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# Synthesis, characterization and biological activities of a novel Mannich base 2-[(3, 4-dimethoxyphenyl)(pyrrolidin-1-yl)methyl]cyclopentanone and its complexes with Cu(II), Co(II), Ni(II) and Fe(II) ions

M. Liaqat[1], T. Mahmud[1*], M. Imran[1], M. Ashraf[2], A. U. Haq[3], M. Muddassar[4], T. Ahmad[5]

[1]*Institute of Chemistry, University of the Punjab, Lahore, Pakistan*
[2]*Department of Chemistry, The Islamia University of Bahawalpur, Bahawalpur, Pakistan*
[3] *College of Pharmacy, Gachon University of Medicinal Sciences, Incheon, South Korea*
[4]*Department of Biosciences, COMSATS Institute of Information Technology, Park Road, Islamabad, Pakistan*
[5]*Department of Chemistry, University of the Sargodha Sub-campus, Mianwali, Pakistan*

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One-pot, three-component Mannich reaction was carried out by condensation of 3,4-dimethoxybenzaldehyde, pyrrolidine and cyclopentanone in the presence of calcium chloride using ethanol as a solvent to afford a novel Mannich base (L). The resulting Mannich base (L) was isolated and complexed with Cu(II), Co(II), Ni(II) and Fe(II) ions. The structures of the synthesized scaffolds were confirmed by IR, $^1$H NMR, $^{13}$C NMR, mass spectroscopy, TGA and elemental analyses. The metal contents were determined by ICP-OES. All compounds showed poor antibacterial activities. The anti-enzymatic activities of the Mannich base (L) and its metal complexes were checked against jack bean urease. The Mannich base ligand (L), its nickel and iron complexes showed potent antiurease activity with $IC_{50}$ values of 9.25±0.002, 1.42±0.003, 5.41±0.005 µM, respectively, and were superior inhibitors than the standard, thiourea ($IC_{50}$ 21.25±0.15 µM). The probable binding mode of the most active Ni(II) complex was determined using molecular docking simulations.

**Keywords:** Mannich base, Metal complex, Antiurease activities, Docking studies

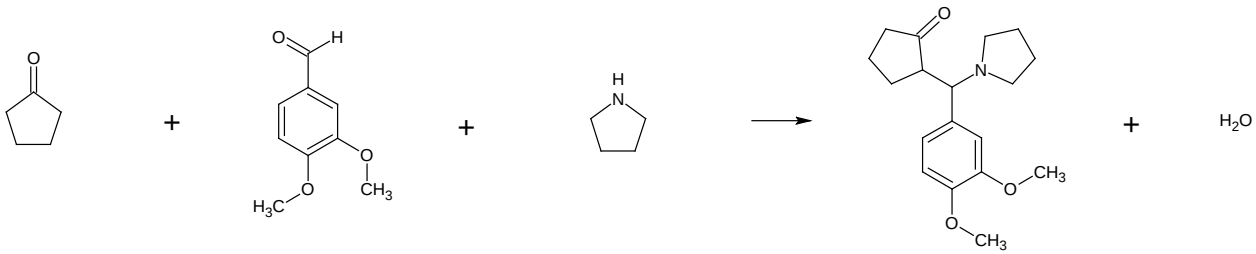
## INTRODUCTION

The Mannich reactions are the most charming tools in the field of organic synthesis which give a quantitative approach for the production of carbon-carbon bonds in organic molecules [1−4]. These tools provide different possibilities to produce new analogues by employing various substituted derivatives of any component present in the reaction mixture. The multidisciplinary chemistry of Mannich bases offers a main role for the construction of novel species used for various commercial purposes. Mannich bases are extensively used as intermediates in the preparation of different natural and pharmaceutical products [5,6]. The growth of novel analytical routes designed for the production of β-amino carbonyl compounds has crucial significance in organic chemistry. Several chemists reported the synthesis of Mannich bases using various catalysts [7]. Chemists are trying to build up environment friendly protocols *via* nontoxic catalyst such as calcium chloride [8]. The production of metal complexes possessing certain ligands of pharmacological importance have their own place in society due to the significance of certain metal ions in several biological processes [9,10]. Transition metals play a vital biological role in association with certain metal-protein complexes [11]. The multidisciplinary applications and novel structures of Mannich bases and their complexes are responsible for their extensive investigations in the present age [12]. In view of the above potential importance of Mannich bases and in continuation of our similar recent studies [13,14] another Mannich base 2-[(3,4-dimethoxyphenyl)(pyrrolidin-1-yl)methyl) cyclopentanone (L) and its four complexes with Cu(II), Co(II), Ni(II) and Fe(II) ions were synthesized. Synthetic, structural, docking, antibacterial and antiurease activities of these compounds are part of this manuscript.

