of 1.0 M solution (80 mL, 80 mmol). The reddish–brown solution was allowed to stir at room temperature for 30 min under N_2, after which terephthaldehyde, 5.10 g (38 mmol), was added in one portion. The mixture was cooled to 0 °C and 160 mL of 0.5 N NaOH were added. Ten minutes later, 80 mL of 30% H_2O_2 were added gradually. Stirring was continued for 20 h, at the end of which time the precipitate was collected and dried: 11.50 g (84%); reported 74%.[16] After two recrystallizations from ethanol/water, the pure product was obtained, mp 190.4–190.7 °C (reported[16] 186.5–187.5 °C).

^{1}H NMR (270 MHz, $CDCl_3$): δ 4.33, s, ppm, 4H, CH_2; 7.10, s, 4H, ArH; 7.5–8.0, m, 8H, H_{5-8}; 8.38, s, 2H, H_3; 9.15, s, 2H, H_1.

p-[Bis(4-isoquinolyl)carbonyl]benzene (8)

A mixture of 7.00 g (19 mmol) of bisisoquinoline **7**, 210 mL of benzene and 70 g of MnO_2 was allowed to reflux for 2

days with a Dean-Stark trap. The oxides were filtered through Celite and the Celite was washed with chloroform. The MnO_2 was Soxhlet extracted for 5 days with $CHCl_3$. The combined extract was dried over $MgSO_4$. The solvent was removed, yielding a golden solid, 4.72 g (72%), which was recrystallized three times from toluene:hexanes, mp 248.2–249.2 °C. FTIR (KBr): 1664.5 cm^{-1} (C=O).

^{1}H NMR (270 MHz, $CDCl_3$): δ 7.70–7.85, m, 4H, H_6 and H_7; 8.00, s, 4H, phenyl; 8.10, d ($J = 8$), 2H, H_8; 8.25, d ($J = 8$), 2H, H_5; 8.69, s, 2H, H_3; 9.42 ppm, s, 2H, H_1. EI MS: 388 (M^+). ELEM. ANAL., Calcd. for $C_{26}H_{16}N_2O_2 \bullet 1/3\ C_7H_8$: C 81.19, H 4.49, N 6.68; found: C 80.77, H 4.47, N 6.68.

p-Bis[4-{1-cyano-2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinolyl}carbonyl]benzene (9)

Diketo bisisoquinoline **8** (4.00 g, 11.1 mmol) was dissolved in 200 mL of DMF with 3.87 g (24.4 mmol) of *p*-fluorobenzoyl chloride. After 30 min of stirring, 2.42 g (24.4 mmol) of TMSCN were added, along with a catalytic amount of $AlCl_3$. The flask was stoppered and stirred for 4 days. The solution was poured into water (500 mL) and filtered: 7.62 g (89%). The crude product was purified by column chromatography (silica gel, 40:60 hexanes/ethyl acetate) and recrystallized from chloroform:hexanes, mp 249.0–249.5 °C. FTIR (KBr); 1677.2 cm^{-1}, 1651.1 cm^{-1} (C=O).

^{1}H NMR (270 MHz, $CDCl_3$); δ 6.47, s, 2H, H_1; 7.16–7.18, m, 8H, *o* to F and H_5 and H_8; 7.26, s, 4H, ArH; 7.68–7.78, m, 4H, H_6 and H_7; 7.82, s, lH, H_3. EI MS: 686 (M^+). ELEM. ANAL., Calcd. for $C_{42}H_{24}F_2N_4O_4$: 73.46, 3.52, 8.16; found: C 73.20, H 3.65, N 8.16.

Attempted Synthesis of *p*-Bis{4-[1-(*p*-fluorobenzoyl) isoquinoly]carbonyl}benzene (10) from Diketo Reissert Compound 9

To a stirring solution of 0.50 g (0.73 mmol) of the diketo Reissert compound **9** in 20 mL of DMF at 0 °C NaH (0.07 g of 60% dispersion, 2 mmol) was added. The reaction mixture was stirred for 2 days at 0 °C, poured onto ice, filtered, and dried: 0.30 (68%) of dark solid. FTIR (KBr): 1670.4 cm^{-1}(broad). The ^{1}H NMR (270 MHz, $CDCl_3$) spectrum was complicated due to side products resulting from the presence of the carbonyl group, but did indicate the presence of some desired product **10**. However, no pure compound could be isolated by either recrystallization or column chromatography.

