CHAPTER 13: The Birth and Fate of Glycine: The the Interstellar Medium to Primitive Earth

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CHAPTER 13

The Birth and Fate of Glycine: From the Interstellar Medium to Primitive Earth

A. RIMOLA[a], M. SODUPE[a] AND P. UGLIENGO⋆[b]

[a]Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Catalonia, Spain; [b]Dipartimento di Chimica and Nanostructured Interfaces and Surfaces (NIS) Centre, Università degli Studi di Torino, via P. Giuria 7, IT-10125, Torino, Italy
⋆E-mail: piero.ugliengo@unito.it

13.1   Introduction

Glycine (NH_2CH_2COOH, hereafter referred to as Gly) is the simplest amino acid and accordingly it is a paradigmatic compound to investigate the primordial chemical evolution of bio-molecular building blocks, namely, from its synthesis to its transformation into biopolymers under abiotic conditions.

Amino acids are organic compounds that contain amine ($-NH_2$) and carboxyl ($-COOH$) functional groups. Polymerization of amino acids through condensation reactions leads to the formation of peptides, the building blocks of proteins. Proteinogenic amino acids (*i.e.*, those forming proteins) are α-amino acids, in which both the amine and the carboxyl groups are attached to the first (α-) carbon. The generic formula is $NH_2CHRCOOH$, in which $NH_2CHCOOH$ is the backbone chain and R the side chain. R is an organic substituent (normally an aliphatic chain ended by a particular

functional group) that allows one to differentiate a type of amino acid
from the rest and dictates its chemical properties, *e.g.*, non-polar, polar,
acidic, basic, *etc.* For Gly, R = H, is the simplest case. An amino acid
exhibits either a canonical (*i.e.*, with NH_2/COOH groups) or a zwitterionic
(*i.e.*, with NH_3^+/COO^- groups) state. The prevalence of one state over the other
depends on the environmental conditions. In the gas phase, the canonical
state is the most stable because the intramolecular charge separation of
the zwitterion is not stable. In contrast, in solution at pH = 7 (*e.g.*, in bio-
logical media), the zwitterion predominates due to the Coulomb screening
power of water.

In an astrochemical context, Gly is considered to be a complex organic mol-
ecule (COM), due to its size (10 atoms). COMs are molecules between 6 and
12 atoms, among which at least one is C.[1,2] COMs have been detected in dif-
ferent astrophysical environments by means of astronomical observational
measurements based on rovibrational emission spectroscopy.[3–6] Although
there is currently a hot debate on COM formation, one paradigm postulates
that their synthesis can occur on the surfaces of interstellar grains.[7–10] These
grains are submicron dust particles consisting of a refractory core of silicates
or carbonaceous materials usually covered in ice mantles, predominantly of
H_2O "dirtied" by other simple volatile species like CO, CO_2, NH_3 and CH_3OH.
The "on-grain" synthesis route states that simple reactants, coming from the
gas phase, adsorb on the surfaces of the ice mantles, diffuse on them and,
upon encountering, react to form COMs. Since observational detections of
interstellar molecular species can only be possible if they are in a gaseous
state, COMs formed by "on-grain" should move from the solid to the gas
phase. For Gly this final step is problematic. Interstellar desorption of ice-
adsorbates into the gas phase normally occurs by energetic processes such as
UV or electron irradiation and shocks. Gly is sensitive to UV and electrons[11]
and accordingly its survival in the gas phase after the desorption process is
unlikely. Moreover, as Gly is a large COM, its detection in the microwave is
hampered by a large number of rotational transitions resulting in a forest of
weak lines that are hard to interpret. These two problems may well explain
why unambiguous direct detections of interstellar Gly have not been success-
fully achieved so far.[12–15]

In carbonaceous chondrites, *i.e.*, the most pristine, less altered meteorites
known so far, a rich suite of complex organic compounds have been identi-
fied,[16–21] some of them of biological relevance, such as amino acids, sugars
and nucleobases. Nevertheless, in contrast to the interstellar COMs detected
in observational measurements, these meteoritic organic compounds are
chemically more complex. That is, molecules with more than 12 atoms and
with a larger variety of chemical functional groups ~~are abundant~~, includ-
ing aliphatic and aromatic hydrocarbons, alcohols, carbonyl compounds,
amines, amides, nitrogen heterocycles, carboxylic and hydroxycarboxylic
acids, sulfonic and phosphonic acids, amino acids and carbohydrates.[22] In
comets, although the chemical content is not so complex as the meteoritic
one, there is also clear evidence of the presence of more evolved organic

compounds than the interstellar COMs. For instance, large organic entities with elemental composition of C, H, N and O (and ~~inlesser~~ amounts, P and S) have been identified, which have been tentatively associated with polymeric materials.[23–25] Moreover, organic volatiles have also been identified, the most relevant one being undoubtedly Gly in the Stardust's Wild 2 [26,27] and Rosetta's 67P[28] comets. Due to this enhanced chemical complexity, it is believed that most of these compounds were synthesized in the same asteroidal bodies, where they were trapped. In that respect, hydrothermal alteration processes undergone by the asteroidal bodies are of particular importance because they could have facilitated the occurrence of organic reactions in water solution that led to the formation of these more complex molecules.[29–32] Remarkably, all these organic compounds (among them Gly) formed and/or present in the asteroidal bodies could have well chemically fed the primordial Earth. Indeed, meteoritic bombardment in the first billion years of the Earth's existence could have been an important source of abiogenic important molecules. Along this line, the Earth late heavy bombardment (that occurred *ca.* 4.1–3.8 Ga ago) was of significant importance, in which a disproportionate large number of asteroids collided with the early planets belonging to the inner Solar System.

In the sequence of organizational events that led to the origin of life on early Earth, biomolecular building blocks, irrespective of their origin (*i.e.*, *via* exogenous delivery or endogenous synthesis), had to transform into more complex systems, in which at each step they gained more biological relevance. A crucial step was the formation of biopolymers essential for life such as peptides, polynucleotides and polymeric carbohydrates. Peptides result from the linking of different amino acids through the nucleophilic attack of the NH_2 end of one amino acid with the COOH end of another amino acid, giving rise to the peptide bond plus a water molecule (condensation reaction). The simplest case of a peptide bond is the joining of two Gly molecules, giving rise to glycylglycine, $NH_2CH_2-C(=O)-NH-CH_2COOH$: the $-C(=O)-NH-$ moiety is almost planar due to electron delocalization and its structural rigidity imparts specific conformations to peptides.