## EXPERIMENTAL SECTION

3,4-Dimethoxybenzaldehyde, pyrrolidine, cyclopentanone, metal salts and solvents used were all of analytical grade and were used without further purification. Melting points were determined on a Gallen Kamp apparatus. FT-IR spectra were measured on a Perkin Elmer IR spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded by Brucker Avance 400. Mass spectra were measured on JEOL JMS−600. Elemental analyses were performed using a EuroEA elemental analyzer. UV-visible spectra were taken using the T90+UV/VIS spectrometer PG instrument within the range of 200 – 400 nm. SDT-Q 600 V20.9

*) To whom all correspondence should be sent:
E-mail: tariqm06@yahoo.co.uk



**Scheme 1**: Synthetic route for the synthesis of Mannich base ligand (L)

Build 20 instrument was used for TGA. Magnetic susceptibility measurements of the complexes were made by using a Gouy magnetic balance at room temperature.

*Synthesis of Mannich base ligand (L):*

According to a reported procedure [8], an ethanolic solution of 3, 4-dimethoxy-benzaldehyde, pyrrolidine and cyclopentanone were mixed in 1:1:1 mole ratio followed by addition of one equivalent of calcium chloride. The contents were mixed under ice cold conditions for ten min. Resulting mixture was then heated at 70−90oC for 1.5 h. The mixture was then stirred at room temperature for 24 h. The progress of reaction was monitored by TLC. $NaHCO_3$ solution (5%) was added to the mixture, which resulted in a yellow precipitate, which was filtered, washed with distilled water, ethanol and finally dried.

*General procedure for the synthesis of metal complexes*

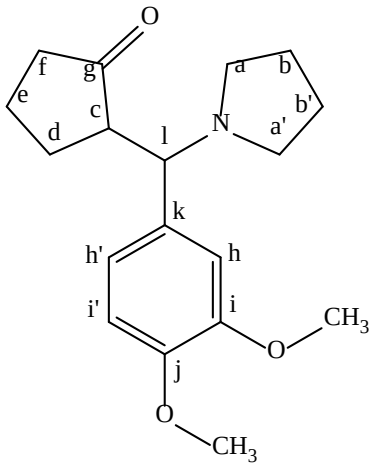
Hot ethanolic solution of the Mannich base and respective metal chlorides were mixed in 1:1 mole ratio. The contents were gently heated at 50oC for 10 min. The resulting mixtures were then stirred at room temperature for about 2.5 h. The resulting solids formed were filtered, washed with distilled water, ethanol and finally dried under vacuum.

*Characterization of ligand and its metal complexes*

*Mannich base (L):* Molecular formula: $C_{18}H_{25}NO_3$ g/mole, yellow solid, Yield: 59%, m.p.: 188–190oC Molecular weight: 303.35. IR ($cm^{-1}$): 1598 (C-N-C stretching), 1508 (C=C stretching); 1678 (C=O stretching).

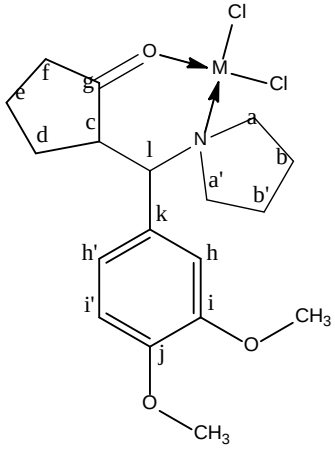
*Labeling of Mannich base for $^1H$ and $^{13}C$ NMR spectra*

