Enabling LIFDI-MS measurements of highly air sensitive organometallic compounds: a combined MS/glovebox technique
Enabling LIFDI-MS measurements of highly air sensitive organometallic compounds: a combined MS/glovebox technique†‡

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A new setup combining a ThermoFisher Exactive Plus Orbitrap Mass Spectrometer with a liquid injection field desorption ionization (LIFDI) source directly connected to an inert atmosphere glovebox is presented. The described setup allows for the analysis of very air- and moisture sensitive samples. Furthermore, the soft nature of LIFDI ionization gives access to the molecular ions of fragile molecules. This new setup is therefore especially useful for sensitive organometallic complexes. The functionality of the new setup is tested against [(Cp)2TiCl], which is known for its notorious sensitivity to air and moisture. Its drastic colour change from green to orange upon exposure to air further supports the easy detection of traces of oxygen during the experiment. In addition, we applied this setup to the mass spectrometric analysis of the qualitative composition of a Cu/Al cluster mixture, which is not accessible by other analytical methods.

Introduction

Intermetallic materials of catalytically active late transition metals with abundant main group metals such as Cu/Al, Cu/Zn, Fe/Al or Ni/Ga have attracted widespread interest as cost-efficient substitutes for precious metal catalysts.1–3 In nanoparticulate (NP) form they exhibit high activities in various catalytic reactions such as the semi-hydrogenation of alkynes. Christoph Janiak developed synthetic protocols for the preparation of ligand-free NPs from organometallic precursors in ionic liquids with remarkable catalytic activities and selectivities, e.g. Ni/Ga NPs with up to 100% selectivity for the semi-hydrogenation of alkynes to alkenes.4–6

Much effort has been devoted to studying catalytic processes on intermetallic material surfaces.7–8 In the course of a long lasting cooperation with Christoph Janiak we became interested in the employment of atom-precise intermetallic clusters as molecular surface models in the investigation of catalytic reaction mechanisms.9–12 In this regard, liquid injection field desorption ionization mass spectrometry (LIFDI-MS) was used as a key method giving direct in-situ access to the composition of highly reactive and complex reaction solutions. Nevertheless, since a majority of intermetallic clusters are extremely sensitive to air and moisture, a new mass spectrometric setup is required.

Although mass spectrometry (MS) is a very important and well-established method for the structural elucidation of organic and biochemical molecules,13–15 it has not yet reached the same level of importance in the analysis of organometallic compounds. Elemental analysis data are frequently cited rather than MS data. Multiple parameters may be made accountable for this. The analysis of fragmentation patterns of organometallic compounds for example does not have the same degree of importance for structural elucidation as for organic molecules,16 while the observation of molecular ion signals is more essential. On the other hand, organometallic compounds are very often sensitive to air and moisture, which severely limits instrumental opportunities. McIndoe and co-workers have developed an electrospray ionization MS setup coupled to a glovebox for measurements under inert conditions.17,18 However, ionization in nonpolar solvents remains challenging.

One of the softest ionization methods established in mass spectrometry is field desorption (FD) also being nearly solvent
independent. Due to a high electric field, the weakest bound electron is removed and the formed ions are detectable. This does not transfer excess energy to the formed ions leading to mass spectra with almost no fragmentation signals.\textsuperscript{19–21} An excellent primer on the method including practical considerations was recently given by Gross.\textsuperscript{22} One limitation of this method is rooted in the demanding sample application. For each experiment, the mechanically fragile emitter is coated with a solution of the sample, before the system is evacuated to $10^{-7}$ mbar. This procedure is time consuming and causes a high consumption of emitters. In addition, reproducibility of sampling is difficult to control. Another technique was constructed by McEwen where the front area of the MS instrument was wrapped with a plastic bag filled with nitrogen.\textsuperscript{23} Evacuating and flushing the bag with inert gas several times lead to almost inert conditions. By this construction [$\text{FeH(\eta}^5\text{-toluene})(\text{P(OMe)\_2})_2]\text{\textsuperscript{+}}$ was detected as main peak of the spectra. However, due to its highly demanding and time consuming procedure, this construction did not become a standard technique for measuring highly air and moisture sensitive metalorganic compounds.

