Aryl Fluoride Monomers in Nucleophilic Aromatic Substitution Polymerization: Evaluation of Monomer Reactivity by ^{19}F NMR Spectroscopy

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ABSTRACT: The reactivity of a number of aryl fluoride monomers used in nucleophilic aromatic substitution polymerization was explored utilizing ^{19}F NMR experiments. NMR is a valuable tool for evaluating the electron-withdrawing effect of substituents present on phenyl rings. When an electron-withdrawing group is present on a phenyl ring, a partial positive charge develops at the ortho and para positions through resonance interactions. While both ^{13}C and ^{19}F NMR were used to probe the electron density at the actual site of nucleophilic reaction, ^{19}F NMR chemical shifts proved to be the most sensitive probe with a chemical shift range spanning 2500 Hz between the most activated monomer examined, difluorodiphenyl sulfone, and nonactivated fluorobenzene. The ^{19}F shifts reflect the reactivity of the individual monomers examined. Taft inductive and resonance parameters were calculated for a series of monomers from ^{19}F data and used to identify activating forces for the monomers. NMR data were compared with calculated net atomic charges. Relative reactivity studies were also performed in order to verify the utility of this fast and convenient NMR probe of monomer reactivity.

Introduction

Among the many classes of high-performance materials available, poly(aryl ethers) have been shown to be useful, thermally stable polymers. One common route toward obtaining these polymers is through nucleophilic aromatic substitution polymerization. This route, first reported by Johnson and co-workers[1] in 1967, involves the nucleophilic displacement of activated dihalo aryl derivatives by bis(phenol) salts to yield high molecular weight poly(aryl ethers) where the generation of an aryl ether linkage is the polymer-forming reaction. This type of polymerization has been investigated in the intervening years, and the reaction mechanisms and conditions leading to most of the common poly(aryl ethers) (e.g. polysulfones and poly(ether ketones)) are rather well understood.[2,3]

The nucleophilic displacement of a halogen from an activated aryl halide system occurs in a two-step addition−elimination reaction (S_NAr). The nucleophile adds to the electron-deficient aryl halide, forming a negatively charged Meisenheimer complex from which the halide is eliminated, leading to the formation of an aryl−ether linkage. The activating group present in the aryl halide serves two purposes. The group must be an electron-withdrawing moiety, which decreases the electron density at the site of the reaction, and secondly, its presence must lower the energy of the transition state for the reaction by stabilizing the anionic intermediate formed. These S_NAr reactions only proceed if the electron-withdrawing substituent is located either in ortho or para positions relative to the halide.

The most commonly employed activating groups in these reactions have been sulfones, ketones, and more recently, phosphine oxides, which are all strongly electron withdrawing substituents. Aryl fluorides have been observed to be the most effective substrates of all the aryl halides for a number of reasons.[4] Poly(aryl ethers), made by nucleophilic aromatic substitution polymerization, contain the activating group as a part of the main chain of the polymer. Consequently, the resulting poly(aryl ethers) properties are often influenced by the activating group, as well as any other functionalities, present in the monomers.[5]

It has been demonstrated that other functional groups, some weakly electron withdrawing, can also activate aryl fluorides toward nucleophilic aromatic substitution.[1,6] Certain heterocycles (for examples, see refs 1 and 7−12) as well as other functional groups (e.g. perfluoroalkyl groups,[13] azines,[14] acetylenes,[15] etc.) can effectively activate aryl fluorides toward S_NAr reactions and many of these groups have been successfully used in the preparation of the corresponding poly(aryl ethers).

Though a number of different activating groups have been employed in poly(aryl ether) syntheses, there is little information available on relative reactivities of various monomers. No compilation of monomer reactivity exists, though certain trends have been noted. Hay and co-workers have reported Huckel molecular orbital calculations for the determination of the net charge densities at the C−F carbon atoms of a number aryl fluoride monomers.[15−17] They have stated that they were able to qualitatively correlate these calculated values with the relative reaction rates of the monomers in nucleophilic substitution, though no actual relative reaction rates were reported. Nonetheless, credible predictions of monomer reactivity containing several different types of activating groups were made on the basis of HMO calculations.

In our laboratory, it was of interest to find a spectroscopic probe that would allow the evaluation of a large number of potential monomers in regard to their ability to undergo these S_NAr-type polymerization reactions. Work performed in the preparation of poly(aryl ether triazoles)[8] and poly(aryl ether quinoxalines)[9] indicated that ^{19}F NMR could be used as a sensitive and convenient probe of a monomers ability to undergo transformation under standard S_NAr conditions. A preliminary report of the use of ^{19}F NMR in the evaluation of monomer reactivity has appeared recently.[18]

For this study, a wide range of aryl fluoride monomers were studied by ^{19}F NMR spectroscopy and it was shown

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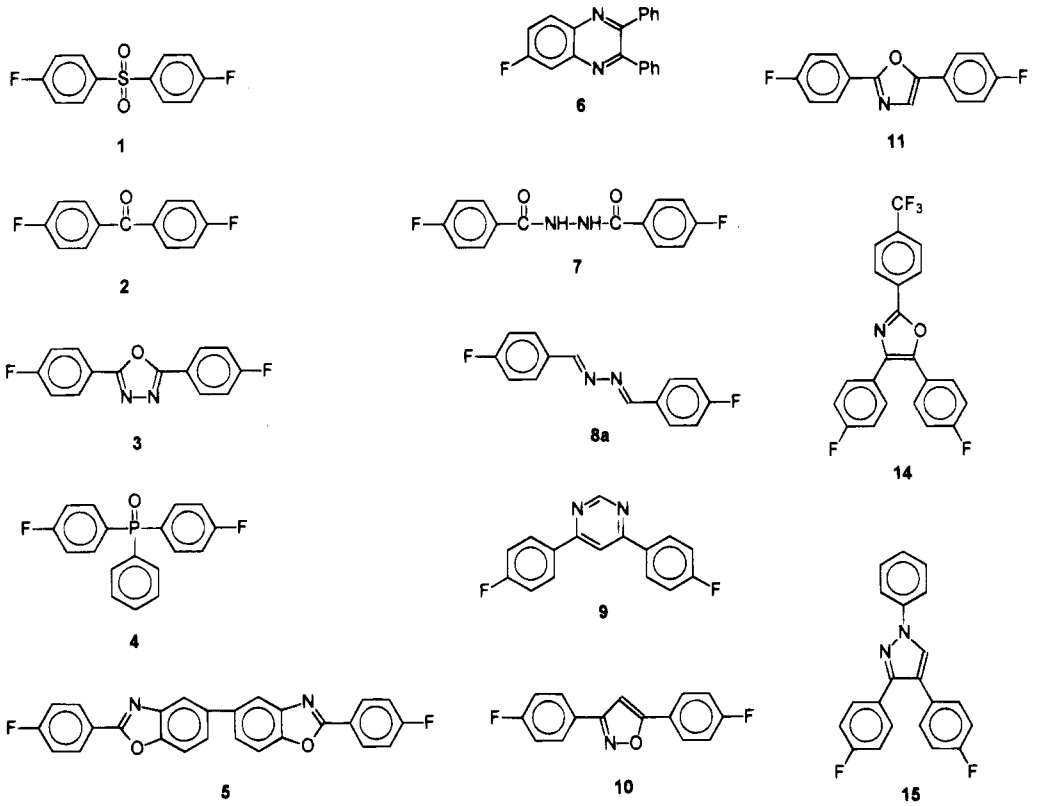


Figure 1. Structures of various aryl fluorides.

that there is indeed a correspondence between the observed chemical shifts and monomer reactivity. Competitive relative reactivity studies were performed in order to corroborate the observed ^{19}F NMR chemical shift correlations. The MNDO-PM3 semiempirical method was also used to calculate charge densities of the C–F carbons of selected aryl fluorides. These values were compared to experimentally measured ^{19}F NMR chemical shifts.

