Lewis acid activation of Weiss' Reagents ($[PhI(Pyr)_2]^{2+}$) with boranes and isolation of $[PhI(4\text{-}DMAP)]^{2+}$

Aseel Bakro,[a#] Lachlan Sharp-Bucknall,[a#] Tiffany B. Poynder,[a] Jack K. Clegg[b], David J. D. Wilson,[a] and Jason L. Dutton[a]*

[a] Department of Chemistry and Physics, La Trobe University, Melbourne 3086, Victoria, Australia

[b] School of Chemistry and Molecular Biosciences, The University of Queensland, St Lucia, Queensland, Australia, 4072

# these authors contributed equally

j.dutton@latrobe.edu.au

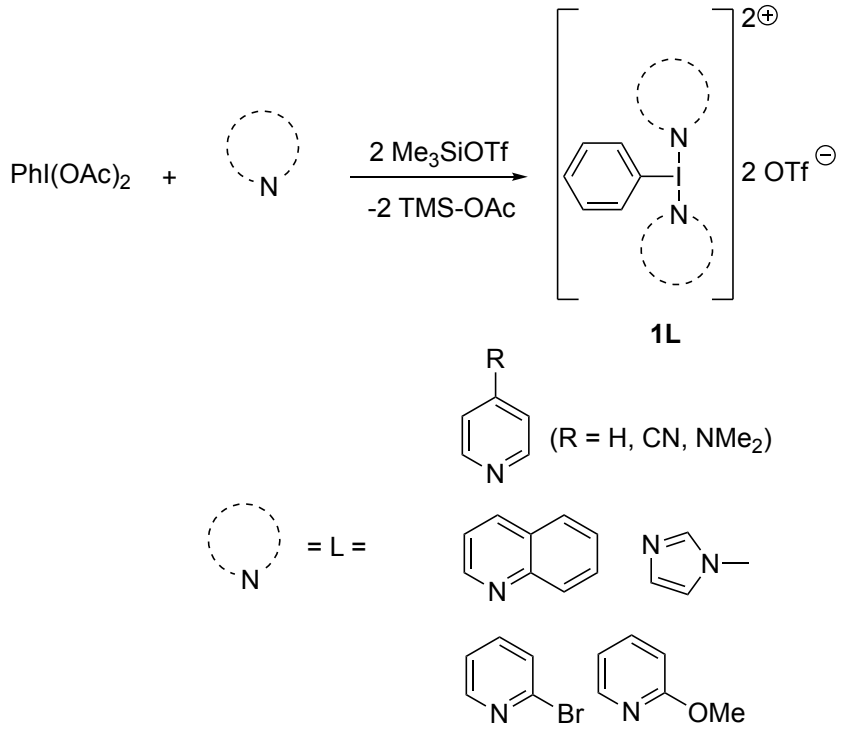
ABSTRACT

Abstraction of a pyridine ligand from Weiss' reagent ($[PhI(Pyr)_2]^{2+}$) using BF_3-Et_2O was found to activate Weiss' reagent towards electrophilic aromatic substitution reactions. The activated species can be isolated when 4-DMAP is used as the pyridine ligand and was determined to be a $[PhI(4\text{-}DMAP)]^{2+}$ in solution, and is associated with a triflate counterion in the solid state. The isolated cation was reactive in electrophilic aromatic substitution reactions towards mesitylene, xylene and toluene that Weiss' reagent itself does not react with. If pyridine is used as the ligand the intermediate that results from abstraction cannot be isolated but is even more active, being observed to react with benzene.

