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Original Research Article

Reaction between Thiouracil derivatives and Chloroasetic acid in gas and soluble phases:A theoretical study

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ABSTRACT

Thiouracilis a historically relevant anti-thyroid preparation. Because of its structure you can find it in various chemical reactions differently. In this study, the reaction of Thiouracil with Chloroacetic acid and the formation of their additive products has been investigated. This reaction is aconcerted process, and it has not been determined yet by exhaustive mechanisms. From the potential energy profile, two possible mechanisms as well as two NH bonds dissociations are examined. Density Functional Theory (DFT) was used to compare these mechanisms. Calculation results for comparing these two pass ways were indicated byB3LYP/6-311g (d,p) levels of theory. The activation energies to 2-(6-oxo-1,6-dihydropyrimidin-2-ylthio) acetic acid and 2-(4-oxo-1,4-dihydropyrimidin-2-ylthio) acetic acid formation were obtained 55.78 and 72.9 kcal.mol-1, respectively. These calculations were also carried out for ethyl and

methyl Thiouracil derivatives. The calculation results indicate that removal of hydrogen from nitrogen to sulfur group at the ortho position is more favorable.

Keywords: Thiouracil**,** Chloroacetic acid, DFT**,** B3LYP**,** activation energy

Introduction

Thiouracil is a specific molecule that consists of sulfated uracil and its derivatives (Fig. 1). This is a suitable anti-thyroid drug. For the first time Astwood, E.B. (1943) used it as therapy of Grave's disease [1, 2]. Thiouracil blocks the thyroid peroxidase enzyme in order to inhibit thyroid activity. Thiouracil is a minor chemical component of natural tRNA that is Thio analogue of RNA base uracil. Researchers have used derivatives of Thio as melanoma seekers (tumor derived from melanin forming cells); they have covalent bond to the growing melanin through sulfur. Other derivatives of Thiouracil have been used as a diagnosis and chemotherapy for metastatic melanoma. [2].

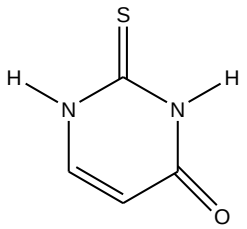

Fig 1. Thiouracil scheme, it consists of sulfated uracil ($C_4H_4N_2OS$)

Thiouracilis produced via the condensation of Ethyl Feormylacetate and Thiourea. In 1943 it was marketed as the first anti-thyroid Ethionamide product.

Due to the high number of side effects, it has been discontinued in favor of other drugs that are less toxic, such as propyl. Currently, this product is not used as a Thyrostatic drug in humans and Tetracycline compounds is used as an active drug; also cattle men give it orally to their cattle for gaining weight before slaughter. These compounds cause livestock gain weight through the water retention in tissues [3]. In fact, Thiouracils contain nucleoside analogues which replace sulfur with one or more oxygen atoms. These compounds play important roles in molecular biology and pharmacology because of their specific structure. Naturally they are present in T-RNA structure, and have been used as fluorescent probes for thyroid disease treatment in DNA