Some Commonly Used Ionization Techniques

- Electron Ionization (EI)
- Chemical Ionization (CI)
- Electrospray (ESI) / Nanospray
- Desorption Techniques
  - Matrix-Assisted Laser Desorption/Ionization (MALDI)
  - Fast Atom Bombardment (FAB)
- Ambient: DESI / DART
- Ionization for Elemental Analysis
  - Thermal Ionization Source
  - Spark Source
  - Glow Discharge
  - Inductively-Coupled Plasma (ICP)

Q: why are so many ionization techniques used in MS?
Effect of Ionization Techniques

- Same molecule analyzed by 4 techniques
- Clicker Q: which is preferable: A, B, C, D, or E: it depends

Chemical Ionization (CI)

Introduced in 1966 by Munson and Field, it was a direct outgrowth of fundamental studies of ion/molecule interactions.

Where other techniques rely on interaction of molecule and electron, photon, or electric field, ionization of the analyte molecule, M, is achieved through reaction with a reagent ion, R⁺

CI Method of Munson & Field (Still used)

1. Reagent species is ionized by high-pressure* electron ionization
   \[ e^- + R \rightarrow R^+ + 2e^- \]
2. Collision of reagent ion with gas-phase analyte (present at <1% abundance of reagent) yields analyte ion
   \[ R^+ + M \rightarrow M_i^+ + R_1 \]
3. Potential fragmentation of M⁺ by one or more pathways
   \[ M_i^+ \rightarrow M_2^+ + N_2 \rightarrow M_3^+ + N_3 \]
   \[ \rightarrow M_4^+ + N_4 \]

*: how high P? Remember prob of an electron leading to ionization is \(~3 \times 10^{-7}\) at P = \(10^{-7}\) Torr

1. Munson and Field, JACS, 1966, Suggested reading on course web page
Clicker Q: Pressure in CIMS?

- If a typical ionizer for atmospheric chemistry CIMS is 50 cm$^3$ and with a residence time of 100 ms and a reagent ion mole fraction of 100 ppb, what pressure should it be operated at?
  
  A. 0.1-1 atm
  B. 1-100 mbar
  C. 0.01-mbar
  D. 0.001 mbar
  E. I don’t know

CI Ion Source

From Barker

Similar to EI source.
- Higher P
- Simultaneous introduction of M and R
Many different chemistries used depending of what one wants

A CU ANYL student developed a new chemistry as part of his PhD:

- CH$_3$COO$^-$ + R-COOH $\rightarrow$ CH$_3$COOH + R-COO$^-$

  - proton abstraction by acetate ion
  - http://dx.doi.org/10.1016/j.ijms.2008.04.032
  - Used by multiple groups now, including ours
Gas-Phase Ion-Molecule Reactions

\[ \text{Cl}^- + \text{CH}_3\text{Br} \rightarrow \text{CH}_3\text{Cl} + \text{Br}^- \]

From Hoffmann

Figure 1.36
Potential energy diagram for a substitution reaction in the gas phase and in solution in water\(^5\)

Gas-Phase IMRs Notes

- **Condensed Phase**
  - Molecules are strongly **solvated**
  - Ions even more so
  - High activation energies to break the solvation cage
  - Also **continuous exchange of energy from collisions**

- **Gas Phase**
  - Interaction of naked ion with molecule is exothermic
    - Ion-molecule complex formation
  - Energy remains in the complex due to lack of collisions (low-pressure), allowing it to overcome the barrier
  - Non-equilibrium!!
Solvation in IMRs

Figure 1.37
(A) CH₃Br; (B) CH₃OH. Potential energy profile for differently solvated ions reacting with molecules. (Reproduced (modified) from Ref. 76 with permission)

Efficiency of IMRs

- Approx. every collision leads to a proton transfer, if $\Delta G^0 < 0$

Figure 1.38
The natural logarithm of the number of reactions per collision ratio indicates that the proton transfer is almost 100% efficient when the process is exergonic. When it becomes endergonic, the efficiency drops sharply. (Reproduced (modified) from Ref. 77 with permission)
Proton transfer reaction - mass spectrometry

\[ H_3O^+ + VOC \rightarrow VOCH^+ + H_2O \quad \text{PA(VOC)} > \text{PA(H}_2\text{O)} \]

Clicker Question

\[ \Delta H_{\text{react}} = \text{PA(H}_2\text{O)} - \text{PA(VOC)} \]

The reaction will proceed if:
(a) If \( \Delta H \) is \text{VERY, VERY POSITIVE}
(b) If \( \Delta H \) is \text{POSITIVE}
(c) If \( \Delta H \) is \text{NEGATIVE}
(d) If \( \Delta H \) is zero
(e) If \( \Delta H \) is \text{VERY, VERY NEGATIVE}

\text{Note: PA = Proton Affinity: energy released (or absorbed if < 0) when a proton attaches to a molecule}
- Note sign convention is reversed!
### Reagent Gases Used in H+ Addition CI

<table>
<thead>
<tr>
<th>Reagent gas</th>
<th>Predominant reactant ions</th>
<th>Proton affinity (kcal/mol)</th>
<th>Hydride affinity (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>He-H⁺</td>
<td></td>
<td>101.2</td>
<td>270</td>
</tr>
<tr>
<td>CH₃⁺</td>
<td></td>
<td>82</td>
<td>266</td>
</tr>
<tr>
<td>CH₂⁺</td>
<td></td>
<td>159</td>
<td>269</td>
</tr>
<tr>
<td>CH⁺</td>
<td></td>
<td>196.5</td>
<td>225.1</td>
</tr>
<tr>
<td>H⁺</td>
<td></td>
<td>204.0</td>
<td>225.1</td>
</tr>
</tbody>
</table>

From Watson

TABLE 8.1: Characteristics of reagent gases for CI

http://www.kore.co.uk/paffinities.htm
The analyte molecule M is known to be ionized by a proton transfer mechanism with both methane or isobutane. **Which of the options below is true?**

(A) PA(M) > 8.5 eV  
(B) 5.7 eV < PA(M) < 8.5 eV  
(C) PA(M) < 5.7 eV  
(D) None of the above  
(E) I don’t know

---

Which reagent gas is more likely to yield fragmentation of M?

