International Journal of Pharmaceutical Chemistry

ISSN: 2249-734X (Online)
Journal DOI:10.7439/ijpc
CODEN:IJPCI4 (American Chemical Society)

Research Article

Synthesis and spectroscopic characterization of transition metal complexes of methyl and methoxy substituted 2-sulfamoylbenzamides

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Abstract

This research work described the synthesis of transition metal complexes with methyl and methoxy substituted 2-sulfamoylbenzamides. All the ligands were synthesized from readily available benzisothiazole. Various solvent systems, under different sets of reaction conditions were tried to develop a method for complex formation. Methanol solvent was proved to be best solvent for complexation. The newly developed methodology was then applied to the synthesis of transition metal complexes which were identified by spectroscopic techniques. The structural assignments, of the ligands and the complexes were carried out by spectroscopic studies. Conclusively, higher activation energy was found to be involved in the synthesis of ligand molecule whereas the complexation appears to be a direct function of reaction time.

Key words: Synthesis, Characterization, Transition metal complexes, Aminoaryl derivatives

1. Introduction

Amines are ammonia derivatives in which alkyl or aryl groups are added by replacing one or more hydrogen atoms. These are divided into primary, secondary and tertiary amines according to the number of alkyl or aryl groups attached to the nitrogen atom [1,2]. Some of the main examples of amines are amino acids, biogenic amines, trimethylamine and aniline. One of the hydrogen atoms in the ammonia is replaced by an alkyl or aryl group in primary amines. Examples include methylamine. Secondary amines have two alkyl or aryl substituents bound to nitrogen atom together with one hydrogen atom. Examples include dimethylamine. All the three hydrogen atoms in tertiary amines are replaced by organic substituents. Examples include N-methylpiperidine. Cyclic amines have either secondary or tertiary amines. The nitrogen atom is connected to an aromatic ring in aromatic amines as in anilines. The basicity of the amine is decreased, depending on the substituent's by the presence of nitrogen atom. Due to electron-donating effect of the amine group the reactivity of the aromatic ring increases strongly. Derivatives of amines are excellent inhibitor of the viral polymerases. Amines substituted with 3-piperidyl derivatives of rifamycin-SV are particularly active against viral infections. Murine sarcoma virus causes cell transformation by obstruction of viral polymerase derivatives. Inhibition of DNA-directed DNA polymerase was less as compared to the virion polymerase[3].

Now-a-days a major problem faced by medical world is the evolution of microorganisms that have more opposition to already available antimicrobial agents. So medical science requires the development of antimicrobial agents with enhanced pharmacological and pharmacokinetics characteristics as well as with broad range activity. For this purpose in the

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past many amine derivatives have been used as valuable antibacterial and antiviral agents. Pharmacological and pharmacokinetics characteristics are due to carbamate residue which is important constituent of these amine derivatives. The cytotoxic pre-screening of platinum (II) complexes have ligands resulting from 1,2-phenylenediamine, *N*-benzyl ethylenediamine and 2- or 4-picoline in seven human cancer cell lines showed that the above compound is much less active than cisplatin. Cisplatin is most generally used and successful oncological agents against cancers. Due to severe side effects its medical use has become limited, e.g ototoxicity, nephrotoxicity, neurotoxicity and the emergence of drug resistance [4]. Considering that complexes having diamine as chelated ligands have shown antitumor activity and that many aromatic compounds have demonstrated the ability to intercalate between DNA bases [5].

The transition metals of 3d series (Cr, Mn, Fe, Co, Ni, Zn) and some from 4d series as Cd &Pd have been found human friendly metals in biological system .Hence these have been utilized extensively in complexation reaction with organic ligands. Therefore we selected these to react with o-sulfomoyl benzoic acid and get the transition metal complexes respectively. Following properties are common among transition metal complexes: Due to the potential applications as catalysts, liquid crystals and antitumoral drugs, transition metal compounds having pyrazole ligands have gained much consideration. Because of the coordination versatility and the hydrogen bonding possibilities, pyrazolyl ligands make these systems good candidates to generate refined inorganic structures[6].

