Heterocycle-Activated Aromatic Nucleophilic Substitution: Poly(aryl ether phenylquinoxalines). 2

J. Hedrick,* R. Twieg, T. Matray, and K. Carter

IBM Research Division, Almaden Research Center, 650 Harry Road, San Jose, California 95120-6099

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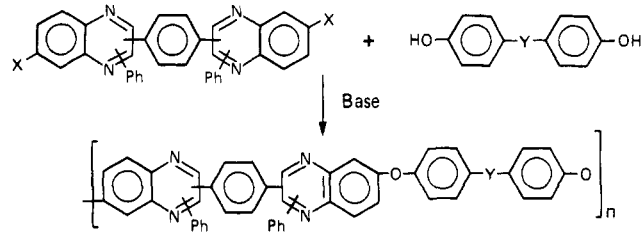
ABSTRACT: A synthetic approach for the preparation of poly(aryl ether phenylquinoxalines) has been developed wherein the generation of an aryl ether linkage is the polymer-forming reaction. Fluorines located on the para position of the benzene rings of various 2,3-diphenylquinoxaline heterocycles were found to be activated toward nucleophilic aromatic substitution. Model reactions demonstrated that these fluorine atoms on the phenyl groups of the diphenylquinoxaline were displaced by phenoxides in high yield, and the process was deemed suitable as a polymer-forming reaction. Thus, the pyrazine component of the phenylquinoxaline heterocycle has an activating effect on both the annulated benzo ring and the pendant phenyl groups, albeit to a lesser extent in the latter case. The extent of activation of the diphenylquinoxaline aryl fluorides was evaluated by both ^{1}H NMR and ^{19}F NMR spectroscopy. Appropriately substituted bis(fluorophenyl)-quinoxaline monomers were prepared and polymerized with bisphenols in high-boiling aprotic dipolar solvents containing potassium carbonate. High molecular weight polymers were obtained with glass transition temperatures ranging from 190 to 240 °C. Enhanced polymer solubility was achieved.

Introduction

Poly(phenylquinoxalines) (PPQs) were first reported by Hergenrother and co-workers in the late 1960s and have since been shown to possess many desirable properties including excellent thermal stability, low dielectric constant, high glass transition temperature (T_g), and good mechanical properties.[1-3] PPQs have been most often synthesized by the formation of the quinoxaline ring via the polycondensation of an aromatic bis(*o*-diamine) with a bis(phenyl-α-dicarbonyl) compound either in *m*-cresol at elevated temperatures or in a *m*-cresol/xylene solvent mixture at ambient temperature. The polymer generated in the synthesis is a fully cyclized structure and requires no further curing. Although PPQs are soluble in selected chlorinated solvents and *m*-cresol, the toxicity of these solvents may limit the use of PPQs in many applications.

It has been shown that aryl ethers containing PPQs generally show better solution and melt processing characteristics than their counterparts containing only directly linked aromatic rings. Ether linkages in these polymers have usually been introduced at an early stage of the synthesis by use of bis(phenyl-α-dicarbonyl) monomers already containing an aryl ether linkage. These ether-containing monomers are themselves prepared by a Friedel–Crafts route[4] or by nucleophilic aromatic nitro displacement.[5] An alternative method for the introduction of aryl ether linkages into PPQs is through a polyether synthesis wherein the monomers already contain the quinoxaline ring. For instance, Connell and co-workers have polymerized bisphenols containing a preformed quinoxaline heterocycle with activated difluorides (e.g., 4,4′-difluorobenzophenone, 4,4′-difluorodiphenyl sulfone, etc.).[6] High molecular weight poly(aryl ether phenylquinoxalines) were obtained from a dimethylacetamide/*o*-dichlorobenzene solvent mixture containing potassium carbonate. In addition, a heterocycle-activated PPQ synthesis has been shown to be an effective route to poly(aryl ether phenylquinoxalines). Here, bis(6-fluorophenylquinoxalines) were shown to polymerize readily with biphenols to give a high molecular weight polymer in *N*-methyl-2-pyrrolidone (NMP) containing potassium carbonate (Scheme I).[7] The resulting poly(aryl ether phenylquinoxalines) displayed high glass transition temperatures and tough ductile mechanical properties and were processable from either the melt or solution.

Scheme I. Synthesis of Poly(phenylquinoxalines) by a Heterocycle-Activated Reaction between a Biphenol and a Bis(6-fluorophenylquinoxaline)



The synthesis of poly(aryl ethers) most often involves the nucleophilic displacement of an aryl halide with a phenoxide in polar aprotic solvents.[8,9] Conventionally, the aryl halide is activated by an electron-withdrawing group such as carbonyl or sulfone which increases the electrophilicity of the fluorine-bearing carbon. In addition, these activating groups can accept a negative charge by resonant interaction, thus lowering the activation energy for the displacement through a Meisenheimer complex. The reaction used for the synthesis of the poly(aryl ether phenylquinoxalines) involved the nucleophilic aromatic substitution of a fluorine atom at the 6- or 7-positions of a quinoxaline heterocycle with a phenoxide. Aromatic nucleophilic substitution at these positions in a quinoxaline heterocycle resulted from activation of the aryl fluoride by the electron-poor pyrazine ring and formation of a Meisenheimer-like complex, presumably formed as a stabilized intermediate during the transformation (Scheme II).[7] NMR spectroscopy was found to be a useful probe to determine the electronic perturbations due to substituents on aromatic rings. The electronic effect of the pyrazine component of the quinoxaline heterocycle has been evaluated by ^{1}H NMR, by observing the magnitude of the deshielding of the protons ortho to the pyrazine.[7] It has been observed that the deshielding increases with increasing electron withdrawal. Utilizing this probe, appropriately substituted monomers were evaluated. For example, in oxazole-activated displacement for the preparation of poly(aryl ether benzoxazoles), the protons on the 2-phenyl group of the benzoxazole were found to be

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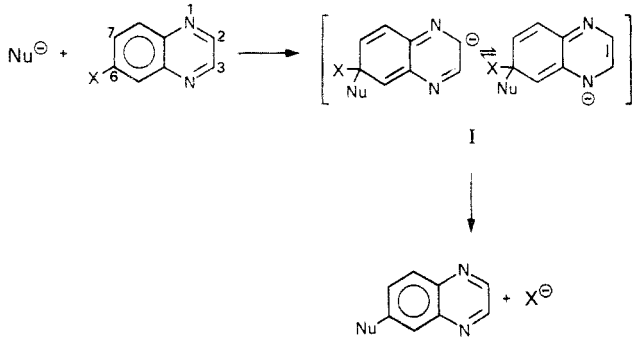
Scheme II. Meisenheimer Complex Stabilization of the Transition State Involved in the Reaction between a Phenoxide and a 6-Fluorophenylquinoxaline



shifted further downfield than the ortho protons of the benzo ring.[10] Interestingly, in the case of the 2,3-diphenylquinoxalines, the pyrazine ring was found to have a greater electron-withdrawing effect upon the benzo ring than on the appended phenyl groups. This does not, however, exclude the possible activation of fluorine atoms at the para positions of either the 2-phenyl or 3-phenyl groups of 2,3-diphenylquinoxalines.[11] In this study, this latter reaction as a route to poly(aryl ether phenylquinoxalines) is evaluated.

