



## Review

# Retention models for ionizable compounds in reversed-phase liquid chromatography

## Effect of variation of mobile phase composition and temperature

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## ABSTRACT

General models in reversed-phase liquid chromatography that have been extended to relate retention of ionizable compounds to mobile phase composition, pH and/or temperature are reviewed. In particular, the fundamentals and applications of the solvation parameter model, the polarity parameter model and several classical models based on empirical equations are presented and compared. A main parameter in all these models is the degree of ionization of the acid–base compound, which depends on both the pH of the mobile phase and the acid–base constant of the compound. Thus, on one hand, the different procedures for pH measurement in the mobile phase and their influence on the performance of the models are outlined. On the other hand, equations that relate the variation of the pH of the buffer and the  $pK_a$  of the compound with the mobile phase composition and/or temperature are reviewed and their applicability to the retention models critically discussed.

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## 1. Introduction

The chromatographic retention of ionizable compounds is strongly dependent on the pH of the mobile phase. In a reversed-phase liquid chromatographic system (RPLC), neutral compounds are much more retained than ionic compounds. For an ionizable analyte, i.e. a compound with acid–base properties in the working range of pH, the ratio between the concentrations of neutral

and ionic forms, and therefore chromatographic retention, depends on the pH of the mobile phase and on the  $pK_a$  of the compound. This rate can be easily calculated from the well-known mathematical definitions of the acid–base equilibrium constants, which for a monoprotic acid (HA) or base (A) takes the form:



where the electrical charges of HA and A species have been omitted for simplicity. If the compound is a neutral acid, HA has no charge, whereas A has a negative charge ( $A^-$ ), so the latter it is usually poorly retained as compared with the former. But if the studied

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