Antimicrobial screening tests gave good results in the presence of metal ion in the ligand system. The nuclease activity of the above metal complexes shows that Cu, Ni and Co complexes cleave DNA through redox chemistry whereas other complexes are not effective[7].

2. Experimental

All the reagents used were pure synthetic and solvents employed were purified according to the standard procedures. $CuSO_4.5H_2O$ and Cobalt salts were obtained from Merck Germany. The melting points were taken by using Gallenkamp digital melting point apparatus (MFB-595-010M). The UV spectra were measured on a Schimadzu UV240 spectrophotometer. FT-IR spectra were recorded on a Schimadzu IR Prestige-21 infrared spectrophotometer. Since all the synthesized products were found as solids, the IR spectra were taken as KBr discs. Reactions were monitored by Thin Layer Chromatography (TLC) using aluminium backed plates coated with silica gel 60 mesh (0.25 mm) containing a fluorescent indicator active at 254 nm. The mobile phase systems used for the purpose mostly employed *n*-hexane, ethyl acetate, methanol, chloroform etc [8].

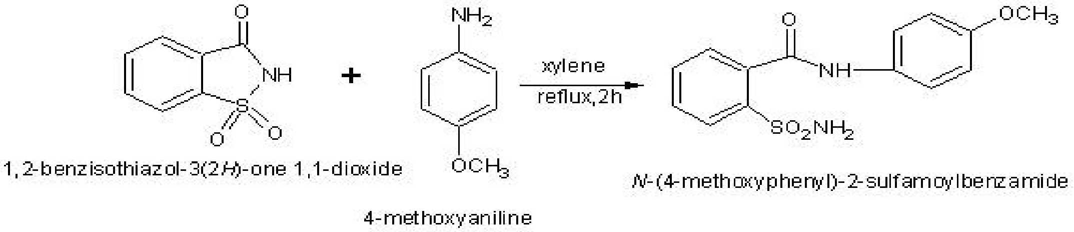
2.1 Synthesis of the ligands

The ligands were synthysized as described in Fig. 1-8.

2.1.1 Synthesis of *N*-(4-methoxyphenyl)-2-sulfamoylbenzamide

Soluble saccharin I (1.0 g, 5.46 mmol) and *p*-anisidine (0.846 g, 5.46 mmol) were dissolved in xylene in a round bottom flask. The reaction mixture was mixed and then subjected to reflux for 3 hrs. After this reaction was filtered and its TLC run by checking the solubility of both reactants and product in suitable solvents (Fig. 1)[9].

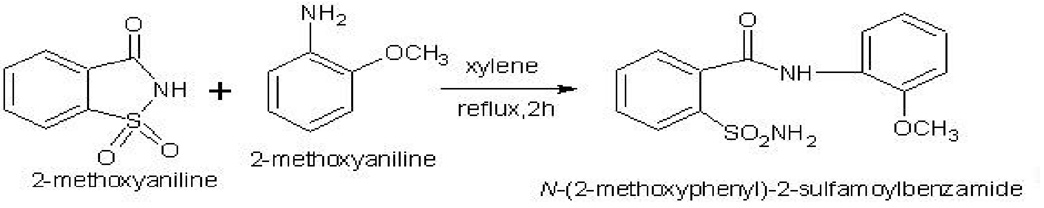
Fig. 1 Scheme for the Synthesis of *N*-(4-methoxyphenyl)-2-sulfamoylbenzamide



TLC indicated that some saccharin remains unreacted so 0.5% NaOH solution was prepared and 25 mL of this solution is added into reaction mixture. Then reaction mixture was stirred and after stirring two layers appeared and then filtered. After this the purity of the expected product was checked.

