



Original articles

Research article

<https://doi.org/10.17308/kcmf.2022.24/9060>

Polycondensation in a spray of aqueous-alcoholic solution of lactic acid

V. B. Fedoseev¹✉, E. N. Fedoseeva²

¹G. A. Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences,
49 Tropinina str., Nizhny Novgorod 603950, Russian Federation

²Lobachevsky State University of Nizhny Novgorod,
23 pr. Gagarina, Nizhny Novgorod 603950, Russian Federation

Abstract

The removal of low molecular weight products of the reaction and heat withdrawal is one of the problems of bulk polycondensation. Polycondensation under spray conditions is an effective way to solve these problems.

Based on the example of the reversible reaction of lactic acid polycondensation, it was shown that size effects can significantly affect the conversion rate, the degree of polymerization, and the rate of processes. Chemical thermodynamics suggests that chemical equilibrium in a spray shifts towards the formation of polylactide. In addition, the recondensation of volatile components (water, lactic acid, solvent) stabilizes the concentration of reagents and the temperature in the spray drops throughout the entire process. Model experiments confirming the obtained regularities are presented. Microscopic observation of sessile drops of aqueous and aqueous-alcoholic lactic acid solutions demonstrated the formation of polylactide under normal conditions (without heating, catalyst, evacuation).

The described regularities are of a thermodynamic nature and are relevant for polymerization and polycondensation processes involving volatile monomers and solvents.

Keywords: Polycondensation, Spray, Polylactide, Microencapsulation, Phase transitions

Funding: The work was carried out in accordance with the state assignment of the G. A. Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences.

For citation: Fedoseev V. B., Fedoseeva E. N. Polycondensation in a spray of aqueous-alcoholic solution of lactic acid. *Kondensirovannye sredy i mezhfaznye granitsy = Condensed Matter and Interphases*. 2022;24(1): 101–108. <https://doi.org/10.17308/kcmf.2022.24/9060>

Для цитирования: Федосеев В. Б., Федосеева Е. Н. Поликонденсация в условиях спрея водно-спиртового раствора молочной кислоты. *Конденсированные среды и межфазные границы*. 2022;24(1): 101–108. <https://doi.org/10.17308/kcmf.2022.24/9060>

✉ Victor B. Fedoseev, e-mail: vbfdoseev@yandex.ru

© Fedoseev V. B., Fedoseeva E. N., 2022



1. Introduction

The increased interest in spray technologies is due to the possibility of obtaining products and materials with unique properties. The ease of implementation and the efficiency of spray technologies allow using them in the production of polymeric materials [1, 2], pharmaceutical preparations [3], and in organic synthesis [4]. There are good prospects for spray technologies in which polymerization and other chemical processes occur inside or on the surface of aerosol particles [5]. This allows creating functional materials with a special morphology, for example, inorganic particles coated with a polymer shell [6, 7] or organic particles with an oxide shell [8], hollow spheres [9] and polymer microcapsules filled with components for various purposes [10].

Features and benefits of spray technologies are based on size effects, which contribute to the emergence of conditions and states not typical for macroscopic systems. Size effects are understood as the dependence of the properties and dynamics of processes on the size or volume of the system. In the spray, they become significant for submillimeter drops. In particular, size effects during phase transformations of the liquid–liquid type allow reagents to be involved in the processes for which their interactions with each other is complicated by low mutual solubility [11, 12]. Thermodynamic estimates show that a decrease in volume can lead to the complete mutual solubility of low-soluble components [13, 14].

The assessment of the use of the spray technology in organic synthesis was provided in [15], where the synthesis of polylactide (PLA) was one of the examples.

PLA has a wide range of applications as a biocompatible, biodegradable, and thermoplastic polymer. One of the methods for its production is direct synthesis using aqueous organic solutions of lactic acid [16, 17]. The main difficulties of the technology are associated with the removal of a low molecular weight polycondensation product (water), which, like the formation of a high molecular weight product, is accompanied by an increase in viscosity and a slowdown in the heat and mass transfer processes. The consequence is local overheating of the reaction mixture, tarring, and other undesirable chemical transformations.

In the spray, the problems associated with an increase in the viscosity of the reaction mixture

are effectively removed due to interfacial heat and mass transfer, and the removal of a low molecular weight product is facilitated by a large specific surface area and surface curvature.

The vapour pressure above the surface of spray drops is higher than in a macrosystem of the same composition, and the concentration of water in the reaction mixture equilibrium with the gaseous medium, decreases with a decrease in the radius of drops (Kelvin equation). This should shift the equilibrium in the polycondensation reaction towards polymer formation.

