The SPE International Award Address—1979

Recent Aspects of Research in Macromolecules

C. G. OVERBERGER

Department of Chemistry and the Macromolecular Research Center
The University of Michigan
Ann Arbor, Michigan 48109

I am very honored to be selected as the 1979 recipient of the Society of Plastics Engineers International Award.

The science and technology of macromolecules has occupied most of my scientific life. A major part of this effort has been related to the synthesis of macromolecules and the mechanisms of their formation. I list here a number of areas in which I had major interests at one time:

 • Side Chain Crystallization;
 • Catalyst Research. Synthesis and Decomposition of Azo Compounds—Free Radical Initiators;
 • Cationic Catalyzed Polymerization;
 • Polymers Containing Mercaptan Groups;
 • Anionic Catalyzed Polymerization;
 • Transition Metal Catalysis.

I might comment briefly about our contributions in ionic polymerization primarily in the cationic area but also in the anionic catalyst area as well. In the late 1940's and early 1950's, we really had very little knowledge of the details of ionic polymerization so that practically everything one did was new and novel. Clearly, there is a close connection between basic information in ionic polymerization and plastics. Our work on mercaptan polymers was directly applicable to rapid curing systems for coatings and plastics. From my point of view, it was an exciting time.

The growth of primary research and development from 1945 to 1965 was exceptional. The enormous resources of the chemical industry were brought to bear on many outstanding problems in polymer science and engineering. In more recent times, our work has been focused around three general topics:

(1) Optically active polymers and their conformation in solution (1-20).

(2) The use of polymers as catalysts and reactants in organic reactions (21-39).

(3) The preparation of polymers with an electrophilic main chain to which is grafted an amino acid or nucleic acid base (40-46).

It is not possible for me to discuss in detail these three topics. Concerning the first topic, I will only say the following: Our initial goal in the synthesis of asymmetric polymers, largely polyamides and polyesters, was to determine the effect of asymmetry on the solution and solid state properties of these polymers. We were very much aware of the increasing effort in the study of the conformation of polyproline in solution and we believed that we could also determine the structure and conformation of other asymmetric polyamides in solution. In a series of over 40 papers we have shown that with the use of high resolution nuclear magnetic resonance spectrometry, dipolar measurements, semi-empirical energy calculations, intrinsic viscosity, and circular dichroism, that the conformation of many rigid asymmetric polyamides can be well-defined in solution. One of our most exciting discoveries has been the conformational transition of the polymers derived from *trans* optically active dicarboxylic cyclopropanes and diamines such as piperazine. In this example we show the first convincing evidence of two rather well-controlled conformations with a reasonably sharp transition between them, much like the polyproline case. We have begun a systematic study of the effect of substituents on the conformation of polyproline type polymers. We can influence markedly the activation energy for the rotation of the amide bond in polyprolines by appropriate substitution on the pyrrolidine ring. By introducing a methyl substituent in the 2-position of proline we can prepare a polymer which does not mutarotate under ordinary conditions. We expect to continue research in this area.

Concerning the second topic, I should like to make the following general comments. We discovered some years ago that polymers derived from polyvinylimidazoles are catalysts for esterolytic reactions. A systematic study of this type of system has revealed that this catalytic activity can be attributed to three factors: (a) cooperative effects, (b) electrostatic interactions, and (c) hydrophobic interactions. The concept of hydrophobic interactions contributing to large acceleration of catalytic activity in ester hydrolysis has provided us with a unique discovery which may be applicable to many other kinds of organic reactions. This area of chemistry has become much more popular in more recent years and now there is an active group of investigators working in the general field which has been expanded to all types of modifications of these systems including micellar reactions. We believe we have made a substantive original contribution to this area and intend to pursue it with increased activity.

