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Petroleomics by Direct Analysis in Real Time-Mass Spectrometry

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23

24 **Abstract**

25 The analysis of crude oil and its fractions applying ambient ionization techniques is
26 yet under explored in mass spectrometry (MS). Direct Analysis in Real Time (DART) in
27 positive ion mode detection was coupled to linear ion trap quadrupole (LTQ) and Orbitrap
28 mass spectrometer and optimized to analyze crude oil and paraffin samples. The ionization
29 and acquisition parameters of the DART-MS such as the template substrates (paper, TLC
30 plate and glass), temperature (from 100 up to 400 °C), carrier gas (helium and nitrogen),
31 concentration of analyte (from 0.33 to 6 mg mL⁻¹) and acquisition time (from 1 to 10 μscans)
32 were optimized for crude oil analyzes. DART-MS rendered the optimum conditions of
33 operation using paper as a substrate, T = 400 °C, helium as a carrier gas, sample concentration
34 ≥ 6 mg mL⁻¹, and acquisition time < 2 μscans. For crude oils analyzes, DART(+)-Orbitrap
35 mass spectra detected nitrogen-containing protonated species, whereas for paraffin samples,
36 hydroxylated HCs species (O_x classes, where x = 1-4) with DBEs of 1-4 were detected, being
37 their structures and connectivity confirmed by CID experiments (MS²). The DART(+)-MS
38 and CID experiments (MS² and MS³) were also able to identify porphyrin standard
39 compounds as [M + H]⁺ ions of *m/z* 615.2502 and 680.1763, where M = C₄₄H₃₀N₄ and
40 C₄₄H₂₈N₄OV, respectively.

41 **Key-words:** ambient mass spectrometry, DART-MS, crude oil, paraffin, porphyrin.

42

43 **1. Introduction**

44

45 A paragraph on interest of what you have done

46 A paragraph on other analytical techniques that were applied to what you have done
47 and their limitations.

48 The objective of this work was to investigate the application of a direct analysis in
49 real time (DART) for this purpose. DART developed by Cody and Laramée,¹ is a type of
50 ambient pressure ionization technique. Its coupling with mass spectrometry has allowed
51 many applications in different fields such as forensic,²⁻⁶ pharmaceutical,⁷⁻⁹ food,¹⁰⁻¹⁴ analysis,
52 in biology,¹⁵⁻¹⁷ chemistry,¹⁸⁻²⁰ In crude oil analysis ²¹ there are no application of DART
53 except the work of Rummel et al.,²² where it was coupled to Fourier Transform Ion Cyclotron
54 Resonance (FT-ICR) mass spectrometer . Here, the DART source was coupled to a hybrid
55 mass analyzer (LTQ Orbitrap Velos Pro™) and the ionization and acquisition parameters
56 (substrates, temperature and type of gas heater, concentration of analyte and acquisition time)
57 were optimized for crude oil analyzes. The ability of DART source in paraffin and porphyrin
58 compounds ionization was also evaluated.

59

60 ***2. Procedure***

61 ***2.1 Reagents and samples***

62 Dichloromethane, heptane, and tetrahydrofuran, THF, (analytical grades with purity
63 higher than 99.5%) were supplied by Sigma–Aldrich Chemicals USA and were used to
64 prepare solutions of crude oil, paraffin and porphyrin standard compounds.

65 Seven crude oil samples, named samples A to G, were supplied by PETROBRAS and
66 characterized to determine the API degree (ASTM D1298-99) and saturates, aromatics,
67 resins, and asphaltenes (SARA) content. For all the crude oils evaluated, API degree values

68 ranged from 26 to 30, classifying them as medium crude oils (API degree = 22-30). Saturates
69 content ranged from 51 to 65 wt %. To evaluate the detection sensibility of DART technique,
70 samples were diluted in dichloromethane in five different concentrations: 0.33; 1.0; 1.6; 3.3
71 and 6 mg mL⁻¹. A volume of 10µL was spotted on the paper surface and analysed by DART-
72 MS. Two other surfaces were tested as substrates: glass and a thin layer chromatography
73 (TLC) plate. The stationary phase of TLC is composed of silica gel.

74 Three saturated hydrocarbon samples were also studied in this work, named paraffin
75 A, B and C. The first two samples, paraffins A and B, were purchased from Sigma–Aldrich
76 Chemicals USA and Vetec Química Fina Ltda, respectively, whereas the paraffin C was
77 obtained from a food grade process. The organic solutions were prepared in heptane at ≈ 10
78 mg mL⁻¹ and a volume of 10µL was spotted on the TLC plate.

79 The porphyrin standard compounds such as 5,10,15,20-tetraphenyl-21H,23H-
80 porphine and 5,10,15,20-tetraphenyl-21H,23H-porphine vanadium(IV) oxide, with
81 molecular formula (M) equal to C₄₄H₃₀N₄ and C₄₄H₂₈N₄OV and molecular weight of
82 614.2471 and 679.1703, respectively, were also studied. Both porphyrin standard compounds
83 were purchased from Sigma–Aldrich Chemicals USA. Solutions were prepared at 100 mg L⁻¹
84 in THF and after, a volume of 10µL was spotted on paper substrate and analysed by
85 DART(+)-MS.

86

87 **2.2 DART(+)-MS**

88 For the experiments, DART–MS system consisting of a DART ion source (IonSense,
89 Saugus, MA, USA) was coupled with a hybrid mass spectrometer: LTQ Orbitrap Velos Pro™
90 (Thermo Fisher Scientific, Bremen, Germany). The operating conditions of the DART ion

91 source were as follows: positive ion mode; helium flow: 4.0 L min⁻¹; discharge needle
92 voltage: 3.0 kV; perforated and grid electrode potentials: +150 and +350 V, respectively. The
93 distance between the DART gun exit and mass spectrometer inlet was about 5-10 mm. For
94 glasses and paper surfaces, the sample introductions were carried out manually, whereas for
95 TLC plate substrate it was automatically performed using Dip-it holder samplers. To assess
96 the influence of the gas beam temperature on the signal intensity, crude oil spots were
97 analyzed at different temperatures ranging from 100 to 400 °C using helium and nitrogen as
98 the gas beam.

99 DART(+) mass spectra were acquired using both a LTQ and an Orbitrap mass
100 analyzers. For high resolution experiments using Orbitrap mass analyzer, a mass resolving
101 power of 100,000 (FWHM, at m/z 400; 0.5 s scan cycle time) was reached. As consequence,
102 a mass error about 3 to 5 ppm was measured, where the mass accuracy is determined from
103
$$\text{Error (ppm)} = ((m/z_{\text{measured}} - m/z_{\text{theoretical}})/m/z_{\text{theoretical}}) \times 10^6.$$

104 The maximum ion injection time was about 10 and 300 ms for LTQ and Orbitrap,
105 respectively, with the automatic gain control (AGC, corresponding to the number of changes
106 transferred from the front-stage ion trap to the orbitrap analyzer) target set at 1×10^5 . The
107 full scan mass spectra were acquired over the range of m/z 150–1000. Tandem mass
108 spectrometry (DART-MS/MS) was also performed by collision-induced
109 dissociation with a collision energy of 15–30% (manufacturer's unit) using LTQ as
110 mass analyzer.

