these propylene-rich copolymers. It is interesting that the resonances from the PBPP and BBPB tetrads overlapped so perfectly. Separate resonances could not be resolved even for sample H, which contained 43% butene-1 and had the highest BBPB concentrations of the copolymers examined.

Conclusions

The structural characterization of these propylene–butene-1 copolymers using ^{13}C-NMR techniques is essentially complete. The copolymer composition, dyad distribution, or number average sequence lengths can be accurately measured. Chemical shift assignments, which are internally consistent, are presented for the entire ^{13}C copolymer spectrum. Only the BP-centered tetrad assignments, which are reasonable considering the information available, should be considered tentative. The comonomer distributions, observed for these copolymers, appear to be Bernoullian over the range of compositions examined.

Acknowledgment. The author wishes to express his appreciation to Mr. F. L. Tilley for the experimental ^{13}C-NMR measurements and to Dr. C. M Selman for preparation of the copolymer samples. Appreciation is also expressed to the Phillips Petroleum Co. for permission to publish this work.

References and Notes

(1) C. J. Carman, R. A. Harrington, and C. E. Wilkes, *Macromolecules*, **10**, 536 (1977).
(2) G. J. Ray, P. E. Johnson, and J. R. Knox, *Macromolecules*, **10**, 773 (1977).
(3) J. C. Randall, *J. Polym. Sci., Polym. Phys. Ed.*, **15**, 1451 (1977).
(4) J. W. Cleary, U.S. Patent 3 332 921, July 25, 1967.
(5) M. H. Fisch and J. J. Dannenburg, *Anal. Chem.*, **49**, 1405 (1977).
(6) J. C. Randall, *J. Polym. Sci., Polym. Phys. Ed.*, **12**, 703 (1974).
(7) D. M. Grant and E. G. Paul, *J. Am. Chem. Soc.*, **86**, 2984 (1964).
(8) J. C. Randall, *J. Polym. Sci., Polym. Phys. Ed.*, **13**, 901 (1975).
(9) C. J. Carman and C. E. Wilkes, *Rubber Chem. Technol.*, **44**, 781 (1971).
(10) F. A. Bovey, "Polymer Conformation and Configuration", Academic Press, New York, N.Y., 1969, p 19.
(11) J. C. Randall, *J. Polym. Sci., Polym. Phys. Ed.*, **14**, 2083 (1976).
(12) J. C. Randall, "Polymer Sequence Determination: ^{13}C NMR Method", Academic Press, New York, N.Y., 1977, Chapter 3.

Hydroxamic Acid Polymers. Effect of Structure on the Selective Chelation of Iron in Water

Anthony Winston* and Darrell Kirchner

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506.

Received January 10, 1978

ABSTRACT: Vinyl polymers bearing side chains terminated in hydroxamic acid (HA) groups were prepared by the following method. The reaction between methacryloyl chloride and either glycine, β-alanine, or γ-aminobutyric acid gave the corresponding amides. The terminal carboxyl group was activated by condensation with *N*-hydroxysuccinimide in the presence of dicyclohexylcarbodiimide. Polymerization was effected by azobis(isobutyronitrile) at 60 °C. The polymer was treated with methylhydroxylamine hydrochloride and triethylamine to give the hydroxamic acid polymer. Depending upon which amino acid was used in the first step, the spacing between hydroxamic acid groups along the polymer chain was 9, 11, or 13 atoms, the polymers being designated P-9, P-11, or P-13. The polymers form colored complexes with iron(III), λ_{max} about 430 nm for a 3:1 HA–Fe ratio and about 470 nm for a 2:1 HA–Fe ratio. Mole ratio plots showed that stable 3:1 complexes formed. The stability constants for the iron polymer complexes were measured by competition experiments between iron(III), the polymer, and EDTA or DTPA. The averages of several determinations at various pH values were: 0.42×10^{29} (P-9); 4.86×10^{29} (P-11); and 2.24×10^{29} (P-13). These results show that the stereochemistry of the system (HA spacing) is an important factor in the stability of the complex. Competition between iron and aluminum for the polymers showed that P-11 was about 10 times more selective for iron than P-9 or P-13. The largest stability complex for aluminum was for P-13 (2.96×10^{27}). Evidence is also presented to show that the 3:1 HA–Fe complexes are converted to 2:1 complexes in the presence of excess iron.

Ion exchange resins bearing chelating functional groups have long been of interest for removing specific metals from water. By appropriate selection of functional groups, resins have been designed to complex a variety of transition, alkaline earth, and alkali metals.[1–8] Many of these resins bind several metal ions and thus are somewhat limited in their selectivity.

Hydroxamic acids form well-known colored complexes with iron(III). In the case of certain naturally occurring trihydroxamic acids, the siderochromes,[9–11] which include the ferrioxamines and the ferrichromes, the stabilities of the iron(III) complexes are exceptional.[12] The cause of this high stability can be attributed not only to the high coordinative power of the hydroxamic acid for iron(III) but also to the number and spacing of the coordinative groups. In the evolution of these iron scavengers in living organisms, the spacing of hydroxamic acids became adjusted so that the three hydroxamic acids of the siderochrome fit precisely the required octahedral coordination sphere of the iron.