$^1H$ NMR (400 MHz, $CDCl_3$,$\delta$): 1.196–1.279 (6H, m, $H_b$, $H_{b'}$ $H_f$),2.060−2.130(4H,m,$H_d$,$H_e$), 2.390−2.417 (1H, t, $H_C$), 2.967–2.995(4H, dt, $H_a$, $H_{a'}$), 3.937(6H, s,o$CH_3$), 6.934–6.948 (1H, d, $H_{h'}$ $J$ = 5.6 Hz), 7.134−7.137(1H, d ,$H_l$ , $J$ =*1.2* Hz) , 7.225− 7.239(1H, d, $H_{i'}$, $J$ = 5.6 Hz), 7.543 (1H, s, $H_h$). $^{13}C$ NMR (400 MHz, $CDCl_3$, $\delta$): 20.15($C_d$), 26.46($C_e$), 29.02($C_b$, $C_{b'}$), 30.33($C_f$), 37.74($C_a$, $C_{a'}$), 55.89($C_l$), 55.97($OCH_3$), 111($C_h$), 113($C_{h'}$), 124($C_{i'}$), 135($C_k$), 148($C_j$), 150.26($C_i$), not observed ($C_g$). EI–MS (*m/z)* (%) = 380.2 observed for $[M+ 2K-H]^+$ (100), 365.2 $[C_{17}H_{22}NO_3+2K-H]^+$ (39), 349.2$[C_{16}H_{19}NO_3+2K-H]^+$ (28).



*Characterization of the metal complexes*

*Labeling of metal complexes of L for $^1H$ and $^{13}C$ NMR spectra*



M = $Cu^{+2}$, $Co^{+2}$, $Ni^{+2}$, $Fe^{+2}$

*Cu (II)-complex:* Molecular formula: $C_{18}H_{25}Cl_2CuNO_3$, light green solid, yield: 51%, m.p.: decomposed above 280oC, molecular weight: 437.85 g/mole, %age metal for $MLCl_2$:

Theoretical/experimental (14.51/13.31). IR ($cm^{-1}$): 1591 (C-N-C stretching), 1512 (C=C stretching); 1660 (C=O stretching), 441 (Cu−N stretching), 528(Cu-O stretching). $^1$H NMR ($CDCl_3$, 400MHz): δ1.566 ($CH_2$, br-m, $H_a$, $H_{a'}$ $H_b$, $H_{b'}$, $H_d$, $H_e$ and $H_f$), 3.125(1H, br, s $H_c$), 3.940 (6H, s,o$CH_3$) 6.947(1H, br-s, $H_l$ ),7.141−7.250(2H, br-d, $H_{h'}$ , $H_{i'}$), 7.550 (1H, S, $H_h$); $^{13}$C NMR (400 MHz, $CDCl_3$, $\delta$): 20.03−26.46 ($CH_2$), 55.90−55.98 ($OCH_3$), 39.16($C_d$), 111.18−113.48 ($C_{h'}$), 114.56($C_h$), 123.03($C_k$), 133.68−135.40 ($C_{i'}$), 148.94 ($C_j$), 151.18 ($C_i$)

*Ni (II)-complex:* Molecular formula: $C_{18}H_{25}Cl_2NiNO_3$, greenish yellow solid, yield: 55%, m.p.: decomposed above 280oC. Molecular weight: 433.00 g/mole, %age metal for $MLCl_2$: Theoretical /experimental (13.56/13.03); IR ($cm^{-1}$): 1589 (C−N−C stretching), 1514 (C=C stretching); 1659 (C=O stretching), 438 (Ni−N stretching), 544(Ni−O stretching); $^1$H NMR ($CDCl_3$, 400 MHz): δ1.260−2.172 (14H, br-m, $H_a$ $H_{a'}$ $H_b$, $H_{b'}$, $H_d$, $H_e$, $H_f$) 3.122(1H, br-t, $H_c$), 3.876 − 3.941(6H, br-s,o$CH_3$), 6.951 (1H, br, d, $H_{h'}$), 7.143 (1H, br, d, $H_l$), 7.245−7.261 (1H, br-d, $H_{i'}$), 7.551(1H, s, $H_h$); $^{13}$C NMR (400 MHz, $CDCl_3$, ($\delta$): 20.26 ($CH_2$), 55.36−55.97 ($OCH_3$), 111.18($C_{h'}$), 113.47 ($C_h$), 124.56($C_k$), 129.03−129.41 ($C_{i'}$), 149.04−150.03 ($C_j$, $C_i$)

