Prebiotic Chemistry

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Formation of Glyoxylic Acid in Interstellar Ices: A Key Entry Point for Prebiotic Chemistry

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Dedicated to Dr. Hans Peter Reisenauer

Abstract: *With nearly 200 molecules detected in interstellar and circumstellar environments, the identification of the biologically relevant α-keto carboxylic acid, glyoxylic acid (HCOCOOH), is still elusive. Herein, the formation of glyoxylic acid via cosmic-ray driven, non-equilibrium chemistry in polar interstellar ices of carbon monoxide (CO) and water (H_2O) at 5 K via barrierless recombination of formyl (HCO) and hydroxycarbonyl radicals (HOCO) is reported. In temperature-programmed desorption experiments, the subliming neutral molecules were selectively photoionized and identified based on the ionization energy and distinct mass-to-charge ratios in combination with isotopically labeled experiments exploiting reflectron time-of-flight mass spectrometry. These studies unravel a key reaction path to glyoxylic acid, an organic molecule formed in interstellar ices before subliming in star-forming regions like SgrB2(N), thus providing a critical entry point to prebiotic organic synthesis.*

In 2007, Eschenmoser postulated in his so-called "glyoxylate scenario" that glyoxylic acid (**1**) and glyoxylate act as fundamental prebiotic starting materials with a chemical constitution for primordial metabolism that could lead to key biologically relevant molecules, such as sugars, amino acids, nucleobases, and constituents of the citric acid cycle.[1] Parts of this scenario have been verified, for instance, the formation of the formal glyoxylate dimer dihydroxyfumarate (DHF, **2**) by treating glyoxylate with hydrogen cyanide (HCN) in an *Umpolung* reaction that further reacts to form tartrate, which might serve as a precursor for oxaloacetic acid and pyruvate;[2] both are constituents of the citric acid cycle. Glycine (**3**), the simplest amino acid, can easily form from the reductive amination of **1** (Scheme 1).[3]

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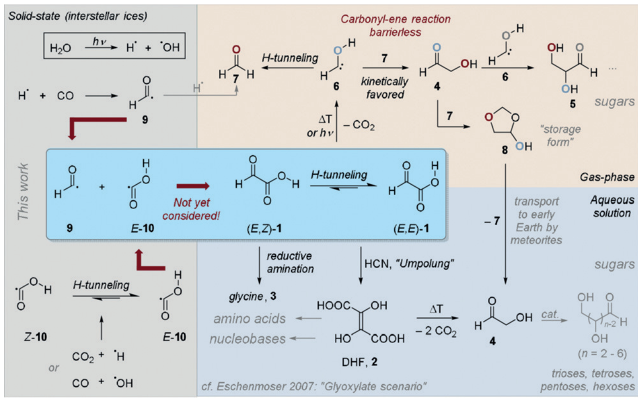


Scheme 1. Presentation of the formation of glyoxylic acid (**1**) in interstellar water (H_2O)–carbon monoxide (CO) ices via ionizing radiation. Glyoxylic acid serves as a precursor for critical biomolecules.

The synthesis of sugars in the field of prebiotic chemistry is in general connected to the formose reaction in aqueous solution, although this reaction is very unselective: various aldoses and branched ketoses form as soon as the autocatalytic formose cycle is initiated.[4] Alternative reactions to address and partially solve these issues were investigated.[5] In the context of the "glyoxylate scenario", Krishnamurthy et al. demonstrated the self-condensation of DHF to pentulosonic acid—a sugar acid that can decarboxylate to form erythrulose.[6] Furthermore, the authors reported the formation of acyclic ketoses up to a C_5 chain length in the reaction of DHF with glycolaldehyde (**4**), glyceraldehyde (**5**), and glyoxylate.[7] DHF thermally bis-decarboxylates in aqueous solution to afford **4**, which may further transform into higher aldoses.[8] Decarboxylation of **1** in the gas-phase yields hydroxymethylene (**6**, H-C̈-OH), which has been identified in an inert gas matrix at cryogenic temperatures around 10 K.[9] Even at these temperatures, **6** undergoes a [1,2]H-shift via tunneling to form formaldehyde (**7**) with a first order tunneling half-life of around 2 h.[9,10] Hydroxymethylene itself is able to react with **7** in a barrierless carbonyl-ene reaction to form **4** and this can further react to form **5**, along with higher acyclic aldoses, thereby offering an uncatalyzed gas phase, base-free, sugar-forming reaction.[11] The hydroxycarbene sugar-forming reactions are faster than the tunneling process and are kinetically favored. As described by Eschenmoser, **1** can be seen as a form of "carboxylated formaldehyde".[1b] Glycolaldehyde reacts in a kinetically favored reaction with **6** to form **5**, or with **7** yielding hemiacetal 1,3-dioxolane-4-ol (**8**), which may be considered as a photostable reservoir of **4** and **7**; **8** immediately releases its building blocks in aqueous solution.[12]