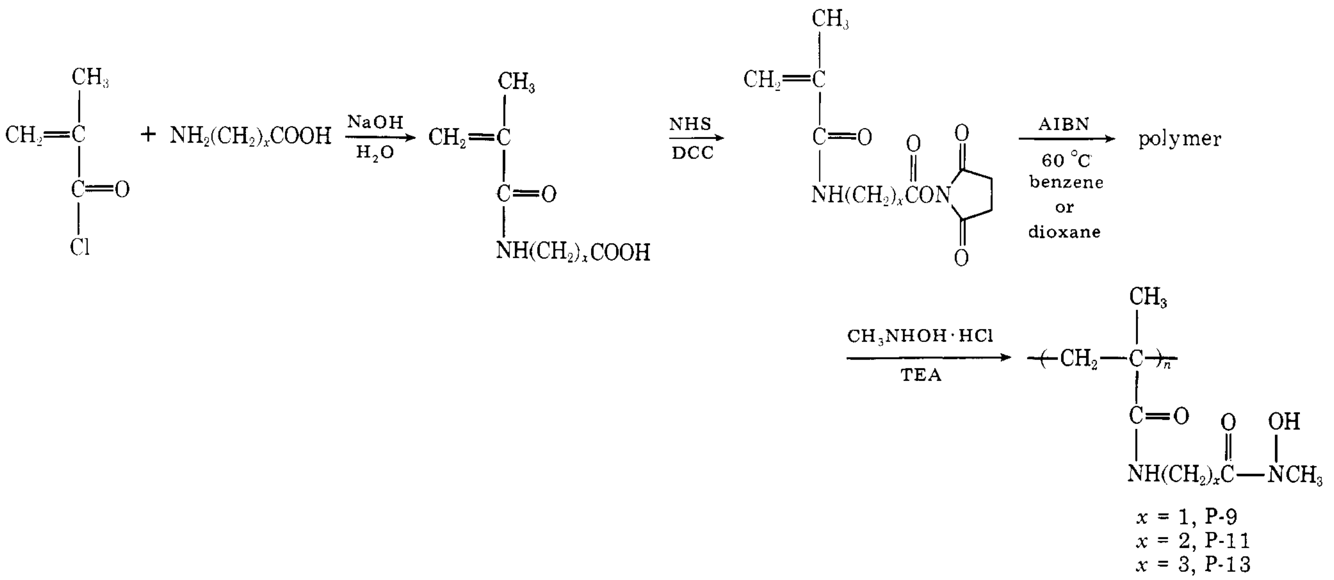
Using the naturally occurring trihydroxamic acids as models, it appeared reasonable that hydroxamic acid polymers would have a high affinity and selectivity for iron if the attached hydroxamic acids could be arranged to fit the octahedron of the iron(III) complex. Although resins based on hydroxamic acids have been synthesized in the past, none have been constructed with the idea of providing a spacing distance favorable for complex formation.

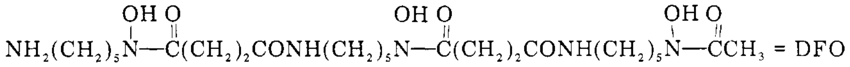
Earlier we showed that in the case of vinyl polymers bearing side chain hydroxamic acid groups, the stability of the iron complex was affected by the atomic chain spacing between neighboring hydroxamic acids.[13] An 11-atom spacing was found to be far superior to a 3-atom spacing, presumably because the larger 11-atom spacing would allow neighboring hydroxamic acids to readily fit the octahedral iron complex, whereas the 3-atom spacing would not. Molecular models had indicated that an 11-atom spacing should be about optimum for formation of the octahedral iron complex.

In order to test this idea and to see to what extent small

0024-9297/78/2211-0597$01.00/0

Scheme I





$$NH_2(CH_2)_5\overset{OH}{N}-\overset{O}{\overset{\|}{C}}(CH_2)_2CONH(CH_2)_5\overset{OH}{N}-\overset{O}{\overset{\|}{C}}(CH_2)_2CONH(CH_2)_5\overset{OH}{N}-\overset{O}{\overset{\|}{C}}CH_3 = \text{DFO}$$

NHS = *N*-hydroxysuccinimide
DCC = dicyclohexylcarbodiimide
TEA = triethylamine
DFO = desferrioxamine
AIBN = azobis(isobutyronitrile)

changes in hydroxamic acid spacing would influence complex stability, it was decided to compare the iron complex stability constants of three polymers in which the hydroxamic acids were spaced by 9, 11, and 13 atoms (to be identified as P-9, P-11, and P-13). In this paper we report the synthesis of these polymers, the determination of the iron-polymer stability constants, and the correlation of these constants with the atomic spacing. Additional information will also be included to further characterize the behavior of these polymers toward iron.

The polymers were synthesized by the procedure shown in Scheme I. The first step was to introduce the spacer amino acids through Schotten–Bauman reactions with methacryloyl chloride. The terminal carboxyl group was then activated by conversion to the *N*-hydroxysuccinimide (NHS) ester through condensation using dicyclohexylcarbodiimide[14] (DCC). Although the NHS ester of *N*-methacryloyl-γ-aminobutyric acid was evidently somewhat impure as indicated by a low carbon analysis, these impurities must have been at least partially eliminated in the polymerization step, since the carbon analysis of the corresponding polymer was satisfactory. Polymerization was initiated by free-radical means to give insoluble polymers. Treatment of the polymers with methylhydroxylamine gave the water-soluble hydroxamic acid polymers P-9, P-11, and P-13.

The polymers were purified by dialysis in water and the water was then removed on a rotary evaporator to give light tan solids. The polymers were extremely difficult to dry thoroughly as evidenced by the change in the carbon analyses on vigorous drying over periods of up to 3 weeks. This tenacity of the polymers for water is undoubtedly due to the fact that the hydroxamic acid group itself is strongly hydrophilic. GPC analysis of the polymers on Sephadex G 25 gave a single peak emerging at the void volume of the column, which indicated that low molecular weight impurities had been largely removed during the dialysis. Addition of iron(III) to aqueous solutions of the polymers produced the characteristic red-brown color of the hydroxamic acid–iron complex. The molecular weight of P-11 was determined by membrane osmometry in water and found to be 56 000.

Experimental Section

Melting points were determined using a Mel-Temp apparatus and are uncorrected. Gel-permeation chromatography (GPC) was carried out using Sephadex-G-25 (Pharmacia Fine Chemicals) in a 2.5 cm by 76 cm glass column. The detector was a Waters Associates Differential Refractometer R403. The pH measurements were made on a Corning Model 10 pH meter. Infrared spectra were recorded on the Beckman IR-8 spectrophotometer. UV–visible spectra were measured on a Beckman DB-G grating spectrophotometer. Proton magnetic resonance spectra were recorded on Varian T-60 and EM-360 spectrometers using Me_4Si as internal standard. Osmometry was run using a Stabin osmometer and membrane B19 from Schleicher and Schuell, Inc. Viscometry was run using a Cannon Ubbelohde dilution viscometer.

N-Methacryloylglycine. A solution of 12.0 g (0.30 mol) of NaOH and 11.5 g (0.15 mol) of glycine in 17 mL of water was cooled to 0 °C and 15.7 g (0.15 mol) of methacryloyl chloride was added cautiously with stirring. When the addition was complete, concentrated H_2SO_4 was added to pH 3. The mixture was extracted ten times with hot $CHCl_3$. The extract was dried over sodium sulfate and evaporated to give a solid. Recrystallization from $CHCl_3$ gave 8.3 g (40%) of product: mp 101–4 °C (lit.[15] mp 104 °C); NMR (Me_2SO-d_6) δ 8.13 (1 H, t, NH), 5.73 (1 H, s, vinyl H), 5.38 (1 H, s, vinyl H), 3.75 (2 H d, methylene), 1.9 (3 H, s, methyl); IR (KBr) 3360 (NH), 1740 (acid C═O), 1642 (C═C), 1580 (amide C═O), and 1540 cm^{-1} (amide NH).