LIFDI-MS overcomes these issues by using a thin fused silica transfer capillary highly facilitating the sample load.\textsuperscript{24–28} The sample is dissolved in an organic solvent with a melting point lower than $-80 \, ^\circ\text{C}$ preventing the solution from solidifying upon contact with vacuum conditions. The solution is applied to the emitter inside of the ion source in a facile and controlled manner (40 µL; 1 mg mL\textsuperscript{-1}). After complete evaporation of the solvent under vacuum conditions, the sample remains on the emitter, covering its large surface area.

This capillary setup allows measurements of air and moisture sensitive compounds to be made more easily.\textsuperscript{26} In a typical procedure, sample preparation is performed under inert conditions (e.g. glovebox) and the sample solutions made available in septum capped vials. At the instrument, the septa of these vials may be penetrated by the LIFDI capillary and the sample is transported to the emitter by the pressure difference. This setup works well for many organometallic compounds.\textsuperscript{24–26} However, when working with very sensitive molecules, as sub-valent compounds, metal alkyl compounds or metals in easily oxidizable oxidation states (e.g. Mn\textsuperscript{6–}), this method reaches its limitations. Through the capillary, the sample vial is connected to the vacuum system of the MS instrument which leads to a constant decrease of the pressure inside the vial, which in consequence results in slow exposure of the sample solution to air and moisture through the vial septum. This not only leads to the failure of the experiment, but can also provoke the irreversible blocking of the capillary due to decomposition of metal containing compounds under formation of solids.

To overcome the described problems, we present in this paper a glovebox-based instrumental setup, which has been developed in cooperation with LINDEN CMS GmbH and GS GLOVEBOX Systemtechnik GmbH (Fig. 1). By inserting the LIFDI capillary through a Teflon-sealed small hole in the back-wall of the glovebox, a sensitive sample may be injected directly from inside the glovebox preventing the contact with air and moisture. The capillary transports the sample solution to the LIFDI probe which is evacuated by an external turbo pump. An isolation valve prevents exposure of the mass analyzer until $10^{-4}$ mbar is reached in the probe. When this pressure is reached, the LIFDI probe is automatically moved into the mass spectrometer by an electric motor and the ionization process is triggered by applying voltage to the emitter. After the measurement, the probe is retracted from the instrument, the isolation valve is closed and the LIFDI setup is again only evacuated by the external turbo pump. It should be noted that to prevent accidental misuse and irreversible damage to the sensitive Exactive Plus mass spectrometer, a plexiglass safety box is installed inside the glovebox, which disables injection when the probe is inserted into the mass analyzer. An additional plexiglass safety box equipped with an electric shutter-type mechanism is installed around the LIFDI apparatus, preventing the probe to be touched while moving.

It should be noted changing the capillary is not further complicated with respect to the common LIFDI setup (without glovebox connection). The capillary, solely, has to be passed through a tiny hole in the back of the glovebox, which is then sealed with a rubber plug and a screw joint similar to the one of the LIFDI probe.

In order to evaluate the functionality of this instrumental setup, we used [(Cp\textsubscript{2})TiCl\textsubscript{2}] (1) as a test substance. 1 is notoriously known for its air sensitivity and its oxidation related intense color change, which has also been widely used as cheap and powerful method for the indication of oxygen in glovebox atmospheres (Fig. 2). An emerald green solution of 1 is obtained by reduction of red [(Cp\textsubscript{2})TiCl\textsubscript{3}] with zinc powder in toluene after 5 min (Scheme 1).\textsuperscript{29} Subsequent filtration gives a clear, green solution which does not lead to change color even when stored in the glovebox for several hours.
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Fig. 2 Color change of the reaction solution upon perforating the sample vial with the LIFDI capillary.

Scheme 1 Reaction of red [(Cp)₂TiCl₂] with excess of zinc to green trimetallic [(Cp)₂TiCl₂ZnCl₂Ti(Cp)₂]. After contact with air an orange suspension containing different Ti/O species is formed.

