New York, N.Y., 1970, p 653.
(27) E. D. Bergman and J. Blum, *J. Org. Chem.*, **24**, 549 (1959).
(28) D. D. Neiswender, W. B. Moniz, and J. A. Dixon, *J. Am. Chem. Soc.*, **82**, 2876 (1960).
(29) J. Van Allan and J. F. Tinker, *J. Org. Chem.*, **19**, 1243 (1954).
(30) L. Horner and E. H. Winkelman in "Newer Methods of Preparative Organic Chemistry", Vol. 3, W. Foerst, Ed., Academic Press, New York, N.Y., 1964, p. 176.
(31) R. Stern, J. English and H. G. Cassidy, *J. Am. Chem. Soc.*, **79**, 5792 (1957).
(32) C. Burkhard, *J. Org. Chem.*, **22**, 592 (1957).
(33) D. Bailey, Ph.D. Thesis, University of Massachusetts, 1975.
(34) B. M. Gallo and S. Russo, *J. Macromol. Sci., Chem.*, **8**, 521 (1974).
(35) B. Stutzel, T. Miyamoto, and H. J. Cantow, *Polym. J.*, **8**, 247 (1976).
(36) H. W. Gibson and F. C. Bailey, *Macromolecules*, **9**, 688 (1976).
(37) R. H. Still and A. Whitehead, *J. Appl. Polym. Sci.*, **21**, 1199 (1977).
(38) J. C. Bevington and T. Ho, *Trans. Faraday Soc.*, **64**, 1329 (1968).
(39) M. Kato, Y. Takemoto, Y. Nakano, and M. Yamazaki, *J. Polym. Sci., Polym. Chem. Ed.*, **13**, 1901 (1975).
(40) J. G. Pacifici and H. L. Browning, *J. Am. Chem. Soc.*, **92**, 5231 (1970).
(41) P. J. Flory, "Principles of Polymer Chemistry", Cornell University Press, Ithaca, N.Y., 1953.

Soluble Functional Polymers. 2. Utilization of Water-Insoluble Chromophores in Water-Soluble Polymeric Dyes[1]

Daniel J. Dawson,* Kenneth M. Otteson, Patricia C. Wang, and Robert E. Wingard, Jr.*

Chemical Synthesis Laboratories, Dynapol, Palo Alto, California 94304.
Received October 20, 1977

ABSTRACT: Two simple and practical routes have been developed for the preparation of water-soluble polymers having water-insoluble anthraquinone chromophores incorporated into their structure. Bonding of chromophore to polymer backbone was attained in both cases via copper(I)-catalyzed nucleophilic substitution of bromoanthraquinones by polymeric amines. The first route involved treating poly(vinylamine) with 0.5 equiv of bromoanthraquinone, followed by converting unreacted backbone amines into water-solubilizing sulfamate groups (Me_3N–SO_3 treatment). The second route employed a 60:40 vinylamine–vinylsulfonate copolymer for the direct preparation of water-soluble products. The copolymer was prepared by copolymerization of *N*-vinylacetamide and sodium vinylsulfonate, followed by acid hydrolysis. The copolymer exhibited an upper limit for chromophore attachment of 50–55% available amines. The reasons for this are discussed in terms of monomer sequencing.

Synthetic polymers have long been employed advantageously for their physical–mechanical properties rather than their chemical properties. Chemical modifications of polymers (unlike the chemistry of their preparation) were little studied until the 1950's. During recent years, however, the development and utilization of specifically functionalized polymers has received attention from chemists in a variety of fields.[2-4] Research has shown, for example, that polymeric reagents,[5] which consist of reactive functionality bound to an insoluble support, are particularly useful and valuable because of their nonpolluting and recyclable nature,[6] and because of the mechanical and operational advantages inherent in solid–liquid systems. Biologically active molecules, such as drugs,[7] enzymes,[8] hormones,[9] and insect sex attractants,[10] have been immobilized on polymers for a number of uses.[11] Polymeric organometallics have been shown to have excellent semiconducting properties.[12] Functionalized resins have found numerous applications as insolubilized chelating agents,[13] supports for organic synthesis,[14] protecting groups,[15] agents for ion exchange[16] and affinity chromatography,[17] catalysts,[18] and immobilizing media for the detection of unstable reaction intermediates.[19]

Much less attention has been focused on *soluble* functionalized polymers even though materials of this type suggest advantages in a variety of applications. Polymeric water-soluble dyes, which are of considerable biological and technological interest because of their various properties,[20] are examples of materials in this class which have been little investigated.[21] One reason for this is that the vast majority of chromophores are not available in a water-soluble (e.g., sulfonated) form,[22] and thus cannot be converted into water-soluble materials by the polymerization of easily prepared monomers. In order to prepare water-soluble polymeric dyes constructed of fundamentally water-insoluble chromophores, the chromophore must somehow be attached to, or be made a part of, a polymeric system which otherwise contains the required solubilizing functionality.

Nucleophilic polymeric amines provide two straightforward synthetic approaches to materials of this type. One route involves preparing an amine homopolymer, utilizing a portion of the amines for chromophore attachment, and converting the remainder into solubilizing groups. An equally viable method involves preparing a copolymer of both amine and sulfonate containing monomers and attaching chromophores to the amines. We report here the successful implementation of both of these routes for the preparation of water-soluble polymeric dyes using water-insoluble anthraquinone chromophores.

