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Small Molecule Reaction Monitoring Using Open Access Atmospheric Pressure Gas Chromatography-Mass Spectrometry (APGC-MS)

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APPLICATION BENEFITS

"Soft" ionization using APGC generated $[M+H]^+$ ion followed by an automated chemical compound target interpretation.

WATERS SOLUTIONS

SQ Detector 2 Mass Spectrometer

Atmospheric Pressure Gas Chromatography (APGC) ionization source

MassLynx™ Software with OpenLynx™ Open Access Application Manager

KEYWORDS

Reaction monitoring, medicinal chemistry, small molecule discovery, APGC-MS, open access software, MassLynx v4.1

INTRODUCTION

Identification of target compounds in chemical reactions is a major challenge for a chemist in a medicinal chemistry laboratory. Obtaining this compound reaction information quickly from a self-service analytical application is of great value for a modern research department. Atmospheric Pressure Gas Chromatography (APGC) is an ionization source that allows coupling of a gas chromatograph to a mass spectrometer with an atmospheric pressure chemical ionization (APCI) source. This allows GC separation combined with soft ionization, often yielding molecular or quasi-molecular ions. This system combined with MassLynx Software with OpenLynx is a powerful tool for monitoring and identifying small molecules.

A chemical target hit $[M+H]^+$ is found through an automatic interpretation process under protonation ionization conditions. The application is optimized for chemical intermediates and compounds which do not show optimal response in electrospray ionization (ESI). The combination of APGC-MS systems with an automatic interpretation and reporting process gives the research chemist a very powerful self-service analytical application tool. The purpose of this application note is to demonstrate the advantages of speed and ease of use that a self-service APGC-MS system brings for monitoring chemical reactions.

EXPERIMENTAL

Chromatographic separations were carried out using CTC-GC-PAL on 6890N GC oven.

Atmospheric pressure APGC System coupled to a SQ Detector 2 Mass Detector.

GC conditions

Column:	Restek RTX-35MS, 15 m × 200 µm × 0.33 µm
Carrier gas:	Helium at 1.2ml/L
Liner:	Agilent 4 mm tap GW
Injection temp.:	200 °C
Injection mode:	Split 1/100
GC oven temp.:	Start 60 °C Ramp 30 °C/min Hold 3.33 min
Total run time:	11 min

MS conditions

Ionization mode:	API+
Scan range:	50–500 *m/z*
Acquisition mode:	MS
Source temp.:	150 °C
Interface temp.:	300 °C
Cone voltage:	40 V
Cone gas:	50 L/h
Auxiliary gas:	200 L/h
Corona current:	4.0 µA

Data management

MassLynx v4.1

RESULTS AND DISCUSSION

MONITORING CHEMICAL REACTION (BORYLATION OF AROMATICS)

To illustrate the functionality of such a system, the synthesis of an arylboronic (Figure 1) was used as a reaction model. Arylboronic is an important educt in chemical reactions (Suzuki reaction). These reactions are often used in medicinal chemistry projects to combine building blocks in palladium catalyzed couplings.

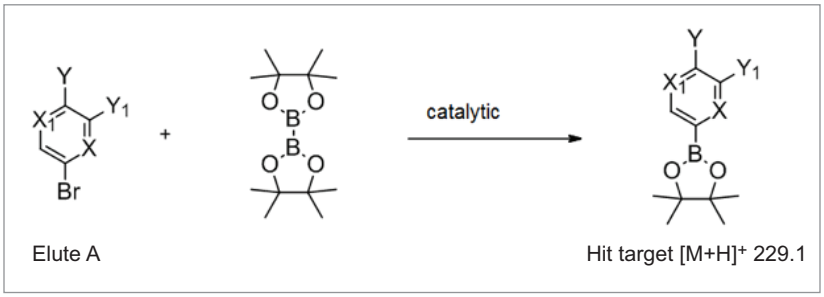

Figure 1. Structures of arylboronic and synthesis.

The increase in the formation of an arylboronic was monitored, as was the decrease from educt A. See in summary result report Figure 4.

SAMPLE PREPARATION

The reaction mix is diluted with acetonitrile to optimal sample concentration from 0.05 mg/mL to 0.1 mg/mL.

