Effect of the Stereochemical Structure of Poly(methacrylic acid) Molecules on Their Interaction with Organic Ions in Aqueous Solutions

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Introduction. The stereochemical structure of organic compounds including those of polymeric nature can profoundly affect their intermolecular interactions. Thus, the biological activity of many substances is often related to their stereochemical structure. This structure is recognized by stereospecific receptors, active enzyme centers, or bonding parts of various transport systems.[1,2]

The contribution of stereochemical structure and related conformational state of carbon chain macromolecules which do not contain truly asymmetric carbon atoms to intermolecular interactions can be manifested when these interactions involve groups of units adjoining each other along the chain contour or located close to each other.

A well-known example of intermolecular interactions, the efficiency of which depends on the stereochemical structure of carbon chain macromolecules, is the formation of interpolymer complexes stabilized by contacts of various nature between long sequences of polymer chain units, which differ in chemical and/or stereochemical structures.[3–5] It may be assumed that the influence of the stereochemical structure of carbon chain molecules on the efficiency of their interaction with low molecular weight compounds can also be manifested in those cases when the molecules of the low molecular weight compound interact with several units of the macromolecule.

In the present work the relationship between the stereochemical structure of carbon chain macromolecules and their interaction with low molecular weight compounds is investigated on the interaction between poly(methacrylic acids) (PMAA) with different microtacticities and luminescent organic ions in aqueous solutions. The choice of these compounds is based on the following considerations.

In many cases the wide use of linear and cross-linked (co)polymers based on the methacrylic acid (MAA) is related to their ability to undergo reversible interactions in aqueous media with various compounds of low or high molecular weight. The activity of PMAA in intermolecular interactions is due to the presence in each monomer residue of a polar proton-donating carboxylic group and a nonpolar hydrophobic methyl group and to the presence in the ionized PMAA of carboxylate groups interacting with positively charged compounds including organic ions. However, even in the un-ionized state PMAA molecules can interact in aqueous media with organic ions of Acridine Orange (AO), Auramine O (Au), the magnesium salt of 8-anilinonaphthalene-1-sulfonic acid (ANS), proflavine, etc.[6] The predominant role in these interactions is, without a doubt, played by the compact conformation peculiar to the molecules of un-ionized PMAA[6,7] which is characterized by the presence of parts with a high local density of nonpolar methyl groups. The destruction of this compact structure of the entire PMAA molecule upon the introduction of an organic solvent to the aqueous solution[6] drastically decreases the fraction of organic ions bound to PMAA. This indicates that the hydrophobic contacts of an organic ion with hydrocargon fragments of PMAA units adjoining each other within the structured part of the chain provide a predominant contribution to the bonding of organic ions by un-ionized PMAA molecules.

Table I. Polymerization of MAA in Aqueous Media and Properties of PMAA Obtained

no.	pH of the reaction medium	polymn temp (°C)	$\bar{M}_\eta \times 10^{-4}$	stereochem composn of PMAA (triad %) S (syndio)	H (hetero)	I (iso)
1	2.2	30	54.7	61	37	2
2		40	66.2	57	40	3
3		50	28.3	62	35	3
4		60	8.8	56	40	4
5		70	5.8	57	38	5
6		80	12.0	53	44	3
7	6.4	50	19.5	72	27	1
8	10.5	30	28.6	78	21	1
9		40	19.0	78	20	2
10		50	38.6	75	23	2

The role of the high local concentration of nonpolar groups of polymer chains interacting with organic ions in aqueous solutions and the importance of multiple contacts that ensure ion bonding by macromolecules are also manifested for polymers with a different chemical structure. Thus, the molecules of water-soluble poly(*N*-alkylmethacrylamides) (PAMA) in the random-coil state do not react with ions of AO or Au. However, on passing from a random coil to the compact globular structure as the temperature of the aqueous solution is raised, the PAMA molecules which do not contain any ionogenic groups begin to bind effectively these organic ions.[8]

Experimental Section. Synthesis and Determination of the Characteristics of Poly(methacrylic acids) with Different Stereoregularities. PMAA samples with different stereoregularities were obtained by free-radical polymerization of MAA in aqueous media at different pHs and temperatures (Table I) and in different organic media (Table II). MAA, organic solvents (Table II), and initiators (AIBN, potassium persulfate) were purified by standard procedures. Immediately before use MAA was distilled under reduced pressure.

