

## Notes

## Coupling an Electrospray Ionization Mass Spectrometer with a Glovebox: A Straightforward, Powerful, and Convenient Combination for Analysis of Air-Sensitive Organometallics

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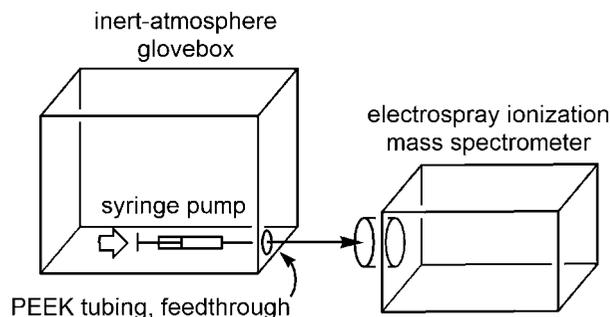
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**Summary:** The study of highly air- and moisture-sensitive organometallic complexes by ESI-MS is greatly facilitated by interfacing the instrument to an inert-atmosphere glovebox, a modification that requires no special precautions beyond proximity.

Electrospray ionization mass spectrometry, ESI-MS, has had a checkered history in organometallic chemistry. Subsequent to its commercial introduction in the early 1990s, organometallic chemists took notice of the technique and demonstrated its potential as a tool for analyzing speciation of charged compounds in solution.<sup>1–3</sup> Fast, extremely sensitive, and capable of dealing with complex mixtures, ESI-MS occupied a niche that ought to have made it a highly attractive, routine method for analysis. Interpretation of data is not difficult: ESI mass spectra of charged compounds typically provide just [cation]<sup>+</sup> or [anion]<sup>−</sup> ions, and the combination of matching experimental isotope patterns with (readily calculated) theoretical isotope patterns, *m/z* value, and, if necessary, MS/MS studies, provides sufficient information for compositional characterization.<sup>4</sup> Most research institutions offer ready access to the instruments, and even quite reactive compounds can be readily analyzed.<sup>5–7</sup> Why then has ESI-MS been only sporadically adopted by organometallic chemists? A major reason is sample decomposition.



**Figure 1.** Inert-atmosphere glovebox situated next to the ESI mass spectrometer. Syringe pump for sample infusion is inside the glovebox; the PEEK tubing passes through a standard glovebox feedthrough sealed with O-rings. See Supporting Information for photographs of the system used herein.

ESI-MS typically analyzes samples at concentrations substantially lower than millimolar, and standard protocols call for the use of polar solvents such as water, acetonitrile, and methanol. Most charged organometallic compounds can be run with ease in aprotic, relatively nonpolar solvents such as dichloromethane (and even in toluene or hexane if mixed with a lipophilic ionic liquid),<sup>8</sup> but if the injection apparatus has been recently exposed to wet, protic, or oxygenated solvent, the ion of interest may interact with these “impurities” resulting in a degraded compound. This is demonstrated by considering a typical ESI-MS experiment: 0.1 mg of an organometallic compound is dissolved in 1 mL of CH<sub>2</sub>Cl<sub>2</sub>; a drop of this solution is added to 1 mL of CH<sub>2</sub>Cl<sub>2</sub> (ca. 20× dilution); 0.02 mL (20 μL) of this solution is analyzed to collect the spectrum. Sample consumption in this experiment is 0.05 × 0.02 × 0.1 mg = 0.01 μg. Assuming a typical molecular weight for the compound of 720 Da, stoichiometric (1:1) reaction of this material requires only 0.25 nanograms of water. Given that most ESI-MS instruments are open-access, trace residual water in the