Size effects at chemical equilibrium can be associated with the difference in the chemical potentials of the components in the bulk and in the near-surface layer. In this case, the effective constant of chemical equilibrium and the rate of processes become a function of the specific surface area, surface activity, and molar volume of the components [15, 18].

In the spray, chemical and phase equilibrium are interconnected through the chemical potentials of the components in different phases. A large specific surface area and small diffusion paths allow to stabilize the temperature and concentrations of reagents due to mass and heat transfer during the recondensation of volatile components between drops [19, 20]. All low molecular weight components of the reaction (water and lactic acid) are present in the gas phase and participate in the recondensation during the polycondensation of lactic acid.

In the formation of insoluble products (polymer) or separation of the solution, size effects change the mutual solubility of the components and lower the upper critical temperature of separation [21, 22]. An increase in the solubility of lactic acid and its oligomers additionally shifts the equilibrium towards polymerization.

The aim of this study was theoretical substantiation of the statement about the advisability of using spray technology as the best alternative to existing methods for the synthesis of PLA. The task of the above model experiments was to experimentally confirm this statement.

2. Results and discussion

2.1. Thermodynamic model of polycondensation under spray conditions

The scheme of equilibrium transformations involving lactic acid, lactide, PLA, and their

thermodynamic properties are given in [23]. The equilibrium constant of the polycondensation reaction K at low degrees of polymerization and low conversion has the form:

$$K = \frac{x_p x_0^{p-1}}{x_1^p} = \frac{x_p}{x_0} \left(\frac{x_0}{x_1} \right)^p, \quad (1)$$

where p is the degree of polymerization, x_0 , x_1 , x_p are the concentration (mole fraction) of water, monomer, and polymer in the solution, respectively.

At high degrees of polymerization, the polymer passes into the solid phase. If no solid solutions are formed, then $x_p = 1$ and the equilibrium constant takes the form:

$$K_* = \left(\frac{x_0}{x_1} \right)^p x_0^{-1}. \quad (2)$$

The values of K and K_* differ by the correction for the transition energy of the polymer into solution. The reactions of the formation of lactide and PLA from lactic acid are characterized by small positive values of the Gibbs energy [23] and, accordingly, by equilibrium constants close to one.

Phase equilibrium and chemical equilibrium are related through the chemical potentials of the components. This relationship determines the state of drops (radius, composition) and the equilibrium concentrations of components in different phases [19, 20]. For ideal solutions, the condition of equality of chemical potentials in coexisting phases is converted to the equations of Kelvin and Freundlich and Raoult's law. For real solutions, the relationship between the solution concentration x_k , drop radius r , partial pressure in the vicinity of the drop $P_k(r, x_k)$ or external environment $P_{ex,k}$ has a more complex form:

$$P_k(r, x_k) = \gamma_k x_k P_{\infty,k} \exp\left(\frac{2\sigma V_k}{rRT}\right). \quad (3)$$

Here σ is the surface tension, V_k is the molar volume of the component k , R is the universal gas constant, T is temperature, $P_{\infty,k}$ is the vapour pressure above the flat surface of the pure component. Values of γ_k and σ in general depend on the composition of the solution. The equilibrium state of the drop corresponds to the condition $P_k(r, x_k) = P_{ex,k}$, where $P_{ex,k}$ is the partial pressure in the external environment. For low-soluble components, the

expression (3) is given in [19,24]. The temperature dependence of the vapour pressure of lactic acid is given in [23]. Its extrapolation to $T = 298$ K gives $P_{\infty,1} \sim 1.5$ Pa. Saturated vapour pressure of water at the same temperature $P_{\infty,0} = 3.2$ kPa.

According to (3) the equilibrium concentration of the volatile component is determined by the droplet radius, vapour pressure, and activity coefficient:

$$x_k = \frac{P_{ex,k}}{\gamma_k P_{\infty,k}} \exp\left(-\frac{2\sigma V_k}{rRT}\right). \quad (4)$$

If all components of the solution are volatile, the following identity is established:

$$\sum x_k = \sum \frac{P_{ex,k}}{\gamma_k P_{\infty,k}} \exp\left(-\frac{2\sigma V_k}{rRT}\right) = 1. \quad (5)$$

Ratios (3)–(5) determine the equilibrium size and composition of the drops corresponding to the composition of the gaseous medium. For volatile components, this identity limits the conditions for the appearance and existence of a spray by the inequality $\sum P_{ex,k}/P_{\infty,k} \gamma_k > 1$, otherwise the drops evaporate completely. The value $S = \sum P_{ex,k}/P_{\infty,k}$ can be interpreted as the relative supersaturation of vapour.

