

## Synthesis and Characterization of Copolymers containing *N,N*-dimethylacrylamide and 2-vinyl-4,4'-dimethylazlactone

Lee G. Stanek<sup>1</sup>, Steven M. Heilmann<sup>2</sup>, and William B. Gleason<sup>1,3</sup> (✉)

<sup>1</sup>Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

<sup>2</sup>Organic Materials Technology Center, 3M Company, St. Paul, MN 55144

<sup>3</sup>Department of Laboratory Medicine & Pathology, University of Minnesota, Minneapolis, MN 55455

Received: 21 April 2005 / Revised version: 8 September 2005 / Accepted: 26 September 2005

Published online: 14 October 2005 – © Springer-Verlag 2005

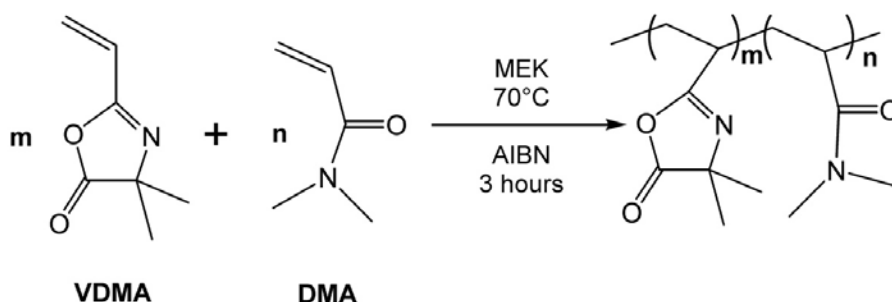
### Summary

We report the synthesis, characterization, and determination of monomer reactivity ratios for the solution copolymerization of *N,N*-dimethylacrylamide (DMA) and 2-vinyl-4,4'-dimethylazlactone (VDMA). The polymerization kinetics were monitored by gas chromatography (GC), structure analysis of the resulting copolymers was determined using <sup>1</sup>H-NMR analysis, and copolymer molecular weights were determined using gel-permeation chromatography (GPC). The reactivity ratios indicate the copolymerization of DMA and VDMA may result in greater mole fraction of VDMA in the copolymer compared to monomer feed compositions, especially when the DMA mole fraction is greater than the VDMA mole fraction. However, the data also indicates an azeotropic copolymerization at a mole fraction of VDMA of 0.78.

### Introduction

Copolymers containing *N,N*-dimethylacrylamide (DMA) have been used in a variety of applications in recent years, with increasing focus in the area of biomaterials.[1-3] The use of these materials for a wide range of applications is facilitated by the hydrophilic properties of DMA and DMA-containing copolymers, and examples include use as DNA sequencing matrices and as hydrogel materials.[4-7] Often times, DMA-containing polymeric materials consist of two or more monomers, and these examples illustrate the utility of copolymerization methods to control the hydrophilic characteristics of the polymeric material. Additionally, copolymerization of monomers bearing reactive functionality is shown to be a reliable and attractive method for further polymer modification. Examples of reactive monomers commonly copolymerized and used in polymer modification include (meth)acrylic acid[8] and glycidyl methacrylate.[9] Recently, 2-vinyl-4,4'-dimethylazlactone (VDMA) has been widely used for a variety of polymer modifications, where some specific applications involved copolymeric systems developed for protein immobilization.[10-14] The copolymerization of DMA with monomers bearing a reactive side group may afford a varying degree of hydrophilicity while allowing for the modification of the material through a variety of potentially simple and useful reactions with the side group.

Here we describe the synthesis and characterization of a series of copolymers of DMA and VDMA with varying monomer mole fractions. Monomer reactivity ratios are reported and the data shows the copolymeric materials possessed a greater mole fraction of VDMA than DMA, when compared to the monomer feed. Also, it was determined that the polymers showed increasing molecular weight and polydispersity with increasing mole fraction of VDMA in the copolymer, which is related to the greater reactivity of VDMA in polymerization with DMA.