MAA was polymerized in sealed ampules in argon at a MAA–solvent volume ratio of 1:4. The polymerization of MAA in aqueous media at pH values ranging from 2.2 to 10.5 was carried out under conditions similar to those in ref 9 using potassium persulfate initiator. The polymers were precipitated from aqueous solutions with a 10-fold excess of 2 N aqueous HCl and purified by precipitating PMAA from methanol solutions with 2 N HCl (3–4 times) and diethyl ether (3–4 times).

For organic solvents, AIBN was used as initiator (4 wt % with respect to MAA), and the reaction was continued for 6 h at 60 °C. The polymer precipitated from the reaction mixture (without solvent, in toluene, dichloroethane, chloroform, and ethyl acetate and partially in dioxane and tetrahydrofuran) was isolated, and that remaining in solution was precipitated with ether. The isolated PMAA was purified by reprecipitating twice from a methanol solution with ether.

Before investigations all PMAA were dissolved in water, the solutions were frozen, and water was removed by vacuum sublimation.

The [η] values for PMAA solutions in 0.002 N HCl at 30 °C were measured in an Ubbelohde viscometer. The $\bar{M}$ value of polymers was calculated by using the equation [η] = $6.6 \times 10^{-4} M^{0.5}$.[10]

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Table II. Polymerization of MAA in Organic Solvents and Properties of PMAA Obtained

			stereochem composn of PMAA (triad %) (^{1}H NMR method)			luminescence method of determn of S-triads in PMAA[a]	
no.	solvent	$M_\eta \times 10^{-4}$	S (syndio)	H (hetero)	I (iso)	$I_{\mathrm{lum}}^{\mathrm{rel}}$ of Au	% of S-triads
1		11.5	45	46	9	1	
2	dichloroethane	30.1	50	43	7	1.7	52
3	chloroform	21.5	52	42	6	2.0	53
4	octane	16.1	52	41	7	2.1	54
5	toluene	19.3	54	40	6	1.6	52
6	ethyl acetate	62.1	55	40	5	3.6	58
7	dioxane	1.9	55	40	5		
8	tetrahydrofuran	13.8	62	35	3	5.0	62
9	ethanol	1.1	67	36	2		
10	dimethylacetamide	9.2	68	30	2	9.4	70

[a] For details, see the text.

The stereochemical structure of synthesized PMAA (Tables I and II) was determined by a traditional procedure[11] by methylating their carboxylic groups with diazomethane[10] and investigating the microtacticity of the poly(methyl methacrylate) by ^{1}H NMR (JEOL C-60 HL spectrometer). The error in the determination of PMAA stereochemical composition with the aid of this method is $\simeq 2\%$.

Measurement of Luminescence Parameters of Organic Ions in PMAA Aqueous Solutions. The luminescence parameters of organic ions in aqueous PMAA solutions were measured at PMAA concentrations of 0.005–0.01 g/dL and at an organic ion–PMAA unit ratio of 1:(500 ÷ 1000).

The luminescence polarization of AO ions in aqueous solutions in the absence or presence of PMAA of different microtacticities was measured on a device described previously.[6a] The investigations were carried out with an ionization degree of PMAA (α) not exceeding 0.1, and the $\lambda_{\max}$ of AO luminescence was 530 nm.[6a] It was shown that $\lambda_{\max}$ and the intensity of AO luminescence measured under these conditions weakly depend on S-triad content: $\lambda_{\max}$ changes from 530 to 527 nm and the intensity increases two times when the content of the S-triads increases from 45 to 78%. When these conditions were not obeyed, the interaction of AO with ionized PMAA ($\alpha > 0.3$) was accompanied by the formation of AO dimers luminescent at a longer wavelength range, $\lambda_{\max} = 640$ nm.[12]

The degree of binding (θ) of AO ions by PMAA molecules was determined from

$$\theta = 100\% \times (P_{\mathrm{meas}} - P_{\mathrm{free}})/(P_{\mathrm{bound}} - P_{\mathrm{free}}) \qquad (1)$$

where P_{meas} and P_{free} are the values of luminescence polarization for AO ions in the presence and absence of PMAA, while P_{bound} is that for AO ions bonded to the un-ionized PMAA ($\alpha < 0.1$) exhibiting hindered rotational mobility. P_{bound} is determined for AO ions fully immobilized in glycerol solution or in aqueous PMAA solution at an AO ion–PMAA monomer residue ratio of 1:10 000.

