Chemical Ionization (CI, PICI, NICI)

Mass spectrometrists have been always searching for ionization methods softer than EI, because molecular weight determination can be important for structure elucidation.

Historically, Chemical Ionization (CI) can be regarded as the second soft ionization method introduced in analytical mass spectrometry.

CI goes back to experiments of Talrose in the early 1950s and was developed to an analytically useful technique by Munson and Field in the mid-1960s.

Note: when a positive ion results from CI, the term may be used without qualification; nonetheless the term positive-ion chemical ionization (PICI) is frequently found in the literature.

When negative ions are formed, the term negative-ion chemical ionization (NICI) should be used.
Basics of (Positive-Ion) Chemical Ionization

In positive-ion chemical ionization (PICI) new ionized species are formed when gaseous molecules interact with ions. CI may involve the transfer of an electron, proton or other charged species between the reactants.

The reactants are:

i) the neutral analyte M

ii) ions from a reagent gas (methane, isobutane, ammonia, etc.)

Bimolecular processes are used to generate analyte ions. The occurrence of bimolecular reactions requires a sufficiently large number of ion-molecule collisions in the ion source, i.e. a non negligible partial pressure of the reagent gas.

Assuming reasonable collision cross sections and an ion source residence time of 1 μs a molecule will undergo 30–70 collisions at an ion source pressure of about $2.5 \times 10^2 \text{ Pa} = 0.002 \text{ atm} = 1.9 \text{ torr}$.

A $10^3$–$10^4$-fold excess of reagent gas is then required; such an excess is also useful to shield the analyte molecules from ionizing primary electrons i.e. to suppress competing direct EI of the analyte.
Four general pathways are hypothesized to form ions from a neutral analyte M in (positive) CI:

\[
\begin{align*}
M + [BH]^+ & \rightarrow [M+H]^+ + B \quad \text{proton transfer} \\
M + X^+ & \rightarrow [M+X]^+ \quad \text{electrophilic addition} \\
M + X^+ & \rightarrow [M-A]^+ + AX \quad \text{anion abstraction} \\
M + X'^+ & \rightarrow M'^+ + X \quad \text{charge exchange}
\end{align*}
\]

✓ A competitive generation of [M-H]⁻ ions, due to proton abstraction, has to be considered in the case of acidic analytes.

✓ Electrophilic addition is typical of NH₄⁺ ions when ammonia is used as reagent gas.

✓ Hydride abstractions are common examples of anion abstraction, typical for aliphatic alcohols.

✓ Charge exchange yields radical ions with low internal energy, which behave similarly to molecular ions in low-energy EI.
Chemical Ionization Ion Sources

CI ion sources are very similar to EI ones. In fact, modern EI ion sources are constructed as EI/CI combined ion sources and can be usually switched to CI operation in seconds:

The CI ion source has to be modified in order to hold a comparatively high pressure of reagent gas (about $10^2$ Pa) without allowing too much leakage into the ion source housing.

During CI operation the pressure in the ion source typically rises by a remarkable factor, compared to the background pressure of the instrument, thus sufficient pumping speed ($\geq 200$ L s$^{-1}$) is necessary to maintain stable operation in CI mode.
Source of Protons in CI: self-CI

A possible source of protons in CI can be the analyte itself: the occurrence of \([M+H]^+\) ions due to bimolecular processes between ions and their neutral molecular counterparts is called autoprotonation or self-CI.

Self-CI is an unwanted phenomenon in EI-MS. \([M+H]^+\) ions from autoprotonation become more probable with increasing pressure and with decreasing temperature in the ion source (the formation of \([M+H]^+\) ions is promoted if the analyte is highly volatile or contains acidic hydrogens).

Self-CI can mislead mass spectral interpretation either by leading to an overestimation of the number of carbon atoms from the M+1 isotopic peak or by indicating a 1 u higher molecular mass.
Methane Reagent Gas Plasma

Methane is a typical source of protons in CI. Indeed, raising the partial pressure of methane to $10^2$ Pa in a typical EI source significantly alters the resulting mass spectrum:
The positive ion CI spectrum of methane can be explained as the result of competing and consecutive bimolecular reactions in the ion source:

\[
\text{CH}_4 + e^- \rightarrow [\text{CH}_4^+], \text{CH}_3^+, \text{CH}_2^+, \text{CH}^+, \text{C}^+, \text{H}_2^+, \text{H}^+ \\
\text{[CH}_4^+ + \text{CH}_4 \rightarrow [\text{CH}_5^+] + \text{CH}_3^+ \\
\text{CH}_3^+ + \text{CH}_4 \rightarrow [\text{C}_2\text{H}_7^+] \rightarrow \text{C}_2\text{H}_5^+ + \text{H}_2 \\
\text{CH}_2^+ + \text{CH}_4 \rightarrow \text{C}_2\text{H}_4^+ + \text{H}_2 \\
\text{CH}_2^+ + \text{CH}_4 \rightarrow \text{C}_2\text{H}_3^+ + \text{H}_2 + \text{H}^+ \\
\text{C}_2\text{H}_3^+ + \text{CH}_4 \rightarrow \text{C}_3\text{H}_5^+ + \text{H}_2 \\
\text{C}_2\text{H}_5^+ + \text{CH}_4 \rightarrow \text{C}_3\text{H}_7^+ + \text{H}_2
\]

