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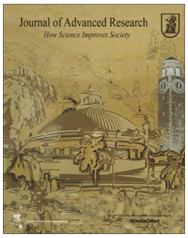

REVIEW

Bis[(L)prolinate-N,O]Zn: A water-soluble and recycle catalyst for various organic transformations

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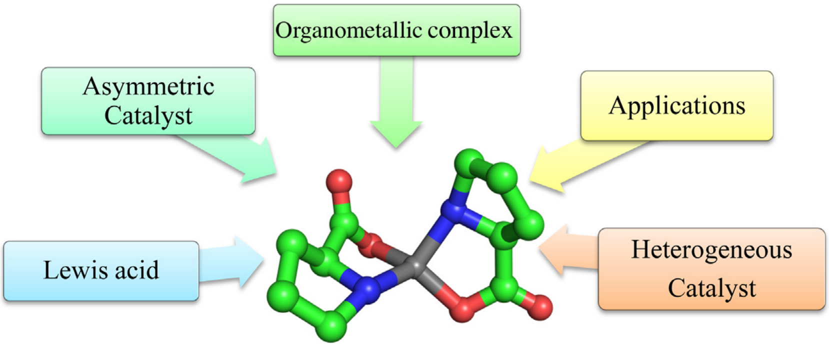
GRAPHICAL ABSTRACT



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ABSTRACT

Under the green chemistry perspective, bis[(L)prolinate-N,O]Zn (also called zinc–proline or Zn $[(L)\text{-pro}]_2$) has proven its competence as a promising alternative in a plethora of applications such as catalyst or promoter. Owing to its biodegradable and non-toxic nature of bis[(L) prolinate-N,O]Zn, it is being actively investigated as a water soluble green catalyst for synthetic chemistry. Bis[(L)prolinate-N,O]Zn are readily utilized under mild conditions and have high selectivity and reactivity with broad range of substrate acceptance to make it better reaction

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medium for a wide variety of organic transformations. This Review summarizes the till date literature on its synthesis, characterization, and its catalytic role in various organic reactions.

Roona Poddar is an Assistant Professor of Chemistry and teaches post graduate student in Department of Chemistry, University of Delhi, Delhi, India. She has a Master Degree in Chemistry from Indian Institute of Technology (IIT) Delhi, and a Ph.D. in Chemistry from the University of Delhi (DU). She has worked as Post Doctorate Fellow for three years before joining as faculty in Department of Chemistry, University of Delhi, Delhi, India She has published numerous research papers in peer reviewed journals.

Arti Jain obtained her PhD (Organic Chemistry) from University of Delhi, India, in 2013. She is currently an Assistant Professor in Department of Chemistry, Daulat Ram College, University of Delhi, India. Her research area is based on the exploration of newer environmental benign protocol for various traditional reactions, use of agricultural waste material to apply cradle to cradle approach etc. She has 4 years of teaching experience to the undergraduate students. She is still doing research in the college.

M. Kidwai is working as Professor at the Department of Chemistry, Delhi University, delhi, India. He has 30 years of teaching experience at the university level. Currently he has 260 papers in the Journal of National and International repute and supervised 40 Ph.D. students and 31 M. Phil students. Pioneer in the field of Green Chemistry, who has started first research work in this field in India in 1990. From Asia among 5 members is inclusive of himself in the international Advisory board make Globally figure in the exclusive field of Green chemistry.

Introduction

The recent past scientific and technological advances have provided a great insight regarding the catalytic properties and mechanism of metal-amino acid complexes. Metal salts with chiral amino acid have been used as promising materials for biological as well as chemical advancement as they tend to exhibit the advantage of the metal salts and the asymmetrical organic amino acids [1,2]. α–Amino acids could act as chelating ligands and form five member ring because they have two types of coordination atoms [3–7] due to the presence of proton acceptor amino group (NH_2) and the donor carboxylic acid group (COOH) in them.

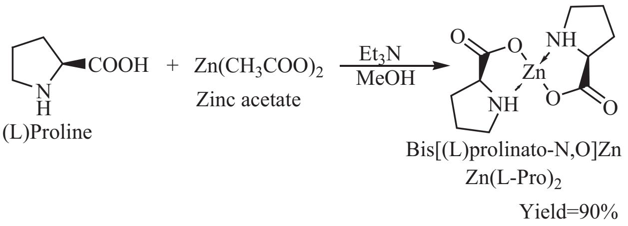
Zinc catches eyes of several researchers due to several reasons, as it can show various coordination geometries, is abundant in nature, is redox-inactive [8], and forms stable complexes with nitrogen. Zinc is an essential micronutrient, which is involved in various biological processes such as transcription, cell signaling catalysis, hormone synthesis, and structural integrity of cell membrane [9,10]. From the biological point of view, more than 300 zinc metallo-enzymes covering all six classes of enzymes have been discovered [11,12]. In most cases, the zinc ion is an essential cofactor for the observed biological function of these metalloenzymes. By the virtue of biological activity, thousands of synthetic zinc complexes have been formed either to mimic natural structure or to completely diverge from the natural platform [13–18]. Moreover zinc is present in active site of class II aldolases (an enzyme) witnessing the bis[(L)prolinate-N,O]Zn as a valid candidate for aldolase mimics.

Deprotonated amino acid coordination chemistry is dominated by the formation of the nitrogen and oxygen chelating motif producing the geometrically (and energetically) favoured five membered metallocyclic compounds [19].

Stability of the zinc complexes varies with different amino acids [20–23]. Metal ion-ligand affinity increases as the polarizability of the donor atom is increased (O < N < S) [24]. So there is an increase in selectivity for the amino acid having (N, S) linkage followed by (N, O). It has been shown that cysteine and its derivatives are more selective for metal ion-ligand binding as compared to other amino acid having (N, O) linkage [25]. The cumulative energy required for the acid dissociation of carboxylic acid to carboxylate ion and ammonium ion to secondary amine for proline with Zinc (II) is lower than other amino acid which has primary amine group and acid group. In secondary amine, there is more inductive effect which makes it more labile for acid dissociation constant [26,27].

Complex synthesis

Originally Darbre and Machuquiero have synthesized this bis[(L)prolinate-N,O]Zn complex. They have synthesized bis[(L)prolinate-N,O]Zn complex by adding small quantity of Et_3N



Scheme 1

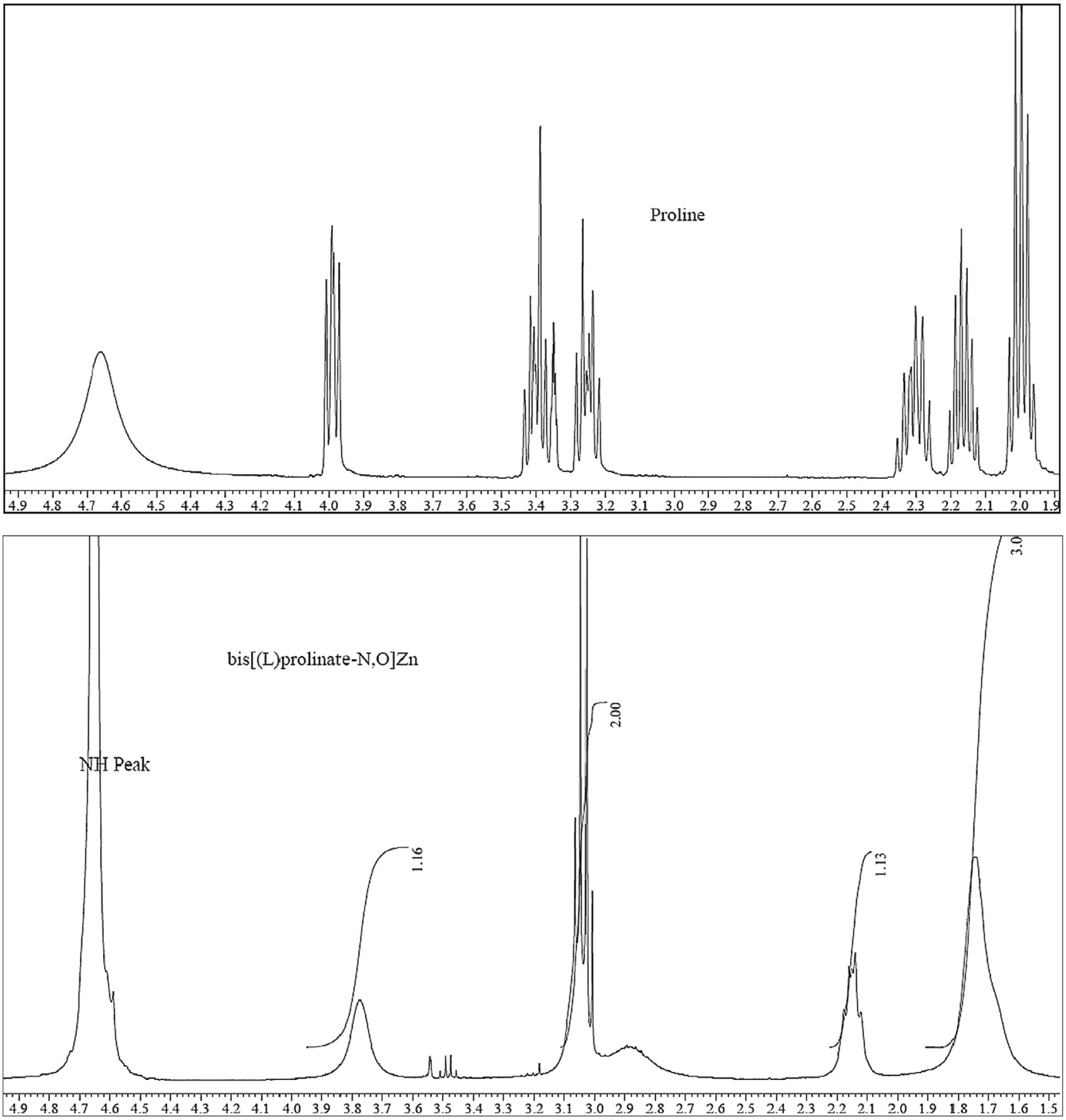


Fig. 1 ^{1}H NMR of proline and bis[(L)prolinate-N,O]Zn.

as base to the proline in methanol followed by zinc acetate (double ratio of amino acid) (Scheme 1). After stirring a white precipitate was obtained which could be separated from reaction medium by simple filtration with good yield [28].

Structure and characterization of the catalyst

^{1}H NMR analysis

In the comparison of ^{1}H NMR of proline and bis[(L)prolinate-N,O]Zn complex in Fig. 1, ^{1}H NMR of the bis[(L)prolinate-N,O]Zn showed that there is proton shielding of protons of proline and the splitting pattern resolved in the presence of Zinc metal ion. Shielding is more in C(2), which indicate the formation of carboxylate ion; moreover, there is a noticeable shielding in C(5) as compared to proline, which further confirms the synthesis of bis[(L)prolinate-N,O]Zn [28].

FTIR analysis

In IR spectra of bis[(L)prolinate-N,O]Zn complex shown in Fig. 2, the shift observed confirms the formation of the target compound in comparison with L-proline. There was decrease in broad band at 3422 cm^{-1} for OH stretching of COOH. The NH stretching band at 3220 cm^{-1} was very prominent while twisting was observed at 1205 cm^{-1}. The COO$^-$ vibration peak appeared comes at 1410 cm^{-1} along with the carbonyl peak of carboxylic group at 1608 cm^{-1} while the in-

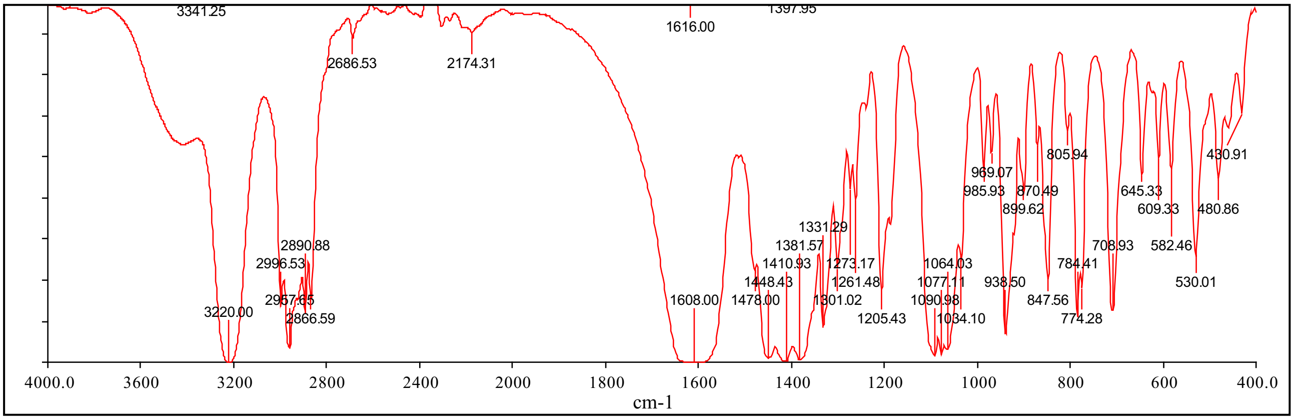


Fig. 2 FTIR of bis[(L)prolinate-N,O]Zn.