In condensation reactions, the release of water represents an important drawback in the prebiotic context: since reactants might have probably been diluted in watery environments, condensation reactions are thermodynamically unfavorable.[33,34] A plausible solution to overcome this "water release problem" advocates that condensation reactions could have taken place in environments where seasonal fluctuations of humidity and temperature allowed repeated periods of wet and dry cycles, the latter conditions being propitious for condensation reactions.[35,36] In addition, J. D. Bernal proposed minerals as central players in the formation of the first biopolymers.[37] He postulated that mineral surfaces were suitable places to adsorb and immobilize the monomers (this way acting as concentrators), to activate them to react (this way acting as catalysts), and to preserve the resulting products from prompt hydrolysis (this way acting as protectors). In this sense, mineral

surfaces can adsorb and retain the water released during the process, in this way favoring the thermodynamics of the reactions.[38,39] This theory has received the support of a great number of investigations for polypeptide and polynucleotide formation, both from the experimental[34,40,41] and theoretical[42,43] sides. Thus, the "polymerization on the rocks" in combination with the fluctuating wet/dry environments opens up the propitious conditions for the occurrence of abiotic condensation reactions yielding the emergence of biopolymers in a prebiotic era.

As mentioned above, Gly has not been directly detected as an interstellar species but paradoxically its presence is recurrent in carbonaceous chondrites. However, the chemical history of Gly, particularly its interstellar formation and its prebiotic polymerization, has been investigated experimentally. There is clear experimental evidence that processing of interstellar ice analogs results in Gly formation, among other amino acids and organic compounds.[44–49] Additionally, experiments have proved that C atom additions are also potential synthetic routes toward Gly formation.[50] In the same way, different experiments devoted to Gly polymerization in the presence of minerals (*e.g.*, silica, alumina, titania) have been successfully carried out.[41,51–57] Despite these positive results, experiments cannot provide atomistic information of these processes, which are mandatory to have unique details on the mechanistic steps, the structures and energetics, and to know the actual role of the surfaces (*e.g.*, ice mantles, minerals) that enable the evolution of the reactions. Such information is currently possible by making use of the tools, methods and techniques of computational chemistry.[43,58,59] In this book chapter, we review exclusively studies based on quantum mechanical simulations devoted to elucidate the possible mechanism related to the birth and fate of Gly, *i.e.*, from its synthesis in the ISM, passing through its transportation and delivery to the early Earth, and finally to its abiotic polymerization.

This chapter is distributed as follows. Section 2 provides a brief description of the quantum chemical methods and the surface modeling techniques usually employed in computational chemistry. Section 3 is the core of the chapter, where dedicated quantum chemical studies on the formation, transportation and delivery, and polymerization of Gly are described. Finally, Section 4 exposes the main conclusions alongside future perspectives on the potentiality of computational chemistry in improving our current know-how on Gly-related events involved in primordial chemical evolution.

13.2   Computational Framework

The chemical processes presented here concern a wide variety of reaction types and mechanisms (*e.g.*, proton/electron transfer, nucleophilic/electrophilic attacks) occurring on structural models mimicking either the surfaces of ice mantles or that of minerals. Accordingly, accuracy of the results relies on (i) the quantum chemical methods describing the chemical reactions, and (ii) the modeling approach describing the surfaces where the reactions occurred.

Within the quantum chemical context, when high accuracy is needed, approaches based on improvement of the wave function such as Møller–Plesset and coupled cluster methods (*e.g.*, MP2 and CCSD(T), respectively) are adopted.[60,61] These methods, however, are extremely expensive for large systems and accordingly hitherto impractical when modeling surface processes. Alternatively, since the late 1990s, approaches based on electron density, the so-called density functional theory (DFT) methods, have become computationally cheaper alternatives to those that are wave function based, as well-designed DFT methods provide acceptable accuracy.[62–66]

In relation to surface modeling, application of the periodic boundary conditions (PBC approach) into a unit cell containing the adsorptive/catalytic sites is the natural method of choice. Alternatively, cutting out from the crystalline model a finite set of atoms containing ~~the catalytic~~ sites, the so-called cluster approach, is also possible.

Powerful computer codes have been developed over the years to solve the PBC problem for infinite systems. However, due to their infinite nature, application of highly accurate, wave function based methods is overwhelming, although recent developments allow MP2 applicability.[67–70] Thus, in practice, they can only be studied using DFT methods. Moreover, localization of transition state structures is less efficiently coded compared with molecular programs, and accordingly characterization of the potential energy surfaces (PESs) is limited to "simple" reactions. In contrast, a large variety of quantum molecular programs can properly handle cluster models, characterizing PESs of complex chemical reactions (like in molecular systems) and using even CCSD(T) if the cluster size and the program allow one to do so.

Despite these methodological advantages, the cluster approach can be limited by: (i) the need to "heal" dangling bonds resulting from cutting covalent/ionic bonds from the extended system, and (ii) the cost of the calculation growing rapidly with the cluster size, which should be large enough to include the surface active sites and the nearest neighbors. Indeed, the cluster sizes can become prohibitively large, particularly for amorphous systems, thereby reducing the aforementioned advantages when adopting molecular computer codes. A possible solution is to use embedding techniques like the ONIOM method,[71] in which the region of main interest (normally the region close to the adsorptive/catalytic sites) is treated at a high level of theory [MP2, CCSD(T)], whereas the surrounding region is treated at a lower level (DFT, semi-empirical or even molecular mechanics).

13.3   Results and Discussion

13.3.1   Gly Formation on ISM: The Role of Water Ice Mantles

Although different gas-phase pathways for glycine formation in the interstellar medium (*i.e.*, through ion–molecule reactions or radical species) have been addressed by quantum chemical calculations,[72–79] in this chapter we will mainly focus on the synthesis of glycine at the surfaces of interstellar

dust grains, since they can act not only as a catalyst but also as a third body
dissipating the released reaction energies. As mentioned in the Introduction,
the core of the interstellar grains is covered by H_2O-dominant ice mantles.
Thus, a reasonable path towards interstellar Gly can be inspired by what is
happening in liquid water, *i.e.*, the Strecker synthesis. This route comprises
the synthesis of amino acids under acidic conditions by the reaction of alde-
hydes/ketones with ammonia and hydrogen cyanide. For the particular case
of Gly, the reaction involves the three steps shown in Figure 13.1A. This
reaction is particularly attractive from an interstellar viewpoint because the
reactants (*i.e.*, $H_2C=O$, NH_3 and HCN) are compounds usually identified as
minor species in the ice mantles, and the $NH=CH_2$ and $NH_2CH_2C\equiv N$ inter-
mediates are compounds experimentally detected in different interstellar
environments.