Keywords: Iodine, hypervalent, oxidants

INTRODUCTION

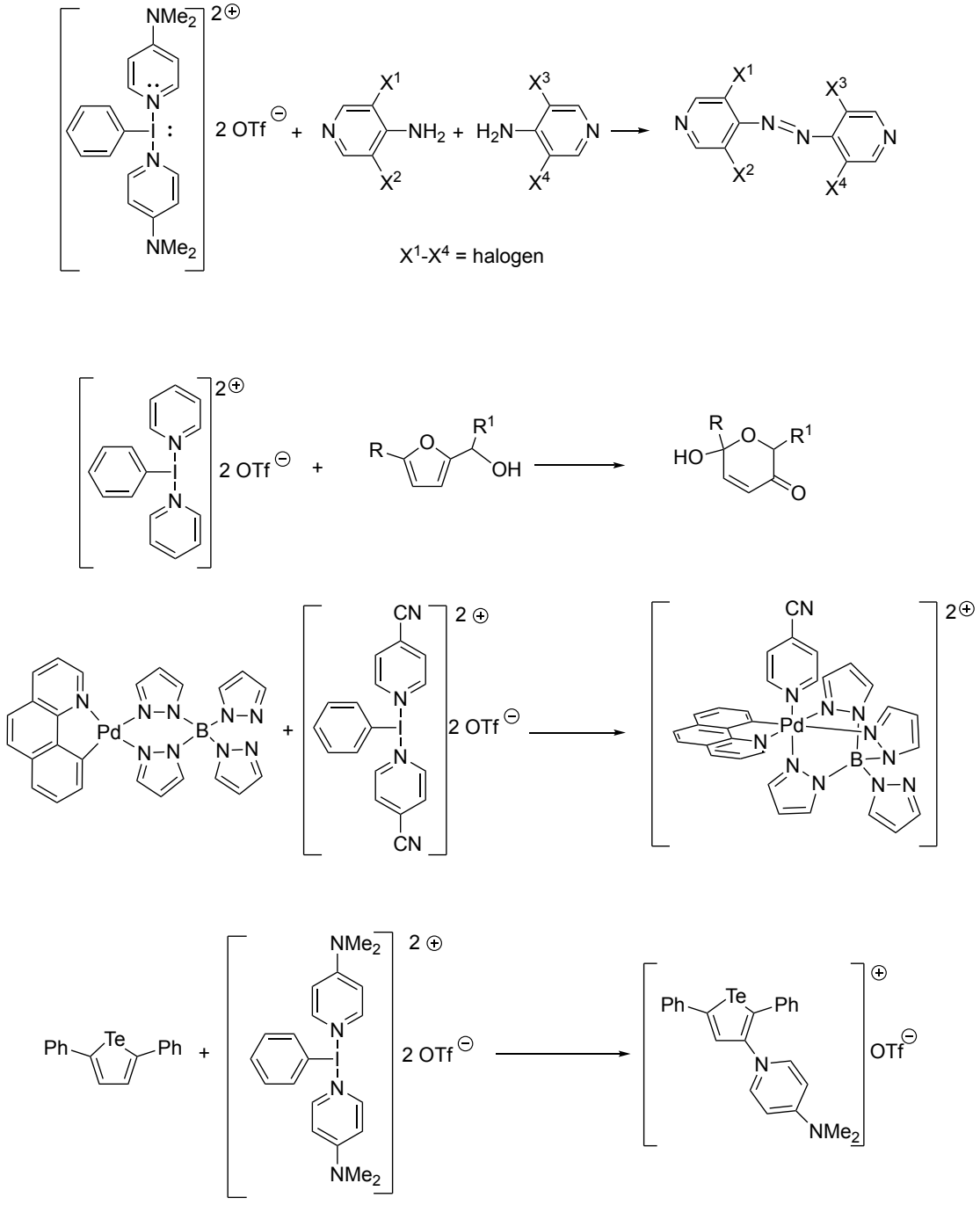
The I(III)-pyridyl family of coordination complexes $[PhI(L)_2]^{2+}$ (**1L**), initially reported by Weiss in 1994 is a versatile oxidant.[1] They are easily synthesized from commercially available $PhI(OAc)_2$, followed by addition of two equivalents of Me_3SiOTf (TMS-OTf) and the desired pyridyl or related N-ligand (Scheme 1).



Scheme 1. Synthesis of Weiss' reagents **1L**.

