



A REVIEW ON MULTI-COMPONENTS REACTIONS FUNCTIONING THROUGH DERIVATIZATION OF CARBONYL COMPOUND AS REACTIVE INTERMEDIATE

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Abstract

The Multi-Component Reaction (MCRs) is a method in which three or more reactants are reacted in single vessel to form a complex cascade of molecule without isolation of intermediate. Here we have focused on various Multi-Component Reaction such as Strecker synthesis of amino acids, Hantzsch synthesis of dihydropyridines, Biginelli Reactions, Mannich reaction, Bucherer-Bergs synthesis and Kabachnik-Fields Reaction. Also discussed the concept map of above reactions which proceed through derivatization of carbonyl compound.

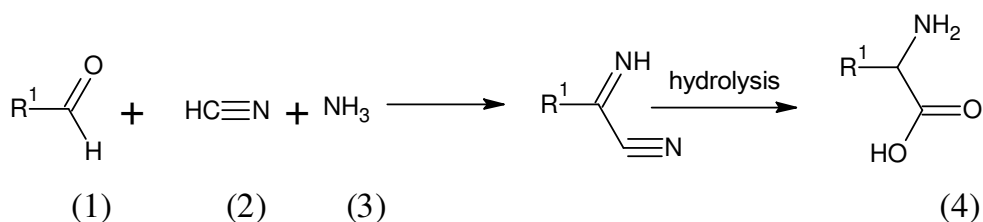
Introduction

Multi-Component Reaction is extremely ideal and eco-friendly reaction system. In scientific literature survey there are many research paper showing one pot synthesis of various heterocyclic compounds fall under the category of MCR's. It is a green tool of organic synthesis which form complex organic compounds within one pot reaction via reacting three or more reactant. There are many advantages of MCR's such as simplicity of operation, minimization of time and cost as there is no isolation of intermediate and its purification. In this article the selected MCR's shows one common pattern that the carbonyl compound reacts with one of the reactant to form a reactive intermediate which is attacked by nucleophile to give desired Product.

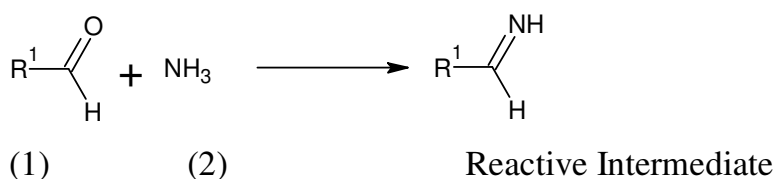
Multi- Component Reactions

1) Strecker Amino Acid Synthesis

This is a first MCR made by Strecker in 1950. In this Reaction Aldehyde (carbonyl Compound) (1) Hydrogen Cyanide (2) and Ammonia (3) are reacted in one pot which upon hydrolysis gives corresponding amino acid(4).

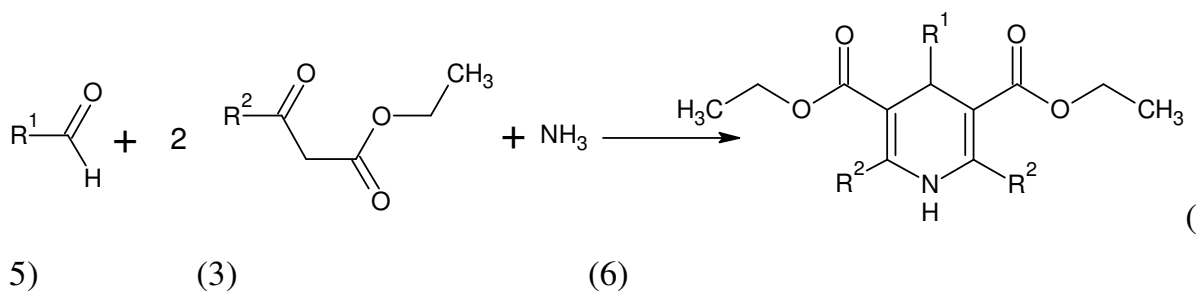


In this reaction Aldehyde (1) react with Ammonia (3) to give reactive imine intermediate which is a derivatization of carbonyl compound.