SELF-SERVICE OPEN ACCESS SAMPLE LOGIN START

The OpenLynx Open Access login screen shown in Figure 2 allows the bench chemist to set up the system so that the user only needs to input the requested information, and then upon completion, the analysis can start.

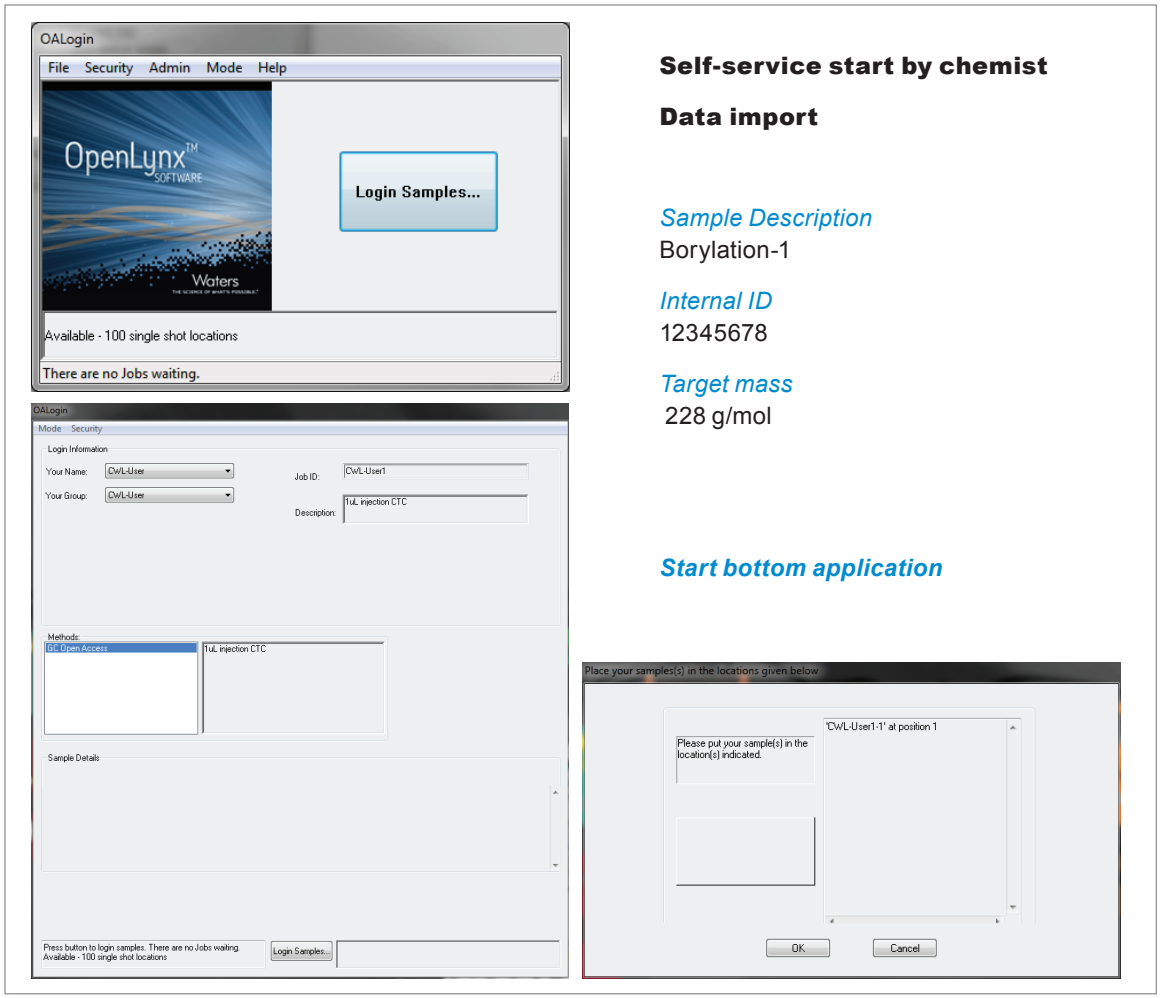

Figure 2. The OpenLynx single page login.

PROTONATION AND HIT FINDING $[M+H]^+$

Protonation occurs when excess water or other modifiers are present in the system and give rise primarily to protonated molecular ion $[M+H]^+$ information. This $[M+H]^+$ ionization is the basis for the automatic hit target interpretation process.