Identity (5) allows to state that the increase in relative supersaturation S leads to a decrease in the equilibrium drop radius. Positive deviation from the ideal behaviour $\gamma_i > 1$ contributes to an increase in the equilibrium drop radius. Negative deviation from the ideal behaviour $\gamma_i < 1$ lowers the equilibrium drop radius. Drops of solutions with a negative deviation from the ideal behaviour can exist at $S < 1$. These patterns are more complex for solutions containing non-volatile or partially soluble components [19, 20].

Equations (1)–(3) describe the relationship between equilibrium concentrations, degree of polymerization, gas phase composition, and spray drop radius:

$$K = x_p \frac{\gamma_0 P_{\infty,0}}{P_{ex,0}} k^p \exp\left(\frac{2\sigma(V_0 + p(V_1 - V_0))}{rRT}\right), \quad (6)$$

here the multiplier $k = \frac{\gamma_1 P_{ex,0} P_{\infty,1}}{\gamma_0 P_{ex,1} P_{\infty,0}}$ depends on the composition of the gas phase and, taking into

account $\gamma_k = \gamma_k(x_i)$, on the concentration of the solution.

The equation (6) describes the main laws of chemical equilibrium in the spray. For example, a decrease in the drop radius (an increase in the exponential) should be compensated by a corresponding decrease in the values of x_p , x_0 or p . The decrease in the value of k (at $r = \text{const}$) is compensated for by the increase in x_p or p shifting the equilibrium towards polycondensation. In other words, the chemical equilibrium in small drops is shifted towards polymer formation, while a decrease in the average radius of spray drops enhances this effect by increasing $P_{ex,1}$ in a spray cloud (3). The transfer of drops in the environment with lower humidity ($P_{ex,0}$) must be accompanied by both a decrease in the radius and an increase in x_p or p .

The decrease in the γ_1/γ_0 ratio leads to a shift of equilibrium towards the formation of a polymer in real solutions. This explains the effectiveness of methods based on the azeotropic distillation of water in the synthesis of PLA [16, 17]. For spray technology, mixtures with $\gamma_0 > 1$, characterized by the lower equilibrium concentration of water in drops are preferable. This further improves the efficiency of the process.

Let us estimate the effect of the solvent composition on the activity coefficients in water–lactic acid–co-solvent mixtures. Let's consider a solution of lactic acid with a concentration of 80 wt. % ($x_0/x_1 = 1.27$) diluted with two volumes of co-solvent. The values of the activity coefficients of water and monomer are equal in the presence of methyl isobutyl ketone – $\gamma_0 = 0.4$, $\gamma_1 = 1.9$ ($\gamma_1/\gamma_0 = 4.75$), ethanol – $\gamma_0 = 1.1$, $\gamma_1 = 0.8$ ($\gamma_1/\gamma_0 = 0.73$), propanol – $\gamma_0 = 1.2$, $\gamma_1 = 0.8$ ($\gamma_1/\gamma_0 = 0.67$), n-butanol – $\gamma_0 = 1.2$, $\gamma_1 = 1.1$ ($\gamma_1/\gamma_0 = 0.92$), 2-butanol – $\gamma_0 = 1.3$, $\gamma_1 = 1.0$ ($\gamma_1/\gamma_0 = 0.77$). The NRTL parameters for the systems water–lactic acid–methyl isobutyl ketone [25], water–propanol [26], water–ethanol [27], water–butanol-2 [28], water–lactic acid–n-butanol [29] were used in the estimates. The interaction parameters for water–lactic acid provided in the literature for different ternary mixtures can differ significantly [25, 28–30]. Missing parameters of the lactic acid–alcohol interaction were replaced by zeros. In addition to butanol, the authors of [29] describe the use of the NRTL model for aqueous

alcoholic solutions of lactic acid with n-pentanol, n-hexanol, and n-heptanol, which form a two-phase system upon such dilution.

From these estimates and equations (3), (4) it follows that in drops of aqueous-alcoholic solutions of lactic acid, the chemical equilibrium will be shifted towards the formation of a polymer. The greatest effect can be expected from solutions containing propanol and 2-butanol.

The use of co-solvents partly solves the problem of viscosity and overheating of the reaction medium [16]. For the azeotropic distillation of water from lactic acid solutions, organic substances of different classes can be used [17].

