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A study on the species present in solutions of hypervalent iodine(III) reagents by electrospray ionization mass spectrometry

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Abstract—Solutions of iodobenzene diacetate in CH_3CN, AcOH, $MeOH/H_2O$ and MeOH (with or without base) were analyzed by electrospray ionization mass spectrometry (ESI-MS) and tandem mass spectrometry (ESI-MS/MS). The major species in CH_3CN, AcOH and $MeOH/H_2O$ solutions are $[PhI(OAc)_2Na]^+$, $[PhI(OAc)_2K]^+$, $[PhI]^{\cdot+}$, $[PhIOAc]^+$, $[PhIOH]^+$, $[PhIO_2Ac]^+$, $[PhIO_2H]^+$ and the dimer $[Ph_2I_2O_2Ac]^+$. On the other hand, MeOH solutions showed $[PhIOMe]^+$ as the most abundant species. A similar result was observed adding 2, 3 or 4 equiv of KOH to MeOH solutions. However, in the presence of 10 equiv of KOH, probably occurs the formation of a polymeric material. Similarly, ESI-MS analysis of the MeOH solution of iodobenzene bis(trifluoroacetate) showed a pattern analogous to that observed for the corresponding solutions of $PhI(OAc)_2$. However, ESI-MS spectral data of $PhI(O_2CCF_3)_2$ of CH_3CN suggests that the main species in solutions is iodosylbenzene, which contrasts with the results obtained for $PhI(OAc)_2$.

1. Introduction

Hypervalent iodine(III) reagents constitute an important class of oxidizers in modern synthetic organic chemistry, promoting a variety of reactions in excellent yield and selectivity.[1] Iodobenzene diacetate, iodobenzene bis(trifluoroacetate), [hydroxy(tosyloxy)iodo]benzene (HTIB or Koser's reagent) and iodosylbenzene are examples of highly used iodine(III) compounds.[1] To understand the reactivity of a chemical reagent it is necessary to have a clear picture of the reactive species present in the reaction medium. With this goal in mind, a detailed study has been performed by Richter et al.[2] concerning the species present in aqueous solutions of [hydroxy(mesyloxy)iodo]benzene (or HMIB) and HTIB. Dissolution of HTIB or HMIB in water lead mostly to the formation of the iodonium $[PhIOH]^+$, which is also found in dimeric forms, such as $Ph(OH)I\text{-}O\text{-}I^+(OH_2)Ph$. Furthermore, this dimeric iodine(III) species undergoes a thermally induced disproportionation reaction giving $PhIO_2$ and PhI. Moreover, a panorama of the species in methanolic solutions of iodosylbenzene was given by Sam and co-workers when the mass spectra of a solution of PhIO in MeOH were acquired using electrospray ionization mass spectrometry.[3] The most important feature of the spectrum is the three peaks with equivalent intensity at *m*/*z* 235, 455 and 501, which were assigned to $[PhIOMe]^+$, $[PhIO{+}PhI^+OMe]$ and $[PhI(OMe)_2{+}PhI^+OMe]$, respectively. On the other hand, information related to the species present in solutions of $PhI(OAc)_2$ and $PhI(O_2CCF_3)_2$ is still scarce.[4] Based on the work of Schardt and Hill[5] toward the preparation of iodobenzene dimethoxide from iodosylbenzene, it has been accepted that the reactive species in oxidations using $PhI(OAc)_2$ or PhIO in MeOH in the presence of KOH is $PhI(OMe)_2$.[6] Recently, Cerioni and Uccheddu[7] have proposed an ion par structure for bis(acetoxy)iodoarenes, such as $PhI(OAc)_2$, based on their chemical shifts in ^{17}O and ^{13}C NMR.

Electrospray ionization mass spectrometry (ESI-MS) and tandem mass spectrometry (ESI-MS/MS) are now well-established tools to study gas phase chemistry[8] and to monitor species present in the solution, including highly reactive intermediates of organic reactions.[9] Thus, in several cases, ESI-MS is the method of choice to determine the mechanism of a reaction.[10] Nevertheless, only a few papers utilized ESI-MS (or the related

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Keywords: Hypervalent iodine; Electrospray ionization mass spectrometry; Iodobenzene diacetate; Iodobenzene bis(trifluoroacetate).