Experimental Section

2,3-Bis(4-fluorophenyl)quinoxaline (3a). Into a 1000-mL round-bottomed flask equipped with a reflux condenser, nitrogen inlet, and stirbar was placed 4,4′-difluorobenzil (**2**; 19.69 g, 80 mmol), *o*-phenylenediamine (**1**; 8.65 g, 80 mmol), and 150 mL of acetic acid. The solution was gradually warmed to 110 °C and allowed to stir for 2.5 h. After cooling, water (700 mL) was added dropwise to give a white solid which was isolated by suction filtration and washed repeatedly with water. Recrystallization from ethanol and water gave 24.3 g (95%) of white fluffy crystals in two crops: mp 133.5–134.0 °C; ^{1}H NMR (DMSO) δ 8.20–8.13 (m, 2H), 7.93–7.87 (m, 2H), 7.58–7.50 (m, 4H), 7.29–7.18 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 163.10 (d, J = 249.8 Hz), 152.05, 141.07, 134.90, 131.73, 130.09, 129.03, 115.41 (d, J = 21.8 Hz). Anal. Calcd for $C_{20}H_{12}N_2F_2$: C, 75.45; H, 3.81; N, 8.80. Found: C, 75.42; H, 3.90; N, 8.79.

2,3-Bis(4-fluorophenyl)-5-azaquinoxaline (3e). Into a 500-mL round-bottomed flask fitted with a reflux condenser, stirbar, and nitrogen inlet was placed 4,4′-difluorobenzil (**2**; 7.38 g, 30 mmol), 2,3-diaminopyridine (**1e**; 3.27 g, 30 mmol), and acetic acid (75 mL). The solution was refluxed for 1 h, and after cooling, water (400 mL) was added dropwise to produce a yellow precipitate. The solid was filtered and washed well with water, and then recrystallization from ethanol and water gave 8.05 g (84%) of fine yellow crystals: mp 148.2–149.2 °C; ^{1}H NMR (DMSO) δ 9.20 (d, J = 4.3 Hz, 1H), 8.61 (d, J = 7.3 Hz, 1 H), 7.97–7.88 (m, 1H), 7.64–7.50 (m, 4H), 7.33–7.20 (m, 4H). ^{13}C NMR (DMSO) δ 163.43 (d, J = 250.8 Hz), 154.88, 154.20, 153.27, 137.92, 136.06, 134.08 (d, J = 24.4 Hz), 131.92 (d, J = 27.9 Hz), 125.31, 115.49 (d, J = 21.8 Hz). Anal. Calcd for $C_{19}H_{11}N_3F_2$: C, 71.46; H, 3.48; N, 13.16. Found: C, 71.51; H, 3.49; N, 13.23.

2,3-Bis(4-fluorophenyl)-6-benzoylquinoxaline (3c). Into a 500-mL round-bottomed flask equipped with a reflux condenser, stirbar, and nitrogen inlet was placed 4,4′-difluorobenzil (**2**; 7.38 g, 30 mmol), 2,3-diaminobenzophenone (**1c**; 6.36 g, 30 mmol), and 100 mL of acetic acid. The solution was allowed to stir for 15 h, and then water (200 mL) was added dropwise. The resulting white solid was filtered and washed repeatedly with water. Recrystallization with acetic acid and water gave 11.46 g (90%) of tan crystals: mp 171.8–172.9 °C; ^{1}H NMR (DMSO) δ 8.38–8.27 (m, 3H), 8.20 (d, J = 8.9 Hz, 1H), 7.87 (d, J = 6.7 Hz, 2H), 7.80–7.70 (m, 1H), 7.67–7.50 (m, 6H), 7.33–7.19 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 195.59, 163.38 (d, J = 250.5 Hz), 163.29 (d, J = 250.5 Hz), 153.71, 153.18, 142.78, 140.04, 138.42, 136.97, 134.41, 132.81, 132.18, 131.86, 131.72, 131.58, 130.03, 129.55, 128.44, 115.57 (d, J = 21.8 Hz). Anal. Calcd for $C_{27}H_{16}N_2OF_2$: C, 76.76; H, 3.83; N, 6.63. Found: C, 76.71; H, 3.83; N, 6.59.

2,3-Bis(4-fluorophenyl)-6-(trifluoromethyl)quinoxaline (3b). Into a 500-mL round-bottomed flask equipped with a reflux condenser, stirbar, and nitrogen inlet was placed 4,4′-difluorobenzil (**2**; 7.38 g, 30 mmol), 3,4-diaminobenzotrifluoride (**1b**; 5.28 g, 30 mmol), and acetic acid (75 mL). The solution was refluxed at 140 °C for 1 h. After cooling, water (500 mL) was added dropwise, causing the formation of a brown precipitate. The solid was filtered and washed with water; then the resulting mixture was dissolved in toluene and filtered through a short bed of silica gel. White crystals formed upon concentration of the filtrate totaling 8.44 g (73%): mp 168.4–169.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.41 (s, 1H), 8.27 (d, J = 9.5 Hz, 1H), 7.95 (d, J = 9.8 Hz, 11H), 7.61–7.47 (m, 4H), 7.14–7.02 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 163.38 (d, J = 250.9 Hz), 153.97, 153.41, 142.03, 140.00, 134.22, 131.81, 131.76, 131.68, 131.62, 131.40, 130.24, 127.11, 127.04, 125.70, 125.65, 115.59 (d, J = 21.8 Hz). Anal. Calcd for $C_{21}H_{11}F_5N_2$: C, 65.29; H, 2.87; F, 24.59; N, 7.21. Found: C, 65.30; H, 2.84; F, 25.01; N, 7.21.

