

MEDICAL
POLYMERS

Copolymerization of Methacryloylguanidine Trifluoroacetate with Styrene in Acetone and Dimethylsulfoxide at High Conversions

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Abstract—Radical copolymerization of methacryloylguanidine trifluoroacetate with styrene has been studied in acetone and dimethylsulfoxide in a wide range of the monomer mixture compositions. For the first time, copolymers (with the yield up to 90%) have been obtained from monomer mixtures with a high total concentration of comonomers (up to 1.7 mol/L). The preliminary biological tests have shown sufficiently high biocide and fungicide activity of the synthesized copolymers.

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In recent years, guanidine-containing polymers have found a wide application for creating biocide and disinfection agents, flocculants, and composite materials with surface bactericidal and fungicidal activity [1–6]; of special importance are biocide preparations differing in the degree of hydrophobicity [3, 7].

The processes of polymerization of guanidine-containing monomers of the methacrylic series, as well as their copolymerization with diallyl and vinyl monomers, were studied previously. It was shown that the obtained polymers demonstrate biocide properties [1, 2, 7–10]. Among the monomers under consideration, methacryloylguanidine trifluoroacetate (MGTFA) occupies a special place. Owing to its solubility in different organic solvents, the synthesis of organosoluble polymers and copolymers of MGTFA with desired physicochemical properties as well as molecular mass, hydrophilic–hydrophobic, biocide, and some other characteristics can be easily performed [2, 11].

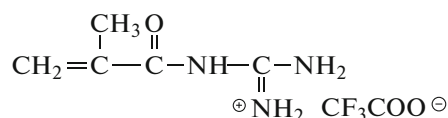
The study of the mechanism of copolymerization of water-soluble methacryloylguanidine trifluoroacetate with styrene insoluble in water will allow one not only to obtain copolymers characteristic of a selective biocide activity but also to facilitate the application of these copolymers as biocide additives to composite materials.

The aim of this work was to study the specific behavior of MGTFA in radical copolymerization with styrene in acetone and DMSO at high conversions as well as to search for ways to synthesize new guanidine-containing amphiphilic copolymers on the basis of MGTFA and to determine the physicochemical properties of these copolymers. This work continues the investigations carried out in the field of synthesis of guanidine-containing monomers and (co)polymers.

EXPERIMENTAL

Acetone, methanol, and DMSO used as solvents were purified via common procedures. Deuterated solvents acetone-d₆, methanol-d₄, DMSO-d₆, and guanidine hydrochloride were used without further purification. 2,2'-Azobisisobutyronitrile (AIBN) was purified by twofold recrystallization from methanol, followed by drying under vacuum. Trifluoroacetic acid was distilled over P₂O₅ at boiling temperature $T_b = 72^\circ\text{C}$; styrene (Merck) was distilled in an argon flow at 30 mmHg, with the monomer sampling in the temperature range of 52–54°C.

MGTFA was obtained by a procedure developed previously [8, 10, 12]. The structure and composition of the synthesized monomer was corroborated by the data of NMR spectroscopy and elemental analysis [10]:



Prepared reaction solutions of MGTFA and styrene in the corresponding solvent were placed in glass reactors or flasks, which were blown with argon and placed in a thermostat to perform polymerization; on attainment of the copolymerization temperature, an initiator was added.

Copolymers were separated via dialysis against distilled water using dialysis bags (Fisher Scientific 3500, USA) or by precipitation. Then the copolymers were dried in a vacuum drier over P₂O₅ at $T = 60^\circ\text{C}$ to constant weight.

