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Versatile Applications of Mannich Base Ligands and their Metal Complexes: A Review Article

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A B S T R A C T

Mannich base is a versatile compound that can be easily modified to introduce different functional groups, allowing for the creation diverse selection of items with varying features. Additionally, the Mannich reaction is a valuable tool in organic synthesis, due to the fact it provides an effortless and efficient approach for synthesizing C-N bonds. Overall, The Mannich base and even its derivatives are essential in many aspects of chemistry and its complexes are in the pharmaceutical industry. Studies have revealed that it shows good anti-cancer, anti-mycobacterial, remarkable anti-HIV, anti-tubercular, anti-convulsant, anti-fungal, antiviral, antitumor, cytotoxic activities and in industrial applications such as in the creation of polymers, surface activity agents, deter gents and resins. The presence of the basic Mannich sidechain has shown marked antimalarial, anti - inflammatory, analgesic and anti - microbial activities. These compounds have also been shown to inhibit corrosion, as well as antioxidant and reducing agents. This review article shows the definition, importance and different applications of Mannich base ligands with transitional metal. These complexes exhibit potent anti-microbial, antiviral, and anti-cancer activities, showcasing their potential in pharmaceutical research and drug development. Moreover, the luminescent properties of Mannich base metal complexes have been harnessed for applications in optoelectronics and sensing. Their tunable emission profiles make them suitable candidates for various sensing platforms and light-emitting devices Mannich base metal complexes.

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1. Introduction

The Mannich reaction, discovered in 1917 [1-6] stands out as a prominent multi-component reaction, involving the simultaneous addition of aldehyde, amine, and ketone in a one-pot condensation to produce amino carbonyl compounds, commonly known as Mannich bases. This reaction holds significant importance as it facilitates the creation of new C-C bonds, enabling the synthesis of diverse amino carbonyl molecules, see Fig. 1.

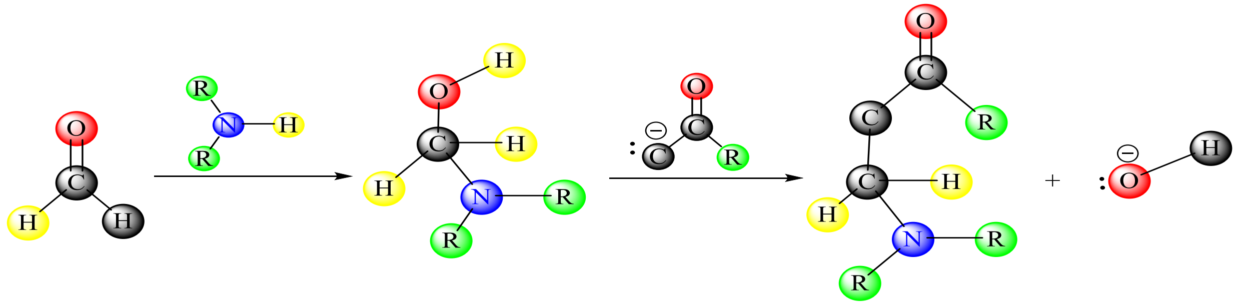


Figure 1: general structure of Mannich bases.

Consequently, the Mannich reaction has a significant effect in the outcome synthesis of essential biomolecules such as peptides, amino alcohols, lactam, amino acids, and other biologically significant compounds. Its versatility and efficiency in forming key chemical bonds make it a fundamental and valuable method in modern organic synthesis, the compounds obtained could be versatile intermediates that help in this [7-12]. In recent years, there has been extensive research on the metallic complexes of Mannich bases, primarily due to the ligands' remarkable selectivity towards different transition metal ions. Notably, these complexes have demonstrated a strong inclination to form, leading to compounds with significant anti-cancer and anti-malarial properties. The straightforward synthesis process, adaptability, and diverse applications have sustained Mannich base complexes as a prominent and widely studied area of research. Their role in advancing coordination chemistry is evident from the existing literature, highlighting the vital contribution of these metallic complexes to the field's development [13-18]. Extensive volume on the toxicological, biological, and chemical features of Mannich bases with broad applications as polymers, dispersants in lubricants, and pharmaceutical agents. This is demonstrated by a review of the literature on Mannich reactions. Studying the structural and binding features of different Mannich base complexes can play a significant role in better understanding complex biological processes [19-22]. A few of the Mannich bases have been studied as corrosion inhibitors in our group. Through the nitrogen atoms π e- and the aromatic ring contained in the Mannich bases molecules, inhibition can be induced by their readily absorbed onto the metal surface. Therefore, as mild steel corrosion preventive in an acidic media, Mannich bases which have been successfully examined, can be used [23-27]. Mannich bases have found diverse and practical applications in various fields, such as treating conventional macro-molecular materials like textiles, leather, paper and synthesizing polymers. They are widely used as additives in petroleum production, cosmetics, water treatment, dyes, and analytical reagents. However, medicinal chemistry is the most significant and noteworthy application of the Mannich reaction. Initially, Mannich bases have shown intriguing biological activities, and with diligent screening processes, many more of their potential medicinal properties are yet to be uncovered. The continuous publication of numerous research papers each year supports the growing interest in exploring the medicinal aspects of Mannich bases and their potential as valuable candidates for drug development and therapeutic interventions. Second, amino methylation of drugs can be used to improve the delivery of drugs to the human body [28-31].

2. Literature Review of Synthesis Mannich Base Ligands and Their Complexes

2.1 [l-(di-n-buty1amine-N-methyl)-mercapto-lH-benzimidazole (L_1) and l-(diphenylamine-N-methy1) mercapto-lH-benzi-midazole] (L_2)

Synthesis of Mannich base ligands, L_1 and L_2 and reacted with metal ions to produce complexes (Co, Ni, Cu, and Zn). To examine the improvement of the reaction, the thin-1ayer method technique purified thin-layer chromatography utilized. Various spectroscopic techniques were used to describe the Mannich base 1igands and their metal complexes, including ^{1}H/NMR, FT/IR, UV/Visible, ICPES, ^{13}C/NMR and AAS. NMR and FT/IR analyses confirmed the monoanionic bi-dentate co-ordination mode of L_1 and L_2, while the tetrahedral geometries of the metal complexes were proposed based on AAS/ICP, electronic spectroscopic and magnetic moment results. Additionally, the luminescent behaviour of the synthesized compounds was investigated, revealing broad emission bands that indicate the involvement of charge transfer transitions [32], see in Fig. 2.

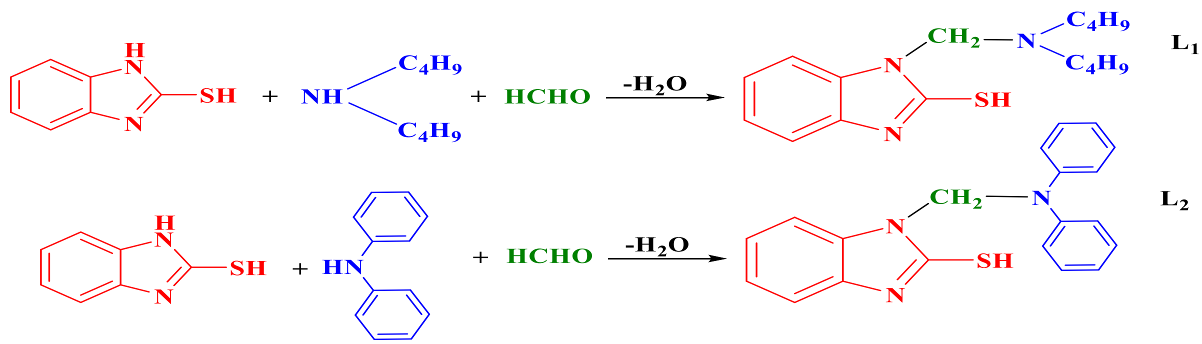


Figure 2: synthesis of two Mannich base ligands [32].

2.2 [1-((diallylamino)methyl)-1H-benzo[d]imidazol-2-ol (A_1) and 1-(((4-chlorophenyl)amino)methyl)-1H-benzo[d]imidazol-2-ol (A_2)]

Mannich base compounds (A_1) and (A_2) were formed and described by reaction O-phenylenediamine and urea with various amine. The hydrogen atom on the nitrogen atom was then swapped through the Mannich reaction employing primary and secondary amines. The synthetic chemicals were then examined using ^{1}H/NMR and FT/IR spectroscopy for their structural organization [33], see Fig. 3.

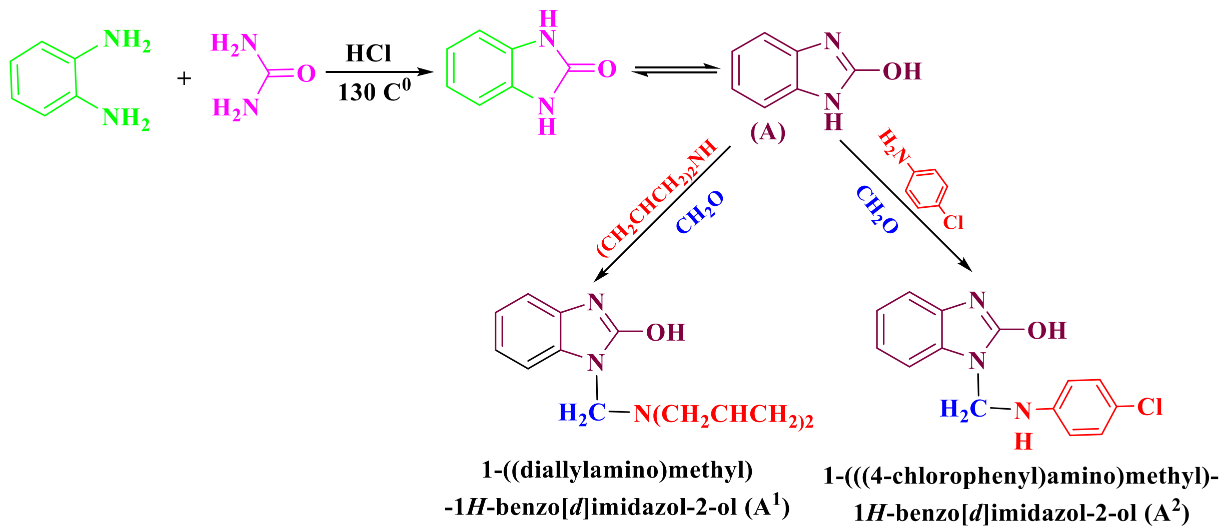


Figure 3: synthesis of compounds [33].

