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$PhI(OTf)_2$ Does Not Exist (Yet)

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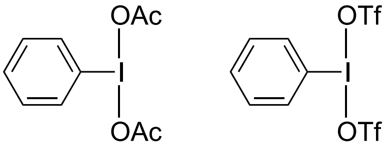
ABSTRACT

$PhI(OTf)_2$ has been used for the past 30 years as a strong I(III) oxidant for organic and inorganic transformations. It has been reported to be generated *in situ* from the reactions of either $PhI(OAc)_2$ or PhI=O with two equivalents of TMS-OTf. In this report it is shown that neither of these reactions generate a solution with spectroscopic data consistent with $PhI(OTf)_2$, with supporting theoretical calculations, and thus this compound should not be invoked as the species acting as the oxidant for transformations that have been associated with its use.

Keywords: Iodine, hypervalent, oxidants

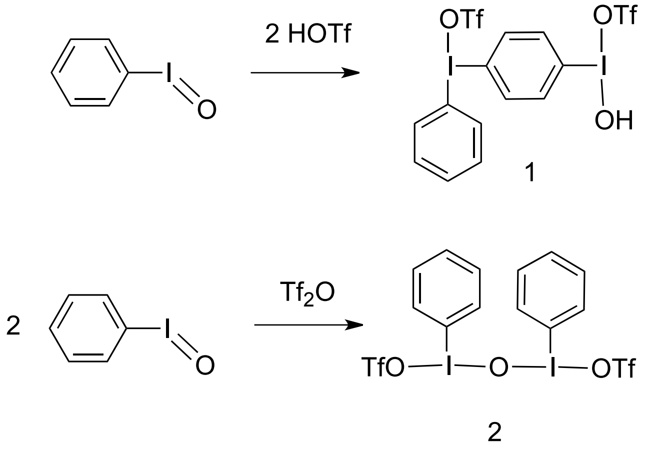
INTRODUCTION

Diacetoxyiodobenzene ($PhI(OAc)_2$) and related species are versatile I(III) oxidants with applications in organic and inorganic chemistry.[1] Replacement of the acetate ligands with more electron poor fragments results in derivatives that are stronger oxidants.[2] One such derivative with an increased oxidative capacity is $PhI(OTf)_2$ which has had reported use as an *in situ* generated species in solution by several groups, including our own. In organic chemistry $PhI(OTf)_2$ has purported use in formation of hydrazones,[3] oxyaminations,[4] dizaeniums,[5] synthesis of functionalized cyclopropane rings,[6] cyclization of hydroxystilbenes or carboxylic acids,[7] functionalization of acetylenes,[8] aryl C-H alkylations,[9] and alpha arylations.[10] We have used it as a starting complex to form Weiss' reagent, $[PhI(Pyr)_2]^{2+}$ via displacement of the triflates.[11]



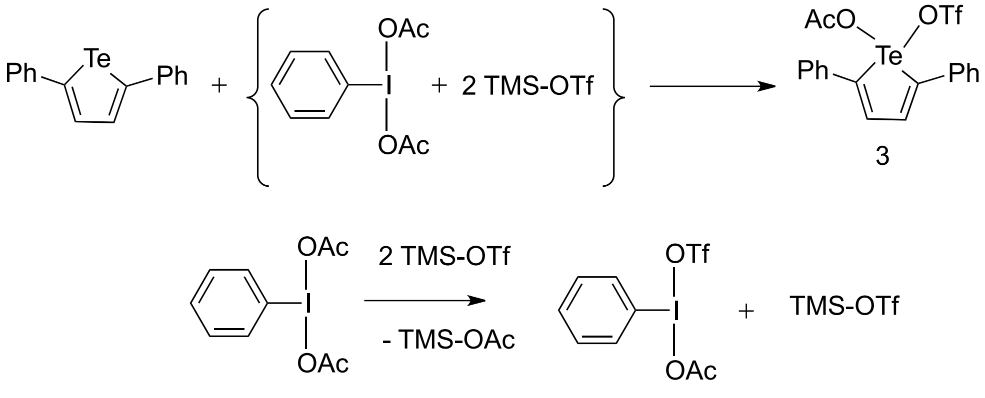
Syntheses of $PhI(OTf)_2$ and a related derivative with methyl ester groups at the 3- and 5-position have been reported by the reaction of two equivalents of TMS-OTf with $PhI(OAc)_2$ or two TMS-OTf with PhI=O,[3-4, 10, 11b, 12] with the first report coming from Zhdankin using TMS-OTf and PhI=O.[13] It was postulated that two equivalents of triflic acid may react with PhI=O to generate $PhI(OTf)_2$ but was found in actuality to generate 1 which could be used to generate bisiodonium salts.[14] Similarly it was suggested that triflic anhydride may react with PhI=O in a 1:1 fashion to generate $PhI(OTf)_2$, but experimental results were inconsistent with

