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Formation of the Heyns rearrangement products in dihydroxyacetone and glycine Maillard reaction: A computational study

Md. Abul Haider Shipar *

Hiroshi Morita Lab, Building No. 08, Room No. 310, Department of Information and Image Sciences, Faculty of Engineering, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

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Abstract

Density functional theory computations at the standard state on the proposed mechanisms of dihydroxyacetone and glycine Maillard reaction under different pH conditions have revealed that dihydroxyacetone + deprotonated glycine and dihydroxyacetone + unprotonated glycine reactions are more favorable than dihydroxyacetone + protonated glycine and dihydroxyacetone + glycine zwitterion reactions for the formation of the Heyns rearrangement products (**HRP**s). The gaseous phase reaction is assumed more feasible than the aqueous phase reaction for the production of **HRP**s. Due to the possibility of the production of both of the enol and keto forms of **HRP**s, the rate of browning in the dihydroxyacetone + deprotonated glycine reaction is assumed higher than that of the others. Dihydroxyacetone + protonated glycine and dihydroxyacetone + glycine zwitterion reactions are not favorable for the formation of **HRP**s and, therefore, the reaction is assumed hindered under these conditions and the rate of browning is supposed to be lower than that of the others. Possibilities for the conversion of dihydroxyacetone to glyceraldehyde and formation of hydroxyacetaldehyde from dihydroxyacetone as a C2-fragmentation product have also been evaluated.

Keywords: Heyns rearrangement products; Dihydroxyacetone; Glycine; Maillard reaction; Density functional calculations.

1. Introduction

Non-enzymatic browning or the Maillard reaction (Maillart, 1912) is one of the most important reactions in controlling food quality and nutritional value. The reaction 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). The reaction can also take place in the human body, and is therefore important in the medicinal arena (Meade, Miller, & Gennard, 2003; Ledl & Schleicher, 1990; Reber et al., 2002). Although about 90 years have passed since the discovery of the Maillard reaction, and many results have been gathered later on, still there is no potential explanation for its mechanism. Several schemes have been proposed to explain the mechanism of the reaction (Hodge, 1953; Namiki & Hayashi, 1983; Tressl, Nittka, & Kersten, 1995). Of these, the Hodge-scheme (Hodge, 1953) is the most accepted and indicates the very complex nature of the reaction. Due to the complexity of the intermediates and the final products (or melanoidines), controlling the Maillard reaction, with respect

* Tel.: +81 043 290 3471; fax: +81 043 290 3490.
E-mail addresses: shipar47@graduate.chiba-u.jp, shipar7@yahoo.com.

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to food quality, nutritional value and medicinal aspects, is still a major challenge. For controlling the reaction, it is necessary that the reaction mechanism is well understood. However, conducting experiments and analyzing the intermediates and final product mixtures for accurate information is complicated. Though a great number of studies have been conducted about the pathways leading to the formation of melanoidines, the mechanism is still obscure and specific pathways, instead of those based on hypothesis, are not available for the formation of Maillard colors, flavors, antioxidants, and so on. Computational chemistry can be applied to such a complex reaction to obtain useful information, helpful to understand and establish proper mechanisms for the reaction. In this paper, mechanisms for the initial stage of dihydroxyacetone and glycine Maillard reaction under different pH conditions are proposed and described, following the Hodge-scheme (Hodge, 1953). During proposing the mechanisms, formation of the Heyns rearrangement products (**HRP**s) is considered as the possible product of the reaction. The aim of the present study is to perform Density Functional computations to evaluate the possibility of the formation of different compounds in the proposed mechanisms through the estimation of the Gibb's free energy changes (ΔG°). The total mass balance for different steps of the reaction has been followed during the calculation of ΔG°. To observe the possible internal energy changes, electronic energy changes (ΔE°) for the formation of different compounds in different steps of the reaction have also been calculated by following the total mass balance of the reaction.

1,3-Dihydroxyacetone or dihydroxyacetone (**DHA**) is the simplest ketose sugar, which can exist in equilibrium with glyceraldehyde (**Gald**) (Fig. 1) (Harrold, 1991; Holum, 1996; Lozynski, Rusinska-Roszak, & Mack, 1997; Moore, 1962; Thornalley, Wolff, Crabbe, & Stern, 1984; Yaylayan, Majors, & Ismail, 1999). With considerable biological importance, both of these compounds provide the basis of carbohydrate chemistry (Kobayashi, Igarashi, Takahashi, & Higashi, 1976). **DHA** is commercially used in cosmetics, and as a food additive (Brown, 2001; Navrátil, Tkáč, Švitel, Danielsson, & Šturdik, 2001; Zhu et al., 2003). **DHA** is used as an intermediate for the production of tanning agents, emulsifiers, plastifiers, alkyl-type resins and X-ray contrast agents (Feige, Ried, & Bachmann, 1996). It has been reported as the active browning ingredient in sunless tanning lotions, and can induce DNA damage, inhibition of lipid accumulation, and blocking of the cell-cycle (Petersen, Wulf, Gniadecki, & Gajkowska, 2004; Stanko & Adibi, 1986). The mechanism of sunless tanning color that develops after dermal application is due to **DHA** binding to amino acids in the stratum corneum (Kurz, 1994). Genotoxicity and mutagenic effects of **DHA** have also been reported (Marnett et al., 1985; Merschsundermann, Schneider, Klopman, & Rosencrantz, 1994; Morita, 1991; Pham, DeMarini, & Brockmann, 1980; Yamaguchi, 1982).

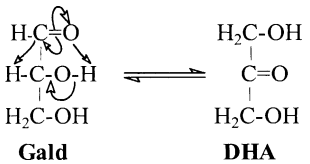


Fig. 1. Interconversion of glyceraldehyde (**Gald**) and dihydroxyacetone (**DHA**).

On the other hand, glycine (**Gly**), the simplest amino acid, can be found in four forms (Eskin, 1990; Harrold, 1991; Holum, 1996; Macrane et al., 1993; Shipar, 2004). 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 ($H_3N^+–CH_2–CO_2H$) and exists as the conjugated acid (Harrold, 1991; Holum, 1996). Hence, under acidic conditions, e.g., pH < 5.5, protonated glycine (**PGly**) becomes the dominant species. Glycine zwitterion (**GlyZ**, $H_3N^+–CH_2–CO_2:^-$) becomes the dominant species at the isoelectric point of glycine (I = pH ≈ 6) (Harrold, 1991; Holum, 1996; Macrane et al., 1993). Production of basic amino groups is facilitated by the alkaline medium and, therefore, deprotonated glycine (**DGly**, $H_2N–CH_2–CO_2:^-$) becomes the dominant species under basic conditions (pH > 8) (Eskin, 1990).

The reaction between **DHA** and **Gly** has not been well studied and, therefore, the mechanism of the reaction is still obscure. However, it can be assumed that the Heyns rearrangement (**HR**) can take place in the initial or early stage of the reaction, leading to the production of **HRP**s (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993; Wrodnigg & Eder, 2001). The initial stage of **DHA** + **UGly** reaction (Fig. 2) may involve firstly the protonation of **DHA** to **PDHA**. Nucleophilic attack by **UGly** on the electron deficient carbon atom of the carbonyl group of **PDHA** may lead to the production of the cation of the dihydroxyacetone–glycine addition compound, **CatDG** (2-hydroxy-2-protonated glycino-1,3-dihydroxy-propane), which can produce the dihydroxyacetone–glycine addition compound, **DGadd** (2-hydroxy-2-glycino-1,3-dihydroxy-propane), through deprotonation. Elimination of one molecule of water (H_2O) from **DGadd** can take place, resulting in the production of the Schiff base of the dihydroxyacetone–glycine addition compound, **DGSB**. Through protonation, **DGSB** can produce the cation of the Schiff base, **CatDGSB**, which can form the enol form of the Heyns rearrangement product, **HRPE** (2-glycino-1,3-dihydroxyprop-l-ene), through deprotonation. Through keto-enolic tautomerization (**KET**), **HRPE** can be rearranged to

