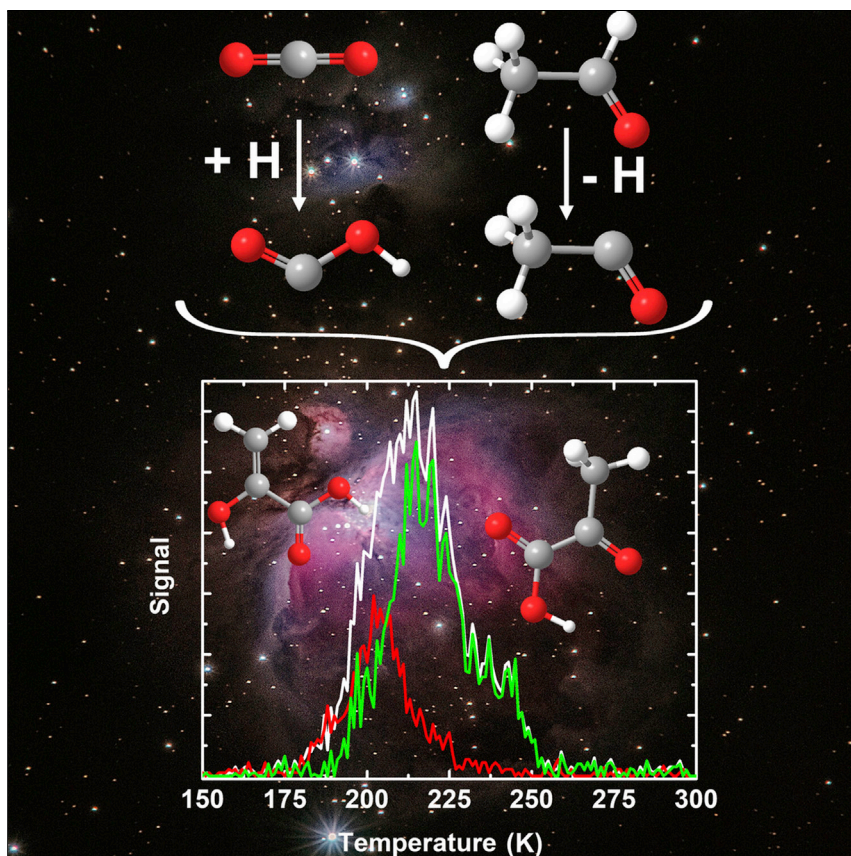


Article

Interstellar Formation of Biorelevant Pyruvic Acid (CH_3COCOOH)

Prebiotic pyruvic acid is unlikely to have formed on the early earth, where liquid water was not present. Hence, it may have formed in space in ices containing acetaldehyde (CH_3CHO) and carbon dioxide (CO_2), whose reactions were triggered by energetic cosmic radiation. We demonstrate a key reaction pathway for pyruvic acid synthesis through non-equilibrium reactions in interstellar cold molecular clouds and star-forming regions, thus offering a unique entry point to abiotic organic synthesis in deep space.

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HIGHLIGHTS

Pyruvic acid, essential to life, forms in the absence of a biochemical machinery

Interstellar ices are breeding grounds for organic molecules

High-energy electrons initiate chemical reactions in interstellar ices

The results guide the radio-astronomical identification of pyruvic acid in space

Article

Interstellar Formation of Biorelevant Pyruvic Acid (CH₃COCOOH)

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SUMMARY

Pyruvic acid represents a key molecule in prebiotic chemistry to form metabolites and amino acids. Without liquid water on the early Earth, endogenous formation of pyruvic acid is unlikely, and an exogenous delivery constitutes an appealing alternative. However, despite the detection of more than 200 molecules in space, pyruvic acid is elusive. Here, we describe its formation by barrierless recombination of hydroxycarbonyl (HOCO•) and acetyl (CH₃CO•) radicals in ices of acetaldehyde (CH₃CHO) and carbon dioxide (CO₂) modeling interstellar conditions driven by cosmic rays. Exploiting isotopically labeled ices and photoionization reflectron time-of-flight mass spectrometry, the reaction products were selectively photoionized in the temperature-programmed desorption phase and isomers discriminated based on their ionization energies. This reveals a key reaction pathway for pyruvic acid synthesis through non-equilibrium reactions in interstellar cold molecular clouds and star-forming regions, thus offering a unique entry point to abiotic organic synthesis in deep space.

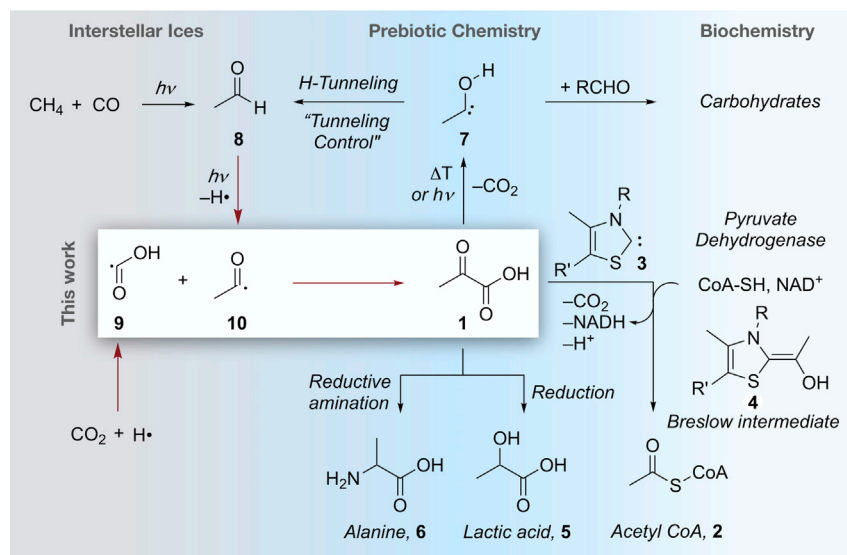
INTRODUCTION

Pyruvic acid (1, CH₃COCOOH) along with its deprotonated pyruvate anion (CH₃COCOO[−]) represent critical molecules in modern biochemistry and plays a key role in contemporary chemical processes that occur within living organisms in order to maintain life (metabolism) (Scheme 1). Serving as the starting material for the Krebs cycle (citric acid or TCA cycle [tricarboxylic acid cycle]) and the pyruvate dehydrogenase complex, 1 links glycolysis with the TCA cycle. After decarboxylation of 1 and nicotinamide adenine dinucleotide (NAD⁺) reduction, acetyl CoA (2) forms with cofactor A (CoA-SH, Scheme 1). Here, the energy is provided via carbon-carbon bond cleavage and the release of carbon dioxide (CO₂) in an oxidative decarboxylation of 1 as the very first step. With thiamine pyrophosphate (TPP, 3)—a thiamine (vitamin B₁) derivative with a N-heterocyclic carbene (NHC) as the active entity—the amino enol structure 4 forms, which is referred to as the *Breslow intermediate*.^{1,2} The polarity of the formerly electrophilic carbonyl carbon atom is switched and now reveals nucleophilic character. Therefore, NHC organocatalysis and such *Umpolung* chemistry has found widespread applications in organic chemistry.^{3–5} Only recently, Berkessel et al. characterized several hitherto elusive Breslow intermediates by NMR spectroscopy and X-ray crystallography.^{6,7}

