THEORETICAL STUDY ON GLUCOSE AND METHYLAMINE MAILLARD REACTION: FORMATION OF THE AMADORI REARRANGEMENT PRODUCTS

Weiwei Huan[1], Hongchen Du[2], Rongkai Pan[2], Jie Li[1*] and Lijuan Feng[2]

[1]Zhejiang Provincial Key Laboratory of Chemical Utilization of Forestry Biomass, College of Chemistry and Materials Engineering, Zhejiang A&F University, Hangzhou 311300, China
[2]Shandong Engineering Research Center of Green and High-Value Marine Fine Chemical, Weifang University of Science and Technology, Weifang 262700, China

ABSTRACT. In the present study, the mechanism of Maillard reaction was investigated using density functional theory calculations. Glucose and aminomethane were used as initial reactants in this study. The calculations show that the Amadori rearrangement reaction is the rate-controlling step with a corresponding energy potential of 402 kJ/mol, the enthalpy change is 219 kJ/mol, which is an endothermic reaction and therefore energy needs to be supplied from outside if the reaction is to proceed. The calculated results are in good agreement with the previous findings and can provide insight into the reaction mechanism of the Maillard reaction. These findings will help further research and find out the correct reaction mechanism.

KEY WORDS: Food chemistry, Mechanism, Transition State, Computational chemistry

INTRODUCTION

The Maillard reaction, also known as non-enzymatic browning reaction, is one of the most important reactions for controlling the quality and nutritional value of food. When food is cooked, the Maillard reaction plays an important role in improving the appearance and flavour of the food. The Maillard reaction (MR) is a complex network of chemical reactions that occur between carbonyl compounds (especially reducing sugars) and compounds with free amino groups such as amines, amino acids, and proteins [1-4].

The Maillard reaction has been a central and major challenge for the food industry due to its association with aroma, flavour and colour, especially in traditional processes such as the roasting of coffee and cocoa beans, the baking of bread and cakes, the roasting of cereals and the cooking of meats. In addition, a wide range of reaction products are produced during martensitisation, which have a significant impact on the nutritional value of food products. Nutritional value can be reduced through reduced digestibility and the possible formation of toxic and mutagenic compounds, or it can be increased through the formation of antioxidant products. The chemistry of the Maillard reaction is very complex. It encompasses not one reaction pathway, but an entire network of various reactions. Since then, food technologists have been developing and elaborating on Hodge's original comprehensive reaction scheme [5], and as a result the understanding of this reaction has steadily evolved. However, the Maillard reaction is notoriously difficult to control. Various factors affecting food processing can act as variables in food processing, and the kinetic approach tends to provide a complementary view of this mechanism because it takes into account the rate-determining step of the reaction, and it is powerful in that the rate-determining step provides a control point. However, little is known about the complex reaction mechanisms that lead to the formation of these Maillard reaction products (MRPs).

The experimental assessment of the role of these complex species in Maillard reaction is quite complex and the tendency of the end products of Maillard reaction to produce complex mixtures

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makes experimental data insufficient. In addition, the specific biological functions of each Maillard reaction product are not fully known because of the difficulty of purification and identification, and therefore the experimental outlook for this area of research has so far not allowed for a detailed explanation of whether these mechanisms are still valid.

The experimental study was accompanied by theoretical calculations of the Maillard reaction mechanism. In 2001, Jokic *et al.* performed a quantum elucidation of some details of the Maillard reaction between D-glucose and glycine [6]. The results show that the initial reaction rate for the formation of Amadori compounds and the reaction rate of fructosylglycine was slow. In 2022, Kato *et al.* tested the feasibility of quantum chemical calculations with different computational levels and aqueous solution models to predict the aldehyde ratio of disaccharides containing d-glucose [7]. In 2021, Wang *et al.* performed DFT studies on the molecular mechanisms of interaction between enzymes and Maillard reaction products, the calculations show that the molecular interactions between MRPs and proteins include parallel misaligned aromatic stacking, T-shaped perpendicular aromatic stacking, H-bond and H-bond coupled aromatic stacking [8].