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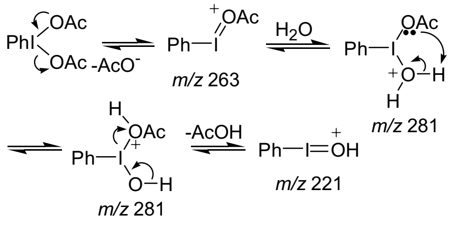
cold-spray ionization) as a tool to monitor iodine(III) or (V) species present in a solution.[11]

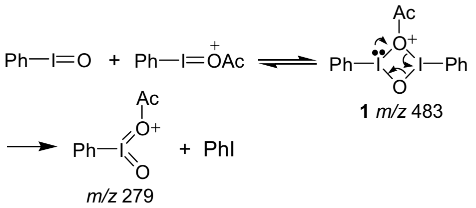
Considering this scenario, we herein present a study on the species present in solutions of $PhI(OAc)_2$ and $PhI(O_2CCF_3)_2$ in MeOH (with or without base), acetonitrile, acetic acid, and $MeOH/H_2O$ by ESI-MS and ESI-MS/MS. This work gives additional information concerning the possible reactive species in oxidations with $PhI(OAc)_2$ and with $PhI(O_2CCF_3)_2$, which will be useful for understanding the reactivity of these important oxidizers.

2. Results and discussion

This work was initiated by acquiring the mass spectra in positive mode of a $PhI(OAc)_2$ solution in acetonitrile. In addition to the expected peaks corresponding to $[PhI(OAc)_2Na]^+$ (at *m*/*z* 345) and $[PhI(OAc)_2K]^+$ (at *m*/*z* 361), we detected the presence of the iodonium $[PhIOAc]^+$ (at *m*/*z* 263) and protonated iodosylbenzene $[PhIOH]^+$ (at *m*/*z* 221), which are presumably formed according to the mechanism shown in Scheme 1. To confirm the metallic adduct structures at *m*/*z* 345 ($M+Na^+$) and *m*/*z* 361 ($M+K^+$) and the correlations among the species present in Figure 1a each individual adduct ion was selected for characterization by ESI-MS/MS using collision induced dissociation (CID). The MS/MS spectrum of *m*/*z* 361 showed the *m*/*z* 39 (K^+) as an abundant peak in addition to the ions at *m*/*z* 263 and 221, that also are present in the ESI-MS spectra (Fig. 1a). The MS/MS spectrum of *m*/*z* 263 showed the fragment ion *m*/*z* 221 only. These data confirm the correlations among the structures PhI, $[PhIOAc]^+$, $[PhI(OAc)_2Na]^+$ and $[PhI(OAc)_2K]^+$ in solution and/or dissociation in the ESI source. Another iodine(III) species present in solution is the dimer **1** (at *m*/*z* 483) that is expected to be formed by reaction of PhIO and $[PhIOAc]^+$. A somewhat similar dimer has been observed by Ochiaiet al.[12] in solutions of (*Z*)-(2-bromo-1-decenyl)(phenyl)iodonium bromide. Through a disproportionation reaction (Scheme 2), the dimer **1** originates PhI and the iodine(V) species $[PhIO_2Ac]^+$, at *m*/*z* 279, that is the most abundant ion in the ESI-MS spectrum.[13] The ion $[PhIO_2H]^+$ (at *m*/*z* 237), which also bears an iodine(V) atom, could be formed either through an equilibrium in solution in the presence of water or by elimination of $H_2C{=}CO$ from *m*/*z* 279. The MS/MS spectrum of *m*/*z* 483 is shown in Figure 2a. As expected, the ions at *m*/*z* 279, 263 and 237 in the MS analysis (Fig. 1a) are also the major ions in the MS/MS spectrum, indicating again a correlation among the structures in solution and/or dissociation in the ESI source.

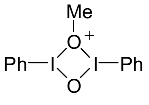


Scheme 1.

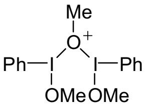


Scheme 2.

