Kinetic Studies on the Nucleophilic Aromatic Substitution of Fluoronitrobenzene Derivatives with Polyvinylamine in Water Mediated by 2,6-*O*-Dimethyl-β-cyclodextrin

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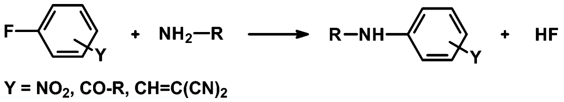
ABSTRACT: Nucleophilic substitution of fluoronitroaromatics with polyvinylamine (PVAm) is a suitable method for producing various nitrophenyl-functionalized PVAm's. This functionalization reaction of PVAm has been studied in detail using kinetic measurements, and the degree of functionalization has been determined using model compounds as the reference system. 2-Fluoronitrobenzene (2-FNB), 4-fluoronitrobenzene (4-FNB), 1-fluoro-2,4-dinitrobenzene (Sanger's reagent), and 1,5-difluoro-2,4-dinitrobenzene (DFDNB) have been used as functionalization reagents. The solubility of the reagents in water was mediated by complexation with 2,6-*O*-β-dimethylcyclodextrin (β-DMCD). UV/vis spectroscopic measurements have been used to determine the degree of functionalization, rate constants, and activation energies of the nucleophilic aromatic substitution reaction. Correlation of structure and reactivity is discussed. On increasing the number of electron-withdrawing groups, the activation energies decrease. Ortho-nitro-substituted reagents require lower activation entropy than the related para-substituted reagents.

Introduction

Polyvinylamine (PVAm) is a commercially available polyelectrolyte with widespread applications.[1−6] The cationic form of the polymer possesses the highest known charge density along the polymer backbone. Furthermore, the primary amino groups of the PVAm units can be used for many chemical postderivatization reactions.[1−4,7] Nucleophilic substitution reactions of fluoroaromatics with PVAm offer great synthetic potential for incorporating chromophoric groups directly into the polymer backbone because a push−pull substituted aromatic system is formed in only one step (Scheme 1).[7]

Scheme 1. General Reaction Scheme for the Nucleophilic Aromatic Substitution of Fluoro Compounds with Primary Amines to Push−Pull Systems (Y: Electron-Withdrawing Group)



Higher molecular weight PVAm (M_n > 1500 g mol^{-1}) is only soluble in water, which makes postderivatization reactions difficult because fluoronitroaromatic compounds are, for example, sparingly soluble or insoluble in water. Thus, the nucleophilic aromatic substitution of water-soluble polymers with water-insoluble reagents is difficult to achieve because the micelle technique cannot be applied cleanly to polyelectrolytes.[8−10] In a related synthesis, Jang et al. precipitated the polyallylamine polymer, and a dissolution in DMSO has also been carried out.[11] This method is impracticable for polyvinylamine because dissolution cannot be effected as the dried polymer only swells in DMSO or alcohol. Unfortunately, hot DMSO is unsuitable as alternative solvent for derivatization reactions of polyvinylamine because of its oxidizing properties. Bellamy et al. investigated the nucleophilic substitution reaction of linear polyethylenimine with picryl chloride in *N*-methylpyrrolidone and of PVAm with picryl chloride in an ethylene glycol/methanol mixture.[12] Because of the high reactivity of picryl chloride, reaction with the alcoholic solvents was also observed.

Cyclodextrins have become established for several applications in polymer science to confer solubility to water-insoluble reagents in aqueous solutions.[13−17] In a previous paper we reported the nucleophilic aromatic substitution of activated fluoroaromatic compounds with PVAm in water mediated by cyclodextrins.[7] According to Ritter, the 2,6-*O*-dimethyl-β-cyclodextrin (β-DMCD) derivative has been found to be suitable. We have also found that only strongly activated fluoroaromatic compounds with strong −M substituents are suitable for successful nucleophilic substitution of PVAm in water.[7] It is expected that with increasing the number of electron-withdrawing groups at the fluoro-substituted benzene ring the fluoride ion is a better leaving group compared to nonsubstituted fluorobenzene.[18−20] Thus, 4-fluorobenzophenone or 4-fluorobenzonitrile is not suitable for this purpose. The nucleophilic substitution of fluoroaromatics is strongly determined by several structural features of the fluoroaromatic compound and the amine as well as environmental effects, such as solvent polarity.[21−28]

To demonstrate the synthetic potential of this elegant reaction to produce chromophoric water-soluble polymers for several applications, a deeper understanding of this reaction is required. To get a better insight into the course of this reaction, a reactivity study has been carried out using kinetic measurements. Because fluoro-substituted benzophenones and fluoronitriles have been found to be less reactive, fluoronitroaromatics have been investigated in detail. The following fluoroaromatic compounds were chosen for the kinetic study: 2-fluoronitrobenzene (2-FNB), 4-fluoronitrobenzene (4-FNB), 1-fluoro-2,4-dinitrobenzene (Sanger's reagent), and 1,5-difluoro-2,4-dinitrobenzene. Figure 1 shows the syn-