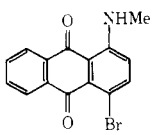
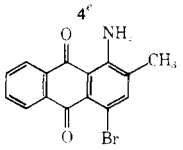
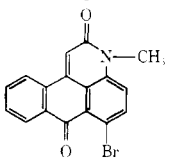
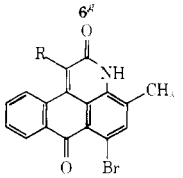
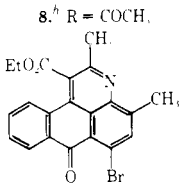
Homopolymer Route

Chromophore Attachment. Halogen atoms appropriately positioned on an anthraquinone nucleus undergo a facile copper(I)-catalyzed nucleophilic displacement by amines (Ullmann condensation).[23] A representative number of bromoanthraquinones were selected for reaction with poly(vinylamine hydrochloride) (1) in such a manner that residual amines would be available for conversion into water-solubilizing groups by sulfamation. This polymeric amine was chosen as the nucleophilic backbone for chromophore attachment because it is an easily prepared and characterized, homogeneous, linear polymer possessing a high density of reactive primary amines.[1,24]

The first step in the homopolymer route to water-soluble polymeric dyes involved an Ullmann condensation between 1 and 0.5 equiv of a bromoanthraquinone (Scheme I). The six water-insoluble bromoanthraquinones employed are listed

0024-9297/78/2211-0320$01.00/0

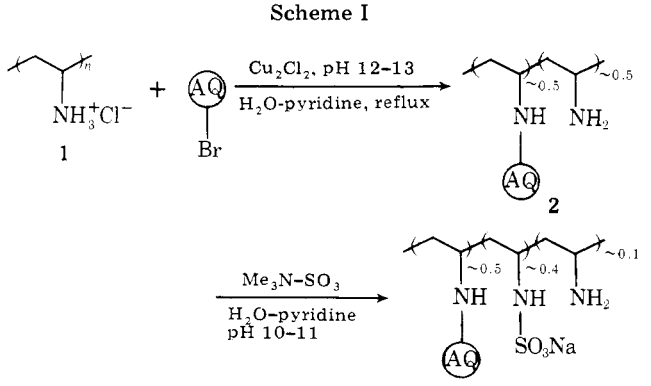
Table I
Water-Soluble Polymeric Dyes Prepared from Water-Insoluble Chromophores

Bromoanthraquinone	Homopolymer route[a]			Copolymer route[b]		
	λ_{max}, nm[c]	a, $(g/L)^{-1}$ cm^{-1} [c]	Chromophore content, mer %[d]	λ_{max}, nm[c]	a, $(g/L)^{-1}$ cm^{-1} [c]	Chromophore content, mer %[d]
 4[e]	595	18.9	48	596	15.3	32
 5[f]	575	13.3	51	573	12.0	32
 6[g]	510	11.9	46	511	10.2	32
 7,[h] R = CO_2Et 8,[h] R = $COCH_3$	518 517	12.9 14.4	49 45	517 517	12.6 13.2	33 30
 9[i]	464	17.3	46	462	14.3	33

[a] Dyes prepared from 0.5 equiv of anthraquinone and excess Me_3N–SO_3. [b] Dyes prepared from 60:40 copolymer **13** and 0.80 equiv of anthraquinone. [c] Water solution at pH 7. [d] See Experimental Section for details of determination. [e] C. V. Wilson, *Org. Synth.*, **29**, 68 (1949). [f] A. Locher and H. E. Fierz-David, *Helv. Chim. Acta*, **10**, 647 (1927). [g] "British Intelligence Objectives Subcommittee Report 1484", Publication Board No. 86139, Library of Congress, Washington, D.C., 1947, p 46. [h] A. Peter, U.S. Patent 1891317 (1932); *Chem. Abstr.*, **27**, 1892 (1933). [i] P. Bücheler and A. Peter, U.S. Patent 2759940 (1956); *Chem. Abstr.*, **50**, 15597i (1956).

in Table I. The key to the successful execution of this reaction was the development of a suitable aqueous solvent system. Polymer **1** is soluble only in aqueous media, while the bromoanthraquinones and condensation products are insoluble in aqueous base. Thus, carrying out the displacement in water resulted in a sluggish reaction with premature precipitation of a very poorly substituted product and concomitant hydrolysis (i.e., substitution by hydroxide) of the unreacted bromoanthraquinone. Precipitation was avoided and chromophore attachment was achieved in 90% yield or greater by adding the bromoanthraquinones portionwise to water–pyridine solutions of **1** at pH 12–13. In order to keep the polymer in solution as the reaction progressed, it was found necessary to steadily increase the percentage of pyridine in the solvent mixture. Cuprous chloride was found to be a potent catalytic agent for this reaction. Although the condensations took place rapidly, reaction times of several hours were required because of the need to carefully adjust the solvent ratio.