Weiss' reagents have been used for the oxidation of transition metals with delivery of the associated pyridine ligands.[2] A number of organic chemistry reactions employ Weiss' reagents for oxidative chemistry, which has been led in recent times by the group of Wengryniuk. Reactions include oxidative couplings,[3] oxidative ring expansion,[4] oxidation of alcohols for complex ring formation,[5] and aminolactonization.[6] In main group chemistry,

reactions with group 16 aromatic rings results in the competing electrophilic aromatic substitution of the nitrogen ligands or $[I\text{-}Ph]^+$ fragments onto the ring (Scheme 2).[7] The umpolung functionalization of carbon atoms via delivery and then displacement of $[I\text{-}Ph]^+$ by nucleophiles has also been reported.[8]



Scheme 2. Representative reactions of Weiss' reagent in transition metal, organic and main group chemistry

Lewis acid activation of I(III) complexes by borane to enhance reactivity has been reported for the general class of $PhIL_2$ (L = ligand) complexes, including $PhICl_2$, $PhIF_2$, and $PhI(OAc)_2$.[9] Borane Lewis acids interact with the lone pairs on the ligand substituents, which has been shown crystallographically by Shafir and co-workers.[10] Using $PhI(OAc)_2$ and BF_3 they reported the generation of $[Ph\text{-}I\text{-}Ar]^+$ cations by the addition of mesitylene to the activated species.

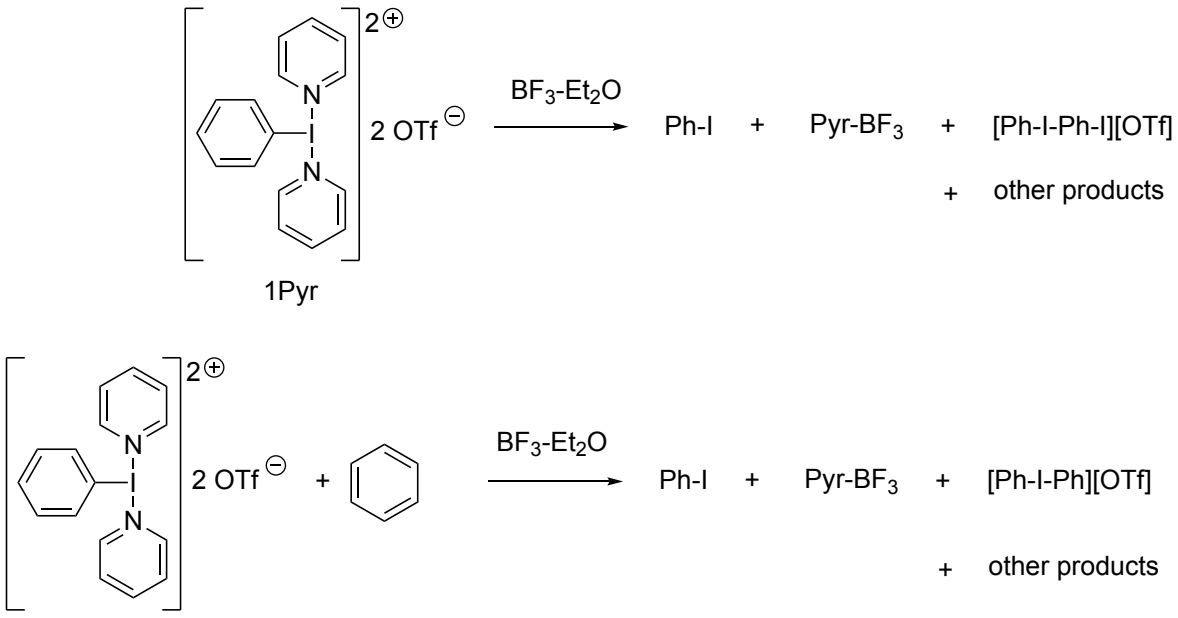
We wondered if activation by borane Lewis acids was possible for Weiss' reagents such as $[PhI(pyr)_2]^{2+}$, that do not bear an available lone pair. With its coordinative bonding properties the pyridine ligand is also potentially labile via a dissociative mechanism.[11] In this report we describe the first examples of Lewis acid activation of Weiss' reagent $[PhI(pyr)_2]^{2+}$ using BF_3-Et_2O and the isolation of $[PhI(DMAP)]^{2+}$ as a more reactive derivative of Weiss' reagent.