**Scheme 1.** Copolymerization of VDMA with DMA

## Experimental

### Materials

DMA was purchased from Aldrich Chemical Company (Milwaukee, WI), and passed through a 1 cm (O.D.) glass column packed with Inhibitor Remover (Aldrich Chemical Company) to remove hydroquinone monomethyl ether (MEHQ) and stored at 4°C. 2-Vinyl-4,4'-dimethylazlactone (VDMA) was obtained from SPNE (Princeton, NJ), and was vacuum distilled as previously reported.[15] Butylated hydroxytoluene (BHT) and 2,2'-azobisisobutyronitrile (AIBN) were obtained from Aldrich Chemical Company (Milwaukee, WI). AIBN was purified by recrystallization from methanol. All other materials were of reagent grade or higher and used as received.

### Polymer Synthesis

Polymerizations, as illustrated in Scheme 1, were conducted according to the following representative procedure. A 250-mL round-bottom 3-neck flask was charged with 2.0 g (14.4 mmol) of VDMA, 8.0 g (80.7 mmol) of DMA, and 90 mL of MEK. The solution was sparged with argon for 15 minutes and heated to 70°C ± 1°C. After temperature equilibration, 0.0250 g (0.152 mmol) of AIBN in 10 mL of MEK was added to initiate the polymerization. After 3 hours of polymerization, heating was stopped and the solution was added drop-wise to stirring petroleum ether to precipitate the polymer. Solid polymer was isolated via vacuum filtration and dried overnight in a vacuum oven at 40°C. Initial and final aliquots (1.0 mL) of the polymerization solution were removed from the flask via Eppendorf pipetter and were each added to a 1.0 mL solution of 2 % (w/v) BHT in a 9:1 (v/v) solution of ethyl acetate and toluene and analyzed following the GC method described below.

## Instrumentation

### *GC Analysis*

Changes in initial monomer feed compositions were monitored by gas chromatography following the method described by Harwood, *et al.*[16] Gas chromatograms were obtained using a HP 5980-II Gas Chromatograph with a HP-1, crosslinked methyl siloxane column (30 m x 0.32 mm with a 0.25 micron coating) with a HP guard column containing a glass wool filter. Data analysis was performed using Chemstation software from Agilent Technologies. Aliquots (1.0 mL) of each polymerization solution were taken at the start and completion of the polymerization, and diluted with 1.0 mL of a 2% (w/v) solution of BHT in ethyl acetate:toluene solution (9:1, v/v) to quench the polymerization. Five microliters of each diluted aliquot were injected into the GC with a heating program as follows: Start temperature, 50°C; 50 to 200°C at 10°C/min; final temperature, 200°C. The peak areas for the monomers were normalized to the toluene peak.

### *<sup>1</sup>H-NMR Analysis*

A Varian Inova 300 or 500 MHz spectrometer was used for the analysis with CDCl<sub>3</sub> as solvent for the copolymers. Distinct peaks for each monomer were visible in the spectra and used for the analysis as follows: For DMA, methyl protons [N(CH<sub>3</sub>)<sub>2</sub>] at approximately 3.0 ppm, and for VDMA, the methyl protons [(CH<sub>3</sub>)<sub>2</sub>] at approximately 1.4 ppm. Integration of these peaks afforded the mole fraction of the respective monomers in the copolymer.

### *GPC Analysis*

GPC analysis was conducted on a HP GPC system with a HP 1074A refractive index detector, an Agilent 35900E analog to digital signal converter with Agilent Technologies software for molecular weight determinations. The system was equipped with a Jordi DVB (divinylbenzene) three-column set and was calibrated using polystyrene standards of molecular weights ranging from 10<sup>3</sup> to 4x10<sup>5</sup> g/mol. All samples were dissolved in degassed, HPLC grade tetrahydrofuran (THF) at concentrations of 10 mg/mL, and filtered using 0.2-μm PTFE filters. The samples were analyzed at a flow rate of 1.0 mL/min, an injection volume of 50 μL, and a column temperature of 40°C.

## Results and Discussion

### *Monomer Reactivity Ratios*

The general observation in copolymerization is that two monomers having similar structural features should copolymerize with approximately random monomer distribution in the resulting copolymer. Therefore, in the system of *N,N*-dimethylacrylamide (DMA) and 2-vinyl-4,4'-dimethylazlactone (VDMA), this result would be expected considering the structural similarity of the two monomers, but the data show this not to be exactly the case.