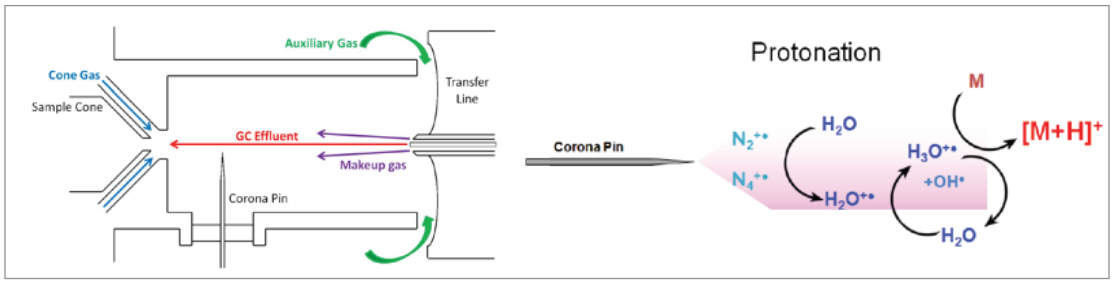

Figure 3. Schematic of APGC ionization source and mechanism of protonation ionization.

A chemical target $[M+H]^+$ is found through the automatic interpretation process under protonation ionization condition (Figure 3).

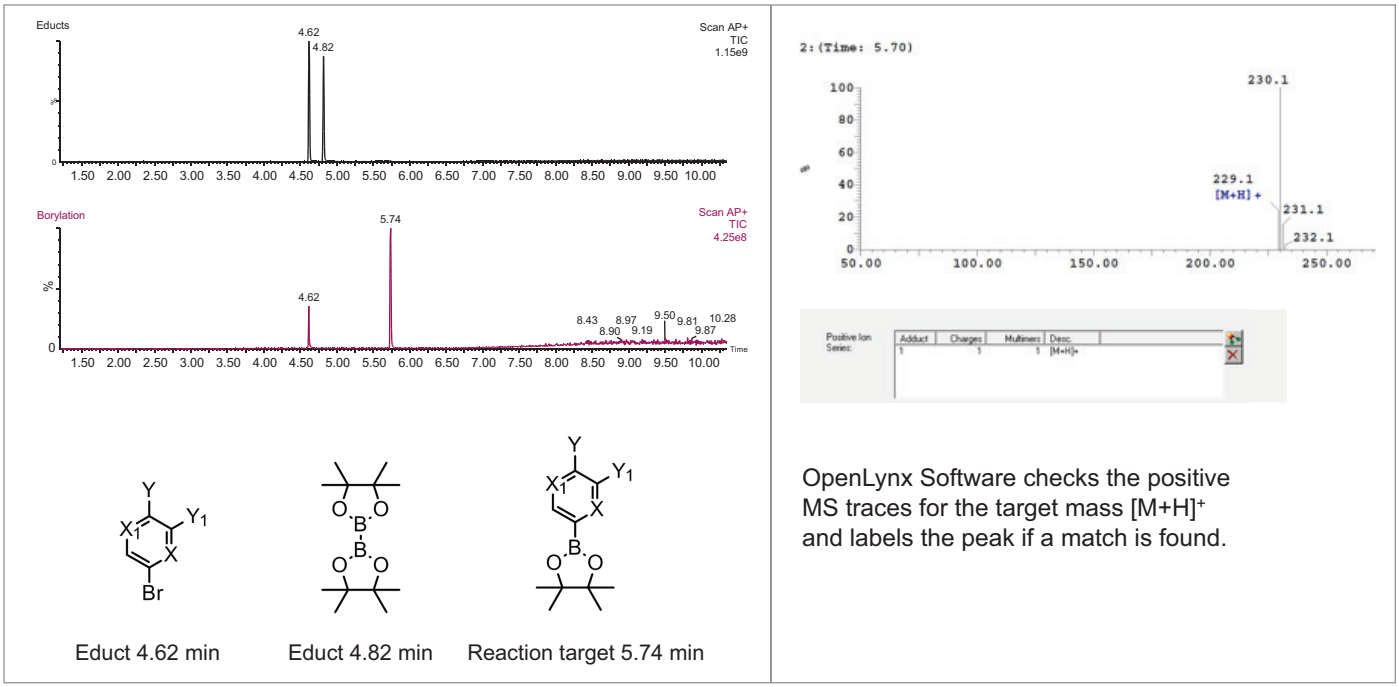

Figure 4. Chemical target hit [M+H]+.