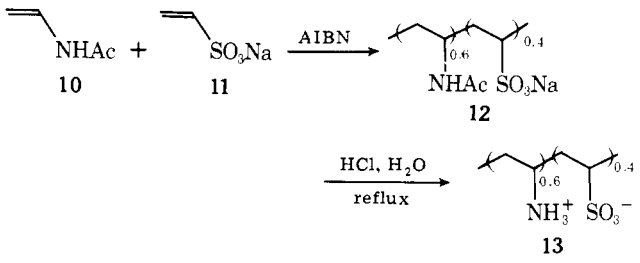
Scheme I



Polymers **2** were found to be soluble in water-miscible organic solvents (e.g., pyridine, dimethylformamide, and dimethyl sulfoxide) containing 10–20% H_2O and in aqueous solutions of low ionic strength at pH 3–5. These solubility properties were found to be somewhat dependent on the particular chromophore attached, the degree of substitution, and the molecular weight of the polymer. Neither purification nor isolation was necessary prior to sulfamation, but both could be accomplished by either preciptation (into 2-propanol or acetone) or dialysis against aqueous pyridine. The elemental analyses of these carefully purified products (see Experimental Section) provided the chromophore content values expressed as mer[25] percent in Table I.

The residual backbone amines could be directly sulfamated

Scheme II



10 11 12 13

by treatment of the aqueous pyridine reaction mixture with excess sulfur trioxide–trimethylamine complex.[26] This was best carried out at moderate temperatures and a pH of 10–11 with stirring for 12–18 h. Higher pH values resulted in decomposition of the SO_3 complex, while lower values afforded poor conversion because of incomplete deprotonation of the amines. Upon completion of sulfamation, residual salts and monomeric impurities were removed by ultrafiltration and isolation was accomplished by lyophilization. Elemental analyses of these polymeric dyes (see Experimental Section) indicated that under these conditions 75–85% of the residual amines were sulfamated.[27]

Dried samples of the dyes rapidly redissolve in water to afford homogeneous solutions. The solutions are clear and bright and are visually very similar to organic solutions of water-insoluble monomeric models. The spectroscopic properties of the materials prepared are listed in Table I.

Copolymer Route

Copolymer Synthesis. This route involved the nucleophilic attachment of water-insoluble chromophores to a copolymer prepared, in principle, from amine and sulfonate containing monomers. The simplest practical linear copolymer possessing both the desired primary amine and sulfonate functionality is one hypothetically derived from the copolymerization of vinylamine and vinylsulfonic acid. It was reasoned that the copolymerization of *N*-vinylacetamide (**10**) with sodium vinylsulfonate (**11**), followed by acid hydrolysis, would provide the vinylamine–vinylsulfonate copolymer.[28]

In preliminary experiments these two monomers were found to undergo free-radical polymerization in water or water–2-propanol in the absence of oxygen with 2,2′-azobis(2-methylpropionitrile) (AIBN) as initiator (Scheme II). Solutions equimolar in both monomers afforded poly(*N*-vinylacetamide-*co*-sodium vinylsulfonate) with a 54:46 mer ratio of vinylacetamide (N) to vinylsulfonate (S) incorporation as determined by elemental analysis. The azeotropic copolymerization ratio (i.e., the ratio of monomers at which the copolymerization can be taken to a high percent conversion without producing a heterogeneous N/S composition) was found to be 60 (±3) mol % *N*-vinylacetamide to 40 (±3) mol % vinylsulfonate. This value was determined in water by a plot of mer percent vinylacetamide in the copolymer (low conversion conditions) vs. mole percent *N*-vinylacetamide in the starting mixture for a series of monomer ratios ranging from 35–70 mol % *N*-vinylacetamide.[29]

The molecular weight of azeotropic copolymer **12** was readily controlled by the polymerization temperature and the use of the chain-transfer solvent 2-propanol. When concentrated solutions of the monomers were copolymerized at 65–70 °C in water, **12** was routinely produced with molecular weights in the range of $0.6–1.0 \times 10^5$. The use of 2-propanol–water (1:1) as solvent at these temperatures resulted in molecular weights of $2.6–2.9 \times 10^4$. Lower molecular weight preparations (1.4×10^4) were obtained with 2-propanol–water (1:1) at 75–80 °C. Copolymer **12** proved soluble in water and aqueous lower alcohols but was insoluble in nonhydroxylic solvents. Isolation and purification were therefore readily accomplished by precipitation from acetone. The yields of **12**, as a white powder, were found to be in the 60–70% range.

The sequence of vinylacetamide and vinylsulfonate residues in **12** is a direct function of the reactivity ratios of each of the monomers. The reactivity ratio may be defined as the preference for a residue composed of any monomer to be followed by another residue of its own type.[29] The reactivity ratios of *N*-vinylacetamide and sodium vinylsulfonate were determined to be 0.48 ± 0.05 and 0.16 ± 0.02, respectively, in pure water.[30] Utilizing these values, it can be calculated[31] that in the azeotropic copolymer 33–36% of the vinylacetamide groups are bracketed by vinylsulfonates, 28–29% of the vinylacetamides are in sequences of two, 17–18% are in sequences of three, 9–10% are in sequences of four, 5–6% are in sequences of five, and the remainder are in sequences of six or higher. These reactivity ratios also allow the calculation of the frequency of vinylacetamide–vinylacetamide (25%), vinylacetamide–vinylsulfonate (69%), and vinylsulfonate–vinylsulfonate (6%) diads. These numbers are in excellent agreement with the respective values of 23, 72, and 4% determined by ^{13}C-NMR spectroscopy.[32] These figures show that although **12** is not predominantly alternating, somewhat over 80% of the vinylacetamide residues are adjacent to at least one vinylsulfonate residue.