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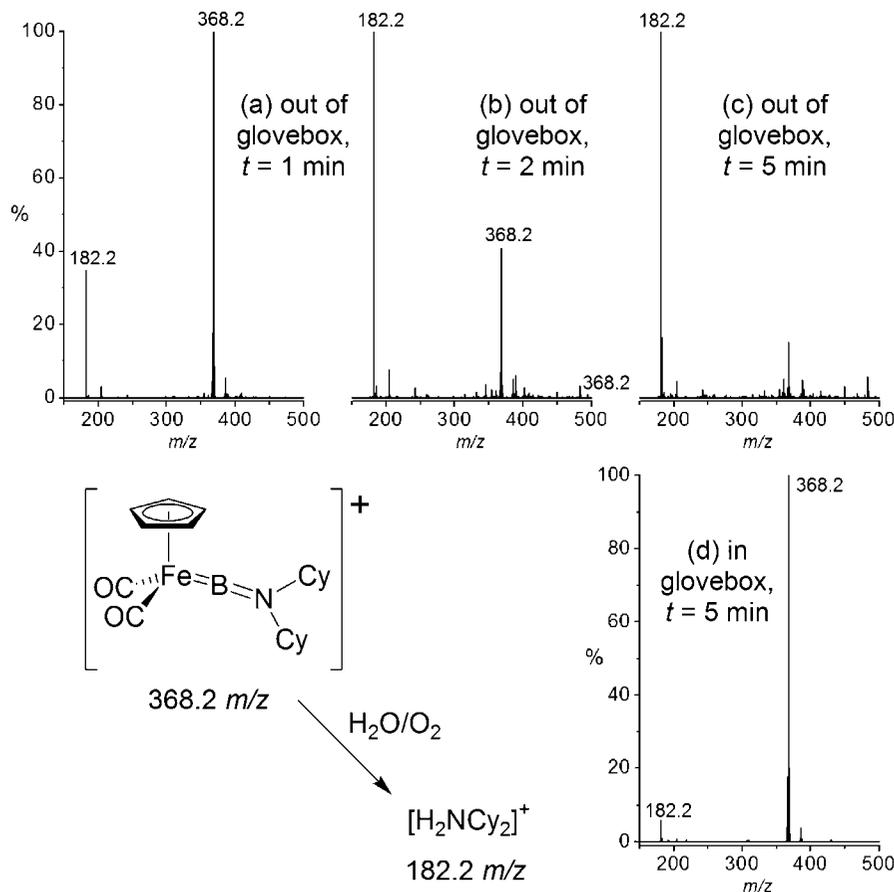
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**Figure 2.** Handling the iron complex  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2\text{BNCy}_2][\text{BAr}^{\text{F}}_4]$  (inset, 368.2  $m/z$ ) outside of the glovebox results in rapid decomposition, primarily to the cation  $[\text{H}_2\text{NCy}_2]^+$  (182.2  $m/z$ ) (a–c). Inside the glovebox, the sample may be handled at leisure and very little decomposition is observed within the same time frame (d). The sample was prepared in  $\text{CH}_2\text{Cl}_2$ .

inlet system is both inevitable and disastrous. Consequently, a sample shown to be pure by other methods can often prove difficult to interpret by ESI-MS.

A variety of precautions may be taken to improve the situation. Making up the sample in a glovebox (or on a Schlenk line) is, of course, essential. The cheapest and easiest method to ensure that cross-contamination is minimized is by using an exclusive-to-each-user inlet system (where samples are infused via syringe pump; this involves a gastight syringe, some tubing, and associated fittings). Exhaustive rinsing with dry oxygen-free solvent also attenuates decomposition. However, the best solution is one that eliminates air and moisture entirely from all stages of sample preparation, dilution, and introduction to the mass spectrometer, and this ideal can be achieved by moving these steps inside an inert-atmosphere glovebox. Locating the glovebox within a meter or so of the instrument, installing a syringe pump inside, and passing the tubing out through a standard feedthrough are the only requirements (Figure 1).

This setup is related to Fogg's recent description of the direct integration of a MALDI mass spectrometer with a glovebox for the purposes of analyzing air-sensitive organometallic compounds.<sup>9</sup> MALDI in many ways is complementary to ESI-MS: it deals with solids rather than solutions and works better with neutral than charged compounds. Treatment of the problem of sample decomposition does not address the problem of analyzing neutral compounds by ESI-MS, especially in nonpolar solvents and with compounds lacking basic sites with which to

associate charged species such as protons or alkali metals. Finding some other way to attach a charge is necessary, and derivatization methods such as addition of alkoxides to carbonyl complexes<sup>10</sup> or silver ions to metal–metal bonds<sup>11</sup> work only in a limited number of cases. Other strategies, such as using ligands specially designed to contribute a charge,<sup>12–14</sup> may be required in certain cases. Even without tackling neutral compounds, there are a huge number of cationic complexes ripe for analysis, many of catalytic significance.<sup>15–19</sup>

The effect of excluding air and moisture from samples for ESI-MS analysis is often quite dramatic, especially for more reactive compounds. For example, the iron borylene complex  $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})_2=\text{B}=\text{N}(\text{cyclo-C}_6\text{H}_{11})_2][\text{BAr}^{\text{F}}_4][\text{Ar}^{\text{F}}=\text{C}_6\text{H}_3(\text{CF}_3)_2]$  368.2  $m/z$  is highly moisture-sensitive and rapidly