$PhI(OTf)_2$ and more consistent with that of structure 1.[15] Reactions of PhI=O with half an equivalent of triflic anhydride are known to give Zefirov's reagent (2).[16]



Scheme 1. Reactions of PhI=O with triflic acid and triflic anhydride

While investigating the chemistry of "$PhI(OTf)_2$" with tellurophenes we isolated the mixed acetate/triflate Te(IV) species 3.[17] This led us to closely examine the $CDCl_3$ proton NMR spectrum of the mixture of the reaction of $PhI(OAc)_2$ with two equivalents of TMS-OTf, which clearly showed the species generated under these conditions is in fact PhI(OTf)(OAc) (Scheme 2). The identity of the PhI(OTf)(OAc) (generated from the reaction of equimolar amounts of $PhI(OAc)_2$ with TMS-OTf) was shortly thereafter confirmed in a remarkable piece of crystallography on this reactive species by Shafir *et al*.[18]



Scheme 2. Reaction of $PhI(OAc)_2$ with two TMS-OTf stopping at PhI(OTf)(OAc).

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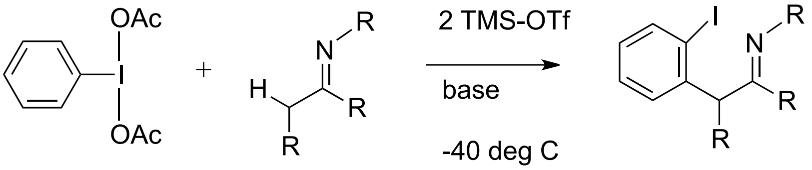
A series of recent papers published in *The Journal of The American Chemical Society* and *Angewandte Chemie* from the Peng group has reported the arylation of 2-oxazolines or aryl alkylations, and employs $PhI(OAc)_2$/ 2 TMS-OTf as the oxidant (Scheme 3 for example), using $PhI(OTf)_2$ as a starting point for theoretical calculations on the reaction mechanism in each study.[9-10] However, as detailed above, the reaction of $PhI(OAc)_2$ with two equivalents of TMS-OTf does not result in generation of $PhI(OTf)_2$ either at room temperature or at -40 °C as specified in the study. The outcomes of their syntheses are not at all in question here, but rather the starting point of $PhI(OTf)_2$ in their theoretical studies cannot be correct.



Scheme 3. Reaction of $PhI(OAc)_2$ with 2-oxazolines in the presence of two TMS-OTf, which was proposed to proceed via $PhI(OTf)_2$ as an intermediate.

Given the continued use of $PhI(OAc)_2$/2 TMS-OTf as a purported method of generating $PhI(OTf)_2$ we decided it was timely for a detailed study on the possible synthesis and existence of $PhI(OTf)_2$ from both a synthetic and theoretical perspective using this method and the original method from PhI=O and 2 TMS-OTf.

