

The expressRT™-100 HPLC system samples directly from your reaction vessel for real-time reaction analysis

introduction

Chemical process development and optimization require quality analytical data taken over the course of the reaction. Traditionally this sampling is done manually and the samples then submitted for analysis. Data from overnight time-points may be lost. With integrated reaction sampling and chromatography, the ExpressRT-100 allows for continuous unattended monitoring of your chemical process. The ExpressRT-100 is a mobile system and can be brought to the reaction. Automated in-line dilution makes this an effective tool for understanding small-, up to full-scale reactions. Proven low-flow LC technologies allow for efficient, precise and sensitive measurements. Rapid separations with 300 micron I.D. columns generate short turnaround times for a fast sampling rate. Low sample volumes and fast re-equilibration of gradient methods provide the performance you need for the most demanding of reaction analyses.

method

10 g of salicylic acid was dissolved in 200 mL of methanol. 5 mL of concentrated sulfuric acid was added and the mixture brought to a boil in a 500 mL round bottom flask. The reaction was monitored for 12 hours. 18 uL of sample was drawn directly from the reaction vessel and diluted 100-fold with methanol. This dilution was delivered to the chromatography module's sample loop where 40 nL was then injected. Chromatography was performed on a 50 x 0.3 mm Eksigent ChromXP™ 3C18-EP-120 column with an isocratic mobile phase composition of 40:60 0.1% TFA in H₂O:MeOH. Salicylic acid and methyl salicylate were detected @ 214 nm. Retention times for salicylic acid and methyl salicylate were 1.9 and 2.4 minutes respectively.

figure 1. esterification of salicylic acid to form methyl salicylate.

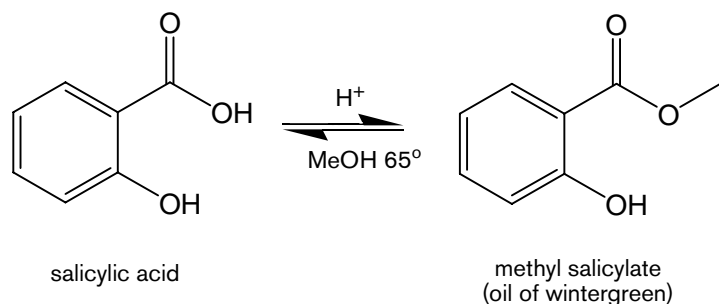
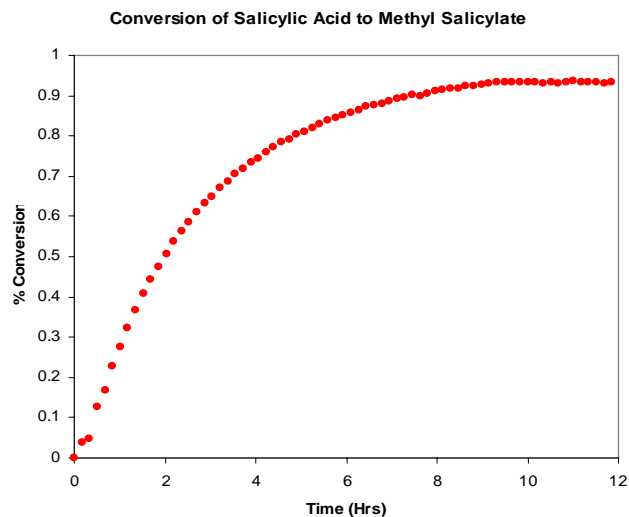


figure 2. percent conversion vs. time for a 12 hour overnight reaction.



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results

Continuous monitoring of an overnight reaction was achieved with automated sampling, dilution, and chromatography. Real-time reaction data was generated and saved over 12 hours. The hundred-fold dilution performed by the sampler allowed direct injection of diluted sample from the reaction vessel onto the column. High performance micro-scale chromatography generated a resolution of >2 , under isocratic conditions, within 3 minutes. Initial rate kinetics and final equilibrium can be determined from Figure 2. Quick turnaround time and constant sampling generated 72 data points in 12 hours. The amount of mobile phase consumed was less than 3 mL, despite constant pumping over 12 hours. Total sample volume used for analysis was less than 2 mL. Scheduling features of the software allow for user-determined sampling intervals and lower total sample volume. This data can be used in conjunction with other reaction data including pH, temperature, and spectroscopic data in order to optimize reaction rates or equilibrium points. Process conditions can be changed on the fly with real-time chromatographic feedback. Different dilution and chromatographic methods can be run on the same reaction. Fast equilibration, dilution options and low delay volumes afford the ability to analyze for conversion and low level impurities with separate methods.

figure 3. Conversion of salicylic acid (1st peak) to methyl salicylate (2nd) over time ($t = x$ hours). Equilibrium (93 % conversion) is reached at 9.2 hours.