RESULTS AND DISCUSSION

The reaction of the pyridine derivative of Weiss' reagent **1Pyr** and BF_3-Et_2O in C_6D_6 (Scheme 3) resulted in a clear solution with a white suspension. In the ^{19}F NMR spectrum the predominant BF_3 peak was consistent with the pyridine adduct of BF_3, confirmed by comparison of the ^{19}F NMR spectrum of a mixture of pyridine and BF_3 in C_6D_6. The proton NMR spectrum showed a variety of phenyl containing species in the aryl region, in addition to signals consistent with the pyridine adduct of BF_3. The mass spectrum included a major positive ion at m/z = 286, which is 5 mass units heavier than the $[Ph\text{-}I\text{-}Ph]^+$ cation. Repeating the experiment in C_6H_6 returned a mass of m/z = 281. This cation could be identified in the ^1H NMR spectrum, in addition to iodobenzene. Without the addition of BF_3-Et_2O **1Pyr** is

unreactive towards benzene, although **1Pyr** has been previously reported to react with more activated anisole to give pyridiyl substitution on the para C-H of anisole.[7b] In combination these experiments suggest that BF_3-Et_2O activates **1Pyr** by abstracting a pyridine group, rendering a transient $[PhI(Pyr)]^{2+}$ species (**2Pyr**) active as a substrate for electrophilic aromatic substitution on benzene via the iodine atom. It was subsequently found that the reaction can be performed in acetonitrile with stoichiometric benzene, although in this case a signal that can be attributed to the $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ also becomes apparent in the mass spectrum.

The reaction of **1Pyr** with BF_3-Et_2O in acetonitrile in the absence of benzene gives $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ as the dominant species in the mass spectrum, which was also observed in the proton NMR spectrum along with PhI. No $[Ph\text{-}I\text{-}Ph]^+$ was observed. We have previously reported that $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ formed in the attempted synthesis of $PhI(OTf)_2$, which suggests that $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ may be a sink when I(III) reagents in this general class become too electrophilic and react with themselves.[12]



Scheme 3. Reaction of **1Pyr** with BF_3 in the absence and presence of benzene.

Reaction of the 4-DMAP analogue of Weiss' reagent **1DMAP** with BF_3-Et_2O in CD_3CN resulted in a yellow solution. PhI and other phenyl containing species as well as the DMAP adduct of BF_3 could be identified via multinunclear NMR spec troscopy. In the mass spectrum the signals arising from $[Ph\text{-}I\text{-}Ph]^+$ and $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ were absent. Addition of benzene did not result in generation of $[Ph\text{-}I\text{-}Ph]^+$ as was observed in the reaction with the pyridine analogue.

Single crystals were grown via vapour diffusion of Et_2O into a CH_2Cl_2 solution of the mixture at -30 ^oC. X-ray diffraction studies revealed the crystals to be cation **2DMAP**, with a single 4-DMAP bound to the iodine atom, another triflate associated with iodine and a free triflate anion (Figure 4). In the solid state the I-O bond distance was found to be 2.36 Å. This can be compared to the I-OTf bond in PhI(OAc)(OTf) determined by Shafir and co-workers of 2.35 Å and the I-OAc bond distance of 2.06 Å, where they proposed the compound as an ionic pair of [PhI(OAc)][OTf].[10] The I-N bond distance is 2.09 Å, shortened from the 2.18-2.22 Å observed in **1DMAP**.[3a]

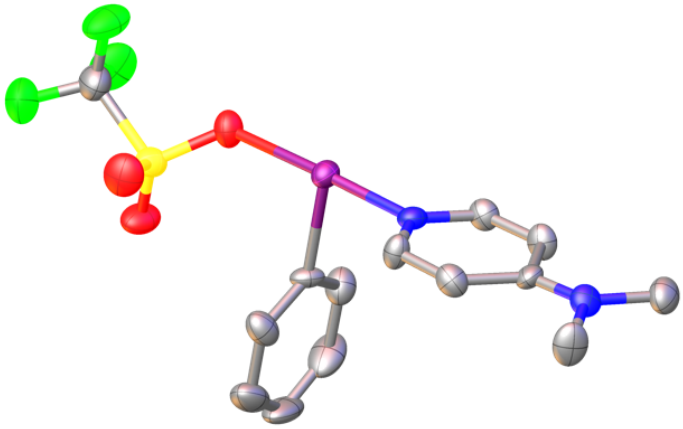


Figure 1. Solid state structure of the cationic unit of **2DMAP**. Ellipsoids are depicted at the 50% probability level. Triflate anion, dichloromethane solvate and hydrogen atoms are omitted. Selected bond distances (average of two independent molecules in asymmetric unit) (Å): I-N 2.085(8), I-O 2.358(6).

