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Investigation of pyridine carboxylic acids in CM2 carbonaceous chondrites: Potential precursor molecules for ancient coenzymes

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Abstract

The distribution and abundances of pyridine carboxylic acids (including nicotinic acid) in eight CM2 carbonaceous chondrites (ALH 85013, DOM 03183, DOM 08003, EET 96016, LAP 02333, LAP 02336, LEW 85311, and WIS 91600) were investigated by liquid chromatography coupled to UV detection and high resolution Orbitrap mass spectrometry. We find that pyridine monocarboxylic acids are prevalent in CM2-type chondrites and their abundance negatively correlates with the degree of pre-terrestrial aqueous alteration that the meteorite parent body experienced. We also report the first detection of pyridine dicarboxylic acids in carbonaceous chondrites. Additionally, we carried out laboratory studies of proton-irradiated pyridine in carbon dioxide-rich ices (a 1:1 mixture) to serve as a model of the interstellar ice chemistry that may have led to the synthesis of pyridine carboxylic acids. Analysis of the irradiated ice residue shows that a comparable suite of pyridine mono- and dicarboxylic acids was produced, although aqueous alteration may still play a role in the synthesis (and ultimate yield) of these compounds in carbonaceous meteorites. Nicotinic acid is a precursor to nicotinamide adenine dinucleotide, a likely ancient molecule used in cellular metabolism in all of life, and its common occurrence in CM2 chondrites may indicate that meteorites may have been a source of molecules for the emergence of more complex coenzymes on the early Earth.

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1. INTRODUCTION

Carbonaceous chondrites are meteorites that contain significant amounts of organic carbon (*e.g.*, 2% by weight) with some variable amount of this organic carbon in soluble form (Sephton, 2002). The organic compounds contained in these chondrites are thought to be formed either by aqueous reactions in meteorite parent bodies or via

reactions occurring in the interstellar medium (on energetically-processed, icy-organic dust grains) and later incorporated into meteorite parent bodies (Cronin and Chang, 1993; Cronin et al., 1993), or possibly by a combination of the two processes. The soluble organic content of carbonaceous chondrites is highly complex and is known to contain biologically relevant molecules such as amino acids (Kvenvolden et al., 1970; Cronin and Moore, 1971; Cronin and Pizzarello, 1997; Meierhenrich et al., 2004), nucleobases (Stoks and Schwartz, 1979, 1981; Martins et al., 2008; Callahan et al., 2011), and metabolic intermediates (Pizzarello et al., 2001, 2004; Cooper et al., 2011).

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Numerous investigations involving the analysis of soluble organic compounds in meteorites have relied heavily on gas chromatography–mass spectrometry and, to a lesser extent, liquid chromatography–mass spectrometry. In one of our earlier studies, we had applied liquid chromatography coupled to triple quadrupole mass spectrometry to investigate nitrogen heterocyclic compounds in a variety of carbonaceous chondrites (Callahan et al., 2011). Many nitrogen heterocycles are components of RNA/DNA nucleotides as well as coenzymes (cofactors), which make these compounds of significant interest for origin of life and astrobiology studies. We demonstrated that multiple reaction monitoring (MRM) mode (via triple quadrupole mass spectrometry) served as a highly sensitive means for the targeted analysis of nitrogen heterocycles. However, the low mass resolution and mass accuracy with MRM acquisitions prevented an unambiguous identification of compounds in some cases, and this led us to employ high resolution/accurate mass measurements to rectify these cases. Coupled with liquid chromatography, the high mass accuracy and high mass resolution of an Orbitrap mass spectrometer eliminates most, if not all, of the matrix interferences in the extracted ion chromatograms, which allows for the unambiguous identification and quantitation of targeted compounds. Thus, we have expanded our investigation of meteoritic organic compounds by applying these state-of-the-art techniques to target additional nitrogen heterocycles such as nicotinamide, nicotinic acid, and other pyridine carboxylic acids. The delivery of these classes of compounds to the early Earth via meteorites may have been significant for the synthesis of more complex coenzymes (such as nicotinamide adenine dinucleotide, NAD) that are used throughout modern metabolism.

Fig. 1 shows nicotinic acid (3-pyridinecarboxylic acid) and its structural isomers, picolinic acid (2-pyridinecarboxylic acid) and isonicotinic acid (4-pyridinecarboxylic acid), which have been identified in only a few carbonaceous chondrites to date, such as Murchison, a CM2 chondrite, and Tagish Lake, a C2 ungrouped chondrite (Pizzarello et al., 2001, 2004; Pizzarello and Huang, 2005). The compound-specific isotope ratio values for nicotinic acid were $\delta D = 129\text{‰}$ and $\delta^{13}C = 20\text{‰}$ in the Murchison meteorite, which strongly suggests that these compounds are extraterrestrial in origin because these values are well outside of terrestrial ranges (Pizzarello et al., 2004; Pizzarello and Huang, 2005). In addition, the presence of nicotinic acid, its two structural isomers, as well

as several other methyl and dimethyl homologs of pyridine carboxylic acids, also points to an abiotic and extraterrestrial origin for these molecules because the observation of extensive structural diversity of organic compounds in meteorites is interpreted as indicative of an extraterrestrial origin (Sephton, 2002). The mechanism of synthesis of these pyridine carboxylic acids has yet to be determined because the Murchison and Tagish Lake meteorites are carbonaceous chondrites with dissimilar organic content, yet they contain approximately the same abundances of pyridine monocarboxylic acids (Pizzarello et al., 2006). Furthermore, the prevalence of nicotinic acid and its isomers in carbonaceous chondrites is unknown; therefore, we devised a method to conduct a systematic study of these compounds in several meteorites of one class (*i.e.*, a systematic study of several CM2 chondrites rather than several ungrouped carbonaceous chondrites).

