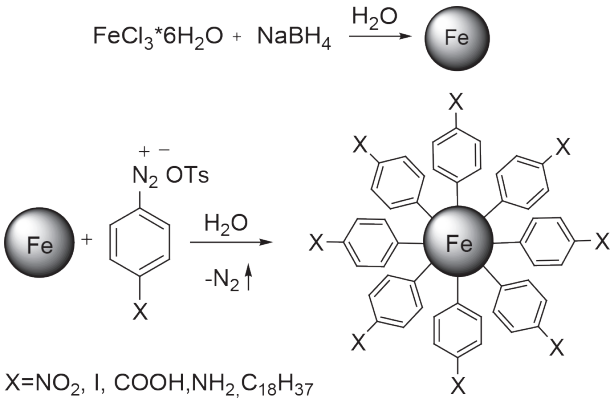
SYNTHESIS OF MULTIFUNCTIONAL MODIFIED PARTICLES OF ZEROVALENT IRON USING DIAZONIUM SALTS

V.V. Kurtukov, A.S. Shvyrkova, S.S. Vlasov
Scientific advisor – Ass. Prof., PhD P.S. Postnikov
Linguist – Ass. Prof., PhD I.A. Matveenko

National Research Tomsk Polytechnic University
634050, Russia, Tomsk, 30 Lenin Ave., kurtukov@tpu.ru

Surface modification with diazonium salts has received a lot of attention in the last years because of its simplicity, reliability and a wide variety of applications of this method [1]. It can be used in a considerable number of fields, including but not limited to drug delivery, catalysis, biosensors, theranostics, magnetic resonance imaging (MRI), material enhancement and many more [2]. The research group of P.S. Postnikov has worked out a method for acquisition of stable zerovalent iron (ZVI) particles covered with various aromatic functional groups using aromatic diazonium salts (ADS) [3]. The method is described in Scheme 1.

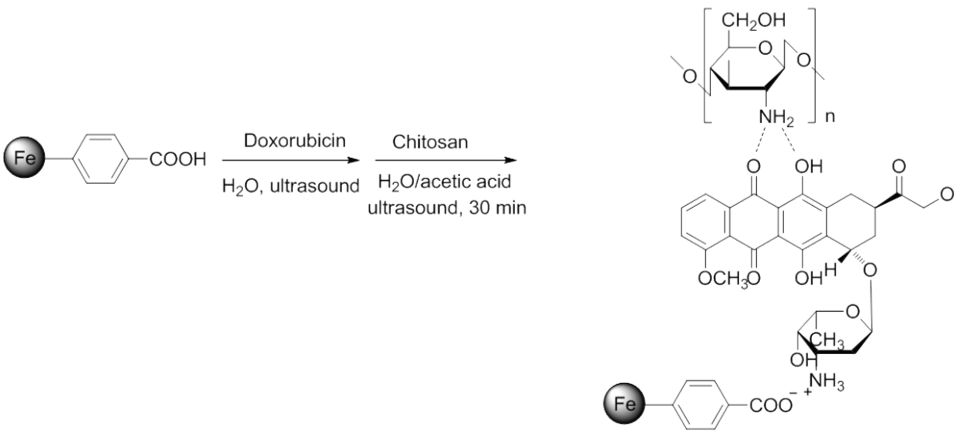


Scheme 1. *Synthesis of ZVI NPs using p-aminobenzenediazonium tosylate*

Incorporating this method, our group managed to start working in several different directions. First, after noticing that gadolinium has excellent magnetic properties, as well as the ability to form chelates, it was decided to acquire Gd-based MRI theranostic agent. The product of this research is now passing the stage of preclinical trials. Second, an attempt to attach manganese to the particles was made, but it didn't lead to any results deserving consideration. One of the latest focus areas for the group has become a development of a pharmaceutical composition with complex effect on malignant tissue for the treatment of liver cancer based on zerovalent iron microparticles. The method for their acquisition is described in Scheme 2.