111 For crude oil samples, the DART(+)-Orbitrap mass spectra were acquired and processed
112 using Composer software (Sierra Analytics, Pasadena, CA, USA). The MS data were
113 processed and the elemental composition of the sample was determined by measuring the

114 m/z values. Class and DBE distributions, and carbon number (CN) *versus* DBE graphs were
115 plotted to better analyze the results. DBE is defined as the number of rings added and the
116 number of double bonds in each molecular structure. The unsaturation level of each
117 compound can be deduced directly from its DBE value according to equation 1:^{23,24,25}

$$118 \quad \text{DBE} = c - h/2 + n/2 + 1 \text{ (equation 1)}$$

119 Where c , h , and n are the numbers of carbon, hydrogen, and nitrogen atoms,
120 respectively, in the molecular formula.

121

122

123

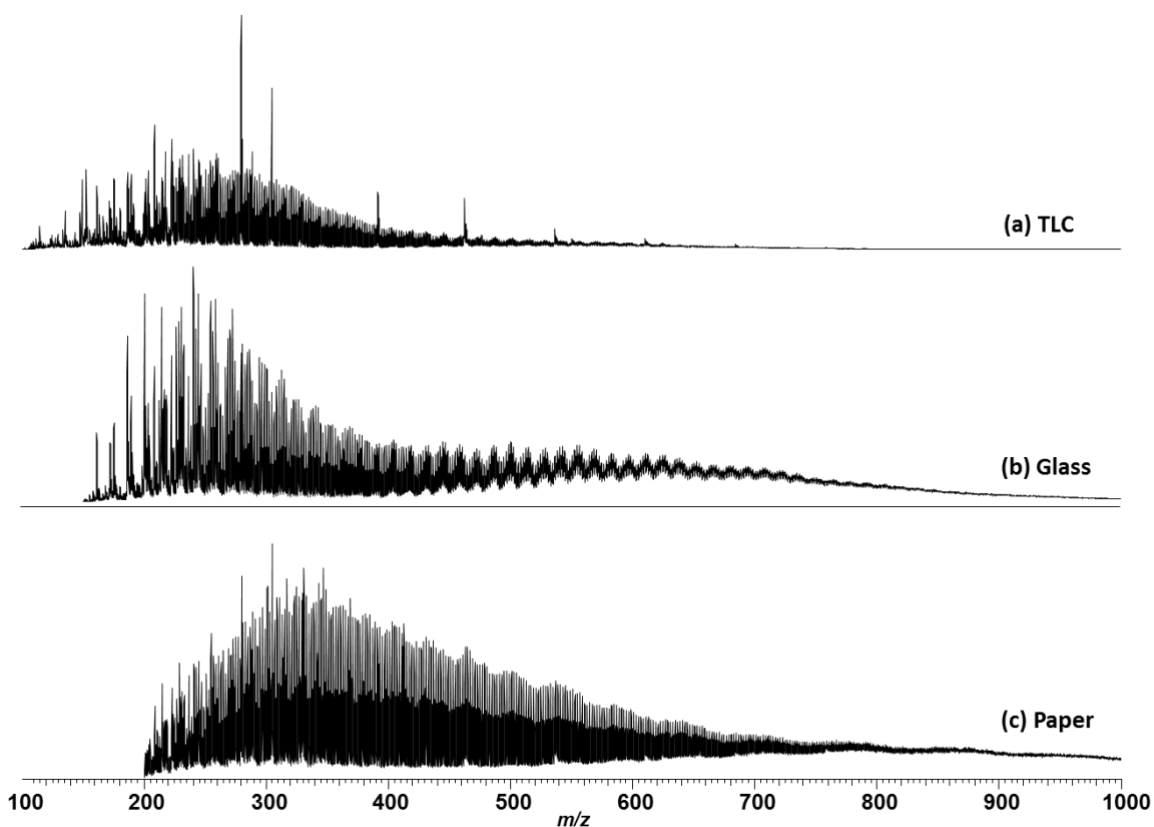
124 **3. Results**

125 **3.1 DART(+)-MS Optimization**

126 The sensibility of DART(+)-MS technique for crude oil analyzes as function of some
127 parameters were evaluated such as: substrate (TLC plate, glass and paper, **Figure 2**);
128 temperature (from 100 to 400 °C, **Figure 3**); type of gas heater (He and N₂, **Figure 4**);
129 concentration of analyte (from 0.33 to 6 mg mL⁻¹, **Figure 5**); and acquisition time for
130 Orbitrap experiments (number of microscans, **Figure 8**).

131 **Figures 2a-c** show DART(+)-LTQ mass spectra (using Helium as heater at 400 °C) of
132 a typical Brazilian crude oil (sample A at 10 mg mL⁻¹) as a function of different substrates:
133 **(a)** TLC; **(b)** glass; and **(c)** paper. A higher amplitude and distribution of signals with profiles
134 ranging from m/z 200-800 was observed when paper substrate was applied. The sensibility
135 of DART(+) source increased in the following order: TLC < glass < paper. As consequence,

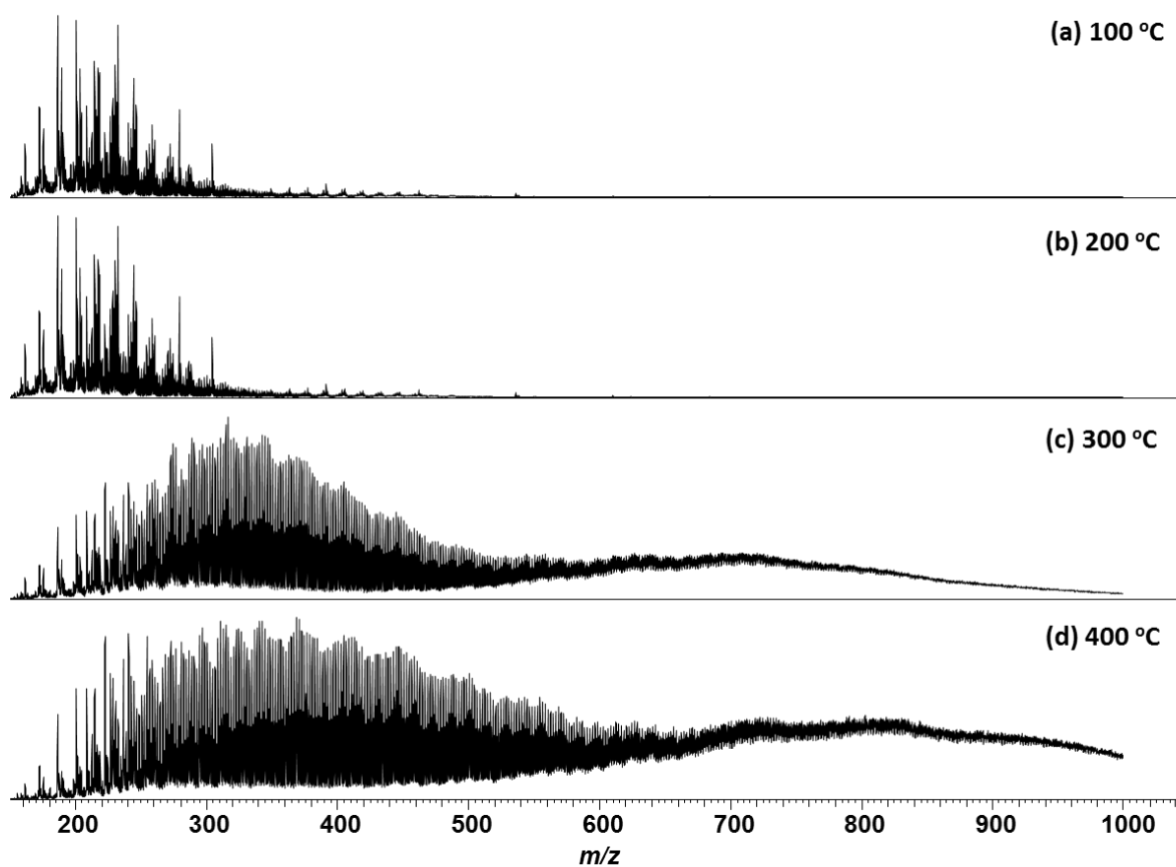
136 the average molar mass distribution (M_w) was shifted for higher values of m/z (from m/z 280
137 to 360). A lower chemical interaction between polar organic compounds and the cellulose
138 $((C_6H_{10}O_5)_n)$ was the key contributor to have a better ionization efficiency using paper as
139 substrate.