Anal. Calcd for $C_6H_9NO_3$: C, 50.34; H, 6.34; N, 9.79. Found: C, 50.21; H, 6.21; N, 9.77.

N-Methyacryloyl-β-alanine. This procedure is a modification of that given previously.[13] A solution of 24.0 g (0.592 mol) of NaOH and 26.7 g (0.300 mol) of β-alanine in 40 mL of water was prepared and cooled to 0–5 °C. Methacryloyl chloride (31.3 g, 0.300 mol) was added with vigorous stirring over a 15-min period. The reaction mixture was stirred for 40 min and then concentrated HCl was added to a pH of 3, whereupon a light oil separated. The reaction mixture was immediately filtered by suction with addition of $CHCl_3$ as necessary to extract the oily product and to reduce viscosity. The two layers were separated and the aqueous layer was again extracted with $CHCl_3$. The $CHCl_3$ layers were combined, dried over Na_2SO_4, and concentrated on a rotary evaporator. Careful addition of hexane caused precipitation of the product to give 35.5 g (75%) of crude solid.

Recrystallization of the solid from benzene gave 28.4 g (60%) of *N*-methacryloyl-β-alanine, mp 75–77 °C (lit.[13] mp 76–78 °C). IR and NMR data were reported previously.[13]

***N*-Methacryloyl-γ-aminobutyric Acid.** A solution of 12.0 g (0.30 mol) of NaOH and 15.4 g (0.15 mol) of γ-aminobutyric acid in 17 mL of H_2O was cooled to 0 °C and 15.7 g (0.15 mol) of methacryloyl chloride was added cautiously, with stirring, over a 20-min period. When the addition was complete, concentrated HCl was added to attain pH 3. The solution was filtered and extracted twice with $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4.

The monomer could not be isolated because of its rapid polymerization when the $CHCl_3$ solution was concentrated. Therefore, the $CHCl_3$ was partially removed and the monomer solution was used to form the succinimidyl ester in the next step.

***N*-Hydroxysuccinimide (NHS) Ester of *N*-Methacryloylglycine.** To a stirred solution of 10.24 g (0.089 mol) of *N*-hydroxysuccinimide and 12.7 g (0.089 mol) of *N*-methacryloylglycine in 100 mL of dry dioxane was added 18.63 g (0.096 mol) of *N,N'*-dicyclohexylcarbodiimide (DCC) at 13 °C. After 2 h, 0.13 g of 4-*tert*-butylcatechol was added and stirring was continued for 2 h at room temperature. *N,N'*-Dicyclohexylurea was removed by filtration. Addition of hexane to the dioxane solution caused the product to precipitate. The crude product was dissolved in acetone, filtered, and reprecipitated with hexane to give 12 g (56%) of ester: mp 158–162 °C; NMR (Me_2SO-d_6) δ 8.55 (1 H, t, NH), 5.75 (1 H, s, vinyl H), 5.5 (1 H, s, vinyl H), 4.3 (2 H, d, CH_2), 2.8 (4 H, s, succinimide H), 1.9 (3 H, s, CH_3); IR (KBr) 3300 (NH), 1820 and 1775 (succinimide C=O), 1730 (ester C=O), 1650 (C=C), 1610 (amide C=O), and 1525 cm^{-1} (amide NH). Anal. Calcd for $C_{10}H_{12}N_2O_5$: C, 50.00; H, 5.04; N, 11.66. Found: C, 49.73; H, 4.99; N, 11.47.

NHS Ester of *N*-Methacryloyl-β-alanine. This compound was prepared according to the previously reported procedure.[13]

NHS Ester of *N*-Methacryloyl-γ-aminobutyric Acid. The $CHCl_3$ solution of *N*-methacryloyl-γ-aminobutyric acid was partially evaporated. To this solution was added 13.8 g (0.12 mol) of *N*-hydroxysuccinimide, 25.2 g (0.13 mol) of *N,N*-dicyclohexylcarbodiimide, and 125 mL of dry dioxane at 13 °C. The solution was stirred for 2 h, 0.13 g of 4-*tert*-butylpyrocatechol was added, and the solution was stirred at room temperature for an additional 2 h. The *N,N'*-dicyclohexylurea was removed by filtration. Addition of hexane to the dioxane solution caused the precipitation of a solid. The solid product was dissolved in acetone, filtered, and reprecipitated with hexane to give 10 g (2%) of the ester: mp 100–102 °C; NMR ($CDCl_3$) δ 6.5 (1 H, NH), 5.7 (1 H, s, vinyl H), 5.3 (1 H, s, vinyl H), 3.5 (2 H, m $NHCH_2$), 2.7 (6 H, CH_2C=O and succinimide H), 2.0 (5 H, CH_3 and CH_2); IR (KBr) 3350 (NH), 1820 and 1785 (succinimide C=O), 1725 (ester C=O), 1660 (C=C), 1615 (amide C=O), and 1535 cm^{-1} (amide NH). Anal. Calcd for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.01; N, 10.44. Found: C, 52.58; H, 6.18; N, 10.79.

Polymerization. General Procedure. A solution of the succinimidyl monomer in dry dioxane was heated at 60 °C and purged with N_2. Azobis(isobutyronitrile) (AIBN) (30 mg) was added, and the reaction mixture was stirred under N_2 for 24 h. The white precipitate was filtered and dried.

Polymer of NHS Ester of *N*-Methacryloylglycine. From 1.9 g (7.9×10^{-3} mol) of monomer was obtained 1.7 g (89%) of polymer: IR (KBr) 3400 (NH), 1825 and 1790 (succinimide C=O), 1740 (ester C=O), 1630 (amide C=O), and 1525 cm^{-1} (NH). Anal. Calcd for $C_{10}H_{12}N_2O_5$: C, 50.00; H, 5.04; N, 11.66. Found: C, 51.98, 50.13; H, 6.77, 6.19; N, 10.64.

