Application Note

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Temperature-Dependent Reaction Monitoring of an Ester Hydrolysis

Fast reaction monitoring using an Agilent 1260 Infinity II Prime Online LC

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Abstract

This application note demonstrates the capability of the Agilent 1260 Infinity II Prime Online LC System to monitor chemical reactions by drawing samples from the reaction vessel. Monitoring can be done in a fast cycle time to cope even with the speed of a fast hydrolytic reaction at elevated temperature. From the obtained data, typical curves will be drawn by the online plot functionality. The temperature of the hydrolytic reaction was controlled by the Mettler-Toledo EasyMax 102 reactor. The Agilent Online LC Monitoring Software controls the entire experiment and enables complete automation of monitoring experiments in a safe and economic manner.

Introduction

A main field of the chemical industry is the large-scale synthesis of building blocks for the synthesis of fine chemicals, pharmaceuticals, and modern polymer materials. These compounds must be characterized for their behavior under typical conditions faced during transportation and storage and to ensure that they provide desired characteristics in the final product, for example, the bacterial degradation behavior of polymer materials in the environment.

This application note demonstrates the use of the Agilent 1260 Infinity II Prime Online LC System for the exploration of hydrolysis conditions and their influence on degradation of a succinic acid monovinyl ester (4-oxo-4-(vinyloxy) butanoic acid, Figure 1), which is a first-order reaction. For this study, different temperatures were applied at a defined pH to determine the speed of the hydrolysis.

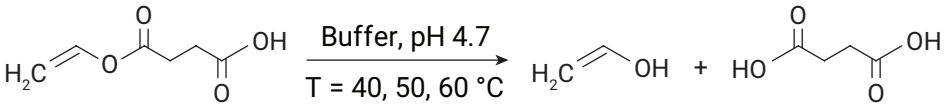

Figure 1. Hydrolysis of succinic acid monovinyl ester.

Experimental

Instrument

- Agilent 1260 Infinity II Flexible Pump (G7104C)
- Agilent 1260 Infinity II Online Sample Manager Set (G3167AA): Agilent 1260 Infinity II Online Sample Manager (G3167A) clustered with external valve (part number 5067-6680) located at the Agilent 1290 Infinity Valve Drive (G1170A) and Agilent Online LC Monitoring Software
- Agilent 1290 Infinity II Multicolumn Thermostat (G7116B)
- Agilent 1290 Infinity II Diode Array Detector (G7117B) with Agilent InfinityLab Max-Light Cartridge Cell (10 mm, G4212-60008)

Column

Agilent InfinityLab Poroshell 120 PFP, 2.1 × 50 mm, 1.9 µm (part number 699675-408)

Software

- Agilent OpenLab CDS, version 2.6 or later
- Agilent Online LC Monitoring Software, version 1.0

Analytical method

Solvents	A) Water + 0.1% formic acid (FA) B) Acetonitrile (ACN) + 0.1% FA
Analytical Flow Rate	0.8 mL/min
Isocratic	10% B Stop time: 1.0 min
Column Temperature	40 °C
Agilent Feed Injection (Automatic)	80% of analytical flow rate
Flush Out Solvent	Water:ACN 9:1 + 0.1% FA (S2)
Flush Out Volume	Automatic
Injection Volume	1 µL
Needle Wash	3 seconds, water:ACN 1:1 + 0.1% FA (S1)
Sampling	See sampling method
Diode Array Detector	200 ± 4 nm, Ref.: 360 ± 16 nm, 20 Hz data rate

Sampling

Direct injection from the reactor interface of the Agilent 1260 Infinity II Online Sample Manager every 2 minutes.

Sample delivery pump

- Pump used: Agilent 1260 Infinity II Isocratic Pump (G7110B)
- Flow rate: 5 mL/min
- Solvent stream from the reaction vessel to the 1260 Infinity II Online Sample Manager reactor interface, and back to the reaction vessel

Mettler-Toledo EasyMax 102

For adjustment of temperature conditions for the hydrolysis reaction, the Mettler-Toledo EasyMax 102 equipped with a 50 mL reaction vessel and internal temperature control was used. The reaction solution was pumped to the reactor interface valve of the 1260 Infinity II Online Sample Manager and from there back to the reaction vessel.

