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L-Proline an efficient catalyst for synthesis of Triazole, Tetrazole derivatives: A Review

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Abstract

L-Proline, an a-amino acid, has emerged as an efficient organocatalyst for the synthesis of various heterocyclic compounds. In recent years, several studies have reported the use of L-Proline as a catalyst in different synthetic protocols for the preparation of diverse heterocyclic structures including triazole, tetrazole, and other heterocyclic compounds. The unique structure of L-Proline allows it to act as both a Brønsted acid and a chiral auxiliary, making it a versatile catalyst for a range of reactions. In addition to its catalytic properties, L-Proline is inexpensive, readily available, and environmentally friendly, making it an attractive alternative to other conventional catalysts. This review summarizes recent advances in the use of L-Proline as a catalyst for the synthesis of heterocyclic compounds, highlighting its versatility and potential applications in organic synthesis.

Keywords: L-Proline , organocatalyst, 1,2,3- triazole, tetrazole, heterocyclic compounds

1. INTRODUCTION:

Heterocyclic compounds, which contain at least one atom other than carbon in the ring, constitute an important class of organic compounds due to their wide range of applications in medicine, agrochemicals, materials science, and other fields. The development of efficient synthetic methods for the preparation of heterocyclic compounds has therefore been an active area of research in organic chemistry[1]. Over the past few decades, there has been growing interest in the use of catalysts to facilitate these synthetic processes, as they can enhance the rate, selectivity, and efficiency of reactions[2]. L-proline is a natural non-essential and important amino acid, one significant starting materials of amino acid transfusion, the crucial intermediate of synthesizing antihypertensive such as captopril and enalapril, and has been popularly utilized in food and medicine industry[3]. Especially, L-proline, which is an organic chiral molecular, and contains basic and acidic center Fig.1, has been used to catalyze various reactions[4]. To date, these reactions can be mainly divided to three types: (1) Asymmetric reactions. Such as asymmetric α-amination, asymmetric[5], Aldol reaction[6],and asymmetric Michael reaction[7], (2) Two and multicomponent reactions[4] (3) L-proline as the ligand coordinated with metal to catalyze reactions. For examples, C-X (C, N, O, S, and etc.) coupling, asymmetric reaction, and cascade reaction[8]. L-proline is a readily obtainable naturally occurring amino acid and is easy to obtain in high

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enantiomeric purity it has been reported as an eco- friendly catalyst for the synthesis of several heterocycles with high efficient, also L-proline used is a favorable way for addition, accompanied by cyclization or cycloaddition, of various one or more heteroatoms with heterocyclic compounds of different ring sizes that are of interest as antibacterial agents, herbicides, pharmaceuticals and as dyes[9]

In recent years, organocatalysis has been a subject of great interest due to the ease of obtaining, easily stored, stable, non-toxic and inexpensive. In addition, organocatalysis is a type of catalysis that can be done without the need for inert atmosphere or anhydrous conditions in mild conditions[10]. Organocatalysis has now seen an exponential growth in many publications, the interest in new catalysts and reactions in which asymmetric products can be produced in classical and valuable reactions using organocatalysts, such as Diels–Alder, Mannich, Michael reactions and others[11].

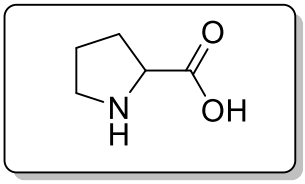


Fig.1 L-proline structure

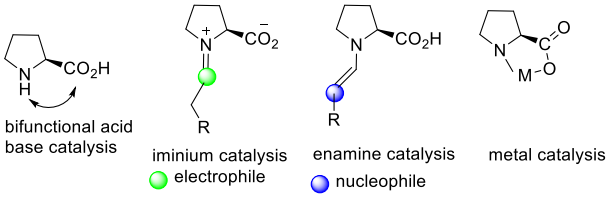


Fig.2 types of catalysis by proline

2. L-proline-catalyzed for triazole derivatives synthesis

1,2,3-Triazole is an important compound with a wide range of biological properties and chemical application[3]. The 1,2,3-triazole nucleus is a privileged structural motif that has been widely applied in the materials, chemical, and biological sciences , In particular, triazole rings are extremely attractive owing to their remarkable pharmaceutical and biological functionalities which have been reported to show good serine protease inhibition activity, antimicrobial effects, and promising anticancer properties[12].