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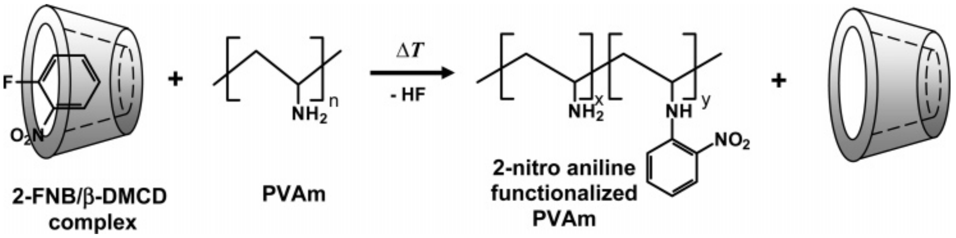


Figure 1. Cyclodextrin-mediated nucleophilic aromatic substitution with PVAm in water shown for the reaction of the 2-fluoronitrobenzene/β-DMCD complex with PVAm to 2-nitrophenyl-functionalized PVAm ($n = x + y$).

thetic concept for the example of the nucleophilic aromatic substitution of the 2-FNB/β-DMCD complex with PVAm in water.

The choice of the fluoronitroaromatic reagents is also based on the fact that introduction of nitroaniline derivatives in polymers is of special interest because these functionalities have been widely used in materials science (NLO)[21,22] and analysis (solvatochromism).[23−28] There are a large number of substituted 4-nitroaniline derivatives which are used as solvent-sensitive indicators for setting up polarity scales,[23−25] as lipophilic indicators in micelles and bilayers and in biological membranes.[27−29] Therefore, water-soluble polymers bearing those functionalities are suitable candidates for the construction of sensor layers and pH-responsive membranes.

In the work described here we show that the reactivity and therefore the degree of functionality are strongly determined by the nature of the fluoroaromatic compound. Different degrees of functionality as a function of time controlled by kinetic analyses of the β-DMCD-mediated nucleophilic aromatic substitution are of importance for the applications. The knowledge of kinetic parameters is then of help in adjusting precisely the experimental conditions for postfunctionalization of PVAm under ambient conditions.

During the nucleophilic substitution reaction the color of the aqueous solution changes from colorless to yellow due to the formation of the push−pull substituted aromatic in the polymer backbone.[7] The appearance of the new UV/vis absorption band of the chromophoric moiety in the polymer can be readily detected by means of UV/vis spectroscopy. Unfortunately, the solubility of PVam and functionalized PVAm is limited in water and D_2O. Therefore, it is not easy to achieve detailed information on structure formation using high-resolution ^1H and ^{13}C NMR spectroscopic investigations. For this reason, alternative methods are required to elucidate the functionalization reaction of PVAm with chromophoric moieties.

In this basic study we establish the kinetic procedure and the utilization of model studies to determine the degree of functionalization of polyvinylamine with nitroaniline derivatives.

Experimental Part

Determination of the Degree of Substitution of Nitrophenyl-Functionalized PVAm. Low molecular weight model compounds were synthesized for the UV/vis spectroscopic determination of the degree of substitution of the nitrophenyl-functionalized PVAm. 4-Fluoronitrobenzene, 2-fluoronitrobenzene, Sanger's reagent, and 1,5-difluoro-2,4-dinitrobenzene were converted into the corresponding nitro-*N*-isopropylanilines using isopropylamine.[30] The degree of substitution s can be determined by a known method, using eq 1 if the molar absorption coefficient of the model compound and those of the functionalized PVAm are known from UV/vis spectroscopic determination.[31]

$$s = \frac{\epsilon' M_{\mathrm{eq}}}{\epsilon_{\mathrm{model}} - \epsilon' M_{\mathrm{s}}} \tag{1}$$

In eq 1, s is the degree of substitution (number of substituents per basic building block), ϵ' the molar absorption coefficient of the polymer [L g^{-1} cm^{-1}], M_{eq} the molecular weight of the basic building block (chromophoric unit), $\epsilon_{\mathrm{model}}$ the molar absorption coefficient of the model compound [L mol^{-1} cm^{-1}], and M_{s} the molecular weight of the incoming substituent (without fluorine).

Kinetic Investigations. The nitrophenyl-functionalized polyvinylamines formed during the substitution of activated fluoroaromatics with PVAm are characterized by a UV/vis absorption spectrum in the region of 400−450 nm. To determine the rate constant k, time-dependent UV/vis absorption spectra were run. At the appropriate absorption maximum $\lambda_{\max}$ of the newly formed absorption bands, the absorbance was plotted against the reaction time for each fluoroaromatic used. Using nonlinear regression according to the model for pseudo-first-order reactions (eq 2), the rate constant k was determined at different reaction temperatures.

$$y = A_0 + A_1 \mathrm{e}^{-kt} \tag{2}$$

The regression coefficients are A_0 the final absorption at t = infinity, A_1 the total change in absorption between $t = 0$ and $t =$ infinity, and k the rate constant in s^{-1}.

