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Boronic Acid Analysis by Mass Spectrometry – II: Atmospheric Solids Analysis Probe (ASAP)

by CM Williams, EPSRC National Mass Spectrometry Service Centre, Swansea University, SA2 8PP, UK
<http://www.nmssc.ac.uk/>

Introduction

Boronic acids have been notoriously difficult to analyse without the need for derivitisation^[1]. Until recently, the method utilised at the NMSSC required the use of 1,2-ethanediol to create an ester that could be analysed by electron ionisation (EI) or chemical ionisation CI^[1]. Previously, a study was instigated to investigate the ideal conditions for the generation of a molecular or pseudo-molecular species using atmospheric pressure ionisation (API) techniques and mass spectrometry^[4]. Boronic acids are used widespread throughout the chemical, and biochemical world. The need for an easy, rapid method of generating an intact (pseudo-) molecular species has been a goal for many years. There has been a recent literature report of the analysis of boronic acids by nano liquid chromatography-direct electron ionization mass spectrometry, using a system built in-house^[2]. The authors showed that their system was able to produce a molecular species with the added benefit of chromatographic separation. Presented here is a method which any modern APCI instrument can be modified to perform.

Experimental methodology

Instrumentation

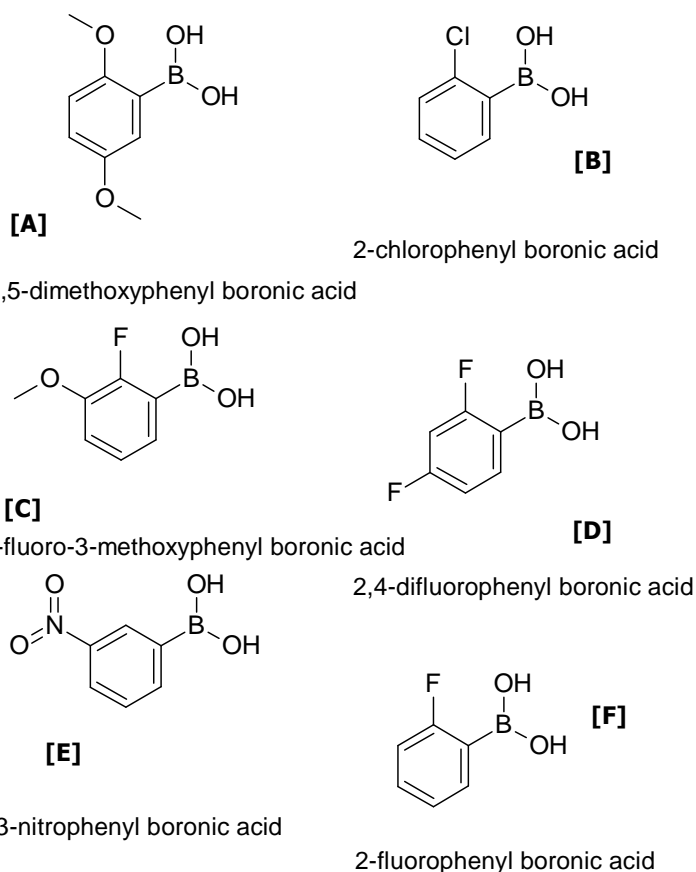
- Thermo Fisher Scientific LTQ Orbitrap XL (Thermo Fisher Scientific Inc., CA, USA).
- ASAP-MS probe^[1] for Thermo Fisher Ion Max source (In APCI mode).
- All data acquisition, processing and reporting was achieved using Xcalibur v2.0.7.

Materials and Reagents

- Six standard samples, structure [A] to [F], were donated by Dr A.W.T. Bristow, AstraZeneca for an inter-laboratory study on the ionisation of boronic acids^[4].

Method

- ASAP was performed as described in NMSSC Application Note 7.
- Samples were ionised as solids with no additives.
- The APCI vaporiser temperature was increased slowly until the boronic acid ionised.



Results and Discussion

- All six boronic acids were successfully analysed using ASAP with no modification.
- Results presented previously showed that the use of nano-electrospray ionisation, electrospray ionisation and APCI ionisation gave varying success and the choice of solvent was crucial^[4].
- The analyses of 2,5-dimethylphenyl boronic acid, with the theoretical isotope pattern below can be seen in Figure 1.
- Due to the two isotopes of boron, ions are observed for both the ¹⁰B and ¹¹B. It can be seen that the ions correspond to the [M+H]⁺ species.
- The analysis of 2-chlorophenyl boronic acid can be seen in Figure 2. The presence of Cl and B can clearly be observed from the isotope pattern, shown in the bottom spectrum.
- It was essential that the APCI vaporiser temperature was low when the probe was inserted into the source.