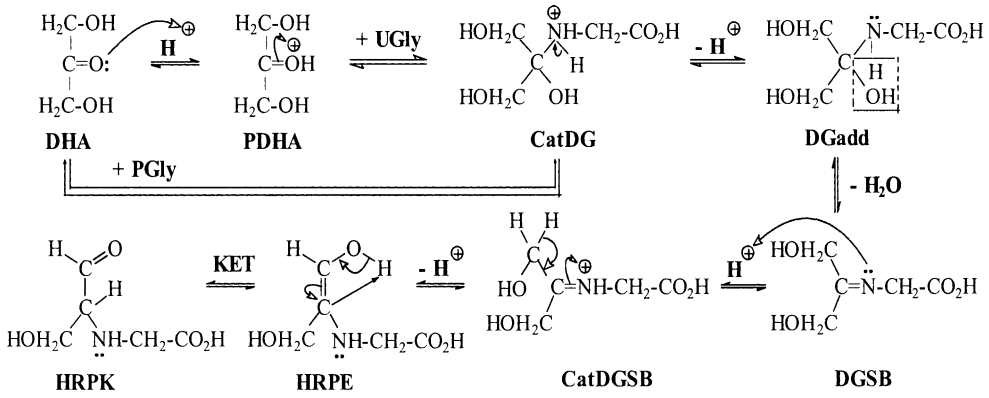


Fig. 2. Proposed mechanism for the formation of the Heyns rearrangement products (**HRPs**) in the initial stage of **DHA + UGly** and **DHA+PGly** Maillard reactions. *Abbreviations*: **DHA**, dihydroxyacetone (l,3-dihydroxy-prop-2-one); **UGly**, unionized or unprotonated glycine; **PGly**, protonated glycine; **PDHA**, protonated form of dihydroxyacetone; **CatDG**, cation of dihydroxyacetone–glycine addition compound (2-hydroxy-2-protonated glycino-1,3-dihydroxy-propane); **DGadd**, dihydroxyacetone–glycine addition compound (2-hydroxy-2-glycino-1,3-dihydroxy-propane); **DGSB**, Schiff base of dihydroxyacetone–glycine addition compound; **CatDGSB**, cation of the Schiff base of dihydroxyacetone–glycine addition compound; **HRPE**, enol form of the Heyns rearrangement product (2-glycino-1,3-dihydroxy-prop-1-ene); **HRPK**, keto form of the Heyns rearrangement product (2-glycino-3-hydroxy-prop-1-al); **KET**, keto-enolic tautomerization.

its more stable keto form, **HRPK** (2-glycino-3-hydroxy-prop-1-al).

Production of **CatDG** in the **DHA + PGly** reaction (Fig. 2) may occur through the direct nucleoplic addition of **DHA** and **PGly**, instead of the formation of **PDHA**. Consequently, **HRPE** and **HRPK** can be formed from **CatDG** through the mechanism proposed for the **DHA + UGly** reaction (Fig. 2).

In the initial stage of the **DHA + DGly** reaction (Fig. 3), nucleophilic addition of **DHA** and **DGly** may lead first to the formation of the ionic addition adduct, **CatDG(DGly)**, which can form the dihydroxyacetone–deprotonated glycine addition compound, **DGadd(DGly)** [2-hydroxy-2-deprotonated glycino-1,3-dihydroxy-propane], through intramolecular rearrangement (**IMR**). The Schiff base, **DGSB(DGly)**, can be formed through the elimination of one molecule of H_2O from **DGadd(DGly)**, and protonation of **DGSB(DGly)** can lead to the production of **CatDGSB(DGly)**. Deprotonation of **CatDGSB(DGly)** can produce the enol form of the Heyns rearrangement product, **HRPE(DGly)** [2-deprotonated glycino-1,3-dihydroxy-prop-1-ene]. Through **KET**, **HRPE(DGly)** can be rearranged to its keto form, **HRPK(DGly)**.

In the initial stage of the **DHA + GlyZ** reaction (Fig. 3), nucleophilic addition of **DHA** and **GlyZ** may produce firstly the ionic addition adduct, **CatDG(GlyZ)**, which can lead to the formation of the addition

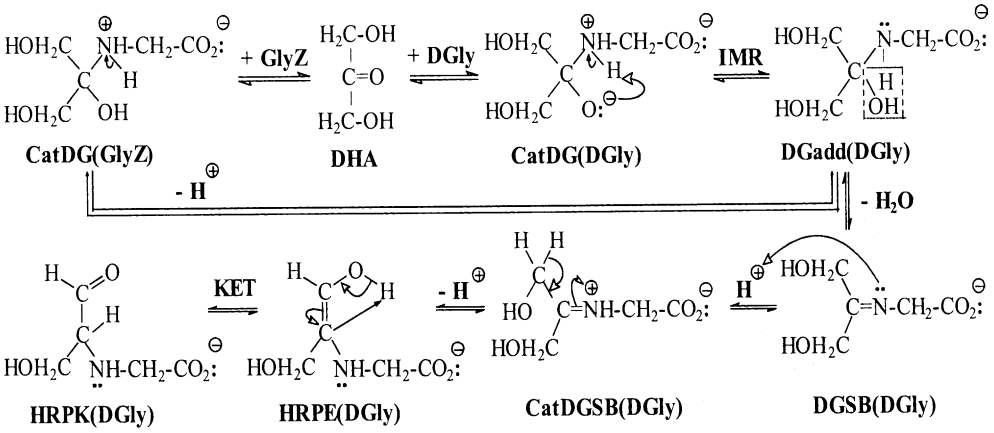
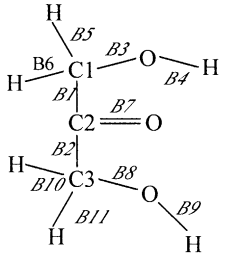


Fig. 3. Proposed mechanism for the formation of the Heyns rearrangement products (**HRPs**) in the initial stage of **DHA + DGIy** and **DHA+GlyZ** Maillard reactions. *Abbreviations*: **DHA**, dihydroxyacetone (l,3-dihydroxy-prop-2-one); **DGly**, deprotonated glycine; **GlyZ**, glycine zwitterion; **CatDG(GlyZ)**, ionic addition adduct of **DHA** and **GlyZ**; **CatDG(DGly)**, ionic addition adduct of **DHA** and **DGly**; **DGadd(DGly)**, dihydroxyacetone–deprotonated glycine addition compound (2-hydroxy-2-deprotonated glycino-1,3-dihydroxy-propane); **DGSB(DGly)**, Schiff base of **DGadd(DGly)**; **CatDGSB(DGly)**, ionic adduct **of DGSB(DGly)**; **HRPE(DGly)**, enol form of the Heyns rearrangement product (2-deprotonated glycino-1,3-dihydroxy-prop-1-ene); **HRPK(DGly)**, keto form of the Heyns rearrangement product (2-deprotonated glycino-3-hydroxy-prop-1-al); IMR, intramolecular rearrangement; KET, keto-enolic tautomerization.

compound, **DGadd(DGly)**, through deprotonation. Subsequent production of **HRPE(DGly)** and **HRPK(DGly)** from **DGadd(DGly)** can occur through the mechanism proposed for the **DHA** + **DGly** reaction (Fig. 3). Information regarding **DHA** + **DGly** Maillard reaction under different pH conditions is still not available. Previous studies were related mainly to the role of unprotonated amino groups in the Maillard reaction, and generally overlooked the function of protonated, deprotonated amino groups, and amino groups at the isoelectric points. The present study will be helpful to evaluate the role of different **Gly** species (**UGly**, **PGly**, **DGly** and **GlyZ**) in the Maillard reaction under different pH conditions involving **DHA**. Experimental evaluation of the role of these complex species in the Maillard reaction is quite complicated and, therefore, computational methods are used.

2. Methodology

All compounds in the proposed mechanisms (Figs. 2 and 3) have been studied in their gaseous and aqueous phases at the standard state. **DHA** and **Gly** can have many conformations in both of the gaseous and aqueous states (Csazer, 1992; Hu, Shen, & Schaefer, 1993; Jensen & Gordon, 1991; Kobayashi & Takahashi, 1979; Lelj, Adamo, & Barone, 1994; Lozynski et al., 1997; Palla, Petrongolo, & Tomasi, 1980; Ramek, Cheng, Frey, Newton, & Schäfer, 1991; Wagen et al., 1994; Yaylayan et al., 1999). 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, general optimized structures of **DHA** and **Gly** (Figs. 4 and 5) at a specific method (RB3LYP) (Becke, 1992a, 1992b, 1993, 1996; Foresman & Frisch, 1996; Frisch & Foresman, 1998; Hehre, Radom, Schleyer, & Pople, 1986) have been used in both of the gaseous and aqueous phases to avoid complexities and simplify the calculation. The same procedure has been followed for all other compounds in the proposed mechanisms (Figs. 2 and 3). However, many compounds in the proposed mechanisms are assumed to be unstable in the gaseous



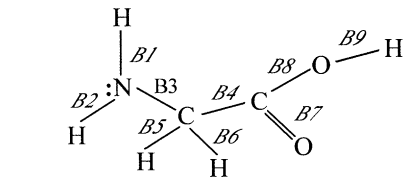
B1 = 1.53 A°, *B2* = 1.5308 A°,
B3 = 1.4132 A°, *B4* = 0.9739 A°,
B5 = 1.1048 A°, *B6* = 1.0934 A°,
B7 = 1.2139 A°, *B8* = 1.4303 A°,
B9 = 0.969 A°, *B10* = 1.0965 A°,
B11 = 1.1016 A°, C1-C2-C3 = 117.4°,
C2-C1-O 113.8°, C1-C2-O = 122.4°,
C1-O-H = 105.7°, H-C1-H = 107.3°,
H-C1-C2 = 107.7°, C2-C3-O = 109.7°,
C3-C2-O = 120.2°, C3-O-H = 108.4°,
O-C1-C2-O = -147.3°, O-C3-C2-O = -148.6°.