Here we report the detection and quantitation of meteoritic nicotinic acid and its structural isomers, picolinic acid and isonicotinic acid. We also report the first detection of pyridine dicarboxylic acids in meteorites. We analyzed extracts from the following eight meteorites for pyridine carboxylic acids by liquid chromatography coupled to UV detection and high resolution Orbitrap mass spectrometry (LC-UV/MS): Allan Hills (ALH) 85013, Dominion Range (DOM) 03183, Dominion Range (DOM) 08003, Elephant Moraine (EET) 96016, LaPaz Ice Field (LAP) 02333, LaPaz Ice Field (LAP) 02336, Lewis Cliff (LEW) 85311, and Wisconsin Range (WIS) 91600. All of these meteorites are CM2 type carbonaceous chondrites, which typically contain the most diverse organic compounds (Schmitt-Kopplin et al., 2010) including nitrogen heterocycles (Stoks and Schwartz, 1982; Callahan et al., 2011). To our knowledge, these meteorites have never before been investigated for pyridine carboxylic acids. In addition, we carried out experiments simulating cosmic ray processing of mixed-molecular ices, which may take place in dense interstellar clouds. From these results, we discuss the potential relationship between interstellar ice chemistry and meteoritic pyridine carboxylic acids.

2. EXPERIMENTAL

2.1. Chemicals and reagents

All glassware and ceramics were rinsed with ultrapure water (18.2 M Ω cm, <5 parts-per-billion total organic carbon from a Millipore Milli-Q Integral 10 system), wrapped

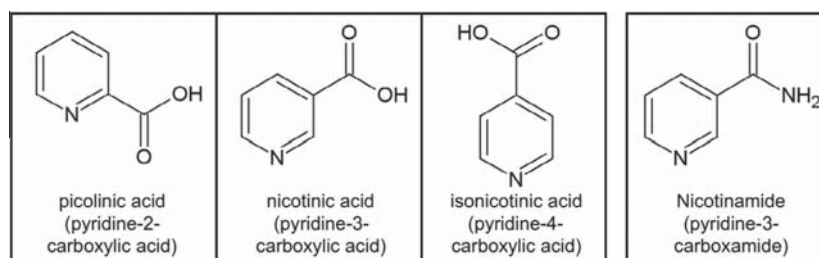


Fig. 1. Structures of the three pyridine monocarboxylic acid isomers and nicotinamide.

in aluminum foil, and heated to 500 °C overnight. Ultra-pure water was used exclusively for this study. Pyridine mono- and dicarboxylic acid standards (minimum 97% purity) were purchased from Sigma–Aldrich and nicotinamide was purchased from ICN Biomedicals, Inc. Acetonitrile (99.5+%) and sulfuric acid (95–98% purity) were purchased from Sigma Aldrich, and methanol (Optima® grade) was purchased from Fisher Scientific. A standard solution of mono- and dicarboxylic acids and nicotinamide was prepared by first making individual standards in water, then mixing those standards into one solution ranging from 1–100 µM. For liquid chromatographic separation, a 0.05% by volume sulfuric acid solution was prepared. A solution of 6 M hydrochloric acid (HCl) for the acid hydrolysis extraction was double vacuum distilled.

2.2. Meteorites

The following Antarctic CM2 carbonaceous chondrites analyzed in this study were interior fragments selected by the meteorite sample curator at the NASA Johnson Space Center: ALH 85013 (parent 23, specific 65, mass 1.134 g), DOM 03183 (parent 15, specific 25, mass 1.196 g), DOM 08003 (parent 9, specific 14, mass 1.126 g), EET 96016 (parent 0, specific 16, mass 1.116 g), LAP 02333 (parent 16, specific 24, mass 1.061 g), LAP 02336 (parent 3, specific 11, mass 1.078 g), LEW 85311 (parent 24, specific 74, mass 1.138 g), and WIS 91600 (parent 59, specific 61, mass 1.069 g). Individual meteorite chips, free of fusion crust, were pulverized into a fine powder using a ceramic mortar and pestle under a positive pressure High-Efficiency Particulate Air (HEPA) filtered Class 100 laminar flow hood (Labconco). The control blank for this study was crushed serpentine (a hydrated magnesium silicate mineral) heated to 500 °C for 3 h, which was processed using identical protocols.

2.3. Extraction and sample work-up

2.3.1. Hot water and acid-hydrolyzed hot water extracts

For the extraction of pyridine carboxylic acids, samples of ALH 85013 (105.9 mg), DOM 03183 (108.7 mg), DOM 08003 (98.1 mg), EET 96016 (110.0 mg), LAP 02333 (96.8 mg), LAP 02336 (99.3 mg), LEW 85311 (100.2 mg), and WIS 91600 (100.0 mg) were transferred to individual glass ampoules and flame-sealed with 1 mL water each and heated to 100 °C for 24 h. The hot water extracts were then centrifuged and the supernatant was split into two 500 µL portions. One 500 µL portion of the supernatant was transferred to a 10 mm glass test tube, dried under vacuum and placed into a larger 20 mm test tube. The test tube was flame-sealed and the hot water extracted dried residue was acid-hydrolyzed using 6 M HCl vapor at 150 °C for 3 h in order to liberate any pyridine carboxylic acids that might have been in an acid-labile “bound” form, which is typical for some meteoritic organic compounds (Cronin and Moore, 1971). The acid-hydrolyzed hot water extracts were dried under vacuum then re-dissolved in 1 mL of water. The hot water and acid-hydrolyzed hot water meteorite extracts (unknown pH, but the latter was likely acidic) were desalted

using conditioned cation exchange columns (Biorad Poly-Prep® AG® 50 W-X8 resin, 100–200 mesh, hydrogen form). Meteorite extracts were loaded onto the columns, rinsed with water, and the pyridine carboxylic acids were eluted with 2 M NH₄OH. Only the (basic) elute fraction was kept and analyzed. The desalted extracts were then dried down under vacuum and re-dissolved with 100 µL water. All meteorite extracts were stored in a –86 °C freezer until analysis.

2.3.2. Formic acid extracts

Samples of ALH85013 (206.9 mg), DOM03183 (204.8 mg), DOM08003 (204.6 mg), EET96016 (214.5 mg), LAP02333 (215.7 mg), LAP02336 (211.1 mg), LEW85311 (206.6 mg), and WIS91600 (211.9 mg) were transferred to individual glass ampoules and flame-sealed with 2 mL formic acid and heated to 100 °C for 24 h. The ampoules were frozen in liquid nitrogen before opening (to minimize the risk of explosion), centrifuged, and the supernatant transferred to a test tube. The meteorite powder was rinsed with 1 mL formic acid; the supernatants were combined and then dried under vacuum. After the residue was dry, it was dissolved in 2 mL 0.1 M ammonium hydroxide. Meteorite extracts were loaded onto a conditioned Waters solid phase extraction (SPE) cartridge (Oasis Max 6 cc, 150 mg sorbent) and rinsed with 6 mL 5% ammonia in water followed by 6 mL methanol. Pyridine monocarboxylic acids were then eluted using 6 mL 5% formic acid in methanol. The purified extracts were dried under vacuum and dissolved in 400 µL 0.1 M ammonium hydroxide. All meteorite extracts were stored in a –86 °C freezer until analysis.