Notwithstanding the central role of **1**, its formation in interstellar environments has remained elusive. Its structure is C_s symmetric and displays two conformers: (*E*,*Z*) and the thermodynamically preferred (*E*,*E*) conformation.[13] Both rotamers can be photochemically interconverted with the (*E*,*E*) conformer being enriched through H-tunneling rotamerization.[13] The prebiotic origin of **1** has remained elusive, and Eschenmoser concluded that hitherto unknown reservoirs of **1** must exist as a major prerequisite for the "glyoxylate scenario". Glyoxylic acid has been suggested to form via ultraviolet (UV) exposure of water and acetylene solutions.[14] Recently, **1** was identified in the polymerization of hydrogen cyanide in aqueous solution as proposed by Eschenmoser.[15] Mohammed et al. demonstrated the synthesis of glyoxylate in non-enzymatic transamination reactions of **3** and **7** under prebiotic liquid conditions,[16] but these transformations bear only little relevance to reactions in the interstellar medium, where liquid water is unlikely to exist.

Here, we report the very first directed synthesis of **1** in models of extraterrestrial environments via the barrierless radical–radical recombination of the formyl (**9**) and hydroxycarbonyl (**10**) radicals (Scheme 1) by exposing low-temperature interstellar model ices to ionizing radiation with energetic electrons, thus mimicking secondary electrons generated in the tracks of galactic cosmic ray (GCR) particles as they interact with solid matter in deep space.[17] These model ices are comprised of carbon monoxide (CO) and water (H_2O) revealing that **1** can be synthesized abiotically by interaction of ionizing radiation with polar interstellar ices in molecular clouds. Water represents the dominant component of icy mantles of interstellar grains, reaching up to 58 % of the total ice abundance[18] with carbon monoxide being present in fractions up to 13 %, as detected in the Young Stellar Object NGC 7538 IRS 9.[18] Cold molecular clouds represent the nurseries of stars and planetary systems,[19] where nanometer-sized carbonaceous and silicate-based grain particles store icy layers of primarily water (H_2O), methanol (CH_3OH), carbon dioxide (CO_2), and carbon monoxide (CO), at temperatures as low as 10 K. As the ices are chemically processed by GCRs and the internal UV field, organic molecules, such as acetaldehyde, acetone, and acetic acid can form.[20] Once the molecular cloud transits into a star-forming region, this matter is transferred to circumstellar disks—reservoirs of material out of which planets, planetoids, and comets may form. Isotopic studies reveal that carbonaceous chondritic material carries a significant fraction of interstellar organic matter.[21] Consequently, organic molecules, such as **1**, which might have been formed in interstellar ices, can be incorporated into matter of Solar Systems, such as our own, ultimately unraveling how and where in the universe the molecular precursors to the origins of life might have been synthesized.