Cooperative interactions between catalytically active imidazole groups and other functional groups have been well documented. Poly[4(5)-vinylimidazole] was found

to be a better catalyst (2- × 3-fold) than imidazole towards the neutral ester p-nitrophenyl acetate (PNPA) when the reaction was carried out at high pH. This enhanced reactivity was attributed to multiple catalysis by a combination of anionic and neutral imidazole groups along the backbone of the polymer. Also, under somewhat different reaction conditions, a bifunctional interaction of neutral imidazole units was observed. The total rate equation for the polymeric catalysis can be expressed by the following equation:

$$k_{cat} = k_1\alpha_1 + k_2\alpha_1^2 + k_3\alpha_2 + k_4\alpha_1\alpha_2 \qquad (1)$$

where k_1 is a simple nucleophilic catalysis rate constant, k_2 is an imidazole-catalyzed imidazole nucleophilic constant, k_3 is a catalysis rate constant for imidazole anion, and k_4 is a rate constant for anionic imidazole-catalyzed imidazole catalysis; α_1 and α_2 are fractions of neutral and anionic imidazole, respectively. We have found that the bifunctional effect is primarily between neighboring imidazole units, such as 1, 3, 1, 4, and 1, 5, rather than between remote groups brought together via folding of the macromolecule. We investigated a series of oligo[4(5)-vinylimidazoles] and found that the oligomers of $ca.$ 5 units had about 71 percent of the catalytic activity of high molecular weight polymer.

The distance and conformation between imidazole groups is apparently critical for cooperative interaction. We have found that graft copolymers of L-histidine on polyethylenimine (PEI) showed no cooperative interaction. It has been proposed that this is due to lack of close proximity between neighboring imidazole units.

By designing systems in which electrostatic and bifunctional effects could be utilized, we have been able to considerably improve the catalytic efficiency of polymeric catalysts based on 4(5)-vinylimidazole. Rate enhancements of up to 50 times the rate exhibited by monomeric imidazole were observed in the poly[4(5)-VIm]-catalyzed hydrolysis of the negatively charged substrates 3-nitro-4-acetoxybenzoic acid (S_2^-) or NABS. Bell-shaped pH-rate profiles were observed for the hydrolysis of these esters (*Fig. 1*). The maximum occurred at pH 7 where about 25 percent of the imidazole residues were protonated. The catalytic activity of oligo[4(5)-vinylimidazole] towards NABS generally increased with increasing molecular weight. The oligomers with a degree of polymerization (DP) more than eight showed higher reactivity than imidazole and a bell-shaped pH-rate profile. We concluded that electrostatic interactions between the cationically charged imidazole groups in the oligomer and the anionic substrate were important only for high molecular weight oligomers. We further concluded that short-range interactions between neutral imidazole residues also enhanced the catalytic activity of the oligomer.

Analogous to poly[4(5)-VIm], the histidine copolymer also displayed a bell-shaped pH-rate profile (*Fig. 1*).

It is interesting to note that while the maximum rate for poly[4(5)-VIm] occurred at $ca.$ pH 7, the maximum for the graft copolymer occurred at $ca.$ pH 6. This is possible because the graft copolymer contains amine
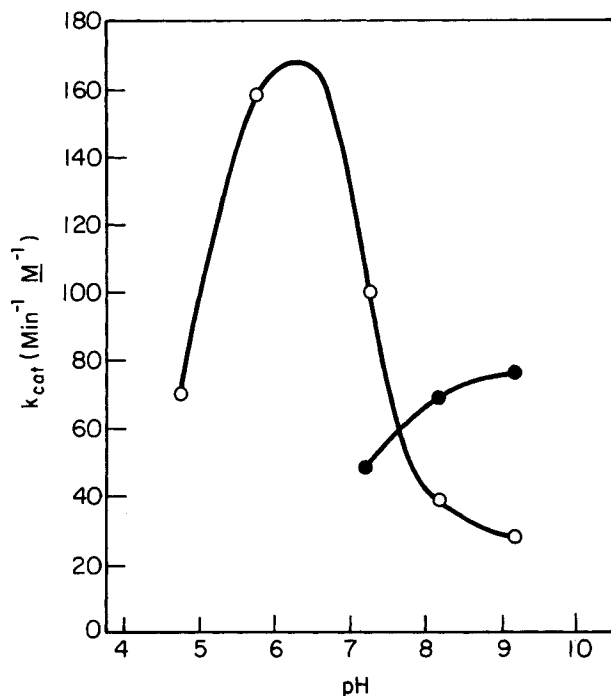

Fig. 1. *Second-order rate constant for the hydrolysis of S_2^- catalyzed by imidazole (●) and by the histidine graft copolymer (○) in 96.7 percent H_2O, 3.3 percent acetonitrile, $[S_2^-] = 5 \times 10^{-5}$ $\underline{M}$, $\mu = 0.02$, 26°C.*

groups β to the imidazole, which are protonated, thus it is not necessary that some of the imidazoles be protonated for electrostatic attraction of the substrate.

