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Application of direct analysis in real time to a multiphase chemical system: identification of polymeric arsanes generated by reduction of monomethylarsenate with sodium tetrahydroborate

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ABSTRACT

Direct analysis in real time (DART) has been applied in conjunction with high-resolution Orbitrap mass spectrometry to characterize the products of the aqueous reduction of monomethylarsenate by tetrahydroborate (B/As molar ratio ≈ 4 mol/mol). Under these conditions, the reaction gives rise to a complex mixture of arsenic compounds which result in the formation of a reddish precipitate. The use of the DART revealed the presence of a number of polymeric arsanes – up to eight arsenic atoms – associated with the liquid/solid phase of this reaction system. These polymers exhibit an uncommon ionization behavior similar to alkanes, where the action of the DART results in the generation of $[M - H]^+$ ions. Furthermore, for each polymer $\text{MeHAs}-(\text{AsMe})_n-\text{AsHMe}$ ($n = 0-8$), a series of oxidation products $[(M + nO) - H]^+$ was also identified and their formation has been discussed.

FIGURE FOR TABLE OF CONTENT ONLY (TOC)

ARSANE GENERATION

MeHAs-(AsMe)_n-AsHMe
n = 0 - 8

DART - ORBITRAB

MASS SPECTRUM

Hydride extraction
Oxidation products

INTRODUCTION

In the field of mass spectrometry, direct analysis in real time (DART) is regarded as the most significant invention since the introduction of electrospray (ESI) and matrix assisted laser desorption ionization (MALDI).¹ DART is a non-destructive ambient ionization source able to yield desorption/ionization – directly in open air – of low molecular weight analytes present on the surface of liquid/solid materials or in the gas-phase.^{1,2} Relative to the fundamentals of its ionization mechanism, DART is among the best understood of the ambient ionization techniques. In fact, alike other atmospheric pressure ionization techniques,³ the action of the DART on a molecule (M) results in the production of $M^{+•}$ and $[M + H]^+$ positive ions and $[M - H]^-$ negative ions.¹ Since its introduction in 2005,² DART has witnessed an increasing number of applications in many fields of analytical science,^{1,4} including analysis of pharmaceuticals,⁵ warfare agents,⁶ drug discovery monitoring⁷ and food testing.^{8–10}

In this study, we present use of the DART source interfaced with an Orbitrap high resolution mass spectrometer for monitoring the constituents of a complex-multiphase chemical system. The reaction under study is the aqueous reduction of a solution of monomethylarsenate with sodium tetrahydroborate. This chemistry – hydride generation – has been utilized in analytical chemistry for many years^{11,12} and applied to the determination and speciation of trace levels of arsenic compounds.¹³ Under analytical conditions (i.e., trace and ultratrace levels of As), borohydride converts simple arsenic oxoacids into their corresponding arsanes through a concerted reduction.¹⁴ However, when the concentration of arsenic increases, a complex scenario of side reactions occurs, resulting in the formation of condensation by-products which can result in the precipitation of compounds containing arsenic.¹⁵ Most of the analytical work to date on the characterization of this chemical system has been performed by GC/MS analysis of the reaction headspace.^{14,16} No direct confirmation of compounds associated with the liquid/solid phase of this reaction system has been achieved. Considering the complex nature of this chemistry, direct chromatographic investigation of the liquid/solid phase is unfeasible. Here, we propose use of DART for the identification of the compounds associated with the condensed phase of this aqueous system.

EXPERIMENTAL SECTION

Reagents and materials. An aqueous standard solution of monomethylarsenate was prepared from its sodium salt [$w(\text{MeAsO}(\text{ONa})_2) = 0.99 \text{ g/g}$, ChemService, PA, USA] in 0.1 M HCl at a mass fraction of 1000 $\mu\text{g/g}$ as As. A reducing solution of sodium tetrahydroborate (1% w/w) was prepared by dissolving the solid salt ($w(\text{NaBH}_4) \geq 0.98 \text{ g/g}$, Alfa Aesar, Word Hill, MA, USA) in aqueous 0.1 M NaOH.

Instrumentation. A DART (Direct Analysis in Real Time) ion source (IonSence, Saugus MA, USA) was placed 17 mm away from the orifice of a LTQ linear ion trap-Orbitrap mass spectrometer working in positive ion mode (Thermo Fisher Scientific Inc., Bremen, Germany). The mass spectrometer was tuned and calibrated according to the manufacturer's operating instructions. The DART functioned using helium as carrier gas at 3.5 mL/min. Operating temperature was set at 100 °C and all other DART operating conditions were standard settings: needle current = 9990 μA ; needle voltage = 3500 V; discharge electrode current = 7 μA ; discharge electrode voltage = 150 V; grid electrode current = 10 μA ; grid electrode voltage = 250 V.

