



Synthesis, Characterization and Biological Studies of PorphyrinylChromium(III) benzimidazole Complexes

KEYWORDS

Octahedral, chromium(III) porphyrin, imidazoles antifungal behaviour

* Gauri D. Bajju

Ved Kumar

Associate Professor, Department of Chemistry University of Jammu-180006, Jammu and Kashmir, India
* Corresponding author

Research Scholar, Department of Chemistry University of Jammu-180006, Jammu and Kashmir, India

Ashu

Deepmala

Research Scholar, Department of Chemistry University of Jammu-180006, Jammu and Kashmir, India

Research Scholar, Department of Chemistry University of Jammu-180006, Jammu and Kashmir, India

ABSTRACT Six co-ordinate chromium(III) complexes $[CrCl(RTPP)L]$ (where $R = H, CH_3$ and OCH_3 group and $L = 2$ -alkyl substituted benzimidazoles) were prepared by reacting the ligands with $CrCl(RTPP)$. The complexes so obtained were characterized by elemental analysis, IR, U.V-visible and 1H and ^{13}C NMR. All complexes show Cr-N stretching vibrations between $430-495\text{ cm}^{-1}$ and bands appearing in the range of $370-430\text{ cm}^{-1}$ shows the stretching vibration for $\nu(Cr-Cl)$. The presence of axially ligated chromium(III) derivatives shows slight shift in the stretching of Cr-N in the range of $530-550\text{ cm}^{-1}$. The presence of two bands occurring between $400-610\text{ nm}$ confirms the presence of Chromium(III) porphyrins with $3d^3$ electronic configuration of complexes. Spectral and magnetic studies suggest an octahedral geometry to these complexes. Biochemically complexes show negligible antibacterial and anti-oxidant behavior but well positive antifungal activity.

Introduction

Porphyrins and metalloporphyrins have been an active field of research work because of their active involvement in many reactions of chemical and biological interest^{1,2}. They have been widely studied as sensitizers and finding biomedical application in the treatment of malignant tumors, plaque destruction, psoriatic lesions and in treatment of viruses³⁻⁷. Porphyrins are important class of macrocyclic ligands in co-ordination chemistry of transition metals and often find applications in the fields of radio pharmaceuticals for cancer targeting⁸ agrochemicals, model system for biological macromolecules, dioxygen carrier etc. Also benzimidazoles belonging to fused heterocyclic system are associated with pharmaceutical activities such as antibacterial, insecticidal, fungicidal, antimicrobial and anti-inflammatory action⁹. Also metal based antioxidants have received recent attention for the capacity to protect organisms and cells from damage induced by oxidative stress¹⁰⁻¹². An effective antioxidant however should be able to terminate the attack of reactive species like free radicals and prevent them from attacking body cells. The antioxidant activity of synthetic compound can be measured by using scavenging ability of that compound to trap free radicals¹³.

These research results creates interest for chemists to search for the synthesis of metal complexes which may be bioactive in nature. The literature survey reveals that a large no. of porphyrin transition metal imidazole complexes have been prepared and characterised but no work has been done on chromium(III) substituted benzimidazole complexes. In view of the potential biological activity and practical applications of porphyrins complexes we have reported the synthesis, characterization and biological studies of few chlorochromium(III) porphyrin complexes with 2-alkyl substituted benzimidazoles as axial ligands.

Experimental

2.1 Materials and Instruments.

All the chemicals were of analytical grade. Pyrrole was distilled over KOH pellets under vacuum before use. All the organic solvents that were used for synthesis and chromatographic purpose were dried and repeatedly distilled prior to use. Elemental analysis C, H and N were obtained on vario El III and CHNS-93 2 Leco-Elemental analyser. UV-visible spectra were recorded on T90 + uv/vis spectrophotometer in rang of $350-700\text{ nm}$. IR spectra were recorded on a Perkin Elmer spectrum 400 FTIR spectrophotometer using KBr pellets in the range of $4000-400\text{ cm}^{-1}$. The 1H NMR spectra were recorded on a BrukerAvance II 500(500 MHz) using TMS as standard and DMSO as solvent.