Hydrolysis of all the *N*-acetyl groups of **12** was readily effected with 3–4 equiv of aqueous HCl at reflux for 24–48 h. The amine–sulfonate copolymer **13** is represented in Scheme II as containing only ammonium and sulfonate groups for reasons of simplicity. The thorough analysis of a 60:40 copolymer, prepared and purified as described above, revealed 38 mer % each of these two units plus an additional 20 mer % of ammonium chloride units. The remaining 4 mer % was equally divided between unprotonated amine and sodium sulfonate units.

Chromophore Attachment. Copolymer **13** was found to be less reactive than poly(vinylamine) in the Ullmann condensation with bromoanthraquinones **4–9** (Table I). The reaction proceeded satisfactorily with 0.80 equiv of anthraquinone (relative to amine) in refluxing water–pyridine (9:1). The use of the pyridine cosolvent was necessary because of the water insolubility of the bromoanthraquinones. An excess of sodium hydroxide was employed in this condensation as the negatively charged sulfonates on the backbone make deprotonation of the amines a much less favorable process than was the case with **1**. Cuprous chloride was determined to be the best catalyst for this reaction, although a variety of cuprous salts (e.g., Cu_2O, Cu_2Br_2, CuOAc) performed well.

Unexpectedly, chromophore attachment to **13** was found to have an upper limit of 30–33 mer % (determined by elemental analysis). Thus, approximately one-half of the amines were unreactive. This result was not significantly altered by employing more forcing reaction conditions. In order to gain some insight into this result, a series of copolymers ranging in composition from 44 to 64 mer % amine were prepared (under conditions of low conversion to minimize heterogeneity) and treated with bromoanthraquinone **8** under identical conditions. The percentage of unreactive amines varied from 80 in the lowest amine content polymer to 39 in the highest. The general trend evident is that the greater the N/S ratio, the lower the percentage of unreactive amines. *This observation suggests that the monomer sequence of the copolymer determines the limit of reactivity.*

There are three types of amines in this series of copolymers. There are those flanked by two sulfonates (SNS), those between an amine and sulfonate (NNS), and those between two amines (NNN). The least reactive copolymers (in terms of percent unreactive amines) were those with low N/S ratios. Intuitively, these copolymers should possess the highest de-

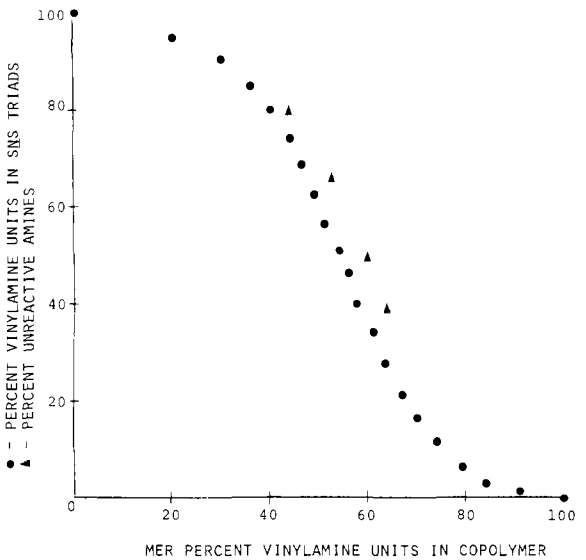
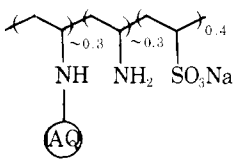


Figure 1. Plots of mer percent vinylamine units in copolymer vs. both percent vinylamine units present as SNS triads and percent unreactive amines.

gree of alternation (i.e., SNS fraction). For this series of copolymers, a plot of the calculated[31] percent of amine units present as SNS triads vs. the mer percent amine units in the copolymer was compared with a plot of percent unreactive amines vs. the mer percent amine units in the copolymer (Figure 1). The agreement between these two lines is quite reasonable. These results indicate that polar, steric, and field effects combine to render those amines which are bracketed by sulfonates unreactive. The discongruence between the two lines suggests that other factors, perhaps configurational in nature, are also involved in limiting the reactivity.[33]

The dyes prepared from **13** are represented by **14.** The products were purified and isolated as described previously.



14

Their spectroscopic properties are listed in Table I. Dried samples of these polymeric dyes rapidly redissolve in water to produce clear, homogeneous solutions.

In summary, we emphasize that two convenient and straightforward methods are now available for the preparation of water-soluble polymers comprised, in part, of water-insoluble functional groups. Both methods successfully employed polymeric amines for the attachment of water-insoluble anthraquinone dye functional groups. In the first method, approximately one-half of the amines in poly(vinylamine) were used for the bonding of chromophore, with the remaining amines being employed to obtain water solubilization by conversion into sulfamate groups. The second method involved the utilization of a vinylamine–vinylsulfonate copolymer. The attachment of anthraquinones to the amino groups of this material provided water-soluble products directly. Both methods are envisioned as being valuable for the preparation of a wide range of specifically functionalized, water-soluble polymers.