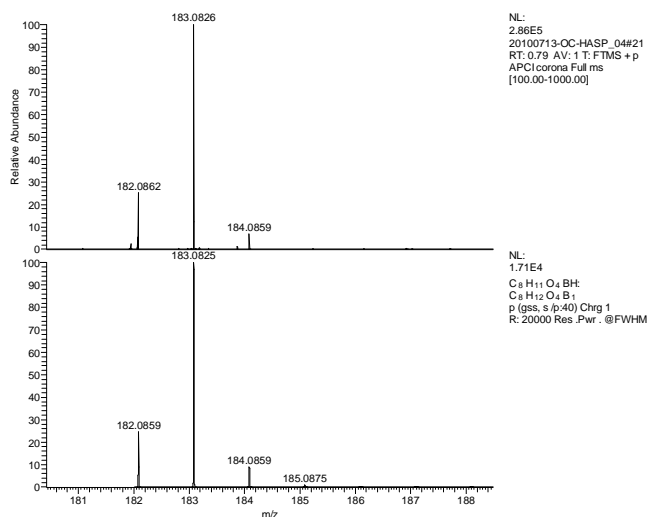


Figure 1: ASAP analysis of 2,5-dimethoxyphenyl boronic acid. Ions observed are $[M+H]^+$ ^{10}B at 182, $[M+H]^+$ ^{11}B at 183 and their respective isotopes.

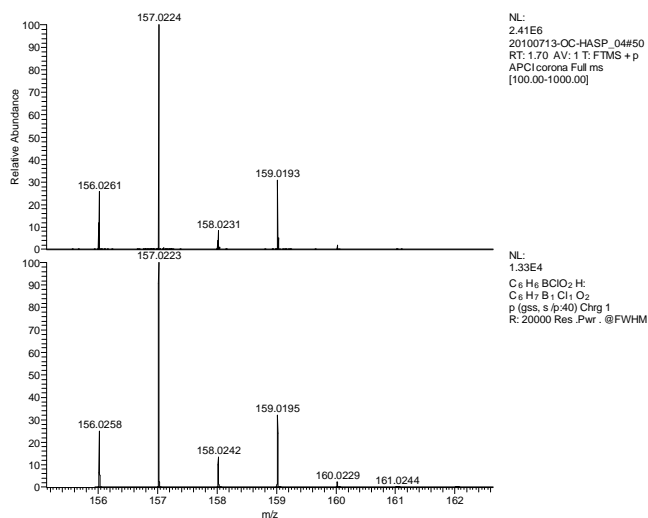


Figure 2: ASAP analysis of 2-chlorophenyl boronic acid. The isotope pattern clearly shows the presence of both boron and chlorine.

- Failure to keep the temperature low resulted in the formation of the boroxine from the boronic acid, as shown in Figures 3 and 4.

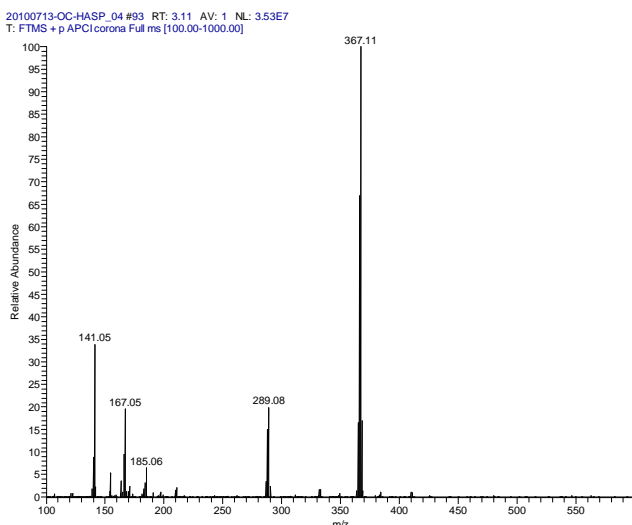


Figure 3: ASAP analysis of 2-fluorophenyl boronic acid. Note the formation of the boroxine at high temperature.

- The observed spectrum vs the theoretical isotope pattern for the boroxine formed from 2-fluorophenyl

boronic acid clearly shows that 3 $-OH$ groups have been lost in the boroxine formation, Figure 4.

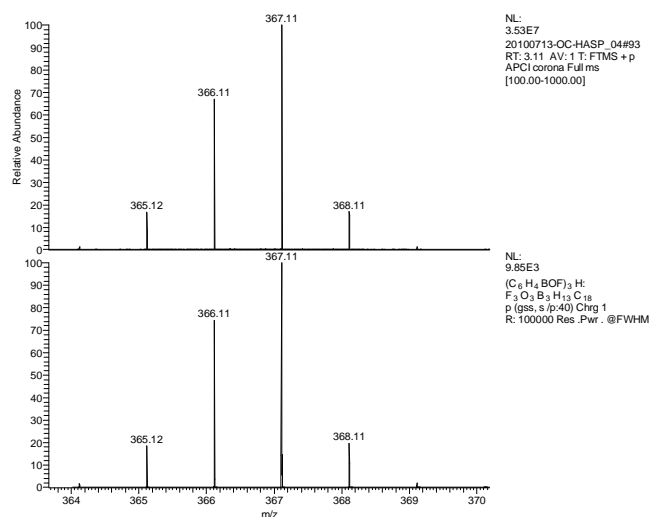


Figure 4: ASAP analysis of 2-fluorophenyl boronic acid. Note the formation of the boroxine, showing observed, top, and theoretical isotope pattern, bottom, of the formed boroxine.

Conclusion

- ASAP has been shown to aid the analysis of boronic acids.
- Analysis was rapid and required no sample preparation.
- Careful experimental conditions must be observed to avoid over heating of the sample.
- The protonated molecular species was observed in positive mode.
- The method is far simpler than previous methods used^[1,4].

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- Dr A. W. T. Bristow (Astra Zeneca)

References

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