# On the activation of $PhICl_2$ with pyridine

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ABSTRACT

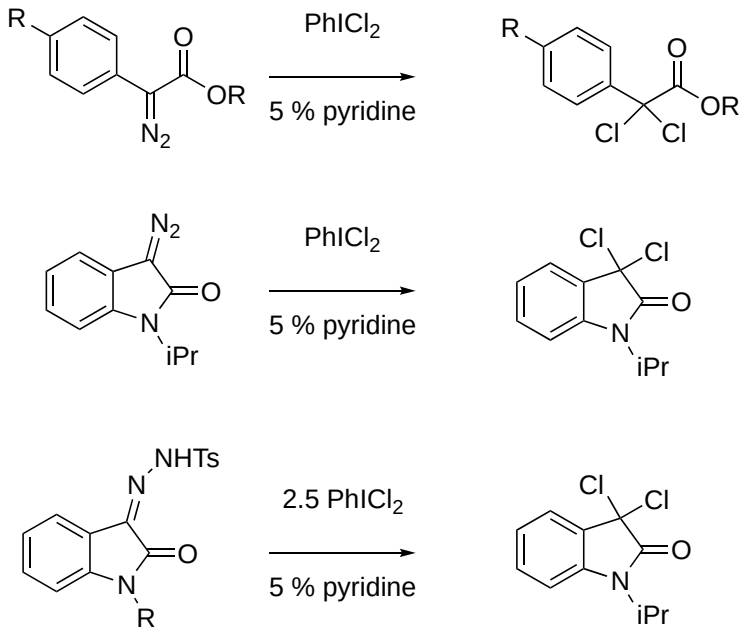
It has been previously proposed that pyridines can activate $PhICl_2$ by displacing a chloride and forming the $[PhI(Pyr)(Cl)]^+$ cation as a reactive intermediate. Here we show that pyridine does not displace chloride, but rather forms a weak complex with the iodine via halogen bonding along the C-I bond axis. This interaction is investigated by NMR, structural, charge density and theoretical investigations, which all indicate the pyridine does not activate $PhICl_2$ as proposed.

Keywords: Iodine, hypervalent, oxidants, halogen bonding, charge density

INTRODUCTION

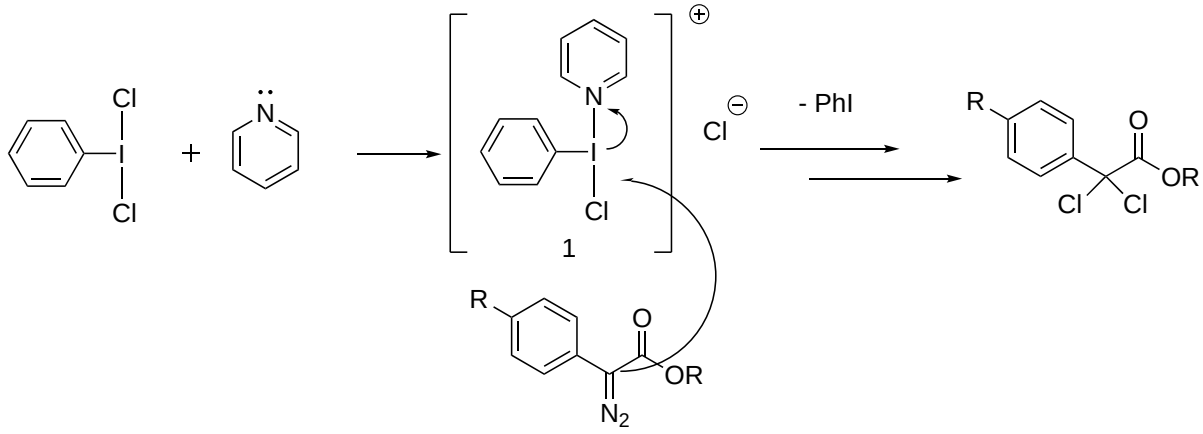
$PhICl_2$ is a versatile oxidant, primarily acting as a chlorinating agent representing a convenient substitute for $Cl_2$. $Cl_2$ is a highly corrosive, toxic gas, which in addition to being hazardous, is challenging to deliver in a stoichiometric fashion. $PhICl_2$ conversely is an easily weighed solid and has been used widely in the oxidation of organic and inorganic compounds.[1-3]