2.3 [$Co_3(L_2)(NO_3)_4$].CH_3CN (1) and [$Ni_3(L_2)(NO_3)_4$].CH_3CN (2)

Produced trinuclear cobalt (1) and nickel (2) compounds. These complexes were made using the ligand H_2L_2, which was made by reacting HL_1 as Mannich base in a [tow: one] mole ratio with propylene diamine. Reacting 5-bromo-salicyaldehyde with N, N, N'-trimethyl-ethylene diamine affords the Mannich base HL_1 precursor. In the ensuing complexes, metal ions are connected by NO and OC_6H_5 atoms. Two of each compound's 4 nitrato groups behave as che1ating ligands towards the termina1 meta1 ions. Compounds l and 2 have their core metal ions accommodated within the sa1en-1ike cavity of the organic ligand. End-on azido or end-on nitrato bridges can be applied in place of nitrato bridges; N-thiocyanato groups are formed, resulting in the compounds [$Ni_3(L_2)(N_3)_2(NO_3)_2$] (3), [Co_3 (L_2) $(NCS)_2$ $(NO_3)_2$]$_2$ (5) and [Co_3 (L_2) $(N_3)_2$ $(NO_3)_2$] (4). The magnetic characteristics of these five compounds were examined, and it was discovered that compounds l and 2 had intramolecular antiferromagnetic interactions, whereas compounds 3, 4, and 5 exhibit ferromagnetic connections. The nature and amplitude of these interactions are addressed and compared to prior research on similar systems [34] see Fig. 4.

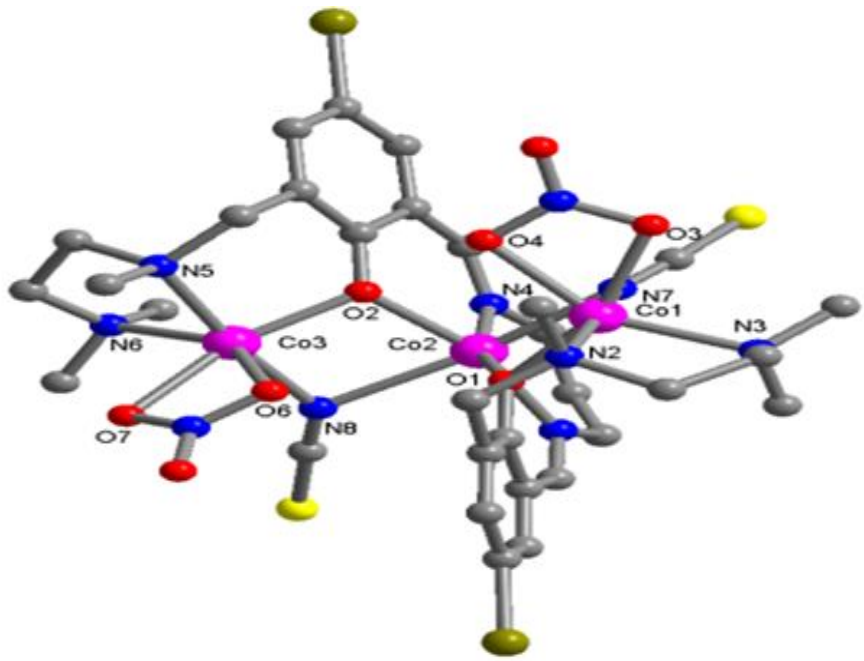
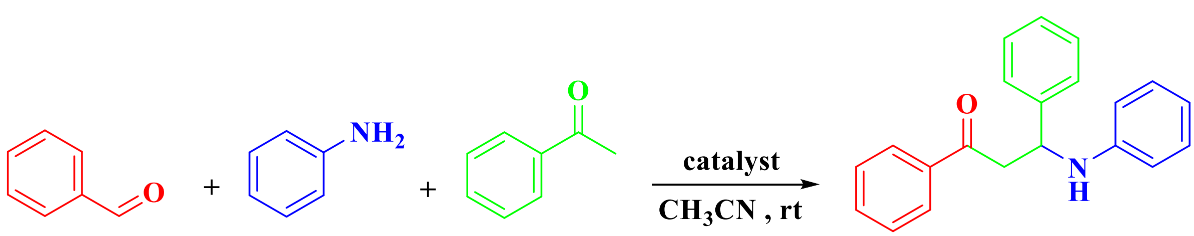


Figure 4: the tri-nuclear complex 5 [34]

2.4 [1,3-diphenyl-3-(phenylamino)propan-1-one (1)]

Hf $(OTf)_4$ was discovered to be a very effective catalyst for the Mannich process. Under solvent-free conditions, as little as (0.1-0.5) mol percent Hf $(OTf)_4$ may catalyze the high-yielding synthesis of a variety of aryl and alkyl ketone-based Mannich bases. The inclusion of Hf $(OTf)_4$ resulted in good region- and diastereo-selectivity in the synthesis of alkyl ketone-based Mannich bases. The ^{1}H-NMR tracing of the H/D exchange reactions of cyclopentanone and acetophenone in MeOH-d_4 revealed that the coordination of Hf $(OTf)_4$ with ketone might permit its quick keto-enol tautomerization, hence contributing to the overall promotion of the Mannich reaction. [35], see Fig. 5.



1,3-diphenyl-3-(phenylamino)propan-1-one (1)

Figure 5: the catalytic effect on Mannich reaction [35].

2.5 Mannich Bases and Bis-(Mannich bases) of Isoindolin-1,3-dione (1)

Synthesized novel Mannich bases compounds through reaction of formalin with the appropriate amine or di-amine and iso indolin-1,3- di one (1). By using dihydrazide or hydrazide as amino compounds in the reaction of Mannich base with 1, both (bis-Mannich and Mannich) bases were synthesized. The preparation of Mannich bases involved the incorporation of 1, showcasing the compositional potential of sec-Mannich bases is described as a precursor. The ketonic Mannich bases with N-alkylation of 1 was examined [36], see in Fig. 6.

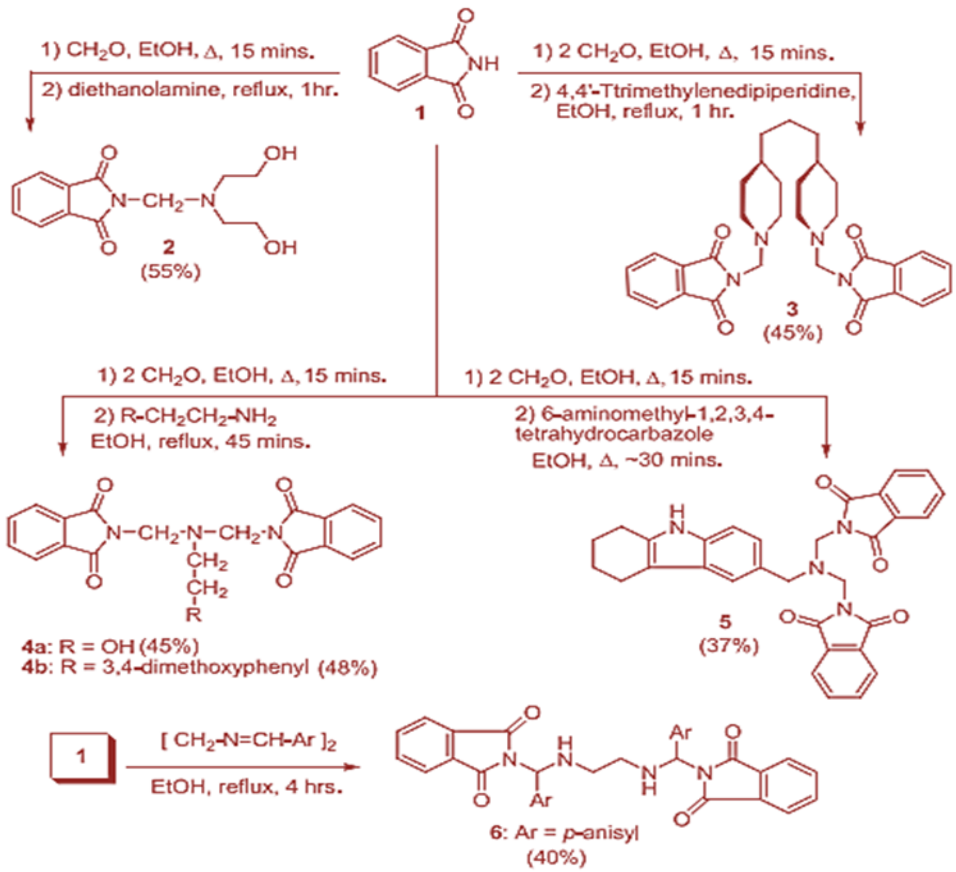


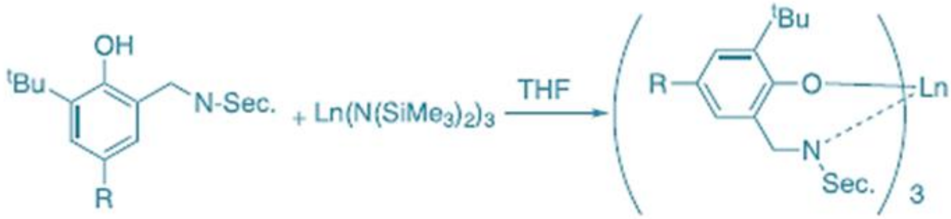
Figure 6: Mannich bases and compound (1) [36].

