Precursors of Biological Cofactors from Ultraviolet Irradiation of Circumstellar/Interstellar Ice Analogues

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Abstract: Biological cofactors include functionalized derivatives of cyclic tetrapyrrole structures that incorporate different metal ions. They build up structural partnerships with proteins, which play a crucial role in biochemical reactions. Porphyrin, chlorin, bacteriochlorin, and corrin are the basic structures of cofactors (heme, chlorophyll, bacteriochlorophyll, siroheme, F 430, and vitamin B_{12}). Laboratory and theoretical work suggest that the molecular building blocks of proteins (α-amino acids) and nucleic acids (carbohydrates, purines, and pyrimidines) were generated under prebiotic conditions. On the other hand, experimental data on the prebiotic chemistry of cofactors are rare. We propose to search directly for the pathways of the formation of cofactors in the laboratory. Herein we report on the detection of N-heterocycles and amines in the room-temperature residue obtained after photo- and thermal processing of an interstellar ice analogue under high vacuum at 12 K. Among them, hexahydro-1,3,5-triazine and its derivatives, together with monopyrrolic molecules, are precursors of porphinoid cofactors. Hexahydropyrimidine was also detected. This is the first detection of these compounds in experiments simulating circumstellar/interstellar conditions. Except for 2-aminopyrrole and 2,4-diaminofuran, which were only found in ^{13}C-labeled experiments, all the reported species were detected in both ^{12}C- and ^{13}C-labeled experiments, excluding contamination. The molecules reported here might be present in circumstellar/interstellar grains and cometary dust and could be detected by the Stardust and Rosetta missions.

Keywords: chemical evolution · cofactors · photochemistry · stellar dust · tetrapyrroles

Introduction

Dense interstellar clouds are cold regions, $T \approx 10$ K, mainly composed of gas and dust. Dust particles in dense clouds accrete ice mantles containing mostly H_2O, but also CH_3OH, CO, CO_2, and NH_3. The aim of our experiments is to simulate the physical conditions of low pressure, low temperature, and UV irradiation that circumstellar/interstellar ice mantles coating dust particles may experience.[1,2] For this, an ice layer with a composition analogous to that of interstellar ices was deposited on a substrate while being irradiated by UV photons. After irradiation, the sample was slowly warmed up to room temperature leaving a residue containing the most refractory products of photo- and thermal processing. Previous laboratory work shows that the sample contains a rich variety of organic molecules.[1,3–6] These studies suggest that circumstellar/interstellar ices might contain a rich mixture of organic compounds.

The grain material from dense clouds will eventually enter circumstellar disks. In addition, photoprocessing of ice mantles may take place at different stages of the protostellar

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evolution, for instance, during the T Tauri phase (i.e., the stage between deeply embedded protostars and low-mass main sequence stars, characterized by ultraviolet and infrared excesses with respect to a main sequence star of the same effective temperature), and in the outer regions of protoplanetary disks around young stellar objects (ref. [1] and references therein). Comets were presumably formed by aggregation of dust particles in the solar nebula, the interstellar cloud from which our solar system formed, and could contain the products of ice processing. These objects are thought to host the most pristine material in our solar system.[7,8] The similarity between the compounds produced in our experiments and the oxygen-rich complex organic molecules found abundantly in comet Halley[9,10] suggests that presolar energetic processing in the interstellar medium, and/or the solar nebula, could play an important role in determining the organic inventory of the early solar system. The organic fraction of comets may have important implications for the origin of life on Earth, as first predicted by Oró.[11]

Herein we present the products obtained by UV irradiation and subsequent warm up of the $H_2O/CH_3OH/NH_3/CO/CO_2$ (2:1:1:1:1) ice mixture characteristic of circumstellar regions.[1,12–14]