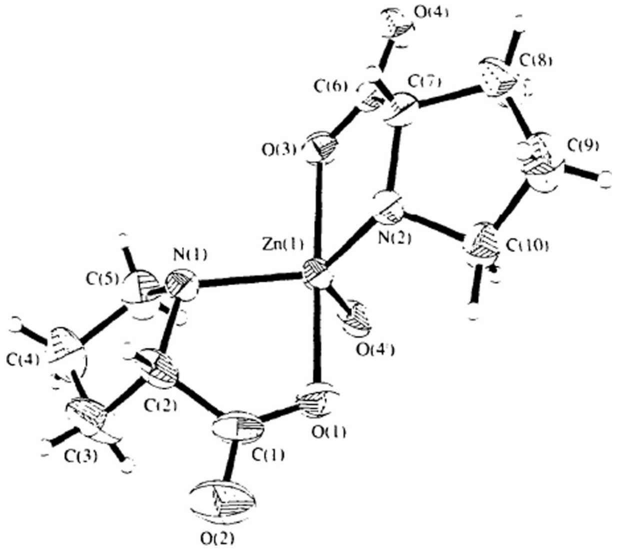


Fig. 3 Single crystal X-ray diffraction of bis[(L)prolinateo-N,O] Zn.

plane deformation at 774 cm^{-1}, scissoring at 703 cm^{-1} and rocking vibrational peak o at 530 cm^{-1} were also observed. The CH$_2$ stretching, wagging, and rocking were observed at 2800–3216, 1330–1300, and 938–847 cm^{-1} respectively. The C—N stretching was observed in between 1330 and 1450 cm^{-1} while the C—N stretches due to absorption were noticed at 1077 and 1064 cm^{-1} [29].

Single crystal X-ray diffraction

Structure of bis[(L)prolinate-N,O]Zn complex was first shown by Chew H-N, and he described *trans* complex [Zn (C$_6$H$_7$NO$_2$)$_2$] in Fig. 3 [30], as a spiral structure formed along the 2_1 direction with atoms O4 (2−x, y$^{-1/2}$, −z), Zn, N(2), C(7) and C(6) constituting a repeating unit. The Zn atom is pentacoordinate, the fifth coordination site being occupied by the symmetry related atom O(4 i) [symmetry code: (i) 2−x, y−i ∼, −z] of a neighboring proline molecule so that an infinite polymeric chain is generated. The polymer shows a helical structure along the 2∼ direction. The zinc coordination here is unique, as most zinc-amino acid complexes are hexacoordinate. The Zn atom has trigonal bipyramidal geometry with O(4 i), N(1) and N (2) while O(1) and O(3) occupying the axial position and the pyrrolidine rings are transformed from planner to 3-dimension shape. The distance Zn—O and Zn—N and all the bond lengths of the proline unit were comparable and normal for metal-coordinated amino acids [31–34]. The angle between O(3)—Zn(1)—O(1) is nearly linear with value of 173.8 (1)°.

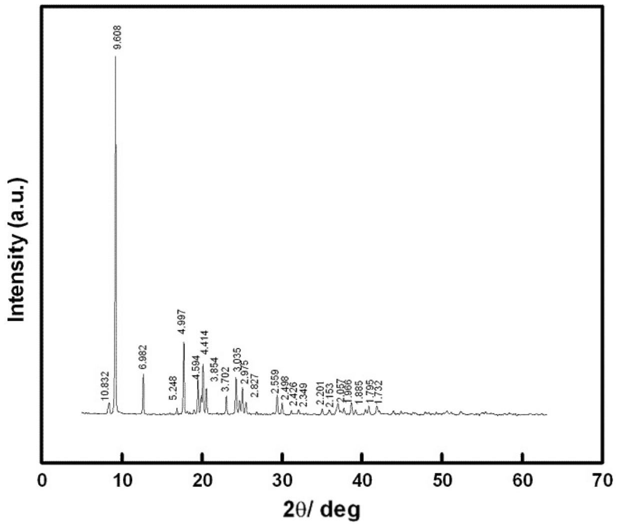


Fig. 4 Powder XRD of bis[(L)prolinate-N,O]Zn.

Powder X-ray diffraction

Kidwai and his coworkers group have shown for the first time X-ray diffraction of the complex in the range 2θ = 0–100 as shown in Fig. 4. The characteristic peak obtained from powder XRD of bis[(L)prolinate-N,O]Zn of specific *d* value has showed that the complex is orthorhombic in structure since it is in agreement with data card 47-1919JCDPS [35,36].

TEM image

For crystal assessment of bis[(L)prolinate-N,O]Zn, TEM technique was used. Kidwai and his co-workers (2011) had

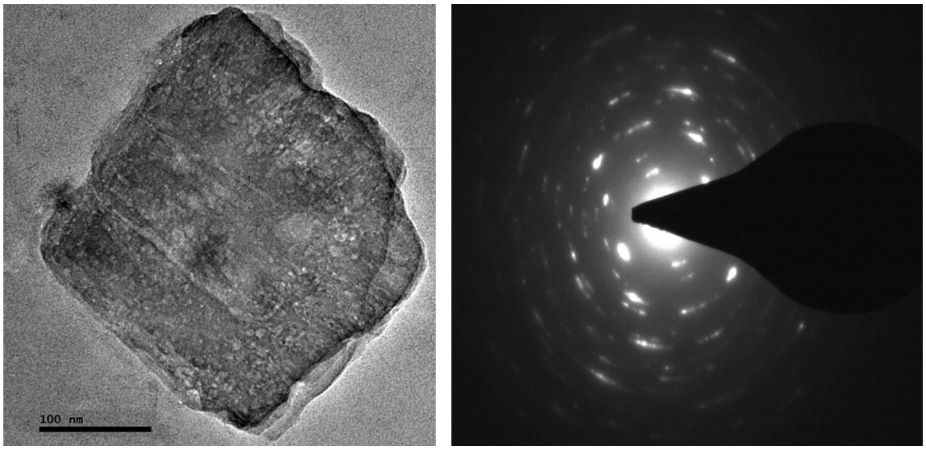


Fig. 5 TEM images of fresh bis[(L)prolinate-N,O]Zn.

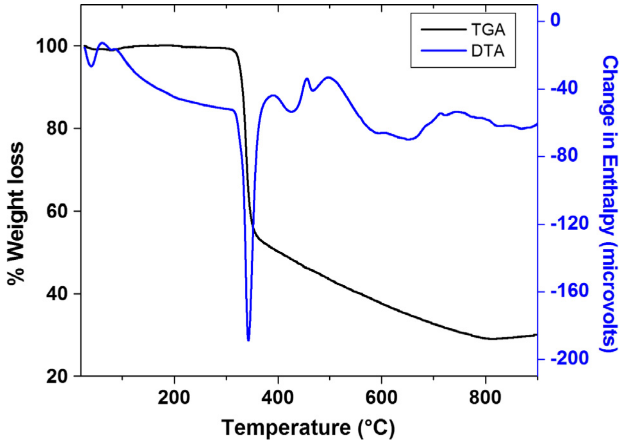


Fig. 6 TGA/DTA graph of bis[(L)prolinate-N,O]Zn.

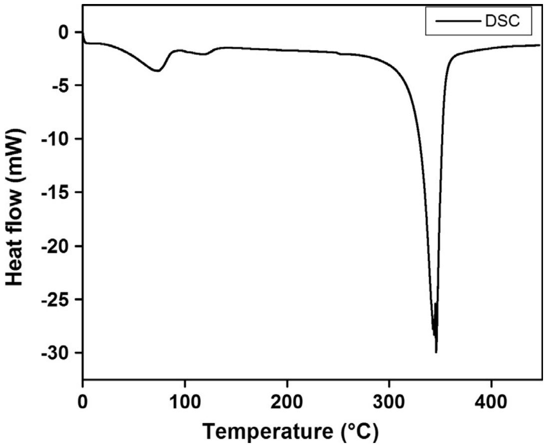


Fig. 7 DSC graph of bis[(L)prolinate-N,O]Zn.

acquired various images of complex on carbon coated grid and confirmed the crystalline in nature of the complex as depicted in Fig. 5 [37].

Thermal analysis

The thermal stability of bis[(L)prolinate-N,O]Zn complex was evaluated by TG/DTA and DSC experiments as described by kidwai and research group in Figs. 6 and 7 [38]. Briefly the complex was heated at the rate of 10 K min^{-1} in N_2 atmosphere. A blunt endothermic peak due to the release of adhered water molecules was observed at 100.62 °C in the DTA curve. The purity of crystal was further confirmed by the sharpness of endothermic peak at 342.81 °C in the DTA curve which matches the melting point of bis[(L)prolinate-N,O]Zn. TGA curve showed the detailed decomposition of the complex (Fig. 6). Differential scanning calorimetry (DSC) study was carried in the inert atmosphere from the temperature range 20–500 °C with a heating rate of 10 K min^{-1}. Bis[(L)prolinate-N,O]Zn undergone through an irreversible endothermic transition at its melting point 342.81 °C. Henceforth it was confirmed that the material is stable up to its melting point making it suitable for various applications, where the complex is utilized at high temperatures.

Solubilities of bis[(L)prolinate-N,O]Zn

Bis[(L)prolinate-N,O]Zn is highly soluble in water and insoluble in organic solvent due to its ionic nature. The N, O and Zn atoms form H-bond with water molecules and make it hydrated which is not possible in organic solvent. The recyclability of complex depends upon its solubility in the reaction medium. Majority of the reactions with complex are performed in aqueous medium and extracted with organic solvent (Ethyl acetate, ether, chloroform or DCM) from the aqueous layer and reused for further reaction [29,36,37]. In aqueous medium the reactivity of metal complexes is restricted because water molecules can participate as substrate for metal bonding. Criterion for water stable Lewis acids (improbable to hydrolysis) has been investigated based on the relationship between the catalyst activity with two parameters *viz* water exchange rate constant and hydrolysis constant [26]. Zinc complexes are found to be appropriate for various organic reactions in aqueous medium.

Bis[(L)prolinate-N,O]Zn distribution in biological system

Although metal ions and complexing agents occur ubiquitously in biological tissues and fluids, few studies have been done for the distribution of the metal ions among the competing ligands in such systems [39,40]. First time equilibria of complex were understood in Bjerrum's book "Metal Ammine Formation in Aqueous Solution" that was published in Denmark in 1941 [42]. It has been confirmed that the equilibrium between a complex forming agent and an ion is usually thermodynamically reversible and occurs instantaneously without significant energy of activation. So equilibria can be written in mass-action equations. Furthermore, Bjerrum has established that complex formation is occurred in stepwise course. Quantitative studies by Albert (1950) for the avidity of L-proline for Zn(II) ion have been reported [41]. It was found that pKa value for L-proline is 10.68 and stability constant of the bis[(L)prolinate-N,O]Zn complex is 10.2, implying that L-proline has the greatest avidity for Zn(II) ion and forms a stable complex with it.

The computed distribution of Zn(II) ion among seventeen amino acids present in human blood plasma had been studied and approximately 50% of the Zn(II) is coordinated to cysteine and histidine (as their stability constant is highest among all amino acids), but considerable amino acid complex formation occurs with most of the other amino acids [43].

Recently, metal ions have been used in metallization of biomacromolecules [44]. These processes rely upon the specific metal ion amino acid interaction, which allow an efficient metal deposition and attachment to biological systems. The molecular mechanism of the metallization process was studied by means of chemical quantum calculations of metal ion-amino acid interaction [45]. An interesting feature of the zinc (II) ion is its ability to adopt a tetrahedral, a trigonal bipyramidal, or an octahedral geometry depending on the ligands bonded to the ion. On the other hand the Zn^{2+} aqua ion, as well as Zn^{2+} complexed to two N donors, is six-coordinated [46,47]. Zinc(II) ion coordinated by at least three N or S donor forms either tetrahedral or trigonal bipyramidal complexes [48]. A theoretical study of Zn(II) interaction with L-proline was carried out using density functional theory method with Becke's three parameter, hybrid exchange functional and the Lee-Yang-Parr correlation functional (B3LYP). A moderately high affinity ($-13.4\ \mathrm{kJ\ mol^{-1}}$) was predicted for the proline residue complexing a zinc ion *via* the nitrogen atom of the five membered ring [49].

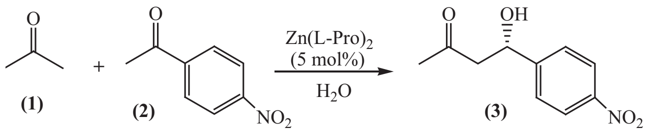
In plant, there is increase in concentration of proline to get rid of heavy metals which are toxic in nature. To check the importance of proline in plant reactions to heavy metal stress, Sharma et al. have studied the effect of proline on Zn-induced inhibition of glucose-6-phosphate dehydrogenase and nitrate reductase *in vitro*. Proline appeared to protect both enzymes against Zinc. There were no indications of any significant role for proline-water or proline-protein interactions. The significance of these findings with regard to heavy metal-induced proline accumulation *in vivo* has been discussed [50]. A synergistic immunological adjuvant formulation having bis[(L)prolinate-N,O]Zn complex as synergist has been patented which showed the pharmaceutical properties associated with the complex [51].

Bis[(L)prolinate-N,O]Zn in organic synthesis as catalyst

Bis[(L)prolinate-N,O]Zn has received immense attention over the last eight years which provided intriguing opportunities in organic synthesis because of its ability to act as Lewis acid and ease of preparation. The following section illustrates various synthetic approaches exploiting bis[(L)prolinate-N,O]Zn as a catalyst. In most cases, water had been used as a part of the reaction media. Henceforth, in each synthetic approach, examples related to the use of this organometallic complex in biphasic systems, water saturated organic solvents and even water as a sole reaction media have been described. This section examines the growing opportunities and applications of bis[(L)prolinate-N,O]Zn catalyzed reactions. Originally Darbre et al. (2003) have shown bis[(L)prolinate-N,O]Zn as a selective catalyst for the direct aldol reaction in aqueous media. They have investigated that 5 mol% of the Zn complexes of lysine, arginine and proline are catalysts for the aldol addition of acetone **(1)** and *p*-nitrobenzaldehyde **(2)** in aqueous medium, giving considerable yields and enantiomeric excess up to 56% at room temperature (Scheme 2) [28].