In prebiotic chemistry, 1 may have served as a fundamental building block for key biological compounds.^{8,9} Pyruvic acid can be reduced to lactic acid (CH₃CH(OH)COOH, 5)¹⁰ or acts as a precursor for the amino acid alanine (6) formed in the reductive amination of 1.¹¹ Recently, Muchowska et al. reported a captivating chemical reaction network promoted by Fe(II), in which 1 and glyoxylate (HCOCOO[−]) build up nine of the 11

The Bigger Picture

One of the key questions is how life could have emerged on early Earth and what chemicals and key reactions were involved. Terrestrial biomolecules, such as DNA, RNA, and peptides, formed from building blocks like nucleobases and amino acids. But where do these come from? Simple chemical building blocks could have formed on icy grains in space and may have survived comet impact on the early Earth. Pyruvic acid is widely accepted as a key prebiotic starting material, as it may have served as a fundamental building block for biorelevant molecules. This is underlined by the identification of pyruvic acid in carbonaceous meteorites. This study investigates the formation of pyruvic acid under interstellar conditions to encourage scientists in other fields to consider pyruvic acid as a potential interstellar molecule and include it in their radio-astronomical line searches. For chemists, the study will lead to a better understanding of the fundamental processes of abiotic syntheses of organic molecules.



Scheme 1. Interstellar Formation of Pyruvic Acid

Interstellar formation of pyruvic acid (1) in low-temperature ices containing acetaldehyde (8) and carbon dioxide by energetic processing through simulated galactic cosmic rays. Pyruvic acid serves as a precursor for critical biomolecules, including the amino acid alanine (6, bottom middle). In biochemistry, pyruvic acid is part of the citric acid cycle and forms acetyl CoA (2) in an enzymatic catalyzed reaction by pyruvate dehydrogenase (bottom right) with the Breslow intermediate 4 as the key intermediate (top right).

intermediates of the TCA cycle.⁹ Adding hydroxylamine (NH₂OH) and metallic iron into the system produces four biological amino acids (6, glycine, aspartic acid, and glutamic acid). In this reaction network, both α -ketocarboxylic acids along with hydroxylamine serve as fundamental starting materials. Further, Powner et al. highlighted the critical role of 1 by synthesizing 2-phosphoenolpyruvate (PO₄²⁻C(CH₂)COO⁻, PEP)—the highest energy phosphate found in living organisms—from simple prebiotic nucleotide precursors: glycolaldehyde (HOCH₂CHO) and glyceraldehyde (HOCH₂CH(OH)CHO).¹² Pyruvate synthesis may occur during the abiotic degradation of carbohydrates and their phosphates,^{13,14} by the oxidation of lactic acid in aqueous media,¹⁵ and in the presence of iron sulfides in very low yields of only 0.07% under hydrothermal vent conditions, e.g., at elevated temperatures (523 K) and pressures (200 MPa) or in the presence of other transition metals. However, these scenarios rely on very specific reaction conditions to produce labile components, such as 1, which might not have been widespread under prebiotic conditions on the early Earth.^{16–19}

In the gas phase, 1 thermally decarboxylates (Scheme 1) at elevated temperatures yielding carbon dioxide and methylhydroxycarbene (7, HO- $\ddot{C}$ -CH₃); the latter undergoes isomerization via [1,2]H-tunneling to acetaldehyde (8, CH₃CHO), an observation that leads to the tunneling control reactivity paradigm.^{20–22} In general, hydroxycarbenes undergo barrierless carbonyl ene reactions with carbonyl compounds in the gas phase, yielding biorelevant molecules, including the carbohydrates glycolaldehyde and glyceraldehyde.²³ Eckhardt et al.²⁴ and Turner et al.^{25,26} recently demonstrated the formation of glyoxylic acid (HC(O)COOH) and even (di)phosphates (PO₄³⁻/P₂O₇⁴⁻) in ices modeling interstellar conditions, providing compelling evidence that essential biorelevant molecules, together with their precursors, might form in deep space. At least a fraction of these abiotically synthesized compounds might be incorporated into meteoritic parent bodies and could have survived successive meteorite or comet impact on the Earth, thus

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reinforcing the theory of an exogenous source of key prebiotic molecules on the Earth.²⁷ This setting defines an appealing alternative to competing theories like the formation of biorelevant molecules in hydrothermal vents on the prebiotic Earth. Although pyruvic acid is prone to decarboxylation, especially in the presence of transition metals and at elevated temperatures, Cooper et al. identified pyruvic acid in carbonaceous meteorites at 15 nmol g⁻¹, indicating that even such potentially unstable compounds are able to survive the entrance of the meteorite into the atmosphere and participate in further prebiotic processes.²⁸ Therefore, abiotic formation in the interstellar medium and delivery to the early Earth by meteorites constitutes another plausible source of prebiotic molecules on the Earth. This finding clearly underlines the importance of non-equilibrium processes in the fields of astro- and prebiotic chemistry.^{29,30}

