The ribose and glycine Maillard reaction in the interstellar medium (ISM): A theoretical study

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Abstract.   Possibility of the Maillard reaction to take place in the gaseous phase in the interstellar medium was investigated by using Density Functional Theory (DFT) computations. Cyclic ribose (**c-Rib**)/ open-chain ribose (**c-Rib**) and glycine were taken as the model. Mechanisms have been proposed, and possibility of the formation of different compounds have been evaluated through calculating the Gibb's free energy changes for different steps of the reaction by following the total mass balance. The result reveals that both **c-Rib** and **Rib** can participate in the reaction, and **c-Rib** is more efficient than **Rib**. The reactions under basic and neutral conditions are supposed to be the first and second most favourable. Acidic conditions and the isoelectric point of glycine were unfeasible for the reaction. The kinetics of the mechanics are briefly addressed in this work.

Keywords.   Density functional computational study; ribose; glycine; Maillard reaction; gaseous phase interstellar medium.

1.   Introduction

Non-enzymatic browning, also known as the Maillard reaction,[1] occurs between carbonyl compounds, especially reducing sugars, and compounds with free amino groups, such as amines, amino acids, and proteins. The reaction in aqueous solution is usually vital to foods as well as to general biochemistry and even to medicine.[2–5] The gaseous phase Maillard reaction has not been well studied, and therefore, the role of the reaction under this condition is obscure. It is evident from theoretical and experimental studies to form larger sugars, such as ribose, from simple organic precursors in the gaseous phase.[6,7] However, no clear-cut evidence is still available. Ribose might have played an important role during the creation of the first living organism, could be in the gaseous phase interstellar medium, in the early history of earth or in the 'pre-RNA or RNA-world'.[8,9] Ribose can be formed from simple organic precursors, formaldehyde and glycolaldehyde.[10] Formaldehyde is a significantly abundant interstellar molecule, and glycolaldehyde has been detected in the interstellar medium.[11] Therefore, 'RNA world' is assumed to have a large

pre-biotic source of ribose, formed through the 'formose reaction' of formaldehyde and glycolaldehyde.[10,11]

Meteorites impact on Earth have been shown to carry many amino acids.[12] The amino acid, glycine, might have been detected in the gaseous phase in the interstellar medium.[13] However, this report has recently been challenged.[14] Blagojevic *et al* have proposed a possible ion–molecule reaction pathway to interstellar amino acid synthesis.[15] Jackson *et al*[16] have investigated the possibility of forming glycine from interstellar species through the ion–molecule reactions of ionized amine fragment compounds with neutral carboxylic acid and ester species. By taking these findings in mind, we can assume that ribose (from formaldehyde and glycolaldehyde) and glycine (from simple atmospherically abundant molecules) can be formed in the gaseous phase in the interstellar medium, and therefore, the Maillard reaction between ribose and glycine can take place under this condition. While bulk solvation effects have not been taken into consideration we believe that the scarce nature of the free solvents in the ISM will prevent such conditions from affecting the outcome. However, test calculations by our group reveal that such effects shall account statistically for less than 5% of ISM mediated mechanism.

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It is well known that organic molecules comprise more than 75% of known interstellar chemical species.[2] Therefore, a variety of gas phase interstellar reactions dominated by two-body, exothermic, ion–molecule reactions permit reactions that lead to synthesis of larger molecules in the interstellar medium (up to 12 atoms). There are many atmospherically abundant molecules, including molecular hydrogen (H_2), H_3^+, and H_3O^+ (H_2 is the most abundant interstellar chemical species) suggesting protonation may be an important ion–molecule reaction. Several different reaction conditions can be applied to catalyse the effective transformation of formaldehyde to ribose (Simonov *et al* 2007). There are many possible routes for this mechanism, among which α-hydroxy ketones can catalyse the reaction.

Due to the fact that formaldehyde ($CH_2=O$) is significantly abundant amongst the ~ 140 known interstellar molecules as well as the fact that protonated formaldehyde ($CH_2=OH^+$) has been detected we can use this to focus on similar reactions. In these experiments with formaldehyde[7] a gas phase protic variant of the formose reaction is generally explored at 2 mbar using hydronium ion (H_3O^+) as a proton donating source to formaldehyde. Therefore, by using gas-phase conditions of standard temperature and pressure with zero-point corrections we can develop a simulated environment of the ISM.

