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Understanding the regioselectivite of the Baeyer-Villiger reaction of bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one: A DFT Study

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ABSTRACT

A density functional theory study was performed on the Baeyer-Villiger reaction of bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one with hydrogen peroxide. The thermodynamic and kinetic parameters were analyzed by considering the regio-isomeric Pathways, we found that the regioisomers P_1 *and* P_3 *are kinetically and thermodynamically favored.*

Keywords: Baeyer-Villiger, bicyclo[4.2.0]octan-7-one, bicyclo[3.2.0]heptan-6-one, TST, DFT.

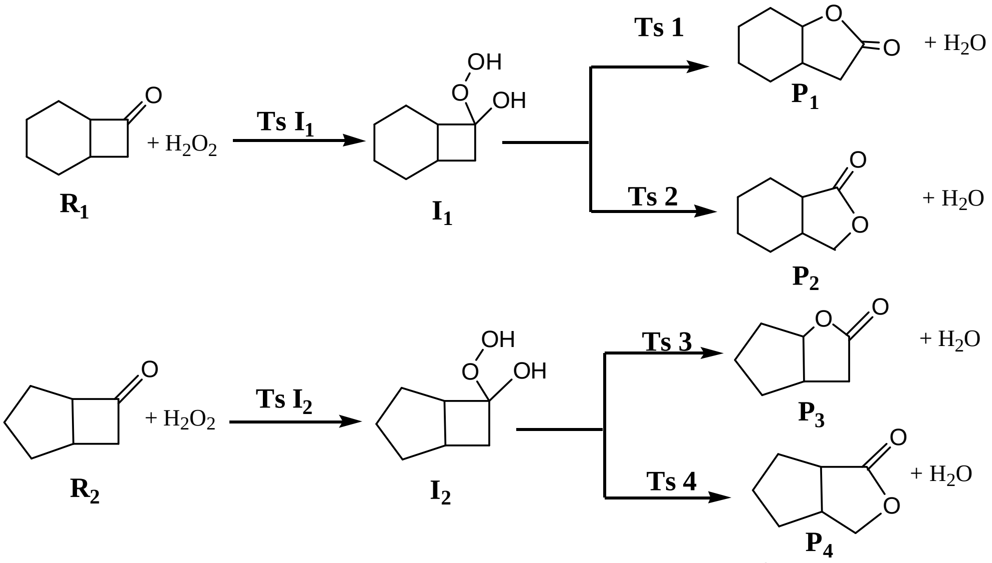
INTRODUCTION

The Baeyer-Villiger (B.V) oxidation is the oxidative cleavage of a carbon-carbon bond adjacent to a carbonyl, which converts ketones to esters and cyclic ketones to lactones [1, 2]. The B.V oxidation can be carried out either with peroxyacids, such as MCBPA (*meta*-chloroperbenzoic acid), or with H_2O_2 and O_2 as Green Oxidants. [3-6]

The reaction is of great importance for the manufacture of lactones. The regiospecificity of the reaction depends on the relative migratory ability of the substituents attached to the carbonyl group. Substituents which are able to stabilize a positive charge migrate more readily, so that the order of preference is *tert*-alkyl > cyclohexyl > *sec*-alkyl > phenyl > *primary*-alkyl > CH3. [7]

C. Mazzini *et al.* experimentally studied the B-V reaction between bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one with hydrogen peroxide, [8] finding that these reaction s are regioselective yielding the corresponding lactone P_1 and P_3 as the majority regioisomere (see Scheme 1).

In this paper, the mechanism and the regioselectivity of the BV reaction of bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one with hydrogen peroxide, is modelled at reliable levels of theory.



Scheme 1: Competitive regio-isomeric pathways associated with the Baeyer-Villiger reaction of bicyclo[4.2.0]octan-7-one (R_1) and bicyclo[3.2.0]heptan-6-one (R_2)

MATERIALS AND METHODS

DFT computations were carried out using the B3LYP functional, [9] together with the standard 6-31G/(d) basis set. [10] The optimizations were carried out using the Berny analytical gradient optimization method. [11] The stationary points were characterized by frequency computations in order to verify that TSs have one and only one imaginary frequency. The IRC paths [12] were traced in order to check the energy profiles connecting each TS to the two associated minima of the proposed mechanism using the second order González–Schlegel integration method. [13]

The electronic structures of stationary points were analyzed by the natural bond orbital (NBO) method. [16] All computations were carried out with the Gaussian 09 suite of programs. [17]

RESULTS AND DISCUSSION

The present study has been divided into two sections: i) first, the Baeyer-Villiger reaction between bicyclo[4.2.0]octan-7-one $\mathbf{R_1}$ and hydrogen peroxide is studied; ii) in the second part, the Baeyer-Villiger reaction between bicyclo[3.2.0]heptan-6-one and hydrogen peroxide is theoretically investigated. In each part, energetic aspects, geometrical parameters of the TSs and their electrostatic potential maps are analyzed.

