

Mass Directed Fraction Collection by Normal Phase Flash Chromatography Coupled to the expression CMS



Introduction

The Advion expression Compact Mass Spectrometer (CMS) was coupled to a Normal Phase Flash Chromatography system for mass directed fraction collection. Typically a UV detector is used to monitor compounds eluting from Normal Phase columns. A limitation of the UV detector is that it relies on compounds having a chromophore in the chemical structure, hence an analyte of interest may not be detectable if it lacks a suitable UV chromophore or coelutes with another compound. In addition, solvent systems can interfere with and hinder UV absorbance. The Advion expression CMS provides the ultimate in selectivity, unambiguously identifying residual starting materials, desired product ions, side reactants and impurities by their molecular weight despite co-eluting compounds and solvent peaks. Mass directed fraction collection greatly speeds up the chemist's work flow with confidence in the content and purity of the collected fractions by eliminating off-line TLCs, workup and core lab LC/MS assays.

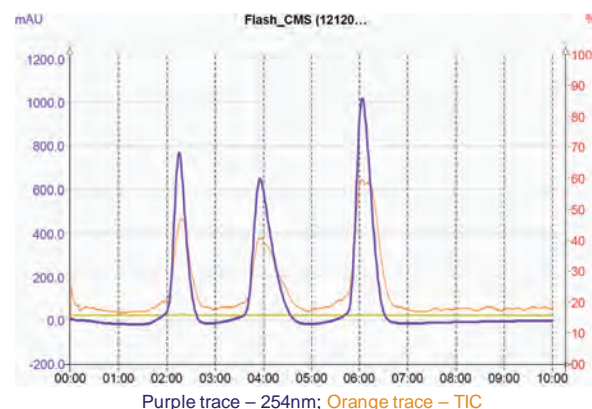
Experimental

Mass spectrometer: expression CMS
Flash system: Interchim PuriFlash
Column: PURIFLASH COLUMN 15
SILICA HC 25G
20mL/min (gradient method - 10 minutes)

Time	% HEX	% EtOAc
0:00	80	20
2:30	80	20
7:30	0	100
8:30	0	100
8:35	80	20
10:00	80	20

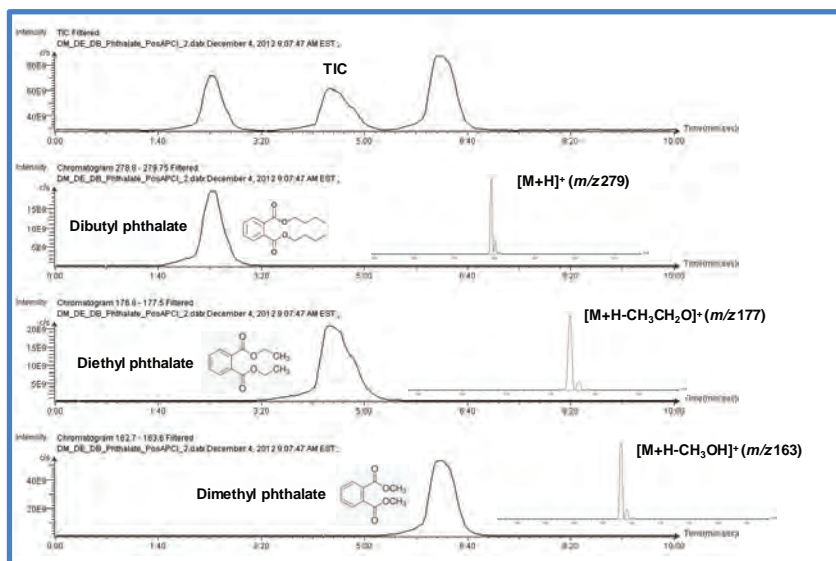
Sample mixture: Mixture of 1mL dimethyl phthalate (1.2g/mL), 1mL diethyl phthalate (1.1g/mL) and 1mL dibutyl phthalate (1.05g/mL)
Injection volume: 0.5mL injection (0.55g total loaded on-column)
MRA valve set to 38: 13300:1 (1.5 µL/min transfer rate)
Eluent flow rate: 500 µl/min
Eluent make-up flow: Acetonitrile + 0.1% FA
MS scan range: m/z 100 - m/z 1200
MS scan time: 1000 ms

