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Synthesis of Some Novel Ligands of Benzimidazole Derivatives

KEYWORDS

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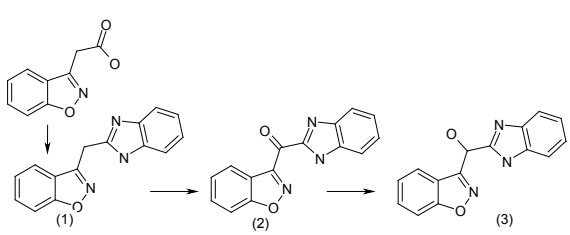
ABSTRACT *Synthesis of new benzimidazole derivative were described. 3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole was oxidized and subsequently reduced to get the ligands. Complexation of the ligand with copper and nickel was studied.*

Imidazole is of considerable interest as a ligand in that its presence in many biological systems provides a potential binding site for metal ions [1, 2]. Imidazole itself is usually a unidentate ligand and forms complexes with metal ions through its tertiary nitrogen atom. Some complexes of imidazole and its derivatives with transition-metal ions have been reported [3-5].

Complexes of nickel (II) and imidazole ligand have been studied as models for copper proteins that contain both functionalities in the side chain [6]. Some of these nickel (II) complexes were found to exhibit a variety of pharmacological activity and superoxide dismutase activities [7]. The adducts and their formation reactions have also been found useful in a variety of ways, such as in biological applications and as both ultraviolet absorbers and antioxidants.

These compounds play an important role in the development of coordination chemistry related to their potential applications in catalysis and enzymatic reactions, magnetism and molecular architecture. For this, we studied complexation of some compounds with ions like Copper and Nickel. Synthetic scheme could be presented as follows.



Scheme-1

Experimental:-

Synthesis of 3-(1H-benzimidazol-2-ylmethyl)-benzo[d] isoxazole (1)

3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole(1) was prepared from benzo[d]isoxazole 3- acetic acid(10) using Phillip's [8] method for synthesis of benzimidazoles as per literature.[9]Yield: - 81 %. M.p: - 174^0 C.IR (KBr)- Showed peak at 3400 cm^{-1}(Broad imidazole –NH-). H^1 NMR showed peak at δ 12.5 (s, 1H, -NH), δ7.0 -7.8 (m, 8H, Ar proton), δ 4.6 (s, 1H,-CH_2).

Oxidation of 3-(1H-benzimidazol-2-ylmethyl)-benzo [d] isoxazole(1)/

OR Synthesis of Benzo [d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone (2)

3-(1H-benzimidazol-2-ylmethyl)-benzo[d] isoxazole (6) was oxidized using selenium dioxide as oxidizing agent. 3-(1H-benzimidazol-2-ylmethyl)-benzo [d]isoxazole (6) (2.5g, 10 mmoles) was dissolved in dioxan (10 ml). Selenium dioxide (1.65g, 15mmoles) was added to above solution. Reaction mixture was refluxed (100^{0}C) for 5hrs. Reaction progress was monitored on Thin Layer chromatography .After completion; reaction mixture was filtered hot to remove selenium. Filtrate was concentrated to remove excess of dioxan. Reaction mixture was decomposed in cold water to get the solid product. Product was filtered, dried and recrystallised from ethanol.Yield - 75.75%. M.p.181-182^{0}C. IR(KBr) showed peaks at 3500 cm^{-1}(Broad imidazole –NH-), 1667cm^{-1} (carbonyl). H^{1}NMR showed peaks at δ 14.0 (s, 1H, NH), δ 7.0-8.2 (m, 8H, Ar proton). Compound identified as Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone (2)

Synthesis of Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanol (3) / OR reduction of Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone(2)

Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone(2) was reduced by sodium borohydrate as reducing agent. Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone(2) (2.6g, 10 m.mol) was dissolved in methanol 10ml. Above solution was cooled to about 10^{0}C and sodium borohydrate (0.4g, 10 m.mol) was added in small portions maintaining the temp below 15^{0}C. Reaction mixture was stirred for 1 hr. Reaction progress was monitored on Thin Layer chromatography. After completion, reaction mixture was decomposed in water. Reaction mixture was neutralized with sodium carbonate. Solid product was filtered and washed with water. Product crystallized with methanol. Yield - 52.3%. M.p. 220-222^{0}C. IR (KBr) showed peaks at 3419 cm^{-1} (Broad imidazole NH-), 2956 cm^{-1} (-OH), 2853 cm^{-1}(-CH- stretching). H^{1}NMR showed peaks at 12.2 (s, 1H, NH), δ 6.3-7.8 (m, 9H, Ar proton), δ 4.4 (d, 1H,-CH). δ3.8 (s, 1H, broad - OH)

