

PAPER • OPEN ACCESS

## Influence of Side Chain Length on the Properties of Alkylated Copolymers Based on N-Methyl-N-Vinylacetamide

To cite this article: O A Dommes *et al* 2019 *IOP Conf. Ser.: Mater. Sci. Eng.* **500** 012017

View the [article online](#) for updates and enhancements.

## Influence of Side Chain Length on the Properties of Alkylated Copolymers Based on N-Methyl-N-Vinylacetamide

O A Dommes<sup>1</sup>, A A Gosteva<sup>1</sup>, G F Kolbina<sup>1</sup>, O V Okatova<sup>1</sup>, I I Gavrilova<sup>1</sup>,  
E F Panarin<sup>1,2</sup>, G M Pavlov<sup>1,3</sup>

<sup>1</sup> Institute of Macromolecular Compounds, Russian Academy of Sciences,  
Bolshoy pr. 31, St. Petersburg 199004, Russia

<sup>2</sup> Department of Medical Physics and Bioengineering, Peter the Great St. Petersburg  
Polytechnic University, Polytechnicheskaya str. 29, St. Petersburg 195251, Russia

<sup>3</sup> Saint Petersburg State University, Universitetskaya nab. 7/9 St. Petersburg 199034,  
Russia

E-mail: oljaspb552@gmail.com, georges.pavlov@mail.ru

**Abstract.** A series of alkylated statistical copolymers of N-methyl-N-vinylacetamide and N-methyl-N-vinylamine hydrochloride containing  $C_6H_{13}$  –  $C_{12}H_{25}$  side aliphatic group in the chain were studied by the methods of molecular hydrodynamics (velocity sedimentation, translational diffusion and viscous flow) in 0.1M NaCl and salt free water solutions, and by flow birefringence. The competition between electrostatic and hydrophilic/hydrophobic interactions manifests differently depending on the ionic strength and the length of the side chains. It was found that the radical length noticeably affects the characteristics of copolymer macromolecules. The hydrodynamic volume decreases and the shear stress optical coefficient increases considerably for the samples with  $C_{12}H_{25}$  side chain groups. This is explained by drastic increase in the hydrophobic interactions which dominate over the electrostatic interactions.

### 1. Introduction

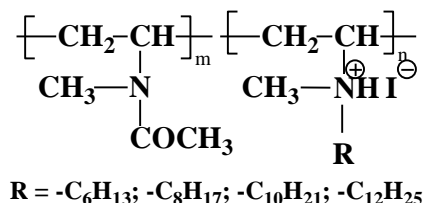
The interest in synthesis and study of new molecular carrier containers based on polymers and polymer systems for targeted transport of various biologically active substances to living organisms [1] is still ongoing. In the frame of the original “drug delivery” concept, significant efforts have been made to increase the efficiency of pharmaceutically active compounds by attempting to control the temporal as well as spatial drug distribution in vivo [2],[3].

Such biologically active substances are often hydrophobic meanwhile the efficiency of their therapeutic application is determined by the delivery to targeted organ. Accordingly, molecular systems combining hydrophobic and hydrophilic fragments are promising for use in medicine. Amphiphilic copolymers based on N-methyl-N-vinylacetamide are one of examples of such macromolecular systems. Alkylation of charged hydrophilic copolymers of N-methyl-N-vinylacetamide and N-methyl-N-vinylamine hydrochloride (MVAA-MVAH) leads to the formation of amphiphilic copolymers with a specified length of the lateral radicals. Such macromolecules have hydrophilic backbone and a number of hydrophobic side radicals and possibly may form hydrophobic internal domains in macromolecular coils.



## 2. Experimental part

The initial MVAA-MVAH copolymers were synthesized and then alkylated by alkyl iodides  $C_6H_{13}$ – $C_{12}H_{25}$  as described in [4] in the laboratory of hydrophilic polymers in the Institute of Macromolecular Compounds, Russian Academy of Sciences. The composition was 85(m):15(n) mol. %. The content of halide ions was determined by argentometric titration on a TVL-1 conductivity meter. The chemical structure is shown below.



The nonalkylated MVAA-MVAH copolymers with similar composition and the alkylated ones with 20 mol. % of charged side aliphatic groups (from  $C_2H_5$  to  $C_{12}H_{25}$ ) were investigated earlier [5],[6],[7].

