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Speacore X50, Multivapor, Melting Point M-565

SHORT NOTE

Separation, concentration, and identification of aspirin and salicylic acid

Work-up procedures of after chemical synthesis are indispensable but time consuming. Here we demonstrate a semi-automatized work-up procedure for the separation, concentration and identification of aspirine and salicylic acid.

Introduction

Separation and purification, concentration and identification of substances are indispensable steps in lab- and industrial scale chemical synthesis. Since these work-up procedures are often more time consuming, and thus more costly, than the reaction itself, they are true bottlenecks, for example in the pursuit of new drugs [1]. Furthermore, due to the many and repetitive steps, post reaction operations are sources of errors and sample confusion.

The aim of this note is to show how the separation, concentration and identification of multiple samples can be performed efficiently and reproducible. Therefore, flash chromatography is used for the product separation, parallel vortex evaporation for the concentration and melting point determination for identification. Employed BUCHI equipment was designed to automate these processes.

In an example case, aspirin (acetylsalicylic acid, ASA) and salicylic acid (SA) are separated from a liquid mixture, concentrated, dried and finally analysed by measuring the melting point.

Experimental

1 mM SA and 1 mM ASA were dissolved in 10 ml of a 3:1 vol. solution of cyclohexane:ethyl acetate, and 1 Vol. % of formic acid. Isocratic feed of the mobile phase to the cartridge was achieved by two independent controlled pumps C-605 and consisted of 75 vol % cyclohexane and 24 % ethyl acetate and 1 % formic acid.

The mobile phase flow rate for separation was 20 ml/min. Prior to the separation the cartridge was conditioned for 5 min using the same mobile phase. Separated substances were detected by a C-640 UV-Vis detector. For the detection the signal maxima at 303 nm for SA and 277 nm for ASA, were recorded in parallel.

From the chromatographic fractions containing the SA and ASA the solvent was removed by vortex evaporation. For evaporation the vacuum was reduced from 300-140 mbar in 5 min using a gradient function and evaporated to dryness at 140 mbar. Vortex speed was set to 7. Obtained samples were dried in the drying oven at 90 °C until a constant sample weight was obtained.

The melting process was recorded using the M-565 equipped with the Melting Point Monitor Software. A temperature gradient of 1 °C/min was applied and started about 10 °C below the expected melting point.

Results and Conclusion

Combination of the Sepacore X50 flash chromatography system, the Multivapor P-12 and the Melting Point M-565 led to an efficient and semi-automated work-up. Following key results were achieved:

- SA and ASA were successfully isolated from solution phase in high purity using flash chromatography; the separation process was finished in less than 10 minutes.
- Fractions of the isolated substances were automatically collected using two independent detection wavelengths.
- The solvents of the two fractions were evaporated by applying a vacuum gradient. No supervision was necessary and the process was finished within 20 minutes.
- Unambiguous identification of the substances was done by comparison of the measured melting point with the values from literature.
- It was demonstrated that the semi-automated processes widened the bottleneck for post synthetic processes by shortening the work-up time.

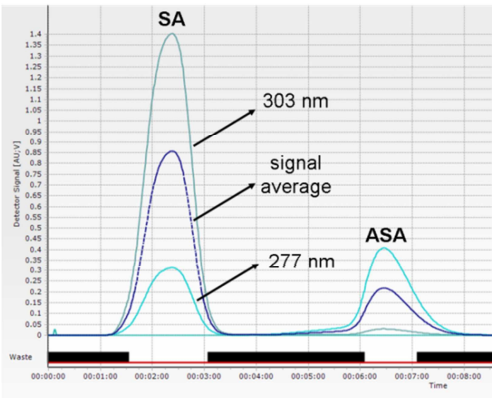

Figure 1. Chromatogram of the separation of SA and ASA recorded using the Sepacore Control software.

References

[1] Cork D., Hird N. (2002) *Work-up strategies for high-throughput solution synthesis,* Drug Discovery Today, Vol. 7, No.1 , p 56-63.