The luminescence intensity, I_{lum}, of Au in aqueous PMAA solutions was measured using excitation at 436 nm and recording the emission at 546 nm. The I_{lum} value of Au in solutions was measured at pH = 4.0 (biphthalate buffer). Considerable deviations from this pH value are accompanied by a marked decrease in I_{lum}. This is confirmed by the following data:

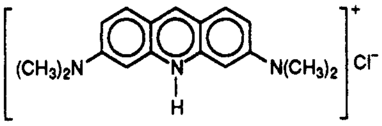
pH (ionic strength 0.05)	1.9	3.0	4.0	4.7	5.2
I_{lum} (relative units)	1.5	5.0	28.0	22.0	12.0

A decrease in I_{lum} leads to a lower precision of measurements as a result of an increasing contribution of scattering light.

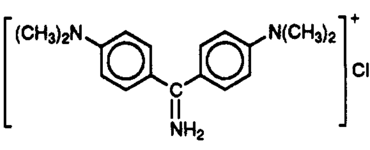
It was shown that $\lambda_{\max}$ of AO luminescence measured under these conditions is practically independent of S-triad content: $\lambda_{\max}$ changes from 505 to 503 nm when the content of the S-triads increases from 45 to 78%.

Results and Discussion. In order to investigate the relationship between the stereochemical PMAA structure and the efficiency of its interaction with organic ions, a series of PMAA samples with a relatively wide stereoregularity range were used. It is known that when PMAA is obtained by free-radical polymerization, the stereotactic triads in the polymer chains are mainly syndiotactic.[13-15] The content of syndiotactic triads in PMAA samples varied from 45 to 78%. PMAA with a higher content of S-triads and isotactic PMAA are usually obtained by the anionic polymerization of readily split MAA esters with subsequent removal of protective groups. The remaining small quantity of hydrophobic protective groups, even though it cannot be determined by traditional methods of structural analysis (NMR, IR spectroscopy, etc.), can influence the interaction between PMAA and organic ions because the number of ions is very small as compared to that of polymer units in solution, 1:(500–1000). Hence, these polymers have not been investigated in the present work.

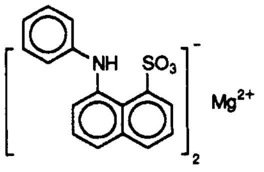
Organic ions of AO, Au, and a magnesium salt of ANS were used as water-soluble luminescent ions which under certain conditions can interact with un-ionized PMAA.



AO



Au



ANS

The interaction between ANS ions and macromolecules in aqueous solutions is also known to increase their luminescence intensity.[16] In contrast to AO and Au ions which are cations, ANS ions bear a negative charge.

It may be assumed that the study of interaction of these differently charged ions with PMAA having different

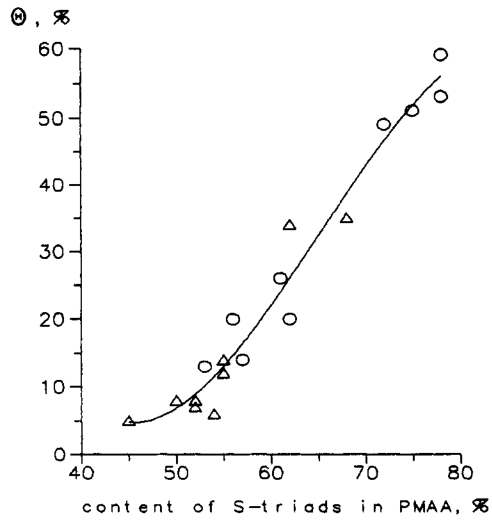


Figure 1. Fraction of AO ions bound to un-ionized PMAA in aqueous solution vs the content of syndiotactic triads. PMAA were obtained by free-radical polymerization in organic (△) or aqueous (○) media. PMAA content 0.06 mg/mL, 1 AO ion per 500 PMAA units, pH = 4, ionic strength 0.05.