Experimental Section

Materials. All materials were commercially available and used as received unless otherwise noted. The materials utilized are shown in Figures 1–3. 2,5-Bis(4-fluorophenyl)-1,3,4-oxadiazole (**3**) and 2,5-Bis(4-methylphenoxy)-1,3,4-oxadiazole,[19a] the 2,5-bis(4-fluorophenyl)-1-aryl-1,3,4-triazoles (**12a–h**) and related model compound,[8] 2,3-bis(4-fluorophenyl)-quinoxaline as well as other related quinoxalines (**13a–e**),[9] 1,4-bis(4-fluorophenyl)-2,3-diaza-1,3-butadiene (azine) (**8a**),[8] and 3,4-bis(4-fluorophenyl)-1-phenylpyrazole (**15**)[19b] were prepared as described in the noted references. 2,3-Bis(4-fluorophenyl)-5-[4-(trifluoromethyl)phenyl]oxazole (**14**) was prepared in a manner similar to that described for other functional azoles.[19c]

Analyses and Instrumentation. NMR spectra were recorded on either an IBM WP 250 spectrometer operating at 250.1 MHz (^1H) or 62.9 MHz (^{13}C) or an IBM WP 300 spectrometer operating at 282.3 MHz (^{19}F). Tetramethylsilane (Me_4Si) was used as a reference for ^1H and ^{13}C NMR measurements while $CFCl_3$ was used as an internal standard for the ^{19}F NMR measurements with the reference peaks being assigned at 0.0 ppm. Chemical shifts upfield of the reference are assigned a negative sign and are reported in ppm. All samples for ^{19}F NMR were carefully prepared as dilute solutions (5% w/w) in DMSO-d_6. ^{13}C NMR measurements were performed using $CDCl_3$ as the solvent. Elemental analyses were performed by Oneida Research Services, Oneida, NY. HPLC was performed using a Waters 590 system (UV detector at 256 nm) fitted with a 30 cm Waters μ Bondpack C_{18} column with 20:80 acetonitrile/water as the eluent. Molecular geometries and net charge densities were calculated using the

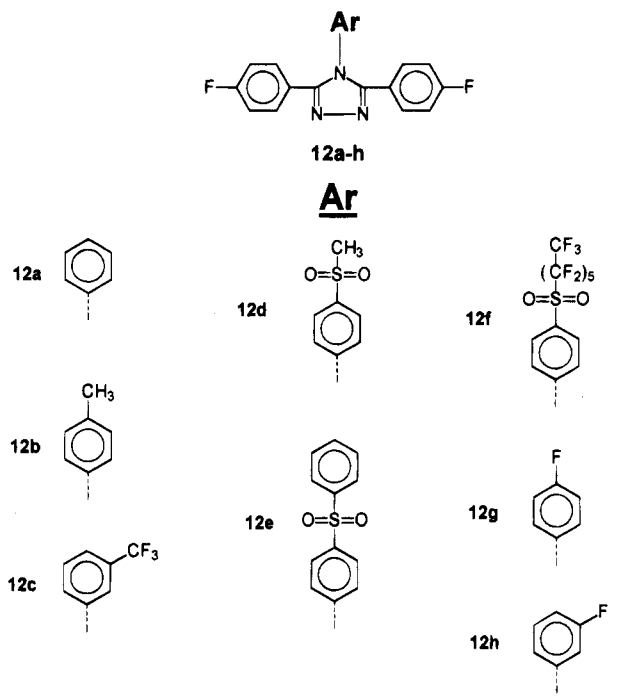


Figure 2. Structures of 2,5-bis(4-fluorophenyl)-1-aryl-1,3,4-triazoles (**12a–h**).

semiempirical PM3 procedure[20] within the commercially available MOPAC package. Initial molecular geometries were obtained by MMX molecular mechanics techniques contained within the ALCHEMY molecular graphics package.

Model Compounds. Model compounds were synthesized by reacting the desired aryl fluoride with *m*-cresol under standard S_NAr conditions. The compounds wer used as standards for relative reactivity studies.

4,4′-Bis(3-methylphenoxy)diphenyl Sulfone. A 15 mL three-neck flask fitted with an overhead stirrer and Dean-Stark trap was charged with 1.284 g (5.05 mmol) of **1**, 1.258 g

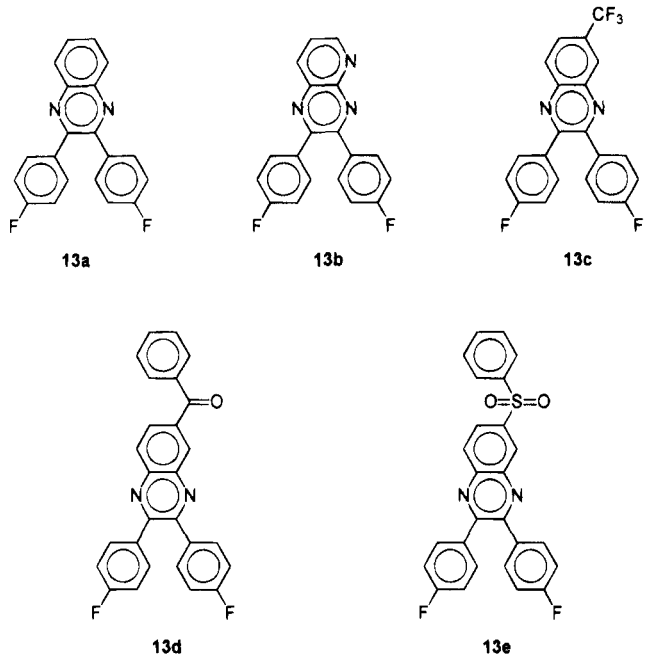


Figure 3. Structures of 2,3-bis(4-fluorophenyl)quinoxalines (**13a**–**e**).

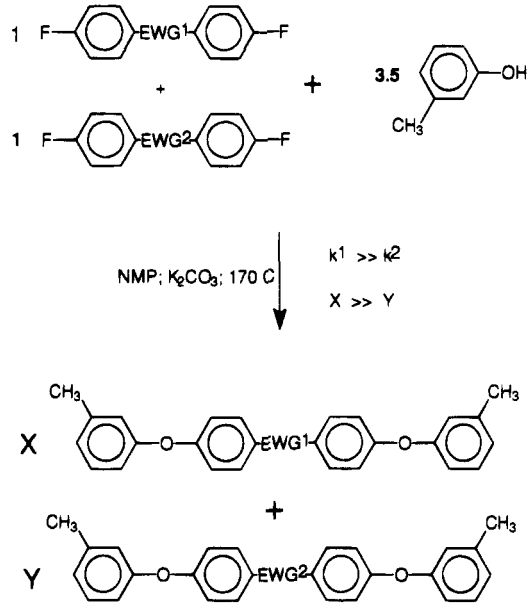
(11.63 mmol) of *m*-cresol, 1.95 g of K_2CO_3, and 6.2 mL of *N*-methyl-2-pyrrolidinone (NMP). A small amount of toluene was added to effect the azeotropic removal of water. This mixture was stirred and heated to 140 °C, at which point toluene was collected and removed from the system. The temperature was maintained for 5 h; more toluene was added periodically and subsequently collected and drained from the trap. The mixture was then heated to 165 °C for 4 h. The reaction mixture, which contained one product as indicated by HPLC, was cooled, diluted with 100 mL of $CHCl_3$, and washed successively with 10% HCl solution, saturated $NaHCO_3$ solution, and water. The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo to give a clear oily solid. The product was recrystallized from ethanol to give 1.82 g (84% yield) of white crystals: mp 83.5–84.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.86 (d, 4H), 7.27 (m, 2H), 7.02 (m, 6H), 6.85 (m, 4H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 161.96, 154.80, 140.39, 135.25, 129.73, 129.57, 125.71, 120.84, 117.54, 117.18, 21.21. Anal. Calcd for $C_{26}H_{22}O_4S$: C, 72.54; H, 5.15. Found: C, 73.10; H, 5.15.