2.4. Irradiated pyridine + CO₂ ice experiments

Proton irradiation experiments were performed in the Cosmic Ice Laboratory at the NASA Goddard Space Flight Center. The system consisted of a stainless steel high vacuum chamber ($P \sim 10^{-7}$ torr) containing a polished aluminum substrate attached to the cold finger of a closed-cycle helium cryostat (ARS model DE-204). This rotatable substrate can face a deposition tube, a beam of 0.8-MeV protons from a Van de Graaff accelerator, or an FTIR spectrometer (Hudson and Moore, 2003, 2004). Gases (CO₂ and pyridine vapor) were mixed in a separate gas manifold, and ice films were produced by leaking them into the vacuum chamber in front of the cold substrate over the course of ~15 min. Final sample thicknesses were ~1 µm, as measured by laser interferometry. This thickness is well below the stopping range for 0.8-MeV protons and ensures that the entire ice sample is processed. Contaminants (mainly H₂O) made up no more than 1% of the final ice, based on our estimates of the background gases present and the rate at which the sample was grown. After deposition, the pyridine + CO₂ (1:1) ice was exposed to a 0.8-MeV proton beam with a current of 150 nA until a fluence of 1.2×10^{15} protons cm⁻² was achieved. The average energy dose (energy absorbed) was 36 eV per initial molecule deposited (plausible for dense interstellar clouds), which was determined using a proton stopping power for the

pyridine + CO₂ mixture of 2.73×10^8 eV cm² g⁻¹ proton⁻¹. This value was calculated using the SRIM software package (Ziegler et al., 2010), assuming a density for the pyridine + CO₂ mixture of 1 g cm⁻³.

To aid in the interpretation of the IR spectra of the irradiated ice, we also measured the IR spectra of the possible irradiation products nicotinic acid, isonicotinic acid, and picolinic acid at ~20 K. These reference spectra may also be useful for interpretation of observational data. Since these three substances are supplied as powders, a sublimation oven inside the vacuum chamber (described by Gerakines et al., 2012) was used in each case to vaporize the chosen compound and produce an ~1 μm thick film on the cold substrate whose IR spectrum could then be measured.

After irradiation, the ice was allowed to warm up slowly to room temperature overnight, allowing volatile products to be pumped away. The remaining non-volatile (refractory) material was removed by repeatedly pipeting 250 μL water on the aluminum substrate until the yellow-colored residue was observed to be completely removed. The refractory solution was analyzed immediately by LC-UV/MS.

2.5. Sample Analysis by LC-UV/MS

All samples and controls were analyzed using a Thermo Scientific Accela high performance liquid chromatograph coupled to a Thermo Scientific Accela photodiode array detector (PDA) and a Thermo Scientific LTQ Orbitrap XL hybrid mass spectrometer. Separation of pyridine carboxylic acids was accomplished by injecting 5 μL sample solution onto an SIELC Primesep 100, 150 × 2.1 mm column (5 μm particle size) with a Primesep 100, 10 × 2.1 mm guard column (5 μm particle size). Mobile phase (A) consisted of water with 0.05% sulfuric acid and mobile phase (B) was 100% acetonitrile. Samples were eluted at 200 μL/min using the following gradient: 0–3 min. 100% A, 3–10 min. 100–95% A, 10–20 min. 95% A, and 20–30 min. 100% A. The UV spectrum (200–400 nm) was collected using the Accela PDA. UV ($\lambda = 260$ nm) retention time was used as additional confirmation for identification and not for quantitation due to high UV-absorbing background and complexity.

The Thermo Scientific LTQ Orbitrap XL hybrid mass spectrometer was equipped with an electrospray ionization (ESI) source and operated in positive ion mode. Parameters for ESI were as follows: the nitrogen gas for desolvation of the electrospray was set to 35 for the sheath gas, 15 for the auxiliary gas, and 1 for the sweep gas, all in arbitrary units. The ion transfer capillary voltage and temperature were 21 V and 275 °C, respectively. The tube lens was set to 55 V. Full scan mass spectra were taken over a range of m/z 50 to 500. The mass resolution was set to 30,000 (at full-width-half-maximum for m/z 400) in order to maintain an appropriate number of data points across chromatographic peaks. MS/MS data was collected in the Orbitrap mass analyzer (HCD energy 60% and 100%, isolation width 1 Da, and resolution 7500). External calibration was performed using a mixture of caffeine, MRFA (L-methionyl-arginyl-phenylalanyl-alanine acetate hydrate)

peptide, and Ultramark 1621 (a mixture of fluorinated phosphazines) in an acetonitrile–methanol–water solution containing 1% acetic acid, which resulted in a typical mass accuracy of <2 parts-per-million (ppm).

Abundances were calculated only for pyridine monocarboxylic acids. The error for these measurements was estimated to be <10%, which was calculated as the relative standard deviation from 21 measurements of each pyridine monocarboxylic acid standard (63 measurements in total) and verified by three measurements of each pyridine monocarboxylic acid (9 measurements in total) in the meteorite LAP 02333. Very low (or zero) recoveries of pyridine dicarboxylic acids (due to the desalting and SPE procedures employed here) prevented accurate measurements of abundances and were not reported here. In addition, 2,6-pyridinedicarboxylic acid exhibited poor ESI efficiency, which resulted in poor sensitivity for this compound.

3. RESULTS AND DISCUSSION

3.1. Measurements of pyridine carboxylic acids in standard solutions and meteorite extracts

We performed a seven-point linearity study using standard solutions of the three pyridine monocarboxylic acid isomers using a concentration range of 1–100 μM (or 5 pmol to 500 pmol on column). The calibration curves were highly linear ($R^2 > 0.99$) for nicotinic acid, isonicotinic acid, and picolinic acid using the integrated peak area of the extracted ion chromatogram at the theoretical protonated mass of 124.0393 ± 0.0006 Da (5 ppm mass window), and enabled accurate quantitation of these compounds in a sample. Our estimated limit of detection for each pyridine carboxylic acid isomer is ~1 part-per-billion (ppb or ng isomer/g meteorite).

