

Mechanochemical reactions of fluorides with hemin

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Abstract

Hemin has two potential sites to react with fluorides, the peripheral acid groups and the central Fe^{III} cation. The mechanochemical reactions of hemin with fluorides (LiF , NaF , KF , CsF , NH_4F and AgF) were monitored using X-ray diffraction (XRD), and IR and Mössbauer spectroscopies. LiF and NaF were found inert when milled with hemin, however KF , CsF , NH_4F and AgF react at both hemin sites. At the iron site Cl^- is replaced by F^- with formation of KCl , CsCl , NH_4Cl , and AgCl , as detected by XRD, while with the peripheral acid groups, fluorides collect the acidic protons to form KHF_2 , CsHF_2 , NH_4HF and AgHF_2 . The reactions of hemin with the reactive fluorides take place first at the iron site and then at the propionic acid groups. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Hemoglobin, the oxygen carrier of blood, is composed of a large protein moiety, globin, linked to a Fe^{III} -porphyrin IX center, the heme, by the coordination of Fe to a histidine residue. The hemin molecule, depicted in Fig. 1a, has been used as a simple model to understand hemoglobin chemistry and as a starting reagent in the synthesis of pharmaceutical products for the treatment of anemia [1,2]. It has the Fe^{III} atom coordinated to the porphyrin IX ring. According to the crystallographic studies [3] the Fe^{III} atom is slightly out the plane formed by the porphyrin ring (Fig. 1b). The fifth ligand in axial position is loosely coordinated to a Cl^- anion, while the sixth axial position is vacant for coordination to oxygen and other nucleophilic ligands.

Hemin has two potential sites to participate in reactions with basic substances, the two peripheral acid groups and the central Fe^{III} cation. These reactions are important in the study of hemoglobin biochemistry as well as in the synthesis of complexes with pharmaceutical properties in the treatment of anemia [4,5]. The two propionic acid residues can interact by hydrogen bonding with other OH groups and Fe atoms in neighbor molecules leading to dimeric and polymeric structures [6]. The modification of these interactions is

paramount in the synthesis of pharmaceuticals capable to be transported by the blood and assimilated by the cells [7]. The studies of bonding properties of iron at the sixth axial position with a wide variety of ligands have been related with its role as oxygen carrier in biological systems [8]. The absolute majority of reactions with hemin have been carried out in solutions with only a minimum in the solid state [8]. However, the reactions in solid state can shed light on some particularities of hemin complexes of biological importance [8].

In this communication we report reactions of hemin with fluorides by milling together the solid reagents. As reference, the reactions were also carried out in methanolic solutions. The reactions products were characterized by IR, XRD and Mössbauer techniques.

2. Experimental

Li , NaF , KF , CsF , NH_4F , AgF and hemin were commercial reagents of analytical grade (from Sigma) and methanol absolute (from Merck). For IR measurement KBr of spectroscopic grade (also from Sigma) was used. As reference compounds, LiFHF_2 , NaHF_2 and KHF_2 were prepared from HCl and the corresponding fluorides and then purified from methanolic solutions. Their nature and purity were established using IR spectroscopy and XRD.

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