A primary motivation for this research involves the fact that even mechanisms with high reaction barriers can potentially lead to interesting experimentally viable biological products.[7] While the barriers observed are present (in the order of 50–60 kJ/mol) it must be noted that errors in the calculation exist. These computational faults lie in the order of 7–10 kcal/mol which in some cases would lead to a barrier-less chemical process. Experimentally important ISM product has been shown to form from the scheme we proposed and from further ISM observations we believe it to be a viable starting point for our model calculations.

In the present study, Density Functional Theory (DFT) computations have been applied to investigate possibility of the formation of the Amadori rearrangement products (**ARP**s) in the Maillard reaction between ribose and glycine in the gaseous phase. Mechanisms (figures 1 and 2) are proposed for the formation of **ARP**s in ribose + glycine Maillard reaction, followed usually the most accepted Hodge-scheme.[17] Ribose can exist in its open and closed chain or cyclic forms (**Rib** and **c-Rib**, respectively),[3,4,8,18,19] and therefore, both of these forms of

ribose have been considered in the present study to evaluate their activities in the reaction. Four forms of glycine (**Gly**), i.e. unionized or unprotonated glycine (**UGly**, $H_2N-CH_2-CO_2H$), protonated glycine (**PGly**, $H_3N^+-CH_2-CO_2H$), deprotonated glycine (**DGly**, $H_2N-CH_2-CO_2:^-$) and glycine zwitterion (**GlyZ**, $H_3N^+-CH_2-CO_2:^-$) under neutral (pH = 7), acidic (pH < 5·5), and basic (pH > 8) conditions and at the isoelectric point of glycine (I = pH ≈ 6), respectively,[3,4,18,19] are considered in the present study.

2. Computational methodology

All compounds in the proposed mechanisms (figures 1 and 2) have been optimized at RB3LYP/6-31G(*d*) in GAUSSIAN 98 program.[20] All RB3LYP/6-31G(*d*) optimized structures have been taken for RB3LYP/6-31G(*d*) frequency calculations to achieve the relevant zero point energy (ZPE) and the Gibb's free energy ($G°$) in the gaseous phase.[21] Opt = Z-matrix and/or Freq = No Raman keywords have been used when necessary.[21] By using RB3LYP/6-31G(*d*) on the RB3LYP/6-31G(*d*) optimized structures, relevant electronic energies in the gaseous have been
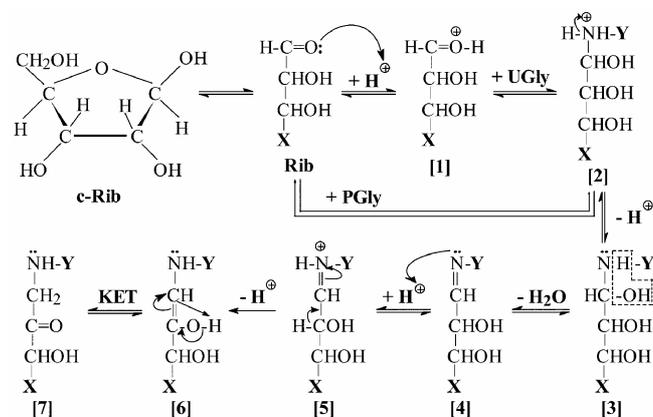
Figure 1. Proposed mechanisms for the formation of the Amadori rearrangement products in **c-Rib** + **UGly/Rib** + **UGly** and **c-Rib** + **PGly/Rib** + **PGly** Maillard reactions. Abbreviations: **c-Rib** = cyclic ribose; **Rib** = open-chain ribose; **KET** = keto-enolic tautomerization. Numerical 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$_2$OH and –CH$_2$–CO$_2$H groups, respectively. For other abbreviations, see the caption of figure 1.

