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Identify Low Mass Volatile Organic Compounds from Cometary Ice Analogs using Gas Chromatography coupled to an Orbitrap mass spectrometer associated to Electron and Chemical Ionizations

Thomas Javelle¹, Michel Righezza¹ and Grégoire Danger^{1,2,3,*}

¹ Aix-Marseille Université, Laboratoire de Physique des Interactions Ioniques et Moléculaires, UMR 7345, CNRS, Marseille, France

² Aix Marseille Université, CNRS, CNES, LAM, Marseille, France

³ Institut Universitaire de France (IUF)

ABSTRACT: Analysis of organic matter extracted from meteorites showed that solar system objects present an important molecular diversity. To improve our understanding of such organic matter, new analytical technologies must be developed. The present study displays the first experiments using a GC-FT-Orbitrap-MS to decipher the molecular diversity observed in experiments simulating the evolution of cometary ices. The proposed analytical strategy focuses on the analysis of 110 volatile organic compounds (VOC) with mainly 1 to 6 carbon atoms generated in such cometary ice analogs. Electron ionization (EI) and chemical ionization (CI) modes with methane (CH₄) or ammonia (NH₃) were optimized and compared. Those developments maximized the intensity of molecular, protonated or deprotonated ions and improved high-resolution molecular formula unambiguous identification: EI mode is too energetic to provides there detection, while it is not the case in CI mode. Particularly, NH₃ as a reagent gas improves amine identification in positive mode (PCI) and esters, alcohols, carbonyls, amides, carboxylic acids and nitriles in negative mode (NCI). The combination of both EI and CI mass spectrum analysis improves molecular identification, thanks to the detection of molecular, deprotonated or protonated ion of highest intensity and fragment formula assignments. The EI and NCI NH₃ combination allows formula assignments up to 94 % of our database with limit of detection up to 7 ppm. This procedure has been validated for untargeted GC-FT-Orbitrap-MS analysis of VOC coming from the processing of cometary ice analogs.

Keywords: chemical ionization, electron ionization, FT-Orbitrap-MS, GC-MS, high resolution mass spectrometry, volatile organic compound, cometary ice analogs.

1. INTRODUCTION

Meteorites are the daughters of interplanetary bodies, comets and asteroids. Their soluble organic compounds were first analysed in 2010 by high resolution mass spectrometry (HRMS) using FT-ICR-MS technology [1]. This analysis within a 150–2,000 Da mass range showed the presence of more than 14,000 organic molecules. Further analytical developments using UPLC-Orbitrap showed that for each detected ion up to 31 different isomers can be present, which suggests the presence of hundreds of thousands of different molecules [2]. To understand the origin of this molecular diversity, laboratory experiments are developed.

In the case of the study of the cometary parent body, the chemistry that led to the organic matter can be simulated in laboratory by starting from ice analogs composed by the primitive and the most abundant compounds (H₂O, CO, CO₂,

37 CH₃OH, NH₃ and H₂S). Those cometary ice analogs are formed at low temperatures (20 K to 77 K), low pressure (10⁻⁹ to 10⁻⁸ mbar) and then irradiated (ultraviolet photons at Lyman α , ions or electrons) to simulate their processing when exposed to the surrounding stars or to the Sun irradiation. This alteration leads to the formation of new molecules mainly through the recombination of radicals.

41 To simulate a comet approaching the Sun, the processed cometary ice analogs is then warmed up. It releases many volatile organic compounds (VOC) into the gas phase and a solid organic material remains. Its HRMS analyse (m/z 50-590) revealed the presence of an important molecular diversity with around 10,000 ions with masses up to 4,000 Da [5] presenting similarities with the organic matter observed in meteorites [1,6–8].

45 The composition of the gas phase were still poorly characterized up to 2016 when VOCs was analysed using gas chromatography coupled to mass spectrometry (GC-MS). Thirty-three compounds with m/z up to 102 were identified in the gas phase after the processing and the warming of a cometary ice analog containing only methanol [10]. However, after improvements of the VOC recovery, more than 100 species were still not identified mainly due to the increase of the number of isobars with the rise of molecular masses [9–12]. In this context, the use of HRMS coupled to a gas chromatography will allow the identification of isobars and a better chromatographic reconstruction. It will improve compound identifications and provide information on the chemistry occurring in cometary ice analogs, especially when they contain other heteroatoms like nitrogen (from NH₃) or sulfur (H₂S).

53 Invented in the early 2000s [13], the FT-Orbitrap-MS was first coupled with gas chromatography (GC) in 2010 [14] and is only commercially available since 2015 [15]. Nowadays, the FT-Orbitrap-MS is the mass analyser providing the highest resolution when coupled to gas chromatography (120,000 at m/z = 200 Th). The high precision of less than 5 ppm in mass measurement leads to two major enhancements for GC-MS analysis: LOD improvement in full mode thanks to mass deconvolution [15–19], and unambiguous ion formula assignment deduced from ion detection [15–19]. This new technology was already used for pesticide, wastewater pollutants, glyceraldehyde and toxicologic analysis [15–18,20] and for developments aiming to combine mass accuracy to soft ionization to identify unknown [21].

60 In the present work, a GC-FT-Orbitrap-MS is used for the first time to analyse low mass volatile organic compounds formed during experiments simulating the evolution of cometary ices. Conditions involving electron impact ionization (EI) tested at different electron voltage and chemical ionization (CI) with a set of reagent gas are optimized based on standard mixtures. Once the optimal detection of high mass ions was found out, a strategy was developed coupling ionization modes to improve molecular identifications. Limits of detection of various chemical families were also estimated using a semi-quantitative approach. Finally, the identification strategy developed was applied to the analysis of VOC generated by the UV alteration of a cometary ice analogs, demonstrating the interest of using a GC-FT-Orbitrap-MS compared to a classical GC-MS analysis.

68 2. MATERIAL AND METHODS

69 2.1 Chemicals, database construction and LOD measurement.

70 110 chemicals were purchased from Sigma-Aldrich, Aldrich, Fluka, Fisher, Carlo Ebra, Acros and Riedel-de Haën with the purity of 80 to 99.9 % (see supplementary information TS1 for details). They were chosen according to their astrophysical interest [10,22,23] contains #C = 0 to 6, #O = 0 to 3 and #N = 0 to 1 from 12 different chemical functions (see

73 supplementary information Figure S1). The 500 mg/L standards mixtures methanol (Fisher Chemicals, 99.99 %) solutions
74 were designed to avoid co-elutions. EI identifications were confirmed with fragment comparison to NIST MAINLIB
75 database (267376 spectra). CI spectral identification was done using retention time (RT). NIST HR Databases were created
76 using Deconvolution Plugin 1.3 for TraceFinder 4.1 and NIST MS Search 2.3. Fragment formula are first attribution of
77 Thermo Scientific Xcalibur 4.1.31.9 within 5 ppm and +1 charge for EI and PCI, and 10 ppm and -1 charge for NCI. LOD
78 were calculated using dilutions of 40, 8, 4, 0.8 and 0.4 µg/L. LOD are measured on extracted (± 5 ppm) most intense peaks
79 and uncertainty are 95 % Student's t-distribution.