While **2DMAP** is an interesting compound as potentially a more reactive derivative of Weiss' reagent, **2DMAP** was clearly not the main component of the reaction mixture. Using the BF_3 4-DMAP abstraction method we were unable to isolate a pure sample. However, with the knowledge that **2DMAP** can be crystalized, we sought an alternative route to make **2DMAP** in a manner where it could be isolated.

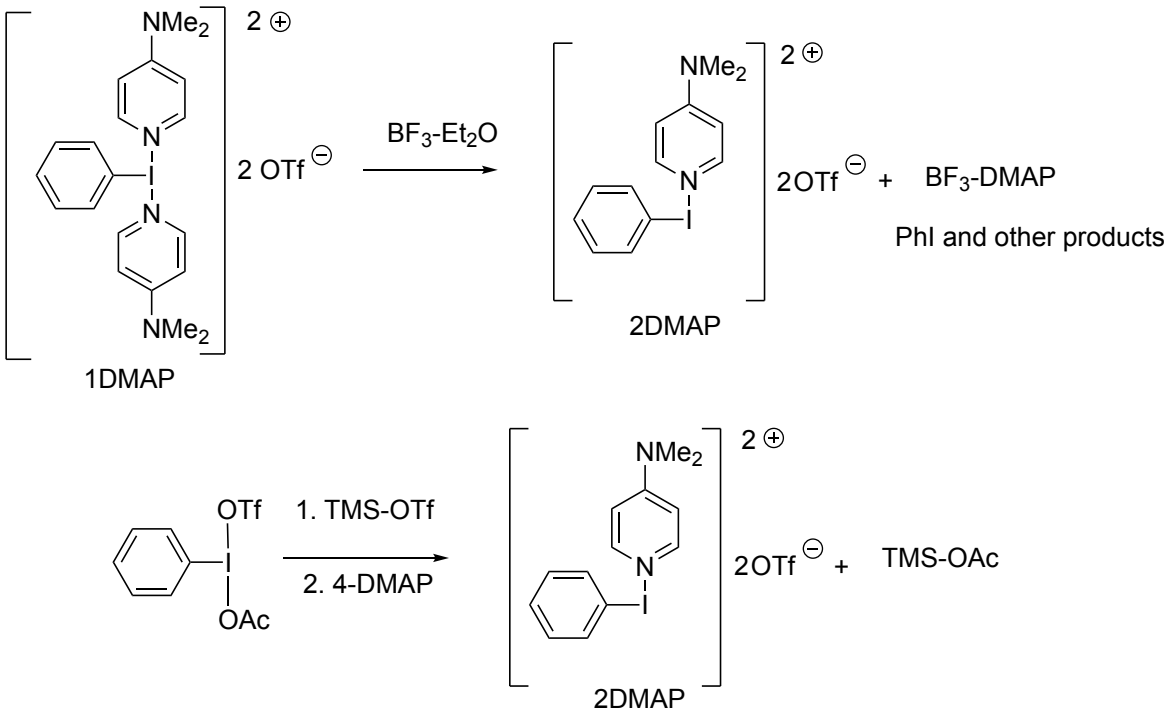
Weiss' reagents are most conveniently synthesized from the reaction of $PhI(OAc)_2$ with two equivalents of TMS-OTf, followed by addition of two equivalents of a suitable pyridine ligand. The first step of the reaction stops at PhI(OAc)(OTf);[12] displacement of the triflate by pyridine presumably activates the bound acetate allowing for TMS-OTf to abstract it and permit binding of the second pyridine ligand.

