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Density functional computational studies on ribose and glycine Maillard reaction: Formation of the Amadori rearrangement products in aqueous solution

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Abstract

By following the Hodge-scheme, and considering the formation of the Amadori rearrangement products (**ARP**s) as one of the possible intermediates in the early stage, density functional theory calculations have been performed at the standard state on the proposed mechanisms of the Maillard reaction of cyclic ribose (**c-Rib**)/open-chain ribose (**Rib**) and glycine species under different pH conditions in aqueous solution. The result reveals that both **c-Rib** and **Rib** can participate in the reaction. **Rib** has been found as more reactive than **c-Rib** in the reaction. The reactions under basic and neutral conditions are supposed to be the most and second most favourable for the formation of **ARP**s. Production of both of the enol and keto forms of **ARP** have been found as feasible under basic condition, whereas the neutral condition is only favourable for producing the enol form of **ARP**. Therefore, the rate of browning under basic condition is assumed higher than that of the neutral condition. Formation of all intermediates in the proposed mechanisms has been found as unfeasible in the reaction under acidic condition and at the isoelectric point of glycine. Therefore, production of **ARP**s under these conditions is assumed to be stalled under these conditions, resulting into lower browning rate. Formation of **Rib** through the cleavage of glucose has been assumed less feasible than the formation of glucose from **Rib** and formaldehyde in aqueous solution.

Keywords: Density functional computational study; Ribose; Glycine; Maillard reaction; Amadori rearrangement product

1. Introduction

Complexity of nonenzymatic browning or the Maillard reaction (Maillard, 1912) is well known. The reaction is a complex series of chemical reactions that occurs between carbonyl compounds, especially reducing sugars, and compounds with free amino groups, such as amines, amino acids, and proteins. It occurs on heating or on prolonged storage, and is one of the deteriorative processes that take place in stored foods (Davídek, Velíšek, & Pokorný, 1990; Eskin, 1990; Macrane, Robinson, & Saadler, 1993). More recently, it has been realized that the reaction actually occurs in the human body, and is therefore, important in medicinal arena (Ledl & Schleicher, 1990; Meade, Miller, & Gerrard, 2003; Reber et al., 2002). Although more than 90 years have passed since the first research on the Maillard reaction, and many results have been gathered later on, still there is no potential explanation of the mechanism. Several schemes for the explanation of the mechanism of the Maillard reaction have been proposed (Hodge, 1953; Namiki & Hayashi, 1983; Tressl, Nittka, & Kersten, 1995), out of which the Hodge-scheme (Hodge, 1953) is still seemed to be the most acceptable, and has consequently been reviewed by many authors. According to the Hodge-scheme (Hodge, 1953), the Amadori rearrangement (**AR**) can take place in

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the early or initial stage of the Maillard reaction between aldose sugars and amino compounds, which can lead to the formation of the Amadori rearrangement products (**ARP**s) (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). This stage in the Maillard reaction is reversible and well understood (Ames, 1992). **ARP**s are the primary precursors of final products or melanoidines, and therefore, having great importance in the Maillard reaction. **ARP**s readily undergo further reactions to produce melanoidines through the formation of relative deoxyosones. **ARP**s have been reported as less reactive than reductones, and about 10 to 100 times more reactive than the parental reducing sugars (Davídek et al., 1990; Wrodnigg & Eder, 2001). A number of studies have been reported which show that **AR** can occur at physiological conditions if sufficient reactants are present and the reaction time is long enough (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). Moreover, direct cleavage or retro-aldolization of **ARP**s or Schiff bases may also take place in the reaction (Bell, 1997; Davídek et al., 1990; Eskin, 1990; Hodge, 1953; Macrane et al., 1993; Namiki & Hayashi, 1983; Tressl et al., 1995). Due to comparatively less stability, isolation and detection of these species in the Maillard reaction is assumed complicated. Computational model chemistry could successfully be applied on such a complex reaction to obtain useful information, which will be helpful to find out proper mechanism to understand the reaction. Thus, it will be useful to control the reaction potentially in foods and other systems, such as in the human body.

Ribose, a functional five-carbon sugar, is not only important in foods, but also in human body (Blank & Fay, 1996; Cerny & Davidek, 2004; Chen & Ho, 2002; Chen, Xing, Chin, & Ho, 2000; Cuzzoni, Stoppini, Gazzani, & Mazza, 1989; Ho, 1996; Litchfield, Thorpe, & Baynes, 1999; Meynier & Mottram, 1995; Mottram & Leseigneur, 1990; Roger, Matthew, & Elizabeth, 2005; Thorpe & Baynes, 1996). Ribose is present at micromolar concentrations in blood, and is a potent protein-browning agent, which can contribute to the chemical modification, cross-linking, browning and fluorescence of tissue proteins during aging and in disease through the Maillard reaction (Litchfield et al., 1999; Thorpe & Baynes, 1996). Ribose is used for the commercial production of riboflavin (Park, Choi, Bennett, & Seo, 2006). D-ribose can be used to synthesize D-ribose and L-apiose via stereoselective cis-dihydroxylation and C2-hydroxymethylation, respectively, and these L-sugars can serve as versatile intermediates for the synthesis of L-nucleosides (Yun et al., 2005).