Therefore, in this study, we applied density-functional theory (DFT) calculations to investigate the possibility of the formation of Maillard reaction products (MRPs) in the gas phase for the glucose and methylamine model systems.

COMPUTATIONAL METHODS

All the geometries and energies of the Maillard reactions presented in this study were calculated by B3LYP density functional theory method with 6-31g* basis set [9-13]. Frequency analysis was also performed at the same level to ensure that the frequencies are all positive and the structure belongs to a minimum in the potential energy surface. All transition states were verified as the presence of a single imaginary frequency and the linkage between the specified reactants and products was verified. The linkage between the specified reactants and products was verified by intrinsic reaction coordinates (IRC) analysis. The path of a chemical reaction can be traced from the transition state (TS) to the products and/or reactants using the Intrinsic Reaction Coordinate (IRC) method. The method assumes that the initial geometry is a good approximation of the TS. A minimum energy profile (MEP) is defined as the steepest descent on the potential energy surface from the transition state down to a local minimum. An IRC path is defined similarly but in mass-weighted coordinates, i.e. it follows the direction of maximum instantaneous acceleration instead of the steepest descent. Based on the basis of the principle of statistical thermodynamics, standard molar heat capacity ($C_{p,m}^{\ominus}$), entropy ($S_m^{\ominus}$), and enthalpy ($H_m^{\ominus}$) from 200 to 800 K were evaluated using the scaled frequencies. All calculations are implemented in the Gaussian09 package [14]. The changes in enthalpy (ΔH_{298}°) of the reactions were evaluated using the following equation:

$$\Delta H_{298}^{\circ} = \sum \Delta_f H_{298,P}^{\circ} - \sum \Delta_f H_{298,R}^{\circ} = \Delta E_0 + \Delta E_{ZPE} + \Delta H_T^{\circ}$$

where $\sum \Delta_f H_{298,P}^{\circ}$ and $\sum \Delta_f H_{298,R}^{\circ}$ are the sum of the heats of formation of the products and reactants, respectively; ΔE_0 is the difference between the total energies of the products and the reactants at 0 K; ΔE_{ZPE} is the difference between the zero-point vibrational energy of the products and the reactants; ΔH_T^0 is the difference between the thermal correction from 0 K to 298 K of the products and the reactants.

RESULTS AND DISCUSSION

Based on previous studies, a possible mechanism for the Maillard reaction between glucose and glycine has been suggested [15]. In this article, amino acids are substituted by methylamine and

2,3,4,5,6-pentahydroxyhexanal is used as reducing sugar. The initial stage of Maillard reaction in this study has been investigated using density functional theory method.

As shown in Figure 1, firstly, the two reactants undergo a reaction in which the hydrogen atom in the amino group attacks the carbonyl oxygen atom and passes through the transition state (TS1) to produce an addition product (a1). The energy released by this process is about 71.7 kJ/mol, which is an exothermic reaction with an activation energy of 62.9 kJ/mol.
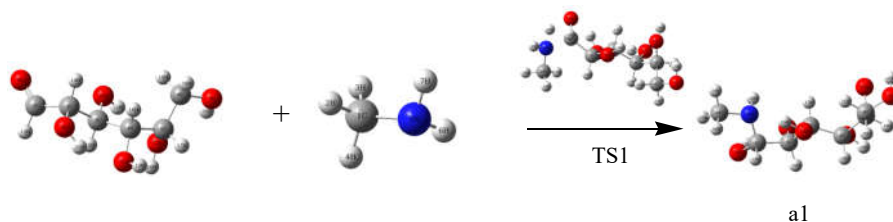
Figure 1. The first step of the Maillard reaction.