RESULTS AND DISCUSSION

Ice Preparation

Here, we demonstrate the first abiotic synthesis of **1** under conditions mimicking extraterrestrial environments via the barrierless radical-radical reaction of the hydroxycarbonyl (HOCO•, **9**) and acetyl (CH₃CO•, **10**) radicals (Scheme 1) by exposing low-temperature model ices to ionizing radiation with high-energy electrons simulating secondary electrons formed in the path of galactic cosmic ray (GCR) particles penetrating ices on interstellar grains in molecular clouds.^{31,32} Cold molecular clouds encompass the raw material of stars and planetary systems with nanometer-sized grain particles consisting of amorphous and polyaromatic carbon³³ and olivine-type silicates³⁴ ("interstellar dust") accumulating icy layers of mainly water (H₂O), methanol (CH₃OH), carbon dioxide (CO₂), and carbon monoxide (CO) at temperatures as low as 10 K.^{35–37} These ices are chemically processed by the internal ultraviolet (UV) field³⁸ and by energetic GCRs, leading to the synthesis of an array of organic molecules, such as the simplest sugar-related compound—glycolaldehyde,³⁹ other aldehydes⁴⁰ (e.g., Abelson,⁸ Bennett et al.,^{31,32}), ketones (e.g., acetone), and carboxylic acids^{41,42} (e.g., formic acid⁴³ and acetic acid⁴⁴).³⁵ When a molecular cloud transits into a star-forming region, matter is incorporated into circumstellar disks, which, in turn, contain the material out of which planets, planetoids, and comets may form. Therefore, **1**, initially formed in interstellar ices, can be integrated into matter of solar systems eventually untangling the fundamental chemical reaction(s) of how and where in the universe the molecular precursors to the origins of life can arise.

In contrast to the complex mixture of ice constituents found in the interstellar medium, laboratory model ices typically only consist of binary or ternary mixtures of molecules detected in interstellar ices to facilitate the assignment of newly formed molecules based on mass-to-charge ratios, isotopic shifts, and ionization energies. Therefore, only a fraction of the molecules expected to form in interstellar ices are typically found in lab-based experiments. However, molecules formed in different individual simplified mixtures can be expected to form in interstellar ices, based on the availability of the reactants used.

The experiments were conceived to unravel the abiotic synthesis of **1** upon exposing polar model ices of **8** and carbon dioxide (CO₂) to proxies of galactic cosmic rays in the form of high-energy electrons under conditions mimicking the lifetime of molecular clouds of up to a few million years.⁴⁵ These anhydrous model ices were chosen to explore the proof-of-concept that **1** can be synthesized via interaction of interstellar ices with ionizing radiation. Accounting for data from the Spitzer space

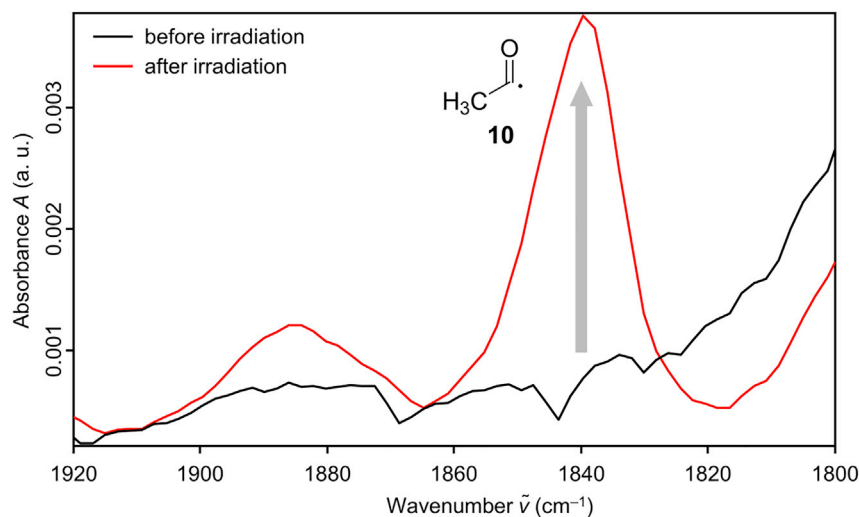


Figure 1. Infrared Spectra before and after Exposure of the Ice to Ionizing Radiation

Observed infrared absorptions between $1,800\text{--}1,900\text{ cm}^{-1}$ before (black) and after (red) the exposure of the acetaldehyde (CH_3CHO) carbon dioxide- $^{18}\text{O}_2$ (C^{18}O_2) ice to ionizing radiation. The new observed IR absorption can be assigned to the acetyl radical ($\text{CH}_3\text{CO}\cdot$, $1,840\text{ cm}^{-1}$).

telescope, ices containing carbon dioxide at levels of up to 37% relative to water were observed toward low- and high-mass stars, field stars, and Galactic center sources^{46–48}; **8** was only detected tentatively on grains,^{49,50} but laboratory experiments verified that **8** forms easily on interstellar grains containing carbon monoxide (CO) and methane (CH_4).^{31,40} During the radiation exposure of **8** and carbon dioxide or **8** and carbon dioxide- $^{18}\text{O}_2$ (C^{18}O_2) ices, multiple novel infrared (IR) absorption features emerged (Figures 1 and S1–S5; Table S1).

IR Analysis

These absorptions can be linked to four discrete molecules: carbon monoxide (CO, $2,131\text{ cm}^{-1}$), carbon monoxide- ^{18}O (C^{18}O , $2,086\text{ cm}^{-1}$), the acetyl radical (**10**, $1,840\text{ cm}^{-1}$, Figure 1), and methane (CH_4 , $1,304\text{ cm}^{-1}$).^{51–53} The assignment of **10** is further supported by the isotopic shift in a mixture of acetaldehyde- d_4 (CD_3CDO) and carbon dioxide- $^{18}\text{O}_2$, where the acetyl- d_3 radical is detected at $1,851\text{ cm}^{-1}$, which agrees well with matrix isolation studies of acetyl and previous studies on the irradiation of pure acetaldehyde ices.^{51,53} However, since electron irradiation can produce a significant array of new species and isomers with close vibrational absorptions, infrared spectroscopy is capable of determining only newly formed functional groups, but often does not allow further identification of individual complex organic molecules. In contrast to inert gas matrix isolation spectroscopy, no inert host gas was used in our experiments, since they aim to replicate interstellar ices; therefore, all observed infrared absorptions were typically very broad and not sharp, which made assignments of specific molecules extremely challenging. The features at 954 cm^{-1} and $1,052\text{ cm}^{-1}$ can be linked to CH_2 wagging and C–O stretching vibrations, respectively. In addition, a broad absorption feature between $1,200$ and $1,300\text{ cm}^{-1}$ was observed after irradiation that was probably connected to C–O–H deformation vibrations. Due to the low concentration, broad absorptions, and signal overlaps in the critical regions, we could not identify **1** unambiguously. However, since the formation of **10** from **8** released suprathermal hydrogen, which could easily overcome the barrier of addition to carbon dioxide to form **9**,⁵⁴ it is very likely that **9** formed in the ices. Unfortunately, in both isotopically labeled and the unlabeled

ices, the absorption features of **9** coincided with acetaldehyde absorption features at 1,796 cm⁻¹ and the acetyl feature at 1,833 cm⁻¹, respectively.⁵⁵ Moreover, no absorptions associated with vinoxy radicals (2-oxoethyl, CH₂CHO, 1,542 cm⁻¹) were observed. This is in agreement with a recent study on radical-radical reactions in pure acetaldehyde ices, revealing that reaction products from vinoxy radicals did not form.⁵³ Comparing the molecular structure of **1** with the radical building blocks **9** and **10** suggests that **1** could have formed in the ices via a barrierless radical-radical recombination (Scheme 1). However, an alternative analytical technique is required for the firm identification of **1**.