140
141 **Figure 2.** DART(+)-LTQ MS for a typical Brazilian crude oil sample on the (a) TLC plate,
142 (b) glass and (c) paper substrates.

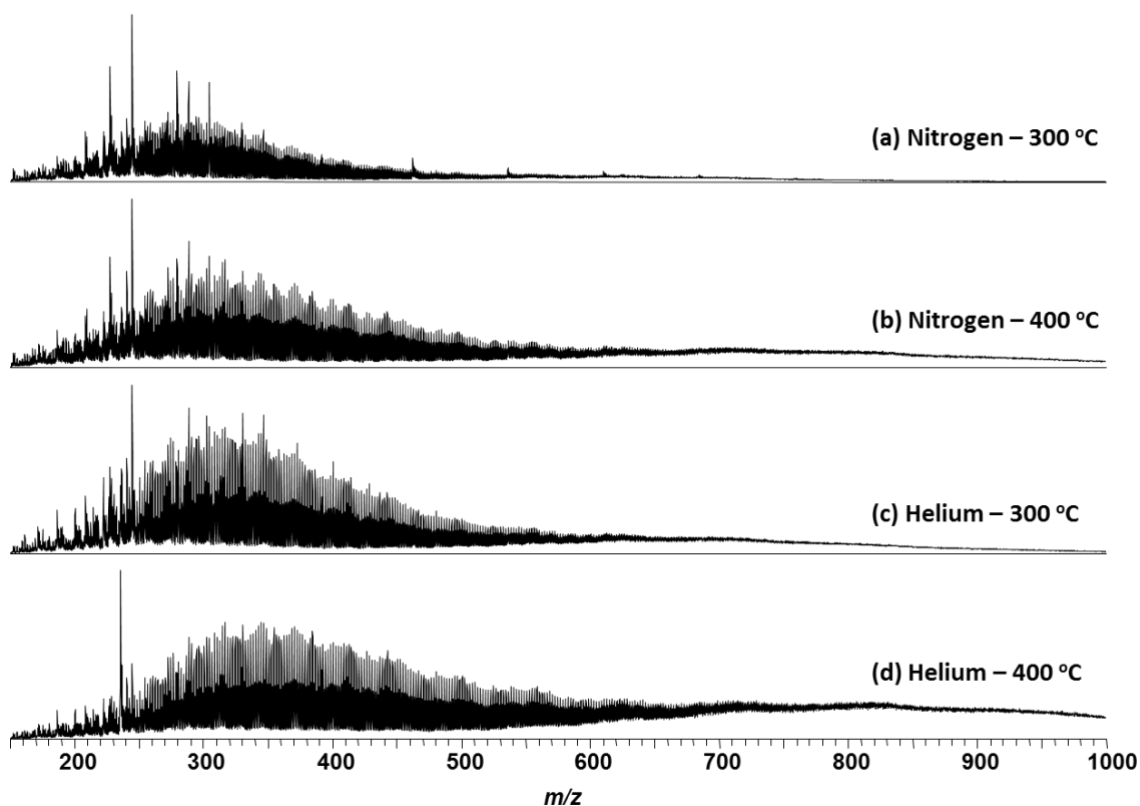
143 The ionization efficiency of DART source was also tested as a function of
144 temperature, **Figure 3**, and the type of the gas heater (Helium or N_2), **Figure 4**. **Figure 3**
145 shows the DART(+)-LTQ mass spectra as a function of temperature using Helium at (3a)
146 100°C, (3b) 200°C, (3c) 300 °C, and (3d) 400 °C. It is possible to note that a higher sensibility
147 and a higher amplitude of signals with m/z from 200-1000 and $M_w = 400$ Da was observed

148 with 400 °C as the optimum temperature, **Figure 3d**. Changing the He gas heater to N₂
149 (**Figures 4a-b**), the DART(+)-LTQ mass spectrum at 400 °C, **Figure 4b**, showed a similar
150 performance to that one with He at 300 °C, **Figure 4c**, thus proving the better efficiency of
151 molecules ionization in presence of He due to its higher internal energy of ionization (He =
152 19.8 eV *versus* N₂ = 15.6 eV).



153
154 **Figure 3.** DART(+)-LTQ MS on a Brazilian crude oil solution spot (concentration of 10 mg
155 mL⁻¹) as a function of temperature using He as gas heater at (a) 100, (b) 200, (c) 300 and (d)
156 400 °C.

