IARJSET ISSN (O) 2393-8021, ISSN (P) 2394-1588

International Advanced Research Journal in Science, Engineering and Technology

Impact Factor 8.066 ⁜ Peer-reviewed / Refereed journal ⁜ Vol. 10, Issue 10, October 2023

DOI: 10.17148/IARJSET.2023.101017

A review: L- Proline as an organocatalyst

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Abstract: Organocatalysis will be a ability in Synthetic Green Chemistry and Synthesis mainly expressed to be utilized for speeding up the rate of synthetic reaction with a sub stoichiometric measure of a natural compound which does not contain a metal and not a macro molecule like protein, nucleic acid or polymer [1,2].

The area of as a L-Proline organocatalysis has been one of the most powerful and quickly developing fields in organic synthesis throughout the last decade, generally because of its incredible potential for acknowledging extremely complex , successful , specific asymmetric changes and amine derivatives likewise utilized for different reactions like asymmetric Aldol reactions, Asymmetric Michael reactions, organocatalytic H stimulation , assymetric anti 1,2 diol, epoxide development, transamination, Mannich reaction , asymmetric α-hydroxyamination, polymerization, One pot Multi-component reaction.

These review articles gives update data on current reports and describe effectiveness of L-Proline organocatalysis and its productivity for this methodology and extension. The information on the procedure of synthesis, compound responses, and work on this in different publications is presented.

Keywords: Proline, Organocatalyst, Asymmetric Synthesis, aldol reaction.

I. INTRODUCTION

The term 'organocatalysis' was presented by Ostwald [1] back in 1900 in relative to chemically active small organic compounds, therefore recognizing them as a unique group from enzymes and inorganic catalysts.

A significant achievement in the historical backdrop of organocatalysis was the revelation of the Robinson asymmetric annulation catalyzed by (S)- proline (1) made in the mid-1970s by two autonomous gatherings of specialists. The reaction was called the Hajos ± Parrish ± Eder ± Sauer ± Wiechert reaction after the authors.[10-12]

In organic synthesis when little organic molecules are utilized as catalyst then the reaction is supposed to be organocatalysis. Without a doubt, the credits the disclosure of first organocatalytic reaction goes to J. Von Liebig, who found accidently the change of dicyanon to oxamide in the presence of a aqueous solution of acetaldehyde [18].

Numerous organocatalysts are latent towards humidity and oxygen, this benefit gives its significance for such challenging reactions conditions over latent atmosphere, low temperature, complete solvents and so on are in many examples, not needed and it very well may be utilized in drugs [34-35] also.

L Proline as an organocatalyst:

B. List and colleagues have describe the first model of the asymmetric Mannich reaction utilizing L-proline in year 2000 and its utility as an organocatalyst.[39] eg. At the point when acetone (overabundance), p-nitrobenzaldehyde, and p-anisidine are treated with L-proline (35 mol%) gave the embattled adduct in half yield with 94% ee nature of item as displayed in scheme 2. The B. List and W. Notz have established the simple anti 1,2 diol reaction[40] as displayed in reaction scheme 3.