The addition compound a1 loses 1 molecule of H_2O to generate Schiff base (number a2) (Figure 2). The calculated activation energy (E_a) of this process is 216 kJ/mol, which is significantly higher than the previous reaction, indicating that this reaction is difficult to carry out and maybe a rate control step. In order to make the reaction proceed, external energy is needed (such as baking heating), and the enthalpy change of the reaction ΔH = 44.5 kJ/mol which is an endothermic reaction.
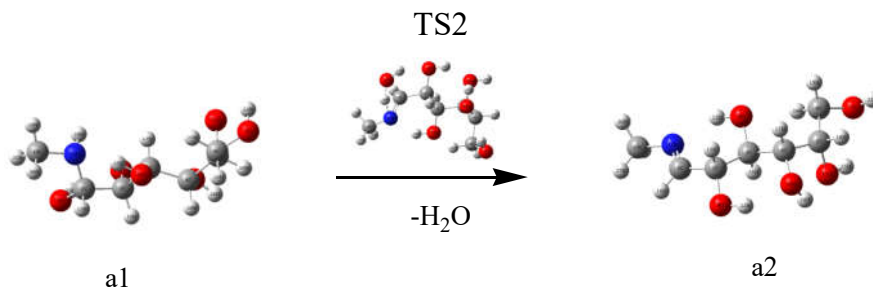

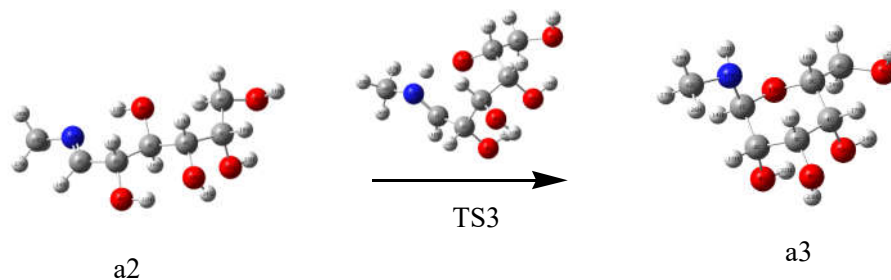Figure 2. The second step of the Maillard reaction.

Figure 3. The third step of the Maillard reaction.

Schiff base (a2) undergoes cyclisation to form glucosylamine (a3), tetrahydro-2-(hydroxymethyl)-6-(methylamino)-2H-pyran-3,4,5-triol (Figure 3). The activation energy of the process is 175 kJ/mol.

25H of (11N) on the N atom of compound a3 (N-substituted glucomylamine) combines with 13O to form compound a4 (Figure 4). The activation energy of this process is 183 kJ/mol, and the transition state (TS4) is shown in the figure below with a enthalpy change of 24.9 kJ/mol, which belongs to endothermic reaction.
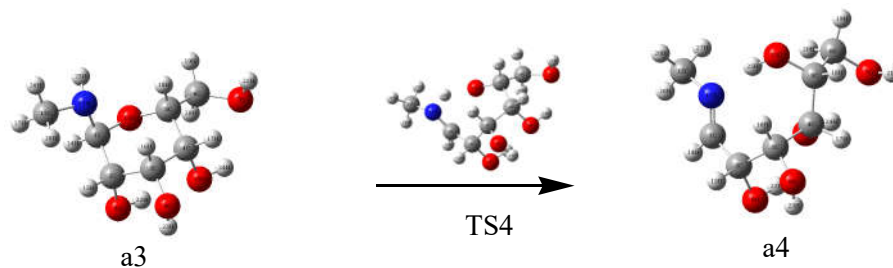
Figure 4. The fourth step of the Maillard reaction.