It is only in recent years that the importance of apolar or hydrophobic interactions to enzymatic and synthetic catalysts has been recognized. Apolar binding is perhaps the most important factor in obtaining rate enhancements with polymeric catalysts. Our results strongly support such a possibility. We have studied the solvolytic reactions of p-nitrophenyl acetate and p-nitrophenyl heptanoate catalyzed by poly[4(5)-VIm] and imidazole. The kinetics were studied as a function of temperature, pH, and the ethanol-water composition of the solvent (*Fig. 2*). It was found that the conformation of the polymer chain of poly[4(5)-VIm] was dramatically affected by the ethanol-water composition and by the degree of neutralization of the pendant imidazole residues.

The enhanced catalytic activity of poly[4(5)-VIm] towards the neutral substrate p-nitrophenylacetate in buffer solutions of high and low ethanol composition at pH $ca.$ 8 (*Fig. 3*) was attributed to increased bifunctional catalysis with the shrinkage of the macromolecule in solution. The enhanced solvolysis of p-nitrophenylheptanoate in pH $ca.$ 8 buffer solutions of low ethanol composition (*Fig. 3*) was attributed to an increased accumulation of substrate in the polymer domain due to hydrophobic interactions between the polymer and the substrate.

Large rate enhancements, which have been attributed to hydrophobic effects, have also been observed for the histidine graft copolymer (*Fig. 4*).

I now want to comment on the third topic. Preparation of new model polymers of polynucleotides with a linear polyethylenimine (PEI) backbone and optically
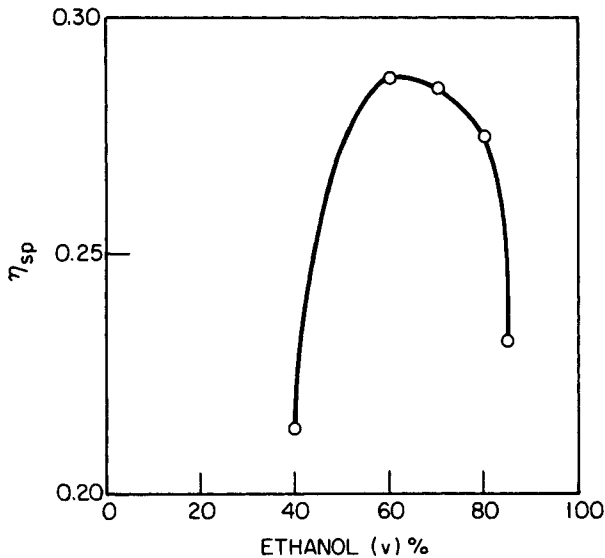
Fig. 2. Solution viscosity of poly [4(5)-VIm] as a function of ethanol composition (EtOH/H₂O), poly[4(5)-VIm] = 0.4229 (g/dl), μ = 0.02, 26°C.
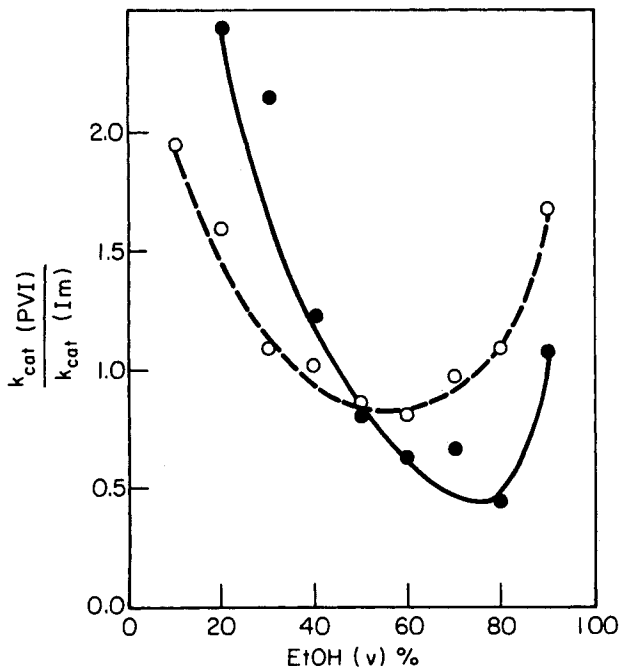

Fig. 3. Poly[4(5)-VIm] catalyzed hydrolysis of PNPA (●) and PNPH (○) in varying ethanol composition, pH 8, μ = 0.02, 26°C.