calculated.[21] Relevant ZPE have been added to the electronic energies to get the total electronic energies ($E°$).[21]

Finally, electronic and free energy changes ($\Delta E° = E°_{\text{Product(s)}} - E°_{\text{Reactant(s)}}$, and $\Delta G° = G°_{\text{Product(s)}} - G°_{\text{Reactant(s)}}$, respectively) for different compounds in the proposed mechanisms 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. Relevant dipole moments (μ_{Gas}, in Debye) of different compounds in the gaseous phase have been obtained from the electronic energy calculations on the RB3LYP/6-31G(*d*) optimized structures at RB3LYP/6-31G(*d*).[21] Relevant heats of formation ($\Delta H°_f$) of different compounds have been obtained by performing AM1 semi-imperical calculations[21] on the RB3LYP/6-31G(*d*) optimized structures.

3. Results and discussion

3.1 *Thermochemistry*

At constant temperatures and pressures, ΔE and ΔG of a reaction indicate the internal energy changes
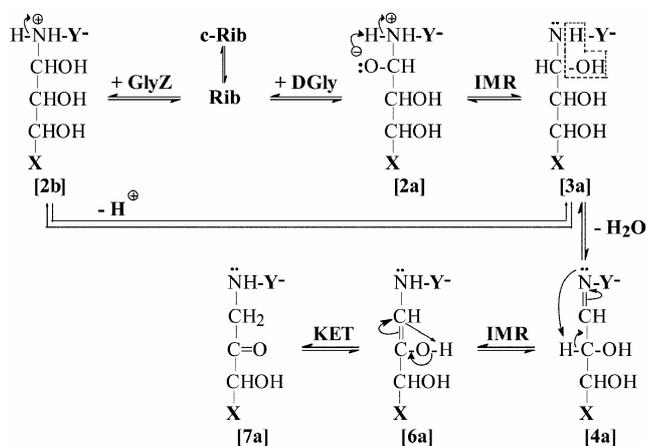
Figure 2. Proposed mechanisms for the formation of the Amadori rearrangement products in **c-Rib + DGly/Rib + DGly** and **c-Rib + GlyZ/Rib + GlyZ** Maillard reactions. Abbreviations: **IMR** = intramolecular rearrangement. Numerical abbreviations: **2a** = ionic addition adduct of **Rib** and **DGly**; **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). **Y⁻** Refers the $-CH_2-CO_2$:⁻ group. For other abbreviations, see the caption of figures 1 and 2.

and spontaneity of the reaction, respectively. $\Delta G°$ for the formation of different compounds in the proposed mechanisms for **c-Rib + Gly** (**Gly** refers **UGly**, **PGly**, **DGly** and **GlyZ**) and **Rib + Gly** reactions (figures 1 and 2) are presented in table 1. During calculating $\Delta G°$, **c-Rib+Gly** and **Rib+Gly** total free energies ($G°_{\text{c-Rib}} + G°_{\text{UGly/PGly/DGly/GlyZ}}$ and $G°_{\text{Rib}} + G°_{\text{UGly/PGly/DGly/GlyZ}}$, respectively) have been used as the standard in the equation $\Delta G° = G°_{\text{Product(s)}} - G°_{\text{Reactant(s)}}$. Table 1 also represents $\Delta E°$ for the formation of different compounds in the proposed mechanisms (figures 1 and 2), obtained by using **c-Rib + Gly** and **Rib + Gly** total electronic energies ($E°_{\text{c-Rib}} + E°_{\text{UGly/PGly/DGly/GlyZ}}$ and $E°_{\text{Rib}} + E°_{\text{UGly/PGly/DGly/GlyZ}}$, respectively) as the standard in the equation $\Delta E° = E°_{\text{Product(s)}} - E°_{\text{Reactant(s)}}$. Dipole moments (in Debye) and $\Delta H°_f$ (in kJ/mol) for different compounds in the proposed mechanisms (figures 1 and 2) are also presented in table 1. Table 2 represents some RB3LYP/6-31G(*d*) geometric parameters of different compounds presented in figures 1 and 2.