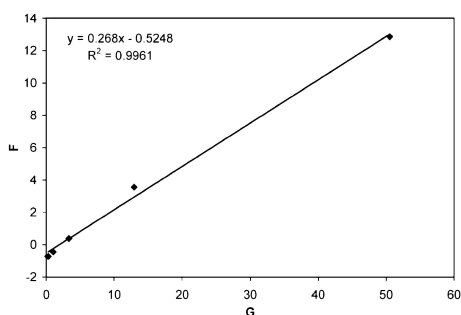
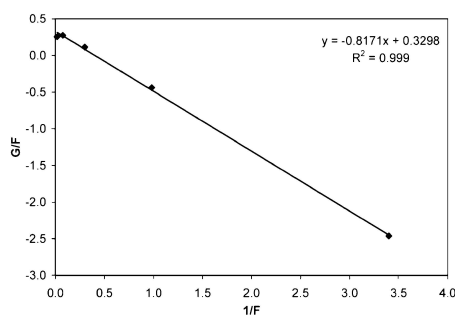
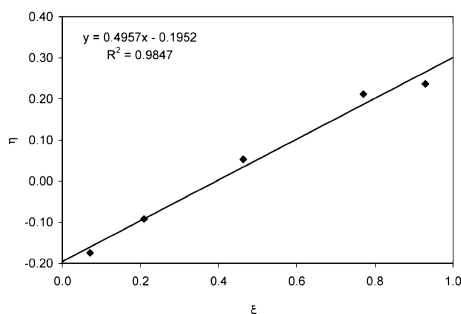
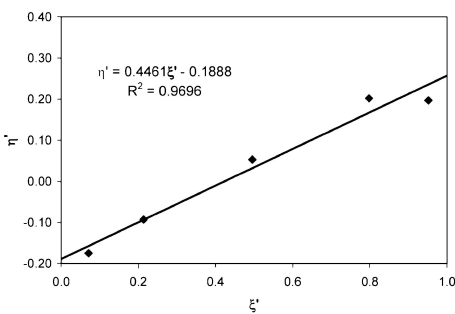
Data in Table 1 was used to determine monomer reactivity ratios for the DMA-VDMA system using linearization methods of Fineman and Ross (F-R)[17] and Kelen and Tudos (K-T)[18], and a non-linear least squares (NLLS) method using the computer program developed by van Herk known as Contour.[19] A full description of the linearized equations used in this paper is given in our previous work.[15]

**Table 1.** Parameters for the F-R, inverted F-R, and K-T methods for reactivity ratio determination for DMA-co-VDMA<sup>a</sup>

Trial	$f_2^b$	$F_2^c$	$X^d$	$Y^e$	G	F	G/F	1/F	$\eta$	$\xi$
DV1	0.06	0.16	16.0	5.08	12.86	50.52	0.255	0.02	0.24	0.93
DV2	0.15	0.28	5.79	2.59	3.555	12.94	0.275	0.08	0.21	0.77
DV3	0.33	0.45	2.02	1.23	0.381	3.324	0.114	0.30	0.05	0.46
DV4	0.55	0.61	0.81	0.64	-0.448	1.019	-0.440	0.98	-0.09	0.21
DV5	0.78	0.78	0.29	0.29	-0.724	0.294	-2.461	3.40	-0.17	0.07

<sup>a</sup>  $\alpha = 3.854$ ; <sup>a</sup> Mole fraction of VDMA ( $f_2$ ) in the monomer feed at completion of the polymerization as determined by GC; <sup>b</sup> Mole fraction of VDMA ( $F_2$ ) in the copolymer as determined by <sup>1</sup>H-NMR; <sup>c</sup>  $X = f_1/f_2$ ; <sup>d</sup>  $Y = F_1/F_2$ ;

Figures 1-4 show the plots of the F-R, Inverted F-R, K-T, and Extended KT methods that were used to estimate the monomer reactivity ratios for the DMA-VDMA system, and Figure 5 shows the 95% joint confidence interval (JCI), as determined using the method described by Kelen, *et al.*[20] The JCI was used as a measure of the accuracy to which the values obtained by the linearization methods compare with respect to the

