

## Video Article

# Analysis of Volatile and Oxidation Sensitive Compounds Using a Cold Inlet System and Electron Impact Mass Spectrometry

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URL: <https://www.jove.com/video/51858>

DOI: [doi:10.3791/51858](https://doi.org/10.3791/51858)

Keywords: Chemistry, Issue 91, mass spectrometry, electron impact, inlet system, volatile, air sensitive

Date Published: 9/5/2014

Citation: Sproß, J. Analysis of Volatile and Oxidation Sensitive Compounds Using a Cold Inlet System and Electron Impact Mass Spectrometry. *J. Vis. Exp.* (91), e51858, doi:10.3791/51858 (2014).

## Abstract

This video presents a protocol for the mass spectrometrical analysis of volatile and oxidation sensitive compounds using electron impact ionization. The analysis of volatile and oxidation sensitive compounds by mass spectrometry is not easily achieved, as all state-of-the-art mass spectrometric methods require at least one sample preparation step, e.g., dissolution and dilution of the analyte (electrospray ionization), co-crystallization of the analyte with a matrix compound (matrix-assisted laser desorption/ionization), or transfer of the prepared samples into the ionization source of the mass spectrometer, to be conducted under atmospheric conditions. Here, the use of a sample inlet system is described which enables the analysis of volatile metal organyls, silanes, and phosphanes using a sector field mass spectrometer equipped with an electron impact ionization source. All sample preparation steps and the sample introduction into the ion source of the mass spectrometer take place either under air-free conditions or under vacuum, enabling the analysis of compounds highly susceptible to oxidation. The presented technique is especially of interest for inorganic chemists, working with metal organyls, silanes, or phosphanes, which have to be handled using inert conditions, such as the Schlenk technique. The principle of operation is presented in this video.

## Video Link

The video component of this article can be found at <https://www.jove.com/video/51858/>

## Introduction

The analysis of compounds, such as metal organyls, silanes, or phosphanes by mass spectrometry is not always feasible. Several of these compounds are known to decompose rapidly when in contact with air. Therefore the most crucial steps when measuring mass spectra are sample preparation, the transfer of the analyte into the mass spectrometer and ion generation in the absence of air. In this protocol, we describe a strategy to meet these requirements and present an inlet system, which makes it possible to obtain mass spectra of volatile compounds previously not to be analyzed by mass spectrometry due to their difficult handling and rapid decomposition under ambient conditions. Thereby, unambiguous identification of novel or existing volatile metal organyls, silanes and phosphanes, susceptible to oxidation or hydrolysis, can now be performed with the assistance of mass spectrometry. There are two requirements which have to be met in order to analyze compounds which are susceptible to oxidation or hydrolysis: sample preparation and ion generation under inert conditions. The last premise can be easily met using a mass spectrometer with an ion source operating under vacuum. This is the case with most matrix-assisted-laser-desorption/ionization (MALDI) mass spectrometers and with all electron impact ionization (EI) mass spectrometers<sup>1,2</sup>. Electrospray ionization (ESI) is not readily compatible for the analysis of compounds susceptible to oxidation or hydrolysis, as the ionization process takes place under ambient conditions<sup>3</sup>. However, for some compounds which react not vigorously with oxygen or water, the drying and nebulizing gas with which most ESI sources are operated is sufficient for analysis by mass spectrometry<sup>4</sup>. This is also the case for ionization strategies similar to ESI, e.g., low-temperature ESI, low-temperature atmospheric pressure ionization, and low-temperature liquid secondary ion mass spectrometry<sup>5-7</sup>. In contrast, sample preparation and transfer into the ion source under inert conditions is much more challenging. Both MALDI and ESI instruments have been coupled with glove boxes in order to enable sample preparation of compounds susceptible to oxidation and/or hydrolysis in an inert atmosphere<sup>4,8</sup>. The mass spectrometer is interfaced to the glove box either with a transfer capillary (ESI) or directly attached to the glove box (MALDI). The coupling of a glove box to a mass spectrometer via a transfer capillary would also be possible using another ionization strategy – liquid injection field desorption/ionization (LIFDI) – with which the analysis of sensitive compounds was reported<sup>9,10</sup>.