80 **2.2 Chemical Synthesis.**

81 Methoxy ethane was synthesized using the Williamson synthesis described by Schmidt et al. [24] using absolute ethanol
82 (Sigma-Aldrich, ≥ 99.8 %), iodomethane (Aldrich) and solid sodium (Aldrich).

83 **2.3 Experimental setup.**

84 Data were recorded using a modified GC-FT-Orbitrap-MS (Trace 1310 Gas Chromatograph with an Q-Exactive
85 Orbitrap™ MS analyser from Thermo Fisher Scientific). 1 µL is injected in a GC split/splitless (SSL) injector (250 °C) using
86 an AI 1310 sampler from Thermo Fisher Scientific. For gas injection, a modified GC SSL injector (280 °C) was used using a
87 vent-free GC/MS adapter (Frontier Laboratories LTD, 0.15 mm, c.a. 50 cm length, column ultra-ALLOY metal capillarity).
88 Then the gaseous sample was focused using a MicroJet Cryo-Trap MJT-1035E from Frontier Laboratories LTD
89 implemented on Rxi® guard column from Restek (20 cm \times 0.25 mm) at 10 cm from the head of the separative column for 45
90 s using liquid nitrogen (purchased from Linde).

91 GC-FT-Orbitrap-MS has been coupled to a vacuum chamber whose characteristics are detailed elsewhere [4]. Shortly 13.8
92 mbar of methanol gas (prepared from Fisher Chemicals, 99.99 %) was deposited during 70.2 h on a MgF₂ windows cooled at
93 77 K using liquid nitrogen (Linde) at low pressure ($2 \cdot 10^{-7}$ mbar). Concomitantly, the ice was irradiated (mainly Lyman α)
94 with a H₂ discharge lamp (121 nm, $\sim 10^{14}$ photons.cm⁻².s⁻¹). FT-IR transmission spectrometer (BRUKER Vector 22 FTIR
95 Spectrometer, 4000-910 cm⁻¹, 20 scans, 2 cm⁻¹ resolution) allows to monitor the evolution of the ice while formed and
96 irradiated. Modifications of the vacuum chamber were based on previously reported studies [9,12]. The photo processed ice
97 is then warmed up at 300 K and VOC were transferred to the GC-FT-Orbitrap-MS using the previously reported procedure
98 [9]. The only modification is that both sample injection loops are connected to a unique modified SSL injector.

99 GC analysis was performed using a Rxi®-Sil624MS column (60 m \times 0.25 mm i.d. \times 1.4 µm d.f. from Restek) for all the
100 analysis. Helium (scientific 6.0 from Linde-France) carrier flow was fixed to 1 mL/min with vacuum compensation,
101 5.0 mL/min purge flow and split flow of 10.0 mL/min. Temperature into the oven was 35 °C (3 min) up to 130 °C at
102 2 °C/min to finally reach 280 °C for 2 min at 30 °C/min. Aux Heater 1 and 2 were set at 280 °C and the MS Transfer line at
103 250 °C.

104 Methane (Alphagaz, Air Liquide) or ammonia (Alphagaz, Air Liquide), in positive (PCI) or negative (NCI) modes were
105 used. Tuning of PCI CH₄ and NCI CH₄ was done using FT43 and corresponding tune files were used for PCI and NCI NH₃
106 analysis. EI source was heated up to 250 °C, PCI CH₄ to 350 °C with 2.0 mL/min gas flow, NCI CH₄ to 200 °C with
107 1.5 mL/min, PCI NH₃ to 300 °C and 1.5 mL/min and NCI NH₃ to 150 °C with 2.0 mL/min. Except when specified electron
108 voltage was set at 70 eV (otherwise 10, 30, 50 eV). Data were recorded with resolution $m/\Delta m = 60\ 000$ at $m/z = 200$ Th (from

109 142 360 at $m/z = 45.02146$ Th to 87 795 at $m/z = 116.08373$ Th, see supplementary information TS2 and TS3). Automated
110 gain control (AGC) target was 106, maximum precursor ion injection time (ITmax) was 200 ms and maximum IT C-trap
111 parameters. MS transfer line was set at 250 °C. For gas injections the mass spectrometer recorded within the mass range
112 $m/z = 30$ to 200 Th, while liquid injection mass range was 40 to 200 Th. All data analyses were monitored using Qual
113 Browser Thermo Xcalibur 4.1.31.9.

114 3. RESULTS

115 The combination of retention time (RT) and low resolution mass spectrometry has been sufficient to identify 33 VOCs
116 from methanol irradiated ice [10]. Analytical improvement of such analysis shows that many compounds remain unknown
117 [12]. Extending the database containing such specific compounds is highly expensive and time consuming. In this context,
118 stoichiometric formula assignments using HRMS improve identification [21,25,26] and optimize standard analysis. The first
119 step to obtain this information is to optimize high mass ions detection on a set of standard molecules.

120 3.1 Optimization of ionization modes for high mass ion detection.

121 EI is the simplest and most sensitive ionization method used for GC-MS analysis. Unfortunately, this technique produces
122 unstable excited $M^{+\bullet}$ radical molecular ions leading to fragmentation. The random detection of those molecular ions prevent
123 detection of the molecular formula of unknown. A usual way to improve molecular ion detection is to use a “softer”
124 ionization mode such as CI. In this case proton exchange forms protonated or deprotonated ions which formula are related to
125 M by the gain or loss of one proton.

126 3.1.1 Electron impact versus chemical ionization global intensity.

127 The low total ion current (TIC) intensity is the principal issue for the use of CI in trace analyses. To investigate the relative
128 impact of each ionization mode on our targeted molecular families, Figure 1 displays the percentage of TIC for the same
129 sample for each method (EI at 70 eV, PCI CH₄, NCI CH₄, PCI NH₃ and NCI NH₃) relative to the sum of the total ion current
130 (TIC) of all methods normalized to 100 for compounds at the same concentration (see supplementary information TS2). It
131 shows that CI can be more intense than EI for some species. For instance, TIC of NCI NH₃ represents 86 % of the whole
132 summed TIC of valeraldehyde (64), while TIC of EI at 70 eV, PCI CH₄, NCI CH₄ or PCI NH₃ corresponds to 7 %, 1 %, 5 %
133 or 0 % respectively. Consequently, valeraldehyde presents the highest sensitivity with NCI NH₃. This ionization mode is
134 optimal for the detection of aldehydes, as well as esters, alcohols, amides or carboxylic acids. On the contrary, EI contributes
135 to 90 % of the global TIC of 1-methoxypropane (14) versus 2 %, 8 % and 0 % for PCI CH₄, NCI CH₄ and PCI NH₃,
136 respectively. EI at 70 eV is also the optimal ionization mode for the other ethers as well as nitriles and amines. In the case of
137 these later families, some CI ionization techniques are contributing to more than 5 %. Despite this low TIC intensity, the use
138 of CI can be considered to obtain interesting structural information: PCI CH₄ for nitriles and amines, PCI NH₃ for amines and
139 NCI NH₃ for nitriles.

140 3.1.2 Molecular ion in electron impact mode.

