

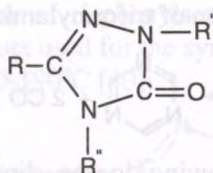
Synthesis of 1,2,4-triazolin-5-one derivatives

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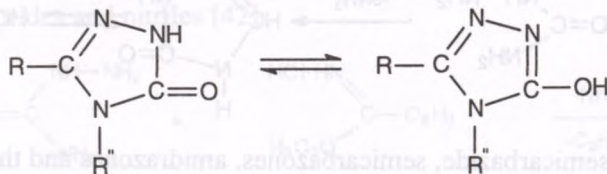
This paper is a review of the methods used for preparation of 1,2,4-triazolin-5-one derivatives. The initial products were semicarbazide and semicarbazone derivatives, amidrazones and their salts, aminoguanidine salts.

1,2,4-triazolin-5-one derivatives have the general formula:



were: R, R', R'' can be hydrogen, alkyl, aryl, amine group.

In the case when R' = H or R'' = H, in this type of compounds tautomerism is likely to occur as can be seen in the formulae:

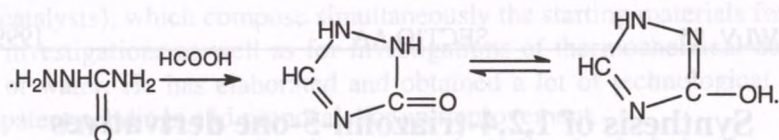


As reported in the literature these compounds are applied as herbicides [1-26] or fungicides [27-33].

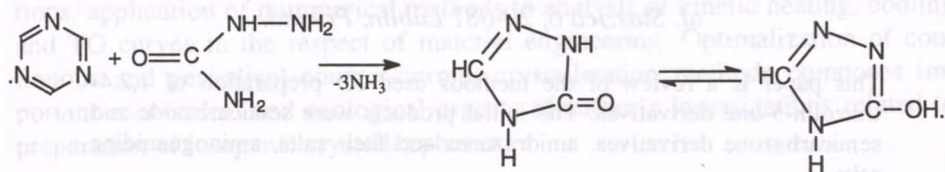
This paper is a review of the methods used for preparation of 1,2,4-triazolin-5-one derivatives.

1,2,4-Triazolin-5-one was obtained using semicarbazide as an initial product. One of the methods consists in cyclization of semicarbazide with formic acid in

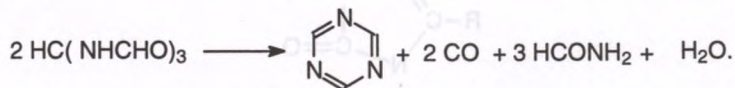
the presence of concentrated H_2SO_4 which was carried out at 95-100 °C with the yield of about 90 % [34-37]:



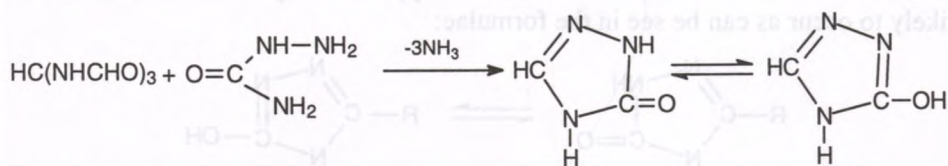
While studying chemical properties of *s*-triazine, Grundmann [38] carried out the reaction with semicarbazide according to the scheme:



This reaction was characterized by a small yield and same difficulties with the synthesis of *s*-triazine. As follows from the literature reports *s*-triazine is formed during the thermal decomposition of triformylaminomethane [39]:



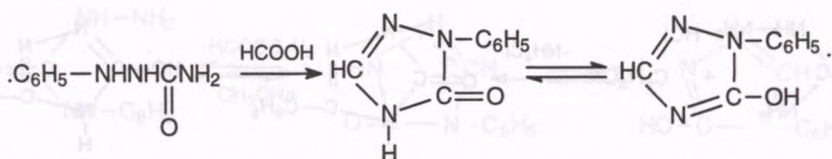
This method was shortened owing to the direct reaction of triformylaminomethane at the temperature of its decomposition (about 180-190 °C) with semicarbazide without separation of *s*-triazine. The reaction yield was about 90 % [40].