Reaction conditions

- Educt: succinic acid monovinyl ester
- Buffer: 0.2 M ammonium acetate at pH 4.7
- Stirring at different temperatures: 40, 50, or 60 °C
- Reaction start: add the educt dissolved in 1 mL ethanol for a final concentration of 100 ppm

Hydrolysis reaction chemicals

- Succinic acid monovinyl ester, provided by Dow
- Ammonium acetate, glacial acetic acid

HPLC solvents and chemicals

- All solvents were purchased from Merck, Germany.
- Chemicals were purchased from VWR, Germany.
- Fresh ultrapure water was obtained from a Milli-Q Integral Water Purification System equipped with LC-Pak polisher and a 0.22 µm membrane point-of-use cartridge (Millipak).

Results and discussion

For the determination of the temperature dependence of the hydrolysis of succinic acid monovinyl ester, a pH value of 4.7 was chosen and three different temperature values (40, 50, and 60 °C) were applied. The reaction was started by the addition of succinic acid monovinyl ester. The ester was dissolved in 1 mL of ethanol to 49 mL of buffer at the chosen temperature for a final concentration of 100 ppm. From the reaction, a sample was drawn every 2 minutes for direct injection without subsequent dilution or quenching. For relative quantification, the first data point, where the sample was drawn immediately after the start of the reaction, was defined to be 100 ppm (100%).

For the reaction temperature of 40 °C, it took about 11.25 minutes to hydrolyze 50% of the succinic acid monovinyl ester (Figure 2).

The corresponding chromatograms show the declining educt succinic acid monovinyl ester at a retention time of 0.577 minutes from samplings 1, 7, and 27 (Figure 3).

Overall, with a total run time of only one minute, excellent performance with a retention time of only 0.577 minutes (void = 0.179 min, k' = 2.22) could be achieved with the short Agilent InfinityLab Poroshell 120 PFP column and the applied chromatographic method.

By increasing the temperature of the decomposition reaction to 50 and 60 °C, the speed of the reaction was increased drastically (Figure 4). At 50 °C, the educt was consumed to 50% in approximately 4.26 minutes and at 60 °C in 2.15 minutes. The reaction was considered complete in 18.29 minutes at 50 °C (educt level below 5%) and in 8.28 minutes at 60 °C.

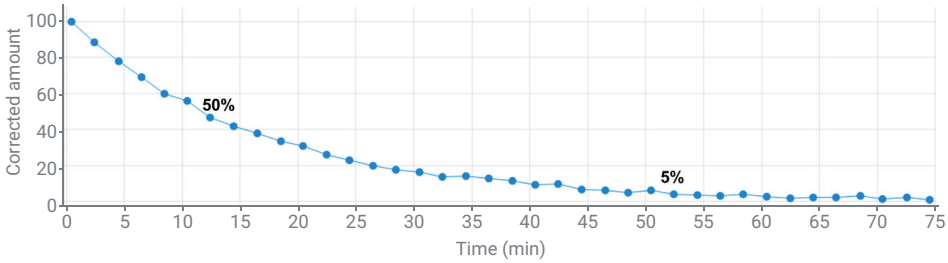

Figure 2. Hydrolysis of succinic acid monovinyl ester at pH 4.7 and 40 °C. Fifty percent of the educt was consumed at approximately 11.25 minutes between sampling 6 and sampling 7. The educt falls below the value of 5% in sampling 27 at approximately 52.26 minutes.

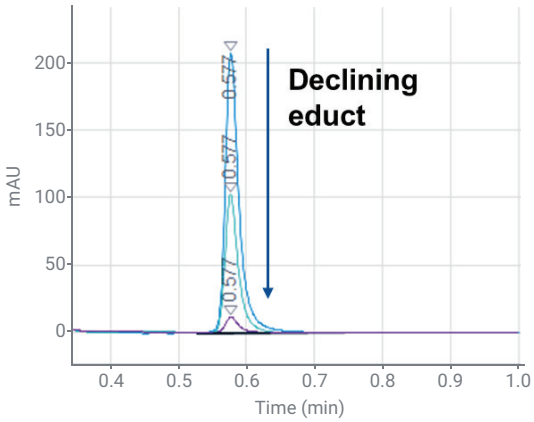

Figure 3. Chromatogram of declining educt succinic acid monovinyl ester from samplings 1 (blue), 7 (turquoise), and 27 (purple).

