

# Search for New Three-, Four-Component Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi Reactions with Organic Compounds of Phosphorus, Arsenic, Antimony and Bismuth

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**Abstract:** It is discovered a new three-, four-component Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi reactions with of arsine, stibine and bismuthine in organometallic chemistry. Modifications were replaced to a nitrogen atom of classical reactions of atoms of phosphorus, arsenic, antimony and bismuth. It has been proposed a new mechanism for possible reactions.

**Key words:** Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi reactions, phosphorus, arsenic, antimony, bismuth.

## 1. Introduction

In recent years, it has been actively investigated nucleophilic reaction organilgalogenidami phosphine and with electrophilic geterilalkenami allowing to obtain primary, secondary and tertiary phosphines, selectively and with high yield. Most of these reactions are realized under mild conditions at a pressure atmlosfernom phosphine.

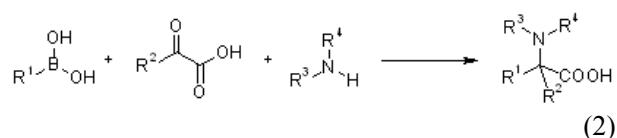
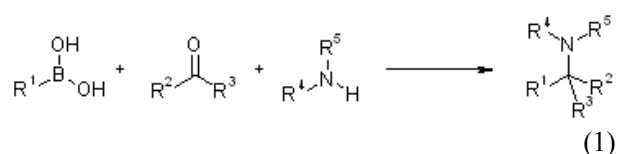
Although the chemistry of organophosphorus compounds devoted a considerable number of monographs, but the reaction of organic compounds of arsenic, antimony and bismuth are very limited. The aim of this work searches for new three-, four-component reactions Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi reactions with organic compounds of phosphorus, arsenic, antimony and bismuth.

The purpose of this work, search for new three-,

four-component reactions Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi reactions with organic compounds of phosphorus, arsenic, antimony and bismuth.

## 2. Theory

It is known that the Petasis reaction is a MCR (multi component reaction) that enables the preparation of amines and their derivatives such as  $\alpha$ -amino acids.

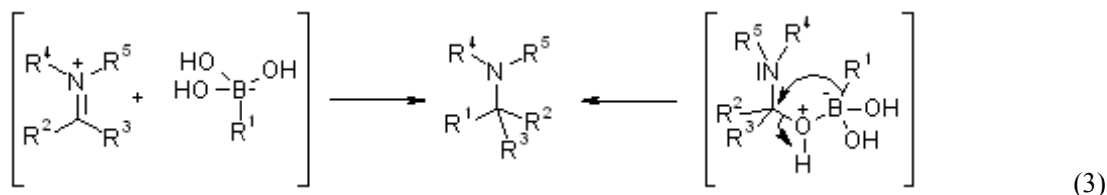


The reaction is also referred to as the Boronic Acid Mannich reaction, since it proceeds via an imine with the organic ligand of the boronic acid acting as the nucleophile, similar to the role of the enolizable

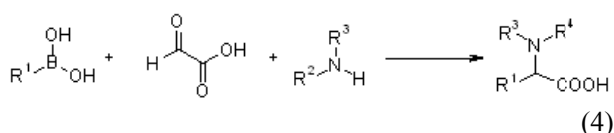
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ketone component in the original Mannich reaction. One proposal is that the transfer is actually

intramolecular, and takes place via the adduct pictured below:



The direct reaction with glyoxylic acid merits particular mention, since it leads to interesting, unnatural  $\alpha$ -amino acids in a single step, while avoiding the appearance of toxic byproducts such as seen with the Strecker Synthesis.

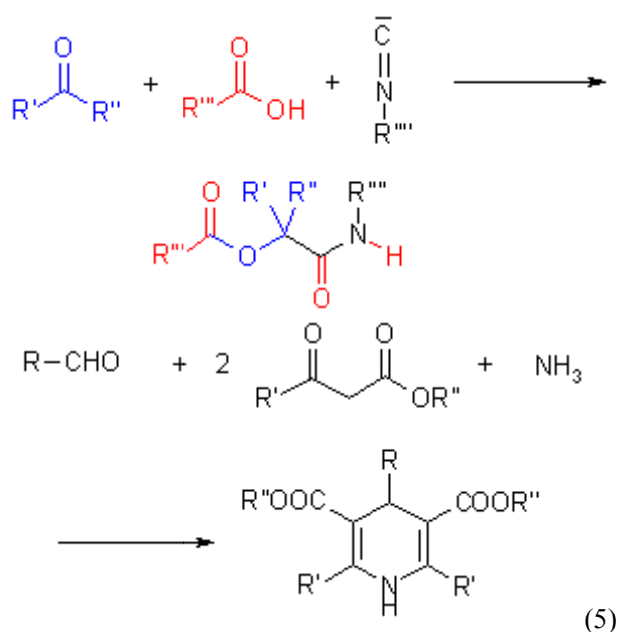


This reaction can be carried out with secondary amines, sterically hindered primary amines, hydrazines or anilines in dichloromethane at room temperature. The range of potential nucleophilic partners includes alkenylboronic acids, and electroneutral as well as electron-rich (hetero-)arylboronic acids. The conversion of electron-poor boronic acids can be effected at elevated temperatures MW (microwave) in suitable solvents.