1-(*p*-Fluorobenzoyl)isoquinoline (12)

To a stirring solution of 1.00 g of 2-(*p*-fluorobenzoyl)-1,2-dihydroisoquinaldonitrile (**11**)[25] in 40 mL of DMF at 25 °C, NaH (0.17 g of 60% dispersion in oil, 4.3 mmol) was added. The reaction mixture was stirred for 36 h, poured onto ice, and extracted with CH_2Cl_2: 1.63 g (90%) of viscous brown oil, which was purified by column chromatography (silica gel, 60:40 hexanes:ethyl acetate) and recrystallized twice from ethyl acetate:hexanes, yellow solid, mp 91.0–92.2 °C. FTIR (KBr): 1664.1 cm^{-1} (C=O).

^{1}H NMR (270 MHz, $CDCl_3$): δ 7.12–7.18, m, 2H, *o* to F; 7.61–8.04, m, 6H, ArH; 8.22, d ($J = 8$), 1H, H_3; 8.59, d ($J = 8$), 1H, H_4. ELEM. ANAL., Calcd. for $C_{16}H_{10}NOF$: C 76.49, H 4.01, N 5.57; found C 76.38, H 4.00, N 5.53.

4-Benzoylisoquinoline (14)

4-Benzylisoquinoline (**13**),[15] 5.00 g (22.8 mmol), 150 mL of benzene, and 50 g of MnO_2 were allowed to reflux for 2 days using a Dean-Stark trap. The mixture was filtered through Celite and the Celite was washed with chloroform. The MnO_2 was Soxhlet extracted for 4 days with $CHCl_3$. The combined extract was dried over $MgSO_4$. The solvent was removed, producing a viscous yellow oil, 3.54 g (66%), which was triturated with ethanol and recrystallized three times from ethyl acetate:hexanes and twice from toluene:-hexanes, mp 77.4–78.7 °C. FTIR (KBr): 1657.6 cm^{-1} (C=O).

^{1}H NMR (270 MHz, $CDCl_3$): δ 7.48–7.53, m, 2H, *m* to C=O; 7.62–7.81, m, 3H, H_6,H_7 and *p* to C=O; 7.87–7.91, m, 2H, *o* to C=O; 8.09, d ($J = 8$), 1H, H_5; 8.17, d ($J = 8$), H_8; 8.65, s, 1H, H_3; 9.41, s, 1H, H_1. ELEM. ANAL., Calcd. for $C_{16}H_{11}NO$: C 82.38, H 4.75, N 6.00; found: C 82.37, H 4.81, N 5.93.

2-(*p*-Fluorobenzoyl)-4-benzoyl-l,2-dihydroisoquinaldonitrile (15)

Ketone **14** (1.00 g, 4.3 mmol) was dissolved in 20 mL of CH_2Cl_2, after which 0.745 g (4.7 mmol) of *p*-fluorobenzoyl chloride was added. After 30 min of stirring, 0.466 g (4.7 mmol) of TMSCN was added along with a catalytic amount of $AlCl_3$. The reaction was stoppered and stirred for 7 days. The solution was poured into 500 mL of water, stirred overnight, and filtered: 1.40 g (85%). After three recrystallizations from toluene:hexanes, the pure product was obtained, mp 170.4–171.7 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 8.49, s, lH, H_3; 7.13, d ($J = 8$), 1H, H_5; 7.38–7.46, m, 5H, ArH; 7.54, d ($J = 8$), 1H, H_8; 7.64–7.80, m, 6H, ArH. ELEM. ANAL., Calcd. for $C_{24}H_{15}N_2O_2F$: C 75.38, H 3.95, N 7.33; found: C 75.38, H 3.96, N 7.33.

Attempted Synthesis of 4-Benzoyl-l-(*p*-fluorobenzoyl) isoquinoline (16) by Rearrangement of Bis(Reissert Compound) 15

To a stirring solution of 0.50 g (1.3 mmol) of the Reissert compound **15** in 20 mL DMF at 25 °C NaH (0.07 g of 60% dispersion, 2 mmol) was added. The reaction mixture was stoppered and stirred for 1 day, poured onto ice, filtered and dried: 0.15 g (33%). TLC indicated that there were at least seven components in the product mixture. The ^{1}H NMR spectrum was complicated due to side products resulting from the presence of the carbonyl group.

2-(*p*-Fluorobenzoyl)-4-benzyl-l,2-dihydroisoquinaldonitrile (17)

4-Benzylisoquinoline (**13**)[15] (5.00 g, 22.8 mmol) was dissolved in 50 mL of CH_2Cl_2. Then, 4.45 g (68.4 mmol) of KCN dissolved in 11 mL of water were added. The resulting mixture was stirred for 15 min prior to the dropwise addition of 7.23 g (45.6 mmol) of *p*-fluorobenzoyl chloride over 2 h. The mixture was stirred for 20 h, after which 100 mL of water were added. The layers were separated. The organic layer was washed with water 3×, 10% HCI 3×, H_2O 3×, 10% $NaHCO_3$ 3×, and water 3×. The solution was dried

over $NaSO_4$ for 1 day and concentrated: 6.96 g (83%). The crude product was purified by column chromatography (silica gel, 90:10 hexanes:ethyl acetate) and recrystallized from hexanes:ethyl acetate, mp 148.3–149.3 °C. FTIR (KBr): 1664.1 cm^{-1} (C=O).