Fig. 4. RB3LYP/6-31G(d) geometric parameters of dihydroxyacetone (**DHA**).

state, and due to the large size and complex nature, the PCM model with RB3LYP or RHF method has been used to simplify the optimization of some compounds in the GAUSSIAN 98 program (Becke, 1992a, 1992b, 1993, 1996; Foresman & Frisch, 1996; Frisch & Foresman, 1998; Hehre et al., 1986; Larid, Ross, & Ziegler, 1996; Miertus & Tomasi, 1982; Miertus, Scrocco, & Tomasi, 1981; Salahub et al., 1991; Springborg, 1995; Young, 2001). 6-31G(d) polarized basis set (Foresman & Frisch, 1996; Frisch & Foresman, 1998; Hehre et al., 1986; Young, 2001) 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). Many of the compounds in the proposed mechanisms may be favorable in their cyclic forms (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993) and, therefore, special care has been taken to avoid the possible intramolecular cyclization during the optimization. All RB3LYP/6-31G(d), PCM/RB3LYP/6-31G(d) or PCM/RHF/6-31G(d) optimized structures have been taken for RB3LYP/6-31G(d) and PCM/RB3LYP/6-31G(d) frequency calculations to achieve the relevant zero point energy (ZPE) and the Gibb's free energy (G°) in the gaseous and aqueous states, respectively (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). Single point energy calculations in the gaseous and aqueous states have been performed on the RB3LYP/6-31G(d), PCM/RB3LYP/6-31G(d) or PCM/RHF/6-31G(d) optimized structures by using RB3LYP/6-31 G(d) and PCM/RB3LYP/6-31G(d), respectively (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 single point energies to obtain the total electronic energies (E°). Finally, electronic and free energy changes ($\Delta E^{\circ} = E^{\circ}_{\text{Product(s)}} - E^{\circ}_{\text{Reactant(s)}}$, and $\Delta G^{\circ} = G^{\circ}_{\text{Product(s)}} - G^{\circ}_{\text{Reactant(s)}}$, respectively) for different compounds in the proposed mechanisms (Figs. 2 and 3) have been calculated by following the total mass balance of the reaction. Thus, the possibility and internal energy changes for the formation of different compounds in the proposed mechanisms have been investigated.

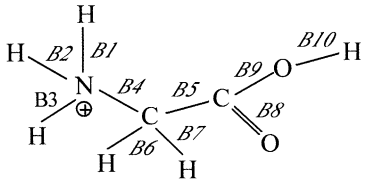
3. Results and discussion

At a constant temperature and pressure, ΔE and ΔG of a reaction indicate the internal energy changes and spon-



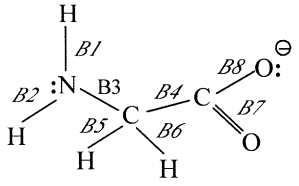
B1 = 1.0177 A°, *B2* = 1.0179 A°, *B3* = 1.4614 A°, *B4* = 1.5174 A°, *B5* = 1.093 A°, *B6* = 1.1079 A°, *B7* = 1.2094 A°, *B8* = 1.3568 A°, *B9* = 0.9757 A°, H-N-H = 107°, N-C-C = 112.2°, C-O-H = 106.1°, C-C-O-H = -178.8°.

UGly



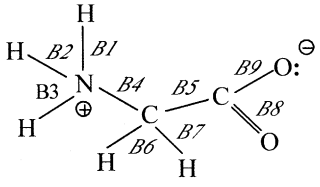
B1 = 1.0484 A°, *B2* = 1.026 A°, *B3* = 1.026 A°, *B4* = 1.511 A°, *B5* = 1.5332 A°, *B6* = 1.0917 A°, *B7* = 1.0917 A°, *B8* = 1.2135 A°, *B9* = 1.3177 A°, *B10* = 0.9795 A°, N-C-C = 105.4°, C-O-H = 110°, C1-C2-O = 108.4°, C-C-O-H = -180°.

PGly



B1 = 1.03 A°, *B2* = 1.0239 A°, *B3* = 1.4818 A°, *B4* = 1.5731 A°, *B5* = 1.1022 A°, *B6* = 1.0979 A°, *B7* = 1.2532 A°, *B8* = 1.2635 A°, H-N-H = 101.4°, N-C-C = 114.1°, H-C-H = 105.89°, N-C-C-O = -168.3°, N-C-C-O = 13.5°.

DGly



B1 = 1.02902 A°, *B2* = 1.02907 A°, *B3* = 1.0548 A°, *B4* = 1.50323 A°, *B5* = 1.55 A°, *B6* = 1.0974 A°, *B7* = 1.0949 A°, *B8* = 1.2666 A°, *B9* = 1.24535 A°, N-C-C = 106.7°, C-C-O = 114.9°, C-C-O = 116.5°, N-C-C-O = -7.4°, N-C-C-O = 173.2°.

GlyZ

Fig. 5. RB3LYP/6-31G(d) geometric parameters of unprotonated glycine (**UGly**), protonated glycine (**PGly**), deprotonated glycine (**DGly**) and glycine zwitterion (**GlyZ**).

Table 1
ΔG° (in kJ/mol) for the formation of different compounds during the Heyns rearrangement (**HR**) in the initial stage of **DHA + Gly** Maillard reaction under different conditions, calculated by using **DHA + Gly** total free energies ($G^{\circ}_{\mathrm{DHA}} + G^{\circ}_{\mathrm{uGly/PGly/DGly/Glyz}}$) as the standard in the equation $\Delta G^{\circ} = G^{\circ}_{\mathrm{Product(s)}} - G^{\circ}_{\mathrm{Reactant(s)}}$

Reactions →	**DHA + UGly**		**DHA + PGly**	
	Gaseous	Aqueous	Gaseous	Aqueous
PDHA	25.1	154.7	–	–
CatDG	−270.5	175.3	−77.5	229.2
DGadd	−14.0	8.7	179.1	62.7
DGSB	−12.6	−3.6	180.4	50.4
CatDGSB	−253.0	173.3	60.0	227.3
HRPE	−0.54	10.0	192.5	64.4
HRPK	−48.1	−36.0	145.0	82.4
	DHA + DGly		**DHA + GlyZ**	
CatDG(DGly)	−73.2	−32.8	–	–
CatDG(GlyZ)	–	–	339.5	395.7
DGadd(DGly)	−86.2	−16.1	639.5	161.5
DGSB(DGly)	−101.4	−19.5	624.3	158.1
CatDGSB(DGly)	−275.6	−326.4	450.1	503.9
HRPE(DGly)	−127.8	−44.7	597.8	132.8
HRPK(DGly)	−130.0	−82.5	595.7	95.2

For abbreviations and details of the compounds, see the captions and mechanisms of Figs. 2 and 3.

taneity of the reaction, respectively. ΔG° for the formation of different compounds in the proposed mechanisms under different pH conditions (Figs. 2 and 3) are presented in Table 1, and were calculated by using **DHA + Gly** total free energies ($G^{\circ}_{\mathrm{DHA}} + G^{\circ}_{\mathrm{uGly/PGly/DGly/Glyz}}$) as the standard in the equation $\Delta G^{\circ} = G^{\circ}_{\mathrm{product(s)}} - G^{\circ}_{\mathrm{Reactant(s)}}\Delta E^{\circ}$ for the formation of different compounds in the proposed mechanisms are presented in Table 2, and were calculated by using **DHA + Gly** total electronic energies ($E^{\circ}_{\mathrm{DHA}} + E^{\circ}_{\mathrm{uGly/pGly/DGly/Glyz}}$) as the standard in the equation

Table 2
ΔE° (in kJ/mol) for the formation of different compounds during the Heyns rearrangement (**HR**) in the initial stage of **DHA + Gly** Maillard reaction under different pH conditions, calculated by using **DHA + Gly** total electronic energies ($E^{\circ}_{DHA} + E^{\circ}_{uGly/PGly/DGly/Glyz}$) as the standard in the equation $\Delta E = E^{\circ}_{Product(s)} = E^{\circ}_{Reactant(s)}$

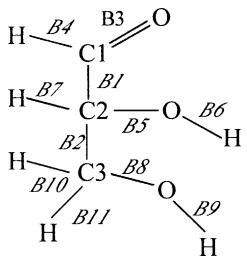
Reactions →	**DHA + UGly**		**DHA + PGly**	
	Gaseous	Aqueous	Gaseous	Aqueous
PDHA	20.1	149.8	–	–
CatDG	−324.6	−67.4	−110.1	−12.6
DGadd	−71.1	−10.5	143.3	44.4
DGSB	−21.9	11.8	192.5	66.6
CatDGSB	−263.7	−40.7	−49.2	14.3
HRPE	−10.8	23.7	203.6	78.6
HRPK	−55.6	−24.1	158.8	30.8
	DHA + DGly		**DHA + GlyZ**	
CatDG(DGly)	−63.6	−6.8	–	–
CatDG(GlyZ)	–	–	130.9	218.2
DGadd(DGly)	−81.3	4.9	587.3	109.0
DGSB(DGly)	−57.4	40.8	611.2	144.8
CatDGSB(DGly)	−61.2	557.1	607.3	661.2
HRPE(DGly)	−83.0	16.6	585.6	120.7
HRPK(DGly)	−80.6	−16.4	587.9	87.5

For abbreviations and details of the compounds, see the captions and mechanisms of Figs. 2 and 3.