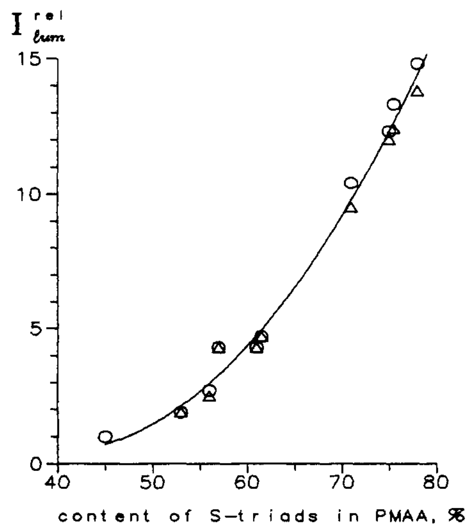


Figure 2. Relative luminescence intensity $I_{\rm lum}^{\rm rel}$ of Au ions in aqueous PMAA solutions in a biphthalate buffer (pH = 4.0) vs the content of syndiotactic triads of PMAA. PMAA content 0.1 mg/mL, 1 Au ion per 500 (○) or 1000 (△) PMAA units.

stereochemical structures and carried out by different luminescence methods reflects information about the phenomenon under investigation.

The high sensitivity of the luminescence methods enables us to carry out investigations at very low concentrations of PMAA and organic ions ($C_{\rm PMAA}$ = 0.05–0.1 mg/mL or 0.005–0.01 wt %, 1 organic ion per 500–1000 PMAA monomer residues). The absence of dependence of PMAA ability to bond organic ions on polymer concentration in this range of concentrations indicates that the investigations were carried out on a monomacromolecular level.

It was found that un-ionized PMAA with different stereochemical structures exhibit different abilities of bonding of AO, Au, and ANS ions (Figures 1 and 2). The data in Figures 1 and 2 show that the ability of PMAA which are obtained both in aqueous and in organic media to bind organic ions correlates with the S-triad content, greatly increasing with polymer syndiotacticity. Thus, when the S-triad content in PMAA increases from 45 to 78%, other conditions being equal, the degree of AO bonding increases from 5 to 60%, and the luminescence intensity of Au ions increases 15-fold. The tacticity of PMAA influences not only the efficiency of their interactions with organic cations but also that with anions (ANS). Thus, the intensity of luminescence of ANS in aqueous PMAA solutions, which increases with the degree of their bonding by polymer chains, increases by a factor of 1.6 when the S-triad content in PMAA increases from 58 to 72% (at pH = 2.9 in 0.5 M NaCl).

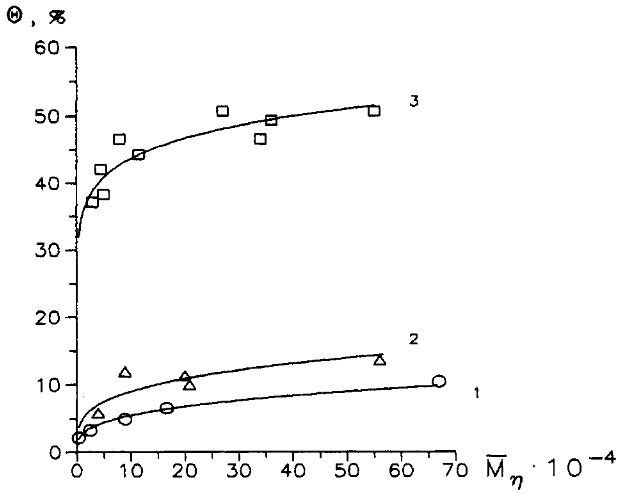


Figure 3. Fraction θ of AO ions bonded in an aqueous solution by un-ionized PMAA vs the molecular weight of the polymers. Content of S-triads in PMAA: 48% (curve 1), 54% (curve 2), and 68% (curve 3). PMAA content of 0.06 mg/mL, 1 AO ion per 500 PMAA units, pH = 4, ionic strength 0.05.