On the other hand, glycine (**Gly**), the simplest amino acid, can be found in its four forms. Unionized or unprotonated glycine (**UGly**, $H_2N–CH_2–CO_2H$) becomes the dominant species in the gaseous state, and can exist at a very low concentration in neutral (pH = 7) aqueous solution (Harrold, 1991; Holum, 1996). In acidic solution, glycine is completely protonated and exists as the conjugated acid (Harrold, 1991; Holum, 1996). Hence, under acidic conditions, e.g. pH < 5.5, protonated glycine (**PGly**, $H_3N^+–CH_2–CO_2H$) becomes the dominant species. At the isoelectric point of glycine (I = pH ≈ 6), glycine zwitterion (**GlyZ**, $H_3N^+–CH_2–CO_2:^-$) becomes the dominant species (Harrold, 1991; Holum, 1996; Macrane et al., 1993). Production of basic amino groups is facilitated by the alkaline medium, and therefore, under basic conditions (pH > 8), deprotonated glycine (**DGly**, $H_2N–CH_2–CO_2:^-$) becomes the dominant species (Eskin, 1990).

As ribose can exist in equilibrium mixture of its open and closed chain or cyclic forms (**Rib** and **c-Rib**, respectively) (Eskin, 1990; Harrold, 1991; Holum, 1996), both of these forms can participate in the reaction, and therefore, the reaction is assumed more complex. Both of these forms of ribose have been considered in the present study to evaluate their activities in the Maillard reaction involving **Gly** species (i.e. **UGly**, **PGly**, **DGly** and **GlyZ**). Possible mechanisms for the formation of **ARP**s in **c-Rib** + **UGly**, **Rib** + **UGly**, **c-Rib** + **PGly** and **Rib** + **PGly** reactions are presented in Fig. 1, and **c-Rib** + **DGly**, **Rib** + **DGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are in Fig. 2. The gaseous state **c-Rib**/**Rib** + **Gly** reaction is assumed relevant to astrobiology (Breslow, 1959; Halfen, Apponi, Woolf, Polt, & Ziurys, 2006), and the aqueous solution to foods (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). Therefore, density functional computational calculations have been performed on the proposed mechanisms (Figs. 1 and 2) to test the possibility of the formation of different compounds under different pH conditions in aqueous solution by estimating the free energy changes for different steps of the reaction. In addition, glucose (**Glu**) is the most

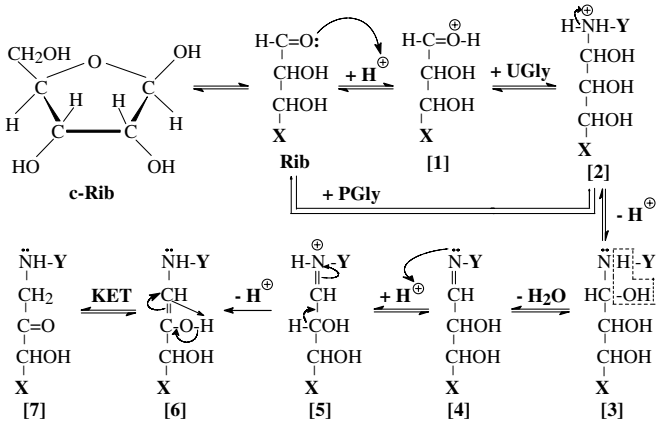

Fig. 1. Proposed mechanisms for the formation of the Amadori rearrangement products in **c-Rib** + **UGly**/**Rib** + **UGly** and **c-Rib** + **PGly**/**Rib** + **PGly** Maillard reactions. *Abbreviations*: **c-Rib** = cyclic ribose; **Rib** = open-chain ribose; **UGly** = unionized or unprotonated glycine; **PGly** = protonated glycine; **KET** = keto-enolic tautomerization. *Numerical abbreviations*: **1** = protonated form of **Rib**; **2** = ionic addition adduct of **Rib** and **UGly** or **PGly** (1-protonated glycino-pent-1,2,3,4,5-ol); **3** = addition compound of **Rib** and **UGly** or **PGly** (1-glycino-pent-1,2,3,4,5-ol); **4** = Schiff base of **3**; **5** = ionic adduct of **4**; **6** = enol form of the Amadori rearrangement product (1-glycino-pent-2,3,4,5-ol-1-ene); **7** = keto form of the Amadori rearrangement product (1-glycino-pent-3,4,5-ol-2- one). **X** and **Y** refer the –CH(OH)–CH_2OH and –CH_2–CO_2H groups, respectively.