(A) Isobutane  
(B) Methane  
(C) Depends on structure of M  
(D) It cannot be determined without additional info  
(E) I don’t know
Fragmentation

**EI**

**Cl, R= Methane (PA=5.7 eV)**

**Cl, R= Isobutane (PA=8.5 eV)**

**NOTE**

- Many instruments include dual sources: CI for molecular weight; EI for ID by fragmentation
- The not fully predictable nature of CI fragmentation prevents development of spectral libraries.

---

Selective Detection by choosing CI reagent

**Q:** the proton affinity of butyl methacrylate is:

(a) Lower than that of hydrocarbons
(b) Higher than that of hydrocarbons
(c) Equal to that of hydrocarbons
(d) I don’t know

---

Figure 1.5
The EI (top), methane CI (middle) and isobutane CI (bottom) mass spectra of butyl methacrylate. The ionization techniques (EI vs. CI) and the reagent gases (methane vs. isobutane) influence the amount of fragmentation and the prominence of the protonated molecular ions detected at 143 Th.

From de Hoffmann

Figure 1.10
Gas chromatography/mass spectrometry total ion current (TIC) traces of butyl methacrylate dissolved in C11–C12 saturated hydrocarbon. (A) Electron ionization. The peak corresponding to butyl methacrylate is marked by a dot. The peaks following are C11 saturated hydrocarbons. (B) Same trace obtained by chemical ionization using methane as the reagent gas. Butyl methacrylate (dot) is still well detected, and the hydrocarbon peaks are attenuated. (C) Chemical ionization using isobutane as the reagent gas. Butyl methacrylate is detected well but the hydrocarbon peaks are virtually non-existent.

From de Hoffmann
Potential Complexity of Reagent Ions

 Relevant reaction:
\[ \text{CH}_4 + \text{H}^+ \rightarrow \text{CH}_5^+ \]
\[ \text{PA(\text{CH}_4)} = \Delta \text{H} = 131 \text{ kcal mol}^{-1} \]

 Relevant reaction:
\[ \text{C}_2\text{H}_5^+ + \text{CH}_4 \rightarrow \text{C}_2\text{H}_5^+ + \text{H}_2 \]
\[ \text{PA(\text{C}_2\text{H}_5^+)} = \Delta \text{H} = 162.6 \text{ kcal mol}^{-1} \]
1. Generation of ions
2. Ion selection: H₂O⁺, NO⁺ and O₂⁻
3. Sample introduction and reaction
4. Selection of reaction products
5. Detection.

---

Proton-Transfer Reaction MS

http://www.ptrms.com/
Switchable Reagent Ions in PTRMS

<table>
<thead>
<tr>
<th>REAGENT</th>
<th>ION</th>
<th>TECHNOLOGY</th>
<th>MAIN BENEFITS, DETECTABLE SUBSTANCES AND EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O⁺</td>
<td>PTR-MS</td>
<td></td>
<td>Most common volatile organic compounds (VOCs), e.g. aldehydes, ketones, acids, esters, alcohols, aromatic compounds, nitriles, amines, oximes, fumaric, fumins, sulfoxides, with a detection limit down to the sub-ppt range.</td>
</tr>
<tr>
<td>NO⁺</td>
<td>SRI</td>
<td></td>
<td>Similar to H₂O⁺, especially advantageous for the separation of aldehydes and ketones, carboxylic acids and esters, carboxylic acids and alcohols, etc.</td>
</tr>
<tr>
<td>O₃⁺</td>
<td>SRI</td>
<td></td>
<td>Additionally e.g. ethylene and acetylene and nearly all halocarbons (chlorine, bromine, iodine and iodine) can be detected.</td>
</tr>
<tr>
<td>Kr⁺</td>
<td>SRI*</td>
<td></td>
<td>The Universal Trace Gas Analyzer: e.g. CO, CO₂, SO₂, NO, NO₂ and all above mentioned can be detected with IONICON instruments incl. SR-I.</td>
</tr>
</tbody>
</table>


Aerodyne ToF-CIMS

Fig. 1. Schematic of the chemical ionization source and four stage (S1–S4) differentially pumped interface coupled to the time-of-flight mass spectrometer (TOFMS, 5 × 10⁻⁷ mbar). The high pressure interface consists of (i) ion-molecule reaction (IMR) chamber (S1, 85 mbar), (ii) collisional dissociation chamber (CDC) (S2, 2 mbar), (iii) stage 3 that houses a second RF-only segmented quadrupole (S3, 1.5 × 10⁻⁵ mbar), and (iv) stage 4 that houses a series of DC optics that focus and accelerate the primary beam into the TOFMS (S4, 3.5 × 10⁻⁷ mbar). DC voltages applied to the focusing electrodes under different dechannelling conditions, are shown in the inset figure, as a function of the distance from the entrance aperture.

An Aircraft CIMS Instrument

**Figure 1.** Schematic of the Caltech CIMS instrument as utilized on the NASA DC-8.

Atmospheric Pressure CI (APCI)

- A method for coupling CI to liquid chromatography
- Heat and gas flow desolvate nebulizer droplets, yield dry vapor of solvent and analyte molecules.
- Corona discharge ionizes solvent, which in turn acts as CI reagent.
- Not suitable for very nonvolatile or thermally labile samples. For these, electrospray is the method of choice.