REPORTING

The view report style was designed with the MassLynx report editor. This report style gives the chemist all necessary information in one view designed for his experiment.

Gas chromatograph conditions guaranteed a high separation for many substance classes to this research task.

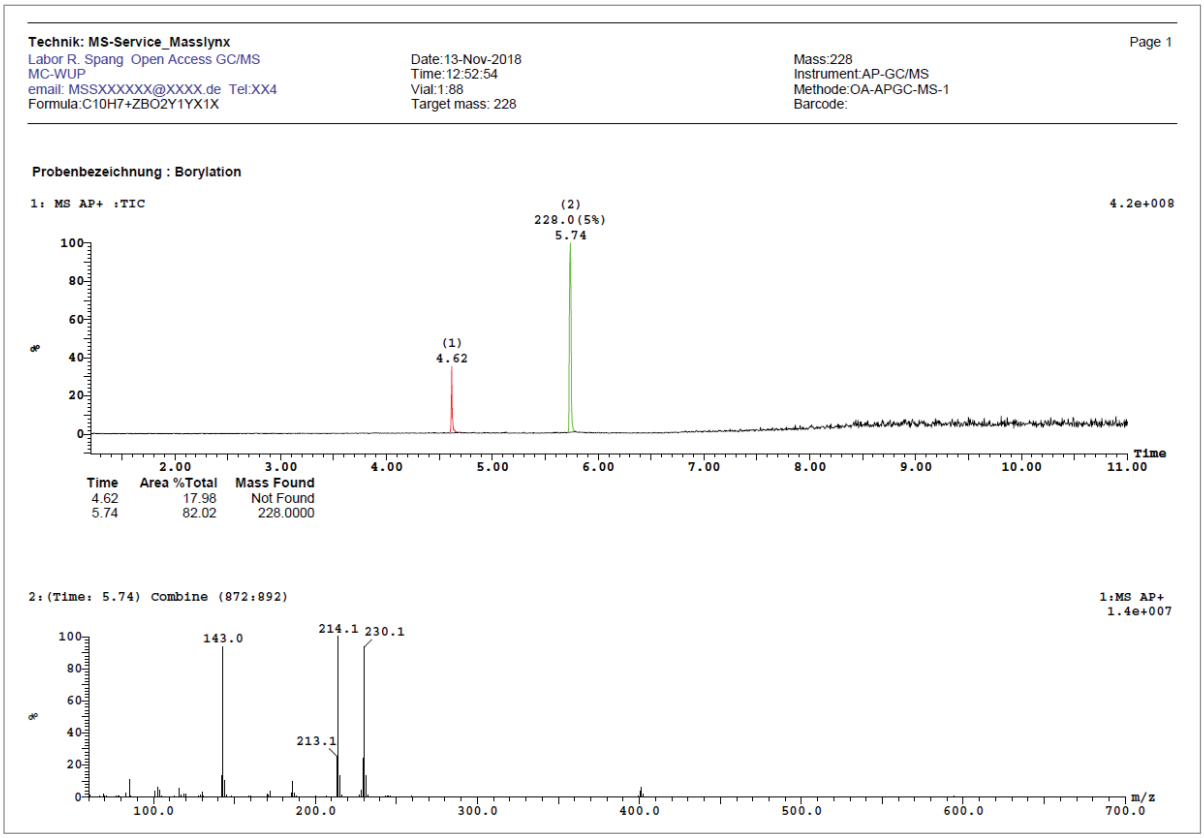

Figure 5. Summary report styles.

CONCLUSIONS

By using an Open Access APGC-MS System, the medicinal chemists were able to quickly and easily monitor their reactions. Open Access gives the chemist a GC-MS system that is flexible for analytical data acquisition. The mass spectrometry and gas chromatography conditions generated good separation and soft ionization yielding protonated molecules. This system allows a very robust automatic hit finding workflow. With the single page report style (Figure 4) the bench chemist gets the formation status for the chemical reaction in a compact manner to ensure a fast interpretation of the analytical results.

References

1. Waters.com. Hints and Tips – Guidance for APGC users.

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