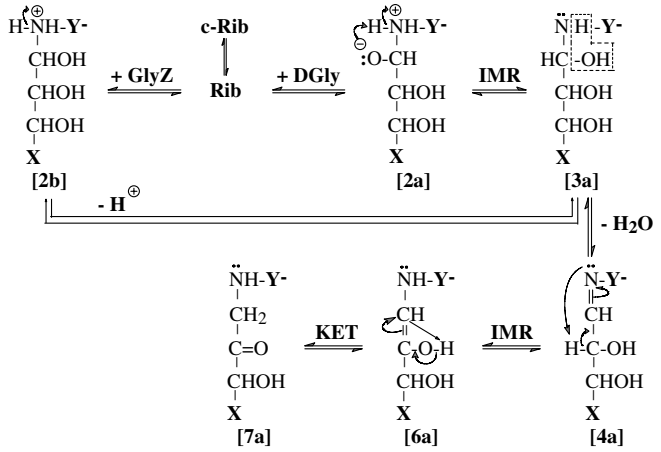

Fig. 2. Proposed mechanisms for the formation of the Amadori rearrangement products in **c-Rib** + **DGly**/**Rib** + **DGly** and **c-Rib** + **GlyZ**/**Rib** + **GlyZ** Maillard reactions. *Abbreviations*: **DGly** = deprotonated glycine; **GlyZ** = glycine zwitterion; **IMR** = intramolecular rearrangement. *Numerical abbreviations*: **2a** = ionic addition adduct of **Rib** and **DGly**; **2b** = ionic addition adduct of **Rib** and **GlyZ**; **3a** = addition compound of **Rib** and **DGly** or **GlyZ** (1-deprotonated glycino-pent-1,2,3,4,5-ol); **4a** = Schiff base of **3a**; **6a** = enol form of the Amadori rearrangement product (1-deprotonated glycino-pent-2,3,4,5-ol-1-ene); **7a** = keto form of the Amadori rearrangement product (1-deprotonated glycino-pent-3,4,5-ol-2-one). $\mathbf{Y}^-$ Refers the $-CH_2-C\,O_2{:}^-$ group. For other abbreviations, see the caption of Fig. 1.

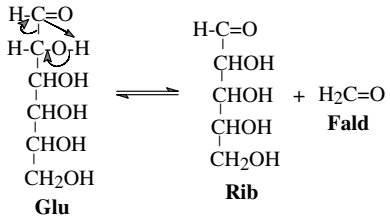

Fig. 3. Formation of ribose (**Rib**) through the cleavage of glucose (**Glu**).

abundant organic species in foods and human body, and therefore, is the most important reducing sugar (Eskin, 1990; Harrold, 1991; Holum, 1996). **Rib** can be produced through the cleavage of **Glu**, in which formaldehyde (**Fald**) can be produced as a by-product (Fig. 3). This possibility has also been tested by using density functional computations in aqueous solution.

2. Methodology

At the standard state, possibility of the formation of all compounds in the proposed mechanisms (Figs. 1–3) has been studied in their aqueous solution. As all compounds in the proposed mechanisms (Figs. 1–3) can have many conformations in aqueous solution, it is not possible to consider all of these conformations during the calculation of energy changes for different steps in a reaction, especially when it is a complex one, such as the Maillard reaction. Therefore, only general low energy structures, optimized at a specific method (RB3LYP) (Foresman & Frisch, 1996; Frisch & Foresman, 1998) by using GAUSSIAN 98 program (Frisch, Trucks, & Schlegel, 2001), of the compounds have been used to avoid complexities and simplify the calculation (Shipar, 2004). The 6-31G(*d*) polarized basis set (Foresman & Frisch, 1996; Frisch & Foresman, 1998) has been used for all calculations. During the optimization, all structural parameters, e.g. bond-lengths, bond-angles and dihedral angles, have been used as variables. The term "Stationary point found" has been verified in the geometry output to confirm the ground state (Foresman & Frisch, 1996; Frisch & Foresman, 1998). Fig. 4 represent the RB3LYP/6-31G(*d*) geometric parameters of the reactants **c-Rib**, **Rib** and **Gly** species (**UGly**, **PGly**, **DGly** and **GlyZ**), respectively. Moreover, many of the intermediates in the proposed mechanisms (Figs. 1–3) can have their stable cyclic forms, and therefore, especial care has been taken during the optimization to avoid the possible intramolecular cyclization of the compounds (Shipar, 2004). All RB3LYP/6-31G(*d*) optimized structures have been taken for PCM/RB3LYP/6-31G(*d*) frequency calculations to achieve the relevant zero point energy (ZPE) and the Gibb's free energy (G^0) in aqueous solution (Foresman & Frisch, 1996; Frisch & Foresman, 1998). Opt = *Z*-matrix and/or Freq = NoRaman keywords have been used when necessary (Foresman & Frisch, 1996; Frisch & Foresman, 1998). By using PCM/RB3LYP/6-31G(*d*) on the RB3LYP/6-31G(*d*) optimized structures, relevant electronic energies in aqueous solution have been calculated (Foresman & Frisch, 1996; Frisch & Foresman, 1998). The dielectric constant, $\varepsilon = 78.39$ has been used to represent the aqueous solution (Foresman & Frisch, 1996; Frisch & Foresman, 1998). Relevant ZPE have been added to the electronic energies to get the total electronic energies (E^0). Finally, electronic and free energy changes ($\Delta E^0 = E^0_{\text{Product(s)}} - E^0_{\text{Reactant(s)}}$, and $\Delta G^0 = G^0_{\text{Product(s)}} - G^0_{\text{Reactant(s)}}$, respectively) for different compounds in the proposed mechanisms (Figs. 1–3) have been calculated by following the total mass balance of the reaction. Thus, the