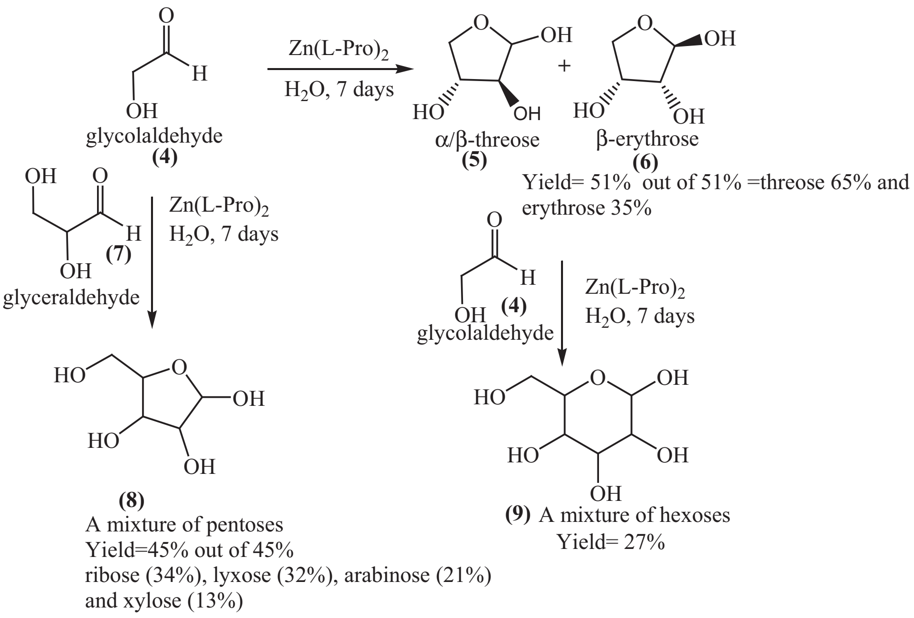
The catalytic ability of other with 5 mol% Zn-(L)-amino acid complexes had been studied in water-acetone medium. The complexes were prepared and isolated as described for Zn-proline [52–57]. In the absence of zinc, product **(3)** was obtained in 74% yield and 6% *ee* with the *R*-1 enantiomer in excess. The higher *ee* values were observed with different amino acids requiring chiral Lewis acid as catalyst. Moreover in 2004, Darbre and Reymond et al. together explored the bis[(L)prolinate-N,O]Zn complex catalyzed pathway for the formation of sugars [58]. Bis[(L)prolinate-N,O]Zn complex catalyzed the aldolization of unprotected glycolaldehyde **(4)** in water to give tetroses **(5,6)** in 51 % yield which further aldolization gave hexoses **(9)** with 10% enantiomeric excess of the D-isomer (Scheme 3). A mixture of pentoses **(8)** was produced by the reaction of glycolaldehyde with glyceraldehyde **(7)** in the presence of bis[(L)prolinate-N,O]Zn complex in water.

The aldol reaction of 4-nitrobenzaldehyde catalyzed with three different ketones (2-butanone, cyclopentanone and cyclohexanone) in three different combinations with aqueous media, has been studied to explore selectivity of environmentally benign reaction. The combination included conditions are bis[(L)prolinate-N,O]Zn complex, $NaHCO_3$/bis[(L)prolinate-N,O]Zn complex and L-proline/bis[(L)prolinate-N,O]Zn complex. For the synthesis of *β*-hydroxy ketones $NaHCO_3$ was surprisingly found to be a proficient catalyst, showing high-quality diastereo- and regioselectivity within 9 h. Cyclopentanone **(17)** were mainly found to give *syn* diastereoisomers while cyclohexanone **(19)** produced *anti* isomers being the major product which was an exceptional result (Scheme 4) [59].

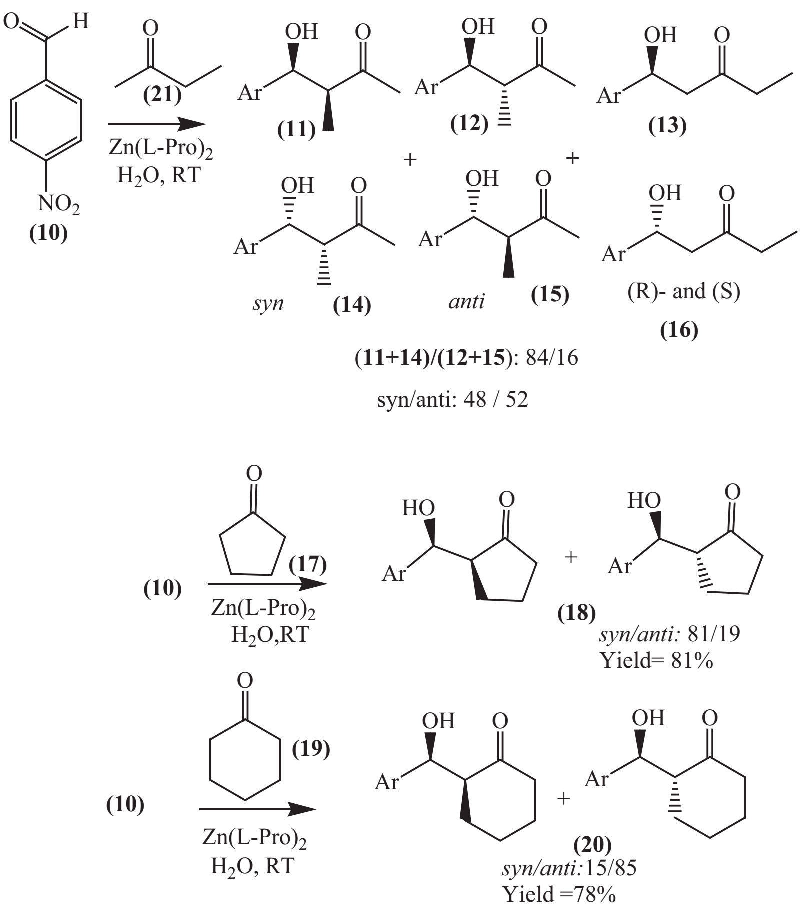


S Yield = 100%
ee= 56%

Scheme 2

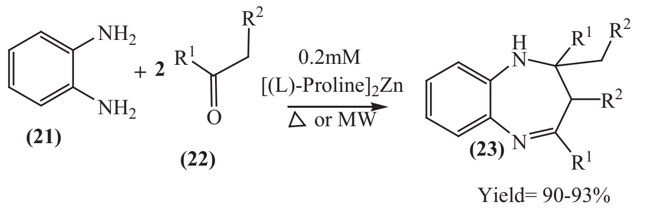


Scheme 3



Scheme 4

Sivamurugan and his research group have performed the reaction of *o*-phenylene diamine **(21)** and α-hydrogen carbonyl **(22)** with 0.2 mmol of bis[(L)prolinate-N,O]Zn as catalyst to produce 1,5-benzodiazepine derivatives a one pot reaction under solvent-free conditions [60]. The effectiveness of the catalyst has been checked by microwave irradiation technique as



a: R^1 = $-CH_3$; R^2=H

b: R^1 = $-CH_3$; R^2=CH_3

c: R^1 = $-CH_2CH_3$; R^2 = CH_3

d: R^1 =$-CH_2CH_2CH_3$;R^2=$-CH_2CH_3$

e: R^1 = CH_3;R^2=$-CH_2CH_3$

f: R^1 = R^2 = $-(CH_2)_4-$

g: R^1 = R^2 = $-(CH_2)_5-$

h: R^1 = C_6H_5 ; R^2 = H

i: R^1 = 4-ClC_6H_4; R^2 = H

j: R^1 = 4-BrC_6H_4 ; R_2 = H

k: R^1 = 4-OHC_6H_4 ; R^2 = H

Scheme 5

well as conventional method. 1,5-Benzodiazepine **(23)** was obtained in moderate to good yield (90–93%) in all the reactions within a shorter reaction time (2–3 mins) under microwave irradiation while in conventional the yield (80–88%) was lower and had in longer reaction time (2 h). The catalyst was recycled up to five times with marginal loss of its catalytic reactivity (Scheme 5).

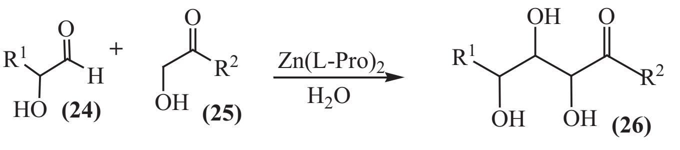
To explore the wide applicability of bis[(L)prolinate-N,O] Zn, the aldolization of different hydroxyl aldehydes and ketones was studied by Darbre group using the complex [61]. Glycolaldehyde **(4)** gave mainly tetroses whereas in the cross-aldolization of glycolaldehyde and *rac* glyceraldehydes **(7)**, pentoses accounted for 60% of the sugars formed with 20% of ribose. They suggested that generally, unprotected α-hydroxy aldehydes and ketones could undergo aldol additions in the presence of bis[(L)prolinate-N,O]Zn as catalyst in water. Depending on the starting aldehyde, the products formed may include tetroses, pentonse, hexoses, keto-pentoses, keto-hexoses with smaller yields of higher sugars. For the simplicity of analysis, the sugars were also reduced to polyols using $NaBH_4$ (Schemes 6 and 7) [62].

An appropriate mechanism was proposed by darbre for bis [(L)prolinate-N,O]Zn to catalyze the aldol reaction shown in Fig. 8. The chelating enolate formation took place by bonding of glycolaldehyde **(4)** to the zinc. This is similar step which occurs in class II aldolase enzyme having zinc (II) in active site as cofactor. The electron deficient carbonyl reacted with the enolate which does not require to coordinating with zinc.

The main difficulty to use pentoses as probable prebiotic reagents was the lack of stabilities in earlier days. Previously, the self condensation of formaldehyde in basic medium was used to synthesize pentoses to yield less than 1% of riboses [63]. So the investigations were carried out to escalate the amount and stability of pentoses. The results showed that synthesis of pentoses should be done using Lewis acid and maximum stability of products could be achieved at room temperature in aqueous.

In another publication by Lopez et al. [64], bis[(L)prolinate-N,O]Zn complex was depicted to catalyze the very famous aldol reaction of acetone **(1)** and broad range of aromatic aldehydes **(32)** in aqueous media, and even less reactive aromatic aldehydes such as methoxybenzaldehyde gave good yields. The reaction was also comprehensive to hydroxyacetone and dihydroxyacetone as donors (Schemes 8 and 9).

Heterocyclic aldehydes with acetone were also established to be appropriate substrate for the aldol reaction. Variation in molar concentration acetone was also done and good to better yields were achieved with even cyclopentanone. Moreover e 2-butanone and cyclohexanone underwent aldol reaction with 4-nitrobenzaldehyde. They also extended bis[(L)prolinate-N,O]



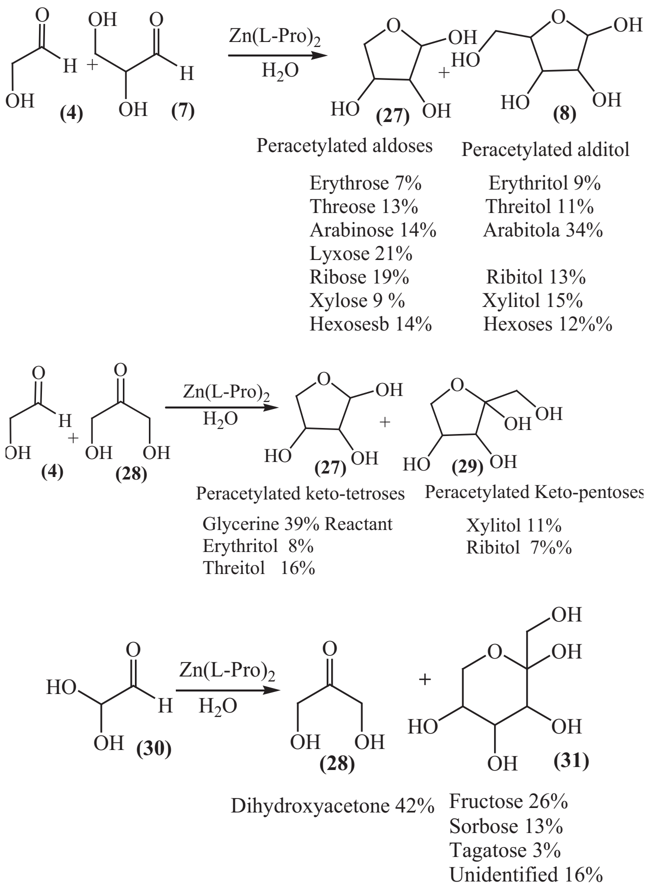
R^1 = H
R^1 = CH_2OH

R^2 = H
R^2 = CH_2OH

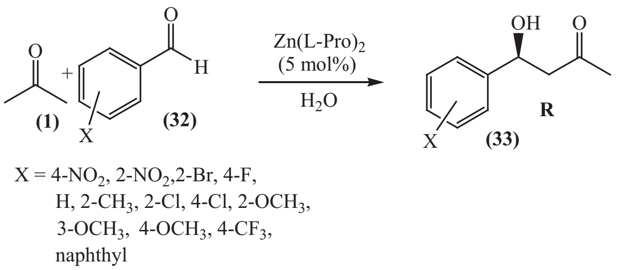
R^1 = R^2 = H
R^1 = CH_2OH, R^2 = H
R^1 = $CHOHCH_2OH$, R^2 = H
R^1 = H, R^2 = CH_2OH
R^1 = R^2 = CH_2OH

The product consisted of tetroses (51%), hexoses (27%) and unidentified compounds (22%). The tetroses consisted of 65% threose and 35% erythrose.The hexose mixture contained mainly glucose, galactose (together 40% of the hexose mixture) and talose (10% of the hexose mixture)

Scheme 6



Scheme 7



Scheme 8

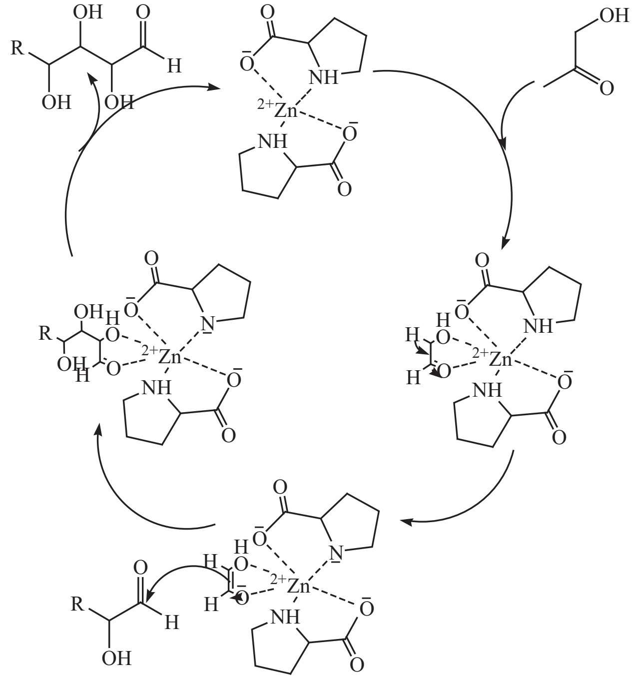


Fig. 8 Plausible mechanism for the bis[(L)prolinate-N,O]Zn catalyzed the formation of ribose and other pentoses.