Additionally, MALDI and LIFDI are not suitable for the analysis of highly volatile compounds. MALDI requires the co-crystallization of the analyte with a matrix and LIFDI requires the deposition of the analyte onto an emitter from a solution. With both ionization strategies it is very likely that the analyte will evaporate along with the solvent. In contrast to MALDI instruments, EI mass spectrometers usually offer several methods for introducing the sample into the ion source: the direct inlet probe (small amounts of solids, oils, or waxes are deposited into an aluminum crucible which is introduced using a push rod), a septum inlet (for liquids), or coupling with a gas chromatograph. Again, at least part of the sample transfer takes place under ambient conditions and is difficult to perform under an inert atmosphere.

In the 1960's, a sample inlet system was presented which enables the introduction of samples under vacuum into the ion source of an EI instrument – the all-glass heated inlet system (AGHIS)<sup>11,12</sup>. Here, the sample was located inside a sealed piece of glass capillary, which was

inserted into the AGHIS. Subsequently, the AGHIS was evacuated and the glass container with the sample was broken. The AGHIS was then heated to evaporate the sample which reached the ion source of an EI mass spectrometer by means of a leak. When the glass capillary with the sample was prepared inside a glove box, the sample could be introduced into the mass spectrometer without any contact to air. However, the AGHIS is an apparatus which is not commercially available and difficult to assemble even for a skilled glassblower workshop. Due to the large dimensions switching between direct inlet using a push rod and AGHIS is not straight forward.

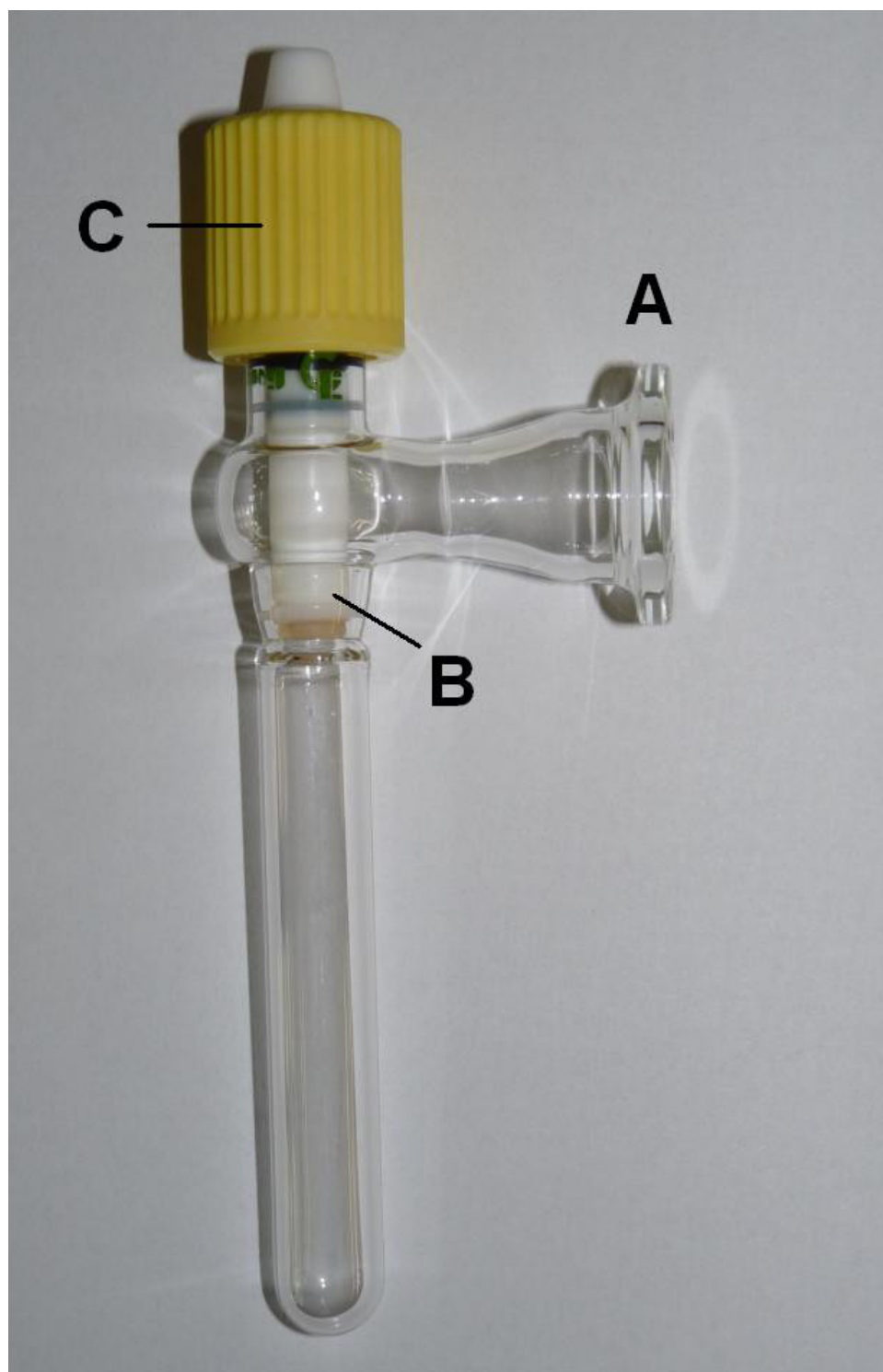
In our mass spectrometry lab, we developed a similar inlet system in the style of the AGHIS. However, as it is not possible to heat the inlet system, the analyte has to exhibit a certain volatility in order to enter the ion source of the mass spectrometer. The volatility of the analyte has to be sufficient, to allow for the transfer of the compound under vacuum at liquid nitrogen temperature – either by boiling or sublimation. The custom-made inlet system consists of a stainless steel plate, which is positioned at the direct inlet system, a stainless steel tube with a needle valve, and a flange, to which a lockable test tube containing the sample can be attached. The installation of the cold inlet system requires no modifications to the mass spectrometer (Autospec X, Vacuum Generators, now Waters Corp., Manchester, UK) – switching between cold inlet system and direct inlet using a push rod can be performed easily within seconds.