Then a4 combined with proton H under acidic conditions to form a5 (Schiff base cation) (Figure 5), release a large amount of heat, enthalpy change -990 kJ/mol, indicating that the process is easy to occur and is a spontaneous reaction.
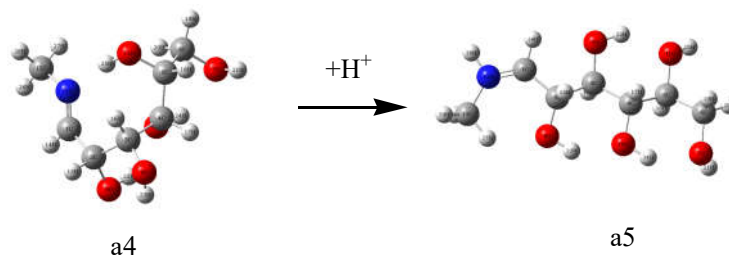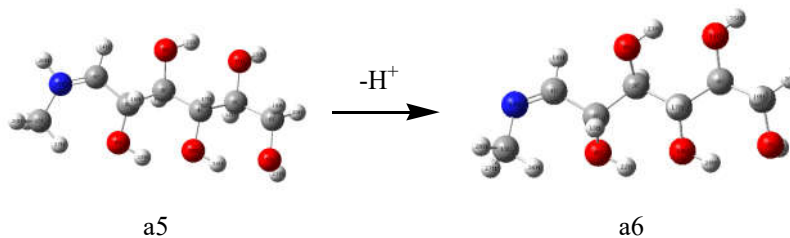

Figure 5. The fifth step of the Maillard reaction.

Figure 6. The sixth step of the Maillard reaction.

Then, the Schiff base cation (a5) first loses H+ and forms compound a6 (Figure 6), the H atom (15H) on the 2C atom in a6 is transferred to the 1C atom to form compound a7 (Figure 7). The activation energy barrier is 402 kJ/mol and the enthalpy change is 219 kJ/mol. The molecular

rearrangement process is difficult to occur on the surface, and it is an endothermic reaction from a thermodynamic point of view. In order to make the reaction occur, it needs to provide higher energy. In the pecan roasting process, the reaction needs to be at a higher temperature. To make sure it goes smoothly.
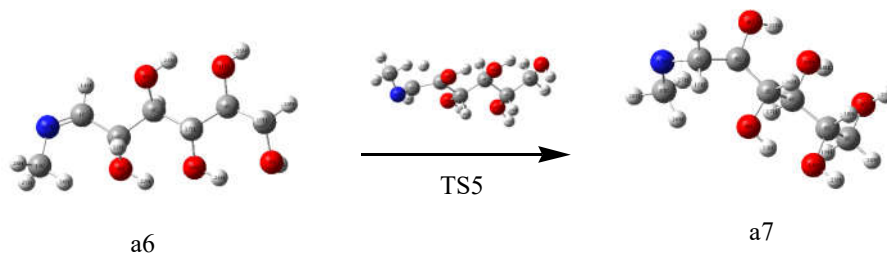

Figure 7. The seventh step of the Maillard reaction.

In a7, there is a single electron on each of the 2C and 12N atoms that is not bonded, and then the 15H atom on 1C is transferred to the 12N atom, at which point there is another single electron on 1C, which forms a single bond with the single electron on 2C, and with the addition of the original single bond between 1C-2C, 1C-2C becomes a double bond, and the activation energy of this process is 81.5 kJ/mol, thermodynamic enthalpy change is -195 kJ/mol. to this point, the enolic structure was generated (a8) (Figure 8).
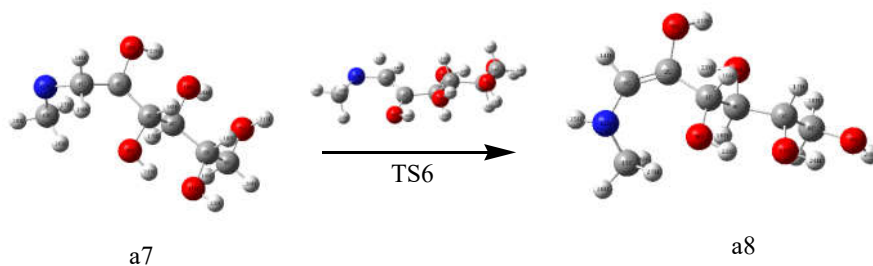

Figure 8. The eighth step of the Maillard reaction.