141 One possibility to improve the intensity relative to the base peak of the radical molecular ions ($M^{+\bullet}$) in EI is to modulate
142 the electron energy to limit the amount of energy received by the parent molecule. Indeed, while the total ion formation rate
143 is optimal at 70 eV, relative abundances of ions with high mass would be higher at 10 eV. When this ion is not detected, the
144 ideal configuration for molecular formula identification is to detect an ion of high intensity as close as possible to it. In

145 variable electron voltage (VeV) ion resulting from rearrangement like deprotonated cation ($[M-H]^+$) is often detected (see
146 supplementary information TS3).

147 A standard mixture (see experimental section) was analysed using variable electron voltage from 70 to 10 eV. The
148 corresponding responses and $M^{+\bullet}$ or protonated or deprotonated ions detection is displayed in Figure 2. At lower electron
149 energy, the intensity impacting molecules is weaker allowing to increase the stability of ions with high mass and their
150 relative abundance without any chemical family discrimination. For instance, from 70 to 10 eV the intensity of the $M^{+\bullet}$
151 radical cation of 2-pentanone ($M^{+\bullet}$, $[C_5H_{10}O]^+$, $m/z = 86.0726$ Th) rises from 9 % to 49 % (Figure 2 a). Thus, for some
152 analytes, a decrease of the electron energy limits molecule fragmentation and increase the $M^{+\bullet}$ radical cation intensity.
153 However, for many other analytes, such as 2-propanol (21, $M = C_3H_8O$), valeric acid (95, $M = C_5H_{10}O_2$) or isopropyl
154 acetate (49, $M = C_5H_{10}O_2$), $M^{+\bullet}$ is never detected (TS3) and deprotonated cation relative intensity is also not improved.
155 Moreover, an important loss of base peak intensity is observed at low electron energy (Figure 2 b). For instance, even with a
156 significant increase of the relative intensity of molecular or deprotonated cation compared to 70 eV, at 10 eV 2-pentanone
157 (60) presents a 95 % decrease of the intensity of its base peak. This sensitivity is an issue for analyte identification in trace
158 analysis. Therefore, the modulation of the electron energy in EI is not relevant to analyse our targeted VOC due to its lack of
159 selectivity and sensitivity.

160 3.1.3 Molecular related ions in chemical ionization modes.

161 To improve the compound identification in CI, one way is to define an ionization mode allowing us to detect an ion of high
162 intensity as close as possible to the molecular ion. It corresponds to the detection of the protonated or deprotonated cation
163 ($[M\pm nH]^+$) in PCI or anion ($[M\pm nH]^-$) in NCI of highest intensity. The protonated molecule ($[M+H]^+$, $n = 1$, where n
164 corresponds to the number of hydrogens) in PCI or the deprotonated molecule in NCI ($[M-H]^-$, $n = 1$) may not be detected
165 because it may be unstable or rearrangements may occur. That is why, we extend this study to deprotonated and protonated
166 ions from $n = -5$ up to 5.

167 Figure 3 presents the intensity of molecular, deprotonated or protonated ions of highest intensity relative to the base peak
168 of a standard molecule grouped according to their chemical families. As shown previously, the detection of molecular ion,
169 deprotonated or protonated ions of highest intensity in EI mode is difficult due to their fragmentation (Figure 3 a). In general,
170 NCI modes give the most valuable information on molecular ions, since they allow the detection of either the molecular ion,
171 or a deprotonated or protonated ion of highest intensity for all families except for ethers (Figure 3 c and e). PCI is much more
172 selective (Figure 3 b and d). Indeed, PCI NH_3 only provides the detection of one of them for amines, while PCI CH_4 is
173 selective to esters, amides, carboxylic acids, nitriles and amines. For instance, the detection of one of them of valeraldehyde
174 (64) is only possible using NCI with NH_3 or CH_4 . PCI CH_4 can only provide its detection for 1-methoxypropane (14) (41 %).
175 These results confirm that, contrary to variable electron voltage in EI, CI can provide the detection of one of those ions with
176 a sufficient intensity relative to base peak. However, except for amines with PCI NH_3 , the PCI modes give the lowest TIC
177 response and it is thus not relevant for our VOC (Figure 2).

178 Once the molecular ion, deprotonated or protonated ions of highest intensity is identified for various analytes, correlations
179 should be drawn between their chemical structure and their nature. The nature of those ions obtained in CI modes is highly
180 dependent to their chemical family (see supplementary information TS2). NCI seems to be the most reliable mode. Like in

181 previous studies [21], in NCI, most of them correspond to the deprotonated anions ($[M-H]^-$) for all chemical families except
182 for ethers and amines. Next to NCI modes, two useful pieces of information can be extracted from PCI modes: amines form
183 exclusively protonated cation with NH_3 and ethers provide deprotonated cation $[M-H]^+$ with CH_4 . However, PCI, contrary to
184 NCI, provides ion of highest mass and highest intensity of different natures for a given family. For instance, in case of
185 valeraldehyde (64, $M = C_5H_{10}O$) it corresponds to deprotonated cation $[M-H]^+$ ($[C_5H_9O]^+$, $m/z = 85.06477$ Th) while 2-
186 methyl pentanal (80, $M = C_6H_{12}O$) provides protonated cation $[M+H]^+$, ($[C_6H_{13}O]^+$, $m/z = 101.09607$ Th) with PCI CH_4 . In
187 the same way, valeraldehyde and 2-methyl pentanal provide either the protonated cation $[M+H]^+$ ($[C_5H_9O]^+$,
188 $m/z = 85.06473$ Th) and/or the tri-deprotonated cation $[M-3H]^+$ ($[C_6H_9O]^+$, $m/z = 97.06470$ Th) with PCI NH_3 , respectively.

189 The NCI NH_3 mode thus produces the highly valuable deprotonated anion in high intensity for esters, alcohols, carbonyls
190 (aldehydes and ketones), amides, carboxylic acids and nitriles. This technique should give the most valuable molecular
191 formula information for unknown identification. PCI NH_3 for amines and PCI CH_4 for ethers could be used to obtain the easy
192 detection of protonated cation in complement to EI for formula identification. For the rest, no CI technique with high TIC
193 intensity gives molecular ion, deprotonated or protonated ions with sufficient intensity.

194 3.2 Semi-quantitative analysis.