3. Versatile applications of Mannich bases

3.1 Catalytic properties

3.1.1 The catalytic properties of complexes for the ring-opening polymerization of ε-caprolactone

Synthesized a chain of Mannich base ligands HA = [2, 4 - t Bu_2 –6-CH_2 N Me_2 –PhOH , HB= 2, 4–t Bu_2 -6 - CH_2NEt_2–PhOH (HB), HC= 2, 4-tBu_2-6-CH_2 Py- Ph OH, HD= 2-tBu-4-Me-6-CH_2 Py- Ph OH, HE= 4-tBu- 2, 6-$(CH_2Py)_2$–Ph OH] through (Mannich reaction) by used form aldehyde and phenol reaction with amine (secondary). A chain of the ligands' amine elimination interactions with Ln[N$(SiMe_3)_2$ guided in the formation of homo-leptic complexes [$LaA_{3\ (1)}$, $LaB_{3\ (3)}$, $GdA_{3\ (2)}$, $GdB_{3\ (4)}$, $GdC_{3\ (6)}$, $LaC_{3\ (5)}$, $LaD_{3\ (7)}$, $GdE_{3\ (10)}$, Gd $D_{3\ (8)}$ and $LaE_{3\ (9)}$]. NMR spectra were used to describe Complexes 1, 3, 5, 7, and 9, and single-crystal X-ray diffraction was included to identify the structures of Complexes 3 and 5. Complexes 3 and 5 has same structure, with distorted octahedral geometry in the lanthanum core. Under this geometry, $O_{(1)}$, $O_{(2)}$, and $O_{(3)}$ atoms occupied two platforms, although $N_{(1)}$, $N_{(2)}$, and The NMR spectra of a -caprolactone oligomer indicated that the ROP of -caprolactone occurred via a coordination-insertion process. These Mannich base monophenolate lanthanide complexes' catalytic characteristics for ROP of -caprolactone have been investigated. For -caprolactone polymerization, all complexes show strong catalytic activity. The NMR spectra of a -caprolactone oligomer indicated that the ROP of -caprolactone occurred via a coordination-insertion process. $N_{(3)}$ atoms occupied the remaining three spaces. All complexes were analyzed by integratingelemental analyses and infrared spectroscopy. The catalytic properties of these Mannich base monophenolate lanthanide complexes for ROP of ε-caprolactone have been studied. All complexes showed high catalytic activity for ε-caprolactone polymerization. The NMR spectra of a -caprolactone oligomer indicated that the ROP of -caprolactone occurred via a coordination-insertion process. These Mannich base monophenolate lanthanide complexes' catalytic characteristics for ROP of -caprolactone have been investigated. For -caprolactone polymerization, all complexes show strong catalytic activity. The NMR spectra of a -caprolactone oligomer indicated that the ROP of -caprolactone occurred via a coordination-insertion process. [37], see Fig. 7.



1: R = tBu, N-Sec. = Me_2N, Ln = La; 2: R = tBu, N-Sec. = Me_2N, Ln = Gd
3: R = tBu, N-Sec. = Et_2N, Ln = La ; 4: R = tBu, N-Sec. = Et_2N, Ln = Gd
5: R = tBu, N-Sec. = pyrrolidyl, Ln = La 6: R = tBu, N-Sec. = pyrrolidyl, Ln = Gd
7: R = Me, N-Sec. = pyrrolidyl, Ln = La 8: R = Me, N-Sec. = pyrrolidyl, Ln = Gd

Figure 7: synthesis of complexes 1–8 [37]

3.1.2 The Trinuclear Copper Complexes as Catalysts in Oxidation Reactions.

In 2018, Avijit *et al*.,[38] successfully synthesized three ligands, namely The ligands used in this study, Namely H_2L_1, H_2L_2 and H_2L_3 where N, N – bis (3, 5-dime thy1-2-hydroxy benzy1)- N', N' -dimethyl-l,3-diamino propane , H_2L_1; N ,N -bis(3,5-dimethy1-2-hydroxy benzy1)-N', N'-dimethy1-l,2-diaminoethane], H_2L_2 and N,N-bis(3,5-dime thy1-2-hydroxy benzy1)-N', N'-diethy1-l,2-diaminoethane, H_2L_3 were reacted with [Cu.$(CH_3COO)_2$ .H_2O] to form dinuclear compounds [Cu_2L_2] (1-3). Subsequent reactions of these dimeric compounds with [Cu $(ClO_4)_2$. $6H_2O$], and [NaN_3] resu1ted in the formation of trinuc1ear compounds, [$(CuL_1)_2$(μL,l-N_3)$_2$.Cu(H_2O)].CH_3OH (l), [$(CuL_2)_2$(μL,l-N_3)$_2$.Cu(H_2O)].2CH_3OH (2), and [$(CuL_3)_2$.(μL,l-N_3)$_2$. Cu(H_2O)] .CH_3OH (3), in a 1 to 1 manner. The structures of these complexes were characterized using X-ray diffraction and CHNS analysis. All complexes exhibited catecho1ase-1ike and phenoxazine synthase-1ike activities in the presence of 3 ,5 –di - tert-buty1catechol and aminophenol, respective1y. The catalytic oxidation reactions resulted in the production of H_2O and H_2O_2 during the catecholase - 1ike and phenoxazine synthase activities respectively. These findings demonstrate the potential of these trinuclear copper complexes as catalysts in oxidation reactions and highlight their promising applications in various catalytic processes, see Fig. 8.

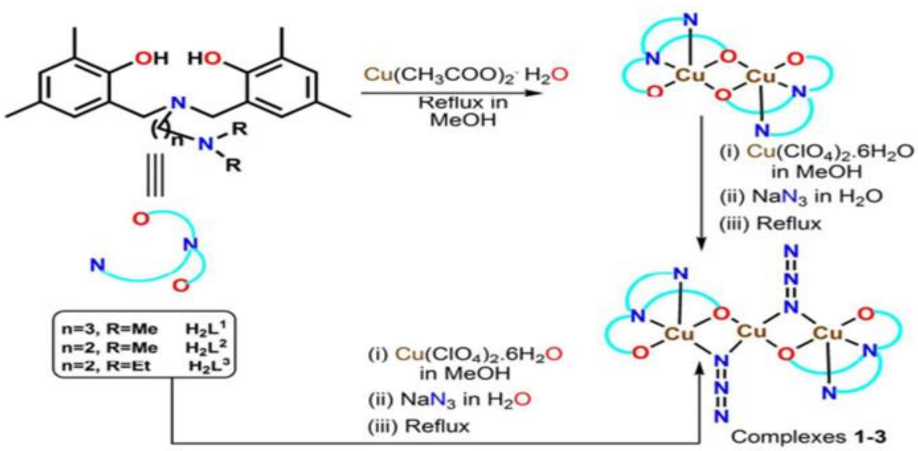


Figure 8: syntheses of complexes 1-3

3.2 Biological Activity

3.2.1 The anti-microbial Activity of Prepared Compounds Towards Selective Bacteria and Fungi

In 2016 Rehab *et al*., [39] synthesized novel compound [N-(4- morpholino methyl)-1,8–naphthal imide] =Mannich base ligand, reacted with metallic ion Pd^{+2}, Pt^{+4}, Ru^{+3}, Rh^{+3}, and were diagnosis through FTIR, UV-Vis and ^{1}HNMR spectroscopy, A.A., C.H.N.S, as well as conductance and magnetic measurements. The results display for all complexes were create in [Metal: Ligand] [1: 2] mole ratio but for Palladium^{+2} complex which was create in [Metal: Ligand] [1:1] mole ratio. The anti-microbial action of prepared compounds has been tested towards some selective bacteria, for example *P. aerugionosa*), *B. Subtilis* and some selective fungi *C. albicans*), A. flavus through diffusion method [39], see Fig. 9.

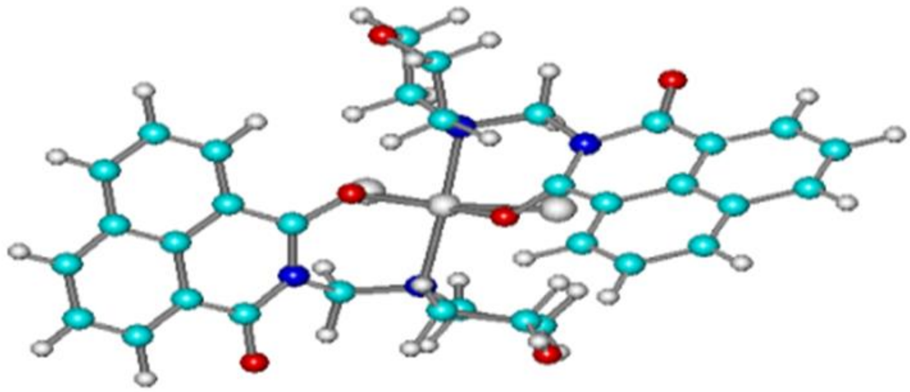


Figure 9: synthesis of [RuL_2] complex [39].