Elemental analysis was carried out with the use of pyrolysis chromatography on a Flash 2000 CHNS

Table 1. Copolymerization of MGTFa (M_1) and styrene (M_2); $T = 60^\circ\text{C}$ (in acetone, $T = 58^\circ\text{C}$), AIBN concentration of 5×10^{-3} mol/L, copolymerization time of 20–22 h

| Experiment no. | Initial mixture | | Conversion, % | $M_1 : M_2$, mol % | $[\eta]$, dL/g | |
|----------------|---------------------|--------------------|---------------|---------------------|-----------------|-------|
| | $M_1 : M_2$, mol % | M_Σ , mol/L | | | Methanol | DMSO |
| 1 | 60 : 40 | 0.8 | 86 | 53 : 47 | 2.03 | 2.21 |
| 2 | 50 : 50 | 0.8 | 86 | 48 : 52 | 3.17 | 2.96 |
| 3 | 20 : 80 | 0.8 | 54 | 34 : 66 | 3.63 | 3.44 |
| 4 | 70 : 30 | 1.7 | 64 | 68 : 32 | 19.25 | 32.72 |
| | 70 : 30 | 1.7 | 21 | 69 : 31 | 2.24 | 5.23 |
| 5 | 60 : 40 | 0.8 | 61 | 51 : 49 | 2.01 | 4.50 |
| 6 | 50 : 50* | 0.8 | 68 | 45 : 55 | — | 2.48 |
| 7 | 20 : 80 | 0.8 | 48 | 30 : 70 | — | 3.61 |
| 8 | 20 : 80** | 0.8 | 11 | 36 : 64 | 5.10 | 7.58 |

In experiments 1–3 and 4–8, acetone and DMSO were used as solvents, respectively.

*AIBN = 10×10^{-3} mol/L.

**AIBN = 0.5×10^{-3} mol/L.

analyzer (Thermo Scientific, USA); helium was the carrier gas; samples were 1–4 mg; the burning was performed at 2000°C .

^1H NMR spectra were recorded on a Bruker MDS-300 spectrometer (300 MHz) in D_2O , acetone- d_6 , methanol- d_4 , and DMSO- d_6 at 25°C ; the chemical shifts were determined relative to the residual protons of solvent.

The intrinsic viscosity of polymers was measured on an Ubbelohde viscometer in a 0.25 N NaCl solution in water or in DMSO at 30°C or in methanol at 20°C .

The procedures of biocide tests are given in [10].

RESULTS AND DISCUSSION

Radical copolymerization of MGTFa (M_1) with styrene (M_2) was carried out in acetone and DMSO. The reaction mixture was blown with argon at 60°C (with acetone, $T = 58\text{--}59^\circ\text{C}$), whereupon the appropriate amount of initiator AIBN ($(0.5\text{--}10) \times 10^{-3}$ mol/L) was added. The ratio of MGTFa and styrene comonomers was varied in the range from 70 : 30 to 20 : 80 mol %; the total concentrations of comonomers were 0.8 and 1.7 mol/L. The copolymerization time comprised 20–22 h. The composition of the synthesized copolymers was determined by NMR spectroscopy (Table 1). As reference signals, bands of protons of groups which appeared in separate spectral regions and were not overlapped with the signals of protons of other groups were used. For copolymers with styrene, the integral of signals of the styrene phenyl group (five protons) in the region of 6.5–7.5 ppm was assumed as a basis (Fig. 1). The residual signals of comonomers were mutually overlapped and appeared in the spectral region of 0.3–3.0 ppm.

The reaction system retains the homogeneity in DMSO up to high conversions. On attainment of ~20% conversion in acetone, independently of the comonomer ratio gel-like, fractions of copolymers insoluble in acetone are formed (as was shown previously with the example of MGTFa polymerization and its copolymerization with methyl methacrylate [10]).

Based on the data obtained, the following regularities were revealed. At the identical concentration and ratio of comonomers, the yield of copolymers in acetone is higher as compared with that in DMSO.