Polymer of NHS Ester of *N*-Methacryloyl-β-alanine. This polymer was prepared as previously reported.[13]

Polymer of NHS Ester of *N*-Methacryloyl-γ-aminobutyric Acid. From 2.1 g (7.8×10^{-3} mol) of monomer was obtained 1.6 g (76%) of polymer: IR (KBr) 3400 (NH), 1815 and 1780 (succinimide C=O), 1725 (ester C=O), 1640 (amide C=O), 1520 cm^{-1} (NH). Anal. Calcd for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.28; H, 6.80; N, 9.20.

Conversion of NHS Ester Polymers to Hydroxamic Acid Polymers. General Procedure. To a solution of methylhydroxylamine hydrochloride in 10 mL of dry DMF was added an equimolar amount of triethylamine. The precipitate was removed by filtration and the solution was added to a DMF solution of succinimidyl ester polymer. The mixture was stirred for 24 h, dialyzed in Spectrapor membrane tubing (mol wt cutoff 6000–8000), and analyzed for purity by GPC using Sephadex G-25. The solution was evaporated to dryness and the polymer was dried under reduced pressure.

Poly(*N*-methacryloylglycine hydroxamic acid). From 1.0 g of the succinimide ester polymer and a threefold excess of methylhydroxylamine was obtained 0.4 g (56%) of hydroxamic acid polymer: IR (KBr) 3400 (OH), 1620 (C=O), and 1530 cm^{-1} (NH). Anal. Calcd for $C_7H_{12}N_2O_3$: C, 48.82; H, 7.03; N, 16.27. Found (after drying for 2 days): C, 47.34; H, 7.61; N, 15.05. Found (after drying for 3 weeks under vacuum at room temperature): C, 48.59; H, 7.58; N, 15.92.

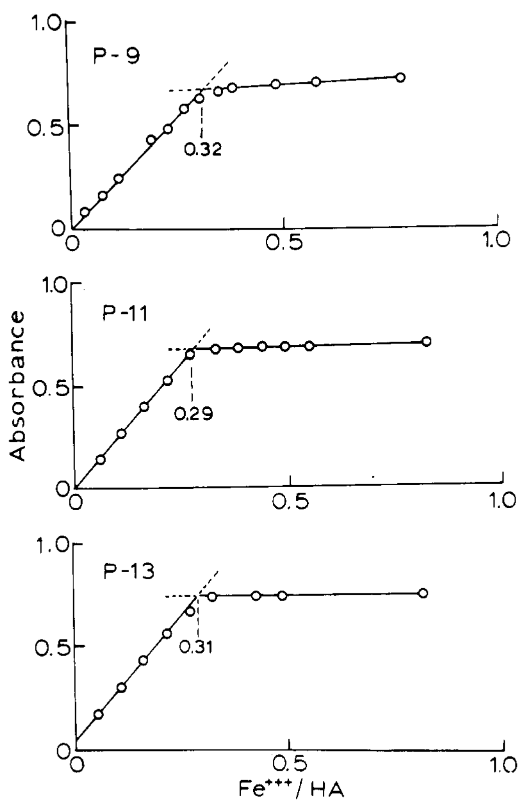


Figure 1. Absorbance vs. the mole ratio of iron(III) to hydroxamic acid for polymers P-9, P-11, and P-13.

Poly(*N*-methacryloyl-β-alanine hydroxamic acid). this polymer was prepared as previously reported.[13]

Poly(*N*-methacryloyl-γ-aminobutyric acid hydroxamic acid). From 1.2 g of the succinimidyl ester polymer and a threefold excess of methylhydroxylamine was obtained 0.54 g (60%) of hydroxamic acid polymer: IR (KBr) 3380 (OH), 1630 (C=O) and 1530 cm^{-1} (NH). Anal. Calcd for $C_9H_{16}N_2O_3$: C, 53.98; H, 8.05; N, 13.99. Found (after drying for 2 days at room temperature): C, 51.37; H, 7.91; N, 12.52. Found (after drying under vacuum for 2 weeks): C, 52.69; H, 8.14; N, 13.53.

Mole Ratio Determination. Fe^{3+}–Hydroxamic Acid (HA). Aqueous stock solutions of P-9, P-11, and P-13 were prepared at concentrations of 0.025 monomer equiv/L. Ferric perchlorate solutions of approximately 2.7×10^{-2} M were prepared, acidified with nitric acid, and standardized with EDTA (bismuth method).[16] Aliquots (0.4 mL) of the polymer solution were placed in each of a series of 10-mL volumetric flasks, varying amounts of iron solution (0.02 to 0.40 mL) were added, and the resulting solutions were diluted to 10 mL with water. The pH was 3.5. The absorbance of each solution was measured at λ_{max} (430–440 nm) and plotted against the Fe^{3+}–HA ratio, Figure 1.

The following procedure was carried out to see whether or not the ionic strength of the solution would have an appreciable affect on the measurements. A series of solutions was prepared to contain iron, polymer, and varying amounts of KNO_3 (0.0, 0.1, and 0.3 N). Absorbance readings at 444 nm were all identical. A second series was prepared as before but also containing DTPA. Absorbance readings at 444 nm for this series were also identical. Thus, it appears that in this range ionic strength has little influence on either the absorbance measurements or on the competition equilibrium.

Potentiometric Titration of P-11. A solution of P-11 (1.075×10^{-2} M in hydroxamic acid units) and KNO_3 (0.1 N) was prepared and adjusted to pH 3.0 with nitric acid. The solution was titrated with 0.1026 N KOH at 25 °C under a wet nitrogen purge.

Results and Discussion

Effects of Structure on the Stability of Hydroxamic Acid (HA) Polymer–Iron(III) Complexes. In order to

Table I
Equilibrium Constants, K_I, for the Distribution of Iron(III) between Siderochrome and DTPA

Siderochrome	pH	λ_{max}, nm	a,[a] mM	K_I[b]	SD[c]
P-9	2.0	452	1.68	148.4	6.2
P-9	4.0	452	1.68	25.82	8.9
P-9	6.0	452	1.68	0.528	0.094
P-11	2.0	446	1.96	11.67	0.99
P-11	4.0	444	1.96	1.97	0.17
P-11	6.0	444	1.96	0.0404	0.0059
P-13	2.0	440	2.00	25.84	0.28
P-13	4 0	440	2.00	4.49	0.47
P-13	6.0	440	2.00	0.0934	0.0091
DFO	2	430	2.48	21.42	1.54

[a] Millimolar absorptivity. [b] Average of three determinations. [c] Standard deviation.