The presented inlet system is of particular use when metal organyls, silanes, or phosphanes, susceptible to oxidation or hydrolysis, have to be analyzed. These compounds are commonly analyzed using nuclear magnetic resonance (NMR) spectroscopy or infrared (IR) spectroscopy. Unfortunately, these methods allow not always for an unambiguous identification of a compound because they yield incomplete information, e.g., when elements such as chlorine or bromine are part of the molecule. Gas electron diffraction on the other hand is able to provide detailed information about the analyte, however, the method is very time consuming, sample preparation is difficult, and only few groups are able to conduct these analysis<sup>13,14</sup>. Here, the cold inlet system for the analysis of metal organyls, silanes, or phosphanes, susceptible to oxidation or hydrolysis by EI mass spectrometry is of great use for (in)organic chemists enabling the unambiguous identification of novel compounds by supplying them with information regarding the mass of a molecule and of characteristic fragment ions. The only prerequisite for the measurement of mass spectra for a substance is a certain volatility at reduced pressure.

## Protocol

### 1. Sample Preparation

1. Use custom-made lockable test tubes with a flange (**Figure 1**) for transportation and transfer of the samples into the mass spectrometer. Prior to filling with sample, evacuate the lockable test tubes attached to a multiple manifold Schlenk line and remove residual water by heating with a heat gun. Vent the test tube with dry Argon and evacuate again, while heating.
2. Immerse the lockable test tube into a cold trap filled with liquid nitrogen (CAUTION: Be careful when working with liquid nitrogen). Condense the sample into the test tube from a sample container attached to a manifold of the Schlenk line, close the lock on top of the test tube as well as the manifold and remove the locked test tube from the nitrogen bath. As mass spectrometry is very sensitive, a small amount is sufficient. Most of the analyte will remain in the lockable test tube during the analysis and is available for further experiments after the measurement.