The relative abundances of the reported product ions are influenced dramatically by the ion source pressure and temperature.
The effects can be observed by comparing the contribution to the total intensity of ions with m/z > 12 (% $\Sigma_{12}$) of different product ions arising from EI (at 100 eV) on methane under different pressure/temperature conditions:

It is apparent that ions generated by ion-molecule interactions (and not by direct EI) increase their amount at higher pressures.
Fortunately, the typical ion source pressure in CI, about $10^2$ Pa, is in the plateau region of the pressure dependence, thus ensuring reproducible CI conditions.

Interestingly, the amount of very unstable species, like $\text{CH}_5^+$, is slightly increased at higher temperatures.
“Exotic” ions involved in methane-Cl: CH$_5^+$ and C$_2$H$_7^+$

Protonated methane and ethane, CH$_5^+$ and C$_2$H$_7^+$, represent reactive and fascinating species present in the methane reagent gas plasma. Their structures have been predicted by calculations and experimentally verified.

The chemical behavior of the CH$_5^+$ ion, also called methanium, appears to be compatible with a stable structure involving a three-center/two-electron bond, associating 1 hydrogen atom, 1 proton and the carbon atom:

Rearrangement of this structure due to the exchange between one of the hydrogen atoms involved in the three-center/two-electron bond and one of the three remaining hydrogen atoms, often called pseudorotation, appears to be a fast process that is induced by interactions with the chemical ionization gas.
Several isomers can be hypothesized for the C$_2$H$_7^+$ ion, also called ethanium. The bridged isomer shown in the figure, with a H$^+$ ion placed between the two carbon atoms, is considered the most stable one.

It is worth noting that a three-center/two-electron bond has to be invoked also to explain the structure of the methane radical cation, CH$_4^+$, the precursor of methane-related ions, generated through electron ionization:
Energetics of Protonation

The tendency of a (basic) molecule B to accept a proton is quantitatively described by its proton affinity PA.

The protonation process can be described as follows:

\[ B_g + H_g^+ \rightarrow [BH]_{g}^+; \quad -\Delta H_f^0 = PA_{(B)} \]

Under the conditions of CI the PA of the neutral analyte M has to be compared with that of the complementary base, B, of the proton-donating reactant ion \([BH]^+\) (Brønsted acid).

Protonation will occur as long as the process is exothermic, i.e., if \(PA(B) < PA(M)\). The heat of reaction has to be distributed basically among the degrees of freedom of the \([M+H]^+\) analyte ion.

As a result, the minimum internal energy of the \([M+H]^+\) ions is determined by:

\[ E_{int(M+H)} = PA_{(M)} - PA_{(B)} \]
If the proton affinities are known predictions can be made about the possibility that a particular analyte will be protonated under certain CI conditions.

**PA for compounds usually adopted as reactant gases in CI are:**

<table>
<thead>
<tr>
<th>Reagent Gas</th>
<th>Reactant Ions</th>
<th>Neutral from Reactant Ions</th>
<th>PA of Neutral Product</th>
<th>Analyte Ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂</td>
<td>H₃⁺</td>
<td>H₂</td>
<td>424</td>
<td>[M+H]⁺, [M−H]⁺</td>
</tr>
<tr>
<td>CH₄</td>
<td>CH₃⁺, (C₂H₅⁺ and C₃H₅⁺)</td>
<td>CH₄</td>
<td>552</td>
<td>[M+H]⁺ ([M+C₂H₅]⁺ and [M+C₃H₅]⁺)</td>
</tr>
<tr>
<td>NH₃</td>
<td>NH₄⁺</td>
<td>NH₃</td>
<td>854</td>
<td>[M+H]⁺, [M+NH₄]⁺</td>
</tr>
</tbody>
</table>
These values can be directly compared with those relevant to other compounds (including possible reagent gases):

