Bioorganic & Medicinal Chemistry Letters 18 (2008) 6494–6500

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

Five-coordinated oxovanadium(IV) complexes derived from amino acids and ciprofloxacin: Synthesis, spectral, antimicrobial, and DNA interaction approach

M. N. Patel *, S. H. Patel, M. R. Chhasatia, P. A. Parmar

Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar, 388 120, Gujarat, India

ARTICLE INFO

Article history:
Received 15 May 2008
Revised 9 September 2008
Accepted 13 October 2008
Available online 21 October 2008

Keywords:
Oxovanadium
DNA intercalation
Ciprofloxacin
Gel electrophoresis
Viscometric studies
SOD-like activity

ABSTRACT

Five-coordinated oxovanadium(IV) complexes with ciprofloxacin and various uninegative bidentate amino acids have been prepared. The structure of complexes has been investigated using spectral, physicochemical, mass spectroscopy, and elemental analyses. The antimicrobial activities (MIC) of the complexes, ligands, metal salt, and some standard drugs have been evaluated using the doubling dilution technique against *Staphylococcus aureus, Baccilus subtilis*, *Serratia marcescens* (*Gram-positive*), and *Pseudomonas aeruginosa*, and *Escherichia coli* (Gram-negative) bacteria. The result shows the significant increase in the antibacterial activity of the ligand, metal, and ciprofloxacin on complexation. The interaction of the complexes with pBR322 DNA has been investigated using spectroscopic, gel electrophoresis, and viscometric techniques. This shows that the complexes can bind to pBR322 DNA by the intercalative mode. The superoxide dismutase-like activity of the complexes has been determined.

The development of metal complexes as artificial nucleases is an area of burgeoning interest. The metal complexes as pharmaceuticals[1] have gained access over traditional organic dominated drugs, due to their potential use as regulators of gene expression and tools of molecular biology.[2] The major intracellular target of anticancer metallodrugs is DNA; therefore metal complexes that can bind to specific nucleotides of DNA are of interest. Studies of metal complexes, which react at specific sites along a DNA strand as reactive models for protein–nucleic acid interactions, provide routes toward the rational development of chemotherapeutic agents,[3] sensitive chemical probes for DNA structure in solution,[4] and tools for the molecular biologist to dissect genetic systems.[5] In this regard, transition metal complexes are outstanding as an artificial nuclease for DNA due to their diverse ability to recognize and react selectively with individual target sites.[6] Moreover, ciprofloxacin a quinolone-type compound is widely used as an anti-bacterial drug that targets the DNA topoisomerase (gyrase) of bacterial type II. Treatment with this drug leads to the breaking up of DNA double-strand leading to cell death. The cytotoxicity of the drug is achieved via strong binding of the complex to the gyrase–DNA in the presence of metal. At the same time, its therapeutic mode does not have a purely organic path; some are activated by biotransformation, while others have a direct or indirect effect of metal ion on its metabolism.[7–9] To continue research in DNA-binding model of the fluoroquinolones and their transition metal complexes,[10] in this letter, we have prepared the VO(IV) mixed-ligand complexes of ciprofloxacin and DL-alanine (L^1) or L-tyrosine (L^2) or L-tryptophan (L^3) or glutamic acid (L^4) or L-leucine (L^5). The DNA-binding properties of the complexes have been investigated by ultraviolet spectroscopy, viscosity measurements, and gel electrophoresis. Experimental results indicated that the complexes and ciprofloxacin can bind to DNA by intercalation modes, but the binding affinity of the complexes is much higher than that of the ligand.

All the chemicals used were of analytical grade. Vanadylsulphate, DL-alanine, L-tyrosine, L-tryptophan, glutamic acid and L-leucine were purchased from, E. Merck (India) Ltd., Mumbai. Ciprofloxacin hydrochloride was purchased from Bayer AG (Wuppertal, Germany). Luria broth, ethidium bromide, sucrose, and tris(hydroxymethyl)methylamine were purchased from Hi-media Laboratories Pvt., Ltd., India. Agarose was purchased from Sisco Research Lab., India. Bromophenol blue, acetic acid, and EDTA were purchased from SD Fine Chemicals, India. The organic solvents were purified by standard methods.[11]

Perkin-Elmer elemental analyzer (240) was used to analyze carbon, hydrogen, and nitrogen. Thermogravimetric analysis and differential scanning calorimetric study were performed with a model 5000/2960 SDTA, TA instrument (USA). Infrared spectra were recorded on an FT-IR Shimadzu spectrophotometer as KBr pellets in the range 4000 to 400 cm^{-1}. The electronic spectra of the complexes were recorded in the range 800 to 200 nm on UV-160A UV–vis spectrophotometer, Shimadzu, Japan. The magnetic moments were measured by Gouy's method using mercury tetrathiocyanatocobaltate(II) as the calibrant ($\chi_g = 16.44 \times 10^{-6}$ cgs

* Corresponding author.
E-mail addresses: jeenenpatel@yahoo.co.in, jeenen@gmail.com (M.N. Patel).