157

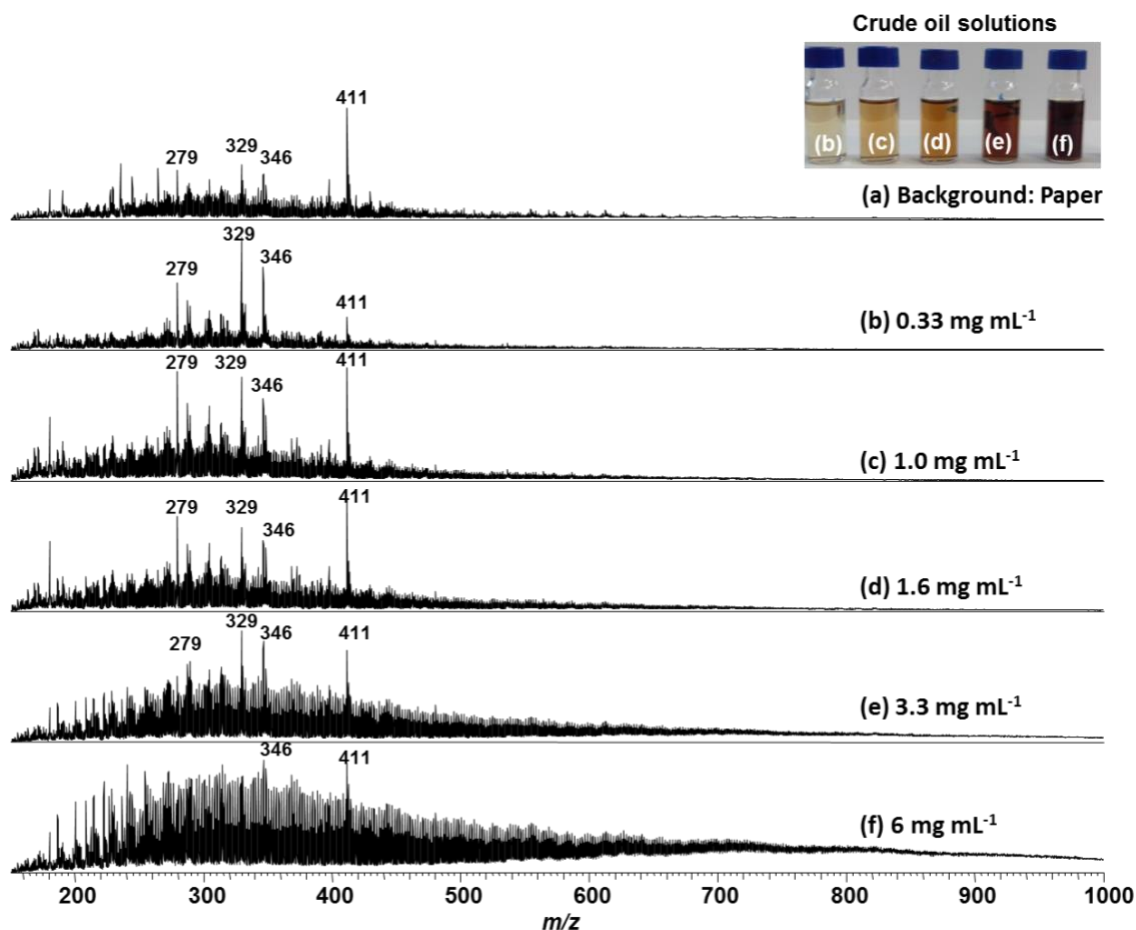


158

159 **Figure 4.** DART(+)-LTQ MS for a crude oil solution spot as a function of gas heater:
 160 nitrogen and helium at 300 (a and c) and 400 °C (b and d), respectively.

161

162 The sensibility of DART(+)-MS technique was also evaluated as a function of
 163 concentration of crude oil (from 0.33 to 6 mg mL⁻¹). As consequence of increasing crude oil
 164 concentration, a higher signal-to-noise ratio and amplitude of signals were easily observed
 165 (see the decreasing of relative intensity of ions of m/z 279, 329, 346 and 411 formed from
 166 the paper substrate). Therefore, it is suggested that concentrations higher than 6 mg mL⁻¹
 167 must be used for crude oil analysis.



168

169 **Figure 5.** DART(+)-LTQ MS as a function of crude oil concentration: (a) 0, (b) 0.33 (c) 1.0,
 170 (d) 1.6, (e) 3.3 and (f) 6 mg mL⁻¹. He at 400 °C was used as gas heater.

171

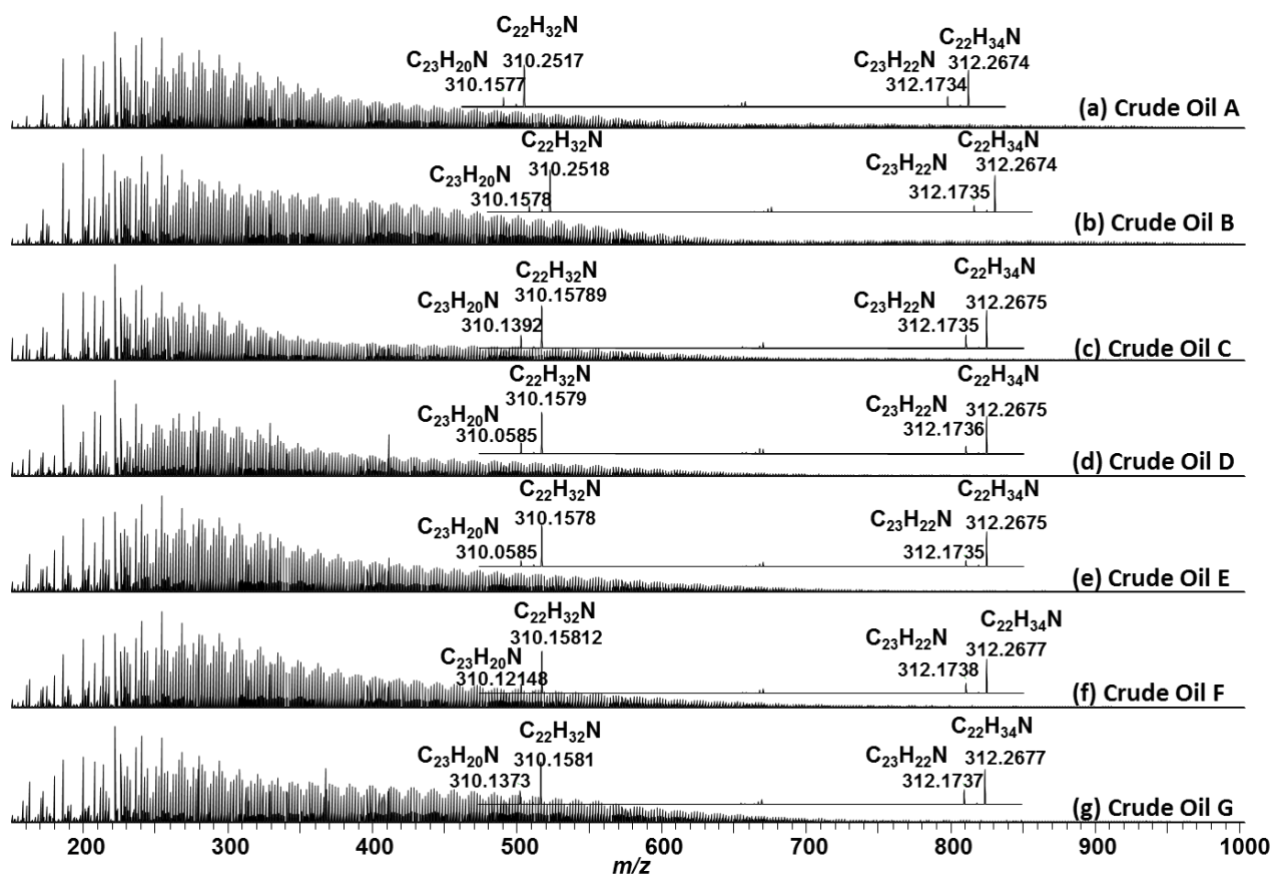
172 **3.2 Crude oil analyzes**

173 After optimization of DART source ionization conditions as following: substrate
 174 (paper), temperature (T = 400 °C), gas heater (Helium) and concentration (≥ 6 mg mL⁻¹),
 175 DART(+) mass spectra at high resolution (FWHM $\approx 100,000$ at *m/z* 400) were acquired for
 176 seven crude oil samples (samples A-G), using Orbitrap mass analyzer, **Figure 6.**

177 **Figures 6a-g** show the DART(+)-Orbitrap mass spectra of seven typical Brazilian
178 crude oil samples, showing peaks profile from m/z 200-700 with M_w centered from m/z 374
179 to 453. Nitrogen-containing species were detected as protonated molecules, that is, $[M-H]^+$
180 cations, according to the proposed mechanism of **equation 3**. The magnified region near m/z
181 310-312 indicates that DART(+) detected pyridine analogous compounds (N class):
182 $[C_{23}H_{21}N + H]^+$, $[C_{22}H_{31}N + H]^+$, $[C_{23}H_{21}N + H]^+$ and $[C_{22}H_{33}N + H]^+$ ions with m/z
183 310.1577, 310.2517, 312.1734 and 312.2674, and DBEs of 15, 8, 13 and 7, respectively. The
184 theoretical m/z values for these ions are 310.1590, 310.2529, 312.1734 and 312.2674, thus
185 providing a medium mass error of about -4.02 ppm. In Petroleomic, ultra-high resolution and
186 accuracy mass spectrometry with FWHM > 400,000 and exact mass < 1 ppm is required for
187 the identification of complex organic mixtures, thus ensuring an excellent recalibration data
188 from Composer *software*. Accurate mass measurements define the unique elemental
189 composition ($C_cH_hN_nO_oS_s$) and DBE from singly charged ions.^{26,27} To correct the mass
190 deviation (Error > 1 ppm), DART(+)-Orbitrap mass spectra were further processed with the
191 Composer *software*, especially designed for formula attribution via automatic recalibration
192 for known homologous series from the measured m/z values of polar crude oil markers.^{28,29}
193 A medium of approximately 350 molecular formula (where $n = 7$) were assigned from
194 monoisotopic components for the Orbitrap mass spectra, corresponding to a medium
195 percentage of 70 % of all assignments.