<table>
<thead>
<tr>
<th>Conjugate base (B)</th>
<th>Reagent ion</th>
<th>$PA(B) \text{ kJ mole}^{-1}$†</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H}_2$</td>
<td>$\text{H}_3^+$</td>
<td>423</td>
</tr>
<tr>
<td>$\text{CH}_4$</td>
<td>$\text{CH}_5^+$</td>
<td>536</td>
</tr>
<tr>
<td>$\text{C}_2\text{H}_6$</td>
<td>$\text{C}_2\text{H}_7^+$</td>
<td>585</td>
</tr>
<tr>
<td>$\text{H}_2\text{O}$</td>
<td>$\text{H}_3\text{O}^+$</td>
<td>712</td>
</tr>
<tr>
<td>$\text{CH}_3\text{OH}$</td>
<td>$\text{CH}_3\text{OH}_2^+$</td>
<td>762</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CN}$</td>
<td>$\text{CH}_3\text{CNH}^+$</td>
<td>782</td>
</tr>
<tr>
<td>$(\text{CH}_3)_2\text{C} = \text{CH}_2^*$</td>
<td>$(\text{CH}_3)_3\text{C}^+$ *</td>
<td>810</td>
</tr>
<tr>
<td>$\text{NH}_3$</td>
<td>$\text{NH}_4^+$</td>
<td>847</td>
</tr>
<tr>
<td>$\text{CH}_3\text{NH}_2$</td>
<td>$\text{CH}_3\text{NH}_3^+$</td>
<td>884</td>
</tr>
<tr>
<td>$\text{NH}_2(\text{CH}_2)_2\text{NH}_2$</td>
<td>$\text{NH}_2(\text{CH}_2)_2\text{NH}_3^+$</td>
<td>936</td>
</tr>
</tbody>
</table>

* Reagent ion from isobutane.
† $100 \text{ kJ mole}^{-1} = 23.9 \text{ kcal mole}^{-1} = 1.04 \text{ eV}$.

Any reagent ion is able to protonate the conjugate base placed in a lower row of the table.

In case several analytes are present in the sample, reagent ions with higher PAs will provide a better selectivity.
As an example, CH$_5^+$ will protonate C$_2$H$_6$ because:

\[ \Delta PA = PA(\text{CH}_4) - PA(\text{C}_2\text{H}_6) = 536 - 585 = -49 \text{ kJ mol}^{-1} \]

The product of this process is C$_2$H$_7^+$. In fact, C$_2$H$_7^+$ is easily stabilized by H$_2$ loss to yield C$_2$H$_5^+$, i.e. protonated ethene.

When ammonia is used as reagent gas, only amines and amides can be actually protonated, yet positive ionization can occur also by electrophilic addition of NH$_4^+$.

On the other hand, molecular hydrogen is the most exothermic of all the protonating reagent gases, leading to a considerable fragmentation. The latter is complicated by hydrogenation processes, making CI spectra less predictable.

Nonetheless, H$_2$ - based CI has proved to be of practical value in special cases, i.e. to ionize hardly ionizable molecules, for example in the MS analysis of tetrapyrroles.
It is worth noting that the difference in PAs also influence the internal energy deposited into the analyte ion. Higher differences lead to higher internal energies and, consequently, to a significant fragmentation.

As an example, CI of methyl stearate by methane and by isobutane leads to slightly different fragmentation extents:
Use of milder reagent gases in CI: effect of source temperature

When milder reagent gases, like isobutane or ammonia, are used in CI additional thermal energy can be transferred by raising the source temperature.

The final effect is increasing fragmentation, although the molecular ion is still present in the mass spectrum:

![Effect of temperature on CI spectra of geraniol](image)

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<table>
<thead>
<tr>
<th>Ion source temperature (°C)</th>
<th>CH₄ CI Ion mass (intensity)</th>
<th>NH₃ CI Ion mass (intensity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>170</td>
<td>M - 1 (9)</td>
<td>M + 18 (2)</td>
</tr>
<tr>
<td></td>
<td>M - 17 (100)</td>
<td>M (29)</td>
</tr>
<tr>
<td></td>
<td>+ other fragment ions</td>
<td>M - 17 (100)</td>
</tr>
<tr>
<td>135</td>
<td>M - 1 (7)</td>
<td>M + 18 (7)</td>
</tr>
<tr>
<td></td>
<td>M - 17 (100)</td>
<td>M (56)</td>
</tr>
<tr>
<td></td>
<td>+ other fragment ions</td>
<td>M - 17 (100)</td>
</tr>
<tr>
<td>110</td>
<td>M - 1 (9)</td>
<td>M + 18 (28)</td>
</tr>
<tr>
<td></td>
<td>M - 17 (100)</td>
<td>M (100)</td>
</tr>
<tr>
<td></td>
<td>+ other fragment ions</td>
<td>M - 17 (88)</td>
</tr>
</tbody>
</table>
Impurities with higher PA than the reagent gas: the case of water

If present, impurities of the reagent gas having a higher PA are protonated by the reagent ion. Residual water is a frequent source of contamination. High concentrations of water in the reagent gas may alter its properties remarkably. In fact, $\text{H}_3\text{O}^+$ becomes the predominant species in a CH$_4$/H$_2$O mixture under CI conditions:
Methane Reagent Gas: PICI Spectra

Methane is one of the most common reagent gases used in CI: as a result, a \([M+H]^+\) quasi-molecular ion is obtained and often represents the base peak in PICI spectra obtained using methane as a reagent gas.

Since \(\text{CH}_4\)-mediated protonation is generally exothermic by 1–4 eV the extent of fragmentation of the resulting \([M+H]^+\) ions is much lower than that observed for the same analyte under 70 eV EI conditions:
The possible explanations for such behaviour are:

✓ [M+H]$^+$ ions have a narrow internal energy distribution

✓ fast radical-induced bond cleavages are prohibited, because only intact molecules are usually eliminated from even-electron ions like [M+H]$^+$.