Experimental Section

Visible spectra were obtained with a Cary Model 118 spectrophotometer. The ^{13}C NMR spectrum (0–200 ppm, proton decoupled) of an alkaline H_2O–D_2O–dioxane (15:5:1) solution of **13** was recorded with a Varian XL-100 instrument by the NMR Laboratory, Stanford University, Stanford, Calif. The scale was calibrated using a value of 67.4 ppm for dioxane. Elemental analyses were performed by the Microanalytical Laboratory, Stanford University. Molecular weights were determined by gel permeation chromatography and were calculated from peak elution volumes recorded relative to either sulfonated polystyrene standards (M_p^{PSS}) eluting with 0.05 M aqueous phosphate buffer (pH 7.0)[34a] or polystyrene standards (M_p^{PS}) eluting with 0.01 M LiBr in dimethylformamide.[34b] Silanized glass columns were employed for both methods.

Polymeric dyes **3** and **14** were purified by ultrafiltration with an Amicon Model 202 stirred cell (Amicon Corp., Lexington, Mass.) employing a 63-mm diameter PM 10 membrane (molecular weight cutoff 1×10^4). The device was operated at 40 psi Ar pressure. Ultrafiltration was carried out with 15% aqueous pyridine made up to 0.02 N with NaOH (pH 12) until the ultrafiltrate was colorless and then with H_2O until the pyridine had been expelled and the pH had fallen to neutrality. Polymeric dyes **2** were purified by sequential bag dialysis (regenerated cellulose, average pore radius 24 Å, estimated molecular weight cutoff 2×10^4) against 25% aqueous pyridine containing 0.1% NaCl (10 days), 0.1% saline solution (2 days), and pure H_2O (2 days). The dialysates were changed daily.

The mer percents of chromophore substitution and sulfamation for the dyes were calculated entirely from elemental analysis data. For **2**, a plot for each chromophore of C/N ratio (mequiv/g basis) vs. mer percent substitution enabled the experimentally determined C/N ratio to be correlated with substitution. The mer percent sulfamation for each **3** could then be determined from a plot of N/S ratio (mequiv/g basis) vs. mer percent sulfamation for the degree of chromophore substitution obtained. The chromophore substitution for **14** was found with a plot of N/S ratio (mequiv/g basis) vs. mer percent substitution.

Preparation of Polymeric Dye 3 with 1-Methylamino-4-bromoanthraquinone (4). A 250-mL, three-neck flask, equipped with overhead stirrer, reflux condenser, and Ar inlet, was charged with 1.19 g (15.0 mmol) of poly(vinylamine hydrochloride) (prepared[1] from poly(*N*-vinylacetamide) of M_p^{PS} 3.0×10^4), 0.60 g (15.0 mmol) of NaOH, 1.60 g (15.0 mmol) of Na_2CO_3, and 50 mL of H_2O. The mixture was stirred until homogeneous (pH 12.5) and treated with 476 mg (1.50 mmol) of **4**, 10 mg of Cu_2Cl_2, and 30 mL of pyridine and heated to reflux. The following treatments were made to the refluxing reaction mixture at the times indicated: (a) 1 h, 1.5 mmol of **4**, 20 mL of pyridine; (b) 2 h, 1.5 mmol of **4**, 10 mL of pyridine, 5 mg of Cu_2Cl_2; (c) 3.5 h, 1.5 mmol of **4**, 10 mL of pyridine, 3 mmol of NaOH; (d) 5 h, 1.5 mmol of **4**, 20 mL of pyridine, 5 mg of Cu_2Cl_2, 3 mmol of NaOH.

At 6.5 h the reaction was diluted with 160 mL of pyridine, transferred to a 1-L flask equipped with magnetic stir bar and pH probe, and cooled to room temperature. A 15-mL sample was withdrawn at this point for purification and analysis. The pH was maintained at 10–11 by the addition of 2.5 N NaOH as the remainder of the solution was treated as follows with Me_3N–SO_3 (Aldrich Chemical Co.) and H_2O: (a) initial, 5.0 g of Me_3N–SO_3; (b) 0.5 h, 5.0 g Me_3N–SO_3, 50 mL of H_2O; (c) 1.0 h, 5.0 g of Me_3N–SO_3, 50 mL of H_2O; (d) 1.5 h, 6.0 g of Me_3N–SO_3, 100 mL of H_2O. The mixture was stirred for an additional 14 h, heated to 50 °C for 3 h, and filtered. The product was purified by ultrafiltration and the resulting solution was freeze dried to afford 2.12 g of polymeric blue dye: vis λ_{max} (H_2O) 595 nm, a 18.9 $(g/L)^{-1}$ cm^{-1}; elemental analysis of the purified intermediate provided a C/N ratio (mequiv/g basis) of 6.21 corresponding to 48 mer % chromophore substitution; elemental analysis of the sulfamated product afforded an N/S ratio (mequiv/g basis) of 3.75 which corresponds to 40 mer % sulfamation for this degree of chromophore substitution.