Bis[4-(3-methylphenoxy)phenyl]methanone. A 15 mL three-neck flask fitted with an overhead stirrer and Dean-Stark trap was charged with 1.945 g (8.91 mmol) of **2**, 2.138 g (19.77 mmol) of *m*-cresol, 3.45 g of K_2CO_3, and 7.0 mL of NMP. The reaction was allowed to proceed as above. The solvent was removed in vacuo to give a clear oily solid. The product was recrystallized from ethanol to give 1.75 g (88% yield) of white crystals: mp 62–64 °C; ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 4H), 7.26 (m, 3H), 7.03 (m, 6H), 6.90 (m, 3H), 2.38 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 191.83, 171.53, 161.39, 155.52, 140.12, 132.10, 129.62, 125.22, 120.63, 117.06, 116.97, 21.28. Anal. Calcd for $C_{26}H_{22}O_4S$: C, 82.21; H, 5.62. Found: C, 82.03; H, 5.67.

Bis(3-methylphenoxy)phenylphosphine Oxide. A 15 mL three-neck flask fitted with an overhead stirrer and Dean-Stark trap was charged with 1.295 g (4.30 mmol) of **4**, 1.061 g (9.81 mmol) of *m*-cresol, 1.75 g of K_2CO_3, and 7.0 mL of NMP. The reaction was allowed to proceed as above. The solvent was removed in vacuo to give a pale yellow oil. The product did not recrystallize from ethanol but instead gave a clear thick liquid, 1.75 g (98% yield), which solidified at temperatures below 0 °C: ^{1}H NMR ($CDCl_3$) δ 7.65 (m, 1H), 7.60 (m, 4H), 7.48 (m, 3H), 7.24 (m, 3H), 6.99 (m, 6H), 6.84 (m, 4H), 2.33 (s, 6H). Anal. Calcd for $C_{26}H_{22}O_3P$: C, 75.53; H, 5.36. Found: C, 74.88; H, 5.96.

Competitive Relative Reaction Rates. A series of experiments was performed in which equimolar amounts of two aryl difluorides were reacted with a limited amount of *m*-cresol under standard S_NAr conditions (NMP, K_2CO_3, 170 °C, azeotropic removal of water by toluene) (Scheme 1). A known amount of biphenyl was added in each experiment as an internal standard. Aliquots of the reaction mixtures were taken every 15 min and analyzed by HPLC for product formation, so that plots of product formation vs reaction time could be made. These reactions were performed with pairs of monomers of varying reactivity: {**1** + **2**}; {**2** + **3**}; {**3** + **4**}, {**4** + **13a**}. The conditions employed in the competitive reaction of 2,5-bis(4-fluorophenyl)-1,3,4-oxadiazole (**3**) and bis(4-fluorophenyl)phenylphosphine oxide (**4**) with *m*-cresol are described as an example.

Scheme 1. Competitive Relative Reactivity Experiment



Reaction of 2,5-Bis(4-fluorophenyl)-1,3,4-oxadiazole and Bis(4-fluorophenyl)phenylphosphine Oxide with *m*-Cresol. To a 25 mL three-neck flask, fitted with an overhead stirrer and Dean-Stark trap, was added 0.892 g (3.31 mmol) of **3**, 0.998 g (3.31 mmol) of **4**, 0.511 g (3.31 mmol) of biphenyl, 1.08 g (9.99 mmol) of *m*-cresol, 2.6 g of K_2CO_3, and 14.0 mL of NMP. The reaction was allowed to proceed as in the above reactions. Small aliquots (0.5 mL) were removed from the reaction mixture every 15 min. Each aliquot was cooled, diluted with 5 mL of $CHCl_3$, and washed successively with 10% HCl solution, saturated $NaHCO_3$ solution, and water. The organic layer was dried over $MgSO_4$ and filtered. The samples were then examined by HPLC, and concentrations of products were determined. Since *m*-cresol was purposely employed at insufficient levels to allow for all reactants to be converted directly to the bis(3-methylphenoxy) products, the reactions were allowed to continue until all *m*-cresol was consumed. Product formation vs reaction time plots were generated for each experiment (Figure 4).

Results and Discussion

NMR is a valuable tool for evaluating the electron-withdrawing effect of aryl substituents.[21] When an electron-withdrawing group is present on a phenyl ring, a partial positive charge develops at the ortho and para positions through inductive and resonance interactions. Since the electron-withdrawing effect activates various aryl fluorides toward nucleophilic substitution (S_NAr) reactions, NMR can be used as a sensitive and convenient technique for the evaluation of substrates that may undergo transformation under S_NAr conditions. NMR chemical shifts are very sensitive to the electron density of particular nuclei of interest, and in the case of the aryl fluoride monomers, there are three NMR probes that can be utilized: ^{1}H, ^{13}C, and ^{19}F.

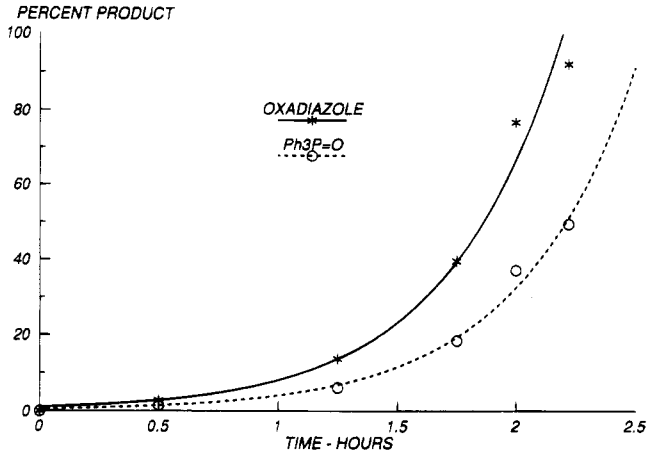


Figure 4. Plot of product formation vs reaction time in a competitive relative reactivity experiment involving an oxadiazole, **3**, and a phosphine oxide, **4**.

The magnetic shielding or chemical shift of a particular nucleus, A, in solution is dependent upon the shielding tensor σ^A. This magnetic shielding has a strong dependence on the electronic atmosphere around the nucleus due to the electrical currents and local magnetic fields generated by the circulation of electrons in local orbitals. This term can be represented as the sum of several terms:

$$\sigma^A = \sigma^{AA}_{dia} + \sigma^{AA}_{para} + \sum \sigma^{BA}_{intera} + \sigma'$$

The first term in the expression, the diagmagnetic term, takes into account the effect of electrons circulating about the nucleus in spherically symmetrical orbitals. This term is most important for the ^1H nucleus.

$$\sigma^{AA}_{dia} = \frac{\mu_0 e^2}{12m\pi} \sum_i \left\langle \frac{1}{r_i} \right\rangle$$

The second term, the paramagnetic term takes into account the effect of electrons in orbitals of nonspherical symmetry. This term is of primary importance for ^{13}C and ^{19}F nuclei.

$$\sigma^{AA}_{para} = -\frac{\mu_0 e^2 \hbar^2}{6m^2\pi} \langle \Delta E \rangle^{-1} \langle 1/r^3 \rangle_{2p} \sum q$$

The last two terms of the σ^A equation deal with interatomic contributions, such as intramolecular anisotropy and ring current effects, and solvent effects.

When performing experiments investigating effects such as the electron-withdrawing nature of a series of substituents, it is important to keep as many of the shielding terms constant as possible. Certain effects can be minimized by studying samples from dilute solutions and using the same solvent and internal standards when comparing data.