Less common pathways in CH$_4$-Cl are:

✓ Hydride abstraction, leading to [M–H]$^+$ ions;

✓ Electrophilic addition, giving rise to [M+C$_2$H$_5$]$^+$ and [M+C$_3$H$_5$]$^+$ adduct ions, corresponding to [M+29] and [M+41] peaks.
Other Reagent Gases in PICl

Molecular hydrogen and hydrogen-containing mixtures, isobutane, ammonia, di-methyl-ether, di-isopropyl-ether, acetone, acetaldehyde, benzene, and iodomethane are also adopted as reagent gases in CI.

The choice will depend on the fragmentation extent required.

Even transition metal ions such as Cu$^+$ and Fe$^+$ can be employed as reactant ions, usually to locate double bonds.

Isobutane is an especially versatile reagent gas, because:

- it provides low fragmentation PICl spectra;
- it generates almost exclusively one well-defined adduct ([M+C$_4$H$_9$]$^+$, [M+57]), if any;
- it can be also employed for electron capture.
Comparison between EI and CI spectra of isobutane and ammonia:
Comparison between EI (70 eV) and isobutane-Cl spectra: glycerol
A complex sample: isobutane-Cl spectrum for the gastric content in an overdose case.

Only quasi-molecular ions ([M+H]^+) are obtained for most drugs. The only drug undergoing fragmentation is aspirin.
Charge Exchange Chemical Ionization

Charge exchange (CE) or charge transfer ionization occurs when an ion-neutral reaction takes place and the ionic charge is transferred to the neutral:

\[ X^{+•} + M \rightarrow M^{+•} + X \]

In principle, any of the reagent systems discussed so far is capable to effect CE-CI because the respective reagent molecular ions \( X^{+•} \) are also present in the source.

However, other processes, in particular proton transfer, are prevailing with methane, isobutane, and ammonia, for example.

Reagent gases suitable for CE should exhibit abundant molecular ions even under the conditions of CI, whereas potentially protonating species have to be absent or at least have minor abundance.
Energetics of Charge Exchange

The energetics of CE are determined by:

✓ the ionization energy (IE) of the neutral analyte, IE(M),

✓ the recombination energy of the reagent ion, RE(X⁺⁺).

Recombination of an atomic or molecular ion with a free electron is the inverse of its ionization. RE(X⁺⁺) is defined as the exothermicity of the gas phase reaction:

\[ X^{++} + e^- \rightarrow X; \quad -\Delta H_r = RE_{(X^{++})} \]

For monoatomic ions RE has the same numerical value as the IE of the neutral atom; for diatomic or polyatomic species differences due to storage of energy in internal modes or electronic excitation may occur.

Ionization of the analyte via CE is effected if:

\[ RE_{(X^{++})} - IE_{(M)} > 0 \]
The heat of reaction, and thus the minimum internal energy of the analyte molecular ion, is given by:

\[ E_{\text{int}(\text{M}^+\cdot)} \geq \text{RE}_{(\text{X}^\ast\ast)} - \text{IE}_{(\text{M})} \]

where the ≥ symbol indicates a possible thermal energy contribution.

In summary:

- no CE is expected if \( \text{RE}(\text{X}^\ast\ast) < \text{IE}(\text{M}) \);
- predominantly \( \text{M}^{++} \) ions are expected if \( \text{RE}(\text{X}^\ast\ast) \) is slightly above \( \text{IE}(\text{M}) \);
- extensive fragmentation will be observed if \( \text{RE}(\text{X}^\ast\ast) \) is much greater than \( \text{IE}(\text{M}) \).

Accordingly, the “softness” of CE-CI can be adjusted by choosing a reagent gas of suitable RE. Fortunately, the differences between REs and IEs are small, and, unless high accuracy is required, IE data may be used to estimate the effect of a CE reagent gas.
Reagent gases for charge exchange – chemical ionization (CE-CI)

Typically, pure compounds are employed for CE-CI.

Occasionally, they are diluted with nitrogen, acting as an inert or, sometimes, reactive, buffer gas:

<table>
<thead>
<tr>
<th>Reagent Gas</th>
<th>Reactant Ion</th>
<th>RE or RE range [eV]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₆H₅NH₂</td>
<td>C₆H₅NH₂⁺⁺</td>
<td>7.7</td>
</tr>
<tr>
<td>C₆H₅Cl</td>
<td>C₆H₅Cl⁺⁺</td>
<td>9.0</td>
</tr>
<tr>
<td>C₆H₆</td>
<td>C₆H₆⁺⁺</td>
<td>9.2</td>
</tr>
<tr>
<td>NO⁺ : N₂ = 1:9</td>
<td>NO⁺</td>
<td>9.3</td>
</tr>
<tr>
<td>C₆F₆ : CO₂ = 1 : 9</td>
<td>C₆F₆⁺⁺</td>
<td>10.0</td>
</tr>
<tr>
<td>CS₂ : N₂ = 1 : 9</td>
<td>CS₂⁺⁺</td>
<td>9.5–10.2</td>
</tr>
<tr>
<td>H₂S</td>
<td>H₂S⁺⁺</td>
<td>10.5</td>
</tr>
<tr>
<td>COS : CO = 1 : 9</td>
<td>COS⁺⁺</td>
<td>11.2</td>
</tr>
<tr>
<td>Xe</td>
<td>Xe⁺⁺</td>
<td>12.1, 13.4</td>
</tr>
<tr>
<td>N₂O : N₂ = 1 : 9</td>
<td>N₂O⁺⁺</td>
<td>12.9</td>
</tr>
<tr>
<td>CO₂</td>
<td>CO₂⁺⁺</td>
<td>13.8</td>
</tr>
<tr>
<td>CO</td>
<td>CO⁺⁺</td>
<td>14.0</td>
</tr>
<tr>
<td>Kr</td>
<td>Kr⁺⁺</td>
<td>14.0, 14.7</td>
</tr>
<tr>
<td>N₂</td>
<td>N₂⁺⁺</td>
<td>15.3</td>
</tr>
<tr>
<td>H₂</td>
<td>H₂⁺⁺</td>
<td>15.4</td>
</tr>
<tr>
<td>Ar</td>
<td>Ar⁺⁺</td>
<td>15.8, 15.9</td>
</tr>
<tr>
<td>Ne</td>
<td>Ne⁺⁺</td>
<td>21.6, 21.7</td>
</tr>
<tr>
<td>He</td>
<td>He⁺⁺</td>
<td>24.6</td>
</tr>
</tbody>
</table>

COS: carbon oxy-sulphide
In CE-CI the reagent gas is typically admitted at somewhat lower pressure (15–80 Pa) compared to CI based on proton transfer.

The comparison of CE-CI spectra obtained for cyclohexene using different reagent gases shows how the fragmentation extent can be modulated by exploiting their differences in recombination energies:
Gases having high RE values, such as N$_2$ and Ar, cause extensive fragmentation, so that they are principally used as components of mixed reagent gas systems such as argon-water and nitrogen-nitric oxide.

EI of Ar containing a small percentage of water affords abundant ions with $m/z$ 40 ($\text{Ar}^{+}$) and $m/z$ 19 ($\text{H}_3\text{O}^+$).

$\text{Ar}^{+}$ causes charge exchange followed by fragmentation.

$\text{H}_3\text{O}^+$ acts as a proton transfer reagent giving abundant quasi-molecular ($\text{M+H}$)$^+$ ions that undergo little fragmentation.
CE-CI selective towards compound classes

The energy distribution upon CE-CI largely differs from that obtained upon EI in that the CE process delivers an energetically well-defined ionization of the neutral.

Choosing the appropriate reagent gas allows for the selective ionization of a targeted compound class contained in a complex mixture. The differentiation is possible due to the characteristic range of ionization energies for each compound class.

This property of CE-CI can also be applied to construct breakdown curves from a set of CE-CI mass spectra using reactant ions of stepwise increasing $\text{RE}(X^{++})$, e.g. $\text{C}_6\text{F}_6^{++}$, $\text{CS}_2^{++}$, $\text{COS}^{++}$, $\text{Xe}^{++}$, $\text{N}_2\text{O}^{++}$, $\text{CO}^{++}$, $\text{N}_2^{++}$. 
CE-CI allows for the direct determination of the molecular weight distributions of the major aromatic components in liquid fuels and other petroleum products.

The approach involves selective CE between $C_6H_5Cl^+$ and the substituted benzenes and naphtalenes in the sample:
Regio- and Stereo-selectivity in CE-CI

Small differences in activation energy (AE) can be exploited in CE-CI to distinguish between regio- or stereo-isomers, using a fine control of internal energy.

As an example, the CE-CI spectra obtained for epimeric 4-methylcyclohexanols using C₆F₆⁺⁺ as reagent gas differ substantially in the extent of water loss (M⁺⁺/[M–H₂O]⁺⁺ ratios: 0.09 for trans, 2.0 for cis)

Indeed, the 1,4–H₂O elimination proceeds quite easily in the trans isomer, whereas internal energy afforded by CE-CI is not high enough to promote the more energetically demanding elimination from the cis isomer.
Negative Ion Chemical Ionization (NICI)

Under CI conditions, negatively charged ions can be generated by using:

✓ electrons having near thermal energy;

✓ negatively charged reagent ions, if stable anions can be formed from the reagent gas.

If their increase is promoted such species can trigger NICI through the following mechanisms:

❖ capture of thermal electrons by the sample molecules

❖ ion-molecule reactions between sample molecules and reagent gas negative ions.
Electron capture: generating thermal electrons

Thermoionic emission from a heated metal filament is the standard source of free electrons in EI or related techniques. However, emitted electrons are highly energetical and need to be decelerated in order to promote subsequent electron capture.

Gases such as methane, isobutane, or carbon dioxide, filling the ionization chamber, are suitable for this purpose. Such gases yield almost no negative ions themselves, while moderating the energetic electrons energy to thermal energy.

