Journal of Molecular Structure 1063 (2014) 145–152

Contents lists available at ScienceDirect

Journal of Molecular Structure

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

The NMR and X-ray study of L-arginine derived Schiff bases and its cadmium complexes

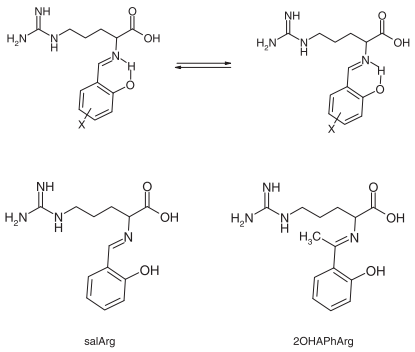
B. Kołodziej [a,*], E. Grech [a], W. Schilf [b], B. Kamieński [b,c], A. Pazio [d], K. Woźniak [d]

[a] Department of Inorganic and Analytical Chemistry, West Pomeranian University of Technology, Piastów 42, 71-065 Szczecin, Poland
[b] Institute of Organic Chemistry, Polish Academy of Science, Kasprzaka 44/52, 01-224 Warszawa, Poland
[c] Institute of Physical Chemistry, Polish Academy of Science, Kasprzaka 44/52, 01-224 Warszawa, Poland
[d] Department of Chemistry, University of Warsaw, Pasteura 1, 02-093 Warszawa, Poland

HIGHLIGHTS

- Five Schiff bases were examined using NMR in solution, two of them were studied by CPMAS NMR.
- Two Schiff base complexes were studied in solution and solid state by NMR.
- The structures of two Schiff base ligands were defined using X-ray method.
- The positions of tautomeric equilibrium were defined for all ligands.
- The comparison of X-ray and NMR data has been done.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 25 November 2013
Received in revised form 15 January 2014
Accepted 22 January 2014
Available online 30 January 2014

Keywords:
Schiff bases
Heteronuclear NMR
X-ray
Hydrogen bonds
Cd^{2+} complexes

ABSTRACT

The structure study of five Schiff bases derived from L-arginine (*L-Arg*) and 2-hydroxy carbonyl compounds were performed in both solution and solid state using NMR and X-ray methods. Both analytical methods applied to the solid state sample of two Schiff bases showed a significant difference in molecular structures of unsubstituted and 7-CH_3 substituted compounds. This effect was explained as a steric interaction of methyl group. Additionally the structure of two Cd^{2+} complexes with some Schiff bases were determined by NMR methods in DMSO solution and in the solid state. On the base of heteronuclear NMR measurement (^{13}C, ^{15}N and ^{113}Cd) it was possible to define the complexation site on nitrogen atom. The large set of spectral parameters: chemical shifts, homo- and heteronuclear coupling constants, were used in structure study.

1. Introduction

Schiff bases, named imines or azomethines, are products of condensation of primary amines and active carbonyls [1–3]. From a variety of structures of Schiff bases, very interesting are o-hydroxyaldehyde or o-hydroxyketone derivatives having the opportunity to form intramolecular hydrogen bonds [4]. Their ability to form intramolecular hydrogen bonds and hydrogen transfer process from phenolic oxygen atom to iminic nitrogen atom makes imines a very attractive compounds for various areas of science and industry [5]. To a large extent this is related to the presence of two tautomeric forms of Schiff bases: enol-imine and keto-amine, which are responsible for the thermo- and photochromic properties of these compounds [6,7].

* Corresponding author. Tel.: +48 793117101.
E-mail address: beatakolodziej7@wp.pl (B. Kołodziej).

0022-2860/$ - see front matter © 2014 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.molstruc.2014.01.058

Imines are considered as optical devices (molecular switches, ophthalmic lenses, optical memories) [8,9], dyes, temperature sensors, corrosion inhibitors, homogenous catalysts, intermediates in organic synthesis, or as ligands with excellent donor abilities for various metal ions in coordination chemistry [10–15]. Schiff bases are formed in living organisms in enzymatic reactions [16] and exhibit biological activity, which is associated with azomethine linkage (CH=N) responsible for anticancer [17], antibacterial, anti-HIV, anti-inflammatory [18], antifungal, herbicidal and antimalarian properties, and also for clinical and analytical applications of imines [19–22].

During a few last decades Schiff bases derived from biologically active chiral compounds are of great interest because of their possibility to form complexes which can be used as chiral catalysts in enantioselective reactions [23–25]. They also play a role of structural and/or functional models of compounds found in living organisms [26]. Particular interest in this group of organic compounds is focused on Schiff bases derivatives of amino acids [27], building blocks for proteins and polypeptide synthesis [28]. One of α-amino acids found in living organisms is L-arginine (*L-Arg*), conditionally essential amino acid. *L-Arg* is involved in various biochemical processes, including ammonia detoxification, immune modulation, polyamine synthesis, secretion of hormones such as insulin, glucagons and growth hormone. Its structure contains guanidine fragment, which affects the biological activity of *L-Arg*. Numerous examples found in nature explain the specific effects of *L-Arg* with carboxylates, phosphates, guanine and peroxides. Hence the interest in designing of drug and artificial receptors based on guanidine [26].