2.2. Experimental observations of polycondensation in sessile drops

Direct monitoring of the physical and chemical processes occurring in the spray is practically impossible. However, microscopic observations of the behaviour of sessile drops obtained by the deposition of a spray on a solid surface provide some notions. The conducted experiments qualitatively confirmed the possibility of obtaining PLA in a spray and also allowed to reveal some kinetic regularities.

The result of the evolution of drops of lactic acid solutions on a hydrophobized glass slide is shown in Fig. 1. The method described in [15] was used. The drops were in the air gap between the glass slides, which reduced the evaporation rate and eliminated convective currents.

In the general case, after the creation of the spray, rapid evaporation of the droplets occurred, then they were covered with a shell slowing down the evaporation. On the surface of large drops, the appearance, growth and movement of folds was noted. These changes indicated the formation of polymeric capsules in which the processes of polycondensation continued.

The surface shell can be a PLA layer or a saturated solution of oligomers [31].

To test this assumption, a layer of distilled water was applied on a glass slide with capsules formed from an aqueous solution of lactic acid (80 wt%). Drops that fell into the distilled water, without dissolving, were destroyed and detached from the slide, and moved around inside the water layer. The state of the system after water evaporation is shown in Fig. 1a. It shows particles wetted with a

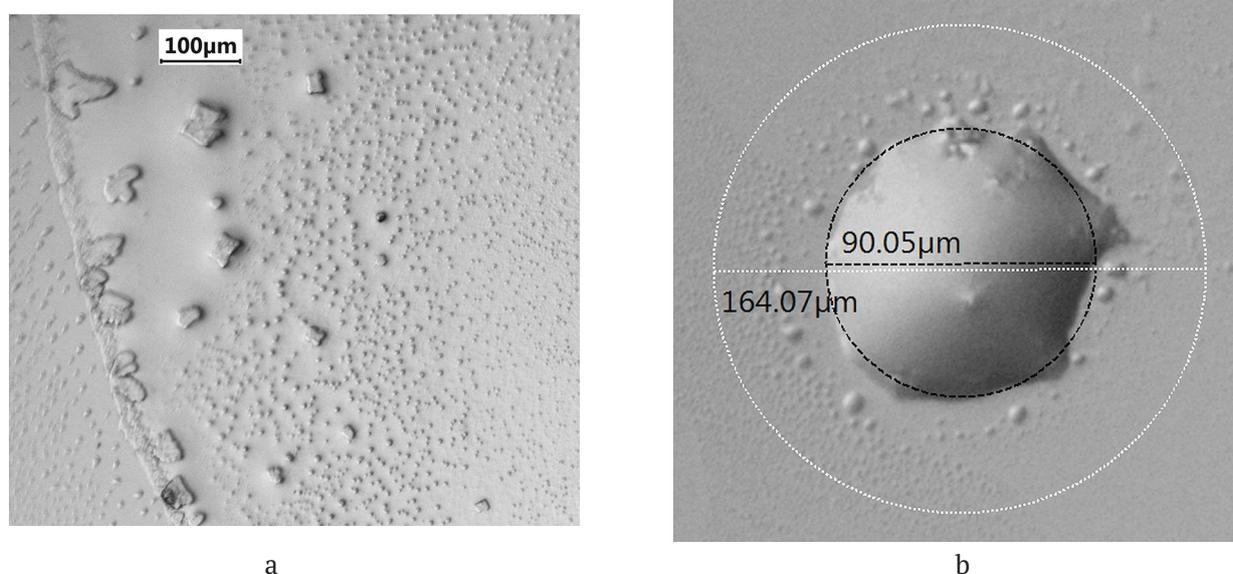


Fig. 1. Structures formed during the destruction of encapsulated drops with distilled water after the evaporation of water (a); the result of the evolution of a large drop of water-alcohol (isopropyl alcohol) lactic acid solution with an indication of the initial and final diameter of the drop (b)

thin layer of non-evaporating solution. The water-insoluble dispersed phase was probably formed by the shells of the destroyed capsules, and the solution surrounding the particles was probably formed by the soluble components (monomer and oligomers) released during the destruction of the capsules. The faceting of individual particles of the dispersed phase (Fig. 1a) shows that the capsule shell was formed either by crystalline PLA or low-soluble oligomers.