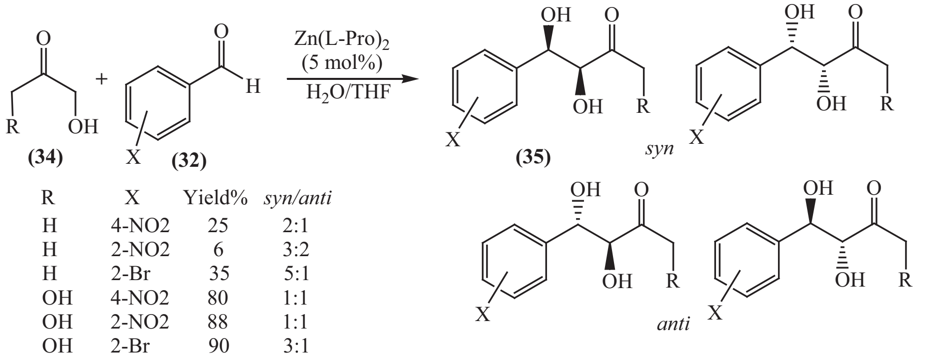
Zn complex catalyzed reaction with Hydroxyacetone and Dihydroxyacetone. Encouraging results were obtained with ketones too. They postulated a mechanism linking a formation zinc-assisted enamine, where zinc complexation stabilized the enamine intermediate [65]. Coordination to zinc stabilized the enamine in aqueous, possibility of the condensation with the aldehyde shown in Fig. 9.

In 2006, Kofoed et al. have explored the dual mechanism of bis[(L)prolinate-N,O]Zn complex catalyzed aldol reactions in water. They found that the aldol condensation of aldehydes with acetone in water medium under numerous catalyst *e.g.* proline, bis[(L)prolinate-N,O]Zn complex, (S)-(+)-1-(2-pyrrolidinomethyl)pyrrolidine and (2S,4R)-4-hydroxyproline progressed *via* an enamine mechanism, while the aldol reaction of dihydroxyacetone catalyzed by bis[(L)prolinate-N,O]Zn complex and by organic bases such as *N*-methylmorpholine occured under rate-limiting deprotonation of the α-carbon and formation of an enolate intermediate [66]. Bis[(L)prolinate-N,O]Zn complex appeared to be a particularly efficient catalyst for both enamine and enolate type catalyses. Addition of a base to bis[(L)prolinate-N,O]Zn complex induced precipitation of $Zn(OH)_2$ above pH 9, implying that the conjugate base $[(OH)((L)prolinate-N,O)_2]Zn$ was not available as a general base for deprotonating dihydroxyacetone, while the pH curve showed that proline could easily disintegrate from zinc upon protonation from pH 8 to pH 6 (Scheme 10).

Bis[(L)prolinate-N,O]Zn complex was shown to be an capable catalyst for the Hantzsch synthetic route for the synthesis of 1,4-Dihydropyridine (DHP) **(41)** derivatives using a broad variety of aromatic aldehydes **(39)** and dicarbonyl compounds **(40)** in aqueous medium under microwave irradiation. The Bis[(L)prolinate-N,O]Zn exhibited greater catalytic activity even with low MW power (≈200 W) and gave excellent yield (90–98%) in short reaction times (< 5 min) [67] (Scheme 11).

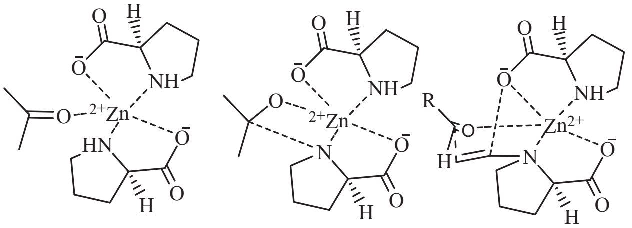
Quinoxaline derivatives show broad spectrum of biological activities. They have been used in dyes [68,69], pharmaceuticals [70,71] and building blocks for the synthesis of organic semiconductors [72]. An ecofriendly straightforward, proficient method for the preparation of quinoxalines **(44)** by the condensation of 1,2-diamines (**43**) with various 1,2-diketones (**42**) using bis[(L)prolinate-N,O]Zn as a catalyst has been reported by Heravi et al. in 2007 [73]. In his reaction acetic acid was used as a solvent which was unable to precede the reaction (Scheme 12).

Direct nitroaldol reaction by bis[(L)prolinate-N,O]Zn complex was performed in 2007 by Reddy et al. [74]. The Henry reaction or nitroaldol is one of the influential Carbon-Carbon bond formation reactions in organic chemistry to



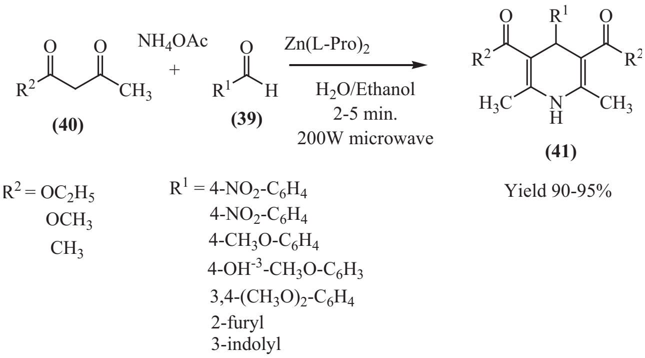
R	X	Yield%	*syn/anti*
H	4-NO2	25	2:1
H	2-NO2	6	3:2
H	2-Br	35	5:1
OH	4-NO2	80	1:1
OH	2-NO2	88	1:1
OH	2-Br	90	3:1

Scheme 9

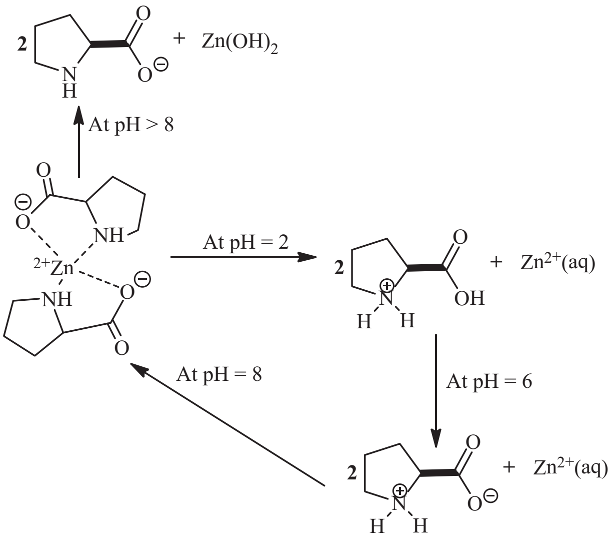


(36) (37) (38)

Fig. 9 Proposed intermediates for the zinc-supported enamine mechanism of the bis[(L)prolinate-N,O]Zn complex-catalyzed aldol reaction.



Scheme 11



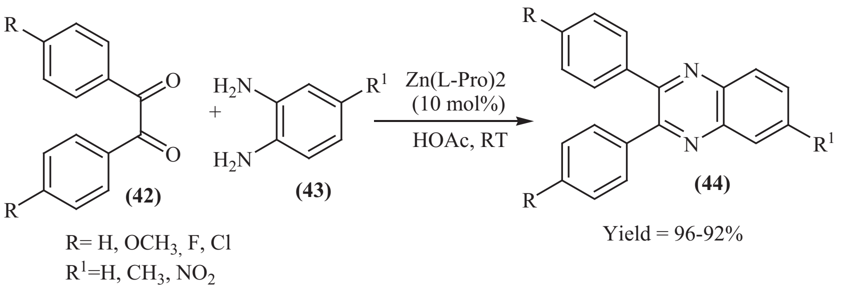
Scheme 10

produce important functionalized skeletons such as α-hydroxy carboxylic acids and 1,2-amino alcohols [75,76]. The standard nitroaldol reaction is carried out in the presence of inorganic (alkali metal hydroxides, calcium hydroxide, alkoxides, aluminum ethoxides, carbonates, bicarbonates) or organic base (primary, secondary, and tertiary amines) in an organic solvent [77]. To conquer some of the inconveniences associated, the selective, homogeneous and reusable catalysts are highly recommended. Hence, bis[(L)prolinate-N,O]Zn complex was used as a catalyst for this reaction (Scheme 13).

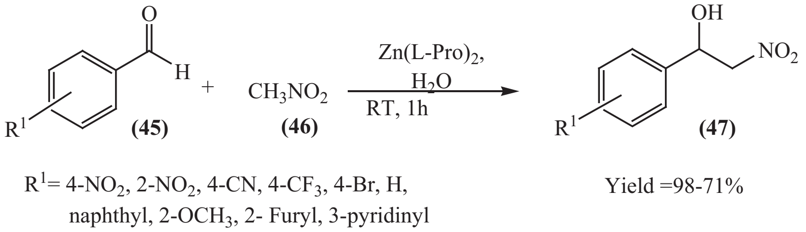
Bis[(L)prolinate-N,O]Zn complex also acted as a water-soluble and recyclable Lewis acid catalyst for the selective synthesis of 1,2-disubstituted benzimidazoles via the reaction of substituted *o*-phenylenediamines **(48)** and aldehydes **(49)** in moderate to excellent isolated yields (42–92%) using water as solvent at ambient temperature [78]. Under the optimized reaction conditions, in all cases the yields were high and 1,2-disubstituted product **(50)** was formed selectively rather than 2-substituted product **(51).** This selectivity could be useful in synthesizing a mini library of biologically relevant 1,2-disubstituted benzimidazoles in moderate to excellent yields (Scheme 14).

Shah and co-worker have revealed [79] that the bis[(L) prolinato-N,O]Zn, a Lewis acid catalyst under microwave irradiation could afford 3-methyl-1-substituted-phenyl-1*H*-chromeno[4,3-*c*]pyrazol-4-ones (**54**) by cyclization of hydrazones of 3-acetyl-4-hydroxycoumarin. The range of yields of various products was obtained to be 82–93%. In the absence of the catalyst, no reaction occurred. There was no remarkable increase in the yields of product at high temperatures and at high microwave power (Scheme 15).

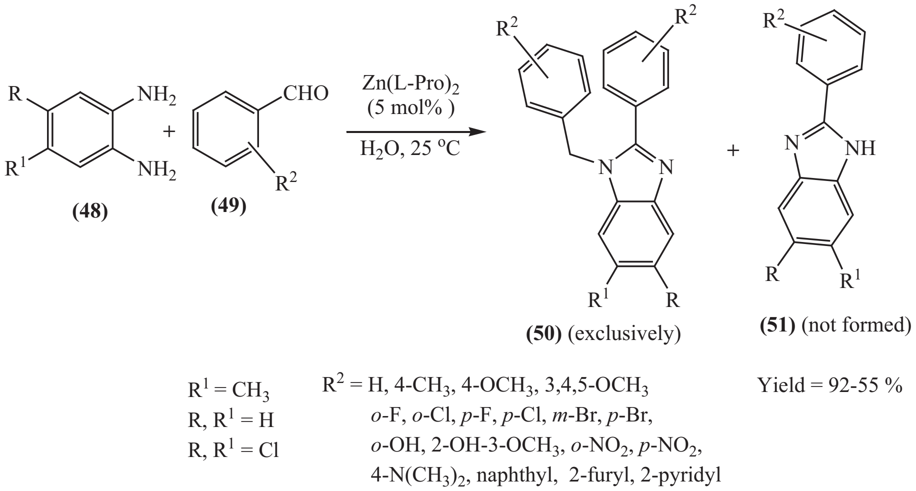
Itoh et al. have utilized the concept that that stereospecific aldol reactions are catalyzed by aldolase enzymes in a reversible manner. Aldolases enzymes are subdivided into two classes aldolase I (on catalyzing stereospecific aldol reaction through the enamine intermediates) and aldolase II (in which Zn^{2+} enolates of substrates react with acceptor aldehydes) [80] in Fig. 10. Mechanistic studies suggested that the amino acid part



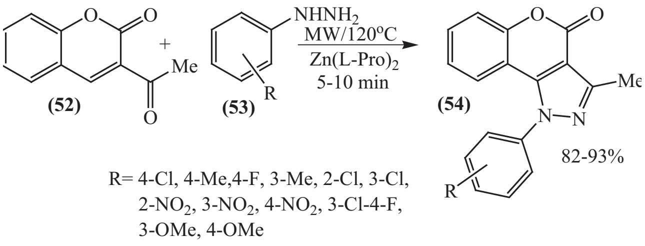
Scheme 12



Scheme 13



Scheme 14



Scheme 15

and the Zn^{2+} ion of the catalyst function in a cooperative manner to generate Zn^{2+} - enolates to give aldol adducts (Fig. 11).