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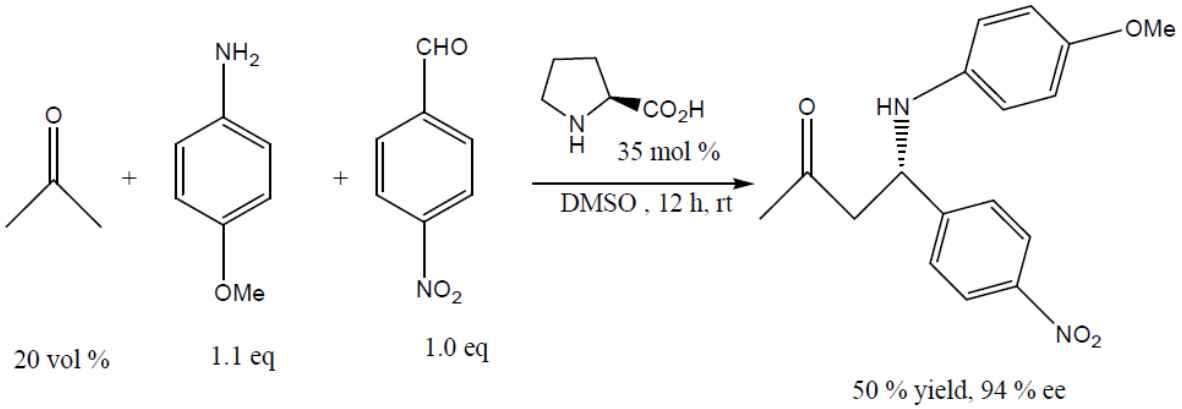
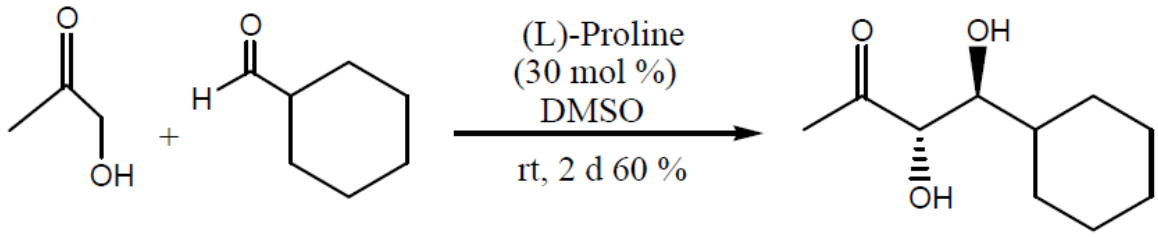
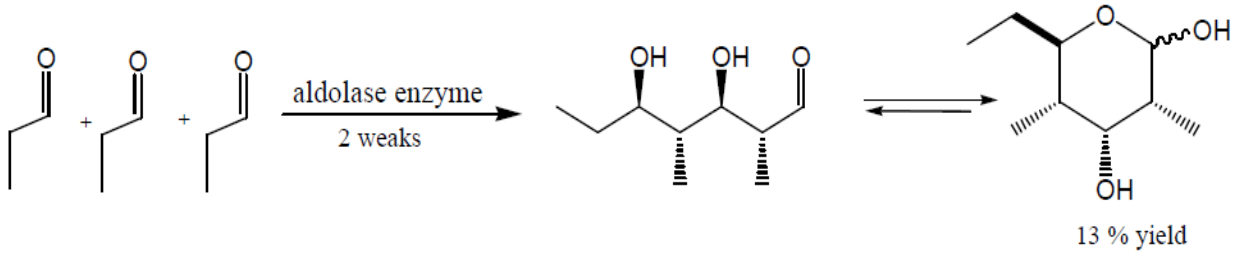


Scheme 2: Asymmetric Mannich reactions catalyzed by L-Proline



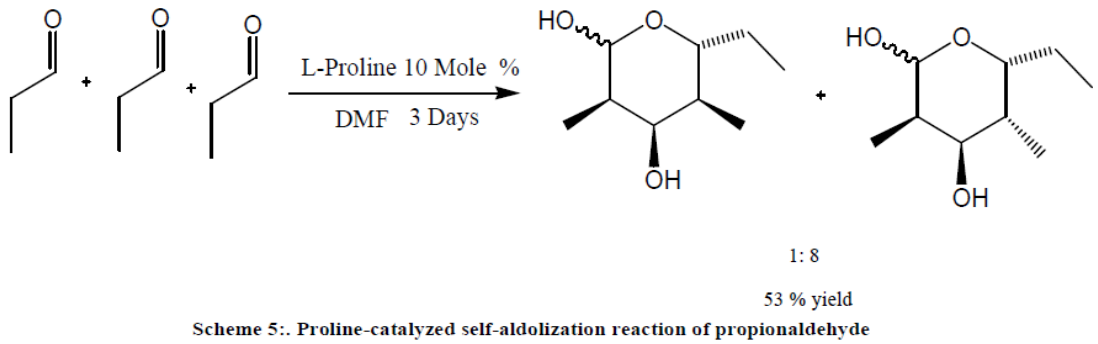
Scheme 3 : Asymmetric Diol Formation

The L-Proline is extremely adaptable reagent for Asymmetric Synthesis in Organic Chemistry and utilizing such sort of nature of L-proline we can perform self aldol condensation reactions. Rise in yields is likewise announced [41].