The experiments were designed to unravel the abiotic formation of **1** upon exposing interstellar model ices to ionizing radiation with energetic electrons, at radiation doses equivalent to the lifetime of molecular clouds of a few million years. During radiation exposure, multiple novel infrared (IR) absorptions emerged (Figure 1 and Supporting Information, Figures S1–S8, Tables S1–S4). As verified by isotopic substitution experiments, these features can be assigned to six

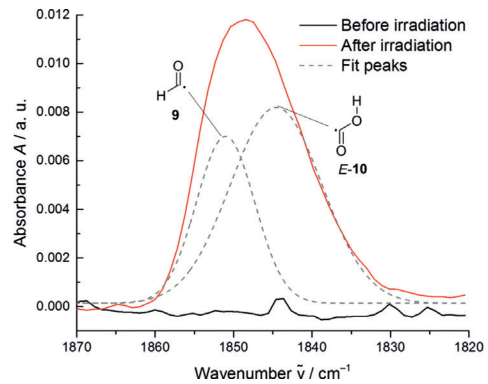
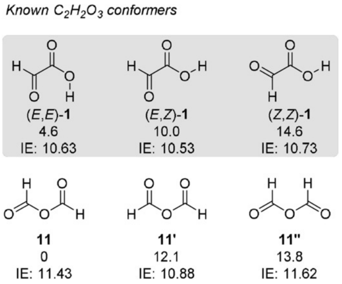


Figure 1. Observed infrared absorptions around 1850 cm^{-1} after (red) and before (black) the exposure of the water (H_2O)–carbon monoxide (CO) ice to ionizing radiation.

discrete molecules: carbon dioxide (2344, 660 cm^{-1}), the formyl radical (**9**; 1852, 1095 cm^{-1}),[22] the hydroxycarbonyl radical ((*E*)-**10**; 1847 cm^{-1}),[23] formaldehyde (**7**; 1718, 1499, 1250, 1175 cm^{-1}), formic acid (1700, 1224 cm^{-1}), and methanol (1023 cm^{-1}).[24] The hydroxycarbonyl radical exists in two conformers, namely *Z* and the thermodynamically preferred *E* form. Both conformers can be interconverted by IR irradiation.[25] In the dark, the *E*-**10** conformer enriches due to H-tunneling rotamerization of *Z*-**10** (Scheme 1).[25] The overlap of the fundamentals of **1** with those of the detected dominating species prevents the unambiguous identification of **1** via IR spectroscopy. However, a comparison of the molecular structure of **1** with the building blocks detected by IR spectroscopy suggests that **1** might have been formed in the ices via a barrierless radical–radical recombination of **9** with **10** (Scheme 1). Nevertheless, an alternative analytical technique is required for the firm identification of **1**.

Therefore, we exploited photoionization reflectron time-of-flight mass spectrometry (PI-ReTOF-MS) during the temperature-programmed desorption (TPD) phase of the irradiated ices. This method represents a unique approach to detect gas-phase molecules isomer-selectively via soft photoionization based on their distinct ionization energies, without dissociatively fragmenting the molecular parent ion, as often experienced with traditional electron impact (EI) ionization techniques. Considering the computed adiabatic ionization energies at the CCSD(T)/CBS//MP2/cc-pVTZ level of theory (see the Supporting Information) of **1** and formic anhydride (**11**) of 10.53–10.73 eV and 10.88–11.62 eV, respectively (Scheme 2), 10.82 eV photons can only ionize **1**, but not **11**. Therefore, the subliming molecules in the irradiated ices were photoionized in the TPD phase first with 10.82 eV photons (Figure 2). The ions were then extracted and mass-resolved based on their arrival times. Figure 3 a shows the TPD profile of ions recorded at mass-to-charge (*m*/*z*) of 74. Upon lowering the photon energy to 10.23 eV, which is below the



Scheme 2. Distinct conformers of glyoxylic acid (**1**, top) and of formic anhydride (**11**, bottom). The zero-point vibrational energy (ZPVE) corrected relative energies (in $kJ\,mol^{-1}$) and adiabatic ionization energies (IE in eV) at CCSD(T)/CBS//MP2/cc-pVTZ level of theory are included.