RESULTS AND DISCUSSION

From $PhI(OAc)_2$ and 2 TMS-OTf

Experimental reports on this reaction in $CDCl_3$ are detailed in our previous paper,[17] which show that this reaction stops at PhI(OTf)(OAc). The structure of PhI(OTf)(OAc) was later corroborated in a separate study by Shafir and co-workers.[18] A referee for this report suggested that performing the chemistry in acetonitrile solvent would promote metathesis of the second acetate group with TMS-OTf. To probe this we isolated PhI(OTf)(OAc) as per Shafir's procedure and recorded a ^1H proton NMR spectrum in CD_3CN, which showed peaks in the phenyl region at 8.37, 7.83 and 7.68 ppm as well as an acetate peak at 2.17 ppm. Addition of one equivalent of TMS-OTf to this acetonitrile solution of PhI(OTf)(OAc) resulted in no change to the chemical shifts and no generation of TMS-OAc.

Theoretical calculations on the free energy change for the reaction were performed at the wPBE/def2-TZVP level of theory with an acetonitrile PCM solvent model. We found that many common theoretical methods do a poor job of reproducing the geometry for bound triflate in comparison to experimental reports. The wPBE/def2TZVP method gives results consistently close to experimentally reported values across the species of interest in this study.

The calculated ΔG for the reaction $PhI(OAc)_2$ + TMS-OTf $\rightarrow$ PhI(OTf)(OAc) + TMS-OAc is – 67 kJ/mol, consistent with experimental observation that this reaction proceeds to completion. From this point however, the reaction of PhI(OTf)(OAc) + TMS-OTf $\rightarrow$ $PhI(OTf)_2$ +TMS-OAc has a calculated ΔG of + 30 kJ/mol. Considering the overall reaction $PhI(OAc)_2$ + 2 TMS-OTf $\rightarrow$ $PhI(OTf)_2$ + 2 TMS-OAc gives a value of -37 kJ/mol. This theoretical data is consistent with our experimental observation that the reaction stops at PhI(OTf)(OAc) and the 30 kJ/mol free energy well this product is in compared to $PhI(OTf)_2$ solidly supports that $PhI(OTf)_2$ should not be invoked as a species in this reaction system.

DiMagno and co-workers reported isolation and use of a derivative of $ArI(OTf)_2$ containing methyl ester groups at the 3- and 5- positions of the phenyl ring.[12] Gas phase wPBE/def2TZVP theoretical calculations on this system show the reaction of $ArI(OAc)_2$ + TMS-OTf → ArI(OAc)(OTf) + TMS-OAc is favourable with a ΔG of – 43 kJ/mol. A second metathesis giving $ArI(OTf)_2$ is also negative at – 58 kJ/mol, unlike the parent phenyl system most often used. This indicates $ArI(OTf)_2$ may be viable with these electron withdrawing groups present in the backbone of the phenyl ring. It should however be noted that this species was not structurally determined by X-ray crystallography in the report and only characterized by NMR spectroscopy. In the ^1H NMR spectrum in CD_3CN a substantial unassigned peak at 2.18 ppm is present, which is a virtually identical chemical shift to the 2.17 ppm observed for the acetate resonance in PhI(OAc)(OTf). We repeated their synthetic procedure using only one equivalent of TMS-OTf and obtained a spectroscopically identical material to what DiMagno and co-workers reported, with the signal at 2.17 ppm integrating consistently with an acetate group, and downfield from the signal in the starting $ArI(OAc)_2$ material that is coincident with the residual CHD_2CN. Addition of another equivalent of TMS-OTf to this material resulted in no change to the spectrum, with the exception of the full equivalent of TMS-OTf remaining unreacted. Thus we conclude that this compound, reported as $ArI(OTf)_2$, is in fact also ArI(OAc)(OTf).

From PhI=O

The reaction of 2 TMS-OTf with PhI=O in CH_2Cl_2, the original report of $PhI(OTf)_2$, was described to rapidly generate a yellow solution from which low melting crystals or oily substances of $PhI(OTf)_2$ could be isolated.[13] The byproduct was Me_3Si-O-$SiMe_3$ and the proton NMR chemical shifts at 60 MHz in CD_2Cl_2 were reported to be multiplets at 8.2 (2H) and 7.5 ppm (3H).