$\Delta E^{\circ} = E^{\circ}_{product(S)} - E^{\circ}_{Reactant(s)}$. The total mass balance of any reaction is important as it is related to the energy changes. The total mass balance of **DHA + Gly** reaction under different conditions has been maintained during the calculation of ΔG° and ΔE°. The main problem in balancing the total mass arises for the protonation ($+H^{+}$) and deprotonation ($-H^{+}$). Therefore, the following equation has been applied during balancing the total mass:

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

According to ΔG° (Table 1), protonation of **DHA** to **PDHA** is not favorable in both of the gaseous and aqueous state **DHA+UGly** reactions. It is difficult to explain the unfeasibility of the protonation of **DHA** to **PDHA**. According to ΔE° (Table 2) **PDHA** is electronically more unstable in the aqueous state than in the gaseous state. In comparison, previous computational study revealed that protonation of **Gald** is favorable in the gaseous phase **Gald + UGly** reaction (Shipar, 2004). Except **PDHA**, formation of all other compounds in the proposed mechanism for **DHA + UGly** reaction has been found to be feasible in the gaseous state (Table 1). Therefore, it is possible that instead of the protonation of **DHA** to **PDHA**, direct nucleophilic addition of **DHA** and **UGly** occurs in the gaseous phase **Gald + UGly** reaction leading to formation of **CatDG**, which can consequently produce **HRP**s. It is also possible that some other compounds, such as 1,2,3-10 trihydroxypropane [$H_2C(OH)HC(OH)H_2C(OH)$] formed through the nucleophilic addition of **DHA** and H_2O, are involved in the initial step. Interconversion of **DHA** to **Gald** (Fig. 1) is found not to be favorable in both of the gaseous and aqueous states. ΔG°_{gas} and ΔG°_{aq} for the interconversion of **DHA** to **Gald**, have been calculated as 20.5 kJ/mol (relative $\delta E^{\circ}_{gas} = 20.1$ kJ/mol) and 1.1 kJ/mol (relative $\Delta E^{\circ}_{aq} = 0.8$ kJ/mol), obtained by using **DHA** free energy and electronic energy (G°_{DHA} and E°_{DHA}) as the standard in the equations $\Delta G^{\circ} = G^{\circ}_{Product(s)} - G^{\circ}_{Reactant(s)}$ and $\Delta E^{\circ} = E^{\circ}_{Product(s)} - E^{\circ}_{Reactant(s)}$, respectively. As **DHA** is a ketose and **Gald** is an aldose sugar, and ketoses are naturally more stable than aldoses, interconversion of **DHA** to **Gald** is assumed naturally not to be favorable, and the result is consistent with this assumption. The same values for ΔG° and ΔE° with negative signs (−20.5, −1.1 kJ/mol and −20.1, −0.8 kJ/mol, respectively) have been found for the interconversion of **Gald** to **DHA**, which reveal that interconversion of **Gald** to **DHA** is more favorable in the gaseous state reaction than that of the aqueous state, and it is also in agreement with the above natural postulation. However, adequate experimental data are still not available to evaluate this assumption. Some



B1 = 1.5236 A°, *B2* = 1.53655 A°,
B3 = 1.20501 A°, *B4* = 1.114 A°,
B5 = 1.41903 A°, *B6* = 0.97026 A°,
B7 = 1.105068 A°, *B8* = 1.41162 A°,
B9 = 0.973733 A°, *B10* = 1.096114 A°,
B11 = 1.1048 A°, C1-C2-C3 = 109.9°,
C2-C1-O = 125°, C1-C2-O = 108.4°,
C2-O-H = 107.7°, C1-C2-O-H = -167.1°,
O-C1-C2-O = 3.3°, C2-C3-O-H = -42.2°.

Fig. 6. RB3LYP/6-31G(d) geometric parameters of glyceraldehyde (**Gald**).

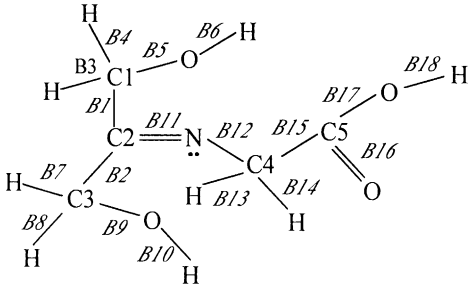
important geometric parameters of **DHA** and **Gald**, used in the present study, are presented in Figs. 4 and 6, respectively.

DHA + UGly aqueous phase reaction is found not to be favorable for the formation of **PDHA**, **CatDG**, **DGadd**, **CatDGSB** and **HRPE** (Table 1). Therefore, it is possible that nucleophilic addition of **DHA** and **UGly** immediately follows the elimination of one molecule of H_2O to form **DGSB**, which will directly rearrange to **HRPK** through intramolecular rearrangement in the aqueous phase **DHA + UGly** reaction. It is also possible that some other mechanisms are involved in this case, and sufficient information is still not obtainable. According to ΔE° (Table 2), **CatDG** and **CatDGSB** have been found electronically to be more stable species than the others in the **DHA + UGly** gaseous phase reaction, whereas **CatDG** appears to be a more stable species than the others in the aqueous phase **DHA + UGly** reaction.

Except **CatDG** in the gaseous state, formation of all other compounds in the proposed mechanism for **DHA + PGly** reaction (Fig. 2) has been found not to be favorable in both of the gaseous and aqueous states (Table 1). Therefore, it is assumed that the reaction is hindered for the formation of **HRP**s under this condition. Some other mechanisms may also be involved in this case. **CatDG** has been found electronically to be the most stable species in both of the gaseous state **DHA + PGly** reactions (Table 2).

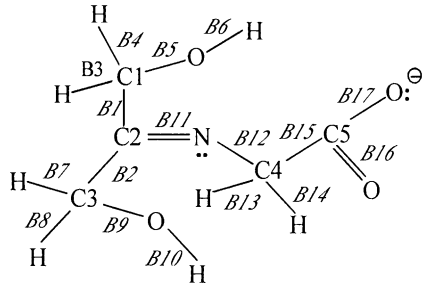
The Schiff bases (**SB**s) are one of the most common intermediates in the Maillard reaction (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). **DHA + PGly** and **DHA + GlyZ** reactions are not favorable for the formation of **SB**s, whereas, **DHA + UGly** and **DHA + DGly** reactions are supposed to be favorable for the formation of **SB**s, i.e., **DGSB** and **DGSB(DGly)**, respectively (Table 1). The gaseous phase reaction is assumed more favorable for the formation of **SB**s (Table 1). **DGSB** and [**DGSB(DGly)**] are supposed to electronically be more stable in the gaseous phase **DHA + UGly** and **DHA + DGly** reactions, respectively (Table 2). Some important RB3LYP/6-31G(d) optimized geometric parameters of **SB**s, used in the present study, are presented in Fig. 7.