2,3-Bis(4-fluorophenyl)-6-(phenylsulfonyl)quinoxaline (3d). Into a 250-mL round-bottomed flask equipped with a reflux condenser, stirbar, and nitrogen inlet was placed 4,4′-difluorobenzil (**2**; 3.23 g, 13.1 mmol), 3,4-diaminodiphenyl sulfone (**1d**; 3.26 g, 13.1 mmol), and acetic acid (100 mL). The solution was warmed to 100 °C and allowed to stir for 1 h. After cooling the reaction mixture was precipitated with stirring into water (500 mL), and the resulting white solid was filtered and washed with water. Recrystallization from acetic acid and water gave 4.43 g (74%) of white crystals: mp 199.8–201.0 °C; ^{1}H NMR (DMSO) δ 8.72 (s, 1H), 8.37–8.23 (m, 2H), 8.11 (d, J = 7.3 Hz, 2H), 7.76–7.61 (m, 3H), 7.60–7.48 (m, 4H), 7.31–7.18 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 163.52 (d, J = 250.9), 163.46 (d, J = 252.2), 154.57, 153.79, 142.65, 142.51, 140.74, 140.02, 134.01, 133.56, 131.84, 131.75, 131.70, 131.62, 130.75, 129.99, 129.39, 127.90, 126.88, 115.66 (d, J = 22.0 Hz). Anal. Calcd for $C_{26}H_{16}F_2N_2O_2S$: C, 68.11; H, 3.52; F, 8.29; N, 6.11; S, 6.99. Found: C, 67.83; H, 3.84; F, 8.62; N, 6.10; S, 6.91.

2-Amino-4-fluoronitrobenzene (5). In a 500-mL pear-shaped flask equipped with a stirbar, addition funnel, and nitrogen inlet was placed 2,4-difluoronitrobenzene (**4**; 31.8 g, 200 mmol) and *N*-methylpyrrolidinone (100 mL). The solution was stirred at room temperature, and ammonium hydroxide (20 mL) was added. Additional ammonium hydroxide (10 mL) was added after 16 h, and a final addition of ammonium hydroxide (10 mL) and NMP (50 mL) was made after 40 h. Six hours after the final addition, thin layer chromatography showed only a trace of the 2,4-difluoronitrobenzene remaining so the slurry was chilled in an ice bath and brought up to 500 mL by dropwise addition of ice water. The resulting yellow solid was isolated by suction filtration and washed with water. Recrystallization from 2-propanol and water gave 30.0 g (96%) of yellow needles: mp 96 °C (lit.[12] mp 97 °C); ^{1}H NMR (DMSO) δ 8.11–8.02 (m, 2H), 7.61 (br s, 2H), 6.76 (d, J = 10.7 Hz, 1H), 6.49 (t, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 129.36, 129.17, 105.85, 105.46, 103.76, 103.35. Anal. Calcd for $C_6H_5FN_2O_2$: C, 46.16; H, 3.23; F, 12.17; N, 17.94. Found: C, 45.80; H, 3.24; F, 12.05; N, 17.58.

2-Amino-4-(phenylsulfonyl)nitrobenzene (6). Into a 500-mL round-bottomed flask fitted with a stirbar, reflux condenser, and nitrogen inlet was placed 2-amino-4-fluoronitrobenzene (**5**; 10.0 g, 64 mmol), the sodium salt of benzenesulfinic acid (11.57 g, 70 mmol), and 100 mL of dimethyl sulfoxide. The slurry was gradually warmed in an oil bath to 125 °C. After 2 h the reaction was cooled and water (300 mL) was added dropwise, resulting in an orange–yellow solid. The solid was filtered, washed with water, and air dried. The isolated material (16.37 g, 91.9%) was analytically pure and used without further purification: mp 179.8–181.2 °C; ^{1}H NMR ($CDCl_3$) δ 8.23–8.12 (m, 3H), 6.54–6.38 (m, 5H), 6.21 (br s, 2H); ^{13}C NMR (acetone) δ 148.24, 146.43, 141.39, 134.65, 133.81, 130.36, 128.53, 128.29, 119.55, 113.63. Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 51.77; H, 3.42; N, 10.24; S, 11.49. Found: C, 51.79; H, 3.62; N, 10.06; S, 11.52.

3,4-Diaminodiphenyl Sulfone (1d). In a 500-mL round-bottomed, two-neck flask equipped with a stirbar, reflux condenser, and gas inlet fitted with a balloon was placed 2-amino-4-(phenylsulfonyl)nitrobenzene (**6**; 5.56 g, 20 mmol), 10% palladium hydroxide on activated carbon (0.28 g), and acetic acid (75 mL). The system was flushed first with nitrogen and then with hydrogen and the balloon filled with hydrogen. The

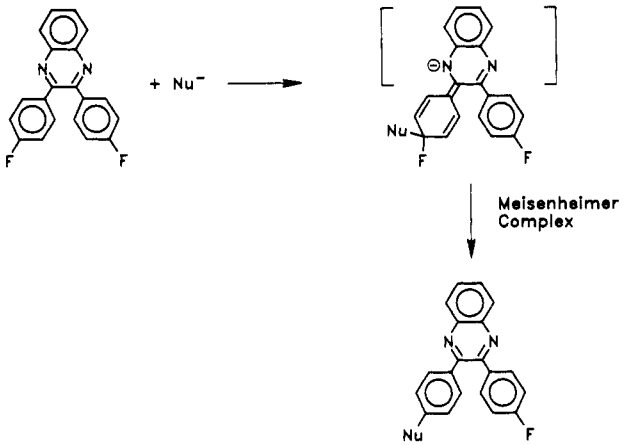
reaction mixture was briefly warmed to 100 °C for 20 min to dissolve all of the nitro compound, and then the heat was removed and the reaction was maintained under a hydrogen atmosphere at room temperature for 48 h. After this time thin layer chromatography indicated the reaction was complete and the system was flushed with nitrogen. The mixture was filtered through a short bed of silica gel to remove catalyst and concentrated by rotary evaporation. Purification by silica gel chromatography (5% → 50% gradient of EtOAc/hexane) gave a dark solid which was used directly in the synthesis of **3d**: ^{1}H NMR (DMSO) δ 7.80–7.76 (m, 2H), 7.60–7.52 (m, 3H), 7.00–6.96 (m, 2H), 6.56 (d, 2H), 5.46 (br s, 2H), 4.92 (br s, 2H); ^{13}C NMR (DMSO) δ 143.46, 140.6, 134.7, 132.5, 129.4, 126.6, 126.4, 118.0, 112.5, 112.0.