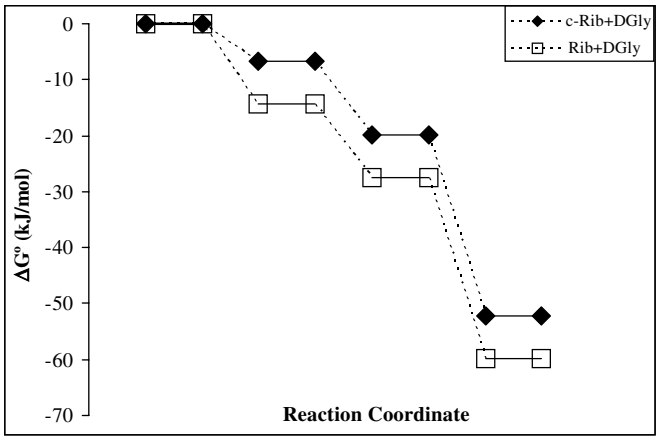

Fig. 4. Possible low energy (ΔG^0_{Aq}) diagram for the formation of the Amadori rearrangement products (**ARPs**) in **c-Rib** + **DGly** and **Rib** + **DGly** reactions, obtained by using **c-Rib** + **DGly** and **Rib** + **DGly** total free energies ($G^0_{\text{c-Rib}} + G^0_{\text{DGly}}$ and $G^0_{\text{Rib}} + G^0_{\text{DGly}}$, respectively) as the standard (**STD**). For numerical abbreviations and details of the compounds, see the caption and mechanism of Fig. 2.

possibility and internal energy changes for the formation of different compounds in the proposed mechanisms have been investigated. Relevant dipole moments (μ, in Debye), related to the internal energy of the molecule, of different compounds in aqueous solution have been obtained from the electronic energy calculations on the RB3LYP/6-31G(d) optimized structures at PCM/RB3LYP/6-31G(d) (Foresman & Frisch, 1996; Frisch & Foresman, 1998). Relevant heats of formation (ΔH_f^0) of different compounds have been obtained by performing AM1 semi-imperical calculations (Foresman & Frisch, 1996; Frisch & Foresman, 1998) on the RB3LYP/6-31G(d) optimized structures.

3. Results and discussion

At constant temperatures and pressures, ΔE and ΔG of a reaction indicate the internal energy changes and spontaneity of the reaction, respectively. ΔG^0 for the formation of different compounds in the proposed mechanisms for **c-Rib + Gly** and **Rib + Gly** reactions under different pH conditions in aqueous solution (Figs. 1 and 2) are presented in Table 1, calculated by using **c-Rib + Gly** and **Rib + Gly** total free energies ($G^0_{\text{c-Rib}} + G^0_{\text{UGly/PGly/DGly/GlyZ}}$ and $G^0_{\text{Rib}} + G^0_{\text{UGly/PGly/DGly/GlyZ}}$, respectively) as the standard in the equation $\Delta G^0 = G^0_{\text{Product(s)}} - G^0_{\text{Reactant(s)}}$. Table 2 represents ΔE^0 for the formation of different compounds in the proposed mechanisms (Figs. 1 and 2), obtained by using **c-Rib**, **b0 + Gly** and **Rib + Gly** total electronic energies ($E^0_{\text{c-Rib}} + E^0_{\text{UGly/PGly/DGly/GlyZ}}$ and $E^0_{\text{Rib}} + E^0_{\text{UGly/PGly/DGly/GlyZ}}$, respectively) as the standard in the equation $\Delta E^0 = E^0_{\text{Product(s)}} - E^0_{\text{Reactant(s)}}$. Dipole moment ($\mu$) of a molecule indicates its polarity, and ΔH_f^0 indicates the thermal changes during its formation. Dipole moments (in Debye) and ΔH_f^0 (in kJ/mol) for different compounds in the proposed mechanisms (Figs. 1 and 2) are presented in Table 3. Table 4 represents some RB3LYP/6-31G(d) optimized geometric parameters of different compounds in the proposed mechanisms (Figs. 1 and 2).

Table 1
ΔG^0_{Aq} (in kJ/mol) for different compounds presented in Figs. 1 and 2

Compounds	Reactions			
	c-Rib + UGly	**Rib + UGly**	**c-Rib + PGly**	**Rib + PGly**
Rib	7.7	–	7.76	–
1	6.2	−1.4	–	–
2	39.3	31.6	93.3	85.5
3	83.3	75.6	137.2	129.5
4	29.8	22.1	83.7	76.0
5	5.3	−2.4	59.3	51.6
6	56.4	48.7	110.4	102.7
7	−1.5	−9.2	52.4	44.7
	c-Rib + DGly	**Rib + DGly**	**c-Rib + GlyZ**	**Rib + GlyZ**
Rib	7.63	–	7.72	–
2a	109.7	102.0	–	–
2b	–	–	102.1	94.4
3a	132.9	125.2	310.5	302.8
4a	−6.6	−14.3	171.0	163.3
6a	−19.8	−27.5	157.8	150.1
7a	−52.1	−59.8	125.5	117.8