The interstellar Strecker synthesis on water ice mantles has been fully
simulated[80] (namely, accounting for all the reaction steps) using a cluster
of $18H_2O$ molecules as a model for the surface of an interstellar water ice
mantle (see Figure 13.1B). The water cluster was generated by extracting
a cluster from the crystalline P-ice (the proton-ordered analog to hexago-
nal Ih ice), which has been successfully used in the past to simulate water
ice features.[81] The outermost water molecules of the cluster, envisaging the
classical hexagonal organization, exhibits an ideal H-bond network that
allows the proton transfer, which is usually advocated in proton transfer
processes in which water (normally as solvent) acts as a catalyst[82] (see
Figure 13.1C). In the interstellar Strecker synthesis of the Gly formation, the
catalytic role of water is involved in all the reaction steps. Indeed, in both
the formation of NH_2CH_2OH, its dehydration to form $NH=CH_2$, the reac-
tivity of $NH=CH_2$ with HCN to give $NH_2CH_2C\equiv N$ and its final hydrolysis,
surface ice water molecules act in proton transfer processes. This process is
fundamental in reducing the kinetic energy barriers, when compared to the
gas-phase analog processes. Figure 13.1D shows the localized transition
states for the first and second Strecker steps, in which the proton trans-
fer catalysis was found to be more relevant. All the steps of the simulated
interstellar Strecker synthesis were found to be thermodynamically favor-
able. However, the problem of this synthetic route is related to its kinetics.
Despite the proton-relay mechanism, the kinetic barriers are exceedingly
high for the 10–20 K temperatures occurring in dense molecular clouds,
being 60, 73 and 163 kJ mol^{-1} for steps (i), (ii) and (iii) of Figure 13.1A. For
temperatures in the 100–200 K range, occurring in regions surrounding a
newly born massive star (hot molecular cores) steps (i) and (ii) (*i.e.*, forma-
tion of $NH=CH_2$ and NH_2CH_2CN) become feasible, providing a plausible
explanation for the experimental detection of these species in astrophysi-
cal environments.[83] However, step (iii), that related to the actual Gly forma-
tion by hydrolysis of NH_2CH_2CN, is unlikely to occur even in these warmer
regions. The main conclusion is that, in dark and cold molecular clouds,
the Strecker-type mechanism occurring at the water ice surfaces seems to
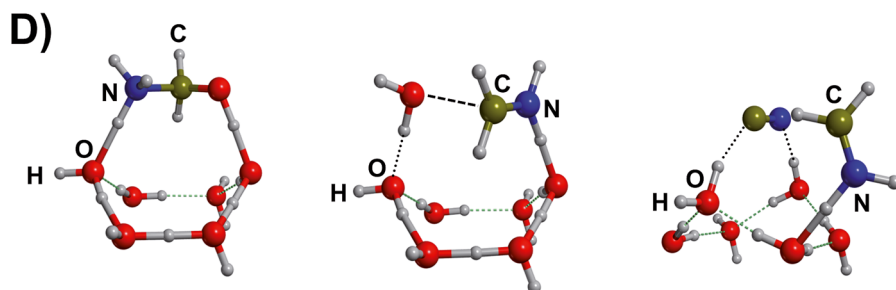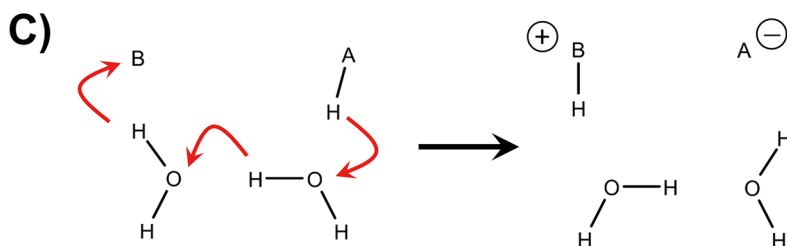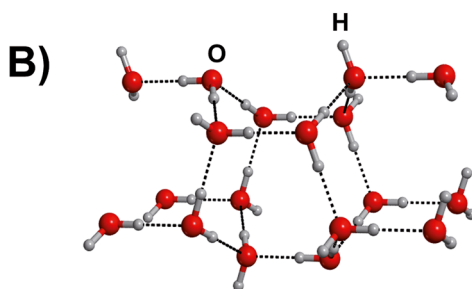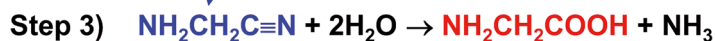be not feasible for the synthesis of Gly by kinetic reasons.

A)   **Step 1)** $H_2C=O + NH_3 \rightarrow NH_2CH_2OH \rightarrow NH=CH_2 + H_2O$

Step 2) $NH=CH_2 + HCN \rightarrow NH_2CH_2C\equiv N$

Step 3) $NH_2CH_2C\equiv N + 2H_2O \rightarrow NH_2CH_2COOH + NH_3$

B)

C)

D)

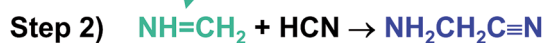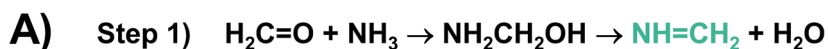**Figure 13.1**   (A) Steps involved in the Strecker synthesis for the formation of Gly. (B) Molecular cluster of 18H$_2$O molecules as a model to represent the surface of an interstellar water, *i.e.*, mantle. (C) Motion of the protons in a proton relay mechanism assisted by two H$_2$O molecules. HA and B are the generic proton donating and receiving species, which convert into A$^-$ and HB$^+$ after the process. (D) Transition state structures for the formation of NH$_2$CH$_2$OH, NH=CH$_2$ and NH$_2$CH$_2$C≡N assisted by the external waters of the ice cluster model. Note that the waters at the bottom of the cluster are not shown for the sake of clarity. Adapted from ref. 80 with permission from the Royal Society of Chemistry.

As mentioned in the Introduction, Gly is easily formed in the laboratory
when ices are energetically processed, normally by irradiation of UV photons
and high-energy particles. The underlying idea is that energetic fluxes of UV
photons and particles activate the iced species, *e.g.*, by generating reactive
radicals, hence allowing their fast reactivity and, perhaps Gly synthesis. This
idea has been investigated through *ab initio* computer simulations.[84] Two
cases were considered: (i) UV ice irradiation causing homolytic cleavage of
water molecules, and (ii) ionization of water ice by cosmic rays. UV effects
were modeled by removing one H atom of one water molecule belonging to
the $(H_2O)_8$ water cluster mimicking the grain ice, ending up with a water clus-
ter exhibiting an OH· radical group (*i.e.*, becoming a radical neutral cluster).
Cosmic rays' effects were modeled by removing one electron of the $(H_2O)_8$
cluster (*i.e.*, becoming a radical cation cluster). Remarkably, for the latter
case, geometry optimization of the cluster collapsed to a system exhibiting
an OH· (responsible for the radical character) and a H_3O^+ (responsible for
the cation character). The structures of all the considered cluster models are
shown in Figure 13.2A. By using these two "processed" cluster models, Gly
formation was simulated at DFT BHLYP level through two steps: (i) reaction
of the OH· radical with an incoming CO to form the ·COOH radical, and
(ii) reaction of the formed ·COOH radical with an incoming NH=CH$_2$ molecule.
It is worth mentioning that, according to this mechanism, the final product
is not Gly, but one of its radical forms, ·NHCH$_2$COOH. However, due to the H
atom abundance in ISM, the radical species can (barrierless) be transformed
in Gly. When considering the radical neutral cluster, the first step (OH· + CO
→·COOH) exhibits an energy barrier of about 13 kJ mol^{-1}. However, the sec-
ond step (·COOH + NH=CH$_2$ →·NHCH$_2$COOH) exhibits a high energy barrier,
about 52 kJ mol^{-1}, kinetically hampering the reaction.