We then analyzed the species present in solutions of $PhI(OAc)_2$ in other solvents. The mass spectrum registered from a solution of $PhI(OAc)_2$ in acetic acid or in a mixture of $MeOH/H_2O$ indicated the same species when acetonitrile was used as solvent. The only difference refers to the most abundant peak when AcOH is used as solvent, that is that corresponding to $[PhIOAc]^+$ instead of $[PhIO_2Ac]^+$. Contrasting with these results, the mass spectrum of $PhI(OAc)_2$ in MeOH has a very prominent peak at *m*/*z* 235, which was assigned to the iodonium $[PhIOMe]^+$. The mechanism for the formation of this cation should be analogous to that described for $[PhIOH]^+$ in Scheme 1, but with MeOH instead of H_2O. Other intense signals in the spectrum were that corresponding to $[PhI]^{\cdot+}$ (*m*/*z* 204), $[PhIOH]^+$ (*m*/*z* 221), $[PhIOAc]^+$ (*m*/*z* 263), the iodine (V) $[PhIO_2Ac]^+$ (*m*/*z* 279), $[PhI(OAc)_2Na]^+$ (*m*/*z* 345) and $[PhI(OAc)(OMe)Na]^+$ (*m*/*z* 317), as shown in Fig. 1b. These data suggest that the reactive species in oxidations with $PhI(OAc)_2$ in MeOH is the iodonium $[PhIOMe]^+$. This result is slightly different from that found by Sam and co-workers for methanolic solutions of PhIO, because dimeric species are not the major species for $PhI(OAc)_2$ solutions in the same solvent. Based on the dimeric species **1** that was found in solutions of $PhI(OAc)_2$, we herein suggest that the ions at *m*/*z* 455 and 501 that were detected by Sam[3] may be assigned to the structures **2** and **3**, respectively.



2 *m*/*z* 455



3 *m*/*z* 501

As several iodobenzene diacetate-mediated oxidations are performed in the presence of base,[1] we decided to acquire the mass spectrum of $PhI(OAc)_2$ with different amounts of KOH. Thus, the spectra obtained from solutions of $PhI(OAc)_2$ in MeOH in presence of 2, 3 or 4 equiv of KOH were similar to that obtained in absence of base, with the most abundant peak corresponding to $[PhIOMe]^+$. However, when a higher excess of base was added (10 equiv), the profile of the spectra changed completely, due to the formation of a polymeric form of iodine(III), such as iodosylbenzene (Fig. 1c). This modification has great consequences in the reactivity, as a simple control experiment showed. The $PhI(OAc)_2$ promoted α-hydroxylation of ketones is a well-known reac-