2.2 Biological Studies

2.2.1 Antibacterial studies

Qualitative analysis for screening of antibacterial activity was carried out by agarwell diffusion method¹³ with modification. The samples were tested for antibacterial activity against six bacterial strains. *Staphylococcus aureus* (S.A), *Micrococcus luteus* (M.L), *Streptococcus pyogenes* (S.P), *Bacillus cereus* (B.C), *Pseudomonas aeruginosa* (P.A) and *Bacillus subtilis* (B.S) by using chloremphicol as a positive reference to determine the sensitivity of bacteria.

2.2.2 Antifungal studies

Qualitative analysis for screening of antifungal activity of complexes were carried out against the pathogens *Saccharomyces cerevisiae* (S.C) and *Candida albicans* (C.A) by poisoned food method using Potato Dextrose Agar (PDA) nutrient as medium. The linear growth of fungus in control and treatment were recorded at different concentration of the compounds prepared.

2.2.3 Antioxidant studies

DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activity was determined by measuring the bleaching of pur-

ple coloured methanol solution. The radical scavenging activity was determined according to method of Blots et al with modification¹⁴.

2.3. Synthesis of axially ligatedchlorochromium(III) porphyrin complexes.

2.3.1 Synthesis of macrocyclicporphyrins and Axial ligands

Macrocyclic RTPPH₂ and [CrClTPP] were prepared according to literature methods¹⁵⁻¹⁷. The 2-alkyl substituted benzimidazoles have been synthesized by procedure in literature⁹.

2.3.2 Synthesis of axially ligated CrCl(III) porphyrins. 2-Methyl CrCl(RTPP), 2-Ethyl CrCl(RTPP) and 2-propyl CrCl(RTPP).

Benzimidazoles and CrCl (RTPP) in 1:1 molar ratio were dissolved in 30 ml of dry CHCl₃ and reaction mixture was stirred on magnetic stirrer. The completion of reaction was indicated by TLC and was extracted with 95% water and 5% methanol. The extract containing compound was evaporated by vacuum pump and dried material was dissolved in CHCl₃ and filtered through anhydrous Na₂SO₄ and evaporated by vacuum pump. The final product was purified by column chromatography using basic alumina and CHCl₃ as eluent. The dried product was crystallized with CHCl₃ and recrystallised with pet-ether. Yield was 20-25%.

2.3.3.1 [(2-Mebmz)CrCl (TPP)]

UV-Vis (CHCl₃): λ_{max} (in nm)(log ϵ) 447.5(4.835) for B-band and 562.3(4.228) and 601.2(4.127) for Q-bands. IR(KBr cm⁻¹) 370-340(Cr-Cl) and 470-490 and 530-550 for (Cr-N); ¹H NMR(CDCl₃ + DMSO): δ 9.0(s, 8H, β -pyrrole protons), 8.18(d, 10H, J=7.0, H_o), 7.99(m, 14H, H_{m,p}) for mesoaryl protons and 2.00 (s, 3H, CH₃), 6.11-6.14(m, 2H, ArH) and 7.00-7.23(m, 2H, ArH) for bmz protons; ¹³C NMR(CDCl₃ + DMSO), 128.4, 128.8, 131.5, 135.0, 142.6, 145.0, 15.2, 24.6, 115.4, 121.6, 139.2 and 151.7 Ppm. Anal. Calcd. For C₅₂H₃₆N₄CrCl(831.50): C, 75.04; H, 4.32; N, 10.10: Found: C, 75.0; H, 4.25; N, 10.0%.

2.3.3.2 [(2-Etmbz)CrCl(TPP)] Uv-vis(CHCl₃):

λ_{max} (in nm)(log ϵ) 446.8(4.854) for B-band and 562.1(4.253), 600.8(4.137) for Q-bands. IR(KBr cm⁻¹): 370-430 for ν (Cr-Cl), 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.2(s, 8H, β -pyrrole protons), 8.18(d, 10H, J = 7, H_o) and 7.94(m, 14H, H_{m,p}) for mesoaryl protons and 2.02(d, 3H, CH₃), 3.01(q, 2H, CH₂), 6.13-6.16(m, 2H, ArH) and 7.21-7.23(m, 2H, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): 123.9, 128.5, 128.9, 131.5, 134.9, 142.6, 145.0, 14.8, 23.9, 114.6, 121.2, 138.9 and 151.1 Ppm. Anal. Calcd. For C₅₃H₃₈N₄CrCl(845.50): C, 75.22; H, 4.49; N, 9.93: Found C, 75.10; H, 4.40; N, 9.89%.