Knowing the rate constant at different temperatures, ln(k) was plotted against T^{-1} according to the Arrhenius equation (eq 3), and the activation energy E_{A} was determined from the gradient of the curve and the preexponential factor A determined from the intercept with the y axis.

$$k = A\mathrm{e}^{-E_{\mathrm{A}}/RT} \tag{3}$$

The activation enthalpy $\Delta_{\mathrm{R}}H^{\ddagger}$ was calculated using eq 4. Knowing the preexponential factor A from eq 3 and combining eqs 3 and 5 (Eyring equation) and rearranging them for $\Delta_{\mathrm{R}}S^{\ddagger}$ gives the activation entropy.

$$\Delta_{\mathrm{R}}H^{\mp} = E_{\mathrm{A}} - RT \tag{4}$$

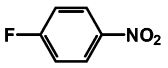
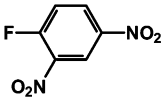
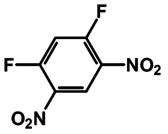
$$k = \frac{k_{\mathrm{B}}T}{h}\mathrm{e}^{\Delta_{\mathrm{R}}S/R}\mathrm{e}^{-\Delta_{\mathrm{R}}H/RT} \tag{5}$$

A prerequisite for using eq 2 for pseudo-first-order two-component reactions is that one of the reactants is in large excess. Table 1 shows the activated fluoroaromatics used, the starting concentration c_0 of both reaction partners, and the reaction conditions of the nucleophilic aromatic substitution of the PVAm with β-DMCD complexes at pH 11 in water.

Materials. The aqueous solution samples of polyvinylamine (PVAm, $M_{\mathrm{n}} = 15\,000$ g mol^{-1}, pH = 11) were kindly provided by BASF AG (Ludwigshafen, Germany). 2,6-*O*-Dimethyl-β-cyclodextrin (β-DMCD) was donated by Wacker Chemie (Burghausen, Germany).

2-Fluoronitrobenzene (2-FNB), 4-fluoronitrobenzene (4-FNB), 1-fluoro-2,4-dinitrobenzene (Sanger's reagent), and 1,5-

Table 1. Reaction Conditions Used for the Kinetic Studies of the Nucleophilic Aromatic Substitution of Fluoro Nitrobenzene Derivatives with PVAm in Water

fluoro compound (FC) used	initial concentration FC/β-DMCD complex [mol·l^{-1}]	initial concentration c_0(PVAm) [mol·l^{-1}]	ratio of PVAm to FC	reaction temperature [°C]
	$1.031 \cdot 10^{-3}$	0.3375	327	50 60 70 80
	$1.031 \cdot 10^{-3}$	0.3375	327	50 60 70 85
	$2.577 \cdot 10^{-4}$	0.3375	1310	0 23 28 32
	$2.577 \cdot 10^{-4}$	0.3375	1310	0 22 29 33

difluoro-2,4-dinitrobenzene (DFDNB) were commercially available products (Aldrich). For purification 2-FNB, 4-FNB, and Sanger's reagent were distilled under vacuum. White crystals of DFDNB were used without further purification.

Syntheses of the Cyclodextrin Complexes. For the cyclodextrin complex formation, stoichiometric amounts of the fluoronitro-substituted aromatic compound and of β-DMCD were dissolved in methanol and stirred overnight at room temperature.[14] The solid complex was isolated by removing methanol in a vacuum.

Syntheses of the Nitrophenyl-Functionalized Polyvinylamines. For functionalization of PVAm in water the solid β-DMCD complex was dissolved in 50 mL of distilled water, and 4.4 mL of aqueous solution of PVAm containing 0.5 g of the polymer was added. The mixture was refluxed for 8 h. After this time the chromophoric functionalized PVAm was precipitated in ice-cold acetone (refrigerator) and dried in a vacuum.

For the kinetic studies 4.4 mL (0.5 g of polymer) of the aqueous solution of PVAm was dissolved in 20 mL of distilled water and heated to a constant temperature. After adding an aqueous solution of the fluoro compound/β-DMCD complex, time-dependent UV/vis absorption spectra were measured.

Syntheses of the Nitroaniline Derivatives (Model Compounds). Syntheses of the model compounds *N*-isopropyl-4-nitroaniline, *N*-isopropyl-2-nitroaniline, and *N*-isopropyl-2,4-dinitroaniline were accomplished by reaction of isopropylamine with the corresponding fluoronitroaromatics.[30]

Synthesis of *N,N′*-Diisopropyl-2,4-dinitrobenzene-1,5-diamine. 1.0 g (4.9 mmol) of 1,5-difluoro-2,4-dinitrobenzene was dissolved in 70 mL of toluene, and 4.2 mL of isopropylamine (49 mmol) was added. The reaction mixture was heated for 24 h at 80 °C. Excess isopropylamine and the solvent were then distilled off at 140 °C. The solid yellow residue was recrystallized from methanol to give yellow needles in 93% yield with a melting point of 163 °C. ^{1}H NMR (400 MHz, δ, ppm, CD_2Cl_2): 9.15 (s, 1H, *m*-Ar*H*), 8.20 (d, 2*H*, −N*H*), 5.71 (s, 1*H*, *o*-Ar*H*), 3.77 (m, 2*H*, −C*H*-(CH_3)$_2$), 1.34 (d, 12*H*, −CH−(CH_3)$_2$).