Table II
Equilibrium Constants, K_I, for Distribution of Iron(III) between Polymer and EDTA[a]

Polymer	pH	λ_{max}, nm	a, mM	K_I	SD[c]
P-9	2	452	1.68	1165	
	4	452	1.68	122[b]	47
P-11	2	444	1.97	116.2	
	4	444	1.97	13.23[b]	2.4
P-13	2	440	2.00	236.2	
	4	440	2.00	26.65[b]	3.8

[a] A time delay of from 140 to 300 min was required to achieve equilibrium. [b] Average of three determinations. [c] Standard deviation.

Table III
pK Values of Ligands and Iron Complexes[a]

Ligands and complexes	pK_1	pK_2	pK_3	pK_4	pK_5	pK_0	log K_{FeZ}
DTPA	10.58	8.60	4.27	2.64	1.5		
EDTA	10.26	6.16	2.67	2.00			
Fe(DTPA)						>10	27.40
Fe(EDTA)						7.5	25.1
Fe(HDTPA)	3.56						
Fe(HEDTA)	<1						
DFO	9.70	9.03	8.39				
Fe(HDFO)	0.94						
P-11[b]	8.7						
Fe(HP-11)[b]	0.6						

[a] Reference 12 except where indicated. [b] This work. The values for P-11 were also assumed for P-9 and P-13.

confirm that the hydroxamic acid groups of the polymers would form the normal 3:1 complexes with iron, the compositions of the complexes were analyzed by the mole ratio method using the characteristic absorption band at 430–450 nm. The results are shown in Figure 1. The sharp intersections in the region of 0.3 Fe–HA indicate stable complexes at the 3:1 ratio. Molecular models show that in all three cases the spacings of the HA units are sufficiently large to permit complete utilization of hydroxamic acids in forming the iron complexes. Although the sharp intersections of Figure 1 indicate that the complexes are hightly stable, the mole ratio method is not sensitive to small changes in stability constants and does not reveal any differences in the three polymers. Thus, in order to reveal the effects arising from small changes in HA spacing, a more sensitive method had to be employed.

Earlier, Anderegg, L'Eplattenier, and Schwarzenbach[12] had shown that the stability constants of iron complexes of a series of naturally occurring hydroxamic acids, called siderochromes, could be determined conveniently through competition experiments involving ethylenediaminetetracetic acid (EDTA) and diethylenetriaminepentaacetic acid (DTPA). This work gave results having an appropriate degree of sensitivity to structural variations and so was selected with the expectation that similar structural effects would be revealed in the case of the hydroxamic acid polymers. The methods were described in detail by Schwarzenbach and only the essential features will be repeated here. For consistency, the notation will be the same as that used by Schwarzenbach.

The procedure is based on eq 1–13. The initial step is to measure the equilibrium constant K_I, eq 2, for the equilibrium shown in eq 1,

$$\mathrm{Fe(Sid)}' + \mathrm{Z}' \rightleftharpoons \mathrm{FeZ}' + \mathrm{Sid}' \quad (1)$$

$$K_I = \frac{[\mathrm{FeZ}]'[\mathrm{Sid}]'}{[\mathrm{Fe(Sid)}]'[\mathrm{Z}]'} \quad (2)$$

where Sid stands for siderochrome, either polymer or desferrioxamine, and Z is the competing complexing agent EDTA or DTPA. The concentrations of the species of eq 1 are indicated by the sign ′ and are defined, eq 3–6, as the sums of the species at all degrees of protonation. The concentrations are also given in terms of the nonprotonated species and α, the reciprocal of the fraction nonprotonated.

$$[\mathrm{Sid}]' = \sum[\mathrm{H}_j\mathrm{Sid}] = [\mathrm{Sid}]\cdot\alpha_{\mathrm{Sid}} \quad (3)$$

Table IV
α Values for Ligands and Iron Complexes at Various pH Levels[a]

Ligand or complex	α pH 2	α pH 4	α pH 6
DTPA	1.90×10^{18}	4.45×10^{11}	1.54×10^{7}
EDTA	2.72×10^{13}	2.77×10^{8}	
Fe(DTPA)	37.3	1.36	1.00
Fe(EDTA)	1.00	1.00	
DFO	1.32×10^{21}		
Fe(DFO)	1.09	1.00	1.00
P-11[b,c]	1.26×10^{20}	1.26×10^{14}	1.26×10^{8}
Fe(HP-11)[b]	1.04	1.00	1.00

[a] Calcd from pK data of Table III. [b] This work. [c] The pK_1 of 8.7 was used three times in eq 13 to calculate α.

$$[\mathrm{Z}]' = \sum[\mathrm{H}_j\mathrm{Z}] = [\mathrm{Z}]\cdot\alpha_{\mathrm{Z}} \qquad (4)$$

$$[\mathrm{Fe(Sid)}]' = \sum[\mathrm{Fe(H}_p\mathrm{Sid)}] = [\mathrm{Fe(Sid)}]\cdot\alpha_{\mathrm{FeSid}} \qquad (5)$$

$$[\mathrm{FeZ}]' = \sum[\mathrm{Fe(H}_p\mathrm{Z)}] = [\mathrm{FeZ}]\cdot\alpha_{\mathrm{FeZ}} \qquad (6)$$

The absorbance, D, of the Fe–HA complex is determined both in the absence and presence of the competing chelating agent Z (EDTA or DTPA) at known pH values. From the equilibrium concentration of Fe(Sid)′, as measured by the absorbance, and from the total concentrations of Fe, Sid, and Z, the quantities required for evaluating K_{I} may be determined, eq 7–10, where ϵ' is the molar absorbtivity and d the path length (1 cm).

$$D = \epsilon'_{\mathrm{FeSid}}\cdot[\mathrm{FeSid}]'\cdot d + \epsilon'_{\mathrm{FeZ}}\cdot[\mathrm{FeZ}]'\cdot d \qquad (7)$$

$$[\mathrm{Fe}]_t = [\mathrm{FeSid}]' + [\mathrm{FeZ}]' \qquad (8)$$

$$[\mathrm{Sid}]_t = [\mathrm{Sid}]' + [\mathrm{FeSid}]' \qquad (9)$$

$$[\mathrm{Z}]_t = [\mathrm{Z}]' + [\mathrm{FeZ}]' \qquad (10)$$

Polymers P-9, P-11, and P-13 were analyzed by this procedure using both DTPA and EDTA at pH levels of 2, 4, and 6. For comparison, the naturally occurring desferrioxamine (DFO, Scheme I) was also run. The results are shown in Tables I and II.