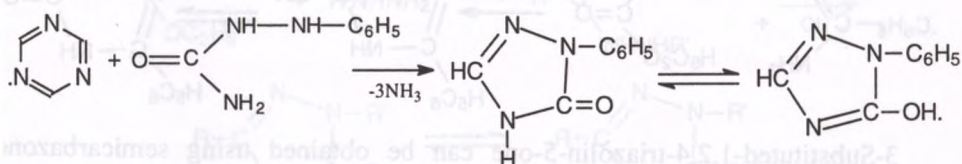
Derivatives of semicarbazide, semicarbazones, amidrazones and their salts were the initial products used for preparation of alkyl or aryl derivatives of 1,2,4-triazolin-5-one.

1-Substituted 1,2,4-triazolin-5-one was obtained using the above mentioned methods.

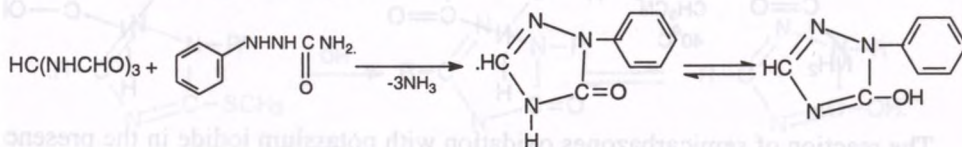
Cyclization of 1-phenylsemicarbazide with formic acid led to 1-phenyl-1,2,4-triazolin-5-one proceeding at 120-130 °C with the yield of 80 % [34]:



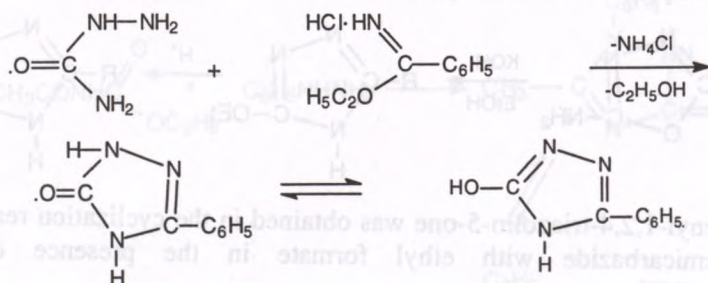
A better yield (90 %) was obtained heating 1-phenylsemicarbazide with formic acid for 6 hours in the presence of concentrated H_2SO_4 at $95\text{-}100^\circ\text{C}$ [41]. The same compound with the yield of about 18 % was obtained in the way similar to the synthesis of 1,2,4-triazolin-5-one in the cyclization reaction of 1-phenylsemicarbazide with s-triazine [38]:

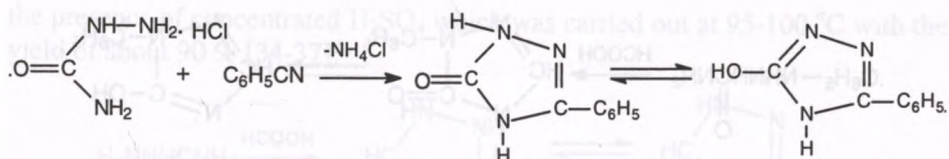


A better yield (93 %) of this compound was obtained by means of a shortened method of direct cyclization of 1-phenylsemicarbazide with trimethylamine which was a product used for the synthesis of s-triazine. The reaction proceeded at $180\text{-}190^\circ\text{C}$ [40]:

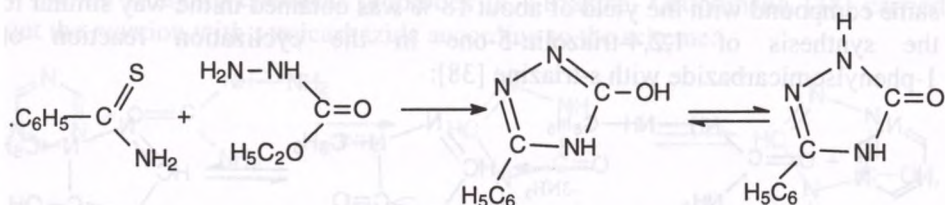


Semicarbazide was also used as an initial product to prepare 3-substituted-1,2,4-triazolin-5-one. A good yield was obtained in the reaction with imidoester hydrochlorides and nitriles [42]:

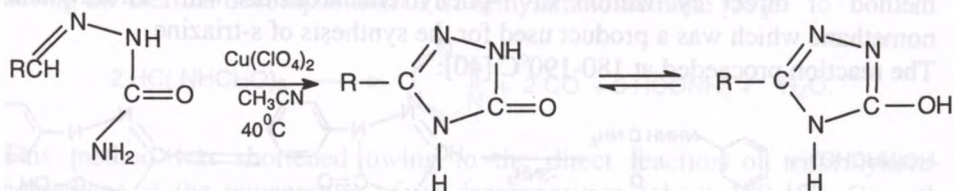




The same derivatives can be obtained in the reaction of thiobenzamide with ethyl hydrazine formate but with a smaller yield [43]:

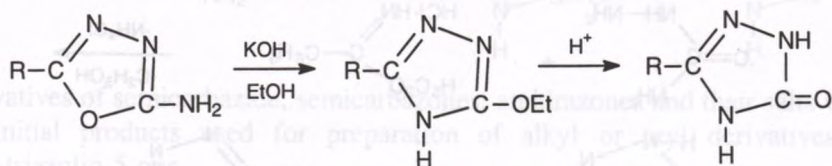


3-Substituted-1,2,4-triazolin-5-one can be obtained using semicarbazone derivatives as the initial products. A good yield was provided by the reaction of semicarbazones oxidation with copper perchlorate in acetonitrile at 40°C [44].

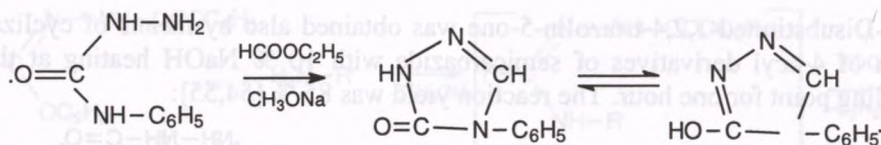


The reaction of semicarbazones oxidation with potassium iodide in the presence of Na_2CO_3 had a similar course [45].

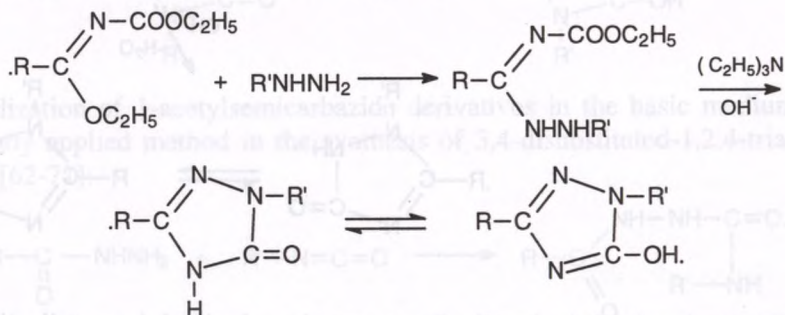
3-Substituted-1,2,4-triazolin-5-one can be obtained with the yield of about 90 % due to the transformation of oxadiazoles carried out at the ethanol boiling point in the presence of KOH [46]:



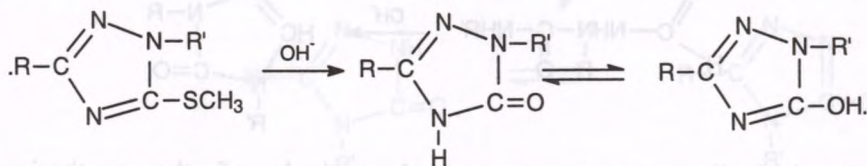
4-Phenyl-1,2,4-triazolin-5-one was obtained in the cyclization reaction of 4-phenylsemicarbazide with ethyl formate in the presence of sodium methylete [47]:



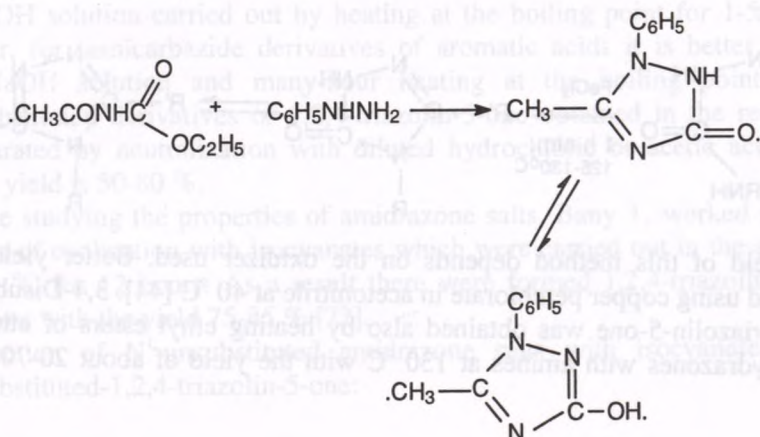
1,3-Disubstituted-1,2,4-triazolin-5-one was obtained with 70 % yield heating ethoxycarbonylimidoesters with hydrazine derivatives in toluene with the addition of Et_3N at 100°C for three hours [48,49]:

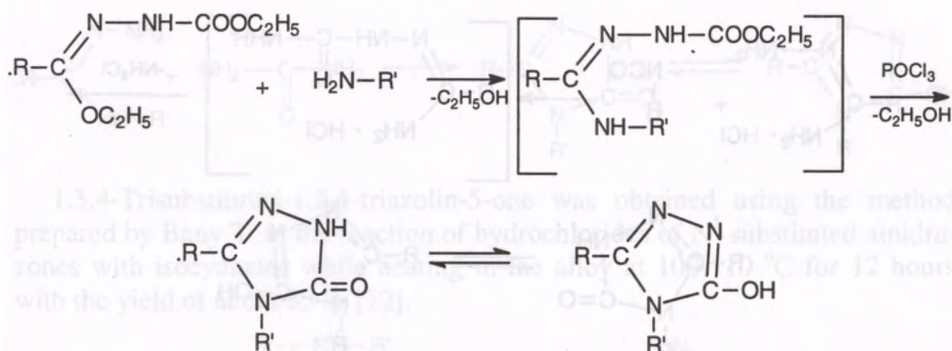


A similar yield can be obtained for 1,3-disubstituted-1,2,4-triazolin-5-one heating suitable 3-methylthio derivatives of 1,2,4-triazole in the basic medium [50]:

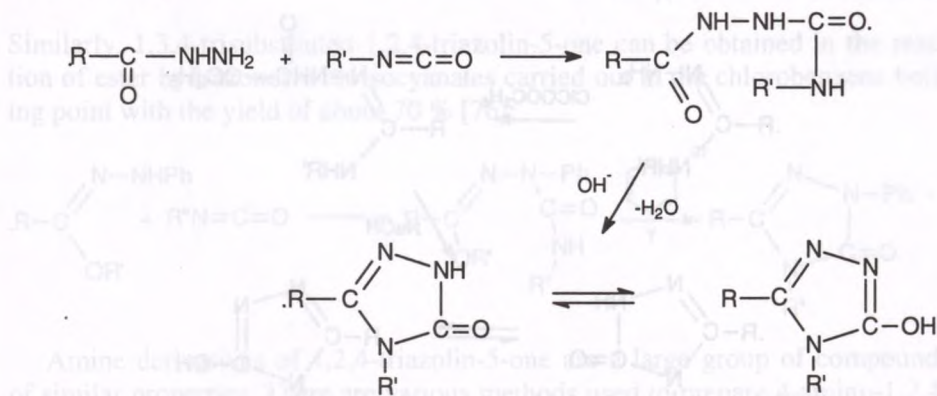


The reaction of acetylurethane with phenylhydrazine gave 2-phenyl-3-methyl-1,2,4-triazolin-5-one [51-53]:





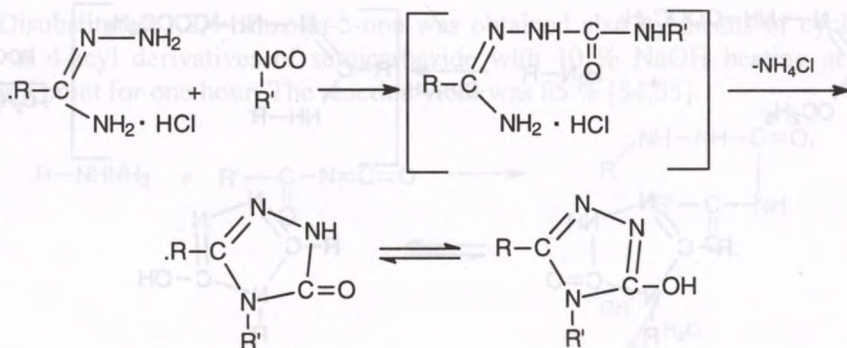
Cyclization of 1-acetylsemicarbazide derivatives in the basic medium is a frequently applied method in the synthesis of 3,4-disubstituted-1,2,4-triazolin-5-one [62-71]:



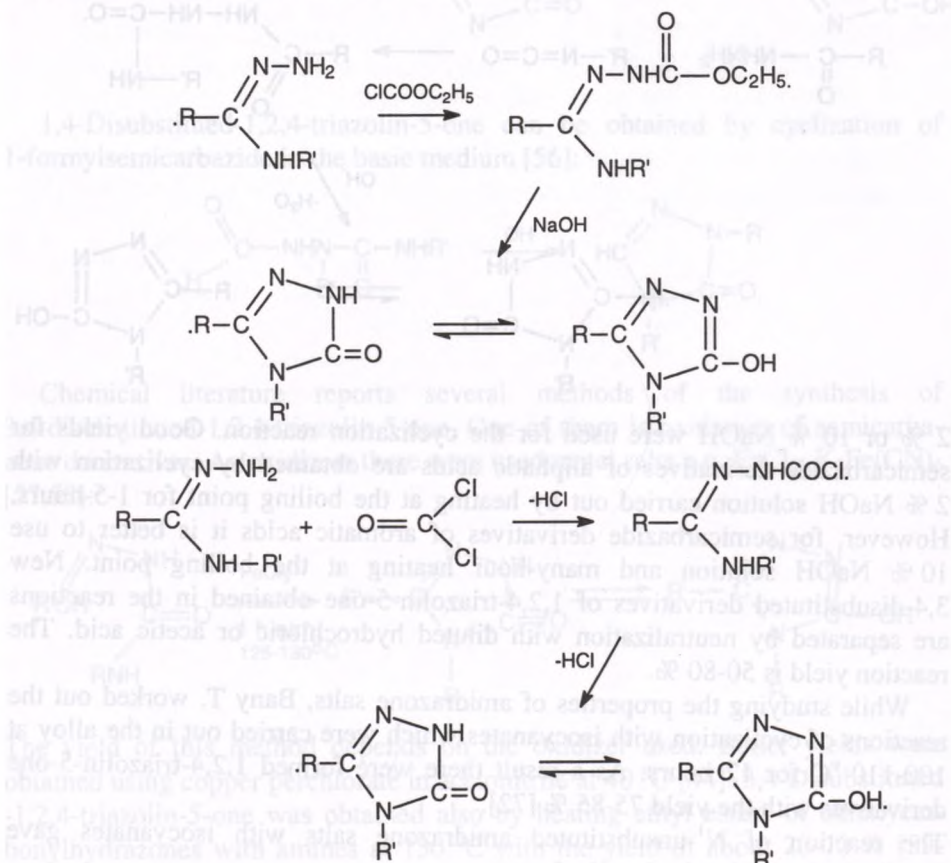
2 % or 10 % NaOH were used for the cyclization reaction. Good yields for semicarbazide derivatives of aliphatic acids are obtained by cyclization with 2 % NaOH solution carried out by heating at the boiling point for 1-5-hours. However, for semicarbazide derivatives of aromatic acids it is better to use 10 % NaOH solution and many-hour heating at the boiling point. New 3,4-disubstituted derivatives of 1,2,4-triazolin-5-one obtained in the reactions are separated by neutralization with diluted hydrochloric or acetic acid. The reaction yield is 50-80 %.

