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Formation of Lactic Acid ($CH_3CH(OH)COOH$), a Metabolic Keystone for the Molecular Origins of Life, in Interstellar Ice Analogues

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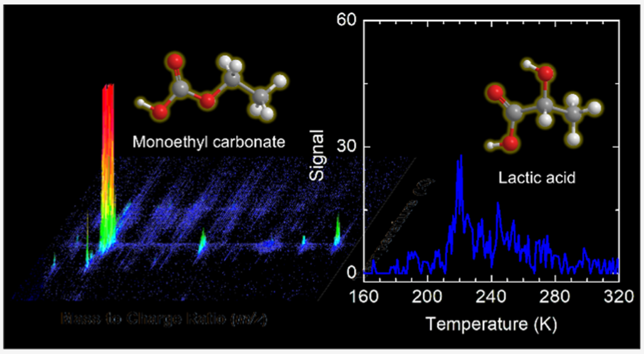

ABSTRACT: Lactic acid ($CH_3CH(OH)COOH$)—a key biorelevant hydroxycarboxylic acid—is ubiquitous in living organisms and critically linked to the molecular origins of life due to its fundamental role in metabolic pathways. With the anoxic conditions of early Earth, anaerobic metabolic pathways such as lactic acid fermentation may have served as an essential mechanism for primordial cellular metabolisms. Although lactic acid has been detected in high abundances in carbonaceous asteroid Ryugu and various meteorites like Murchison, its formation pathways under extreme conditions of the interstellar medium (low temperature, radiation) have remained elusive. Here, we report the first bottom-up formation of racemic lactic acid via a barrierless radical−radical recombination between the hydroxycarbonyl ($HO\dot{C}O$) radical and the 1-hydroxyethyl ($CH_3\dot{C}HOH$) radical in interstellar analog ices composed of carbon dioxide (CO_2) and ethanol (CH_3CH_2OH). These results provide a first step toward a fundamental understanding of the abiotic formation of biorelevant hydroxycarboxylic acids via nonequilibrium reactions from ubiquitous precursor molecules in extraterrestrial environments. Utilizing isomer-selective vacuum ultraviolet photoionization reflectron time-of-flight mass spectrometry and isotopic substitution experiments, lactic acid and its isomer monoethyl carbonate (CH_3CH_2OCOOH) were identified in the gas phase during temperature-programmed desorption. These findings suggest that they can likely form in interstellar ices containing carbon dioxide and ethanol in cold molecular clouds via galactic cosmic rays-mediated nonequilibrium chemistries.

■ INTRODUCTION

Since the first identification of the chiral biomolecule lactic acid ($CH_3CH(OH)COOH$, **1**) in the Murchison meteorite by Peltzer and Bada over 40 years ago,[1] **1** has received extensive attention from the laboratory astrophysics, astrochemistry, and astrobiology communities due to its importance for the molecular origins of life.[2−5] In contemporary biochemistry, **1** and the deprotonated lactate anion ($CH_3CH(OH)COO^-$) serve as the primary carbon source for the tricarboxylic acid (TCA) cycle[6] and play a vital role in cellular metabolisms such as fermentative glycolysis.[7] During lactic acid fermentation, a central anaerobic metabolic pathway, glucose ($C_6H_{12}O_6$) undergoes glycolysis to produce pyruvic acid ($CH_3COCOOH$, **2**),[8] which is subsequently reduced by nicotinamide adenine dinucleotide (NADH) to yield **1** (Figure 1); this reaction regenerates NAD^+ and represents a critical step for sustaining glycolysis and producing adenosine triphosphate (ATP) in the absence of oxygen (O_2).[6] Glycolysis and the TCA cycle are among the earliest biochemical processes associated with the origins of life.[9,10] Considering the anoxic (oxygen-poor) conditions of early Earth, the earliest life would have been dominated by anaerobic metabolic pathways;[11] among these pathways, lactic acid fermentation may have served as an essential mechanism for primordial cellular metabolisms.

Hydrothermal vents in the deep ocean and warm ponds are considered as possible scenarios for the emergence of life,[12−14] however, a substantial amount of crucial prebiotic organic molecules including amino acids,[15] nucleobases,[16] sugars,[17] and hydroxycarboxylic acids[18] could have been delivered to early Earth via meteorites and comets.[19,20] Although more than 300 molecules have been reported in interstellar and circumstellar regions,[21,22] the underlying mechanisms of their formation remain poorly understood. These compounds may form in diverse interstellar environments including diffuse clouds, dense molecular clouds and star-forming regions, which have typical number densities of $10-10^2$, 10^2-10^4, and 10^6-10^9 atom cm^{-3}, respectively.[23] In diffuse clouds, molecule