The K_{I} values were then used to determine the stability constants K_{FeSid}, eq 12, for the equilibrium, eq 11

$$\mathrm{Fe} + \mathrm{Sid} \rightleftharpoons \mathrm{FeSid} \qquad (11)$$

$$K_{\mathrm{Fe(Sid)}} = \frac{[\mathrm{Fe(Sid)}]}{[\mathrm{Fe}]\cdot[\mathrm{Sid}]} = \frac{K_{\mathrm{FeZ}}\cdot\alpha_{\mathrm{FeZ}}\cdot\alpha_{\mathrm{Sid}}}{K_{\mathrm{I}}\cdot\alpha_{\mathrm{Z}}\cdot\alpha_{\mathrm{FeSid}}} \qquad (12)$$

To do this, K_{Fez} and the α values for the various species must be known. K_{Fez} for DTPA and EDTA were reported by Schwarzenbach,[12] Table III. The α values were calculated at the three pH levels from the pK values of the various species by means of eq 13.

$$\alpha = \ldots[\mathrm{H}]^{-1} \times 10^{-\mathrm{p}K_0} + 1 + [\mathrm{H}] \times 10^{\mathrm{p}K_1} + [\mathrm{H}]^2 \times 10^{\mathrm{p}K_1+\mathrm{p}K_2}\ldots \qquad (13)$$

The pK values for EDTA, DTPA, DFO, Fe-EDTA, Fe-DTPA, and Fe-DFO were reported by Schwarzenbach[12] and are included in Table III. The α values derived therefrom are included in Table IV. The pK of polymer P-11 and of its protonated iron complex Fe(HP-11) were determined independently as follows.

Table V
Effect of Degree of Neutralization, θ, on pK_a for P-11[a]

θ	pK_a	θ	pK_a
0.19	9.1	0.67	10.1
0.38	9.5	0.84	10.4
0.50	9.7		

[a] Titrated with standard NaOH. Ionic strength 0.10 in KNO_3.

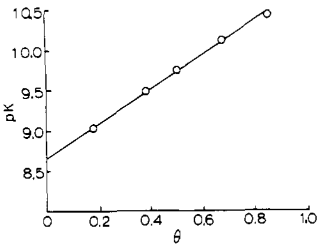


Figure 2. Apparent pK vs. degree of neutralization, θ, for polymer P-11; ionic strength 0.1 KNO_3.

It has long been known that the apparent pK of polyacids increases with increasing degrees of neutralization, this effect being caused by the build up of negative charge during the course of the titration, making it more and more difficult to remove additional protons. This effect was observed in the case of polymer P-11, the pK_a increased steadily during titration, Table V. The question then arises as to what pK_a value should be used in order to calculate an α value for the polymer. Now a basic difference exists between the neutralization of the polymer with base and its complexation with iron. In the complexation reaction the polymer would not accumulate negative charges, for as the hydroxamic acid groups ionize the charge would be neutralized by the complexing iron and hence, we should not expect the pK_a to change much as the complexation proceeds. Thus, it would be reasonable to use the pK_a value for zero degree of neutralization. This value can be obtained from a plot of pK vs. the degree of neutralization, θ, according to the method of Bak.[17] The plot for polymer P-11, Figure 2, is linear and extrapolation to zero θ gives 8.7 for pK_a, a very reasonable value when compared with the results of Schwarzenbach for similar systems.

The pK for the protonated iron complex Fe(HP-11) can be determined spectroscopically as shown by Schwarzenbach.[18] The expressions applicable to this procedure are shown in eq 14–18.

$$\mathrm{Fe(HP\text{-}11)} \overset{K^{\mathrm{H}}}{\rightleftharpoons} \mathrm{Fe(P\text{-}11)} + \mathrm{H}^+ \qquad (14)$$

$$K^{\mathrm{H}} = \frac{[\mathrm{Fe(P\text{-}11)}][\mathrm{H}^+]}{[\mathrm{Fe(HP\text{-}11)}]} \qquad (15)$$

$$[\mathrm{Fe(P\text{-}11)}] + [\mathrm{Fe(HP\text{-}11)}] = c \qquad (16)$$

$$D = \epsilon_1[\mathrm{Fe(P\text{-}11)}] + \epsilon_2[\mathrm{Fe(HP{=}11)}] \qquad (17)$$

$$\begin{aligned} D &= c\cdot\epsilon_2 + K^{\mathrm{H}}\cdot(c\cdot\epsilon_1 - D)/[\mathrm{H}^+] \\ &= c\cdot\epsilon_2 + K^{\mathrm{H}}\cdot(D' - D)/[\mathrm{H}^+] \end{aligned} \qquad (18)$$

$D' = D$ of curve "a", Figure 3, and $= c\cdot\epsilon_1$. Equations 15, 16, and 17 are combined to give eq 18. The value of K^{H} was determined from a series of spectra taken of the iron complex at various pH levels. The spectral series for polymer P-11 is shown in Figure 3. The plot of D at $\lambda_{\max}$ vs. $(D' - D)/[\mathrm{H}^+]$, eq 18, Figure 4, is linear and the slope gives a value of 0.6 for p$K^{\mathrm{H}}_{\mathrm{Fe(HP\text{-}11)}}$. This value is listed in Table III and the α values calculated therefrom are given in Table IV. The α values for Fe(HP-11) turn out to be 1.00 except at very low pH. But even at pH 2, the α is only 1.04. Any minor errors in determining p$K^{\mathrm{H}}_{\mathrm{Fe(HP\text{-}11)}}$ thus would have little effect either on the α or on the final stability constant. The α values were assumed to be the same for all three polymers P-9, P-11, and P-13. All the

Table VI
Stability Constants for Fe–Hydroxamic Acid Complexes

	$K_{\text{Fe-Sid}} \times 10^{-29}$					
	Using DTPA			Using EDTA		
Sid	pH-2	pH-4	pH-6	pH-2	pH-4	Av
P-9	0.40	0.37	0.39	0.48	0.47	0.42
P-11	5.12	4.91	5.09	4.83	4.33	4.86
P-13	2.31	2.15	2.20	2.37	2.15	2.24
DFO	27.9					
DFO[a]	31.6					
FCHO[a,b]	1.12					

[a] Data of Schwarzenbach. [b] FCHO-Ferrichrome.