In both of the gaseous and aqueous states, **DHA + DGly** reaction has been found as favorable for the formation of all compounds in the proposed mechanism, whereas **DHA + GlyZ** reaction has been found not to be feasible for the formation of all compounds in the proposed mechanism (Table 1). Therefore, like **DHA + PGly** reaction, **DHA + GlyZ** reaction is also postulated to be stalled for the production of **HRP(DGly)**s in both of the gaseous and aqueous states, and **DHA + DGly** reaction is assumed to be the most favorable for the production of **HRP(DGly)**s. In both of the gaseous and aqueous states, **DHA + DGly** reaction is assumed favorable for the formation of **HRP(DGly)**s (Table 1), which is in consistent with the previous report for the formation of the Amadori rearrangement products [**ARP(DGly)**s] in the **Gald + DGly** reaction (Shipar, 2004). However, production of **HRP(DGly)**s in the **DHA + DGly** reaction is assumed to be more favorable than the production of **ARP(DGly)**s in the **Gald + DGly** reaction (Shipar, 2004). Formation of **HRPK** in the **DHA + UGly** reaction appears to be favorable in both of the gaseous and aqueous states, whereas formation of **HRPE** is favorable in the gaseous state **DHA + UGly** reaction (Table 1). In comparison, both of the gaseous and



B1= 1.5154 A°, *B2*= 1.5271 A°, *B3*= 1.0937 A°, *B4* = 1.0948 A°, *B5*= 1.4392 A°, *B6*= 0.9707 A°, *B7*= 1.0984 A°, *B8*= 1.1063 A°, *B9*= 1.4096 A°, *B10*= 0.9756 A°, *B11*= 1.2766 A°, *B12*= 1.4584 A°, *B13* = 1.1023 A°, *B14*= 1.097 A°, *B15*= 1.5205 A°, *B16*= 1.2109 A°, *B17*= 1.3501 A°, *B18*= 0.9759 A°, C_1-C_2-C_3 = 116.3°, C_2-C_1-O = 110.8°, C_1-O-H = 107.4°, C_3-O-H = 106.6°, C_2-N-C_4 = 118.5°, C_1-C_2-N-C_4 = 179.1°, C_2-N-C_4-C_5 = 176.8°, C_4-C_5-O-H = -179.1°.

DGSB



B1= 1.5122 A°, *B2*= 1.5346 A°, *B3*= 1.0952 A°, *B4*= 1.0973 A°, *B5*= 1.4431 A°, *B6*= 0.998 A°, *B7*= 1.1 A°, *B8*= 1.0961 A°, *B9*= 1.4248 A°, *B10*= 0.9796 A°, *B11*= 1.2779 A°, *B12*= 1.4376 A°, *B13*= 1.1 A°, *B14*= 1.0961 A°, *B15*= 1.6176 A°, *B16*= 1.2422 A°, *B17*= 1.2637 A°, C_1-C_2-C_3 = 114.9°, C_2-C_1-O = 104°, C_1-O-H = 105.1°, C_3-O-H = 104.1°, C_2-N-C_4 = 118.8°, C_1-C_2-N-C_4 = 148°, C_2-N-C_4-C_5 = -74.6°.

DGSB(DGly)

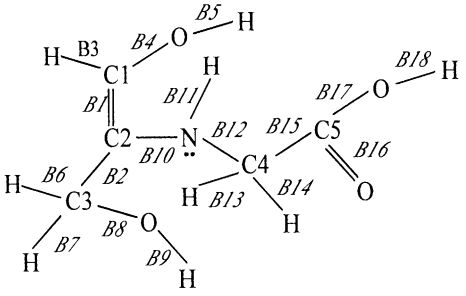
Fig. 7. RB3LYP/6-31G(d) geometric parameters of the Schiff bases.

aqueous phase **Gald + UGly** reaction were reported as not feasible for the formation of the enol form of the Amadori rearrangement product (**ARPE**) (Shipar, 2004). Both **DHA + PGly** and **DHA + GlyZ** reactions are not favorable for the formation of **HRP**s [**HRPE** or **HRPE(DGly)** and **HRPK** or **HRPK(DGly)**] in both of the gaseous and aqueous states (Table 1) and, therefore, formation of **HRP**s under these conditions is assumed to be impeded. Some other mechanisms may also be involved in these cases. The gaseous phase **DHA + Gly** reaction is assumed more feasible for the production of **HRP**s than the that of the aqueous phase, which is consistent with the previous report that the gaseous phase **Gald + Gly** reaction is more plausible for the production of **ARP**s than that of the aqueous phase (Shipar, 2004).

According to ΔE° (Table 2), **HRPE** is electronically more stable in the **DHA + UGly** gaseous phase reaction than that of the aqueous phase, whereas it is more stable in **DHA + PGly** aqueous phase reaction than that of the gaseous phase. **HRPK** has also been found to be electronically more stable in the gaseous phase than the aqueous phase **DHA + UGly** reaction, and more stable in the aqueous phase **DHA + PGly** reaction than that of the gaseous phase. It also reveals that **HRPK** is electronically more stable than **HRPE** in both of the gaseous and aqueous state reactions. **HRPK(DGly)** has also been found to be electronically more stable than **HRPE(DGly)** in both of the gaseous and aqueous phase reactions (Table 2).

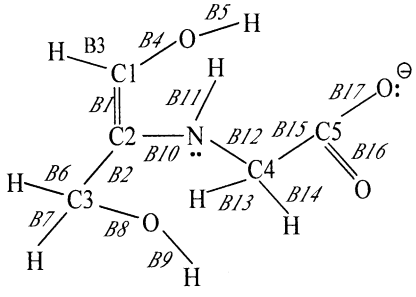
HRPs are the primary precursors of melanoidines and, therefore, have great importance in the Maillard reaction involving ketose sugars and amino compounds (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993; Wrodnigg & Eder, 2001). However, due to comparatively lower stability of these species, isolation and detection of **HRP**s in the Maillard reaction is assumed complicated. **HRP**s possess strong reducing properties (Davídek et al., 1990), and readily undergo further reactions to produce melanoidines through the formation of relative deoxyosones (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). **HRP**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). They crystallize in open chain forms but mainly as β-pyranoses (Davídek et al., 1990). A number of studies have been reported which show that if sufficient reactants are present and the reaction time is long enough, then **ARP**s can be formed under physiological conditions (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993), whereas such reports on **HRP**s are still not available. Some important RB3LYP/6-31G(d) optimized geometric parameters of **HRP**s, used in the present study, are presented in Figs. 8 and 9.

Ionic adducts, such as **CatDG**, **CatDGSB**, etc., may play an important role during the formation of the melanoidines, especially in **DHA + PGly** and **DHA + GlyZ** reactions. As these species are supposed to be formed readily in the reaction, they may have an outstanding role in the production of melanoidines. Direct cleavage or retro-aldolization of these species or other intermediates, **HRP**s as well as the parental sugars, may occur readily during the formation of melanoidines (Davídek et al., 1990; Eskin, 1990; Hodge, 1953; Hollnagel & Kroh, 1998; Macrane et al., 1993; Namiki & Hayashi, 1983; Tressl et al., 1995; Hayashi & Namiki, 1986; Weenen & Tjan, 1994). For example, hydroxyacetaldehyde (**Hald**) can be formed from **DHA** by C2-fragmentation



B1= 1.3472 A°, *B2*= 1.5137 A°, *B3*= 1.0852 A°, *B4* = 1.3658 A°, *B5*= 0.9803 A°, *B6*= 1.0962 A°, *B7*= 1.1007 A°, *B8*= 1.4366 A°, *B9*= 0.9721 A°, *B10*= 1.4255 A°, *B11*= 1.0194 A°, *B12*= 1.4418 A°, *B13* = 1.1 A°, *B14*= 1.097 A°, *B15*= 1.54 A°, *B16*= 1.204 A°, *B17*= 1.359 A°, *B18*= 1.972 A°, C_1-C_2-C_3 = 121.9°, C_2-C_1-O = 125.8°, C_1-O-H = 107.01°, H-C_1-C_2 = 123.1°, C_3-O-H = 107.04°, C_2-N-C_4 = 118.3°, H-C_1-O-H = -169.9°, C_2-N-C_4-C_5 = 75.3°, C_4-C_5-O-H = 4.9°.

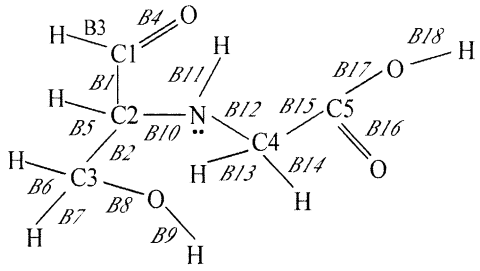
HRPE



B1= 1.3547 A°, *B2*= 1.5142 A°, *B3*= 1.0835 A°, *B4*= 1.3932 A°, *B5*= 0.9768 A°, *B6*= 1.0966 A°, *B7*= 1.0986 A°, *B8*= 1.4497 A°, *B9*= 0.9725 A°, *B10*= 1.3891 A°, *B11*= 1.0306 A°, *B12*= 1.453 A°, *B13*= 1.0982 A°, *B14*= 1.06 A°, *B15*= 1.5797 A°, *B16*= 1.2644 A°, *B17*= 1.2467 A°, C_1-C_2-C_3 = 119°, C_2-C_1-O = 124.07°, C_1-O-H = 105.8°, H-C_1-C_2 = 123.4°, C_3-O-H = 105.1°, C_2-N-C_4 = 121.8°, H-C_1-O-H = -160.4°, C_2-N-C_4-C_5 = 147.2°.