^1H NMR (270 MHz, $CDC1_3$): δ 3.82, AB q (J = 14), 2H, $ArCH_2$; 6.37, s, lH, H_3; 6.52, s, 1H, H_1; m, 7.08–7.63, 11H, ArH; m, 8.09–8.15, 2H, α to CO. ELEM. ANAL., Calcd. for $C_{24}H_{17}N_2OF$: C 78.25, H 4.65, N 7.60; found: C 77.99, H 4.71, N 7.53.

1-(*p*-Fluorobenzoyl)-4-benzylisoquinoline (18)

To a stirring solution of 0.63 g (1.7 mmol) of the 4-benzylisoquinoline Reissert compound **17** in 40 mL of DMF at 25 °C, NaH (0.08 g of 60% dispersion, 2 mmol) was added. The mixture was stirred for 2 days, poured onto ice, and filtered: 0.46 g (79%). The crude product was purified by column chromatography (silica gel, 60:40 hexanes:ethyl acetate) and recrystallized from ethyl acetate:hexanes, mp 135.0–136.3 °C. FTIR (KBr): 1723.0 cm^{-1} (C=O).

$^l H$ NMR (270 MHz, $CDCl_3$): δ 4.47, s, 2H, $ArCH_2$; 7.07–7.42, m, 7H, *o* to F and ArH; 7.76–7.79, m, 2H, *m* to F; 8.03–8.39, m, 4H, $H_{5–8}$; 8.53, s, 1H, H_3. EI MS: *m/z* 341 (M^+), 340 $(M-H)^+$. HR ESI MS: *m/z* 364.1127 $(M + Na)^+$, Calcd. for $C_{23}H_{16}FNO$ + Na: 364.1108, error 5.2 ppm; 342.1299 $(M + H)^+$, Calcd. for $C_{23}H_{16}FNO$ + H: 342.1289, error 2.9 ppm.

α,α′-Bis[1-cyano-2-(*o*-toluyl)-1,2-dihydroisoquinolin-4-yl]-*p*-xylene (19)

Bisisoquinoline **7** (8.00 g, 22.2 mmol) was dissolved in 150 mL of DMF, after which 7.55 g (48.8 mmol) of *o*-toluyl chloride were added. After 30 min of stirring, 4.84 g (43.3 mmol) of TMSCN were added, along with a catalytic amount of $AlCl_3$. The flask was stoppered and stirred for 5 days. The solution was poured into water and the precipitate was filtered: l8.6 g (93%). After three recrystallizations from chloroform:hexanes, the pure product was obtained, mp 220.5–221.5 °C. FTIR (KBr): 1672 cm^{-1} (C=O).

^1H NMR (270 MHz, $CDCl_3$): δ 2.27, s, 6H, CH_3; 3.60, AB q (J = 14), 4H, $ArCH_2$; 6.11, s, lH, H_3; 6.76, s, lH, H_1; 7.04–7.32, m, 22H, Ar. ELEM. ANAL., Calcd. for $C_{44}H_{34}N_4O_2$: C 81.21, H 5.27, N 8.61; found C: 81.19, H: 5.33, N: 8.56.

α,α′-Bis[4-{1-(*o*-Toluyloxy-*p*-fluorobenzyl)isoquinolyl}]-*p*-xylene (20)

To a stirring solution of 8.00 g (12 mmol) of Reissert compound **19** and 2.88 g (0.23 mmol) of *p*-fluorobenzaldehyde in 150 mL of DMF, NaH (1.06 g of 60% dispersion in oil, 26 mmol) was added at 25 °C. The reaction mixture was stirred for 2 days, poured into water, and filtered: 8.38 g (86%). The crude product was purified by column chromatography (silica gel, 50:50 hexanes/ethyl acetate) and recrystallized once from ethyl acetate:hexanes, mp 145.6–146.7 °C. FTIR (KBR): 1714 cm^{-1} (C=O).