3.1. Study of the B-V reaction between ketone R_1 and hydrogen peroxide

The values of the Gibbs free energies and the relative of the stationary points involved in the B-V reaction between ketone R_1 and hydrogen peroxide are summarized in Table 1. The Gibbs free energy profile of the B-V reaction between ketone R_1 and hydrogen peroxide is given in Figure 1.

Table 1. DFT/6-31G(d) Gibbs free energies (G, in a.u.), and the relative [a] (ΔG in kcal mol^{-1}), computed at 298.15 K and 1 atm, for the stationary points involved in the B-V reaction between ketone R_1 and hydrogen peroxide

System	G	ΔG
$R_1 + H_2O_2$	-538,58357	-------
TS in1	-538,53293	21,776
I 1	-538,56111	14,093
TS 1	-538,532562	32,007
TS 2	-538,53255	32,015
P 1 + H_2O	-538,724556	-88,468
P 2 + H_2O	-538,719555	-85,330

[a]: $R_1 + H_2O_2$

The B3LYP/6-31G(d) activation energies associated with the two reactive channels of the B-V reaction between ketone R_1 and hydrogen peroxide are 32.007 (**TS1**), and 32.015 (**TS2**) kcal mol^{-1}, these energy results indicate that this B-V reaction between ketone R1 and hydrogen peroxide is a moderate regioselectivity and product P_1 is kinetically favored.

The formation of the products P1 and P2 being exothermic by 88.468 and 85.330 kcal mol^{-1} respectively. Consequently, due to the strong exothermic character of the reaction, which makes the formation of the two BVs irreversible, the differences between the formation energies suggest that this reaction would lead to an isomeric mixture.

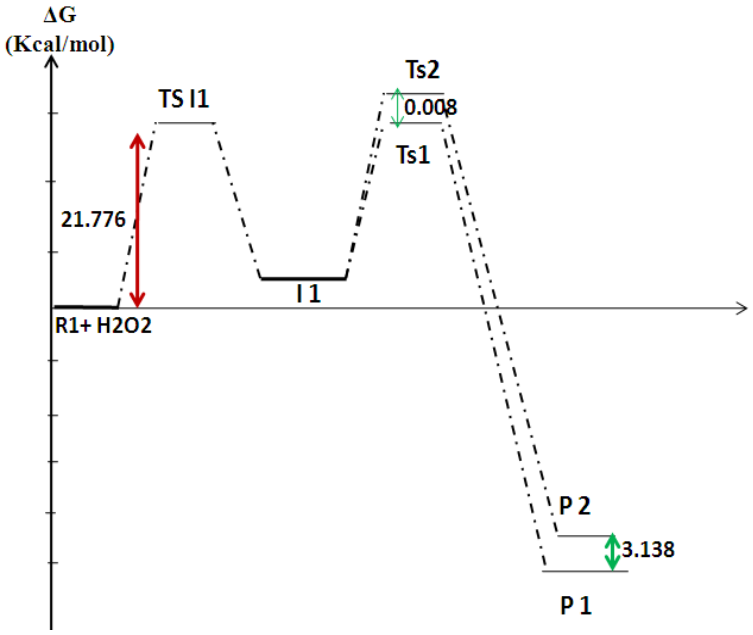


Figure 1. Gibbs free energy profile (ΔG, in kcal mol−1) of the B-V reaction between ketone R1 and hydrogen peroxide

3.2. Study of the B-V reaction between ketone R_2 and hydrogen peroxide

The values of Gibbs free energies and the relative one associated with the two reactive channels belonging to the BV reaction of bicyclo[3.2.0]heptan-6-one with hydrogen are summarized in Table 2. The Gibbs free energy profile of the BV reaction of bicyclo[3.2.0]heptan-6-one with hydrogen is given in Figure 2.

