

# MEDICINAL CHEMISTRY RESEARCH

An International Journal for  
Communications on Design  
and Mechanisms of Action  
of Biologically Active Agents

Indexed/Abstracted: Current Contents, SciSearch,  
Research Alert, Chemistry Citation Index,  
Biochemistry & Biophysics Citation Index.

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Volume 12, Numbers 4 and 5, 2003  
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Special Issue: Current Trends in Drug Discovery  
Research Symposium

February 17–20, 2004, Lucknow, India

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# TWO ALTERNATIVE GENERAL SYNTHETIC APPROACHES FOR PREPARATION OF BIOLOGICAL ACTIVE BENZO- AND AZOLOPYRIDAZINE'S DERIVATIVES

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Condensed pyridazines are very attractive systems in searching of compounds with high and various biological activities. One of the approaches to the synthesis of condensed heterocyclic systems based on the Richter reaction - thermal cyclization of vicinal alkynylphenyldiazonium chlorides.

Only a few papers were devoted to this reaction, which is known as method of synthesis of 4-hydroxycinnolines. We carried out comparative investigation of behavior of the Richter reaction in series of benzene and azoles. We have found some peculiarities of behaviour of vicinal alkynylazolediazonium halogenides in thermal cyclization in comparison with their benzene analogies.

Understanding of new synthetic and mechanistic aspects of the Richter reaction allowed us to prepare series of fused pyridazines with all possible variants of the arrangements of benzene's and azole's ring with diazine's one. Unexpected result we found by the cyclization of 3-alkynylpyrazolyl-4-diazonium halogenides. The formation of pyridazine ring was accompanied by migration the N- methyl group towards the neighbouring nitrogen atom of the pyrazole cycle.

Thus, in the present work we showed that the Richter reaction in the series of pyrazole is general route to the chloro-, bromo- and hydroxyderivatives of pyrazolo/3,4-c/- and -/4,3-c/pyridazines.

We found unexpected [1,2]-methyl shift in the Richter cyclization of the pyrazole diazonium salts.

Also we carried out comparative investigation unknown type of heterocyclization, namely, isomerization of acetylenic derivatives of hydrazides of vic.-functionally substituted acetylenylaryl- and -hetaryl carboxylic acids.

The study of the hydrazides of vicinal phenyl- and azolyethynyl derivatives showed that nucleophilic intramolecular addition of function to triple bond in arene and heteroarene series occurred by different way. Phenyl derivatives are cyclized under the effect of basis into corresponding 5-membered *N*-aminolactams in yields of 60-90%, which then were recycled into benzodiazinones by boiling in presence of CuCl.

Both benzene- and azole derivatives (pyrroles, indoles and pyrazoles) are underwent to isomerization to corresponding diazinones (60-85%) under action of different transition metals catalysts, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, NiBr<sub>2</sub>·3H<sub>2</sub>O, CuC≡CPh and CuCl in boiling DMF or Pyridine.

Thus, we found that in the benzene and the azole series the direction of heterocyclization strongly depends on the mutual arrangement of acetylenic and another functional groups.

In conclusion, we have formulated some rules of a direction of an addition of the functions to triple bond depending on structure of substrates, electronic and steric parameters and the reaction conditions.

Critical review of biological activity of condensed diazines will be presented

This work was supported by RFBR grant 02-03-32229, grant CRDF No 008-XI.