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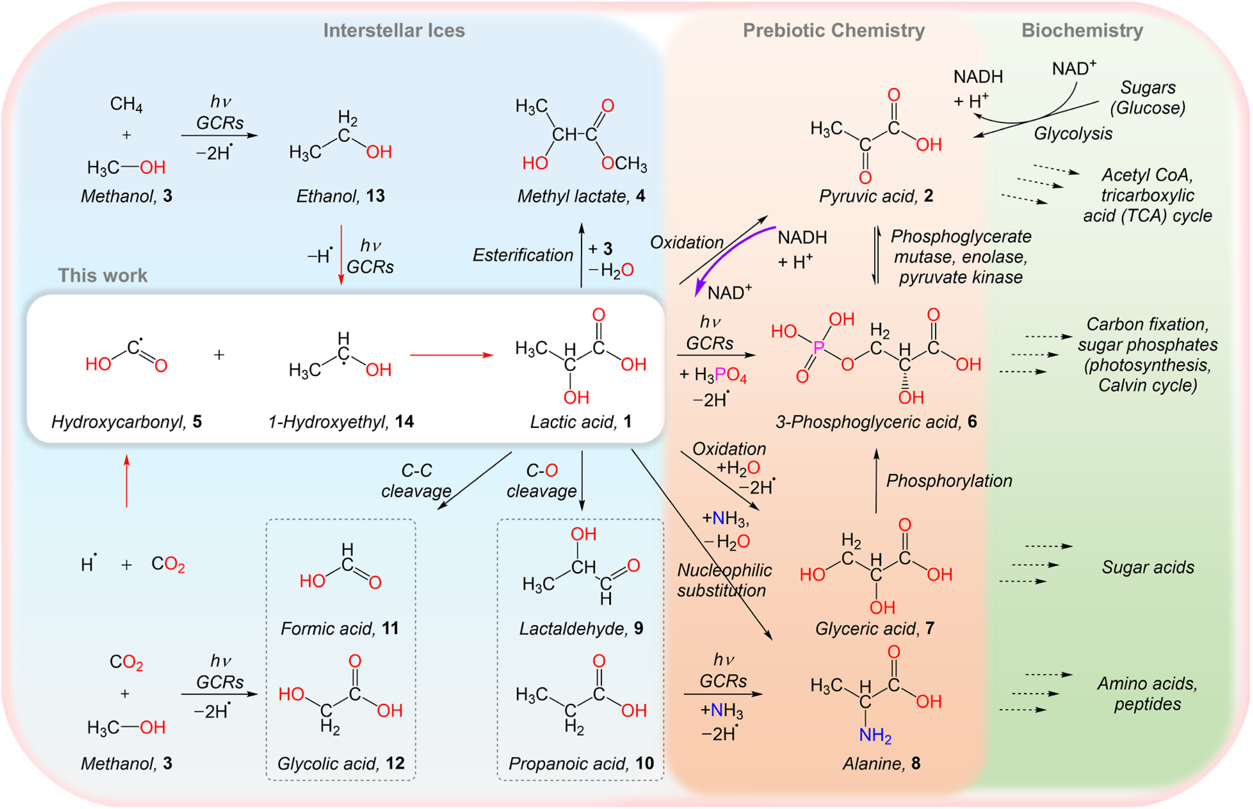

Figure 1. Proposed formation pathway of lactic acid in interstellar ices and its potential role as a key precursor to crucial biorelevant molecules. The white-background region highlights the reaction pathway investigated in this study. Lactic acid (**1**) is formed through radical−radical recombination of the hydroxycarbonyl radical ($HO\dot{C}O$, **5**) with the 1-hydroxyethyl radical ($CH_3\dot{C}HOH$, **14**) in interstellar ice analogs composed of carbon dioxide (CO_2) and ethanol (**13**) exposed to energetic electrons, which simulate the secondary electrons produced by GCRs as they penetrate interstellar ices. Lactic acid (**1**) serves as a central building block of glyceric acid (**7**) and alanine (**8**) contributing to the synthesis of sugar acids and complex amino acids. In contemporary biochemistry, **1** plays a fundamental role in the lactic acid fermentation (purple arrow) and serves as a key precursor to crucial biomolecules such as pyruvic acid (**2**) and 3-phosphoglyceric acid (**6**), linking to the tricarboxylic acid (TCA) cycle and Calvin cycle, respectively.

formation is mainly driven by gas-phase photochemistry and photoionization,[23] although efficient formation can also occur on grain surfaces through different processes, including atom addition.[24] However, gas-phase-only astrochemical models significantly underpredict the abundances of complex organics such as methanol (CH_3OH, **3**) compared to astronomical observations.[25] It has been suggested that in dense molecular clouds, icy dust particles shield molecules from the destructive ultraviolet radiation, allowing the formation of complex organics on the surfaces of interstellar ices through ultraviolet (UV) photons interactions, and within the bulk ice as a result of energy deposition by galactic cosmic rays (GCRs).[26,27] Laboratory simulation experiments have provided compelling evidence for the formation of biorelevant aldehydes,[28] amino acids,[29] sugars[4] and sugar derivatives[30] in interstellar ice analogues under astrophysically relevant conditions. These biorelevant compounds and their precursors can form abiotically in processed interstellar ices composed of simple molecules such as water (H_2O), carbon dioxide (CO_2), carbon monoxide (CO), **3**, ammonia (NH_3), and methane (CH_4).[31] This synthesis can occur through nonequilibrium chemistry driven by GCRs and vacuum ultraviolet (VUV) radiation.[4,32−34] The main constituents of GCRs are energetic protons (H^+) and helium nuclei (He^{2+}), which span a broad kinetic energy range from MeV to PeV.[35,36] Upon gravitational collapse, dense molecular clouds transition into star-forming regions, where the temperatures rise to up 100−300 K, leading to the release of complex organics into the gas phase.[21,23] During the star formation, ices containing these species may become integrated into circumstellar disks, which provides the raw materials for the formation of comets, planets, and planetoids.[37] Therefore, once synthesized in interstellar ices, these organics may be incorporated into planetesimals and ultimately delivered to planets like early Earth via meteoritic or comet impact.[38] In fact, **1**—an α-hydroxycarboxylic acid—has been detected in multiple meteorites such as Murchison, Bells, and Ivuna[1,18,39] with abundances up to 736 nmol g^{-1};[39] the high abundance of **1** suggests that it survives the entry of the meteorite into the early Earth's atmosphere when embedded in a matrix.[30] Additionally, enantioselective analyses of the Murchison meteorite revealed a tentative chiral bias toward the L-enantiomer of hydroxycarboxylic acids such as lactic acid (**1**); the enantiomer ratio (D/L) of **1** was determined to be 0.92 ± 0.10.[1] Notably, the L-enantiomer of **1** is the predominant form found in plants and higher organisms.[5] The connection between extraterrestrial molecular asymmetry and biological homochirality highlights the critical question of whether the chiral bias essential for life originated in deep space.[40] Understanding whether homochirality evolved in interstellar environments or later on planets like Earth is a primary motivation for astrochemical studies of chiral molecules.[5,41,42]