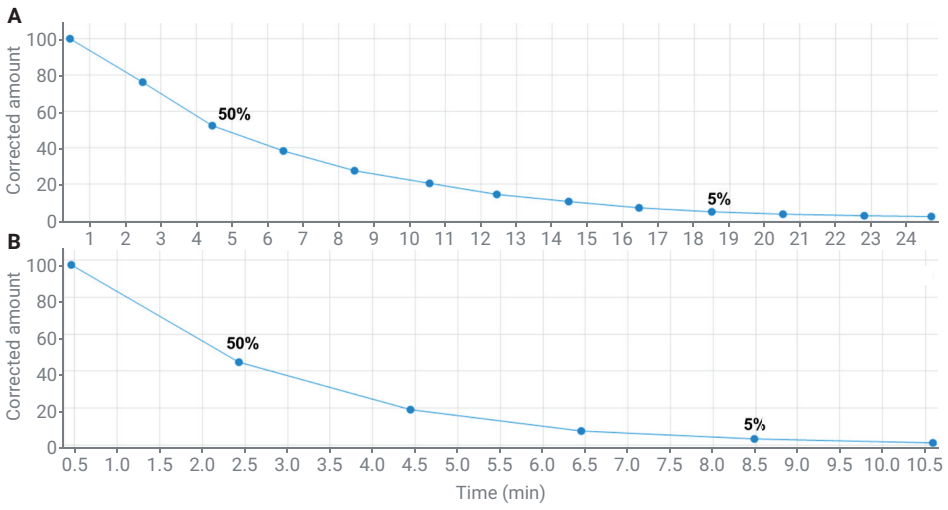

Figure 4. Hydrolysis of succinic acid monovinyl ester at pH 4.7 at 50 °C (A) and 60 °C (B). (A) Fifty percent educt consumption at sampling 3 at 4.26 minutes. Educt below 5% at sampling 10 at 18.29 minutes. (B) 50% educt consumption before sampling 2 at 2.15 minutes. Educt below 5% at sampling 5 at 8.28 minutes.

Table 1 shows a summary of the times to reach the 50% educt level and the 5% educt level at the applied reaction temperatures.

Table 2 summarizes the sampling times, the relative educt amounts, and peak details based on the data points measured for the fast hydrolytic reaction at 60 °C (Figure 4B). In the first sampling, there was already educt consumption measured, and the 50% level was near sampling point 2 at approximately 2.25 minutes.

Conclusion

This application note demonstrates the capability of the Agilent 1260 Infinity II Prime Online LC System for monitoring chemical reactions where the reaction speeds may vary. The hydrolysis reaction of succinic acid monovinyl ester was monitored at different temperatures – showing the capability to generate data even when the reaction is completed within 10 minutes. This fast reaction monitoring enables the determination of the half-life time under the given conditions. The Agilent Online LC Monitoring Software controls the entire experiment and enables completely unattended sampling and data acquisition in a safe and economic manner.

Table 1. Reaction summary of time to reach the 50% educt consumption and the 5% residual educt level.

Reaction Temperature (°C)	Time to 50% Educt Consumption (min)	Time to 5% Educt Level (min)
40	11.25	52.26
50	4.26	18.29
60	2.15	8.28

Table 2. Summary of the experimental data collected for the fast hydrolytic reaction at 60 °C.

Sample	Sampling Time (min:s)	RT (min)	Amount (%)	Area	Height
1	0:27	0.579	97.44	255.29	175.67
2	2:25	0.578	44.86	117.54	80.60
3	4:26	0.578	19.27	50.50	35.15
4	6:26	0.578	7.81	20.46	15.24
5	8:28	0.577	3.32	8.72	6.48
6	10:34	0.578	1.43	3.76	2.77

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