Poly(*N*-vinylacetamide-*co*-sodium vinylsulfonate) (12). A 2-L, four-neck flask, equipped with overhead stirrer, thermometer, reflux condenser, and Ar inlet, was charged with 104 g (1.22 mol) of 2-propanol-free *N*-vinylacetamide (**10**),[1] 107 g (0.82 mol) of sodium vinylsulfonate (**11**, Air Products and Chemicals) as a 25% aqueous solution, 5.0 g (0.03 mol) of AIBN, and 500 mL of H_2O. The mixture was thoroughly deoxygenated and heated at 65 °C (internal) for 3.5 h. After cooling, the solution was filtered, evaporated to a volume of 100 mL , and diluted with 300 mL of CH_3OH. The slow addition of this mixture to 14 L of rapidly stirred acetone provided 142 g (67.3%) of **12** (M_p^{PSS} 6.6×10^4) after filtration and drying in vacuo. Anal. $(C_4H_7NO)_{0.6}(C_2H_3O_3SNa)_{0.4}$: C, H, N, S.

Preparation of Copolymer 13. A 1-L, three-neck flask, equipped with overhead stirrer and reflux condenser, was charged with the 142 g of **12** (0.83 mol of amide) prepared in the preceding step, 300 mL of H_2O, and 250 mL of 12 N HCl (3 mol). The solution was refluxed for 48 h, cooled, and allowed to stand for 24 h. The precipitated product was isolated by decantation, dissolved in 250 mL of 2 N NaOH, and

reprecipitated by slow addition to 14 L of rapidly stirred methanol containing 100 mL of 12 N HCl. The precipitate was filtered, washed with methanol, and dried in vacuo to afford 29.5 g of **13** as a white granular solid: ^{13}C NMR 31.5 (CS–C–CS), 39.9 (CS–C–CN), 45.7 (CN–C–CN), 46.6 (CN), and 55.2 (CS). Elemental analysis showed the N/S ratio (mequiv/g basis) to be 1.5. Proton titration and ^{13}C NMR showed that the hydrolysis was complete.

Preparation of Polymeric Dye 14 with 1-Methylamino-4-bromoanthraquinone (4). A 50-mL, two-neck flask, equipped with magnetic stir bar, reflux condenser, and Ar inlet, was charged with 564 mg of **13** prepared in the preceding step (7.10 mequiv of N/g by elemental analysis), 23 mL of H_2O, and 2 mL of 4 N NaOH. The mixture was stirred until homogeneous (pH 13.0) and treated with 1.01 g (3.20 mmol) of **4**, 10 mg of Cu_2Cl_2, and 3 mL of pyridine and heated to reflux. Additional 1-mL portions of 4 N NaOH were added at reaction times of 1 and 2 h. After 3 h the deep-blue solution was diluted with 25 mL of 10% aqueous pyridine, cooled to room temperature, and filtered. The product was purified by ultrafiltration and the resulting solution was lyophilized to afford 710 mg of polymeric dye: vis λ_{max} (H_2O) 596 nm, a 15.3 $(g/L)^{-1}$ cm^{-1}; elemental analysis provided an N/S ratio (mequiv/g basis) of 2.29 corresponding to 32 mer % chromophore substitution.

Acknowledgment. Helpful and stimulating discussions with Drs. G. A. Crosby, W. J. Leonard, Jr., and N. M. Weinshenker are gratefully acknowledged. The authors also thank the Analytical and Polymer Sciences Departments at Dynapol for their skillful assistance. An especial debt of gratitude is owed M. Kronstadt and Drs. P. L. Dubin and R. Phillips for providing their results on the structures of the amine–sulfonate copolymers in advance of publication.