^1H NMR (270 MHz, $CDCl_3$): δ 2.58, s, 6H, CH_3; 4.31, s, 4H, $ArCH_2$; 7.02, t (J = 10), 4H, *o* to F; 7.09, s, 4H; 7.2–7.7, m, 14H; 7.77, s, 2H, methine; 7.95, d (J = 8), 2H; 8.10, d (J = 8), 2H; 8.31, d (J = 8), 2H; 8.39, s, 2H, H_3. ELEM. ANAL., calcd for $C_{56}H_{42}F_2N_2O_4 \bullet 1/5\ (C_4H_8O_2)$: C 79.11, H 5.07, N 3.25; found: C 78.72, H 4.88, N 3.23.

α,α′-Bis[4-{1-α-hydroxy-*p*-fluorobenzyl)isoquinolyl}]-*p*-xylene (21)

Bisisoquinoline Reissert compound **19**, 10.00 g (15.4 mmol), 4.21 g (33.9 mmol) of *p*-fluorobenzaldehyde, and 1.07 g of benzyltrimethylammonium chloride were dissolved in 113 mL of acetonitrile. After 30 min of stirring, 14 mL of 50% NaOH were added. The reaction was allowed to stir for 6 h with heating in an oil bath to reflux the acetonitrile. The mixture was diluted with 1 L of water. The product was extracted with $CHCl_3$ and washed 3× with water, dried over Na_2SO_4 and concentrated by evaporation: 8.84 g; FTIR: ester C=O at 1715.6 cm^{-1} and no OH group, signifying incomplete hydrolysis. The crude product was dissolved in 200 mL ethanol, 100 mL H_2O, and 40 g (0.71 mol) of KOH were added. After refluxing overnight, the product was isolated by precipitation into water: 6.45 g (73%); recrystallized from CH_2Cl_2:hexane, colorless crystals, mp 174.2–175.5 °C. FTIR (KBr): 3378 cm^{-1} (OH).

^1H NMR (270 MHz, $CDCl_3$): δ 4.37, s, 4H, $ArCH_2$; 6.21, br, 2H, OH; 6.32, br, 2H, methine; 6.96, t (J = 9), 4H, *o* to fluorine; 7.14, s, 4H, ArH; 7.29, m, 4H, *m* to fluorine; 7.46, t (J = 8), 2H, H_6; 7.60, t (J = 8), 2H, H_7; 7.92, m, 4H, H_5, and H_8; 8.37, s, 2H, H_3. ELEM. ANAL., Calcd. for $C_{40}H_{30}F_2N_2O_2 \bullet 1.5\ H_2O$: C 75.57, H 5.23, N 4.41; found C: 75.94, H: 4.86, N: 4.52. Analogous hydrolysis of diester **20** afforded the diol **21** in 79% yield.

p-Bis[4-{1-(*p*-fluorobenzoyl)isoquinoly}carbonyl] benzene (10)

A mixture of 12.76 g (16 mmol) of diol **21**, 300 mL benzene, and 100 g MnO_2 was allowed to reflux for 12 h using a Dean-Stark trap. The oxides were filtered through Celite and washed with CH_2Cl_2 in a Soxhlet extractor for 5 days. The combined extract was dried over $MgSO_4$. The solvent was removed: yellow solid, 6.13 g (61%). The crude product was recrystallized 3× from ethanol, light yellow crystals, mp 228.2–230.2 °C. FTIR (KBR): 1664.1 cm^{-1}, (C=O); 1598.7 cm^{-1} (C=C).

$^l H$ NMR (270 MHz, $CDCl_3$): δ 7.18, t (J = 9), 4H, *o* to F; 7.72, t (J = 8), 2H, H_6; 7.84, t (J = 8), 2H, H_7: 8.03, m, 8H, phenyl and *m* to F; 8.24, m, 4H, H_5 and H_8; 8.71, s, 2H, H_3. ELEM. ANAL., Calcd. for $C_{40}H_{22}F_2N_2O_4 \bullet 1/4\ H_2O$: C 75.17, H 3.55, N 4.38; found C 75.28, H 3.49, N 4.37.

N,N′-(4,4′-Oxybisbenzoyl)-bis{4,4′-(*p*-fluorobenzyl)-1,2-dihydroisoquinaldonitrile} (24)

A solution of 6.55 g (27.6 mmol) of 4-(*p*-fluorobenzyl)isoquinoline, (**23**),[23] and 3.01 g (10.5 mmol) of 4,4′-oxybis(benzoyl chloride) (**22**, made by treatment of the diacid with $SOCl_2$) in (dry) CH_2Cl_2 was stirred under N_2 for 20 min before 3.01 mL (22.6 mmol) 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 2 h of stirring, the organic phase was

washed in a separatory funnel: 3× water, 3 × 10% HCl, 3 × 10% $NaHCO_3$, 3 × 5% NaOH. After drying over Na_2SO_4, the solvent was removed via rotary evaporation and the compound dried under vacuum: 5.42 g (67%). Four recrystallizations from EtOH:hexanes (small amount of toluene) afforded a light yellow powder, mp 156.3–160.5 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 3.80, AB q (J = 14), 4H, $ArCH_2$; 6.43, s, 2H, H_3; 6.53, s, 2H, H_1; 6.96, t (J = 9), 4H, *o* to F; 7.05, d, (J = 7) 4H, *o* to O; 7.18–7.39, m, 12H, ArH; 7.63, d (J = 7), 4H, *o* to C=O. ELEM. ANAL., Calcd. for $C_{48}H_{32}F_2N_4O_3$: C 76.79, H 4.30, N 7.46; found: C 76.29; H 4.35; N 7.26.