Experimental Section

The experimental setup consisted of a high-vacuum chamber ($P \approx 1 \times 10^{-7}$ torr) at room temperature, in which a gas mixture was deposited onto an aluminium block at the cold finger tip and irradiated with UV photons. The system was pumped by a turbo pump (Pfeiffer Balzers TSH 280H) backed up by a diaphragm pump (Vacuubran MD4T). A temperature of 12 K, typical of dense clouds, was achieved by means of a closed-cycle helium cryostat (Air Products Displex DE-202). For a detailed description, see ref. [15]. The gas mixtures were prepared in a gas line with a vacuum pressure of $\approx 10^{-5}$ torr, containing the following components: H_2O (liquid), distilled; CH_3OH (liquid), Janssen Chimica, 99.9%; NH_3 (gas), Praxair, 99.999%; CO (gas), Praxair, 99.997%; CO_2 (gas), Praxair, 99.996%. CO_2 was kept in a separate bulb in order to prevent it from reacting with the ammonia, NH_3, with deposition through two independent tubes. Simultaneously to deposition, the ice layer was photoprocessed with a microwave-stimulated hydrogen-flow discharge lamp. The lamp output was $\approx 1.5 \times 10^{15}$ photons per second;[16] the emission spectrum of the lamp ranged from 7.3 to 10.5 eV, with the main emission at Lyman-α (10.2 eV) for a hydrogen pressure (P_H) of 0.5 torr.

The deposition and irradiation time was typically 24 h, with a gas flow of $\approx 10^{16}$ molecules per second, corresponding to an average dose of ≈ 0.15 UV photons per molecule. A long simultaneous deposition and irradiation was required to obtain enough organic residue material for the analysis. After irradiation, the system was warmed up gradually by means of a temperature controller (Scientific Instruments Inc. 9600-1) at $1\,K\,min^{-1}$ until $T = 40$ K, in order to prevent explosive reactions caused by UV-produced free radicals embedded in the ice.[17] Subsequently, the warm up proceeded at $\sim 4\,K\,min^{-1}$ up to room temperature, at which point the refrigerator and temperature controller were turned off and the system slowly reached thermal equilibrium with the environment. The Al block containing the residue was removed from the system and stored in a capsule filled with nitrogen. Experiments using ^{13}C-labeled gases (^{13}CO (gas), Cambridge Isotope Laboratories Inc. (C.I.L.), 99% ^{13}C; $^{13}CO_2$ (gas), C.I.L., 99% ^{13}C; $^{13}CH_3OH$ (liquid), Sigma, 99% ^{13}C) were performed to deduce the number of C atoms in the organic products and to exclude the possibility of contamination.

Analytical procedure: Water extracts of the residues were prepared for GC–MS analyses. The analyses were performed by using an Agilent 6890 GC system equipped with a 5973N MS detector. A 12 m Varian-Chrompack Chirasil-L-Val capillary column (Lexington, MA) with 0.25 mm inner diameter and 0.12 μm layer thickness was applied for gas chromatographic separations with a 1:2 split injection and $1.5\,mL\,min^{-1}$ constant flow of He carrier gas. Under standard conditions, the temperature program of the oven was 3 min at 70 °C, then increased at a rate of $5\,°C\,min^{-1}$, followed by 17.5 min at 180 °C. Mass spectrometric operating conditions were 72 eV for electron-induced ionization and mass windows between 50 and 550 amu for the total-ion-current mode. All calculations were performed using the ChemStation and Data Analysis software from Agilent.

The sample extracts were dissolved in HCl (30 μL, 0.1 M) and derivatized using the procedure of Abe et al.,[18] which transforms alcohols into ethyl esters, amines into *N*-ethoxycarbonyl derivatives, and amino acids into *N*-ethoxycarbonyl ethyl esters (ECEE). The analytical protocol differs from our previous work[5] because a 24 h hydrolysis step with 6 M HCl at 110 °C was not included.

By using the single-ion monitoring mode (SIM) it was possible to select a given ion mass, in order to increase both chromatographic resolution and sensitivity.