The composition of copolymers is close to the composition of the initial reaction mixture, with a weak enrichment in styrene in all cases except the initial mixture 20 : 80 mol %, when the copolymer is enriched in MGTFa (Table 1, experiment 3). This regularity is obeyed both for acetone and for DMSO. The mentioned specific features can be explained by the difference in permittivity of the solvents, which is two times higher for DMSO than for acetone ($\epsilon = 49.0$ and 20.7, respectively) [13]. This is probably the reason for a reduced activity of MGTFa in copolymerization in the presence of DMSO. The above distinctions may also be due to the structure of the initial monomers. Although MGTFa is of methacrylate nature and styrene is a vinyl monomer, in both cases, the $\pi\text{--}\pi$ conjugation takes place [14]; i.e., the behavior upon copolymerization may be similar, but, as was shown by the data obtained, styrene is more active in copolymerization.

The formation of MGTFa copolymers was proven previously by the NMR and DSC methods [10] as well as by the data on solubility [8]. For additional corroboration of the copolymerization implementation, the intrinsic viscosity of copolymers was measured in a

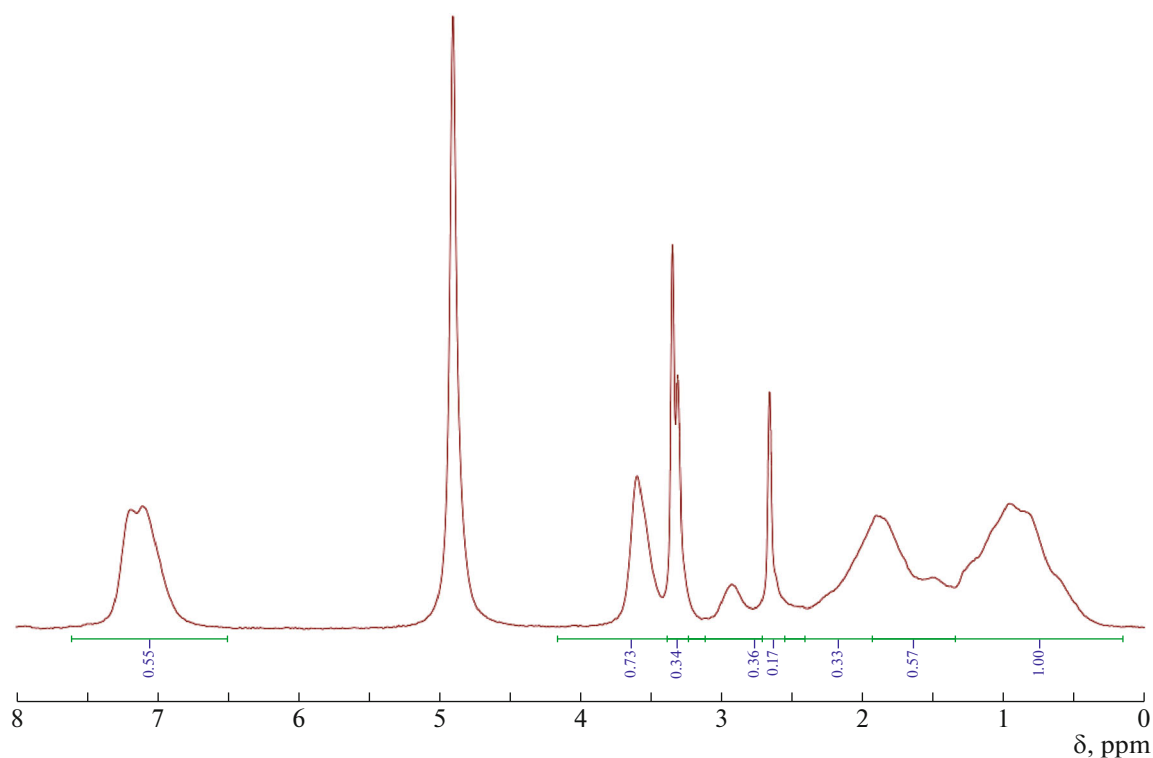


Fig. 1. (Color online) NMR spectrum of MGTFA–styrene copolymer in CD_3OD (3.31 ppm indicates residual signals of solvent).

