Matrix Isolation and Photorearrangement of *Cis*—and *Trans*—1,2-Ethenediol to Glycolaldehyde

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1,2-Ethenediols are deemed key intermediates in prebiotic and interstellar syntheses of carbohydrates. Here we present the gas-phase synthesis of these enediols, the high-energy tautomers of glycolaldehyde, trapped in cryogenic argon matrices. Importantly, upon photolysis at λ = 180–254 nm, the enols rearrange to the simplest sugar glycolaldehyde.

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The paradigm of prebiotic chemistry is that life emerged from small molecules, which then self-assembled into larger structures that eventually formed stable networks of interconnected chemical reactions driven by a constant flow of energy.^{1, 2} In this respect, the formose reaction³ has been suggested to play a role in the abiological synthesis of carbohydrates, including ribose, the sugar component of RNA.^{4, 5} This aqueous reaction converts formaldehyde (H₂C=O) into a variety of sugars in the presence of (organic) bases or minerals.⁶ The mechanism of the formose reaction had been proposed by Breslow⁷ in 1959 to occur through a series of base-catalyzed aldol reactions, with autocatalysis of glycolaldehyde (**1**, Scheme 1). The mechanism for the initial formation of **1** from two formaldehyde molecules was a riddle until 2018,⁸ when we showed that **1** can form in the gas phase by a nearly barrierless carbonyl-ene reaction ($\Delta H^{\dagger} \approx 1$ kcal mol⁻¹) using nucleophilic hydroxycarbene (H–C–OH) as the nucleophilically reactive formaldehyde isomer.⁹

The follow-up steps in the formose reaction rely on facile enolizations that allow aldol additions with H_2CO , eventually leading to a variety of aldoses and ketoses. *cis*-Ethenediol (*cis*-2) and *trans*-ethenediol (*trans*-2) –the enols of glycolaldehyde (1)–, are thereby implied as the first intermediates leading to the formation of prebiotic three- to five-carbon sugars.^{10, 11} The formation of 2 from 1 is likely to be promoted by minerals (*e.g.*, borates), which starts the cycle with the aldol reaction of 2 as the nucleophile with formaldehyde as the electrophile to give glyceraldehyde.¹² Hence, iterative enolization and aldol reactions with H_2CO gives rise to the observed sugars.¹³



Scheme 1. Formation of glycolaldehyde (1) from hydroxycarbene as the reactive formaldehyde isomer.⁸ Generation and subsequent reaction of 1,2-ethenediol (2) with formaldehyde.^{10, 11}

There is little spectroscopic information on *cis*-**2** and *trans*-**2**, considering their role as prime intermediates in the synthesis of biologically relevant compounds.¹⁰ Both diastereomers of **2** were observed and analyzed by solution NMR and IR spectroscopy at low temperatures after flash-vacuum pyrolysis of anthracene-based precursors.¹⁴ Structures with the mass and ionization potentials of *cis*-**2** and *trans*-**2** were prepared through exposing methanol-carbon monoxide ices to ionizing radiation and were subsequently identified *via* photoionization reflectron time-of-flight mass spectrometry.¹⁵ More recently, *cis*-**2** has been prepared in the gas phase and its rotational spectrum recorded.¹⁶ There are several theoretical studies on *cis*-**2** and *trans*-**2**,¹⁷⁻¹⁹ each having several conformers.

Here we report the preparation and matrix isolation of the two most stable conformers of the Z and E isomers of **2** and present detailed IR as well as UV/Vis spectroscopic data together with their unexplored photochemistry that leads to the simplest sugar **1** that has been detected in interstellar space⁴¹ but the search for higher sugars has not been successful.³⁹ Compound **1** has also been identified in the Murchison and Murray meteorites^{42, 43} and in comets

(*e.g.*, 67P/Churyumov–Gerasimenko),³⁸ and **1** is considered a key prebiotic intermediate in the production of important biomolecules such as glycolaldehyde phosphates, amino acids, and ribonucleotides.⁴⁴

The formation of **2** and **1** via [1,3]H-shift in abiotic environments potentially plays a pivotal role in the formation of carbohydrates. However, [1,3]H-shifts in keto-enol tautomerizations are often associated with high barriers (40-45 kcal mol⁻¹)²⁰⁻²² and can be excluded under the cryogenic conditions in space. In such environments, excess energy is mostly available through light to promote such isomerizations.^{23, 24} Hence, our results can aid the identification and reactivity of **2** in interstellar media and shed light on the poorly understood processes of prebiotic syntheses of **1** and higher sugars at low temperatures in interstellar media with **2** as the key intermediate.

