

Positive Ion Mode LCMS Retention of Polar Compounds - Tips and Suggestions

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Assuring Retention of Polar Compounds in Aqueous Normal Phase (ANP) Gradients for Positive-Ion LC-MS

Developing reliable LC-MS methods for polar analytes often presents challenges—insufficient retention, poor peak shape, or unstable ionization. When using a **Cogent TYPE-C™ column**, such as the Cogent Diamond Hydride™, Aqueous Normal Phase (ANP) provides a highly *effective* mode for separating these compounds, particularly in positive-ion electrospray workflows.

The following enhanced guidance expands on the original MICROSOLV technical note to help analysts establish robust, reproducible ANP gradients.

1. Prepare Solvents for Positive-Ion LC-MS

Proper mobile-phase composition is essential for achieving retention and optimal ionization:

- Solvent A: 50% methanol / 50% DI water + 0.1% formic acid
- Solvent B: 90% acetonitrile / 10% DI water + 0.1% formic acid

These compositions promote strong initial retention of polar analytes while supporting stable protonation efficiency in positive-ion MS detection.

2. ANP Gradient Setup for Polar Compound Retention

To retain highly polar species, ANP gradients must start with a very high organic content:

- Begin at 100–90% Solvent B This high-acetonitrile environment enhances surface interactions on TYPE-C™ silica, enabling polar compounds to retain effectively.
- Gradually reduce the percentage of Solvent B, down to 20% Solvent B This transition is appropriate when Solvent A is 50/50 methanol–water and allows controlled elution of polar compounds without early breakthrough.

This behavior is unique to ANP and differs significantly from reversed-phase (RP) or HILIC, making TYPE-C™ columns particularly powerful for analytes that struggle to retain under traditional methods.

3. Rapid Column Re-Equilibration—A Major Advantage

One of the operational strengths of Cogent TYPE-C™ columns is their fast equilibration time:

- Column re-equilibration: ~5 minutes
- Comparable HILIC columns: 20–30 minutes or more

This substantial time savings improves throughput, reduces idle instrument time, and leads to more consistent retention, especially in high-volume LC-MS laboratories.

4. WHY TYPE-C™ Columns Excel in ANP for LC-MS

The silicon-hydride surface of TYPE-C™ columns offers several benefits:

- Strong retention of polar molecules in high-organic environments
- Rapid switching and equilibration between gradient runs
- Cleaner baselines and improved ionization efficiency compared to traditional silica surfaces

This unique behavior helps analysts create robust, reproducible methods with minimal trial-and-error.



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