2.1.2 Synthesis of *N*-(2-methoxyphenyl)-2-sulfamoylbenzamide

Fig. 2 Scheme for the Synthesis of *N*-(2-methoxyphenyl)-2-sulfamoylbenzamide

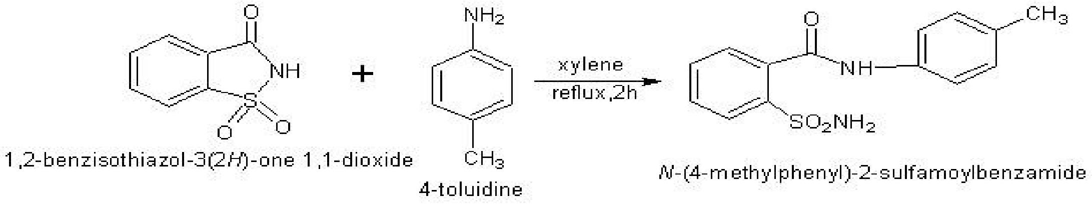


Soluble saccharin I (1.0 g, 5.46 mmol) and o-anisidine (0.8 mL, 5.46 mmol) were dissolved in xylene in a round bottom flask. Then the reaction mixture was subjected to reflux for 10 hrs but before this mixing was done. After this reaction was filtered and its TLC run by checking the solubility of both reactants annd product in suitable solvents.

Basic treatment was given to it by following the same procedure mentioned above (Fig. 2).

2.1.3 Synthesis of *N*-(4-methylphenyl)-2-sulfamoylbenzamide

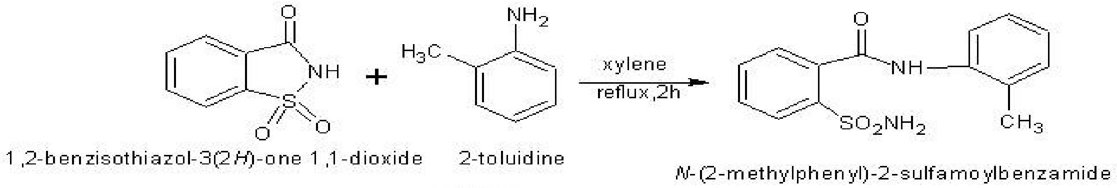
Fig. 3 Scheme for the Synthesis of *N*-(4-methylphenyl)-2-sulfamoylbenzamide



Soluble saccharin I (1.0 g, 5.46 mmol) and p- toludine (0.642 g, 5.46 mmol) were taken and subjected to reflux using xylene for 2.5 hrs. After this TLC run and purity of the product was checked. Then it was filtered and residue was washed with xylene and allowed for drying. After some time crystals of the product were obtained (Fig. 3).

2.1.4 Synthesis of *N*-(2-methylphenyl)-2-sulfamoylbenzamide

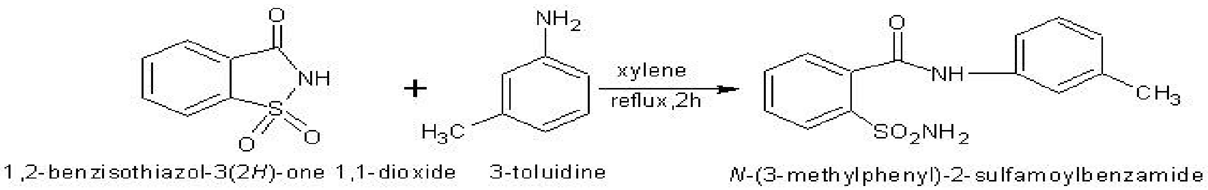
Fig. 4 Scheme for the Synthesis of *N*-(2-methylphenyl)-2-sulfamoylbenzamide



Soluble saccharin I (1.0 g, 5.46 mmol) and o- toludine (0.642 mL, 5.46 mmol) were dissolved in xylene in a round bottom flask. The reaction mixture was mixed and then subjected to reflux for 10 hrs. After this reaction was filtered and its TLC run by checking the solubility of both reactants and product in suitable solvents (Fig. 4).