195 Limits of detection (LOD) were evaluated for some of our standards (see supplementary information TS1). LOD are
196 contained in a very wide range between 7 and 4000 $\mu g/L$ (ppm) for nitriles, alcohols, carbonyls and esters. High LOD can be
197 related to the low sensitivity of gas chromatography with respect to certain chemical families. Amines such as ethylamine (9)
198 or carboxylic acids like formic acid (37) are usually derivatized before GC-MS analysis [27,28]. For other compounds with
199 low molecular masses such as ethanol ($46 \text{ g}\cdot\text{mol}^{-1}$) (12) or 1-propanol (60 g/mol) (32) high LOD are due to detector
200 limitation as the Orbitrap has inherent low sensitivity around and below $m/z = 50$ Th. CI and EI LODs are generally in the
201 same order of magnitude (ratio between 10 and 0.1, Figure S2). Exceptions are alkanes, ethers, nitriles, formic acid (37) and
202 methyl isobutyrate (56) which are detected more sensitively using EI. Alkanes, ethers and nitriles are often very basic species
203 that cannot be deprotonated by NH_2^- , this strong Brønsted base forming deprotonated anion. The lowest LOD are recorded for
204 4-methyl-2-pentanone (71) within around 7 ppm for EI and $18 \pm 4 \mu g/L$ (ppm) for NCI NH_3 . This is comparable to analyses
205 of organics containing 10 C to 13 C in pesticide trace analyses (LOD from 0.5 to 1 ppm - 1 μL , splitless injections [15,16]),
206 toxicology (LOD from 10 to 20 ppm - 2 μL , splitless [17]). LOD up to 10 ppb (gas injection, splitless) for wastewater
207 pollutants detection are only improved thanks to extra preconcentration during sample preparation [18].

208 4. DISCUSSION

209 The use of GC-HRMS for the analysis of COV from cometary ice analogs allow molecular formula assignment for
210 qualitative analysis and enhances LOD thanks to extraction of accurate masses for quantitative analysis. However, HRMS
211 libraries are not fully available yet. Strategies such as high resolution filtering of low resolution mass spectra hits [29] can be
212 proceeded, but the comparison of intensity of mass spectra recorded in different conditions is not rigorously possible. Thus,
213 homemade libraries must be used for compound identifications. The use of soft ionization (CI) for molecular weight
214 measurement can improve compound identification [25,26]. A common CI method for GC-HRMS identification is PCI CH_4
215 [26]. However, as shown in this work, in the case of C1 to C6 VOCs analysis PCI CH_4 provides low deprotonated cation
216 detection with much lower TIC than other CI methods. The combination of EI and NCI NH_3 provides more valuable data for
217 compound identification with optimal LOD. They allow reliable protonated or deprotonated ion detection, maximal intensity

218 and specific fragmentation features. To improve compound identification, we propose a strategy combining EI and NCI NH₃
219 mass spectra for HRMS library search.

220 **4.1 Qualitative analysis.**

221 To exhaustively characterize remaining unknown compounds after database comparison, we propose a workflow
222 (Figure 4) to combine GC-HRMS analysis from different ionization methods. Step 1 to step 3 are classical steps for
223 compound identification in GC-MS: acquisition, step 1, mass trace deconvolution and peak detection, step 2, and mass
224 spectra extraction and library search, step 3. Retention time (RT) alignment, step 4, is a key step to compare different
225 ionization modes using characteristics found in the present study. We must improve this step because no internal standards
226 can be used for cometary ice analogs VOCs analysis. Finally, steps 5 and 6 aim to restrict possibilities before standard
227 analysis confirmation step 7.

228 **4.1.1 Simple ionization mode GC-HRMS analysis.**

229 After recording the chromatographic data using different ionization sources, step 1, a list of detected compounds with their
230 corresponding identification is separately edited: chromatographic peaks are listed thanks to peak detection on narrow
231 (± 5 ppm) extraction of mass traces, step 2. The corresponding mass spectra and RT are compared with the existing database.
232 Mass spectrum comparison is obtained thanks to the mass spectrum similarity index defined as

$$233 \quad SI = \left(1 - \frac{\sum_{m/z} |I_u(m/z) - I_l(m/z)|}{\sum_{m/z} |I_u(m/z) + I_l(m/z)|} \right) \times 100 \quad \text{Eq. 1 [30]},$$

234 with $I_u(m/z)$ the intensity of the unknown at exact mass m/z and $I_l(m/z)$, the intensity of the compound referenced in the
235 library at same exact m/z , and the RT difference.

236 As shown previously using reference spectra, NCI NH₃ is used for esters, alcohols, carbonyls, amides, carboxylic acids
237 and nitriles analysis. During unknown analysis of such compounds, deprotonated anion can be identified as an ion of highest
238 mass with intensity relative to base peak higher than 2.5 %. This is true for 94 % of analysed standards (see supplementary
239 material Table S1). If the second highest mass ion is considered, this ion is included for 94 % of them. The remaining 6 %
240 contain trimethylacetaldehyde (35) that forms adduct induced by hyperconjugation of its tert butyl group, methyl formate (6)
241 and ethyl formate (19) that are the smaller esters and it still present but at lower threshold (1.19 and 1.60 resp., see
242 supplementary material Table S5). From its detection, direct measurement of the number of #O, #N, #C and #H and DBE can
243 help to characterize unknowns.

244 Furthermore, NCI NH₃ can give information on primary neutral fragments helping to characterize chemical structures by
245 allowing discriminations between different chemical families. The presence of a fragment with a mass loss of 16.03132 Th (1
246 C + 4 H) relative to the deprotonated anion is characteristic to compounds with a vicinal methyl (alcohols, carbonyls or
247 nitriles). This mass loss is consistent with alcohol groups in position 2. For example, 1-pentanol (83) and 3-pentanol (67) do
248 not produce such loss, while 2-pentanol (68) does. 2-methyl-2-butanol (48), 2-propanol (21) and 3-methyl-2-butanol (61)
249 follow the same rule. This mass loss is also recorded for 2-ketones. Indeed, 2-pentanone (60) provides it but not 3-pentanone
250 (65). This rule is consistent with acetone (18) and 4-methyl-2-pentanone (71) fragmentation patterns. Finally, methyl groups
251 in β or γ -position of aldehydes or nitriles can also be lost. This is the case for isovaleraldehyde (53), isovaleronitrile (78) and
252 2-methyl butyronitrile (72). Isobutyraldehyde (27) is the only unexplained exception. These observations are useful to

253 understand most of the NCI NH₃ fragmentation patterns observed for our standards and to restrict possible structures. The
254 protonated or deprotonated ion detection (using PCI NH₃ for amines and NCI NH₃ for the others) and identification of mass
255 loss with NCI NH₃ can therefore give information on possible structures. Once the formula of the molecular ion and its
256 branching are known, the last unknown information is the chemical family. This can be obtained by matching information
257 from multiple ionization modes.

258 **4.1.2 Multiple ionization mode GC-HRMS analysis.**

259 Combining information from multiple ionization modes requires the possibility to match peak lists containing both
260 identified and remaining unknown from two GC-HRMS analysis. The step allowing to match lists is known as RT
261 alignment, step 4. Indeed, a direct match is not possible because of the usual RT shift between two recorded data. RT can be
262 corrected either using the retention index relative to an internal standard [31] or by cross comparison of RT and mass spectra
263 [32]. Unfortunately, none of those two usual techniques can be used in the context of GC-HRMS analysis of ice analogs with
264 multiple ionization modes. Internal standards cannot be used during ice analog synthesis or added before VOC analyses.
265 Furthermore, mass spectra and retention times cannot be fitted to align RT because of the different ionization modes.
266 Consequently, we chose to align RT by matching identified compounds and using a narrow RT uncertainty window $\pm 1\%$
267 for unknown peaks. The matched list can then be used to characterize unknown compounds combining the different
268 ionization sources properties.

