Solvents and Caveats for ESI MS

Solvents are typically chosen based on a compound of interest's solubility and compatibility with various ionization techniques used in ESI MS. Volatility and the solvent's ability to donate a proton are important in ESI and other atmospheric ionization techniques.

Protic primary solvents like MeOH and mixtures with H_2O, such as 1:1 MeOH/H2O or 1:1 ACN/H_2O, are used. Water's relatively low vapor pressure can be detrimental to sensitivity when employed at 100%. Better sensitivity results when surface tension is decreased through addition of a volatile organic solvent. Surfactants with higher proton affinity, though they increase ion liberation from nebulized droplets, can also reduce sensitivity.

Aprotic co-solvents like 10% DMSO in water and isopropyl alcohol improve solubility for some compounds. Formic acid is often added at low levels (0.1%) to facilitate ionization by ensuring the analyte is more basic than the solvent. Even in small amounts, however, some acids, like TFA, though necessary for otherwise insoluble compounds, can limit sensitivity.

In the ESI ionization mode, **buffers and salts (Na+, K+, and phosphate) cause a reduction in the vapor pressure and consequently a reduced signal**. The increased surface tension of the droplets, and resultant reduction of volatility, can be remedied by using relatively more volatile buffers like ammonium acetate, formed by a weak acid-base pair.

Solvent considerations

- Useful Solvents
    - **Water**
    - **Acetonitrile (ACN)**
    - **Methanol (MeOH)**
    - Ethanol
    - Propanol
    - Isopropanol
- Acceptable additives
    - Acetic acid
    - Formic acid
    - Ammonium hydroxide
    - Ammonium formate (salt concentration = 10 mM or less)
    - Ammonium acetate (salt concentration = 10 mM or less)
- Nonvolatile salts (phosphate, borate, citrate, etc.)
    - Can deposit in source and plug capillaries thus requiring more cleaning and maintenance operations
    - Modern source designs can handle nonvolatiles better than older designs
- Surface-active agents (surfactants/detergents) suppress electrospray ionization
- Inorganic acids are corrosive

- Trifluoroacetic acid (TFA)
    - To some extent suppresses positive-ion electrospray at levels exceeding 0.01%.
    - Greatly suppressed negative-ion electrospray.
- Triethylamine (TEA)
    - High PA (232 Kcal/mole) yields an intense [M+H]+ ion at m/z 102
    - Suppresses positive ion electrospray of less basic compounds.
- Tetrahydrofuran (THF)
    - 100% THF is highly flammable, so APCI and most interface techniques use nitrogen as the nebulizer gas. (Using air creates an explosion hazard).
    - Reacts with PEEK® tubing.