The LIFDI mass spectrum of this solution indicates the presence of several species which can be traced to the complex [(Cp)₂TiCl₂]²⁻, reported as the major reaction product of this reduction. 29,30 Thus, the weakly detected molecular ion is observed at m/z 561.8522 (calc. 561.8549) (s. Fig. 3, Fig. S2‡). In addition, the fragment ions [(Cp)₂TiCl₃]⁻ (m/z 425.9890, calc. 425.9896), [(Cp)₂TiCl⁴]²⁻ (m/z 391.0205, calc. 391.0207), [(Cp)₂TiCl⁵]⁻ (m/z 212.9936, calc. 212.9945) or the toluene adduct [(Cp)₂TiCl(Tol)]⁻ (m/z 240.0175, calc. 240.0180) are assigned. Very small patterns in this spectrum can be also attributed to oxygen containing products, e.g. [(Cp)₂TiCl(OH)(OH₂)]⁻ (m/z 231.0050, calc. 231.0051), [(Cp)₂TiCl₂(OH)₂]⁻ (m/z 200.9349, 200.9348) or [(Cp)₂TiCl₂(OH)(OH₂)]⁻ (m/z 182.9686, calc. 182.9687). Surface-oxidation of the zinc used in the reaction is most probably the oxygen source for the formation of these species. However, the spectra recorded after keeping this solution in the glovebox for 5 min and for 45 min are identical based on the distribution as well as quantity of the patterns (see ESI‡). In contrast, when this measurement is repeated with the traditional LIFDI setup without glovebox connection, a color change of the solution becomes apparent after a few seconds. Already 15 s after puncturing the septum of the sample vial with the LIFDI capillary and a needle, the solution becomes slightly yellow and patterns attributable to Ti-O species become more prominent in the mass spectrum, i.e. [(Cp)₂TiCl₂(OH)]⁻ (m/z 407.0148, calc. 407.0156, Ti/O ratio: 2/1) and [(Cp)₂TiCl₃]²⁻ (m/z 570.9646, calc. 570.9665, Ti/O ratio: 3/2). These rather Ti-rich compounds disappear after prolonged measurement time and new species with higher oxygen content become very prominent. Among these oxygen rich species are [(Cp)₂TiCl(OH)(OH₂)]⁻ (m/z 182.9680, calc. 182.9687, Ti/O ratio 1/2), or [(Cp)₂TiCl₂(OH)₂]⁻ (m/z 231.0054, calc. 231.0051). After allowing an excess of air to get in contact with the sample solutions, the color changes to dark orange, along with precipitation of an orange solid. The spectra now consists of [(Cp)₂TiCl(OH)(OH₂)]⁻ (m/z 182.9689, Ti/O ratio: 1/2) as the main signal in addition to [(Cp)₂TiCl₂]⁻ (m/z 542.8914, calc. 542.8967, Ti/O ratio: 3/2), [(Cp)₂TiCl₃(OH)₂]⁻ (m/z 200.9354, calc. 200.9348, Ti/O ratio: 1/2), and [(Cp)₂TiCl₃(OH)]⁻ (m/z 376.9465, calc. 376.9453, Ti/O ratio: 2/1). In summary, the more the reaction solution was exposed to air, the larger the amount of oxygen containing species emerged (Fig. 3). These experiments clearly outline the usefulness of a LIFDI/glovebox connection for the analysis of very air- and moisture sensitive organometallic compounds. The major advantage of submitting samples directly from a glovebox to the emitter, is the fact, that the sample as well as the capillary remains under constant inert atmosphere. However, the benefits of working with gloveboxes with respect to handling sample vials capped with septa outside of gloveboxes is not only the increased duration of sample stability, but also the practical simplification of many work steps inside gloveboxes, e.g. sample preparation and dilution or application of the sample solutions to the LIFDI emitter, guaranteeing high experimental reproducibility. This becomes especially important for automation of experiments by e.g. synthesis robots, which is an essential future perspective for our research on intermetallic cluster compounds (vide infra).

While the classical LIFDI setup was able to detect the molecular ion peak, it however led to a very fast decay of the green Ti(m) compound [(Cp)₂TiCl₂ZnCl₂]. Our new setup prevents any contact between sample and air. There are species even more reactive or prone to oxidation than 1, such as catalytic intermediates or low-valent metal complexes or clusters. Connecting LIFDI to the protective atmosphere of a glovebox is an important step towards in-situ identification of such highly reactive species.