2.1.5 Synthesis of *N*-(3-methylphenyl)-2-sulfamoylbenzamide

Fig. 5 Scheme for the Synthesis of *N*-(3-methylphenyl)-2-sulfamoylbenzamide



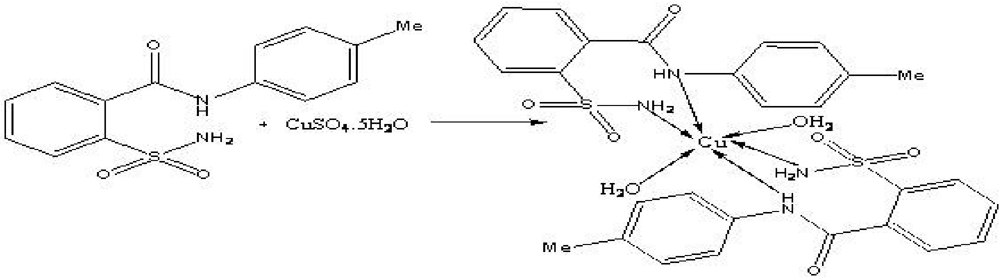
Soluble saccharin I (1.0 g, 5.46 mmol) and m-toludine (0.655 mL, 5.46 mmol) were dissolved in xylene in a round bottom flask. Then the reaction mixture was subjected to reflux for 8 hrs but before this mixing was done. After this reaction was filtered and its TLC run by checking the solubility of both reactants annd product in suitable solvents.

Basic treatment was given to it by following the same procedure mentioned above (Fig. 5).

2.2.Synthesis of M--L Complexes:

2.2.1 Synthesis of Diaquabis[(*N*-(4-methylphenyl)-2-sulfamoylbenzamide]copper Complex

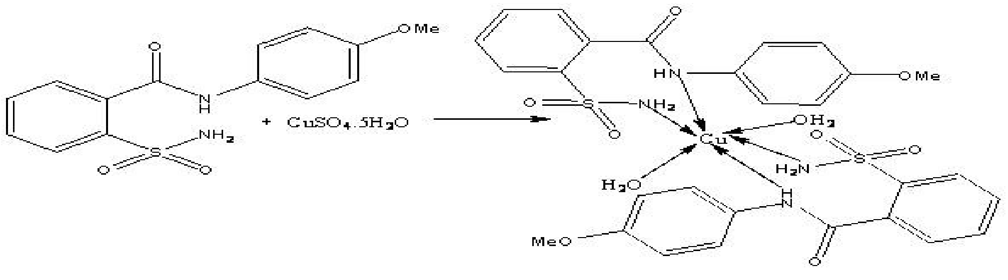
Fig. 6 Synthesis of Diaquabis[(*N*-(4-methylphenyl)-2-sulfamoylbenzamide]copper Complex



A mixture of N-(4-methylphenyl)-2-sulfamoylbenzamide (2.3g, 0.0094 moles) and copper acetate pentahydrate (0.59g, 0.0094 moles) were taken separately in aqueous methanol (25 mL). Then put both the solutions in 100 mL round bottom flask and was subjected to reflux for 2 hours under constant stirring. The volume of the reaction mixture was reduced to half by evaporating the reaction mixture. The dark blue crystals were filtered, washed with cold water and dried at room temperature. I checked the purity of the product by TLC (Fig. 6).

2.2.2 Synthesis of Diaquabis[*N*-(4-methoxyphenyl)-2-sulfamoylbenzamide]copper Complex

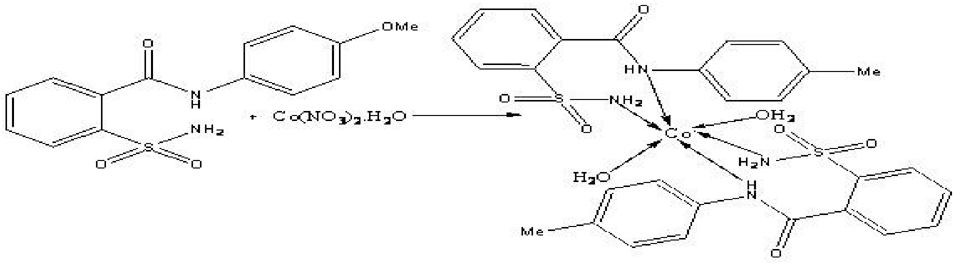
Fig 7: Synthesis of Diaquabis[*N*-(4-methoxyphenyl)-2-sulfamoylbenzamide]copper Complex



