

Synthesis, characterization and some properties of lanthanum complex of N,N'-bis-(2-butyl-5-chloro-3H-imidazol-4-ylmethylene)-ethane-1,2-diamine, a salen type ligand

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Diamagnetic lanthanum complex was prepared with a salen type ligand “imidozalen”, bis(2-*n*-butyl-4-chloro-imidazole)-5-iminoethane and the complex was characterized by elemental analyses, magnetic studies, UV-Vis and IR, spectroscopy, NMR, thermal and conductance studies. Antifungal and antibacterial properties were also studied. The complex has a potential as an epoxidation catalyst.

Key words: lanthanum, imidozalen, salen-type complex, epoxidation, antifungal, antibacterial activity.

INTRODUCTION

Salen ligands form a variety of complexes with almost all kinds of metals [1–4]. Lanthanum complexes of salen and its derivatives have also been studied [5–7]. Lanthanum complexes are generally noted to have higher coordination number and the reported crystalline structure of such complexes helps in understanding the mode of coordination in these complexes [8–10]. The most common coordination numbers of lanthanum are 8 and 9. A coordination number of 8 is probably the most characteristic of lanthanum with square antiprism being the preferred stereochemistry. Many previously accepted examples of coordination number 6 are actually invalid because some coordinated solvent molecules are present and they raise the true coordination number to 7, 8 or 9.

Remarkably high asymmetric amplifications (positive nonlinear effects) were realized in some chiral lanthanide complex-catalyzed organic reactions [11] such as the asymmetric hetero-Diels–Alder reaction, Michael’s addition reaction, epoxidation, *etc.* These phenomena may be explained by the autogenetic formation of the enantio-pure lanthanide complexes as the most active catalysts. The high coordination numbers of the lanthanides seem to play an important role through the formation of aggregates of the heterochiral complexes as less active catalysts. Chiral lanthanum complexes [12] have been used in the asymmetric catalysis and highly enantio-selective epoxidation has been achieved *via* this mode. It is found that imidazole and its derivatives are biologically active molecules

[13], which emphasizes that antibacterial, antifungal and antimitotic studies of metal complexes are also an interesting area of research.

Inspired by the applicability of salen complexes and biological activity of imidazole derivatives, we studied a new salen type of Schiff base “imidozalen” and its complex. Imidozalen, the salen type of Schiff base was derived from 2-*n*-butyl-4-chloro-5-formyl imidazole with ethylene diamine and the structure of the ligand was studied by X-ray diffraction crystal studies [14]. We further studied the activity of the prepared imidazolene and its complex against a set of fungi by using potato dextrose agar medium and we also checked its antibacterial activity. We report in this paper the synthesis, application and the probable structure of imidozalen lanthanum complex, based on spectral and analytical studies.

MATERIALS AND METHOD

All reagents were of AR grade of purity and used without any further purification. Imidozalen was derived from 2-*n*-butyl-4-chloro-5-formyl imidazole and ethylene diamine [14]. Elemental analysis for C, H, and N was performed on an Elementar Vario EL III device. Electronic absorption spectra were recorded on an Analytik Jena, Specord-50 spectrometer. IR spectra were obtained on a Jasco FTIR-4100 instrument. Magnetic moment was measured in the solid state using a Guoy Balance with mercury tetrathiocyanatocobaltate(II) as standard at room temperature. The molar conductivity was measured using an Elico CM-180, conductivity meter. ¹H NMR spectra were recorded on Bruker AMX-400 NMR spectrometer.

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The antibacterial activity was studied by well known method. 20 ml of nutrient agar was poured into 9 cm Petri plates. The medium was allowed to cool down and kept overnight. These plates were swabbed with the test bacteria. The concentration of bacterial cells in the inoculums was maintained at a minimum of 1×10^4 cells/ml in 0.5% of peptone solution. Using a flame cork borer, 5 mm diameter wells were made in the nutrient agar plates at a distance of 2 cm from the periphery of the plates. These wells were filled with 50 μ l suspension of the complex and the ligand in DMF. Sterile distilled water and DMF served as control. These plates were incubated at 28°C in an upright position in a BOD incubator for 24 h. After a period of incubation, the plates were inspected for inhibition zone, if any, and measured using an mm scale.