269 An exhaustive analysis of normalized TIC intensity, step 5, combining different ionization methods allows to sort
270 unknowns into four distinct groups, alkanes/ethers, amines, nitriles and others (esters, alcohols, aldehydes, amides and
271 carboxylic acids), using two steps (Table 1). First, the comparison of EI to NCI NH₃ classifies molecules into three groups
272 according to the normalized TIC contribution of NCI NH₃: high, medium and low (Figure 1). One of them contains esters,
273 alcohols, aldehydes, amides and carboxylic acids having high NCI NH₃ normalized TIC contribution: ~93, 87, ~92, 98 or
274 92 %, respectively. The other only nitriles (32 % of NCI NH₃ contribution). The last one corresponds to alkanes, ethers and
275 amines with low NCI NH₃ contribution (0, ~7 and ~4 % resp.). Second, extra comparison of PCI NH₃ with EI can isolate
276 amines: the contribution of PCI NH₃ relative to EI for such molecules is around 33 % for tested compounds (Figure 1).

277 The combination of the chemical group with HRMS spectral data, step 6, allows more precise unknown identification,
278 thanks to formula identification (6a) and mass spectra analysis (6b). Step (6a) can split the groups alkanes/ethers and others
279 (Table 1). The presence of an oxygen atom into the chemical formula of an unknown contained into the group alkane/ethers
280 proves it is an ether. Using the same arguments one can split the chemical group others into amides ($\#O = 1$ and $\#N = 1$),
281 esters/carboxylic acids ($\#O = 2$ and $\#N = 0$) and carbonyls ($\#O = 1$ and $\#N = 0$). At this step, seven groups exist: alkanes,
282 ethers, amines, nitriles, amides, esters/carboxylic acids and carbonyls (Table 1).

283 During mass spectra analysis (6b), primary mass loss must be considered. Indeed, the mass loss of 2.01557 Th (2 H) with
284 respect to the deprotonated anion is interesting to distinguish alcohols from carbonyls mass spectra. The formation of this ion
285 is highly efficient for alcohols and corresponds to their base peak ($DBE = 1.5$ for saturated alcohols) while the deprotonated
286 anion ($DBE = 0.5$ in case of saturated alcohols) corresponds to a much lower intensity peak (from 3 to 10 % of intensity).
287 This way, 2-methyl-1-propanol (44) can be distinguished from isobutyraldehyde (27) because it produces such ions very
288 efficiently (100 %) while only traces (0.64 %) for isobutyraldehyde (see supplementary information Table S4).

289 Finally, mass spectra of esters and carboxylic acids can be distinguished thanks to mass spectra analysis. The presence of
290 any fragment is characteristic to esters because of the breakable C(=O)-O-R bound (see supplementary information Table
291 S5) while carboxylic acids do not provide any fragment (only adducts sometimes, see supplementary information Table S6)
292 using NCI NH₃. These elements show that the combination of multiple ionization modes can provide a full characterization
293 of an unknown compound. Moreover, as previously described, branching information can also be described using NCI NH₃.
294 Finally for ethers and alkanes that are the only molecular families undetectable using CI, exhaustive analysis of EI mass
295 spectra can help to further interpretation and enable standard proposition to definitive identification.

296 **4.2 Application to VOCs identification from cometary ice analogue.**

297 In part 4.1, we proposed a workflow combining different ionization modes to develop an analytical strategy for an
298 exhaustive identification of VOC. In this section, we test this strategy to identify VOC formed from a methanol ice
299 previously irradiated at Lyman α and at low temperature (77 K). Once irradiated, this ice is warmed up to 300 K and the
300 VOCs desorbing during this warming are recovered to be analyzed with the GC-HRMS (details in methods section).

301 **4.2.1 Standard identification.**

302 The classical identification process was monitored using the database (see supplementary information Table S12) with the
303 *SI* (Eq. 1) indicator for high resolution mass spectra ($\Delta m/m < 5$ ppm) and retention time comparison. This allowed the
304 identification of dioxygen (2), carbon dioxide (3), ether (4), acetaldehyde (5), methanol (8), methyl formate (6), ethanol (12),
305 diethyl ether (11) and methyl acetate (22) (Figure 5). Identifications are commonly confirmed using both EI and NCI NH₃
306 ionization methods. The only exception is dioxygen (2) that has been only detected by EI because of its better sensitivity, and
307 methyl acetate (22) because NCI NH₃ has better sensitivity for esters than EI.

308 Monitoring both EI and NCI NH₃ analysis enables deconvolution of coeluting species while extracted ion chromatograms
309 cannot distinguish them. For instance, Peak@9.31 with a NCI NH₃ normalized TIC relative to EI of 60 % can be identified
310 as diethyl ether using EI (11, $\Delta RT = -0.04$ min, *SI* = 80 %) coeluting with ethanol using NCI NH₃ (12, $\Delta RT = -0.16$ min,
311 *SI* = 48 %). Again, this can be explained by sensitivity issues: NCI NH₃ has lower sensitivity than EI for ethers, while it is
312 the contrary for alcohols (Figure 1).

313 **4.2.2 Cross-validation.**

314 To cross-validate the strategy, dimethyl ether (4) and acetaldehyde (5) were removed from the mass spectra library
315 (Table 2). Consequently, after steps 1 to 4 (identification and mass extraction, Figure 4), two extra unidentified peaks were
316 present in both chromatograms: Peak@5.81 and Peak@6.90. The description of the multiple ionization modes showed that
317 for the peak at 5.81 min the normalized TIC of NCI NH₃ relative to EI was 2 %. This unknown is part of “low normalized
318 TIC contribution of NCI NH₃” i.e. alkanes, ethers and amines. However, as the chemical formula of its NCI NH₃ major
319 fragment (CH₃O, *DBE* = 0.5, see supplementary information Table S10) contains one heteroatom (*#O* = 1 and *#N* = 0),
320 Peak@5.81 must be an ether. As discussed previously, ethers do not provide deprotonated anions using NCI NH₃, but the EI
321 mode can help to identify it. Indeed, the only EI fragments with intensity higher than 2.5 % are [C₂H₅O]⁺
322 (*m/z* = 45.03350 Th, *DBE* = 0.5) and [C₂H₆O]⁺ (*m/z* = 46.04130 Th, *DBE* = 0, see supplementary information Table S11).
323 [C₂H₆O]⁺ is the ion with the highest mass having a *DBE* as an entire. In EI mass spectrometry, such clues show that it could
324 be the M⁺ radical cation [33]. Consequently, Peak@5.81 can be an ether with *M* = C₂H₆O, i.e. dimethyl ether.