Fig. 4. Second-order rate constants for the hydrolysis of the S_n^- series by imidazole (●) and by the histidine graft copolymer (○) in 96.7 percent water, 3.3 percent acetonitrile, pH = 8.06, $[S_n^-]$ = $5 \times 10^{-5} \underline{M}$, μ = 0.02, 26°C.

in an ordered conformation with base stacking not unlike poly A and poly U.

Over the past decade, there has been considerable interest in the syntheses and properties of model polymers of polynucleotides to help elucidate the structures and properties of polynucleotides. Investigations on these synthetic model systems have been expected to provide useful information on the types of possible polynucleotide structures and the forces which control their secondary and tertiary structures. In view of the fact that most of the structural studies on the polynucleotides have been performed by means of ORD and CD, the synthetic models which have been reported so far could not be suitable models in a sense because of the lack of optically active center in the structure.

The 2-(thymin-1-yl)propionalyl group was grafted onto a linear polyethylenimine backbone according to the following synthesis:

active nucleic acid base derivatives as pending side chains are described. 3-(Adenin-9-yl)propionic acid (I) and 3-(thymin-1-yl)propionic acid (II) were prepared by the Michael reaction of ethyl acrylate and the corresponding nucleic acid base and subsequently grafted onto linear PEI by the *p*-nitrophenyl active ester method.

Optically active (−)- and (+)-2-(thymin-1-yl)propionic acid (IV, V) was grafted onto linear PEI by direct coupling with diethylphosphoryl cyanide (DEPC) to give optically active polymer. Related monomer and dimer model compounds were also prepared from diethylamine and dimethylethylendiamine, respectively. The evidence indicates that these polymers exist
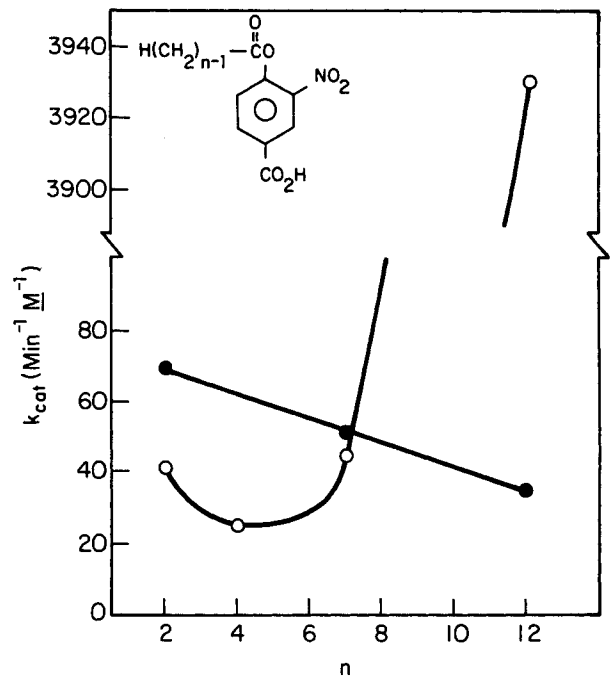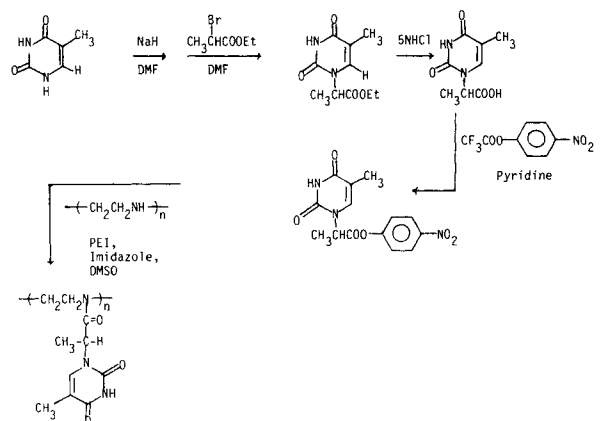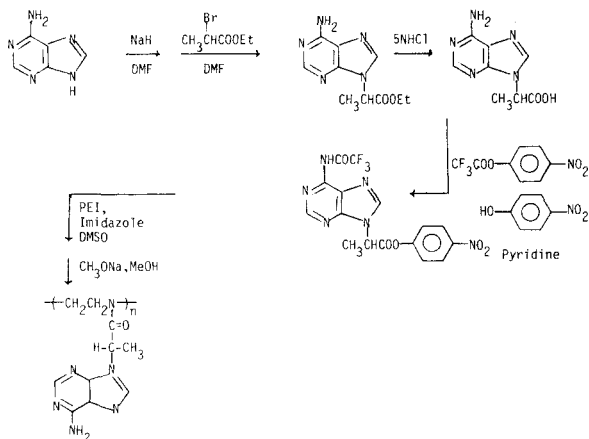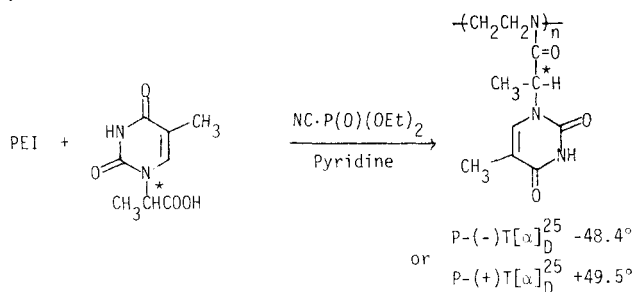
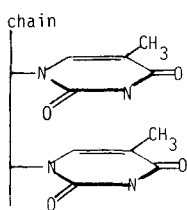The corresponding adenine polymer was prepared in an analogous manner.