Despite inverse polarity of the extraction voltage, the same conditions as those for PICI can be usually applied. However, EC is sensitive to ion source conditions, in particular temperature.

Lowering the ion source temperature provides lower-energy electrons: assuming Maxwellian energy distribution the mean electron energy is 0.068 eV at 250 °C and 0.048 eV at 100 °C.
Negative ion formation by electron capture

When a neutral molecule interacts with an electron of high kinetic energy, a positive radical ion is generated by EI.

If the electrons have less energy than the IE of the respective neutral, EI is prohibited. As the electrons approach thermal energy, EC can occur instead.

Three different mechanisms of ion formation are hypothesised under EC conditions:

\[
\begin{align*}
M + e^- \rightarrow M^*; & \quad \text{resonance electron capture} \\
M + e^- \rightarrow [M-A]^- + A^* & \quad \text{dissociative electron capture} \\
M + e^- \rightarrow [M-B]^- + B^+ + e^- & \quad \text{ion-pair formation}
\end{align*}
\]

The electron energy ranges for the three processes are, respectively:
- resonance EC $\Rightarrow 0 - 2$ eV
- dissociative EC $\Rightarrow 0 - 10$ eV
- Ion pair formation $\Rightarrow > 10$ eV
Three subsequent stages can be hypothesised for electron capture-NICI. As an example, negative ionization of nitrobenzene in the presence of methane as reagent gas can be visualized as follows:

\[
\begin{align*}
\text{e}^- & \xrightarrow{\text{CH}_4} \text{e}^-_{\text{th}} & \text{production of thermal electrons by \text{CH}_4-}\text{-mediated deceleration of emitted electrons} \\
\text{e}^-_{\text{th}} + \text{C}_6\text{H}_5\text{NO}_2 & \rightarrow \text{C}_6\text{H}_5\text{NO}_2^- \cdot * & \text{resonance capture process} \\
\text{C}_6\text{H}_5\text{NO}_2^- \cdot * & \xrightarrow{\text{\text{CH}_4}} \text{C}_6\text{H}_5\text{NO}_2^- & \text{collisional stabilization} \\
\text{C}_6\text{H}_5\text{NO}_2^- + \text{e}^- & \rightarrow \text{C}_6\text{H}_5\text{NO}_2 + \text{e}^- & \text{electron auto-detachment}
\end{align*}
\]

Electron auto-detachment, leading to loss of sensitivity, can occur when the energy excess born by the generated anion is not stabilized through collisions with the reagent gas, that are favoured by relatively high pressures inside the ionization source.
Energetics of electron capture

The potential energy curves for a neutral molecule AB and for the potential ionic products generated after different electron capture processes help in making predictions about EC-NICI:

- the formation of negative molecular ions, $AB^-$, is energetically much more favorable than homolytic bond dissociation of AB

- the $AB^-$ ions (negative molecular ions) from EC are less excited than their positive counterparts arising from 70 eV EI.
A typical example of EC-NICI in which resonance electron capture is the predominant EC process is provided by polycyclic aromatic hydrocarbons (PAH):

Only the isotopic distribution of the negative molecular ion is observed in the NICI spectrum of benzo[a]pirene, obtained using isobutane as buffer gas and an ion source temperature of 200 °C.
The energetics of EC are determined by the electron affinity (EA) of the neutral. The EA is the inverse of the enthalpy of reaction for the capture of a zero kinetic energy electron by a neutral molecule or atom:

\[ M + e^- \rightarrow M^-; \quad -\Delta H_r = EA_{(M)} \]

<table>
<thead>
<tr>
<th>Compound</th>
<th>EA [eV]</th>
<th>Compound</th>
<th>EA [eV]</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbon dioxide</td>
<td>-0.600</td>
<td>pentachlorobenzene</td>
<td>0.729</td>
</tr>
<tr>
<td>naphthalene</td>
<td>-0.200</td>
<td>carbon tetrachloride</td>
<td>0.805</td>
</tr>
<tr>
<td>acetone</td>
<td>0.002</td>
<td>biphenylene</td>
<td>0.890</td>
</tr>
<tr>
<td>1,2-dichlorobenzene</td>
<td>0.094</td>
<td>nitrobenzene</td>
<td>1.006</td>
</tr>
<tr>
<td>benzonitrile</td>
<td>0.256</td>
<td>octafluorocyclobutane</td>
<td>1.049</td>
</tr>
<tr>
<td>molecular oxygen</td>
<td>0.451</td>
<td>pentafluorobenzonitrile</td>
<td>1.084</td>
</tr>
<tr>
<td>carbon disulfide</td>
<td>0.512</td>
<td>2-nitronaphthalene</td>
<td>1.184</td>
</tr>
<tr>
<td>benzo[e]pyrene</td>
<td>0.534</td>
<td>1-bromo-4-nitrobenzene</td>
<td>1.292</td>
</tr>
<tr>
<td>tetrachloroethylene</td>
<td>0.640</td>
<td>antimony pentafluoride</td>
<td>1.300</td>
</tr>
</tbody>
</table>

If EC occurs on a neutral having negative EA, the electron–molecule complex will have a short lifetime (electron auto-detachment occurs).
Dissociative electron capture

Dissociative electron capture is the typical pathway followed by negative chemical ionization of chloro-fluoro-carbides.