The following methods of molecular hydrodynamics and optics have been used: velocity sedimentation, translational diffusion, viscometry and dynamic flow birefringence (DFB). The molar masses were calculated from the data of sedimentation-diffusion analysis as described in [7]. The full complex of measurements was carried out in 0.1 M NaCl under suppression of polyelectrolyte effects. Additionally, the intrinsic viscosity  $[\eta]$  values at minimal ionic strength ( $\approx 10^{-6}$  M, pure water) were obtained from the initial slope of  $\ln \eta_r$  dependence on concentration  $c$  [8], [9].

One of the substantial properties of macromolecules is their optical anisotropy, i.e. the difference of optical properties in two orthogonal directions. The optical anisotropy of the macromolecular coil (or dispersed nanoparticle) is determined by the internal structure of the particle, by their shape and artificially induced orientation, and, finally, by the difference in refractive indices of particle and solvent [10].

Optical properties of alkylated MVAA-MVAH copolymer dilute solutions were studied in 0.1 M NaCl at 21 °C by DFB which is the most sensitive method both to the structure of the repeating unit of the macromolecule and to the conformation of its chain.

DFB was investigated on the device with a visual recording system in a dynamooptimeter [10]; the parameters of device could be found in [11].

## 3. Results and Discussion

Two series of samples were investigated. Each series was obtained from one MVAA-MVAH sample. The hydrodynamic data are presented in table 1 (a, b). Series 1 – samples with higher molar mass (numbers 1 – 4), series 2 – samples with lower molar mass (numbers 5 – 8).

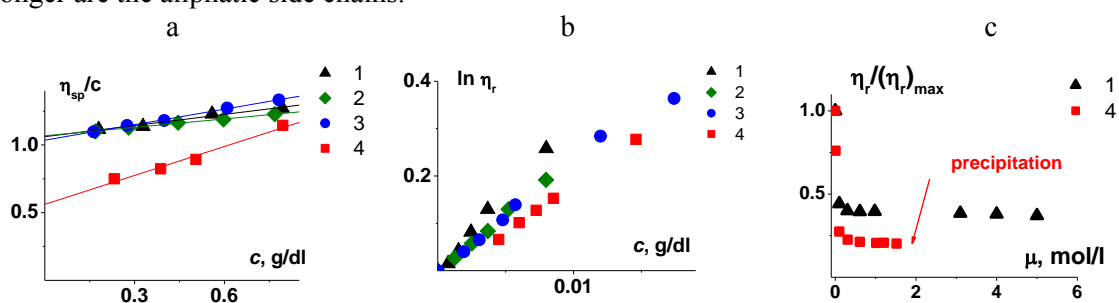
As follows from table 1 and figure 1 (a, b), intrinsic viscosity decreases significantly when radical length is  $N_C=12$  as in 0.1M NaCl as in  $H_2O$  due to hydrophobic interactions.

**Table 1.** Hydrodynamic characteristics of alkylated MVAA-MVAH copolymers in 0.1M NaCl at 25 °C

Sample no.	Radical length, $N_C$	Molar mass, $M \cdot 10^{-3}$ , g/mol	Intrinsic viscosity $[\eta]$ in 0.1M NaCl, $\text{cm}^3/\text{g}$	Intrinsic viscosity $[\eta]$ in $\text{H}_2\text{O}$ , $\text{cm}^3/\text{g}$	Diffusion coefficient $D_0 \cdot 10^7$ , $\text{cm}^2/\text{s}$	Sedimentation coefficient $s_0 \cdot 10^{13}$ , s	Mass of a unit length $M_L \cdot 10^{-9}$ , g/mol·cm	Contour length $L \cdot 10^8$ , cm
1	6	79	106	4500	2.4	1.9	4.18	1890
2	8	119	107	2600	2.0	2.28	4.35	2740
3	10	126	104	2700	1.91	2.32	4.52	2790
4	12	163	56	2300	2.40	3.62	4.68	3480
5	6	28	33	500	4.1	1.16	4.18	670
6	8	31	31	480	4.2	1.24	4.35	710
7	10	33	29	360	4.3	1.35	4.52	730
8	12	47	22	310	4.1	1.80	4.68	1000

Additionally the relative viscosity of solution was monitored during titration with NaCl solutions to investigate the interplay between hydrophobic/hydrophilic and electrostatic interactions. Two samples were chosen (samples 1 and 4 in table 1). The initial ionic strength of solution was  $\approx 10^{-6}\text{M}$  (pure water). Then 1 M and subsequently 6 M NaCl was added and the relative viscosity  $\eta_r$  was measured. The polymer concentration was kept virtually constant, as  $0.976 \pm 0.004$  g/dl. The relative viscosity  $\eta_r$  of sample 4 ( $\text{C}_{12}\text{H}_{25}$  radical) decreased more significantly, and finally the polymer precipitated after 1.8 M NaCl in contrast to sample 1 ( $\text{C}_6\text{H}_{13}$  radical) which remained soluble up to 5 M NaCl. Even dry salt addition didn't cause polymer precipitation. The results are presented in figure 1c.