During the calculation of $\Delta G°$ and $\Delta E°$, 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. Molecular hydrogen (H_2), H_3^+, H_3O^+ etc. are present in the interstellar medium.[22] Therefore, the following equation has been applied during balancing the total mass:

$$H^+ + H_2O \leftrightarrow H_3O^+$$
Proton   water   hydroxonium ion
(protonation and deprotonation)
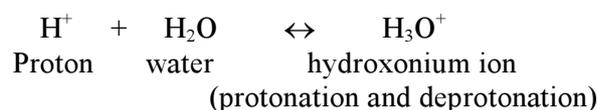
According to $\Delta G°$ (table 1), production of **Rib** from **c-Rib** is probable in **c-Rib + UGly** and **c-Rib + PGly** reactions, and not in **c-Rib + DGly** and **c-Rib + GlyZ** reactions. Possibility of producing **Rib** from **c-Rib** in **c-Rib + UGly** and **c-Rib + PGly** reactions is supposed to be almost same (table 1). Based on $\Delta E°$ (table 1), **Rib** is electronically more stable in **c-Rib + UGly** reaction than that of the others. Based on $\Delta G°$, protonation of **Rib** in **c-Rib + UGly** reaction is found to be more favourable than **Rib + UGly** reaction (table 1). Protonated ribose (**1**), formed in **c-Rib + UGly** reaction, is electronically more stable than that of **Rib + UGly** reaction.

Based on $\Delta G°$ (table 1), **c-Rib + UGly** and **Rib + UGly** reactions are found to be feasible for the formation of the ionic addition adduct, **2** (1-protonated glycino-pent-1,2,3,4,5-ol), ionic adduct of the Schiff base, **5** (ionic adduct of the Schiff base

Table 1. $\Delta G^{\circ}_{\text{gas}}$, $\Delta E^{\circ}_{\text{gas}}$, μ_{Gas}, and $\Delta H^{\circ}_{\text{f}}$ for different compounds presented in figures 1 and 2.

Compounds ↓	$\Delta G^{\circ}_{\text{Gas}}$ (kJ/mol)				$\Delta E^{\circ}_{\text{Gas}}$ (kJ/mol)				μ_{Gas} (Debye)	$\Delta H^{\circ}_{\text{f}}$ (kJ/mol)
	c-Rib + UGly	Rib + UGly	c-Rib + PGly	Rib + PGly	c-Rib + UGly	Rib + UGly	c-Rib + PGly	Rib + PGly		
Rib	−21·3	–	−21·28	–	−22·66	–	−22·6	–	2·0969	−979·4
1	−94·3	−73·0	–	–	−101·7	−79·2	–	–	7·261	−264·4
2	−167·9	−146·6	45·5	66·9	−222·4	−199·8	−7·9	14·6	7·4653	−788·4
3	37·8	59·0	251·3	272·6	−11·1	11·5	203·4	225·9	3·8739	−1381·9
4	4·3	25·6	217·8	239·1	−0·5	22·1	214·0	236·6	2·0875	−1105·8
5	−181·9	−160·6	31·6	52·9	−193·5	−170·9	21·0	43·6	4·2938	−515·9
6	25·3	46·6	238·8	260·1	13·2	35·8	227·7	250·3	3·3578	−1136·0
7	−32·7	−11·4	180·9	202·1	−40·7	−18·1	173·8	196·3	1·0744	−1149·5
Compounds ↓	c-Rib + DGly	Rib + DGly	c-Rib + GlyZ	Rib + PGly	c-Rib + UGly	Rib + UGly	c-Rib + GlyZ	Rib + GlyZ	–	–
Rib	7·63	–	7·72	–	−22·5	–	−22·41	–	–	–
2a	43·3	64·6	–	–	−27·9	−5·3	–	–	4·2724	−1511·5
2b	–	–	46·9	68·2	–	–	−0·7	21·9	8·5114	−1296·6
3a	42·4	63·7	768·1	789·4	−28·8	−6·2	623·3	645·9	7·9653	−1590·7
4a	−109·7	−88·4	616·0	637·3	−96·4	−73·8	602·2	624·7	8·8492	−1220·6
6a	−127·8	−106·6	597·8	619·1	−112·9	−90·3	585·6	608·2	9·0894	−1247·3
7a	−122·1	−100·8	603·6	624·9	−102·3	−79·7	596·2	618·8	11·3309	−1251·5