In earlier investigations of heterocyclic activation of aryl fluorides, the predictive use of ^1H NMR chemical shift data, involving the protons ortho to the electron-withdrawing group, was reported.[22] In those examples, the ortho proton resonances of potential monomers were compared with those found in aryl fluoride systems containing conventional activating groups (e.g. ketones or sulfones). While some information about a substituents electron-withdrawing ability can be obtained by ^1H NMR, the technique suffers from several disadvantages. There is a small chemical shift range of this nucleus, amounting to only about $\Delta\delta = 1$ ppm observed between nonactivated compounds and highly activated ones. Additionally, ^1H NMR shielding can vary significantly due to local intramolecular anisotropic effects, and the technique only surveys the site ortho to the electron-withdrawing gruop rather than the actual site of the substitution reaction. For these reasons, other NMR probes were sought (Figure 5a, ^1H NMR of **13a**).

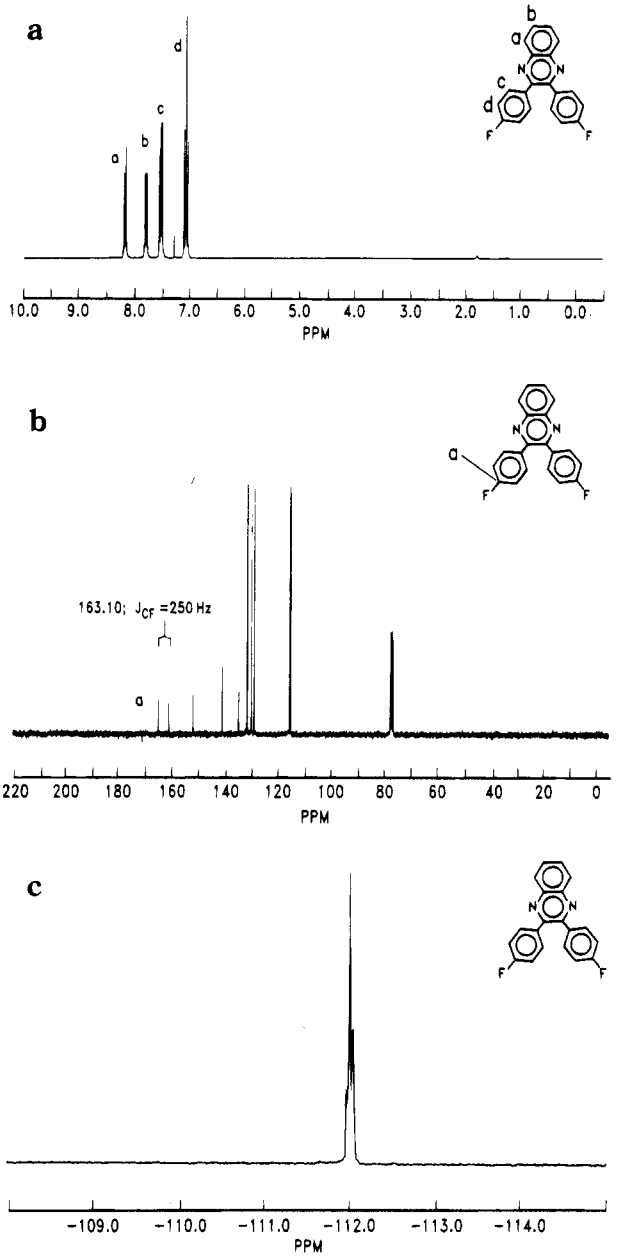


Figure 5. (a) ^1H NMR spectrum of **13a**. (b) ^{13}C NMR spectrum of **13a**. (c) ^{19}F NMR spectrum of **13a**.

Both ^{13}C and ^{19}F NMR can be used to probe the electron density at the actual site of nucleophilic reaction, i.e. the C–F bond of aryl fluorides. A large number of studies involving the use of ^{13}C NMR spectroscopy in the study of substituent effects have been reported and reviewed.[21,23,24]

For the aryl fluorides of interest in this study, the ^{13}C NMR chemical shifts of the carbon atoms para to electron-withdrawing groups in monomers which successfully undergo polymerization were found to range from δ 164.5 to 166.2 ppm, while the resonance of the unreactive molecule, fluorobenzene, is observed at δ

Table 1. NMR Chemical Shifts of Various Aryl Fluorides[a]

compound	^{13}C chemical shift[b]	^{19}F chemical shift[c]
4,4′-difluorodiphenyl sulfone (**1**)	165.31	−104.08
bis(4-fluorophenyl)methanone (**2**)	165.27	−106.01
2,5-bis(4-fluorophenyl)-1,3,4-oxadiazole (**3**)	165.55	−106.71
bis(4-fluorophenyl)phenylphosphine oxide (**4**)	165.05	−106.71
2,2′-bis(4-fluorophenyl)bibenzoxazole (**5**)		−106.83
2,3-diphenyl-6-fluoroquinoxaline (**6**)	164.8	−107.81
bis[(4-fluorophenyl)carbonyl]hydrazine (**7**)		−107.81
azine (**8a**)	164.50	−108.00
4,6-bis(4-fluorophenyl)pyrimidine[10] (**9**)		−109.42
3,5-bis(4-fluorophenyl)isoxazole[10] (**10**)		−109.81
		−110.73
2,5-bis(4-fluorophenyl)oxazole[11] (**11**)	164.07	−109.91
	162.70	−112.76
2,5-bis(4-fluorophenyl)-1-phenyl-1,3,4-triazole (**12a**)	163.38	−110.49
2,3-bis(4-fluorophenyl)quinoxaline (**13a**)	163.10	−111.99
4,5-bis(4-fluorophenyl)-2-[4-(trifluoromethyl)-phenyl]oxazole (**14**)		−110.54
		−112.27
fluorobenzene	162.82	−112.77
3,4-bis(4-fluorophenyl)-1-phenylpyrazole (**15**)		−113.29
		−114.88

[a] ^{13}C chemical shifts are reported in ppm relative to TMS = 0.0 ppm. ^{19}F chemical shifts are reported in ppm relative to CCl_3F = 0.0 ppm. [b] Performed on dilute solutions in $CDCl_3$. [c] Performed on dilute solutions in DMSO-d_6.

162.8 ppm. This corresponds to a usable frequency range of about 213 Hz when measured on a 250 MHz instrument, with a resolution of ±2 Hz. ^{13}C chemical shift data correspond well with the strength of various electron-withdrawing groups, as shown in Table 1. Unfortunately, when ^{13}C NMR experiments are performed on dilute samples, many scans are required due to the low sensitivity and low natural abundance of ^{13}C nuclei (Figure 5b). Quite often, the C−F carbon can be difficult to detect since it is a quaternary carbon atom and has a strong C−F coupling (J_{CF} = 250 Hz). For these reasons the use of ^{19}F NMR was explored.

Since we are concerned with the level of activation of the aryl fluoride bond, it is possible to use the fluoride atoms as probes of the strength of various electron-withdrawing groups. The use of ^{19}F NMR chemical shifts proved to be the most sensitive probe of reactivity with a chemical shift range spanning 9 ppm (2500 Hz) between the most activated monomer, 4,4′-difluorophenyl sulfone (−104.08 ppm) and nonactivated fluorobenzene (−112.77 ppm). Due to the high sensitivity of ^{19}F NMR and the ease of detection, this technique was used to study a series of aryl fluoride monomers (Figure 5c).