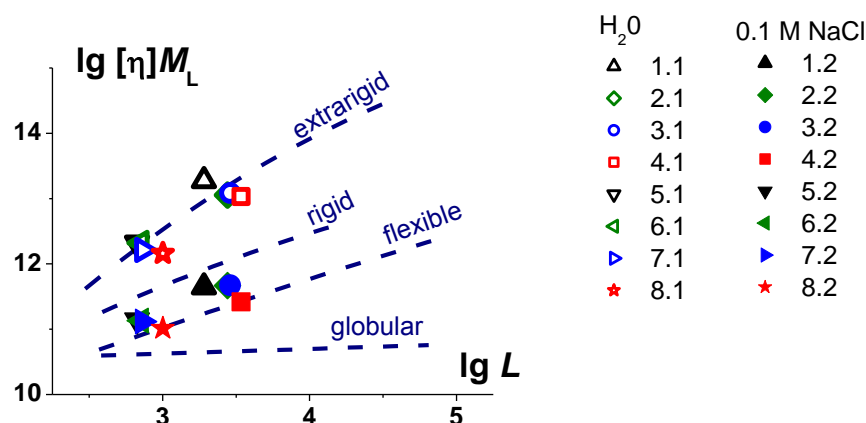
At low ionic strength the electrostatic interactions are dominating in solution, and macromolecules of both copolymers have the maximal dimensions in pure water solutions. An increase in ionic strength with the gradual addition of salt leads to the progressive screening of electrostatic interactions, which in turn leads to a decrease in the coil dimensions. The latter causes an increase in hydrophobic interactions of side aliphatic chains. The hydrophobic interactions are the stronger the longer are the aliphatic side chains.



**Figure 1.** Viscometry data for MVAA–MVAH alkylated copolymers (samples 1 – 4 in table 1) **(a)** – Huggins [12] plot in 0.1M; **(b)** – logarithmic dependence of relative viscosity  $\eta_r$  on polymer concentration  $c$  in salt free  $\text{H}_2\text{O}$ ; **(c)** – viscosity titration data for MVAA–MVAH alkylated copolymers (samples 1 and 4 in table 1): dependence of relative viscosity  $\eta_r$  normalized to its maximal value on ionic strength of solution  $\mu$  (polymer concentration  $c = 0.976 \pm 0.004$  g/dl). The initial (in  $\text{H}_2\text{O}$ ) relative viscosity was  $\eta_r = 5.2$  for sample 1 and  $\eta_r = 8.4$  for sample 4. The measurements of sample 4 solution were finished after ionic strength  $\mu = 1.5$  mol/l because of polymer precipitation.

A powerful tool for interpreting hydrodynamic, especially viscometric, data are the Kuhn-Mark-Houwink-Sakurada plots normalized to the mass per unit length  $M_L$  [13]. The Flory-Fox relationship [14] gives a molecular meaning of the intrinsic viscosity value:  $[\eta] = \Phi \langle h^2 \rangle^{3/2} / M$ , where  $\langle h^2 \rangle$  is the root-mean-square distance between the chain ends,  $\Phi$  is the Flory viscosity parameter. The product  $[\eta]M_L = \Phi \langle h^2 \rangle^{3/2} / L \sim V/L$  characterizes the volume  $V$  occupied by a part of macromolecule per unit of its contour length  $L$ . For linear macromolecules, the  $[\eta]M_L = f(L)$  dependence (figure 2) can be considered as a distribution of linear macromolecules according to their sizes and conformations [13]. The dashed curves in figure 2 represent the dependences obtained for different linear chains and structures with different equilibrium rigidity values; the minimum values correspond to globular structures (statistical segment length  $A \sim 1$  nm), and the maximum values correspond to multi-stranded structures ( $A \sim 200$  nm). Use of this plot for new polymer systems allows to obtain qualitative estimations of their size and conformation.

It can be noted that the data for alkylated MVAA-MVAH copolymers in 0.1M NaCl are located between flexible and rigid macromolecules, and the data in pure water solution – near extra-rigid uncharged macromolecules (figure 2).