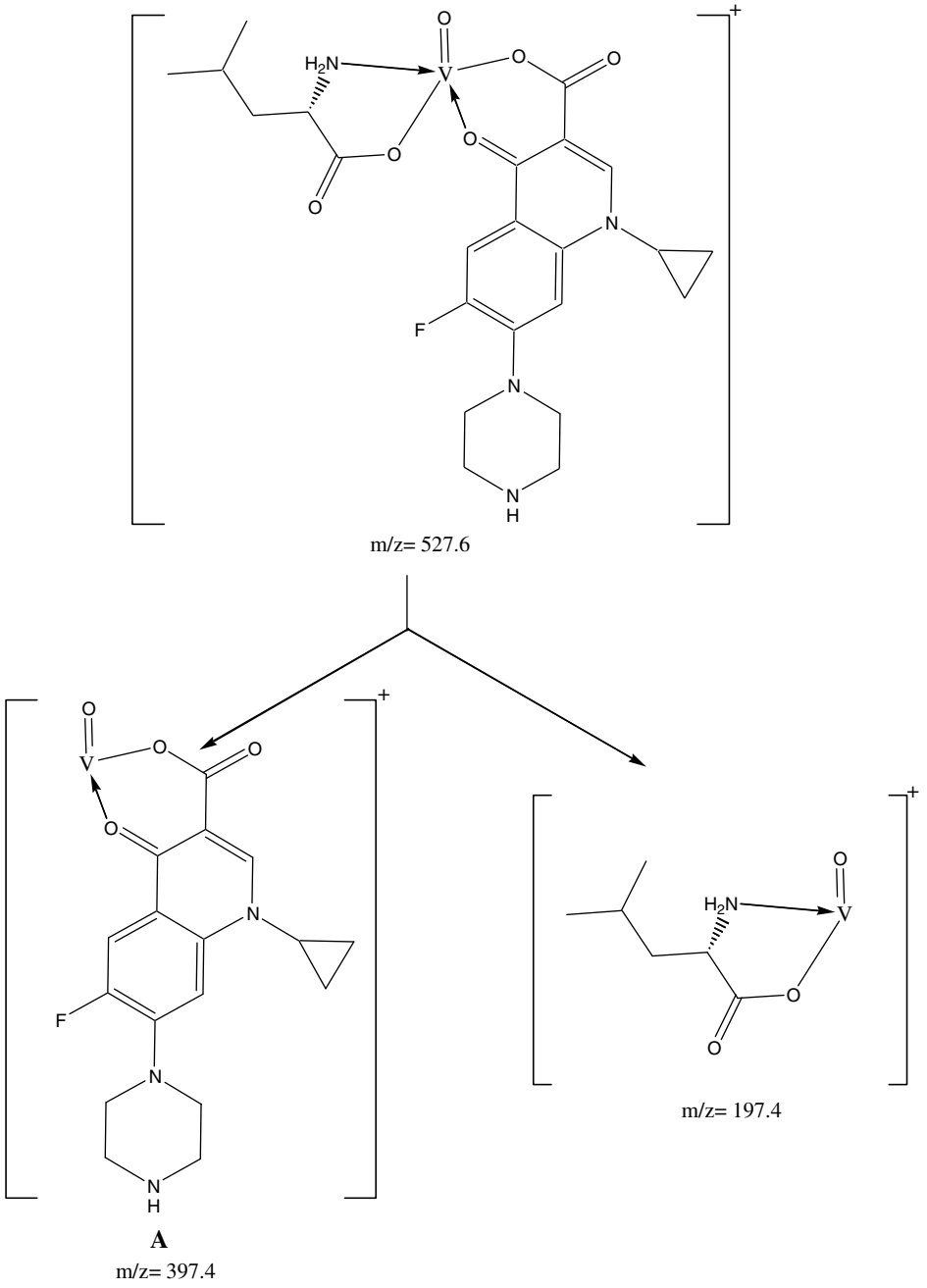
0960-894X/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bmcl.2008.10.068

Table 1
Infrared spectral data of the complexes(cm^{-1})

Complexes	ν(C=O) pyridone	$\nu(COO)_{sy}$	$\nu(COO)_{as}$	$\Delta\nu$	$\nu(M-O)_{Carbo}$	ν(M–N)	ν(C–F)	ν(C–N)	ν(V=O)
I	1619	1375	1587	212	426	530	1276	1356	1001
II	1620	1371	1586	215	427	525	1275	1357	1020
III	1635	1370	1589	219	428	531	1277	1356	1021
IV	1625	1373	1587	214	427	534	1278	1354	1020
V	1677	1371	1585	214	426	535	1274	1357	1020

units at 20 °C), Citizen Balance. The diamagnetic correction was made using Pascal's constant.[12] Mass spectra were recorded on Shimadzu LCMS 2010.

All the synthesized complexes are stable to air for an extended period of time and soluble in DMSO, slightly soluble in ethanol and water; insoluble in benzene, acetone, acetonitrile, and diethyl ether. Elemental analyses of the complexes are in good agreement with theoretical expectation. They possess high melting points indicating that the complexes are stable in air.



Scheme 1. Proposed fragmentation pattern of $[C_{23}H_{33}FN_4O_8V]$.