NaCl aqueous solution, methanol, DMSO, and methyl ethyl ketone (MEK). The data allow one to make the following conclusions. The intrinsic viscosity of copolymers prepared in acetone is lower than the value for samples obtained in DMSO under the same conditions. A gain in the initial total concentration of comonomers leads to an increase in the intrinsic viscosity (see, for example, Table 1, experiments 4 and 6). The same result was obtained with a decrease in the initiator content. It should be noted that the yield of copolymers declines as intrinsic viscosity increases (Table 1, experiments 6–8).

The measurements of the viscosity of copolymer samples with a high content of styrene in MEK failed (Table 1, experiments 3, 7, and 8), although it is well known that the styrene homopolymers are soluble in ketones [15]. There is evidence that the above copolymers are of random type: the copolymers obtained in acetone demonstrate a higher intrinsic viscosity upon measurements in methanol rather than in DMSO. In this case, a decrease in the MGTFA content in copolymer results in a gain in the sample viscosity. For samples synthesized in DMSO, the intrinsic viscosity is higher upon measurements in DMSO than in methanol.

An interesting fact was revealed during the synthesis of copolymer at the initial comonomer ratio of 70 : 30 mol % (Table 1, experiment 4): on dialysis against water, copolymers with the identical comonomer

composition but with different solubilities were obtained. One of the above copolymers characteristic of a high viscosity (experiment 4, yield of 64%) was formed as a precipitate, which was filtered and dried. A copolymer with a lower viscosity (experiment 4, yield of 21%) contained in the aqueous contents of the bag proved to be a unique copolymer involving styrene, the intrinsic viscosity of which was measured in a low-molecular-mass electrolyte (0.25 N NaCl aqueous solution). The viscosity value was equal to 0.34 dL/g. Thus, for these samples, it is believed that the solubility of copolymers depends not only on the comonomer ratio in copolymer but also on their molecular mass.

Unfortunately, up to now, the search for a procedure of molecular mass determination by the GPC method has failed, which is related to the specific structural features of guanidine groups, which form high-strength bonds with a column-filling phase, and in this case, the copolymers remain bound in the column and do not elute in the course of analysis. From analysis of NMR spectra, it is impossible to determine the content of end groups which originate from the initiator, which would allow one to evaluate the number-average molecular mass.

The preliminary biological tests showed rather high bactericidal (*E. coli*, *S. aureus*) and fungicidal (*Candida albicans*) activity of the synthesized copolymers. It is comparable with the previously obtained data [10]

Table 2. Bactericidal and fungicidal properties of copolymers (minimum suppressed concentrations, wt %)

| Comonomer ratio, mol % | Test culture | | |
|----------------------------|----------------|------------------|--------------------|
| | <i>E. coli</i> | <i>S. aureus</i> | <i>C. albicans</i> |
| MGTFA : styrene = 53 : 47 | 1.7 | 0.9 | 0.8 |
| MGTFA : styrene = 68 : 32 | 1.8 | 0.9 | 0.9 |
| MGTFA : MMA = 60 : 40 [10] | 1.5 | 1.0 | 0.8 |

for MGTFA–MMA copolymers and probably is determined by the fact that the biocide effect is mainly due to the presence of MGTFA units in the chain (Table 2).

As a result of the investigations performed, samples of MGTFA–styrene copolymers differing in comonomer composition and molecular mass (viscosity) characteristics were obtained for the first time with a high yield (up to 90%). It was shown that the copolymerization of MGTFA with styrene is governed by the basic regularities of radical polymerization: a gain in the concentration of comonomers in the initial solution leads to an increase in conversion and intrinsic viscosity, and a significant decrease in the radical initiator concentration is accompanied by an abrupt drop in the copolymer yield (to 11%). It was found that, at high conversions, the copolymers with styrene are enriched in styrene both in acetone and in DMSO except when the MGTFA content in the initial reaction mixture is 20 mol %. As was shown, the bactericidal and fungicidal properties of MGTFA–styrene copolymers are comparable with the analogous characteristics for MGTFA–MMA copolymers.

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