In a series of recent papers Murphy and co-workers have reported on the activation of $PhICl_2$ using catalytic amounts of pyridine ligands to achieve chlorination of diazo compounds or hydrozones (Scheme 1).[4-8]




Scheme 1. Reported reactions of $PhICl_2$ with diazo or hydrozone compounds using catalytic pyridine.

The mechanism presented for the initial report regarding the chlorination of diazo compounds proposed that pyridine displaces a chloride from $PhICl_2$ giving activated cationic complex **1**, which is then susceptible to attack by the nucleophilic carbon of the diazo (Scheme 2).[4]




Scheme 2. Proposed activation of $PhICl_2$ with pyridine.

Evidence for activated complex **1** was provided by a downfield shift in the $^1H$ NMR resonance of the methyl protons in the proposed adduct with lutidine of ~ 0.5 ppm.[4] 4-DMAP is also used as an activating pyridine ligand in the reports.[5] As part of our interest in the coordination chemistry of I(III) with N-ligands the proposed active species **1** caught our attention as we have been attempting unsuccessfully to isolated such a complex for some time. In this report we describe our findings on the interaction of $PhICl_2$ with pyridine ligands.

RESULTS AND DISCUSSION

$PhICl_2$ was prepared by oxidation of iodobenzene with $H_2O_2$ in the presence of concentrated HCl (ESI) and crystallised from a saturated $CH_2Cl_2$ solution (-20 °C). While the crystal structure of $PhICl_2$ has been previously reported,[9] the high quality of the crystals obtained allowed the collection of diffraction data to better than 0.38 Å resolution and refinement of a multipole model (Figure 1).[10] In the solid state the iodine atom has the expected T-shaped geometry with a slight asymmetry due to the presence of different intermolecular interactions involving each Cl atom (see ESI). The full deformation of the static electron density (Figure 2) and 2D-Lapacian maps (Fig. S3-S5, ESI) indicates a local partial positive charge (σ-hole) on the iodine atom opposite the phenyl group.[11] The σ-hole acts as a halogen bond acceptor from an adjacent chlorine (Cl2 ⋯ I1 = 3.42 Å, $R_{ClI}$ = 0.92, $\psi = 0.31$).[12,

[13] The presence of this type $\beta$ halogen-bond was confirmed by a (3, -1) bond critical point (Fig. S6, ESI) with a density of $\rho$= 0.16 e·Å$^{-3}$ (Table S5, ESI).

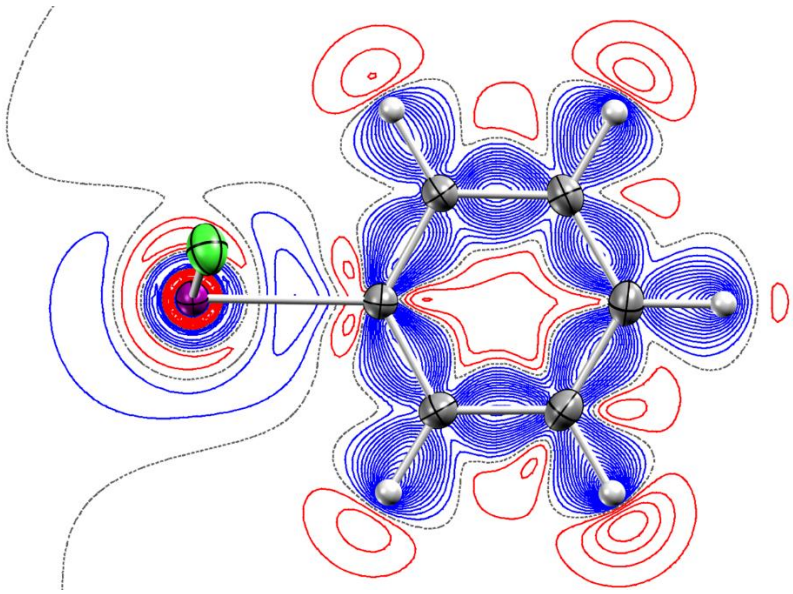
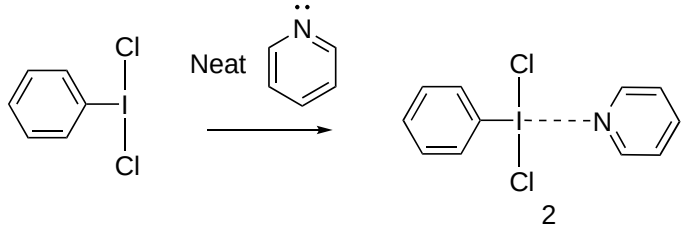


