Available online at www.sciencedirect.com
ScienceDirect
Coordination Chemistry Reviews 250 (2006) 2295–2307
COORDINATION CHEMISTRY REVIEWS
www.elsevier.com/locate/ccr

Review

The coordination chemistry of Vitamin C: An overview

B. Zümreoglu-Karan *

Department of Chemistry, Hacettepe University, Beytepe Campus, 06800 Ankara, Turkey

Received 27 July 2005; accepted 2 March 2006
Available online 17 April 2006

Contents

Abstract

An overview is presented of aspects of the coordination chemistry of Vitamin C (L-ascorbic acid) and up-to-date information about the structures and properties of a selection of ascorbate complexes covering the literature from the first synthetic reports which emerged about two decades ago. After a brief introduction concerning the ligand characteristics of ascorbic acid, the review includes pure complexes with transition metals with special attention to the recently described polynuclear complexes, complexes with rare earth metals and mixed ligand complexes. Finally, a section is devoted to the biomedical importance of the complexes. The highlights in these topical areas are briefly discussed.

Keywords: Vitamin C; Ascorbic acid; Ascorbate complexes; Coordination compounds; Bioinorganic chemistry

Abbreviations: A, ascorbate dianion $(C_6H_6O_6)^{2-}$; baea, bis(aminoethyl)amine; bipy, bipyridine; Bu, butyl; $CDCl_3$, deutorated chloroform; CD_3OD, deutorated methanol; Cp, cyclopentadiene; CP/MAS, cross-polarization/magic angle spinning; 3D, three dimensional; 2D, two dimensional; dach, diaminocyclohexane; DHA, dehydroascorbic acid; DEPT, distortionless enhancement by polarization transfer; DMF, dimethylformamide; DMSO, dimethylsulfoxide; D_2O, deutorated water; en, ethylenediamine; Et, ethyl; HA, ascorbate monoanion $(C_6H_7O_6)^-$; H_2A, ascorbic acid $(C_6H_8O_6)$; HETCOR, heteronuclear correlation; H_2Or, orotate monoanion; Me, methyl; MeOH, methanol; NaHA, sodium ascorbate; *n*-Bu, *n*-butyl; *n*-Pr, *n*-propyl; ox^{2-}, oxalate; ph, phenyl; phen, 1,10-phenanthroline; salen, *N*,*N*′-bis(salicylidene)ethylenediamine; STM, scanning tunneling microscopy; TMEDA, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine; trimen, *N*,*N*,*N*′-trimethylethylenediamine

* Tel.: +90 312 2977951; fax: +90 312 2992163.
E-mail address: bkaran@hacettepe.edu.tr.

0010-8545/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.ccr.2006.03.002

1. Introduction

Vitamin C was first isolated in 1928 by the Hungarian biochemist and Nobel Prize winner Szent-Györgyi [1]. In the nearly 80 years since its discovery, Vitamin C has become "the most famous but yet least understood of the vitamins". The most vital role of Vitamin C is no doubt that of the primary, water-soluble antioxidant in the human body.

Vitamin C is the L-enantiomer of ascorbic acid (meaning "without scurvy", the disease caused by a Vitamin C deficiency). The defining part of the substance is the ascorbate monoion, which possesses both acid and base properties. The term "Vitamin C" is not only used to refer to "L-ascorbic acid" but also for its first oxidation product "dehydroascorbic acid". The monoclinic crystal structure of the acid itself was established in the 1960s by X-ray and neutron diffraction analyses [2–4] and is approximated by the 2D structure given in Fig. 1. A 3D STM image on gold coated mica substrate given in Fig. 2 correlates well with crystallography. The image corresponds to the HOMO orbital of the L-ascorbic acid molecule for both of its keto- and enol-tautomeric forms and also for the anionic form [5].