Scheme 4. Aldolase-catalyzed self-aldolization of propionaldehyde

The reaction displayed in scheme 4 is a basic enzymatic reaction yet when it is performed with L-Proline then it goes quick with moderate yield [42].



Scheme 5:. Proline-catalyzed self-aldolization reaction of propionaldehyde

The result of scheme 5 showed Pyranoses four asymmetric focuses when catalysed under proline catalysis which is phenomenal diastereoselectivity catalyst and enantioselectivity (47% ee) from three aldehyde molecules. The character of every aldehyde component might conceivably be completely altered giving admission to a wide scope of molecules. Above technique is a basic one-pot scheme giving direct admittance to carbohydrates and polyketides that are normally prepared by utilizing multi-step response methodology.

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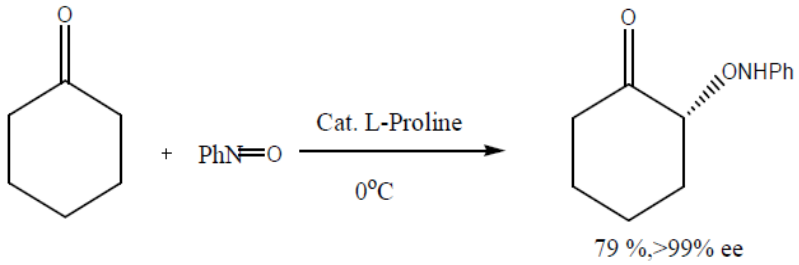
Scheme- 6a showed α-hydroxyaldehydes are optically dynamic and vital in intermediates for organic synthesis. Therefore, numerous techniques are newly produced for this utility and their preparation [43, 44] for fast, transformation from chiral regular sources. eg. amino acids, sugars, and chiral α-hydroxy acids. Such a need emerges for improvement of direct catalytic enantioselective α-aminooxylation of aldehydes utilizing nitrosobenzene and L proline as catalyst. [45]

Because of L-proline as impetus and nitroso benzene as oxidant the above reaction was conveyed at low temperature. In this reaction the side reaction and dimer preparation of nitroso benzene just as aldol responses is stifled [46]



Scheme 6 a. Direct asymmetric α-aminooxylation of cyclohexanone

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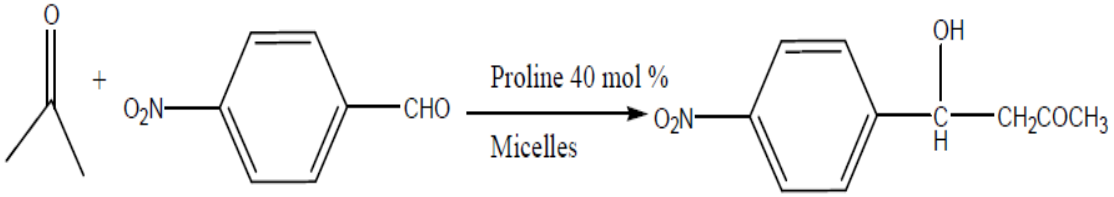
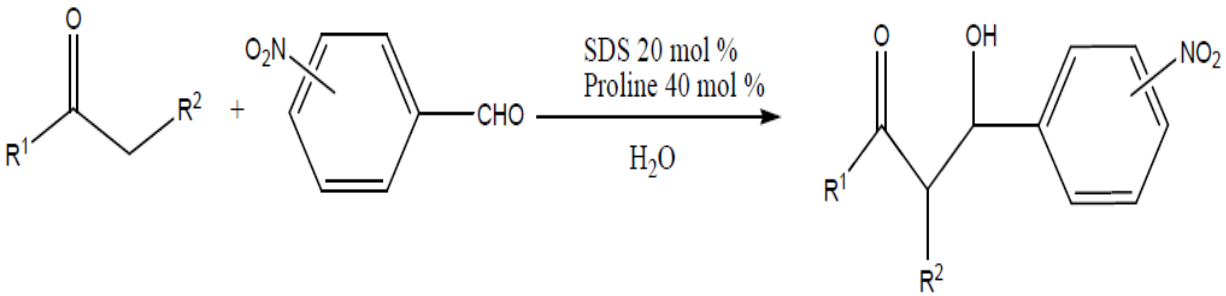
The little organic molecule can achieve enhance organocatalytic reaction in this way, L-proline additionally assumes a significant part in aldol intramolecular condensation and furthermore asymmetric α-hydroxyamination of α-branched Aldehydes[47].The reaction is fluid aldol condensation in which acetone responds with 4-nitrobenzaldehyde without surface active agent. The reaction is conveyed by blending acetone (20 mmol), 4-nitrobenzaldehyde (4 mmol) and L-proline (0.16 mmol, 40 mol%) in unadulterated water (15 ml). The reaction was saved for five days at 40°C, the expected aldol item was acquired with yield of up to 15%. Henceforth need to be raised to increase the yield of the product.