**Figure 2.** The double logarithmic dependence of normalized hydrodynamic volume  $[\eta]M_L$  on contour length  $L$ . The curves correspond to extra rigid, rigid, flexible, and globular uncharged linear chains [13]. The data for alkylated MVAA-MVAH copolymers (samples 1–8 in table 1) in salt-free water solution are shown as open points 1.1 – 8.1 and in 0.1 M NaCl – as filled points 1.2 – 8.2. Black symbols correspond to samples containing  $C_6H_{13}$  aliphatic side chain, green symbols –  $C_8H_{17}$ , blue symbols –  $C_{10}H_{21}$ , red symbols –  $C_{12}H_{25}$ .

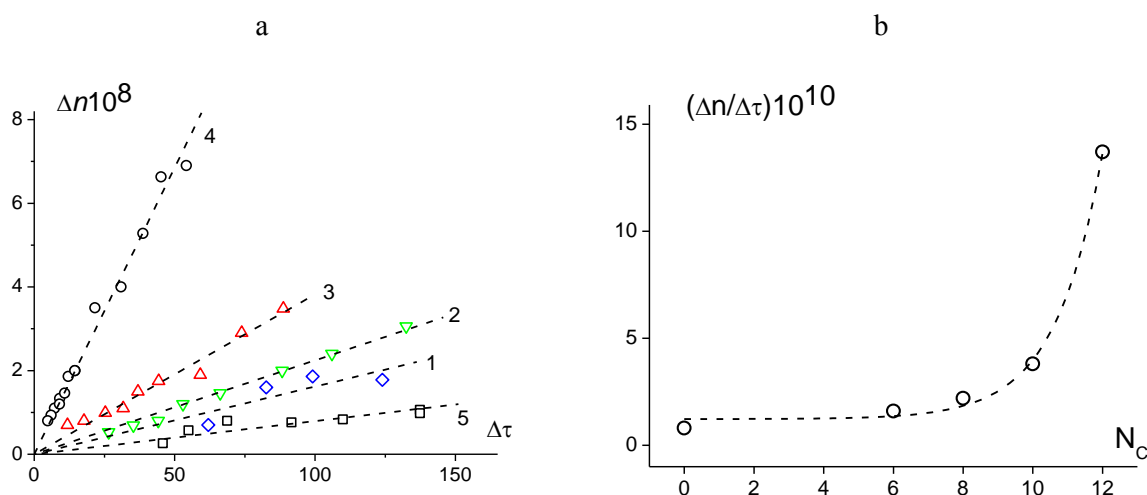
The most important characteristic of dissolved macromolecules in DFB is the value of shear optical coefficient  $[n]/[\eta] = \Delta n / \Delta \tau$ . It is related to the anisotropy of the intrinsic optical polarizability of the statistical segment  $((\alpha_1 - \alpha_2)_0)$  by the following relation:

$$[n]/[\eta] = \{4\pi(n_s^2 + 2)^2 / 45kTn_s\} \times \{(\alpha_1 - \alpha_2)_0 + [2.60\Phi(\Delta n / \Delta c)^2 / \pi^2 N_A^2]M/[\eta]\} \quad (1),$$

here  $[n] = \lim_{g,c \rightarrow 0} (\Delta n / g\eta_0 c)$ ,  $\Delta n$  is the observed DFB effect,  $\Delta \tau$  is the shear stress,  $g$  is the shear rate gradient,  $\Phi$  is Flory viscose parameter;  $n_s$  and  $\eta_0$  are the refractive index and dynamic viscosity of the solvent;  $\Delta n / \Delta c$  is the refractive index increment of the polymer-solvent system;  $k$  is Boltzmann constant;  $N_A$  is Avogadro number;  $T$  is Kelvin temperature. The second term on the right-hand side of equation (1) is the contribution of the so-called macroform effect.

Figure 3a shows the dependencies of  $\Delta n$  on the shear stress  $\Delta\tau = g(\eta - \eta_0)$ , the slope of which gives the desired value  $\Delta n/\Delta\tau$  ( $\eta$  is viscosity of the solution). The dependence of shear stress  $\Delta n/\Delta\tau$  on side radical length  $N_C$  is shown in figure 3b. The sign of the DFB value is positive and increases significantly for samples with long side chains ( $N_C > 10$ ). This effect was observed for both molecular masses series. The large DFB value can be explained both by an increase in the order of anisotropic elements in the direction of a larger coil axis, and by an increase in the macroform effect due to the greater asymmetry of the macromolecule. The separation of these contributions requires further study in a series of polymer homologues with a fixed length of side chains and their composition.