Results

Figure 1 shows the chromatogram corresponding to the residue obtained from photo- and thermal processing of the ^{13}C-labeled ice mixture ($H_2O/^{13}CH_3OH/NH_3/^{13}CO/^{13}CO_2$ 2:1:1:1:1), henceforth referred to as the ^{13}C residue. A similar chromatogram was obtained for the residue of a similar experiment using unlabeled ices, the ^{12}C residue. The abundance of glycine was obtained by integrating the peak area calibrated with a standard. The abundances of the other species were calculated assuming the same sensitivity for each compound. The quantum yield (Φ) was obtained by dividing the abundance by the number of photons. Table 1 gives the identification of the products corresponding to both the ^{12}C and ^{13}C residues. The next column gives the quantum yield (Φ in molecules per photon) of these species relative to hexahydro-1,3,5-triazine, Φ(tri), where $\Phi(\text{tri}) \approx 1.6 \times 10^{-4}$. For comparison, the quantum yield of hexamethylenetetramine (HMT, $(CH_2)_6N_4$), the most abundant component in the infrared spectrum of these residues, is $\Phi(\text{HMT}) \approx 0.01$.[1] The mass fragments of the elutants in the ^{12}C and ^{13}C residues are given along with their retention times, t_R, in minutes. Except for 2-aminopyrrole and 2,4-diaminofuran, which were not detected in the ^{12}C residue, the same species were found in both samples. The reported molecules are, therefore, true products of photo- and thermal processing of the ices, and organic contamination can be excluded. A common contaminant, bis(2-ethylhexyl)phthalate, present in vinyl gloves, was detected; however, its presence is not expected to affect the results. N-Heterocycles and amines are the dominant components in the chromatogram. The N-heterocycles include, in order of abundance, (diaminomethyl)hexahydro-1,3,5-triazine, hexahydro-1,3,5-triazine, (1-aminoethyl)hexahydro-1,3,5-triazine, hexahydropyrimidine, 2,5-diaminofuran, 2-aminopyrrole, and 2,4-diaminofuran; the amines detected are 1,1,2,2-tetraminoethane, 1,1,2-

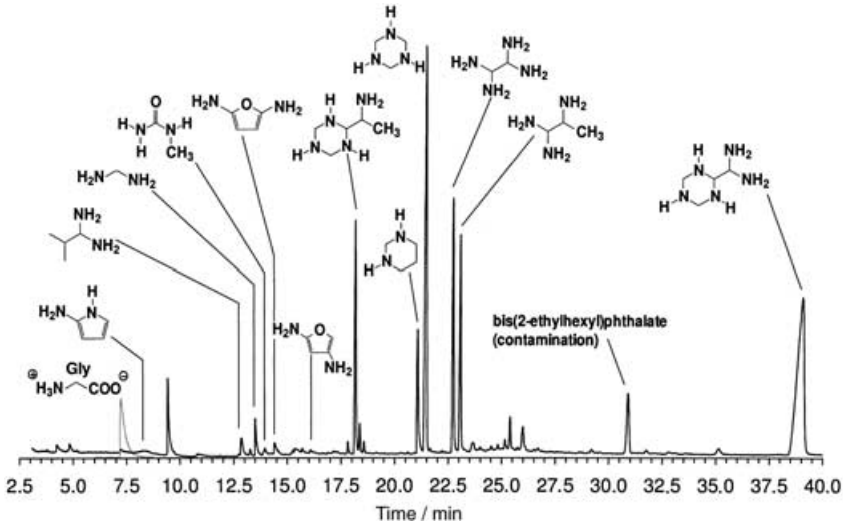


Figure 1. Gas chromatogram showing the N-heterocyclic molecules and the amines generated under simulated interstellar conditions, corresponding to the ^{13}C residue (photolyzed $H_2O/^{13}CH_3OH/NH_3/^{13}CO/^{13}CO_2$ 2:1:1:1:1 ice). The inset peak (gray, enlarged for clarity) shows the abundance of glycine in the ^{13}C residue recorded in the extract ion mode for 103 amu of the GC–MS system.

triaminopropane, diaminomethane, and 1,1-diamino-2-methylpropane. Also, *N*-methylurea was identified as a component of the residues. The small peak eluting at 7.23 min for the ^{13}C residue (Figure 1) corresponds to glycine. Shown superposed onto this peak (gray inset, enlarged for clarity) is the same peak in the extract ion mode for 103 amu of the GC–MS data, corresponding to derivatized glycine.