References and Notes

(1) For the first paper in this series, see D. J. Dawson, R. D. Gless, and R. E. Wingard, Jr., *J. Am. Chem. Soc.*, **98**, 5996 (1976).
(2) E. M. Fettes, Ed., "Chemical Reactions of Polymers", Interscience, New York, N.Y., 1964.
(3) M. Okawara, T. Endo, and Y. Kurusu, *Prog. Polym. Sci. Jpn.*, **4**, 105 (1972).
(4) J. A. Moore, Ed., "Reactions on Polymers", D. Reidel Publishing Co., Boston, Mass., 1973.
(5) Reviews on polymeric reagents are available: (a) C. G. Overberger and K. N. Sannes, *Angew. Chem., Int. Ed. Engl.*, **13**, 99 (1975); (b) C. C. Leznoff, *Chem. Soc. Rev.*, **3**, 65 (1974); (c) A. Patchornik and M. A. Kraus, *Pure Appl. Chem.*, **43**, 503 (1975); (d) N. M. Weinshenker and G. A. Crosby, *Annu. Rep. Med. Chem.*, **11**, 281 (1976).
(6) (a) G. A. Crosby, N. M. Weinshenker, and H.-S. Uh, *J. Am. Chem. Soc.*, **97**, 2232 (1975); (b) N. M. Weinshenker, G. A. Crosby, and J. Y. Wong, *J. Org. Chem.*, **40**, 1966 (1975).
(7) (a) P. Cuatrecasas, *Proc. Natl. Acad. Sci. U.S.A.*, **63**, 450 (1969); (b) C. Sorg, E. Rüde, and O. Westphal, *Eur. J. Biochem.*, **17**, 85 (1970); (c) G. S. Banker, German Patent 1944694 (1970); *Chem. Abstr.*, **73**, 18482a (1970); (d) V. V. Korshak, M. M. Teplyakov, and R. D. Fedorova, *J. Polym. Sci., Part A-1*, **9**, 1027 (1971); (e) J. R. Dombrowski and L. G. Donaruma, *J. Appl. Polym. Sci.*, **15**, 1219 (1971); (f) H.-G. Batz, G. Franzmann, and H. Ringsdorf, *Angew. Chem., Int. Ed. Engl.*, **11**, 1103 (1972); (g) T. Nagai, *Kobunshi*, **21**, 190 (1972); (h) H.-G. Batz, G. Franzmann, and H. Ringsdorf, *Makromol. Chem.*, **172**, 27 (1973); (i) B.-Z. Weiner and A. Zilkha, *Isr. J. Chem.*, **11**, 567 (1973).
(8) (a) R. Goldman, L. Goldstein, and E. Katchalski in "Biochemical Aspects of Reactions on Solid Supports", G. R. Stark, Ed., Academic Press, New York, N.Y., 1971; (b) G. J. H. Melrose, *Rev. Pure Appl. Chem.*, **21**, 83 (1971); (c) G. Manecke, *Biotechnol. Bioeng. Symp.*, **3**, 185 (1972); (d) R. Axen, J. O. Porath and E. S. Ernbach, U.S. Patent 3645852 (1972); *Chem. Abstr.*, **73**, 111203v (1970); (e) N. E. Franks, U.S. Patent 3647630 (1972); *Chem. Abstr.*, **75**, 22975x (1971); (f) W. R. Vieth and K. Venkatasubramanian, *Chem. Technol.*, **3**, 677 (1973); (g) R. Epton, J. V. McLaren, and T. H. Thomas, U.S. Patent 3761357 (1973); *Chem. Abstr.*, **80**, 15671v (1974); (h) S. Emi, D. V. Myers, and G. A. Iacobucci, *Biochim. Biophys. Acta*, **445**, 672 (1976).
(9) (a) J. M. Schuck and B. S. Wildi, U.S. Patent 3679653 (1972); *Chem. Abstr.*, **77**, 105588r (1972); (b) M. S. Yong, *Science*, **182**, 157 (1973).
(10) C. C. Leznoff, presented at the Table Ronde Roussel U.C.L.A.F., Paris, March 4, 1976.
(11) A review of synthetic biologically active polymers is L. G. Donaruma, *Prog. Polym. Sci.*, **4**, 1 (1974).
(12) (a) D. O. Cowan, J. Park, C. U. Pittman, Jr., Y. Saski, T. K. Mukherjee, and N. A. Diamond, *J. Am. Chem. Soc.*, **94**, 5110 (1972); (b) C. U. Pittman, Jr., and B. Surynarayanan, *ibid.*, **96**, 7916 (1974).
(13) (a) A. Warshawsky, *Talanta*, **21**, 962 (1974); (b) L. R. Melby, *J. Am. Chem. Soc.*, **97**, 4044 (1975).
(14) (a) R. B. Merrifield, *J. Am. Chem. Soc.*, **85**, 2149 (1963); (b) J. M. Stewart and J. D. Young, "Solid Phase Peptide Synthesis", W. H. Freeman Co., San Francisco, Calif., 1969; (c) G. R. Stark, Ed., "Biochemical Aspects of Reactions on Solid Supports", Academic Press, New York, N.Y., 1971; (e) E. C. Blossey and D. C. Neckers, Ed., "Solid Phase Synthesis", Halsted Press, New York, N.Y., 1975.
(15) (a) C. C. Leznoff and J. Y. Wong, *Can. J. Chem.*, **51**, 3756 (1973); (b) J. M. J. Fréchet and L. J. Nuyens, *ibid.*, **54**, 926 (1976); (c) E. Seymour and J. M. J. Fréchet, *Tetrahedron Lett.*, 1149 (1976).
(16) F. Helfferich, "Ion Exchange", McGraw-Hill, New York, N.Y., 1962.
(17) P. Cuatrecasas and C. B. Anfinsen, *Annu. Rev. Biochem.*, **40**, 259 (1971).
(18) (a) J. P. Collman, L. S. Hegedus, M. P. Cooke, J. R. Norton, G. Dolcetti, and D. N. Marquardt, *J. Am. Chem. Soc.*, **94**, 1789 (1972); (b) R. H. Grubbs, C. Gibbons, L. C. Kroll, W. D. Bonds, Jr., and C. H. Brubaker, Jr., *ibid.*, **95**, 2375 (1973); (c) H. Bruner and J. C. Bailar, Jr., *Inorg. Chem.*, **12**, 1465 (1973); (d) Y. Nakamura and H. Hirai, *Chem. Lett.*, 809 (1974); (e) T. Kitamura, T. Joh, and N. Hagihara, *ibid.*, 203 (1975); (f) K. Kaneda, M. Terasawa, T. Imanaka, and S. Teranishi, *ibid.*, 1005 (1975); (g) C. U. Pittman, Jr., L. R. Smith, and R. M. Hanes, *J. Am. Chem. Soc.*, **97**, 1742 (1975).