The above reaction on a larger scale using 22.30 g (94 mmol) of **23** produced 24.25 g (70%) of crude product.

4,4′-Sulfonylbis(benzoic Acid) (26)

A solution of 40.12 g (120 mmol) of dimethyl 4,4′-sulfonylbis(benzoate) (**25**) and 19.64 g (0.350 mol) of KOH in 300 mL of absolute ethanol was heated at reflux overnight. The dipotassium salt was filtered, dissolved in water and acidified by adding conc. sulfuric acid dropwise until pH 2. The acid was filtered, washed with water and dried: 35.16 g (96%), mp > 400 °C. FTIR: COOH, 3200–2500 cm^{-1}; C=O, 1690 cm^{-1}; SO_2, 1284 and 1160 cm^{-1}.

4,4′-Sulfonylbis(benzoyl Chloride) (27)

A solution of 34.16 g (111.5 mmol) of **26** and 84.0 mL (1.12 mol) of $SOCl_2$ was allowed to reflux for 2 h, after which a 2–3 drops of DMF were added as a catalyst and refluxing was continued for an additional 22 h. At the end of the reaction, the excess $SOCl_2$ was removed via reduced pressure distillation. Recrystallization from toluene gave 35.52 g (93%) of a white fluffy solid, mp 159–160 °C. FTIR: no carboxyclic acid band at 3200 cm^{-1}.

N,N′-[4,4′-Sulfonylbis(benzoyl}]-bis{4,4′-(*p*-fluorobenzyl)-1,2-dihydroisoquinaldonitrile} (28)

To a solution of 3.63 g (15.3 mmol) of 4-(*p*-fluorobenzyl)isoquinoline (**23**)[23] and 2.51 g (7.3 mmol) of diacid chloride **27** in 75 mL of dry CH_2Cl_2 2.10 mL (15.8 mmol) of TMSCN were added via syringe, followed by a cat. amount of $AlCl_3$. The mixture was stirred under N_2 for 6 days, quenched with 300 mL of water and stirred for 2 h. The organic layer was washed 3× water, 3 × 5% NaOH, 3 × 10% $NaHCO_3$, 3 × 10% HCl, and 3× water and dried over Na_2SO_4 for 1 day. Solvent removal and drying afforded 3.08 g (53%) of crude solid, which after three recrystallizations from EtOAc/hexane produced a yellow solid, mp 165.8–166.7 °C. The reaction was repeated using 18.51 g of **23**, yielding 17.70 g (58%).

^{1}H NMR (270 MHz, $CDCl_3$): δ 3.82, AB q (J = 14), 4H, $ArCH_2$; 6.22, s, 2H, H_1; 6.56, s, 2H, H_3; 6.92, t (J = 9), 4H, *o* to F; 7.16–7.38, m, 16H, ArH; 7.72, d (J = 8), 2H, H_5; 8.03, d (J = 8), 2H, H_8. FTIR: C=O, 1670 cm^{-1}; C=C, C=N, 1598–1507 cm^{-1}; —SO_2—, 1395, 1330 cm^{-1}. ELEM. ANAL., Calcd. for $C_{48}H_{32}N_4O_4SF_2$: C 72.17, H 4.04, N 7.01; found: C 71.93, H 4.09, N 6.94.

p-{1-[4-(*p*-Fluorobenzyl)isoquinolyl]carbonyl}diphenyl Ether (29)