3.2.2 The Anti-microbial Activity of Prepared Compounds Towards Selective Bacteria and Fungi

Mannich bases been synthesized from (TBB)= N-(phenyl(thiomor pho1ino) methy1) benzamide, (TBA)= N-(pheny1(thiomorpholino)methyl) acetamide, (TBC)= 1-N-(phenyl (thiomorpholino)methyl) carb amide and (TBN)= N-(phenyl (thiomor pholino) methyl) nicotin amide. TLC, FTIR, MS Spectra, ^{1}H, ^{13}C-NMR and C.H.N.S. The antibacteria1 and antifunga1 activity of the prepared compounds was tested against specific types of bacteria and fungi. (TBC) show very good efficiency towards *S. aureus*, *P. aeruginosa* and *E. coli*; (TBA) show very good efficiency towards *P. species*, *A. niger* and *C. albicans*, compared to other Mannich bases [40], see Fig. 10.

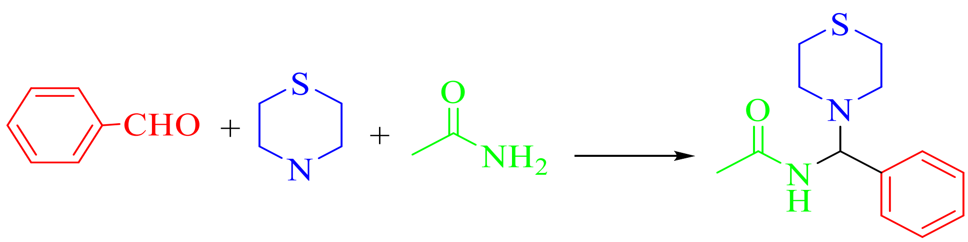


Figure 10: synthesis of (TBA) [40].

3.2.3 The Anti-bacterial Activity of Prepared Compounds

Prepared a novel ligand BTBPBO = [3-4-[4-(Benzo thiazol-2-yl-amino)-benzyl]–phenyl iminobutan-2-one oxime] from the reaction of 4 ,4-dia aniline methane with 2-mercpto benzo thiazole, then the produce of this period reacted with diacetylmonoxime. The compounds were organized from reaction of (BTBPBO) with metal ion (ii) [Co, Cu, Cd and Hg] and diagnosis through the spectral and physical ways to govern the stereo-geometries of prepared compounds, which showed that it has a shape tetra hederal but Co(ii), Cu(ii) compounds were octahedral. The prepared compounds display good anti-bacterial efficiency [41], see Fig. 11.

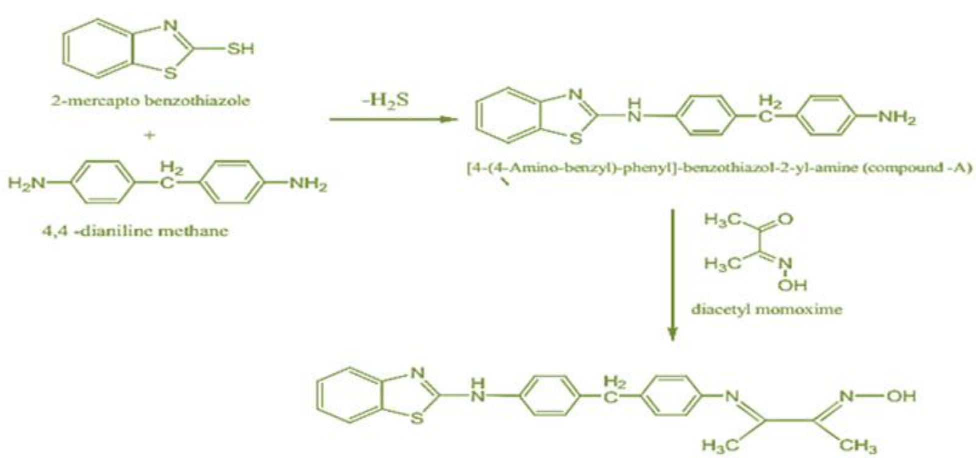


Figure 11: synthesis of Mannich bases [41].

3.2.4 Anti-bacterial Activity of Compounds Towards Several Choices Bacterial

Novel chain compounds of mixed ligands contained (La)= 1,10-phenanthroline and Mannich ligand (Lb), where Lb= The compounds Lb_1, Lb_2, and Lb_3 were synthesized as N-[1-Morpholino-(3-methoxy-4-hydroxy)benzyl] acetamide (M.B.A); N- [l-Morpholino-(3-methoxy-4-hydroxy) benzy1] urea (M. B.U) and N-[l-Morpholino-(3-methoxy-4-hydroxy) benzy1] benzamide (M.B.B) respectively with Fe(ll), Ni(ll), Co(ll), Zn(ll) and Cu(ll) ions. General formula with preparing complexes: [M $(Lb)_2$ (La)] n H_2O and octahedral structure. The compounds were diagnosis by UV/Vis, conductance, FT/IR, and CHN as well as magnetic data. Through the resu1ts of the measurements, the ligands showed a bidentate coordination with the metal ions by O /atom for the CO-NH_2 group, and N/atom for the C_4H_9NO group, while the ligand La is coordinated through the two nitrogen atoms. Anti-bacterial actions of compounds were studies towards several choice bacterial [42], see Fig. 12.

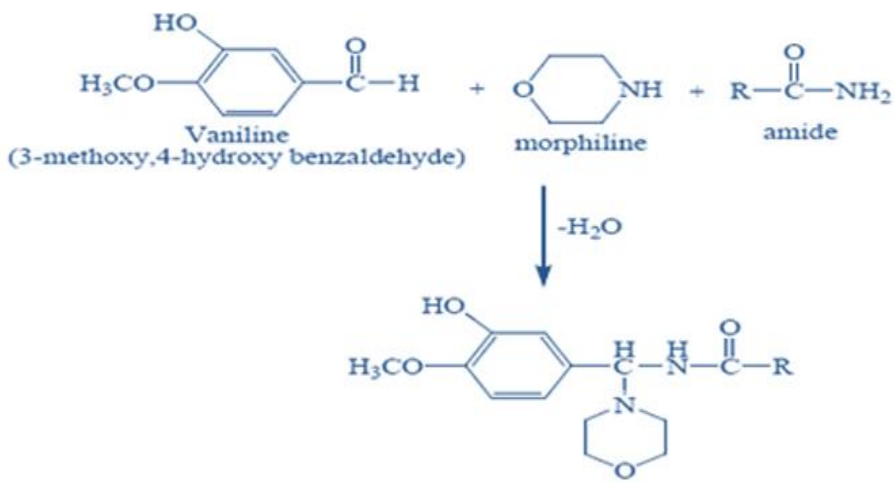


Figure 12: preparation of ligand [42].

3.2.4 The Anti-microbial Activity of Mannich Bases

Reacted aldehyde and produce primary aliphatic amines with (5-methyl -1Hs -triazo1e-3- thiol)(1) to generate the Schiff-Mannich base [2-methy1-6-substituted-6,7-dihydro-5H-s-tri azolo[5,l-b]-l,3,5-thiadiazines] (cyclic), When primary aromatic amines were coupled with 3-methy1-l-((substituted-amino)methy1)-1H-s-triazole-5-thiols (unicycles), methanol (formaldehyde) specifically interacted with 4-amino-3-methy1-s-triazole-5-thio1 (8) in the laboratory or boiling ethano1. Without integrating the secondary amine, this reaction produced 3-methyl-5,6-dihydro-s-triazo1o[3,4-b]-l,3,4-thiadiazol. These reactions followed the Mannich reaction criteria. Furthermore, Schiff's bases (unicycles) were synthesized by reacting aromatic aldehydes with compound (8) under varied circumstances. All unique compounds' structures were proven by C.H.N.S. In addition to the anti-microbial activity, some prepared derivatives showed a high ability to remove certain ions (Pb(ii), Mg(ii), Ca(ii) and Cd(ii)) from aqueous solutions [43], see Fig. 13.

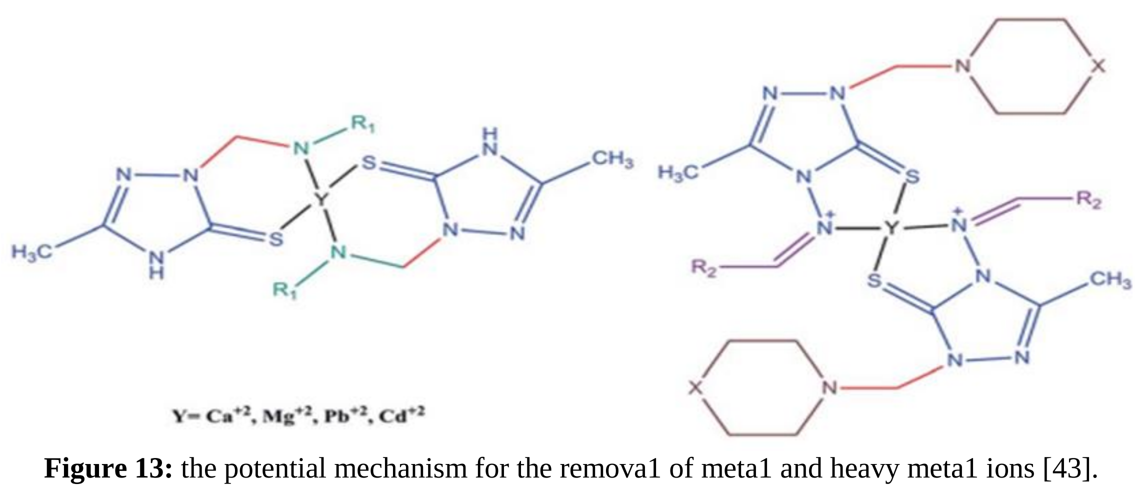


Figure 13: the potential mechanism for the remova1 of meta1 and heavy meta1 ions [43].