196

197



198

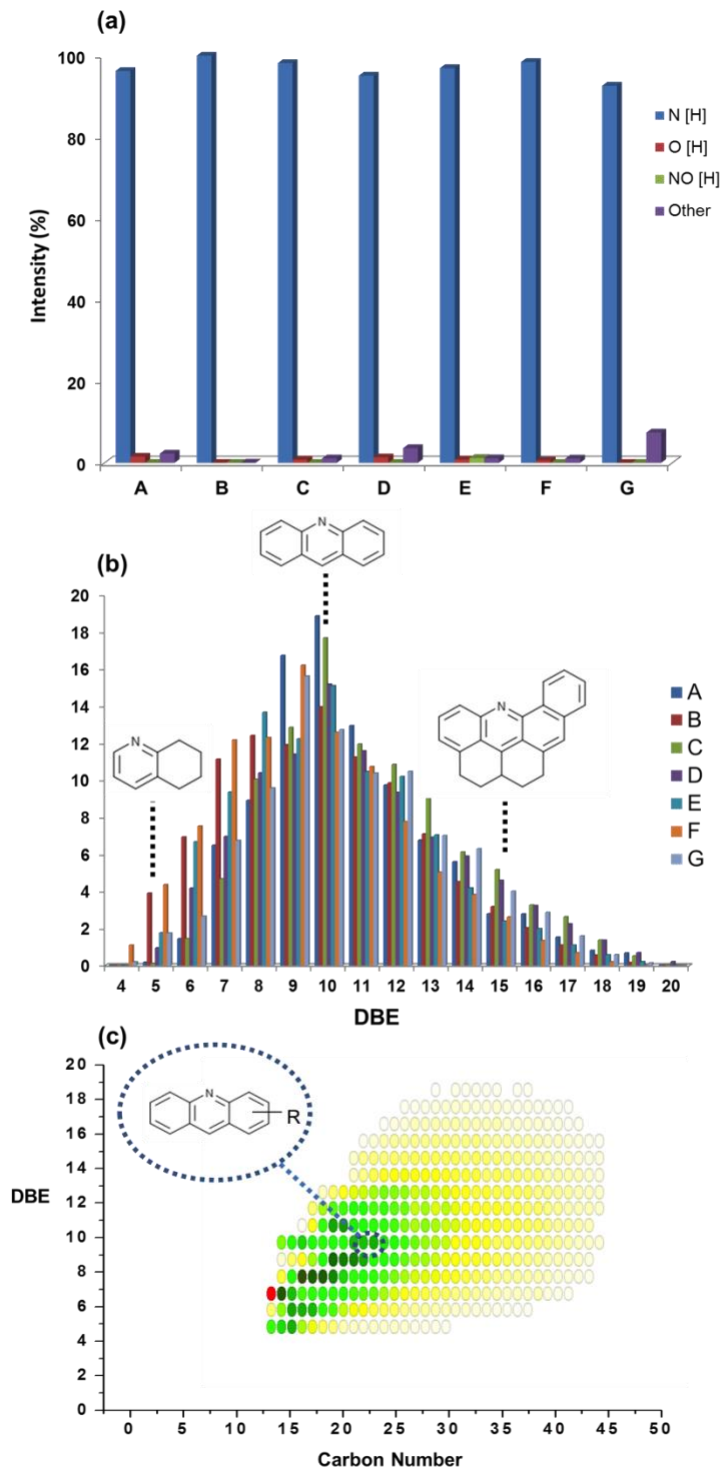
199 **Figure 6.** DART(+)-Orbitrap MS for seven crude oil samples (A-G). He was used as gas
 200 heater at 400 °C. Acquisition time of 1 microscan.

201

202 One way to display the similarities or differences between the signal patterns of crude
 203 oil samples is the construction of certain types of plots, such as the plots of the relative
 204 abundances of different classes of compounds, DBE vs intensity and DBE vs CN,³⁰ **Figure**
 205 **7a-c.** **Figure 7a** displays the distribution of polar compound classes (NH), NO[H], and O[H])
 206 obtained from DART(+)-Orbitrap MS. In all cases, DART(+) seems to efficiently promoted
 207 the ionization of polar compounds, as protonated cations ($[M + H]^+$), with their magnitude
 208 following the order: N[H] > O[H] > NO[H]. The DBE relative abundance distributions of

209 N[H] class for samples A-G were also evaluated, **Figure 7b**, in which a distribution ranging
210 from 4 to 20 was observed. **Figure 7c** presents the DBE *versus* CN for the majority class,
211 N[H] class, for the sample F. Carbon numbers ranged from C₁₂ to C₄₅ for pyridine compound
212 species (DBEs = 4-20), with maximum abundance around C₁₆ and DBE = 8 were observed.