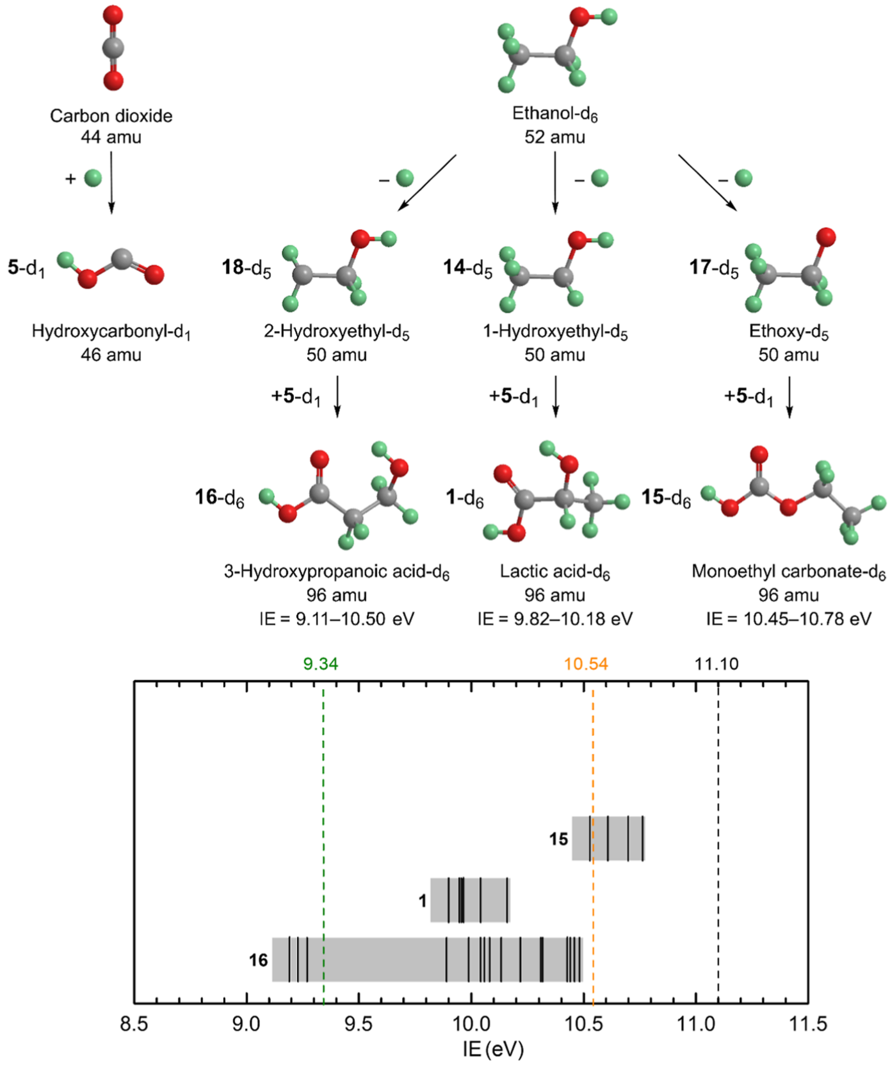

Figure 2. Proposed formation pathways of isomers **1**, **15**, and **16** in irradiated carbon dioxide–ethanol ices. (a) Barrierless radical–radical recombination of **5** with **14**, **17**, and **18** form isomers **1**, **15**, and **16**, respectively. (b) The computed adiabatic ionization energies (IEs; black solid line) and the IE ranges (gray area) of isomers **1**, **15**, and **16** are compiled after error analysis. VUV photon energies at 11.10, 10.54, and 9.34 eV were used to photoionize sublimed molecules during TPD of irradiated ices. Atoms are color-coded in light green for deuterium, gray for carbon, and red for oxygen.

In prebiotic chemistry, **1** can form **2** and methyl lactate ($CH_3CH(OH)COOCH_3$, **4**) through oxidation and esterification, respectively (Figure 1). The formation of **2** has been demonstrated via the barrierless recombination of hydroxycarbonyl (HO$\dot{C}$O, **5**) and acetyl ($CH_3\dot{C}O$) radicals in electron-irradiated interstellar analog ices containing carbon dioxide and acetaldehyde (CH_3CHO).[43] **1** can react with phosphoric acid (H_3PO_4), which forms in irradiated phosphine (PH_3)-containing ices,[44] to synthesize 3-phosphoglyceric acid ($C_3H_7O_7P$, **6**) thus providing a compelling link to photosynthesis in the Calvin cycle.[45] Oxidation of **1** results in the simplest sugar acid, glyceric acid ($HOCH_2CH(OH)COOH$, **7**), which can be produced in irradiated carbon dioxide–ethylene glycol ($HOCH_2CH_2OH$) ices.[30] Through nucleophilic addition, **1** can react with ammonia to form the proteinogenic amino acid alanine ($CH_3CH(NH_2)COOH$, **8**),[46] contributing to the synthesis of peptides. Additionally, undergoing carbon–oxygen bond cleavage, **1** can be converted into lactaldehyde ($CH_3CH(OH)CHO$, **9**) and propanoic acid (CH_3CH_2COOH, **10**). Further, carbon–carbon bond cleavage in **1** produces formic acid ($HCOOH$, **11**) and glycolic acid ($HOCH_2COOH$, **12**), which are precursors to amino acids. Therefore, **1** may have served as a key precursor to crucial biorelevant molecules, eventually seeding the evolution of life on early Earth. However, despite the detection of various hydroxycarboxylic acids and their derivatives in laboratory simulations,[3,4,30,33,47] meteorites[1,9,18,48] and asteroid,[49] the fundamental formation mechanisms of **1** in interstellar environments have, to the best of our knowledge, remained largely unexplored. An elucidation of interstellar formation pathways of **1** would critically advance our fundamental understanding of the synthesis routes of astrobiologically relevant molecules for the origins of life.[28]

Given the chemical and physical complexity of interstellar environments, laboratory experiments have to begin with well-defined model ices to enable a systematic investigation of specific reaction pathways. Carbon dioxide–ethanol ice serves as a suitable model system to investigate the low-temperature formation of $C_3H_6O_3$ isomers (Figure 2), as both molecules have been detected toward multiple environments in the