Table 2
ΔE^0_{Aq} (in kJ/mol) for different compounds presented in Figs. 1 and 2

Compounds	Reactions			
	c-Rib + UGly	**Rib + UGly**	**c-Rib + PGly**	**Rib + PGly**
Rib	6.5	–	6.4	–
1	−1.1	−7.6	–	–
2	−15.2	−21.6	39.7	33.2
3	34.4	27.9	89.3	82.8
4	−254.3	−260.7	199.4	−205.8
5	−6.2	−12.6	48.7	42.3
6	44.4	38.0	99.3	92.9
7	−9.6	−16.0	45.3	38.9
	c-Rib + DGly	**Rib + DGly**	**c-Rib + GlyZ**	**Rib + GlyZ**
Rib	6.8	–	6.3	–
2a	38.5	32.1	–	–
2b	–	–	54.5	48.1
3a	61.7	55.3	165.7	159.3
4a	6.7	0.2	157.1	150.7
6a	−4.8	−11.2	145.7	139.2
7a	−32.3	−38.7	118.2	111.8

During the calculation of ΔG^0 and ΔE^0, the total mass balance of the reaction under different conditions has been maintained. The main problem in balancing the total mass arises for protonation and deprotonation, and therefore, the following idea has been applied during balancing the total mass (Shipar, 2004):

$$\underset{\text{Proton}}{H^+} + \underset{\text{water}}{H_2O} \leftrightarrow \underset{\text{hydroxonium ion}}{H_3O^+} \quad \text{(protonation and deprotonation)}$$

According to ΔG^0 (Table 1), production of **Rib** from **c-Rib** is not probable under all pH conditions. This reveals that instead of the production of **Rib**, **c-Rib** may directly be involved in the reaction. The relevant pH and presence of **Gly** species (**UGly**, **PGly**, **DGly** and **GlyZ**) in the system may be responsible in this case. Due to lacking of adequate exper-

Table 3
Dipole moments in aqueous solution (μ_{aq}, in Debye) and heats of formation (ΔH_f^0, in kJ/mol) for different compounds presented in Figs. 1 and 2

Compounds	μ [PCM/RB3LYP/6-31G(d)]	ΔH_f^0 [AM1]
c-Rib	6.3423	−992.6
Rib	2.9455	−979.4
1	9.6144	−264.4
2	9.4572	−788.4
2a	5.2643	−1511.5
2b	11.5921	−1296.6
3	5.5831	−1381.9
3a	10.9188	−1590.7
4	2.953	−1105.8
4a	11.0414	−1220.6
5	5.3815	−515.9
6	3.7491	−1136.0
6a	10.9163	−1247.3
7	1.4758	−1149.5
7a	13.8162	−1251.5

Table 4
Some RB3LYP/6-31G(*d*) geometric parameters of different compounds presented in Figs. 1 and 2

Compounds	Bond lengths (Å)						Bond angles (°)			Dihedral angles (°)
	C–C	C–O	O–H	C–H	N–C	N–H	H–C–O	C–N–C[e]	C–C–C	C–C–C–C[f]
c-Rib	1.544, 1.5367, 1.5468, 1.5235	1.3882, 1.4028, 1.4301	0.9724, 0.9737, 0.9686, 0.9687	1.0979, 1.0984, 1.0983, 1.0999	–	–	101.9, 102.9, 113.5	–	–	−31.8
Rib	1.5152, 1.5542	1.215[b]		1.1075	–	–	114.3	121.6	–	84.3
1	1.5384, 1.5479	1.3599[b]	0.975	1.1209	–	–	109.6	117.8	–	68
2	1.5546	–	–	–	1.5381, 1.4827[d]	1.0333, 1.0262	108.6	–	112.8	−172.3
2a	1.5669	1.2952	–	1.1303	1.6177, 1.47[d]	1.0167, 1.0218	116.2	117	114.2	−61.7
2b	1.5544	–	–	–	1.5195, 1.4872[d]	1.0197, 1.0278	111.4	–	111.4	−75
3	1.5515	–	0.9749	1.0921	1.4641, 1.448[d]	1.0162	111.6	108	118	−176.8
3a	1.5566	–	0.9643	1.1376	1.4543, 1.4471[d]	1.003	111.3	104	115.3	−72.8
4	1.5106	–	–	1.0962	1.269[c], 1.4495[d]	–	109.6	–	119.2	177.7
4a	1.5147	–	–	1.0918	1.2727[c], 1.4447[d]	–	112.2	–	118.2	86.7
5	1.5155	–	–	1.1209	1.3032[c], 1.455[d]	1.0173	109.2	–	124.2	−165.1
6	1.3461[a]	1.3785	0.9764	1.0849	1.4167, 1.4503[d]	1.0154	124	–	117.3	−102.7
6a	1.3565[a]	1.3497	1.05	1.0876	1.4226, 1.4755[d]	1.0203	122.7	–	115.6	−96.1
7	1.5125	1.2245[b]	–	1.0989, 1.1113	1.4461, 1.4456[d]	1.0166	116.6	–	115.5	158.7
7a	1.4765	1.2389[b]	–	1.101, 1.1287	1.4528, 1.4762[d]	1.02	117.1	–	111.4	140.7

[a] C=C.
[b] C=O.
[c] N=C.
[d] N–C(**Y**/**Y**$^-$).
[e] C–N–C(**Y**/**Y**$^-$).
[f] C–C–C–C(**X**).

imental data, providing proper explanation on this point is difficult. However, **c-Rib** + **DGly** and **c-Rib** + **PGly** reactions are assumed as the most and least favourable for the production of **Rib** from **c-Rib**, respectively (Table 1). Based on ΔE^0, **Rib**, produced from **c-Rib**, is electronically more stable in **c-Rib** + **GlyZ** reaction than that of the others. The calculated μ of **Rib** is found lower than **c-Rib** (Table 3).