Similar energetics were computed in the presence of the radical cation
cluster adopting the same mechanism, and accordingly, Gly formation is not
expected to occur through this process. However, on the radical cation clus-
ter, an alternative route concerning the second step was identified as more
favorable. It involves NH=CH$_2$, a species detected experimentally in the ISM,
reacting first with the H_3O^+ species at the cluster surface, to give the NH_2^+=CH$_2$
cation, which then reacts with ·COOH, leading to the formation of Gly in its
radical cation state. Figure 13.2B shows this entire path (first and second
steps) on the radical cation cluster. The energetics of this alternative second
step were found to be more favorable than the direct NH=CH$_2$ + ·COOH cou-
pling, the energy barrier of the proton transfer and of the final NH_2^+=CH$_2$
+ ·COOH reaction being about 4 and 26 kJ mol^{-1}, respectively. To assess its
kinetic plausibility, rate constants using the classical Eyring equation at
T = 10, 50, 100 and 200 K were calculated. Results indicate that at 10–50 K the
path is actually slow but, in contrast, at 100–200 K the reaction could evolve
at reasonable speeds. These results clearly point out that defects on water ice
surfaces caused by the impact of cosmic rays can activate, trigger and enable
interstellar Gly formation, although its actual occurrence requires thermal
energy, like that present in warmer regions such as hot molecular cores and
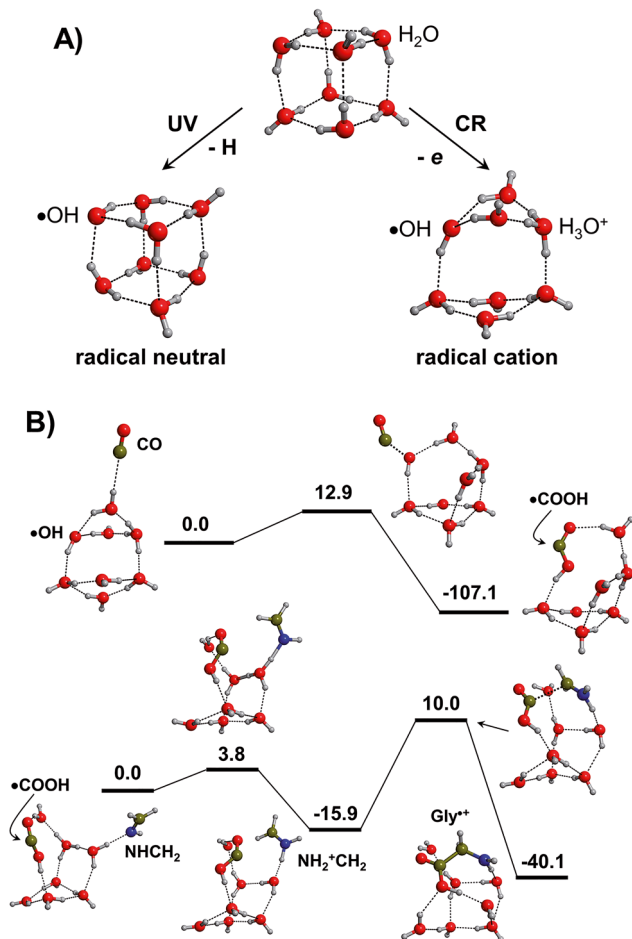protostellar envelopes, rather than in cold dense interstellar clouds.

Figure 13.2 (A) Cluster models for neutral $(H_2O)_8$, when removing a H atom (radical neutral) and when removing one electron (radical cation). (B) Reaction energy profiles (potential energies including zero-point energy corrections) calculated at BHLYP/6-311++G(d,p) theory level for the Gly formation on the radical cation cluster. The first step is the reaction of OH· + CO → ·COOH and the second step the reaction of ·COOH + NH_2^+=CH_2 → NH_2CH_2COOH·+ (Gly·+), in which previously the NH=CH_2 molecule is protonated by the surface H_3O^+ species. Relative energy units are in kJ mol^{-1}. Adapted from ref. 84 with permission from the American Astronomical Society, Copyright 2012.

13.3.2 Gly Transportation and Delivery to Early Earth by Micro-asteroidal Bodies

Once formed, the next step of Gly is to evolve into a more biochemical complex form in terrestrial environments. Therefore, it should be transported and delivered to the primitive Earth through asteroidal grains, either of cometary, meteoritic or any other cosmic origin. The mineral components

of these micro-asteroidal bodies are highly complex and heterogeneous, but
examples of the most identifiable families are silica based materials, metal
oxides like sulfides, apatites and carbonates. The adsorption of Gly at the
surfaces of specific minerals of that kind has already been investigated the-
oretically,[85–93] showing moderate to very strong Gly/mineral interactions.
Thus, the problem is not attaching Gly on these carriers, but rather its release
once landed on the Earth's crust.

This "Gly release problem" (which can be extended to any other amino
acids) has been investigated by studying the role of water in the release of Gly
from the asteroidal grains. It has been found that the Gly/water/silicate(for-
sterite) system is more stable compared to Gly directly attached to the silicate
surface (the water molecules solvating the attached Gly molecule).[94] Simi-
lar results were found for the Gly/water/hydroxyapatite interface.[95] However,
these two interfaces were limited on the adopted number of water molecules.
This implies that the desorbed state of Gly is unstable compared to the case
of full solvation. This aspect was also accounted for in the simulation of the
desorption of Gly from the FeS_2 surfaces immersed in bulk aqueous solvent.[88]
Indeed, the desorbed Gly was fully solvated by water solvent, resulting in a
more stable state (between 125 and 200 kJ mol^{-1}) compared with the solvated
Gly/FeS_2 complexes. This implies that, when solvent is properly taken into
account, the fully solvated desorbed Gly state is stabilized over the adsorbed
complex attached to minerals of micro-asteroidal bodies.