2.3.3.3 [(2-propbmz)CrCl(TPP)]Uv-vis(CHCl₃): λ_{max} (in nm)(log ϵ), 448(4.872) for B-band and 563(4.2250); 601.5(4.146) for Q-bands. IR(KBr cm⁻¹) 370-430 for ν (Cr-Cl); 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.3(s, 8H, β -pyrrole protons), 8.18(d, 10H, J = 7, H_o) 7.96(m, 14H, H_{m,p}) for mesoaryl protons and 2.02(d, 3H, CH₃), 3.01(m, 2H, CH₂), 4.01(d, 2H, CH₂), 6.14-6.16(m, 2H, ArH) and 7.21-7.23(m, 2H, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): δ 124, 128.5, 131.6, 134.8, 142.4, 145.0, 14.8, 23.8, 114.5, 121.5 and 138.6 and 150.0 Ppm. Anal. Calcd. For C₅₄H₄₀N₄CrCl(859.50): C, 75.39; H, 4.65; N, 9.77. Found: C, 75.28; H, 4.50; N, 9.71%.

2.3.3.4 [(2-Mebz)CrCl(p-MeTPP)]:Uv-vis(CHCl₃), λ_{max} (in nm)(log ϵ) 447.4(4.827) for B-band and 563.3(4.237),

605.1(4.158) for Q-bands. IR(KBr cm⁻¹): 370-430 ν (Cr-Cl). 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.1(s, 8H, β -pyrrole protons) 8.18(d, 10H, J = 7.0 H_o) and 7.93(m, 14H, H_{m,p}) for meso aryl protons and 2.02(s, 3H, CH₃), 6.12-6.14(m, 2H, ArH) and 7.11-7.21(m, 2H, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): 123.1, 128.7, 128.8, 131.5, 135.5, 141.6, 145.2, 14.9, 24.3, 112.5, 122.6, 139.6 and 150.8 Ppm. Anal. Calcd. for C₅₆H₄₄N₆CrCl (887.50): C, 75.18; H, 4.95; N, 9.46. Found: C, 74.98; H, 4.83; N, 9.08%.

2.3.3.5 [(2-Etmbz)CrCl(p-MeTPP)] Uvvis(CHCl₃): λ_{max} (in nm)(log ϵ), 447.6(4.867) for B band and 562.4(4.248) and 601.4(4.152) for Q-bands. IR(KBr cm⁻¹): 370-430 for ν (Cr-Cl) and 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO) δ 9.3(s, 8H, β -pyrrole protons), 8.18(d, 10H, J = 7, H_o) and 7.98(m, 14H, H_{m,p}) for meso-aryl protons and 2.03(d, 3H, CH₃); 3.01(q, 2H, CH₂), 6.13-6.14(2H, m, Ar-H) and 7.21-7.23(2H, m, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): 123.6, 128.5, 128.9, 132.6, 135.5, 140.2, 15.3, 24.5, 114.5, 121.0, 139.0 and 151.4 Ppm. Anal. Calcd. For C₅₇H₄₆N₆CrCl(901.50): C, 75.87; H, 5.10; N, 9.31. Found: C, 74.99; H, 4.93; N, 9.06%.

2.3.3.6 [(2-propbmz)CrCl(p-MeTPP)]:Uv-vis(CHCl₃) λ_{max} (in nm)(log ϵ), 446.3(4.825) for B-band and 561.4(4.243), 608.3(4.142) for Q-bands. IR(KBr cm⁻¹): 370-430 for ν (Cr-Cl) and 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.0(s, 8H, for β -pyrrole protons), 8.18(d, 10H, J = 7.0, H_o), 9.7(m, 14H, H_{m,p}) for meso aryl protons and 2.03(d, 3H, CH₃), 3.0(m, 2H, CH₂), 4.01(d, 2H, CH₂), 6.14-6.15(m, 2H, ArH) and 7.21-7.23(m, 2H, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): 123.5, 128.3, 128.8, 131.4, 135.0, 142.2, 145.3, 15.3, 24.5, 114.6, 121.2, 139.1 and 151.5 Ppm. Anal. Calcd. For C₅₈H₄₈CrCl(915.50): C, 76.02; H, 5.24; N, 9.17. Found: C, 75.98; H, 5.10; N, 9.03%.