Figure 1. ORTEP representation (90% probability level) and 2D-deformation electron density of compound $PhICl_2$ viewed perpendicular to the ZX plane of the phenyl ring (contour 0.05 e Å$^{-1}$). Positive density is shown in blue and negative in red; grey dotted lines represent zero density. I1-C1 = 2.0977(4) Å, I1-Cl1 = 2.48319(12) Å and I1-Cl2 = 2.505926(11) Å); Cl1-I1-Cl2 = 176.701(4) °.

The reaction of $PhICl_2$ with pyridine was then investigated. A sample of $PhICl_2$ was dissolved in $CDCl_3$. One stochiometric equivalent of pyridine was added and an NMR spectrum was taken. The $^1H$ NMR spectrum showed no significant change in the chemical shift for either the pyridine or $PhICl_2$ moieties, but a slight broadening was observed as compared to the separate species under the same conditions. We also reproduced the work with 1 equivalent of lutidene from Murphy showing the same slight change in chemical shift as they reported.[4] This is in contrast to a related pyridine complex of I(III), Weiss' reagent, $[PhI(Py)_2]^{2+}$, in which pyridine is unambiguously bound, where the ortho pyridine C-H protons are shifted to 9.00 ppm, as compared to 8.57 ppm for free pyridine.[14] The sample was placed in the freezer at -30 deg C and pale yellow needle-like crystals formed overnight. Single crystal X-ray analysis returned a structure of only $PhICl_2$.

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Scheme 3. Reaction of $PhICl_2$ with neat pyridine.

A sample of $PhICl_2$ was then dissolved in neat pyridine and held at -30 °C overnight which resulted in the precipitation of bright yellow block-like crystals. Single crystal X-ray analysis (Figure 2) confirmed the formation of a $PhICl_2$·Py complex (**2**).

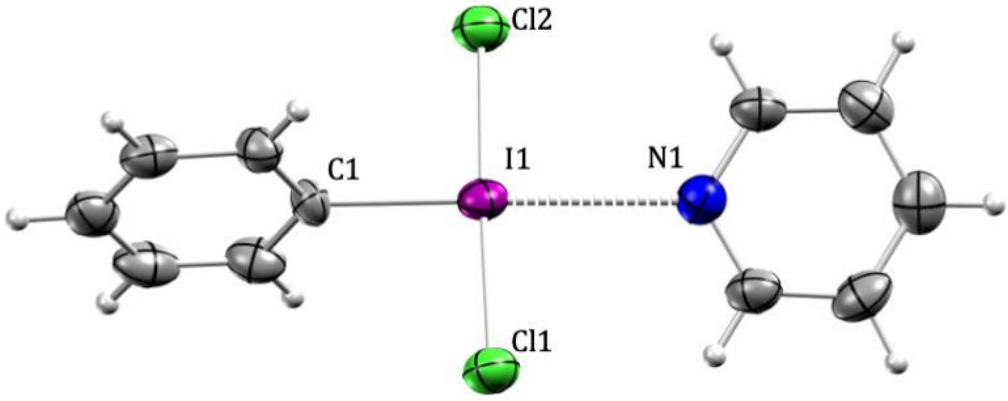
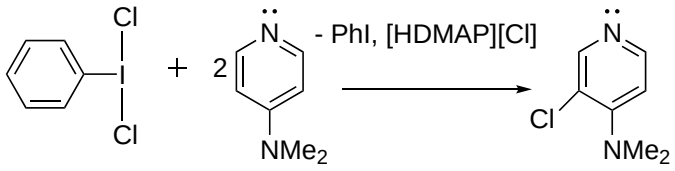