3.2.4 The Anti-bacterial Activity Testing Against Specific Types of Bacteria

Reacted salicylaldehyde and 1,3-cyclohexanedione with urea to prepare Mannich base, 1-((2,6- dioxo cyclohexyl) (2-hydroxyl phenyl) methyl) urea and through its reaction with metal ions a group of complexes (1a-1e) were prepared, where the prepared compounds were identified by different spectroscopic methods EPR, UV-visib1e, FT-IR, ^{1}H-^{13}CNMR and from the resu1ts of the measurements the octahedral geometry of complexes was determined. Using the diffusion method. The prepared compounds were subjected to biological activity testing against specific types of bacteria *S. aureus*, *P. aeruginosa*, *K. pneumaniae* and *E. coli* as the results showed that the effectiveness of the complexes was higher than the reference (Ciprofloxacin) used [44], see Fig. 14.

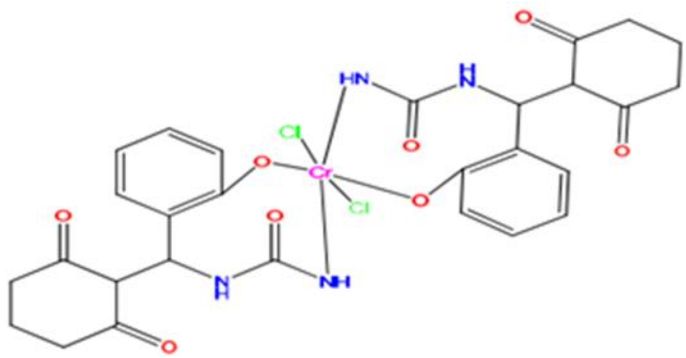


Figure 14: structure of Cr complex [44].

3.2.5 The anti-bacterial Activity of the Prepared Compounds

Prepared Ni(II), Cd(II), Co(II), Cu(II) and Fe(III) complexes derived from tri-azole new tri-dentate ligands and diagnosis using various spectro-scopic ways. As proposed by the conductivity data, all the compounds were of an electrolytic nature. Ligand trizol is coordinated with the meta1 ions in the complexes through an atom (N) in a group (amino) and an atom (S) in a group (thiophenolic) and this is confirmed by the measurements of (FTIR). The thermal stability of the prepared compounds was studied, which was found to have an octahedral geometry. When testing the bacterial activity of the prepared compounds, it was found that the compounds containing ions (Nickel(ii), Cobalt(ii), and Copper(ii)) as a metal centre showed good results against the selected bacterium types (*B. subtilis, S. pyogenes* and *P. vulgaris*) compared to the standard [45], see Fig. 15.

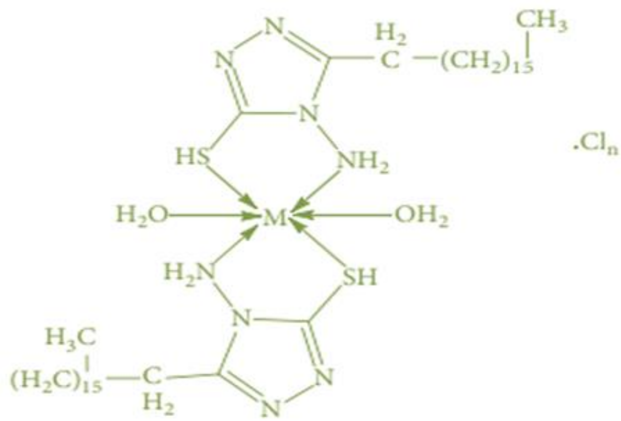


Figure 15: proposed structure of complexes [45].

3.2.6 The anti-bacteriaI Activity of Ligand and CompIexes

Reacted 4-N, N-dimethyl benzaIdehyde A Schiff-Mannich base, 5-((lH–indol-1-yl)methyl thio)–N-(4-(dimethyl amino)benzylidene)-1 ,3 ,4–thiadiazol-2-amine (L), was synthesized by combining 2-amino-5-mercapto-1, 3, 4-thiadazole with indole. This ligand, L, was then reacted with various meta1 ions including Co(II), Pd(II), Ni(II), Cu(II), Au(III), and Pt(IV) to form complexes. Using different spectroscopic techniques such as ^{1}H - ^{13}C /NMR, UV/Vis, CHNS, and FT-IR, complexes have been identified. Based on the measurement results, it was determined that the ligand L exhibited a tridentate behavior when interacting with the metal ions. The antibacterial activity of the prepared compounds was evaluated against specific strains including Klebsiella pneumoniae (G^-), Bacillus subtilis, and Staphylococcus aureus (G^+). The results indicated that the complexes demonstrated higher anti-bacterial activity compared to the ligand alone. Furthermore, the HyperChem 8.0.7 program was utilized to study the compounds in the gas phase and calculate the binding energy, HOMO, LUMO, heat of formation, infrared vibration of the bond, and the electrostatic potential [46], see Fig. 16.

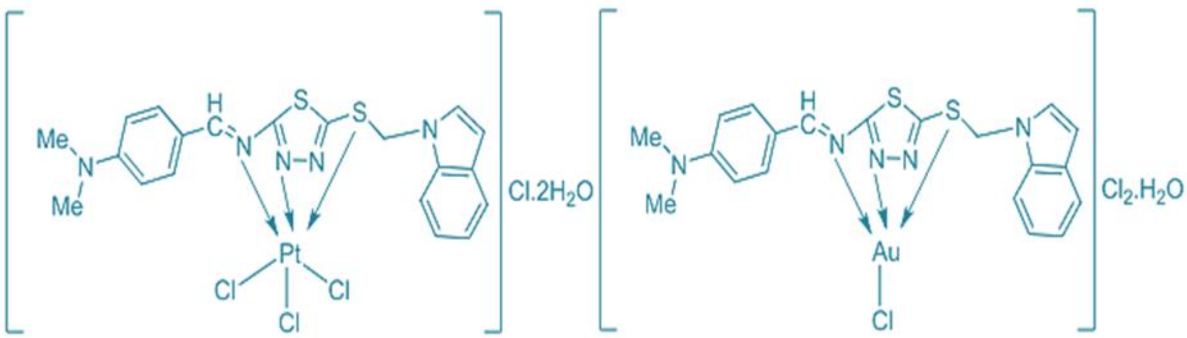


Figure 16: structure of complexes (Pt and Au) [46].

3.3 Corrosion inhibition

3.3.1 The effect Mannich Base as Corrosion Inhibition on Copper in 1 M HCl Medium

Synthesized a Mannich base= MFC= N-(4-(Mor pho lino methyl Carbamoyl Phenyl) furan-2-carbox amide and dignosis through [1]H, [13]C-NMR and FT-IR. By measuring electrochemical impedance spectroscopy (EIS), Periodic voltage measurement, weight loss wt., and active dynamic polarization (CV), the effect of MFC inhibition on copper in 1 M HCl medium was studied. To describe the corrosion inhibitor mechanism, thermo dynamic parameters, for example, enthalpy, free energy and entropy were personalized. With increasing Adding an inhibitor to the copper metal controls this copper oxidation, as revealed in the CV. Significant morphological improvement over the copper surface with the addition of the inhibitor. This was demonstrated by surface analysis using SEM [47], see Fig. 17.

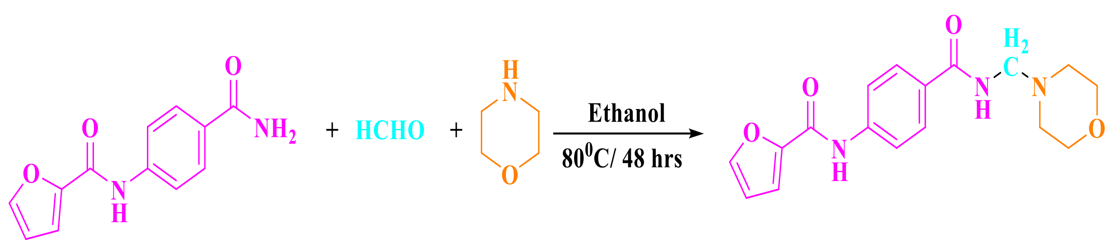


Figure 17: Synthesis of MFC [47].

3.3.2 Mannich-base H.M.P as a corrosion inhibitor for mild steel in a 0.2 M

A new Mannich base called 2-((4-(2-hydroxy-4-methylbenzyl)-pipera.zin-1-yl)methyl)-5-methyl.phenol (H.M.P) was successfully synthesized. The compound's characterization was carried out using various spectroscopic techniques such as C.H.N.S, UV-Vis, [1]H, and [13]C-NMR. To assess its effectiveness as a corrosion inhibitor for mild steel in a 0.2 M A substance has been evaluated for weight loss and potential dynamic polarization methods in an H_2SO_4 solution. The results revealed that the compound's inhibitory activity increased with increasing inhibitor concentrations. However, the inhibitory impact faded within 96 hours. Analysis of potential dynamic polarization data revealed that the inhibitor acted as a mixed-type corrosion inhibitor; density functional theory (D.F.T) calculations were performed to gain a more accurate recognizing of the relationship between the molecular structure of H.M.P and its inhibitory properties. This research sheds light on the synthesis, characterization, and prospective use of the new Mannich-base H.M.P as a mild steel corrosion inhibitor in acidic situations. The findings on its inhibitory properties and the relationship with its molecular structure offer important insights for future research and the development of effective corrosion inhibitors for various industrial applications [48]; see Fig. 18.