Isolation of PhI(OAc)(OTf) followed by addition of one equivalent of 4-DMAP led to the immediate generation of Weiss' reagent **1DMAP**. Isolation of PhI(OTf)(OAc), followed by addition of one equivalent of TMS-OTf in CH_2Cl_2, and then addition of one equivalent of 4-DMAP led to the observation of a new set of signals in the ^{1}H NMR spectrum of a CD_3CN solution after workup, which were present as a minor product in the reaction mixture from BF_3 abstraction of 4-DMAP from **1DMAP** (Scheme 4). Finally, it was found that the most convenient synthesis arose from addition of two equivalents of TMS-OTf to $PhI(OAc)_2$ followed by dropwise addition of a solution containing one equivalent of 4-DMAP at -35 °C to furnish the target compound. The product was isolated as a yellow powder, and regrowing crystals from CH_2Cl_2 via vapour diffusion of Et_2O at -35 °C confirmed the identity of the material as **2DMAP**. We surmised that 4-DMAP was reacting with TMS-OTf to give [TMS-4-DMAP][OTf],[13] which then reacts with PhI(OTf)(OAc) to give **2DMAP**. This was confirmed by performing the reaction of PhI(OTf)(OAc) with a separately prepared sample of [TMS-4-DMAP][OTf], which generates **2DMAP** as the dominant product as monitored by ^{1}H NMR spectroscopy.

The ortho protons on the 4-DMAP in **2DMAP** are shifted significantly downfield from parent **1DMAP** in the ^{1}H NMR spectrum from 8.29 to 8.46 ppm, consistent with the stronger binding of 4-DMAP to iodine in **1DMAP** as compared to **2DMAP** due to the higher potential electrophilicity of the iodine atom.

The chemical shift of the OTf^- fragments in the ^{19}F NMR spectrum was -78.62 ppm in CD_3CN. Only one sharp signal was observed and this shift is nearly identical to that observed in $[NBu_4][OTf]$ at -78.78 ppm. If an OTf^- remained bound to the iodine in solution, two signals, or a broadening and more substantive downfield shift would be expected.[14] **1DMAP**, having no available sites to bind with OTf^- also has a chemical shift at -78.78 ppm. This result suggests

that **2DMAP** is mostly ionized in solution with only a weak association with OTf^- and can be considered as $[PhI(4\text{-}DMAP)]^{2+}$.

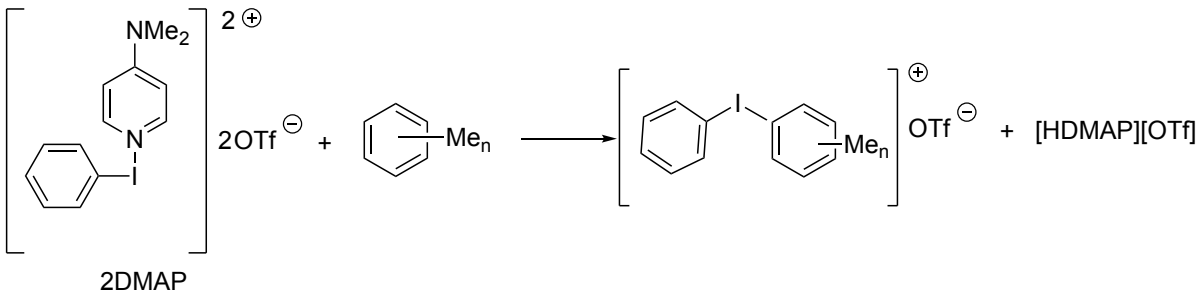


Scheme 4. Generation of **2DMAP** by abstraction of 4-DMAP from **1DMAP** and synthetic route for isolation of **2DMAP** from PhI(OAc)(OTf).

Attempting isolation of **2Pyr** by adding one equivalent of pyridine to a mixture of PhI(OAc)(OTf)/TMS-OTf gave **1Pyr**, indicating that the pyridine analogue is not favourable, which is consistent with the differing reactivity observed in the BF_3 abstractions with the pyridine and 4-DMAP analogues of Weiss' reagent.