Scheme 6b

In this alteration anionic surface dynamic specialist sodium dodecyl sulfate (20 mol% SDS), was included the reaction, which gave 87% yield of aldol condensation product , just in 24 hr this yield is relatively higher than that of the comparing reaction which was made in natural solvents (68 %) scheme 6c.



Scheme 6c: Aldol reactions of ketones with nitrobenzaldehydes in SDS micelle

In the above reaction , it was found that just the pyrrolidine ring (in L-proline) was valuable in micelles and the carboxylic acid group (in L-proline) didnot participate in the reaction mechanism. The L-proline methyl ester and Lhydroxyproline can catalyze similar aldol reaction micelles, giving the aldol product yields 82 and 70%, individually when acetone responds with P-Nitro benzaldehyde in previously mentioned conditions. The L-amino and a few D-amino acids are additionally utilized as catalyst yet the product was acquired in less amount. The above outcomes show that the reaction mechanism in micelle might be not the same as that in natural solvents. On this premise, an amine catalyzed instrument is proposed for the aldol reaction in micelles [47].

The S. Chandrasekhar et al played out the Asymmetric aldol reaction in poly(ethylene glycol) L-proline as catalyst. It is a fast and direct aldol reaction. L-proline catalyzed the PEG as solvent with practically identical enantioselectivitie item.

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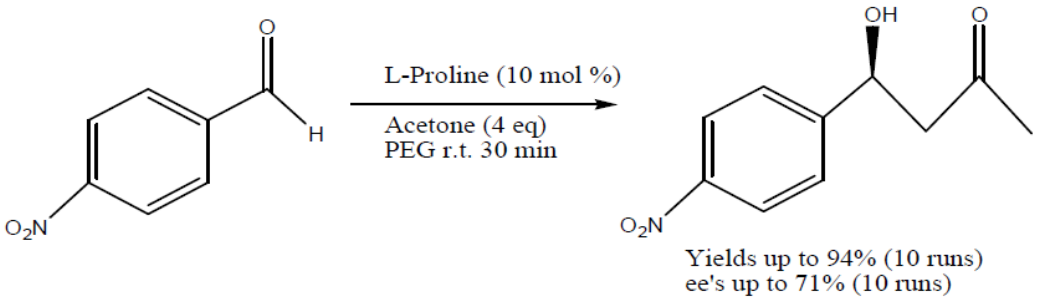
It was accomplished by responding different aldehydes and acetone. One can incorporate most remarkable C-C bond formation by the asymmetric aldol reaction of an aldehyde and an adjusted or unmodified ketones[48]. Since a few amide subsidiaries of L-Proline can likewise be utilized for aldol condensation [49,50] (scheme:7).



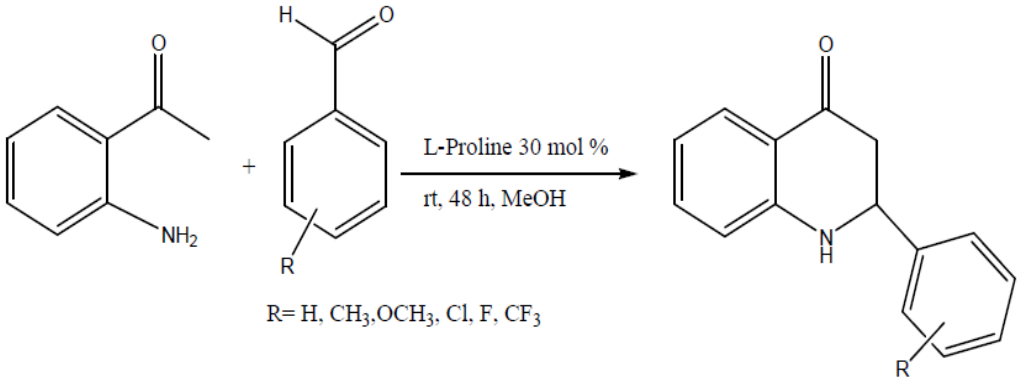
Scheme 7 : L-Proline catalyzed asymmetric aldol reactions in PEG