Complexation studies of 3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole (1)

Copper complex :-(1a)

3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole (6) (2 m.mol), was added in 10 ml of ethanol. Cuprous chloride (2 m.mol) in 5.ml of ethanol was added to the above solution and refluxed for two hours. After reaction was com-

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plete, the reaction mixture was cooled to about 10^0C. Precipitated dark green colored complex was filtered, washed thoroughly with water and cold ethanol.IR (KBr) showed 3439 cm^{-1}(-C=N-lower frequency than ligand 3500 cm^{-1}), 2925 cm^{-1} (-CH_2- stretching) 1610 cm^{-1} (Aromatic stretching) peaks. H^1NMR showed peaks at δ 7.1-7.4 (m, 8H, Aromatic protons), δ 3.5 (s, 2H, CH_2) (NH present in ligand was absent). Following similar procedure, other complexes were prepared.

Nickel complex :-(1b)
IR (KBr):-3410 cm^{-1}(-C=N-lower frequency than ligand 3500 cm^{-1}), 2924 cm^{-1} (-CH_2- stretching) 1611 cm^{-1} (Aromatic stretching,),Mass- m/z 559 $(M+2)^+$, 250 (base peak)

Complexation of Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl)-methanone (2)
Copper complex :-(2a)
IR (KBr) Showed Peaks at 3400 cm^{-1}(-C=N-lower frequency than ligand 3500 cm^{-1}), 1609 cm^{-1} (Aromatic stretching, carbonyl at 1667 cm^{-1}in ligand was absent), Mass m/z- 590.6 $(M)^+$, 263.9 (base peak)

Nickel - complex (2b)
IR (KBr)- 3420 cm^{-1}(-C=N-lower frequency than ligand 3500 cm^{-1}), 1608 cm^{-1} (Aromatic stretching, carbonyl at 1667 cm^{-1}in ligand was absent)

Complexation studies of Benzo[d]isoxazo-3-yl-(1H-benzoimidazol-2-yl methanol (3)
Copper complex :-(3a)
IR(KBr) Showed 3444 cm^{-1}, 3322 cm^{-1}, 2956 cm^{-1} (Broad band OH-present in ligand disappears), 1228 cm^{-1}(C-O-) Shifts lower frequency due to complex formation.(1231 cm^{-1} in ligand) [10] H^1NMR Showed δ 4.9 (s, 1H, CH), δ7.2-7.8 (m, 8H, Aromatic), Mass- m/z 592 $(M+2)^+$, 264(base peak)

Conclusion:-
Synthesized Ligands form stable 2:1 complexes with copper and nickel. -NH- of the Benzimidazole participates in the complex formation of all the three ligands, whereas nitrogen of Benzoxazole participates only in the complexation of 3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole (1).

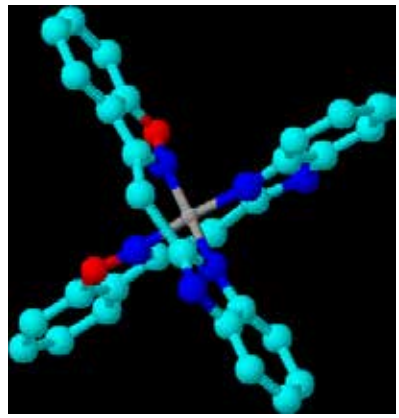

fig-1:-complex of 3-(1H-benzimidazol-2-ylmethyl)-benzo [d]isoxazole (1) 3d view.

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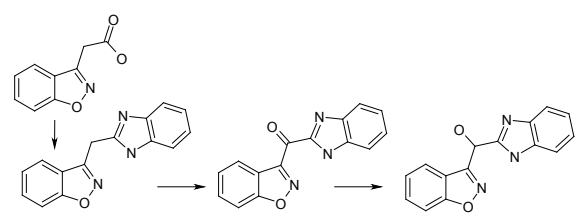
Graphical abstract: -
Some benzoxazole imidazole derivatives and their complexes are studied.



Abstract :-
Synthesis of new benzimidazole derivative were described. 3-(1H-benzimidazol-2-ylmethyl)-benzo[d]isoxazole was oxidized and subsequently reduced to get the ligands. Complexation of the ligand with copper and nickel was studied.

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