Synthesis and Characterization of Homo- and Heteroleptic Niobium(V) Complexes. Exploration of Their Catalytic and Biochemical Potential

Abstract

The thesis presents an account of the findings of investigation on synthesis, characterization and catalytic activity of a variety of new mixed-ligand niobium(V) complexes, including peroxidoniobium (pNb) complexes immobilized on various polymer supports. The thesis also deals with the bio-chemical studies on *in vitro* activity of water-soluble oxido- and peroxidoniobium(V) complexes as inhibitors of the enzyme acid phosphatase. The contents of the thesis have been distributed over six chapters.

Chapter 1 presents a general introduction and a literature review of the work embodied in the thesis. In addition to delineating the outline and scope of the present study in the background of the known aspects of niobium and its compounds, recent advances in the peroxido chemistry of niobium are being presented. This chapter also highlights the importance of the immobilization of metal complexes on various polymer supports, *viz*., biopolymers, insoluble cross-linked polymers and water-soluble polymers, from chemical and biological perspectives. It has been emphasized that despite the substantial advancement in the field of metal containing polymers, there is a paucity of data on polymer immobilized peroxidometallates. Attention is also being drawn to the fact that potential of discrete peroxidoniobium compounds as biologically active agents remains relatively unexplored notwithstanding the favourable bio-relevant characteristics of niobium and its compounds.

Chapter 2 provides a detailed account of chemicals used, methods of elemental analysis, and techniques employed for characterization and structural evaluation of the newly synthesized complexes. The details of instruments used for catalytic activity studies are also described herein.

Chapter 3 presents the synthesis and characterization of a set of new heterogeneous catalysts comprising of peroxidoniobium(V) complexes immobilized on amino acid grafted cross-linked poly(styrene-divinylbenzene) resin (**MR**), of the type $[Nb(O_2)_3L]^{2-}$–**MR**, [L = valine (**3.1**), asparagine (**3.2**) or glycine (**3.3**)]. Results of spectral studies [FT-IR, Raman, solid-state ^{13}C NMR, diffuse reflectance UV-Vis, X-ray

photoelectron spectroscopy (XPS)], powder X-ray diffraction (PXRD) studies, scanning electron microscopy (SEM), Brunauer-Emmett-Teller (BET), thermogravimetric analysis (TGA), and elemental analysis [CHN, inductively coupled plasma optical emission spectroscopy (ICP-OES), energy dispersive X-ray spectroscopy (EDX)] confirmed the successful anchoring of triperoxidoniobium(V), $[Nb(O_2)_3]^-$ species to the host polymer *via* the pendant amino acid groups.

The supported catalysts exhibited excellent performance in epoxidation of styrene as well as a range of cyclic and terpenic compounds, in particular: limonene, norbornene, cyclooctene and cyclohexene, under environmentally acceptable solvent-free condition, with aqueous H_2O_2 as oxidant. The catalytic protocols provided excellent conversion to the desired epoxide (up to 100%) with selectivity > 99%, TON as high as 1000, and high H_2O_2 utilization efficiency (92-97%). Moreover, the catalysts efficiently facilitated chemoselective solvent-free oxidation of a variety of thioethers to sulfones at room temperature. Simple operational strategy, free from halogenated solvents, easy recyclability for multiple reaction cycles with the consistent activity-selectivity profile are the additional significant attributes of the developed catalytic processes.

In **Chapter 4**, we report the preparation of a new pNb complex anchored to a linear water-soluble polymer (WSP), poly(sodium methacrylate (**PMA**). The complex, $[Nb(O_2)_3(carboxylate)]^{2-}$–**PMA** (**4.1**) was well-characterized by elemental analysis, ICP-OES, NMR (^{13}C and ^{93}Nb), FTIR, Raman, SEM, EDX, UV-Visible and TGA analysis.

