Application Note

REACTION MONITORING

by Direct Analysis Probe on a Compact Mass Spectrometer

Advion

INTRODUCTION

The expression CMS provides essential compound information quickly and improves the chemist's workflow. The Atmospheric Solids Analysis Probe (ASAP) permits fast analysis of solid and liquid samples and is a simple, faster and lower cost alternative to LC/MS methods. This direct analysis probe method has been shown to be useful for the analysis of volatile and semivolatile compounds. ASAP is available as a combined ASAP-APCI source, or existing APCI sources can be easily modified to become dual APCI-ASAP capable.

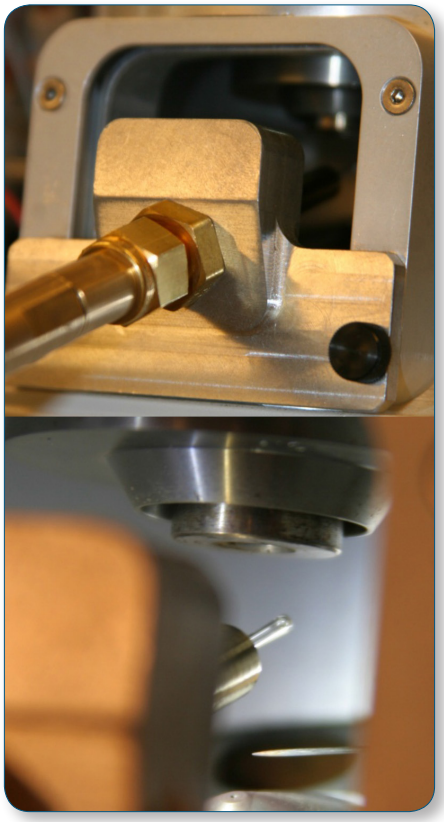


Figure 1:
Photos of ASAP probe and glass capillary tip which supports the sample for analysis

EXAMPLE

Two examples are demonstrated. Following the synthesis of 4-iodoisoquinoline from the corresponding bromide, using the methods of Artis and Buchwald, TLC could not be used to monitor the reaction. The product and starting material have the same retention factor (Rf) on the silica plate and thus could not be differentiated by TLC. The second was to determine the optimum stop time for the reaction based on Yaetko et al.'s work.

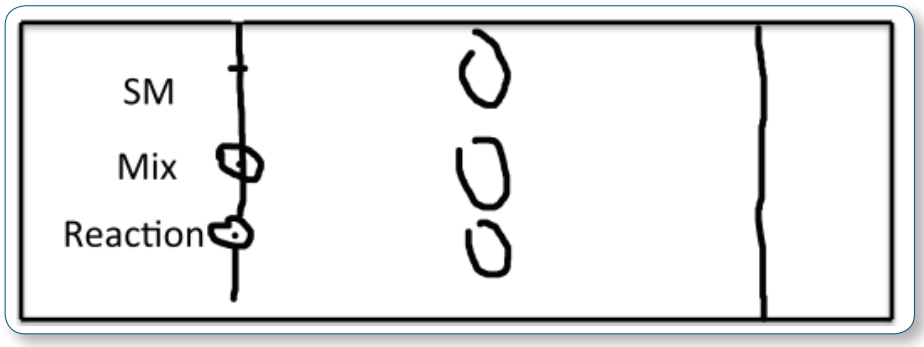
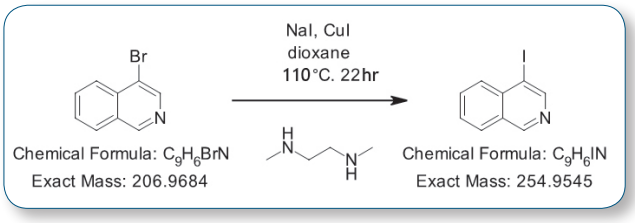


Figure 2: SM: 4-iodoisoquinoline, Reaction: is the reaction mixture containing both the starting material and the 4-iodoisoquinoline (if it has formed), Mix: is a spot of the starting material and the reaction mixture

The ASAP probe was dipped into the reaction mixture, wiped with a KimWipe and analysed in the CMS via the ASAP probe employing APCI as the mode of ionization.



RESULTS

The reaction product is readily seen in the mass spectrum after reacting at 110 °C for 22 hours (Figure 3). The relative ionization efficiency of the two compounds is unknown; if one assumes that they have similar ionization efficiency, there is approximately 33% conversion, and the ASAP analysis took only 30 seconds from sampling to analysis completion. No reaction was visible by TLC separation.

The product of the reaction to form 6-iodotryptophan following the method of Yaeko et al, could not be identified unequivocally, as being formed by standard methods prior to the standard workup and purification. To determine when the reaction could be stopped, the reaction mixture was sampled over time and analysed by CMS using the ASAP probe. The ions associated with the starting material, 6-iodoindole, and the two possible products of the reaction 6-iodotryptophan and the acetamide protected version of the 6-iodotryptophan were monitored over time.