Model Reaction. A 15-mL three-neck flask fitted with a nitrogen inlet and Dean–Stark trap with condenser was charged with 2,3-bis(4-fluorophenyl)quinoxaline (**3a**; 1.2725 g, 3.90 mmol), *m*-cresol (7; 0.9800 g, 8.90 mmol), and anhydrous K_2CO_3 (2.000 g, 14.50 mmol) and carefully rinsed into the flask with 8 mL of a NMP/CHP (50/50) solvent mixture. The reaction mixture was heated to 150–160 °C to effect the dehydration of the system, and the water generated by phenoxide formation was collected in the Dean–Stark trap. After complete dehydration of the system (4–6 h), the reaction was heated to 180 °C for 18 h, at which time TLC analysis (ethyl acetate/hexane (1/3)) showed complete conversion of **3a** and the formation of a single product. The reaction mixture was partitioned between chloroform and water, and the chloroform layer was washed five times with water, dried ($MgSO_4$), and concentrated on a rotary evaporator (~95% yield). The crude product was purified by flash chromatography (10% ethyl acetate/hexane, silica gel) and recrystallized (methanol) to afford **8** as a light brown crystalline powder: mp 124–126.5 °C; ^{1}H NMR (DMSO-d_6) δ 8.08–8.16 (m, 2H), 7.82–7.90 (m, 2H), 7.49 (d, 2H), 7.23–7.32 (m, 2H), 6.94–7.03 (m, 6H), 6.80–6.87 (m, 4H), 2.28 (s, 6H); ^{13}C NMR (DMSO-d_6) δ 157.43, 156.15, 152.47, 140.49, 139.92, 133.71, 131.64, 130.34, 129.88, 128.76, 124.63, 119.47, 117.98, 116.07, 20.94. Anal. Calcd for $C_{34}H_{26}N_2O_2$: C, 82.56; H, 5.29; N, 5.66. Found: C, 81.95; H, 5.44; N, 5.41.

Polymer Synthesis. A typical synthesis of a poly(aryl ether phenylquinoxaline) was conducted in a three-neck flask equipped with a nitrogen inlet, mechanical stirrer, and Dean–Stark trap with a condenser. A detailed synthetic procedure designed to prepare a poly(aryl ether phenylquinoxaline) based on **9c** is provided. The flask was charged with 1.8041 g (5.6 mmol) of **3a** and 1.7056 g (5.60 mmol) of **10**, and the resulting mixture was carefully washed in with 16 mL of a NMP/CHP solvent mixture. Toluene (20 mL) was added, followed by 2.1568 g (0.0156 mol) of K_2CO_3. The reaction mixture was then heated until the toluene began to reflux. An optimum reflux temperature range was achieved when the oil bath was maintained between 140 and 150 °C. Toluene was periodically removed from the Dean–Stark trap and replaced with deoxygenated dry toluene to ensure dehydration. The reaction mixture was maintained at 140 °C until the presence of water was no longer observed in the Dean–Stark trap, which may take 4–8 h. During this stage of the reaction the solution underwent severl color changes. For example, during the initial formation of the phenoxide, a yellow–brown color was observed, and as the refluxing proceeded, the color changed to dark brown. Upon dehydration the temperature was slowly increased to 180 °C, and the toluene was removed through the Dean–Stark trap. The reaction mixture was heated to 180 °C for approximately 20 h. Completion or near completion was qualitatively estimated by the point where the viscosity increased dramatically. The reaction mixture was diluted with NMP and filtered hot to remove inorganic salts. The filtered solution was cooled, and several drops of weak acid (e.g., acetic acid) were added to neutralize phenoxide end groups. The polymer solution was then coagulated in about a 10-fold volume of methanol and then boiled in water to remove any trapped salts. The polymer was then dried in a vacuum oven (80 °C) to a constant weight. The yield of polymer **12a** was essentially quantitative.

Characterization. Glass transition temperatures, taken as the midpoint of the change in slope of the base line, were measured on a Du Pont DSC 1090 instrument with a heating rate of 10 °C/min. Intrinsic viscosity measurements were determined by using a Cannon–Ubbelohde dilution viscometer in NMP (25 °C). NMR spectra were recorded on either an IBM WP250 instrument operating at 250.1 MHz (^{1}H) and 62.9 MHz (^{13}C) or an IBM WP300 instrument operating at 282.3 MHz (^{19}F). Tetramethylsilane was used as a reference for ^{1}H and ^{13}C measurements, while $CFCl_3$ was used as an internal standard for the ^{19}F measurements. The reference peaks are assigned 0.0 ppm, chemical shifts upfield of the reference are assigned as negative and reported in ppm, and the coupling constants are reported in hertz. Elemental analyses were performed at Galbraith Laboratories, Inc., Knoxville, TN.

Scheme III. Meisenheimer Complex Stabilization of the Transition State Involved in the Reaction between a Phenoxide and a 2-(4-Fluorophenyl)quinoxaline



Materials

All materials were commercially available and used as received unless otherwise noted. The solvents *N*-cyclohexyl-2-pyrrolidinone (CHP) and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) were obtained from Aldrich and were vacuum distilled from calcium hydride. The bisphenol monomers 2,2-bis(4′-hydroxyphenyl)propane (Bisphenol A) and 2,2-bis(4′-hydroxyphenyl)hexafluoropropane (Bisphenol AF) were also obtained from Aldrich and recrystallized from toluene and toluene/ethyl acetate (95/5), respectively.

Results and Discussion

The reaction utilized for the synthesis of poly(aryl ether phenylquinoxalines) was the nucleophilic aromatic substitution by a phenoxide on a halide at the para positions on the 2-phenyl and 3-phenyl groups of phenylquinoxaline. The rationale for the nucleophilic aromatic substitution on the pendent phenyl groups of the quinoxaline was similar to that described before for the halide on the 6- or 7-positions of the heterocycle. First, the electron-poor pyrazine ring would have the effect of an electron-withdrawing group, and second, due to resonance of the negative charge in the pyrazine ring, a Meisenheimer complex would form as a stabilized intermediate during the transformation (Scheme III). The electronic effect of the pyrazine ring on the 2-phenyl group could be evaluated by ^{1}H NMR, as the deshielding of the protons ortho to a substituent is indicative of an electron-withdrawing group. Comparison of the ^{1}H NMR spectral assignments of 2,3-bis(4-fluorophenyl)quinoxaline with 2,3-diphenyl-6-fluoroquinoxaline shows that the protons ortho to the pyrazine have a chemical shift of δ 8.2 (Figure 1b), as previously reported for the synthesis of poly(aryl ether phenylquinoxalines), as compared to δ 7.55 for the ortho protons of the 2-phenyl group (Figure 1a).[7] This demonstrates the electron-withdrawing effect of the pyrazine ring on the fused benzo ring in the ground state is substantially greater than the 2-phenyl group. However, other weakly electron-withdrawing groups (i.e., perfluoroalkyl) have comparable ^{1}H NMR chemical shifts (δ 7.6) and were shown to