UV/vis Spectroscopic Measurements. UV/vis absorption spectra of functionalized PVAm solutions were measured by means of a UV/vis MCS 400 diode-array spectrometer (Carl Zeiss) connected to an immersion cell (TSM 5) via glass-fiber optics.

Results and Discussion

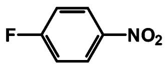
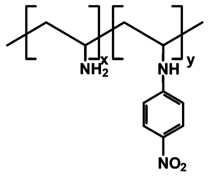
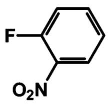
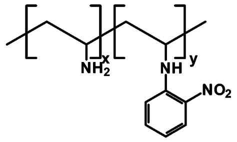
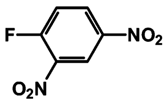
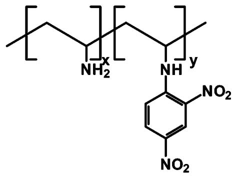
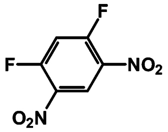
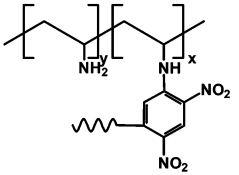
Functionalization of Polyvinylamines in Water Mediated by 2,6-*O*-Dimethyl-β-cyclodextrin (β-DMCD). The fluoroaromatics with *o*- and/or *p*-nitro groups were complexed with β-DMCD and converted into colored nitrophenyl-functionalized PVAm via nucleophilic aromatic substitution in water. Table 2 shows the nitro-substituted fluoroaromatics chosen, the reaction conditions, and the UV/vis absorption maxima of the nitrophenyl-functionalized PVAm formed.

The nitrophenyl-functionalized PVAms show varying solubility behavior. While the PVAm treated with 2-FNB/β-DMCD and 4-FNB/β-DMCD are readily soluble in both water and methanol, the 2,4-dinitrophenyl-functionalized PVAm is only partially soluble in water and methanol with swelling in the latter. The PVAm treated with DFDNB is only sparingly soluble in water and insoluble in methanol. This indicates that cross-linking of the polymer chain has occurred as a result of the second substitution, a theory that is investigated more precisely by the kinetic measurements. Therefore, the kinetic measurements were carried out in the temperature range between 0 and 33 °C. Higher reaction temperatures give rise to spontaneously cross-linking and precipitation of the functionalized polymer when DNFB or DFDNB was used for functionalization. This result was an additional reason to use a large excess of PVAm for the kinetic measurements of the highly reactive fluoroaromatics.

However, PVAm can also undergo cross-linking with CO_2 or residual formamide groups react with amino groups to amidinium ions. The influence of those reactions plays no role among the nucleophilic substitution reaction.

To determine the degree of substitution of the nitrophenyl-functionalized PVAms using UV/vis spectroscopy, the following model compounds were synthesized because their structures are related to the chromophoric units in the polymer: *N*-isopropyl-4-nitroaniline, *N*-isopropyl-2-nitroaniline, *N*-isopropyl-2,4-dinitroaniline, and *N,N′*-diisopropyl-2,4-dinitrobenzene-1,5-diamine. As the model compounds are insoluble in water, the molar absorption coefficients were determined in methanol. The degree of substitution could only be determined by UV/vis spectroscopy using eq 1 for 2- and 4-nitrophenyl-

Table 2. Reaction Conditions Used for the Synthetic Procedure and UV/vis Spectral Data of the Functionalized PVAm Formed (Ratio of the Reactants n_{FC} to n_{PVAm}: 0.0763, 0.1527, 0.2289, and 0.3053)

fluoro compound (FC) used	Reaction conditions	Functionalized PVAm	UV/vis absorbance in water at pH 11 λ_{max}
	T = 100°C 8 h H_2O pH = 11		413 nm
	T = 100°C 8 h H_2O pH = 11		450 nm
	T = 100°C 8 h H_2O pH = 11		358 nm (shoulder: 423 nm)
	T = 100°C 8 h H_2O pH = 11		double band: 338 nm 423 nm

