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DFT study of condensation mechanisms of 4-pyridinecarboxaldehyde with o-, m-, p-aminobenzoic acids

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Abstract. It was theoretically studied the mechanism of the condensation reaction of 4-pyridinecarboxaldehyde with o-, m- and p-aminobenzoic acids. Theoretical calculations represent a primary advantage in studying these reactions, along with the determination of a wide range of molecular properties. The studied reactions take place in two stages, each stage is accompanied by a transition state and for each stage it is calculated the activation energy. Thermodynamically speaking, all reactions are endothermic and the most convenient from an energetic point of view is the reaction for obtaining 4-(pyridine-3-yl-methylene amino) benzoic acid in methanol with an energy value of 9.98 kcal/mol.

Keywords: mechanism, DFT calculations, Schiff bases, energetic stability, transition state.

Studiul DFT al mecanismului de condensare a 4-piridincarboxaldehidei cu acizii o-, m-, p-aminobenzoic

Rezumat. A fost studiat teoretic mecanismul reacției de condensare a 4-piridincarboxaldehidei cu acizii o-, m- și p-aminobenzoici. Calculele teoretice reprezintă un avantaj primordial în studierea acestor reacții, cu determinarea a unei game largi de proprietăți moleculare. Reacțiile studiate decurg în două etape, fiecare etapă este însoțită de câte o stare de tranziție și pentru fiecare etapă calculându-se energia de activare. Termodinamic vorbind, toate reacțiile sunt endoterme și cea mai convenabilă din punct de vedere energetic este reacția de obținere a acidul 4-(piridin-3-il-metilenamino)benzoic în metanol cu valoarea energiei de 9,98 kcal/mol.

Cuvinte cheie: mecanism, calcule DFT, baze Schiff, stabilitatea energetică, stare de tranziție.

1. INTRODUCTION

Current chemical engineering has the task of developing new chemical compounds that would allow obtaining materials with useful properties for various fields. A rapidly developing field at the intersection of inorganic and organic chemistry is coordination chemistry, which offers effective solutions for various fields: agriculture, industry, pharmaceuticals etc. [1]. One of the most important components in the synthesis of coordination compounds is coordination agents (ligands), the nature of which can radically influence the structure and properties of new metal-organic molecules.

Schiff Bases present valuable coordination agents in the synthesis of coordination compounds, which allow diversification of the composition and structure of the final products. The geometric peculiarities of organic molecule, the presence of electron-donating atoms, as well as the nature of metal ions generating the complex, create the prerequisites for the assembly of new molecular architectures with distinct properties. To obtain organic molecules that would have a greater interest in the coordination process, precursors are used that would ensure the presence of various functional groups: pyridinic, carboxylic etc. [2].

The compounds obtained from the condensation which contain a pyridinic nucleus possess a series of pharmacological properties, being described in the literature as antimicrobial [3], anti-inflammatory [4], antioxidant [5], etc. There are a variety of mechanisms by which condensation occurs and this depends on the chemical nature of the reactant groups and the environment in which the reaction occurs (temperature, presence of catalysts, the solvent used etc.).

Condensation of different organic molecules and obtaining Schiff bases allowed the synthesis of coordination compounds with a special composition and molecular architecture, which manifest various useful properties such as luminescence, absorption of small molecules etc. [6-9]. The theoretical study of Schiff bases with tautomeric forms was previously carried out in a series of papers [10, 11]. Theoretically, the mechanism of the condensation reaction was studied in the papers [12, 13] where the general mechanism and energy profile of the reactions are described. The thermodynamic parameters are also studied with the estimation of thermal effect values.

Different solvents can influence the equilibrium constant of a reaction by stabilizing the reactant or product. The equilibrium is shifted in the direction of the substance that is preferably stabilized. Stabilization of the reactant or product can occur through various non-covalent interactions with the solvent, such as hydrogen bonding, dipole-dipole interactions and Van der Waals interactions [14].

In this research, the condensation mechanisms of 4-pyridinecarboxaldehyde with o-, m-, and p-aminobenzoic acids will be studied, studying the influence of the solvent on the energy profile of the reaction.