Addition of benzene to **2DMAP** in CD_3CN solvent resulted in no reaction as monitored by ^1H NMR spectroscopy, which is consistent with the absence of $[Ph\text{-}I\text{-}Ph]^+$ in the BF_3 abstraction reaction from **1DMAP**. However addition of more activated mesitylene, xylene, or toluene to **2DMAP** (Scheme 5) resulted in immediate generation of $[Ph\text{-}I\text{-}Ar]^+$ as evidenced

by the ^{1}H NMR and mass spectra, with the other product being protonated 4-DMAP from electrophilic aromatic substitution. Addition of mesitylene, 1,2-xylene, or toluene to **1DMAP** gave no reaction, confirming increased reactivity in **2** as compared to Weiss' reagent. The observation of $[Ph\text{-}I\text{-}Ph]^+$ in the mass spectrum of the reaction of BF_3 with **1Pyr** in the presence of benzene implies the pyridine bound analogue of **2** is generated *in situ* for this derivative, even though it cannot be isolated, and likely decomposes to $[Ph\text{-}I\text{-}Ph\text{-}I]^+$ in the absence of benzene as was observed in attempted syntheses of $PhI(OTf)_2$.



Scheme 5. Reaction of **2DMAP** with mesitylene, 1,2-xylene and toluene.

Theoretical calculations at the B3LYP-D3(BJ)/def2-TZVPPD(CPCM,dichloromethane) [15] level of theory with RIJCOSX[16] were performed in Orca[17] to rationalize the observed behavior in the system. The optimized geometries are consistent with the X-ray structures; **2DMAP** and **2pyr** give I-N bond distances of 2.05 and 2.10 Å, respectively, while the I-O bond distance in **2DMAP**[OTf] is 2.30 Å. For both **1DMAP** and **2DMAP** the LUMO is a sigma-symmetric antibonding orbital orientated along the I-N bond axis (Figure 2). With **2DMAP** the LUMO is more sterically accessible and 2.0 eV lower in energy than in **1DMAP**, explaining the increased electrophilic activity in **2DMAP** (HOMO-LUMO gap is also 1.34 eV smaller in **2DMAP** compared to **1DMAP**). The LUMO in **2Pyr** is 0.62 eV lower in energy than in **2DMAP**, which explains the increased reactivity of the presumed transient dication arising from BF_3

abstraction of pyridine from **1Pyr**, which is reactive towards benzene, whereas DMAP ligated **2DMAP** is not reactive. The calculated NPA[18] partial charge on I in **2DMAP** (1.24) is slightly increased from **1DMAP** (1.21), also consistent with the increased electrophilic reactivity in **2DMAP**.

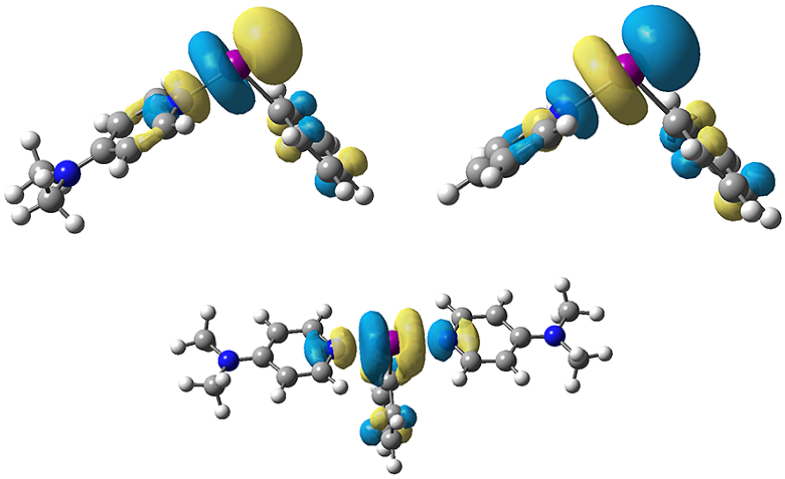


Figure 2. Plots of the LUMO of **2DMAP** and **2Pyr** (top) and **1DMAP** (bottom).

CONCLUSIONS

We have demonstrated that the Weiss' reagents can be activated by addition of borane Lewis acids. In the case of the pyridine derivative the transient cation generated is sufficiently reactive to react with unactivated benzene to give $[Ph\text{-}I\text{-}Ph]^+$ cations. The intermediate arising from abstraction of the pyridine ligand, **2L**, can be isolated in a straightforward procedure when 4-DMAP is used as the ligand. This derivatize is more reactive than the parent Weiss reagent, readily reacting with methyl substituted benzenes giving $[Ph\text{-}I\text{-}Ar]^+$ cations. We are currently exploring the scope of its potential reactivity towards inorganic and organic substrates.

Acknowledgements

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