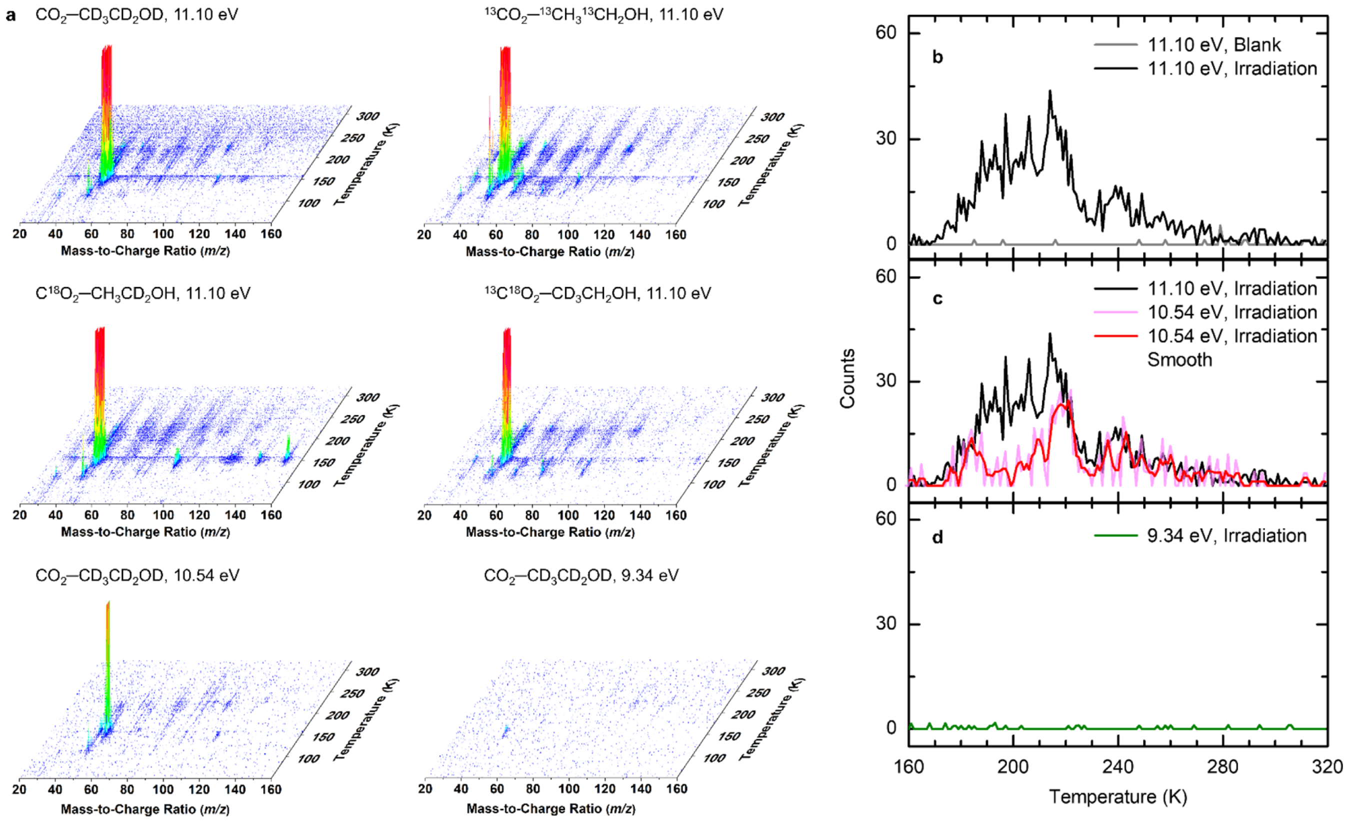

Figure 3. PI-ReToF-MS data during TPD of processed carbon dioxide−ethanol ices. Data were recorded at 11.10 eV for the irradiated CO_2−CD_3CD_2OD ice, irradiated $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice, irradiated $C^{18}O_2$−CH_3CD_2OH ice, and irradiated $^{13}C^{18}O_2$−CD_3CH_2OH ice, and recorded at 10.54 and 9.34 eV for the irradiated CO_2−CD_3CD_2OD ice (a). TPD profiles of $m/z = 96$ in CO_2−CD_3CD_2OD ice were measured at 11.10 eV (b and c), 10.54 eV (c), and 9.34 eV (d).

interstellar medium (ISM). While carbon dioxide is ubiquitous throughout the ISM, ethanol (CH_3CH_2OH, **13**) has been identified in the gas phase toward multiple sources including the molecular cloud associated with the ultracompact HII region G34.3 + 0.15,[50] as well as star-forming[51] and hot-core regions.[52] Carbon dioxide is among the most abundant species in interstellar ices at fractions of up to 40% relative to water;[53] **13** has been inferred in ices by the James Webb Space Telescope (JWST) toward background stars[54] and young protostars with an abundance reaching up to 1.8% relative to water.[55] This simplified ice mixture may enable the identification of specific reaction products through a combination of Fourier-transform infrared (FTIR) spectroscopy and VUV photoionization reflectron time-of-flight mass spectrometry,[56] facilitating a controlled investigation of fundamental reaction mechanisms leading to biorelevant molecules such as **1** under astrophysical conditions. Here, we report the first formation of lactic acid ($CH_3CH(OH)COOH$, **1**) in interstellar analog ices composed of carbon dioxide and ethanol (**13**) through the barrierless recombination of hydroxycarbonyl (**5**) and 1-hydroxyethyl ($CH_3\dot{C}HOH$, **14**) radicals (Figures 1 and 2). The carbon dioxide−ethanol ice mixtures were exposed to 5 keV electrons at temperatures as low as 5 K. These electrons mimic the secondary electrons produced by GCRs as they interact with icy mantles on interstellar nanoparticles (grains) in cold molecular clouds. The irradiation conditions correspond to processing time scales equivalent to molecular cloud lifetimes of up to 7×10^5 years.[57] GCRs primarily lose energy through the ionizing molecules in interstellar ices, producing secondary electrons with kinetic energies ranging from a few eV to approximately 10 keV, depending on the energy of the incident GCR particles.[58,59] In this study, 5 keV electrons were selected because their linear energy transfer is comparable to that of low-energy (10−20 MeV) GCR protons interacting with ices.[60,61] Utilizing VUV photoionization reflectron time-of-flight mass spectrometry (PI-ReToF-MS) and isotopic labeling experiments, **1** and its isomer monoethyl carbonate (CH_3CH_2OCOOH, **15**) were identified in the gas phase during temperature-programmed desorption (TPD) of the processed ices based on their desorption profiles and computed adiabatic ionization energies (IEs) along with their fragment ions. These results advance our fundamental understanding of the interstellar formation mechanisms of key biorelevant organics—hydroxycarboxylic acids—in the ISM. Both carbon dioxide and **13** are ubiquitous in deep space. Our results suggest that **1** and **15** are plausibly formed in interstellar ices containing carbon dioxide and **13** in cold molecular clouds via GCR-mediated nonequilibrium chemistries. During the transition of a molecular cloud toward star formation, these organics sublimate into the gas phase. Once synthesized in interstellar ices, **1** could be also incorporated into planetesimals of solar systems and delivered to planets like early Earth, thus providing an exogenous source of prebiotic molecules[62] and serving as a key molecular precursor to biomolecules (Figure 1) necessary for the biological processes of early life on prebiotic Earth.