In spite of the simplicity of this sugar molecule, its biochemistry is poorly understood due to a very complicated redox chemistry which makes the molecule both an interesting and intriguing reducing agent in inorganic systems. The interaction of Vitamin C with metal ions goes back almost 50 years to the early work of Udenfried et al. [6] about the oxidation of Vitamin C by dioxygen. Many solution studies have since been carried out on reactions between ascorbic acid and metal ions. The important work of Martell in this field established the catalytic role of metals in the oxidation of Vitamin C ([7] and the references therein) and was followed by several other studies involving equilibria between ascorbate and metal ions [8,9]. Relatively fewer studies have been reported regarding the isolation and characterization of solid complexes of ascorbic acid. The first synthetic reports emerged in the 1980s [10–12] however the coordination chemistry of Vitamin C has not progressed in a steep rise due to the problems associated with (i) the chemical instability of ascorbic acid [13–15], (ii) the low stability constants [7] and (iii) the reluctance of the complexes toward crystallization.

The reactions of L-ascorbic acid with transition metal complexes were reviewed by Davies in 1992 [16]. The present article is mainly confined to the advances in the coordination chemistry of Vitamin C, with particular attention to the synthesis and structural description of isolated complexes, notably during the period 1990–2005, including also the earlier literature related to the subject.

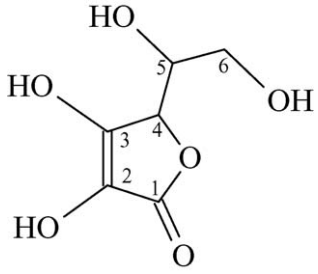

Fig. 1. L-Ascorbic acid.

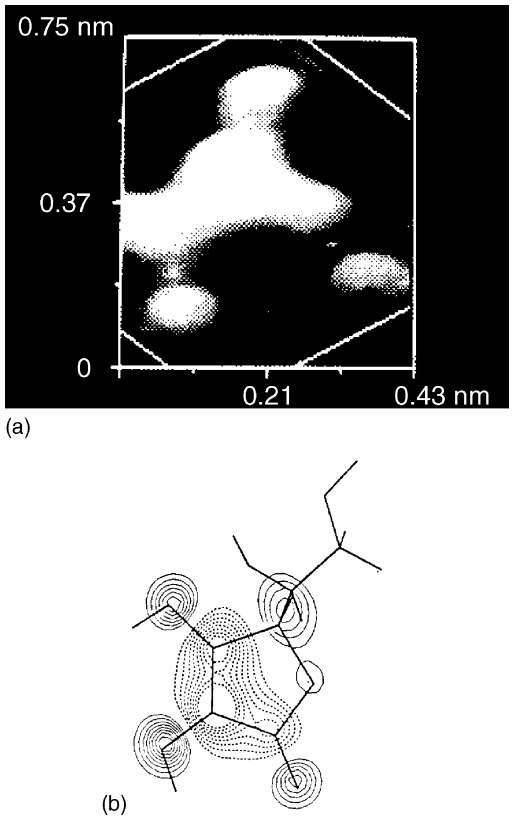

Fig. 2. (a) 3D STM image and (b) contour plot of the charge density of the HOMO orbital of ascorbic acid [5].

2. Ligand characteristics of Vitamin C

Structurally, ascorbic acid (H_2A) is a sugar acid, a γ-lactone and an ene-diol. As a weak dibasic acid ($pKa_1 = 4.25$ and $pKa_2 = 11.79$), the monoanion (HA) forms at pH 4–5 with deprotonation of O(3)–H and the dianion (A) forms at pH 11–12 with deprotonation of the O(2)–H [17]. The mono-anionic form is more stable due to the delocalization of the negative charge between the oxygen atoms at the 1- and 3-positions [18]. At physiological pH, the resonance stabilized HA undergoes two separate one-electron transfer steps to dehydroascorbic acid (DHA) via ascorbate free radical [19,20]. DHA (Fig. 3), is reduced back to H_2A by various cellular reductants. It retains the nutritional and physiological activity of H_2A but with different biological roles in cell-culture systems [21].

Although H_2A has several donor atoms capable of metal complex formation, the interaction of HA with metals mainly occurs monodentately through the O(3) atom [22–26] or by chelation via O(3) and O(2) [10,27], as shown in Fig. 4, depending on the nature of the metal cation and the pH of the solution. O,O′-chelation should be the normal kind of coordination for A as concluded by NMR studies [28–30]. In the solid state, several other bonding modes have been proposed including the participation of the carbonyl oxygen and side chain OH groups [31–36].