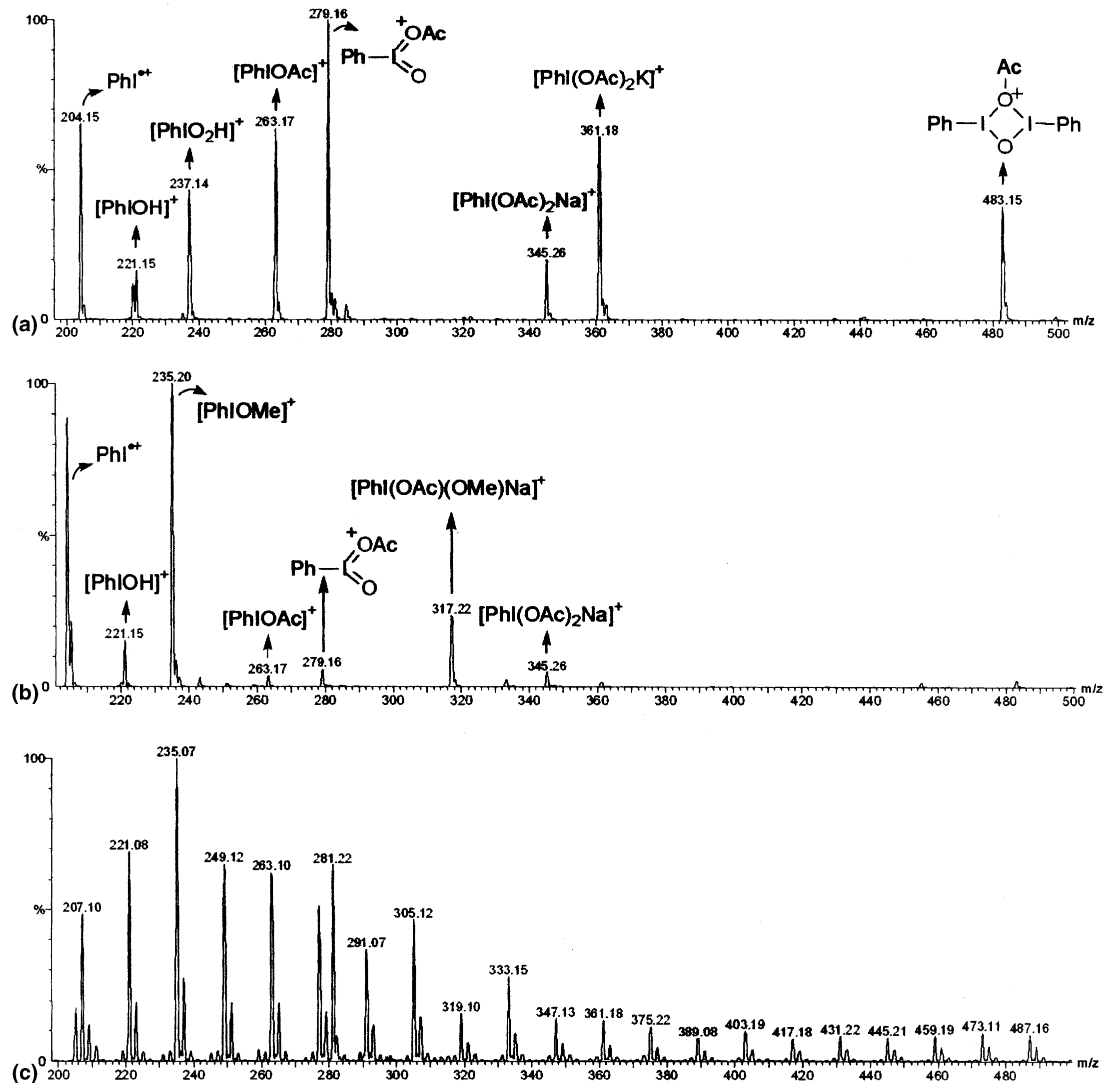
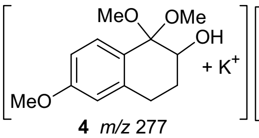
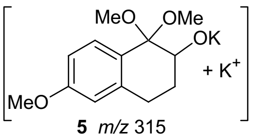


Figure 1. ESI(+)-MS spectra for solutions of $PhI(OAc)_2$ in (a) Acetonitrile; (b) MeOH; (c) MeOH with 10 equiv of KOH.



4 *m/z* 277



5 *m/z* 315

tion.[6] When we used the protocol described by Moriarty and co-workers[6] in the oxidation of 6-methoxy-1-tetralone, a clean mass spectrum was obtained in the positive ion mode, showing the presence of the acetals **4** and **5**. However, when the same ketone was added to a mixture of 10 equiv of KOH and $PhI(OAc)_2$ in MeOH that was previously stirred for 14 h, a complex mass spectrum was registered but ions corresponding to the expected products were not detected. Thus, the formation of the polymeric iodine(III) using excess of base may preclude an oxidation reaction.

The mass spectrum of a solution of iodobenzene bis(trifluoroacetate) in MeOH was also acquired, showing a pattern analogous to that observed for the corresponding solutions of $PhI(OAc)_2$. Thus, the most prominent peak of hypervalent iodine(III) is $[PhIOMe]^+$. It was also detected that iodosylbenzene is in the form of $[PhIOH]^+$ and of $[PhIOK]^+$, as well as $[PhI]^{\cdot+}$. On the other hand, the mass spectrum obtained from a solution of $PhI(O_2CCF_3)$ in CH_3CN showed protonated iodosylbenzene as the most abundant ion, instead of $[PhIO_2Ac]^+$, as in the case of $PhI(OAc)_2$ solution. The dimer **6**, which could be formed from PhIO and $[PhIOH]^+$ by a mechanism similar to that shown in Scheme 2, was also detected. Finally, the MS/MS spectrum of *m/z* 441 is in full agreement with the proposed structure (Fig. 2b).