Fig. 2 shows typical extracted ion chromatograms of the serpentine procedural blank (bottom trace), the standard mix of all three pyridine monocarboxylic acid isomers (middle trace), and the LAP 02336 meteorite (top trace). These data are representative of our results from the other CM2 carbonaceous chondrites. Nicotinic acid, isonicotinic acid, and picolinic acid in the meteorite were unambiguously identified based on chromatographic retention time, accurate mass measurements, and product ion spectra. We did not detect nicotinic acid, isonicotinic acid, or picolinic acid in our procedure blank (above our detection limits), which suggests that our laboratory analytical protocols did not introduce additional pyridine carboxylic acids. The abundances of nicotinic acid and its isomers were adjusted based on recoveries of standards processed using our desalting or SPE procedure (see Supporting Information for table).

Fig. 3 shows typical extracted ion chromatograms of the serpentine procedural blank (bottom trace), the standard mix of pyridine dicarboxylic acid isomers (middle trace), and the LAP 02333 meteorite (top trace). Additionally, product ion spectra for these compounds are shown in Fig. 4. We unambiguously identified 3,4-pyridinedicarboxylic acid, 2,5-pyridinedicarboxylic acid, and 3,5-pyridinedicarboxylic acid in multiple meteorite extracts. To our

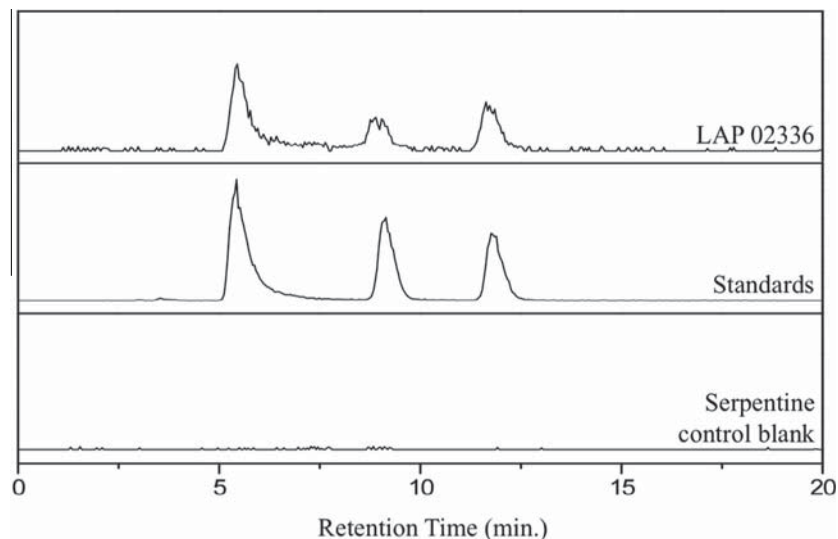


Fig. 2. Extracted ion chromatograms (m/z 124.0393 with a 5 ppm window corresponding to the protonated molecular ion) of picolinic acid (5.4 min), isonicotinic acid (9.0 min), and nicotinic acid (11.6 min) of the LAP 02336 carbonaceous chondrite formic acid extract (top trace) and reference standards (middle trace). Pyridine monocarboxylic acids were not detected in the serpentine control blank (bottom trace).

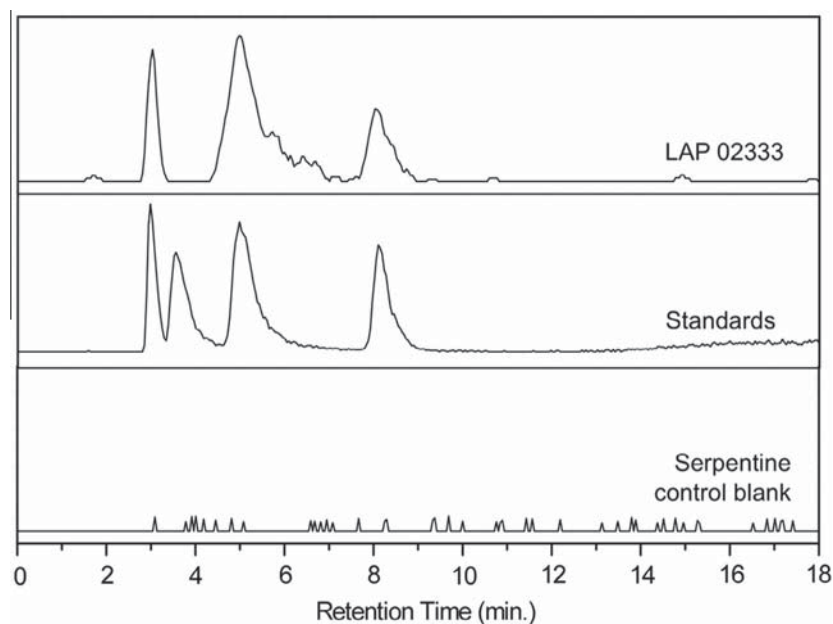


Fig. 3. Extracted ion chromatograms (m/z 168.0291 with a 5 ppm window corresponding to the protonated molecular ion) of 3,4-pyridinedicarboxylic acid (3.0 min), 2,5-pyridinedicarboxylic acid (5.0 min), and 3,5-pyridinedicarboxylic acid (8.1 min) of the LAP 02333 carbonaceous chondrite acid-hydrolyzed hot water extract (top trace) and reference standards (middle trace). Note that 2,3-pyridinedicarboxylic acid (3.6 min) was not detected in LAP 02333 and other meteorites. Pyridine dicarboxylic acids were not detected in the serpentine control blank (bottom trace).

knowledge, this is the first report of pyridine dicarboxylic acids in meteorites, and these organic compounds appear to be common in CM2 chondrites as well. However, we were unable to detect 2,3-pyridinedicarboxylic acid (quinolinic acid) in our meteorite extracts. The lack of detection for quinolinic acid may have been attributed to very poor recoveries during the desalting procedure (~7%). On the

other hand, other pyridine dicarboxylic acids were detected despite similar low recoveries.

One interesting observation is that we did not detect nicotinamide in any of the meteorite extracts, which suggests that CM2 carbonaceous chondrites might not have been a significant source of this compound for early Earth (see [Supporting Information](#) for more details).