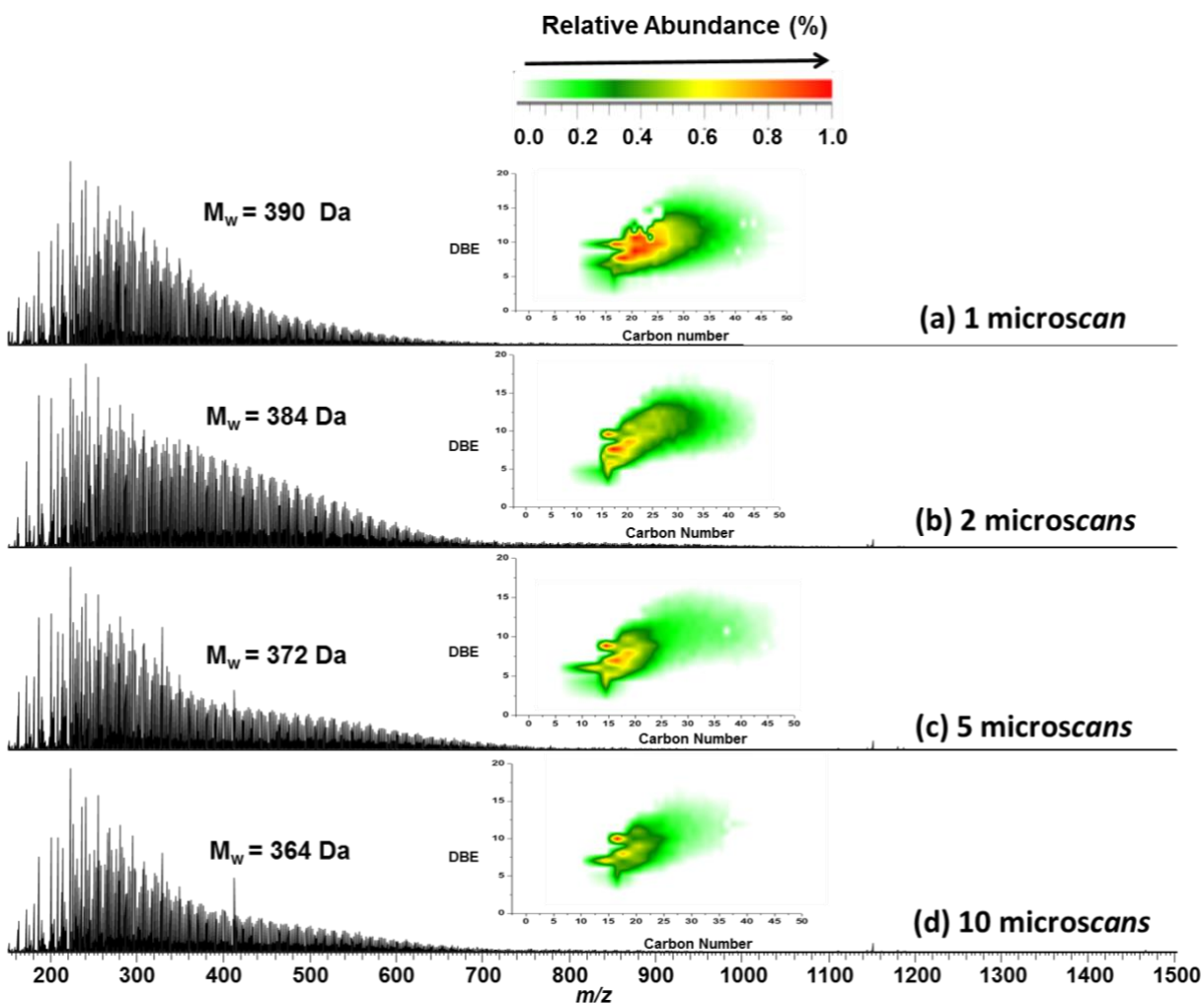
213 An attempt to improve the exact mass and consequently the signal-to-noise ratio in
214 an Orbitrap analyzer was made by increasing its acquisition time. **Figure 8** shows the
215 DART(+)-Orbitrap mass spectra as a function of the acquisition time (number of microscans)
216 for sample F. The M_w decreased as the number of microscan increased (1 \rightarrow 10) as well as
217 the population of nitrogen compounds assignments, depicted by the DBE vs CN plot (see the
218 insert of **Figure 8**). The number of assigned molecular formulas decreases from 288 (for 1
219 μ scan) to 199 (for 10 μ scans). Probably, the ions transmission from the LTQ to Orbitrap was
220 affected by fact that desorption and ionization mechanism of DART acts only in a specific
221 point. Hence, the ionic population was reduced as function of time.



222

223 **Figure 7.** Class distribution, DBE *versus* intensity of seven crude oil samples (A-G) and

224 DBE *versus* CN plots of sample F generated from DART(+)Orbitrap data.



225

226 **Figure 8.** DART(+)-Orbitrap mass spectra as a function of acquisition time (number of
 227 microscans) for crude oil sample A. Note that M_w decreases as the number of microscan
 228 increases as well as the nitrogen compounds assignments decreases as showed by DBE vs
 229 CN plot (see the insert of **Figure 8**).

230

231 3.3 Paraffin Analyzes

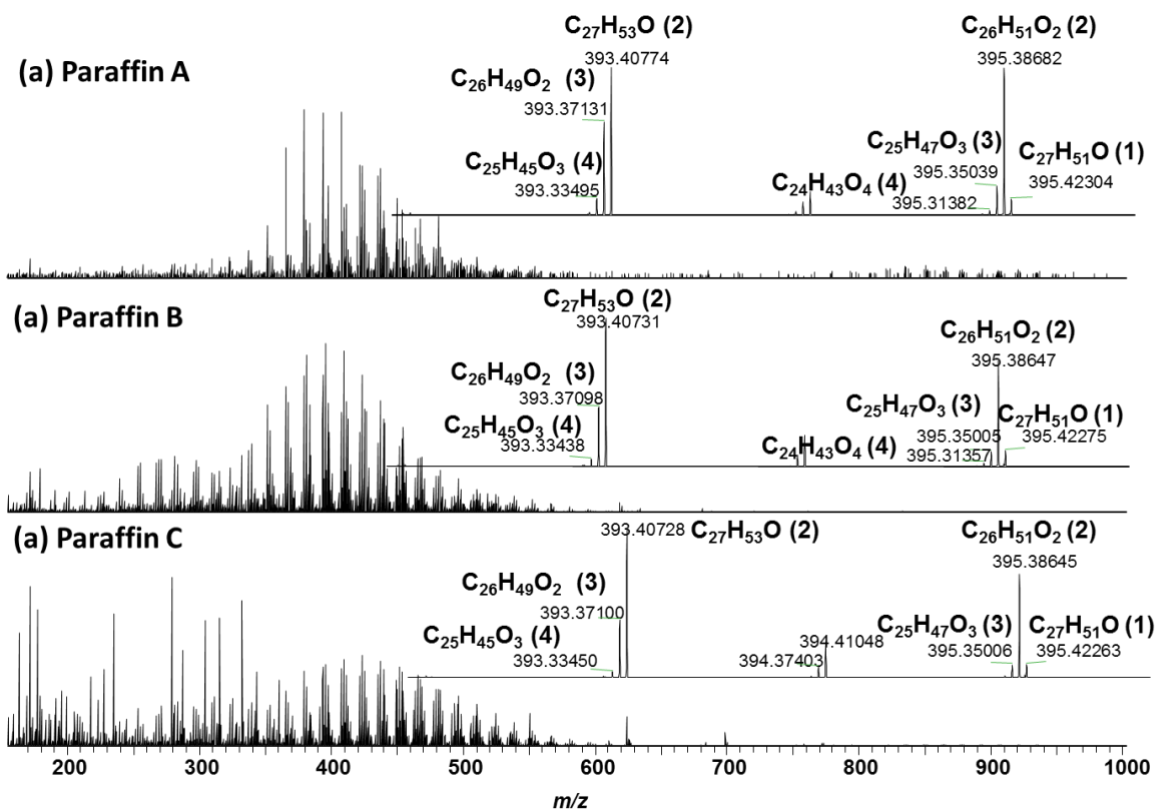
232 The analysis of hydrocarbons (HCs) using atmospheric or ambient ionization
 233 techniques still remain a challenge in mass spectrometry.³¹ **Figure 9** shows DART(+)-
 234 Orbitrap mass spectra for the three paraffin samples evaluated. The right side inserts show

235 paraffin detection as oxygenated HCs species (O_x classes, where $x = 1-4$) with DBEs of 1-4
236 and a mass error of - 3-4 ppm. In all cases, a similar Gaussian profile from m/z 250-600 was
237 observed. The oxidized HCs species were generated at high temperature and atmospheric
238 pressure from short-life time oxygen-based species such as OH and OOH radicals and also
239 H_3O^+ ion in contact with HCs compound species, producing oxidized HCs (O_x classes).^{31,32}

240 In 2009, Cooks et al.³³ has also analyzed saturated hydrocarbons ($C_{15}H_{32}$ to $C_{30}H_{62}$)
241 using discharge-induced oxidation in desorption electrospray ionization. Multiple oxidations
242 and dehydrogenations occurred during the DESI discharge, but no hydrocarbon
243 fragmentation was observed. DESI-Orbitrap mass spectrum of a petroleum distillate
244 containing vacuum gas oil saturates (boiling point > 316 °C) showed HCs species containing
245 two oxygen additions in alkanes structures from $C_{21}H_{44}$ to $C_{36}H_{74}$, similar to observed for
246 DART(+)-Orbitrap data.