The potential energy curves for CF₂Cl₂ and for its dissociation products F⁻ and •CFCl₂ provide useful information on the process:

The predicted ΔH for the process is 1.48 eV, yet the appearance energy (AE) is 1.8 eV: a minimum excess energy of 0.32 eV can be estimated.
When a dissociative negative ionization occurs, NICI spectra show a significant fragmentation, becoming similar to EI spectra. In the case of 2,3,4,5-tetrachloro-nitrobenzene, ionised in the presence of methane as buffer gas, losses of NO or NO$_2$ are observed:

Note that the isotope distributions for the molecular ion and for the two main fragments show the peculiar abundance of the M+2 and M+4 isotopologues, due to the presence of several chlorine atoms on the molecular structure.
Negative ion formation by ion-molecule reactions

Ion-molecule reactions leading to negative ions in NICI can be classified into four categories:

(1) Proton transfer \[ M + X^{-} = (M-H)^{-} + XH \]

(2) Charge exchange \[ M + X^{-} \cdot = M^{-} \cdot + X \]

(3) Nucleophilic addition \[ M + X^{-} = MX^{-} \]

(4) Nucleophilic displacement \[ AB + X^{-} = BX + A^{-} \]
Proton transfer

The tendency of an anion $X^-$ to accept a proton from a particular analyte may be assessed from a knowledge of proton affinity (PA) values for $X^-$ and for the anion related to the analyte ($Y^-$).

The proton affinity of anion $X^-$ is the inverse of the change in enthalpy or heat content accompanying the following reaction:

$$X^- + H^+ \Rightarrow HX \quad \text{PA} (X^-) = -\Delta H$$

If PA($X^-$) > PA($Y^-$) a HY molecule will be able to transfer its proton to $X^-$:

$$X^- + HY \Rightarrow HX + Y^-$$
Proton affinity values for typical anions can be used to predict the evolution of proton transfers:

Each anion in the table will be able to generate any of the anions of the lower rows from the corresponding neutral species.

<table>
<thead>
<tr>
<th>Anion</th>
<th>PA(X⁻) (kJ mole⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NH₂⁻</td>
<td>1689</td>
</tr>
<tr>
<td>H⁻</td>
<td>1676</td>
</tr>
<tr>
<td>OH⁻</td>
<td>1636</td>
</tr>
<tr>
<td>O⁻</td>
<td>1595</td>
</tr>
<tr>
<td>CH₃O⁻</td>
<td>1583</td>
</tr>
<tr>
<td>(CH₃)₂CHO⁻</td>
<td>1565</td>
</tr>
<tr>
<td>CH₂CN⁻</td>
<td>1556</td>
</tr>
<tr>
<td>F⁻</td>
<td>1554</td>
</tr>
<tr>
<td>C₅H₅⁻</td>
<td>1480</td>
</tr>
<tr>
<td>O₂⁻</td>
<td>1465</td>
</tr>
<tr>
<td>CN⁻</td>
<td>1462</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>1395</td>
</tr>
</tbody>
</table>

As an example, the CH₃O⁻ anion, generated by electron ionization of methyl-nitrite:

CH₃ONO + e⁻ → CH₃O⁻ + NO

is able to generate the cyclopentadienilic anion from cyclopentadiene:
Charge exchange

The charge exchange reaction:

$$M + X^- \rightarrow M^- + X$$

will occur if the electron affinity of $M$ is greater than that of $X$.

As an example, the relatively low electron affinity of the oxygen molecule means that $O_2^-$ is able to ionize molecules with higher electron affinities by charge exchange:

\[
\begin{align*}
\text{NO}_2^- + \text{O}_2^- & \rightarrow \left[\text{NO}_2^-\right]^- + \text{O}_2 \\
\text{Cl} & \\
\text{Cl}
\end{align*}
\]

In some cases, collateral charge exchanges can lead to loss of sensitivity, as it occurs when $F^-$ radicals are present in the ion source:

$$M^- + F^- \rightarrow M + F^-$$
Nucleophilic addition

Anions having low proton affinities, thus unable to give proton transfer, like Cl\(^-\) and O\(_2\)\(^{2-}\), may form stable addition complexes by nucleophilic attack to analyte molecules.

The Cl\(^-\) ion, formed by electron ionization of CH\(_2\)Cl\(_2\), CH\(_2\)Cl\(_2\)/CH\(_4\) mixtures or Cl\(_2\)CF\(_2\), forms stable, hydrogen-bonded complexes with several acids, amides, aromatic amines and phenols.