The copper-catalyzed multicomponent reaction for the synthesis of 1H-[1,2,3]triazolo[4,5-c]quinolone derivatives in the presence of L-proline as catalyst was developed to prepare 1,2,3-triazole ringsas showed in the (figure 2). [12]

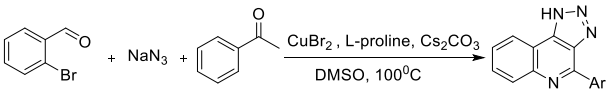


Fig.3 Copper-Catalyzed Multicomponent Reactions in the presence of L-proline as catalyst

The CuI/L-proline system in glycerol was used as a solvent to perform the CuAAC reaction to synthesis of triazole derivatives without an inert environment as showed in the (figure 3)[13].

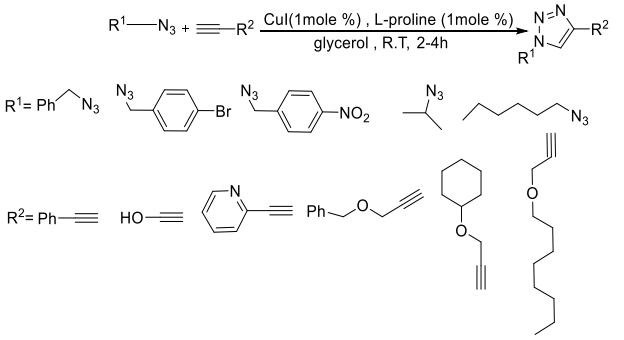


Fig.4 Synthesis of 1,4-disubstituted 1,2,3-triazoles

The synthesis of a series of 4,5-diaryl-2H-1,2,3-triazoles from cyanostilbene analogs of benzo[b]thiophene, benzo[b]furan, and indole, catalyzed by L-proline via Lewis base-catalyzed one-step [3+2]cycloaddition of azide as showed in the(figure 4)[14].

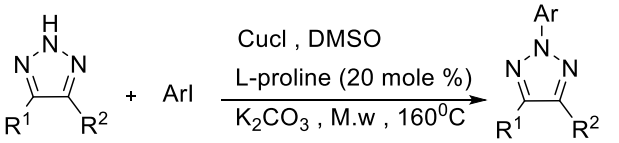


Fig.5 N2 Arylation of substituted 1,2,3-triazoles is catalyzed by copper

2-Iodobenzamides, terminal alkynes, and NaN_3 were involved in an intermolecular domino C-N coupling/azide alkyne cycloaddition reaction that was aided by an in-place copper catalyst made of CuBr and L-proline.The necessary chemicals were produced in this reaction in high yields, although only iodobenzamides were compatible with the process. The transformation produced the desired 2-(1,2,3-triazolyl) benzamide in DMSO at 90 0C with an 82% yield, but no product was seen without L-proline, as shown in the (figure 5)[15].

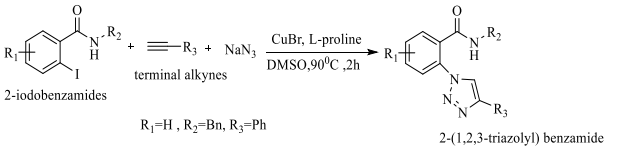


Fig.6 CuBr-catalyzed tandem reaction in the presence of L-Proline

The efficient method was established to synthesis series of 4,5-diaryl-2H-1,2,3-triazoles from cyanostilbene analogs of benzo[b]thiophene, benzo[b]furan and indole, catalyzed by L-proline via Lewis base-catalyzed one-step [3+2]cycloaddition of azide as showed in the (figure 6)[16].

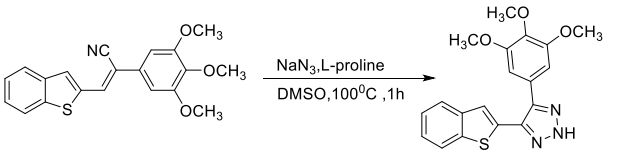
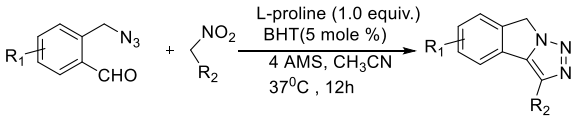