*Co (II)-complex:* Molecular formula: $C_{18}H_{25}Cl_2CoNO_3$, off-white solid, yield: 51%, m.p.: decomposed above 280oC, molecular weight: 433.24 g/mole, %age metal for $MLCl_2$: Theoretical/experimental (13.60/12.98); IR ($cm^{-1}$): 1593 (C−N−C stretching), 1515 (C=C stretching); 1661 (C=O stretching), 441(Co−N stretching), 531 (Co−O stretching); $^1$H NMR ($CDCl_3$, 400MHz): δ1.262−1.454 (4H, br-m, $H_b$, $H_{b'}$), 1.583-2.659 (2H, br-t, $H_f$), 2.043−2.244 (4H, br−m, $H_e$, $H_d$), 2.992−3.195(1H, br-t, $H_c$), 3.812-3.857(6H, br-s,o$CH_3$), 3.939−4.015(4H,br-t, $H_a$, $H_{a'}$), 6.825−6.869(1H, br−d, $H_{h'}$), 7.013−7.140(1H, br-d, $H_l$), 7.232−7.245(1H, br-d, $H_{i'}$), 7.549−7.624(1H, br-s, $H_h$); $^{13}$C NMR (400 MHz, $CDCl_3$, $\delta$): 20.43−26.66 ($CH_2$), 55.85−55.98 ($OCH_3$), 111.17−111.86 ($C_{h'}$), 124.57($C_h$), 133.87−133.92 ($C_k$, $C_{i'}$), 149.97−150.34 ($C_i$, $C_i$)

*Fe (II)-complex:* Molecular formula: $C_{18}H_{25}Cl_2FeNO_3$, light brown solid, yield: 56%, m.p.: decomposed above 280oC, molecular weight: 430.15 g/mole, %age metal for $MLCl_2$: Theoretical/experimental: (12.98/11.92); IR ($cm^{-1}$): 1595 (C−N−C stretching), 1512 (C=C stretching); 1664 (C=O stretching), 427(Fe−N stretching), 519 (Fe−O stretching);$^1$H NMR ($CDCl_3$, 400MHz): δ 1.255-2.567(14H, br- m, $H_a$, $H_{a'}$ $H_b$ ,$H_{b'}$ $H_d$, $H_e$, $H_f$), 3.122 (1H, br-s, $H_c$),3.941(6H, S,o$CH_3$), 6.948 (1H, br-d, $H_{h'}$)7.143 (1H, br−d, $C_l$) , 7.248(1H, br-d, $H_{i'}$), 7.552(1H, s, $H_h$ ); $^{13}$C NMR (400 MHz, $CDCl_3$, $\delta$): 20.45−26.46 ($CH_2$), 55.05−55.95 ($OCH_3$), 111.11 ($C_{h'}$), 112.41 ($C_h$), 58.37($C_f$), 123.31 ($C_k$), 133.47−133.58 ($C_{i'}$), 149.75−150 ($C_j$, $C_i$)

### *Biological evaluation*

*Antiurease activity:* Measurement of antiurease activity was carried out by Berthelot assay with minor modifications [15-16]. Ten µL of 50 mM phosphate buffer (pH 7.0), 10 µL of respective test compound and 25 µL of jack beans urease (0.015 units, from Sigma) were mixed and pre-incubated at 37ºC for 10 min. Then, 40 µL of 20 mM urea was added to each well as a substrate and incubation continued at 37ºC for further 10 min followed by pre-read at 625 nm using the 96-well plate reader Synergy HT (BioTek Inc. USA). Then freshly prepared phenol hypochlorite (115 µL) reagent was added in each well (by mixing 45 µL of phenol reagent with 70 µL of alkali reagent). Incubation was further continued for another 10 min followed by the measurement of absorbance. The percentage enzyme inhibition was calculated by the formula: Inhibition (%) = 100 – [(Abs. of test sample / Abs. of control) × 100]. $IC_{50}$ values of active compounds were determined by measuring activities at further dilutions and the data were computed by using EZ-Fit Enzyme software (Perrella Inc., USA).

### *Molecular docking studies*

*Structures preparation and docking protocol:* For molecular docking simulations of the most active compound, Surflex-Dock program implemented in Sybyl-X 2.12 by CARTRA Company was used under Centos-6.6 Linux operating system [17]. The structure of the most active compound was drawn by the sketching tool available in SYBYL; proper atom type for each atom in the most active compound was assigned. Compound was minimized using the Powell method until the gradient reached to 0.05 kcal/mol and the maximum iteration reached was 10000 with the Tripos force field. Similarly, the crystal structure of urease (4ubp.pdb) [18] from Protein Data Bank was retrieved. This structure was solved at the 1.5Å resolution and had all residues available in the active site. For docking simulations, the structure was refined and prepared using the protein preparation wizard. All heteroatoms were removed except the nickel ions that acted as the catalytic center for hydrolysis of urea in the active site of the enzyme. Similarly, missing hydrogen atoms were

added and protonation states were fixed at the termini of the protein. The protomol was generated near the active site residues containing Ni(II) ions and other amino acids. Surflex-Dock was employed to generate 20 docked conformers of the compound. Finally, C-Score was calculated for each conformer and the best binding pose was selected based on the best score.