325 The Peak@6.90 contains two fragments in its NCI NH₃ spectrum with intensity higher than 2.5 %: [C₂HO]⁻
326 ($m/z = 41.00352$ Th, $DBE = 2.5$) and [C₂H₃O]⁻ ($m/z = 43.01918$ Th, $DBE = 1.5$). As discussed previously, this ion of highest
327 mass and highest intensity corresponds to the deprotonated anion on NCI NH₃ mass spectra. Consequently, C₂H₃O = M-H
328 i.e. its molecular formula is C₂H₄O. Peak@6.90 is consequently an unsaturated molecule ($DBE = 1$). To improve information
329 upon this unknown, EI and NCI NH₃ normalized TIC response can be compared. This molecule is part of the “high
330 normalized TIC contribution of NCI NH₃” (90 %). Its chemical family can correspond to esters, alcohols, aldehydes, amides
331 or carboxylic acids. While for Peak@6.90 #O = 1 and #N = 0, one can directly exclude esters (#O = 2), amides (#N = 1) and
332 carboxylic acids (#O = 2) from the last list. The two remaining families are carbonyls or alcohols. To argue for one or the
333 other, one must look for the relative intensity of the mass loss of 2.01566 Th (2 H) with respect to ion of highest mass
334 ([C₂HO]⁻, 4 %) versus the deprotonated anion (100 %). The fact that the intensity of the second one is higher than this mass
335 loss indicates that this chromatographic peak is not alcohol but carbonyls. Consequently, Peak@6.90 is acetaldehyde. These
336 identifications are consistent with the previous.

337 Finally, using the same strategy, we propose an assignment to the five remaining unknown that has not been identified
338 previously (Table 2). Two must be removed, as they are peaks containing ions from the column and are present into blanks.
339 Then, from the five remaining unknowns, Peak@6.74 contains the same ions as acetaldehyde. It is a double injection peak,
340 certainly due to slow heating of the cryotrapping. The last unidentified peaks are only detected using the EI mode. They may
341 be out of detection limits obtained with NCI NH₃. Peak@5.30, Peak@7.22 and Peak@9.01 can be part of groups alkanes,
342 ethers, amines or nitriles (Table 1). Peak@5.30 EI mass spectrum is consistent with C₃ alkane formation (propane or
343 propene): [C₃H_n]⁺ the major peaks with n from 2 to 7. Comparison with standard mass spectrum shows that Peak@5.30
344 cannot be propane. Peak@7.22's ion of highest mass is [C₃H₇O]⁺ ($m/z = 59.04922$ Th, $DBE = 0.5$). Methoxy ethane is the
345 only unsaturated ether with this molecular mass. This attribution has been confirmed with the presence of masses
346 45.03347 Th and 59.04920 Th at the right RT after comparison with the analysis of the products of a Williamson synthesis.
347 Finally, the only ion present in the EI-MS of Peak@9.01 is [C₃H₇O]⁺ ($m/z = 59.04922$ Th, $DBE = 0.5$). This implies that it is
348 an ether with $M = C_3H_7O-R$ with unknown alkyl chain R with fragment 59 which must be more intense than fragments 31,
349 43 or 49. Comparing RT with the one recorded in our database and the intensity of fragment 59 intensity relative to the three
350 others fragments in mass spectra from the NIST database 2-methoxy propane seems to be the most probable identification of
351 Peak@9.01.

352 5. CONCLUSION

353 In the present study, a GC-FT-Orbitrap-MS was used for the first time to analyse VOCs containing 1 to 6 carbon atoms
354 produced during the photo-processing of cometary ice analogs. The recovery of these VOCs was allowed by the specific
355 coupling of the GC-FT-Orbitrap-MS to the vacuum chamber where ices are processed. Different ionization modes (EI, PCI or
356 NCI with NH₃ or CH₄) were first tested. Their combination with the FT-Orbitrap-MS high-resolution (full width at half
357 maximum over 100.000 at $m/z = 200$) and precision (less than 5ppm) provides unambiguous formula identifications and
358 untargeted identification of molecular ions. Variable electron voltage ionization methods cannot provide molecular ion
359 improvement without drastic loss of TIC intensity. With chemical ionization modes (methane or ammonia in positive or
360 negative ionization modes), we demonstrate that NCI NH₃, generally poorly used, is the best mode to use for compounds
361 having less than six carbon atoms. The best compromise for sensitivity and easy molecular formula identification consists in

362 combining EI with NCI NH₃, for all compounds, except amines, alkanes and ethers, with an accuracy of formula detection of
363 94 %. Semi-quantitative analysis shows that NCI NH₃ and EI have similar LODs up to 7 ppm (database of 110 compounds
364 containing 1 to 6 carbon atoms Table S1). In the case of amine identification, the ideal combination is EI with PCI NH₃,
365 while only EI can ionize alkanes and ethers.

366 From those results, a workflow (Figure 4) has been built up using formula identification thanks to high resolution mass
367 spectra and chromatographic normalized TIC comparison of CI with respect to EI. This workflow has been cross-validated
368 on the identification of unknown VOCs generated by the photo-processing of an ice analog of methanol. Specially, dimethyl
369 ether (4), acetaldehyde (5) and methoxy ethane were identified and validated while propene and 2-methoxy propane were
370 identified without standard analysis validation. Further improvements of this method will be to identify compounds from
371 nitrogen containing cometary ices analogs.

372

373 **ASSOCIATED CONTENT**

374 **Supporting material**

375 Figure S1. Composition of the library.

376 Figure S2. EI over NCI LOD ratio.

377 Figure S3. Summary of the relative intensity of the ions of highest mass and intensity related to the chemical formula for
378 NCI NH₃ ionization of the total database analysis.

379 Figure S4. Infrared spectrum of CH₃OH after 2.7h irradiation while deposition.

380 Table S1. Calculated and measured data for the 110 analytes included in the database.

381 Table S2. Summary of EI/CI ion of highest mass and intensity related to the chemical formula.

382 Table S3. Summary of VeV ion of highest mass and intensity related to the chemical formula.

383 Table S4. Comparison of intensity of ion of highest mass and intensity related to the chemical formula detected in NCI
384 NH₃ for carbonyls and alcohols.

385 Table S5. Comparison of NCI NH₃ detected ions intensity for esters.

386 Table S6. Comparison of NCI NH₃ detected ions intensity for carboxylic acids.

387 Table S7. Comparison of NCI NH₃ detected ions intensity for ethers.

388 Table S8. Comparison of NCI NH₃ detected ions intensity for amines.

389 Table S9. Comparison of NCI NH₃ detected ions intensity for nitriles.

390 Table S10. NCI NH₃ extracted unknown mass spectra.

391 Table S11. EI extracted unknown mass spectra.

392 **AUTHOR INFORMATION**

393 **Corresponding Author**

394 *E-mail: gregoire.danger@univ-amu.fr

395 **Author Contributions**

396 TJ performed the experiments, treated the data and developed the methodology. TJ, GD and MR wrote the manuscript and

397 GD managed the program.

398

399 **Notes**

400 The authors declare no competing financial interest.

401

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504

Identify Low Mass Volatile Organic Compounds from Cometary Ice Analogs using Gas Chromatography coupled to an Orbitrap mass spectrometer associated to Electron and Chemical Ionizations

Thomas Javelle¹, Michel Righezza¹ and Grégoire Danger^{1,2,3,*}

¹ Aix-Marseille Université, Laboratoire de Physique des Interactions Ioniques et Moléculaires, UMR 7345, CNRS, Marseille, France

² Aix Marseille Université, CNRS, CNES, LAM, Marseille, France

³ Institut Universitaire de France (IUF)