The activity of the soluble complex **4.1** as well as the **MR** supported complexes **3.1**-**3.3** as homogeneous or heterogeneous catalysts in the targeted synthesis of 5-hydroxymethyl-2-furancarboxylic acid (HMFCA) *via* 5-hydroxymethylfurfural (HMF) oxidation with H_2O_2 as oxidant, under eco-compatible reaction condition has been investigated. Both types of catalysts displayed excellent activity with 100% conversion of HMF to yield HMFCA (100% selectivity) with high TON and TOF values. The heterogeneity of the insoluble catalysts was confirmed by a hot filtration test. The heterogeneous catalysts showed impressive recyclability for multiple consecutive cycles without any significant alteration in its activity or HMFCA selectivity. Overall, the use of water as a solvent, environmentally benign H_2O_2 as oxidant, relatively low catalyst: substrate ratio, workable reaction temperature, and acceptable reaction time are the distinct green attributes of the developed catalytic HMF oxidation procedure.

Chapter 5 illustrates the synthesis of a new structurally well-defined triperoxido derivative of Nb(V) immobilized on chitosan, an abundant and renewable support material. The complex was extensively characterized by various spectroscopic and analytical techniques, *viz*., elemental analysis, SEM-EDX, powder XRD, XPS, BET, TG-DTG, FT-IR, Raman and ^{13}C NMR analysis.

We report in this chapter an account of our findings on activities of newly synthesized pNb catalyst, $[Nb(O_2)_3(NH_2)(OH)]^-$-chitosan (**5.1**) as well as a previously obtained chitosan-supported peroxidotantalate $[Ta(O_2)_3(NH_2)(OH)]$-chitosan (**ChpTa**), in the oxidation of three distinct types of organic substrates, *viz*., phenol, styrene and sulfides using aqueous H_2O_2 as oxidant under ecologically sustainable organic-solvent-free condition. The supported catalysts showed excellent activity in the non-solvent epoxidation of styrene with H_2O_2 to provide 96% conversion with nearly 100% selectivity of the desired epoxide and a high TON value of 260 at room temperature. Moreover, phenol was selectively converted into 100% dihydroxybenzene (HQ:CT=2:1) at ambient temperature, in absence of organic solvent, with a TON value of 80. In addition, both the catalysts were highly active towards the oxidation of a diverse range of sulfides such as aromatic, aliphatic, vinylic, allylic, and alcoholic sulfides to chemoselectively produce the desired sulfoxides in an aqueous medium with a TON value as high as 1900. The heterogeneous nature of the insoluble catalysts was confirmed by a hot filtration test. The catalysts are stable, water tolerant and easily recyclable at least up to five successive cycles of epoxidation and sulfoxidation with undiminished activity and selectivity.

Chapter 6 describes the facile synthesis and comprehensive characterization of new oxido and peroxidoniobium(V) complexes with biogenic ligands, maltol (malt) and deferiprone (def) in their co-ordination sphere, *viz*., $[NbO(malt)_3]_2 \bullet 9H_2O$ (**6.1**), $Na_2[Nb(O_2)_3(malt)] \bullet H_2O$ (**6.2**) and $Na_2[Nb(O_2)_3(def)] \bullet 2H_2O$ (**6.3**). The complexes were well-characterized by various analytical and spectroscopic techniques (FTIR, Raman, NMR, UV-visible, TGA, ICP-OES and elemental analysis). The charge neutral complex **6.1** was further characterized by single crystal XRD analysis, and the proposed structures of the peroxidoniobium (pNb) complexes **6.2** and **6.3** were validated by density functional theory (DFT) studies.

A comparative investigation on the *in-vitro* effect of the title compounds as well as the polymer-anchored peroxidoniobium complex, $[Nb(O_2)_3(carboxylate)]^{2-}$–**PMA** (**4.1**) [PMA=poly(sodium methacrylate)] on the activity of the model enzyme wheat thylakoid acid phosphatase (ACP) is also elaborated in this chapter. ACP is used as an excellent model to investigate the toxic metal inhibitory effect in membrane proteins. Employing established enzyme assay system, it has been demonstrated that each of the tested species is a potent inhibitor of the enzyme with the IC_{50} values varying within the range 6-64 μM. Furthermore, results of the detailed enzyme kinetic study demonstrated that the compounds induce their inhibitory effect *via* distinct pathways. The oxidoniobium complex **6.1** and the polymer-anchored pNb complex **4.1**, acted as classical non-competitive inhibitors of ACP, whereas the monomeric pNb complexes emerged as mixed inhibitors of the enzyme ($K_{ii} > K_i$).

The work described in this thesis in chapters 3-6 has already been published.