Discussion

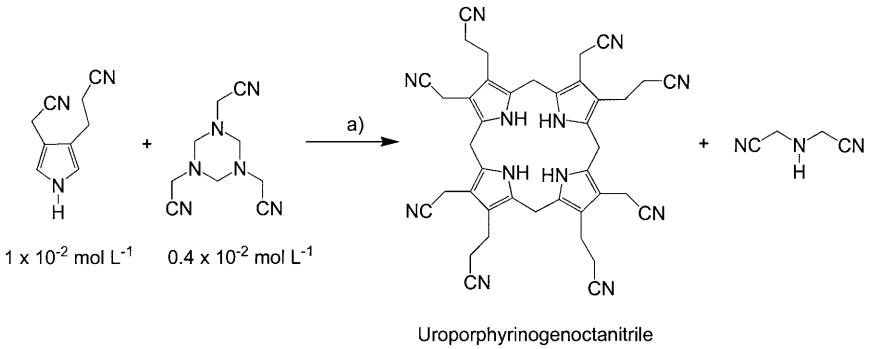
We report the detection of a number of N-heterocyclic molecules as products of photo- and thermal processing of circumstellar/interstellar ices. Previously, 2,5-diaminofuran and 2,5-diaminopyrrole were reported.[5] A number of these molecules are of biogenic interest. For the molecular origin of the biological cofactor family, on the one hand, an autotroph origin was discussed considering that organisms are capable of synthesizing all their carbon constituents from carbon dioxide (or other C_1 units). On the other hand, a heterotroph origin was proposed which assumes that structural prototypes of cofactors were of prebiological origin and taken from the environment by biological systems, used as catalysts, genetically fixed, copied, and structurally optimized. Important types of cofactors were probably not modified during the phases of biological evolution.[19,20] The key building block of all porphinoid cofactors, with the exception of a few hexahydroporphyrins, is the macrocyclic molecule uroporphyrinogen (constitutional type

Table 1. Peak identification for ^{12}C and ^{13}C products from the photolyzed $H_2O/CH_3OH/NH_3/CO/CO_2$ (2:1:1:1:1) ice shown in Figure 1.[a]

Molecule	Φ[b] ^{13}C residue $\Phi\times100/\Phi$(tri)	MS fragmentation ^{12}C residue [amu]	MS fragmentation ^{13}C residue [amu]	t_R[c] [min] ^{12}C residue	t_R[c] [min] ^{13}C residue
glycine	1.76	102	177, 132, **103**	7.51	7.23
2-aminopyrrole	2.50	$\leq$ d.l.[d]	158, 135, 113, **85**	$\leq$ d.l.[d]	8.42
unidentified	18.6	189, **131**, 117, 103	193, **133**, 121, 105	9.61	9.43
1,1-diamino-2-methylpropane	6.16	189, 161, 145, **117**, 102, 89	236, 220, 207, 191, 190, 162, 147, 118, 103, 91, **63**	12.97	12.85
diaminomethane	8.08	161, **117**, 102, 89	191, 190, 162, **118**, 103, 90	13.60	13.52
N-methylurea	2.71	102, 73	220, 205, 204, 176, 159, 147, **103**, 87, 74	13.95	13.95
2,5-diaminofuran	3.84	242, 169, 153, 125, **97**, 81, 69, 53	246, 173, 157, 129, **101**, 85, 72, 56	14.58	14.42
2,4-diaminofuran	1.01	$\leq$ d.l.[d]	246, **173**, 157, 129, 101, 85, 56	$\leq$ d.l.[d]	16.08
(1-aminoethyl)hexahydro-1,3,5-triazine	43.1	272, 230, 171, **143**, 129, 116	277, 233, 175, **146**, 131, 118	18.15	18.17
hexahydropyrimidine	26.7	230, 214, **189**, 170, 158, 143, 129, **115**, 102, 85	234, 217, **190**, 174, 161, 146, 131, **117**, 103, 88	21.03	21.08
hexahydro-1,3,5-triazine	100	274, 258, **230**, 202, 157, 129, 102	277, 261, **233**, 204, 159, 131, 103	21.42	21.49
1,1,2,2-tetraminoethane	49.9	203, **189**, 117, 102	205, **190**, 118, 103	22.70	22.74
1,1,2-triaminopropane	39.0	290, 246, 231, 217, 202, **189**, 117, 102	293, 249, 234, 219, 204, **190**, 118, 103	23.04	23.08
unidentified	5.13	330, 229, 214, 201, 170, 143, 129, 116, **100**	337, 235, 219, 207, 174, 146, 131, 118, **104**	25.37	25.39
bis(2-ethylhexyl)phthalate (contamination)	(19.5)	279, 167, **149**, 113, 104, 83, 71, 57	279, 167, **149**, 113, 104, 83, 71, 57	30.81	30.89
(diaminomethyl)hexahydro-1,3,5-triazine	147	315, 302, 258, 230, 215, 202, 189, **187**, 157, 129, **115**, 102	319, 305, 261, 233, 218, 204, **190**, 159, 131, 117, 103	38.81	39.07