Tureček and coworkers^{50, 51} described several simple neutral enols through retro-Diels-Alder reactions of norbornene precursors and characterization by mass spectrometry and ionization energy measurements in the gas phase. Our strategy for the preparation of **2** was FVP of $(1R^*, 2R^*, 3S^*, 4S^*)$ -bicyclo[2.2.1]hept-5-ene-2,3-diol (**3**) in the reaction **3** \rightarrow *cis*-**2** + C₅H₆ (C₅H₆ = cyclopentadiene, **4**) and *trans*-9,10-dihydro-9,10-ethanoanthracene-11,12-diol (**5**) in the reaction **5** \rightarrow *trans*-**2** + C₁₄H₁₀ (C₁₄H₁₀ = anthracene, **6**) (Scheme 2).

Compound **3** and its deuterated isotopologue were synthesized according to the literature (see ESI).⁵² Pyrolysis of **3** at 700 °C and subsequent trapping of the pyrolysis products at 10 K led to large amounts of **4** in the corresponding matrix isolation spectra, indicating nearly complete consumption of **3** and confirming the dissociation pathway (Fig. 1 and Fig. S1). Structure **4** was unambiguously identified by comparison with matrix-isolated data of an authentic sample.⁵³



Scheme 2. 1,2-Ethenediols (2) generated from 3 and 5 through pyrolysis and trapping in argon matrix. Subsequent photorearrangement to glycolaldehyde (1).

The IR spectrum of the FVP products of **3** shows several new absorptions, next to some unreacted starting material and the usual impurities (e.g., H_2O) (Fig. S1). We also observed new unreported signals that we assign to *cis*-**2**. Notably, a medium intensity band at 1711 cm⁻¹ is attributed to the C=C stretching mode in *cis*-**2** (Fig. 1) that agrees well with previous IR measurements for other enols (*e.g.*, 1667 cm⁻¹ for ethenol;⁵⁴ 1712 cm⁻¹ for 1,2-ethenediol;²⁰ 1680 cm⁻¹ for 1-aminoethenol).²¹ The very prominent bands at 3667 and 3592 cm⁻¹ can be assigned to the OH stretching modes of *cis*-**2** (Fig. S2). The strongest band at 1084 cm⁻¹ in *cis*-**2** corresponds to the most characteristic C–O stretching vibration. Intense C–H and CCO deformation modes are at 742 and 709 cm⁻¹ along with bands at 525 and 418 cm⁻¹ for the C–C and C–O twisting modes (Table S1). *Cis*-**2** had been characterized using IR spectroscopy in solid films at 77 K,¹⁴ with C=C and C–O stretching modes at 1705 and 1095 cm⁻¹, consistent with our data.

The assignment of these bands was also verified with a d_2 -*cis*-**2** labelled derivative, which results in characteristic isotopic shifts. For example, the prominent IR band at 1711 cm⁻¹ is red-shifted by 7 cm⁻¹ (calc.: -11 cm⁻¹) in d_2 -*cis*-**2**; the OH stretching modes at 3667 and 3592 cm⁻¹ show large red-shifts of 957 and 942 cm⁻¹ (calc.: -1066 and - 1031 cm⁻¹) for d_2 -*cis*-**2**. The OH deformation mode at 1718 cm⁻¹ is red-shifted by 284 cm⁻¹ (calc.: -305 cm⁻¹). The good match between the AE-CCSD(T)/cc-pVTZ computed and experimentally observed frequencies and shifts of underscores their successful preparation (Fig. 1, Fig.s S1-S3, Table S1 in the ESI).



Fig. 1. (a) IR spectrum showing the pyrolysis products of 3 with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of 4 was subtracted (downward bands). (b) IR spectrum of *cis*-2 computed at AE-CCSD(T)/cc-pVTZ (unscaled).