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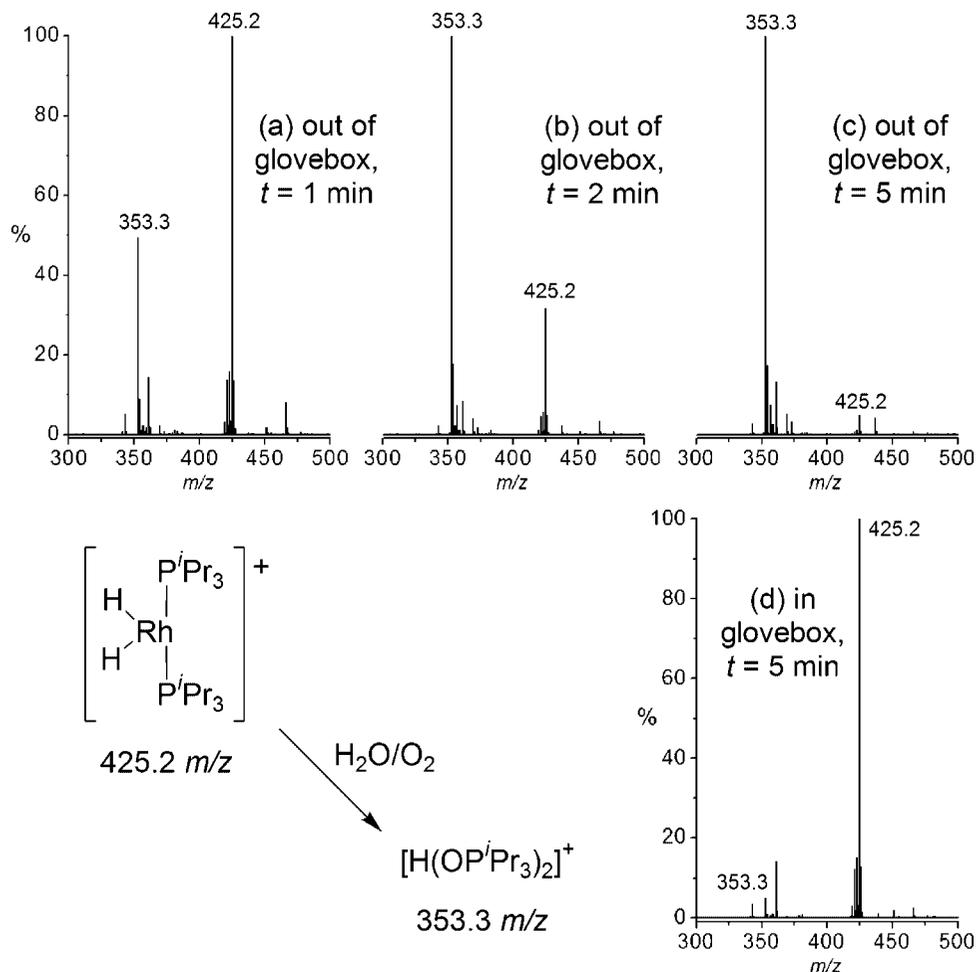
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**Figure 3.** Handling the rhodium complex  $[\text{H}_2\text{Rh}(\text{P}^i\text{Pr}_3)_2][\text{BAR}^{\text{F}}_4]$  (inset, 425.2  $m/z$ ) outside of the glovebox results in rapid decomposition, primarily to the cation  $[\text{H}(\text{OP}^i\text{Pr}_3)_2]^+$  (353.3  $m/z$ ) (a–c). Inside the glovebox, the sample may be handled at leisure and very little decomposition is observed (d). The sample was prepared in  $\text{CH}_2\text{Cl}_2$ .

decomposes in solutions exposed even briefly to the air.<sup>20</sup> We made up a dilute solution of this compound in an argon-filled glovebox in  $\text{CH}_2\text{Cl}_2$  and removed an aliquot using a 250  $\mu\text{L}$  gastight syringe. Portions of this solution were infused into the mass spectrometer at 1, 2, and 5 min (Figure 2a–c), and the spectra compared with that of the same solution infused directly from the glovebox (Figure 2d), which shows virtually no decomposition over the same time period. Evidence of decomposition appears in the first spectrum and worsens over time, the primary cationic product of hydrolysis being  $[\text{H}_2\text{N}(\text{cyclo-C}_6\text{H}_{11})_2]^+$ . Other species observed in the spectrum are not so easily identified, and we have found this to be a typical situation: decomposition leads to messy, difficult to interpret spectra that drastically lower the confidence of the analyst in the quality of the data.