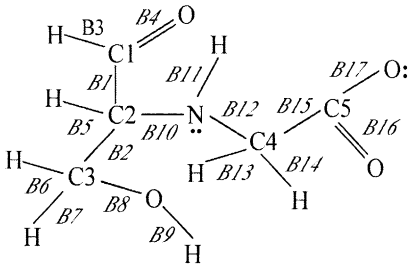
HRPE(DGly)

Fig. 8. RB3LYP/6-31G(d) geometric parameters of the enol form of the Heyns rearrangement products.



B1= 1.5328 A°, *B2*= 1.5357 A°, *B3*= 1.1141 A°, *B4*= 1.2076 A°, *B5*= 1.1121 A°, *B6*= 1.0921 A°, *B7*= 1.1029 A°, *B8*= 1.4161 A°, *B9*= 0.9698 A°, *B16*= 1.4648 A°, *B11*= 1.0185 A°, *B12*= 1.4507 A°, *B13*= 1.0961 A°, *B14*= 1.095 A°, *B15*= 1.517 A°, *B16*= 1.2113 A°, *B17*= 1.3491 A°, *B18*= 0.9761 A°, C_1-C_2-C_3 = 111.5°, C_2-C_1-O = 125°, H-C_1-C_2 = 114.4°, H-C_2-N = 111.4°, C_3-O-H = 107.8°, C_2-N-C_4 = 116°, H-C_1-C_2-C_3 = 179.3°, C_2-N-C_4-C_5 = 154.3°, C_4-C_5-O-H = 177.4°.

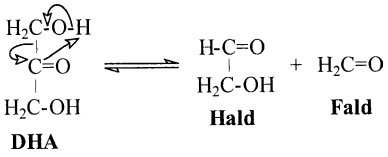
HRPK



B1= 1.5257 A°, *B2*= 1.5369 A°, *B3*= 1.1147 A°, *B4*= 1.215 A°, *B5*= 1.1021 A°, *B6*= 1.0939 A°, *B7*= 1.0956 A°, *B8*= 1.4373 A°, *B9*= 0.9695 A°, *B10*= 1.4654 A°, *B11*= 1.0278 A°, *B12*= 1.4759 A°, *B13*= 1.1 A°, *B14*= 1.0977 A°, *B15*= 1.5748 A°, *B16*= 1.2645 A°, *B17*= 1.282A°, C_1-C_2-C_3 = 113.6°, C_2-C_1-O = 126.4°, H-C_1-C_2 = 112.6°, H-C_2-N = 108°, C_3-O-H = 105.9°, C_2-N-C_4 = 115.4°, H-C_1-C_2-C_3 = 172.6°, C_2-N-C_4-C_5 = 94.7°.

HRPK(DGly)

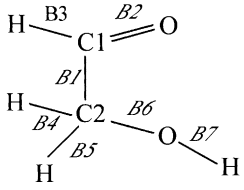
Fig. 9. RB3LYP/6-31G(d) geometric parameters of the keto form of the Heyns rearrangement products.



DHA **Hald** **Fald**

Fig. 10. Fragmentation of dihydroxyacetone (**DHA**) to hydroxyacetaldehyde (**Hald**) and formaldehyde (**Fald**).

(Fig. 10). ΔG°_{gas} and ΔG°_{aq} for the production of **Hald** from **DHA** have been calculated as −0.03 kJ/mol (respective $\Delta E^{\circ}_{gas} = 12.1$ kJ/mol) and −37.6 kJ/mol (respective $\Delta E^{\circ}_{aq} = -8.9$ kJ/mol), respectively. It reveals that formation of **Hald** through the C2-fragmentation of **DHA** is more favorable in the aqueous state than in the gaseous state. This is consistent with the previous findings that **Hald** is produced as a C2-sugar fragmentation product in the early stage of the Maillard reaction, especially in aqueous solution (Namiki & Hayashi, 1983; Hayashi & Namiki, 1986). Computational studies on **Gald** and **Gly** Maillard reaction also revealed that formation of **Hald** from **Gald** is favorable in the aqueous state, and not in the gaseous state (Shipar, 2004). Due to the high browning activity, C2-sugar fragmentation products are important in the Maillard reaction. Higher browning activity of **Hald** than other carbonyl compounds has been reported by Namiki and Hayashi (1983), and Hayashi and Namiki (1986). Though **Hald** is not a reducing sugar, having carbonyl and hydroxyl groups it is structurally similar to sugars and, therefore, can lead to the formation of browning products through the Maillard reaction (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993; Namiki & Hayashi, 1983; Weenen & Tjan, 1994). In **Hald**, the H atoms are electrophilic, and due to the existence of only one hydroxyl group, which is a nucleophile, the electron flow to the carbonyl carbon is assumed lower than that of **Gald**, glucose, etc. Therefore, positive charge on the carbonyl carbon of **Hald** might be higher than that of other carbonyl compounds, and hence, the carbonyl carbon of **Hald** might be more suitable for nucleophilic attack. The nucleophilic amino groups of amino compounds with the loan pair electron on the nitrogen atom can readily attack the electron deficient carbonyl carbon of **Hald**, leading to the formation of melanoidines. For the formation of **Hald** as a C2-sugar fragmentation product, the rate of browning in the sugar–amino compound reaction, such as in **DHA** + **Gly** reaction, can be enhanced. By using PCILO semi-emprical quantum-chemical method, some electronic structures of **Hald** have been studied by Fedoronko, TemKovic, Konigstein, Kovacik, and Tvaroska (1980). Peräkylä (1997) used Ab initio quantum mechanical calculations up to MP4(SDQ)/6-31+G**// HF/6-31+G*, and the solvent effect has been observed by using the polarisable continuum method (PCM). Some important RB3LYP/6-31G(d) geometric parameters of **Hald**, used in the present study, are presented in Fig. 11.



B1= 1.5112 A°, *B2*= 1.2139 A°, *B3*= 1.1089 A°, *B4*= 1.1049 A°, *B5*= 1.3987 A°, *B6*= 1.1045 A°, *B7*= 0.9767 A°, O-C_1-C_2 = 121.5°, H-C_1-C_2 = 116.9°, C_1-C_2-O = 111.8°, O-C_1-C_2-O = 0°, C_1-C_2-O-H= 0°.

Fig. 11. RB3LYP/6-31G(d) geometric parameters of hydroxyacetaldehyde (**Hald**).

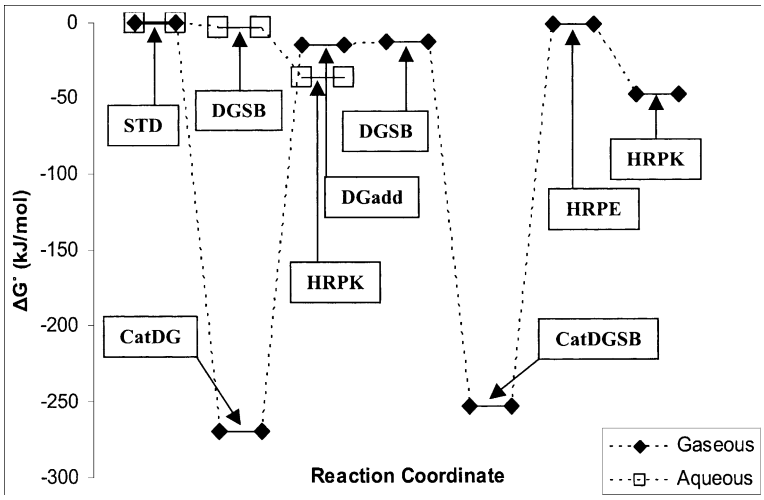


Fig. 12. Possible low energy (ΔG°) diagram for the formation of the Heyns rearrangement products (**HRP**s) in the initial stage of **DHA + UGly** reaction in the gaseous and aqueous states, obtained by using **DHA + UGly** total free energies ($G^{\circ}_{\mathrm{DHA}} + G^{\circ}_{\mathrm{uGly}}$) as the standard (**STD**). For abbreviations and details of the compounds, see the caption and mechanism of Fig. 2.