The final state of one of the drops of an aqueous-alcoholic solution of lactic acid, prepared by diluting an aqueous solution (80 wt%) with isopropyl alcohol in a ratio of 1 to 2 is shown in Fig. 1b. This state remained unchanged for several days. In the process of evaporation and

polycondensation, in the drop appeared inclusions, and many small non-evaporating drops were detected around it. The formation of a fraction of small drops was observed in experiments with both water-alcohol and aqueous solutions of lactic acid. They originate both in the vicinity of large drops and at a considerable distance from them. The causes and examples of the appearance of such satellite drops are described in [20, 32, 33].

The dynamics of the evaporation of drops of a water-alcohol solution of lactic acid at $t = 23-25\text{ }^\circ\text{C}$ and humidity $\sim 35\%$ is shown in Fig. 2. The radius of drops was determined based on a sequence of micrographs. The shape of the contact spot of most drops initially differed from round and changed during evaporation;

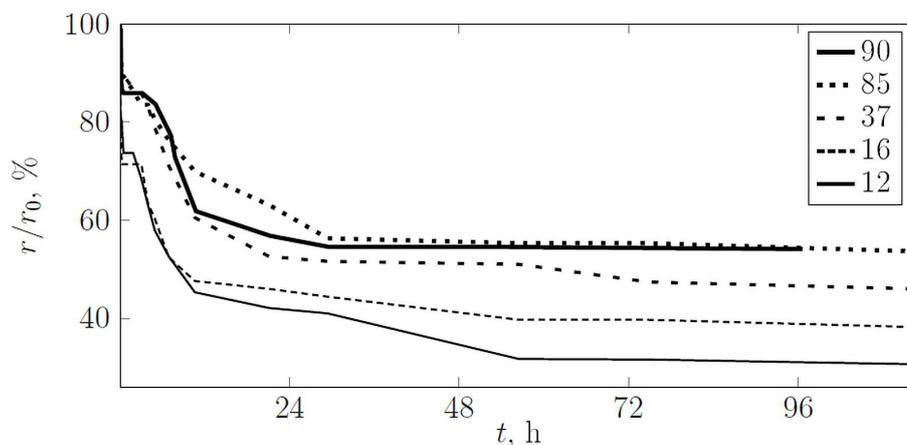


Fig. 2. Dynamics of changes in the relative radius of drops of an aqueous-alcoholic lactic acid solution

therefore, the radius was calculated as half the sum of the maximum and minimum diameters. Normalization of drop sizes by to the initial radius r_0 allows to compare the evaporation rates of drops of different sizes.

The plots shown in Fig. 2 reflect the non-monotonic nature of the process. The evaporation rate was determined based on the change in the drop radius $d(r / r_0) / dt$. The maximal evaporation rate was revealed in the first 5-10 min after the creation of the spray (~ 4%/min). Probably, at this stage, the excess of isopropyl alcohol evaporates, and the solution in drops approaches the azeotrope. After that, the drop sizes stabilized for some time, then decreased again, and the rate increased from zero to ~3%/h. In the last section of the plots, it again asymptotically decreased to 0.

Heterogeneities in the solution, indicating the onset of polycondensation, appeared in large drops 10–15 min after creating the spray. The subsequent decrease in the size of the drops was obviously associated with the processes of polycondensation and azeotropic distillation of the water released in the reaction. The asymptotic slowdown of the processes can be explained by the encapsulation of the drops, which complicated the removal of water, and the increase in conversion.

As can be clearly seen in Fig. 2, the described stages have different durations for large and small drops. In the first minutes, the radius of drops with a radius of 10–20 μm decreased 2 times faster than that of drops with a radius of 40–90 μm . The transition to the asymptotic stage occurred 4–5 h after the creation of the spray for small drops and 5–8 h after the creation of the spray for large drops.

The non-monotonic change of the rate can be explained by the action of at least two reasons:

1. The influence of conversion on the rate of polycondensation. From $x_0 = n_0 / (n_0 + n_{1,\Sigma} - pn_p + n_s)$, where n_0 , n_s , and $n_{1,\Sigma}$ are the number of moles of water, alcohol, and the total number of moles of monomer in a drop, we obtain $n_0 \sim (n_{1,\Sigma} - pn_p + n_s)$. Whence it follows that the increase in conversion (pn_p) and removal of the co-solvent (n_s) during azeotropic distillation leads to a decrease in the amount of water in the drop and, accordingly, to a decrease in its radius.