The UV/Vis spectrum of matrix-isolated *cis*-**2** displays a strong transition at 191 nm, which correlates well with the computed value of 186 nm (f = 0.142) at TD-B3LYP/6-311++G(2d,2p). The absorption band at 191 nm arises from a HOMO \rightarrow LUMO+3 excitation, corresponding to a π - π * transition (Fig. 2). Aside from *cis*-**2**, another strong band located at 237 nm provides evidence for the presence of **4** formed as a byproduct of the retro-Diels-Alder reaction of **3**⁵³ and agrees with reported data.⁵³

Studying the photochemistry of *cis*-2, is challenging because of the rich unimolecular photochemistry of 4, which has been studied previously: bicyclo[2.1.0]pent-2-ene, allylacetylene, and vinylallene form by 180 > λ > 200 nm irradiation of matrix-isolated 4.⁵³ Even though *cis*-2 absorbs in this range, we envisaged that two subsequent irradiation steps at appropriate wavelengths would nevertheless allow us to excite *cis*-2 exclusively. Considering the intense absorption at 237 nm for 4, we first irradiated the pyrolysis products matrices at λ > 200 nm, which selectively bleached the IR bands of 4, while those of *cis*-2 remained unchanged. Thereafter, the matrix was subjected to irradiation at 180–254 nm, which resulted in the disappearance of all IR absorptions assigned to 2. Simultaneously, the appearance of new IR bands matched well with 1 (Fig. S4). Along with IR bands of 1, we also observed a strong IR band at 2139 cm⁻¹ due to carbon monoxide (C=O) as a decomposition product of 1. It has been shown that the photolysis of 1 in low-temperature matrices produces a CH₃OH–CO molecular complex; these results were readily reproduced here.⁵⁵

The photochemistry of *cis*-**2** was also followed by UV/Vis spectroscopy (Fig. 2). In accordance with the IR experiments, irradiation of the matrix with wavelengths $\lambda > 200$ nm leads to the disappearance of the observed UV band at 237 nm. Upon further irradiation with wavelength $\lambda = 180-254$ nm, the intensity of the UV band at 191 nm decreased as well.



Fig. 2. Solid line: UV/vis spectrum showing the pyrolysis product of **3** with subsequent trapping in an argon matrix at 10 K. Dashed line: after irradiation at $\lambda > 200$ nm for 30 min in argon at 10 K. Inset: computed [TD-B3LYP/6-311++G(2d,p)] electronic *trans*itions for *cis*-**2**.

Rearrangements on the potential energy surface of **2** have been studied computationally employing DFT methods.¹⁷ For comparison, we reinvestigated the most important intramolecular reactions of **2** at the AE-CCSD(T)/cc-pVTZ level of theory (Fig. 3). According to our computations, *cis*- and *trans*-**2** each display several conformers: *cis*-*syn*-*anti*-**2** (*cis*-**2sa**) where the OH groups have an *anti* and *syn* orientation leading to an unsymmetric (C_1) structure and *cis*-*anti*-*anti*-1,2-**2** (*cis*-**2aa**) with an *anti* orientation of the two OH groups that shows C_{2v} symmetry. *Cis*-**2sa** conformer is predicted to be 4.2 kcal mol⁻¹ more stable than *cis*-**2aa** (including ZPVE, denoted as ΔH_0), which can be rationalized

by stabilization of the former through intramolecular hydrogen bonding between the hydroxyl groups on the adjacent carbons. The activation enthalpy for the *cis*-**2sa**/*cis*-**2aa** conformational isomerization is 4.8 kcal mol⁻¹ (**TS1**) (Fig. 3). According to computations, the *trans*-isomer has three distinct conformers: *trans*-*syn*-*syn*-1,2-**2** (*trans*-**2ss**) with C_{2h} symmetry, unsymmetric *trans*-*anti*-*syn*-1,2-**2** (*trans*-**2as**), and *trans*-*anti*-*anti*-1,2-**2** (*trans*-**2aa**) of C_2 symmetry. The relative energies compared (in kcal mol⁻¹, Fig. 3) to the most stable structure *cis*-**2sa** are *trans*-**2ss** (3.7) > *trans*-**2as** (4.2) > *trans*-**2aa** (4.6). The barriers for stepwise conformational changes for *trans*-**2ss** \rightarrow *trans*-**2aa** are 5.0 (**TS3**) and 5.5 (**TS4**) kcal mol⁻¹, respectively. As anticipated, the retro-Diels-Alder reaction of **3** in the gas phase leads to the formation of *cis*-**2**. The experiment IR spectrum of the pyrolysis products matches the computed spectrum of *cis*-**2sa**, which is the only conformer present in the matrix.