Hydride generation. A 1 mL volume of 1000 $\mu\text{g/g}$ As as monomethylarsenate in 0.1 M HCl was introduced into a 4 mL borosilicate vial. The vial was then closed with a holed screw cap equipped with a teflon/silicone septum. A 200 μL volume of borohydride solution (1% w/w NaBH_4 in 0.1 M NaOH) was then injected into the solution of the monomethylarsenate with a plastic syringe.

Safety considerations. Because of the high toxicity and volatility of the arsenic compounds generated, all experiments were conducted in a vented lab, using adequate PPE.

RESULTS AND DISCUSSION

When a dilute aqueous solution of monomethylarsenate ($w(\text{As}) < 1 \mu\text{g/g}$) is mixed with an excess of tetrahydroborate (B/As molar ratio $> 10^3 \text{ mol/mol}$), complete conversion of the arsenic oxoacid into monomethylarsane is normally expected:^{11,14}

However, when the same reaction is conducted at high concentration of arsenic (e.g., $1000 \mu\text{g/g As}$), the reaction medium immediately becomes yellowish following injection of the reducing agent, and the subsequent formation of a reddish precipitate reveals a peculiar chemistry unexplained by reaction (1) alone (see Figure 1). Obviously, this is an unwanted phenomenon from an analytical point of view.

An interpretation of this observation was recently advanced based on GC/MS analysis of the reaction headspace.¹⁵ The identification of polymeric arsenic compounds yields the conclusion that, under non-analytical conditions, hydride generation of MeAsH_2 (1) becomes competitive with that of condensation between arsanes and arsenic oxoacids not yet reduced, which are simultaneously present in the reaction medium:

Using GC/MS it was possible to identify only arsane dimers (As-As) and trimers (As-As-As) which are sufficiently volatile to be sampled *via* the headspace;¹⁷ unfortunately, it was not possible to achieve identification of heavier compounds. Furthermore, due to the complex multiphase nature of the reaction medium, the implementation of other chromatographic techniques is precluded. A DART-Orbitrap setup was thus investigated as a means to identify any higher molecular weight by-products that may be produced as a consequence of this hydride generation chemistry.

Figure 1. An aqueous solution of monomethylarsenate ($w(\text{As}) = 1000 \mu\text{g/g}$) in 0.1 M HCl (A) is reacted with $[\text{BH}_4]^-$. After 30 s the solution becomes yellowish (B) and after 30 min a precipitate appears (C).

Positive ion DART mass spectrum of Me₂As₂H₂. The reduction of monomethylarsenate by tetrahydroborate under non-analytical conditions was achieved as described in the experimental section. The headspace of the reaction vessel was sampled with a gas-tight syringe and the content injected directly into the DART source. As reported previously,¹⁵ the GC/MS analysis of this headspace revealed the presence of methylarsane (MeAsH₂, the expected analytical product) and two volatile condensation by-products: 1,2-dimethyl diarsane (MeHAs-AsHMe), and 1,2,3-trimethyl triarsane (MeHAs-AsMe-AsHMe). Accordingly, use of the DART-Orbitrap for analysis of the reaction headspace was aimed at identifying the ionization pathway typical for this class of compounds. The resultant mass spectrum of volatile reaction products is shown in Figure 2 and is dominated by the presence of 1,2-dimethyl diarsane. The mass spectrum of MeHAs-AsHMe (M) does not exhibit intense signals for the expected [M + H]⁺ ion or the molecular ion M⁺. Surprisingly, the most characteristic signal associated with the MeHAs-AsHMe molecule is [M – H]⁺ which can be detected at 180.8964 Da (Figure 2):

In this respect, the spectral characteristic of 1,2-dimethyl diarsane is similar to that of alkanes, which also ionize in positive mode yielding [M – H]⁺ species.³ Furthermore, the mass spectrum of 1,2-dimethyl diarsane exhibits an intense signal at 164.8651 Da, corresponding to the [MeAs-As]⁺ fragment. It is interesting to note that ions at *m/z* = 165 Da and 185 Da are, respectively, the first and second most abundant ions in the EI⁺ spectrum obtained by GC/MS.¹⁶ Table 1 reports all fragments identified in the DART mass spectrum shown in Figure 2. The signals identified with accurate mass measurements include most of the products of fragmentation that MeHAs-AsHMe can yield.