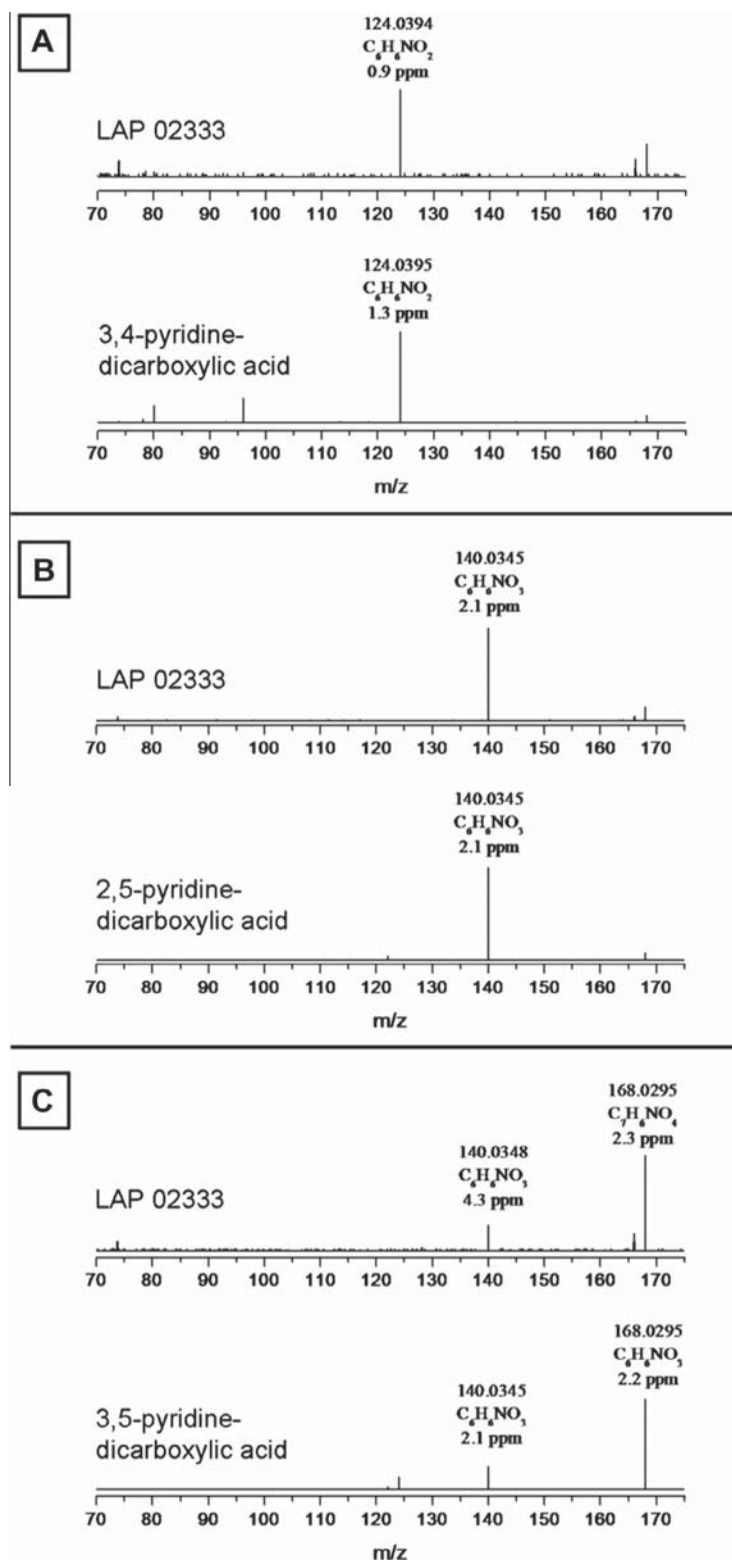


Fig. 4. Product ion spectra (HCD 60%, resolution 7,500) of reference standards and compounds found in LAP 02333. Three compounds were identified: 3,4-pyridinedicarboxylic acid (A), 2,5-pyridinedicarboxylic acid (B), and 3,5-pyridinedicarboxylic acid (C).

3.2. Abundances of pyridine carboxylic acids in meteorite extracts

We analyzed two different hot water extracts, non acid-hydrolyzed and acid-hydrolyzed, of eight CM2 carbonaceous chondrites in order to determine the abundances of nicotinic acid and its two isomers, picolinic acid and isonicotinic acid. Seven of the eight CM2 chondrites in this study, with the exception of WIS 91600, contained all three pyridine monocarboxylic acid isomers in both extracts. The abundances of pyridine monocarboxylic acid isomers in the hot water extract were approximately equivalent. This result is similar to what was observed in earlier studies of hot water extracts of two carbonaceous chondrites (a CM2 chondrite and a C2 ungrouped chondrite) (Pizzarello et al., 2006). WIS 91600 was the only meteorite that did not contain any pyridine monocarboxylic acids above our detection limits (<1 ppb), which was likely due to thermal alteration on the parent body (Choe et al., 2010) that led to the decomposition of organic compounds. Of the meteorites that contained pyridine monocarboxylic acids in both extracts, DOM 03183 contained the least amount of total pyridine monocarboxylic acids (61 ppb), also likely due to thermal alteration of the meteorite parent body (Alexander et al., 2012). Fig. 5a shows the abundances of pyridine monocarboxylic acids in the hot water extracts, which range from approximately 61–253 ppb total pyridine monocarboxylic acids (excluding WIS 91600). Fig. 5b shows the abundances of pyridine monocarboxylic acids in the acid-hydrolyzed hot water extracts, which are noticeably higher than the values for the hot water extracts ranging from 128 ppb to 497 ppb total pyridine monocarboxylic acids (excluding WIS 91600). The difference in the hot water vs. the acid-hydrolyzed hot water extracts is the release of approximately 23–166% more pyridine monocarboxylic acids likely from an acid-labile bound form (e.g., precursor molecules, complex bonded species). However, another possibility for the lower abundances of pyridine monocarboxylic acids in the hot water extracts compared to the hot water acid-hydrolyzed extracts might be due to the desalting step. Hot water meteorite extracts were (likely) neutral to basic pH, which might have resulted in some loss of pyridine monocarboxylic acids during the water rinse rather than the elution step. We investigated both 3-cyanopyridine and nicotinamide, which can be hydrolyzed to nicotinic acid, as a potential precursor molecule (see Supporting Information).