Transition metal ion catalyzed coupling reaction is one of the most significant reactions to form a carbon–heteroatom bond. Out of carbon-heteroatom, the C—S bond formation has received much attraction due to its occurrence in many molecules that are of pharmaceutical used in drugs, building block material interests and biologically active. In 2009, Sheng-Rong et al. reported a palladium-free and mild synthetic procedure for the cross-coupling reaction of thiols **(66)** and aryl chlorides **(65)** with bis[(L)prolinate-N,O]Zn with K_2CO_3 as inorganic base, in ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) (Scheme 16) [81].

Multicomponent reactions (MCRs) are one pot processes in which three or more reactants come together in a single reaction vessel to form a product containing substantial elements of all the reactants [82]. Pyrano[2,3-*d*]pyrimidines derivatives

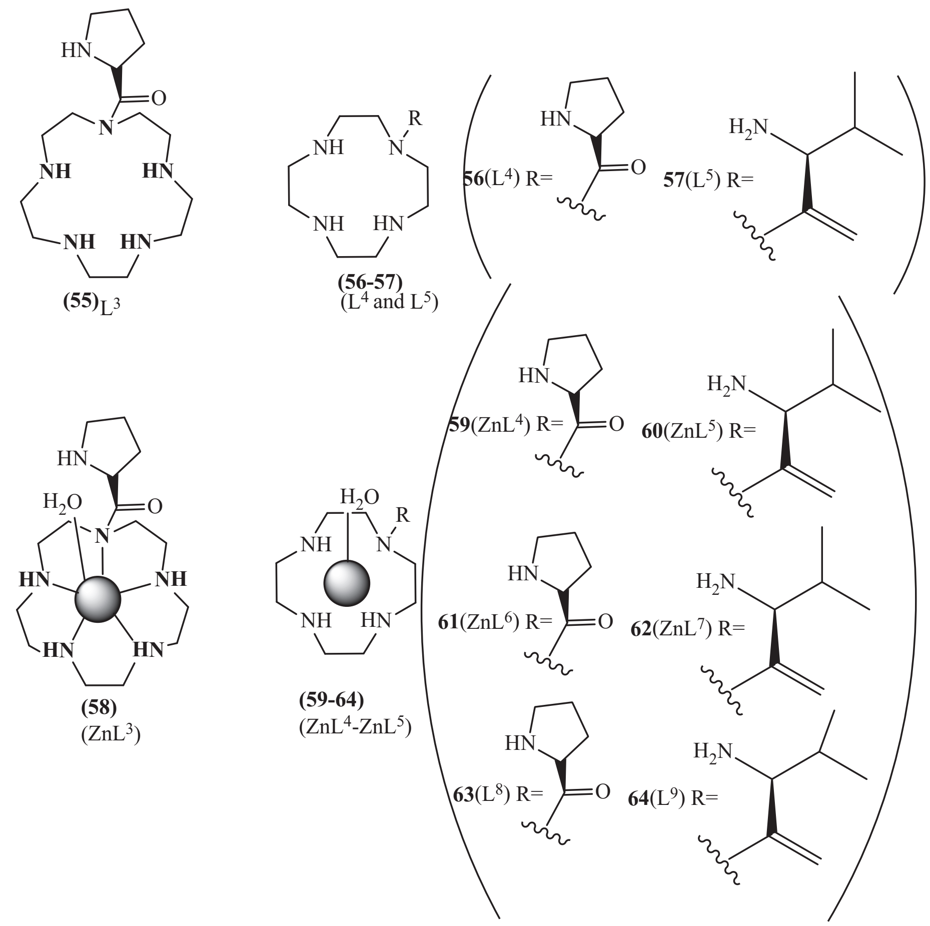


Fig. 10 Ligands that can bind to Zn^{2+} to form mimic of aldolase enzymes that catalyze stereospecific aldol reactions in a reversible manner.

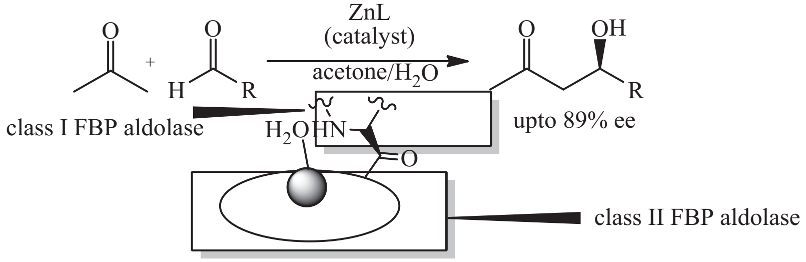
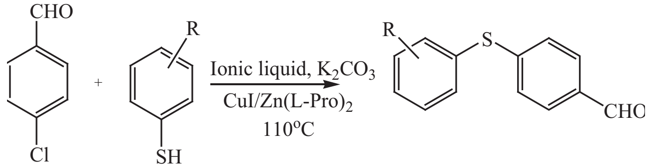


Fig. 11 Initially hypothesized scheme for aldol reactions catalyzed by the amino acid part and the Zn^{2+} ion of the catalyst function in a cooperative manner to generate Zn^{2+} - enolates.



(65) **(66)** **(67)**

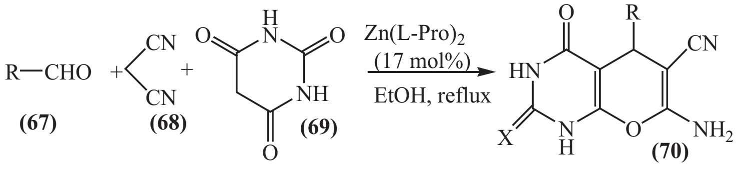
R= H, 2-*i*-propyl, 4-F, 4-Me, 2,4-$(OMe)_2$, 4-F-3-Me, 3-F-4-OMe, 2,5-$(F)_2$, 2,6-$(OEt)_2$, 2-Cl-6-Me, 3-Et-4-OH

Yield= 90-75%

Scheme 16

have acquired much attraction during the last decade owing to their broad spectrum of biological activities. Uracil derivatives have shown antibacterial, antitumor, antihypertensive, bronchiodilator, vasodilator, cardiotonic, hepatoprotective and antiallergic activities. Some of them also demonstrate herbicidal, analgesic, antifungal and antimalarial properties [83–91]. Influenced by this attractive importance of pyrano[2,3-*d*] pyrimidine derivatives, Heravi et al. in 2010 have synthesized these compounds using bis[(L)prolinate-N,O]Zn complex as a catalyst [92] (Scheme 17).

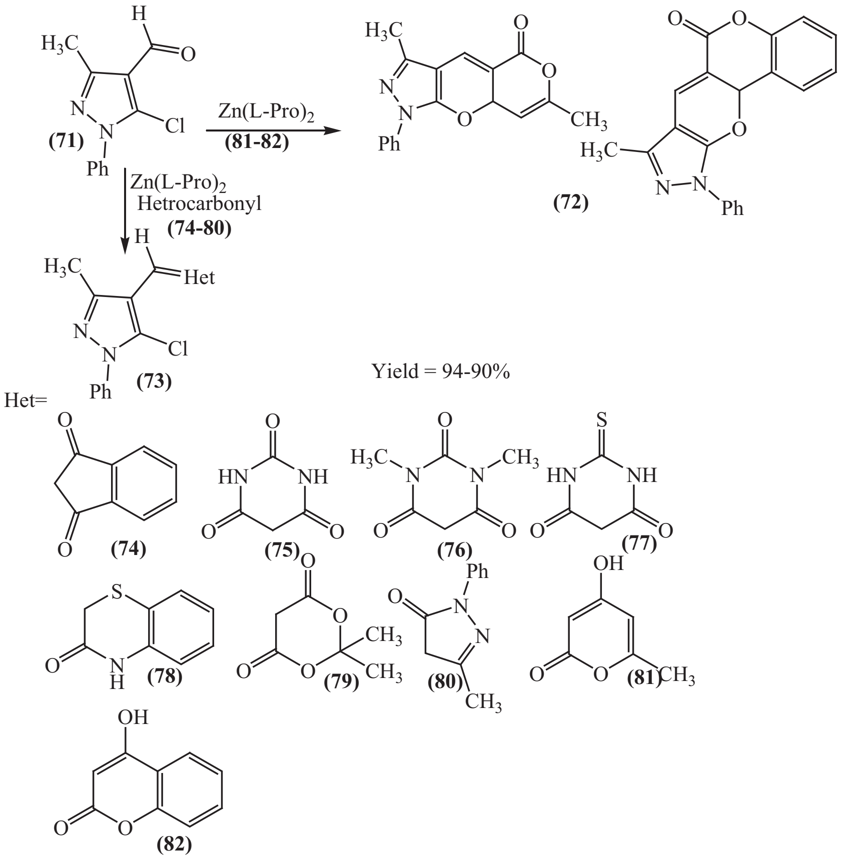
Siddiqui and her research groups have further explored the activity of bis[(L)prolinate-N,O]Zn as a Lewis acid catalyst in



R= C_6H_5, 4-$CH_3C_6H_4$, 2-$CH_3C_6H_4$,
4-$OCH_3C_6H_4$, 2-$OCH_3C_6H_4$,
3-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 4-ClC_6H_4,
4-$CF_3C_6H_4$, 3,4-$(OCH_3)_2C_6H_3$,
4-$N(CH_3)_2C_6H_3$, C_2H_5, CH_3

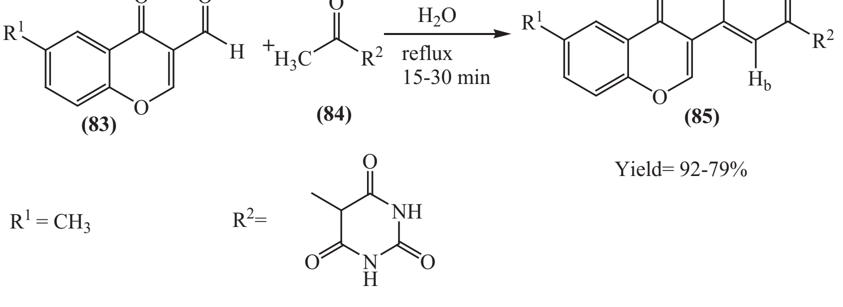
Yield= 78-91%

Scheme 17



Yield = 94-90%

Scheme 18



Yield= 92-79%

R^1 = CH$_3$

Scheme 19

Knoevenagel condensation. The Knoevenagel condensation products from 5-chloro-3-methyl-1-phenylpyrazole-4-carboxaldehyde **(71)** with different cyclic active methylene compounds, using water soluble and recyclable bis[(L)prolinate-N,O]Zn both are under solvent-free conditions and using water as a reaction medium in good yields [93,94] (Scheme 18).

Naturally origin as well as synthetic chromone derivatives forms an important constituent of pharmacophores of a variety of biologically active molecules having significant medicinal applications [95–102]. On the other side, chalcones family correspond to flavanoid class and have shown a remarkable range of biological activities [103]. Bis[(L)prolinate-N,O]Zn catalyzed the preparation of a library of chromonyl chalcones (**85**) from different cyclic active methyl groups (**84**) and 3-formylchromones (**83**) [104]. The yield of substituted chromonyl chalcones was found to 79–92% in 15–30 mins (Scheme 19).

From the point of view of green chemistry to use green solvent, water is the best option for reaction solvent to proceed and there is no requirement to mention properties of water [105,106]. Since water has specific properties [107–114] a disadvantage comes with the insolubility of organic compounds [115–117]. A novel, greener approach was adopted for the synthesis [118] of dicoumarols (**88**) using bis[(L)prolinate-N,O]Zn as a mild, non-toxic, Lewis acid catalyst in water employing 4-hydroxycoumarin (**86**) and aromatic/heteroaromatic aldehydes (**87**) (Scheme 20).

Kidwai and his research group [37] have done more progress toward the catalytic evaluation of bis[(L)prolinato-N,O] Z, they synthesized χ, δ-Acetylenic ketones **(91)** from phenylacetylene **(89)** and benzalacetophenone **(90)** using *bis*[(L) prolinato-N,O]Zn as a catalyst and Et_3N as an additive (Scheme 21) and the yield of product was up to 85%.

It was also indicated that only bis[(L)prolinate-N,O]Zn was capable of acting as an efficient catalyst for the synthesis of γ, δ-acetylenic ketones. The reason is only in bis[(L)prolinato-N, O]Zn, and amino acid contains secondary amine which ultimately enhances the catalytic efficiency of bis[(L)prolinato-N, O]Zn. The use of zinc reagent to affect the 1,4 - addition of an alkynyl group to an α,β-unsaturated ketone could be explained by the tendency with which zinc binds to alkyne ligand. It suggests that highly water soluble catalyst could coordinate with the alkyne easily and could transform it into product *via* intermediate. A plausible pathway involves the intramolecular delivery of an alkynyl group through a six membered transition state [A], which has been shown in the mechanism in Fig. 12. This on further rearrangement gives desirable product. Mechanism illustrates that there is no scope for the formation of side product. Furthermore, it is also shown that Et_3N was added in fractional amount to deprotonate the terminal alkyne and could be recovered back in the aqueous layer, when product was extracted.