Another representative example is the ion  $[\text{Rh}\{\text{P}(\text{C}_3\text{H}_7)_3\}_2\text{H}_2]^+$ , a reactive unsaturated species derived from facile loss of  $\text{H}_2$  from the precursor dihydrogen complex  $[\text{Rh}\{\text{P}(\text{C}_3\text{H}_7)_3\}_2\text{H}_2(\eta^2\text{-H}_2)][\text{BAR}^{\text{F}}_4]$  ( $\text{Ar}^{\text{F}} = \text{C}_6\text{H}_3\{\text{CF}_3\}_2$ ),<sup>21</sup> seen in the mass spectrum at 425.2  $m/z$  (Figure 3). It rapidly decomposes upon exposure to air to the phosphine oxide, observed in the spectrum at 353.3  $m/z$  as the  $[\text{H}\{\text{OP}(\text{C}_3\text{H}_7)_3\}_2]^+$  ion, in which

two phosphine oxides coordinate to a single proton (Figure 3a–c). However, exclusive handling of the sample in the glovebox provides a clean spectrum largely free of breakdown products (Figure 3d).

Sensitivity is rarely a problem in organometallic applications of ESI-MS; indeed, for the most part the problem is with solutions that are too concentrated rather than those that are too weak. The temptation to run very concentrated samples is often great; it is tempting, for example, to inject the same solution that was just used to collect an NMR spectrum. This strategy has one advantage but many flaws, but in certain situations may be worthwhile. The advantage of a concentrated sample is that stoichiometric decomposition due to adventitious contaminants (including water and oxygen) is minimized. The disadvantages of a dirty source can be minimized by infusing the sample for a minimum of time (a few seconds), and the detector problems may be avoided by detuning the instrument (there are many ways of doing this of course—far more than there are ways of tuning the instrument—but one simple and easily reversible tactic is to move the capillary from which the spray emerges away from the orifice leading to the mass analyzer). Problems are mostly associated with cross-contamination and spectra quality. A very concentrated sample necessarily deposits material into the mass spectrometer, which can result in a dirty source and problems for subsequent users, who may see evidence of this material in their own spectra. While the organometallic complex itself may readily decompose and

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disappear, it is often accompanied by stable counterions (e.g.,  $\text{NR}_4^+$ ,  $\text{BR}_4^-$ ) that linger in the instrument and are often tenaciously resistant to washing. A more fundamental reason for avoiding high concentration is the possibility of nonlinear detector response at high ion intensity, which may have undesirable effects (especially for the multichannel plates used in TOF mass analyzers) including suppression of high-intensity signals, distortion of isotope patterns, and perturbation of peak shape. This last effect makes it difficult to obtain accurate mass data, so low-intensity spectra should always be collected in this instance.

Calibration in ESI-MS is often carried out using PEG,<sup>22</sup> proteins,<sup>23</sup> salt aggregates,<sup>24</sup> or protonated water clusters.<sup>25</sup> All of these typically utilize polar, protic solvents and are as such undesirable as calibrants in an instrument about to be used to analyze reactive organometallic compounds. We find that a 10 ng/mL mixture of tetraalkylammonium bromides  $[\text{N}(\text{C}_n\text{H}_{2n+1})_4]\text{Br}$  ( $n = 2, 3, 4, 5, 6, 7, 8, 12, 16, 18$ ) in dichloromethane provides a simple way of calibrating the instrument in positive ion mode from  $\sim 100$  to  $1100 m/z$  (see Supporting Information for table of calibration values).

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We have tested a range of other air-sensitive organometallics and found that the necessity for the extra precaution of the glovebox ranges from crucial to unimportant. However, the real utility lies in a system well set up for a mass spectrometry service: samples can be brought to the glovebox sealed appropriately (ampules, Schlenk flasks, well-sealed vials, etc.), stored indefinitely, and opened securely at leisure without fear of mishandling. With this in mind, and given that the cost of a glovebox is low compared to that of a new mass spectrometer, the addition of this facility adds a whole new constituency to the list of users able to exploit the abilities of ESI-MS.

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**Supporting Information Available:** Calibration table, photographs, acquisition parameters. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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