Protonation of **Rib** to its protonated form (**1**) is favourable in **Rib** + **UGly** reaction, and not in **c-Rib** + **UGly** reaction (Table 1). Previous computational studies on glyceraldehyde (**Gald**) and **Gly** (**UGly**, **PGly**, **DGly** and **GlyZ**) Maillard reaction stated that protonation of **Gald** in **Gald** + **UGly** reaction is not feasible in aqueous solution (Shipar, 2004). According to ΔE^0 (Table 2), protonated ribose (**1**), formed through the protonation of **Rib** (Fig. 1) is electronically more stable in **Rib** + **UGly** than **c-Rib** + **UGly** reaction (Table 2). However, sufficient experimental data are still not available, and therefore, offering appropriate information on these points are also complicated.

Both **c-Rib** + **UGly** and **Rib** + **UGly** reactions are not favourable for producing the ionic addition adduct, **2** (1-protonated glycino-pent-1,2,3,4,5-ol), addition compound, **3** (1-glycino-pent-1,2,3,4,5-ol), the Schiff base, **4**, the ionic adduct, **5**, and the enol form of **ARP**, **6** (1-glycino-pent-2,3,4,5-ol-1-ene) [Table 1 and Fig. 1]. Both of the reactions are feasible for the formation of the keto form of **ARP**, **7** (1-glycino-pent-3,4,5-ol-2-one) [Table 1 and Fig. 1]. Previous theoretical study evaluated that **Gald** + **UGly** reaction is only favourable for forming the keto form of **ARP**, and the aqueous solution is less favourable for the production of **ARP** (Shipar, 2004). In **c-Rib** + **UGly** and **Rib** + **UGly** reactions, **7** is electronically more stable than **6**. Both **6** and **7** are electronically more stable in **Rib**+ **UGly** reaction than that of **c-Rib** + **UGly** reaction (Table 2).

c-Rib + **DGly** and **Rib** + **DGly** reactions are seemed to be more feasible for the formation of different compounds in the proposed mechanism (Table 1). Both of the reactions are not favourable for producing the ionic addition adduct, **2a**, and addition compound, **3a** (1-deprotonated glycino-pent-1,2,3,4,5-ol), and favourable for forming the Schiff base, **4a**, enol and keto forms of the **ARP**, **6a** (1-deprotonated glycino-pent-2,3,4,5-ol-1-ene) and **7a** (1-deprotonated glycino-pent-3,4,5-ol-2-one), respectively (Table 1 and Fig. 2). It is also consistent with the previous finding that **Gald** + **DGly** reaction is more favourable for the production of **ARP**s (Shipar, 2004). In comparison, **c-Rib** + **DGly** and **Rib** + **DGly** reactions are supposed to be more suitable for the formation of **ARP**s (**6a** and **7a**) than the formation of **ARP**s (**6** and **7**) in **c-Rib** + **UGly** and **Rib** + **UGly** reactions (Table 1). It is in agreement with the previous reports that the basic condition facilitates the Maillard reaction spontaneously (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). Production of **ARP**s (**6a** and **7a**) is more plausible in **Rib** + **DGly** reaction than **c-Rib** + **DGly** reaction (Table 1). Both of **c-Rib** + **DGly** and **Rib** + **DGly** reactions are not feasible for the formation of **2a** and **3a** (Table 1). Therefore, it is postulated that in **c-Rib** + **DGly** reaction, instead of opening the chain of **c-Rib**, **DGly** may directly be added to **c-Rib** and elimination of one molecule H_2O may be occurred at the same time, leading to the formation of **4a**, which can consequently produce **6a** and **7a** as shown in Fig. 2. In **Rib** + **DGly** reaction, nucleophilic addition of **Rib** and **DGly** and elimination of one molecule H_2O may take place at the same time to produce **4a**, and **6a** and **7a** can be produced from **4a** according to the mechanism as presented in Fig. 2. Both **6a** and **7a** are electronically more stable than **6** and **7** (Table 2). Both **6a** and **7a** are electronically more stable in **Rib** + **DGly** reaction than that of **c-Rib** + **DGly** reaction (Table 2). The calculated μ is found as higher for **6a** and **7a** than **6** and **7**, respectively (Table 3). Amongst **ARP**s (**6**, **6a**, **7** and **7a**), **7a** contains the highest and **6** contains the lowest ΔH_f^0 (Table 3).

Based on ΔG^0 (Table 1), **c-Rib** + **PGly**, **Rib** + **PGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are found not to be favourable for the formation of all compounds in proposed mechanisms (Figs. 1 and 2). It reveals that nucleophilic addition of **c-Rib** or **Rib** with **PGly** or **GlyZ** is not feasible because of the unavailability of lone pair electrons on the glycino-nitrogen. **Gald** + **PGly** and **Gald** + **GlyZ** reactions were also reported as not to be feasible for the production of **ARP**s (Shipar, 2004). It is also in agreement with the previous statement that acidic or protonated forms of amino groups of amino compounds are not favourable for the Maillard reaction (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). However, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are seemed to be more unfeasible than **c-Rib** + **PGly** and **Rib** + **PGly** reactions (Table 1), which is also supported by ΔE^0 values (Table 2).