■ RESULTS

Infrared Spectroscopy. Fourier-transform infrared (FTIR) spectroscopy was exploited to monitor the chemical evolution of isotopically labeled carbon dioxide−ethanol ices (CO_2−CD_3CD_2OD, $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$, $C^{18}O_2$−CH_3CD_2OH, and $^{13}C^{18}O_2$−CD_3CH_2OH) before, during, and after electron irradiation at 5 K (Figures S1−S4). Detailed absorption assignments are provided in Tables S1−S4. The absorption bands of the deposited ices correspond to the fundamental and combination vibrational modes of carbon dioxide[30,63] and ethanol.[28,64,65] After deposition, ice mixtures were irradiated with electrons at a relatively low dose (22 nA, 5 min) to minimize sequential reactions and limit the formation pathways to first generation products.[28] Upon irradiation, several new absorption features emerged. The difference spectra in the 1900−1500 cm^{-1} region were deconvoluted into multiple Gaussian peaks. The stretching vibration of carbon monoxide (CO) was observed at 2090 cm^{-1} ($\nu(^{13}CO)$) in irradiated $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice and 2040 cm^{-1} ($\nu(^{13}C^{18}O)$) in irradiated $^{13}C^{18}O_2$−CD_3CH_2OH ice (Figures S2 and S4).[66,67] Absorptions at 1684 cm^{-1} and 1680 cm^{-1} in irradiated CO_2−CD_3CD_2OD and $C^{18}O_2$−CH_3CD_2OH ices, respectively, are linked to C=O stretching mode (ν_2) of formaldehyde-d_2 (D_2CO); this band shifts to 1702 cm^{-1} ($H_2{}^{13}CO$, ν_2) in irradiated $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice (Figures S1−S3).[67−69] The absorption at 1673 cm^{-1} in irradiated $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice is attributed to acetaldehyde-$^{13}C_2$ ($^{13}CH_3{}^{13}CHO$, ν_4); this is confirmed from the observations of acetaldehyde (CH_3CHO, ν_4) at 1715 cm^{-1} in $C^{18}O_2$−CH_3CD_2OH ice and acetaldehyde-d_3 (CD_3CHO, ν_4) at 1706 cm^{-1} in $^{13}C^{18}O_2$−CD_3CH_2OH ice (Figures S2−S4).[70,71] It is important to note that the absorption at 1764 in irradiated CO_2−CD_3CD_2OD ice can be assigned to the **5**-d_1 ($DO\dot{C}O$, ν_2) radical.[67] Additionally, absorptions at 1642, 1605, 1622, and 1578 cm^{-1} in irradiated CO_2−CD_3CD_2OD, $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$, $C^{18}O_2$−CH_3CD_2OH, $^{13}C^{18}O_2$−CD_3CH_2OH ices, respectively, can be linked to one of more carbonyl-containing (C=O) products.[72] Notably, lactic acid ($CH_3CH(OH)COOH$, **1**) exhibits strong absorption bands at 3380 cm^{-1} and 1720 cm^{-1}, corresponding to the O−H and C=O stretching vibrations, respectively.[73] However, these vibrational modes overlap with absorption bands with ethanol. Therefore, an alternative, more sensitive analytical technique is required to identify individual reaction products.

PI-ReToF-MS. PI-ReToF-MS was employed to identify individual $C_3H_6O_3$ isomers during the temperature-programmed desorption of electron-irradiated carbon dioxide−ethanol ices. In combination with isotopic labeling experiments, PI-ReToF-MS enables the identification of specific structural isomers in the gas phase based on their adiabatic ionization energies and desorption temperatures.[56,70] Separate experiments were conducted at VUV photon energies of 11.10, 10.54, and 9.34 eV to ionize and hence distinguish the first-generation products **1**, **15**, and 3-hydroxypropanoic acid ($HOCH_2CH_2COOH$, **16**) formed via radical−radical recombination after low-dose irradiation (Figure 2). Photons at 11.10 eV can ionize all three isomers if formed (Tables S5−S7), while photons at 9.34 eV can only ionize **16a−16e** (IE = 9.11−9.29 eV); at 10.54 eV, all isomers can be ionized except for **15b−15c** (IE = 10.62−10.78 eV). The PI-ReToF-MS data collected during TPD of the irradiated carbon dioxide−ethanol ices are compiled in Figure 3a.

As ethanol (IE = 10.38−10.52 eV)[74] can be photoionized at 11.10 and 10.49 eV, its sublimation event centered at around 152 K and dominated the ion signals during the TPD. It is worth noting that $C_2H_2O_4$ isomers (m/z = 90) may form via recombination of two hydroxycarbonyl ($HO\dot{C}O$, **5**) radicals, whereas $C_4H_{10}O_2$ isomers (m/z = 90) can result from the recombination of radicals derived from the ethanol (CH_3CH_2OH, **13**). To distinguish $C_3H_6O_3$ isomers (m/z = 90) from these potential isomeric species, experiments were conducted using fully deuterated carbon dioxide−ethanol ice (CO_2−CD_3CD_2OD) to enable unambiguous mass spectral differentiation. At a photon energy of 11.10 eV, the TPD profile of the ion signal at mass-to-charge ratios (m/z) of 96 from CO_2−CD_3CD_2OD ice reveals a broad sublimation event starting from 170 K and extending to 280 K (Figure 3b). A blank experiment with CO_2−CD_3CD_2OD ice was carried out under identical conditions but without electron irradiation; no ion signal of m/z = 96 was detected, confirming that the observed sublimation event originates from electron-induced chemical processing of the ices. To verify the molecular formula, fully carbon-13 labeled precursors were used. Replacing CO_2−CD_3CD_2OD ice with $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice resulted in a mass shift of 3 amu from m/z = 96 to m/z = 93 (Figure 4a); this isotopic shift confirms the incorporation of exactly three carbon atoms. Therefore, the sublimation event at m/z = 96 observed in irradiated CO_2−CD_3CD_2OD ice can be assigned to a molecule with the formula $C_3D_6O_3$.