In summary, the species present in solutions of $PhI(OAc)_2$ and $PhI(O_2CCF_3)$ depend on the solvent utilized. Several species of iodine(III) are present in solutions of $PhI(OAc)_2$ in acetonitrile, in acetic acid and in a mixture of methanol and water. In addition, a disproportionation reaction may take place at these solvents, generating iodine(V) species. Iodosylbenzene is the most important species in solution of $PhI(O_2CCF_3)_2$ in acetonitrile. In contrast, methanolic solutions of either $PhI(OAc)_2$ or $PhI(O_2CCF_3)_2$ consist mainly of the iodonium $[PhIOMe]^+$. These results will be useful for

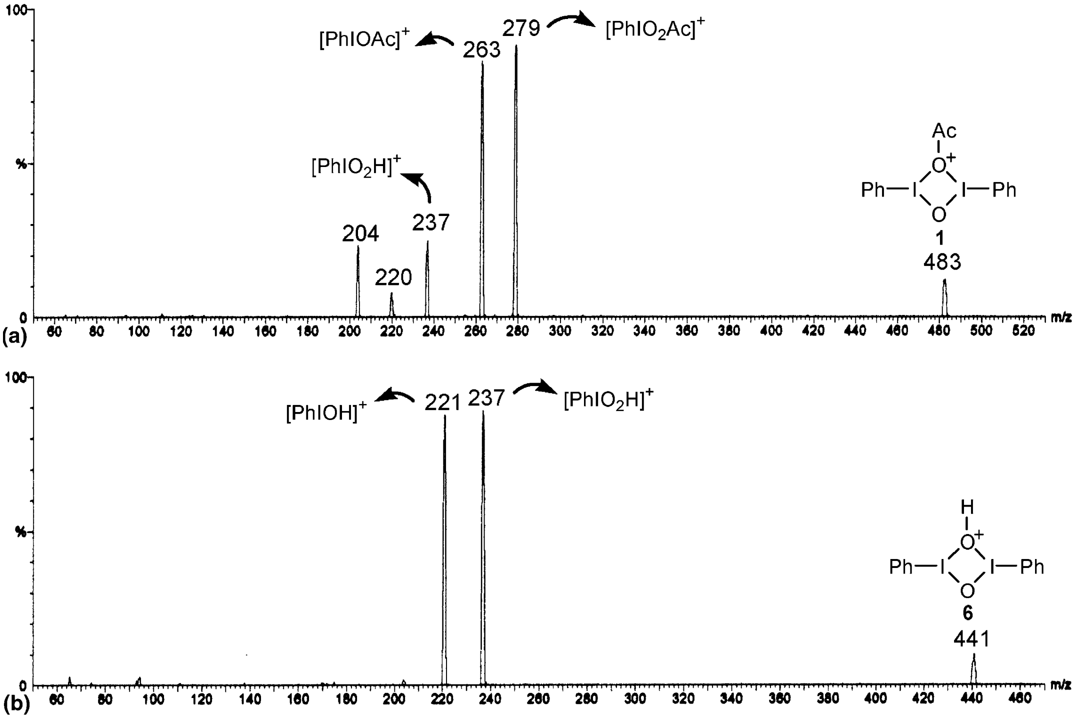


Figure 2. ESI(+)-MS/MS spectra of (a) dimer **1**; (b) dimer **6**.

understanding the reactivity and the mechanisms of iodine(III) promoted oxidations.

3. Experimental section

Iodobenzene diacetate and iodobenzene bis(trifluoroacetate) are commercially available. The solvents used in the preparation of the solutions were HPLC grade. All of the mass spectra were acquired from freshly prepared solutions. ESI analyses were performed on a triple quadrupole mass spectrometer (Quattro-LC, Micromass, Manchester, UK). The samples were infused into the ESI at a flow rate of 10 μL min^{-1} using a Harvard Apparatus model 1746 (Holliston, MA) syringe pump. After a systematic investigation (data not shown) the heated capillary and the voltage were maintained at 250 °C and 3 kV, respectively. Experiments were carried out using cone voltage from 10 to 20 V in the positive ion mode of analysis. CID fragmentation was performed using argon collision gas (7 psi) on an isolated parent ion.

Acknowledgements

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