The steroisomers of the above graft polymer of thymine were synthesized by means of the modified pathway shown below. Efforts to prepare the corresponding stereoisomers of the adenine polymer have not yet succeeded.

Our studies indicate that the hypochromicities of both the thymine and adenine grafted polymers are very similar to poly A and poly U. The circular dichroism study of the thymine grafted system further supports our speculation that we have a very highly ordered conformation due to base stacking in neutral water solution. A schematic of base pairing and base stacking is given.

Thymine Base Stacking   Thymine-Adenine Base Pairing

chain

chain

chain
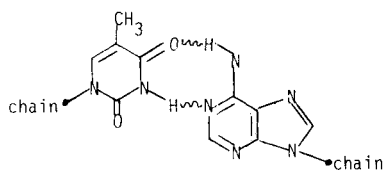
This topic is an exciting one and represents a major effort on our part. I include here the abstracts of four manuscripts which cover this area.

SYNTHESES OF POLYETHYLENIMINE CONTAINING ASYMMETRIC NUCLEIC ACID BASE DERIVATIVES AS GRAFTED PENDANTS

C. B. Overberger and Y. Morishima

Preparations of new model polymers of polynucleotides with a linear polyethylenimine (PEI) backbone and the optically active nucleic acid base derivatives as pending side chains are described. ($\pm$)-2-(Thymin-1-yl)propionic acid (II) and ($\pm$)-2-(adenin-9-yl)propionic acid (IV) were synthesized. These carboxylic acid derivatives were grafted onto PEI at the imino nitrogen by

the *p*-nitrophenyl active ester method. The enantiomeric pairs of II were optically resolved with quinine to yield (–)- and (+)-2-(thymin-1-yl)propionic acid-(VII and VIII). VII and VIII were grafted onto PEI through amide bond by direct coupling with diethylphosphoryl cyanide to give optically active graft polymers. The related monomer and dimer model compounds were also prepared by the same method from diethylamine and dimethylethylenediamine, respectively.

SYNTHESIS AND OPTICAL PROPERTIES OF POLYETHYLENIMINE CONTAINING L-PROLINE AND OPTICALLY ACTIVE THYMINE DERIVATIVES

C. G. Overberger and Y. Morishima

Preparation and optical properties of linear polyethylenimine (PEI) containing L-(–)-N-[(–)-2-(thymin-1-yl)propionyl]propyl group as grafting pendant [P-(–)Pro-(–)T] and its related monomer and dimer model compounds are described. Hypochromic effects and circular dichroism of these compounds were compared with those of PEI containing (–)-2-(thymin-1-yl)propionyl group as grafting pendant [P-(–)T], which has no L-proline ring as spacing group. P-(–)Pro-(–)T showed no exciton coupling of B_{2u} $\pi - \pi^*$ transition although it showed large hypochromicity in neutral aqueous solution, implying the stacking of the bases has no screw sense.