It is known that Passerini reaction three-component between a carboxylic acid, a carbonyl compound such as a ketone or aldehyde, and an isocyanide, offers direct access to  $\alpha$ -hydroxy carboxamides. The Passerini reaction proceeds rapidly if the reaction is performed in aprotic solvents at room temperature. High yields are obtained with high concentrations of the starting materials in the reaction mixture. From these findings, it is assumed that the Passerini reaction does not follow an ionic pathway. Hydrogen bonding is believed to play a crucial role in the formation of the presumed cyclic transition state for this reaction.

It is known that Hantzsch Dihydropyridine (Pyridine) Synthesis allows the preparation of dihydropyridine derivatives by condensation of an

aldehyde with two equivalents of a  $\beta$ -ketoester in the presence of ammonia. Subsequent oxidation (or dehydrogenation) gives pyridine-3,5-dicarboxylates, which may also be decarboxylated to yield the corresponding pyridines.

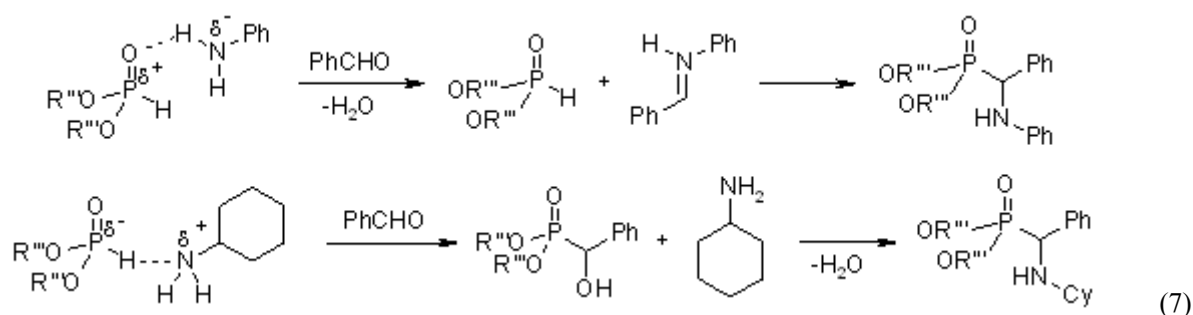
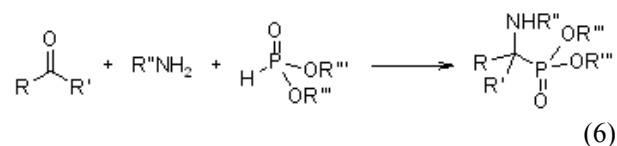


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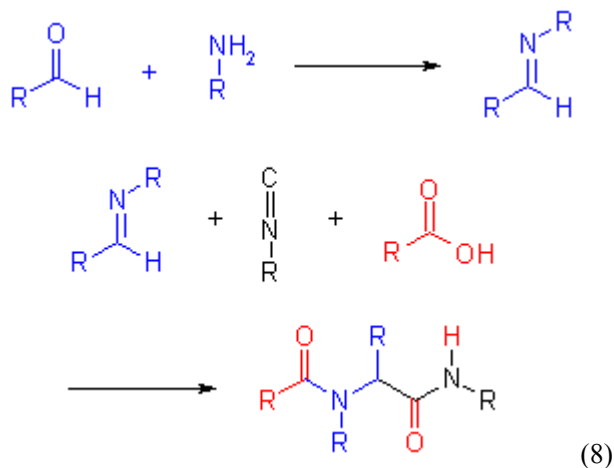
It is known that Kabachnik-Fields reaction three-component coupling of a carbonyl, an amine and a hydrophosphoryl compound leads to  $\alpha$ -aminophosphonates. The Kabachnik-Fields reaction is very important in drug discovery research for generating peptidomimetic compounds.

The pathway of the Kabachnik-Fields reaction depends on the nature of the substrates. The amine and hydrophosphoryl compound form a complex in which either one of the partners may react with the carbonyl compound. Often, the basicity of the amine determines the reaction pathway. Weakly basic amines such as anilines, which can act as proton

donors, favour the formation of an imine, whereas alkylamines such as cyclohexylamines do not form imines.



It is known that the U-4CC (Ugi four-component condensation) between an aldehyde, an amine, a carboxylic acid and an isocyanide allows the rapid preparation of  $\alpha$ -aminoacyl amide derivatives. The Ugi reaction products can exemplify a wide variety of substitution patterns, and constitute peptidomimetics that have potential pharmaceutical applications. This reaction is thus very important for generating compound libraries for screening purposes.



The mechanism is believed to involve a prior formation of an imine by condensation of the amine with the aldehyde, followed by addition of the carboxylic acid oxygen and the imino carbon across the isocyanide carbon; the resulting acylated isoamide

rearranges by acyl transfer to generate the final product.