Antifungal activity was studied by disc diffusion method. Fungal cultures were prepared for antifungal activity one day prior to the experiment. Fungal culture was prepared by mixing mycelium and spores with water; the suspension was properly mixed by using cyclomixer. The final concentration of fungi spores was determined and adjusted at the required concentration. The complex and the ligand were made up to a concentration of 5 mg/100 μ l (5%) in DMSO and studied in regard to antifungal activity. DMSO was also used as a negative control. A systematic fungicide Bavistin (Carbendazim) of 2 mg/ml concentration was prepared in distilled water and used as positive control in antifungal assay. All the fungal cultures were obtained from the Department of Applied Botany and Biotechnology, University of Mysore, Mysore.

EXPERIMENTAL

Preparation of the complex

An ethanolic solution of lanthanum(III) nitrate hexahydrate (0.433 g, 0.01 mol) in 100 ml ethanol was added slowly to an ethanolic solution of imidozalen ligand (0.397 g, 0.01 mol) in 100 ml ethanol at room temperature, stirred continuously for about 30 min. During the addition, the colour changed from pale yellow to bright yellow with immediate formation of a turbid solution, which disappears after stirring and refluxing on a water bath for 3 h yielding an orange-yellow solution. The solution was concentrated to yield a deep orange-yellow precipitate, which was separated, washed with ether and dried over fused CaCl_2 .

The yield was 0.612 g (77%); m.p. 140–143°C, IRS (nujol) ν cm^{-1} : 3550–3332 (br), 3185 (m), 1631 (w), 1511 (m), 1458 (m), 1431 (w), 1326 (m), 1255 (s), 1182 (w), 1032 (s), 1097 (m), 1007 (w), 940

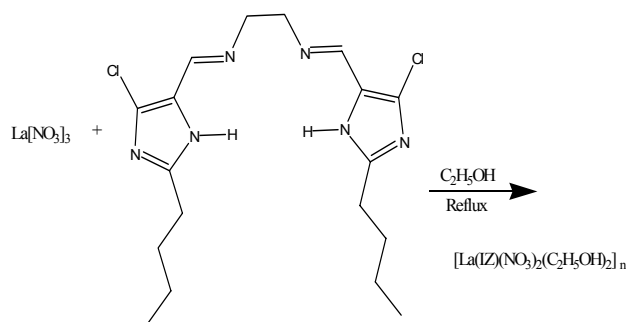
(w), 816 (s), 740 (w), 555 (m), 482 (w), 427 (w), 407 (m). UV-Vis λ_{max} nm, (ν cm^{-1}): 305 (32786), 401 (24937), 470 (21276), 704 (14204). ^1H NMR (CDCl_3): 0.8 (t, 6H, CH_3), 1.30 (m, 4H, CH_2), 1.62 (m, 4H, CH_2), 2.59 (t, 4H, CH_2), 3.78 (s, 4H, $\text{N}-\text{CH}_2$), 13.10 (b, 2H, $-\text{CH}=\text{N}-$). Anal. calcd. for $\text{C}_{24}\text{H}_{42}\text{Cl}_2\text{N}_8\text{O}_9\text{La}$: C, 36.18; H, 5.27; N, 14.07. Found: C, 36.23; H, 5.32; N, 14.19.

Asymmetric epoxidation using the prepared complex as a catalyst

Styrene (0.9 g, 8.64 mmol) was treated with sodium hypochlorite solution, 5 ml, in the presence of 4 mg of lanthanum imidozalen catalyst in 10 ml ethanol, under ice cold conditions. The reaction time was 20 min with continuous stirring. The yield was 0.415 g, 40%, b.p. 192–195°C (Lit. 193–196°C), IRS (neat): 1600, 1010 cm^{-1} . ^1H NMR (CDCl_3) δ : 2.84 (b, 2H, OCH_2), 3.80 (t, 1H, OCH), 7.15 (bs, 5H, ArH). Anal. calcd. for $\text{C}_8\text{H}_8\text{O}$: C, 79.97; H, 6.71. Found: C, 79.15; H, 6.58. Further studies on catalytic activity of this complex are in progress.