functionalized PVAm's which are completely soluble in methanol. The molar absorption coefficients of *N*-isopropyl-4-nitroaniline in methanol (2.23×10^4 L mol^{-1} cm^{-1}) and of *N*-isopropyl-2-nitroaniline (5.95×10^3 L mol^{-1} cm^{-1}) were put into this equation. The prerequisite to use this methodology is that the UV/vis absorption coefficient of the polymer bonded chromophore is unaffected by neighboring amine functionalities or free PVAm because the NH substituent in nitroaniline derivatives can undergo interactions with hydrogen bond accepting molecules which have an effect on both position and intensity of the UV/vis absorption bands.[32,33] To prove this effect, isopropylamine was used in combination with the model compounds *N*-isopropyl-2-nitroaniline and *N*-isopropyl-4-nitroaniline. Matching the experimental conditions for determination the degree of substitution of the nitrophenyl-functionalized PVAm, no measurable effect of isopropylamine addition on the nitroaniline model compounds was observed. An increase of the UV/vis absorption band of the model compound *N,N'*-diisopropyl-2,4-dinitrobenzene-1,5-diamine is only observed when a large excess of isopropylamine was used. Therefore, we think it is justified using this methodology to determine the degree of substitution. For the PVAm functionalized with DFDNB and Sanger's reagent the polymers were not completely soluble in either water or methanol; the degree of substitution could not be determined using this method. Table 3 shows the degree of substitution of the PVAm determined using UV/vis spectroscopy. The order of magnitude of the degree of substitution determined via UV/vis spectroscopy accorded with the ^{1}H NMR spectroscopic determination using another PVAm batch.[34] However, at low degree of substitution the error is high using the ^{1}H NMR spectroscopic determination because the signals of the aromatic protons of the functionalized PVAm are very small compared to those of the polymer chain.

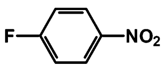
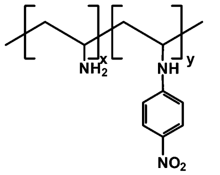
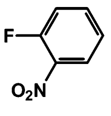
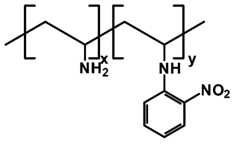
In Table 3 as can be seen that about a third of the 4-fluoronitrobenzene added actually reacts with PVAm. This means that for less reactive aromatics, such as 4-FNB, very long reaction times are necessary in order to achieve a high conversion. In the case of 2-fluoronitrobenzene under the same reaction conditions almost complete conversion is achieved. The degree of substitution of 2-nitrophenyl-functionalized PVAm is thus about 3 times higher than that of 4-nitrophenyl-functionalized PVAm under the same reaction conditions.

To understand the difference in the reactivity in nucleophilic aromatic substitution between 4-FNB/β-DMCD and 2-FNB/β-DMCD with PVAm in water more precisely, kinetic investigations were carried out.

Kinetic Investigations: Determination of the Rate Constant *k* and the Activation Energy E_A. Figure 2 shows a series of characteristic UV absorption spectra taken during the nucleophilic aromatic substitution of 4-FNB/β-DMCD with PVAm as a function of the reaction time at 60 °C in water at pH 11. The UV/vis absorption band which appears at $\lambda_{max} = 413$ nm shows the formation of 4-nitrophenyl-functionalized PVAm. It should be mentioned at this point that the β-DMCD has no effect on the UV/vis absorption band of 4-nitrophenyl-functionalized PVAm. This result shows that β-DMCD does not interact with the bonded chromophores.[32,33]

The plot of the absorbance at a particular absorption maximum λ_{max} against the reaction time t gives curves typical of pseudo-first-order reactions. Figure 3 shows the absorbance as a function of the reaction time at 50, 60, 70, and 80 °C for the reaction of 4-FNB/β-DMCD with PVAm in water. Using nonlinear regression according to eq 2, the rate constant k is determined, which,

Table 3. Quantitative Results Given for the Reactions of 4-FNB/β-DMCD and 2-FNB/β-DMCD Complexes with PVAm in Water (Reaction Conditions: T = 100 °C, 8 h, pH = 11)

fluoro compound (FC) used	Ratio of FC to PVAm	Functionalized PVAm	UV/vis absorbance in methanol λ_{max}	Degree of substitution % (UV/vis)
	0.0763 0.1527 0.2289 0.3053		390 nm	3.3 3.7 8.2 9.1
	0.0763 0.1527 0.2289 0.3053		434 nm	7.3 14.5 22.7 28.3

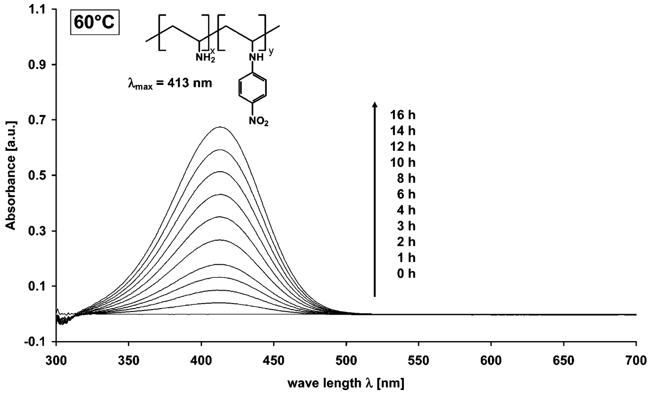


Figure 2. Typical UV/vis absorption spectra series measured during the reaction of the 4-FNB/β-DMCD complex with PVAm (pH = 11, T = 60 °C) in water.

