Polyhedron 73 (2014) 37–44

Contents lists available at ScienceDirect

Polyhedron

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

# Copper catalyzed oxidation of amino acids

Szabina Góger [a], József S. Pap [a], Dóra Bogáth [a], A. Jalila Simaan [b], Gábor Speier [a], Michel Giorgi [c], József Kaizer [a,*]

[a] Department of Chemistry, University of Pannonia, H-8200 Veszprém, Hungary
[b] Aix Marseille Université, CNRS, Centrale Marseille, iSm2 UMR 7313, 13397 Marseille, France
[c] Aix-Marseille Université, FR1739, Spectropole, Campus St. Jérôme, Avenue Escadrille Normandie-Niemen, 13397 Marseille cedex 20, France

ARTICLE INFO

*Article history:*
Received 27 November 2013
Accepted 5 February 2014
Available online 18 February 2014

*Keywords:*
Biomimetic oxidation
Oxidase activity
Kinetic studies
Amino acids
Copper(II)

ABSTRACT

Copper(II) chloride and novel *bis*(1-amino(cyclo)alkane-1-carboxylato-$\kappa^2N,O$)copper(II) complexes as catalysts were studied in relation with enzymatic oxidation of amino acids. The oxidation of aminophosphonate derivative: (1-amino-1-methyl)ethylphosphonic acid was also investigated. Two *bis*(1-aminocycloalkane-1-carboxylato-$\kappa^2N,O$)copper(II) complexes were structurally characterized. Surprisingly, while the 1-aminocyclobutane-1-carboxylate complex has square planar (*SP*-4) copper(II) center with *trans*-orientated ligands, the 1-aminocyclohexane-1-carboxylate complex has μ-carboxylato dimeric structure with square pyramidal (*SPY*-5) sites, one with *cis*- and one with *trans*-orientated ligands. Redox behavior of the *bis*(1-amino(cyclo)alkane-1-carboxylato-$\kappa^2N,O$)copper(II) complexes was also investigated. Catalytic oxidations were carried out in alkaline DMF-water mixtures using $H_2O_2$ as oxidant and the complexes as catalysts. The observed potentials for the irreversible current peaks associated with the Cu(II) to Cu(I) reduction and the rates of the amino acid oxidations show inverse trend. This suggests that the Cu(II)/Cu(I) redox cycling due to the presence of $H_2O_2$ plays important role in the peroxide/copper activation that in turn provides the observed products.



## 1. Introduction

The oxidative degradation of organic substances such as amino acids under mild conditions is of great interest for industrial and synthetic processes both from an economical and environmental point of view. Amino acids may form potentially harmful disinfection byproducts during the conventional treatment of water and wastewater [1,2]. Removal of these parent compounds by the use of the environmental-friendly oxidant, ferrate(VI) was assessed by studying the kinetics of the oxidation of glycine [3]. Previously, kinetics and mechanism of oxidation of neutral L-amino acids by sodium *N*-chloro-*p*-toluene sulfonamide in acid [4,5] and alkaline medium [6] have been reported.

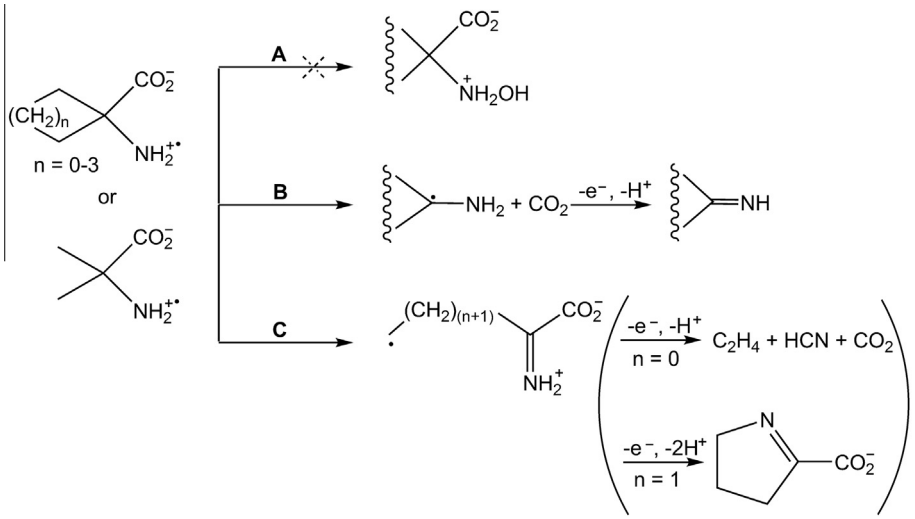
Metal ion-catalyzed oxidations (MCO) of amino acids were also performed by researchers to mimic the deamination of bioactive molecules catalyzed by enzymes. The first example of a biomimetic mononuclear iron complex, ([$Fe^{III}$(Salen)Cl] (Salen = *N*,*N*′-bis (salicylidene)-ethylenediaminato) was described, that highly selectively and efficiently catalyzes the oxidation of a series of acyclic and cyclic amino acids to ethylene or the corresponding carbonyl compounds [7,8] (Scheme 1), mimicking the action of the non-heme iron enzyme 1-aminocyclopropane-1-carboxylic acid oxidase (ACCO) [9]. Kinetics and mechanism of the oxidation of α-amino acids by peroxomonosulphate (PMS) in acetic acid/sodium acetate buffered [10–16], and alkaline medium were also reported [17].