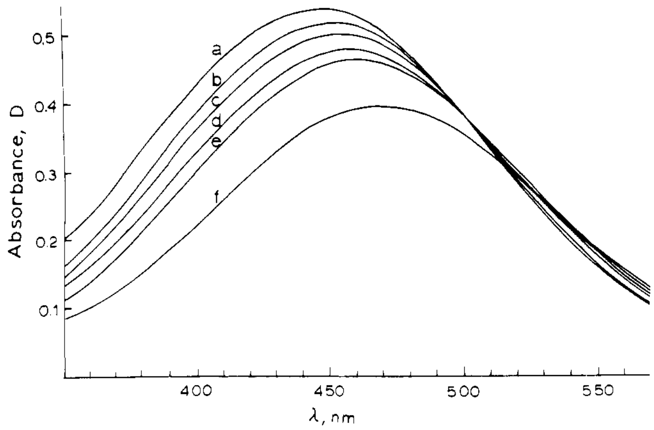


Figure 3. Absorption spectra of polymer P-11 at various pH values. Concentrations: [HA] = 1.002×10^{-3}; [Fe^{3+}] = 3.151×10^{-4}; (a) pH 2.01; (b) pH 1.48; (c) pH 1.21; (d) pH 0.95; (e) pH 0.7; (f) pH 0.2.

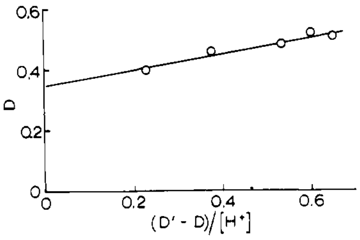


Figure 4. Plot of eq 18 from data taken from Figure 3. Absorbance values taken at λ_{max}.

values are now at hand to calculate the stability constants for the polymers by means of eq 12. The results are shown in Table VI.

The stability constants of the iron–polymer complexes are in the same range as those of the naturally occurring siderochromes ferrioxamine and ferrichrome. This result and the mole ratio data indicate that the hydroxamic acid units are utilized completely in forming the 3:1 HA–Fe complexes. Thus, the side chain is sufficiently short to give the chelate effect, but differences occur because of somewhat different steric arrangements. The fact that the stability constant changes significantly with changing side chain length indicates that the 3:1 iron complex is formed through three *neighboring* hydroxamic acid units. If this were not the case, we should not expect much influence from side chain length and we would also expect the complex to cross-link through the ferric ion and become insoluble.

The stability constants clearly show that the order of stability is Fe(P-11) > Fe(P-13) ≫ Fe(P-9). Molecular models show that in order to make the 3:1 iron complex using neighboring hydroxamic acid units, the side chains must be long enough to wrap around the iron in the required octahedral arrangement. In the model of P-11, the side chains can do this without strain, but for P-9 the fit is not nearly as good and considerable strain is encountered, especially for the attachment of the third side chain onto the iron. In the case of P-13, which has ample side chain length to form the complex, the lower stability is attributed to the greater entropy due to the longer side arm. Thus, the optimum side chain length is the 11-atom spacing of P-11. In comparing the polymer with the natural siderochromes, the constant of the P-11 complex is about one-fifth that of the ferrioxamine complex but about four times greater than for the ferrichrome complex.

Effect of Structure on the Selectivity of the Polymers for Iron over Aluminum. Another question that concerns the three polymers is how selective are the polymers for iron over other metals. A solution of Fe(P-11) was prepared and treated with a variety of metal ions, Hg^{2+}, Pb^{2+}, Al^{3+}, Ca^{2+}, and Mg^{2+}. Of these only aluminum complexed sufficient amounts of polymer, displacing iron, to have any effect on the absorbance. Since aluminum was able to compete effectively with iron to form a colorless complex with the polymer, a series of experiments was set up to measure this competition. Equations 19–22 relate to this procedure.

$$\text{FeSid} + Al^{3+} \rightarrow \text{AlSid} + Fe^{3+} \tag{19}$$

$$K_{II} = \frac{[\text{AlSid}][Fe^{3+}]}{[\text{FeSid}][Al^{3+}]} \tag{20}$$

$$Al^{3+} + \text{Sid} \rightleftharpoons \text{AlSid} \tag{21}$$

$$K_{\text{AlSid}} = \frac{[\text{AlSid}]}{[Al^{3+}][\text{Sid}]} = K_{II} \cdot K_{\text{FeSid}} \tag{22}$$

From the change in absorbance on adding aluminum, K_{II} was determined. K_{II} was then converted to K_{AlSid} by eq 22. Finally the ratio $K_{\text{FeSid}}/K_{\text{AlSid}}$ was evaluated and used as a measure of the selectivity of the polymer for iron as compared with aluminum. The results are shown in Table VII.

Although all three polymers are selective for iron, polymer P-11 is more selective by a factor of 10 than either P-9 or P-13. Thus the side chain length and the hydroxamic acid group spacing are important factors not only in complex stability but also in metal selectivity. It is also interesting that in the case of aluminum, the complex with P-13 is now the more stable of the three.

Conversion of the 3:1 Hydroxamic Acid Complex to the 2:1 Complex. Although the iron–polymer complexes form crystal clear, red-brown solutions in water at the high dilutions required for the spectral measurements, addition of iron to a concentrated solution of polymer causes an immediate precipitation of a red-brown complex. The interesting point is that when additional iron is added to this mixture, the precipitate dissolves over a period of a few minutes to form a clear, red-brown solution. A semiquantitative measurement indicates that the precipitate forms at a 3:1 HA–Fe ratio whereas the clear solution is reached at a 2:1 ratio. The λ_{max}

Table VII
Data for the Competition between Fe^{3+} and Al^{3+} for the Polymer at pH 2

		$K_{M-P} \times 10^{-29}$		$K_{Fe-P}/$
Polymer	$K_{II} \times 10^3$	Fe	Al	K_{Al-P}
P-9	18.4	0.42	0.0077	54.5
P-11	1.43	4.86	0.00695	699
P-13	13.2	2.24	0.0296	75.7

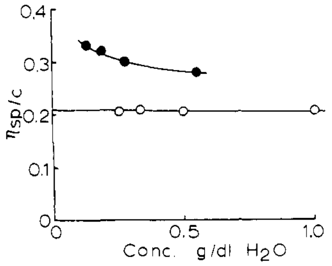
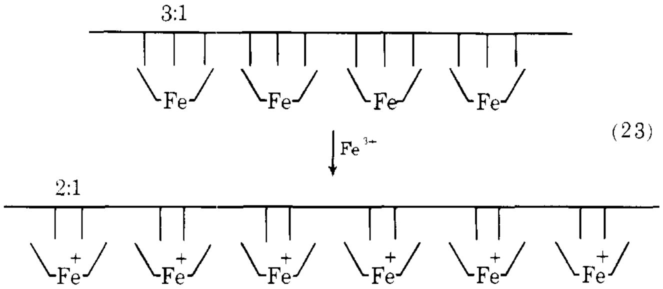


Figure 5. Viscosity of P-11 (○) and of the P-11-Fe(III) complex in water at 2:1 molar ratio of hydroxamic acid to iron (●). The concentration refers to that of the polymer alone.

changes during the process from 430 to 460–470 nm. This effect is not observed on addition of other metal ions or of acids. We suggest that this phenomenon is a result of the conversion of the insoluble 3:1 complex to a soluble 2:1 complex as shown schematically in eq 23.