2. Computational methods

The optimization of the geometric structures of the species participating in the condensation reaction was calculated, using the Density Functional Theory (DFT) with the hybrid exchange-correlation functional B3LYP (Becke with the functional correlation of three parameters: Lee, Yang, and Parr), and the standard basis set 6-31G [15, 16], using the GAUSSIAN 09 program. Through the IRC method, the configurations of reactants and reaction products were obtained, as well as the analysis of intrinsic reaction coordinates was performed to confirm the connectivity between the transition state and a local minimum [17].

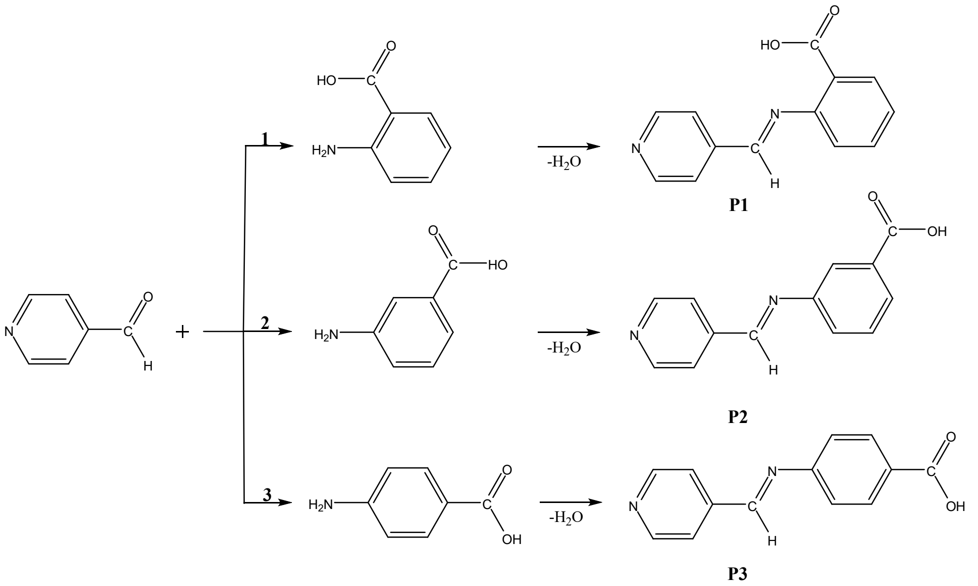

Figure 1. The general mechanism of condensation of 4-pyridinecarboxaldehyde with o-, m-, p-aminobenzoic acids

3. Results and discussion

As part of the research, theoretical studies of the mechanisms of condensation reactions of 4-pyridinecarboxaldehyde with o-, m-, and p-aminobenzoic acids were carried out both in a vacuum and in solvent (methanol). There was studied the mode of interaction of the ligands, in particular, and obtaining three Schiff bases: 4-(pyridine-2-yl-methylene amino) benzoic acid (**P1**), 4-(pyridine-3-yl-methylene amino) benzoic acid (**P2**) and 4-(pyridine-4-yl-methylene amino) benzoic acid (**P3**). The geometric and energetic parameters (stabilization energy, activation energy, caloric effect) of the condensation reactions were also studied.

Theoretical study of the interaction of 4-pyridinecarboxaldehyde with o-aminobenzoic acid. The first reaction studied is the interaction of o-aminobenzoic acid with 4-pyridine carboxaldehyde, as a result of which 4-(pyridine-2-yl-methylene amino) benzoic acid was obtained (Figure 1, **P1**). According to the general scheme in Figure 1, the mechanism of the condensation reaction with the formation of 4-(pyridine-2-yl-methylene amino) benzoic acid shown in Figure 2 was elaborated.