247 To confirm the structures and the connectivity of some oxygenates HCs compound
248 classes (O_x classes), which were identified using DART(+)-Orbitrap MS, the DART(+)-
249 MS/MS spectra were acquired for the ions with m/z 337, 351, 365, 379 and 393. This
250 approach identifies the characteristic neutral loss and confirms the existence of hydroxylated
251 HCs compounds such as alcohols from successive eliminations of 18 Da (H_2O), and 28 Da
252 ($CH_2=CH_2$) along the molecule, **Figure 10**.

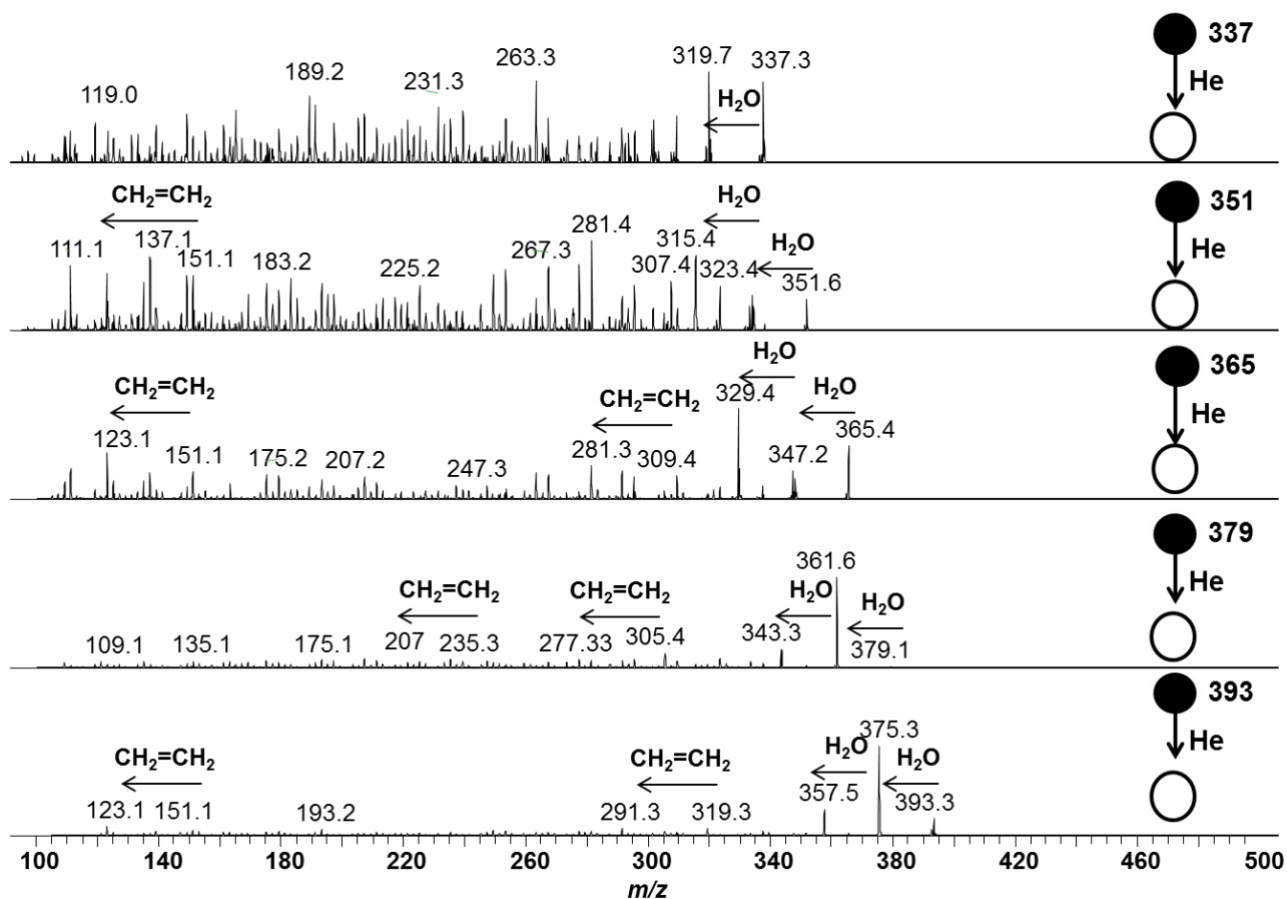
253



254

255 **Figure 9.** DART(+)-Orbitrap mass spectra for paraffin samples. The right side inserts show
 256 paraffin detection in oxygenated form (O_x classes). The number between parentheses
 257 corresponds to DBE value.

258



259

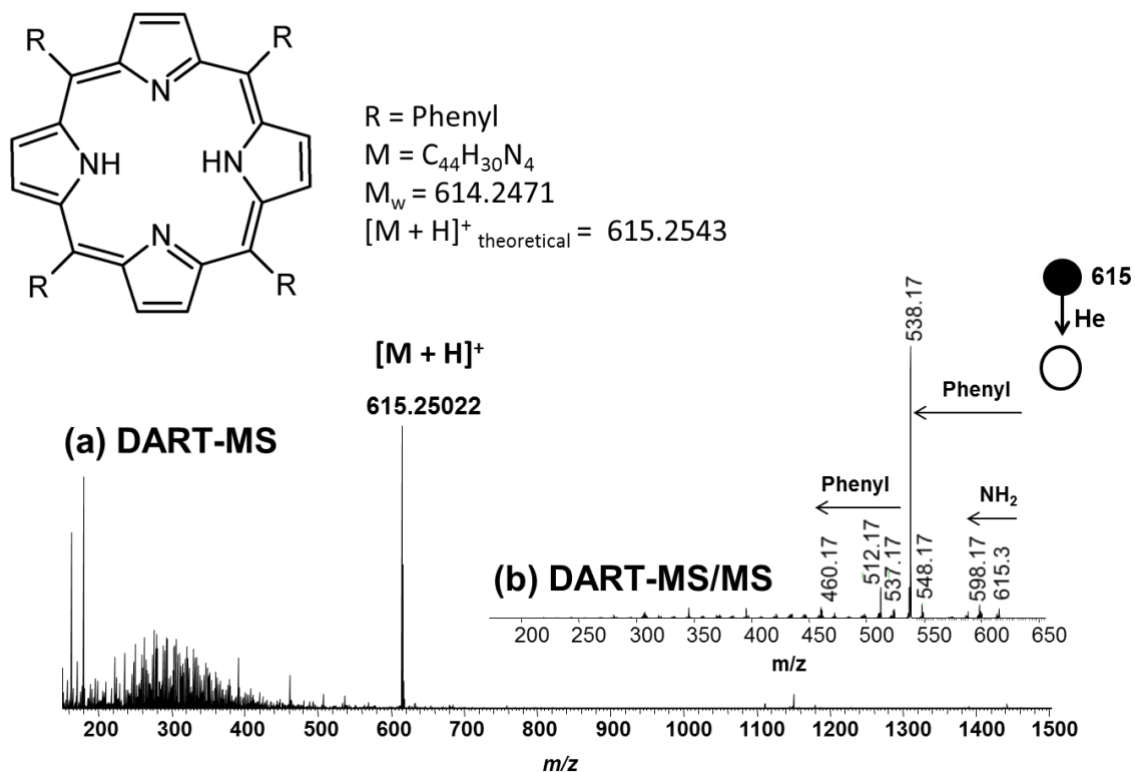
260 **Figure 10.** DART(+)-MS/MS for ions with m/z 337, 351, 365, 379 and 393.