(23)

The 2:1 HA–Fe complex, being a polyelectrolyte, would be expected to be soluble. The λ_{max} of 460–470 nm is intermediate between 430 nm, characteristic of the 3:1 complex, and 520 nm, characteristic of the purple 1:1 complex[9] of iron with acetohydroxamic acid. Even in the presence of a large excess of iron, λ_{max} for the polymer–iron system never approached 520 nm of the 1:1 complex.

In order to further characterize the system, the effect of dilution upon viscosity was observed for both the polymer and its 2:1 iron complex, Figure 5. The viscosity of the 3:1 complex could not be determined because of its low solubility. The polymer itself shows normal viscosity behavior and an intrinsic viscosity of 0.2. The 2:1 iron complex, on the other hand, shows the upward curvature characteristic of a polyelectrolyte. The trend is not particularly pronounced but it is reproducible. Strangely, addition of salt had little effect on the viscosity behavior. These results, whereas not entirely conclusive, would be consistent with a rather stiff polymer which is not much affected by external conditions. This picture would fit the concept of a polymer stiffened by encasement with iron complexes.

Table VIII
Effect of HA–Fe Ratio (P-11) on the Formation of a Precipitate with CMC[a]

Mole ratio HA/Fe	Effect of CMC[b]	Mole ratio HA/Fe	Effect of CMC[b]
7.7	No ppt	2.6	Slight ppt
3.8	No ppt	2.2	Medium ppt
3.1	No ppt	1.5	Heavy ppt

[a] Carboxymethylcellulose, sodium salt. [b] Under the conditions of the experiment iron alone did not form a precipitate with CMC.

The 2:1 HA–Fe complex, because of its cationic nature, should form a precipitate with sodium carboxymethylcellulose (CMC).[19] A series of polymer solutions was prepared in which the HA–Fe ratio was varied from 7.7:1 to 1.5:1. These solutions were treated with a solution of Na-CMC and observed for the appearance of precipitate. The results are shown in Table VIII. No precipitate formed at the 3:1 ratio. Only when the ratio had approached 2:1 was there any observable precipitate.

These results indicate that two hydroxamic acids on neighboring side arms form a tight complex with iron, whereas the third hydroxamic acid is less firmly attached and is capable of displacement to form the stable 2:1 species. Molecular models reveal that in order for the third neighboring hydroxamic acid to become attached to the iron in the octahedral arrangement, one bond of the hydroxamic acid must be positioned to point directly away from the polymer chain. This requires that the third side chain must in a sense reach around the iron to form the final coordinate linkage. This is obviously a less favorable approach than from the other positions which are directed toward the polymer backbone. Hence a lower stability for this third link is reasonable.

Acknowledgments. The authors gratefully acknowledge Dr. James L. Hall, Professor Emeritus of Chemistry, West Virginia University for consultations and generous assistance in determining the stability constants of the iron polymer complexes. We also appreciate the help of students David Golden for osmometry measurements and Melody Lindley for viscosities.

The methane sulfonate salt of desferrioxamine-B (Desferal) was kindly donated by Ciba Pharmaceutical Co., Summit, N.J.

The research was supported through fundings under P1 88-379 establishing the Water Research Institute, West Virginia University and administered by the Office of Water Research and Technology, U.S. Department of the Interior.

References and Notes

(1) J. R. Millar, *Chem. Ind.* (*London*), 606 (1957).
(2) E. Bayer, *Angew. Chem., Int. Ed. Engl.*, **3**, 325 (1964).
(3) G. Schmuckler, *Talanta*, **12**, 281 (1965).
(4) E. Blasius and B. Brozio, *Chelates Anal. Chem.*, **1**, 49 (1967).
(5) S. Kopolow, T. E. Hogen Esch, and J. Smid, *Macromolecules*, **6**, 133 (1973).
(6) S. L. Davydova and N. A. Plate, *Coord. Chem. Rev.*, **16**, 195 (1975).
(7) L. D. Rollman, *J. Am. Chem. Soc.*, **97**, 2132 (1975).
(8) M. M. Jones, H. D. Coble, T. H. Pratt, and R. D. Harbison, *J. Inorg. Nucl. Chem.*, **37**, 2409 (1975).
(9) J. B. Neilands, *Struct. Bonding* (*Berlin*), **1**, 59 (1966).
(10) J. B. Neilands, *Science*, **156**, 1443 (1967).
(11) H. Maehr, *Pure Appl. Chem.*, **28**, 603 (1971).
(12) G. Anderegg, F. L'Eplattenier, and G. Schwarzenbach, *Helv. Chim. Acta*, **46**, 1409 (1963).
(13) A. Winston and G. R. McLaughlin, *J. Polym. Sci., Polym. Chem. Ed.*, **14**, 2155 (1976).
(14) G. W. Anderson, J. E. Zimmernan, and F. M. Callahan, *J. Am. Chem. Soc.*, **86**, 1839 (1964).
(15) D. V. Ioffe and S. G. Kuznetsov, *Zh. Obshch. Khim.*, **29**, 3804 (1959); *Chem. Abstr.*, 54, 19518 d (1960).
(16) C. N. Reilley, R. W. Schmid, and F. S. Sadek, *J. Chem. Educ.*, **36**, 619 (1959).
(17) K. Bak, *Acta Chem. Scand.*, **16**, 229 (1962).
(18) G. Schwarzenbach and K. Schwarzenbach, *Helv. Chim. Acta*, **46**, 1390 (1963).
(19) A. J. Varma and J. Smid, *J. Polym. Sci., Polym. Chem. Ed.*, **15**, 1189 (1977).