**Figure 1** Fineman-Ross plot for low conversion poly(DMA-co-VDMA)**Figure 2** Inverted Fineman-Ross plot for low conversion poly(DMA-co-VDMA)**Figure 3** Kelen-Tudos plot for low conversion poly(DMA-co-VDMA)**Figure 4** Extended Kelen-Tudos plot for monomer reactivity ratios

theoretical values predicted from the experimental data. This plot indicates good agreement between the different calculations used to determine the monomer reactivity ratios. The monomer reactivity ratios for copolymerization of DMA and VDMA are shown in Table 3. The reactivity ratio  $r_D$  indicates greater propensity for cross-propagation of a DMA polymer radical than for self-propagation.

North and Scallan[21] have reported that a propagating DMA radical is very reactive, however a DMA molecule is less reactive, as compared to MMA or styrene. This influences the value of  $r_D$ , decreasing the frequency of self-propagation events as compared to cross-propagation, consuming more VDMA.

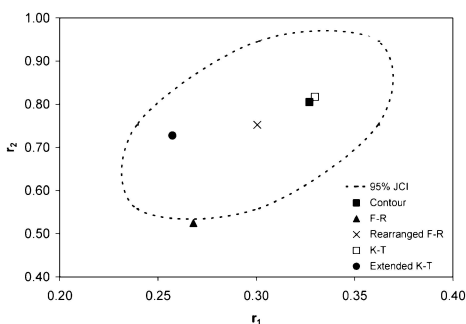
**Table 2.** Monomer Reactivity ratios of poly(DMA-co-VDMA) using different calculation methods

Method	$r_D$	$r_V$	$r_D*r_V$
Fineman-Ross[17]	0.27	0.53	0.14
Inverted F-R[17]	0.33	0.82	0.27
Kelen-Tudos[18]	0.30	0.75	0.23
Extended K-T[18]	0.26	0.73	0.19
Contour program[19]	0.327	0.805	0.22

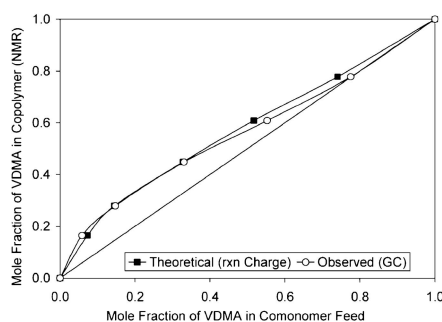
Similarly, it was observed in our previous work that VDMA was more reactive in the copolymerization with MMA, however, carbon-13 chemical shifts of the beta-vinyl carbon of DMA (129 ppm) and VDMA (130 ppm) have similar values, which indicate similar polymerization character according to Hatada *et al.*[22] This case would presumably result in equal consumption of monomer, but the reactivity ratios do not describe such an effect.

Both systems show a similar value for  $r_V$ , which indicates similar reactivity toward homopolymerization of VDMA in the two systems. Examining the reactivity ratios for the DMA-VDMA copolymerization, the  $r_V$  value indicates a propagating VDMA radical will undergo self-propagation more frequently than cross-propagation ( $r_V < 1$ ). This analysis indicates a greater consumption of VDMA, on a qualitative level. However, because  $r_V > r_D$ , a propagating DMA radical will cross-propagate more than a propagating VDMA radical will cross-propagate. Overall, these observations indicate a greater consumption of VDMA into the copolymer.

The data given in Table 1 for polymer DV5 describes a point where the mole fraction of VDMA in the monomer feed ( $f_2$ ) is the same as the mole fraction of VDMA in the copolymer ( $F_2$ ). This point represents an azeotropic copolymerization in the plot of  $F_2$  vs  $f_2$  (Figure 6). As the mole fraction of VDMA is increased in the copolymerization, Figure 6 indicates that the mole fraction of VDMA in the copolymer ( $F_2$ ) gets closer to the mole fraction of VDMA in the feed. The azeotropic point, at a mole fraction of VDMA equal to 0.78, was observed from the data obtained during GC analysis of copolymerization aliquots, and represents a molar monomer composition where the resulting copolymer will have the same ratio of monomer as the initial monomer feed composition.