Following a similar route for the synthesis of *cis*-**2sa**, we prepared *trans*-**2** from **5** by FVP; for the synthesis of **5** and its deuterated isotopologue see the ESI. Pyrolysis of **5** at 700 °C also proceeds through a retro-Diels-Alder reaction, as evident by the appearance of IR bands of anthracene (**6**). Along with **6**, we observed a set of new IR bands that we assign to *trans*-**2**. There is an excellent match of the experimental and the AE-CCSD(T)/cc-pVTZ IR spectrum of *trans*-**2ss**, which is the only conformer present in the matrix (Fig. 4 and Table S2). Notably, strong bands at 1117 and 892 cm⁻¹ are assigned to the C–O stretching and C–H deformation modes in *trans*-**2ss**, showing isotope shifts of +14 and -1 cm⁻¹ (calc.: +13 and -2 cm⁻¹) in *d*₂-*trans*-**2ss**, respectively. The very prominent band at 3637 cm⁻¹ is assigned to the OH stretching mode with an isotope shift of -1094 cm⁻¹ (calc. -1042 cm⁻¹) (Fig.s S6 and S7). Note that we did not observe the C=C stretching mode in the IR spectrum owing to its *C*₂-symmetry, which agrees well with the computations.



Fig. 3. Potential energy profile (ΔH_0) in kcal mol⁻¹ of the reactions of enols 2 at AE-CCSD(T)/cc-pVTZ + ZPVE at 0 K.

The UV/vis spectrum of matrix-isolated *trans*-**2ss** exhibits a broad absorption band at 191 nm (there are also intense bands of **6** as byproduct), which correlates well with the computed value of 198 nm (f = 0.206) (TD-B3LYP/6-311++G(2d,2p)) from a HOMO–LUMO+3 excitation (Fig. S8). In analogy to *cis*-**2sa**, irradiation of matrix-isolated *trans*-**2ss** in solid argon λ = 180–254 nm results in its disappearance and simultaneously appearance of **1** (Fig. S9 and Scheme 2B). The formation of **1** was identified by comparison with an authentic sample.

The relative energy ordering of the $C_2H_4O_2$ isomers shows that *trans*-**2ss** and *cis*-**2sa** are 8.6 and 12.4 kcal mol⁻¹ above 1,1-ethenediol (**7**) at AE-CCSD(T)/cc-pVTZ. The higher stability of **7** over *E*-**2ss** and *Z*-**2sa** is also evident from the HOMO–LUMO energy differences. Changing the position of OH groups leads to an increase of the HOMO energy and a smaller HOMO–LUMO gap (Fig. S10). This implies that *trans*-**2ss** and *cis*-**2sa** should be better nucleophiles than **7**. The NBO charges of these species also are quite different: +0.121e and +0.149e for *trans*-**2ss** and +0.127e at both carbon atoms for *cis*-**2sa**, respectively, whereas in **7**, the methylene carbon atom bears a –0.025e charge, and the carbon atom with two OH groups bears +0.324e charge.

A typical olefin *cis-/trans*-isomerization barrier is ca. 100 kcal mol⁻¹ ^{56, 57} and such an isomerization of **2** therefore would also require a large activation energy to break the π bond and is not considered further here. Instead, the tautomerization of *cis*-**2sa** to **1a** proceeds *via* simultaneous double-hydrogen shift **TS2** with a barrier of 60 kcal mol⁻¹. It involves hydrogen atom transfers from one OH group to the carbon atom, and from the other OH group to oxygen (Fig. 3).¹⁷ The *cis*-**2sa** \rightarrow **1a** interconversion through a conventional [1,3]H-shift mechanism has a higher barrier (**TS2**', 72.2 kcal mol⁻¹), similar to the [1,3]H-shift barrier of **7** to acetic acid.²⁰ The *trans*-**2ss** \rightarrow **1b** reaction requires an activation barrier of 60.4 kcal mol⁻¹ (**TS5**). Our results therefore unravel an important reaction pathway for the photochemical synthesis of glycolaldehyde in space.⁴¹ Very recently, *cis*-**1**,2-ethenediol was detected in the interstellar medium,⁶⁰ and may therefore be considered a key intermediate in the formation of sugars in interstellar space.¹⁵



Fig. 4. (a) IR spectrum showing the pyrolysis product of 5 with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of 6 was subtracted (downward bands). (b) IR spectrum of *trans-*2sa computed at AE-CCSD(T)/cc-pVTZ (unscaled).

Conflicts of interest

No competing financial interests have been declared.

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All data (IR, UV/vis, and NMR spectra) are available in the JLUPub data repository (<u>https://jlupub.ub.uni-giessen.de/handle/jlupub/8394</u>).

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