The anticancer activity of the compound is based on three components: ischaemia, hyperthermia and chemotherapy. Upon entering the malignant tumor, the agent clogs blood capillars because of the particle size. Then, an alternating magnetic field is applied to the particles, causing local hyperthermia. Both those effects are confirmed to be especially harmful for cancer tissue. Following the hyperthermia, chitosan shell of the particles dissipates, letting doxorubicin (widely known chemotherapy drug) enter the tissue and start the local chemotherapy [4].

At the moment, the agent is passing clinical trials and is getting prepared for the in vivo experiments.



Scheme 2. *Synthesis of anticancer composition*

References

1. *O.A. Guselnikova, A.I. Galanov, A.K. Gutakovski, P.S. Postnikov // Beilstein J. Nanotechnol, 2015.– 6.– 1192–1198.*
2. *Ya.N. Ertas, N.N. Jarenwattananon, and L.-S. Bouchard // Chem.Mater., 2015.– 27.– 5371−5376.*
3. *Guselnikova O.A., Gromov M.V., Galanov A.I. // Advanced Materials Research.– Trans Tech Publications, 2014.– Vol.1040.– P.309–313.*
4. *K. Hayashi et al., ACS Biomater. Sci. Eng., 2017.– 3(1).– P.95–105.*

SYNTHESIS OF LACTIC ESTERS

Y.B. Lugovskaya, Y.E. Poharukova

Scientific supervisor – PhD, Associate Professor V.T. Novikov

National Research Tomsk Polytechnic University

634050, Russia, Tomsk, Lenin Avenue 30, julka250393@mail.ru

Nowadays production of lactic esters is one of the challenges in the modern organic chemistry. The esters form a part of essential oils composition specifying their pleasant smell [1], they are used in food and perfumery industry [2]. The esters include a lot of biologically important substances and medications [3]. The most promising esters application results their usage as plasticizers for medical materials production based on polylactide.

Lactic esters are synthesized via the following methods:

1. Esterification of lactic acid with alcohol in the presence of acidic catalyst. Para-toluene sulfonic acid, boric, phosphoric, sulphuric and other acids are used as a catalyst to increase a reaction rate of esterification without affecting an equilibrium state.

To change the equilibrium state and to enhance the yield of esters the following methods are used:

- The use of one of the starting materials in excess. Usually, the concentration of more accessible reagent – an alcohol is increased.
- The ether or water removal forming in situ. For a low-boiling ester synthesis the ester is driven off in situ. For a high-boiling ester synthesis it is preferable to drive off a water in situ. The water is driven off in the form of azeotropic mixture with the vapor of the corresponding alcohol.

It is undesirable to use the 98% of lactic acid as the initial product because its presence in the concentration process leads to a partial lactonization [4].

2. Alcoholysis of polylactic acid. It is very similar to the hydrolysis reaction, only with the alcohol as a substitute for the water. Since the reaction is catalytic, sodium alkoxide, sodium hydroxide and potassium carbonate are used as catalysts.

The first problem of using this method is a relatively low yield of a target product. Moreover, an additional catalyst purification stage is required to eliminate a residue.

3. Esters synthesis from alpha-halogen derivatives of lactic acid. This method is unprofitable, as it requires a high operation costs and complex equipment [5].

As it was presented above, the lactic ester synthetic roots have a number of limitations. In view of this, an improve of existing methods or a search of new techniques is of particular relevance nowadays. This article presents the advanced isopropyl and butyl lactic esters synthetic procedure.

The process is based on esterification reaction of lactic acid with the corresponding alcohol in the presence of acid catalyst.

A solution of 80% L-lactic acid (M.C.D Import&ExportGmbh., Germany) [6, 7], isopropyl or butyl alcohol were chosen as raw materials. Benzene or butyl acetate performed a role of solvent, whereas sulfuric acid acted as a catalyst.

The simple distillation unit was used for ester synthesis during 10–16 hours with the stage of triple mixture removal (the solvent – corresponding alcohol – water) and binary mixture (alcohol – solvent). Calcium carbonate or sodium bicarbonate were additionally introduced into the mixture to remove the excess of alcohol and solvent. The flask content was filtered, the obtained filtrate was distilled.

The isopropyl ester of lactic acid was distilled in the temperature range of 75–80 °C, resulting in 25–30% of product yield. As for the butyl ester,