As noted above, the TPD profile of m/z = 96 ($C_3D_6O_3{}^+$) recorded at 11.10 eV for the irradiated CO_2−CD_3CD_2OD ice exhibits a broad sublimation event spanning from 170 to 280 K (Figure 3b). At this photon energy, all three isomers **1** (IE = 9.82−10.18 eV), **15** (IE = 10.45−10.78 eV), and **16** (IE = 9.11−10.50 eV) can be photoionized (Figure 2 and Tables S5−S7). Therefore, the observed event can be attributed to any of isomers **1**, **15**, and/or **16**. Thereafter, the photon energy was reduced to 10.54 eV; at this energy, isomer **15b−15c** (IE = 10.62−10.78 eV) cannot be ionized. Compared with the TPD profile measured at 11.10 eV, portions of the TPD profiles disappear at 10.54 eV (Figure 3c). The difference in their TPD profiles reveals a sublimation event peaking at 203 K (Figure S5), suggesting that this peak is linked to **15b** and/or **15c**. The remaining ion signals at 10.54 eV can be associated with any isomers **1**, **15** (**15a** and **15d**), and/or **16**. Upon further lowering the photon energy to 9.34 eV—at which only **16a−16e** (IE = 9.11−9.29 eV) can be ionized—no sublimation events were detected (Figure 3d). This absence indicates that **16a−16e** are not formed under the experimental conditions.

Note that other possible $C_3H_6O_3$ isomers such as prop-1-ene-1,1,2-triol ($CH_3C(OH)C(OH)_2$, **19**) and prop-1-ene-1,1,3-triol ($HOCH_2CHC(OH)_2$, **20**) may form via keto−enol tautomerizations of **1** and **16**, respectively. At 9.34 eV, both enols **19** (IE = 7.38−7.71 eV) and **20** (IE = 7.85−8.52 eV) can be ionized if formed. However, no ion signal was detected at m/z = 96 in irradiated CO_2−CD_3CD_2OD ice at this photon energy, ruling out their formation. This is consistent with the previous study on electron-irradiated CO−CH_3CH_2OH ices with a similar irradiation dose,[28] where only first-generation products were detected. Due to the overlap in the IEs between isomers **1** (IE = 9.82−10.18 eV) and **16** (IE = 9.11−10.50 eV), additional experiments were conducted at 11.10 eV using carbon dioxide-$^{18}O_2$−

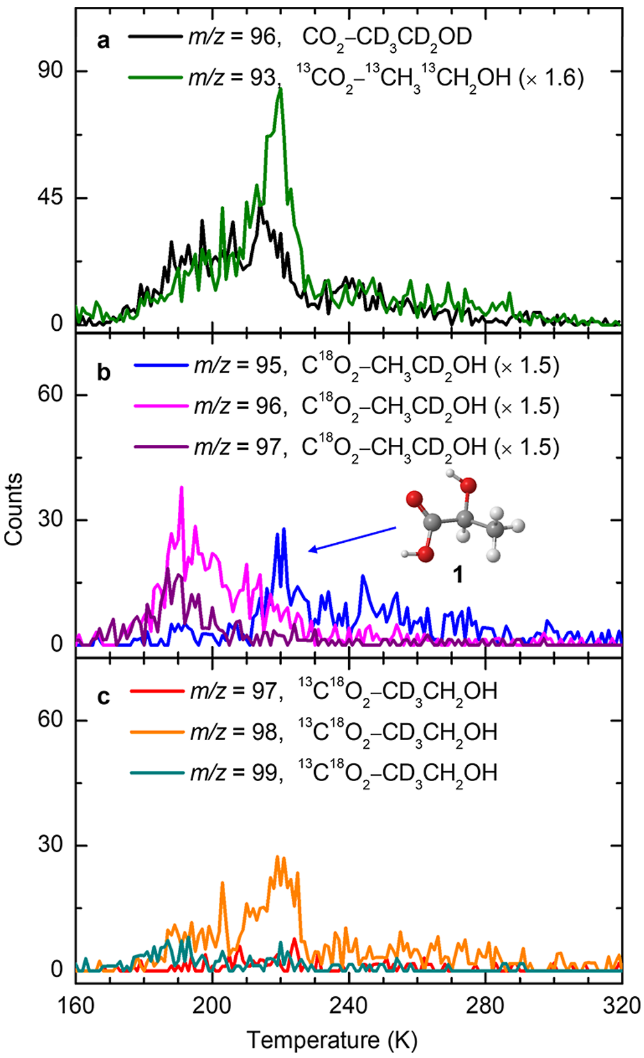

Figure 4. Ion signals recorded at 11.10 eV during TPD of irradiated carbon dioxide−ethanol ices shown as a function of temperature. (a) TPD profiles of irradiated CO_2−CD_3CD_2OD ice (*m*/*z* = 96) and $^{13}CO_2$−$^{13}CH_3{}^{13}CH_2OH$ ice (*m*/*z* = 93). (b) TPD profiles of irradiated $C^{18}O_2$−CH_3CD_2OH ice (*m*/*z* = 95, 96, and 97). (c) TPD profiles of irradiated $^{13}C^{18}O_2$−CD_3CH_2OH ice (*m*/*z* = 97, 98, and 99).