Figure 2. ORTEP representation of the crystal structure of the $PhICl_2$·Py complex (**2**) shown with 70 % probability ellipsoids. I1-C1 2.169(4); I1-Cl1 2.4869(12); I1-Cl2 2.5115(12); I1···N1 = 2.750(4) Å; Cl1-I1-Cl2 = 178.05(4) °.

The $PhICl_2$ part of the molecule in the structure of **2** is very similar to the structure of $PhICl_2$ with a slightly elongated C-I bond (2.169(4) Å in **2** compared to 2.0977(4) Å in **1**). The pyridine is located opposite the phenyl ring resulting in a square planar iodine geometry. The N-I distance is 2.750(4) Å which is indicative of the presence of a much stronger type $\alpha$ halogen bond than in **1** ($R_{NI}$ = 0.78, $\psi = 0.98$),[12, 13] but significant longer than those present in Weiss' reagent (2.22 Å) ,[14, 15] bipyridine adduct of $[ICl_2]^+$ (2.27 Å ),[16] or the 4-coordinate pyridine adduct of iodine triacetate (2.406 Å).[17] NMR titration experiments followed by fitting using BindFit[18, 19] with 1, 2, 3, 4, 5 and 10 equivalents of pyridine relative to $PhICl_2$ in $CDCl_3$ gave a binding constant of 0.7 $M^{-1}$ and binding behavior consistent with a host-guest or coordinative interaction, rather than displacement. Taking together these observations indicate pyridine does not displace a chloride from the iodine in $PhICl_2$ with either stoichiometric or excess pyridine or when dissolved in neat pyridine.

We then investigated the reaction between the stronger base 4-DMAP and $PhICl_2$, which has also been reported to activate $PhICl_2$ albeit with less efficacy than the catalytic reactions

described as pyridine.[5] $PhICl_2$ was dissolved in $CD_3CN$ and a solution of 4-DMAP was added. An aliquot was immediately removed for NMR spectroscopy. Protonated 4-DMAP, PhI and one other species containing 4-DMAP were identified. N-hexane was added to precipitate the protonated 4-DMAP. The solvent was removed and the residue redissolved in $CDCl_3$. PhI was still present and a 4-DMAP containing species contained a singlet, and 2 doublets in the aryl region integrating with a 1:1:1 ratio, and one methyl resonance integrating to 6-protons. This pattern is consistent with substitution of a proton with another atom on the aryl ring. Addition of HOTf resulted in precipitation of a white solid. Redissolving the solid in $CH_3CN$ for mass spectrometry analysis gave a strong signal at m/z = 157, with an isotope pattern consistent with one chlorine. Single crystals were grown from a $CH_3CN$ solution via vapour diffusion of $Et_2O$ and X-ray diffraction analysis gave the pyridinium triflate salt of **3** (Scheme 4, Figure 3), which is consistent with the activation of the ring towards EAS by the amino group, and does not displace chloride from $PhICl_2$ to give $[PhICl(4\text{-DMAP})]^+$ or a 4-coordinate complex analogous to **2**. Use of 2 equivalents of 4-DMAP gives complete conversion. These results indicate that 4-DMAP also cannot activate $PhICl_2$ as proposed, as half of the catalytic amount of 4-DMAP would be converted into **3** and the other half sequestered as the hydrochloride salt.

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Scheme 4. Reaction of $PhICl_2$ with 4-DMAP.