From Figure 2 it is also possible to identify the [M – H]⁺ ion of 1,2,3-trimethyl triarsane at 207.8404 Da. The similar behavior of 1,2-dimethyl diarsane and 1,2,3-trimethyl triarsane toward DART ionization suggests that the hydride abstraction is a characteristic ionization pathway associated with this class of polyarsanes.

Table 1. Ions identified in DART mass spectrum of 1,2-dimethyl diarsane (MeHAs-AsHMe)

Fragment formula	Ion ^(a)	Exact mass (Res 30,000)	Error/ppm
MeH ₂ As-AsHMe	[M + H] ⁺	182.9119	-6.4
MeHAs-AsHMe	[M] ⁺	181.9032	-11.3
MeAs-AsHMe	[M - H] ⁺	180.8964	-5.8
MeAs-AsMe	[M - H ₂] ⁺	179.8884	-6.4
MeHAs-AsH	[M - CH ₃] ⁺	166.8806	-6.7
MeHAs-As	[M - H - CH ₃] ⁺	165.8725	-8.9
MeAs-As	[M - H ₂ - CH ₃] ⁺	164.8651	-6.3
As-AsH	[M - H - (CH ₃) ₂] ⁺	150.8493	-8.0
As-As	[M - H ₂ - (CH ₃) ₂] ⁺	146.8414	-8.0

(a) The most abundant ions are the [M - H]⁺ and the [M - H₂ - CH₃]⁺. The relative abundance of the other fragments is below 2%.

Figure 2. DART-Orbitrap mass spectrum of the reaction headspace generated by mixing 1 mL of monomethylarsenate solution (1000 µg/g As in 0.1 M HCl) with 0.2 mL of tetrahydroborate solution (1% w/w NaBH₄ in 0.1 M NaOH). The error, in part-per-million, of the mass measurement is presented in parentheses.

Identification of polyarsanes. The DART-Orbitrap interrogation of the liquid/solid phase of the monomethylarsane/tetrahydroborate reaction medium was achieved through the use of a glass tip. The tip was immersed in the solution (Figure 1c) and placed close to the helium gas stream exiting the DART to expose the liquid film to the ion source. Figure 3 reports the background subtracted mass spectrum obtained. Polymeric chains of arsanes containing up to eight As atoms ($\text{MeHAs}-(\text{AsMe})_n-\text{AsHMe}$, $n = 0-8$) could be identified through exact-mass measurements. The identification of polymers with more than three arsenic atoms agrees with, and provides further confirmation of, the condensation cascade mechanism proposed by D'Ulivo et al. to describe reduction of monomethylarsenate under non-analytical conditions (2).¹⁵

As expected, for each of these arsenic polymers, the most abundant signal in the DART mass spectrum corresponds to the $[\text{M} - \text{H}]^+$ moiety (Figure 3). For each oligomer, however, it was also possible to identify ions containing an increasing number of oxygen atoms (i.e., $[(\text{M} + \text{O}) - \text{H}]^+$, $[(\text{M} + 2\text{O}) - \text{H}]^+$, $[(\text{M} + 3\text{O}) - \text{H}]^+$, etc.). Such oxygenated ions could result from polymeric arsanes containing As(V) generated in liquid phase by condensation between reaction intermediates. In fact, we can reasonably assume that this condensation cascade reactivity involves not only As(III), but also As(V) species which contain oxygen atoms not reactive towards condensation ($-\text{As}=\text{O}$ moiety). For example, the formation of a fully oxygenated trimer may occur starting from $\text{MeAsH}(\text{O})-\text{OH}$:

The formation of such oxygenated polymers by condensation cascade is also supported by previous identification of $\text{Me}_2\text{As}^{\text{III}}-\text{As}^{\text{V}}(\text{O})\text{Me}_2$ in the headspace after reduction of cacodylic acid under similar experimental conditions.¹⁶

On the other hand, the existence of $[(\text{M} + n\text{O}) - \text{H}]^+$ ions in the DART mass spectra of these polyarsanes may also be justified by possible oxidation reactions of $[\text{M} - \text{H}]^+$ occurring in the ionization/dissolution.