The ^{19}F chemical shifts of the series of monomers studied are listed in Table 1, and where available, the ^{13}C NMR chemical shift of the ipso carbon is also given. The monomers are listed in order of decreasing chemical shift, and Figure 6 shows a plot of ^{13}C and ^{19}F data. The plot shows that there is a good correlation between both the ^{13}C and ^{19}F NMR shifts (r = 0.98). The relative rates of reaction, as experimentally estimated by the time needed to form high molecular weight polymer, is related to the magnitude of the ^{19}F NMR chemical shifts; i.e. the lower the chemical shift, the lower the reactivity of that monomer. A correlation of these observations to actual monomer reactivity was performed and will be discussed below.

The electronic effects of various aryl fluoride monomers were also studied by calculating net charge densities using the semiempirical PM3 procedure within the MOPAC package. Initial molecular geometries were

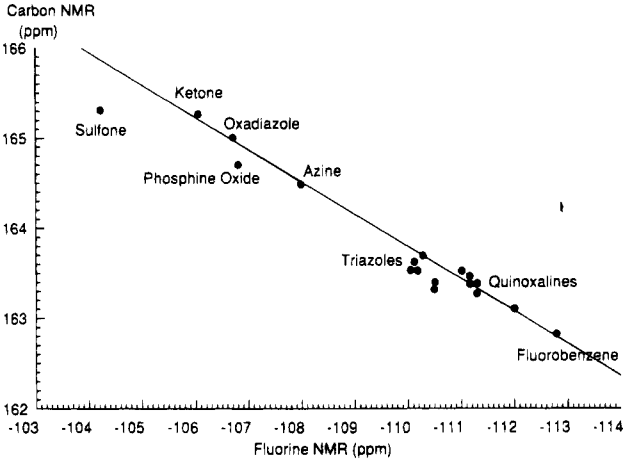


Figure 6. Plot of ^{13}C NMR chemical shifts vs ^{19}F NMR chemical shifts.

Table 2. Calculated Net Atomic Charges

compd	net atomic charge[a]
4,4′-difluorodiphenyl sulfone (**1**)	+0.1175
bis(4-fluorophenyl)methanone (**2**)	+0.0876
2,5-bis(4-fluorophenyl)-1,3,4-oxadiazole (**3**)	+0.0892
azine (**8a**)	+0.083
2,5-bis(4-fluorophenyl)-1-phenyl-1,3,4-triazole (**12a**)	+0.0748
fluorobenzene	+0.0647

[a] Calculated using the semiempirical PM3 procedure within the MOPAC package.

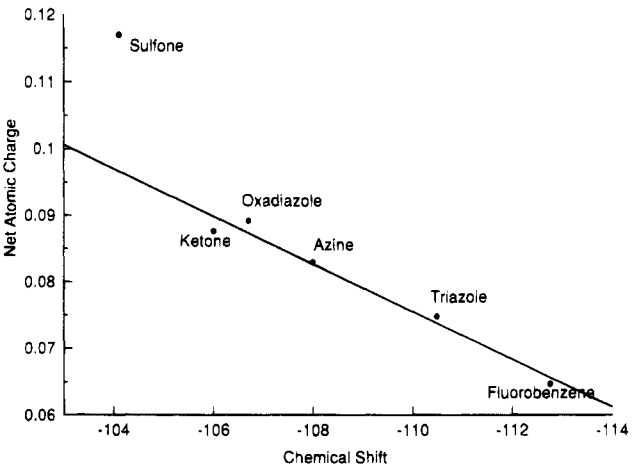


Figure 7. Plot of calculated net atomic charges vs ^{19}F NMR chemical shifts.

obtained by MMX molecular mechanics techniques contained within the ALCHEMY molecular graphics package. The electronic densities of the ispo carbons (C−F carbons) of **1, 2, 3, 8a, 12a,** and fluorobenzene were calculated (Table 2), and the values obtained were plotted against both the ^{19}F shift values (Figure 7) and ^{13}C shift values (Figure 8).

This is a fairly good agreement of the ^{19}F data and the calculated net atomic charge. The correlation is not as good with the ^{13}C data. The ^{13}C shifts of the oxadiazole, **3**, and ketone, **2**, monomers along with the calculate net atomic charges suggests that the oxadiazole monomer possesses a higher positive charge than that of the ketone monomer. If this is the case, then electronic charge cannot be the only quantity affecting the reactivity of aryl fluorides. Experimentally, the ketone monomer is clearly more reactive than the oxadiazole. If the calculated net atomic charge is

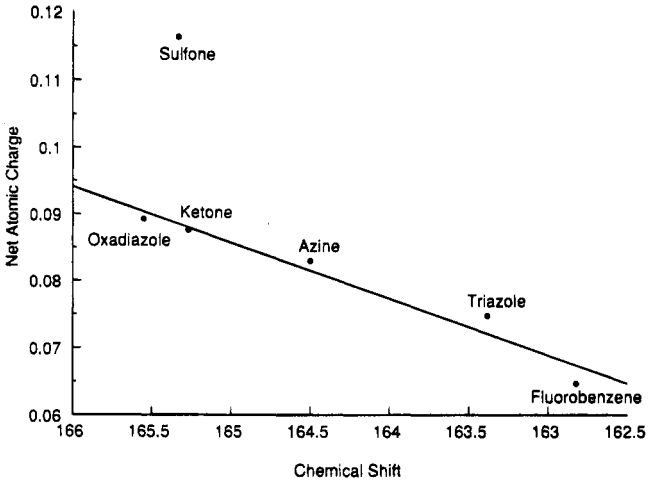


Figure 8. Plot of calculated net atomic charges vs ^{13}C NMR chemical shifts.

accurate, then another effect must be present that allows the ketone to be more reactive than the oxadiazole (e.g. steric effects, etc.). Also the sulfone monomer, which is the most reactive monomer studied, does not correlate with the slope of net atomic charge vs chemical shift magnitude. The C−F carbon of the sulfone monomer, **1**, clearly has a high net atomic charge, but perhaps the PM3 calculations do not necessarily represent the actual electronic nature of all of the monomers studied. In whole, both the ^{13}C and ^{19}F NMR data follow the calculated net atomic charges order fairly well (^{13}C, $r = 0.96$; ^{19}F, $r = 0.98$ when excluding the sulfone monomer), with the ^{19}F data more closely matching the actual experimental data. The calculated net atomic charges of the C−F carbon do not always match the actual monomer reactivities, though the general trends observed are similar. An examination of ^{1}H NMR data in relation to the calculated net atomic charges was also performed. Though there was a tendency of the ^{1}H data to vary with changes in atomic charge, there was a significant degree of scatter in the data.

The ^{19}F NMR technique allowed the screening of a large number of potential fluoromonomers in order to assess the feasibility of usage in nucleophilic substitution polymerization. Aryl fluorides with ^{19}F NMR chemical shifts equal to or less than −112.8 ppm (fluorobenzene) were deemed nonpolymerizable, and indeed, attempts to obtain high molecular weight polymers with these monomers were always unsuccessful regardless of the reaction conditions employed. In cases where the chemical shifts ranged between −110 and −112 ppm, interesting results were found. Two monomer classes studied by our research group fall within this range, the 2,5-bis(4-fluorophenyl)-1-aryl-1,3,4-triazoles[8] (**12a**−**h**) and the 2,3-bis(4-fluorophenyl)-6-quinoxalines[9] (**13a**−**e**). Initial polymerization attempts were carried out utilizing polymerization conditions commonly used with strongly activated monomers: NMP solvent with toluene reflux, K_2CO_3, with reaction temperatures around 180 °C for 24 h. Under these conditions, no high molecular weight polymers were obtained in these systems, due to the weak activating character of the monomers. When the reactions were performed in the solvent DMPU (dimethylpropyleneurea) at higher reaction temperatures (190 °C), high molecular weight polymers were obtained. DMPU has been shown to facilitate nucleophilic substitution reactions in cases where conventional polar aprotic solvents are ineffective.[25] The successful incorporation of these

Table 3. NMR Chemical Shifts of 1,3,4-Triazole Monomers[a]

compd	^{13}C chemical shift[b]	^{19}F chemical shift[c]
4,4′-difluorodiphenyl sulfone (**1**)	165.31	−104.08
bis(4-fluorophneyl)methanone (**2**)	165.27	−106.01
[(phenylsulfonyl)phenyl]triazole (**12e**)	163.54	−110.06
[(methylsulfonyl)phenyl]triazole (**12d**)	163.61	−110.10
[*m*-(trifluoromethyl)phenyl]triazole (**12c**)	163.53	−110.19
[[(perfluorohexyl)sulfonyl]phenyl]-triazole (**12f**)	163.83	−110.28
phenyltriazole (**12a**)	163.38	−110.49
(methylphenyl)triazole (**12b**)	163.32	−110.50
fluorobenzene	162.82	−112.77

[a] ^{13}C chemical shifts are reported in ppm relative to TMS = 0.0 ppm. ^{19}F chemical shifts are reported in ppm relative to CCl_3F = 0.0 ppm. [b] Performed on dilute solutions in DMSO-d_6. [c] Performed on dilute solutions in $CDCl_3$.