A mixture of *N*-(4-methoxyphenyl)-2-sulfamoylbenzamide (0.25g, 0.002 moles) and copper acetate pentahydrate (0.68g, 0.002 moles) were taken separately in aqueous methanol (25 mL). Then put both the solutions in 100 mL round bottom flask and was subjected to reflux for 2 hours under constant stirring. The volume of the reaction mixture was reduced to half by evaporating the reaction mixture at room temperature. The precipitates were filtered, washed with cold water and dried at room temperature and purity of product was checked by the LTC (Fig. 7).

2.2.3 Synthesis of Diaquabis[[(*N*-(4-methylphenyl)-2-sulfamoylbenzamide] cobalt Complex:

Fig 8: Synthesis of Diaquabis[[(*N*-(4-methylphenyl)-2-sulfamoylbenzamide] cobalt Complex



A mixture of ***N***-(4-methylphenyl)-2-sulfamoylbenzamide (0.5g, 0.0046 moles) and cobalt nitrate monohydrate (1.3 g, 0.0046 moles) were taken separately in aqueous methanol (25 mL). Then put both the solutions in 100 mL round bottom flask and was subjected to reflux for 2 hours under constant stirring. The volume of the reaction mixture was reduced to half by evaporating the reaction mixture. The crystals were obtained, washed with cold water and dried at room temperature. I checked the purity of the product by TLC (Fig. 8).

3. Results and Discussion

Various methoxy and methyl substituted amino aryl derivatives were synthesized as described in experimental section and characterized by different techniques as follows:

3.1 Identification of the Ligands and complexes:

Table 1: Identification of the Ligands

Sr. No.	Codes of Ligands	Name of Ligands
1	TA-1	*N*-(4-methoxyphenyl)-2-sulfamoylbenzamide
2	TA-2	*N*-(2-methoxyphenyl)-2-sulfamoylbenzamide
3	TA-3	*N*-(4-methylphenyl)-2-sulfamoylbenzamide
4	TA-4	*N*-(2-methylphenyl)-2-sulfamoylbenzamide
5	TA-5	*N*-(3-methylphenyl)-2-sulfamoylbenzamide

Table 2: Identification of the Complexes

Sr. No.	Codes of Complexes	Name of Complexes
1	TA-6	Diaquabis[(*N*-(4-methylphenyl)-2 sulfamoylbenzamide]copper Complex
2	TA-7	Diaquabis[*N*-(4-methoxyphenyl)-2-sulfamoylbenzamide]copper Complex
3	TA-8	Diaquabis[[(*N*-(4-methylphenyl)-2-sulfamoylbenzamide]cobalt Complex

3.2 Physical Properties

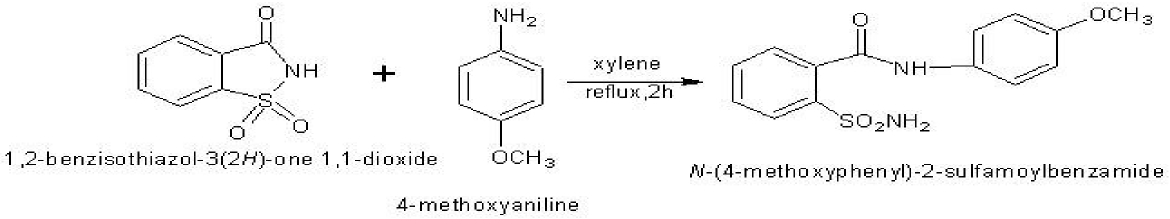
The physical properties such as solubility, color, and melting point were determined. The physical properties of reactants and product are given bellow in table. 3