The study of viscous flow and DFB effect in solutions of alkylated MVAA–MVAH copolymers shows that both in salt-free and in 0.1M NaCl solutions experimental characteristics ( $[\eta]$  и  $\Delta n/\Delta\tau$ ) are noticeably different for samples with long side chains ( $N_C = 12$ ) as compared with those with shorter side groups. This can be interpreted as a phenomenon of self-organization of macromolecules, which occurs due to the prevalence of hydrophobic interactions. Macromolecules of alkylated MVAA–MVAH copolymers have a hydrophilic base, hydrophobic side groups and charges on the chain, and there is a competition of all types of interactions, the contributions of which are determined by the ionic strength of the solutions.



**Figure 3. (a)** – dependence of birefringence  $\Delta n$  on shear rate tension  $\Delta\tau = g(\eta - \eta_0)$  for solutions of amphiphilic alkylated MVAA-MVAH copolymers (samples 1–4 in table 1) and 5 – unalkylated MVAA-MVAH copolymer ( $N_C = 0$ ) in 0.1 M NaCl; **(b)** – dependence of shear stress optical coefficient or reduced birefringence  $\Delta n/\Delta\tau$  on the number of carbon atoms in the side chains  $N_C$  for the same samples.

#### 4. Conclusion

The complex study of hydrodynamic and optical properties of alkylated MVAA-MVAH copolymers containing hydrophilic backbone and hydrophobic side chain (from  $C_6H_{13}$  to  $C_{12}H_{25}$ ) allowed the reliable analysis of their properties. The virtually monotonic change in the intrinsic viscosity and shear optical coefficient up to  $N_C = 10$  followed by the sharp growth of these values for  $N_C = 12$  was observed. At low ionic strength and short aliphatic side chains ( $N_C < 10$ ) the electrostatic interactions prevail, and at medium ionic strength and long aliphatic side chains ( $N_C > 10$ ) dominate the hydrophobic interactions. This statement is supported by comparative titration of samples with  $N_C = 6$

and  $N_C = 12$  by NaCl solutions. When the electrostatic interactions are practically “switched off” (0.1M), the self-organization of the copolymer coils is governed by hydrophobic interactions.

### Acknowledgements

The reported study was funded by RFBR according to the research project № 18-33-00432.

### References

- [1] Vilar G, Tulla-Puche J and Albericio F 2012 *Current Drug Delivery* **9(4)** 367–394
- [2] Qiu L, Bae Y 2006 *Pharm. Res.* **23** 1–30
- [3] Duncan R 2003 *Nat. Rev. Drug Discovery* **2** 347–360
- [4] Panarin E F and Gavrilova I I 1977 *Vysokomol. Soedin., Ser. B* **19** 251–254
- [5] Dommes O A, Okatova O V, Kostina A A, Gavrilova I I, Panarin E F and Pavlov G M 2017 *Polymer Science, Series C* **59(1)**, 125–132.
- [6] Pavlov G M, Dommes O A, Okatova O V, Gavrilova I I and Panarin E F 2018 *Phys. Chem. Chem. Phys.* **20** 9975–9983
- [7] Pavlov G M, Kolbina G F, Okatova O V, Gavrilova I I, Panarin E F 2015 *Doklady Chemistry* **463(1)**, 181–184
- [8] Pavlov G M, Okatova O V, Gubarev A S, Gavrilova I I and Panarin E F 2014 *Macromolecules* **47(8)** 2748–2758
- [9] Pavlov G M, Gubarev A S, Zaitseva I I and Sibileva M A 2006 *J. Appl. Chem.* **79(9)** 1423–1428
- [10] Tsvetkov V 1989 *Rigid-chain Polymers* (New York: Plenum Press) p 490
- [11] Pavlov G M, Kolbina G F, Shtennikova I N, Michailova N A, Korneeva E V 2001 *Eur. Polym. J.* **37** 1219–1225
- [12] Huggins M L 1942 *J. Am. Chem. Soc.* **64(11)** 2716–2718
- [13] Pavlov G M *Eur. Phys. J. E: 2007 Soft Matter Biol. Phys.* **22** 171–180
- [14] Flory P J 1953 *Principles of Polymer Chemistry* (Ithaca, New York: Cornell University Press) p 672