The activation Gibbs free energy corresponding to the formation the products P_3 and P_4 are 32.016 (**TS3**), and 34.853 (**TS4**) kcal mol^{-1}favouring kinetically the formation of $\mathbf{P_3}$ as the single lactones, in good agreement with the experimental outcomes. Note that while formation of the products P_3 and P_4 are exothermic by 90.425 and 86.538 kcal mol−1 respectively; consequently, the product P3 is kinetically and thermodynamically favored.

Table 2. DFT/6-311G(d) Gibbs free energies (G, in a.u.), and the relative [a] (ΔG in kcal mol^{-1}), computed at 298.15 K and 1 atm, for the stationary points involved in the B-V reaction between ketone R2 and hydrogen peroxide

System	G	ΔG
$R2+H_2O_2$	-449,197683	-------
TS I2	-449,148362	30,948
I2	-449,188674	5,653
T3	-449,14666	32,016
T4	-449,142139	34,853
P3+ H_2O	-449,341788	-90,425
P4+ H_2O	-449,335593	-86,538

[a]: *R_2+ H_2O_2*

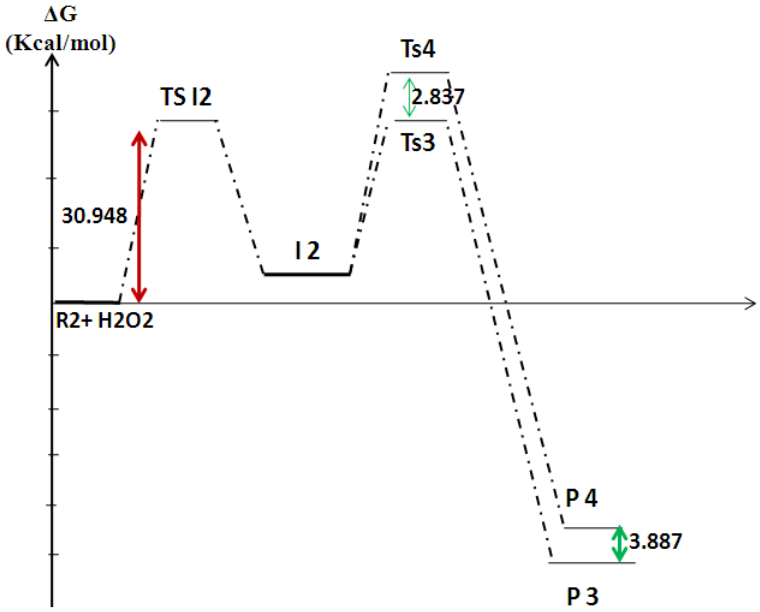


Figure 2. Gibbs free energy profile (ΔG, in kcal mol−1) of the B-V reaction between ketone R2 and hydrogen peroxide

The geometries of the TSs involved in the bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one with hydrogen peroxide are given in Figure 3. The lengths of the O-H and O-C forming bonds at the TSs are 2.480 and 1.887 A at **TS-1**, 2.481 and 2.411 A at **TS-2**, 2.483 and 1.875 A at **TS-3** and 1.916 and 1.898 A at **TS-4**. These geometric parameters suggest an asynchronous bond formation process along the most favourable P_1 and P_3 regioisomeric channel.