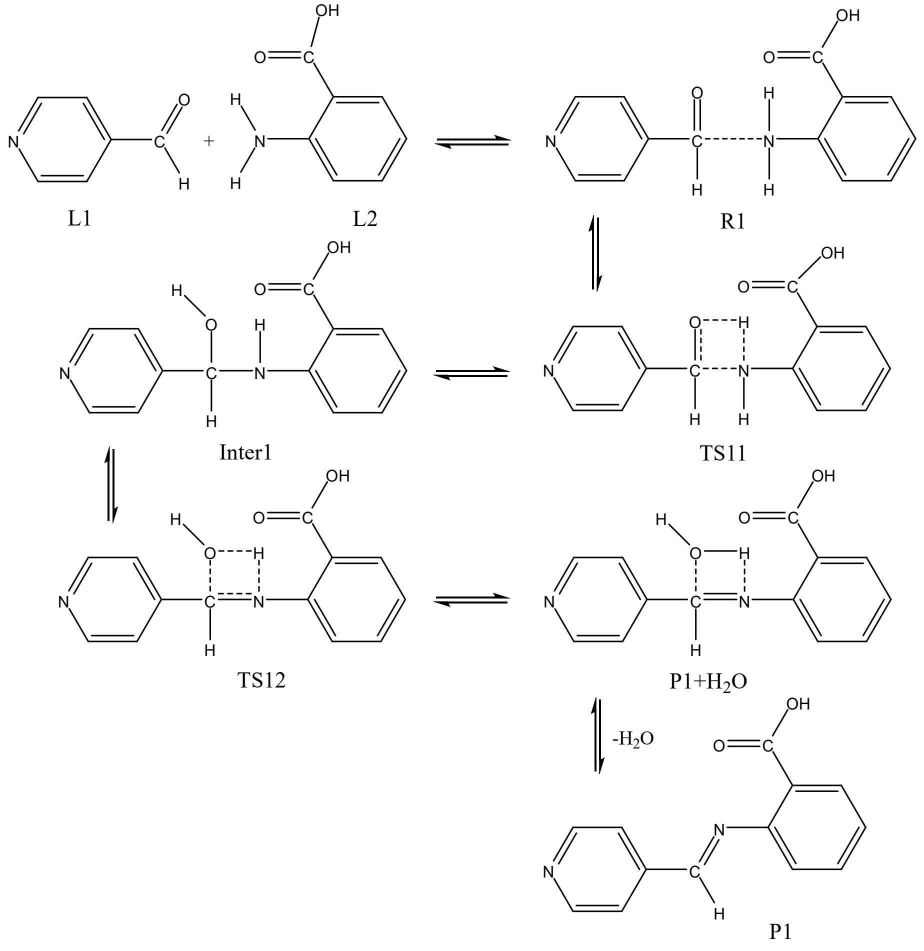

Figure 2. Mechanism of the reaction to obtain the 4-(pyridine-2-yl-methylene amino) benzoic acid (**P1**)

Studying this stage, both in a vacuum and in a solvent, a transition state (**TS11**) is obtained, with the value of the activation energy, respectively, equal to 46.31 kcal/mol and 43.62 kcal/mol and a single imaginary frequency of -1564.43 cm^{-1} and 1569.41 cm^{-1} (Figure 3).

In the second step, the intramolecular transfer of the second hydrogen atom from the group (–NH_2) to the oxygen atom of the group (–OH) takes place. As a result, a water molecule is eliminated, obtaining the final compound (**P1**) which is energetically stable. This step is accompanied by a transition state (**TS12**) with the value of the reaction barrier in a vacuum and solvent, respectively, equal to 56.66 kcal/mol and 54.91 kcal/mol and imaginary frequencies of -1778.92 cm^{-1} and -1785.32 cm^{-1} (Figure 3).

