

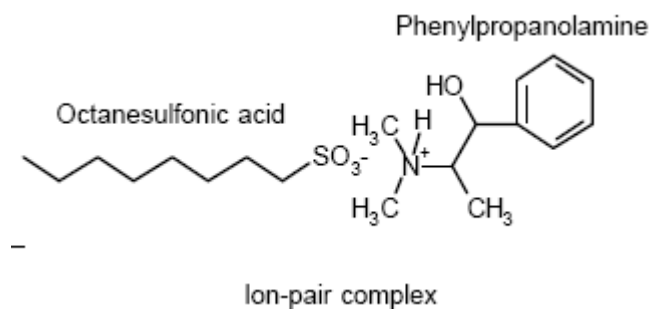
The use of ion-pair reagents can be a handy tool in improving retention and peak shape of ionizable compounds in **HPLC** (typically reversed phase). Here's how:

## Overview

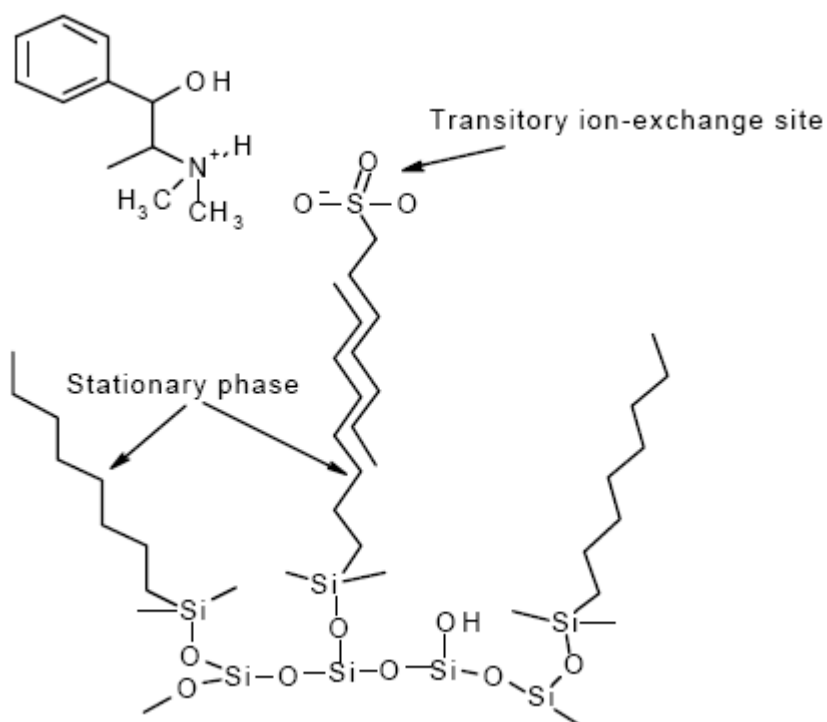
Ion-pairing agents are compounds that contain both an ionic functional group and a hydrophobic portion, such as a hydrocarbon chain. The most common ion-pairing agents are sulfonic acid derivatives such as hexane-, heptane-, octane-sulfonic acids, quaternary ammonium salts such as tetramethyl- or tetrabutylammonium hydroxide, and volatile agents such as trifluoroacetic acid and triethylamine.

## Interaction Mechanisms

As the name implies, ion-pairing agents may exert their principle effect by interacting with any counter-ions in solution, thus forming pseudo-neutral complexes:



Another possible type of interaction can relate to the hydrophobic portions of the ion-pairing agents partitioning into the alkyl bonded phase of the column, forming transitory ion-exchange sites:



## Common Drawbacks

It is sometimes unclear which mechanism is the true or primary occurring, and in most cases it is likely a combination of both in various degrees. This could partly relate to the notorious reputation of some ion-pairing methods yielding inconsistent and irreproducible results. Lengthy equilibration and general mass spec incompatibility are among some of the other commonly noted drawbacks. The additional cost of the ion-pair reagent itself may also be a subtle disadvantage that is frequently overlooked.

## New Technologies

Recent developments in column technology can in some cases overcome the common drawbacks of ion-pair reagents while meeting the chromatographic challenges:

1. pH stable stationary phase technology can allow for improved retention and

peak shape of basic analytes by running at basic mobile phase pHs controlled with buffers instead of utilizing ion-pair reagents.

2. [Hydrophilic Interaction Liquid Chromatography \(HILIC\)](#) stationary phases are improved.
3. HILIC method development techniques can allow for improved retention of polar analytes under mass spectrometry compatible conditions.

## Ideal Ion-Pairing Scenarios

While some of the utility of ion-pairing solutions may be usurped by newer technologies and techniques, there still remain cases where ion-pairing remains the most useful:

1. Samples with a wide range of polar, non-polar, and ionizable compounds that would not otherwise be characterized under the same conditions
2. Ionized compounds lacking a chromophore for UV detection (some ion-pair conjugates absorb UV where the analyte itself would not)
3. Method development familiarity and abundance of literature to reference and extrapolate.

---

### Related resources:

- [Ion-Pairing pH 8.3 LC/MS Oligonucleotides](#)
- [Trityl-on RNA and DNA Purification](#)
- [Basic Compounds by LC/MS Using a High pH Mobile Phase](#)
- [Low Molecular Weight Separation by GFC](#)

- [Synthetic Oligonucleotides by LC/MS](#)
- [pH LC Poster](#)
- [HPLC Column Care Guide](#)

Share with friends and coworkers:

- [Click to email this to a friend \(Opens in new window\)](#)
- [Click to share on Twitter \(Opens in new window\)](#)
- [Click to share on Facebook \(Opens in new window\)](#)
- [Click to share on Pinterest \(Opens in new window\)](#)
- [Click to share on LinkedIn \(Opens in new window\)](#)
- [Click to share on Tumblr \(Opens in new window\)](#)
- [Click to share on Reddit \(Opens in new window\)](#)