At the extreme case, Gly can also be released by the action of water solvent
even when it is chemisorbed, at least on pure silica surfaces, as demonstrated
by quantum chemical simulations.[96] The underlying idea is that strained
ring defects may be present at the silica surfaces, due to the harsh treatment
occurring in the evolution of asteroidal bodies. These structural defects can
chemically react with Gly forming a stable covalently bonded compound.
The question is whether the chemically linked Gly can be restored as a free
molecule upon the action of water. The first step shows the reaction of Gly
with a $(SiO)_2$ ring (so-called S2R), a well-known silica surface defect possess-
ing a high geometrical strain causing high reactivity. In the laboratory, the
S2R motif appears when silica is heated to a temperature of about 600 °C,
because of the surface vicinal silanol groups (Si–OH) condensation.
Figure 13.3A shows the S2R defect at a silica surface as modeled by a cluster
approach. The computed energy profile for the reaction of Gly with S2R
indicates a very favorable process, being almost barrierless with a reaction
energy of −113 kJ mol^{-1} (with respect to the infinitely separated reactants, see
Figure 13.3B). The resulting product is the formation of a chemically bonded
complex called surface mixed anhydride, *i.e.*, Si_{surf}–O–C(=O)–CH_2NH_2, along
with the formation of a SiOH group at the silica surface. Gly can be released
back to the environment by reaction of the surface mixed anhydride with
four water molecules: Gly is detached from the silica grain and released in
the water environment (see Figure 13.3C). The calculated energetics revealed
a free energy barrier and a reaction energy at 298 K of 88 and −60 kJ mol^{-1},
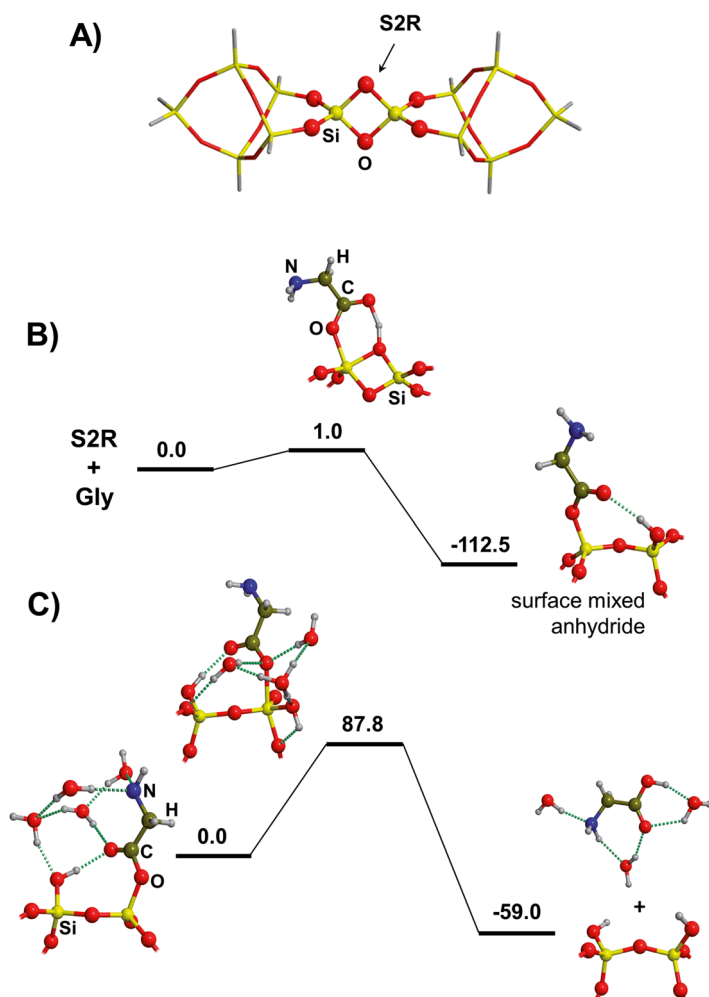respectively, the former easily surmountable under prebiotic conditions.

Figure 13.3   (A) Silica surface cluster model containing a S2R defect. (B) Reaction energy profile (potential energies including zero-point energy corrections) for the reaction of Gly with the S2R defect to give the surface mixed anhydride. (C) Free energy profile at 298 K for the reaction of the surface mixed anhydride with 4H$_2$O molecules simulating the release of Gly alongside the formation of a hydroxylated silica surface. In (B) and (C) only the active part of the silica surface model is shown for the sake of clarity. Both energy profiles were calculated at the B3LYP/6-31+G(d,p)//B3LYP/6-31+G(d,p):MNDO [ONIOM2] theory level. Relative energy units are in kJ mol^{-1}. Adapted from ref. 96 with permission the Royal Society of Chemistry.

13.3.3   Gly "Polymerization on the Rocks" in the Prebiotic Era

The idea pursued by Orgel[97] about the "polymerization on the rocks", in which mineral surfaces may be the cradle of the early peptides through a process analogous to solid-phase synthesis, is based on two concepts: (i) the amino acid/mineral interactions can activate the reactants, hence reducing the kinetic energy barriers to facilitate the peptide bond formation; and (ii) the formed peptide has a mineral surface affinity that grows with the peptide length becoming almost irreversibly adsorbed for the long peptide. The balance between peptide elongation and hydrolysis depends on the chemical nature of the mineral and the pH conditions of the environment. Furthermore, it has been suggested that fluctuating environments of humidity and temperature could have provided a favorable geological setting for amino acid oligomerization through wet and dry cycles.[35,36] Because of that, and also due to the difficulties in modeling mineral-induced processes in aqueous environments, most quantum chemical studies of peptide bond formation at the surface of minerals have been carried out considering dry conditions.

It is worth remembering that the formation of the shortest Gly peptide, glycylglycine through the $2NH_2CH_2COOH \rightarrow NH_2CH_2CH(=O)NHCH_2COOH + H_2O$ reaction in the gas phase exhibits a high free energy barrier (about 190 kJ mol^{-1}) and a slightly exergonic reaction free energy, -13 kJ mol^{-1}, in normal conditions (see Figure 13.4). These figures may vary as a function of the adopted level of theory, especially the reaction free energy. The gas-phase condensation occurs in one step, envisaging a nucleophilic attack of the NH_2 group of a Gly to the C atom of the COOH group of the other Gly. A peptide bond is then formed after the proton transfer from the NH_2 group to the OH group with the release of one water molecule. In the gas phase the mechanism is concerted, while on the mineral surfaces the mechanism is stepwise, the nucleophilic attack and the dehydration steps being well separated.
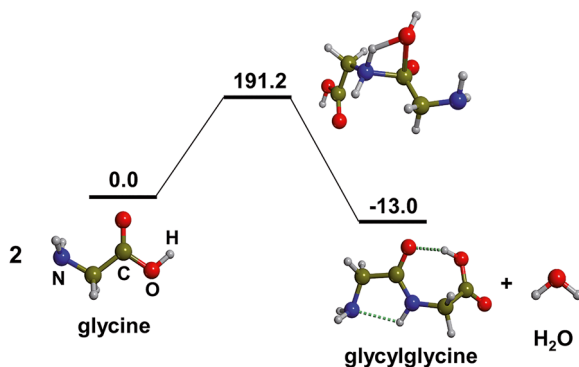

Figure 13.4   Free energy profile at 298 K for the condensation reaction between two gas phase Gly molecules leading to the formation of the glycylglycine dipeptide and one H_2O molecule. Calculated at B3LYP-D3/6-311++G(d,p) theory level. Relative energy units are in kJ mol^{-1}.