**Figure 5** 95% Joint Confidence Interval for poly(DMA-co-VDMA) plotted using the method described by Kelen *et al.*[20]



**Figure 6** Plot of mole fraction of VDMA in copolymer ( $F_{2,VDMA}$ ) versus mole fraction of VDMA in the monomer feed ( $f_{2,VDMA}$ ) for poly(DMA-co-VDMA)

**Table 3.** Comparison of Monomer Reactivity Ratios for Copolymerization of VDMA with Various Monomers<sup>a</sup>

Comonomer with VDMA	$r_{(M \text{ or } D)}$	$r_V$	$r_{(M \text{ or } D)} * r_V$	Reference
MMA (M)	0.44	0.71	0.31	Stanek, <i>et al.</i> [15]
DMA (D)	0.33	0.81	0.22	This work

<sup>a</sup> Reactivity ratios taken from data obtained using the Contour program[19]

### VDMA Homopolymerization Kinetics

Kinetic behavior of polymerization is described by rate constants for propagation ( $k_p$ ) and termination ( $k_t$ ), and the ratio  $k_p^2/k_t$  has been used to characterize the behavior of monomers in radical polymerization.[23] In this work, kinetic data gathered for the homopolymerization of VDMA was used to determine rate parameters valuable in characterizing the polymerization process. Equation 1 describes the rate of polymerization ( $R_p$ ) expression and can be used to probe kinetic parameters such as the propagation and termination rate constants,  $k_p$  and  $k_t$  respectively.[24]

$$-\frac{d[M]}{dt} = k_p [M] \left( \frac{fk_d [I]}{k_t} \right)^{1/2} \quad \text{eq 1}$$

Integration and rearrangement of equation 1, as described by Tobolsky[25], results in equation 2.

$$\ln \left( \frac{[M]_o}{[M]} \right) = \frac{2k_p}{k_t^{1/2}} * (fk_d [I]_o) * (1 - \exp(-k_d t / 2)) \quad \text{eq 2}$$

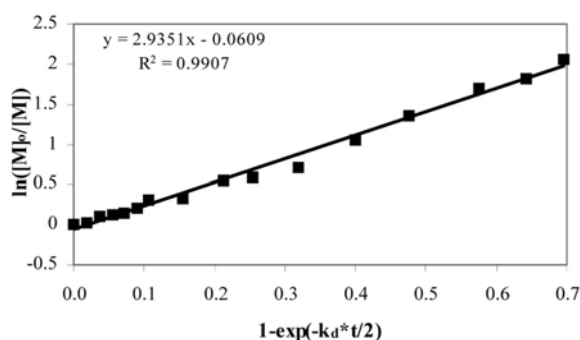
The ratio of  $k_p^2/k_t$  can be easily obtained from the linear plot of  $\ln ([M]_o/[M])$  versus  $1 - \exp(-k_d t / 2)$ , where the slope equals  $[2k_p(fk_d * [I]_o)]/k_t^{1/2}$ . Table 4 shows the experimental data from the GC analysis of the aliquots taken during the

polymerization process. Figure 7 shows a plot of these values and the value of  $k_p^2/k_t$  was determined from the slope and the following parameters:  $f = 0.60$  for AIBN,  $[AIBN]_0 = 0.0348$  M, and  $k_d = 1.25 \times 10^{-4} \text{ s}^{-1}$ . [26] The kinetic ratio  $k_p^2/k_t$  was calculated to be  $12.8 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ .

**Table 4.** Data used to determine  $k_p^2/k_t$  for the radical polymerization of 2-Vinyl-4,4'-dimethylazlactone (VDMA) in MEK solution at 52°C

Aliquot	$[M]_o/[M]$	$\ln ([M]_o/[M])$	Time (min)	$1-\exp(-k_d*t/2)$
0	1.0000	0	0	0.0000
1	1.0284	0.0280	5	0.0186
2	1.1122	0.1063	10	0.0368
3	1.1293	0.1216	15	0.0547
4	1.1605	0.1488	20	0.0723
5	1.2204	0.1992	25	0.0895
6	1.3665	0.3122	30	0.1064
7	1.3847	0.3255	45	0.1553
8	1.7304	0.5484	64	0.2134
9	1.7939	0.5844	78	0.2536
10	2.0388	0.7124	102	0.3178
11	2.8869	1.0602	136	0.3995
12	3.8922	1.3590	172	0.4753
13	5.4519	1.6960	228	0.5747
14	6.1711	1.8199	274	0.6421
15	7.7740	2.0508	316	0.6943

Comparison of  $k_p^2/k_t$  values of the monomers in the DMA-VDMA and MMA-VDMA systems discussed in this paper show DMA to be the most reactive monomer of the three. [15] As shown in work by Guyot, *et al.* [23] acrylates are more reactive than methacrylates.



**Figure 7** Plot of  $\ln ([M]_o/[M])$  versus  $1-\exp(-k_d*t/2)$  according to the data given in Table 4

The values given in Table 5 show the  $k_p^2/k_t$  values for DMA, MMA, and VDMA and describe a lower  $k_p^2/k_t$  for MMA (methacrylate) compared to both VDMA and DMA (acrylates). In general, the greater  $k_p^2/k_t$  value, the more likely the monomer will undergo efficient polymerization in the presence of a comonomer.

**Table 5.** Kinetic parameters for homopolymerization of various monomers

Monomer	$k_p^2/k_t$ ( $M^{-1} s^{-1}$ )	Temp (°C)	Reference
<i>N,N</i> -dimethylacrylamide	3.18	50	North and Scallan[21]
2-Vinyl-4,4'-dimethylazlactone	0.0128	52	This work
Methyl methacrylate	0.0104	60	Matheson <i>et al.</i> [27]

### Molecular Weight Analysis

In addition to determining monomer reactivity ratios for the DMA-VDMA system, and comparing the values to those previously determined for the MMA-VDMA system,[15] the copolymers were characterized by molecular weight analysis using gel-permeation chromatography (GPC). Molecular weight data for the series of DMA-VDMA copolymers, shown in Table 6, indicates decreased molecular weight with decreasing mole fraction of VDMA. In comparison, Tully *et al.*, describe the polymerization character of VDMA in studies of living free radical copolymerization with DMA.[28] Their data for “living” copolymerizations gave higher molecular weight for 50 mole percent DMA than for 25 or 75 percent DMA. In addition, the data reported here gives similar molecular weights despite the lower conversion (<30%) compared to the much higher conversion (95%) using the living free-radical technique.

**Table 6.** Molecular weight data for poly(DMA-co-VDMA)

Polymer	VDMA mole % <sup>a</sup>	$M_n$ ( $kg mol^{-1}$ ) <sup>b</sup>	$M_w$ ( $kg mol^{-1}$ ) <sup>b</sup>	PDI <sup>b</sup>
DV1	16	9.5	18.0	1.89
DV2	28	18.1	32.8	1.81
DV3	45	22.7	37.6	1.66
DV4	61	23.7	43.0	1.82
DV5	78	26.9	49.6	1.84

<sup>a</sup> Determined by <sup>1</sup>H-NMR; <sup>b</sup> Determined by GPC analysis with polystyrene standards (see Experimental Section)

The lower molecular weight in this series of polymers may be a result of chain transfer to monomer by the more reactive radical of DMA as the proportion of DMA radicals to VDMA radicals increased. The hydrogen atoms on the methyl groups of DMA being more susceptible to abstraction than the methyl groups of VDMA, resulting in chain transfer to monomer at high mole fractions of DMA ( $C_M = 1.5 \times 10^{-4}$ , 50°C).[26] However, given the large amount of solvent relative to monomer, it seems likely that chain transfer to solvent may also be occurring.



## Conclusion

This paper describes the synthesis and characterization of copolymers containing *N,N*-dimethylacrylamide and 2-vinyl-4,4'-dimethylazlactone (VDMA). Monomer reactivity ratios show a greater overall consumption of VDMA into the copolymer, and this holds true up to an azeotropic composition of 78 mole percent VDMA. The reactivity ratios describe an approximately random distribution of monomers in the copolymerization of DMA and VDMA.