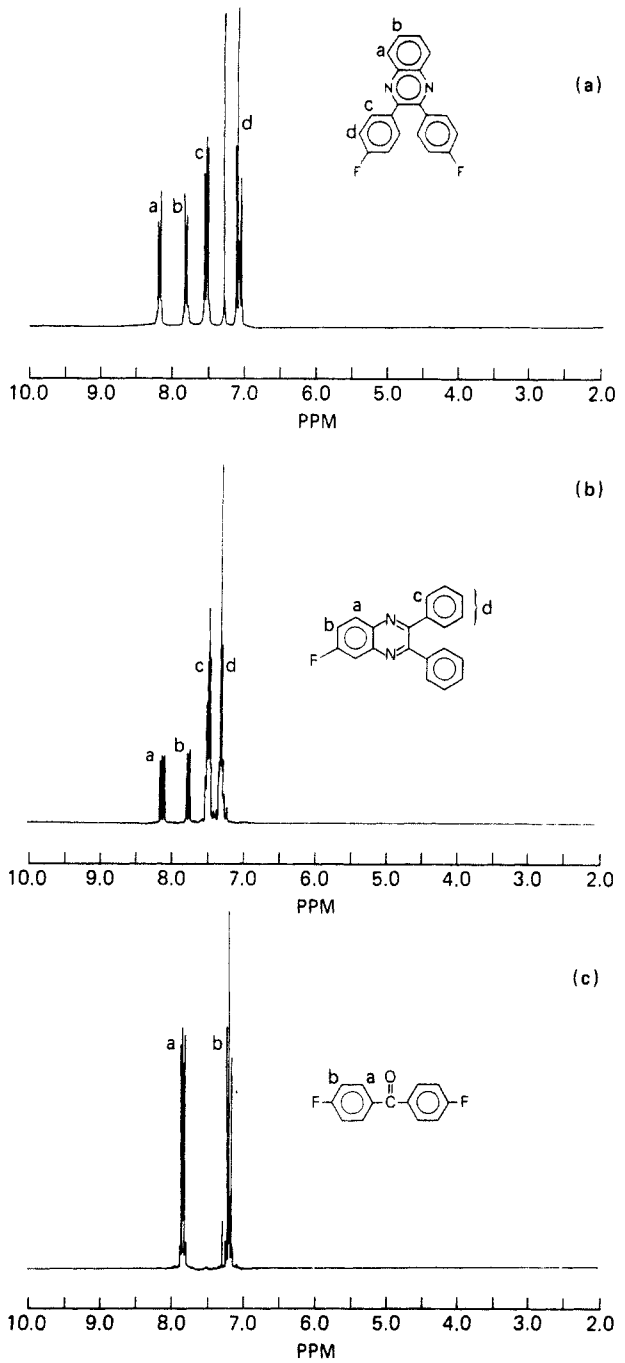


Figure 1. ^{1}H NMR spectra of (a) 2,3-bis(4-fluorophenyl)-quinoxaline, (b) 3,4′-diphenylfluoroquinoxaline, and (c) 4,4′-difluorobenzophenone.

effectively activate nucleophilic aromatic substitution.[13] Furthermore, comparison of the deshielding of the ortho protons of the 2-phenyl group on the phenylquinoxaline to the ortho protons (δ 7.9) of 4,4′-difluorobenzophenone, a conventional activated dihalide, shows them to be comparable with respect to electron affinity and further indicates the possibility of nucleophilic aromatic substitution from the para position on a 2-phenyl ring.

These attempts to relate the reactivity of these fluorinated heterocycles in aromatic nucleophilic substitution reactions with their spectroscopic properties have relied heavily upon ^{1}H NMR. Another potentially superior spectroscopic probe is ^{19}F NMR. Fluorine is an excellent probe due to its high natural abundance and sensitivity to NMR detection. In addition, the fluorine is located at the reaction site of aromatic nucleophilic substitution, unlike the proton probes which are removed from the site of reaction. It is well-known that the ^{19}F chemical shift

Table I. ^{19}F Chemical Shifts for Selected Compounds

compd	chemical shift[a]
4,4′-difluorophenyl sulfone	−104.08
4,4′-difluorobenzophenone	−106.01
2,3-diphenyl-6-fluoroquinoxaline	−107.81
2,3-bis(4-fluorophenyl)-6-(phenylsulfonyl)-quinoxaline (**3d**)	−111.00, −111.16
2,3-bis(4-fluorophenyl)-6-(trifluoromethyl)-quinoxaline (**3b**)	−111.18, −111.31
2,3-bis(4-fluorophenyl)-6-benzoyl-quinoxaline (**3c**)	−111.29, −111.49
2,3-(4-fluorophenyl)-5-azaquinoxaline (**3e**)	−111.30, −111.51
2,3-bis(4-fluorophenyl)quinoxaline (**3a**)	−111.99
fluorobenzene	−112.77

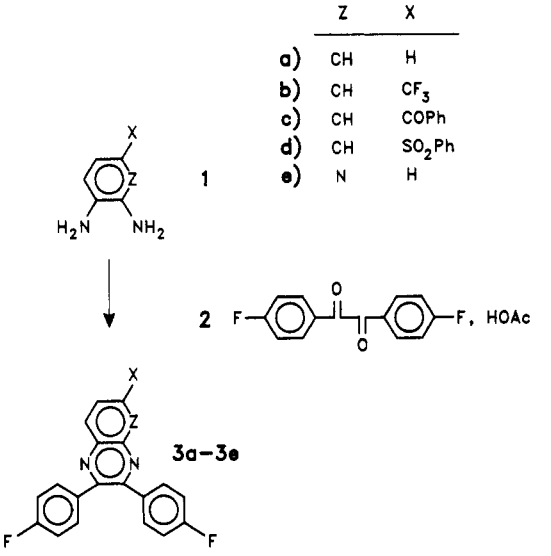
[a] Shifts reported in ppm relative to CCl_3F = 0.0 ppm in DMSO-d_6.

is very sensitive to any perturbations of the aromatic ring electron density arising from both inductive and resonance effects.[14,15] The ^{19}F NMR chemical shifts of fluorines both para and ortho to electron-withdrawing groups are shifted downfield, and the magnitude of this shift can be directly related to the electron density at the carbon to which it is attached. Unlike ^{1}H NMR probes, ^{19}F is not greatly affected by ring current effects or anisotropy.