Table 3: Physical data of the synthesized derivatives

Sr. No.	Codes	Solubility	Recrystalization Solvents	m. p./decomposition point °C
1	TA-1	MeOH, Ethyl acetate	MeOH, Ethyl acetate	193
2	TA-2	MeOH, Ethyl acetate	MeOH	210
3	TA-3	Ethyl acetate	MeOH, Water	298
4	TA-4	Ethyl acetate	MeOH, Water	253
5	TA-5	Ethyl acetate	CHCl3	145

3.2 I.R spectra of Ligands and their metal complexes

3.2.1 I.R spectra of Ligands I.R spectra of *N*-(4-methoxyphenyl)-2-sulfamoylbenzamide

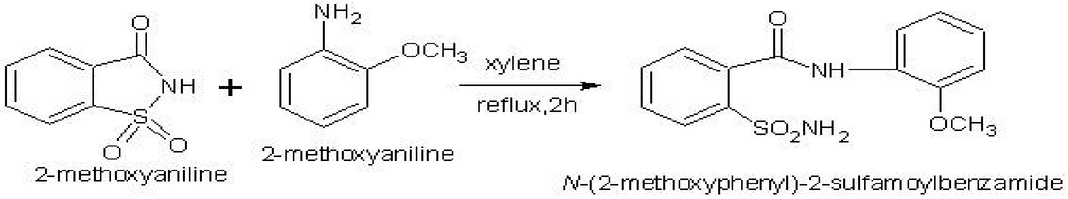


IR= KBr (disc, cm^{-1}), 1165, 1334 (O=S=O), 1531 (NH, *def.*), 1618 (C=O), 3273, 3350 (NH, NH_2), 3002 (*br*) (CH_2)

The synthesis of the ligand has been confirmed by spectroscopic techniques as follows:

IR peaks in the region 3273-3350 cm^{-1} are due to the presence of NH and NH_2 *stretching* frequencies in benzamide and SFA functional group respectively. The C=O peak of the benzisothiazole reactant has shifted to lower wave no. 1618 cm^{-1} indicating the open chain N-sulfamoyl benzamide derivative.

3.2.2 I.R spectra of *N*-(2-methoxyphenyl)-2-sulfamoylbenzamide

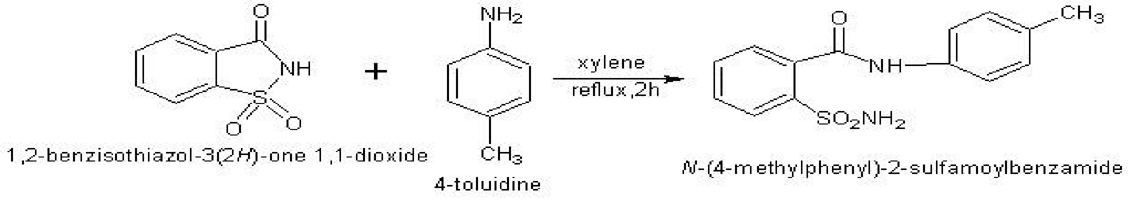


IR= KBr (disc, cm^{-1}), 1157 (O=S=O), 1664 (NH, *def.*), 3269, 3400 (NH, NH_2), 1273 (C-N)

The synthesis of the ligand has been confirmed by spectroscopic techniques as follows:

IR peaks in the region 3269-3400 are due to the presence of NH and NH_2 *stretching* frequencies in benzamide and SFA functional group respectively and thus indicating the open chain N-sulfamoyl benzamide derivative.