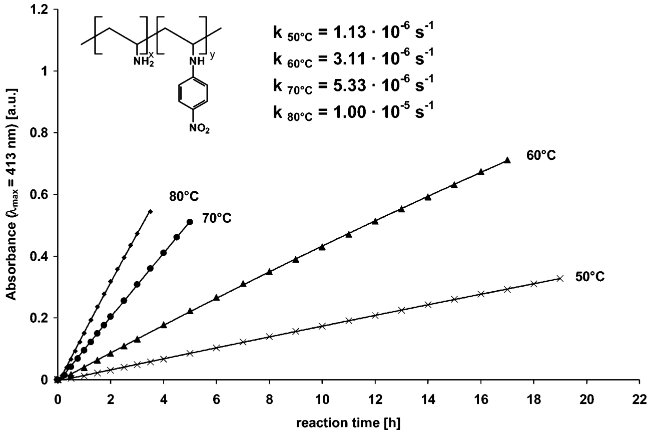


Figure 3. Influence of the reaction temperature on the UV/vis absorption intensity of the formed 4-nitrophenyl-functionalized PVAm moiety as a function of the reaction time (inset: determined rate constants via nonlinear regression analysis).

as expected, increases with an increase in the reaction temperature.

The activation energy E_A of the nucleophilic aromatic substitution of selected fluoroaromatics with PVAm was determined from the gradient of the plot of ln(k) against T^{-1} according to eq 3. Figure 4 shows this for the reaction of 4-FNB/β-DMCD, 2-FNB/β-DMCD, Sangers/β-DMCD, and DFDNB/β-DMCD with PVAm. The deviation from an ideal straight line is reflected in the error margin of the activation energies.

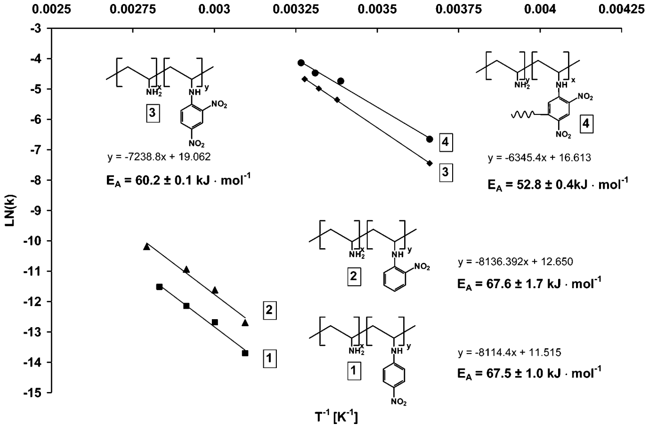


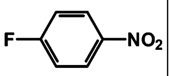
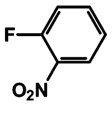
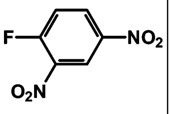
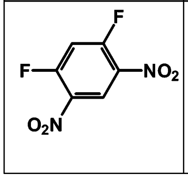
Figure 4. Determination of the activation energies of the nucleophilic aromatic substitution of 2-FNB, 4-FNB, Sanger's reagent, and DFDNB with PVAm in water mediated by β-DMCD.

To gain information on the reactivity of the individual fluoroaromatics toward nucleophilic aromatic substitution by PVAm, the activation energies were determined for the reaction of PVAm with 4-FNB, 2-FNB, Sanger's reagent, and DFDNB. The calculation of the corresponding Eyring parameters was carried out using eqs 4 and 5.

Table 4 gives a summary of the nucleophilic aromatic substitution reactions of the fluoroaromatics with PVAm in water and the corresponding reaction conditions, the UV/vis absorption maxima of the functionalized PVAm's, and the rate constants k, activation energies E_A, enthalpies $\Delta_R H^‡$, and entropies $\Delta_R S^‡$ determined.

Because the same reaction conditions (50, 60, and 70 °C) and the same ratios of the concentrations of the reaction partners are used (PVAm in 327-fold excess), the rate constants for the reaction of 4-FNB/β-DMCD and 2-FNB/β-DMCD with PVAm can be compared directly. The rate constants for the reactions of 2-FNB/β-DMCD at 50, 60, and 70 °C are about 3 times as great as those for the reaction of 4-FNB/β-DMCD. This is supported by a 3-fold increase in the degree of substitution determined by UV/vis spectroscopy compared with 2-nitrophenyl-functionalized PVAm under the same reaction conditions.

