Simultaneous Analysis of Carboxylic Anhydrides and Hydrolysates Using Supercritical Fluid Chromatography

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1. Introduction

Carboxylic anhydrides are easily decomposed by water or alcohol, making analysis by reversed-phase liquid chromatography difficult. Therefore, normal phase liquid chromatography (NPLC) is often used for direct analysis of carboxylic anhydrides. However, NPLC uses a large amount of organic solvent such as hexane and chloroform, which raises concerns about human health and environmental impact.
In this presentation, we examine the use of supercritical fluid chromatography (SFC) for the analysis of carboxylic anhydrides. SFC uses non-polar carbon dioxide as the mobile phase, similar to NPLC with lower solvent cost and environmental impact. In addition, SFC does not require water or alcohol as the mobile phase, which is expected to reduce the influence of decomposition on the analytical results.

2. Methods

2.1. Model compounds

Four isomers of biphthalic anhydride (BPDA) and oxydiphthalic anhydride (ODPA), known raw materials for polyimide, were used as model compounds for carboxylic anhydride (figure 1). These compounds were dissolved in acetonitrile (superdehydrated) to suppress hydrolysis.

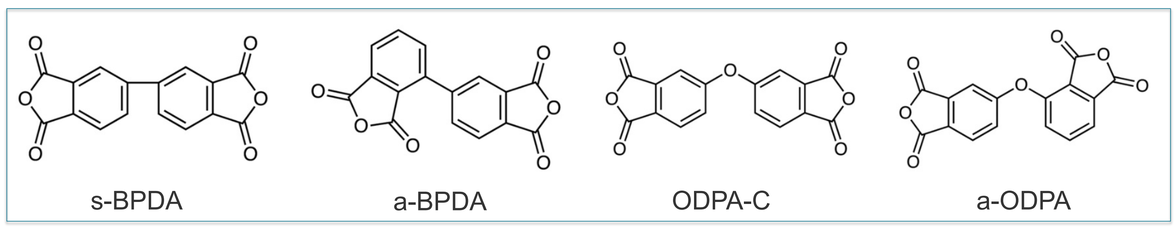


Figure 1: Structure of model compounds

2.2. Column scouting

For efficient method development, column scouting using six stationary phases (Shim-pack™ UC Series) with varying retention mechanisms was carried out to evaluate the most suitable column to separate a mixture of the four model compounds. Table 1 shows the stationary phase structures and features of the columns, while table 2 lists the scouting conditions.

Table 1: Structures and features of stationary phase used for column scouting

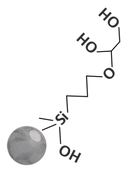
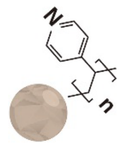
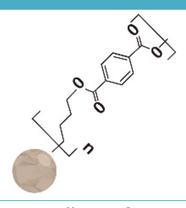
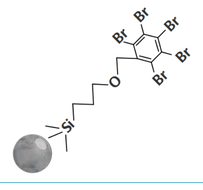
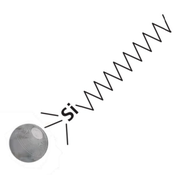
	UC-Diol Ⅱ	UC-Sil Ⅱ	UC-PolyVP
Chemistry			
Feature	The separation mode is normal phase. This inhibits non-specific interactions.	This is excellent for retention of basic compounds and recognition of their tertiary structures.	A favorable peak shape is obtained even without acid-base additives.
	UC-PolyBT	**UC-PBr**	**UC-ODS**
Chemistry			
Feature	This is excellent for resolving aromatic compounds through π-π interactions.	With ODS, separation of poorly retained compounds is improved.	The separation mode is reverse phase. Retention is provided through hydrophobic interaction.

Table 2: Analytical conditions of scouting experiments conditions

Column:	Shim-pack UC-Diol II, UC-Sil II, UC-PolyVP, UC-PolyBT, UC-PBr, UC-ODS (250 mm × 4.6 mm I.D., 5 µm)
Mobile phase:	A: CO_2, B: Acetonitrile
Time program:	B.Conc. 5 % (0 min) → 50 % (8-10 min) → 5 % (10-12 min)
Flow rate:	3.00 mL/min
BPR pressure:	15 MPa
BPR temperature:	50 °C
Column temperature	40 °C
Detection:	300 nm (PDA with a high pressure flow cell)
Injection Volume:	2 µL in acetonitrile (super dehydrated)

2.3. Method Scouting Solution

The Method Scouting Solution software allows to create multiple analytical methods in only five steps, which simplifies and reduces the overall workload to create a method screening experiment and easily determine optimum analytical conditions (Figure 2).

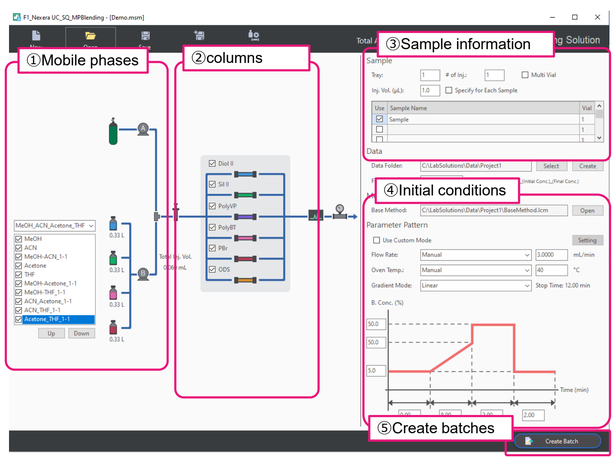


Figure 2: User interface of Method Scouting Solutions and Nexera UC chiral screening system

3. Results and Discussion

3.1. Results of column scouting

Figure 3 shows chromatograms obtained in the column screening experiment. The best separation was achieved using the Shim-pack UC-PolyBT column.