We analyzed formic acid extracts of eight CM2 carbonaceous chondrites in order to obtain the abundances of nicotinic acid, isonicotinic acid, and picolinic acid. All of the eight CM2 chondrites contained all three structural isomers of pyridine carboxylic acids in the formic acid extract. Fig. 5c shows the abundances of pyridine monocarboxylic acids, which are significantly more abundant in the formic acid extract (ranging from 163 ppb to 1377 ppb total pyridine monocarboxylic acids) compared to both of the hot water extracts (non acid-hydrolyzed and acid-hydrolyzed). The elevated abundances may be due to higher extraction

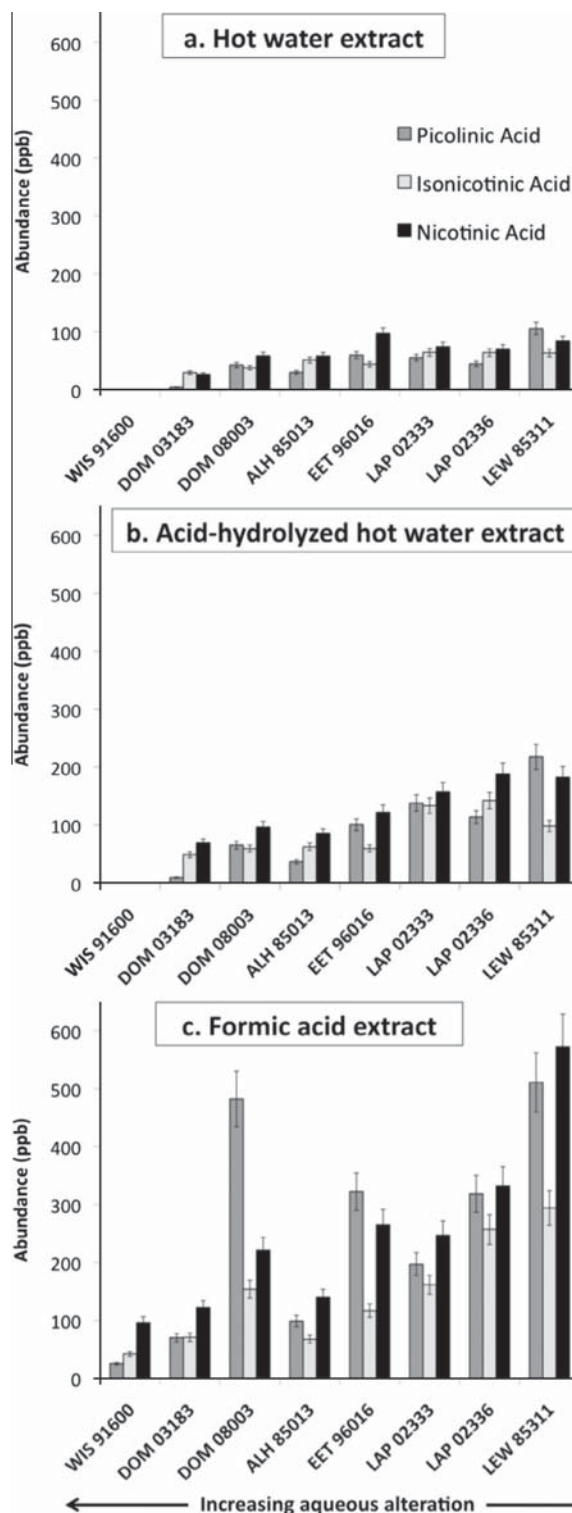


Fig. 5. The abundances and distribution of pyridine monocarboxylic acids in the (a) hot water, (b) acid-hydrolyzed hot water, and (c) formic acid extracts determined by mass detection. Carbonaceous chondrites are ordered from right to left in order of increasing aqueous alteration based on the method by Alexander et al. (2012).

efficiency with formic acid, which has been known to be effective for liberating nitrogen heterocycles from meteorites (van der Velden and Schwartz, 1977; Stoks and Schwartz, 1981; Callahan et al., 2011). In addition, picolinic acid abundance seems to increase significantly, especially in DOM 08003, although the exact reason for this is unknown. A summary of abundances (in numerical form) for pyridine monocarboxylic acids in hot water, hot water acid-hydrolyzed, and formic acid extracts can be found in the [Supporting Information](#).

All CM2 carbonaceous chondrites have experienced some amount of preterrestrial aqueous alteration. Aqueous alteration is a secondary process that occurs for a finite period of time on the meteorite parent body in which ice in the asteroid core melts via heat produced through decay of various radionuclides, such as ^{26}Al (Grimm and McSween, 1989). This period of liquid water on the asteroid alters the chemistry of the mineral matrix and may affect the synthesis or destruction of organic compounds. In Fig. 5a–c, for all extracts, the meteorites are arranged from right to left in order of increasing aqueous alteration based on the method of Alexander et al. (2012, 2013) using previously reported bulk hydrogen abundance, isotopic composition, and C/H ratio information (which also correlates with petrologic indicators for the degree of aqueous alteration) (see [Supporting Information](#) for additional details). In the acid-hydrolyzed hot water and formic acid extracts, there is a noticeable decrease in abundance of pyridine monocarboxylic acids with increasing aqueous alteration. This trend suggests that aqueous alteration may have had an overall destructive effect on these compounds, similar to previous studies involving amino acids (e.g., Glavin et al., 2010) and nucleobases (Callahan et al., 2011). LEW 85311, the least aqueously altered (most primitive) meteorite of this study, contains the highest abundance of total pyridine monocarboxylic acids (>1.3 ppm).

We note that some caution should be used when interpreting organic abundances with the meteorites' inferred degree of aqueous alteration because it is well known that organic abundances can vary considerably across small spatial distances in meteorite stones (Pizzarello et al., 2003; Herd et al., 2011). Consequently, analyses of additional fragments of the same meteorite could lead to much different abundances than those given in our study (since we analyzed only one small fragment for each meteorite) and potentially alter any observed correlations. Nevertheless, intra-meteorite variation in the organic abundances does not change the primary observation of this investigation, which is nicotinic acid and other pyridine carboxylic acids appear to be fairly common, and sometimes in relatively high concentrations, in an inter-meteorite comparison using eight different meteorites.