RESULTS AND DISCUSSION

The lanthanum complex was formed as shown in Scheme 1.



Scheme 1: Synthetic route for lanthanum imidozalen complex.

The electrical conductance measurements were made using chloroform and the values obtained for the blank, ligand and the lanthanum complexes were 0.94×10^{-6} S, 1.35×10^{-6} S and 1.4×10^{-6} S, respectively. The order being the same, the values indicate that the complex can be termed a non-electrolyte. Elemental analyses agree with the empirical formula assigned, viz., $[\text{La}(\text{IZ})(\text{NO}_3)_2(\text{C}_2\text{H}_5\text{OH})_2]_n$ (Fig. 1), where $\text{IZ} = \text{C}_{18}\text{H}_{24}\text{Cl}_2\text{N}_6$.

The very broad peak appearing in the region 3550–3332 cm^{-1} indicates the presence of the ethanol molecule. This band can be attributed to the $-\text{OH}$ stretching frequency of the ethanol molecule. Moreover, the assignment of this peak to the $-\text{OH}$ of water molecules does not fit well with the analytical data and it is also confirmed by thermogravimetric

studies, which indicate that the first step weight loss takes place in the temperature range 85–100°C, which can account for the loss of ethanol molecules. Also, the appearance of an additional band at 1032 cm^{-1} in case of spectra of nitrate complexes suggests the presence of ethanol in the system [15]. The band in the region 1640–1620 cm^{-1} is attributed to C=N stretching vibrations. The free ligand exhibits a peak at 1635 cm^{-1} and its complex shows a band at 1631 cm^{-1} , which suggests that –C=N group may not be involved in the bonding [8].

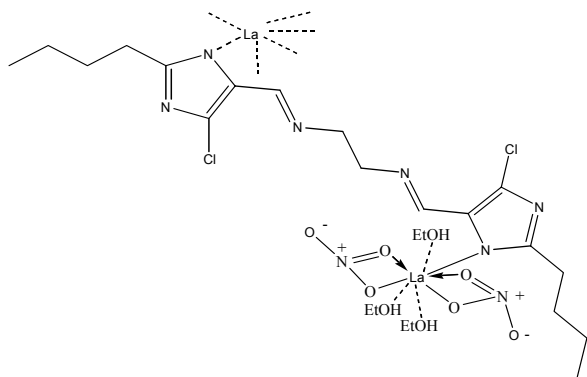


Fig. 1: Possible structure of lanthanum imidozalen complex.

The –NH group of the imidazole ring of the free ligand shows a peak at 3400–3350 cm^{-1} , which is difficult to distinguish in the complex as it overlaps with broad peak of –OH in the region 3550–3332 cm^{-1} , although appearance of another broad peak of medium intensity at 3185 cm^{-1} can be assigned to the shift due to the bonding of –NH. The deprotonation of –NH group may take place and the complex is supposed to have a polymeric form as in the case of salen lanthanum complex [8].

The $\nu_{\text{M-N}}$ and the $\nu_{\text{M-O}}$ vibrations are found at 427 cm^{-1} and at 407 cm^{-1} , respectively, in the titled complex. The nitrate ligand acts as a bidentate ligand and the peaks at 1511 cm^{-1} and 1326 cm^{-1} can be assigned to ν_4 and ν_1 vibrations of nitrate ligand, respectively, as the difference, $\Delta\nu$, is 185 cm^{-1} , which agrees with the literature reports [16, 17]. The absence of a band at 1380 cm^{-1} rules out the possibility of presence of ionic nitrate.