PI-ReTOF-MS Study

This could be achieved by exploiting photoionization reflectron time-of-flight mass spectrometry (PI-ReToF-MS) during the temperature-programmed desorption (TPD) phase, in which, the irradiated ice was heated to 320 K. This approach allowed us to identify different isomers in the gas phase, based on their distinct ionization energies and desorption profiles, which is outlined below. In contrast to electron impact ionization, which can lead to strong fragmentation even of the parent molecule, photoionization is ideally fragmentation free, thereby facilitating the assignment of mass-to-charge ratios of specific isomers. The PI-ReToF-MS experiments were performed using ices of **8** and ¹⁸O isotopically labeled carbon dioxide (C¹⁸O₂). This combination ensured a unique mass-to-charge (*m/z*) ratio for the reaction products investigated as the main reaction products from pure acetaldehyde ices subjected to ionizing radiation were diacetyl (*m/z* = 86), the acetaldehyde dimer (*m/z* = 88), and the protonated dimer (*m/z* = 89), all of which had a lower ionization energy than **1**.⁵³ With the isotopic labeling, however, the mass-to-charge ratio of 1-¹⁸O₂ shifted to *m/z* = 92, at which no reaction products of **8** or C¹⁸O₂ were detected at the photon energies used; at the same time, reaction products from pure acetaldehyde ices were not shifted by the isotopic labeling.

As adiabatic ionization energies of key complex organic molecules have not yet been determined experimentally, they had to be computed with high confidence. All molecular structures were optimized at B3LYP/cc-pVTZ level of theory in their electronic ground state and in their radical cationic form that resembles the most similar conformation. All electronic energies were improved by extrapolated high level *ab initio* coupled cluster CCSD(T)/CBS energies and were corrected by zero-point vibrational energies (ZPVEs). The difference of the ZPVE corrected radical cationic electronic energy and the ZPVE corrected energy of the studied molecule equaled the adiabatic ionization energy. As the difference of deuterated (or heavier) and non-deuterated isotopologs in the ZPVEs is generally marginal, we used the ZPVEs of non-deuterated isotopologs for IE calculations and assumed them to be the same for our experiments with heavier isotopologs. For a comparison and error analysis, the adiabatic ionization energies of selected molecules have been computed and compared with experimental values (Table S2). The comparison showed that the computed values were within an error regime of -0.04 eV to +0.19 eV to the experimentally determined ones. This estimated error and a reduction of ionization energies of 0.03 eV due to the electric field of the extractor plate of the time-of-flight spectrometer⁵⁶ were taken into account for the design of our following experimental studies.

In our PI-ReToF-MS studies, **1** and 2-hydroxyacrylic acid (CH₂(COH)COOH, **11**) could be distinguished based on their experimental (IE = 10.1 eV for **1**)⁵⁷ and computed adiabatic (CCSD(T)/CBS//B3LYP/cc-pVTZ + ZPVE) ionization energies (Table S3) by tuning the photon energy. Utilizing photons at 10.49 eV, all isomers could be photoionized. By tuning the photon energy down to 9.75 eV, **1** (IE = 9.90–10.02 eV) could

not be ionized, leaving only its enol isomer **11** to contribute to the ion signal at $m/z = 92$. Decreasing the photon energy further to 9.20 eV excluded all conformers of 2-hydroxyacrylic acid ($IE = 9.28\text{--}9.84$ eV). The temperature-dependent mass spectra over the range of $m/z = 40\text{--}200$ at each photon energy are shown in Figure 2. As **8** polymerized quickly upon electron irradiation, it desorbed from its sublimation onset at around 90 K up to a maximum temperature of 320 K and hence dominated the ion counts at 10.49 eV. The spectrum recorded at this energy has therefore been scaled to the height of the highest product peak to provide better visibility of the products formed. To exclude contributions from impurities in the ice, a TPD experiment was also conducted at 10.49 eV on unirradiated ice (Figures 3C and S6), revealing $m/z = 117$ as the only significant ion signal apart from the reactants. Figure 3A shows the corresponding TPD profiles of $m/z = 92$ recorded at different ionization energies. At 10.49 eV, a bimodal distribution peaking at 200 K and 235 K was clearly visible, suggesting the formation of both **1** and its enol isomer **11**. This was confirmed when comparing the TPD profile recorded at 9.75 eV, which was below the ionization energy of **1**. Evidently, the second sublimation event vanished at this photon energy. The early sublimation event only disappeared at 9.20 eV. These findings indicate that the first desorption event (175–225 K) was due to **11** and the second event (200–255 K) was linked to the desorption of **1**. The desorption of **1** might have been delayed in comparison with **11** because of one free carbonyl group that might have been involved in an intermolecular hydrogen bonding network within the irradiated ice (see also Figure 3D). In **11**, intramolecular hydrogen bonding (cf. relative energies in Table S3, *anti*-(*Z,Z*) conformer) was dominating the molecular structure.

The individual desorption profiles of **1** and **11** could be extracted from the data by scaling the data collected at 9.75 eV and subtracting them from the TPD profile recorded at 10.49 eV, as visualized in Figure 3B. The assignment of the second desorption event to **1** was further verified when comparing this difference spectrum to that of **1**, as shown in Figure 3D. Pure pyruvic acid desorbed at 175–200 K (green curve), however, when co-deposited with acetaldehyde and C¹⁸O₂ and irradiated using the same parameters as in the experiment (black curve), a second, broad desorption event spanning from 200–235 K became evident. This event originated from **1** trapped inside the polymer matrix of **8**, thereby delaying the desorption. This part of the TPD profile matched with that of the desorption event only seen at 10.49 eV (blue curve, Figure 3D) in our experiments, which further confirmed the synthesis of **1** in the ice. The divergence of the profiles at higher temperatures could be explained by **1** trapped in sites of the polymer matrix that were not accessible to the co-deposited pyruvic acid, whereas the absence of the first desorption event was due to the fact that **10** formed from irradiation was trapped in the polymer matrix. These effects were previously also seen for diacetyl forming in pure ices of **8**.⁵³