The effectiveness of the transformation of item was analyzed by exposing different aldehydes to an aldol reaction in poly(ethylene glycol). Every one of the models contemplated gave comparative outcomes to those announced utilizing traditional solvents what's more different techniques (The 2-and 3-nitrobenzaldehydes). In L-proline catalyzed asymmetric aldol reaction by utilizing poly(ethylene glycol) as recyclable solvent , it runs 10 time quicker without loss of action of either the catalyst or solvent[51].

The one more kind of enantioselective direct intermolecular aldol responses [51] by utilizing L-proline catalyzed reaction of tetrahydro-4H-thiopyran-4-one with various kinds of aldehydes. The reaction which is coordinated aldol reaction [52] has performed enol(ate) subordinates with different aldehydes is among the most remarkable and helpful strategies for stereochemically controlled C-C bond formation[53-54]. The tetrahydro-4H-thiopyranone under goes aldol reactions with various types of Aldehydes which are catalyzed by proline successfully. The wet DMF or DMSO gave the counter adducts in brilliant enantioselectivity great yield as well. By performing desulfurization of these adducts they changed over to items having applications in polypropionate blend [55].

One Pot L-Proline Catalyzed Synthesis:

S. Chandrasekhar et al [83] utilized L-proline as Organocatalyst in one-pot synthesis and they dealt with synthesis of subbed 2-aryl-2,3-dihydroquinolin-4(1H)- ones, with great yields. 2-hydroxyacetophenones and aryl aldehydes go through a smooth one-pot condensation cyclization within the sight of L-proline as organocatalyst to provide flavanones in significant returns. They have represented an overall technique for the blend of aza-analogs of flavones beginning from o-aminoacetophenone(Scheme-14).



Scheme -14: Synthesis of aza-analogs of flavanones starting from o-aminoacetophenone

S. Chandrasekhar et al have detailed that the equivalent molar amounts of o-aminoacetophenone and benzaldehyde on mixing together within the sight of L-proline (30 mol %) and methanol (5 ml) and stir up provided 2-phenyl 2, 3-dihydroquinolin-4(1H)- one in 85% yield. They prerogative that in this mechanism the catalyst can be recuperated toward the end of reaction [83]. Asymmetric synthesis utilizing L-proline was likewise explored by Hiyoshizo Kotsuki considering different reactions like Mannich reaction, Michael expansion reaction, α-oxidation, α-amination and some C-C bond framing reactions. [84].

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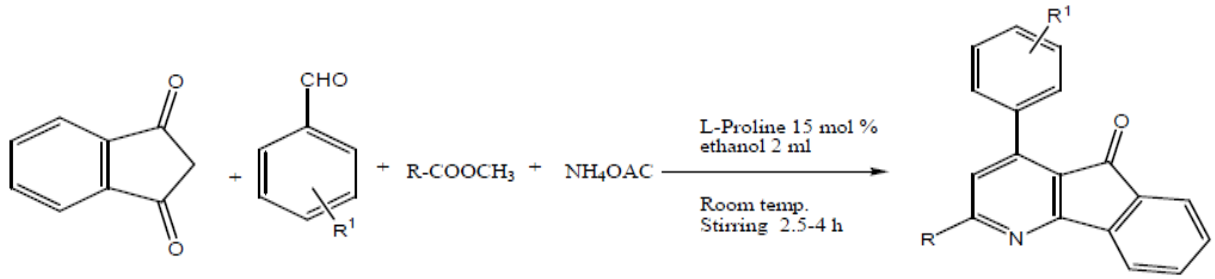
Multicomponent Reactions:

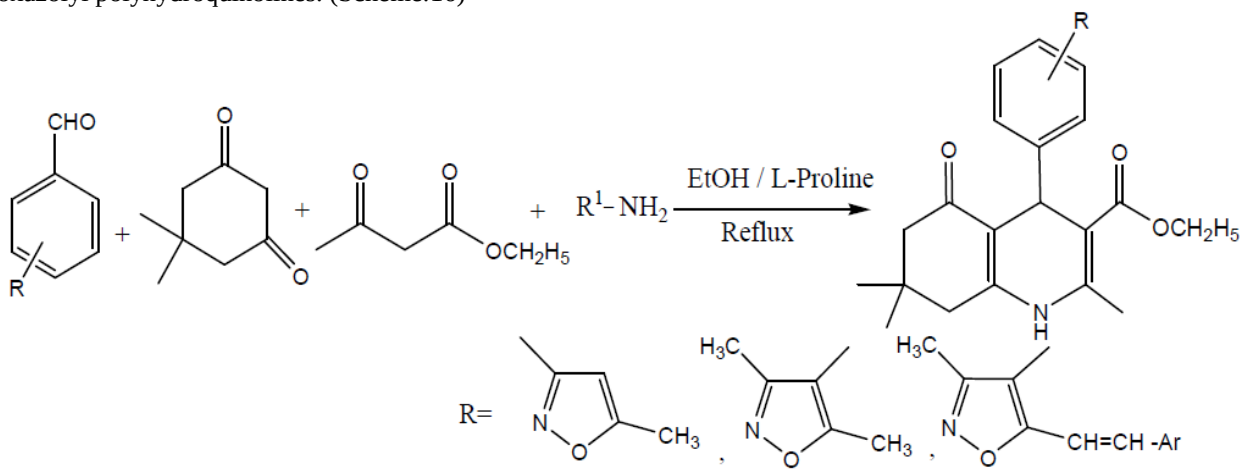
Chhanda Mukhopadhyay and his associates have functioned with the synthesis of different profoundly substituted pyridines at room temperature. This is accounted for interestingly. This gentle and simple efficient synthesis was catalyzed by L-proline (15 mol%) and it gave exceptionally substituted with incredible yields of pyridines at surrounding temperature.



Scheme 15: Synthesis of highly substituted pyridines

The creators at last reason that, this effortless and novel one-pot multicomponent technique catalyzed by L-Proline 15 mol% gave the substituted pyridines [89] as yields.

E. Rajanarendar et al [90] have proposed as the L-Proline catalyst in one pot combination Hantzsch condensation of isoxazolyl polyhydroquinolines. (Scheme:16)



Scheme 16: Synthesis isoxazolyl polyhydroquinolines

The product is generated using the low-cost organocatalyst L-Proline in the aforementioned process. It demonstrates a more efficient and alternative catalyst for one-pot synthesis [90,91].

Three component reactions :

Ali Reza Karimi and colleagues have created a synthetic route to superior diastereoselectivities. cis-isoquinolonic acids[156] catalysed by L-Proline in a three-component one-pot reaction that produced outstanding yields. The reaction between aromatic aldehydes, anilines, and homophthalic anhydride is catalysed by L-Proline (10 mol%) as an organocatalyst in this process.

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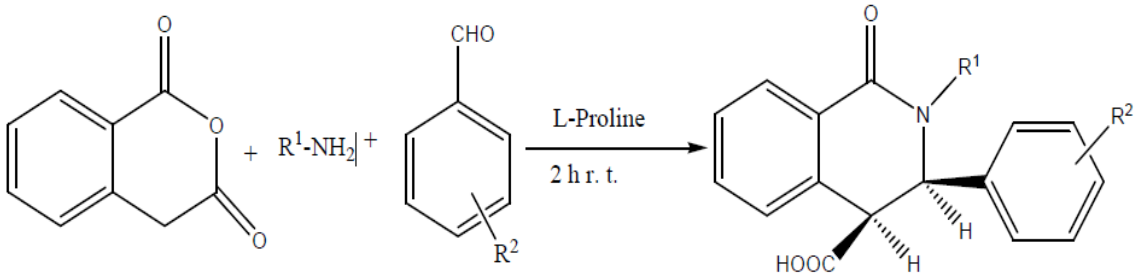
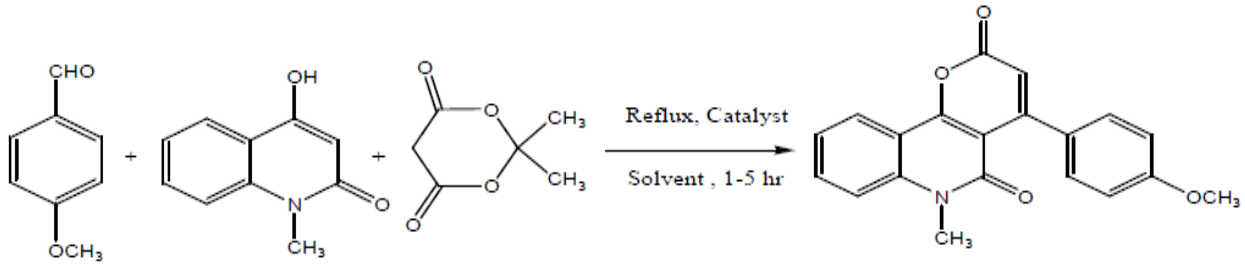