3.3. Irradiation experiments with pyridine–CO₂ ices: connection with meteoritic organics?

The interstellar-parent body hypothesis holds that organic compounds in meteorites may have been produced via radiation- and photochemistry that took place on the icy organic mantles of interstellar grains or via aqueous

phase chemistry in the meteorite parent bodies (Cronin and Chang, 1993; Cronin et al., 1993). For the former scenario, atoms and molecules condense on dust grains in dense interstellar clouds ($T < 30$ K). Energetic processing of icy grains by cosmic rays and/or photons can lead to more complex molecules, as demonstrated by numerous laboratory studies (Bernstein et al., 1999, 2001; Gerakines et al., 2004; Elsila et al., 2007; Hudson et al., 2008; Nuevo et al., 2009, 2010, 2012). Furthermore, theoretical modeling of the dynamical evolution of ice grains in the solar nebula has shown that warming would also occur, which would further enable the production of complex organics (Ciesla and Sandford, 2012). A significant portion of meteoritic organics (e.g., aromatics, carboxylic acids, amino acids) may be relics of interstellar grain processes because they are enriched in deuterium and exhibit a high degree of branching and structural diversity (indicative of reactions involving radicals and ions) (Sephton and Gilmour, 2000; Sandford et al., 2001; Pizzarello and Huang, 2005).

From our investigation and previous studies (Stoks and Schwartz, 1982; Pizzarello et al., 2001), substituted pyridines are structurally diverse in meteorites (with methyl, dimethyl, monocarboxylic acid, and dicarboxylic acid substitutions observed), which suggest that this compound class might be the product of interstellar grain processes. In order to test this hypothesis (which also relates to the interstellar-parent body hypothesis), we proton-irradiated a 1:1 mixture of pyridine and CO₂ held at a very low temperature. This experiment is only a first approximation for the formation of interstellar pyridine carboxylic acids because pyridine has not yet been identified in interstellar ices (though the presence of pyridine in interstellar ice might still be possible). Fig. 6 (top three traces) shows the IR spectra of the deposited sample recorded before and after proton irradiation at ~20 K and the irradiated sample

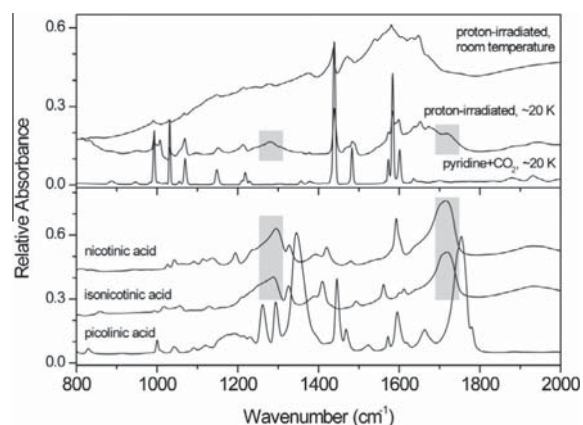


Fig. 6. *In situ* IR spectra of the deposited pyridine + CO₂ sample recorded before and after proton irradiation at ~20 K and the irradiated sample after warm-up to room temperature (top traces). *In situ* IR spectra of nicotinic acid, isonicotinic acid, and picolinic acid deposited (in separate experiments) at ~20 K for reference to the irradiated sample (bottom traces). Common IR bands between the proton-irradiated sample spectra and the nicotinic acid and isonicotinic acid spectra are highlighted in gray.

after warm-up to room temperature. In the non-irradiated pyridine and CO₂ ice sample, the most intense, sharp peaks in the 800–2000 cm⁻¹ range can all be assigned to pyridine (the majority being wagging and bending modes). Fig. 6 (bottom three traces) also shows the IR spectra of nicotinic acid, isonicotinic acid, and picolinic acid (deposited in separate experiments) at ~20 K recorded for reference to the irradiated sample. There are many new IR bands as a result of irradiation, which indicate new products formed. For the irradiated sample at ~20 K, we assign the broad IR bands centered around 1290 cm⁻¹ and 1720 cm⁻¹ to characteristic bands of nicotinic acid and isonicotinic acid, which may have formed *in situ* during the low temperature irradiation of the pyridine–CO₂ ice. These bands correspond to the in-plane deformation of C–H and the carbonyl stretch of nicotinic acid (Kumar and Yadav, 2011) and isonicotinic acid. There do not appear to be any common IR bands between the picolinic acid IR spectrum and the irradiated pyridine–CO₂ ice spectrum at ~20 K. Band broadening in the IR spectrum may be due to increased intermolecular interactions, which supports the notion that pyridine carboxylic acids were synthesized upon irradiation (because there would be strong hydrogen bonding interaction between carboxylic acid groups). After warm-up to room temperature, the IR spectrum becomes very broad and difficult to interpret with respect to the pyridine carboxylic acid isomer reference spectra.

We analyzed the refractory residue of the proton-irradiated pyridine–CO₂ ice by our LC-UV/MS method. A variety of pyridine monocarboxylic acids, pyridine dicarboxylic acids, and hydroxypyridines were identified, the latter may have formed from residual water in the irradiation setup. We find that the distribution of the three pyridine carboxylic acid isomers identified in the refractory residue is similar to the distribution of isomers in the least altered (most primitive) meteorite, LEW 85311 (the abundance of picolinic acid > nicotinic acid > isonicotinic acid). More aqueously altered meteorites generally have a different distribution of pyridine monocarboxylic acids compared to those measured in the irradiated ice residue. We also identified four pyridine dicarboxylic acids (3,4-, 2,3-, 2,5-, 3,5-pyridinedicarboxylic acids) in the irradiated pyridine–CO₂ ice, three of which (3,4-, 2,5-, 3,5-pyridinedicarboxylic acids) we also found in the majority of the CM2 carbonaceous chondrites in this study.

The similar distribution of pyridine carboxylic acid isomers in irradiated pyridine–CO₂ ice and the most primitive meteorite coupled with the extended structural diversity of dicarboxylic acids in both samples is suggestive of radical chemistry and a possible interstellar origin for these molecules. However, previous studies have determined that nicotinic acid in the Murchison meteorite had a $\delta D = +129\%$ and $\delta^{13}C = +20\%$ (Pizzarello et al., 2004; Pizzarello and Huang, 2005), which clearly suggested an extraterrestrial origin but the magnitude of deuterium enrichment did not approach values of interstellar molecules. However, this δD value may be a minimum value because the original H or D on the carboxylic acid group of nicotinic acid would have been removed very quickly after placing the meteoritic pyridine carboxylic acid compounds in water (for

extraction purposes). Additionally, it is unknown whether significant H/D exchange would occur for the four aromatic H or D during aqueous extraction and work-up. Other synthetic routes may have been possible. Fischer–Tropsch type reactions have been previously proposed for the synthesis of alkyl pyridines from aldehydes and ammonia (Stoks and Schwartz, 1982), and similar reactions could be feasible for pyridine carboxylic acids.