It is noteworthy that such oxidations can take place in the gas-phase and have been reported for alkanes.³

These oxidations are also consistent with the chemistry of arsenic because the valence state of arsenic can be raised from III to V by formal addition of oxygen:

In this vein, the generation of ions such as $[(M + n\text{O}) - \text{H}]^+$ can also be interpreted as an ionization by-product of these arsenic polymers, another similarity between alkanes and polyarsanes. Table 3 reports all ions identified in the condensed phase for each of the oligomers.

Table 3. Arsenic compounds identified in the liquid/solid phase of the monomethylarsenate/tetrahydroborate reaction system

Oligomers	Ions ^(a)	Exact Mass (Res 30,000)	Error/ppm
1,2,3-Trimethyl triarsane M = MeHAs-AsMe-AsHMe	[M - H] ⁺	270.8404	-7.7
	[(M + O) - H] ⁺	286.8348	-9.2
	[(M + 2O) - H] ⁺	302.8294	-9.6
	[(M + 3O) - H] ⁺	318.8243	-9.3
	[(M + 4O) - H] ⁺	334.8191	-9.1
1,2,3,4-Tetramethyl tetrarsane M = MeHAs-(AsMe) ₂ -AsHMe	[M - H] ⁺	360.7846	-8.4
	[(M + O) - H] ⁺	376.7793	-8.1
	[(M + 2O) - H] ⁺	392.7735	-9.8
	[(M + 3O) - H] ⁺	408.7682	-10.2
	[(M + 4O) - H] ⁺	424.7627	-10.6
1,2,3,4,5-Pentamethyl pentarsane M = MeHAs-(AsMe) ₃ -AsHMe	[M - H] ⁺	450.7286	-8.9
	[(M + O) - H] ⁺	466.7227	-9.8
	[(M + 2O) - H] ⁺	482.7171	-11.0
	[(M + 3O) - H] ⁺	498.7119	-11.0
1,2,3,4,5,6-Hexamethyl hexarsane M = MeHAs-(AsMe) ₄ -AsHMe	[M - H] ⁺	540.6725	-9.7
	[(M + O) - H] ⁺	556.6674	-9.4
	[(M + 2O) - H] ⁺	572.6616	-10.5
	[(M + 3O) - H] ⁺	588.6567	-9.8
	[(M + 4O) - H] ⁺	604.6508	-10.8
	[(M + 5O) - H] ⁺	620.6472	-8.2
1,2,3,4,5,6,7-Heptamethyl heptarsanes M = MeHAs-(AsMe) ₅ -AsHMe	[M - H] ⁺	630.6162	-10.4
	[(M + O) - H] ⁺	646.6113	-9.7
	[(M + 2O) - H] ⁺	662.6062	-9.7
	[(M + 3O) - H] ⁺	678.6007	-10.0
1,2,3,4,5,6,7,8-Octamethyl octarsane M = MeHAs-(AsMe) ₆ -AsHMe	[M - H] ⁺	720.5607	-9.9

(a) Besides the positive ion arising from hydride extraction, numerous oxidation products could be identified for each oligomer.

Figure 3. DART-Orbitrap mass spectrum of polyarsanes generated by mixing 1 mL of monomethylarsenate solution (1000 µg/g As in 0.1 M HCl) with 0.2 mL of tetrahydroborate solution (1% w/w NaBH₄ in 0.1 M NaOH). The error, in part-per-million, of the mass measurement is presented in parentheses.

CONCLUSIONS

DART-Orbitrap MS has proven to be a powerful tool for the characterization of a multiphase chemical system. This configuration was adopted to study the reduction of monomethylarsenate by sodium tetrahydroborate. Despite the complexity of this reaction mixture, it was possible to identify several oligomers of arsanes originating from a condensation cascade between various reaction intermediates (arsenates and arsanes) present in the medium. These polymers present a peculiar ionization pathway. Similar to the alkanes, the DART mass spectra of polyarsanes are dominated by the positive ion arising from hydride extraction $[M - H]^+$. For each $\text{MeHAs}(\text{AsMe})_n\text{-AsHMe}$ ($n = 0-8$) polyarsane, a series of oxidation products $[(M + nO) - H]^+$ was also observed. The observation of such ions in the DART mass spectrum may represent the fingerprint of oligomers of As(V) generated in the liquid phase by condensation cascade or the formation of $[(M + O) - H]^+$ ions may be attributed to oxidation reactions taking place in the DART source as earlier reported by Cody for the alkanes.

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