To understand the observed effect, it is important to establish the extent to which the influence of the stereochemical structure of PMAA on its interaction with organic ions is due to configurational and conformational factors. If the main contribution to the interaction between the PMAA molecule and the ion is provided by the sequence of neighboring units along the chain contour, then this interaction should not depend on the polymer chain length. When the contribution of long-range effects depending on conformation and increasing the local density of nonpolar groups is considerable, the molecular weight of the polymer can profoundly affect this interaction. In order to investigate the effect of molecular weight of PMAA on its interaction with organic ions, the interaction of AO ions with molecules of fractions of PMAA samples with different contents of S-triads was studied (at pH = 4). These fractions were of different molecular weights (Figure 3), but, according to ^{1}H NMR data, their stereochemical composition was virtually identical.

The analysis of data in Figure 3 shows that PMAA fractions of the same M but with different stereoregularities (content of S-triads: 45, 54, and 68%) bind AO with different efficiency. Thus, for PMAA with M = 100 000, the fraction of bound AO under the investigated conditions was 5, 10, and 45%, respectively. On the other hand, with increasing M from 30 000 to 500 000 and 600 000 for PMAA fractions of the same tacticity, the values of θ increased only 1.2–2 times.

The above data were obtained with the PMAA molecules in the compact state. When DMF (10%) is added to the aqueous solution of PMAA–AO and the compact PMAA structure is destroyed, the AO ions previously bonded to un-ionized PMAA pass into solution.

These data suggest that the greatest correspondence between the steric arrangement of functional groups (structural fragments) participating in the interaction between the PMAA residues and organic ions exists when the PMAA chains are enriched with syndiotactic sequences and the macromolecules are in the compact state. Consequently, the observed phenomenon is due to a combination of the configurational and conformational effects.[17]

The correlation between the ability of PMAA to bind organic ions and its syndiotacticity makes it possible to characterize the syndiotacticity of PMAA by luminescence methods.

The determination of the PMAA syndiotacticity using luminescent organic ions is not absolute and requires previous calibration by using PMAA samples of different stereoregularities. For example, by using Au it is possible to apply as a calibration curve the dependence of relative luminescence intensity $I_{\text{lum}}^{\text{rel}}$ of Au in solutions of PMAA obtained by MAA polymerization in aqueous media (Table I) on the content of S-triads (Figure 2).

The possibilities of using this luminescence method for the determination of PMAA syndiotacticity may be demonstrated, taking as an example the analysis of samples obtained by MAA polymerization in organic solvents with different chemical structures. Table II lists the stereochemical composition of PMAA obtained in this way. Table II also lists the content of S-triads, determined by the luminescence method (measurement of $I_{\text{lum}}^{\text{rel}}$ for an Au solution in the presence of a PMAA under the same conditions as in the determination of calibration data in Figure 2 and the estimation of the fraction of S-triads from the calibration curve). The comparison of these data shows that the mean difference between the results obtained by determination of the S-triad content in PMAA with the aid of luminescence and traditional methods is only 1–2%. The absolute error in the determination of the PMAA stereochemical composition by the ^{1}H NMR method is $\simeq 2\%$. The value of $I_{\text{lum}}^{\text{rel}}$ is determined within ±0.1. Hence, it may be assumed that the precision of this nethod depends mainly on that of the data used for plotting the calibration curves. The error in the determination of the degree of PMAA syndiotacticity by luminescence can slightly increase if the values of M for PMAA used for plotting the calibration data and those for investigated PMAA differe greatly.

Although the luminescence method is not absolute, it exhibits several advantages. Unlike the application of ^{1}H NMR,[11] IR spectroscopy,[18] and X-ray analysis,[19] it does not require PMAA methylation. Therefore, the analysis time decreases from 2–3 days to 15–20 min. Moreover, the X-ray method is applicable only to polymers with a high content of either syndio- or isotriads of monomer units.

The method of direct analysis of PMAA stereoregularity (without its transformation into PMMA) based on ^{13}C NMR[20] involves the use of deuterated solvents and a long period of instrument time because the low natural content of ^{13}C.