Table 4. ^{19}F NMR Chemical Shifts of Quinoxaline Monomers[a]

compd	chemical shift[b,c]
4,4′-difluorodiphenyl sulfone (**1**)	−104.08
bis(4-fluorophenyl)methanone (**2**)	−106.01
2,3-bis(4-fluorophenyl)-6-(phenylsulfonyl)-quinoxaline (**13e**)	−111.00 −111.16
2,3-bis(4-fluorophenyl)-6-(trifluoromethyl)-quinoxaline (**13c**)	−111.18 −111.31
2,3-bis(4-fluorophenyl)-6-benzoylquinoxaline (**13d**)	−111.29 −111.49
2,3-bis(4-fluorophenyl)-5-azaquinoxaline (**13b**)	−111.30 −111.51
2,3-bis(4-fluorophenyl)quinoxaline (**13a**)	−111.99
2,3-diphenyl-6-fluoroquinoxaline (**6**)	−107.81
fluorobenzene	−112.77

[a] NMR performed on dilute solutions in DMSO-d_6. [b] Chemical shifts are reported in ppm relative to CCl_3F = 0.0 ppm. [c] Several compounds have two reasonances due to asymmetry.

monomers into poly(aryl ether) systems shows that even polymers derived from weakly activated monomers, as identified by NMR, can be attained through modification of reaction conditions.

A closer examination of other weakly activated fluoro monomers reveals the sensitivity of the NMR technique. In the case of 1,3,4-triazole monomers, **12a**−**f**, an interesting observation is that the relative rates of reaction, as estimated by the time needed to form high molecular weight polymer, were consistent with the predictions based on the ^{19}F NMR chemical shifts of the monomers.[8] Although actual rates were not measured, the relative reactivity of the triazole monomers was in the order shown in Table 3, with the 1-phenyl and 1-(4-methylphenyl) **12b** being the least reactive and the 1-[(phenylsulfonyl)phenyl] **12e** reacting the fastest. Similarly, the molecular weights of the polymers derived from the more activated triazoles appear to be higher than those from less activated monomers. In that study, it was shown that credible predictions were possible even though the spread of chemical shifts in the triazole monomers was very small ($\Delta\delta$ = 0.44 ppm, ~125 Hz). A similar effect was noted in the study of 2,3-bis(4-fluorophenyl)quinoxalines.[9] These monomers are even more deactivated than the triazoles, with chemical shifts ranging from −111 to −111.99 ppm. The list in Table 4 reflects the qualitative rate of reaction among the quinoxalines, **13a**−**e**. The most active monomer, 2,3-bis(4-fluorophenyl)-6-(phenylsulfonyl)quinoxaline (**13e**), 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 (**13a**) with δ −111.99. Stringent reaction conditions were required to synthesize high molecular weight polymers derived from all of the quinoxaline monomers.

Bass *et al.* have studied some other weakly activated aryl fluoride monomers as well, examining pyrimidine and isoxazole heterocycles as activating groups.[10] The ^{19}F shifts of the isoxazole monomer (**10**) were reported at δ −109.81 and −110.73 (again two resonances are observed due to the nonsymmetrical nature of the monomer) and that of the pyrimidine monomer (**9**) at δ −109.42. These ranges suggest that both should be able to yield high molecular weight poly(aryl ethers) if reaction conditions were altered to account for the low monomer reactivity. Though no information is given about attempts to polymerize the isoxazole monomer, the pyrimidine monomer was successfully incorporated into a poly(aryl ether). The authors do report that the polymer obtained from **9** is of low molecular weight, but the polymerization conditions described in their study were different than those that have been employed by our group. Similarly, Maier *et al.* have reported the successful polymerization of a 2,5-bis(4-fluorophenyl)-oxazole (**11**).[11] In that case, the monomer had ^{19}F shifts at δ −109.91 and −112.76. The low value of −112.76 ppm suggests that the aryl fluoride should have a very low reactivity. That is, in fact, the case with the monomer giving high molecular weights only when the reaction is performed at high temperatures (200 °C), in DMPU, for 20 h. The ability of this monomer to undergo polymerization under these conditions is an indication of its high thermal stability and lack of side reactions that one can experience under these conditions.

Repeated attempts at polymerizations and model reactions were performed on 4,5-bis(4-fluorophenyl)-2-[4-(trifluoromethyl)phenyl]oxazole (**14**) which has ^{19}F δ −110.54 and −112.27. Reaction conditions similar to those employed in the synthesis of the 1,3,4-triazoles and 2,3-bis(4-fluorophenyl)quinoxalines were employed (NMP or DMPU; >180 °C). No desired products were obtained. Model reaction studies revealed that in addition to a variety of degradation products, only one of the fluorophenyl groups of **14** undergoes substitution by the nucleophile, the aryl fluoride resonance at δ −112.27 is still observed in the product of the reaction of **14** and *m*-cresol. The failure of this monomer to polymerize shows that as the activation of the aryl fluoride decreases, a point is reached either where the S_NAr reaction will no longer take place or where other high-temperature degradation reactions preclude the formation of high molecular weight polymer. We examined various other aryl fluorides (e.g. 3,4-bis(4-fluorophenyl)-1-phenylpyrazole (**15**) that were shown to be electron donating as compared to fluorobenzene and found that none of these would undergo nucleophilic aromatic substitution.

In addition to providing relative reactivity information about aryl fluorides, ^{19}F NMR can be used to calculate the Taft substituent parameters σ_I and σ_R^0 [26] (see Table 5). These parameters are a relative measure of inductive and resonance effects in substituted aryl rings, where $\int H^{m-x}$ and $\int H^{p-x}$ are the differences in chemical shift of meta- and para-substituted aryl fluorides as compared to fluorobenzene.[26] The value of σ_R^0 is a better measure of conjugative interactions between the phenyl ring and the substituent than σ_I which is mainly influenced by inductive effects. Many of the more weakly activated monomers rely on their ability to stabilize the anionic intermediate through resonance interactions. These same monomers have little contribution due to electron withdrawal through inductive effects. Conversely, the highly activated monomer, difluorodiphenyl sulfone, has a very large σ_I, +0.52, which accounts for its high reactivity even though its σ_R^0 at 0.14 is not significantly different from values found for other activating groups. The trifluoromethyl group also has a considerable contribution from inductive effects. Indeed, we have shown that trifluoromethyl groups can activate ortho-nitro groups toward S_NAr reactions to yield new poly(aryl ethers).[27] Labadie *et al.* have also shown that other perfluoroalkyl groups can serve as good activating groups for S_NAr reactions.[28]

$$\sigma_I = 0.1409(0.6 - \int H^{m-x})$$

$$\sigma_{R^0} = 0.0339(\int H^{m-x} - \int H^{p-x})$$

Table 5. Taft Inductive and Resonance Parameters

electron-withdrawing group	σ_I	σ_R
NO_2	+0.56	+0.20
COPh	+0.19	+0.18
SO_2Ph	+0.52	+0.14
azine (C=N−N=C)	+0.18	+0.14
CF_3	+0.38	+0.10
2,5-triazole rings	+0.17	+0.05
H	+0.08	0.00
1-triazole ring	+0.49	−0.02
CH_3	−0.08	−0.15
$N(CH_3)_2$	+0.10	−0.54