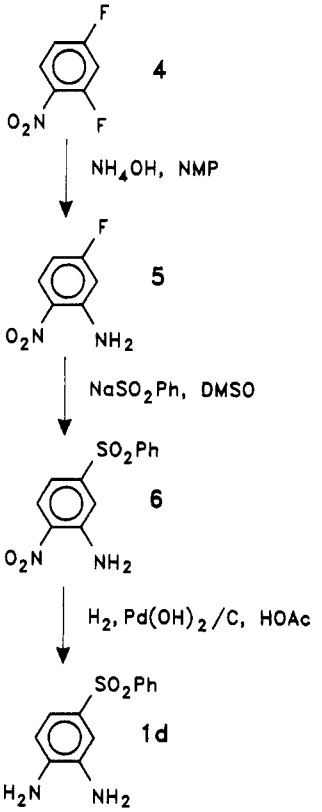
The ^{19}F NMR data further support the fact that the pyrazine ring of the quinoxaline heterocycle is sufficiently electron withdrawing to facilitate nucleophilic substitution of fluorine at the para position in the appended phenyl groups. Table I contains the ^{19}F chemical shifts of several representative fluorinated compounds including the 2,3-bis(4-fluorophenyl)quinoxaline monomers **3a–e**. Comparison of the quinoxaline monomers with conventional activated monomers such as 4,4′-difluorobenzophenone or 4,4′-difluorophenyl sulfone and the relatively unactivated fluorobenzene provides a good approximation of the quinoxalines' overall reactivity and reflects the qualitative rate of reaction among the quinoxalines **3a–e**. The most active monomer, 2,3-bis(4-fluorophenyl)-6-(phenylsulfonyl)quinoxaline (**3d**), has δ −111.00 and −111.16 (two distinct resonances due to the slightly differing influence of the activating phenyl sulfone substituent), and the least active is 2,3-bis(4-fluorophenyl)quinoxaline (**3a**) with δ −111.99. Hence, the monomers are listed in descending order of reactivity in Table I. These values can be compared with the chemical shift of the more activated fluorine of the benzo-substituted monomers which is found at −107.81 ppm. It has been our observation that monomers with $\delta < -110.00$ are weakly activated and require extended reaction times and higher reaction temperatures to affect the displacement reaction. This appears to be the case for many of the quinoxaline-based monomers, and therefore more stringent reaction conditions are required to attain full monomer conversion. Through utilization of NMR spectroscopy, it is becoming possible to better understand the electronic properties of these organofluorine polymer intermediates and their reactivity in aromatic nucleophilic substitution reactions. The refinement of this analysis is underway with the expectation that NMR spectra will provide a predictive insight into searching for new systems useful for polymer synthesis via aromatic nucleophilic substitution chemistry.

One goal of this study was to examine the influence of some additional functionality on the quinoxaline ring on the chemistry of the polymer-forming reaction and the ultimate properties of the resulting polymers. The introduction of the single 6-substituent (and the 5-aza substitution in the pyridine case) is anticipated to produce a more random polymer which depends on the relative disparity of reactivity between the two fluorine atoms in each monomer. All the substituents examined here are electron withdrawing, and it is anticipated that the fluorine

Scheme IV. Quinoxaline Synthesis from a 1,2-Aryldiamine and a 1,2-Dicarbonyl Compound



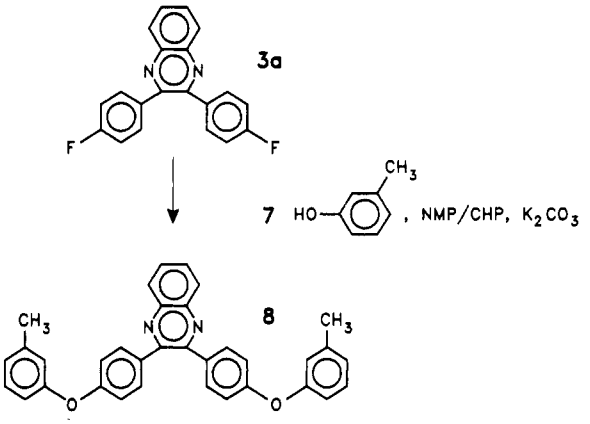
Scheme V. Synthesis of 3,4-Diaminophenyl Phenyl Sulfone (1d)



atom across the pyrazine ring is preferentially activated.

The requisite diphenylquinoxalines were prepared by the well-known condensation between a 1,2-diaminobenzene and a 1,2-dicarbonyl compound (Scheme IV). Among the phenylenediamines utilized, the parent 1,2-phenylenediamine (**1a**), 4-(trifluoromethyl)-1,2-phenylenediamine (**1b**), 3,4-diaminobenzophenone (**1c**), and the pyridine derivative 2,3-diaminopyridine (**1e**) were all commercially available. The 3,4-diaminophenyl phenyl sulfone (**1d**) was synthesized by a four-step procedure (Scheme V) which relied on the regiospecific sequential aromatic nucleophilic substitution of 2,4-difluoronitrobenzene (**4**). This material is first reacted with ammonia to give 2-amino-4-fluoronitrobenzene (**5**). Subsequently a second aromatic nucleophilic substitution is run, this one with sodium benzenesulfinate[16] to form 3-amino-4-nitrophenyl phenylsulfone (**6**). Reduction of the nitro group

Scheme VI. Model Reaction between 2,3-Bis(4-fluorophenyl)quinoxaline (3a) and *m*-Cresol (7)



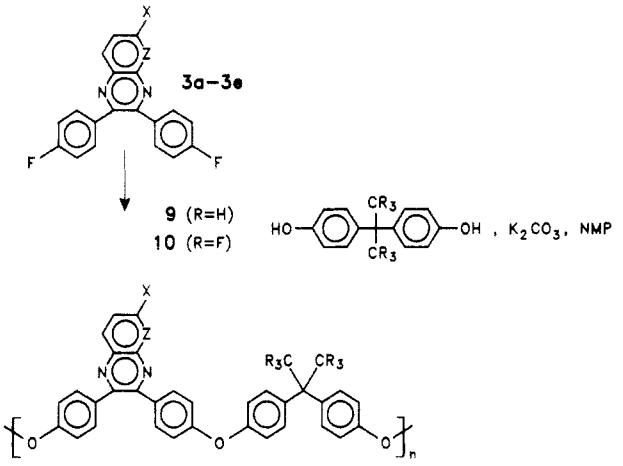
with hydrogen and palladium on charcoal provides the diamine **1d**.