ethanol-d_2 ($C^{18}O_2$−CH_3CD_2OH) ice and carbon dioxide-^{13}C−$^{18}O_2$−ethanol-d_3 ($^{13}C^{18}O_2$−CD_3CH_2OH) ice to investigate their formation via radical−radical recombination pathways (Figures S6 and S7). These two isomers can be distinguished based on the detection of their isotopically shifted ion signals: *m*/*z* = 95 ($CH_3CD(OH)C^{18}O^{18}OH^+$) for **1** in irradiated $C^{18}O_2$−CH_3CD_2OH ice and *m*/*z* = 97 ($HOCH_2CD_2{}^{13}C^{18}O^{18}OH^+$) for **16** in irradiated $^{13}C^{18}O_2$−CD_3CH_2OH ice. In the irradiated $C^{18}O_2$−CH_3CD_2OH ice, the TPD profile at *m*/*z* = 95 reveals a sublimation event from 210 to 280 K (Figure 4b), suggesting the formation of isomer **1**. In contrast, no sublimation event was observed at *m*/*z* = 97 in irradiated $C^{18}O_2$−CH_3CD_2OH ice (Figure 4c), confirming that isomer **16** was not formed. To further confirm the formation of **1**, a gas-phase mass spectrum of lactic acid ($C_3H_6O_3$, *m*/*z* = 90) was measured at 11.10 eV. The spectrum exhibits a prominent ion signal at *m*/*z* = 45 (Figure S8), which can be assigned to the fragment ion $HOCH_2CH_2^+$ and/or $HOCO^+$. Correspondingly, in the irradiated CO_2−CD_3CD_2OD ice, the TPD profiles of *m*/*z* = 50 ($DOCD_2CD_2^+$) and *m*/*z* = 46 ($DOCO^+$) match the sublimation temperature range (210−280 K) of isomer **1** (Figure S9), providing additional evidence for its formation.

■ DISCUSSION

Having provided compelling evidence for the formation of lactic acid (**1**) and its isomer monoethyl carbonate (**15**) in irradiated carbon dioxide−ethanol ices, we now turn to their potential formation mechanisms. In our experiments, low-dose electron irradiation was designed to minimize sequential reactions, thereby constraining the possible formation pathways of $C_3H_6O_3$ isomers. These electrons mimic secondary electrons generated by GCRs as they penetrate ices within cold molecular clouds.[75] Upon interaction with GCRs, unimolecular decomposition of the ethanol (**13**) can form atomic hydrogen ($\dot{H}$) and the 1-hydroxyethyl (**14**) radical (reaction 1), the ethoxy ($CH_3CH_2\dot{O}$, **17**) radical (reaction 2), or the 2-hydroxyethyl ($\dot{C}H_2CH_2OH$, **18**) radical (reaction 3).[28,76,77] The bond cleavages via reactions 1−3 are endoergic by 390, 437, and 422 kJ mol^{-1}, respectively.[28,78,79] The suprathermal hydrogen atom can add rapidly to the carbon−oxygen double bond in carbon dioxide yielding the hydroxycarbonyl (**5**) radical via reaction 4; this process is exoergic by 4 kJ mol^{-1}.[78] Notably, **5** was identified via FTIR absorption at 1764 cm^{-1} ($DO\dot{C}O$, ν_2) in irradiated CO_2−CD_3CD_2OD ice.[67] The entrance barrier for reaction 4 has been calculated to be 106 kJ mol^{-1} at the MRCISD+Q/cc-pVTZ level of theory.[80] The energy provided by suprathermal hydrogen atoms can overcome the entrance barrier to addition.[81] Once formed, these radicals can be preserved within the low-temperature (5 K) ices due to their limited mobility, allowing them to serve as precursors in the formation of $C_3H_6O_3$ isomers upon recombination with neighboring radicals if the appropriate geometry for recombination is in place.

$$CH_3CH_2OH(\mathbf{13}) \rightarrow H + CH_3CHOH(\mathbf{14}) \tag{1}$$

$$CH_3CH_2OH(\mathbf{13}) \rightarrow H + CH_3CH_2O(\mathbf{17}) \tag{2}$$

$$CH_3CH_2OH(\mathbf{13}) \rightarrow H + CH_2CH_2OH(\mathbf{18}) \tag{3}$$

$$H + CO_2 \rightarrow HOCO(\mathbf{5}) \tag{4}$$

The formation of isomers **1** and **15** proceeds via barrierless radical−radical recombination of radical **5** and radicals **14** and **17** via reactions 5 and 6, respectively. It is worth noting that the radical−radical recombination can proceed either during irradiation at low temperatures relevant to cold interstellar clouds or during TPD at higher temperatures relevant to protostellar envelopes and protoplanetary disks. Once formed, they can recombine at low temperatures without diffusion if they have a favorable geometry for recombination in the ice mixtures. Alternatively, radicals can be preserved in the ice due to their limited molecular mobility at low temperatures.[43,82] As the matrix warms during TPD and molecular mobility increases, radical−radical recombination reactions may occur, leading to further product formation. However, our results cannot distinguish between these two possible formation mechanisms. Although **16** may form through the recombination of radical **5** and radical **18**, no evidence of **16** was observed in our experiments; this suggests that radical **18** is either not formed or is present at insufficient concentrations to produce detectable levels of **16**. Radical **18** can isomerize to **14** and **17** with reaction barriers of 165 and 136 kJ mol^{-1}, respectively, computed at the CCSD(T)/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) level of theory.[83] Recent studies on X-ray irradiation of matrix-isolated ethanol demonstrated the predominant formation of **14** and provided evidence for the formation of the **17** radical, too;[76,84] these findings agree with our results that isomers **1** and **15** were formed. Reaction 6, which leads to the formation of isomer **1**, is exoergic by 370 kJ mol^{-1}.[85] Recall that the experimental results from irradiated C^{18}O$_2$−CH$_3$CD$_2$OH ice indicate the formation of **1** involves contributions from one **13** and one carbon dioxide molecule.

$$\mathrm{CH_3CHOH}(\mathbf{14}) + \mathrm{HOCO}(\mathbf{5}) \rightarrow \mathrm{CH_3CH(OH)COOH}(\mathbf{1}) \tag{5}$$

$$\mathrm{CH_3CH_2O}(\mathbf{17}) + \mathrm{HOCO}(\mathbf{5}) \rightarrow \mathrm{CH_3CH_2OCOOH}(\mathbf{15}) \tag{6}$$