A comparison of the Taft parameters calculated for the 2,5-diphenyl and the 1-phenyl rings of the 1,3,4-triazole heterocycle is shown in Table 5. It can be seen that the conjugative electron withdrawal by the triazole ring from the 2,5-diphenyl substituents is small, ranging somewhere between that of CF_3 and H, while inductively, the triazole ring is mildly activating. Both values are smaller than those found in conventional monomers such as ketone or sulfone activated systems. The triazole is actually found to be weakly donating to the 1-phenyl ring, an anticipated result since the substituent is directly attached to the trisubstituted nitrogen atom of the heterocycle.

In the case when an azino group is the activating group (**8a**), one sees a larger value for σ_R^0 than observed with the triazole ring, indicating a greater amount of electron withdrawal through resonance effects with the azino functionality. Experimental results show that aryl fluorides activated by the azino group are much more reactive than the triazole-activated monomers. The calculation of the Taft reactivity parameters σ_I and σ_R^0 from NMR data can give a good deal of information on the degree of activation of various substituent groups.

In order to corroborate the reactivity observations with the NMR data, competitive relative reactivity studies were conducted. The competitive reactions were designed to assess activated fluoro monomers reactivities in relation to each other. The reaction conditions were kept as close to those employed in the synthesis of poly(aryl ethers) as possible. Equimolar amounts of two aryl fluorides were allowed to react with a limiting amount of *m*-cresol. As the nucleophilic aromatic substitution reactions proceeded, small aliquots of the reaction mixture were analyzed by HPLC and quantitative information was obtained by employing the use of a nonreactive internal standard, biphenyl. The study required the synthesis of the appropriate 3-methylphenoxy derivatives of the aryl fluoride monomers studied (**1, 2, 3, 4, 13a**). These derivatives were isolated,

Table 6. Relative Reactivities of Selected Aryl Fluorides

compd	relative reactivity[a]	^{13}C shift	^{19}F shift
4,4′-Difluorodiphenyl sulfone (**1**)	57140	165.31	−104.08
bis(4-fluorophenyl)methanone (**2**)	9080	165.27	−106.01
2,5-Bis(4-fluorophenyl)-1,3,4-oxadiazole (**3**)	510	165.55	−106.71
Bis(4-fluorophenyl)phenylphosphine oxide (**4**)	230	165.05	−106.71
2,3-Bis(4-fluorophenyl)quinoxaline (**13a**)	1	163.10	−111.99

[a] Reactivities relative to **13a**.

purified, and calibrated on the HPLC using biphenyl as an internal standard. The individual relative reactivity reactions were performed between pairs of monomers of decreasing reactivity: {**1** + **2**}, {**2** + **3**}, {**3** + **4**}, {**4** + **13a**}. Though all experiments were carried out under similar reaction conditions (NMP solutions of the monomers, *m*-cresol, biphenyl, heated to 170 °C in the presence of K_2CO_3 with azeotropic removal of water with toluene), small temperature variations during heating and slight concentration differences during heating and slight concentration differences between different reactions prevented the calculation of any absolute reactivity rates. The data obtained were a good measure of relative reactivity between the monomer pairs studied and are shown in Table 6.

The first pair chosen, {**1** + **2**}, are widely used aryl fluoride monomers that are known to undergo facile nucleophilic substitution. From Table 1, it was expected that the sulfone-activated monomer, **1**, with a ^{19}F NMR shift of −104.08 ppm, would be more reactive than the ketone-activated monomer, **2**, which has an observed shift of −106.01 ppm. Indeed this was the case. As the reaction proceeded, it was clear that the sulfone monomer reacted preferentially with the *m*-cresol, with the reaction going to completion in under 1.5 h. The ketone monomer reacted only to 20% in the same period of time. At the first hour of the reaction, the data indicated **1** was reacting approximately 6 times as fast as **2**. This shows that the sulfone is clearly more reactive than the ketone under these reaction conditions.

The next pair studied, {**2** + **3**}, showed the same trend with **2** (^{19}F δ −106.01), being about 18 times more reactive than **3** (^{19}F δ −106.71). In this case, the ketone monomer was quantitatively converted to the 3-methylphenoxy derivative in 2.5 h with only 27% of the oxadiazole monomer reacting in the same amount of time. The reaction {**3** + **4**} was of interest because the chemical shifts of those monomers were both observed at −106.71 ppm. A plot of reaction progress vs time is shown in Figure 4. The oxadiazole monomer, **3**, reacted slightly faster than the phosphine oxide monomer, **4**. The rate of the reaction was only about 2 times greater in this case, which was the smallest observed difference between any two monomer pairs studied. This corresponds well to the ^{13}C NMR data and follows the trend in reactivity expected.

The last pair examined shows the difference between a strongly activating group, the phosphine oxide, **4**, and the weakly activated quinoxaline monomer, **13a**. The chemical shift difference between these two is 5.1 ppm, and we have previously reported the weak activating character of the quinoxaline monomers.[9] In this case the large difference in reactivity was clearly seen with **4** being 230 times more reactive than **13a**. In fact, while complete conversion of **4** was observed in less than 5 h, the quinoxaline monomer did not reach complete conversion until after 24 h.

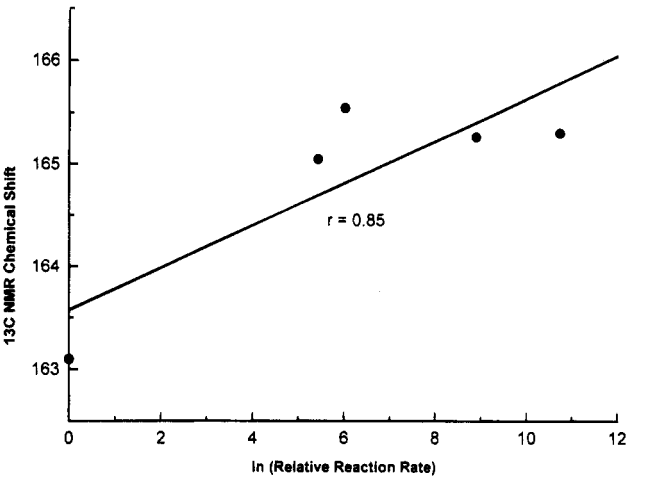


Figure 9. Plot of ^{13}C NMR chemical shift vs ln(relative reaction rate).

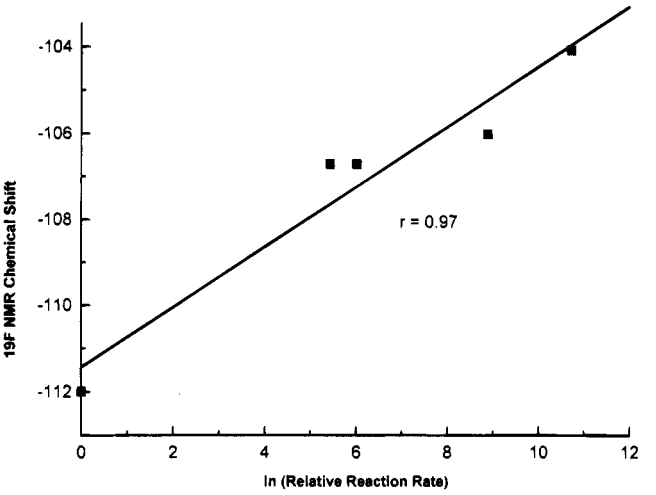


Figure 10. Plot of ^{19}F NMR chemical shift vs ln(relative reaction rate).