The preferential reactivity of the ortho fluorine versus the para fluorine in **4** toward a variety of nucleophiles has already been well established in the synthesis of organofluorine intermediates,[17] pharmaceuticals,[18] and herbicides[19] to mention a few cases. The amount of specificity of reaction at the ortho and para positions is subject to a variety of electronic and steric influences. The addition of alcohols with varying degrees of ortho specificity has been studied in detail.[20] In some cases para addition, such as in the case of malonate addition, can be substantial or even predominate.[21] In the case at hand, the addition of ammonia to 2,4-difluoronitrobenzene (**4**) is highly regiospecific for the ortho position and the 2-amino-4-fluoronitrobenzene (**5**) is easily isolated pure in greater than 90% yield. The product has a melting point in agreement with that previously reported (97 °C) and significantly different from that reported for the other isomer (138 °C).[12] The high ortho specificity of this aromatic nucleophilic substitution on 2,4-difluoronitrobenzene is valuable for the preparation of a range of polymer intermediates, and some additional useful applications are being pursued.

The requisite 2,3-bis(4-fluorophenyl)quinoxalines **3a–d** were all prepared in good yield by reaction of the appropriate 1,2-phenylenediamine **1a–d** with commercially available 4,4′-difluorobenzil (**2**). Given the facile aromatic nucleophilic substitution on this monomer and subsequent elaboration of the benzil to other heterocycles, this material should also prove to be a very useful polymer intermediate.

To demonstrate the feasibility of nucleophilic aromatic substitution of para fluoride on a 2-phenyl ring as a result of activation by a pyrazine group, a model reaction between **3a** and *m*-cresol (**7**) was investigated (Scheme VI) in a NMP/CHP solvent mixture containing potassium carbonate. Since CHP is not miscible with water at elevated temperatures, water generated by phenoxide formation (140–150 °C) was effectively removed through the Dean–Stark trap. Upon dehydration (4–6 h), the reaction mixture was heated to 185 °C to effect the displacement reaction. The displacement of the fluoride at the 6-position of the quinoxaline using similar reaction conditions usually took 12–14 h to achieve quantitative conversion.[7] In contrast, the displacement from the 4-position of the 2-phenyl ring took approximately 36–40 h. TLC analysis (ethyl acetate/hexane) showed that quantitative conversion of **3a** had occurred with the formation of a single product peak. The expected product, **8**, was isolated as a single homogeneous product in high yield (>90%). The model reaction demonstrated that the activated aryl fluoride was cleanly displaced by phenoxides. The high

Scheme VII. Polymerization of Substituted 2,3-Bis(4-fluorophenyl)quinoxalines with Bisphenols



	Z	X	R		Z	X	R
11 a)	CH	H	H	12 a)	CH	H	F
b)	CH	CF_3	H	b)	CH	CF_3	F
c)	CH	COPh	H	c)	CH	COPh	F
d)	CH	SO_2Ph	H	d)	CH	SO_2Ph	F
e)	N	H	H	e)	N	H	F

selectivity and yield observed demonstrated that the transformation is suitable as a polymer-forming reaction.

Polymerization of bis(fluorophenyl)quinoxalines with various bisphenols was carried out in either a NMP/CHP solvent mixture or in DMPU containing potassium carbonate (Scheme VII). The potassium carbonate was used to convert the bisphenol into the more reactive bisphenoxide, and since potassium carbonate is a relatively weak and nonnucleophilic base, no hydrolytic side reactions with the 2,3-bis(4-fluorophenyl)quinoxalines were observed. As for the case of almost all poly(aryl ether) syntheses, dipolar aprotic solvents were used since they effectively solvate the monomers, polar intermediates, and in most cases the subsequent polymer. Furthermore, the formation of the Meisenheimer complex is strongly influenced by the solvent, and polar solvents tend to stabilize this complex, assisting the displacement reaction.[9] For this investigation we investigated two solvent systems: a NMP/CHP (50/50) mixture and DMPU. NMP and CHP allow high reaction temperatures, 200 and 260 °C, respectively, and these high polymerization temperatures are required in the preparation of rigid- or stiff-chain poly(aryl ethers) to maintain solubility. Although NMP tends to be a better solvent and easier to handle, NMP/CHP solvent mixtures are often used since CHP is not miscible with water at temperatures above 100 °C. Thus, nonpolar cosolvents used to azeotrope the water generated during the polymerization are not required. On the other hand, DMPU has been shown to be an excellent solvent for polyether syntheses and, in particular, those polymers which are only marginally soluble in other aprotic dipolar solvents.[22] Furthermore, DMPU allows high reaction temperatures (260 °C). As in the case for most poly(aryl ether) syntheses, the solids compositions were maintained at 20% to avoid side reactions with fluoride ion.[23] Irrespective of the polymerization solvent(s), toluene was used during the initial stages of the polymerizations to remove water generated by bisphenoxide formation as an azeotrope with toluene. This solvent mixture gave a reflux temperature between 150 and 165 °C. In an effort to maintain a dry system, the toluene was periodically removed through the Dean–Stark trap and replaced with deoxygenated dry toluene. Upon completion of bisphenoxide formation and dehydration, the polymerization mixtures were heated to 180–190 °C to effect the displacement reaction. In each case, high molecular weight polymer was attained within 48 h as judged by the dramatic increase in viscosity. The polymers were isolated by precipitation into a 10-fold excess of methanol and boiled in water to remove the remaining salts.

Table II. Polymer Characteristics

sample entry	polymerization solvent	$[\eta]^{25°C}_{NMP}$, dL/g	T_g, °C
11a	NMP/CHP	0.34	N/A[a]
11a	DMPU	0.55	195
12a	NMP/CHP	0.38	N/A[a]
12a	DMPU	0.43	190
11b	DMPU	insol	216
12b	DMPU	insol	212
11c	DMPU	0.40	209
12c	DMPU	0.56	210
11d	DMPU	0.45	225
12d	DMPU	0.75	212
11e	DMPU	0.40	218
11e	NMP/CHP	0.38	221
12e	NMP/CHP	0.40	220
14 ($n = m = 0.5$)	DMPU	0.52	189
14 ($n = 0.33$, $m = 0.67$)	DMPU	0.76	190

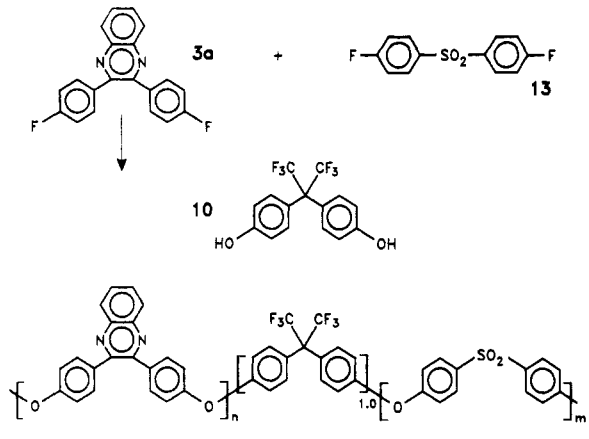
[a] Not available.