The ^1H NMR spectrum of the complex shows a strong peak at δ 3.5 attributed to –CH₂ of ethanol, which supports the IR spectral data. The UV-Vis spectra of the ligand showed absorption maximum at 32786 cm^{-1} , which is also present in the complex. But the appearance of new bands at 24937 cm^{-1} and at 14204 cm^{-1} can be attributed to electron transfer between the metal center and the coordinated ligand. The magnetic moments showed that the complex has diamagnetic nature, as it is expected for any closed shell complex.

The catalytic activity of the complex was checked with styrene as a substrate in the presence of sodium hypochlorite. The control experiment was run without the lanthanum catalyst. However, the yield was low and the percentage of enantiomeric excess obtained was also low. The boiling point of the formed product was checked individually and also as a mixture of the pure readily available product from Aldrich to check the mixed boiling point. The NMR peak at 2.84 δ proved the epoxide formation in case of the sample with the catalyst. The sample without the catalyst took a longer time, compared to the sample with catalyst, to form the expected product.

Lanthanum imidozalen complex and the imidozalen ligand were studied in regard to their toxicity. The ligand, imidozalen and the lanthanum complex were screened against the following bacterial strains: *S. aureus*, *E. coli*, *S. typhi*, *S. typhimurium*, *Salmonella paratyphi. A*, *Salmonella paratyphi. B*, *Shigella boydii*, *Klebsiella*, *Citrobacter*, and *Pseudomonas*. Sterile distilled water and DMF served as control. The ligand did not show any activity. The lanthanum imidozalen complex exhibited very mild activity against *S. aureus* and *E. coli*.

The lanthanum imidozalen complex did not show any antifungal activity. Surprisingly, the ligand showed very mild antifungal activity only for *Fusarium solani*. The tested organisms are *Curvularia Lunata*, *Alternaria alternata*, *Aspergillus niger*, *Aspergillus flavus*, *Fusarium solani*, *Aspergillus ochraceous*. DMSO was used as a negative control. A systematic fungicide Bavistin (Carbendazim) of 2 mg/ml concentration was prepared in distilled water and used as positive control in antifungal assay.

The complex contains –C=N group and a masked –NH groups, which generally, if present, imply activity. A possible explanation of the toxicity of the complexes has been postulated in the light of chelation theory [18]. The importance of toxicity in the compounds containing nitrogen and sulphur has been well established in many fungicides [19]. It was suggested that the chelation reduces considerably the charge of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible n-electron delocalization over the whole chelate ring. This increases the lipophilic character of metal chelate, which favours its permeation through lipid layers of fungus membranes. Furthermore, the mode of action of the compounds may involve the formation of the chelate or the ligand with the active centers of the fungal cell constituents resulting in interference with the normal cell process.

CONCLUSION

The imidozalen was expected to act as a quadridentate ligand [20] but it unexpectedly mimicked the neutral salen lanthanum complex [8].

In conclusion, the salen type imidozalen ligand acts as a unidentate ligand and one of the –NH groups of the ligand binds to one lanthanum ion and the other –NH group is expected to bind to another La ion, thus forming a polymeric chain. Further attempts to obtain the product in crystalline form are in progress, which would help study the complex as a polymeric chain. This complex is also being studied as a catalyst for epoxidation. The basic study of toxicity of this complex raises interesting questions about its mechanism.

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СИНТЕЗ, ОХАРАКТЕРИЗИРАНЕ И НЯКОИ СВОЙСТВА НА ЛАНТАНОВ КОМПЛЕКС НА N,N'-БИС-(2-БУТИЛ-5-ХЛОРО-3Н-ИМИДАЗОЛ-4-ИЛМЕТИЛЕН)-ЕТАН-1,2-ДИАМИН, ЕДИН ЛИГАНД ОТ САЛЕНОВ ТИП

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(Резюме)

Получен е лантанов комплекс с един саленов тип лиганд – „имидозален“, N,N'-бис-(2-бутил-5-хлоро-3Н-имидазол-4-илметилен)-етан-1,2-диамин. Комплексът е охарактеризиран с елементарен анализ, УВ-видима и ИЧ спектроскопия, ЯМР, магнитни, термични и кондуктометрични изследвания. Комплексът има възможно приложение като катализатор при епоксидиране.