The calculated ΔG for the reaction is -41 kJ/mol, indicating the reaction is thermodynamically feasible. It should however be noted the PhI=O is a polymeric, insoluble solid[19] and the energy penalty for breaking up and solubilizing the polymer is not considered in the -41 kJ/mol. A referee suggested that using a model of the hydrated dimer of PhI=O, HO-I(Ph)-O-I(Ph)-OH might better represent the polymer which is terminated by addition of water.[20] Modelling of the reaction HO-I(Ph)-O-I(Ph)-OH + 4 TMS-OTf $\rightarrow$ 2 $PhI(OTf)_2$ + 2 TMS-O-TMS + H_2O gives a ΔG of -100 kJ/mol. The limitation of this model is that more much water is present in the modelled dimer than in the polymer and elimination of water provides a thermodynamic sink. Given the experimental reports and negative ΔG values for both models we revisited the reaction.

PhI=O was suspended in CD_2Cl_2 and two equivalents of TMS-OTf were added resulting in the immediate generation of a colourless solution. A ^1H NMR spectrum was taken which in the upfield region of the spectrum Me_3Si-O-$SiMe_3$ and unreacted TMS-OTf were observed in an approximate 3:1 ratio.[11a] In the aromatic region broad peaks in the locations Zhdankin reported at 8.2 and 7.5 ppm were present. Iodobenzene, however, was the most abundant species, with at least one other compound present. After 16 hours, the compound giving broad signals at 8.2 and 7.5 ppm disappeared and was replaced with signals consistent with a disubstituted and a monosubstituted aryl group. A mass spectrum of a sample of the reaction mixture added to CH_3CN gave a signal with *m/z* at 406.9 in positive ion mode, consistent with the cation $[C_6H_5\text{-I-}C_6H_4\text{-I}]^+$, which is also consistent with signals in the ^1H NMR spectrum. A ^1H NMR taken in DMSO-d_6 to compare with literature data confirmed this cation as the remaining product, with the iodobenzene also remaining present.[21]

Regarding the intermediate, which is consistent with the $PhI(OTf)_2$ spectrum proposed by Zhdankin, in both $CDCl_3$ and CD_2Cl_2, the -ortho aryl protons in $PhI(OAc)_2$ resonate at 8.10 ppm.[22] For PhI(OAc)(OTf) the -ortho protons resonate at a chemical shift of 8.25 ppm.[17] It would be expected that another substitution of acetate for more electron poor triflate would lead to a further downfield chemical shift for these protons, thus a signal at 8.2 ppm is not consistent with $PhI(OTf)_2$. The observation that not all the TMS-OTf is consumed in the reaction is also inconsistent with formation of $PhI(OTf)_2$. In summary, PhI=O reacted with two equivalents of TMS-OTf does not generate a solution of $PhI(OTf)_2$ based on ^1H NMR data.

Triflic anhydride has been suggested to possibly react in equimolar quantities with PhI=O to generate $PhI(OTf)_2$,[15a] but it has also been found to actually give compound 1,[15b] and also gives onward reactions consistent with that class of species. Reaction of half an equivalent of triflic anhydride with PhI=O has been reported to give Zefirov's reagent.[15a] The calculated ΔG for the reaction of PhI=O with one equivalent of triflic anhydride giving $PhI(OTf)_2$ is -166 kJ/mol. The calculated ΔG for the reaction with a half equivalent of triflic anhydride giving Zefirov's reagent is -233 kJ/mol, indicating stopping at this point should be the thermodynamic sink for the reaction.

These ∆G values considered, we decided to revisit the reaction of PhI=O and triflic anhydride in CD_2Cl_2 in an equimolar ratio, to compare the results with our observations for PhI=O and two TMS-OTf. The ^1H NMR spectrum of the reaction mixture showed no peaks consistent with the report of $PhI(OTf)_2$ with no resonances around 8.2 ppm. At least two unique phenyl groups were present in the mixture with the most downfield peak at 8.5 ppm, but being a minor product. The ^{19}F NMR spectrum contained unreacted triflic anhydride at -71 ppm and a resonance at -78 ppm consistent with anionic triflate, and a minor resonance at -76 ppm, which is consistent with a bound triflate and Zefirov's reagent and 1 as previously reported.[15]

Reaction of 2 triflic acid with PhI=O to give $PhI(OTf)_2$ is also calculated to be favourable at -69 kJ/mol, giving water as a byproduct. Reaction of PhI=O with 2 equivalents of TfOH in CD_2Cl_2 gave a ^1H NMR spectrum similar to that of the reaction from triflic anhydride, with a mixture of peaks in the aryl region in the *in situ* NMR spectrum consistent with the general structure of 1 as previously described[14] and no evidence for the presence of $PhI(OTf)_2$.