The luminescence method is very sensitive: when the content of the S-triads of PMAA units increases from 45 to 78%, the measured value of $I_{\text{lum}}^{\text{rel}}$ increases 15-fold.

Consequently, the luminescence method is more suitable than other methods for rapid analyses of stereoregularity of the PMAA samples.

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References and Notes

(1) Ariens, E. *J. Biochem. Pharmacol.* **1988**, *37*, 9.
(2) Pavlinov, S. A.; Piotrovsky, V. K.; Metelitsa, V. I. *Khim.—Pharm. Zh.* **1989**, *23*, 517.
(3) Challa, G.; Tan, Y. Y. *Pure Appl. Chem.* **1981**, *53*, 627.
(4) Litmanovich, A. A.; Papisov, I. M.; Kabanov, V. A. *Eur. Polym. J.* **1981**, *17*, 981.
(5) Nekrasova, T. N.; Anufrieva, E. V.; Krakovyak, M. G.; Lushchik, V. B.; Korshun, A. M. *Vysokomol. Soedin., A.* **1983**, *25*, 133.
(6) (a) Anufrieva, E. V.; Birshtein, T. M.; Nekrasova, T. N.; Ptitsyn, O. B.; Sheveleva, T. V. *J. Polym. Sci., Part C* **1968**, *N16*, 3519. (b) Wang, Y.; Morawetz, H. *Macromolecules* **1986**, *19*, 1925 and references therein.
(7) Horsky, J.; Morawetz, H. *Makromol. Chem.* **1988**, *189*, 2475 and references therein.
(8) Anufrieva, E. V.; Krakovyak, M. G.; Gromova, R. A.; Lushchik, V. B.; Ananieva, T. D.; Sheveleva, T. V. *Dokl. Akad. Nauk SSSR* **1991**, *319*, 895.
(9) Bovey, F. A. *J. Polym. Sci. Part A* **1963**, *N1*, 843.
(10) Katchalsky, A.; Eisenberg, H. *J. Polym. Sci.* **1951**, *N6*, 145.
(11) Bovey, F. A.; Tiers, G. V. D. *J. Polym. Sci.* **1960**, *N44*, 173.
(12) Muller, C.; Fenyo, J. C. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 77.
(13) Lando, I. B.; Semen, I.; Farmer, B. *Macromolecules* **1970**, *3*, 524.
(14) Kabanov, V. A.; Topchiev, D. A. *Polymerization of Ionogenic Monomers*; Nauka: Moscow, 1975.
(15) Krakovyak, M. G.; Sycheva, E. A.; Sheveleva, T. V.; Denisov, V. M.; Anufrieva, E. V. *Vysokomol. Soedin., A* **1989**, *31*, 117.
(16) Semisotnov, G. V.; Rodionova, N. A.; Razgulyaev, O. I.; Uversky, V. N.; Gripas, A. F.; Gilmanshin, R. I. *Biopolymers* **1991**, *31*, 119.
(17) (a) Anufrieva, E. V.; Krakovyak, M. G. *Vysokomol. Soedin., A* **1987**, *29*, 211. (b) Anufrieva, E. V.; Krakovyak, M. G. In *Physical Optics and Dynamic Phenomena and Processes in Macromolecular Systems*; Sedlacek, B., Ed.; W. de Gruyter and Co.: Berlin, New York, 1985; p 251.
(18) Bauman, U.; Schreiber, H.; Tessmark, K. *Makromol. Chem.* **1959**, *36*, 81.
(19) Natta, G. *Makromol. Chem.*, **1960**, *35*, 94.
(20) Chapman, A. I.; Billingham, N. C. *Eur. Polym. J.* **1980**, *16*, 21.

Author Supplied Registry Nos. Dichloroethane, 107-06-2; chloroform, 67-66-3; octane 111-65-9; toluene, 108-88-3; ethyl acetate, 141-78-6; dioxane, 123-91-11; tetrahydrofuran, 109-99-9; ethanol, 64-17-5; dimethylacetamide, 127-19-5; water distilled, 7732-18-5.