Fig.7 Synthesis of 4-(benzo[b]thiophen-2-yl)-5-(3,4,5-tri methoxyphenyl)-2H-1,2,3-triazole

A method involving tandem proline-catalyzed Knoevenagel condensation and intramolecular azide-nitroalkene cycloaddition has been employed to synthesize functionalized *[a]*-fused 1,2,3-triazoles as seen in the (figure 7).[17]



R_1 = H, 4-OMe , 2-OMe , 4-OMe, 2-OH,4-OH , 4-Br

R_2= CO_2Et , SO_2Ph,$CONHCH_3$,$COPh$,$PO(OEt)_2$

Fig.8 Generality of triazole-fused isoindoline synthesis

The present study employs L-proline, a cost-effective and easily accessible organo catalyst, for the direct synthesis of Mannich adducts from an unsubstituted azole, paraformaldehyde, and a ketone. The reaction was conducted using DMSO and H_2O as solvents, as seen in the (figure 8).[18]

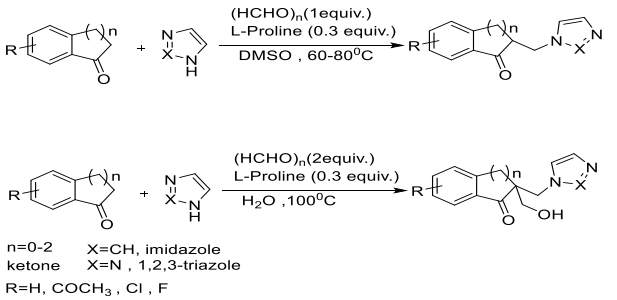
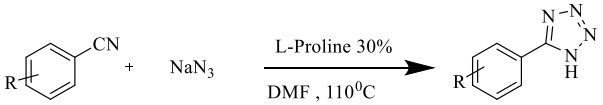


Fig.9 L-Proline-catalyzed direct Mannich adducts prepared from an unsubstituted azole, Paraformaldehyde, and a ketone in DMSO, H_2O as solvent respectively

3. L-Proline-catalyzed for tetrazole derivatives synthesis

Tetrazoles are a significant group of nitrogen-containing heterocycles that have a wide range of uses in a variety of disciplines, such as chemical synthesis, medicinal chemistry, chemistry of coordination and material science.[19] The tetrazole motif is a crucial synthetic scaffold that has found widespread use in a variety of industries as well as in sectors including medical, biochemistry, pharmacology, and industry as materials, such as in photography, imaging chemicals, and military technology.[20]

L-proline acts as a catalyst in the straightforward and effective synthesis of a series of 5-substituted 1H-tetrazoles from structurally different organic nitriles and sodium azide as showed in the (figure 10)[19].



R=H ,CH_3,OCH_3,OH,NO_2,Cl,

Fig.10 L-Proline-Catalyzed Synthesis of tetrazoles

Bhagate and Telvekar[21] was introduced very good applicable way for synthesis of tetrazole from organic nitrile , thiocyanates and cyanamides with sodium azide in one to two hours to yield high percent of products of 5-substituted 1*H*-tertazoles as shown in the figure 11.

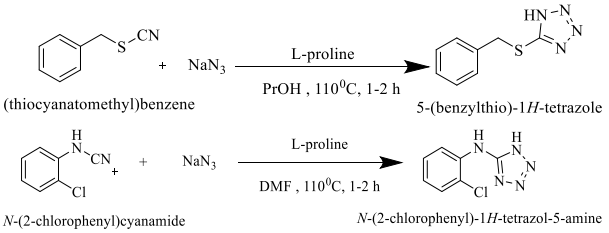


Fig.11 Proline-catalyzed synthesis of 1*H*-Tetrazole

Ugi-tetrazole product 4a was prepared by using protic polar solvent (methanol) , it yielded 78% after 12 hours , figure 12 showed Ugi-tetrazole synthesis[22],

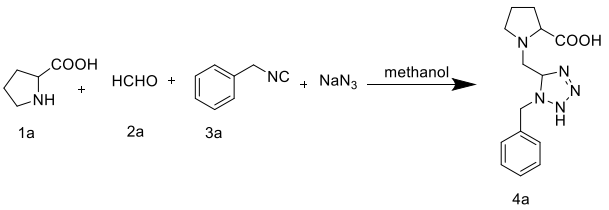


Fig.12 Ugi-tetrazole Synthesis

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