The first modeling attempt to assess the "polymerization on the rock" idea   1
was carried out on a feldspar sanidine ($K_{0.75}Na_{0.25}AlSi_3O_8$) modified model.
The feldspar family of minerals was chosen for their widespread presence on
the early Earth's crust. A cluster was defined from the crystal sanidine bulk,
in which naturally occurring K^+ and Na^+ cations were substituted by protons,   5
giving rise to pairs of Lewis (Al^{3+}) and Brönsted sites (Al–(OH)–Si). These sites
act as a blocker (Lewis) and activator (Brönsted) of adsorbed Gly allowing
for a relatively easy Gly polymerization. A first explorative work[98] adopted a
minimal cluster model of sanidine, in which the key synergic role between
Lewis and Brönsted sites in the Gly oligomerization was proven. In a more   10
extended work,[99] the cluster was enlarged to better understand the role of the
dispersion interactions between the newly formed oligopeptide (up to Gly3)
and the sanidine surface. The main reaction scheme is synthesized in Fig-
ure 13.5. Calculations showed the dispersion interactions having an import-
ant role in stabilizing the adsorbed oligopeptide, while the kinetic barrier to   15
the peptide bond formation is dramatically reduced compared to that in the
gas phase, due to the fact that now the proton transfer from $-NH_2$ to $-OH$ is
not produced directly but through the Brönsted site of the surface, which
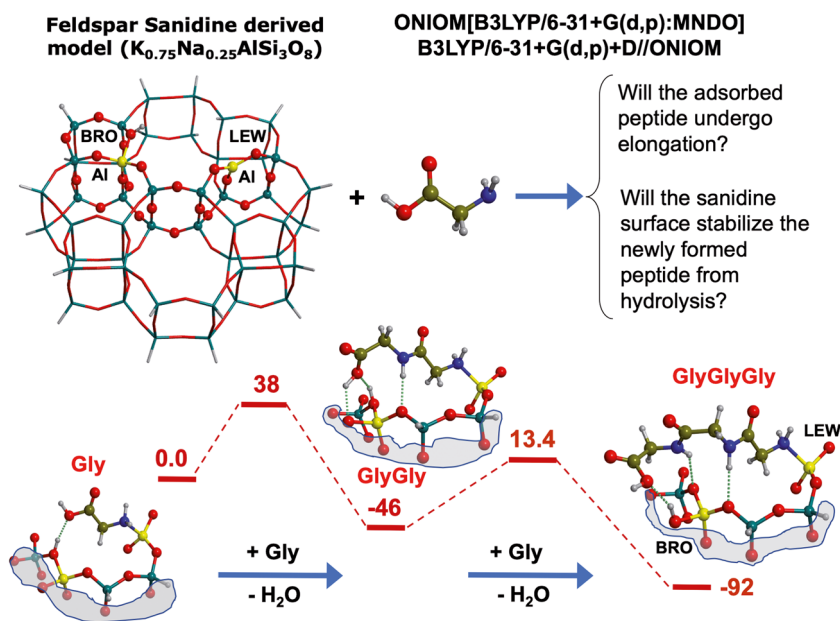
Figure 13.5 Free B3LYP/6-31+G(d,p)+D//ONIOM2 energy profile at 298 K for the
condensation reaction between up to three Gly molecules at the sani-
dine modified cluster model. Grimme's dispersion contribution (+D)
has been included *a posteriori*. Relative energy units are in kJ mol^{-1}.
Adapted from ref. 99, https://doi.org/10.3390/ijms10030746, under
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significantly reduces the geometrical strain of the transition state structure,   1
the value of which remains almost constant across the peptide elongation
steps. It was argued that such an iteration process, possibly due to the Brön-
sted proton mobility at different surface sites, leads to the mineral surfaces to
be covered by an "oligopeptide skin", which may exhibit some pre-enzymatic   5
catalytic power for other biochemically relevant processes.

Other very abundant Earth's crust inorganic materials are those based on
silica minerals shown to facilitate oligopeptides' formation. Indeed, a com-
bined experimental and theoretical study[52] demonstrated that pure silica
surfaces can help the condensation reaction between CH_3NH_2 and HCOOH,   10
used as a reaction model for two Gly molecules. Infrared spectroscopy mea-
surements elucidated that the presence of specific weakly interacting SiOH
pairs is key for the reaction. That is, when these SiOH pairs were present
at the silica surface prior to the reaction, the $CH_3NHC(=O)H$ product was
detected, while when missing, no reaction was observed. This phenomenon   15
was rationalized by theoretical calculations using a silica cluster model, the
active site of which was defined by the specific weakly interacting SiOH pairs
(see Figure 13.6A). The essential phenomenon is that these SiOH groups,
which stay ~5 Å apart (and hence exhibit a weak H-bond interaction), are
sites that allow the adsorption of the reactants in their canonical and ionic   20
states simultaneously, *i.e.*, both the CH_3NH_2/HCOOH and $CH_3NH_3^+$/HCOO$^-$
pairs can be co-adsorbed close to the SiOH sites (see Figure 13.6A). This
coexistence is fundamental for the occurrence of the reaction because the
canonical pair is the reacting one (*i.e.*, they are the condensing constituents),
while the ionic pair acts as the actual catalyst. Specifically, the NH_3^+ group   25
transfers one of its acidic protons to the neutral OH group to form water in
the dehydrating step (see Figure 13.6A). This step was found to be the bottle-
neck of the reaction having a calculated free energy barrier at 323 K (the *T* at
which the experiments were carried out) of 77 kJ mol^{-1}. Moreover, the reac-
tion free energy was computed to be −33 kJ mol^{-1}, in which the surface SiOH   30
groups retain the released water with stable H-bonds (see Figure 13.6A).