Figures and Tables

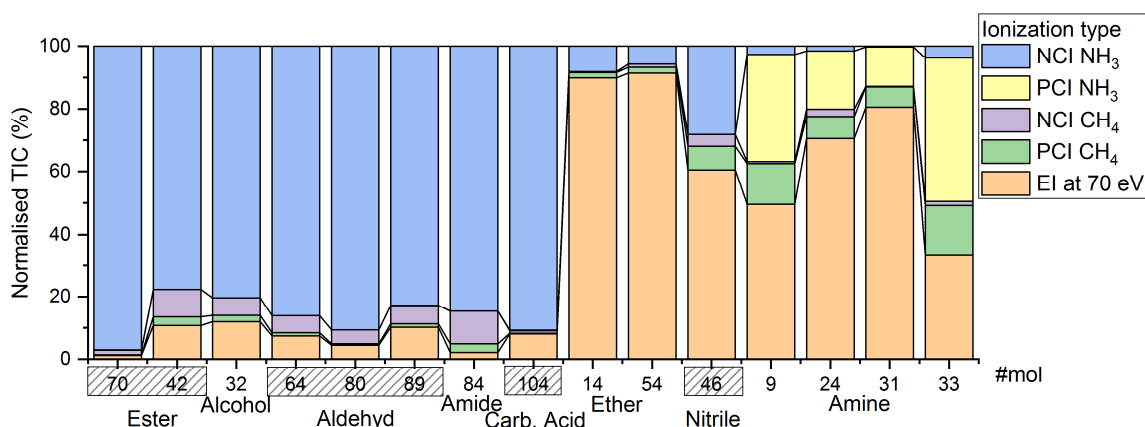


Figure 1. Percentage of TIC for each method normalized to the sum of all TIC modes (EI at 70 eV, PCI and NCI). The

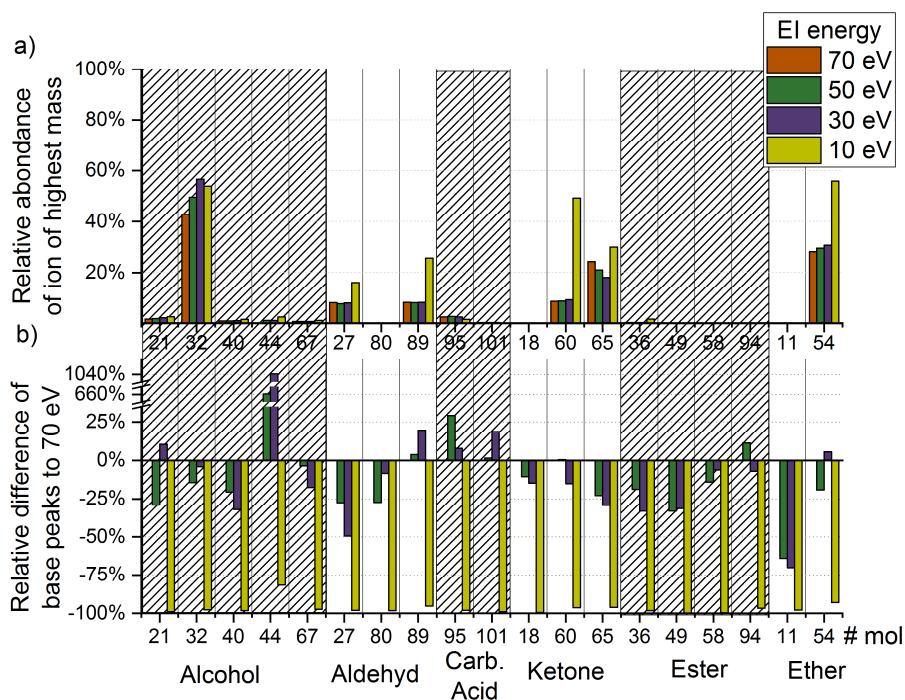
percentage of response for each method is represented for EI at 70 eV, PCI CH₄, NCI CH₄, PCI NH₃ and NCI NH₃

ionizations methods (see supplementary information Table S2): orange EI at 70 eV, green PCI CH₄, purple NCI CH₄, yellow

PCI NH₃ and blue NCI NH₃. Four response types can be classified into amines (with principal contribution of EI at 70 eV

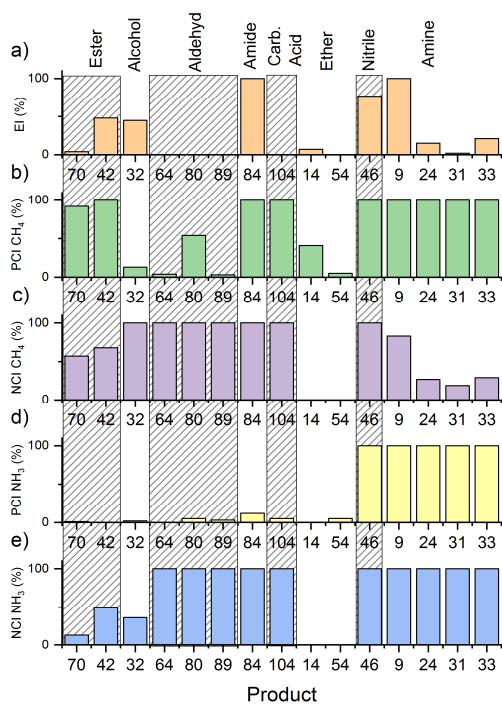
and PCI NH₃), nitriles (EI at 70 eV and NCI NH₃), ethers (EI at 70 eV only) and others (NCI NH₃ only). CH₄ as reagent gas

provides the lowest selectivity.



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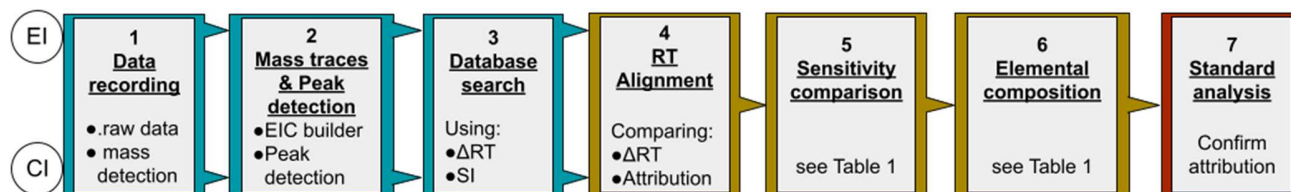
20 Figure 2. Summary of the impact of variable electron voltage (VeV) on VOCs mass pattern (molecular numbering are
 21 extracted from supplementary information Table S1 and more detailed data are displayed in supplementary information
 22 Table S3). Figure a) plots the intensity of ions of high mass and intensity relative to base peak and figure b) plots the relative
 23 intensity difference of the corresponding base peak intensity with respect to 70 eV for all standards.
 24