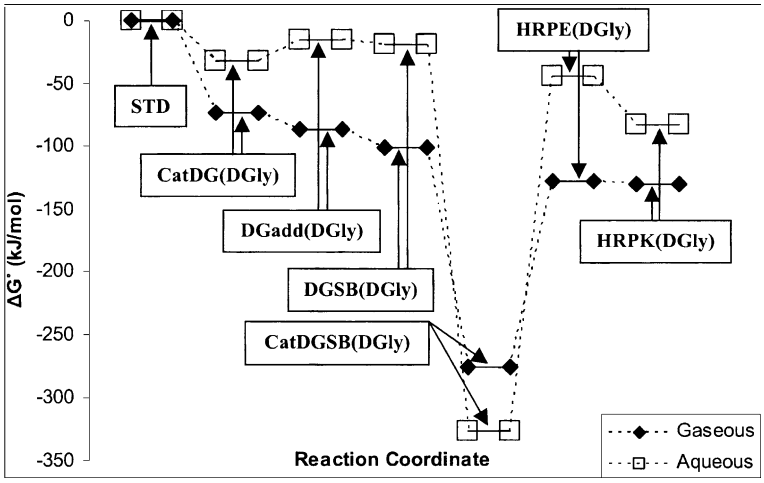


Fig. 13. Possible low energy (ΔG°) diagram for the formation of the Heyns rearrangement products (**HRP**s) in the initial stage of **DHA + DGly** reaction in the gaseous and aqueous states, obtained by using **DHA + DGly** total free energies ($G^{\circ}_{\mathrm{DHA}} + G^{\circ}_{\mathrm{DGly}}$) as the standard (**STD**). For abbreviations and details of the compounds, see the caption and mechanism of Fig. 3.

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

4. Conclusion

Density functional computations have been performed at the standard state on the proposed mechanisms for the Heyns rearrangement during the initial stage of **DHA + Gly** Maillard reaction under different

pH conditions. By following the total mass balance, the possibility for forming different compounds in the proposed mechanisms has been investigated through the estimation of ΔG° and ΔE°. The results reveal that basic conditions play an important role during the production of **HRP**s in the initial stage of the reaction. **DHA + DGly** reaction under basic conditions is supposed to be the most favorable for the formation of **HRP(DGly)**s. The gaseous phase reaction is assumed more favorable for the production of **HRP(DGly)**s than the aqueous phase reaction. As the production of both **HRPE(DGly)** and **HRPK(DGly)** is feasible in **DHA + DGly** reaction, the rate of browning under this condition is assumed to be higher than that of the others. The Maillard reaction can take place in foods as well as in the human body (human blood is slightly basic) and, therefore, these findings are important and consistent with previous statements (Davídek et al., 1990; Eskin, 1990; Ledl & Schleicher, 1990; Macrane et al., 1993; Meade et al., 2003; Reber et al., 2002). **DHA + UGly** reaction under neutral conditions is supposed to be the second most favorable for the production of **HRP**s, and the reaction in the gaseous state is assumed more feasible than that of the aqueous state. However, the aqueous phase **DHA + UGly** reaction has been found not to be feasible for the formation of **HRPE**. Based on ΔG°, the possible low energy diagram for the formation of **HRP**s in **DHA + UGly** and **DHA + DGly** reactions are presented in Figs. 12 and 13, respectively. Formation of **HRP**s in **DHA + PGly** and **DHA + GlyZ** reactions is supposed to be unfeasible and, therefore, the rate of browning under these conditions is assumed to be much more hindered than that of **DHA + UGly** and **DHA + DGly** reactions. This is in agreement with the previous statement that acidic or protonated forms of amino groups of amino compounds are not favorable for the Maillard reaction (Davídek et al., 1990; Eskin, 1990; Macrane et al., 1993). However, some other mechanisms may be engaged under these conditions. Interconversion of **DHA** to **Gald** is assumed not to be feasible, whereas interconversion of **Gald** to **DHA** is more favorable in the gaseous state than in the aqueous state. Production of **Hald** from **DHA** is supposed to be more favorable in the aqueous state than in the gaseous state. Adequate information on the **DHA + Gly** reaction is still lacking and, therefore, to establish a proper reaction mechanism and find out the role of **DHA** and **Gly** in vivo as well as vitro, further extensive theoretical and experimental studies on the reaction are still in demand. In addition, the global minima, maxima and transition states of different compounds on the potential energy surfaces are also necessary . In order to fulfill this intention, the theoretical results, presented in this paper, are thought to be helpful for further theoretical investigations. Computational studies on the intermediate and final stages of the reaction are also necessary. The collective result could provide important clues that will be helpful fore establishing a mechanism leading to approtriate ways of controlling the Maillard reaction in vivo as weel as vitro.

References

Ames, J. M. (1990). Control of the Maillard reaction in food systems. *Trends in food science and Technology, 1*, 150–154.

Becke, A. D. (1992a). Density-functional thermochemistry I, the effect of the exchange-only gradient correction. *The journal of Chemical Physics, 96*, 2155–2160.

Becke, A. D. (1992b). Density-functional thermochemistry II, the effect of the Perdew–Wang generalized-gradient correlation correction. *The Journal of Chemical Physics, 97*, 9173–9177.

Becke, A. D. (1993). Density-functional thermochemistry III, the role of exact exchange. *The Journal of Chemical Physics, 98*, 5648–5652.

Becke, A. D. (1996). Density-functional thermochemistry IV, a new dynamical correlation functional and implications for exact-exchange mixing. *The Journal of Chemical Physics, 104*, 1040–1046.

Brown, D. A. (2001). Skin pigmentation enhancers. *Journal of Photochemistry and Photobiology B: Biology, 63*, 148–161.

Csazer, A. G. (1992). Conformers of gaseous glycine. *Journal of the American Chemical society, 114*, 9568–9575.

Davídek, J., Velíšek, J., & Pokorný, J. (1990). *Development in food science: Chemical changes during food processing* (Vol. 21, pp. 117–152). Amsterdam: Elsevier Science Publishers.

Eskin, N. A. E. (1990). *Biochemistry of foods* (pp. 239–296) (2nd ed.). San Diego: Academic Press, Inc.

Fedoronko, M., TemKovic, P., Konigstein, J., Kovacik, V., & Tvaroska, I. (1980). Study of the kinetics and mechanism of the acid–base-catalyzed enolization of hydroxyacetaldehyde and methoxyacetaldehyde. *Carbohydrate Research, 87*, 35–50.

Feige, K., Ried, T., & Bachmann, K. (1996). Determination of formaldehyde by capillary electrophoresis in the presence of a dihydroxyacetone matrix. *Journal of Chromatography A, 730*, 333–336.

Foresman, J. B., & Frisch, A. (1996). *Exploring chemistry with electronic structure methods* (2nd ed.). Pittsburgh, USA: Gaussian, Inc.

Frisch, Æ, & Foresman, J. B. (1998). *Gaussian 98 user's reference*. Pittsburg, USA: Gaussian, Inc.

Harrold, H. (1991). *Organic chemistry: a short course* (pp. 425–467) (8th ed.). Boston: Houghton Mifelin Company.

Hayashi, T., & Namiki, M. (1986). Role of sugar fragmentation: an early stage browning of amino-carbonyl reaction of sugar and amino acid. *Agriculture and Biological Chemistry, 50*, 1965–1970.

Hehre, W. J., Radom, L., Schleyer, P. V. R., & Pople, J. A. (1986). *Ab initio molecular orbital theory*. New York: John Wiley & Sons.

Hodge, J. E. (1953). Chemistry of browning reactions in model systems. *Journal of Agricultural and Food Chemistry, 1*, 928–943.

Hollnagel, A., & Kroh, L. W. (1998). Formation of α-dicarbonyl fragments from mono- and disaccharides under caramelization and Maillard reaction conditions. *Zeitschrift fur Lebensmittel-Untersuchung und-Forschung, 207*, 50–54.

Holum, J. R. (1996). *Introduction to organic and biological chemistry* (pp. 196–204). New York: John Wiley & Sons Inc.

Hu, C. H., Shen, M., & Schaefer, H. F. (1993). Glycine conformational analysis. *Journal of the American Chemical Society, 115*, 2923–2929.

Jensen, J. H., & Gordon, M. S. (1991). Conformational potential energy surface of glycine: a theoretical study. *Journal of the American Chemical Society, 113*, 7917–7924.

Kobayashi, Y., Igarashi, T., Takahashi, H., & Higashi, K. (1976). Infrared and raman studies of 1,3-dihydroxyacetone, D(+)- and DL-glyceraldehyde. *Journal of Molecular Structure, 35*, 85–99.

Kobayashi, Y., & Takahashi, H. (1979). Conformational studies of glycolaldehyde and 1,3-dihydroxyacetone in solution by ^{1}H-NMR. *Specrochimica Acta A, 35*, 307–314.

Kurz, T. (1994). Formulating effective self-tanners with DHA. *Cosmetics and Toiletries, 109*, 55–61.