CIRCULAR DICHROISM OF POLYETHYLENIMINE CONTAINING OPTICALLY ACTIVE THYMINE DERIVATIVES AS GRAFTED PENDANT

C. G. Overberger and Y. Morishima

Optical properties of linear polyethylenimine containing optically active (+)- or (–)-2-(thymin-1-yl) propionyl group as grafted pendant have been investigated by means of CD and compared with those of the related monomer and dimer model compounds. CD spectra of the polymer in neutral aqueous solution were very different from those of related model compounds, suggesting the polymer exists in some ordered conformation (at least locally) to allow exciton coupling of $\pi - \pi^*$ (B_{2u}) transition in the base chromophores along the polymer chain. This ordered conformation tends to be randomized on heating. The effects of complementary base pairing on the CD spectra have also been studied using a linear polyethylenimine containing ($\pm$)-2-(adenin-9-yl)propionyl grafts and its related monomer and dimer models.

SPECTROSCOPIC STUDIES OF POLYETHYLENIMINE WITH PYRIMIDINE OR PURINE GRAFTS

C. G. Overberger and Y. Morishima

Hypochromic effects of 2-(thymin-1-yl)propionyl graft polyethylenimine (P-T) and its related monomer (M-T) and dimer model (D-T), and 2-(adenin-9-yl)propionyl graft polyethylenimine (P-A) and its monomer (M-A) and dimer model (D-A) have been systematically inves-

tigated and the base-stacked conformation compared with corresponding polynucleotides and dinucleotides has been discussed. The results suggest that the graft polymers and even their dimer models may have a particular preference of a stacked conformation compared with corresponding poly- and dinucleotides. A study of solvent effect on the NMR spectra of dimer model suggests the existence of a preferred base-stacked conformation. Base pairing effects between the complementary basis have also been studied for various combinations among the model systems. Only a combination of P-T/P-A showed a considerable hypochromic effect.

