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ANALYTICAL CHALLENGE

Arsenic speciation challenge

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We would like to invite you to participate in the Analytical Challenge, a series of puzzles to entertain and challenge our readers. This special feature of "Analytical and Bioanalytical Chemistry" has established itself as a truly unique quiz series, with a new scientific puzzle published every three months. Readers can access the complete collection of published problems with their solutions on the ABC homepage at http://www.springer.com/abc. *Test your knowledge and tease your wits in diverse areas of analytical and bioanalytical chemistry by viewing this collection.*

In the present challenge, arsenic is the topic. And please note that there is a prize to be won (a Springer book of your choice up to a value of €100,- given to one winner selected randomly).

Please read on…

Introduction

Arsenic is an element that occurs naturally in the Earth's crust and is distributed throughout the environment. Used by humans for over 2000 years, arsenic was long regarded as a remedy for many maladies [1].However, effective treatments were often accompanied by undesirable side effects, which led to the synthesis of many arsenic-containing compounds in the early 1900s in pursuit of alternatives to the existing arsenic-based therapies. Despite its promise in the medical realm, the notoriety of arsenic is largely due to its use as a toxic substance, both in the form of pesticides and chemical warfare agents. It is now recognized that the toxicity of arsenic is partly dependent on the oxidation state, with inorganic arsenic being considerably more toxic than organic arsenic. Indeed, exposure to inorganic arsenic has been linked to cancer. The ability to distinguish between inorganic and organic forms of arsenic, known as speciation, was recently in the spotlight when concerns about arsenic levels in apple juice and rice received widespread publicity [2].Despite the long history of the use and study of arsenic, new findings continue to be made. For example, the most common organoarsenic compound, arsenobetaine, was not identified until the 1970s [3].More recently, arsenic was in the headlines when it was controversially claimed that a microbe had been discovered in which the DNA contained arsenic atoms where phosphorus atoms had been expected (these findings have been met with strong rebuttals) [4].As we seek to fully understand the roles of arsenic in our world and its impacts on human health, there is a need to identify as many arsenic species as possible.

Meet the challenge

After a renowned arsenic chemist retired from his position in your lab, you were cleaning out his supplies and noticed a vaguely labelled vial containing a solid residue. Knowing that it was likely associated with arsenic, you analyzed the residue using a high-performance liquid chromatography (HPLC) system connected to an inductively coupled plasma mass spectrometer (ICP-MS). You noticed that an arsenic-containing compound eluted from the anion exchange column well after several other anionic species, but this substance did not match any of your reference standards. With the excitement of finding a never-before-seen compound, the HPLC system was then connected to a high-resolution mass spectrometer (HRMS) equipped with an electrospray ionization (ESI) source. At the elution time indicated by the ICP-MS, there was a positively charged ion at *m/z* 258.9291. When the same analysis was repeated in negative polarity, an ion at *m/z* 256.9146 was observed.

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Table 1 ESI-HRMS/MS product ion masses from the pseudo-molecular ions of the mystery substance along with its three main thiolated reaction products

Pseudo-molecular precursor ions, $[M+H]^+$ (*m/z*)	Product ions (*m/z*)
258.9291	240.9186, 228.9182, 210.9077, 192.8972, 164.8661, 138.9734, 136.9578, 118.9838, 104.9683
274.9054	256.8958, 228.9186, 210.9077, 164.8661, 150.9556, 138.9733, 136.9942, 104.9684
290.8830	272.8729, 226.8852, 168.9121, 154.9503, 150.9559, 136.9400, 118.9838, 104.9685
306.8600	272.8727, 226.8852, 170.9278, 168.9121, 150.9556, 136.9401, 118.9839, 104.9684

The challenge

The ESI-HRMS instrument is known to provide accurate mass measurements within an error of 5 parts per million. Thus, the exact molecular mass effectively leads to a unique molecular formula assignment. However, this alone is not enough to identify our mystery substance. Tandem mass spectrometry (MS/MS) of the positive precursor ion at *m/z* 258.9291 was performed to potentially provide structural information about the unknown compound; the observed product ions are listed in the first row of Table 1.

To supplement the structural information gathered from the MS/MS spectrum, you performed additional experiments by treating the substance with H_2S, which results in the progressive exchange of the oxygen atoms with sulfur. Following this treatment, the substance was again passed through the HPLC column and three new major peaks were observed, each of which eluted separately in the chromatogram. Positive polarity ESI-HRMS spectra contained major ions at *m/z* 274.9054, 290.8830, and 306.8600, respectively. These three ions were then individually subjected to MS/MS and the resulting product ions are listed in Table 1.

Given all of these experimental data, can you determine the most likely structure of the unknown compound? And what is the IUPAC name of this compound?

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Declarations

Conflict of interest The authors declare no competing interests.

References

1. Emsley J. Arsenic is everywhere. The Elements of Murder. New York: Oxford University Press; 2005. p. 93–115.
2. Arnaud, CH. Eating Arsenic. Chemical & Engineering News. 2013. https://cen.acs.org/articles/91/i18/Eating-Arsenic.html
3. Edmonds JS, Francesconi KA, Cannon JR, et al. Isolation, crystal structure and synthesis of arsenobetaine, the arsenical constituent of the western rock lobster *Panulirus longipes cygnus* George. Tetrahedron Lett. 1977;18:1543–6.
4. Drahl, C. The Arsenic-Based-Life Aftermath. Chemical & Engineering News. 2012. https://cen.acs.org/articles/90/i5/Arsenic-Based-Life-Aftermath.html

We invite our readers to participate in the Analytical Challenge by solving the puzzle above. Please send the correct solution to abc@springer.com *by October 1, 2022. Make sure you enter "Arsenic speciation challenge" in the subject line of your e-mail. The winner will be notified by e-mail and their name will be published on the "Analytical and Bioanalytical Chemistry" homepage at* http://www.springer.com/abc *and in the journal (volume 415/issue 1) where readers will find the solution and a short explanation.*

The next Analytical Challenge will be published in 414/24, October 2022. If you have enjoyed solving this Analytical Challenge you are invited to try the previous puzzles on the ABC homepage.