The results of the analysis are shown in Table 1.

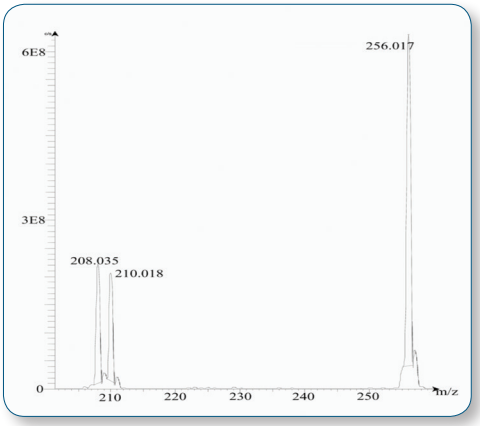


Figure 3: Reaction after 22 hours.

TIME (MIN)	% 6-IODOINDOLE	% 6-IODOTRYPTOPHAN	% 6-IODOTRYPTOPHAN PROTECTED
1	99.73	0.15	0.12
30	94.44	4.62	0.94
60	20.20	65.17	14.63
120	15.20	60.67	24.12

Table 1: The results from the time study indicate that the reaction was reaching a plateau at approximately 60 minutes and that the reaction could have been stopped at 60 minutes.

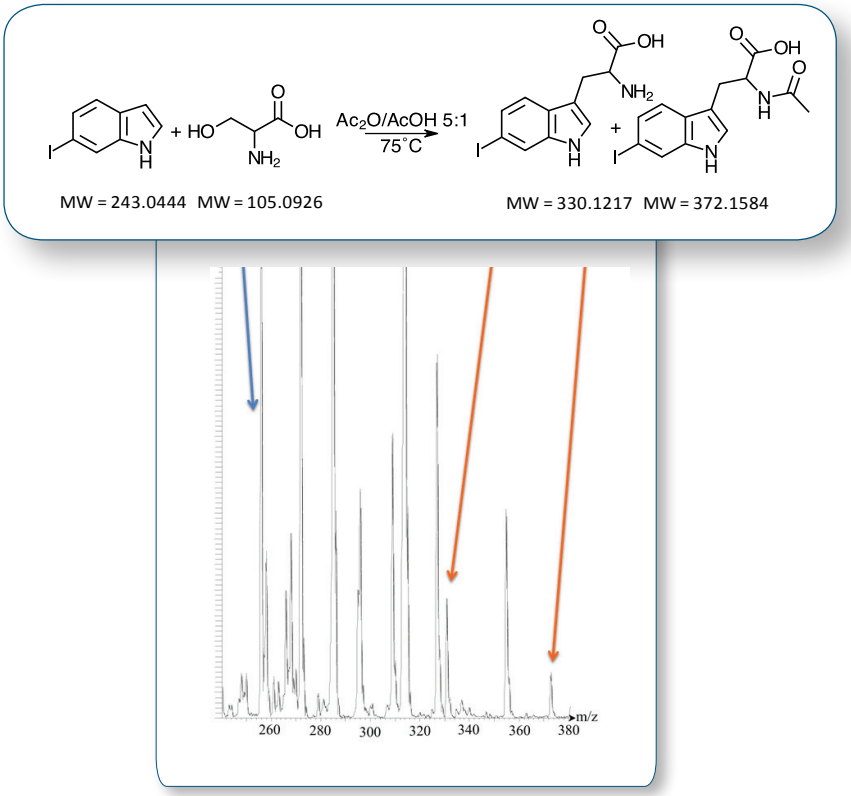


Figure 4:120 minute sample of the reaction for the formation of 6-iodotryptophan, the product and the protected product were seen in the mass spectrum however, the starting material was significantly reduced.

SUMMARY

- Direct analysis of a reaction mixture by a modified APCI source with the ASAP probe provided unequivocal reaction identification.
- Easy-to-use and reliable mass analysis system
- Results are generated in less than 30 seconds

REFERENCES

[i] Klapars Artis, and Stephen L. Buchwald. "Copper-Catalyzed Halogen Exchange in Aryl Halides: An Aromatic Finkelstein Reaction." Journal of the American Chemical Society 124, no. 50 (December 2002): 14844–45. doi:10.1021/ja028865v.

[ii] Yamada Yaeko, Ai Akiba, Shiho Arima, Chiharu Okada, Kiminari Yoshida, Fumihiro Itou, Toshitsugu Kai, Toshiko Satou, Kazuyoshi Takeda, and Yoshihiro Harigaya. "Synthesis of Linear Tripeptides for Right-Hand Segments of Complestatin." Chemical and Pharmaceutical Bulletin 53, no. 10 (2005): 1277–90

[iii] Charles N. McEwen, Richard G. McKay, and Barbara S. Larsen, Anal. Chem. 2005, 77, 7826-7831