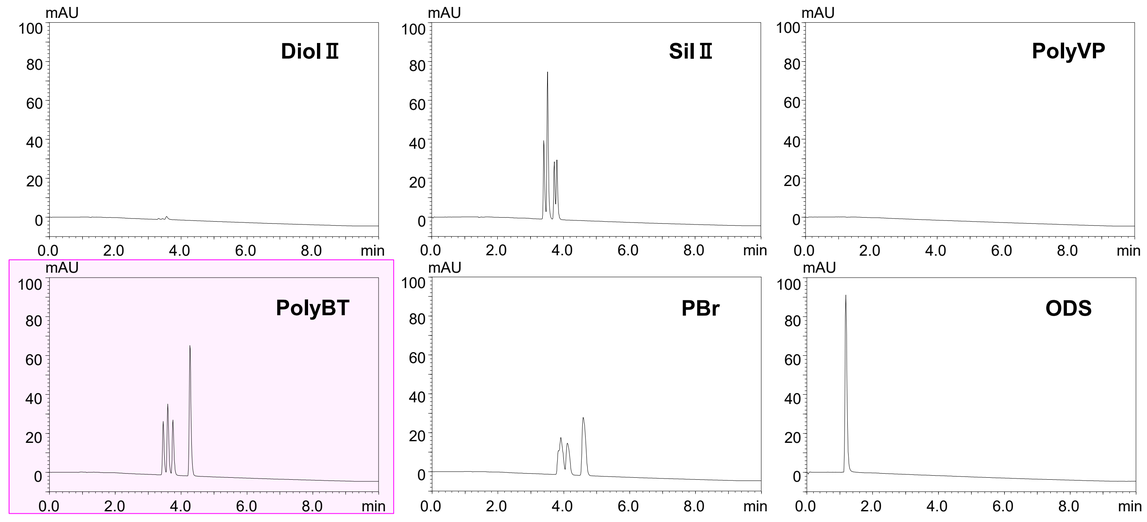


Figure 3: Chromatograms obtained by column screening experiment

3.2. Optimization of analytical conditions

Based on the results obtained, the analytical conditions were optimized to create a method that offers baseline separation of the four model compounds with similar structures in about 7 min (separation > 2.1) (table 3, figure 4). Calibration curves created for concentrations of 5 - 125 mg/L showed good linearity and reproducibility with R^2 > 0.999 and %RSD (n=6) < 1.0 (table 4).

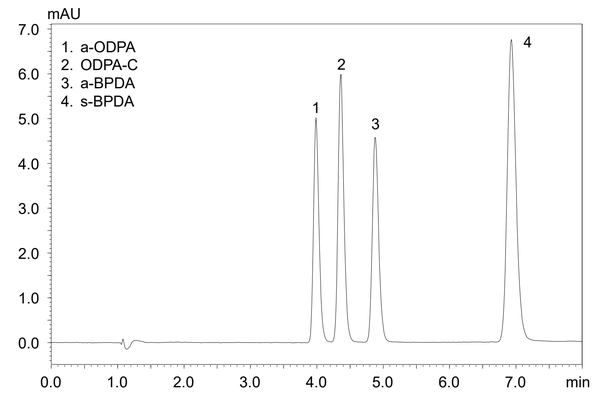


Table 3: Optimized analytical conditions

Column:	Shim-pack UC-PolyBT (250 mm × 4.6 mm I.D., 5 µm)
Mobile phase:	CO_2/Acetonitrile = 90/10
Flow rate:	3.00 mL/min
BPR pressure:	15 MPa
BPR temp.:	50 °C
Column temp.:	40 °C
Detection:	300 nm
Injection Volume:	2 µL in acetonitrile (super dehydrated)

Figure 4: Chromatogram using conditions specified in table 4

Table 4: Repeatability (%RSD) and linearity of calibration curve (R^2)

Compounds	%RSD (peak area, n=6 (50 mg/L))	R^2 (5, 10, 25, 50, 125 mg/L)
a-OPDA	0.68	0.9999
OPDA-C	0.84	0.9998
a-BPDA	0.85	0.9997
s-BPDA	0.93	0.9993

3.3. Simultaneous analysis of carboxylic anhydrides and hydrolysates

The simultaneous analytical method for carboxylic anhydrides and its hydrolyzed products was developed by switching modifiers. After elution of the carboxylic anhydride, the valve with the built-in modifier feed pump was switched, and the modifier was changed from acetonitrile to 0.1 % phosphoric acid in methanol (figure 5). The results show that SFC can be used for simultaneous analysis of compounds with widely different characteristics.

Figure 5: Chromatograms of carboxylic anhydrides (top) and hydrolysates (bottom)

4. Conclusion

This presentation introduces SFC analysis of carboxylic anhydrides without hydrolysis. The simultaneous analytical method for carboxylic anhydrides and its hydrolyzed products was achieved by switching modifiers. This method is expected to be applied to the measurement of impurities and sample degradation indicators.

Method Scouting Solution was used for fast and efficient method development, reducing the risk of human error, by automated creation of multiple screening methods. One big advantage of using SFC is that CO_2 is less expensive and more environmentally friendly than many organic solvents used in LC, and there is no need for waste disposal.