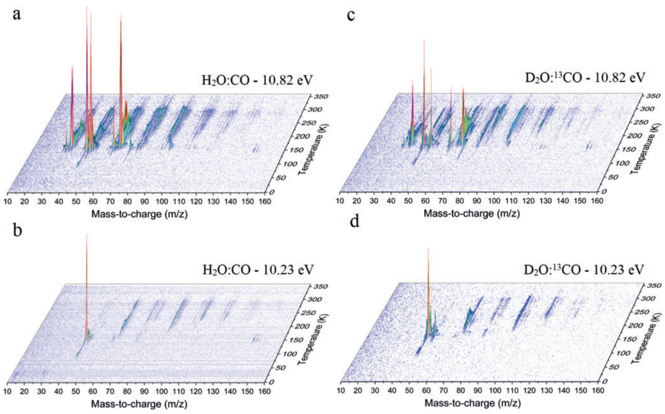


Figure 2. PI-ReTOF-MS data collected in the a) H_2O:CO experiment at 10.82 eV; b) H_2O:CO experiment at 10.23 eV; c) D_2O:^{13}CO experiment at 10.82 eV; d) D_2O:^{13}CO experiment at 10.23 eV.

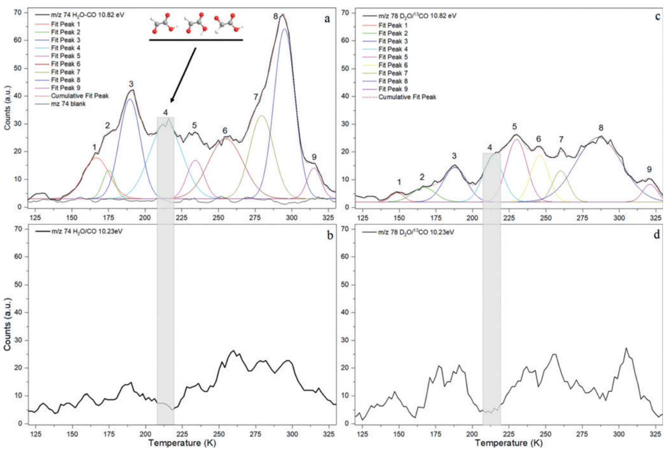


Figure 3. Overview of the PI-ReTOF-MS signals of interest detected in the four main systems: a) H_2O:CO at 10.82 eV; b) H_2O:CO at 10.23 eV; c) D_2O:^{13}CO at 10.82 eV; d) D_2O:^{13}CO at 10.23 eV. The sublimation event 4 in the 208 K to 219 K range recorded at photon energies of 10.82 eV can be linked to conformers of glyoxylic acid ($C_2H_2O_3$, **1**) and its isotopologue ($^{13}C_2D_2O_3$).

adiabatic ionization energy of **1**, only the fourth sublimation event near 210 K disappears completely (Figure 3b). This suggests that this sublimation event can be linked to **1**. To confirm these conclusions, the experiments were repeated using isotopically substituted D_2O:^{13}CO ices. The isotopic shift of the species of interest ($m/z=78$) observed in the PI-ReTOF-MS profiles at 10.82 eV and 10.23 eV are depicted in Figures 3c and d, respectively; these traces support our conclusions: at 10.82 eV, the TPD profile could be well fitted employing nine sublimation events, of which the fourth event disappears at 10.23 eV, thus providing compelling evidence for the formation and detection of **1** ($m/z=74$), along with its deuterated D-^{13}C-**1** counterpart [$D^{13}CO^{13}COOD$] ($m/z=78$).