Conclusion

The results of this study aid in our understanding of how **1** can form abiotically in acetaldehyde-containing interstellar ices upon interaction with ionizing radiation. The molecular structure of **1** suggests a barrierless radical-radical recombination of **9** and **10** as a key formation pathway, since **10** can clearly be identified by infrared spectroscopy and **9** is known to form easily via addition of suprathreshold hydrogen to carbon dioxide. Due to overlap of the main absorptions of **1** with other constituents of the ice, its presence in the irradiated ice at 5 K could, however, not be spectroscopically confirmed, and it remains to be seen whether **1** forms upon irradiation at 5 K or during the warm-up phase when radicals become mobile in the ice and can therefore easily recombine. Exploiting TPD with tunable photoionization

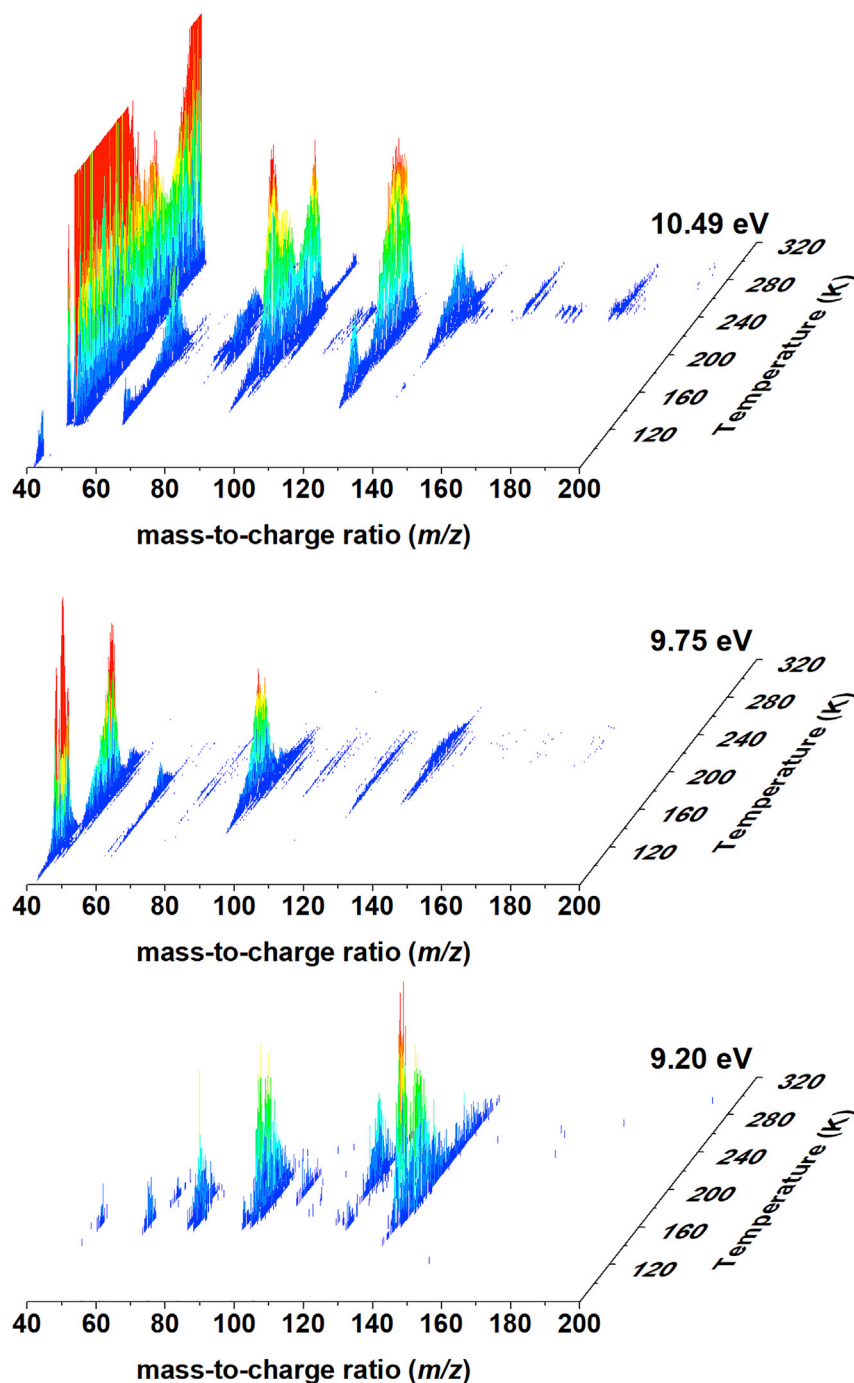


Figure 2. Photoionization Reflectron Time-of-Flight Mass Spectrometric Data of the Radiation Experiments

PI-ReToF-MS data collected at 10.49, 9.75, and 9.20 eV, respectively. Data collected at 10.49 eV have been scaled to the height of the highest visible product peak.

reflectron time-of-flight mass spectrometry and infrared spectroscopy, this study reveals a non-equilibrium pathway for the formation of **1** in interstellar ices. The non-equilibrium nature of this reaction is evident from the endoergic cleavage of the carbon-hydrogen bond in **8** leading to the formation of the acetyl radical **10**