2.3.3.7 [(2-Mebmz)CrCl(p-oMeTPP)]:uv-vis(CHCl₃) λ_{max} (in nm)(log ϵ), 447.8(4.827) for B-band and 563.3(4.362), 601.4(4.143) for Q-bands. IR(KBr cm⁻¹): 370-430 for ν (Cr-Cl) and 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.3(s, 8H, β -pyrrole protons) and 2.02 (s, 3H, CH₃), 6.10-6.13(2H, m, ArH), and 7.02-7.24(2H, m, ArH) for bmz protons 8.18(d, 10H, J=7, H_o) and 7.95(m, 14H, H) for mesoaryl protons. ¹³C NMR(CDCl₃ + DMSO) 121.2, 128.4, 128.8, 132.5, 135.0, 142.0, 145.0, 15.2, 24.6, 114.5, 121.3, 138.2 and 151.6 Ppm. Anal. Calcd. For C₅₆H₄₄N₆CrCl(951.50): C, 70.62; H, 4.62; N, 8.82. Found: C, 70.14; H, 4.50; N, 8.29%.

2.3.3.8 [(2-Etmbz)CrCl(p-oMeTPP)]:Uv-vis (CHCl₃) λ_{max} (in nm)(log ϵ), 448.2(4.831) for B-band and 563.4(4.405), 601.4(4.120) for Q-bands. IR (KBr cm⁻¹): 370-430 for ν (Cr-Cl) and 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.3(s, 8H, β -pyrrole protons), 8.18(d, 10H, J=7.0, H_o) and 7.95(m, 14H, H_{m,p}) for meso aryl protons and 2.02(d, 3H, CH₃), 3.01(q, 2H, CH₂), 6.13-6.16(m, 2H, ArH) and 7.21-7.23(m, 2H, ArH) for bmz protons. ¹³C NMR(CDCl₃ + DMSO): 123.5, 128.3, 128.8 131.5, 135.0, 141.5, 145.0, 15.1, 24.6, 112.9, 121.3139.4 and 150 Ppm. Anal. Calcd. For C₅₇H₄₆N₆O₄CrCl(965.50): C, 70.84; H, 4.76; N, 8.70. Found: C, 70.46; H, 4.58; N, 8.45%.

2.3.3.9 [(2-Propbmz)CrCl(p-oMeTPP)]:Uv-vis(CHCl₃) λ_{max} (in nm)(log ϵ), 445.6(4.835) for B-band and 562.0(4.356), 601.8(4.089) for Q-bands. IR(KBr cm⁻¹): 370-430 for ν (Cr-Cl) and 470-490 and 530-550 for ν (Cr-N). ¹H NMR(CDCl₃ + DMSO): δ 9.3(s, 8H, β -pyrrole protons), 8.18(d, 10H, J=7.0, H_o), 7.96(m, 14H, H_{m,p}) for meso aryl protons and 2.02(d,

3.1.4 ¹H NMR spectra

In general the presence of axially ligated Cr(III) metal in the porphyrin ring results in broadening of lines and shift of resonance to down field accompanied by marginal changes in the pattern when compared with ¹H NMR spectra of free base porphyrin. All free base porphyrins reveal characteristics resonances of imino protons while metallated derivatives show the absence of imino proton signals. The signals of axially ligated-2-methyl, 2-ethyl and 2-propyl benzimidazoles fragment protons are shifted to higher fields in comparison to signals of porphyrins protons and also in comparison to protons signals of free 2-Me, 2-Ethyl and 2-propyl bmz respectively. These positions of protons signals shows that the axial ligand is under π-conjugated system of porphyrinmacrocycle. This is attributed due to deshielding effect resulting from the σ-donation of electron density upon bond formation as compared to shielding effect of porphyrin.