Scheme 17: Synthesis of cis-isoquinolonic acids

They have described a simple and productive procedure for cis-isoquinolonic acid multicomponent reaction. The organocatalyst is LProline, and proline can catalyze productively. Since this reaction result is diastereoselective and has a high return, the novel discovered compounds might have chemotherapeutic potential [92].

Songlei Zhu [93] used L-Proline as an organocatalyst for the synthesis of Pyrano[3,2-c]quinolin-2,5-dione derivatives in another one-pot synthesis.

They have worked on the synthesis of 4-aryl-6-methyl-3,4-dihydro-2H-pyrano[3,2-c]quinolin-2,5(6H)-dione derivatives. Aromatic aldehydes, 4-hydroxy-1-methylquinolin-2(1H)-one, Meldrum's acid, and L-proline in catalytic amounts created the intended result in this three-component reaction [94]. Scheme 18 illustrates the reaction.



Scheme 18 : The typical reaction

The desired compound was obtained in 91 percent yield when the reaction was carried out in the presence of L-proline (10 mol%) in ethanol, and when different solvents were used, the results showed that ethanol performed much better than acetonitrile, chloroform, acetic acid, N,N-dimethylformamide (DMF), and water. The improved condition was then applied to the synthesis of various estimated product derivatives.

In a one-pot three-component aza-Diels–Alder reaction, E. Rajanarendar et al have employed L-Proline[91] in 2012 and PTSA in 2015[93].

They used aromatic or isoxazoleamines and aromatic aldehydes with nitrostyrylisoxazoles with an organocatalyst to synthesise aryl or isoxazole imines in situ, yielding isoxazolyl tetrahydroquinolines or isoxazolo[2,3- a]pyrimidines as end products.

The reaction was initially begun by blending an equi. molar combination of aniline, benzaldehyde, and nitrostyrylisoxazole with of L-Proline (10 mol percent) in acetonitrile as the solvent for 3 hours at room temperature (scheme:19).