The Schiff bases (**SB**s) are one of the most common intermediates in the Maillard reaction, which can undergo further reactions to form intermediates that are more reactive (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993; Nyhammar, Olsson, & Pernemalm, 1983). **c-Rib** + **DGly** and **Rib** + **DGly** reactions are favourable for forming the Schiff-base, **4a**, whereas **c-Rib** + **UGly** and **Rib** + **UGly** reactions are not favourable for producing the Schiff-base, **4** (Table 1). Therefore, it is postulated that **c-Rib** + **DGly** and **Rib** + **DGly** reactions are more favourable for the formation of **ARP**s (**6a** and **7a**) than the formation of **ARP**s (**6** and **7**) in **c-Rib** + **UGly** and **Rib** + **UGly** reactions. However, **Rib** + **DGly** reaction is more suitable for the formation of **4a** than that of **c-Rib** + **DGly** reaction (Table 1). **c-Rib** + **PGly**, **Rib** + **PGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions (Figs. 1 and 2) are not favourable for forming **SB**s, **4** and **4a** (Table 1), and therefore, formation of **ARP**s under these conditions is assumed to be stalled. In **Rib** + **UGly** reaction, **4** is electronically more stable than that of **c-Rib** + **UGly** reaction (Table 2). In **Rib** + **DGly** reaction, **4a** is electronically more stable than that of **c-Rib** + **DGly** reaction. The second lowest and third highest μ values are calculated for **4** and **4a**, respectively (Table 3).

c-Rib + **PGly**, **Rib** + **PGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions (Figs. 1 and 2) are not favourable for the formation of both of **SB**s (**4** and **4a**) and **ARP**s (**6**, **6a**, **7** and **7a**) [Table 1]. Therefore, the rate of browning under these conditions is assumed very low. **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are assumed less favourable for producing **SB**s and **ARP**s than that of **c-Rib** + **PGly** and **Rib** + **PGly** reactions (Table 1). Hence, the browning rate in **c-Rib** + **PGly** and **Rib** + **PGly** reactions is assumed higher than **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions. **Rib** + **PGly** reaction is more favourable for producing **SB**s and **ARP**s than that of **c-Rib** + **PGly** reaction (Table 1). Therefore, the rate of browning in **c-Rib**, **b0 + PGly** reaction is assumed lower than that of **Rib** + **PGly** reaction. **c-Rib** + **GlyZ** reaction is supposed to be less reactive in the browning reaction than that of the others (Table 1). However, some other mechanisms may be involved under these conditions. Adequate data is still not available, and further studies are, therefore, essential. **c-Rib** + **DGly** and **Rib** + **DGly** reactions are suitable for producing both of the enol and keto forms of **ARP** (**6a** and **7a**) [Table 1]. Therefore, the rate of browning in **c-Rib** + **DGly** and **Rib** + **DGly** reactions is assumed higher than that of the others. However, **Rib** + **DGly** reaction is assumed more feasible for producing **ARP**s (**6a** and**7a**) than that of **c-Rib** + **DGly** reaction (Table 1), and therefore **Rib** + **DGly** reaction is supposed as more reactive than **c-Rib** + **DGly** react ion in the browning reaction. **c-Rib** + **UGly** and **Rib** + **UGly** reactions are not favourable for the formation of **SB** (**4**) and the enol form of **ARP** (**6**), and is only feasible for the formation of the keto form of **ARP** (**7**) [Table 1]. Therefore, the rate of browning in **c-Rib** + **UGly** and **Rib** + **UGly** reactions is assumed lower than **c-Rib** + **DGly** and **Rib** + **DGly** reactions. **Rib** + **UGly** reaction is more feasible for producing **ARP** (**7**) than that of **c-Rib** + **UGly**

reaction (Table 1), and therefore, the rate of browning in **Rib** + **UGly** reaction is assumed higher than **c-Rib** + **UGly** reaction.

ΔG^0 and ΔE^0 for the formation of **Rib** through the cleavage of **Glu** (Fig. 3) are calculated as 3.4 kJ/mol and 46.8 kJ/mol, obtained by using **Glu** free energy and electronic energy (G^0_{Glu} and E^0_{Glu}, respectively) as the standard in the equations $\Delta G^0 = G^0_{Product(s)} - G^0_{Reactant(s)}$ and $\Delta E^0 = E^0_{Product(s)} - E^0_{Reactant(s)}$, respectively. The same values for ΔG^0 and ΔE^0 with opposite signs (−3.4 kJ/mol and −46.8 kJ/mol, respectively) are found for the formation of **Glu** through reverse reaction between of **Rib** and **Fald**, calculated by using **Rib** + **Fald** free and electronic energies ($G^0_{Rib+Fald}$ and $E^0_{Rib+Fald}$, respectively) as the standard in the equations $\Delta G^0 = G^0_{Product(s)} - G^0_{Reactant(s)}$ and $\Delta E^0 = E^0_{Product(s)} - E^0_{Reactant(s)}$, respectively. It reveals that formation of **Rib** through the cleavage of **Glu** (Fig. 3) is not feasible in aqueous solution, and **Rib**, formed through this way, is electronically unstable. On the other hand, formation of **Glu** from **Rib** and **Fald** is suitable in aqueous solution, which is also supported by ΔE^0. However, adequate experimental data are still not available to evaluate this assumption.