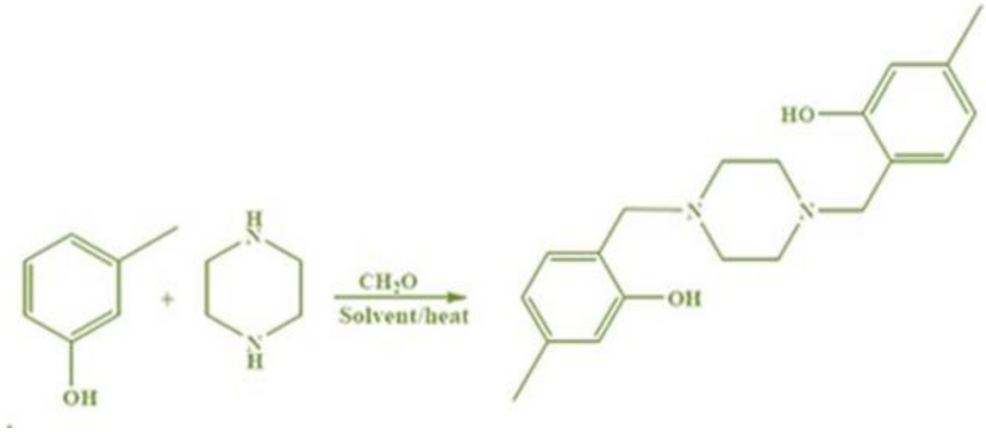


Figure 18: Synthesis of (HMP) [48].

3.4 Antioxidant activity

3.4.1 Antioxidant activity of Mannich-bases

Mannich-bases for cyclovalone derivatives were synthesized, and their antioxidant activity was determined using the D.P.P.H free radical-scavenging assay. Via ^{1}H/NMR, FT/IR, ^{13}C/NMR and MS spectroscopic result, the composition of the compounds was confirmed. The highest antioxidant activity was shown by the complex de Maniche derivative of cyclofalone with diethylamine (2a), with an lC50 value of 39.0 M. According to structure-activity connection research, compounds suffering a higher pKa value for the Mannich base have more activity, as proven by lower IC50 values [49], see Fig. 19.

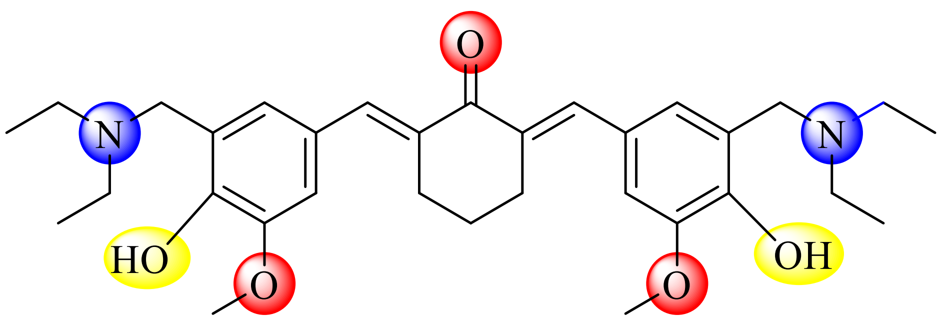


Figure 19: ^{1}H-NMR spectrum of compound 2a [49].

3.4.2 Antioxidant properties of Mannich bases

Three-part Mannich reaction involving benzaldehyde, either acetophenone or 4-iodoacetophenone, and various substituted anilines, catalysed by di-ethanol ammonium chloroacetate. The Mannich bases (MBs) obtained from this reaction showed excellent yields. All compounds were comprehensively characterized using C.H.N.S, ^{1}H, ^{13}C-NMR, UV-Vis, and FT-IR spectral analyses. The in vitro antioxidative potential of the synthesized MBs was evaluated utilized in this study, the antioxidative activity of compounds containing anisidine moiety was investigated using the Thermodynamic investigation of 2,2-diphenyl-1-picrylhydrazyl radical and density functional theory (D.F.T). The results illustrated that these compounds have slight antioxidative implementation. Furthermore, getting rid of iminium ions is required to eliminate water, which was suggested as a key rate-determining step for the overall reaction process. This study provides valuable insights into the synthetic efficiency and antioxidative properties of the produced MBs, offering potential applications in medicinal chemistry and other fields requiring antioxidant agents. The use of diethanol ammonium chloroacetate as a catalyst represents a significant advancement in the Mannich reaction, facilitating the synthesis of diverse MBs with promising biological activities [50]; see Fig. 20.

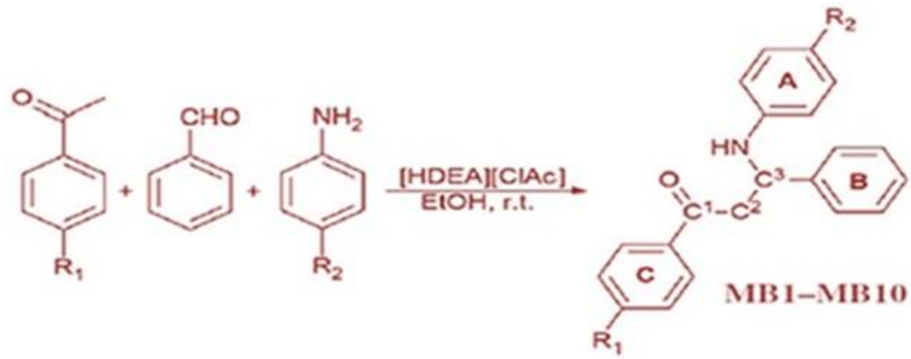


Figure 20: Structure of Mannich bases [50].

3.4.3 Antioxidative Activity of Mixed Ligand Complexes

Synthesized a novel series of mixed ligand complexes containing Coordinated with Co(II), Ni(II), Co(II), and Zn(II) ions, 8-hydroxyquinoline (Q) and a bis-phenolic Mannich base, 2,2'-((2-(dimethyl-amino)ethyl)-azanediyl)-bis(methylene))bis(4-(tert-butyl))bis(4-(tert-butyl)bis(methylene))bis(4-(tert-butyl)bis(phenol), for med complexes. The compounds were characterized using magnetic measurements, spectral studies, conductance measurements, and (CV) cyclic voltammetry. Magnetic and spectral data revealed an octa hederal structure for all the comp1exes. The redox behaviour of meta1 comp1exes was investigated through cyclic vo1tammetry. Using the diffusion method, the synthesized compounds were tested for their anti-bacterial activity against *S. aureus* and *E. coli* their anti-fungal activity against *A Niger* and *Penicilium species*. Remarkably, all the compounds exhibited potent antimicrobial properties against the tested fungi and bacteria. Moreover, the compounds demonstrated significant antioxidant capacity based on antioxidant assays. This indicates their potential as effective antioxidants, which is of great interest for various applications in pharmaceuticals, food preservation, and other fields that require antioxidative properties. The introduction of a bisphenolic Mannich base in combination with 8-hydroxyquinoline resulted in the formation of promising mixed ligand complexes, showing both strong anti-microbial activity and antioxidative potential. This study contributes valuable information for developing novel complexes with potential applications in medicine and other fields [51], seen Fig. 21.

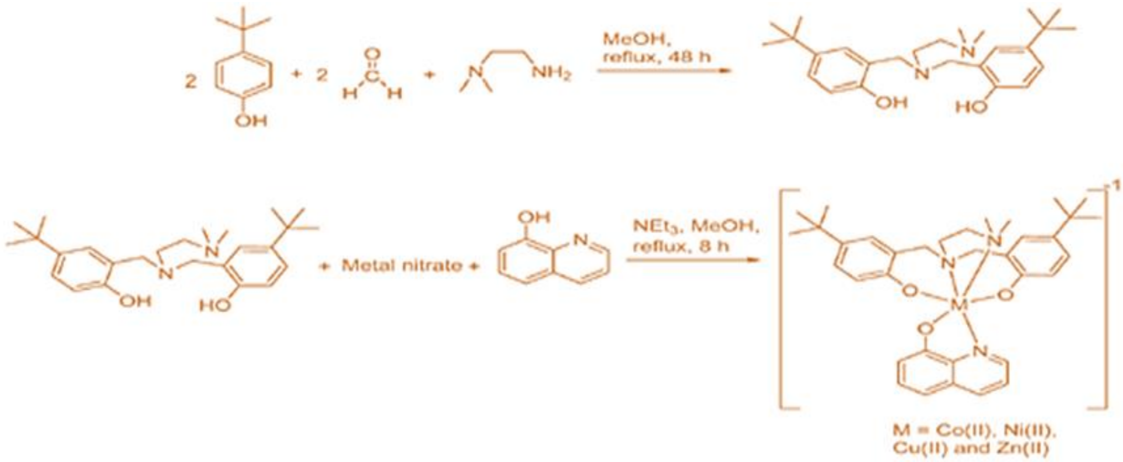


Figure 21: synthesis of new compounds [51].

3.5 Anti-urease Activity of Mannich Bases

Prepared Mannich base {MMP= 1-[(4-methoxy phenyl)(2-methylidene cyclohexyl) methyl]pyrrolidine through reaction (4-methoxy benzaldehyde, cyclohexanone and pyrrolidine). The MMP reaction with chloride salt (ii) (Cu, Ni, Co, and Fe) gives their complexes. The prepared chemicals were ascertained utilizing FT/IR, TGA, ^{1}H/NMR and ^{13}C/NMR measurement, and their potential as anti-urease agents was evaluated. The Mannich base exhibited with an IC-50 value of 224.83, 0.84 M, it has modest anti-urease action. Current research can give an intuitive approach for synthesizing a Mannich base with efficient anti-urease scaffolds [52], see Fig. 22.