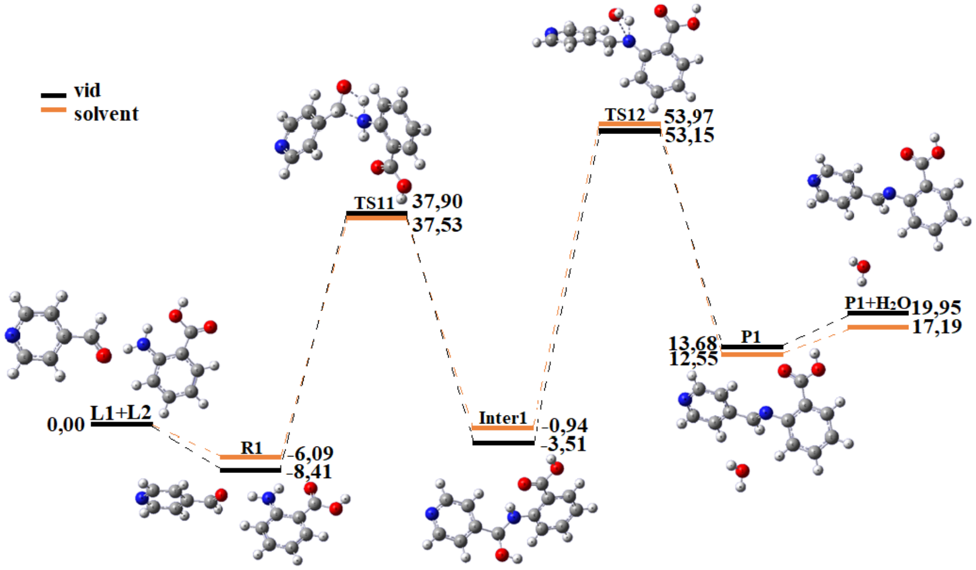

Figure 3. Energy profile of the condensation reaction between 4-pyridinecarboxaldehyde and o-aminobenzoic acid expressed in kcal/mol

Analyzing the structure of the species participating in the first stage of the reaction and their energetic stability, and taking into account the reaction environment, energetically speaking, the reaction barrier in the case of the solvent is lower than in the vacuum one by 2.69 kcal/mol, which shows us that the reaction proceeds more easily in the solvent. We can also conclude that from a thermodynamic point of view, the most energetically favorable reaction is the one that takes place in the solvent, with a gain of 2.76 kcal/mol.

Theoretical study of the interaction of 4-pyridinecarboxaldehyde with m-aminobenzoic acid. The interaction of 4-pyridinecarboxaldehyde with m-aminobenzoic acid was studied, obtaining a new organic product – 4-(pyridine-3-yl-methylene amino) benzoic acid (Figure 1, **P2**). According to Figure 1, the mechanism of condensation reaction was elaborated (Figure 4), with the formation of 4-(pyridine-3-yl-methylene amino) benzoic acid (**P2**) as the final product.

In the first stage of this reaction, the interaction of 4-pyridinecarboxaldehyde with m-aminobenzoic acid takes place according to the mechanism of the condensation reaction (Figure 1, **P2**). Following this interaction, the intermolecular transfer of a hydrogen atom from the amine functional group (–NH_2) to the oxygen atom in the aldehyde group (–CHO) takes place, obtaining a relatively stable intermediate compound (**Inter2**).