A distinctive feature of the Ugi reaction is the possibility of introducing a condensation at the same time four or more components under very mild conditions, and ease of implementation and high yields of the reaction products.

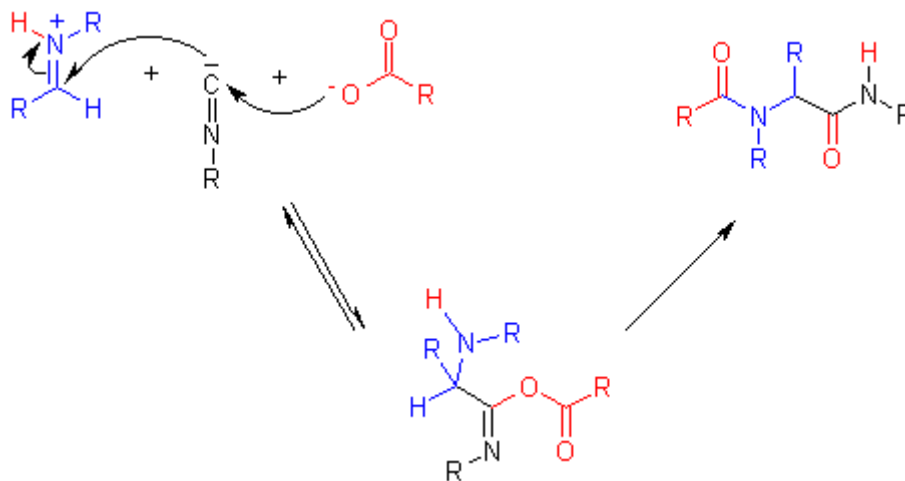
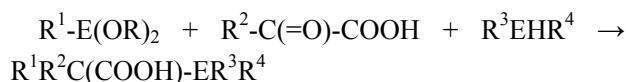
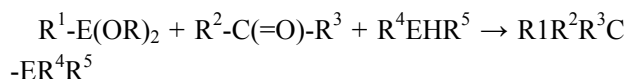
A special activity isonitrils linked due to the presence of divalent carbon atom adjacent to the nitrogen lone pair of electrons carrying the imparting of nucleophilic carbene carbon character.

### 3. Results and Discussion

Comparison of the three-, four-component Petasis, Passerini, Hantzsch, Kabachnik-Fields, Ugi reactions with organic compounds of arsenic, antimony and bismuth showed that they all substitution reactions of amines with a variety of organic compounds which have a labile hydrogen atom.

We proposed a general view of the proposed new three-, four-component Petasis, Passerini, Hantzsch, Kabachnik-Fields, Ugi reactions by replacing nitrogen atoms arsenic, antimony and bismuth.

We propose to extend and modify Petasisa substitution reaction with amines on the nitrogen atom of phosphorus, arsenic, antimony and bismuth.

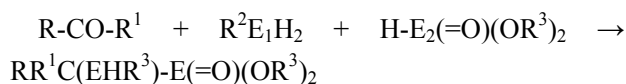


(9)

where, E = N, P, As, Sb, Bi; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> = H, CH<sub>3</sub>, Ar.

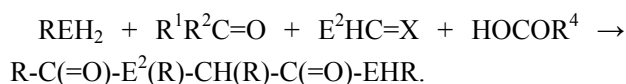
We propose modified Hantzsch condensation reaction of aldehyde with two equivalents of a β-ketoester in the presence of ammonia, phosphine, arsine, stibine, and bismuthine. After oxidation (or dehydrogenation) gave pyridin-3,5-dicarboxylic acid, which can be decarboxylated to give the corresponding pyridine, phosphoridine, arsinidine, stibinidine and vismutinidine.

We propose to expand and change Kabachnik-Fields reactions in connection with the replacement of amines on the phosphines, arsines, stibines and vismutines.



where, E<sub>1</sub>, E<sub>2</sub> = N, P, As, Sb, Bi; R, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = Alk, Ar.

We propose to expand the Ugi reaction and receive bimetallic organic compounds of arsenic, antimony and bismuth:



where, X = O, S, Se; E = P, As, Sb, Bi; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Alk, Ar.

Thus, we first proposed to extend and modify the new three-, four-component Petasis, Passerini,

Hantzsch, Kabachnic-Fields Ugi reactions with arsine, stibine and bismuthine in organometallic chemistry. We proposed a new mechanism for the possible reactions.

## 4. Conclusions

The data presented in this paper show that the organic compound of arsenic, antimony and bismuth are convenient starting materials for the formation of the C-As, C-Sb, C-Bi in obtaining various organometallic compounds which are more widely used as catalysts, pharmaceuticals preparations.

We have opened a new three-, four-component Petasis, Passerini, Hantzsch, Kabachnic-Fields, Ugi reactions with organic compounds of phosphorus, arsine, stibine and bismuthine in organometallic chemistry. We proposed a new mechanism for the possible reactions.

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