To a solution of 12.16 g (16.2 mmol) of bis(Reissert compound) **24** in 170 mL of freshly distilled THF were added 1.42 g (59.3 mmol) of NaH (60% dispersion in mineral oil) in one portion. The mixture was maintained at 60 °C under N_2 for 2 days, diluted with CH_2Cl_2 and then washed with water in a separatory funnel. The solution was dried over $MgSO_4$ for 24 h. Removal of solvent afforded 9.74 g (86%) of the crude product, which was reprecipitated from chloroform into hexane and recrystallized twice from EtOAc/hexane, mp 115.2–117 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 4.44, s, 4H, $ArCH_2$; 6.98 0, t (J = 9), 4H, *o* to F; 7.07–7.21, m, 8H, *o* to O and $ArCH_2$; 7.61, t (J = 8), 2H, H_6; 7.72, t (J = 8), 2H, H_7; 7.98–8.09, m, 6H, *o* to C=O and H_5; 8.26, d (J = 8), 2H, H_8; s, 8.45, 2H, H_3. FTIR: C=O, 1664.1 cm^{-1}; C=C, C=N, 1598.7–1507.1 cm^{-1}; C—O—C, 1238.9 cm^{-1}. ELEM. ANAL., Calcd. for $C_{46}H_{30}F_2N_2O_3$ • 1/3 $C_4H_8O_2$: C 78.23, H 4.52, N 3.86; found: C 78.06, H 4.45, N 4.19. FAB MS (in 3-nitrobenzyl alcohol): *m/z* 697.23, $(M+H)^+$; 236.0, $(C_{16}H_{11}NF)^+$; Calcd. for $C_{46}H_{30}F_2N_2O_3$, M = 696.2.

p-{1-[4-(*p*-Fluorobenzoyl)isoquinolyl]carbonyl}diphenyl Ether (30)

A mixture of 9.00 g (13 mmol) of **29** and 90.0 g (1.03 mol) of MnO_2 in 300 mL of benzene was heated at reflux via oil bath for 24 h using a Dean-Stark trap. The mixture was filtered through a Celite bed, which was washed with $CHCl_3$ and hot EtOAc. The solutions were combined, dried over $MgSO_4$ and evaporated: 5.03 g (57%). An analytically pure sample was obtained after four recrystallizations from EtOH:hexanes, mp 176.8–178.5 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 7.14–7.23, m, 8H, *o* to F and $ArCH_2$; 7.69, t (J = 8), 2H, H_6; 7.79, t (J = 8), 2H, H_7; 7.94–8.11, 8H, *o* to C=O and *o* to O; 8.10, d (J = 8), 2H, H_5; 8.24, d (J = 8), 2H, H_8; 8.65, s, 2H, H_3. FTIR: C=O 1662 cm^{-1}; C—O—C, 1251 and 1151 cm^{-1}. ELEM. ANAL., Calcd. for $C_{46}H_{26}F_2N_2O_5$ • 1/2 C_2H_5OH: C 75.49, H 3.91, N 3.75, F 5.08; found: C 75.30, H 3.74, N 3.83, F 4.57.

p-{1-[4-(*p*-Fluorobenzyl)isoquinolyl]carbonyl}diphenyl Sulfone (31)

To a solution of 14.14 g (17.7 mmol) of bis(Reissert compound) **28** in 200 mL of freshly distilled THF 1.56 g (39.0 mmol) of NaH (60% dispersion in light mineral oil) were added. The mixture was heated at 60 °C under N_2 for 2 days and diluted with CH_2Cl_2. The solution was washed repeatedly with water, dried over $MgSO_4$ for 1 day, and evaporated: 9.69 g (76%) of dried product, which was purified on a silicia gel column using 65:35 EtOAc:hexane, reprecipitated thrice from $CHCl_3$ into hexane and recrystallized twice from EtOAc:hexane, mp 153.7–155.2 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 4.45, s, 4H, $ArCH_2$; 6.99, t (J = 9), 4H, *o* to F; 7.17, m, 4H, Ar-H; 7.66, t (J = 8), 2H, H_6; 7.75, t (J = 8), 2H, H_7; 8.01–8.09, m, 12H, Ar-H; 8.42, s, 2H, H_3. FAB MS (in 3-nitrobenzyl alcohol): *m/z* 745.196, $(M+H)^+$;

634, $(M\text{-}CH_3C_6H_4F)^+$; 526, $(M\text{-}2CH_2C_6H_4F)^+$; isotopic peaks were present in theoretical intensities. Exact mass of $C_{46}H_{30}N_2O_4SF_2$, M = 744.1973.

4,4′-[Sulfonylbis(*p*-phenyleneoxy)]dibenzoic Acid (33)

This compound was prepared in 72% yield by the method reported by Idage.[26]

4,4′-[Sulfonylbis(*p*-phenyleneoxy)]dibenzoyl Chloride (34)

The crude acid **33**, 12.00 g (24.5 mmol), and 18 mL (0.245 mol) of $SOCl_2$ were heated at reflux for 2 h, after which 3–4 drops of DMF were added. The heating was continued for 2 h; the mixture was left overnight at room temperature. The excess thionyl chloride was distilled off under reduced pressure. The crude product was recrystallized from toluene, mp 179–184 °C [lit. mp[26] 184–189 °C]. FTIR: 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 carboxylic acid bands @ 3200–2561 cm^{-1}.