Labuza, T. P., & Saltmarch, M. (1981). The nonenzymatic browning reaction as affected by water in foods. In L. B. Rockland & B. S. Stewart (Eds.), *Water activity influences food quality* (pp. 605–639). New York: Academic Press.

Larid, B. B., Ross, R. B., & Ziegler, T. (1996). Density-functional methods in chemistry:An overview. In B. B. Larid, R. B. Ross, & T. Ziegler (Eds.), *Chemical applications of density-functional theory. American chemical society symposium series* (Vol. 629, pp. 1–19). Washington, DC: American Chemical Society.

Lea, C. H., & Hannan, R. S. (1949). Studies of the reaction between proteins and reducing sugars in the dry state I, the effect of activity of water, of pH and of temperature on the primary reaction between casein and glucose. *Biochimica et Biophysica Acta, 3*, 313–325.

Ledl, F., & Schleicher, E. (1990). New aspects of the Maillard reaction in foods and in the human body. *Angewandte Chemie International Edition in English, 29*, 565–594.

Lelj, F., Adamo, C., & Barone, V. (1994). Role of Hartree–Fock exchange in density functional theory: some aspects of the conformational potential energy surface of glycine in the gas phase. *Chemical Physics Letters, 230*, 189–195.

Lozynski, M., Rusinska-Roszak, D., & Mack, H. G. (1997). MP2 and density functional studies of hydrogen bonding in model trioses: D-(+)-glyceraldehyde and dihydroxyacetone. *The Journal of Physics Chemistry A, 101*, 1542–1548.

Macrane, R., Robinson, R. K., & Saadler, M. J. (1993). *Encyclopedia of food science, food technology and nutrition* (Vol. 1, pp. 146–166). London: Academic Press Limited.

Maillart, L. C. (1912). Action des acides aminés sur les sucres: formation des mélanoides par voi méthodique. *Comptes rendus de l Academie des Sciences Serie I, 145*, 66–68.

Marnett, L. J., Hurd, H. K., Hollstein, M. C., Levin, D. E., Wsterbauer, H., & Ames, B. N. (1985). Naturally occuring carbonyl compounds are mutagens in Salmonella tester strain TA104. *Mutation Research, 148*, 25–34.

Meade, S. J., Miller, A. G., & Gennard, J. A. (2003). The role of dicarbonyl compounds in non-enzymatic crosslinkings: a structure activity study. *Bioorganic and Medicinal Chemistry, 11*, 853–862.

Mersch-sundermann, V., Schneider, U., Klopman, G., & Rosencrantz, H. S. (1994). SOS induction in *Escherichia coli* and *Salmonella mutagenicity*: a comparison using 330 compounds. *Mutagenesis, 9*, 205–224.

Miertus, S., Scrocco, E., & Tomasi, J. (1981). Electrostatic interaction of a solute with a continuum: a direct utilization of ab initio molecular potentials for the prevision of solvent effects. *Chemical Physics, 55*, 117–129.

Miertus, S., & Tomasi, J. (1982). Approximate evaluations of the eletrostatic free energy and internal energy changes in solution processes. *Chemical Physics, 65*, 239–245.

Moore, W. J. (1962). *Physical chemistry* (3rd ed.). New Jersy: Prentice-Hall, Inc., Maruzen Co., Ltd.

Morita, J. (1991). Induction of strand breakage in DNA by hexose derivatives and carbonyl compounds. *Agricultural and Biological Chemistry, 55*, 2407–2408.

Namiki, M., & Hayashi, T. (1983). A new mechanism of the Maillard reaction involving sugar fragmentation and free radical formation. In G. R. Waller & M. S. Feather (Eds.), *The Maillard reaction in foods and nutrition,. American chemical society symposium series* (Vol. 215, pp. 1–46). Washington, DC: American Chemical Society.

Navrátil, M., Tkáč, J., Švitel, J., Danielsson, B., & Šturdik, E (2001). Monitoring of the bioconversion of glycerol to dihydroxyacetone with immobilized *Gluconobacter oxydans* cell using thermometric flow injection analysis. *Process Biochemistry, 36*, 1045–1052.

Nursten, H. E. (1986). Maillard browning reactions in dried foods. In D. MacCarthy (Ed.), *Concentration and drying of foods* (pp. 53–58). London: Elsevier Applied Science.

Palla, P., Petrongolo, C., & Tomasi, J. (1980). Internal rotation potential energy for the glycine molecule in its zwitterionic and neutral forms. A comparison among several methods. *The Journal of Physical Chemistry, 84*, 435–442.

Peräkylä, M. (1997). Ab initio quantum mechanical gas phase and reaction field solvation study on the proton abstraction from hydroxyacetaldehyde by formate: Implications for enzyme catalysis. *Journal of the Chemical Society, Perkin Transactions, 2*, 2185–2189.

Petersen, A. B., Wulf, H. C., Gniadecki, R., & Gajkowska, B. (2004). Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. *Mutation Research, 560*, 173–186.

Pham, H. N., DeMarini, D. M., & Brockmann, H. E. (1980). Mutagenicity of skin tanning lotions. *Journal of Environmental Pathology and Toxicology, 3*, 227–231.

Ramek, M., Cheng, V. K. W., Frey, R. F., Newton, S. Q., & Schäfer, L. (1991). The case of glycine continued: some contradictory SCF results. *Journal of Molecular Structure – Theochem, 235*, 1–10.

Reber, F., Kasper, M., Siegner, A., Kniep, E., Seigel, G., & Funk, R. H. W. (2002). Alteration of the intracellular pH and apoptosis induction in a retinal cell line by the AGE-inducing agent glyoxal. *Graefe's Archive for Clinical and Experimental Ophthalmology, 240*, 1022–1032.

Salahub, D. R., Fournier, R., Mlynarski, P., Papai, I., St-Amant, A., & Ushio, J. (1991). Gaussian-based density functional methodology, software, and applications. In J. K. Labanowski & J. W. Andzelm (Eds.), *Density functional methods in chemistry* (pp. 77–100). New York: Springer.

Shipar, M. A. H. (2004). Computational studies on glyceraldehyde and glycine Maillard reaction. *Journal of Molecular Structure – Theochem, 710*, 45–50.

Springborg, M. (1995). *Density-functional methods in chemistry and materials science*. New York: John Willy & Sons.

Stanko, R. T., & Adibi, S. A. (1986). Inhibition of lipid accumulation and enhancement of energy expenditure by the addition of pyruvate and dihydroxyacetone to a rat diet. *Metabolism, 35*, 182–186.

Thornalley, P., Wolff, S., Crabbe, J., & Stern, A. (1984). The autoxidation of glyceraldehyde and other simple monosaccharides under physiological conditions catalysed by buffer ions. *Biochimica et Biophysica Acta, 797*, 276–287.

Tressl, R., Nittka, C., & Kersten, E. (1995). Formation of isoleucine-specific Maillard products from [1-^{13}C]-D-glucose and [1-^{13}C]-D-fructose. *Journal of Agricultural and Food Chemistry, 43*, 1163–1169.

Wagen, V., Barua, T. K., Anthonsen, H. W., Hansen, L. K., Fossli, D. J., Hough, E., et al. (1994). Dihydroxyacetone dimmers; solution and crystal structure of sterioisomers of 2,5-diethoxy-l,4-dioxane-2,5-dimethanol. *Tetrahedron, 50*, 10055–10060.

Wrodnigg, T. M., & Eder, B. (2001) (pp. 115–152). *Topics in current chemistry* (Vol. 215). Berlin: Springer.

Yamaguchi, T. (1982). Mutagenicity of trioses and methyl glyoxan on *Salmonella typhimurium*. *Agricultural and Biological Chemistry, 46*, 849–851.

Yaylayan, V. A., Majors, S. H., & Ismail, A. A. (1999). Investigation of DL-glyceraldehyde–dihydroxyacetone interconversion by FTIR spectroscopy. *Carbohydrate Research, 318*, 20–25.

Young, D. C. (2001). *Computational chemistry: A practical guide for applying techniques to real world problems*. New York: John Wiley & Sons.

Zhu, Y., Youssef, D., Porte, C., Rannou, A., Ogletree, D., & Somarriba, B. L. M. L. (2003). Study of the solubility and the metastable zone of 1,3-dihydroxyacetone for the drowning-out process. *Journal of Crystal Growth, 257*, 370–377.

Weenen, H., Tjan De Valois, P. J., & Vonk, H. (1994). Mechanism of Pyrazine formation in thermally generated flavors. In T. H. Parliment, M. J. Morello, & R. J. McGorrin (Eds.), *Thermally generated flavours. American Chemical Society Symposium Series* (Vol. 543, pp. 142–157). Washington, DC: American Chemical Society.