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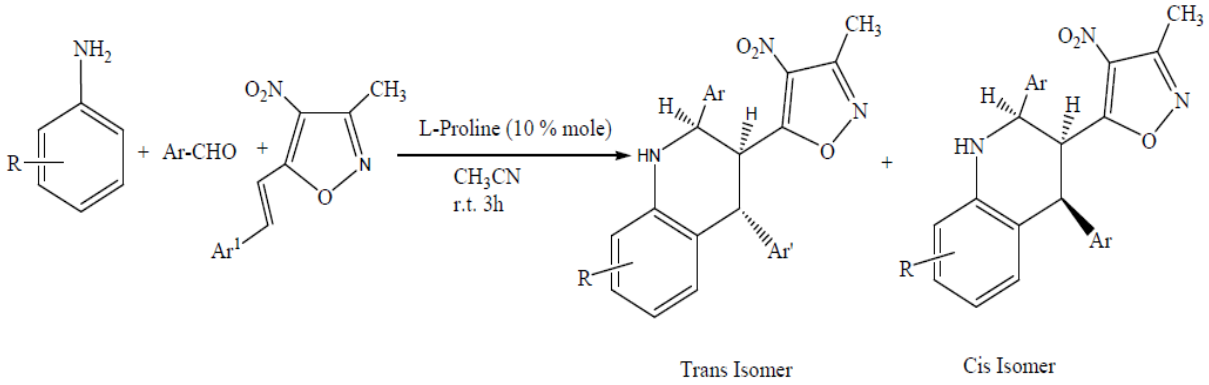
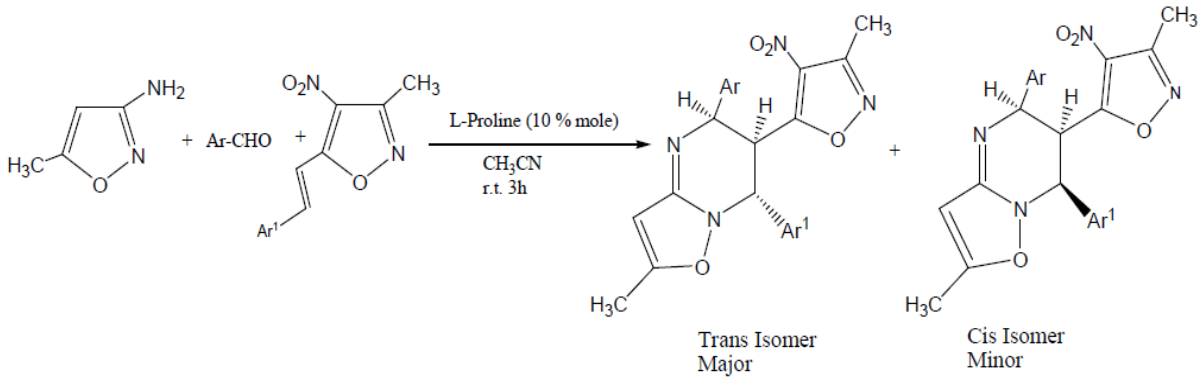


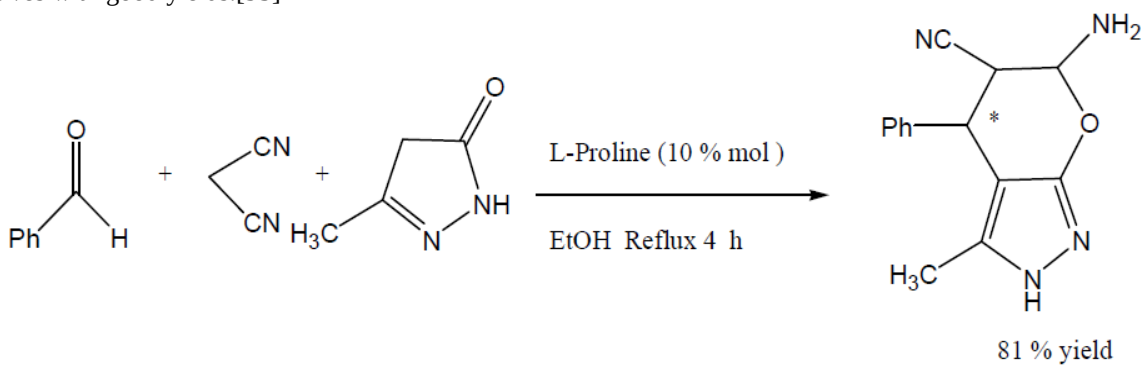
Scheme 19: One-pot synthesis of isoxazolyl tetrahydroquinolines

They examined the three-component reaction of 3-aminoisoxazole and benzaldehyde with nitrostyrylisoxazole in acetonitrile with L-proline (10 mol%) at room temperature. As illustrated in Scheme 20, the reaction produced isoxazolo[2,3-a]pyrimidines[90] as major and minor products in excellent yields.



Scheme 20:One-pot synthesis of isoxazolyl tetrahydroquinolines

Noha M. Hilmy Elnagdi et al. have studied the multicomponent reaction (MCR) of aromatic aldehydes and malononitrile with different active methylenes within the sight of L-proline, which yielded stereospecific pyran and thiopyran derivatives with good yields.[95]



Scheme 21: Synthesis of 6-amino-3,4-dimethyl-4-phenyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

II. CONCLUSION

In conclusion, among all organocalatysts, the invention and application of L-Proline has become the most demanding catalyst. Due to its capacity to conduct a number of transformations, literature and publications over the most recent years have demonstrated its rapidly expanding importance in organic synthesis. It is also complimented by their promptly accessibility, nature friendly, stability, tolerance to moisture and water, easy handling.

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