2. The separation of the solution as a result of the formation and increase in the concentration of low-soluble products (oligomers and polymer). The

core-shell configuration most often occurs in drops as the result of the separation of the solution. In water-organic mixtures, the shell is usually formed by an organic phase with a lower surface tension. A polymer or a concentrated solution of oligomers encapsulate an aqueous solution of low molecular weight components. Encapsulation occurs in experiments with a spray of both aqueous and water-alcohol solutions. The appearance of a new phase should be accompanied by a change in the chemical equilibrium constants (6) from K till K_* , shifting the equilibrium towards PLA formation.

The dependence of water concentration on radius (4) enhances these effects.

The second aspect is also of separate interest. Polymer capsules have many practical applications [34]. For medical applications, it is important that the PLA-coated capsules formed in the spray do not contain catalysts. Their core may contain concentrated aqueous solutions of pharmaceutical dosage forms and biologically active substances added to the spray solution. At the same time, co-solvents partially miscible with water stimulate the formation of capsules even before the polycondensation stage, which allows to control the properties of the shell, taking into account differences in the equilibrium composition of coexisting phases [35].

3. Conclusions

The above theoretical consideration describes the relationship between the equilibrium composition, the volume of condensed phases, the composition of the gaseous medium, and the drop sizes. The performed estimates allowed stating that during the polycondensation of lactic acid solutions in a spray, the chemical equilibrium shifts towards the formation of a polymer and a significant increase in the conversion and the rate of the process are possible.

Size effects increase the conversion and the rate of polycondensation. In particular, the equilibrium concentration of water in drops is lower than in the macrosystem (4), which leads to a shift in the chemical equilibrium towards polymer formation. The recondensation of solvents and reagents stabilizes the temperature of the droplets and the concentrations of the components in them, contributing to the isothermal course of the reaction without overheating of the reaction medium.

The described patterns are reproduced in model experiments with ensembles of sessile drops of aqueous and aqueous-alcoholic solutions of lactic acid. Experiments demonstrate that the polycondensation in a spray of lactic acid solution proceeds without the use of catalysts, heating, and vacuuming. Under the same conditions, the formation of oligomers and PLA do not occur in the macrosystem.

The results of the theoretical consideration and the experiment allowed stating that the spray technology is the basis for the development of an efficient resource-saving production of PLA, including PLA for medical applications.

These regularities are of a thermodynamic nature and should be exhibited in polycondensation processes involving volatile monomers and solvents. They are relevant in the development of new efficient technologies for the production of polymeric materials.

Author contributions

All authors made an equivalent contribution to the preparation of the publication.

Conflict of interests

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

References

1. Hergeth W., Jaeckle C., Krell M. Industrial process monitoring of polymerization and spray drying processes. *Polymer Reaction Engineering*. 2003;11(4): 663–714. <https://doi.org/10.1081/PRE-120026369>
2. Sinha-Ray S. Spray in polymer processing. Droplet and spray transport: Paradigms and applications. 2018: 31–54. https://doi.org/10.1007/978-981-10-7233-8_3
3. Wanning S., Süverkrüp R., Lamprecht A. Pharmaceutical spray freeze drying. *International Journal of Pharmaceutics*. 2015;488(1–2): 136–153. <https://doi.org/10.1016/j.ijpharm.2015.04.053>
4. Zhang Y., Suslick K. S. Synthesis of poly(3,4-ethylenedioxythiophene) microspheres by ultrasonic spray polymerization (USPo). *Chemistry of Materials*. American Chemical Society (ACS). 2015;27(22): 7559–7563. <https://doi.org/10.1021/acs.chemmater.5b03423>
5. Akgün E., Muntean A., Hubbuch J., Wörner M., Sangermano M. Cationic Aerosol photopolymerization. *Macromolecular Materials and Engineering*. 2015;300(2): 136–139. <https://doi.org/10.1002/mame.201400211>
6. Poostforooshan J., Rennecke S., Gensch M., Beuermann S., Brunotte G. P., Ziegmann G., Weber A.

P. Aerosol process for the *in situ* coating of nanoparticles with a polymer shell. *Aerosol Science and Technology*. 2014;48(10): 1111–1122. <https://doi.org/10.1080/02786826.2014.964354>

7. Sigmund S., Akgün E., Meyer J., Hubbuch J., Wörner M., Kasper G. Defined polymer shells on nanoparticles via a continuous aerosol-based process. *Journal of Nanoparticle Research*. 2014;16(8): 2533–2536. <https://doi.org/10.1007/s11051-014-2533-9>

8. Fei B., Lu H., Qi K., Shi H., Liu T., Li X., Xin J. H. Multi-functional microcapsules produced by aerosol reaction. *Journal of Aerosol Science*. 2008;39(12): 1089–1098. <https://doi.org/10.1016/j.jaerosci.2008.07.007>