REFERENCES

1. C. G. Overberger and Y. S. Jon, *J. Polym. Sci., Polym. Chem. Ed.*, **15**, 1413 (1977).
2. C. G. Overberger, Y. Shimokawa, and G. Montaudo, *J. Polym. Sci., Polym. Chem. Ed.*, **15**, 815 (1977).
3. C. G. Overberger and M. J. Han, *J. Polym. Sci.*, Polym. Symp., **51**, 155 (1975).
4. C. G. Overberger and M. J. Han, *J. Polym. Sci., Polym. Chem. Ed.*, **13**, 2251 (1975).
5. C. G. Overberger, Y. Okamoto, and V. Bulacovschi, *Macromolecules*, **8**, 31 (1975).
6. C. G. Overberger and M. J. Han, *Pure Appl. Chem.*, **39**, 33 (1974).
7. G. Montaudo and C. G. Overberger, *J. Polym. Sci., Polym. Chem. Ed.*, **11**, 2739 (1973).
8. G. Montaudo, P. Finocchiaro, and C. G. Overberger, *J. Polym. Sci., Polym. Chem. Ed.*, **11**, 2727 (1973).
9. G. Montaudo and C. G. Overberger, *J. Polym. Sci., Part B*, **11**, 625 (1973).
10. G. Montaudo, P. Finocchiaro, and C. G. Overberger, *J. Polym. Sci., Part B*, **11**, 619 (1973).
11. C. G. Overberger, G. Montaudo, R. C. Glowaky, and M. J. Han, Macromolecular Chemistry—8, IUPAC, International Symposium, Helsinki (1972).
12. C. G. Overberger and John H. Kozlowski, *J. Polym. Sci., A-1*, **10**, 2291 (1972).
13. C. G. Overberger, John H. Kozlowski, and Edward Radlmann, *J. Polym. Sci., A-1*, **10**, 2265 (1972).
14. C. G. Overberger and Thomas J. Pacansky, *J. Polym. Sci., Polym. Symp.*, **45**, 39 (1974).
15. Yoshio Okamoto and C. G. Overberger, *Macromolecules, 7*, 614 (1974).
16. C. G. Overberger, K.-H. David, and J. A. Moore, *Macromolecules*, **5**, 368 (1972).
17. G. Montaudo and C. G. Overberger, *J. Polym. Sci., Part B*, **10**, 433 (1972).
18. G. Montaudo, P. Finocchiaro, P. Maravigna, and C. G. Overberger, *Macromolecules*, **5**, 197 (1972).
19. G. Montaudo, P. Maravigna, P. Finocchiaro, and C. G. Overberger, *Macromolecules*, **5**, 203 (1972).
20. C. G. Overberger, G. Montaudo, Y. Nishimura, J. Sebenda, and R. A. Veneski, IUPAC International Symposium on Macromolecular Chemistry, pp. 127-153 Budapest (1969).
21. C. G. Overberger and Y. Kawakami, *J. Polym. Sci., Polym. Chem. Ed.*, **16**, 1249 (1978).
22. C. G. Overberger and Y. Kawakami, *J. Polym. Sci., Polym. Chem. Ed.*, **16**, 1237 (1978).
23. C. G. Overberger, A. C. Guterl, Jr., Y. Kawakami, L. J. Mathias, A. Meenakshi, and T. Tomono, *Pure Appl. Chem.*, **50**, 309 (1978).
24. C. G. Overberger and A. C. Guterl, Jr., *J. Polym. Sci., Polym. Symp.*, **62**, 13 (1978).
25. C. G. Overberger, Thomas W. Smith, and Kenneth W. Dixon, *J. Polym. Sci., Polym. Symp.*, **50**, 1 (1975).
26. C. G. Overberger and Thomas W. Smith, *Macromolecules*, **8**, 416 (1975).
27. C. G. Overberger and Thomas W. Smith, *Macromolecules*, **8**, 407 (1975).
28. C. G. Overberger and Thomas W. Smith, *Macromolecules*, **8**, 401 (1975).
29. C. G. Overberger and Thomas J. Pacansky, *J. Polym. Sci., Polym. Symp.*, **45**, 39 (1974).
30. C. G. Overberger and K. N. Sannes, *Angew. Chem. Int. Ed.*, **13**, 99 (1974); *Angew. Chem.*, **86**, 139 (1974); *Int. J. Polym. Mater.*, **2**, 271 (1973).
31. C. G. Overberger and C. J. Podsiadly, *Bioorganic Chem.*, **3**, 35 (1974).
32. C. G. Overberger and C. J. Podsiadly, *Bioorganic Chem.*, **3**, 16 (1974).
33. C. G. Overberger and Thomas W. Smith, J. A. Moore, Ed., D. Reidel Publishing Company, Boston, USA, 1973; NATO Adv. Study Inst. Ser., Ser. C, **4**, 1 (1973).
34. C. G. Overberger, *Appl. Polym. Symp.*, **22**, 287 (1973).
35. C. G. Overberger and K. Gerberding, *J. Polym. Sci., Part B*, **11**, 465 (1973).
36. C. G. Overberger and R. C. Glowaky, *J. Am. Chem. Soc.*, **95**, 6014 (1973).
37. C. G. Overberger, R. C. Glowaky, and P.-H. Vandewyer, *J. Am. Chem. Soc.*, **95**, 6008 (1973).
38. Y. Okamoto and C. G. Overberger, *J. Polym. Sci., Polym. Chem. Ed.*, **10**, 3387 (1972).
39. C. G. Overberger and T. J. Pacansky, *J. Polym. Sci., Polym. Chem. Ed.*, **13**, 931 (1975).
40. C. G. Overberger and K. W. Dixon, *J. Polym. Sci., Polym. Chem. Ed.*, **15**, 1863 (1977).
41. C. G. Overberger and Y. Inaki, *J. Polym. Sci., Polym. Chem. Ed.*, in press.
42. C. G. Overberger, Y. Inaki and Y. Nambu, *J. Polym. Sci., Polym. Chem. Ed.*, in press.
43. C. G. Overberger and Y. Morishima, *J. Macromol. Sci., Chem.* (Special Issue), in press.
44. C. G. Overberger and Y. Morishima, in preparation.
45. C. G. Overberger and Y. Morishima, in preparation.
46. C. G. Overberger and Y. Morishima, in preparation.