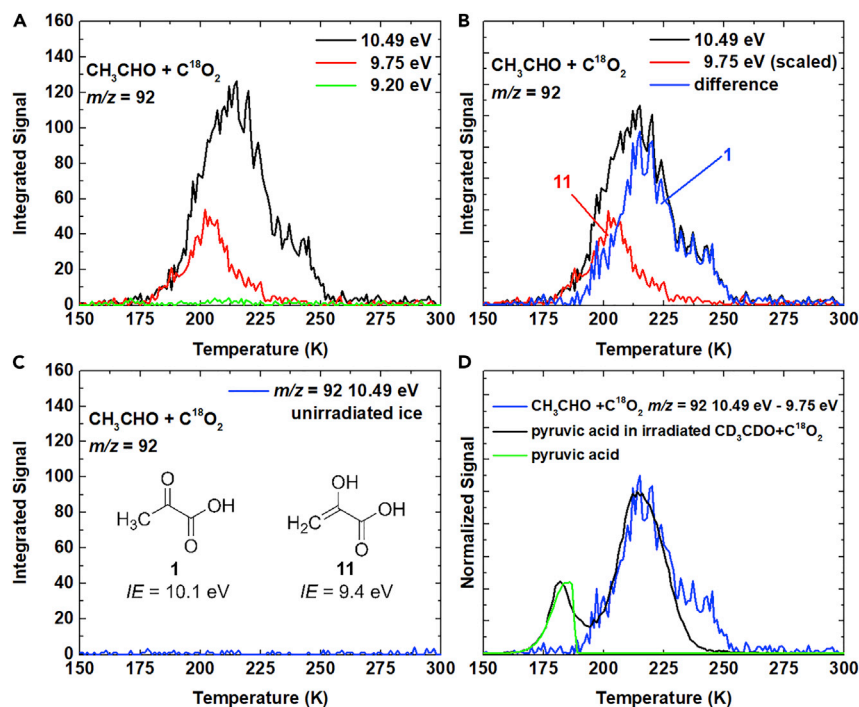


Figure 3. Selected Temperature-Programmed Desorption Profiles

(A–D) PI-ReToF-MS data for $m/z = 92$ collected at 10.49, 9.75, and 9.20 eV, respectively. Collected data (top left, A) and subtraction of signals at 10.49 and 9.75 eV after scaling (top right, B). Blank experiment (bottom left, C) and TPD profiles of pure pyruvic acid (1), pyruvic acid deposited with acetaldehyde- d_4 and carbon monoxide- $^{18}\text{O}_2$, and the desorption profile of $m/z = 92$ in the experiments at 10.49 eV after subtracting the contribution from the enol isomer recorded at 9.75 eV (bottom right, D).

requiring 3.9 eV. Further, the overall reaction leading to the synthesis of 1 from 8 and carbon dioxide is endoergic by 0.8 eV with the energy supplied by the energetic processing of the ice samples.

In cold molecular clouds, once 1 forms within interstellar ices and/or during the annealing phase of the ices when the new star forms (star-forming regions) and temperatures may reach up to 300 K, such as in Sagittarius B2, 1 can sublime to be incorporated into planetoids, asteroids, and comets. Detailed analyses of meteorites like the Murchison meteorite revealed that biorelevant molecules, such as amino acids embedded in meteoric matter, can survive harsh conditions in space as well as impact on the Earth.^{58,59} Even 1, which is a labile compound prone to decarboxylation, has been detected in meteoric samples.²⁸ Therefore, organic molecules formed in molecular clouds could have been delivered to the early Earth, thus highlighting the possibility of an exogenous source of prebiotic molecules as a plausible additional pathway to the formation of biorelevant molecules besides their potential formation in hydrothermal vents on the prebiotic Earth. As 8 has been detected in molecular clouds, such as the Taurus molecular cloud (TMC-1)⁶⁰ and Sagittarius B2⁶¹ as well as toward hot cores like NGC 6334F,⁶² the presence of 1 in these environments seems conceivable. Therefore, the results of this study indicate that directed searches for 1 by the latest generation of telescopes, such as the Atacama large millimeter/submillimeter array (ALMA) toward these regions of space might be successful to further shed light on the origins of prebiotic molecules. This will lead to a better understanding of the fundamental processes of abiotic syntheses of organic molecules in space.

EXPERIMENTAL PROCEDURES

Resource Availability

Lead Contact

Further information and requests for resources should be directed to and will be fulfilled by the Lead Contact, Ralf I. Kaiser (ralfk@hawaii.edu).

Materials Availability

This study did not generate new unique reagents.

Data and Code Availability

The datasets generated during this study are available upon request.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.chempr.2020.10.003>.

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AUTHOR CONTRIBUTIONS

R.I.K. designed the experiments. N.F.K. and A.K.E. performed all experiments and carried out all computations. N.F.K., A.K.E., P.R.S., and R.I.K. co-wrote the manuscript. N.F.K. and A.K.E. contributed equally to this work.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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REFERENCES

1. Breslow, R. (1957). Rapid deuterium exchange in thiazolium salts 1. J. Am. Chem. Soc. 79, 1762–1763.
2. Breslow, R. (1958). On the mechanism of thiamine action. IV. 1 Evidence from studies on model systems. J. Am. Chem. Soc. 80, 3719–3726.
3. Menon, R.S., Biju, A.T., and Nair, V. (2016). Recent advances in N-heterocyclic carbene (NHC)-catalysed benzoin reactions. Beilstein J. Org. Chem. 12, 444–461.
4. Flanagan, D.M., Romanov-Michailidis, F., White, N.A., and Rovis, T. (2015). Organocatalytic reactions enabled by N-heterocyclic carbenes. Chem. Rev. 115, 9307–9387.
5. Hopkinson, M.N., Richter, C., Schedler, M., and Glorius, F. (2014). An overview of N-heterocyclic carbenes. Nature 510, 485–496.
6. Paul, M., Sudkaow, P., Wessels, A., Schlörer, N.E., Neudörfl, J.M., and Berkessel, A. (2018). Breslow intermediates from aromatic N-heterocyclic carbenes (benzimidazolin-2-ylidenes, thiazolin-2-ylidenes). Angew. Chem. Int. Ed. Engl. 57, 8310–8315.
7. Berkessel, A., Elfert, S., Yatham, V.R., Neudörfl, J.M., Schlörer, N.E., and Teles, J.H. (2012). Umpolung by N-heterocyclic carbenes: generation and reactivity of the elusive 2,2-diamino enols (Breslow intermediates). Angew. Chem. Int. Ed. Engl. 51, 12370–12374.
8. Abelson, P.H. (1966). Chemical events on the primitive earth. Proc. Natl. Acad. Sci. USA 55, 1365–1372.
9. Muchowska, K.B., Varma, S.J., and Moran, J. (2019). Synthesis and breakdown of universal metabolic precursors promoted by iron. Nature 569, 104–107.
10. Novikov, Y., and Copley, S.D. (2013). Reactivity landscape of pyruvate under simulated hydrothermal vent conditions. Proc. Natl. Acad. Sci. USA 110, 13283–13288.
11. Goodfriend, G.A., Collins, M., Fogel, M., Macko, S., and Wehmiller, J.F. (2000). Perspectives in Amino Acid and Protein Geochemistry (Oxford University Press).