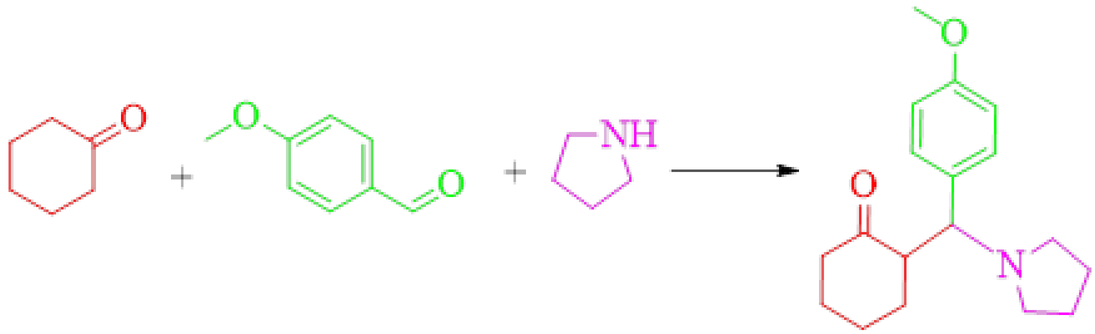


Figure 22: Synthesis of Mannich base (MMP) [52].

3.6 Anticancer activity

3.6.1 Anticancer activity of Mannich bases

Four times higher activity than standard tamoxifen, Mannich's-base compound N-[(diphenyl amino) methyl] acetamide has been shown to be used to overcome drug resistance to estrogen receptor protein. Using Acce1yrs Discovery Studio version 2.5 c1ient software, the X-ray crystal structure of the estrogen receptor protein (PDB 1D 2YAT) was down1oaded from the Protein Data Bank (PDB) and docked with the target Mannich bases. The best compound was also identified, and its anticancer activity was confirmed using in vitro MTS analysis using Raju and Jurkat cell lines based on the results of the in silico ana1ysis of the target compounds with standard tamoxifen [53], see Fig. 23.

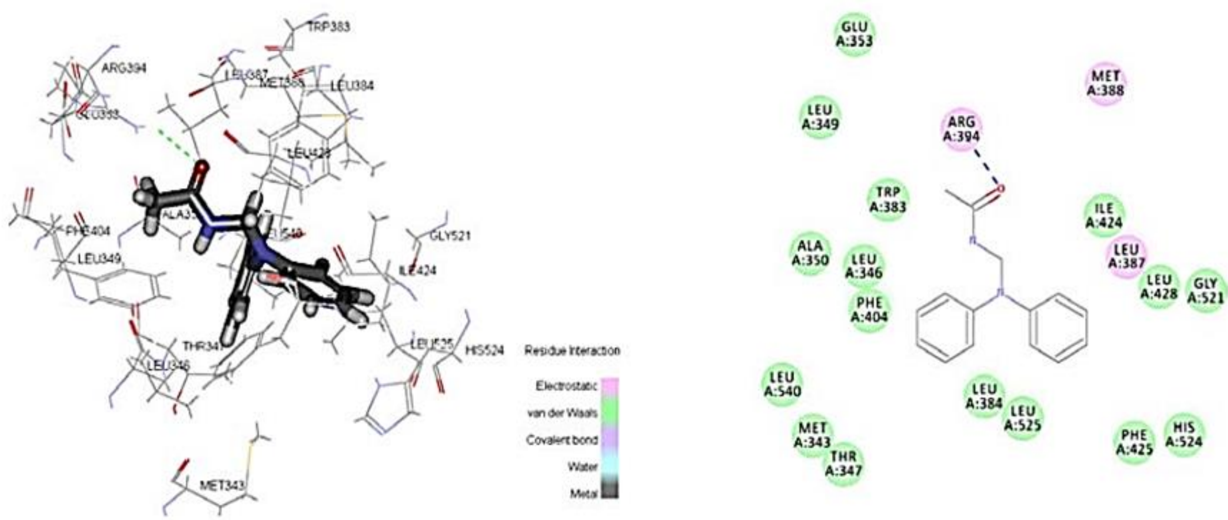


Figure 23: Association of N-[(diphenylamino)methyl] acetamide with amino acids [53].

3.6.2. The anti-cancer Activity of Compounds

Synthesized novel aminonaphthaquinones derived from law sone using Mannich reaction, at lab temperature for anti-cancer use. Munch bases compounds have been prepared, including various amines and aromatic aldehydes with a product yield ranging from medium to high. The anti-cancer efficiency (MTT) with nuclear morphology assessment (DAPI staining or 40, 6-diamidino-2-phenyl indole), apoptosis assessment Tests such as ethidium bromide staining or acridine orange, hemo1ysis, and DNA ladder assay can be conducted on the human liver carcinoma cell Iine Hep-G2 to obtain results. Additionally, one of the basic compounds derived from dried henna (Lawsonia inermis) is available leaves is Lawsone (2-hydroxyl-1,4-naphtha quinone) [54], see Fig. 24.

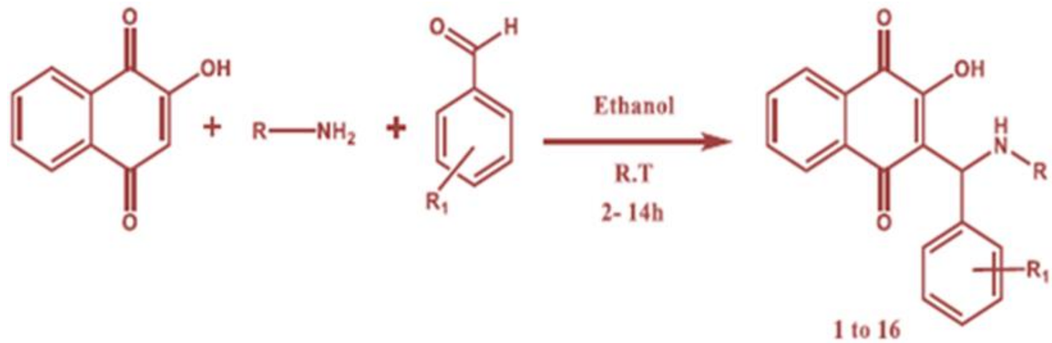


Figure 24: Production of Mannich base compounds [54].

3.6.3 The anti-cancer Activity of Ligand and both Complexes

Synthesized new ligand Mannich base containing the 1,3,4-oxadiaole ring was synthesized and characterized using FT/IR, UV, elemental analysis, ^{1}H/NMR, and ^{13}C/NMR techniques. Subsequently, a comp1ex of Pt^{+4} and Cu^{+2} was prepared by complexation with the synthesized ligand and characterized using UV, FT-IR, flame atomic absorption, magnetic susceptibility, and molar conductivity. The results confirmed the successful synthesis procedure. The antibacterial activity and cytotoxicity. The attributes of the ligand and its metal complexes were investigated. Antibacterial and antifungal activity has been illustrated, and identified against *E. coli* (gram-negative), *S. aureus* (gram-positive), *C. albicans*, and *A. f1avus*. Cytotoxicity was examined on a normal cell line (MDCK), and the findings revealed that the LD50 of L reached 936 g/mL, the toxicity of Pt reached 875 g/mL, and the toxicity of Cu was 1356 g/mL. The ligand and both complexes had been further evaluated for toxicity against a human lung cancer cell line, and the findings disclosed that the LD_{50} of the Pt complex at 615 g/mL. toxicity of Cu complex= 653 µg/mL and toxicity of free ligand= 620 µg/mL. Low MIC was resulted for the ligand and both complexes compared with Amoxicillin and Ampicillin as antibiotic [55], as seen Fig. 25.

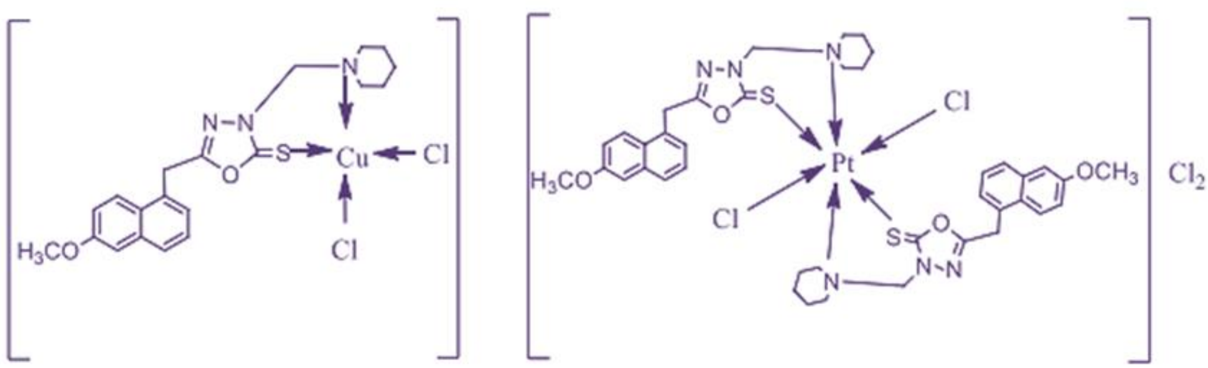


Figure 25: flowchart for the synthesis of ligands and complexes [55].

3.6.4 The anti-cancer Activity of the Prepared Compounds

Prepared ligand Mannich base [3-((3-(4- hydroxyl phenyl)-5-mercapto-4H-1, 2, 4–triazol-4-yl)amino) benzo furan-2(3H)-one] (L), which is derived from acetone and formaldehyde with secondary amine (heterocyclic compound possesses two rings), which in turn interacted with the metal ions Ni(II), Cu(II), Au(III) and Pd(II) to prepare the complexes, where the prepared compounds were identified by different spectroscopic methods C.H.N.S, UV-Vis, TGA and molar conductivity , flame atomic absorption and magnetic susceptibility from the results of the measurements, the square-planar geometric structure was suggested for the metal complexes with chemical formulas $[PdLCl]Cl.2H_2O$, $[NiLCl]Cl.6H_2O$, $[AuLCl]Cl_2.3H_2O$ and $[CuLCl]Cl.H_2O$. Using the MMT method, a toxicity examination of the prepared compounds was carried out on the brain cancer cell line (AMJM), where it was found that the gold complex is the highest toxicity among the tested compounds [56], see Fig. 26.