Note that the PI-ReTOF-MS profiles are complicated by the fact that not only ionized $C_2H_2O_3$, but in principle also molecular ions of $C_3H_6O_2$, $C_4H_{10}O$, and C_6H_2 may contribute to signal at $m/z=74$ (Figure 3a and b). However, extensive isotopic substitution experiments eliminate contributions from $C_4H_{10}O$ and C_6H_2 (Supporting Information, Figure S9). First, in the D_2O:CO and D_2O:^{13}CO systems, ion counts of $C_4H_{10}O$ ($m/z=74$) recorded at a photon energy of 10.82 eV should be shifted to $m/z=84$ ($C_4D_{10}O^+$) and $m/z=88$ ($^{13}C_4D_{10}O^+$), respectively (Supporting Information, Table S5 and Figure S9a,b). However, no signal was detected at these m/z values suggesting that the formation of $C_4D_{10}O$ and $^{13}C_4D_{10}O$, and consequently $C_4H_{10}O$, can be excluded. Considering an adiabatic ionization energy of 10.20 eV of hexa-1,3,5-triyne (C_6H_2),[26] the signal should shift from $m/z=74$ ($C_6H_2^+$) to $m/z=80$ ($^{13}C_6H_2^+$) in H_2O:^{13}CO ices. However, at a photon energy of 10.23 eV, no signal was detected (Supporting Information, Figure S9c) revealing that hexa-1,3,5-triyne did not form. Finally, we explored the potential formation of $C_3H_6O_2$ isomers (Supporting Information, Figure S10). Here, signal should shift from $m/z=74$ to $m/z=77$, 80, and 83 in H_2O:^{13}CO, D_2O:CO, and D_2O:^{13}CO systems, respectively. Data recorded with photon energies of 10.82 eV and 10.23 eV reveal substantial ion counts at temperatures above 210 K (Supporting Information, Figure S10). Therefore, we can conclude that besides **1** subliming at 210 K, some $C_3H_6O_2$ isomers could form as well.

These results represent a critical step toward a systematic understanding of how **1** can form abiotically in interstellar model ices as a consequence of the interaction with ionizing radiation. A comparison of the molecular structure of **1** with those of the C_1 and C_2 building blocks detected spectroscopically suggests that **1** can form via a barrierless radical–radical recombination of **9** with **10** (Scheme 1). This radical–radical recombination can either occur in the ices during the radiation exposure even at 5 K, if both radicals are in close proximity and in a favorable geometry for recombination,[20c] or upon warming when the radicals can diffuse. In H_2O:CO ices, the interaction of ionizing radiation with water molecules can cleave the hydrogen—oxygen bond generating atomic hydrogen and a hydroxyl radical (OH).[27] Suprathermal hydrogen atoms—hydrogen atoms with excess kinetic energy—and vibrationally excited hydroxyl radicals may react with carbon monoxide to form **9** and **10** (Scheme 1). Alternatively, water loses atomic oxygen upon interaction of ionizing radiation in ices[28] upon which the oxygen atom can react with carbon monoxide to form carbon dioxide. About 3% of the carbon monoxide reactant transformed to carbon dioxide (Supporting Information, Figure S11 and Table S6). The latter may react with suprathermal hydrogen atoms within the ice to form **10** and ultimately upon recombination with **9**, glyoxylic acid (**1**) in interstellar ices.

This study was carried out through a novel in situ detection of **1** by exploiting tunable vacuum UV single-photon ionization (PI) coupled with ReTOF mass spectrometry (PI-ReTOF-MS) in an ultra-high vacuum chamber at pressures of a few 10^{-11} Torrs. Since the stability of mineral- and meteorite-embedded biorelevant molecules, such as amino acids and sugars, has been verified,[29] at least a fraction of **1**—once synthesized abiotically in deep space—might survive on meteoritic parent bodies and successive meteorite or comet impact on Earth, therefore reinforcing the theory of exogenous source of prebiotic molecules on Earth. This setting defines an appealing option to rivaling theories like the formation of biorelevant molecules in hydrothermal vents on prebiotic Earth, which require liquid water to exist.[30] Therefore, the formation and detection of **1** in our laboratory simulation experiments should trigger future astronomical searches toward SgrB2(N-LMH)—a hot core in which various organic molecules, such as **4**, have been observed—with the Atacama Large Millimeter/sub-millimeter Array (ALMA).

The exploitation of interstellar model ices represents a substantiated strategy and original step as validated by, for example, Meinert and co-workers and Ehrenfreund and co-workers.[31] Future work may investigate the role of distinct interstellar irradiation fields (for example, photons vs. GRCs) and mineral-catalyzed formation on the yield of glyoxylic acid, thus eventually deciphering the fundamental molecular processes that might have contributed to the inventory of prebiotic, biorelevant compounds from which life could have emerged.

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Conflict of interest

The authors declare no conflict of interest.

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