It is well known, that catalytic and biological properties of Schiff bases are weaker than the corresponding complexes [29–31]. Therefore, Schiff base metal complexes are an area of ongoing interest [32]. Amino acid Schiff base complexes have gained importance from the inorganic point of view and owing to their physiological and pharmacological activities [33]. They are very attractive compounds that mimic metalloenzymes naturally occurring in living organisms [34,35]. These complexes are considered as anticancer [36], as antibacterial, antiviral, and fungicide agents [32,37]. Metal-chelate Schiff base complexes derived from amino acids and o-hydroxynaphtaldehyde have some relationship to ligands involved in a variety of biological processes, e.g. transamination, racemization and carboxylation [38]. Moreover, amino acid Schiff base complexes are used as homogenous and heterogenous catalysts in numerous reactions, such as oxidation, epoxidation, polymerization or decomposition reactions [38,39].

Among the various metallic elements, cadmium is one of the most toxic, produced by industry and naturally present in the environment element [40–43]. Due to the possibility of replacing zinc ions cadmium ions in enzymes present in living organisms sought chelating agents, which may be used in the cadmium intoxication [43,44]. Mobilization and immobilization of Cd in organisms, the environment, and some chemical processes, depend on complexation of this metal ion by coordination with nitrogen donor ligands [42,43].

In this paper we present synthesis of Schiff base ligands and their cadmium complexes obtained from *L-Arg* and some o-hydroxyaldehydes and one ketone – o-hydroxyacetophenone. All of ligands, described in this paper, are able to form intramolecular hydrogen bonds, which together with the shape of potential for the proton motion are of great importance in biological systems [8]. We present here structural studying results using ^{1}H, ^{13}C, ^{15}N and ^{111}Cd NMR in solution and ^{13}C, ^{15}N and ^{111}Cd CPMAS NMR.

The NMR measurements, with special attention on nitrogen NMR, are very good analytical methods for investigation of proton position in hydrogen bonded structures [45]. Signals in the spectral range from about −50 to −220 ppm are assigned to the imine groups in different stages of proton transfer process [5].

2. Experimental

2.1. Synthesis of Schiff bases

Five Schiff bases were obtained from L-arginine (*L-Arg*) and o-hydroxyaldehydes: salicylaldehyde (*salArg*), 5-chlorosalicylaldehyde (*5ClsalArg*), 3-hydroxysalicylaldehyde (*3OHsalArg*), naphthaldehyde (*naphtArg*), and one o-hydroxyketone: 2-hydroxyacetophenone (*2OHAPhArg*).

The imine derivatives of *L-Arg* have been obtained according to the method published previously [46]. Methanolic solution of 1 mmol of appropriate aldehyde or ketone was added to 1 mmol of *L-Arg* was dissolved in hot methanol. Then the mixture was stirred and refluxed for half an hour and then it was cooled to room temperature. After 24 h the obtained precipitate was filtered out and washed by methanol. The authenticity and purity of obtained compounds were examined by proton NMR measurements.

2.2. Synthesis of Cd(salArg) and Cd(5ClsalArg) complexes

Two complexes were synthesized from L-Arg, cadmium acetate hydrate and appropriate aldehyde: salicylaldehyde (*Cd*(*salArg*)) and 5-chlorosalicylaldehyde (*Cd*(*5ClsalArg*)).

Methanolic solution of 1 mmol of *L-Arg* was added to 1 mmol of $(CH_3COO)_2Cd{\cdot}2H_2O$ dissolved in hot methanol. The mixture was stirred vigorously and refluxed for 10 min and afterwards 1 mmol of appropriate aldehyde in methanol was added to the solution. The mixture was stirred and refluxed for an hour. Then it was cooled to room temperature. After 24 h the obtained precipitate was filtered out and washed by methanol. The authenticity and purity of obtained compounds were examined by proton NMR measurements.

2.3. NMR measurements

All liquid state NMR spectra have been run on a Bruker DRX Avance 500 spectrometer using 5 mm TBI Z-gradient probehead at room temperature. The signals assignment has been done on the base of GCOSY, GHSQC and GHMBC experiments using standard Bruker procedures for both acquisition and data processing. The chemical shift of the proton and carbon signals are referred to the internal TMS standard, whereas nitrogen-15 chemical shifts are referred to external nitromethane used as the standard. The CPMAS spectra were collected at room temperature using Bruker 500 Avance II spectrometer equipped with 4 mm MAS ^{1}H/BB probehead. Typical CPMAS experimental conditions for ^{15}N measurements were the following: spectral width 25 kHz, acquisition time 30 ms, contact time 4 ms, rotation rate 6–10 kHz, relaxation delay up to 20 s depending on relaxation properties of the sample. Up to 32,000 scans were collected to obtain good quality spectra. For carbon CPMAS experiment the following conditions were applied: spectral width 31.25 kHz, acquisition time 30 ms, contact time 2 ms, rotation rate 10–11 kHz, relaxation delay 10 s and up to 512 scans were collected. For short contact time CH spectra the contact time 40 μs was applied. The ^{113}Cd NMR spectrum in solid state was recorded in similar conditions as nitrogen spectra. Originally this spectrum was referenced to cadmium acetate ($\delta = -707.34$ ppm) and then the chemical shift was recalculated to the dimethylcadmium scale. A similar procedure was done for solution cadmium spectra.