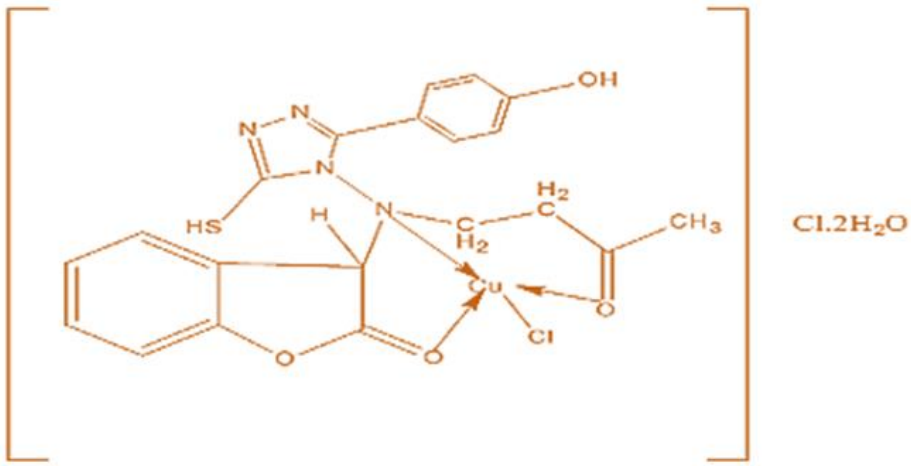


Figure 26: Proposed structure of complexes [56].

3.7 Mannich base Ligand as a Fluorescence Sensor

The complexes were produced by the ligand H_2L (N, N′-di methyl –N, N′ -bis (2- hydroxyl-3-methoxy-5-methyl benzyl) ethylene diamine) responded with Zn (ii) ion in the presence of (bridging co - ligands), azide/acetate or thio cyanate/acetate, chloride. (di-nuclear), $[Zn_2L(SCN)2(H_2O)]H_2O$ (1), $[Zn_2L(N_3)(CH_3CO_2)]$ (2) and $[Zn_2LCl_2 (H_2O)]$ (3), while Cd(ii) ion produced complexes (tetra-nuclear), $[Cd_4L_2(N_3)_2(CH_3CO_2)_2]$. $3H_2O$ (4), $[Cd_4 L_2(SCN)_2 (CH_3CO_2)_2]2H_2O$ (5) ,$[Cd_4L_2Cl_4]H_2O$ (6) with (H_2L) and co-ligands. The possibility of using the ligand (H2L) as a fluorescence sensor that automatically detects the zinc ion $^{(+2)}$ is very effective in the work, as (7.69) nM represents the detection limit for the said ion. it is greater than most of the fluorescence sensors reported for this ion with the correlation constant K =1.508 × 1010 M^{-2} zinc complex $^{(+2)}$ was also used as a sensor. Recently, zinc complexes may be good as a picric acid sensor because of their high sensitivity, structural simplicity, and cost calculation [57], Fig. 27.

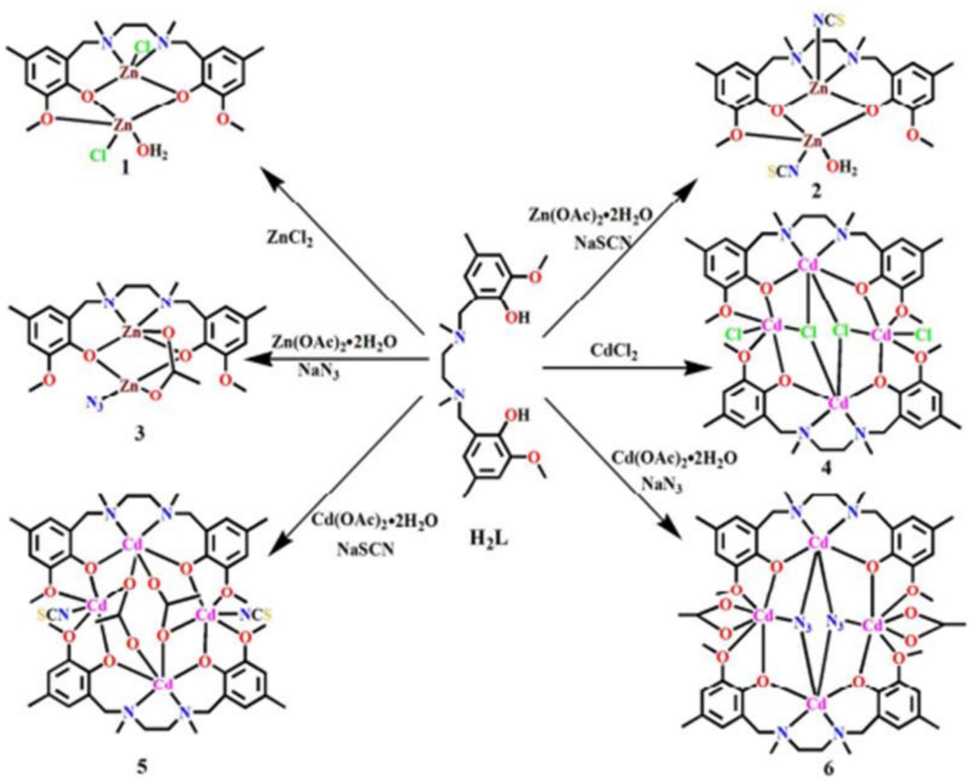


Figure 27: Synthesis of complexes 1-6 [57].

3.8 The potential Applications of Mannich-base in various fields, including Magnetism and Materials Science

Synthesized metal complexes by reacting the Mannich-base ligand H_2L where N , N'-di methyl –N , N' –bis (2 – hydroxy -3- methoxy- 5-methyl benzyl) – ethylene – di amine with the metal ions Co and Ln, where Ln= Dy, Tb, and Gd, resulting in three complexes: Co_2Gd_2 $L_2(\mu 4\text{-}CO_3)_2(NO_3)_2]$ (1), $[Co_2Dy_2L_2$ $(\mu 4\text{-}CO_3)_2$ $(NO_3)_2]$ (3) and $[Co_2Tb_2L_2(\mu 4\text{-}CO_3)_2(NO_3)_2]$ (2) and Measurement results revealed that the geometric structure around the cobalt ions in al complexes is a distorted square pyramid. In contrast, the lanthanum ions exhibit; whole the complexes exhibited a spherical capped square antiprism and spherical tricapped trigonal prism geometry. The magnetization measurements showed a pronounced magnetization relaxation in complexes 2 and 3, whereas the effect was almost negligible in complex 1. This study highlights the distinct geometric arrangements and magnetization behavior of the synthesized metal complexes, providing valuable insights into their structural and magnetic properties. The findings our team in comprehending the coordination chemistry of various metal-ligand interactions, which may have implications for their potential applications in various fields, including magnetism and materials science [58]; see Fig. 28.

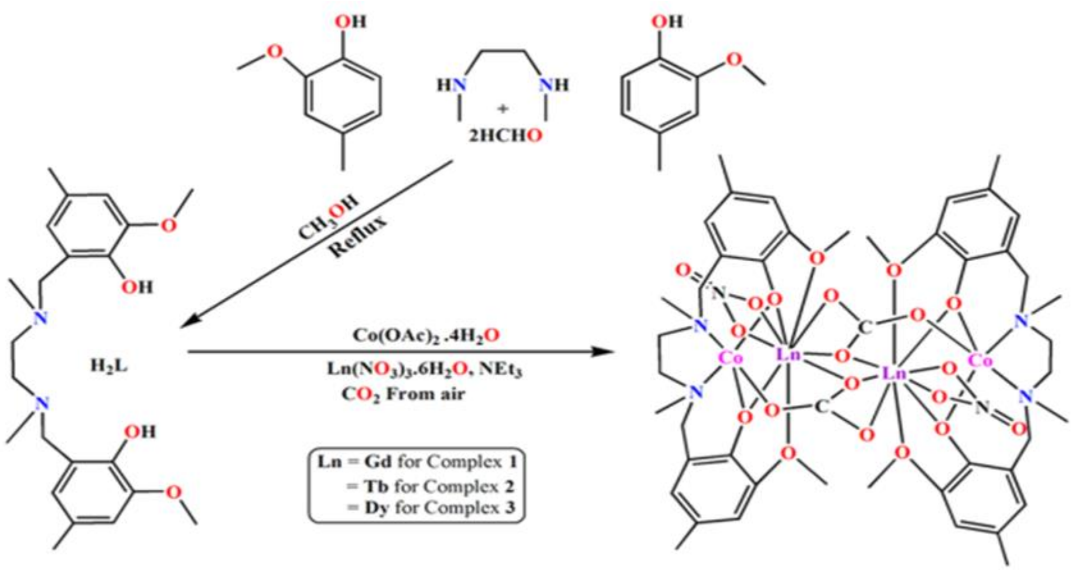


Figure 28: Syntheses of complexes 1−3 [58].

4. Conclusions

Through this article, Mannich-base ligands and their metal complexes were identified, with a study of their different applications in terms of their role in biological activity, as antioxidants, anticancer, urease, as catalysts for some reactions, and as corrosion inhibition for some metals in acidic, alkaline, or neutral mediums, as fluorescence sensors, and in various other fields such as magnetism and materials science.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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