Analysis of Cu/Al cluster libraries

With this instrumental advance we enable reproducible access to complex reaction solutions of mixed-metal clusters. This chemistry offers compounds of unique structures, properties and reactivities. It is, however, affected by challenging product separation and isolation, respectively. This is in line with compounds that simply cannot be isolated in a pure form leading to a loss of information when not characterized in-situ. High resolution mass spectrometry is a way to tackle this problem and follow minor reaction products (former known as by-products). To illustrate our new way of thinking we would like to
draw attention to a recently submitted work, the reaction of [CuMes] (abbreviated for [Cu$_5$]([Mes]$_5$); Mes = mesitylene) with 3.6 eq. of AlCp* (Cp* = pentamethylcyclopentadienyl). The reaction results in a complex mixture of intermetalloid [Cu$_x$Al$_y$](Cp*)$_z$ cluster species. Besides the 18 valence electron cation [Cu$_4$Al$_4$](Cp*)$_4^+$, the species [Cu$_8$Al$_7$](Cp*)$_6$ (2Cu), [Cu$_6$Al$_7$](Cp*)$_6$, [Cu$_7$Al$_7$](Cp*)$_6$–2H (2Al) and an overlapping peak corresponding to a mixture of [HCu$_7$Al$_6$](Cp*)$_6$ (2H) and [Cu$_7$Al$_6$](Cp*)$_6$ (2H) are detected (see Fig. 4). Addition of precise amounts of CuMes (overall final Cu : Al stoichiometry 1 : 1.2) to this mixture, followed by prolonged heating induces subtle spectral changes (see Fig. 4a, middle). Analysis of the peak at $m/z = 1417$ reveals now pure 2 instead of 2H/2. From these reaction solutions, isolation of the composite 2/2H was possible after crystallization and a short work-up procedure (see Fig. 4a, top). Obviously, all the other cluster species, especially those with unligated Al atoms, [Cu$_5$Al$_7$](Cp*)$_6$ and [Cu$_6$Al$_7$](Cp*)$_6$–2H, are removed or decomposed during the work-up procedure, however, we were able to determine these highly reactive and sensitive compounds by mass spectrometry in combination with a glovebox. The results nicely illustrate two key-points: without detailed analysis of reaction solutions by LIFDI-MS, feedback on the reaction design and access to pure 2, as well as its subsequent reactivity assessment would not have been possible. Further, LIFDI-MS analysis of the reaction solution prior to crystallization sheds light on cluster species, which cannot be captured by common crystallization procedures. Due to their naked Al atoms, these species might exhibit unique reactivities, which again can only be detected by MS. Detection likewise reactivity investigation of highly reactive/sensitive molecules require the introduction of a reliable MS setup to exclude any undesired external influence, mainly moisture and air.

Conclusions

In this contribution, we introduced a new coupled glovebox/MS setup for the mass spectrometric detection of molecular ion signals of very air- and moisture sensitive compounds. The setup was tested on the organometallic complex [[(Cp)$_2$TiCl]$_2$ZnCl], known for its extreme air-sensitivity. By a
colour-change from green to orange the oxidation of this complex can also visually be detected. Only by using this new setup, the molecular ion signal of \([((Cp)_2TiCl)_2ZnCl_2]\) is detectable over time. Without the use of a glovebox, oxidation reactions are observed only within a few seconds. The new setup has been further applied to the in-situ analysis of Cu/Al clusters allowing the detection of the highly sensitive open shell cluster \([Cu_7Al_6](Cp^*)_6\) together with its closed shell coordination adducts H\([Cu_7Al_6](Cp^*)_6\), Cu\([Cu_7Al_6](Cp^*)_6\) and Al\([Cu_7Al_6](Cp^*)_6\). We expect this new technique to considerably support our future efforts to employ intermetallic clusters of this type as surface model compounds in mechanistic investigation of catalytic processes.

**Author contributions**

All authors gave approval to submission. P. H. and M. M. contributed equally to this work.

**Conflicts of interest**

We would like to mention that the authors H. B. L. and M. H. L. are the owners of LINDEN CMS GmbH, commercial LIFDI probe manufacturer.

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**Notes and references**