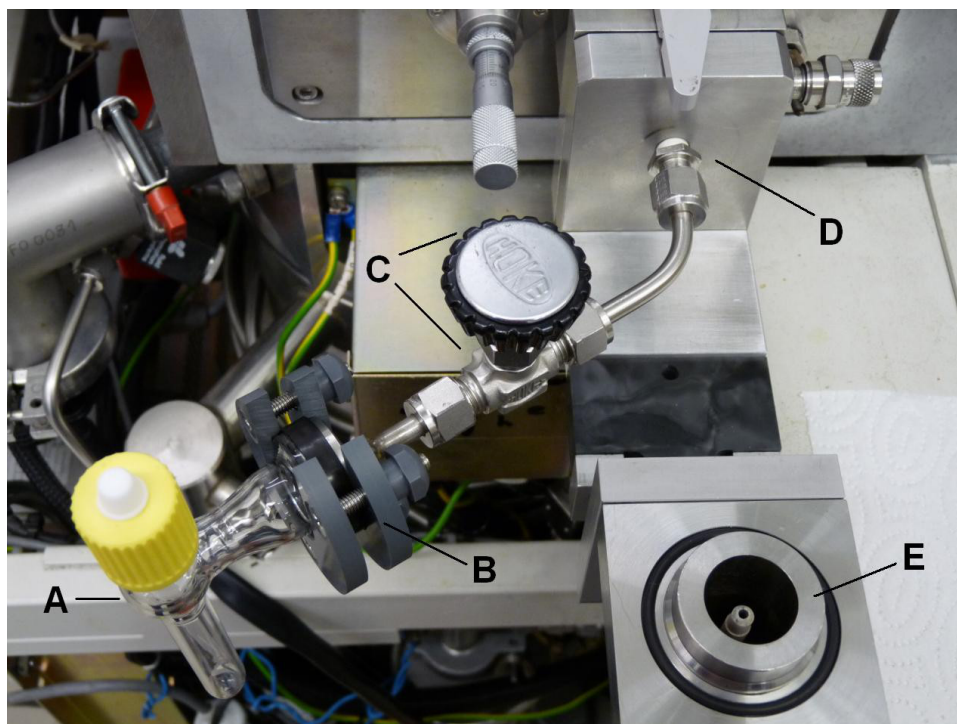


**Figure 1. Lockable test tube used for transfer of samples.** **A)** Flange for attachment to the cold inlet system, **(B)** Teflon tap of the test tube to enable transport of a compound under air-free conditions, **(C)** screw to operate the Teflon tap.

## 2. Measurement of Mass Spectra

1. Prior to sample measurement, tune and calibrate the mass spectrometer according to the instructions supplied by the manufacturer of your mass spectrometer (here, an Autospec X (Vacuum Generators, now Waters Corp., Manchester, UK) is used. Use perfluorokerosene (PFK) as a standard and tune the mass spectrometer to a resolution of ca. 2,800 at  $m/z$  119, 10% valley definition). Remove the push rod of the direct inlet from the ion source and install the outer interface for the test tube (**Figure 2**). To prevent heating of the push rod tip, set the inlet method to "septum" in the control software of the mass spectrometer.

2. Connect the flange of the lockable test tube filled with the sample to the outer interface. Open the needle valve of the outer interface and evacuate the inlet. After evacuation, carefully open the ball valve to the ion source to complete the evacuation step. Close the needle valve of the outer interface. CAUTION: The Teflon tap of the test tube has to be closed in this step.
3. Start a mass measurement in the software of the mass spectrometer. With closed needle valve, open the Teflon tap of the test tube very briefly, allowing gas phase molecules of the analyte to enter the outer part of the interface. Close the Teflon tap again.  
NOTE: The outer part of the interface together with the space between the Teflon tap and the flange of the lockable test tube (compare **Figures 1** and **2B**) serves as an analyte gas reservoir during the analysis.
4. Carefully open the needle valve while observing the vacuum gauge of the ion source. This step allows analyte molecules to enter the ion source of the mass spectrometer. The vacuum should not fall below  $10^{-5}$  mbar during the measurement.  
NOTE: Depending on the volatility of the analyte mass spectra of good quality are obtained at approximately  $10^{-6}$  mbar. The mass spectrum of the sample is now recorded. Usually, the sample amount leaking into the instrument through the needle valve is sufficient to record mass spectra for several minutes. In case the intensity of the ions decreases, opening the needle valve a little more allows for more acquisition time. If the quality of the mass spectra recorded at 70 eV is not satisfying, mass spectra can be recorded using lower kinetic energies of the electrons, e.g., 20 eV.