of 1-glycino-pent-1,2,3,4,5-ol), and the keto form of the Amadori rearrangement product, **7** (1-glycino-pent-3,4,5-ol-2-one). The reactions are found not to be feasible for the formation of the addition compound, **3** (1-glycino-pent-1,2,3,4,5-ol), the Schiff base, **4** (Schiff base of 1-glycino-pent-1,2,3,4,5-ol), and the enol form of the Amadori rearrangement product, **6** (1-glycino-pent-2,3,4,5-ol-1-ene). Therefore, it is assumed that the consequently formed ionic addition adduct, **2** (figure 1), may directly eliminate one molecule of water, leading to the formation of ionic adduct of the Schiff base, **5**, and deprotonation and ketoenolic tautomerization (**KET**) of **5** may take place at the same time to produce **7**. **c-Rib** + **UGly** reaction is assumed more feasible for producing different compounds than **Rib** + **UGly** reaction. Different compounds, produced in **c-Rib** + **UGly** reaction, are found electronically more stable than that of **Rib** + **UGly** reaction (ΔE° in table 1).

Except producing **Rib** from **c-Rib** in **c-Rib** + **PGly** reaction, formation of all other compounds in the proposed mechanisms for **c-Rib** + **PGly** and **Rib** + **PGly** reactions (figure 1 and ΔG° in table 1). **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are not found to be feasible for producing all compounds in the proposed mechanism (figure 2 and ΔG° in table 1). Compounds formed in **c-Rib** + **GlyZ** and **Rib** + **GlyZ** reactions are assumed electronically less sta-

ble than compounds formed in **c-Rib** + **PGly** and **Rib** + **PGly** reactions (ΔE° in table 1).

c-Rib + **DGly** and **Rib** + **DGly** reactions are not feasible for the formation of the ionic addition adduct, **2a**, and the addition compound, **3a** (1-deprotonated glycino-pent-1,2,3,4,5-ol) (figure 2 and ΔG° in table 1). The reactions are feasible for forming the Schiff base, **4a** (Schiff base of 1-deprotonated glycino-pent-1,2,3,4,5-ol), the enol form of the Amadori rearrangement product, **6a** (1-deprotonated glycino-pent-2,3,4,5-ol-1-ene), and the keto form of the Amadori rearrangement product, **7a** (1-deprotonated glycino-pent-3,4,5-ol-2-one) (figure 2 and ΔG° in table 1). Therefore, it is assumed that nucleophilic addition of **c-Rib/Rib** and **DGly** and elimination of one molecule of water may take place at the same time, leading to the formation of the Schiff base, **4a**, which can produce **6a** and **7a** accordingly (figure 2). In producing different compounds, **c-Rib** + **DGly** reaction is assumed more favourable than **Rib** + **DGly** reaction. **c-Rib** + **DGly** and **Rib** + **DGly** reactions are more feasible for the formation of **6a** and **7a** than forming **6** and **7** in **c-Rib** + **UGly** and **Rib** + **UGly** reactions (figures 1 and 2, and ΔG° in table 1). **c-Rib/Rib** + **DGly** reaction facilitates formation of both of **6a** and **7a**, whereas **c-Rib/Rib** + **UGly** reaction facilitates only formation of **7** (ΔG° in table 1). Therefore, it is assumed that the rate of the reaction