3.2.3 I.R. Spectra of *N*-(4-methylphenyl)-2-sulfamoylbenzamide

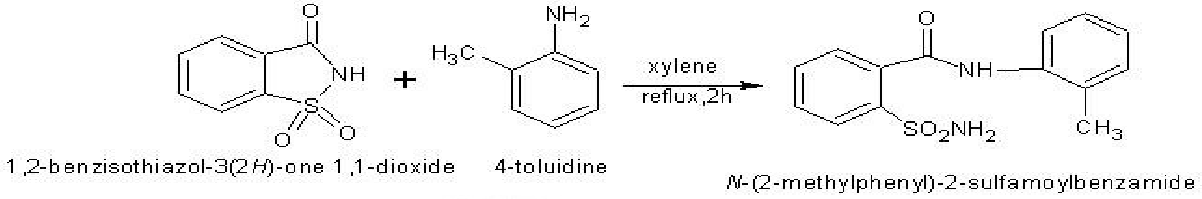


IR= KBr (disc, cm^{-1}), 1330, 1157 (O=S=O), 1539 (NH, *def.*), 1724(C=O), 3228, 3315 (NH, NH_2), 3002 (*br*) (CH_2)

The synthesis of the ligand has been confirmed by spectroscopic techniques as follows:

IR peaks in the region 3228-3315 are due to the presence of NH and NH_2 *stretching* frequencies in benzamide and SFA functional group respectively. The C=O peak of the benzisothiazole reactant has shifted to lower wave No. 1724 cm^{-1} indicating the formation of benzamide derivative.

3.2.4 I.R. Spectra of *N*-(2-methylphenyl)-2-sulfamoylbenzamide

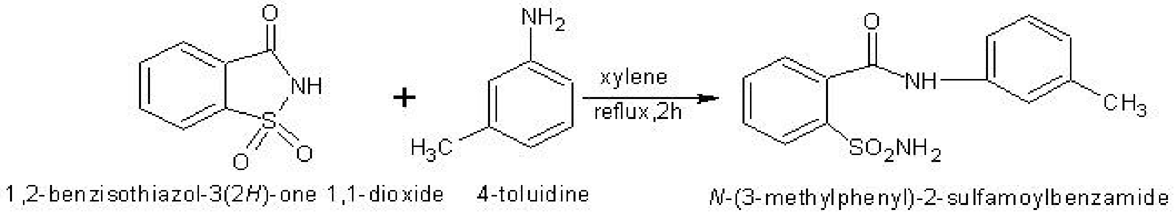


IR= KBr (disc, cm^{-1}), 1590 (O=S=O), 1643(C=O), 3024, 3103 (NH, NH_2)

The synthesis of the ligand has been confirmed by spectroscopic techniques as follows:

IR peaks in the region of 1643 indicate the presence of carbonyl group. Peaks in the region of 3024-3103 are due to the presence of NH and NH_2 *stretching* frequencies in benzamide and SFA functional group respectively. The O=S=O peak of the benzisothiazole reactant appears at 1590 cm^{-1} respectively.

3.2.4 I.R. Spectra of *N*-(3-methylphenyl)-2-sulfamoylbenzamide



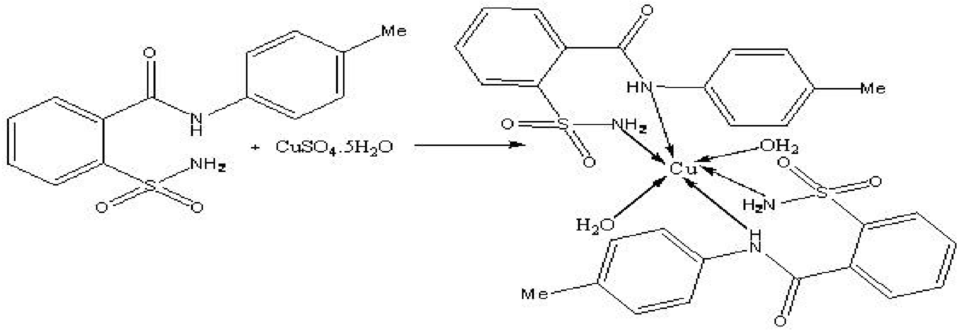
IR= KBr (disc, cm^{-1}), 1541 (O=S=O), 1641(C=O), 3024, 3061 (NH), 3255, 3327 (NH_2)

The synthesis of the ligand has been confirmed by spectroscopic techniques as follows:

IR peaks in the region of 1541 indicate the presence of O=S=O group. Peaks in the region of 3255-3327 indicate NH_2 splitted signal respectively. The C=O peak appears at 1641 respectively.