12. Coggins, A.J., and Powner, M.W. (2017). Prebiotic synthesis of phosphoenol pyruvate by α -phosphorylation-controlled triose glycolysis. *Nat. Chem.* 9, 310–317.
13. Weber, A.L. (2001). The sugar model: catalysis by amines and amino acid products. *Orig. Life Evol. Biosph.* 31, 71–86.
14. Keller, M.A., Turchyn, A.V., and Ralser, M. (2014). Non-enzymatic glycolysis and pentose phosphate pathway-like reactions in a plausible Archean ocean. *Mol. Syst. Biol.* 10, 725.
15. Guzman, M.I., and Martin, S.T. (2009). Prebiotic metabolism: production by mineral photoelectrochemistry of α -ketocarboxylic acids in the reductive tricarboxylic acid cycle. *Astrobiology* 9, 833–842.
16. Cody, G.D., Bocktor, N.Z., Filley, T.R., Hazen, R.M., Scott, J.H., Sharma, A., and Yoder, H.S. (2000). Primordial carbonylated iron-sulfur compounds and the synthesis of pyruvate. *Science* 289, 1337–1340.
17. Roldan, A., Hollingsworth, N., Roffey, A., Islam, H.U., Goodall, J.B.M., Catlow, C.R.A., et al. (2015). Bio-inspired CO₂ conversion by iron sulfide catalysts under sustainable conditions. *Chem. Commun. (Camb)* 51, 7501–7504.
18. Varma, S.J., Muchowska, K.B., Chatelain, P., and Moran, J. (2018). Native iron reduces CO₂ to intermediates and end-products of the acetyl-CoA pathway. *Nat. Ecol. Evol.* 2, 1019–1024.
19. Preiner, M., Igarashi, K., Muchowska, K.B., Yu, M., Varma, S.J., Kleinermaans, K., Nobu, M.K., Kamagata, Y., Tüysüz, H., Moran, J., and Martin, W.F. (2020). A hydrogen-dependent geochemical analogue of primordial carbon and energy metabolism. *Nat. Ecol. Evol.* 4, 534–542.
20. Schreiner, P.R., Reisenauer, H.P., Ley, D., Gerbig, D., Wu, C.H., and Allen, W.D. (2011). Methylhydroxycarbene: tunneling control of a chemical reaction. *Science* 332, 1300–1303.
21. Eckhardt, A.K., Gerbig, D., and Schreiner, P.R. (2018). Heavy atom secondary kinetic isotope effect on H-tunneling. *J. Phys. Chem. A* 122, 1488–1495.
22. Schreiner, P.R. (2017). Tunneling control of chemical reactions: the third reactivity paradigm. *J. Am. Chem. Soc.* 139, 15276–15283.
23. Eckhardt, A.K., Linden, M.M., Wende, R.C., Bernhardt, B., and Schreiner, P.R. (2018). Gas-phase sugar formation using hydroxymethylene as the reactive formaldehyde isomer. *Nat. Chem.* 10, 1141–1147.
24. Eckhardt, A.K., Bergantini, A., Singh, S.K., Schreiner, P.R., and Kaiser, R.I. (2019). Formation of glyoxylic acid in interstellar ices: a key entry point for prebiotic chemistry. *Angew. Chem. Int. Ed. Engl.* 58, 5663–5667.
25. Turner, A.M., Bergantini, A., Abplanalp, M.J., Zhu, C., Göbi, S., Sun, B.J., Chao, K.H., Chang, A.H.H., Meinert, C., and Kaiser, R.I. (2018). An interstellar synthesis of phosphorus oxoacids. *Nat. Commun.* 9, 3851.
26. Turner, A.M., Abplanalp, M.J., Bergantini, A., Frigge, R., Zhu, C., Sun, B.J., Hsiao, C.T., Chang, A.H.H., Meinert, C., and Kaiser, R.I. (2019). Origin of alkylphosphonic acids in the interstellar medium. *Sci. Adv.* 5, eaaw4307.
27. Engel, M.H., and Macko, S.A. (1997). Isotopic evidence for extraterrestrial non-racemic amino acids in the Murchison meteorite. *Nature* 389, 265–268.
28. Cooper, G., Reed, C., Nguyen, D., Carter, M., and Wang, Y. (2011). Detection and formation scenario of citric acid, pyruvic acid, and other possible metabolism precursors in carbonaceous meteorites. *Proc. Natl. Acad. Sci. USA* 108, 14015–14020.
29. Kaiser, R.I., and Roessler, K. (1998). Theoretical and laboratory studies on the interaction of cosmic-ray particles with interstellar ices. III. Suprathermal chemistry-induced formation of hydrocarbon molecules in solid methane (CH₄), ethylene (C₂H₄), and acetylene (C₂H₂). *Astrophys. J.* 503, 959–975.
30. Sutherland, J.D. (2017). Opinion: Studies on the origin of life — the end of the beginning. *Nat. Rev. Chem.* 1.
31. Bennett, C.J., Jamieson, C.S., Osamura, Y., and Kaiser, R.I. (2005). A combined experimental and computational investigation on the synthesis of acetaldehyde [CH₃CHO(X¹A')] in interstellar ices. *Astrophys. J.* 624, 1097–1115.
32. Bennett, C.J., Osamura, Y., Lebar, M.D., and Kaiser, R.I. (2005). Laboratory studies on the formation of three C₂H₄O isomers - acetaldehyde (CH₃CHO), ethylene oxide (c-C₂H₄O), and vinyl alcohol (CH₂CHOH) - in interstellar and cometary ices. *Astrophys. J.* 634, 698–711.
33. Dartois, E. (2019). Interstellar carbon dust. *C* 5, 80.
34. Rogantini, D., Costantini, E., Zeegers, S., Mehdipour, M., Psaradaki, I., Raassen, A., de Vries, C., and Waters, L. (2020). Magnesium and silicon in interstellar dust: an X-ray overview. *arXiv, arXiv:2007.03329v1*.
35. Herbst, E., and van Dishoeck, E.F. (2009). Complex organic interstellar molecules. *Annu. Rev. Astron. Astrophys.* 47, 427–480.
36. Hama, T., and Watanabe, N. (2013). Surface processes on interstellar amorphous solid water: adsorption, diffusion, tunneling reactions, and nuclear-spin conversion. *Chem. Rev.* 113, 8783–8839.
37. Bergin, E.A., and Tafalla, M. (2007). Cold dark clouds: the initial conditions for star formation. *Annu. Rev. Astron. Astrophys.* 45, 339–396.
38. Prasad, S.S., and Tarafdar, S.P. (1983). UV radiation field inside dense clouds - its possible existence and chemical implications. *Astrophys. J.* 267, 603–609.
39. Bennett, C.J., and Kaiser, R.I. (2007). On the formation of glycolaldehyde (HCOCH₂OH) and methyl formate (HCOOCH₃) in interstellar ice analogs. *Astrophys. J.* 661, 899–909.
40. Abplanalp, M.J., Gozem, S., Krylov, A.I., Shingledecker, C.N., Herbst, E., and Kaiser, R.I. (2016). A study of interstellar aldehydes and enols as tracers of a cosmic ray-driven nonequilibrium synthesis of complex organic molecules. *Proc. Natl. Acad. Sci. USA* 113, 7727–7732.
41. Kim, Y.S., and Kaiser, R.I. (2010). Abiotic formation of carboxylic acids (RCOOH) in interstellar and solar system model ices. *Astrophys. J.* 725, 1002–1010.
42. Zhu, C., Turner, A.M., Abplanalp, M.J., and Kaiser, R.I. (2018). Formation and high-order carboxylic acids (RCOOH) in interstellar analogous ices of carbon dioxide (CO₂) and methane (CH₄). *ApJS* 234, 15.
43. Bennett, C.J., Hama, T., Kim, Y.S., Kawasaki, M., and Kaiser, R.I. (2011). Laboratory studies on the formation of formic acid (HCOOH) in interstellar and cometary ices. *Astrophys. J.* 727, 27.
44. Bergantini, A., Zhu, C., and Kaiser, R.I. (2018). A photoionization reflectron time-of-flight mass spectrometric study on the formation of acetic acid (CH₃COOH) in interstellar analog ices. *Astrophys. J.* 862, 140.
45. Moore, M.H., and Hudson, R.L. (2005). Production of complex molecules in astrophysical ices. *Proc. Int. Astron. Union* 1, 247–260.
46. Boogert, A.C.A., Pontoppidan, K.M., Lahuis, F., Jorgensen, J.K., Augereau, J.C., Blake, G.A., Brooke, T.Y., Brown, J., Dullemond, C.P., Evans, N.J., II, et al. (2004). Spitzer space telescope spectroscopy of ices toward low-mass embedded protostars. *Astrophys. J. Suppl. Ser.* 154, 359–362.
47. Nummelin, A., Whittet, D.C.B., Gibb, E.L., Gerakines, P.A., and Chiar, J.E. (2001). Solid carbon dioxide in regions of low-mass star formation. *Astrophys. J.* 558, 185–193.
48. Pontoppidan, K.M., Dullemond, C.P., van Dishoeck, E.F., Blake, G.A., Boogert, A.C.A., Evans II, N.J., Kessler-Silacci, J.C., and Lahuis, F. (2005). Ices in the edge-on disk CRBR 2422.8–3423: Spitzer spectroscopy and Monte Carlo radiative transfer modeling. *Astrophys. J.* 622, 463–481.
49. Öberg, K.I., Boogert, A.C.A., Pontoppidan, K.M., van den Broek, S., van Dishoeck, E.F., Bottinelli, S., Blake, G.A., and Evans, N.J. (2011). The Spitzer ice legacy: ice evolution from cores to protostars. *Astrophys. J.* 740, 109.
50. Schutte, W., Boogert, A., Tielens, A., Whittet, D., Gerakines, P., Chiar, J., Ehrenfreund, P., Greenberg, J., van Dishoeck, E., and Graauw, T. (1999). Weak ice absorption features at 7.24 and 7.41 μ m in the spectrum of the obscured young stellar object W 33A. *Astron. Astro Phys.* 343, 966–976.
51. Jacox, M.E. (1982). The reaction of F atoms with acetaldehyde and ethylene oxide. Vibrational Spectra CH₃CO and CH₂CHO free radicals trapped in solid argon. *Chem. Phys.* 69, 407–422.
52. Das, P., and Lee, Y.-P. (2014). Bimolecular reaction of CH₃ + CO in solid p-H₂: infrared absorption of acetyl radical (CH₃CO) and CH₃-CO complex. *J. Chem. Phys.* 140, 244303.
53. Kleimeier, N.F., Turner, A.M., Fortenberry, R.C., and Kaiser, R.I. (2020). On the formation of the popcorn flavorant 2,3-butanedione (CH₃COCOCH₃) in acetaldehyde-containing