(19) (a) J. Rebek, D. Brown, and S. Zimmerman, *J. Am. Chem. Soc.*, **97**, 454 (1975); (b) P. Jayalekshmy and S. Mazur, *ibid.*, **98**, 6710 (1976).
(20) (a) D. J. Dawson, R. D. Gless, and R. E. Wingard, Jr., *Chem. Technol.*, **6**, 724 (1976); (b) N. M. Weinshenker, *Polym. Prepr., Am. Chem. Soc., Div. Polym. Chem.*, **18** (1), 531 (1977); (c) T. Furia, *Food Technol. (Chicago)*, **31** (5), 34 (1977); (d) W. J. Leonard, Jr., in "Polymeric Delivery Systems", R. Kostelnik, Ed., Gordon and Breach, New York, N.Y., in press.
(21) In addition to ref 1, the following are published accounts of the preparation of water-soluble polymeric dyes: (a) T. Ida, S. Takahashi, and I. Utsumi, *Yakugaku Zasshi*, **89**, 517 (1969); (b) T. Ida, T. Watanabe, S. Takahashi, and I. Utsumi, *ibid.*, **89**, 524 (1969); (c) G. Kalopissis and A. Viout, U.S. Patent 3617165 (1971); *Chem. Abstr.*, **71**, 4127k (1969); (d) S. Machida, H. Narita, and K. Kato, *Angew. Makromol. Chem.*, **25**, 97 (1972); (e) H. Hatanaka, K. Sugiyama, T. Nakaya, and M. Imoto, *Makromol. Chem.*, **175**, 1855 (1974).
(22) H. A. Lubs, Ed., "The Chemistry of Synthetic Dyes and Pigments", Reinhold, New York, N.Y., 1955.
(23) Although generally known as the Ullmann condensation, this reaction is correctly designated the Jourdan–Ullmann–Goldberg synthesis. The amine displacement is not to be confused with the more familiar Ullmann biaryl coupling which is catalyzed by zero-valent copper. Reviews are available: (a) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **48**, 392 (1951); (b) R. M. Acheson, "Acridines", Interscience, New York, N.Y., 1956, pp 161–171; (c) J. W. Schulenberg and S. Archer, *Org. React.*, **14**, 19 (1965).
(24) A preparation of poly(vinylamine) by the Hofmann degradation of poly(acrylamide) has recently appeared: H. Tanaka and R. Senju, *Bull. Chem. Soc. Jpn.*, **49**, 2821 (1976).
(25) A mer unit is a monomeric unit of a polymer.
(26) For a review on sulfamation, see E. E. Gilbert, "Sulfonation and Related Reactions", Interscience, New York, N.Y., 1965, pp 403–424.
(27) The possibility that retained SO_4^{2-} (i.e., SO_4^{2-} associated with nonsulfamated backbone ammonium cations) produces artifically high results for the extent of sulfamation appears unlikely because the dyes were purified under conditions (pH 12) where residual backbone amines are uncharged. In control experiments, various samples of **2** were shown not to retain added SO_4^{2-} under these conditions.
(28) Vinylamine copolymers (excluding those of the graft type) have been prepared with: (a) acrylic acid, M. Vrancken and G. Smets, *J. Polym. Sci.*, **14**, 521 (1954); (b) vinyl alcohol, A. F. Nikolaev, S. N. Ushakov, L. P. Vishnevetskaya, and N. A. Voronova, *Vysokomol, Soedin.*, **5**, 547 (1963); *Chem. Abstr.*, **59**, 2959a (1963); (c) divinylbenzene, L. A. Lomako and V. N. Tolmachev, *Vysokomol. Soedin., Ser. B*, **13**, 49 (1971); *Chem. Abstr.*, **74**, 126646m (1971); (d) 1-vinyl-2-pyrrolidinone, R. I. Gruz, T. Y. Verkhoglyadova, E. F. Panarin, and S. N. Ushakov, *Vysokomol. Soedin., Ser. A*, **13**, 647 (1971); *Chem. Abstr.*, **74**, 142579x (1971). None of these were prepared through copolymerization with *N*-vinylacetamide.
(29) P. J. Flory, "Principles of Polymer Chemistry", Cornell University Press, Ithaca, N.Y., 1953, pp 178–199.
(30) M. Kronstadt, D. J. Dawson, and P. L. Dubin, *Polym. Prepr., Am. Chem. Soc., Div. Polym. Chem.*, in press.
(31) G. E. Ham, Ed., "Copolymerization", Interscience, New York, N.Y., 1964, pp 1–66.
(32) R. Phillips, *J. Appl. Polym. Sci.*, in press.
(33) For an extensive discussion of the factors affecting the chemical reactivity of copolymers, see H. J. Harwood in ref 4, pp 188–225. See also P. Rempp, *Pure Appl. Chem.*, **46**, 9 (1976); N. A. Platé, *ibid.*, **46**, 49 (1976), and references cited therein.
(34) (a) A. L. Spatorico and G. L. Beyer, *J. Appl. Polym. Sci.*, **19**, 2933 (1975); (b) P. L. Dubin, S. L. Koontz, and K. L. Wright, *J. Polym. Sci., Polym. Chem. Ed.*, **15**, 2047 (1977).