3.3. I.R. Spectra complexes

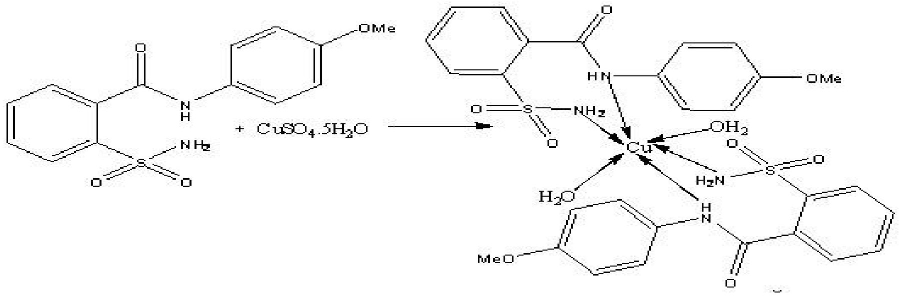
3.3.1 I.R. Spectra of Diaquabis[(N-(4-methylphenyl) -2-sulfamoylbenzamide]copper Complex:



The synthesis of the complex has been confirmed by spectroscopic techniques as follows:

The carbonyl signal in this shifted from 1620 to higher region i.e. 1714 cm^{-1}.A broad signal appear at in the range of 3045-3093 indicating water coordination. The NH_2 value shift to 3213-3516 indicating the coordination. These are the main peaks which indicate the presence of complex formation.

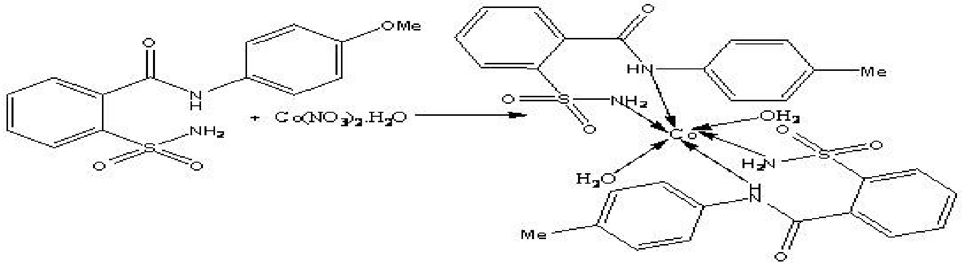
3.3.2 I.R. Spectra of Diaquabis[N-(4-methoxyphenyl)-2-sulfamoylbenzamide]copper Complex



The IR interpretation of the complex was given as:

A change in carbonyl peak appear and it shifts to higher region from 1618-1666 cm^{-1}.The band broadening occurred and the peak appear at 3084 cm^{-1} indicating the presence of water. The two splitted signals of NH_2 are reduced to one indicating the involvement of amine in coordination.

3.3.3 I.R. Spectra of Diaquabis[[(N-(4-methylphenyl)-2-sulfamoylbenzamide]cobalt Complex



A change in carbonyl peak appear from 1620-1786. In this NH_2 prak shift from 3213-3444 and 3338-3512. These are the major peaks which indicate that a change had occurred.

4. Conclusion

The synthesis of transition metal complexes with methyl and methoxy aminoaryl derivatives was carried out in present research work. The ligands in present work were synthesized from readily available benzisothiazole. Various solvent systems, under different sets of reaction conditions were tried to develop a method for complex formation. From the results it was observed that methanol was proved to be best solvent for complexation. The newly develop methodology was then applied to the synthesis of transition metal complexes which were identified by spectroscopic techniques. The structural assignments, of the ligands and the complexes were carried out by spectroscopic studies. Conclusively, higher activation energy was found to be involved in the synthesis of ligand molecule whereas the complexation appears to be a direct function of reaction time.

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