*Acknowledgements.* The authors would like to thank Professor Marc Hillmyer (U of M) and his research group for valuable assistance with polymer characterization and Dr. Letitia Yao (U of M) for assistance in NMR analysis.

## References

- Chiari, M, Cretich, M and Consonni, R (2002) *Electrophoresis* 23:536-541
- Bulai, A, Alencar de Queiroz, A-A, Gallardo, A and San Ramon, J (1999) *Polymer* 40:4953-4960
- Ratner, BD, Hoffman, AS, Schoen, FJ and Lemons, JE (1996) Academic Press San Diego, CA
- Haddad, LC, Hembre, JI, Rasmussen, JK and Sarpong, D (2003) Azlactone-functional Hydrophilic Coatings and Hydrogels, US 2003/0049435:
- Yin, X and Stover, HDH (2003) *Macromolecules* 36:9817-9822
- Gonzalez, N, Elvira, C, San Ramon, J and Cifuentes, A (2003) *J. Chromatogr., A* 1012:95-101
- Albarghouthi, MN, Buchholz, BA, Doherty, EAS, Bogdan, FM, Zhou, H and Barron, AE (2001) *Electrophoresis* 22:
- Kazakov, SV, Muronetz, VI, Dainiak, MB, Izumrudov, VA, Galaev, IY and Mattiasson, B (2001) *Macromol. Biosci.* 1:157-163
- Bicak, N, Sherrington, DC, Sungur, S and Tan, N (2003) *React. Funct. Polym.* 54:141-147
- Drtna, GJ, Heilmann, SM, Moren, DM, Rasmussen, JK, Krepski, LR, Smith II, HK, Pranis, RA and Turek, TC (1996) *Macromolecules* 29:4486-4489
- Heilmann, SM, Rasmussen, JK and Krepski, LR (2001) *J. Polym. Sci. Part A: Polym. Chem.* 39:3655-3677
- Coleman, PL, Walker, MM, Milbrath, DS, Stauffer, DM, Rasmussen, JK, Krepski, LR and Heilmann, SM (1990) *J. Chrom.* 512:345-363
- Rasmussen, JK, Heilmann, SM and Krepski, LR (1988) *Polyazlactones, II*:558-571
- Xie, S, F., S and Frechet, JMJ (2000) *Biotechnol. Bioeng.* 11:30-35
- Stanek, LG, Heilmann, SM and Gleason, WB (2003) *J. Polym. Sci., Part A: Polym. Chem.* 41:3027-3037
- Harwood, HJ, Baikowitz, H and Trommer, HF (1963) *Am. Chem. Soc., Div. Polym. Chem., Preprints* 4:133-141
- Fineman, M and Ross, SD (1950) *J. Polym. Sci.* 5:259-262
- Kelen, T and Tudos, F (1975) *J. Macromol. Sci. Chem.* A9:1-27
- van Herk, AM and Droge, T (1997) *Macromol. Theory Simul.* 6:1263-1276
- Kelen, T, Tudos, K and Turcsanyi, B (1980) *Polym. Bull.* 2:71-76
- North, AM and Scallan, AM (1964) *Polymer* 5:447-455
- Hatada, K, Nagata, K, Hasegawa, T and Yuki, H (1977) *Makromol. Chem.* 178:2413-2419
- Guyot, B, Ameduri, B, Boutevin, B, Melas, M, Viguiet, M and Collet, A (1998) *Macromol. Chem. Phys.* 199:1879-1885
- Odian, G (1991) *Principles of Polymerization* John Wiley & Sons, Inc., New York

25. Tobolsky, AV, Rogers, CE and Brinkman, RD (1960) *J. Am. Chem. Soc.* 82:1277-1280
26. Brandup, J and Immergut, EH (1975) John Wiley & Sons, Inc. New York
27. Matheson, MS, Auer, EE, Bevilacqua, EB and Hart, EJ (1949) *J. Am. Chem. Soc.* 71:497
28. Tully, DC, Roberts, MJ, Geierstanger, BH and Grubbs, RB (2003) *Macromolecules* 36:4302-4308