*In vitro antibacterial screening*: The synthesized Mannich base ligand (L) and its complexes were evaluated for their antibacterial activity against *Bacillus thuringiensis* and *Escherichia coli* by the disc diffusion method [19]. Each compound was used at a concentration of 20 mg/mL in DMSO. The zone of inhibition was measured after 48 h of incubation at 37°C.

## RESULTS AND DISCUSSION

The physico-analytical information of Mannich base ligand (L**)** and its metal complexes is given in the experimental section. All synthesized compounds are stable and coloured solids at room temperature. The ligand and its metal complexes are insoluble in common organic solvents and soluble in chloroform, DMSO and DMF. The complexes exhibited non-electrolytic nature [20].

*IR spectra:* In order to get meaningful information about the connecting modes of L to the metal ion in the complexes, the IR spectrum of Mannich base ligand (L) was compared with the spectral data of its metal complexes. Important peaks at 1598, 1508, 1678 $cm^{-1}$ were attributed to C−N−C, C=C, C=O correspondingly [21-22] in agreement with our ligand. The indication of coordination through oxygen of carbonyl and nitrogen of pyrrolidine was provided by IR spectra of all complexes in which the peaks due to C=O and C-N-C were shifted to lower frequencies (1678−1659 $cm^{-1}$) and (1598−1589 $cm^{-1}$), respectively [23]. Coordination from these sites was further supported by the appearance of some new bands at 431−441 $cm^{-1}$ and 528−544 $cm^{-1}$ assignable to M−N and M−O bonds, respectively [24].

*NMR spectra:* The $^{1}$H-NMR spectrum of the ligand 2-[(3,4-dimethoxyphenyl)(pyrrolidin-1-yl)methyl]cyclopentanone exhibits a multiplet 1.196−1.279 attributed to $H_b$, $H_{b'}$ $H_f$ protons. The $H_e$ and $H_d$ protons appear as multiplet in the range $\delta$ 2.06 – 2.130 ppm. The triplet at $\delta$ 2.390 – 2.417 can be assigned to proton $H_c$. The protons $H_a$ and $H_{a'}$ appear as doublet of triplet at $\delta$ 2.967 – 2.995 ppm. The methoxy protons exhibit a sharp singlet at $\delta$ 3.937 ppm. The aromatic proton $H_{h'}$ exhibits a doublet at $\delta$ 6.934 – 6.948 ppm. The doublet at $\delta$ 7.134 – 7.137 ppm is attributed to proton $H_l$ and is in agreement with literature [25-26]. The doublet at $\delta$ 7.225 – 7.239 is attributed to the aromatic proton $H_{i'}$. The singlet at $\delta$ 7.543 is attributed to the aromatic proton $H_h$. These chemical shifts support well the proposed structure of L. In the metal complexes, the minor changes in chemical shift values of protons, particularly those close to C=O and C-N-C moieties support the involvement of these two groups in coordination with the metal ions [27-28].

The important chemical shifts of different carbon atoms of the ligand L and its metal complexes are also given in the experimental section. Unfortunately, chemical shift of quaternary carbon C=O could not be observed in both ligand and metal complexes, hence it is difficult to comment regarding bidentate coordination mode of ligand towards metal ion on the basis of $^{13}$C NMR data. Therefore, the bidentate mode of the ligand was proposed on the basis of the IR spectra while geometry of complexes was established on the basis of %age of metal by ICP-OES, UV-Vis and magnetic moment data.

*Mass spectrum (EI):* The EI mass spectrum of ligand (L) was recorded. In the said spectrum the base peak was observed at 380.2 which can be attributed to $[M+ 2K-H]^+$ (100), [29]. Some other fragments at 365.2 and 349.2 were also observed and can be attributed to $[C_{17}H_{22}NO_3+2K-H]^+$ (39) and $[C_{16}H_{19}NO_3+2K-H]^+$ (28), respectively.

