

Mechanochemical synthesis of hemin–imidazole complexes

Armando Paneque and José Fernández-Bertran

Center of Pharmaceutical Chemistry, Havana, Cuba and Center for Applied Science and Advanced Technology of IPN (CICATA-IPN), Legaria 694, Col. Irrigacion, 11500 Mexico, D.F., Mexico

Edilso Reguera*

Center for Applied Science and Advanced Technology of IPN (CICATA-IPN), Legaria 694, Col. Irrigacion, 11500 Mexico, D.F., Mexico and Institute of Materials and Reagents, Havana University, Cuba

Hernani Yee-Madeira

School of Physics and Mathematics of IPN, Col. Lindavista, Mexico, D.F., Mexico

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Abstract

Solid state reactions of hemin and imidazole were performed by milling the crystalline materials in an agate mortar. The process was monitored by i.r., x.r.d. and Mössbauer spectroscopies. Samples with different hemin to imidazole molar ratios were studied. The interactions of imidazole with the central Fe atom and with the propionic acid groups in the periphery of the hemin molecule were detected. The latter interactions are suppressed by washing with MeOH. Complexes with 1:2 and 1:4 hemin-to-imidazole molar ratios were identified.

Introduction

Hemoglobin is a complex protein molecule whose center consists of a hemin nucleus, which coordinates an Fe atom in a square planar arrangement (see Figure 1a). The fifth axial position is occupied by coordination with the pyridinic N of the imidazole moiety of the hystidil residue in a side chain of the protein part (see Figure 1b). The sixth axial position is available for O₂ coordination, the basic step of the respiratory process.

Imidazole–hemin complexes have been studied as simple models of hemoprotein molecules [1, 2]. The interactions of hemin with imidazole have been carried out in different media. In aqueous systems, the presence of the μ -oxo-bisiron(III) species and other complexities such as the competition of OH[−] ion for the coordination sites of the iron in hemin have made it difficult to interpret their results [3, 4]. In absence of solvents, the reaction of imidazole with hemin has been conducted at the melting point of imidazole, however there is no report about the nature of the reaction product [5].

In nonpolar solvents such as benzene, *o*-dichlorobenzene and bromobenzene, and in polar solvents such as chloroform, dimethylformamide, dichloromethane, ethyl acetate and acetone, studies have been carried out with deuteroporphyrin (IX) dimethyl ester iron(III) chloride and tetraphenylporphine iron(III) chloride, *etc.*, instead of hemin [6]. In all the media studied, the data available satisfactorily accounted for the existence

of an equilibrium in which two imidazole molecules displace the chloride ion or other ligands to form the low-spin bisimidazole complex with no clear evidence of a stepwise equilibrium. It has been suggested that the excess of imidazole in these reactions may interact with the porphyrin ring of the ferriporphyrins to form π -complexes, or can H-bond to the already coordinated imidazole. The extent of the reactions studied were very dependent upon the nature of the solvents [6].

Little is known about the interactions of imidazole with acidic groups located in the periphery of the hemin molecule. In this paper we present a study of the mechanochemical processes that take place on milling crystalline hemin with imidazole in an agate mortar. Samples with low imidazole content shed light on the Fe–imidazole complexation, while samples with

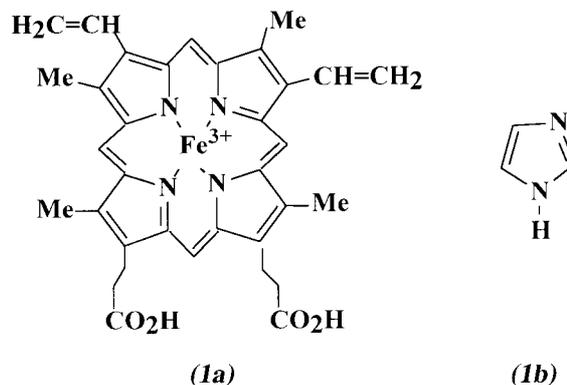


Fig. 1. Structure of: (a) protoporphyrin IX iron(III), (hemin); (b) imidazole.

* Author for correspondence