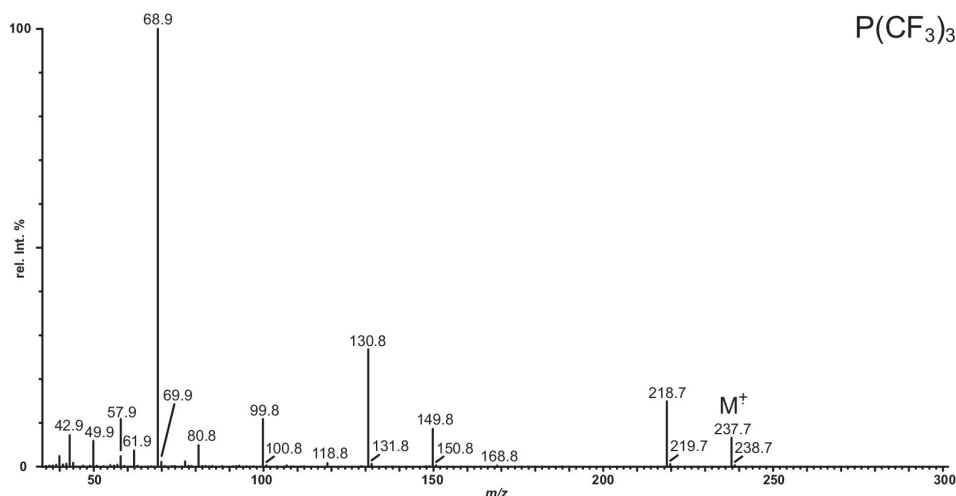
**Figure 2.** Cold inlet system with empty lockable test tube fitted to the ion source of a VG Autospec X. **A)** Lockable test tube, **(B)** flange connection between test tube and cold inlet system, **(C)** needle valve, **(D)** stainless steel plate with seal as connection to the ion source, **(E)** interface of the direct inlet, the ceramic tip of the push rod is visible.

### 3. After the Measurement

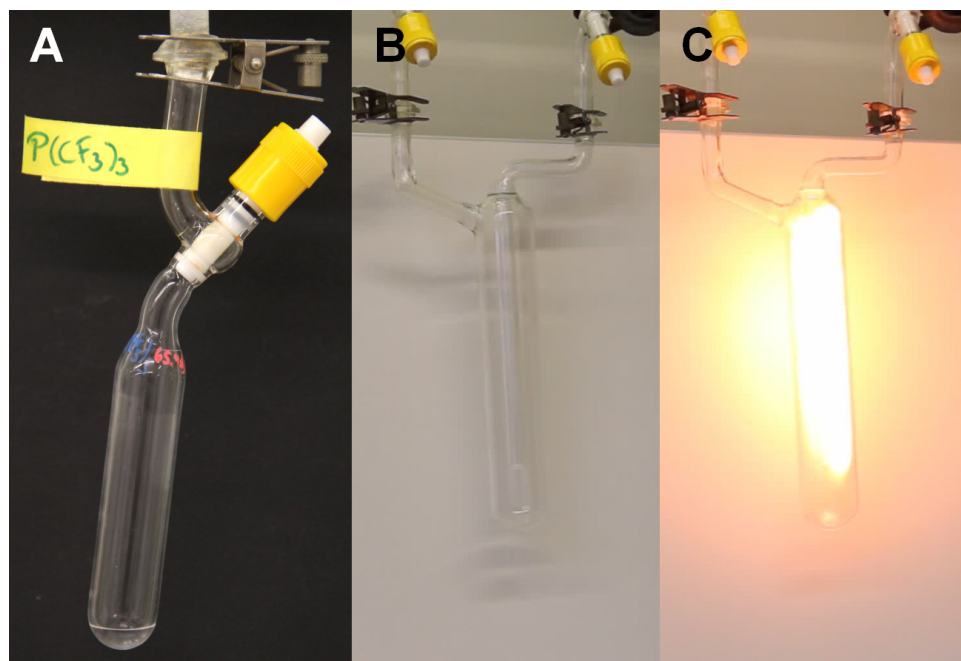
1. Close the needle valve of the outer interface. Close the ball valve to the ion source. Stop the acquisition of mass spectra in the software.
2. Evacuate the inlet system while opening the needle valve completely. Vent the interface while ball valve and needle valve are closed. Evacuate the interface again, open the needle valve during this step in order to remove residual sample vapor in the interface. Repeat this step at least 3x.
3. Remove the lockable test tube from the interface. Continue with next sample or remove the outer interface from the flange of the ion source and replace it with the push rod.

### Representative Results

An EI mass spectrum of tris(trifluoromethyl)phosphane is presented in **Figure 3**, a compound, which decomposes rapidly when in contact with air (**Figure 4**). The presented interface allows for the straight forward measurement of mass spectra for these compounds. The operation of the novel interface is easy and fast and presents no obstacle when operating the mass spectrometer with the routinely applied direct inlet using the push rod.