Notably, both carbon dioxide and **13** are abundant in the ISM.[21] Carbon dioxide is among the most abundant molecules on interstellar nanoparticles (grains), with concentrations reaching up to 40% relative to water.[53] Ethanol (**13**) was detected in multiple comets[86] and has been tentatively identified in interstellar ices toward background stars (NIR38 and J110621) and young protostars (IRAS2A and IRAS23385) with abundances of up to 1.8% relative to water.[54,55] Therefore, the presence of isomers **1** and **15** seems plausible in these environments. During the transition and hence warming from a cold molecular cloud to a star-forming region, these molecules can sublime into the gas phase.[28] The carbon dioxide−ethanol ices used in our simulation experiments serve as model systems to investigate the reaction pathways leading to lactic acid and its isomers. Future experiments can be conducted to explore the effects of varying carbon dioxide to ethanol ratios on the production yield of $C_3H_6O_3$ isomers. While water is the dominant component of interstellar ices,[27] our experiments are not designed to replicate the full chemical complexity of astrophysical environments. Instead, they aim to provide mechanistic insight into fundamental reaction mechanism in well-defined model ices. Future studies could explore the formation of these isomers and other compounds by incorporating water into the ice mixture. For instance, $C_3H_6O_4$ isomers including glyceric acid (**7**) may form in electron-irradiated carbon dioxide−ethanol−water ices.

Besides the sublimation in the hot core stage, once formed in interstellar ices in the early stages of the molecular cloud, **1** may act as a key precursor to crucial biorelevant molecules including pyruvic acid (**2**), 3-phosphoglyceric acid (**6**), and lactaldehyde (**9**), which are considered key intermediates in the TCA cycle, the Calvin cycle, and the methylglyoxal pathway, respectively (Figure 1).[6,45,87] These organics can ultimately be incorporated into comets, asteroids, and planetesimals,[17,28] and may survive the atmospheric entry onto planets such as the early Earth.[20,88] Indeed, detailed sample analyses of carbonaceous asteroid (162173) Ryugu and meteorites such as Murchison, Bells, and Ivuna have identified extraterrestrial biorelevant species including **1** with high abundances.[1,18,39,49] Therefore, **1** could have been delivered to the prebiotic Earth, not only offering an exogenous source toward the synthesis of biomolecules essential to the origins of life, but also potentially contributing to anaerobic metabolic processes such as lactic acid fermentation in the earliest life forms.

Finally, while our simulation experiments investigated the formation mechanisms of racemic **1** in model interstellar ices subjected to GCRs proxies, interstellar ices are also exposed to UV photons.[88] Future studies processing ethanol-containing ices with circularly polarized UV light may help elucidate the enantioselective pathways leading to D- and/or L-enantiomers of **1**.[5] These results would provide crucial insights into the prebiotic evolution of biomolecular homochirality in deep space and predict the potential regions where key precursors essential for the origins of life could exist.

■ CONCLUSIONS

To conclude, the present investigation provides persuasive testimony on the bottom-up synthesis of the key biomolecule lactic acid (**1**) via a barrierless radical−radical recombination of hydroxycarbonyl (**5**) and 1-hydroxyethyl (**14**) radicals in interstellar model ices composed of carbon dioxide and ethanol (**13**). The low-temperature ice mixtures were exposed to proxies of galactic cosmic rays in form of energetic electrons[28] at doses corresponding to exposure time scales up to 7 × 10^5 years; this is equivalent to the early stage of a molecular cloud, which typically have lifetimes of up to a few 10^7 years.[57] Lactic acid (**1**) and its isomer monoethyl carbonate (**15**) were identified in the gas phase during TPD utilizing vacuum ultraviolet photoionization reflectron time-of-flight mass spectrometry (PI-ReToF-MS) and isotopic labeling experiments. The overall reaction leading to **1** (reactions 1, 4 and 5) is endoergic by 17 kJ mol^{-1},[85] highlighting the critical role of nonequilibrium radiation-driven processes for its formation. These findings not only reveal fundamental insights into the abiotic formation of **1** in ethanol-rich interstellar ices under ionizing radiation, but also represent a critical step toward understanding how complex biorelevant acids such as hydroxycarboxylic acids can be synthesized in deep space.

■ MATERIALS AND METHODS

The experiments include the preparation of low-temperature isotopically substituted carbon dioxide−ethanol ice mixtures (CO$_2$−CD$_3$CD$_2$OD, ^{13}CO$_2$−^{13}CH$_3$^{13}CH$_2$OH, C^{18}O$_2$−CH$_3$CD$_2$OH, and ^{13}C^{18}O$_2$−CD$_3$CH$_2$OH) deposited on a polished silver substrate at 5 K in an ultrahigh vacuum chamber at pressures of a few 10^{-11} Torr.[30,89] The ice mixtures were irradiated with energetic electrons to initiate nonequilibrium reactions, followed by the temperature-programmed desorption phase in which the processed ices were heated from 5 to 320 K at a rate of 0.5 K min^{-1}. Although the ratio of carbon dioxide to ethanol (1.6 ± 0.3:1) employed in this study may not reflect their typical abundances in molecular clouds, the ratio was chosen to maximize the production yield of $C_3H_6O_3$ isomers in the experiments, thus facilitating their detection. Infrared spectra of the ices were recorded in situ using the Fourier transform infrared (FTIR) spectrometer before, during, and after irradiation. During the TPD, molecules released into the gas phase were analyzed by vacuum ultraviolet photoionization reflectron time-of-flight mass spectrometry (PI-ReToF-MS) at 11.10, 10.54, and 9.34 eV. Additional experimental and computational details are provided in the Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.5c07637.

Methods (Experimental and Computational), FTIR spectra data of irradiated carbon dioxide−ethanol ice (Figures S1−S4, Tables S1−S4), difference in TPD profiles measured at 11.10 and 10.54 eV (Figure S5), proposed formation pathways for isomers **1**, **15**, and **16** (Figures S6–S7), gas phase mass spectra of isomer **1** (Figure S8), TPD profiles of irradiated CO_2–CD_3CD_2OD ice measured at 11.10 eV (Figures S9), infrared spectra of pure ethanol-d_2 and ethanol-d_3 ices (Figures S10–S11, Tables S8–S9), error analysis of adiabatic ionization energies and relative energies (Tables S5–S9), experimental conditions (Table S12), VUV generation parameters (Table S13), and Cartesian coordinates, vibrational frequencies, and infrared intensities of computed structures (Tables S14 and S15) (PDF)

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Notes

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