Chemists develop a promising drug synthesis method

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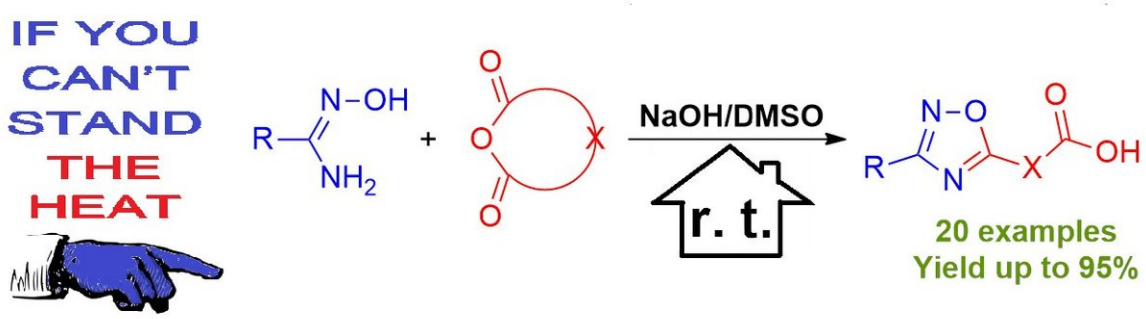

Graphic abstract to the article. Allusion to the saying of Truman. Credit: Anton Sehtnev

Scientists from RUDN University with their colleagues from Yaroslavl have developed a new way to synthesize 1,2,4-oxadiazole derivatives used in many drugs. 1,2,4-oxadiazoles include ataluren, the active ingredient of a drug used in a treatment for genetic disorders. The results of the work are published in *Tetrahedron Letters*.

"Many candidate medications are not developed further and the reasons are often high costs and technological complexity of their production. Moreover, any rise in cost of a chemical process in drug production ultimately affects the consumer. Our latest development simplifies and reduces the cost of one of the stages in active ingredients production,"

says Anton Shetnev, one of the authors of the study from the Research Institute of Chemistry of RUDN.

Many organic compounds are thermosensitive, and classical 1,2,4-oxadiazole production methods that involve heating often lead to resinification of the reaction mass and undesirable side processes. With the new method 1,2,4-oxadiazoles with carboxylic acid, a functional group that enables further modification of the compound, can be produced rapidly, with high yield and without expensive reagents.

The usual method of production of 1,2,4-oxadiazoles is carried out in two stages. Intermediate products of the reaction in the first stage are subsequently converted into the desired 1,2,4-oxadiazoles under relatively high temperature (about 100-140 °C).

The authors of the study offered a method of 1,2,4-oxadiazole production in a single step at room temperature. Chemists came up with a soft and workable synthetic procedure for 1,2,4-oxadiazoles in the amount of several grams. The reaction of the precursors (amidoximes and dicarboxylic acid anhydrides) was carried out in the presence of sodium hydroxide (NaOH) with dimethylsulfoxide as a solvent. The new method is based on superbase catalysis principles. Sodium hydroxide turns into a superbase under the reaction conditions, becoming much stronger than the usual alkali (NaOH dissolved in water). Due to the addition of a superbase, the process of 1,2,4-oxadiazole production can be carried out even at room temperature and without toxic and expensive reagents.

"We have published a series of articles devoted to the application of this methodology, and we are planning to continue the research. All these data are available online, and some scientific groups have already used our work in their studies. If an oxadiazole derivative-based drug appears in the future, I believe that our method will be able to make its

production very effective," the scientist concludes.

More information: Marina Tarasenko et al, Room-temperature synthesis of pharmaceutically important carboxylic acids bearing the 1,2,4-oxadiazole moiety, *Tetrahedron Letters* (2017). DOI: 10.1016/j.tetlet.2017.08.020

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