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

Compounds↓	Bond lengths (Å)						Bond angles (°)			Dihedral angles (°)	
	C–C	C–O	O–H	C–H	N–C	N–H	C–C–C	H–C–O	C–N–C[e]	C–C–C–C[f]	C–C–N–C[g]
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	–84·8
2a	1·5669	1·2952	–	1·1303	1·6177, 1·47[d]	1·0167, 1·0218	116·2	117	114·2	–61·7	133·4
2b	1·5544	–	–	–	1·5195, 1·4872[d]	1·0197, 1·0278	111·4	–	111·4	–75	147·4
3	1·5515	–	0·9749	1·0921	1·4641, 1·448[d]	1·0162	111·6	108	118	–176·8	–67·2
3a	1·5566	–	0·9643	1·1376	1·4543, 1·4471[d]	1·003	111·3	104	115·3	–72·8	130·7
4	1·5106	–	–	1·0962	1·269[c], 1·4495[d]	–	109·6	–	119·2	177·7	178·8
4a	1·5147	–	–	1·0918	1·2727[c], 1·4447[d]	–	112·2	–	118·2	86·7	172·9
5	1·5155	–	–	1·1209	1·3032[c], 1·455[d]	1·0173	109·2	–	124·2	–165·1	–178
6	1·3461[a]	1·3785	0·9764	1·0849	1·4167, 1·4503[d]	1·0154	124	–	117·3	–102·7	113·4
6a	1·3565[a]	1·3497	1·05	1·0876	1·4226, 1·4755[d]	1·0203	122·7	–	115·6	–96·1	93·9
7	1·5125	1·2245[b]	–	1·0989, 1·1113	1·4461, 1·4456[d]	1·0166	116·6	–	115·5	158·7	164·2
7a	1·4765	1·2389[b]	–	1·101, 1·1287	1·4528, 1·4762[d]	1·02	117·1	–	111·4	140·7	162·8

[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**); [g]C–C–N–C(**Y/Y⁻**)

under basic conditions in the gaseous phase interstellar medium is higher than that of neutral conditions. In **c-Rib**/**Rib** + **UGly** reaction, **7** contains the lowest μ_{Gas}, whereas **7a** and **6a** contain the highest and second highest μ_{Gas} in **c-Rib**/**Rib** + **DGly** reaction (table 1). ΔH_f^o for **7** is found as the second highest in **c-Rib**/**Rib** + **UGly** reaction, and the second and third lowest for **6a** and **7a**, respectively, in **c-Rib**/**Rib** + **DGly** reaction (table 1).

3.2 *Kinetics*

While the main purpose of this work is to propose thermochemical mechanisms for the formation of Maillard products in the interstellar medium (ISM) we can also analyse the kinetics of certain paths. Several hundred transition states were attempted to be localized however, we were only able to identify five mechanisms presented here. In reality, many of the ISM reactions occur via barrier-less reactions[7] and can proceed via three body interactions. The transition states that are most probable to be located are for **c-Rib** to **Rib**, **3** to **4**, **6** to **7**, **2a** to **3a**, and **4a** to **6a** transformations (figures 1 and 2). To perform these computations, we have verified the B3LYP/6-31G* frequencies to make sure that the imaginary frequency correspond to the correct reaction route.

Figure 3. Transition state structures for the species depicted for species labelled in table 3 where selected geometrical parameters are shown. Note that bond angles are in degrees (·) and bond lengths in angstroms (Å).

We have calculated the reaction rates using conventional transition state theory (CTST)[23] where the rate has the following form:

$$k(T) = (k_B T/hc^0)e[-\Delta G/RT].$$

In this equation k_B is the Boltmanz constant, T is temperature, c^0 is the concentration (set to 1), R is the ideal gas constant, and ΔG is the free energy of activation. Figure 3 shows transition state structures for the species depicted for species labelled in table 3 where selected geometrical parameters are shown.

Additionally, to evaluate the free energy of activation (E_a) we have used the following equation:

$$\ln k = \ln A - E_a/RT,$$

whereby the slope of the equation corresponds to $-E_a/R$ from which the activation energy can be extracted. This equation was used to define an accurate activation energy based on kinetic factors which is important when analysing ISM behaviour.

Table 3 shows The ΔE_0 values which are the forward batter heights (with zero-point effects inclu-

Table 3. Various thermodynamic and kinetic parameters for the transition state mechanisms shown in figure 3. The E_a is the kinetically derived energies of activation used to describe the processes shown. The ΔE_0 values are the forward barrier heights (with zeropoint effects included), ΔH is the enthalpy of activation, ΔG is the free energy of activation in kcal/mol and k (s^{-1}) is the reaction rate constant. Also shown are the imaginary frequencies that correspond to the mode of the reaction pathway following for the mechanism under consideration.