Normal-Phase PuriFlash - APCI/CMS



Results

Normal-Phase/CMS



Analog Output Signal Smoothing

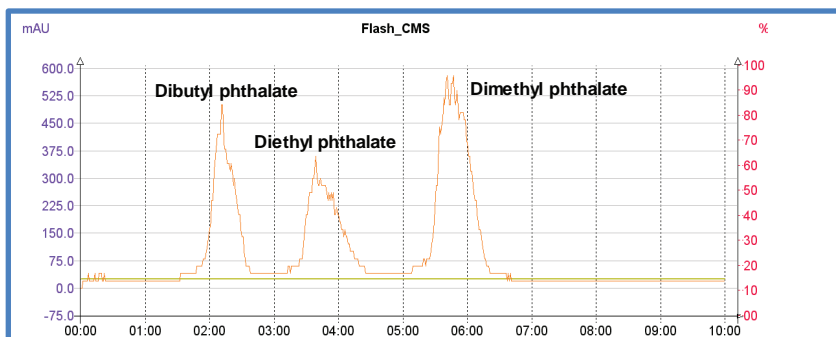


Fig. 1 – AO_SMOOTHING_BACKGROUND REMOVAL_OFF (TIC)

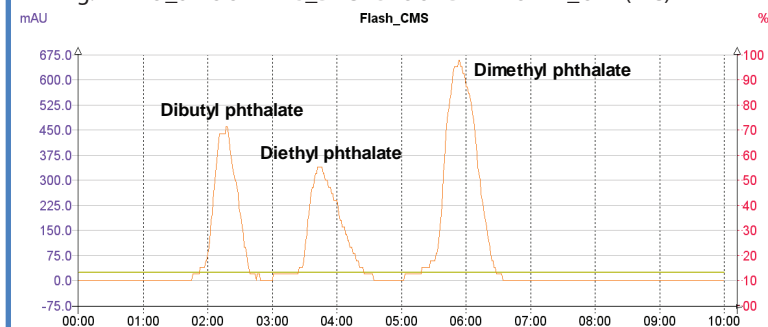


Fig. 2 – AO_SMOOTHING_BACKGROUND REMOVAL_ON (TIC)
Analog output smoothed to provide less noisy chromatographic peaks.

Mass Fractionation

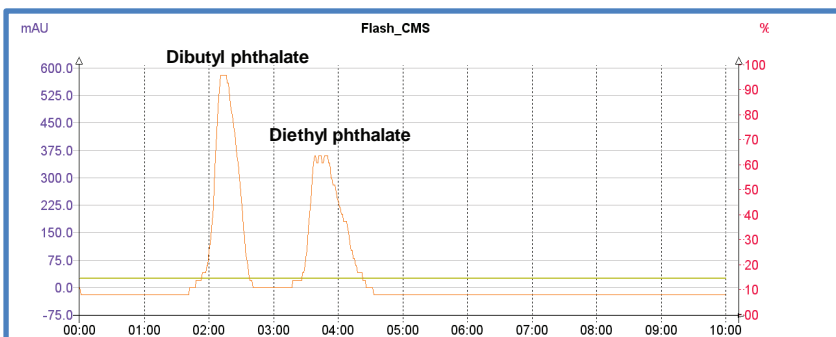


Fig. 3 – Mass fractionation – Dibutyl phthalate and Diethyl phthalate only collected (Analog output configured for m/z 149 - common fragment ion for these two compounds).

Summary

The high flow rate and highly concentrated eluate from the flash chromatography system was continuously sampled using a Rheodyne MRA valve, diluted and introduced to the Advion **expression** CMS using a MS compatible solvent. The mass-to-charge (m/z) ratios of each compound were detected and correlated to the UV peaks. Dibutyl phthalate and Diethyl phthalate fractions were collected based on a common fragment ion (Fig. 3). The affordability and capability of the Advion **expression** CMS makes it the instrument of choice for organic and medicinal synthetic chemists who desire definitive identification of their compounds while optimizing chromatographic separations.