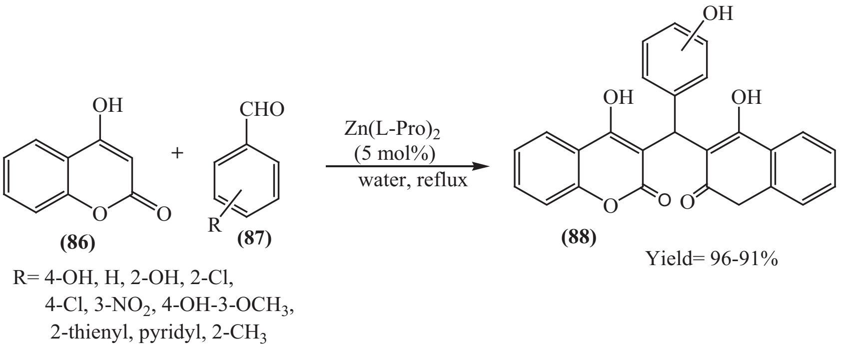
To explore more from bis[(L)prolinate-N,O]Zn as a catalyst to devise greener chemical transformations, kidwai and Jain [38] have further used bis[(L)prolinate-N,O]Zn as a catalyst for the preparation of triazoles by the reaction of alkyne, azide and benzyl halides in water as a solvent (Scheme 22).

A probable mechanism for this reaction is shown in Fig. 13. Since the reaction is carried out in water, hence in bis[(L) prolinate-N,O]Zn complex, metal ion would exist in the form of hydrated cation and the corresponding amino acid in the form of anion. The bis[(L)prolinate-N,O]Zn complex would be abstract proton from alkyne and make it acetylide [119,120]. With the bonding of azide with acetylide, the reaction would take the conduit frequently permitted for this transformation to form a triazolide intermediate, which then ultimately forms the target triazole and the recycling of the catalyst.

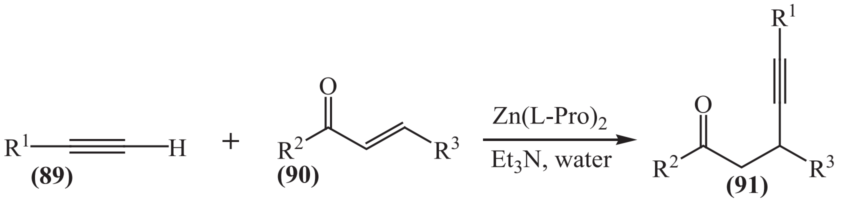
β-Amino carbonyl compounds are found to be attractive targets for various chemical syntheses as they are widely used in biologically active molecules as well as are important reactants for various pharmaceuticals [121]. Kidwai and his research group [29] have reported bis[(L)prolinate-N,O]Zn catalyzed three-component stereoselective Mannich reaction for the synthesis of β-amino carbonyl compounds in aqueous medium (Schemes 23 and 24). One of the most significant rewards of this reaction is the purity of the products. All the products were of very high purity and do not need any additional purification application such as recrystallization or column chromatography.

Products formed showed excellent *anti* selectivity. The *anti* **105** and *syn* **106** isomers were identified by the coupling constants (J) of the vicinal protons adjacent to C=O and NH in their ^1H NMR spectra (Fig. 14).

A plausible transition state was possible in which bonding of imine and enol with zinc produces cyclohexanone (Fig. 15). Transition state **(107)** gives less steric repulsion between the methylene groups of cyclohexanone and aryl group on the carbon atom and more space for the aryl groups of the aldimine, which is the most stable transition state, produces the *anti*-isomer shown in Fig. 16.



Scheme 20



$R^1 = C_6H_5, C_6H_{13}$; $R^2 = C_6H_5, CH_3, C_6H_4Br$; Yield = 78-88 %

$R^3 = C_6H_5, (CH_3)_2CH, C_6H_{13}$, 2-furyl, 1-naphthyl, $(CH_3)_3C$, H, C_6H_4Br

Scheme 21

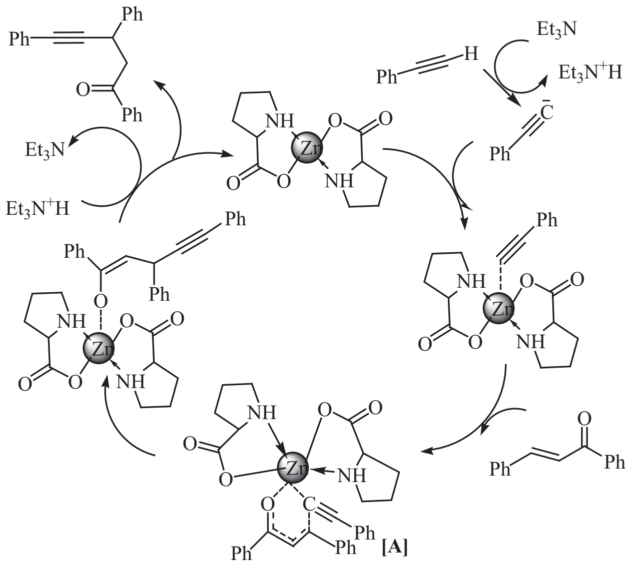


Fig. 12 Plausible mechanism for the bis[(L)prolinate-N,O]Zn catalyzed 1,4-addition of terminal alkyne to conjugated enone.

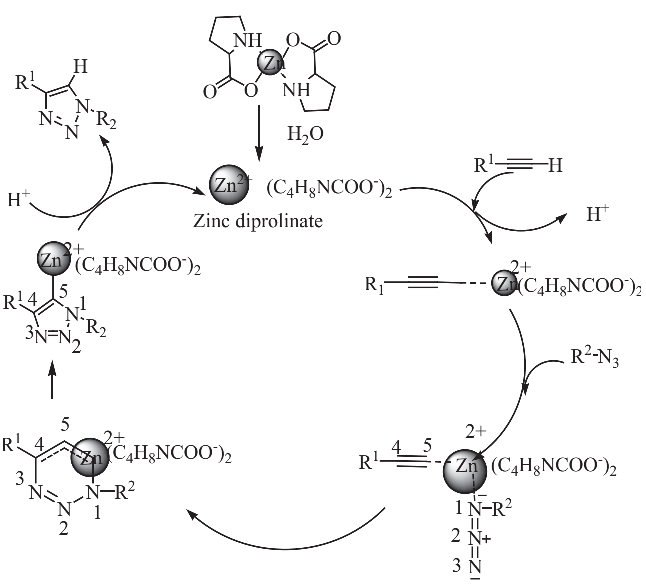
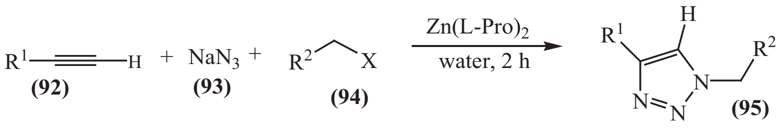


Fig. 13 Proposed mechanism for the preparation of triazoles by the reaction of alkyne, azide and benzyl halides using bis[(L) prolinate-N,O]Zn as a catalyst.

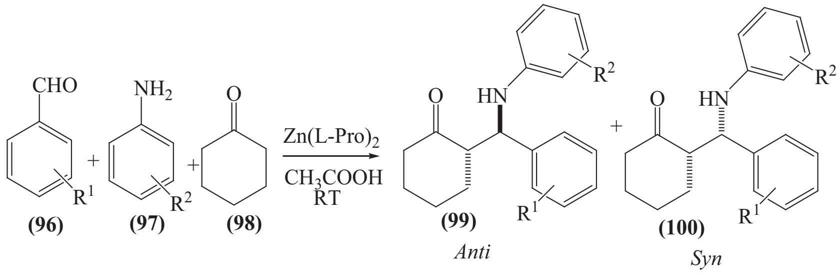
In continuation of further studies on developing economically viable and environmentally benign methodologies for organic reactions and to reveal the efficient utility of transition metals and their derivatives, Kidwai and his research group [36] have reported for the first time bis[(L)prolinate-N,O]Zn catalyzed an efficient synthesis of pyrazoles by the reaction of 1,3 diketone and phenyl hydrazine or hydrazine or hydrazides and 1,3 diketone and o-phenylenediamine in pure water (Schemes 25 and 26). However phenyl hydrazine can give pyrazole in the absence of catalyst in a less amount. But less reactive hydrazines and hydrazides take an evident advantage of the use of this catalyst. Generally 2, 4-dinitrophenylhydrazine with acetylacetone afforded enamine types of compound (**A**) and ethylacetoacetate with hydrazines afforded ***pyrazolones*** [122] (**B**). But by using this catalyst, reaction led to the formation of pyrazole only (Fig. 17). It is remarkable to point out that in the presence of $Zn(OAc)_2$ and in the absence of L-proline, the reaction did not occur. Even L-proline alone was not able to give any desirable product.



$R^1 = C_6H_5, COOC_2H_5, CH_2OH$; Yield= 91-78 %

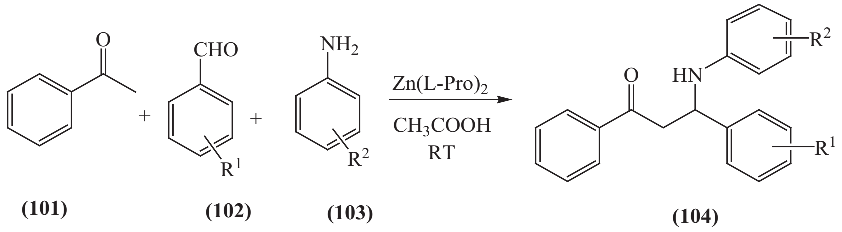
R^2=$C_6H_5CH_2Cl$, n-C_4H_9Br, p-$(NO_2)C_6H_4CH_2Cl$, CH_2=$CHCH_2Br$, CH_3I, n-$C_6H_{13}Br$, $C_6H_5CH_2Br$

Scheme 22



R^1 = H, 4-Cl, 4- CH_3, furyl; R^2 = H, 3-CH_3,4-Cl, 4-OCH_3 Yield= 92-85 % *Anti/Syn*= 92/8

Scheme 23



R^1 = H 4-CH_3, 4-OCH_3, 4-NO_2, 4-Br Yield = 98-70%

R^2 = H, 4-CH_3, 3,4-$(CH_3)_2$, 4-Cl, 4-OCH_3, 4-NO_2, 2-NO_2

Scheme 24

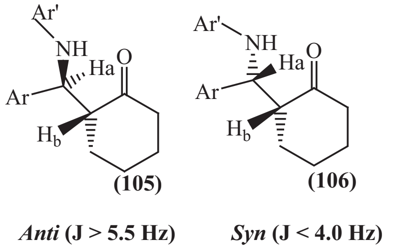


Fig. 14 Identification of *anti* and *syn* isomers by ^1H NMR spectroscopy.

Kidwai and Jain [123] have also extended their work and described a convenient and a resourceful process for the synthesis of xanthenediones with greater stereoselective manner. The prominent features of this protocol are rapid synthesis, simple experimental procedure, mild reaction conditions, manageable work-up, environmental friendliness by avoiding the use of volatile organic compounds as reaction media, reusability of the catalyst, improved yields, and cleaner reaction profile, which make it an efficient, economic and ecofriendly process (Scheme 27).

Friedlander condensation produces heteroannulated pyridines by the condensation–cyclodehydration reaction of reactive active methylene group and an aromatic 2-aminoaldehyde or ketone in acid or base medium. In this context, Siddiqui [124] has reported the preparation of novel benzopyrano [2,3-b] pyridine derivatives **120(a–j)** in aqueous media via Friedlander condensation using 2-amino-3-formyl chromone **118(a–b)** and cyclic active methylene compounds **119(a-e)** (Scheme 28). It was excellent reports on the preparation of

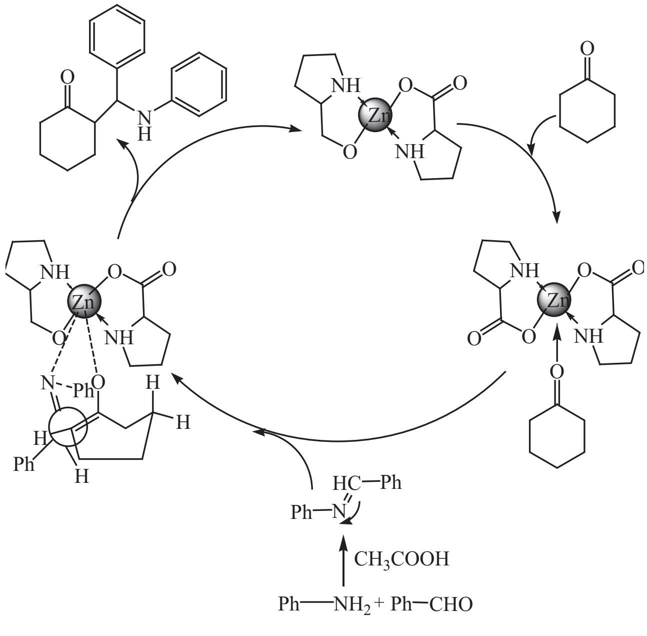


Fig. 15 Plausible mechanism for the bis[(L)prolinato-N,O]Zn catalyzed reaction for β-aminocarbonyl compounds.