261

262 3.4 Porphrin compounds analyzes

263 The detection ability of DART(+)-MS technique regarding standard porphyrin and
 264 metal porphyrin compounds were evaluated, **Figure 11** and **12**, respectively. The **Figure 11a**
 265 shows the DART(+)-Orbitrap MS for the 5,10,15,20-tetraphenyl-21H,23H-porphine
 266 compound, detected as $[\text{M} + \text{H}]^+$ ion with m/z 615.2502, where $\text{M} = \text{C}_{44}\text{H}_{30}\text{N}_4$. Its chemical
 267 structure was confirmed from CID experiments, **Figure 11b**, in which the two neutral losses
 268 of 77 Da and one of 16 Da identifies the presence of two phenyl rings and one amine group
 269 (C_6H_5 and NH_2). The standard metal porphyrin compound was also detected by DART(+)-

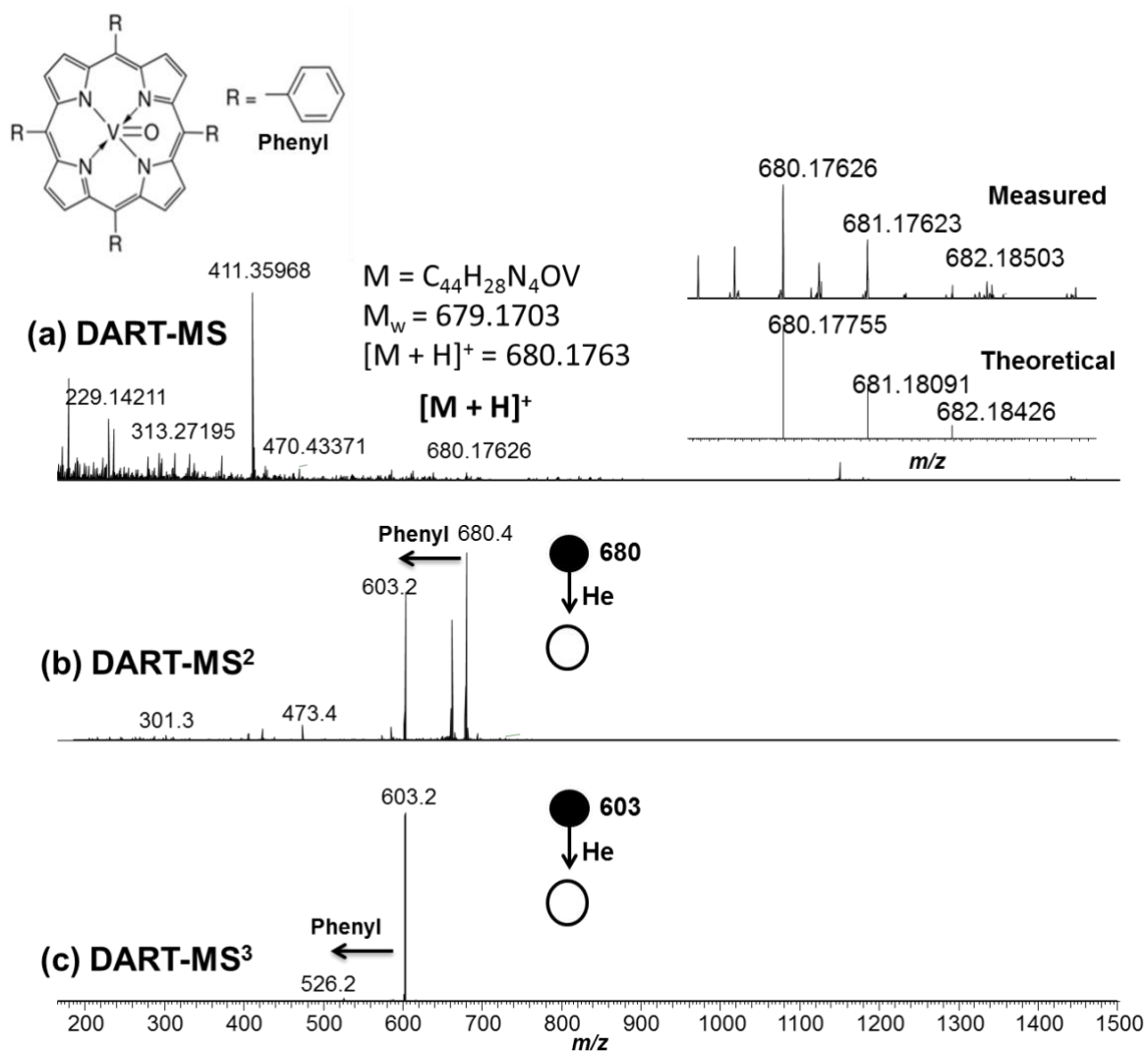
270 Orbitrap MS, with lower ionization efficiency, as $[M + H]^+$ ion with m/z 680.1763, where M
 271 = $C_{44}H_{28}N_4O$, **Figure 12a**. Its connectivity and its structure were confirmed from
 272 DART(+)-MS² and DART(+)-MS³ experiments, in which two neutral losses of 77 Da
 273 happened simultaneously (m/z 680 \rightarrow 603 and m/z 603 \rightarrow 526 transitions **Figures 12b-c**).



274

275 **Figure 11.** (a) DART(+) mass spectrum of porphyrin standard using He at 400 °C and (b)
 276 DART(+)MS/MS for the ion with m/z 615.

277



278

279 **Figure 12.** (a) DART(+) mass spectrum of vanadium porphyrin standard and (b)

280 DART(+)MS² and (c) DART(+)MS³ for ions with m/z 680 and 603, respectively.

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287 **4. Conclusion and Perspectives**

288 The DART(+)-hybruid ion-trap-Orbitrap MS is a powerful, simple, and easy
289 analytical tool that can be applied to petroleum analysis to asses assessing chemical
290 composition at molecular level. Cellulose-based substrates together with high temperature
291 (400 °C), He as a gas heater and crude oil concentrations higher than 6 mg mL⁻¹ increased
292 the sensibility of DART source. Nitrogen-containing species were detected as protonated
293 molecules in crude oil samples, following by NO[H] and O[H] class species.

294 DART(+) also rendered hydroxylated HCs species (O_x classes, where x ranged from
295 1 to 4) with DBEs of 1 to 4 for paraffin samples. Oxidation reactions occur at high
296 temperature and atmospheric pressure between HCs species and generated short-lifetime
297 oxygen-based species such as OH, OOH radicals and H₃O⁺. DART(+)-MS and CID
298 experiments (MS² and MS³) were also able to identify porphyrin standard compounds as [M
299 + H]⁺ ions with *m/z* 615.2502 and 680.1763, where M = C₄₄H₃₀N₄ and C₄₄H₂₈N₄OV,
300 respectively.

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305

306

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