^{1}H–NMR (270 MHz, $CDCl_3$): δ 7.10, d (J = 8), 2H; 7.20, d (J = 8), 2H; 8.05, d (J = 8), 2H; 8.15, d (J = 8), 2H.

N,N′-[Sulfonylbis(*p*-phenyleneoxy)]-bis{4,4′-(*p*-fluorobenzyl)-1,2-dihydroisoquinaldo-nitrile) (35)

To 3.87 g (16.3 mmol) of 4-(*p*-fluorobenzyl)isoquinoline (**23**)[23] and 4.00 g (7.6 mmol) of 4,4′-[sulfonylbis(*p*-phenyleneoxy)]dibenzoyl chloride (**34**) in 75 mL of dry (molecular sieves) CH_2Cl_2 under N_2 2.23 mL (16.7 mmol) of TMSCN were added via syringe along with a cat. amount of $AlCl_3$. After 4 days, the mixture was quenched into water. The organic layer was washed 3× H_2O, 2 × 5% NaOH, 1 × 10% $NaHCO_3$, 3 × 10% HCl, and 3 × H_20, and finally dried over Na_2SO_4. Removal of solvent afforded 4.48 g (60%) of a yellow solid, which was dissolved in $CHCl_3$ and precipitated into to hexane three times, subjected to column chromatography (65:35 EtOAc:hexane) and two recrystallizations from EtOAc:hexane, mp 154–156 °C.

^{1}H NMR (270 MHz, $CDCl_3$): δ 3.83, AB q (J = 14), 4H, $ArCH_2$; 6.37, s 2H, H_1; 6.52, s, 2H, H_3; 6.94, t (J = 8), 4H, *o* to F; 7.03–7.37, m, 26H, ArH 7.60, d, 2H, H_5; d (J = 8), 7.95, 2H, H_8. ELEM. ANAL., Calcd. for $C_{60}H_{40}F_2N_4O_6 \bullet C_4H_8O_2$: C 71.76, H 4.52, N 5.23; found: C 71.62, H 4.12, N 5.21. FAB MS (in 3-nitrobenzyl alcohol): *m/z* 983.26 $(M+H)^+$; 982.26M^+; 956 $(M\text{-}CN)^+$; 719 $(M\text{-}C_{17}H_{12}FN_2)^+$; 665 $(M\text{-}CN\text{-}C_{17}H_{12}FN_2)^+$; $C_{60}H_{40}F_2N_4O_6S$ exact mass 982.2637.

2-Benzoyl-4-(*p*-fluorobenzyl)-l,2-dihydroisoquinaldonitrile (36)

4-(*p*-Fluorobenzyl)isoquinoline (**23**)[23] (42.71 g, 180 mmol) was dissolved in 300 mL of CH_2Cl_2. Then, 35.16 g (540 mmol) of KCN dissolved in 100 mL of water were added. The resulting mixture was stirred for 15 min prior to the dropwise addition of 50.60 g (360 mmol) of benzoyl chloride over 2 h. The mixture was stirred for 20 h, after which 200 mL of water and 300 mL of CH_2Cl_2 were added. The layers were separated. The organic layer was washed with water 3×, 10% HCl 3×, H_2O 3×, 10% $NaHCO_3$ 3×, and water 3×. The solution was dried over $NaSO_4$ for 1 day and concentrated: 73 g (100%). The crude product was recrystallized from ethanol 4×, tan crystals, mp 163.1–163.6 °C. FTIR (KBr): 1677 cm^{-1} (C=O).

^{1}H NMR (270 MHz, $CDC1_3$): δ 3.80, AB q (J = 15 Hz), 2H, $ArCH_2$; 6.40, s, lH, H_1; 6.60, s, 1H, H_3; 6.95, t (J = 8 Hz), 2H, *o* to F; 7.2–7.7 m, 11H, ArH. ELEM. ANAL., Calcd. for $C_{24}H_{17}N_2OF$: C 78.25, H 4.65, N 7.60; found: C 78.29, H 4.66.