These competitive reactivity experiments clearly show that there is a relationship between monomer reactivity and observed ^{19}F NMR chemical shifts. Assuming that the magnitude of the ^{13}C or ^{19}F shift is proportional to the activating energy of the substitution reaction, E_a, and using the relative rates obtained experimentally, one can see if the experimental data obtained follows the Arrhenious equation, $k = Ae^{-E_a/RT}$. Therefore $k \sim$ relative reaction rate $\sim e^{-E_a/RT}$, so ln(relative reaction rate) $\sim E_a$. A comparison of ^{13}C and ^{19}F chemical shifts vs relative reactive rates was performed and shown in Figures 9 and 10. The ^{19}F NMR data fit well ($r = 0.97$) while the ^{13}C NMR data give a much less satisfactory fit ($r = 0.85$). While the series of monomers studied clearly does not represent all of the many classes of activating groups available, it is a good data set to represent monomers with a wide range of relative reactivities. Using this series as a guide, one can measure the ^{19}F NMR shift of a monomer and be able to predict with resonable certainty whether it is strongly, moderately, or weakly activated. More work needs to be done to determine the precise empirical relationship between ^{19}F NMR shifts and E_a.

Conclusions

The use of ^{19}F NMR spectroscopy to evaluate potential aryl fluoride monomers as candidates for nucleophilic aromatic substitution polymerization has been shown

to be an accurate and time-saving technique. Since the ^{19}F shift is controlled by the electron density of the carbon to which it is attached, the magnitude of the ^{19}F chemical shift can be related to the degree of activation of aryl fluorides by various electron-withdrawing groups. The larger the magnitude of the shift, the more activated the compound, with reactivity dropping off as the observed chemical shift approaches that of fluorobenzene.

Net atomic charge calculations were performed on a group of aryl fluorides, and the values obtained were compared to the NMR data. The magnitude of the positive charge that develops on the carbon atom para to an electron-withdrawing groups can be related to the activating strength of the substituent. There was good agreement of calculated data and NMR data, though in some cases the calculated data did not match the actual reactivities of the aryl fluorides. The ^{19}F measurements appear to be a better gauge of reactivity of aryl fluorides than calculated values, ^{1}H shifts, or ^{13}C shifts. The use of ^{19}F shifts to measure reactivity was supported by relative reactivity experiments between selected monomer pairs. In all cases, the reactivity of the aryl fluorides could be predicted by the magnitude of the ^{19}F NMR shifts. Furthermore, ^{19}F NMR data can be used to calculate Taft inductive and resonance parameters for particular electron-withdrawing groups. These values can be used to ascribe the predominate mechanism of electron withdrawal, inductive vs resonance, present in any particular aryl fluoride monomer system.

In order to take advantage of the use of ^{19}F NMR, care should be taken during sample preparation and in interpreting the NMR data. All samples must be prepared at low dilutions, and comparisons can only be made when all spectra are obtained in the same solvent. It is important to note that even though the use of ^{19}F shifts can give a good deal of information about the electron-withdrawing ability of various substituents, an activated aryl fluoride still may not be a suitable monomer if side reactions involving other functional groups present in the molecule preclude successful polymerization.

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References and Notes

(1) Johnson, R. N.; Farnham, A. G.; Clendinning, R. A.; Hale, W. F.; Merriam, C. N. *J. Polym. Sci., Polym. Chem. Ed.* **1967**, *5*, 2375.
(2) Maiti, S.; Mandai, B. K. *Prog. Polym. Sci.* **1986**, *12*, 111.
(3) Rose, J. B. *Polymer* **1974**, *15*, 456.
(4) Bunnett, J. F.; Zahler, R. E. *Chem. Rev.* **1951**, *49*, 273.
(5) Maiti, S.; Mandal, B. K. *Prog. Polym. Sci.* **1986**, *12*, 111.
(6) Labadie, J. W.; Hedrick, J. L. *Makromol. Chem., Macromol. Symp.* **1992**, *54/55*, 313.
(7) Carter, K. R.; Twieg, R.; Hedrick, J. L.; Jonsson, H.; Miller, R. D. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1992**, *33* (1), 388.
(8) Carter, K. R.; Miller, R. D.; Hedrick, J. L. *Macromolecules* **1993**, *26*, 2155.
(9) Hedrick, J. L.; Twieg, R. J.; Matray, T.; Carter, K. R. *Macromolecules* **1993**, *26*, 4833.
(10) Herbert, C. G.; Bass, R. G.; Watson, K. A.; Connell, J. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1994**, *35* (2), 703.
(11) Schneider, J. M.; Maier, G.; Nuyken, O. *Makromol. Rep.* **1994**, *A3*, 179.
(12) Hay, A. S.; Singh, R. *Macromolecules* **1992**, *25*, 1033.
(13) Carter, K. R.; Kim, S. Y.; Labadie, J. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1993**, *34*, 415.
(14) Carter, K. R.; Hedrick, J. L. *Macromolecules* **1994**, *27*, 3426.
(15) Strukelj, M.; Paventi, M.; Hay, A. S. *Macromolecules* **1993**, *26*, 1777.
(16) Yeomans, K. A.; Hay, A. S. *Polym. Mater. Sci. Eng.* **1993**, *69*, 241.
(17) Strukelj, M.; Hamier, J.; Elce, E.; Hay, A. S. *J. Polym. Sci., Polym. Chem.* **1994**, *32*, 193.
(18) Carter, K. R. *Proc. PMSE* **1993**, *69*, 432.
(19) (a) Hedrick, J. L.; Twieg, R. J. *Macromolecules* **1992**, *25*, 2021. (b) Fickes, G. N.; Miller, R. D. Unpublished results. (c) Moylan, C. R.; Miller, R. D.; Twieg, R. J.; Betterton, K. M.; Lee, V. Y.; Matray, T. J.; Nguyen, C. *Chem. Mater.* **1993**, *5*, 1499.
(20) (a) Stewart, J. *Comput.-Aided Mol. Des.* **1990**, *4*, 1. (b) Stewart, J. *J. Comput. Chem.* **1989**, *10*, 209.
(21) Craik, D. J. In *Annual Reports on NMR Spectroscopy*; Webb, G. A., Ed.; Academic Press: London, 1978; Vol. 15, pp 1–104.
(22) Hedrick, J. L.; Labadie, J. W. *Macromolecules* **1990**, *23*, 1561.
(23) Craik, D. J.; Brownlee, R. T. C. *Prog. Phys. Org. Chem.* **1983**, *14*, 1.
(24) Nelson, G. L.; Williams, E. A. *Prog. Phys. Org. Chem.* **1976**, *12*, 229.
(25) Labadie, J. W.; Carter, K. R.; Hedrick, J. L.; Jonsson, H.; Twieg, R. J.; Kim, S. Y. *Polym. Bull.* **1993**, *30*, 25.
(26) (a) Hehre, W. J.; Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 159. (b) Taft, R. W.; Price, E.; Fow, I. R.; Lewis, I. C.; Andersen, K. K; Davis, G. T. *J. Am. Chem. Soc.* **1963**, *85*, 3146. (c) Kaplan, L. J.; Martin, J. C. *J. Am. Chem. Soc.* **1973**, *85*, 793.
(27) Carter, K. R.; Kim, S. Y.; Labadie, J. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1993**, *34* (1), 415.
(28) (a) Kim, S. Y.; Labadie, J. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1991**, *32* (1), 164. (b) Labadie, J. W.; Hedrick, J. L. *Macromolecules* **1991**, *24*, 812.

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