[a] Numbers designated in boldface are the main mass fragments. [b] Quantum yield. For triazine hydrate, $\Phi(\text{tri})\approx1.6\times10^{-4}$. [c] Gas chromatographic retention time. [d] Detection limit.

III, that is, one isomer out of four constitutional isomer types I–IV).[20] The central step in the synthesis of uroporphyrinogen is known to be the tetramerization of monopyrrolic porphobilinogen to uroporphyrinogen.[21,22] Studies on the prebiotic generation of uroporphyrinogen structures in the laboratory of A. Eschenmoser showed that desaminomethylporphobilinogendinitrile reacts with hexahydro-1,3,5-triazinetrinitrile in the presence of montmorillonite to form uroporphyrinogenoctanitrile (Scheme 1). The monopyrrolic reactant desaminomethylporphobilinogendinitrile was proposed to be formed from a previous reaction of glutaminedinitrile and glycinenitrile. Both the monopyrrolic compounds (in small quantities; other constitutional isomers are expected to be detected in the near future) and the macrocyclic hexahydro-1,3,5-triazine (and its derivatives) are now detected in residues made from UV photoprocessing of interstellar/circumstellar ice analogues. In addition, species bearing a nitrile group are produced by energetic processing of interstellar ice analogues: OCN^- is formed by thermal, UV, or ion processing;[23] it is observed in the solid state toward various young stellar objects, while HCN can be formed by ion irradiation,[24] and is present in the gas phase of the interstellar medium and in several cometary comae. These species are potential candidates for prebiological starting reactants to form uroporphyrinogen, which can be transformed, by follow-up reactions of known considerable self-constituting potential,[20] into biological porphinoid cofactors. Hexahydropyrimidine (hexahydro-1,3-diazine) was also detected. Our results support a heterotroph origin of the biological cofactor family, which means that these compounds resulted from abiotic chemical evolution. An autotrophic origin, that is, the synthesis of biological cofactors by biological organisms, is difficult to study experimentally, and might require in vivo experiments.



Scheme 1. The central step in the synthesis of the macrocyclic uroporphyrinogen. Tetramerization of desaminomethylporphobilinogendinitrile with hexahydro-1,3,5-triazinetrinitrile in the presence of montmorillonite. Adapted from Eschenmoser:[20] a) montmorillonite K 10, CH_3CN/180 °C/0.5 h/N_2; 80 % yield.

2-Aminopyrrole was detected in the ^{13}C residue, along with 2,5-diaminofuran and 2,4-diaminofuran.

It was found that several N-bearing molecules detected in the water extracts of our residues (diaminomethane, *N*-methylurea, (1-aminoethyl)hexahydro-1,3,5-triazine, hexahydro-1,3,5-triazine, and 1,1,2,2-tetraminoethane) were also formed by 6 M HCl hydrolysis of standard HMT. As HMT does not decompose in water unless heated to 270 °C,[25] and the abundances in the residues were much larger than those obtained after acid hydrolysis of the standard HMT, these species cannot be decomposition products of the HMT present in our residues. Some of these molecules might, however, be related to HMT formation; such as the case of hexahydro-1,3,5-triazine, which is known to be a precursor of HMT. In addition, the products (1-aminoethyl)hexahydro-1,3,5-triazine and (diaminomethyl)-hexahydro-1,3,5-triazine could lead to formation of HMT-based species.[26] The true number of N-heterocyclic molecules present in the residues is expected to be larger than the values reported here, as the current detection technique is only sensitive to N-heterocycles bearing -NH or -NH_2 groups.