*Thermal study (TGA)*: Thermal analysis was carried out in order to get knowledge about the thermal behavior of the ligand (L) and its complexes. Thermal studies were carried out by means of SDT-Q 600 V20.9 Build 20 by heating up to 1000°C. The TGA curve of the metal complexes showed an endothermic peak at 300°C which was corresponding to the elimination of chlorine coordinated to the metal ion. The organic part decomposed around 400°C. Above 600°C, there was no change in weight, the plateau observed corresponded to the oxide of the respective metal.

*UV/Vis and magnetic moment data:* The absorption band at 13146 $cm^{-1}$ in the Cu (II)-L complex can be assigned to $^{2}T_2$ ----> $^{2}E$ transition revealing tetrahedral geometry. The magnetic moment value of 2.12 B.M. of this complex further supported its tetrahedral geometry [30]. The Ni(II)-L complex showed two absorption bands at 11675 $cm^{-1}$, 15421 $cm^{-1}$ assigned to $^{3}T_1(F)$ -----> $^{3}A_2(F)$,$^{3}T_1(F)$ -----> $^{3}T_1(P)$ transitions supporting tetrahedral environment around the nickel ion. The magnetic moment value (3.21 B.M.) also favored similar environment around the nickel ion [31]. The

electronic spectrum of the Co(II)-L complex exhibited two bands at 11733 $cm^{-1}$, 17357 $cm^{-1}$ assigned to $^4A_2(F)$ -------> $^4T_1(F)$ and $^4A_2(F)$ -----> $^4T_1(P)$ transitions, respectively. The appearances of these bands were in good agreement with the tetrahedral stereochemistry for Co (II) ion which was further supported by its magnetic moment value at 4.29 B.M. [31]. The electronic spectrum of the Fe(II)-L complex showed a single absorption band at 8560 $cm^{-1}$ which was attributed to $^5E$ -----> $^5T_2$ transition of tetrahedral geometry. The room temperature magnetic moment (4.61 B.M.) of this complex corresponded to tetrahedral symmetry [32].

### *Biological activity*

*Antiurease assay*: The synthesized scaffolds were screened for their antiurease activities and their percent inhibitions and $IC_{50}$ values were determined. The enzyme inhibition potential was observed in the following order: L−Ni(II) > L−Fe(II) > L > L−Cu(II) > with $IC_{50}$ values 1.42±0.003 > 5.41±0.005 > 9.25±0.002 > 137.52±0.58 µM, respectively, as compared with standard thiourea with $IC_{50}$ value 21.25±0.15 µM (Table 1). The lower the $IC_{50}$ value, the higher is the inhibitory potential of the compound. Complex L−Co(II) was found inactive and inhibited only 27.87% enzyme activity. This shows that the complexation of L with Ni(II) and Fe(II) improved enzyme inhibitory potential (as shown by the decreased $IC_{50}$ values in comparison with (L) while with Cu(II) antiurease activity decreased considerably (as shown by the increased $IC_{50}$ value) and with Co(II), it completely abolished inhibition. Two nickel atoms are the part of the catalytic centre of the enzyme. The highest inhibition potential of the complex L-Ni (**4**) may be attributed to the catalytic centre by Ni-bound ligand molecule though this statement needs to be justified and possible mechanism of metals in the inhibition of urease enzyme remains to be determined.

### *Antibacterial activity*

The synthesized compounds were also evaluated for their antibacterial activity against *B. thuringiensis* and *E. coli* by the disc diffusion method. The zone of inhibition (mm) was determined as an index of antibacterial activity. These compounds exhibited poor antibacterial potential (Table 2).

### *Molecular docking*

In order to identify the probable binding pose of the most active Ni(II) complex, it was docked in the urease crystal structure of *Bacillus pasteurii* as shown in Figure 1.

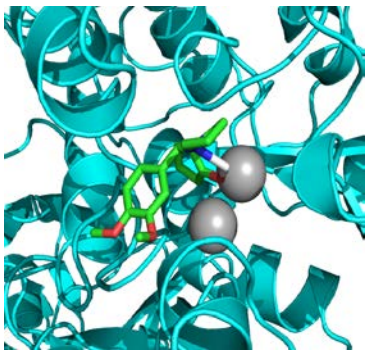


**Figure 1.** Predicted binding mode of the most active compound (green) in the active site (cyan) of urease enzyme. Silver spheres are Ni (II) ions.