Transition state	ν (cm^{-1})	E_a (kJ/mol)	ΔE_0 (kJ/mol)	ΔH_{298} (kJ/mol)	ΔG_{298} (kJ/mol)	k(s^{-1}) $\times 10^{-3}$
c-Rib-ts	1762i	57·40	159·26	159·55	158·67	0·2125
2a-ts	1592i	50·55	136·88	131·44	147·14	3·315
2′-ts	1605i	82·13	192·00	194·43	200·11	$1·052 \times 10^{-5}$
3-ts	1576i	58·94	153·23	148·33	161·21	0·1147
4a-ts	1929i	119·87	266·81	266·35	263·43	$2·815 \times 10^{-12}$
6-ts	2227i	115·46	243·03	249·15	256·02	$1·654 \times 10^{-11}$

ded), ΔH is the enthalpy of activation, ΔG is the free energy of activation in kcal/mol and k (s^{-1}) is the reaction rate constant. Additionally, the imaginary frequency corresponding to the reaction pathway being described has also been displayed. These were used to confirm the assignment that a particular transition state corresponds to a reaction pathway being analysed.

For the first pathway we can see that the ribose isomerization (**c-Rib $\rightarrow$ Rib**) has a forward barrier height of around 159 kJ/mol, a free energy of activation (E_a) of 57·4 kJ/mol and a rate of $0·2125 \times 10^{-3}$ s^{-1}. While the rate of the reaction is a bit slow, under the conditions of the ISM this should occur with at least some frequency. The next step (**2a to 3a**) which has been described in figures 1–2 has a free energy of activation of 147·14 kJ/mol with a much smaller reaction rate constant. This can be attributed to the high polarity of the amino group which prefers the **3a** configuration. This should be definitely possible in the ISM under various adverse conditions and when collisions are taken into consideration. Therefore, if this is the case, possibly this mechanism can proceed via a barrier-less process. Additionally, the energy of reaction suggests that this step is indeed favourable. It is our belief that this pathway can be of direct relevance to chemistry in the ISM. We do believe that this process can occur in the ISM.

A competing mechanism is the formation of a hydrogen bonded complex which is slightly higher in energy and has a free energy of activation of 200·11 kJ/mol (via **2′-ts** shown in figure 3) with a small reaction rate. The activation energy for this process is 50·55 kJ/mol which is still within the margin of error for these calculations to be considered viable in the ISM. While this is a potential mechanism the concentration of this product should

be minimized in an experimental setting. We have presented this result but it is likely that it will not form under typical conditions.

Once **2** is formed from the basic reactions, **3** can form from a change in configuration via the transition state shown in figure 3. As we can see the free energy of activation is 161·2 kJ/mol with a higher reaction rate and therefore it should form experimentally. The first product **2a** has a reaction rate which is about twice as low and should be preferred over structure **4** (which occurs through the transition state labelled as **3-ts** is shown in figure 3). The E_a value of this reaction is 58·94 kJ/mol which is still feasible and can take place in the ISM. Test calculations with a larger B3LYP/6-311++G** basis set yield a value of 43·52 kJ/mol that suggests that this reaction is highly favourable.

The final two isomerization steps (**4a-ts $\rightarrow$ 6a**; **6-ts $\rightarrow$ 7**) are high energy processes with slow reaction rates. The forward barrier heights are elevated, but the activation energies (E_a) suggest that these reactions may not be feasible in the ISM but are a possibility. However, as we will show later the latter step to these products may indeed be barrier-less and not involve a transition state. It is another potential possibility that an external molecule can participate to protonate a structure leading to different chemical structures by external catalysts. Alternatively, the protonation steps can lead to the barrier-height through **4a-ts** and **6-ts** to be reduced since this process involves a high energy hydrogen migration. These steps may be feasible however, from an analysis of the activation energies even within the margin of error they may not occur.