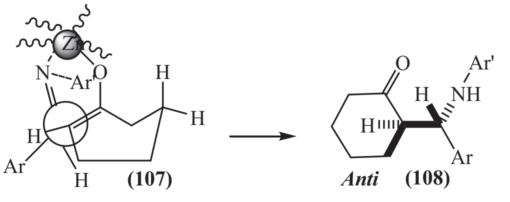
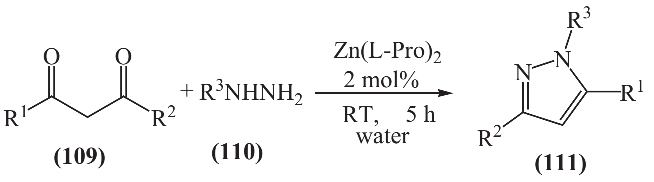


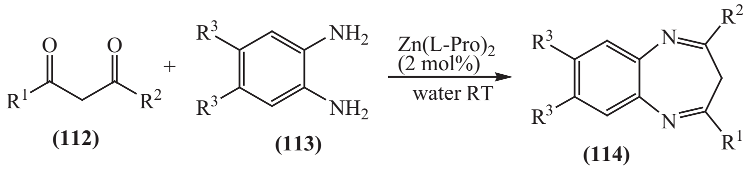
Fig. 16 Possible transition state leading to *anti* product.



Yield = 90-80%

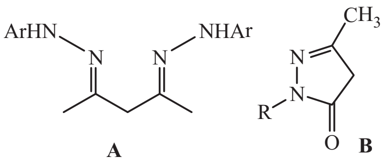
$R^1 = \mathrm{CH_3;\ OC_2H_5,}\ R^2 = \mathrm{CH_3;\ OC_2H_5;}\ R^3 = \mathrm{C_6H_5, H, C_6H_5CO, 2,4\text{-}(NO_2)_2C_6H_3, CH_3CO}$

Scheme 25



$R^1 = \mathrm{CH_3;\ OC_2H_5;}\ R^2 = \mathrm{CH_3;\ OC_2H_5}R^3 = \mathrm{H},\ R^3 = \mathrm{H, CN}$ Yield = 90-40%

Scheme 26



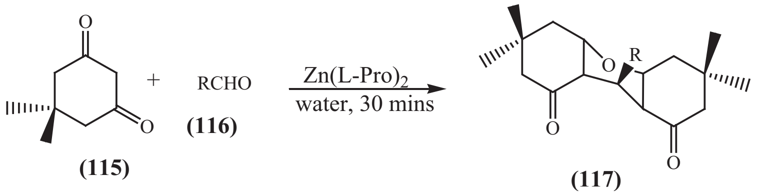
Ar=2,4-dinitrophenyl R= Ph, H

Fig. 17 Enamine(A), Pyrazolone(B).

benzopyranopyridine derivatives using bis[(L)prolinate-N,O] Zn as Lewis acid catalyst.

In continuation of efforts in developing selective, efficient, mild and ecofriendly synthetic methodologies for the preparation of biologically relevant heterocyclic derivatives, Siddiqui and Farooq [125] have reported a simple and convenient method for the synthesis of 4-chromanone derivatives **(123)** by the reaction of 3-formylchromone **(121)** with different primary aromatic and heteroaromatic amines **(122)** using bis[(L)prolinate-N,O]Zn complex as a water-tolerant Lewis acid catalyst in water. The plausible mechanism for the synthesis of (**123**) in the presence of bis[(L)prolinate-N,O]Zn has been shown in Scheme 29. Zn is accomplished of binding with the carbonyl oxygen raising the reactivity of parent carbonyl group in **121** which led to formation of imine with proline takes place in Fig. 18. This is followed by nucleophilic attack of amines **(122)** to the imine to form hydrogen bonded adduct. Finally, water as nucleophile attacks on electrophilic C-2 center with the expulsion of bis[(L)prolinate-N,O]Zn gives the preferred 2-hydroxy chromanones **(123).**

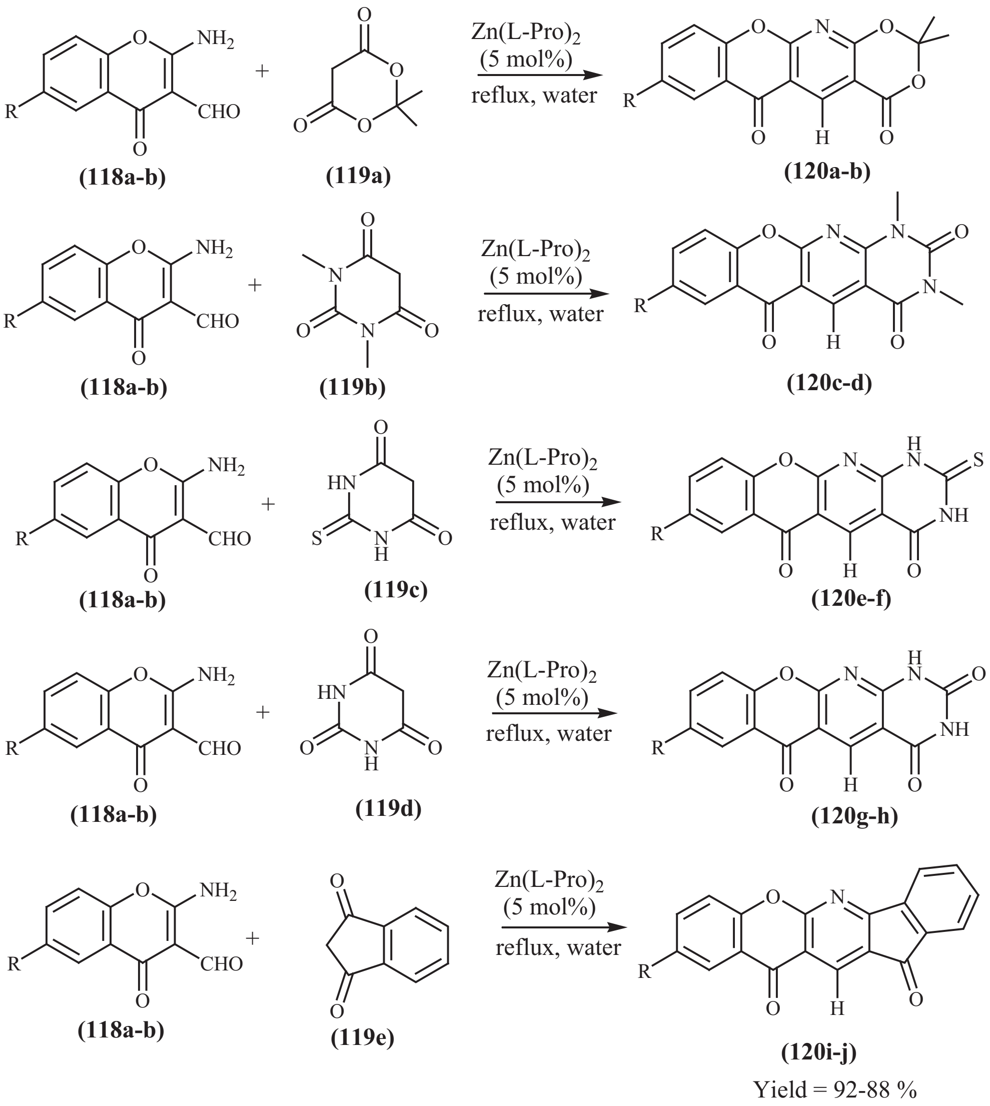
To further explore bis[(L)prolinate-N,O]Zn as heterogeneous Lewis catalyst in microwave, the Pourshamsian and his research group [126] have described the preparation of 1,4-dihydropyridines **(127)** by condensation of ethyl acetoacetate **(125),** ammonium acetate **(126)**, and aldehydes **(124)** under the influence of microwave irradiation in solvent free conditions (Scheme 30). They reported that the reaction offers several advantages, such as the absence of any volatile and hazardous organic solvent, high yields and simple procedure with an easy work-up. Moreover, the catalyst can be easily



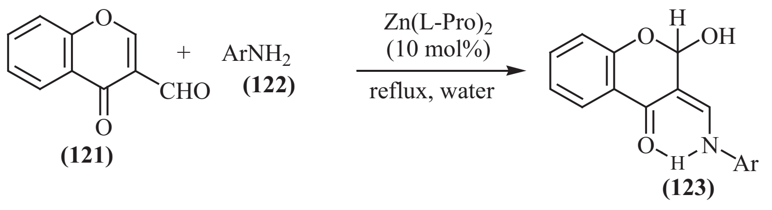
R= $\mathrm{C_6H_5}$, 4-$\mathrm{ClC_6H_4}$, 4-$\mathrm{CH_3OC_6H_4}$, 2-$\mathrm{CH_3OC_6H_4}$, 4-$\mathrm{CH_3C_6H_4}$, Yield = 97-63%

$\mathrm{C_2H_5}$, $\mathrm{CH(CH_3)_2}$, 4-$\mathrm{NO_2C_6H_4}$, 4-$\mathrm{HOC_6H_4}$, 2- thienyl, 2 –hydroxynaphthyl, 2- piperonyl,

Scheme 27



Scheme 28



Ar = 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-$NO_2C_6H_4$, 3-$NO_2C_6H_4$, 4-HOC_6H_4, 4-ClC_6H_4, C_6H_5,1-naphthyl, 2-pyridyl, 2-benzothiazolyl

Yield = 93-87%

Scheme 29

recycled and reused at least three times without appreciable loss of its catalytic activity.

Siddiqui [127] has further investigated the utilities of bis[(L) prolinate-N,O]Zn as heterogeneous Lewis catalyst for the preparation of 3,4-dihydropyrimidin-2(1H)-one derivatives **(136a–j)** by the condensation of 1,3 dicarbonyl **(128),** urea **(129)** and aldehyde **(130)** in Scheme 31. Again they have shown bis[(L)prolinate-N,O]Zn as an suitable catalyst for this transformation.

Recently hybrid materials have seized attention from scientific community mainly as heterogenic catalysts in organic reactions on a large scale succeeding in some organic compounds with high yields. One of the most important classes of hybrid materials used for this purpose involves the complex

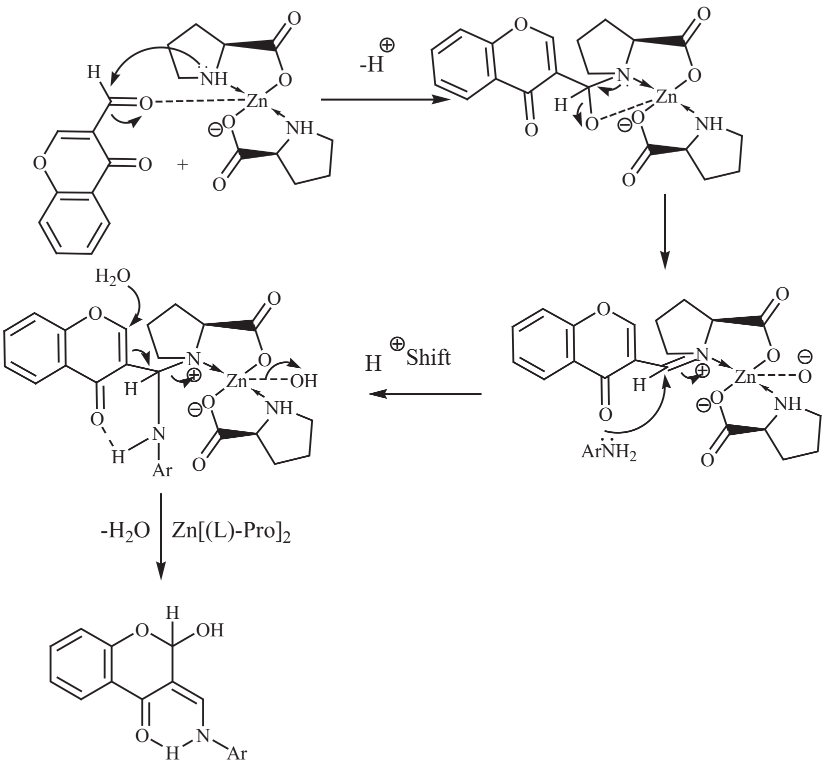
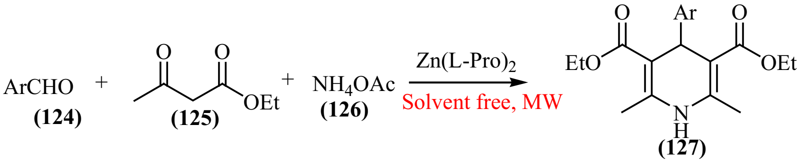
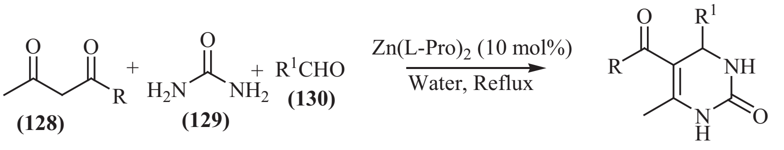


Fig. 18 Plausible mechanism for the bis[(L)prolinato-N,O]Zn catalyzed reaction for 4-chromanone derivative compounds.