The compound docked well in the binding site of the urease enzyme containing two Ni(II) ions, in which one is making trigonal geometries with two histidine residues (HIS137 and HIS139) and one aspartate (ASP363) while other having three coordinate covalent bonds with three histidine residues, (HIS222, His249, and HIS275). It was observed that methoxy groups on the phenyl rings were towards the solvent exposed side of the enzyme. Whereas, oxonium ion was towards one of the histidine residue (HIS222), which might give the binding stability of these compounds along with the van der Waals interactions to show biological response against the enzyme.

**Table 1**. Antiurease activity of L and its metal complexes

| S. No. | Sample code | Inhibition (%) at 0.5 mM | $IC_{50}$ (µM) |
|---|---|---|---|
| 1 | L | 64.87±0.07 | 9.25±0.002 |
| 2 | L-Cu | 64.53±0.92 | 137.52±0.58 |
| 3 | L-Co | 27.87±0.11 | - |
| 4 | L-Ni | 68.85±0.07 | 1.42±0.003 |
| 5 | L-Fe | 68.54±0.09 | 5.41±0.005 |
| | Thiourea | 98.45±0.87 | 21.25±0.15 |

**Table 2.** Antibacterial activity of ligand (L) and metal complexes

| Bacteria | L (mm) | L-Cu (mm) | L-Co (mm) | L-Ni (mm) | L-Fe (mm) | Gentamycine (mm) |
|---|---|---|---|---|---|---|
| *B. thuringiensis* | 3 | 10 | 11 | 6 | 5 | 18 |
| *E. coli* | 4 | 6 | 14 | 4 | 3 | 16 |

## CONCLUSIONS

The present study offers a simple method for the manufacture of *β*-aminoketones. Spectroscopic techniques supported the designed structures. The synthesized scaffolds were screened for their antiurease and antibacterial activities.

Most of the compounds showed poor inhibitory activity against *B. thuringiensis* and *E. coli* and strong inhibitory potential for jack bean urease. It is noteworthy that L−Ni(II) and L−Fe(II) exhibited potent antiurease activities. The docking studies supported the binding mode of the most active compound with the enzyme which is in agreement with the previous reported studies. Additionally, the mild experimental conditions, convenient operation and simple synthetic route made it credible for the production of corresponding scaffolds which may serve as an alternative route of metal containing inhibitors against urease enzyme.

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# Синтез, охарактеризиране и биологична активност на нова Манихова база 2-[(3, 4-диметоксифенил)(пиролидин-1-ил)метил]циклопентанон и комплексите му с Cu(II), Co(II), Ni(II) и Fe(II) йони

М. Лиакат[1], Т. Махмуд[1*], М. Имран[1], М. Ашраф[2], А. У. Хак[3], М. Мудасар[4], Т. Ахмад[5]

*[1]Институт по химия, Пунджабски университет, Лахор, Пакистан*
*[2] Департамент по химия, Исламия университет на Бахавалпур, Бахавалпур, Пакистан*
*[3] Колеж по фармация, Гашонски университет по медицински науки, Инчеон, Южна Корея*
*[4] Департамент по бионауки, COMSATS Институт по информационна технология, Парк роуд, Исламабад, Пакистан*
*[5] Департамент по химия, Университет на Саргодха, Миянвали, Пакистан*

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(Резюме)

Едностадийна трикомпонентна манихова реакция е проведена чрез кондензация на 3,4-диметоксибензалдехид, пиролидин и циклопентанон в присъствие на калциев хлорид и разтворител етанол, като е получена нова манихова база (L). Маниховата база е изолирана и са образувани комплексите й с Cu(II), Co(II), Ni(II) и Fe(II) йони. Структурите на синтезираните съединения са потвърдени чрез IR, $^{1}$H NMR, $^{13}$C NMR, масспектрометрия, термогравиметричен и елементен анализ. Металното съдържание е определено чрез ICP-OES. Всички съединения проявяват слаба антибактериална активност. Антиензимната активност е изследвана по отношение на бобова уреаза. Маниховата база (L), никеловият и железният комплекс проявяват силно антиуреазно действие с $IC_{50}$ стойности съответно 9.25±0.002, 1.42±0.003 и 5.41±0.005 μM, като са по-силни инхибитори от стандарта тиоуреа ($IC_{50}$ 21.25±0.15 μM). Възможният начин на свързване на най-активния никелов комплекс е определен чрез молекулни докинг симулации.