These protonation and deprotonation processes were not completely modelled since we believe these steps may proceeed intermolecularly. The preliminary calculations suggest that the energies shown

are not favourable and other mechanisms should be preferred. The calculation on the KET step may also be problematic due to uncertainty in the mechanism. The intramolecular 1,3-H shift transition state was located however, the intermolecular KET process will proceed more easily with the help of another reactant, solvent, or other possible proton donor and acceptor, as reported by previous studies. This will be the focus of a future study with respect to proton catalysed mechanisms of the reactions studied here.

4. Conclusions

It is clear from the present study that the Maillard reaction between **c-Rib**/**Rib** and **Gly** species may take place in the gaseous phase in the interstellar medium. **c-Rib** is more efficient than **Rib** in the reaction. The basic and neutral conditions are the first 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 the reaction is assumed higher under basic conditions than that of the neutral conditions. Based on our kinetics calculations we have shown that the conversion of **c-Rib** to **Rib** is feasible along with **2a → 3a** and **3 → 4**. Other transition state mechanisms were not able to be located easily and the pathways discussed are the most probable routes for ISM molecule formation. Experimentally, these short lived products can be located by the imaginary frequencies presented and should be able to act as a guide for ISM molecule scans. Other competing reaction paths are probably feasible but this report serves to shed light on potential Maillard reactions in the ISM. These questions are of definite interest to a vast majority of chemists and physicists trying to understand the mistry of origin of life. The primary purpose of this work was to provide thermochemical data supporting this mechanism as a plausible factor for biochemistry in the ISM. However, our brief kinetics study can be of some use. It serves to show that the primary compounds exhibited should form at least in some concentrations under diverse conditions.

From the proposed calculations we have shown that in all cases the energies of reaction are indeed exothermic revealing that the processes that are undergone should be favourable from an energetic standpoint. Single point CCSD(T)/aug-cc-pVQZ calculations (with zero-point effects included) reveal that the barrier-heights through all pathways except for **4a-ts** and **6-ts** are feasible. Within the margin of error for theoretical calculations of transition states and activation barriers (which are in the order of 45–55 kJ/mol) that suggests that potentially these are barrier-less processes.

Our future focus will be on how we can apply these experimental and theoretical methods to investigate the possible formation of ribose and higher sugars. Additionally, the presence of free molecular oxygen in the formose reaction must be examined. Many researchers[24–25] have shown that oxygen can have a definite influence on the reactivity of larger molecular systems. Particularly in steps involving CO groups its seems to favour the formation of oxygen based compounds. However, this is still tentative and needs to be further proved by experimental and theoretical evaluations. Structural determinations based on our experimental set-up will be the area of further investigations from our groups. Few studies that exist investigate the potential formation of ribose and related biomolecules in the ISM. Nevertheless, it is important to be aware that, while these products have not been observed, scientists must not be reluctant to pursue this area of research.

What must be noted is that the energies of reaction are highly favourable for the mechanisms proposed, therefore potentially speaking there are two options to explain this effect. The first is that another lower energy transition state may exist experimentally or the reaction is indeed barrier-less that will occur due to three-body collisions with external molecules. Also, the calculated imaginary frequencies for the transition states can be used in the spectroscopic determination of the relative strengths of a particular reaction pathway. If the frequencies are known that researchers can gear studies aimed at investigating regions of the vibrational spectra in the efforts to locate interesting ISM molecules. The transition states that were not able to locate by our methods probably correspond to processes or reactions that are barrier-less. These barrier-less mechanisms are common in the ISM and can be used to explain the presence of rare molecular species. It is important to note that future studies by our group include the theoretical analysis of external catalyst species that can help for certain chemical mechanisms to occur. However, this work should serve as an important first step in the proposal for the origin of interstellar life.

Under acidic conditions and at the isoelectric point of glycine, the reaction is supposed to be the least and second least favourable. Therefore, the rate of the reaction under these conditions is assumed to be hindered. The theoretical results, presented in this paper, would be helpful for further theoretical and experimental investigations, leading to find out the real possibility of the Maillard reaction to take place in the interstellar medium and the relation of the reaction to the creation of first living organisms.

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