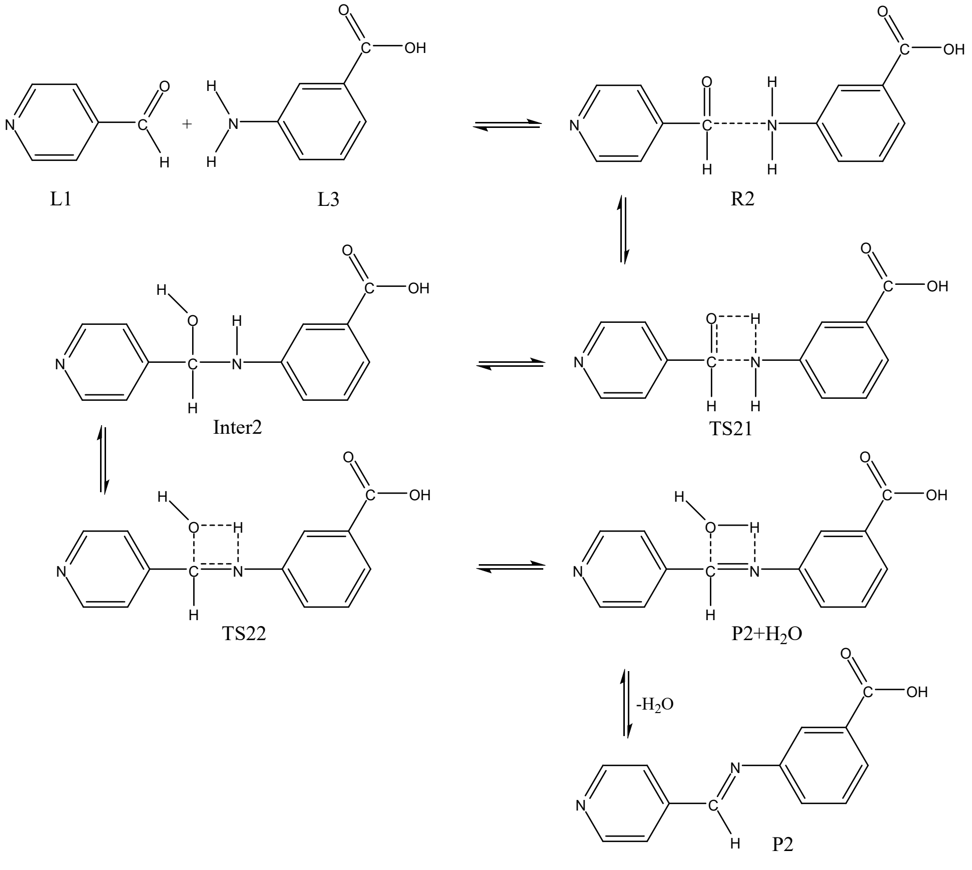

Figure 4. Mechanism of the reaction to obtain the 4-(pyridine-3-yl-methylene amino) benzoic acid (**P2**)

The transition state (**TS21**) at this stage was identified because it has a unique imaginary frequency: -1602.17 cm^{-1} and -1565.04 cm^{-1} in vacuum and solvent, respectively. The value of reaction barrier in vacuum and solvent is equal to 44.18 kcal/mol and 40.01 kcal/mol, respectively. On the basis of the energies obtained, the total energy profile of the condensation reaction was built (Figure 5).

The second step proceeds with the transfer of the second hydrogen atom from the group (–NH_2) to the group (–OH). Also, the elimination of a water molecule takes place and the final compound (**P2**) is energetically stable 4-(pyridine-3-yl-methylene amino) benzoic acid.

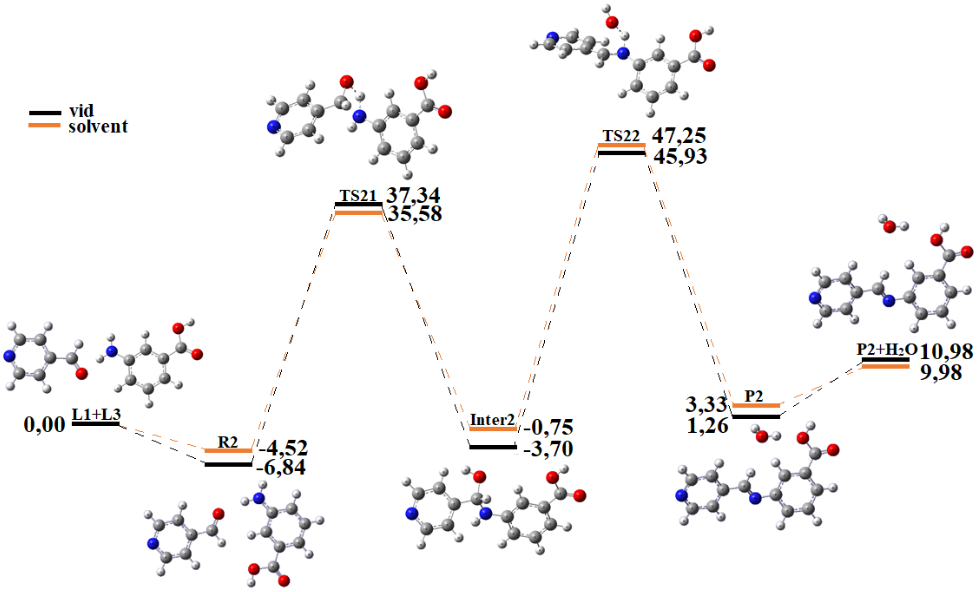

Figure 5. Energy profile of the condensation reaction of 4-pyridinecarboxaldehyde m-aminobenzoic acid expressed in kcal/mol

Analyzing the energetic stability, structure of the species participating in the reaction and taking into account the reaction environment, from the energetic point of view, the activation energy in the case of the solvent at the first stage, is lower than vacuum by 4.08 kcal/mol. Thus, the positive effect was demonstrated of the solvent on the reaction. From a thermodynamic point of view, the most energetically favorable reaction takes place in the solvent, with a gain of 1.0 kcal/mol.