This general procedure was applied to each of the activated difluorides **3a–e** combined with either Bisphenol A (**9**) or Bisphenol AF (**10**), yielding polymer series **11** and **12**, respectively (Scheme VII). Moderately high molecular weight polymer was achieved in each case as indicated by the intrinsic viscosity measurements (Table II). Polymerization of the parent compound 2,3-bis(4-fluorophenyl)quinoxaline (**3a**) with either Bisphenol A (**9**) or Bisphenol AF (**10**) was carried out in both a NMP/CHP solvent mixture and DMPU. Polymerization in NMP/CHP appeared to have limited solubility at the desired solids composition at 190 °C, whereas polymerization in DMPU proceeded readily affording polymers **11a** and **12a**, respectively. There is a considerable difference in the molecular weight of the polymers, as judged by intrinsic viscosity measurements, as a result of the polymerization being performed in different solvents (Table II), and this presumably results from the improved polymer solubility in DMPU. Likewise, polymerization of the benzoyl-substituted monomer **3c** and the phenyl sulfone substituted monomer **3d** afforded high molecular weight polymers **11c** and **12c** by this procedure.

In contrast, the polymerization of the azaquinoxaline **3e** with bisphenols **9** and **10** did not produce as high molecular weight polymers **11e** and **12e** as the other activated difluorides in either DMPU or the NMP/CHP solvent mixture. The intrinsic viscosity values were moderate and in the 0.4 dL/g range (Table II). The limited viscosity buildup in these systems presumably resulted from the limited solubility and premature precipitation prior to quantitative monomer conversion. In the last system, polymerization of the trifluoromethyl-substituted quinoxaline **3b** with either bisphenol **9** or **10** initially produced high molecular weight polymer, but with extended polymerization times, as is required for full conversion, the system appeared to gel, presumably resulting from light cross-linking or polymer precipitation.

The solubility of most PPQs arises, in part, from the constitutional isomers in the polymer backbone. In this case isomers are possible also due to the unsymmetrical substitution at the 6-position (or aza substitution) and the preference for reactivity relative to these positions is unknown. The isomer content can significantly influence the solubility characteristics by disrupting the chain

Scheme VIII. Copolymers Incorporating Diphenyl Sulfone



14 (n=m=0.5 ; n=0.33, m=0.67)

packing precluding an ordered or semicrystalline morphology. Likewise, in the previously reported poly(aryl ether phenylquinoxalines) derived from 1,4-bis(2,3-diphenyl-6-fluoroquinoxalinyl)benzene, three distinct isomers were generated in the monomer-forming reaction and retained in the polymer as is analogous to the multiple isomeric phenylquinoxaline moieties formed in the PPQ synthesis. The resulting poly(aryl ether phenylquinoxalines) were soluble in many aprotic dipolar solvents and could be readily thermoformed via compression molding. Conversely, the poly(aryl ether phenylquinoxalines) **11a–e** and **12a–e** derived from **3a–e** were not as readily soluble in NMP or other common organic solvents at moderate solids compositions (>5%) at ambient temperatures. The limited solubility, even at 200 °C, may be responsible for moderate intrinsic viscosity values. These results are consistent with those of Connell et al. for similar poly(aryl ether phenylquinoxalines).[6] For their approach, bisphenols containing preformed quinoxaline heterocycles were prepared with and without isomers and polymerized with conventional activated dihalide monomers (i.e., 4,4'-difluorobenzophenone, 4,4'-difluorodiphenyl sulfone, etc.). The polymers derived from more symmetrical monomers also precipitated from solution during the polymerization in almost all solvents including NMP, DMAC, and even diphenyl sulfone at elevated temperatures. Once isolated, those polymers were only soluble in *m*-cresol, and intrinsic viscosity values in this solvent were approximately in the 0.5 dL/g range, consistent with the value reported in this paper.

The T_g's of **11a–e** and **12a–e** ranged from 190 to 225 °C depending on the bisphenol and activated difluoride used in the polymer synthesis (Table II). Polymers **11a** and **12a** had the lowest T_g's, while the polymers derived from the substituted monomers **3b–e** had somewhat higher T_g's. The T_g's found were consistent with the values reported by Connell[6] on related structures. The calorimetry measurements showed no evidence of crystallization or melting, consistent with an amorphous morphology. However, compression-molded films were somewhat opaque, indicating at least some low level of crystallinity. Likewise, Connell reported opaque films cast from *m*-cresol, and melting endotherms were observed for several of the polymers.

As a means of preparing a more soluble/processable poly(aryl phenylquinoxaline), random copolymers were synthesized in which the parent phenylquinoxaline containing difluoride **3a** was systematically replaced with 1 or 2 equiv of 4,4'-difluorodiphenyl sulfone (**13**; Scheme VIII). The polymerizations were conducted in an analogous fashion to the synthetic procedure described above, and the characteristics of the subsequent copolymers **14** are shown in Table II. The T_g's of the copolymers were in the 190 °C range depending on the amount of sulfone comonomer, and the molecular weights were high as judged by the intrinsic viscosity measurements (Table II).

Conclusions

Poly(aryl ether phenylquinoxalines) have been prepared by nucleophilic aromatic substitution in which in the generation of an aryl ether linkage is the polymer-forming reaction. We have demonstrated that fluorine at the para position of the phenyl rings of 2,3-diphenylquinoxaline can be displaced with phenoxides and supporting evidence for the reactivity at these sites comes from both ^1H and ^{19}F NMR spectroscopy. A series of fluoro-substituted phenylquinoxalines were prepared and subjected to fluoro displacement with two different bisphenols either in an NMP/CHP solvent mixture or in DMPU containing K_2CO_3. High molecular weight was easily achieved yielding polymers with T_g's ranging from 190 to 250 °C. This represents anoyther example of poly(aryl ether) synthesis based on aryl fluorides activated by a heterocyclic ring, and this synthesis can be considered the quinoxaline analogue of the poly(ether imide) synthesis. Moreover, heterocyclic-activated nucleophilic displacement chemistry should prove effective with monomers derived from other ring systems, providing a general synthetic methodology to high-temperature, high-T_g arylene ether heterocyclic polymers.

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