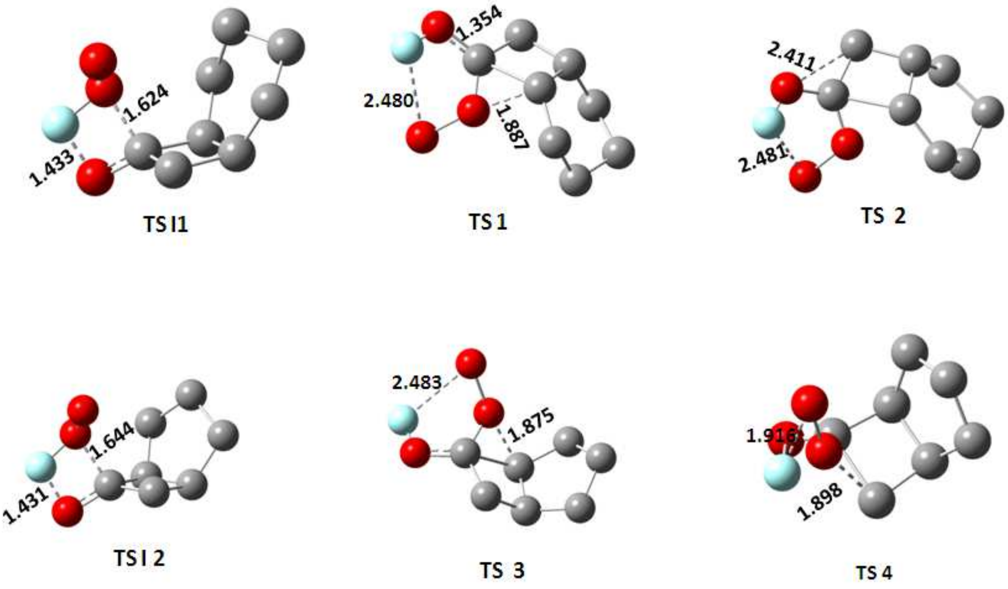


Figure 3. DFT/6-31G(d) optimised structures of the TSs of the bicyclo[4.2.0]octan-7-one and bicyclo[3.2.0]heptan-6-one with hydrogen peroxide. Lengths are given in Angstroms

3.3.Understanding the *regio*selectivity of Baeyer-Villiger reaction using electrostatic potential V(r)

The electrostatic potential is a real property, a physical observable. It can be obtained computationally. [16] While it has been used to interpreting and predicting the regioselectivity. [17]. Regions where V(r)>0 can be expected to be attracted favorably, at least initially, to negative portions of other molecules, while V(r) < 0 predicts attractive interactions with positive portions. In this part we obtain V(r) with the density functional B3LYP/6-31+G(d). (Figure 4)

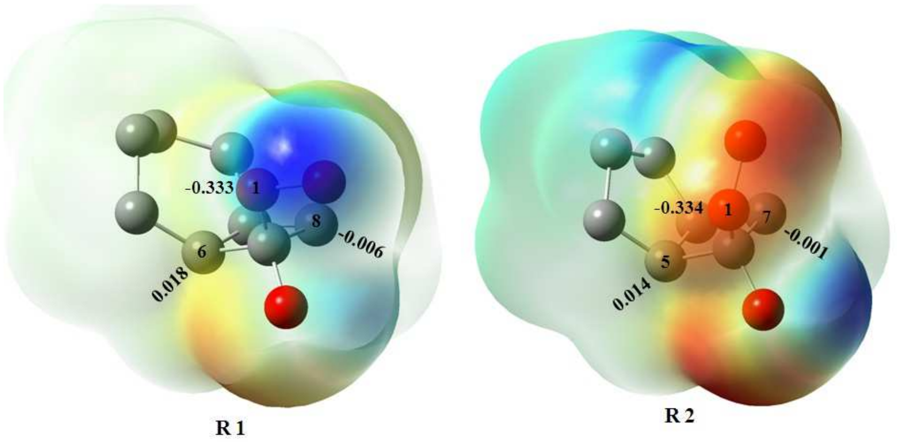


Figure 4. Calculated electrostatic potential on the 0.001 au surface of R_1 and R_2 (Mulliken charges with hydrogens summed: MCHS)

We can observed from figure 4 that the Mulliken charges with hydrogens summed of reactive R_1 and R_2 in the atoms C_6 (R_1) and C_5 (R_2) are (0.018 and 0.014 respectively) is positive than anther carbon, indicating that the interaction between oxygen O_1 and the atoms C_6 (R_1) and C_5 (R_2) are very favored.

CONCLUSION

The high reactivity and regioselectivity of ketone R_1 and R_2 towards the lactones P_1 and P_3 by the B V reaction, has been studied using DFT methods at the B3LYP/6-31G(d). Analysis of the relative Gibbs free energies indicates that while the formation of the products P_1 and P_3 are kinetically and thermodynamically favorable.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper. Also, they declare that this paper or part of it has not been published elsewhere.

CONTRIBUTION OF THE AUTHORS

M. ELIDRISSI: revised and analysed the data.
A. EL HAIB : revised and analysed the data.
M. ZOUBIR : revised and analysed the data.
R. HAMMAL : revised and analysed the data.
A. ZEROUAL: Localisation of transition state, revised the paper.
A. EL HAJBI: revised the draft paper.

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