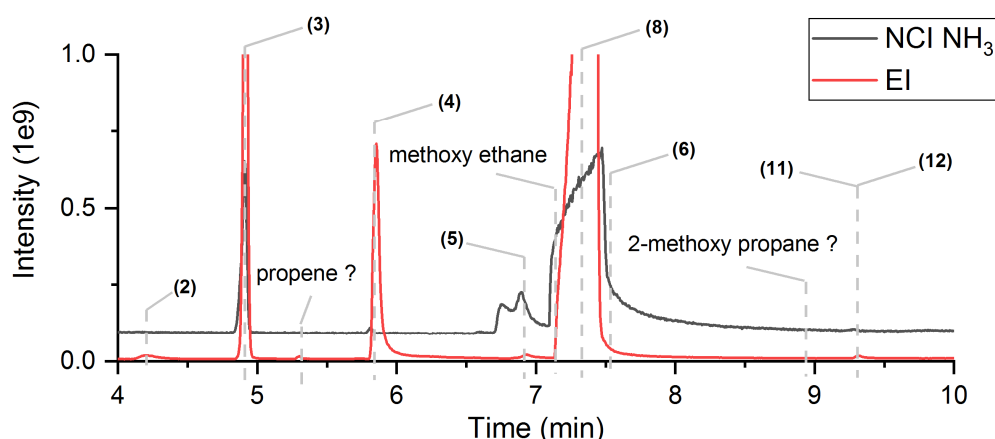
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26 Figure 3. Relative abundance of extracted ions of high mass and intensity with respect to the ionization mode: orange

27 barcharts corresponds to electron ionization (EI), green to positive chemical ionization (PCI) using methane (PCI CH₄),
 28 purple to negative chemical ionization (NCI) using methane (NCI CH₄), yellow to PCI using ammonia (PCI NH₃) and blue to
 29 NCI using ammonia (NCI NH₃) (see Table S2).
 30



31
 32 Figure 4. FT-Orbitrap-MS Identification strategy for unknown identification after library search. The identification workflow
 33 is the following: From the two EI and NCI analysis, step 1, mass traces are extracted building extracted ion chromatograms
 34 (EIC) and a peak list is provided in step 2. Then each extracted spectra are compared to the database using retention time
 35 difference (Δ RT) and similarity index (SI, see Eq. 1) at step 3. Because of the absence of internal standards in interstellar
 36 analogs analysis, retention time alignment must be improved at step 4 using retention time difference and attribution
 37 comparison. Finally, TIC sensitivity of different ionization modes can be compared, steps 5, before as the exact
 38 fragmentation pattern analysis step 6 to propose a precise standard to analyse at step 7.



39
 40 Figure 5. GC-MS chromatograms (TIC) from two analyses (EI at 70 eV and NCI NH₃) of VOCs recovered after the warming
 41 of an ice of pure methanol irradiated during 76 h concomitantly to the gas deposition. Identifications are labeled by following
 42 the strategy described in Figure 4. Dioxygen (2), carbon dioxide (3), methanol (8), methyl formate (6), ethanol (12), diethyl
 43 ether (11) and methyl acetate (22) were detected using library search and confirmed with NCI NH₃ mass spectra
 44 identification. Coupling EI and NCI NH₃ analysis enable coelution separation (ethanol (12), diethyl ether (11)). Dimethyl
 45 ether (4) and acetaldehyde (5), removed from the database for cross-validation, were identified using mass spectra qualitative
 46 analysis and validated with standard identification. Peak@5.30, Peak@7.22 and Peak@9.01 qualitative analysis of HR mass
 47 spectra are respectively consistent with C₃ alkanes (propene ?), methoxy ethane and 2-methoxypropane. IR spectrum is
 48 reported in supplementary information Figure S4 and identification list and workflow are reported Table 2.

49
 50 Table 1. Summary of the parameters used in step 5 and step 6. CI total ion current (TIC) relative to EI is the percentage of
 51 TIC for each method normalized to the sum of EI and NCI NH₃ or PCI NH₃.

Steps:	5a	5b	6a		6b				
	CI TIC relative to EI		ion of highest mass and intensity		NCI NH ₃ [M-H] ⁻		NCI NH ₃ [M-H±2H] ⁻		
	NCI NH ₃	PCI NH ₃	#O	#N	Rel. Ab.	DBE	Rel. Ab.	Nature	DBE
Alkanes	0 %	0 %	0	0	-	-	-	-	-
Ethers	≤ 10 %	0 %	1	0	0 %	-	-	-	-
Amines	≤ 10 %	~ 30 %	0	1	0 %	-	100 %	[M-3H] ⁻	1.5
Nitriles	~ 33 %	0 %	0	1	≥ 90 %	2.5	≥ 8 %	[M-3H] ⁻	3.5
Amides	≥ 90 %	0 %	1	1	-	-	-	-	-
Esters	≥ 90 %	0 %	2	0	3-100 %	1.5	-	-	-
C. Acids	≥ 90 %	0 %	2	0	≥ 90 %	1.5	-	-	-
Carbonyls	≥ 90 %	0 %	1	0	≥ 90 %	1.5	0-9 %	[M-3H] ⁻	2.5
Alcohols	≥ 90 %	0 %	1	0	3-100 %	0.5	≥ 90 %	[M-3H] ⁻	1.5

52 Notes: The sum of TIC for the same subset of standards is normalized to 100 and the percentage of the response for the
53 selected ionization method (Figure 1). At step 5a three normalized TIC response types can be classified into: high, medium
54 and low, grouping different chemical families. Step 5b allows specific identification of amines thanks to the selectivity of
55 PCI NH₃. Step 6a, the presence of O or N in multi-deprotonated anion allows differentiation of amides to esters/carboxylic
56 acids and to carbonyls / alcohols. Then, step 6b, further deprotonate anion characteristics allows M identification with high
57 relative abundance (Rel. Ab.) except for some esters (see supplementary information Figure S3) and amides. In particular,
58 the use of the peak of second intensity next to the deprotonated ion (M-H±H) allows discrimination of alcohols and
59 carbonyls (see supplementary information Table S4). In this study, only unsaturated compounds were analysed. Double bond
60 equivalents (DBE) can thus provide information on the chemical family (see supplementary information Table S4 to Table
61 S9).

62

63 Table 2. Ice analogs VOCs identified from the codeposition of methanol ice irradiated at Lyman α (121 nm) during 76h.

RT		Library		Workflow	
EI	NCI NH ₃	Identification	%EI	% NCI NH ₃	Identification
4.20	-	dioxygen	-	-	-
4.91	4.91	carbon dioxide	85	15	-
5.30	-	Peak@5.30	-	-	propene
5.85	5.81	Peak@5.81	98	2	dimethyl ether*
-	6.76	Peak@6.74	-	-	double peak
6.94	6.90	Peak@6.90	47	53	acetaldehyde*
7.22	-	Peak@7.22	-	-	methoxy ethane*
7.43	7.47	methanol	-	-	-
7.49	-	methyl formate	-	-	-
9.01	-	Peak@9.01	-	-	2-methoxy
-	9.27	ethanol	-	-	propane
9.31	-	diethyl ether	-	-	-
-	11.55	methyl acetate	-	-	-

64 Notes: # corresponds to the id number of the standard (see supplementary information Table S12). *Confirmations are based
65 on standards analysis.

66