Table 4. Activation Parameters (Rate Constants k, Activation Energies E_A, Activation Enthalpies $\Delta_R H^‡$, and Activation Entropies $\Delta_R S^‡$) Determined for the Nucleophilic Aromatic Substitution of Fluoronitrobenzene Derivatives with PVAm in Water Mediated by β-DMCD

fluoro compound (FC) used	ratio of PVAm to FC	λ_{max} of substituted PVAm in reaction mixture	T [°C]	k [s^{-1}]	E_A [kJ·mol^{-1}]	$\Delta_R H^‡$ [kJ·mol^{-1}]	$\Delta_R S^‡$ [J·K^{-1}·mol^{-1}]
	327	413 nm	50 60 70 80	$1.13 \cdot 10^{-6}$ $3.11 \cdot 10^{-6}$ $5.33 \cdot 10^{-6}$ $1.00 \cdot 10^{-5}$	67.5 ± 1.0	64.81 64.73 64.65 64.56	-158.16 -158.41 -158.66 -158.90
	327	450 nm	50 60 70 85	$3.08 \cdot 10^{-6}$ $9.06 \cdot 10^{-6}$ $1.79 \cdot 10^{-5}$ $3.74 \cdot 10^{-5}$	67.6 ± 1.7	64.91 64.83 64.75 64.62	-148.72 -148.98 -149.22 -149.58
	1310	360 nm (shoulder: 423 nm)	0 23 28 32	$5.84 \cdot 10^{-4}$ $4.73 \cdot 10^{-3}$ $6.85 \cdot 10^{-3}$ $9.34 \cdot 10^{-3}$	60.2 ± 0.1	57.93 57.74 57.70 57.66	-94.01 -94.68 -94.83 -94.93
	1310	double band: 350 nm 423 nm	0 22 29 33	$1.29 \cdot 10^{-3}$ $8.74 \cdot 10^{-3}$ $1.14 \cdot 10^{-2}$ $1.60 \cdot 10^{-2}$	52.8 ± 0.4	50.53 50.35 50.29 50.26	-114.22 -114.86 -115.06 -115.17

In contrast, the activation energies for the nucleophilic aromatic substitution of 4-FNB/β-DMCD and 2-FNB/β-DMCD of 67.6 and 67.5 kJ mol^{-1} are approximately equal. The measurable difference in reactivity therefore arises from neighboring group effects and is known from the literature.[18] The dominant factors determining the reactivity of primary amines on nucleophilic aromatic substitution are steric effects rather than the basicity.[19,20]

The activation entropy $\Delta S^‡$ for the reaction of isopropylamine with 4-fluoronitrobenzene in DMSO amounts to about -39 J K^{-1} mol^{-1}.[20] This value is significantly lower than that for the reaction of the 4-fluoronitrobenzene/β-DMCD complex with PVAm in water ($\Delta S^‡ = -158$ J K^{-1} mol^{-1}) which demonstrates the importance of the retarding influence of the polymer chain on the reactivity. Thus, the lower reactivity of PVAm chains compared to isopropylamine and other related compounds in nucleophilic aromatic substitution reactions is likely determined by the accessibility of the amino groups. As the polymer chain is coiled, then a low reactivity results. PVAm is only weakly positively charged at pH = 11 and therefore not stretched. To come loose, the coil requires additional work which is reflected by the strong negative activation entropy term. In further work a systematic study on this complicated feature is planned.

As expected, Sanger's reagent undergoes nucleophilic aromatic substitution with PVAm more readily than 4-FNB or 2-FNB. The activation energy of 60.2 kJ mol^{-1} is consequently significantly lower for the nucleophilic aromatic substitution because of the second −M substituent. Here also the effect of the ortho-activating substituent on the activation entropy can be seen. The introduction of a further fluoro substituent in DFDNB leads to a further lowering of the activation energy to 52.8 kJ mol^{-1}, which can be attributed, without doubt, to the −I effect of the second fluoro substituent. However, the effect on the entropy of activation in comparison with Sanger's reagent is partially compensated for. The reaction of DFDNB with PVAm was subjected to a more precise kinetic and UV/vis spectroscopic analysis, as besides monosubstitution, disubstitution is also possible, which leads to cross-linking and is used in proteins.[35] In tetraethoxysilane, which is moderately polar, only monosubstitution with 3-aminopropylltrialkoxysilane occurs within 30 min at room temperature.[36] Nilsson et al. investigated the nucleophilic substitution reaction of 1-thio-β-galactopyranose with DFDNB in excess to minimize the disubstitution.[37] In a much more polar PVAm/water system and PVAm in excess the reaction is much faster, so a second substitution can take place. However, the UV/vis spectra of the two products only differ marginally. Figure 5 shows the UV/vis spectroscopic progress of the reaction.