**Figure 3.** Mass spectrum of tris(trifluoromethyl)phosphane. [Please click here to view a larger version of this figure.](#)



**Figure 4.** (A) Storage vessel filled with tris(trifluoromethyl)phosphane. (B) Container filled with a small amount of tris(trifluoromethyl)phosphane. (C) Upon contact with air, tris(trifluoromethyl)phosphane ignites spontaneously. (Photographs with courtesy of Dr. J. Bader.)

## Discussion

The acquisition of mass spectra from compounds which decompose under standard sample preparation procedures is presented in this protocol. The presented technique is designed for the analysis of metal organyls, silanes and phosphane, which are highly susceptible to oxidation and/or hydrolysis, making it interesting especially for inorganic chemists. In order to achieve optimal results, vacuum or air-free conditions have to be preserved throughout the analysis. Therefore the protocol should be followed meticulously. In case the analyte comes into contact with air because of leaks in or wrong handling of the inlet system, severe consequences such as explosion of the sample container can be the case depending on the compound to be analyzed (**Figure 4**). Sample preparation should also be performed only by trained personnel used to working with Schlenk lines, as they can implode due to poorly manufactured glass ware when under vacuum. Explosions might be caused by contact of reactive compounds with air, entering the Schlenk line due to poor handling. The danger of liquid oxygen, frozen out from inert gas impurities in a cold trap, should also be considered. Contact of any (in)organic compound with liquid oxygen might lead to vigorous reactions causing explosion of the Schlenk line. During the analysis the pressure in the ion source of the mass spectrometer should be observed carefully, as to high pressure in the ion source might result in damage to the instrument.

As with volatile metal organyls, highly susceptible to oxidation and/or hydrolysis, silanes and phosphane are rarely or impossible to analyze using state-of-the-art mass spectrometers with ESI or MALDI ion sources, where sample preparation and ionization are commonly performed under atmospheric conditions. Here, the cold inlet system presents a valuable extension of the existing methods for analyte introduction. However, the cold inlet system is not compatible with ESI and MALDI ion sources, as it presents a flow of gaseous analyte to the ionization source, while



ESI requires a flow of analyte solution and MALDI analyte co-crystallized with matrix for the generation of ions. As every ionization strategy, EI also has a drawback – due to the high energy of the electron beam, fragmentations occur frequently. Depending on the nature of the analyte this can result in the absence of a molecular ion. However, the analyte can be identified using the fragment ions, especially when the supplied compound is of high purity. For an unambiguous identification, the route of synthesis has to be known in this case. For compounds where the molecular ion is present in the mass spectrum, the fragment ions can be used to confirm the structure of the molecule. Due to the design of the cold inlet system, the presented strategy is limited to compounds with a certain volatility. The volatility of the analyte has to be sufficient, to allow for the transfer of the compound under vacuum at liquid nitrogen temperature – either by boiling or sublimation. Compounds with too low vapor pressure will not yield high-quality mass spectra. Crosstalk between single mass measurements is rarely observed and can be further minimized by pumping out the inlet system carefully.

In general, the measurements can be conducted with every mass spectrometer equipped with an EI ion source and direct inlet system. The presented cold inlet system is operational within seconds and requires no alterations on the mass spectrometer. However, the interface of the cold inlet system has to be custom made, according to the dimensions of the existing inlets of the used EI mass spectrometer. Depending on the capabilities of the available mass spectrometer, additional experiments can be performed, such as accurate mass measurements for the determination or confirmation of elemental compositions or mass-analyzed ion-kinetic-energy spectrometry (MIKES) for the elucidation of fragmentation pathways. Therefore, the cold inlet system represents an additional sample inlet strategy next to the routinely used direct inlet using a push rod in EI mass spectrometry.

## Disclosures

The authors have nothing to disclose.

## Acknowledgements

JS is indebted to Prof. B. Hoge of the Inorganic Chemistry department, Bielefeld University, for the idea of establishing the presented inlet system. The analyzed phosphane was a generous gift from Prof. B. Hoge. Sample preparation of the analyzed compound was performed by M. Wiesemann. Photographs of the phosphane were taken by Dr. J. Bader. The mechanical workshop of the faculty of chemistry is acknowledged for the manufacturing of the interface and the glass workshop of the faculty of chemistry for the manufacturing of the lockable test tubes with flanges. Prof. B. Hoge and Prof. H. Gröger are acknowledged for funding of this publication.

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