The chloride anion also forms stable (M + Cl\(^-\)) complexes with other compounds, like polychlorinated aliphatic compounds, organo-phosphorus pesticides and (oligo) saccharides:
In special cases the $\text{O}_2^-$ ion may behave as a basic species, i.e., it can react by proton transfer with strongly acidic compounds such as nitrophenols:

\[
\begin{align*}
\text{Nitrophenol} + \text{O}_2^- & \rightarrow \text{Product} + \text{HO}_2^- \\
\end{align*}
\]

With less acidic compounds, such as aliphatic alcohols, nucleophilic addition to give $(\text{M} + \text{O}_2)^-$ ions remains the major reaction.
Nucleophilic displacement

OH$^-$ and O$^-$ (formed by electron bombardment of nitrous oxide) are both strongly basic anions so that a proton transfer leading to the formation of a (M-H)$^-$ ion is their major reaction with many compounds.

Both ions can, however, participate in nucleophilic displacement reactions with suitable compounds so that, for example, the NICI spectra of aliphatic esters (RCO$_2$R') also contain carboxylate anions (RCO$_2^-$), resulting from nucleophilic displacement with loss of R'O$^-$ radicals.

O$^-$ is a particularly strong nucleophilic species and can even displace hydrogen atoms from aromatic compounds:

$$\text{ArH} + \text{O}^- \rightarrow \text{ArO}^- + \text{H}^-$$
**Desorption Chemical Ionization (DCI)**

Desorption chemical ionization (DCI) is the definition for chemical ionization in conjunction with a direct exposure probe (or solid probe), i.e. a device able to introduce liquid or solid samples, susceptible of thermal decomposition, directly into the ionization source:

![Diagram of DCI probe](image)

In this case the analyte is applied from a solution or suspension (1-2 μL) to the outer surface of a resistively heated thin wire loop or coil (usually made of platinum).

Afterwards, the analyte is directly exposed to the reagent gas while being rapidly heated (through Joule effect) at rates of several hundreds °C s⁻¹, up to temperatures of 1500 °C.
The rapid heating of the sample plays a key role in generating intact molecular species rather than pyrolysis products. Sometimes a laser can be used to achieve an extremely fast evaporation from the probe prior to chemical ionization.

Analytes that benefit most from the characteristics of DCI are:

- relatively high molecular weight natural compounds, like alkaloids, sugars, steroids
- organometallics, e.g. organo-arsenic compounds in marine or terrestrial environment
- additives in polymer extracts
For some analytes even a rapid heating of the probe leads to pyrolysis, thus making DCI mass spectra (usually labelled as Py-DCI spectra) more complex than typical CI spectra:

As an example, the DCI spectrum (m/z range: 140 to 700) of cellulose acquired using NH$_3$ as reagent gas at 100 eV electron energy is the following:

![NH$_3$-Py-DCI spectrum of cellulose](image)

The consecutive losses of 162 u correspond to subsequent fragmentations of the cellulose chain, with detachment of dehydroglucose units.
Summary of common chemical ionization methods

Chemical ionization (CI)

Positive-Ion CI (PICI)
- Proton transfer
- Charge exchange
- Electrophilic addition
- Anion abstraction

DCI

Negative-Ion CI (NICI)

Electron capture (EC)
- Resonance EC
- Dissociative EC
- Ion-pair formation

Ion-molecule reactions
- Proton transfer
- Charge exchange
- Nucleophilic add.
- Nucleophilic disp.
### Choice between chemical ionization methods

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Thermodynamic Properties$^a)$</th>
<th>Example</th>
<th>Suggested CI Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>low polarity, no heteroatoms</td>
<td>low to high IE, low PA, low EA</td>
<td>alkanes, alkenes, aromatic hydrocarbons</td>
<td>CE</td>
</tr>
<tr>
<td>low to medium polarity, one or two heteroatoms</td>
<td>low to medium IE, medium to high PA, low EA</td>
<td>alcohols, amines, esters, heterocyclic compounds</td>
<td>PICI, CE</td>
</tr>
<tr>
<td>medium to high polarity, some heteroatoms</td>
<td>low to medium IE, high PA and low EA</td>
<td>diols, triols, amino acids, disaccharides, substituted aromatic or heterocyclic compounds</td>
<td>PICI</td>
</tr>
<tr>
<td>low to high polarity, halogens (especially F or Cl)</td>
<td>medium IE, low PA, medium to high EA</td>
<td>halogenated compounds, derivatives, e.g., trifluoroacetate, pentafluorobenzyl</td>
<td>EC</td>
</tr>
<tr>
<td>high polarity, medium to high molecular mass</td>
<td>low to medium IE, high PA and low EA</td>
<td>mono- to tetrasaccharides, low mass peptides, other polar oligomers</td>
<td>DCI</td>
</tr>
<tr>
<td>high polarity, very high molecular mass</td>
<td>decomposition products of low to medium IE, high PA and low EA</td>
<td>polysaccharides, humic compounds, synthetic polymers</td>
<td>Py-DCI</td>
</tr>
</tbody>
</table>

$^a$ IE: ionization energy, PA: proton affinity, EA: electron affinity