Theoretical study of the interaction of 4-pyridinecarboxaldehyde with p-aminobenzoic acid. The theoretical study of the interaction of 4-pyridinecarboxaldehyde with p-aminobenzoic acid was carried out both in vacuum and solvent (methanol), obtaining a new organic product – 4-(pyridine-4-yl-methylene amino) benzoic acid (Figure 1, **P3**) [18]. The general scheme of the condensation reaction mechanism is shown in Figure 1. For all species participating in the reaction, the geometric structure was determined with the calculation of geometric and energetic parameters, which are comparable to those in the specialized literature.

According to the developed mechanism of the reaction represented in Figure 6, the reaction proceeds in two stages. First of all, the interaction of a molecule of

4-pyridinecarboxaldehyde with p-aminobenzoic acid takes place according to the mechanism of the condensation reaction. As a result of the interaction, the intermolecular transfer of a hydrogen atom from the amine functional group (–NH_2) to the oxygen atom in the aldehyde group (–CHO) takes place, forming a new intermediate compound (**Inter3**).

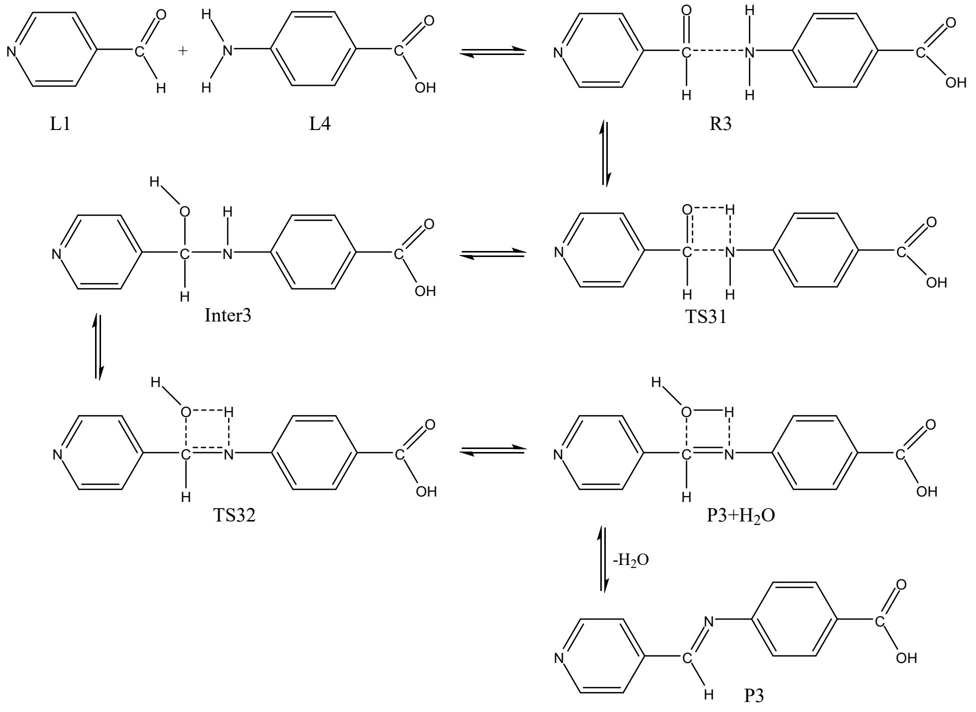

Figure 6. Mechanism of the reaction to obtain the 4-(pyridine-4-yl-methylene-amino) benzoic acid (**P3**)

The first step is accompanied by a transition state (**TS31**), with the value of the reaction barrier in vacuum and solvent, respectively equal to 45.74 kcal/mol and 43.68 kcal/mol, and the imaginary frequencies: -1609.4 cm^{-1} and -1573.12 cm^{-1}, respectively in vacuum and solvent.