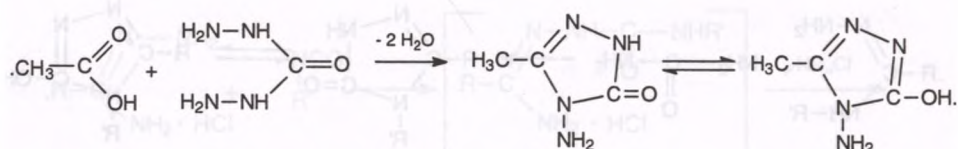
While studying the properties of amidrazone salts, Bany T. worked out the reactions of cyclization with isocyanates which were carried out in the alloy at 100-110 °C for 12 hours. As a result there were formed 1,2,4-triazolin-5-one derivatives with the yield 75-85 % [72].

The reaction of N^1 -unsubstituted amidrazone salts with isocyanates gave 3,4-disubstituted-1,2,4-triazolin-5-one:

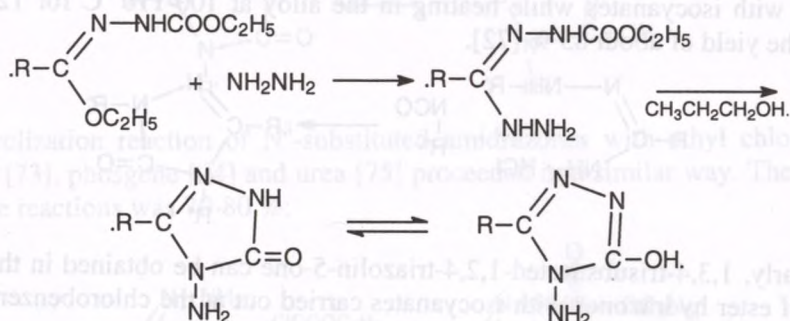


The cyclization reaction of N^3 -substituted amidrazones with ethyl chloroformate [73], phosgene [74] and urea [75] proceeded in a similar way. The yield of these reactions was 70-80 %:



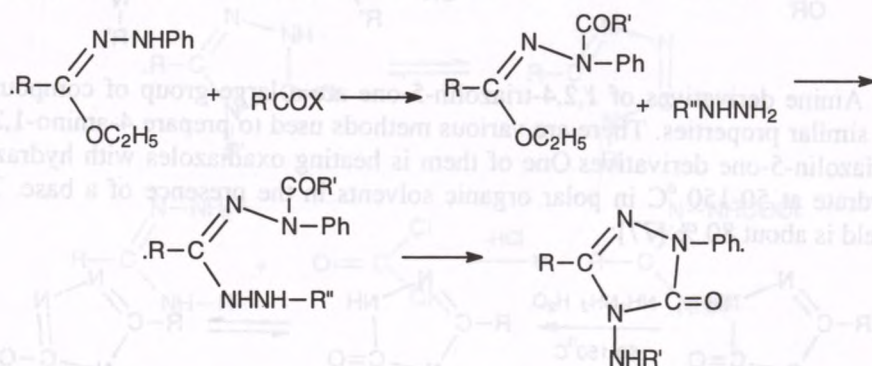


The condensation reaction of ester ethoxycarbonylhydrazones with hydrazine in propanol gives 4-amino-1,2,4-triazolin-5-one derivatives [82]:

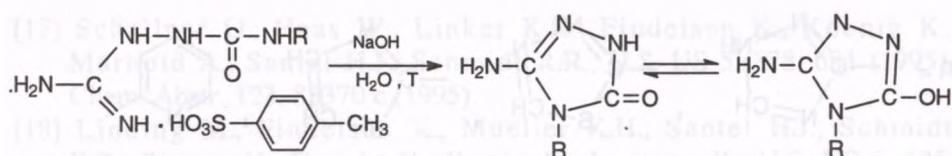


4-Aminosubstituted-1,2,4-triazolin-5-one was obtained with a good yield using hydrazine derivatives in the reaction [83,84].