According to the total mass balance of the reaction, water plays an important role in **c-Rib** + **Gly** and/or **Rib** + **Gly** reactions under all conditions. Water is necessary for the initiation of the reaction. One molecule of water in the initial step for each of **c-Rib** + **UGly**, **Rib** + **UGly**, **c-Rib** + **PGly** and **Rib** + **PGly** reactions is necessary for balancing the total mass, whereas two molecules of water for each are needed in the initial step of **c-Rib** + **DGly**, **Rib** + **DGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions. It is in agreement with the earlier findings that water is essential for the Maillard reaction to take place in foods and other systems, such as in the human body (Ames, 1990; Davídek et al., 1990; Eskin, 1990; Labuza & Saltmarch, 1981; Lea & Hannan, 1949; Macrane et al., 1993; Nursten, 1986). During the formation of **ARP**s, one molecule of H_2O is produced as by-product in the reaction under all conditions. Hence, finally the reaction under neutral and acidic conditions (**c-Rib** + **UGly**, **Rib** + **UGly**, **c-Rib** + **PGly** and **Rib** + **PGly** reactions) contain total three molecules of H_2O, and the reaction under other pH conditions (**c-Rib** + **DGly**, **Rib** + **DGly**, **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions) contain total five molecules of H_2O. It is also in accord to the previous reports that water is a by-product in the Maillard reaction in foods and other systems (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993).

4. Conclusion

Due to much more complexities, conducting experiments for getting information about the role of **c-Rib** and **Rib** in the Maillard reaction involving **Gly** species under different pH conditions are complicated. Therefore, density functional computations at the standard state have been applied on the proposed mechanisms for the early stage of **c-Rib** + **Gly** and **Rib** + **Gly** reactions to evaluate the spontaneity and internal energy changes of the reaction through calculating ΔG^0 and ΔE^0. Hence, possibility of the formation of different compounds during the formation of **ARP**s in the early stage of the reaction has been estimated. From the present investigation, it can be concluded that both **c-Rib** and **Rib** can participate in the reaction. As **Rib** and **c-Rib** can exist in equilibrium mixture, due to the participation of both of these forms in the reaction, the rate o f browning can be enhanced. Production of **Rib** from **c-Rib** is not plausible under different pH conditions, and therefore, it is postulated that instead of producing **Rib**, **c-Rib** can directly participate in the reaction. It is difficult to explain, as sufficient data is still not available. Some other mechanisms may be involved in this case. For example, 1,1,2,3,4,5-hexahydroxypentane [$HC(OH)_2\{HC(OH)\}_3H_2C(OH)$] may be formed through the addition of **c-Rib** and H_2O, which may participate in further reactions. The basic and neutral conditions have been found as the most and second most favourable for the formation of **ARP**s. Formation of the enol form of **ARP** is not feasible under neutral condition, whereas the basic condition facilitates the formation of both of the enol and keto forms of **ARP**. Therefore, the rate of browning is assumed higher in the reaction under basic condition than that of the others. As **SB**s and **ARP**s are the main intermediates in the Maillard reaction, and the basic condition is favourable for producing these species, the reaction under this condition is supposed to be more suitable for following the general Hodge-scheme. The reaction under neutral condition is not suitable for producing **SB** and the enol form of **ARP**. Hence, in following the general Hodge-scheme, the reaction under neutral condition is assumed less suitable than the reaction under basic condition. These findings are important as the Maillard reaction can take place in foods as well as in the human body (human blood is slightly basic). Possible low free energy (ΔG^0) diagrams for the formation of **ARP**s (**6a** and **7a**) in **c-Rib** + **DGly** and **Rib** + **DGly** reactions in aqueous solution is presented in Fig. 4, acquired by using **c-Rib** + **DGly** and **Rib** + **DGly** total free energies ($G^0_{c\text{-}Rib} + G^0_{DGly}$ and $G^0_{Rib} + G^0_{DGly}$, respectively) as the standard (**STD**). At the isoelectric point of glycine and under acidic condition, the reaction is supposed to be the least and second least favourable for producing **ARP**s. Therefore, the rate of browning under these conditions is assumed to be hindered. Water plays an important role for the initiation of the reaction, and water is produced as a by-product during the formation of **ARP**s. Adequate information on **c-Rib** + **Gly** and **Rib** + **Gly** reactions is still insufficient, and therefore, to establish proper reaction mechanism and find out the role of **c-Rib**, **Rib** and **Gly** species (**UGly**, **PGly**, **DGly** and **GlyZ**) in foods and other systems, further extensive theoretical and experimental studies on the reaction are still necessary. In order to establish proper mechanism of the reaction, the theoretical results, presented in this paper, will be helpful for further theoretical and experimental investigations, leading to find out suitable controlling ways of the Maillard reaction in different systems.

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