α,α′-Dihydroxy-α,α′-Bis{1-[4-(*p*-fluorobenzyl)isoquinolyl]}-*p*-xylene (37)

2-Benzoyl-4-(*p*-fluorobenzyl)-1,2-dihydroisoquinaldonitrile (**36**), 14.7 g (40 mmol), 2.95 g (22 mmol) of terephthaldehyde, and 0.20 g of tetrabutylammonium bromide were dissolved in 250 mL of acetonitrile. After 30 min of stirring, 20 mL of 50% NaOH were added. The mixture was heated at reflux for 1.5 h, diluted with 800 mL of H_2O and extracted with CH_2Cl_2 (5 × 50 mL). The extract was washed 5× with water, dried over Na_2SO_4 and concentrated by evaporation: 12.94 g; FTIR: ester C=O at 1715.6 cm^{-1} and no OH group, signifying incomplete hydrolysis. The crude product was dissolved in 265 mL ethanol, 150 mL H_2O, and 52 g of KOH were added. After refluxing 4 h, the mixture was concentrated and precipitated into 750 mL of water: 8.50 g (70%); recrystallized 4× from ethanol, colorless crystals, mp 225.0–225.3. FTIR (KBr): 3545–3600 cm^{-1} (OH).

^{1}H NMR (270 MHz, $CDCl_3$): δ 4.36, s, 4H, $ArCH_2$; 6.15, d (J = 6), 2H, OH; 6.29, d (J = 6), 2H, methine; 6.97, t (J = 9), 4H, *o* to fluorine; 7.15, t (J = 6), 4H, *m* to fluorine; 7.26, s, 4H, ArH; 7.43, t (J = 8), 2H, H_6; 7.58, t (J = 8), 2H, H_7; 8.06, m, 4H, H_5 and H_8; 8.35, s, 2H, H_3. ELEM. ANAL., Calcd. for $C_{40}H_{30}F_2N_2O_2 \bullet H_2O$: C 76.66, H 5.15, N 4.47; found C: 76.48, H: 4.90, N: 4.40.

p-Bis{1-[4-(*p*-fluorobenzoyl)isoquinoly]carbonyl}benzene (38)

A mixture of 5.78 g (9.5 mmol) of diol **37**, 180 mL benzene and 60 g MnO_2 was allowed to reflux for 12 h using a Dean-Stark trap. The oxides were filtered through silica gel, and the latter was washed with CH_2Cl_2 and then methanol. The solvent was removed: yellow product, 2.72 g (45%). (The low yield reflects the fact that the MnO_2 was not Soxhlet extracted in this case.) The crude material was recrystallized from ethanol 2x, light yellow fluffy crystals, mp 237.5–238.5 °C. FTIR (KBR): 1667, 1678 cm^{-1}, (C=O); 1597 cm^{-1} (C=C).

^{l}H NMR (270 MHz, $CDCl_3$): δ 7.20, q (J = 9), 4H, *o* to F; 7.70–7.84, m, 4H, H_6, H_7; 7.97, m, 4H, *m* to F; 8.10, m, 6H, H_5 and xylyl; 8.33, d (J = 8), 2H, H_8; 8.67, s. 2H, H_3. ELEM. ANAL., Calcd. for $C_{40}H_{22}F_2N_2O_4 \bullet 1/4\ H_2O$: C 75.17, H 3.55, N 4.38; found C 75.05, H 3.43, 4.35.

Polymerization of *p*-Bis{4-[1-(*p*-fluorobenzoyl) isoquinoly]carbonyl}benzene (10) with Bis(phenol-A) to form Poly(heteroarylene ether) 39

Tetraketone **10** (1.0000 g, 1.57 mmol) and 0.3584 g (1.57 mmol) of bisphenol-A were dissolved in 9 mL of NMP freshly distilled from CaH_2. Then, 0.2604 g (1.57 mmol) of anhydrous K_2CO_3 and 4 mL of toluene were added. The mixture was heated in an oil bath under N_2 and kept at 140–145 °C for 4 h. The temperature was then raised to 160–170 °C and

maintained for 13 h. The reaction mixture was cooled, diluted with $CHCl_3$, filtered, acidified with acetic acid, and precipitated into methanol to yield 0.95 g of crude tan polymer: $[\eta]$ = 0.16 dL/g ($CHCl_3$, 25 °C); GPC (THF): M_n = 4.9 kDa, M_w = 7.8 kDa; TGA, 5% wt. loss @ 454 °C in air; DSC: T_g = 180 °C and no T_m. FTIR (KBr): 1664.1 cm^{-1} (C=O), 1592.2 cm^{-1}, 1500.6 cm^{-1} (C=C), 1245.4 cm^{-1} (C—O—C).

^1H NMR (270 MHz, $CDCl_3$): δ 1.70, s, 6H, CH_3; 6.90–7.09, m, 8H, *o* to O; 7.2–7.28, m, 4H, *o* to C=O; 7.68, t (J = 8), 2H, H_6; 7.80, t (J = 8), 2H, H_7; 7.92, d (J = 8), 2H, H_5; 8.04, s, 4H, *o* to $C(CH_3)_2$; 8.15, d (J = 8), 2H, H_8; 8.70, s, 2H, H_3.

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