Besides enzymatic reactions, the oxidation of amino acids or amino acid residues in living organisms may occur either by reactive oxygen species (ROS) [18] or as a MCO process [19]. ROS-indicated oxidation reactions of amino acids and the products formed are well described, and understood [20]. Much less is known this far about MCO, however metal-based oxidants have far greater potential [21]. MCO gives rise to highly reactive intermediates such as hydroxyl radicals, which lead to damage in bio-molecules such as proteins that are implicated in aging and the pathogenesis of neurodegenerative diseases, including Alzheimer's disease [22,23].

Here we describe a new copper(II)-catalyzed (Table 1) system for a series of acyclic (α-amino-isobityric acid (AIBH), D,L-alanine (D,L-ALAH)) and cyclic amino acids (1-aminocyclopropane-1-carboxylic acid (ACCH), 1-amino-1-cyclobutanecarboxylic acid (ACBCH), 1-aminocyclopentanecarboxylic acid (ACPCH), and 1-aminocyclohexanecarboxylic acid (ACHCH)), and α-aminophosphonic acid ((1-amino-1-methyl)ethylphosphonic acid (AMEP))

* Corresponding author. Tel.: +36 88 624 720; fax: +36 88 624 469.
*E-mail address:* kaizer@almos.vein.hu (J. Kaizer).

http://dx.doi.org/10.1016/j.poly.2014.02.007
0277-5387/




**Scheme 1.** Pathways leading to different products by ACCO.

**Table 1**
Summary of the isolated complexes.

| Amino acid (AA) | $[Cu^{II}_n(AA)_{2n}]\cdot mH_2O$ |
|---|---|
| ACBC | **1** ($n = 1$, $m = 0$) |
| ACPC | **2** ($n = 1$, $m = 1$) |
| ACHC | **3** ($n = 2$, $m = 2$)[a] |
| AIB | **4** ($n = 1$, $m = 0$) |
| D,L-ALA | **5** ($n = 1$, $m = 1$) |

[a] one water molecule is coordinated.

as surrogates for the corresponding α-aminocarboxylic acids (Scheme 2, Table 1).

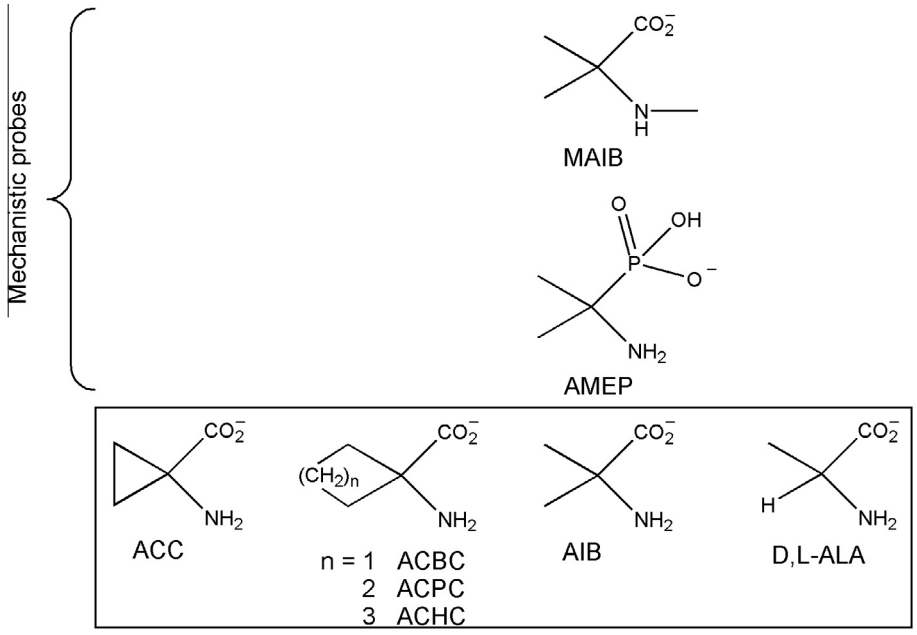
## 2. Experimental

### 2.1. Materials

Solvents used for the reactions were purified by literature methods [24] and stored under argon. All other chemicals were commercial products and were used as received without further purification. The $Cu(ClO_4)_2\cdot 6H_2O$ and the amino acid substrates and AMEPH were purchased from commercial sources.

### 2.2. Analytical and physical measurements

Infrared spectra were recorded on an Avatar 330 FT-IR Thermo Nicolet instrument using samples mulled in in KBr pellets. UV–Vis spectra were recorded on a Cary 60 spectrophotometer equipped with a fiber-optic probe with 1 cm pathlength. Microanalyses were done by the Microanalytical Service of the University of Pannonia. Cyclic voltammograms (CV) were taken on a VoltaLab 10 potentiostat with VoltaMaster 4 software for data process. The electrodes were as follows: glassy carbon (working), Pt (auxiliary), and Ag/AgCl in 3 M KCl (reference). The potentials were referenced *vs.* the ferrocenium ferrocene redox couple (+416 mV in methanol in our setup). The crystal evaluations and intensity data collections were performed on a Bruker-Nonius Kappa CCD single-crystal diffractometer (**1**, **3**) using Mo Kα radiation ($\lambda = 0.71070$ Å) at




**Scheme 2.** Structures and abbreviated names of the substrates used in this study.