The same derivatives were obtained in the reaction of ester hydrazones with carboxylic acid chlorides and then with hydrazine derivatives [85]:

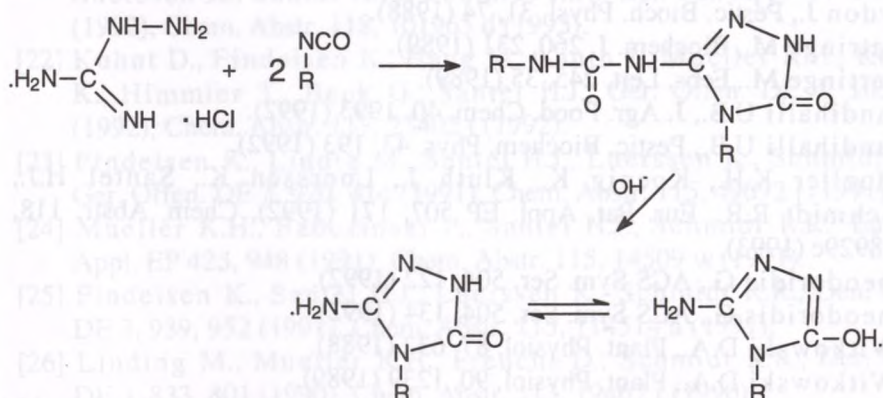


Aminoguanidine salts were the products used to obtain 3-amino-1,2,4-triazolin-5-one derivatives. In the reaction of aminoguanidine salts (hydrochloride or sulfate) with isocyanate there were obtained the linear products of 1-amidine-4-substituted semicarbazide which were isolated in a crystalline form as *p*-toluenesulfonate. Cyclization of these compounds in the basic medium (3N NaOH) gave 3-amino-4-substituted-1,2,4-triazolin-5-one with the yield 51-60 % [86].

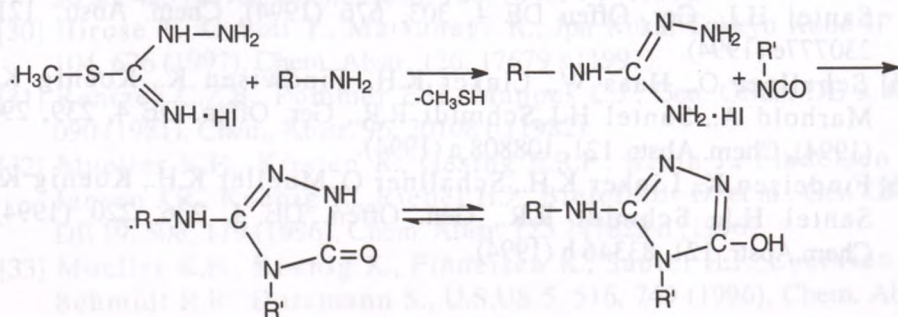


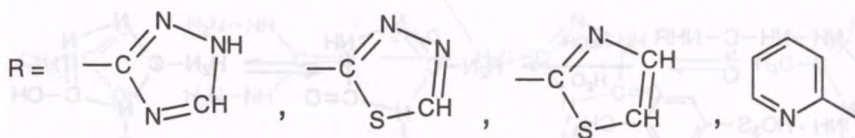
The structure of aminoguanidine salts is similar to that of amidrazone which can cyclize with isocyanate giving 1,2,4-triazolin-5-one derivatives by heating substrates at 110-120 °C for 12 hours [72].

In the reaction of aminoguanidine salts with isocyanate both hydrazine and amidine groups reacted resulting in urea derivatives with 1,2,4-triazole system of the yield 82-96 % [87]. Hydrolysis of these compounds with 20 % NaOH solution for 5 hours gave 3-amino-4-substituted-1,2,4-triazolin-5-one with the yield of 85 %:



3-Aminosubstituted-1,2,4-triazolin-5-one was obtained using this method. Hydroiodide of 3-thiocarbamic acid methyl ester was the initial product [88]. In the reaction of this compound with the first order amines there were formed hydroiodide of 2-amino-1-substituted guanidine which, on heating with isocyanates at 75-100 °C for 12-15 hours, gave 3-aminosubstituted-1,2,4-triazolin-5-one derivatives with the yield of 82-87 % [89-92]:





Based on the ^1H NMR and IR spectra it was stated that the compounds obtained in the reaction of aminoguanidine salts and its derivatives with isocyanates occurred in one of the possible tautomeric forms Δ^2 -1,2,4-triazolin-5-one.

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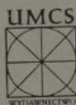
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