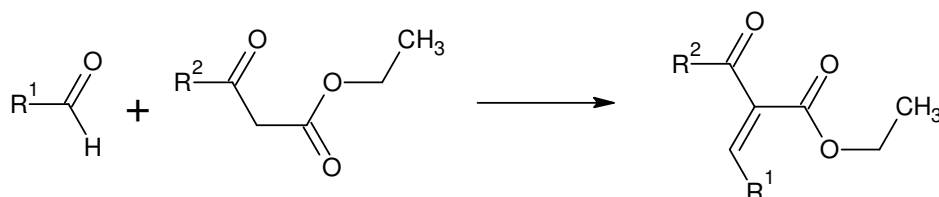


2) Hantzsch synthesis of dihydropyridines

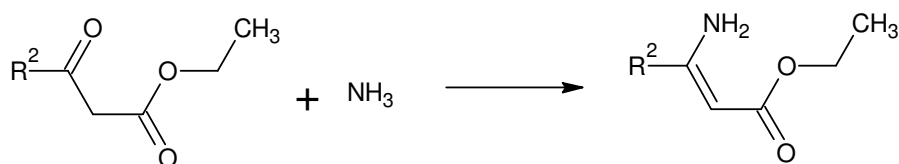
Hantzsch in 1882 synthesized a dihydropyridine (6) via MCR of Aldehyde (1), β -Ketoester (5) and Ammonia (3).



First reactive intermediate is believed to be formed by Condensation of aldehyde with β -Ketoester.

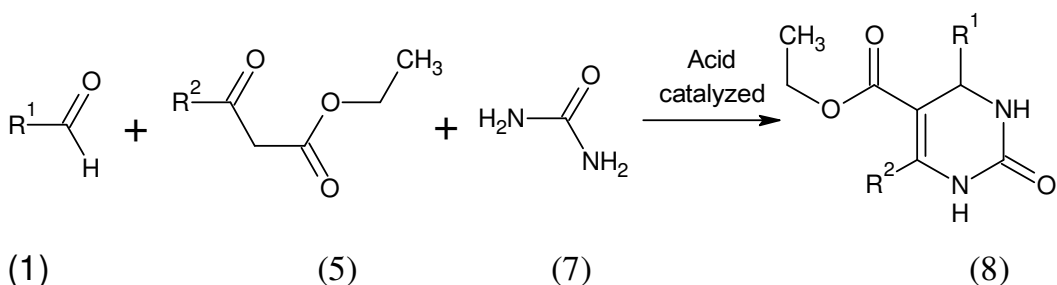


Another reactive intermediate is believed to be formed by Condensation of Ammonia and β -Ketoester.

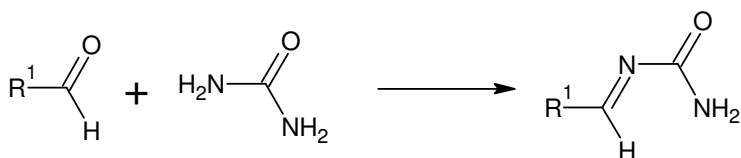


3) Biginelli Reaction

This reaction was first described in 1893. It is acid catalyzed three component reaction between Aldehyde (1), β -Ketoester (5) and Urea (7) to give Dihydropyrimidone (8)



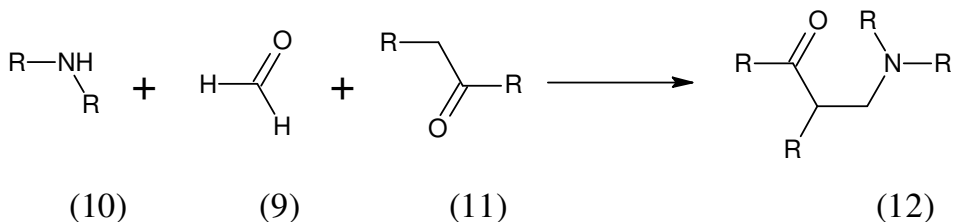
First step in the reaction is believed to be the condensation of Urea and aldehyde to give reactive iminium intermediate



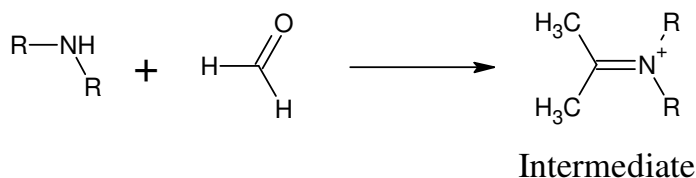
Iminium Intermediate

4) Mannich Reaction

This reaction was discovered by Carl Mannich in 1912. It is a multi-component condensation reaction between formaldehyde (9), Primary or secondary amine (10) and enolizable carbonyl compound (11) to give β -amino carbonyl compound (12) known as mannich base.

