

STRUCTURE OF MATTER AND QUANTUM CHEMISTRY

Mechanistic Insight into Alkylation of the Ethyl Acetoacetate Anion with Different Ethyl Halides¹

S. Marković, J. Đurđević, M. Vukosavljević, and Z. Petrović

Faculty of Science, University of Kragujevac, 34000 Kragujevac, Serbia

e-mail: mark@kg.ac.rs

Received November 6, 2012

Abstract—The alkylation reactions of the ambident ethyl acetoacetate anion with C_2H_5X ($X = F, Cl, Br$, and I) in the O2, C3, and O4 positions of the anion were investigated at the B3LYP/6-311+G(*d,p*) level of theory. It was found that the ethylation reaction does not occur in the position O4, as well as with ethyl fluoride in any position of the anion, due to very high activation energies and thermodynamic instability of the hypothetical products. The activation energies for the reactions in the position O2 are lower in comparison to the position C3, but the products of the reactions in the C3 position are more stable than those in the position O4, implying that the C/O products ratio is controlled by both thermodynamic and kinetic factors, leading to the O2-product with the chloride, and C3-product with the iodide as leaving group.

Keywords: ambident nucleophile, ethylation, reaction mechanism, DFT.

DOI: 10.1134/S0036024413130165

INTRODUCTION

Ethyl acetoacetate (EAE), also called acetoacetic ester, is a chemical that is usually prepared through the base-mediated condensation of ethyl acetate. This condensation is the method of synthesis of 1,3-dicarbonyl compounds, which was extensively explored by Rainer Ludwig Claisen [1, 2]. Industrially, EAE is prepared by treating diketene with ethanol. The molecule of EAE actually exists in two tautomeric forms, keto (92.5%) and enol (7.5%). In 1911, another German chemist, Knorr, succeeded to isolate EAE in pure keto and pure enol forms [3].

EAE is widely used compound in the synthesis of variety of organic chemical compounds [4, 5]. Chemists are familiar with the fact that sodioacetoacetic ester reacts with many alkyl halides, giving a variety of ketones and acids. Pleasant and fruity aroma makes EAE popular in manufacture of flavoring and fragrance products, as in the case of fructose [6]. In addition, food manufacturers use EAE as a component of resinous and polymeric coatings. In other applications EAE can be utilized as a solvent, stabilizer or catalyst. When more extensively modified, acetoacetic acid derivatives find application in the manufacture of drugs, vitamin B, dyes, pigments, heterocycles, and agrochemicals [7–10].

EAE anion is an ambident nucleophile, as it can perform nucleophilic attack using two or more different modes, leading to two or more possible alternative products, depending on the reaction conditions. Alkylation of the EAE anion with ethyl halides reflects its ambident nature. This reaction occurs at either O2 or C3, where the yield of the O-product decreases, whereas the yield of the C-product increases with increasing atomic number of the halogen [11] (Scheme 1). This result is commonly explained by the HSAB (hard–soft–acid–base) rationale [12]. Namely, of the two nucleophilic sites in the enolate anion, oxygen is harder nucleophile than carbon, due to the fact that oxygen is more electronegative than carbon.

Nucleophilic substitution reactions of the S_N2 type proceed best when the nucleophile and leaving group are either both hard or both soft [13]. Because of the polarized low-energy C–X bonds, alkyl halides are soft acids. The predominant product of an ambident nucleophile with the soft alkyl halide results in the C-alkylation, which is orbital controlled. Electron density redistribution between molecules in the C-ethylation can be thought of as electron movement between electron donor (HOMO) and electron acceptor (LUMO) molecular orbitals [14]. Variation of leaving group X leads to different product ratios. Namely, pronounced electronegativity of X leads to the O-alkylation, which is charge controlled.

¹ The article is published in the original.