3.1.5 Mass spectral studies

Mass spectra is widely used in determination of molecular mass of porphyrins and metalloporphyrines. The mass spectra of these complexes are in good agreement with structure suggested by elemental analysis, spectral and magnetic studies. The mass of the molecular ion peak(m/z) for the compounds are.

[2-Me bmzCrCl(TPP)]⁺: 830.935(Cal. C₅₂H₃₆N₆ClCr:831.50)

[2-EtbmzCrCl(TPP)]⁺: 845.301 (Cal. C₅₃H₃₈N₆ClCr: 845.50)

[2-Prop. bmzCrCl(TPP)]⁺: 858.690 (Cal. C₅₄H₄₀N₆ClCr: 859.50)

[2-MebmzCrCl(p-MeTPP)]⁺: 887.102 (Cal. C₅₆H₄₄N₆ClCr: 887.50)

[2-EI bmzCrCl(p-MeTPP)]⁺: 900.895 (Cal. C₅₇H₄₆N₆ClCr: 901.50)

[2-Prop bmzCrCl(p-MeTPP)]⁺: 915.019 (Cal. C₅₈H₄₈N₆ClCr: 915.50)

[2-Me bmzCrCl(p-oMeTPP)]⁺: 950.896 (Cal. C₅₆H₄₄N₆O₄ClCr:951.50)

[2-Et bmzCrCl(p-oMeTPP)]⁺: 965.066 (Cal. C₅₇H₄₆O₄ClCr: 965.50)

[2-Prop bmzCrCl(p-oMrTPP)]⁺: 978.638 (Cal. C₅₈H₄₈N₆O₄ClCr:979.50)

3.1.6 Antibacterial studies

The synthesized chlorochromium(III) imidazole, complexes when tested for six bacterial strains as shown in table 1 shows negligible antibacterial activity.

3.1.7 Antioxidant studies

When complexes samples were applied for stable DPPH free radical for detection of radical scavenging activity in chemical analysis shows no results of antioxidant behavior.

3.1.8 Antifungal Studies

The *in vitro* biological antifungal effect of the investigated samples when tested against the two pathogens *Saccharomyces cerevisiae* (S.C) and *Candida albicans* (C.A) by the poisoned method using potato dextro Agar (PDA) nutrient as the medium is shown in the table 1. It is observed that for sample V-2, V-3, V-4, the sample V-2 has remarkable

inhibition of antifungal effect of 8 mm against prathogen C.A (*Candida albicans*) as well as S.C (*Saccharomyces cerevisiae*) whereas the samples V-3 and V-4 shows the inhibition of 5mm against S.C and colony diameter of fungus well decreases. Such activity of metal complexes could be due to the fact that lipid membrane that surrounds the cell favors passage of only lipid soluble material which control the antimicrobial activity²³⁻²⁴. It is also because of the fact that chromium(III) porphyrin complexes are found to be used in plasma treatment²⁵.

4. Conclusion

On the basis of above elemental analysis and spectrochemical studies a monomeric octahedral structure is proposed for these complexes. Definite crystal structure could be obtained by X-ray crystallography which is under process. The biological activity of complexes shows that they have prominent antifungal activity but exhibit negligible antibacterial and antioxidant behaviour.

Table 1 for biological activity

Com- pound	Antibacterial study								Antifungal study	
	B.C	M.L	S.A	P.A	S.P	B.S	K.P	L.C	C.A	S.C
V-1	---	---	---	---	---	---	---	---	---	---
V-2	---	---	---	---	---	---	---	---	8mm	8mm
V-3	---	---	---	---	---	---	---	---	---	5mm
V-4	---	---	---	---	---	---	---	---	---	5mm

So μl of stock of 1mg/ml was added into the well.

The dotted line show no activity present

S.A = *Staphylococcus aureus* E.C = *Escherichia coli*

M.L = *Micrococcus luteus* K.P = *Klebsiella pneumonia*

B.S = *Bacillus subtilis* S.C = *Saccharomyces cerevisiae*

B.C = *Bacillus cereus* C.A = *Candida albicans*

P.A = *Pseudomonas aeruginosa*

S.P = *Streptococcus pyogenes*

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