The UV/vis spectrum of the disubstituted model compound (inset shown in Figure 5) supports the theory that with increasing reaction time the UV/vis band at ca. 417 nm corresponds to the disubstituted product. Kinetic evaluation of the time-dependent formation of the UV/vis bands at 350 and 423 nm shows that slightly different rate constants result, which indicates unambiguously that two different processes, mono- and disubstitution, are occurring. As the two products have very similar UV/vis spectra, this is only an estimate. The rate constants determined at 350 and 423 nm reflect both the second and first substitution because

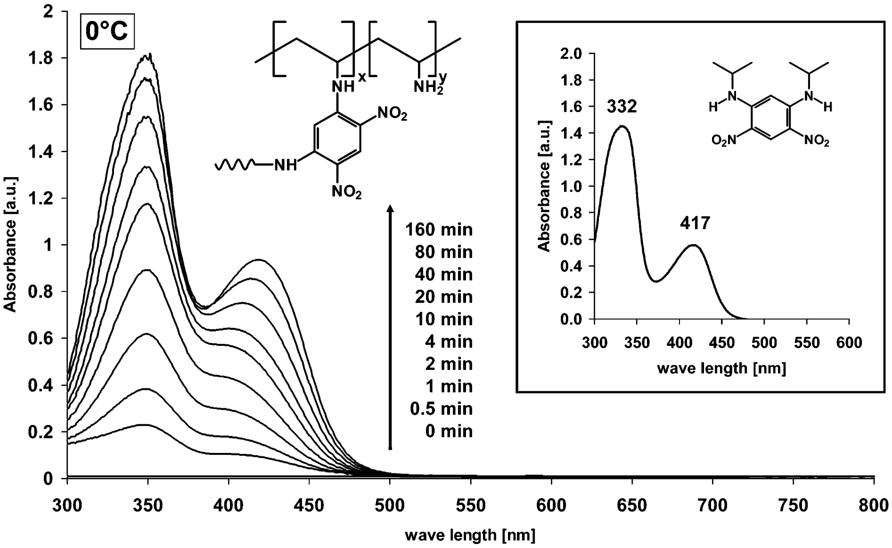


Figure 5. UV/vis absorption spectra series measured during the reaction of DFDNB with PVAm in water at 0 °C and pH 11. Inset: UV/vis absorption spectrum of the model compound *N,N′*-diisopropyl-2,4-dinitrobenzene-1,5-diamine in methanol.

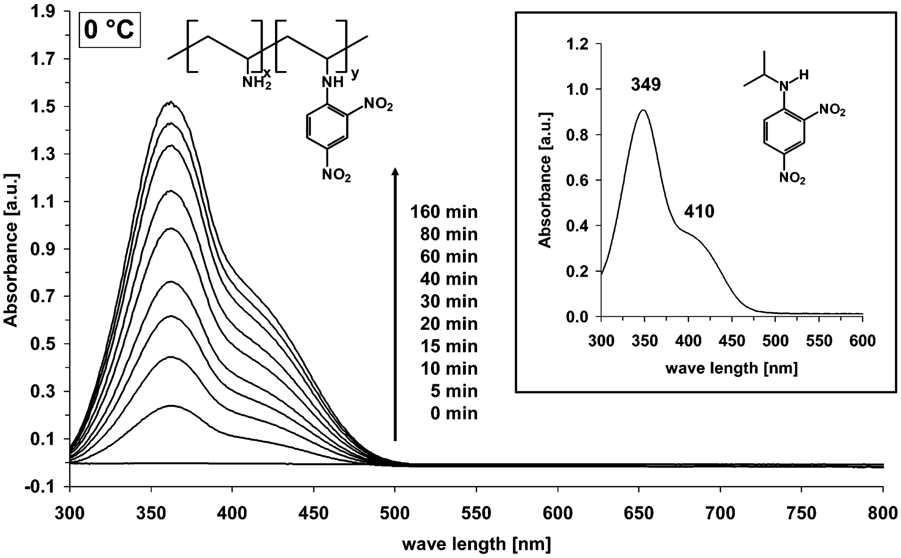


Figure 6. UV/vis absorption spectra series measured during the reaction of Sanger's reagent with PVAm in water at 0 °C and pH 11. Inset: UV/vis absorption spectrum of the model compound *N*-isopropyl-2,4-dinitrobenzene in methanol.

the activation energy determined is independent of the wavelength used.

As a good approximation the rate constants for the reaction of Sanger's reagent/β-DMCD and DFDNB/β-DMCD can be compared with each other. Rate constants for the reaction of DFDNB/β-DMCD are about twice those of the reaction of Sanger's reagent with PVAm in water. The exceptionally high reactivity of DFDNB was somewhat surprising, as we had only expected monosubstitution to occur at 0 °C. The original plan was to only induce cross-linking at higher temperatures.

Conclusions

The results of this work have shown that kinetic investigations allow the reaction of fluoronitrobenzene derivatives with PVAm to be understood and structures to be assigned using model compounds. This is particularly useful as routine ^{1}H and ^{13}C NMR spectroscopic investigations of functionalized polymers is not easily possible because of solubility problems.

In further work the reactivity and structure of nitrofluoroaromatics can be adapted in order to introduce new NLO chromophores, such as stilbene derivatives or azo compounds into polyvinylamines.

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