Some open questions include: (1) do irradiation experiments with more realistic ice compositions (*e.g.*, starting from simpler precursors and the addition of H₂O) still lead to the production of nicotinic acid (and other pyridine carboxylic acids) or will compounds such as hydroxypyridines dominate instead, and (2) what are the compound-specific isotope ratios of pyridine carboxylic acids in other CM2 carbonaceous chondrites (in particular LEW 85311, which experienced a low degree of aqueous alteration yet contained the highest abundances of pyridine carboxylic acids)? We will address these questions in future investigations.

3.4. Implications for prebiotic chemistry on early Earth

Nicotinamide adenine dinucleotide may be one of the most ancient molecules in modern cells and was likely present very early in the evolution of life (Raffaelli, 2011). There are two ways in which modern cells can synthesize NAD: the *de novo* pathway or the Preiss–Handler salvage pathway (Preiss and Handler, 1957a,b,c, 1958a,b). Both pathways involve formation of a nicotinic acid mononucleotide (NaMN) intermediate, which gets enzymatically converted to NAD; however, only the salvage pathway uses existing nicotinic acid as a substrate. The first organisms on early Earth are widely thought to have been anaerobic, so it is possible that the first pathway to NAD was either an anaerobic *de novo* pathway or a salvage pathway in which an abiotic synthesis of nicotinic acid would be required.

Several laboratory studies have investigated the endogenous formation of pyridine carboxylic acids under plausibly prebiotic early Earth conditions. For example, Friedmann et al. (1971) demonstrated that the pyridine ring could be synthesized in the form of nicotinonitrile (3-cyanopyridine) by sending an electrical discharge through a mixture of ethylene and ammonia. Nicotinonitrile is an important molecule because it can be converted to nicotinamide (Fig. 1), the redox active moiety in NAD, and nicotinic acid by hydrolysis of the cyano group. In addition, Cleaves and Miller (2001) demonstrated a possible nonenzymatic early Earth synthesis of nicotinic acid and its metabolic precursor, quinolinic acid (2,3-pyridinedicarboxylic acid), by reacting dihydroxyacetone phosphate with aspartic acid.

CM2-type carbonaceous chondrites may have been an important exogenous source for organic compounds on the early Earth. The measurement of nicotinic acid in many different CM2 carbonaceous chondrites suggests that this compound (and more generally speaking, this class of compounds) was common in these types of meteorites. Nicotinic acid and other pyridine carboxylic acids are readily soluble in water, which suggests that these compounds could be easily removed from the meteorite and possibly participate in chemical reactions on early Earth. It is

interesting to point out that nicotinic acid and adenine, both of which are molecular precursors to NAD, have been measured in meteorites. However, adenine was reported in very low ppb abundances in meteorites (Callahan et al., 2011), which makes it difficult to envision how useful concentrations built up on early Earth without complementary endogenous synthesis or the use of alternative molecules.

Finally, the synthesis of NAD or its intermediates, such as nicotinic acid β -riboside, may be challenging under prebiotic conditions. For example, the synthesis of nicotinic acid β -riboside is difficult in the laboratory, and it is usually produced using multiple synthetic organic steps (without relevant, plausibly prebiotic conditions) (Franchetti et al., 2004). Also, NAD-mediated reactions in living organisms require the β -configuration, and a stereoselective synthesis presents additional difficulties. Nevertheless, alternative routes to synthesize NAD may be feasible. For example, nucleotides have been successfully synthesized using multi-component synergetic reactions, which bypasses trying to couple ribose to a nitrogen heterocycle in the sequential fashion traditionally employed (Powner et al., 2009). A similar scenario may be applicable to the synthesis of NAD, although it may not involve pyridine carboxylic acid.

4. CONCLUSIONS

1. Liquid chromatography coupled to Orbitrap mass spectrometry permitted the unambiguous identification of pyridine carboxylic acids in meteorites based on chromatographic retention time and accurate mass measurements. The linear response over a wide concentration range, along with high recoveries from both desalting and solid phase extraction protocols, enabled the quantitation of pyridine monocarboxylic acids in meteorites. Low recoveries of pyridine dicarboxylic acids inhibited accurate quantitation and revised purification techniques will be needed for these molecules in future studies; however, to our knowledge, this is the first report of pyridine dicarboxylic acids in carbonaceous meteorites.
2. Pyridine carboxylic acids were identified in all eight of the CM2-type carbonaceous chondrites (formic acid extract). The highest abundance of pyridine monocarboxylic acids was found in formic acid extract of LEW 85311, which is the most primitive (least aqueously altered) meteorite in this study.
3. Pyridine monocarboxylic acids negatively correlate with the degree of aqueous alteration of CM2-type meteorite parent bodies (acid-hydrolyzed hot water extract and formic acid extract). There is a decrease in abundance of pyridine carboxylic acids as aqueous alteration of the meteorite parent body increases, which suggests that aqueous phase reactions in the meteorite parent body may have destroyed some of these compounds.
4. The abundance of pyridine monocarboxylic acids significantly increased in the acid-hydrolyzed hot water and formic acid extracts (compared to the hot water extract). These observations suggest that some of the pyridine monocarboxylic acids existed in an acid-labile bound form.
5. The full suite of pyridine monocarboxylic acids and a variety of pyridine dicarboxylic acids were identified in the non-volatile residue of proton-irradiated pyridine + CO₂ ice. A similar suite of pyridine mono- and dicarboxylic acids was measured in CM2 carbonaceous chondrites (only 2,3-pyridinedicarboxylic acid was absent among the targeted compounds) and suggests a connection between interstellar chemistry and the pyridine carboxylic acids observed in meteorites. However, more realistic interstellar ice compositions (e.g., the inclusion of H₂O and simpler organic precursors) are needed in future studies.
6. Nicotinamide was not identified in any of the 24 different meteorite extracts we analyzed. One possible explanation for this might be that the nicotinamide (if it existed on the meteorite parent body) was hydrolyzed to form nicotinic acid during the period of aqueous alteration on the meteorite parent body.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.gca.2014.04.001>.

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