In the second step, the transfer of the second hydrogen atom from the (–NH_2) group to the (–OH) group takes place. This way a water molecule is removed and it is obtained the final compound (**P3**) stable from the energetic point of view.

Analyzing the energy scheme in Figure 7, the reaction barrier in the case of the solvent in the first step is lower than in a vacuum by 2.06 kcal/mol, which shows that the solvent favours the faster course of the reaction.

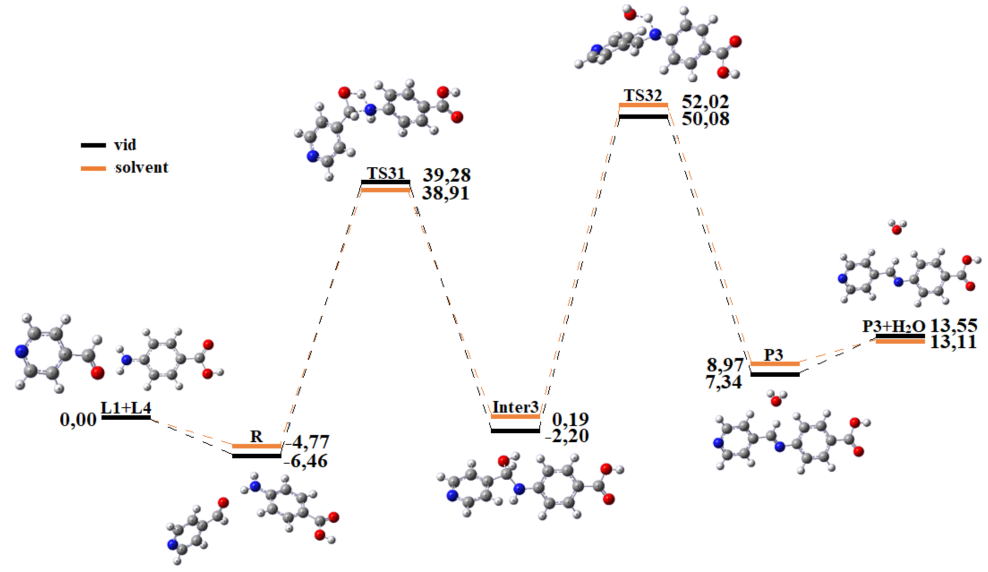

Figure 7. Energy profile of the condensation reaction of 4-pyridinecarboxaldehyde with p-aminobenzoic acid expressed in kcal/mol

Analyzing the structure of the species participating in the reaction and their energetic stability, and taking into account the reaction environment, it can be concluded with certainty that the most energetically convenient reaction is the one that takes place in solvent, with a gain of 0.44 kcal/mol.

The study carried out allows the formulation of conclusions about the energetics of the condensation process of 4-pyridinecarboxaldehyde o-/m-/p-aminobenzoic acid in the perspective of using the reaction products as coordinating agents for the assembly of new coordinating compounds with various properties. In turn, the coordination process is of interest from the point of view of the coordination of the functional groups of the new organic compound to various metal ions.

4. Conclusions

Quanto-chemical calculations are a theoretical way to determine the probability of a reaction occurence, anticipating some processes and applying them practically, we can obtain synthetically new compounds of high purity, saving time and reagents needed for a possible repetition of the condensation process in case there was not obtained the expected product. The mechanisms of the condensation process of 4-pyridinecarboxaldehyde with o-, m- and p-aminobenzoic acids in vacuum and solvent (methyl) were developed where the solvent favours the faster course of the reaction, having lower activation energy compared to the vacuum one.

All the studied reactions take place in two stages and each stage is accompanied by a transition state. It should be noted that in the first stage the activation energy for the o-, m-, and p- reactions are respectively equal to 46.31, 44.18 and 45.74 kcal/mol, indicating higher values compared to the activation energy of the reaction in methanol – 56.66, 49.63 and 52.78 kcal/mol.

Studying these reactions thermodynamically, we can state that all reactions are endothermic and the most convenient from an energetic point of view is the reaction to obtain 4-(pyridine-3-yl-methylene amino) benzoic acid in methanol with an energy value of 9.98 kcal/mol.

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