However, it has been reported that the surface SiOH groups can also have
a direct catalytic role in the Gly condensation reaction rather than being
indirect spectators.[100] Indeed, silica rings of moderate strain present at the
silica surfaces, such as the $(SiO)_3$ ones (so-called S3R defects), can react   35
with Gly forming a surface mixed anhydride (in the same way as S2R, see
above and Figure 13.6B). This surface mixed anhydride has been suggested
to be an activated form of Gly and accordingly it could easily react with a
second Gly molecule to form a GlyGly dipeptide. However, calculations indi-
cate that, for the occurrence of this reaction, surface SiOH groups have to   40
assist the proton transfer involved in the condensation (see Figure 13.6B).
Such a proton transfer mechanism is the same as that promoted by water
solvent molecules (see above) and accordingly, hydroxylated silica surfaces
can be categorized as solid solvents. This SiOH-assisted condensation reac-
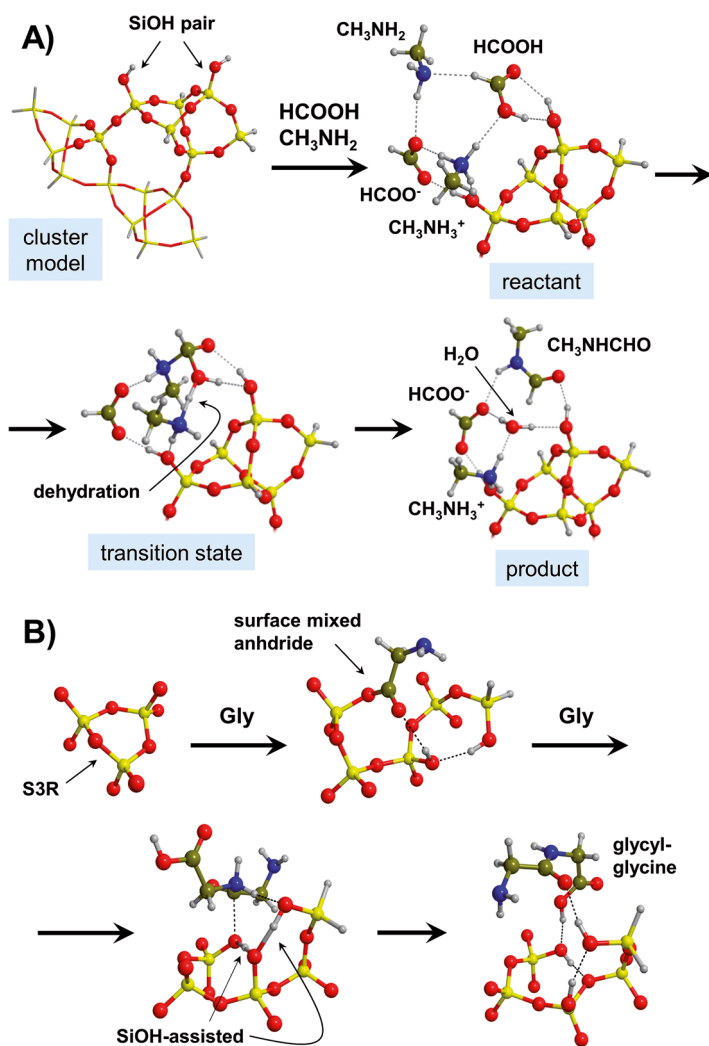tion between the surface mixed anhydride and a second Gly molecule was   45

Figure 13.6 (A) Sequence of the condensation reaction between HCOOH and CH$_3$NH$_2$ in the presence of a silica surface presenting specific weakly interacting SiOH groups. Adapted from ref. 52 with permission from American Chemical Society, Copyright 2018. (B) Sequence of the condensation reaction between two Gly molecules on a silica surface presenting a defective (SiO)$_3$ ring (S3R). The first step is the reaction of Gly with S3R to form a surface mixed anhydride intermediate. The second step is the reaction of the surface mixed anhydride with a second Gly, which is assisted by surface SiOH groups. Adapted from ref. 100 with permission from American Chemical Society, Copyright 2016.

computed to present a free energy barrier (T = 298 K) of 105 kJ mol^{-1}, thus
demonstrating the catalytic role of the surface SiOH groups in the reaction.
Moreover, since the reaction does not release water but forms a new SiOH
group (see Figure 13.6B), the reaction free energy was found to be largely
favorable, −68.8 kJ mol^{-1}.

The Earth's crust also contains certain minerals, which although not
being abundant, possess very attractive catalytic properties. This is the case
of TiO$_2$, whose exclusive physicochemical and catalytic features have been
extensively investigated for industrial and technological purposes. Interest-
ingly, for the cases in which the main feature of the minerals is their cata-
lytic properties, the amount of catalyst is not particularly relevant but its
effectiveness and reusability is. The significance of TiO$_2$ minerals in prebi-
otic chemistry has been addressed elsewhere.[101–103] In the particular case of
Gly polymerization, IR and mass spectrometry experiments carried out by
Martra *et al.*[57] revealed the formation of up to Gly16 oligopeptide on ana-
tase TiO$_2$ nanoparticles from the gas phase Gly adsorption on TiO$_2$. Atom-
istic interpretations of these experiments by means of quantum chemical
calculations have been reported by simulating the condensation of two Gly
molecules on the TiO$_2$ (101) anatase surface.[104] It was found that adsorption
of Gly on the TiO$_2$ surface enhances the electrophilicity of the C atom of the
C=O group, which leads to a moderate decrease of the free energy barrier
at normal conditions, to ≈150 kJ mol^{-1} (see Figure 13.7A). This free energy
barrier is, however, exceedingly high to be surmountable under these condi-
tions. However, it was discovered that a third Gly molecule can act as a cat-
alyst, indeed reducing dramatically the free energy barriers to peptide bond
formation. Specifically, the third Gly catalysed the initial proton transfer
(see Figure 13.7B), reducing the free energy barrier down to 8 kJ mol^{-1}. The
origin of the energy barrier decrease is due to a combination of facilitated
proton transfer and the reduced geometrical strain in the transition state
structure. The remaining bottleneck of the entire condensation reaction is
the dehydration step, with a free energy barrier of 74 kJ mol^{-1}. Remarkably,
the released water molecule is kept adsorbed on the TiO$_2$ surface with a very
favorable reaction free energy (−87 kJ mol^{-1}) due to the large water adsorp-
tion energy onto Ti sites.

13.4   Conclusions and Perspectives

In this book chapter, a plausible journey of the Gly's life, from its likely forma-
tion in the ISM, passing through its transportation and release on a primitive
Earth by bombardment of micro-asteroidal grains, up to its final evolution in
the form of polypeptide, is described by means of quantum chemical simu-
lations. The chapter is dedicated to different theoretical works focusing on
aspects concerning the birth and fate of Gly, and has put them together follow-
ing a consistent organizational sequence that provides evidence on the fea-
sibility of the "formation → transportation and delivery → polymerization"
along the Gly's voyage.