- interstellar ices. *ChemPhysChem* 21, 1531–1540.
54. Holtom, P.D., Bennett, C.J., Osamura, Y., Mason, N.J., and Kaiser, R.I. (2005). A combined experimental and theoretical study on the formation of the amino acid glycine (NH₂CH₂COOH) and its isomer (CH₃NHCOOH) in extraterrestrial ices. *Astrophys. J.* 626, 940–952.
55. Milligan, D.E., and Jacox, M.E. (1971). Infrared spectrum and structure of intermediates in the reaction of OH with CO. *J. Chem. Phys.* 54, 927–942.
56. Bergantini, A., Abplanalp, M.J., Pokhilko, P., Krylov, A.I., Shingledecker, C.N., Herbst, E., et al. (2018). A combined experimental and theoretical study on the formation of interstellar propylene oxide (CH₃CHCH₂O)—a chiral molecule. *Astrophys. J.* 860, 108.
57. Komorek, R., Xu, B., Yao, J., Ablikim, U., Troy, T.P., Kostko, O., Ahmed, M., and Yu, X.Y. (2018). Enabling liquid vapor analysis using synchrotron VUV single photon ionization mass spectrometry with a microfluidic interface. *Rev. Sci. Instrum.* 89, 115105.
58. Cronin, J.R., and Moore, C.B. (1971). Amino acid analyses of the Murchison, Murray, and Allende carbonaceous chondrites. *Science* 172, 1327–1329.
59. Shimoyama, A., and Ogasawara, R. (2002). Dipeptides and diketopiperazines in the Yamato-791198 and Murchison carbonaceous chondrites. *Orig. Life Evol. Biosph.* 32, 165–179.
60. Matthews, H.E., Friberg, P., and Irvine, W.M. (1985). The detection of acetaldehyde in cold dust clouds. *Astrophys. J.* 290, 609–614.
61. Fourikis, N., Sinclair, M.W., Robinson, B.J., Godfrey, P.D., and Brown, R.D. (1974). Microwave emission of the Z₁₁→Z₁₂ rotational transition in interstellar acetaldehyde. *Aust. J. Phys.* 27, 425–430.
62. Nummelin, A., Dickens, J.E., Bergman, P., Hjalmarson, A., Irvine, W.M., Ikeda, M., and Ohishi, M. (1998). Abundances of ethylene oxide and acetaldehyde in hot molecular cloud cores. *Astronomy and Astrophysics* 337, 275–286.