A similar experiment was performed using H_2O/^{13}CO/NH_3 (2:1:1) as the starting ice, in order to test the role played by CH_3OH ice in the formation of refractory species. The resulting chromatogram, not shown, was dominated by 1,1,2,2-tetraminoethane and hexahydro-1,3,5-triazine (the peak area of the latter is 27 % that of the former), and a unidentified product eluting at 14.45 min. It can thus be concluded that CH_3OH plays an important precursor role in the formation of most of the products reported in Table 1. The effect of adding H_2S to the initial gas composition will be discussed elsewhere.

Urea, along with several other amides known to be products of ice photoprocessing,[3,27] were not found in our samples, while *N*-methylurea was detected (Table 1). This difference might be due to the different ice composition or analysis protocol.

The analysis of these residues after hydrolysis with 6 M HCl and derivatization led to a large variety of amino acids as well as 2,5-diaminofuran and 2,5-diaminopyrrole.[5] Of these, only glycine, the simplest amino acid, and 2,5-diaminofuran were detected in the present analysis. The glycine abundance is enhanced from a factor of ~7 to 100 after acid hydrolysis. For 2,5-diaminofuran, the abundance after acid hydrolysis is increased from a factor of 1 to 30. For both molecules, this enhancement is not quantitatively reproducible and the cause of the increase itself is actually unknown. This effect is also observed in the analysis of amino acids[28] and diamino acids[29] in meteorites.

Astrophysical implications: It is important to bear in mind that the products reported here were detected at room temperature after dissolving the residues in water. Thus, the formation temperature of these species, ranging from cryogenic

temperatures to room temperature, is unknown, as well as any possible effects of dissolving the residues in water. As a result, it is not possible to derive any conclusions on the initial abundance of these products in photolyzed ice mantles in the interstellar medium. The reported species should be searched for in environments where annealing of icy grains took place, like hot cores or our solar system, where the agglomeration of such grains might have led to the formation of asteroids and comets. Interplanetary dust particles of asteroidal or cometary origin could host some of these products, but their small mass (of the order of nanograms) would currently prevent their detection in individual particles.

Following the abiotic synthesis of adenine from hydrogen cyanide,[30] other nucleic bases were produced under simulated primitive Earth conditions,[31] as well as different N- and O-heterocycles. A large number of N-heterocyclic molecules were found to be constituents of the Murchison meteorite, among them biochemical compounds, such as purines and uracil.[32] To our knowledge, there is no exact correspondence between the N-heterocycles currently detected in our samples and those found in Murchison. Nevertheless, the N-heterocyclic compounds reported here are similar to those which are very likely to be present in the dust of comet Halley, that is, pyrrole, pyridine, pyrimidine, and its derivatives.[9] Similar N-heterocycles were also observed in comet 81P/Wild 2.[33]

Recently, the positive detection of glycine was reported,[34] although it is still under debate. The column density upper limit for pyrrole in the dark cloud TMC-1 is 6×10^{12} cm^{-2}.[35] The detection of ethylene oxide (cyclic C_2H_4O) may herald the interstellar presence of furan (cyclic C_4H_4O), the next largest similar ring.[36]

Part of the Stardust and Rosetta missions is to analyze cometary material. The Stardust spacecraft aims to collect the dust surrounding comet 81P/Wild2 and return it to Earth for analysis in 2006. The COSAC experiment on board the Rosetta mission is designed to perform in situ GC–MS analysis of a comet nucleus.[37] A comparison between the laboratory results and the cometary data will provide information on the chemical composition of the solar nebula and the physical/chemical processes that played a role prior to comet formation. The similarity between the N-heterocycles tentatively found in comets and those produced in our experiments suggests that photoprocessing of icy dust particles may have been a common phenomenon in the local molecular cloud and/or the solar nebula. The previous detection of amino acids as products of combined photo- and thermal processing of circumstellar/interstellar ice,[5,6] coupled to the heterocyclic molecules reported here, among them a cofactor precursor, suggests that these biogenic species might be present in comets and interplanetary dust particles. The delivery of extraterrestrial organic matter on Earth might have contributed to the emergence of the first living organisms.[11,38]

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