A)

149.0

73.2

Gly **0.0**
+

48.1

H C O
N

TiO$_2$

-98.7

B)

74.1

0.0   **8.4**   **9.6**
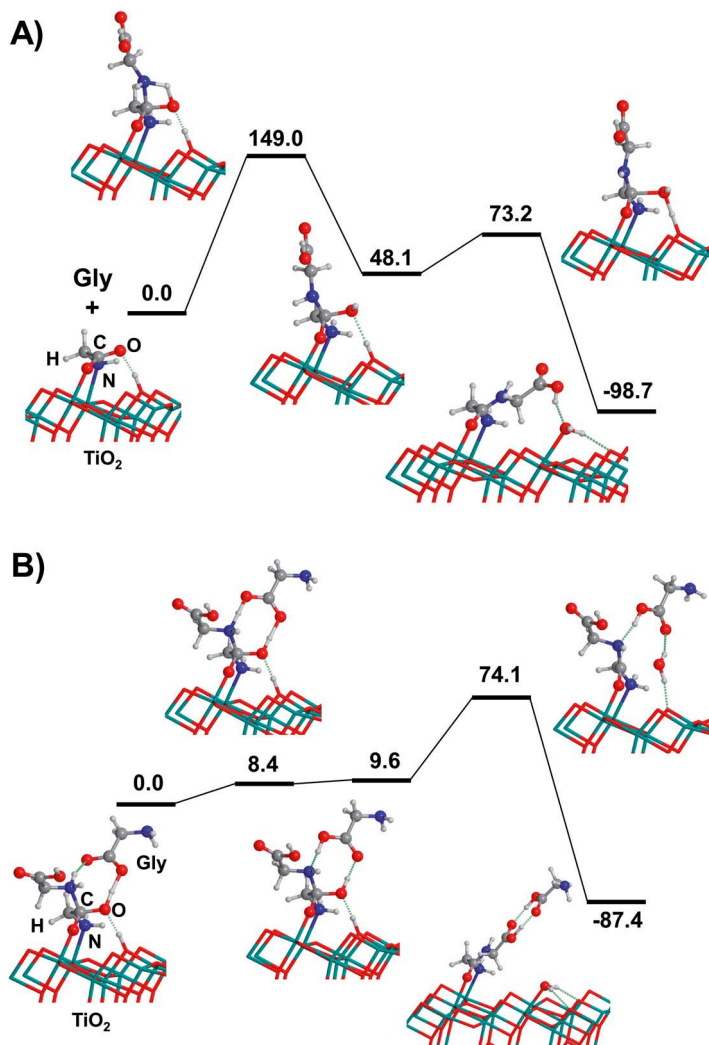
Gly

H C O
N

-87.4

TiO$_2$

Figure 13.7   Free energy profiles at 298 K for the condensation reaction between two Gly molecules on the TiO$_2$ (101) anatase surface, in the absence (A) and in the presence (B) of a third Gly molecule acting as a proton transfer assistant. Calculated at PBE0-D2*//PBE-D2* theory level. Relative energy units are in kJ mol^{-1}. Adapted from ref. 104 with permission from John Wiley & Sons, Copyright © 2018 Wiley – VCH Verlag GmbH & Co. KGaA, Weinheim.

It is shown that Gly can be formed in the ISM through the role of water ice mantles activated by UV radiation and cosmic rays. The ionising capability of this high energy flux brings about both ·OH and H$_3$O$^+$ defective species, which trigger the formation of Gly starting from simpler molecules (CO, NH$_3$, HCN). Calculations allowed one to speculate that Gly in the ISM can be efficiently trapped on asteroidal grains, since Gly can be chemisorbed at the

mineral surfaces exposed at asteroidal grains. Calculations also showed the
essential role of water in primordial oceans to hydrolyse the chemisorbed
Gly at grains. This step is essential for the abiotic polymerization of Gly into
a polypeptide, a process helped (both thermodynamically and kinetically)
by the mineral surfaces, such as silica, aluminosilicates and TiO_2. The role
played by these minerals is to immobilize, activate or capture the released
water, depending on the type of mineral and the structural and chemical
surface features.

Despite these positive results, the route to elucidate this particular aspect
of the prebiotic chemistry remains long and winding. Thus, there is still a
large space to be explored, both theoretically and experimentally, even for
the rather limited "Gly birth and fate" topic. In relation to Gly formation
in the ISM on water-dominated ice mantles, other synthetic routes should
be explored. Gly is a molecule of 10 atoms so different formation reaction
channels are expected. The problem here is to identify these different chan-
nels. In this sense, computational strategies that allow the elucidation of
different Gly formation pathways in an automatic way, such as the transition
state search using chemical dynamics simulations (TSSCDS) method,[105,106]
will be highly welcome. Also, in relation to Gly formation, a completely open
field is its synthesis on micro-asteroidal bodies, namely, cometary/meteor-
itic grains and interplanetary dust particles. In view of the large amount and
variety of amino acids identified in meteoritic samples, the occurrence of
their formation in the same meteorite is a highly probable hypothesis to be
explored. In spite of this, to the best of our knowledge, there are no theoret-
ical works dealing with this topic. Here, in addition to assessing if asteroi-
dal minerals play any role in the chemical reactions, an important point to
address is if hydrothermal alteration is also of fundamental relevance, either
directly (*i.e.*, the presence of "hot" water) or indirectly (*i.e.*, the presence of
minerals that can only be formed by water alteration). As mentioned in this
chapter, the interaction of Gly with mineral surfaces in dry conditions has
already been investigated in different degrees of detail. However, this is not
the case of its release in prebiotic watery environments. Works dedicated to
determining the energetic features of Gly desorption from mineral surfaces
immersed in bulk water are hitherto very scarce and, consequently, cur-
rently much required. They would be very useful in order to provide robust
evidence that liquid water was also essential in the exogenous delivery of
cosmic Gly. Finally, Gly condensation on mineral surfaces is certainly one of
the topics most investigated theoretically in the field of prebiotic chemistry.
However, an important gap remains to be filled: Gly polymerization in clays.
Indeed, although in Bernal's original hypothesis clays were advocated to be
the main minerals facilitating the reaction, to the best of our knowledge,
only very few theoretical studies dealing with peptide bond formation cata-
lysed by mineral clays have been developed, as recently done using the force
field method only.[107] Furthermore, the role of layered double hydroxides,
an important class of layered minerals on the prebiotic chemistry of bio-
polymers has recently been reviewed.[108] Therefore, although some efforts

have been dedicated to improve our understanding on the birth and fate of Gly, it seems evident that there is still a lot of work to do in order to have a deeper understanding on this topic, which certainly will be addressed in due course.

Acknowledgements

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