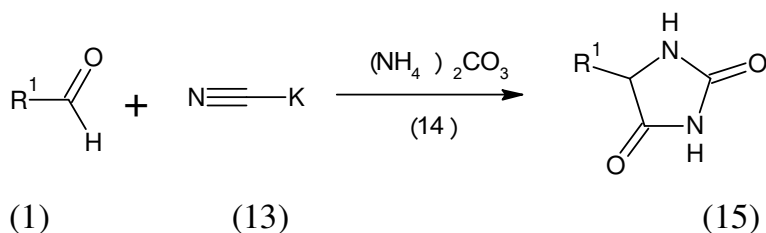


It is believed that the first step is generation of Schiff's base by reaction between formaldehyde and secondary amine which is a reactive intermediate and act as electrophile.

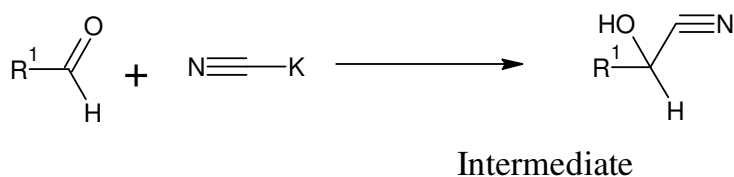


5) Bucherer–Bergs reaction

It is discovered in 1934. It is a MCR between Carbonyl Compound (1), Potassium Cyanide (13) and Ammonium Carbonate (14) to give hydantoins (15).

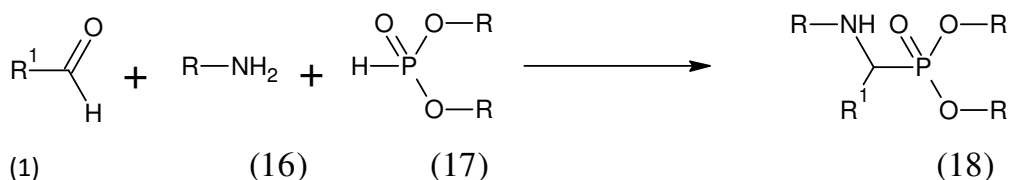


It is believed that formation of Cyanohydrin as intermediate in above reaction via derivatization of carbonyl compound with Pot. Cyanide.

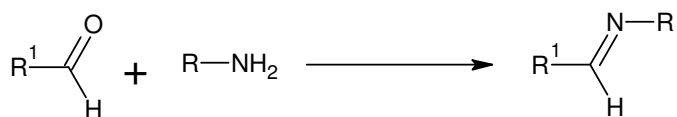


6) Kabachnik-Fields Reaction

This MCR was discovered by Martin I. Kabachnik and Elis K. Fields independently in 1952. In this reaction there is three component condensation of carbonyl Compound(1), Amine (16) and DialkylPhosphonate (17) to give α -amino phosphonates (19).



First step in the reaction is formation of imine intermediate by reaction of amine and carbonyl compound which is attacked by DialkylPhosphonate