In this step, molecular rearrangement is involved and according to the literature 15, the most important step in the Maillard reaction is molecular rearrangement (also known as Amadori rearrangement), the processes of a6 to produce a7 and a7 to produce a8 are molecular rearrangement processes. According to calculations, this process requires the highest activation energy, is the most difficult to carry out, and is a rate-controlling step. Therefore, the Amadori rearrangement reaction plays a very important role in the Maillard reaction.

The H atom (21H) on 2C of the enolitic structure (a8) is transferred to the C atom No. 1 to form the ketone structure (a9) - N-substituted 1-amino-1-deoxy-2-ketose (Figure 9). The activation energy of this process Ea = 193 kJ/mol.

At this point, all intermediate transition states as well as activation energy and thermodynamic enthalpy change data have been obtained in the primary reaction stage of the Maillard reaction, and by quantum chemical calculations, the transformation from the Schiff base cation to an enol-type structure is found to be crucial (highest activation energy) in the primary stage, and this process involves a molecular rearrangement reaction. Thus, amadori molecular rearrangement is among the critical steps (rate-controlling steps) in the primary phase.
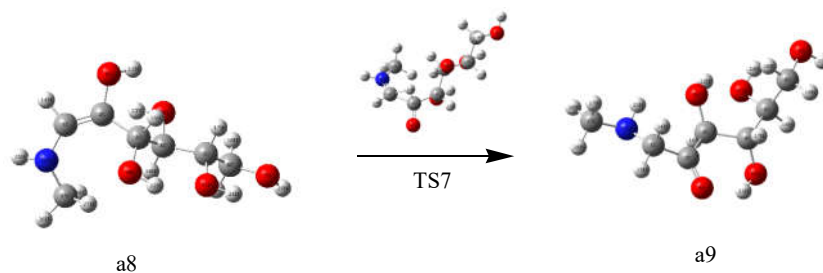
Figure 9. The ninth step of the Maillard reaction.

Figure 10 shows the relative energies of all the intermediates in the proposed mechanisms by following the total mass balance of the reaction, we can see from Figure10 that the barrier of the Amadori rearrangement reaction is the largest and indicates that the Amadori rearrangement reaction is the rate-controlling step.
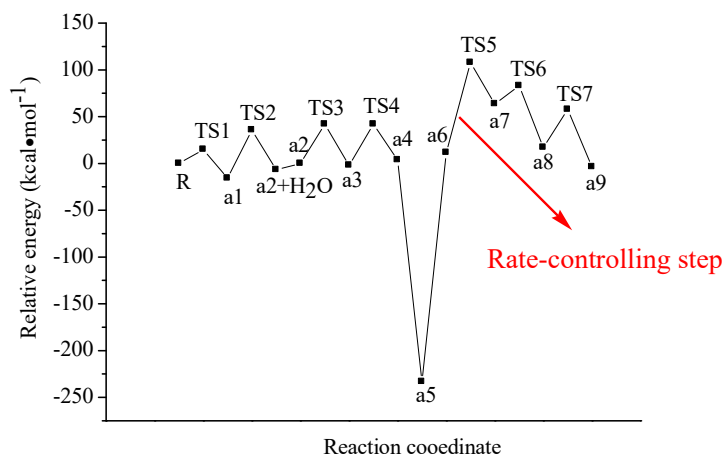

Figure 10. The potential energy profiles (kcal·mol^{-1}) for the Maillard reaction.

CONCLUSION

In this study, density functional theory method has been used to investigate the Maillard reaction mechanism. The calculated results reveal that the Amadori rearrangement reaction is the rate-determining step in the initial stage of Maillard reaction, with the activation barriers of about 402 kJ/mol. The calculated results are in good agreement with previous studies and could provide insights into the reaction mechanism of Maillard reaction, because experimental evaluation of the role of intermediates in the Maillard reaction is quite complicated.

ACKNOWLEDGMENTS

FUNDINGS

AUTHORS CONTRIBUTION

The first two authors contributed equally to this work.

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