9. Berdonosov S. S., Baronov C. B., Kuz'micheva Ju. V., Berdonosova D. G., Melihov I. V. Solid dispersed phases of multilayer and tubular inorganic microparticles. *Rossiiskij himicheskij zhurnal*. 2001;45(1): 35–42 (In Russ). Available at: <http://www.chem.msu.ru/rus/jvho/2001-1/35.pdf>

10. Chicheva P. A., Kurbangaleev V. R., Levchenko K. S., Shmelin P. S., Grebennikov E. P. Preparation of polystyrene microspheres filled with rhodamine G. *Rossiiskij himicheskij zhurnal*. 2020;64(4): 46–50 (In Russ., abstract in Eng.). <https://doi.org/10.6060/rcj.2020644.5>

11. Shishulin A. V., Fedoseev V. B. Thermal stability and phase composition of stratifying polymer solutions in small-volume droplets. *Journal of Engineering Physics and Thermophysics*. 2020;93(4): 802–809. <https://doi.org/10.1007/s10891-020-02182-9>

12. Fedoseev V. B. The size effect for liquid–liquid phase equilibrium in a ternary system. *Technical Physics Letters*. 2021;47(2): 135–138. <https://doi.org/10.1134/S1063785021020036>

13. Fedoseev V. B., Fedoseeva E. N. States of a supersaturated solution in limited-size systems. *JETP Letters*. 2013;97(7): 408–412. <https://doi.org/10.1134/S0021364013070059>

14. Fedoseev V. B., Fedoseeva E. N. Size effects during phase transformations in stratifying systems. *Russian Journal of Physical Chemistry A*. 2014;88(3): 436–441. <https://doi.org/10.1134/S0036024414020083>

15. Fedoseeva E. N., Fedoseev V. B. Possibilities and peculiarities of spray technologies in organic synthesis. *Kondensirovannye sredy i mezhfaznye granitsy = Condensed Matter and Interphases*. 2020;22(3): 397–405. <https://doi.org/10.17308/kcmf.2020.22/3001>

16. Poharukova Y. E., Novikov V. T., Glotova V. N. Polycondensation of lactic acid to oligomers in the solution. *Bulletin of the Kuzbass State Technical University*. 2017;(1): 134–139. (In Russ., abstract in Eng.). <https://www.elibrary.ru/item.asp?id=28897134>

17. Glotova V. N. Improvement of lactide synthesis and purification technology. Cand. tech. sci. diss. Thesis. Tomsk: TPU, 2016. 129 p. (In Russ). Available at: https://elar.urfu.ru/bitstream/10995/40461/1/urfu1572_d.pdf

18. Pavlyukevich N. V., Fisenko S. P., Khodyko Yu. A. Coalescence and diffusion growth of nanoparticles in

closed microvolume of supersaturated solution. *Colloid Journal*. 2010;72(6): 825–829. <https://doi.org/10.1134/S1061933X10060141>

19. Fedoseev V. B., Fedoseeva E. N. Formation of bi- and polymodal distributions and the non-ostwald behavior of disperse systems. *Journal of Engineering Physics and Thermophysics*. 2019;92(5): 1191–1200. <https://doi.org/10.1007/s10891-019-02033-2>

20. Fedoseev V. B., Fedoseeva E. N. Formation of monodisperse and narrow disperse ensembles of droplets of aqueous organic solutions in the vapor of volatile components. *Journal of Engineering Physics and Thermophysics*. 2020;93(5): 1116–1122. <https://doi.org/10.1007/s10891-020-02212-6>

21. Shishulin, A. V., Fedoseev V. B. Features of the influence of the initial composition of organic stratifying mixtures in micro-sized pores on the mutual solubility of components. *Technical Physics Letters*. 2020;46(9): 938–941. <http://dx.doi.org/10.1134/S1063785020090291>

22. Shishulin A. V., Fedoseev V. B. On some peculiarities of stratification of liquid solutions within pores of fractal shape. *Journal of Molecular Liquids*. 2019;278: 363–367. <https://doi.org/10.1016/j.molliq.2019.01.050>

23. Emel'yanenko V. N., Verevkin S. P., Schick C., Stepurko E. N., Roganov G. N., Georgieva M. K. The thermodynamic properties of s-lactic acid. *Russian Journal of Physical Chemistry A*. 2010;84(9): 1491–1497. <https://doi.org/10.1134/S0036024410090074>