Concept Map

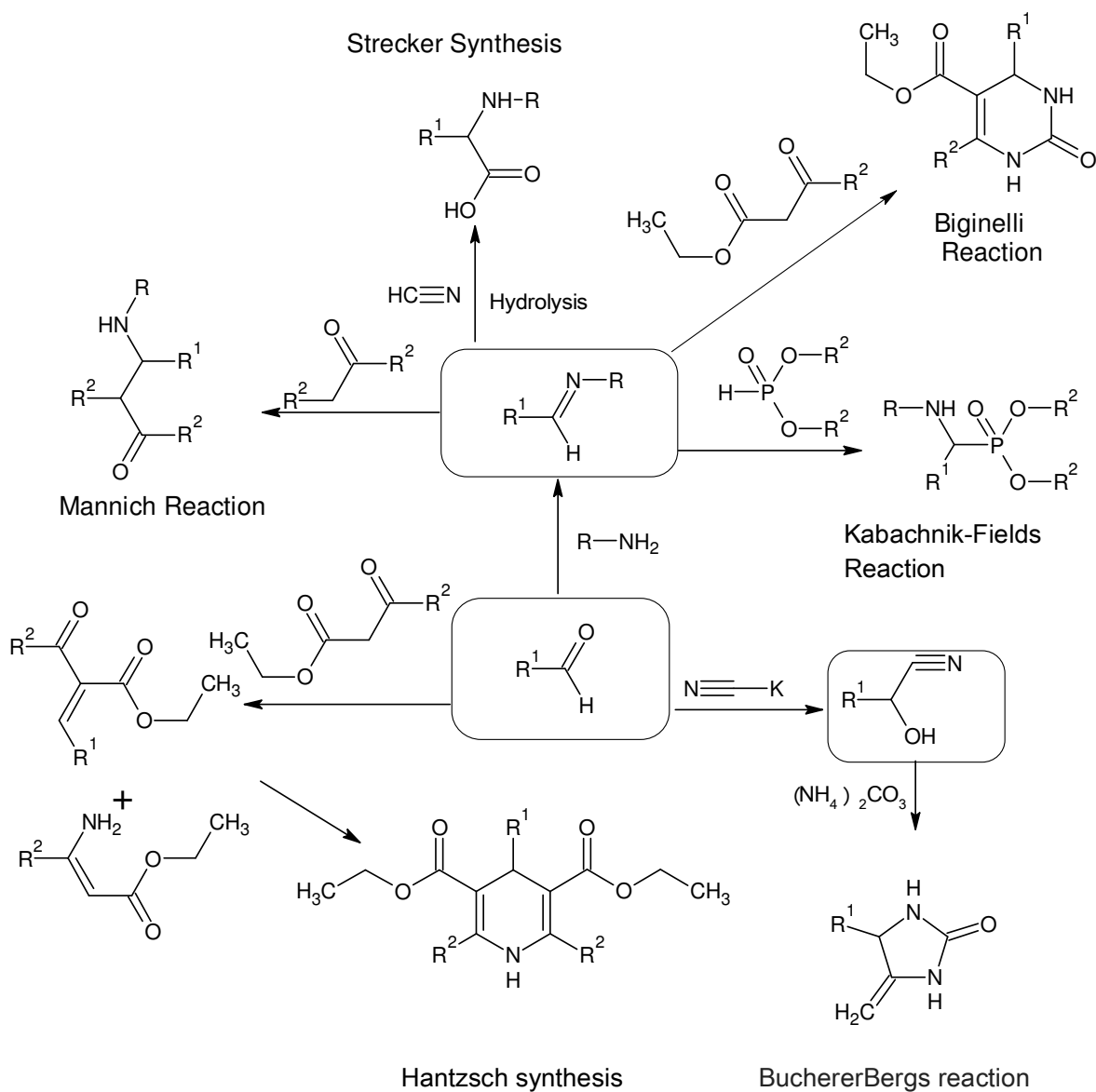


Fig 1

In Fig 1 for Mannich Reaction $R^1 = -\text{H}$,

For Strecker Synthesis $R = -\text{H}$,

For Biginelli Reaction $R = -\text{CONH}_2$,

In above Concept Map carbonyl compound (generally aldehyde) is at center which on derivatization by amine (1^0 , 2^0 , 3^0 , NH_3 or NH_2CONH_2) gives imine type of intermediate. This intermediate acts as electrophile which is attacked by H-CN and upon hydrolysis gives amino acid which is a Strecker Amino Acid Synthesis. This intermediate is attacked by enolizable carbonyl compound to give β -amino carbonyl compound and reaction is Mannich Reaction. Such intermediate is attacked by β -ketoester and upon cyclocondensation its gives product of Biginelli Reaction. Dialkylphosphonate react with this imine type of intermediate and reaction is Kabachnik-Fields Reaction.

In Bucherer–Bergs reaction Potassium Cyanide react with Carbonyl compound to form Cyanohydrin as intermediate which is attacked by ammonium carbonate to give hydantoins. In Hantzsch Synthesis of dihydropyridine two intermediate formed by carbonyl compound one by reaction of aldehyde and β -ketoester and another is β -ketoester and ammonia react each other.

Conclusion

This article has given attention on Multi-Component Reaction Proceed through derivatization of carbonyl compound which act as reactive intermediate through literature survey. Also it focuses on relation between them via Concept Map. As most of the intermediate are formed in *situ* which cannot be isolated but is strong belief that reaction must Proceed through it.

References

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