Yield = 93-87%

Scheme 30

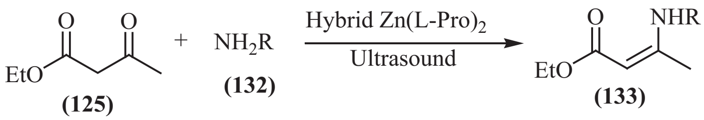


R= CH_3, OEt,

R^1= C_6H_5, 3-$NO_2C_6H_4$, 4-HOC_6H_4, 4-ClC_6H_4, 2-ClC_6H_4

Yield = 91-82%

Scheme 31



R= C_6H_5, 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, $CH_2C_6H_5$, C_4H_9, cyclohexyle Yield = 93-60%

Scheme 32

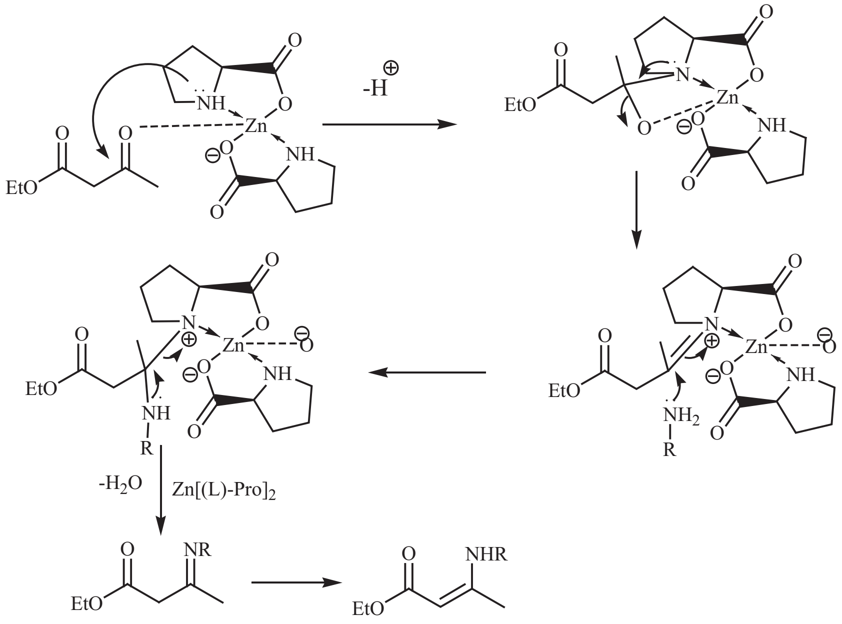
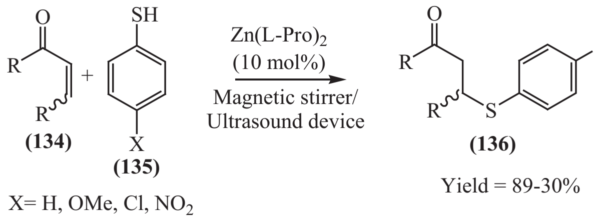


Fig. 19 Plausible mechanism for the bis[(L)prolinato-N,O]Zn catalyzed reaction for β-enaminone compounds.



Scheme 33

of Zn and amino acids. Winck and his research group [128] have introduced bis[(L)prolinate-N,O]Zn and Zn[Gly]$_2$ hybrid materials for the synthesis of several β-enaminones via solvent free protocol under the influence of ultrasound (Scheme 32).

β-enaminones are known for their flexible reactivity, as nucleophiles and electrophiles. In mechanistic point of view there is a nucleophilic attack of the nitrogen from the catalyst on the ketone carbonyl which has methyl group (Fig. 19). This attack produced the iminium ion which was attacked by the amine. The obtained N,N acetal produced the corresponding imine which finally rearranged itself resulting in the β-enaminone while there is no nucleophilic attack on the ester carbonyl group.

Recently Darbem [129] and his research group further extent catalytic property of bis[(L)prolinate-N,O]Zn as a heterogeneous catalyst in a thio-Michael reaction using the ultrasound method (Scheme 33). The 80% yield is obtained in 1 h for the thio-Michel adduct when 10 mol% of the bis [(L)prolinato-N,O]Zn was employed at the same time the

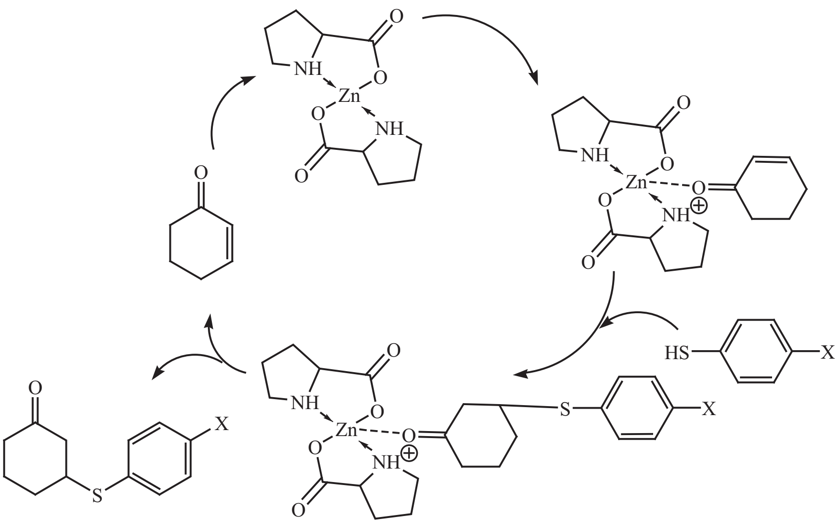
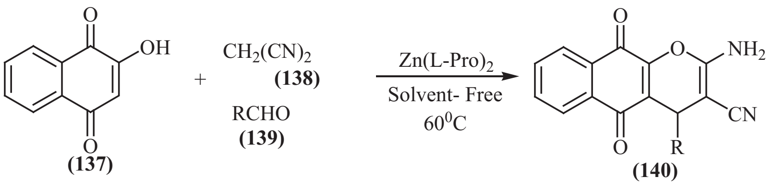


Fig. 20 Plausible mechanism for the bis[(L)prolinate-N,O]Zn catalyzed reaction for thio-Michael reaction.



R= C_6H_5, 4-$OCH_3C_6H_4$, 3-$OCH_3C_6H_4$, 3,4-$OCH_3C_6H_3$, 4-ClC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 4-FC_6H_4, 4-Pyridyl, 4-$CH_3C_6H_4$, 3-$NO_2C_6H_4$, 2-$NO_2C_6H_4$, 2,4-ClC_6H_3, 4-OHC_6H_4, 2,3,4-$OCH_3C_6H_2$, 4-$NO_2C_6H_4$, 2-thienyl,

Yield = 94-78 %

Scheme 34

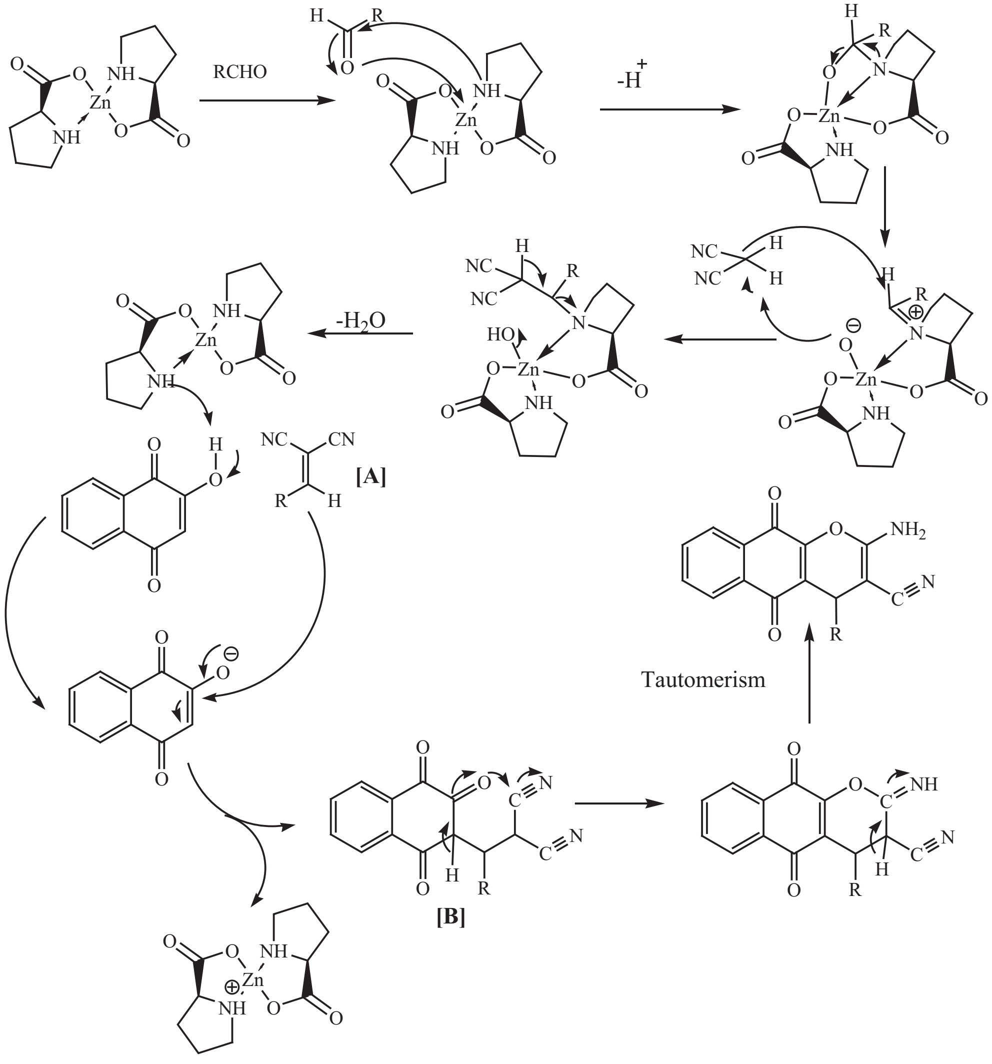
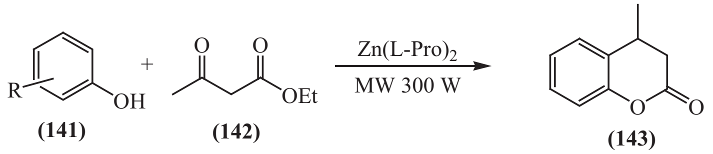


Fig. 21 Plausible mechanism for the bis[(L)prolinate-N,O]Zn catalyzed 2-amino-4H-benzo[g]chromene by reaction of aldehydes, malononitrile and 2-hydroxy-1,4-naphthaquinone.

Ultrasound device used. It is worth noting that when using a chiral hybrid catalyst, bis[(L)prolinato-N,O]Zn, a dextro thio-Michael adduct was obtained. This result is important and contrary to the results from porcine pancreatic lipase [130]. However, the use of the ultrasound device did not result in a substantial increase in the yields for thio-Michael adducts. The reaction using isophorone did not produce the thio-Michael adduct, and to the best of their knowledge, they attributed this effect to the presence of dimethyl groups bonded to carbon 5, which made it impossible for a nucleophilic attack to occur in the transition state following the reaction between bis[(L)prolinate-N,O]Zn and isophorone. This fact was confirmed by the result of 3-methyl-cyclohexen-2-one, which also shows a hindered effect but in



R= 3-OH, 3-MeOH, 2-Me-3-OH, 3,5-OH, 3-OH-5-Me, 2,3-OH,
4-NO$_2$, 2-NO$_2$, 3-OH-4-MeO

Yield = 98-72 %

Scheme 35

the C3 position. For this compound, yields were lower when compared to the other Michael acceptor. Taking into account all results, they presented a mechanism involving the thiophenol and cyclohexen-2-one (Fig. 20).

Maleki and his research group [131] have reported a simple, clean and environmentally friendly process for the synthesis of 2-amino-4H-benzo[g]chromene derivatives by reaction of various aldehydes, malononitrile and 2-hydroxy-1,4-naphthaquinone in the presence of 20 mol% of bis[(L)prolinate-N,O]Zn under solvent-free conditions at 60 °C (Scheme 34). A plausible mechanism of the reaction is shown in Fig. 21 exhibits that bis[(L)prolinate-N,O]Zn complex facilitates cyanoolefin formation and synthesis of 2-amino-4H-benzo[g]chromenes. The reaction occurs via initial formation cyanoolefin [A] from condensation of aldehydes and malononitrile, which reacts with 2-hydroxynaphthalene-1,4-dione to give intermediate [B] which subsequently underwent cyclization to afford the desired products. There was no effect observed on the reaction time and the yield of the corresponding products when electron-donating groups and electron-withdrawing groups on benzaldehydes are used. On further examination it was found that aliphatic aldehydes such as butanal instead of benzaldehydes in the reaction, showed no desired products after 1 h. In addition to the aromatic aldehydes, the reaction also precedes smoothly using heterocyclic aldehydes in high yield.

The author Chavan and his research group [132] have reported the Pechmann condensation reaction of phenols and β-ketoesters employing bis[(L)prolinate-N,O]Zn complex as a simple, efficient, eco-friendly, organometallic catalyst under solvent free condition. They carried out a series of substituted phenols with ethylacetoacetate to obtain corresponding coumarin derivatives in a very good yield (72–98%) (Scheme 35). The catalyst is reusable up to five cycles with marginal loss of its catalytic activity.

Conclusions and future perspectives

This review demonstrates the synthesis, characteristics and catalysis of bis[(L)prolinato-N,O]Zn. This study shows the organic synthetic applications of bis[(L)prolinate-N,O]Zn in water provide alternative, environmentally friendly methods that can be easily prepared and stored as stable solids in non-inert conditions and can be used to substitute a host of traditional Lewis acid applied along with VOCs (Volatile organic compounds) [133–137]. The increased application of bis[(L)prolinate-N,O]Zn in organic reactions will definitely develop in the future as our thinking of this complex and new complexes are revealed and brought to market. Concerning the catalysts, the tendency toward reusable solids will accelerate in the near future. It is anticipated that the reaction conditions under which bis[(L)prolinate-N,O]Zn performs will be broadened and this will open further research opportunities. Given societies demand for green chemistry solutions and the creativity opportunities surrounding this unique amino acid-complex, it is believed that the next decade will give one of the most productive and hopeful sections in the long history of metal-complexes. In future, there are chance that formation of complex alike bis[(L)prolinate-N,O]Zn where zinc metal ion can be substituted with other transition metal dications i.e. Fe^{2+}, Cu^{2+}, Mn^{2+}, Mg^{2+} or proline with other α-amino acid in which amine is secondary which will create a series of green and economic metal complexes.

Conflict of Interest

The authors have declared no conflict of interest.

Compliance with Ethics Requirements

This article does not contain any studies with human or animal subjects.

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