24. Kuni F. M., Shchekin A. K., Grinin A. P. Theory of heterogeneous nucleation for vapor undergoing a gradual metastable state formation. *Physics-Uspokhi*. 2001;44(4): 331–370. <http://dx.doi.org/10.1070/PU2001v044n04ABEH000783>

25. Laiadi D., Housseine A., Merzougui A. Homotopy method to predict liquid-liquid equilibria for ternary mixtures of (water+carboxylic acid+organic solvent). *Fluid Phase Equilibria*. 2012;313(January): 114–120. <https://doi.org/10.1016/j.fluid.2011.09.034>

26. Toikka M., Samarov A., Toikka A. Solubility, liquid-liquid equilibrium and critical states for the system acetic acid+n-propanol+n-propyl acetate+water at 293.15K and 303.15K. *Fluid Phase Equilibria*. 2014;375: 66–72. <https://doi.org/10.1016/j.fluid.2014.04.034>

27. Toikka M., Samarov A., Trofimova M., Golikova A., Tsvetov N., Toikka A. Solubility, liquid-liquid equilibrium and critical states for the quaternary system acetic acid-ethanol-ethyl acetate-water at 303.15K and 313.15K. *Fluid Phase Equilibria*. 2014;373: 72–79. <https://doi.org/10.1016/j.fluid.2014.04.013>

28. Ghanadzadeh Gilani H., Golpour M., Abbasi Souraki B. Ternary equilibrium data of mixtures consisting of 2-butanol, water, and heavy alcohols at $T = 298.2$ K. *The Journal of Chemical Thermodynamics*. 2012;49: 39–45. <https://doi.org/10.1016/j.jct.2012.01.003>

29. Domingues L., Cussolin P. A., da Silva J. L., de Oliveira L. H., Aznar M. Liquid-liquid equilibrium data for ternary systems of water+lactic acid+C4-C7 alcohols at 298.2K and atmospheric pressure. *Fluid Phase Equilibria*. 2013;354: 12–18. <https://doi.org/10.1016/j.fluid.2013.06.007>

30. Faraji S., Mokhtarpour M., Behboudi E., Sadrmousavi A., Shekaari H., Zafarani-Moattar M. T. Vapor-liquid equilibria and computational study for aqueous solutions of novel deep eutectic solvents (amino acid/lactic acid) at 298. *Journal of Chemical and Engineering Data*. 2020;65(7): 3262–3269. <https://doi.org/10.1021/acs.jced.9b01169>

31. Izhenbina T. N. The solubility of the lactic acid oligomer. *Eurasian Union of Scientists*. 2014;7: 71–72. (In Russ). Available at: <https://www.elibrary.ru/item.asp?id=27642469>

32. Littringer E. M., Paus R., Mescher A., Schroettner H., Walzel P., Urbanetz N. A. The morphology of spray dried mannitol particles — The vital importance of droplet size. *Powder Technology*. 2013;239: 162–174. <https://doi.org/10.1016/j.powtec.2013.01.065>

33. Burlakov V., Goriely A. Thermodynamic limit for particle monodispersity: How narrow can a particle size distribution be? *EPL (Europhysics Letters)*. 2017;119(5): 50001–6. <https://doi.org/10.1209/0295-5075/119/50001>

34. Wu C., Ying A., Ren S. Fabrication of polymeric micelles with core-shell-corona structure for applications in controlled drug release. *Colloid and Polymer Science*. 2013;291(4): 827–834. DOI: <https://doi.org/10.1007/s00396-012-2794-8>

35. Toikka A. M., Samarov A. A., Toikka M. A. Phase and chemical equilibria in multicomponent fluid systems with a chemical reaction. *Russian Chemical Reviews*. 2015;84(4): 378–392. <http://dx.doi.org/10.1070/RCR4515>

Information about the authors

Victor V. Fedoseev, DSc in Chemistry, Leading Researcher, G. A. Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences (Nizhny Novgorod, Russian Federation).

<https://orcid.org/0000-0001-9281-3137>

vbfedoseev@yandex.ru

Elena N. Fedoseeva, PhD in Chemistry, Research Fellow, the Laboratory of Applied Chemistry and Ecology, Lobachevsky State University of Nizhny Novgorod (Nizhny Novgorod, Russian Federation).

<https://orcid.org/0000-0002-5066-2331>

el.nik.fedoseeva@gmail.com

Received September 11, 2021; approved after reviewing October 20, 2021; accepted February 15, 2022; published online March 25, 2022.

Translated by Valentina Mittova

Edited and proofread by Simon Cox