These observations, with triflic acid and triflic anhydride giving different products than the reaction of PhI=O with 2 TMS-OTf, indicate that the intermediates generated in the TMS-OTf reaction must differ. This is also consistent with reported reactions on the ring contraction of alcohol appended cyclobutanes where reaction of $PhI(OAc)_2$ with TMSOTf promoter gives a substantially different yield than the reaction of $PhI(OAc)_2$ or PhI=O with triflic anhydride as the promoter.[6b]

CONCLUSION

In this study we have shown that the methods reported to generate $PhI(OTf)_2$ do not give solutions of this species. The most common modern purported method, $PhI(OAc)_2$ + 2 TMS-OTf stops at one metathesis conclusively giving PhI(OTf)(OAc), and $PhI(OTf)_2$ should not be invoked from this mixture. For the reaction of 2 TMS-OTf with PhI=O, while calculated to be thermodynamically feasible, we do not believe $PhI(OTf)_2$ is generated and then decomposes as only half of the TMS-OTf is consumed when the reaction ceases at room temperature and the NMR data of the reaction mixture is not consistent with $PhI(OTf)_2$. In summary, while reactions using the above methods previously reported in the literature all result in compounds containing oxidizing I(III) sources which have been used effectively for organic transformations, the molecule $PhI(OTf)_2$ itself does not (yet) exist. We would again clarify that the organic transformations induced by the I(III) in these systems are not in question. Rather the I(III) oxidant is incorrectly identified which impacts theoretical studies if the incorrect starting energies are used due to an incorrect compound being used, as well as the potential of the unintended presence of acetate possibly being a confounding factor in the desired chemistry.

Acknowledgements

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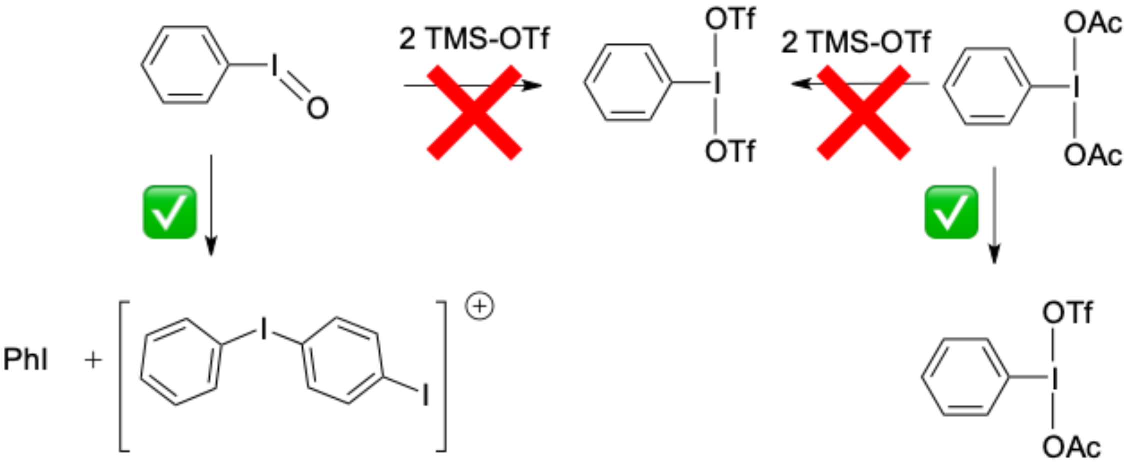
TOC Fig



$PhI(OTf)_2$ has been invoked as an intermediate in I(III) mediated oxidations. In this communication we show that the methods proposed to generate $PhI(OTf)_2$ do not give solutions spectroscopically consistent with this species.