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REGULAR ARTICLE

A Density Functional Theory Study of the Hydrolysis Mechanism of Sulfachloropyridazine

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Abstract: Sulfonamide antibiotics are an important class of organic pollutant in the aquatic environments. To understand the hydrolysis behavior of sulfonamides, the hydrolysis mechanisms of a typical sulfonamide sulfachloropyridazine (SCP) were investigated using the density functional theory (DFT) at the B3LYP/6-31+G (d, p) level. SCP hydrolysis resembles nucleophilic substitution by water molecule attacking sulfonyl group (pathway 1) and heterocyclic aromatic ring (pathway 2) respectively. Due to the electrophilic center sulfur atom in pathway 1 carrying much larger positive charge than the carbon atom in the pathway 2, the sulfonyl group can be easily attacked by water molecule, and thus the pathway 1 can be dominant. By comparing the hydrolysis energy barrier of different forms of SCP, it was found that the SCP hydrolysis in neutral and once-protonated state are much more energetically favorable to proceed than the double protonated form. In addition, the hydrolysis path is not found for the dissociated anionic SCP. As the pH values in solution decreases, the corresponding neutral and once-protonated SCP increases, then the hydrolysis rate becomes faster, which is consistent with the experimental observations that the hydrolytic degradation rate at pH=4 is much faster than those of pH=7 and 9.

AMS subject classifications: 92E10, 80A30,

Key words: Hydrolysis Mechanism, Sulfonamides, Sulfachloropyridazine, the Density Functional Theory (DFT)

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1 Introduction

Sulfonamides (SAs) are a group of synthetic antimicrobial agents [1](e.g., sulfachloropyridazine, sulfathiazole, sulfadiazine and sulfapyridine) which have been widely used in healthcare and veterinary antibiotics for decades [2,3]. All the sulfonamides, apart from sulfaguanidine, are compounds containing two basic and one acidic functional group [4]. The basic functional groups are the amine group of aniline and the heterocyclic base, and the acidic functional group is the sulfonamide group. The mechanism action of SAs is to inhibit the conversion of *p*-aminobenzoic acid and interrupt bacterial utilization of the compound in the synthesis of folic acid and ultimately of protein, purine and DNA [2,5]. Due to the low cost and broad spectrum of activity in preventing or treating bacterial infections and the effectiveness of growth promotion, SAs are extensively prescribed today as the popularly used antibiotic drugs or growth promoter with the increasing need of pharmaceuticals and veterinary medicine [6].

As SAs are persistent and non-biodegradable, the contamination of environment has recently raised concern in aquatic environments [7]. Although the SAs concentrations in the environmental samples are quite low ($ng \cdot L^{-1}$-$\mu g \cdot L^{-1}$), its high biological activity could cause significant changes in biosphere [2,6,8]. Thus, it is very important to understand the possible degradation ways of SAs for helping evaluate their environmental fate or the treatment of these kinds of substance. Many experimental studies reported that SAs are resistant to natural biodegradation, but they undergo abiotic degradation such as hydrolysis and photolysis. Like most of other organic substances [9], SAs may experience photolysis degradation with the presence of catalysts like TiO_2, Fe(III) or H_2O_2 in water solutions under the illumination of UV radiation[10]. Recently, the photolysis mechanisms of sulfachloropyridazine (SCP) and Sulfadiazine (SDZ) have been well investigated using quantum chemical approach [11,12]. Furthermore, as one of the most common reactions controlling abiotic degradation, hydrolysis is an important degradation path for most organic pollutants in the environment. Recently, Kumirska et al made a detailed experimental investigation on the hydrolysis of sulfonamides in aqueous solutions [4], the results indicate that SA hydrolysis was closely depending on the temperature and pH values. At 70°C, the hydrolytic degradation rate for SCP at pH=4 is much higher than those of pH=7 and 9. Two independent hydrolysis paths of SCP were proposed by Kumirska as shown in **Scheme 1**[4]. In the case of path 1, the nucleophilic substitution takes place in the sulfonyl group with sulphanilic acid and the corresponding heterocyclic base as the main products. In path 2, the nucleophilic aromatic substitution occurs in the heterocyclic aromatic ring with sulfanilamide as the primary product.