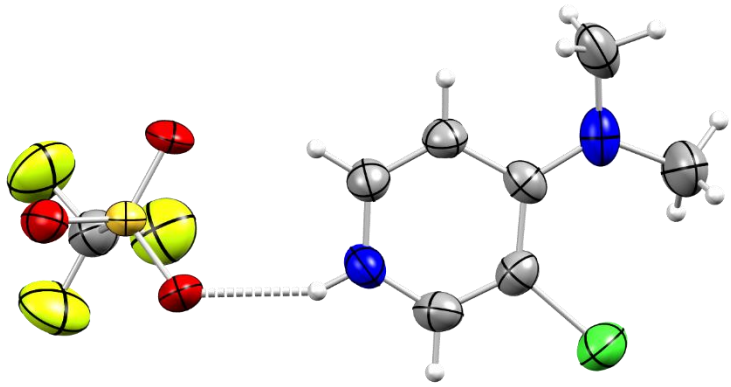

Figure 3. ORTEP representation of **3** shown with 70 % probability ellipsoids.

The interaction of $PhICl_2$ and **2** were then investigated through DFT calculations. The optimized geometry for **2** (B3LYP-D3(BJ)/def2-TZVPPD with acetonitrile solvation) gives a slightly elongated I-N bond and slightly shortened C-I bond at 2.856 and 2.118 Å, respectively, as compared to the experimental results. The calculated $\Delta G$ for the addition of pyridine to $PhICl_2$ is +12.1 kJ/mol at the B3LYP-D3(BJ)/def2-QZVPPD(SMD,acetonitrile)//B3LYP-D3(BJ)/def2-TZVPPD(SMD,acetonitrile) level of theory. With other methods (DSDPBEP86, ωB97XD, DLPNO-CCSD(T)), solvents (dichloromethane, pyridine), and employing a quasi-harmonic model the calculated $\Delta G$ remains consistently positive in sign but small in magnitude with values in the range of +9.8 to +18.2 kJ/mol. The small positive $\Delta G$ is consistent with experimental observations with crystals of **2** only produced in neat pyridine that drives equilibrium towards formation of **2**, with low temperature for crystallization reducing the effect of entropy, and is also consistent with the binding constant of 0.7 $M^{-1}$ from the NMR titration experiments between $PhICl_2$ and pyridine

The displacement of chloride by pyridine to give $[PhI(Pyr)Cl]^+$ as previous proposed is thermodynamically unfavourable, with $\Delta G$ of +30.0 kJ/mol. With dichloromethane or pyridine

solvent models $\Delta G$ is +70.3 and 52.5 kJ/mol, respectively. At all levels of theory considered the calculated $\Delta G$ for displacement of chloride is much more unfavourable than for coordination of pyridine to $PhICl_2$ to form compound **2**.

We also considered alternative pathways to produce the hypothesized $[PhI(Pyr)Cl]^+$ intermediate. Loss of $Cl^-$ from $PhICl_2$ is unfavourable by 94.9 kJ/mol ($\Delta G$), while loss of $Cl^-$ from **2** to yield $[PhI(Pyr)Cl]^+$ is unfavourable by 17.9 kJ/mol.

In combination with the results from the synthetic studies described above it is concluded that displacement of a chloride by pyridine is not the mechanism by which $PhICl_2$ is activated. It is possible that complex **2** is the activated species, so we examined the calculated properties of the pyridine adduct and compared them to free $PhICl_2$.

Calculated CM5 and NPA atomic charges (B3LYP-D3(BJ)/def2-TZVPPD(SMD,acetonitrile)) indicate that the atomic charges on $C_{Ph}$ (bonded to I), I, and Cl, vary by less than 0.04 e between **2** and $PhICl_2$ (Figure 3). The optimised I-C and I-Cl bond distances are also similar in $PhICl_2$ and **2**, with I-C bond distances of 2.107 and 2.118 Å, and I-Cl bond distances of 2.543 and 2.549 Å, respectively. The similar atomic charges and bond distances indicate that the electronic environment in $PhICl_2$ is not significantly impacted by coordination of pyridine in **2**.

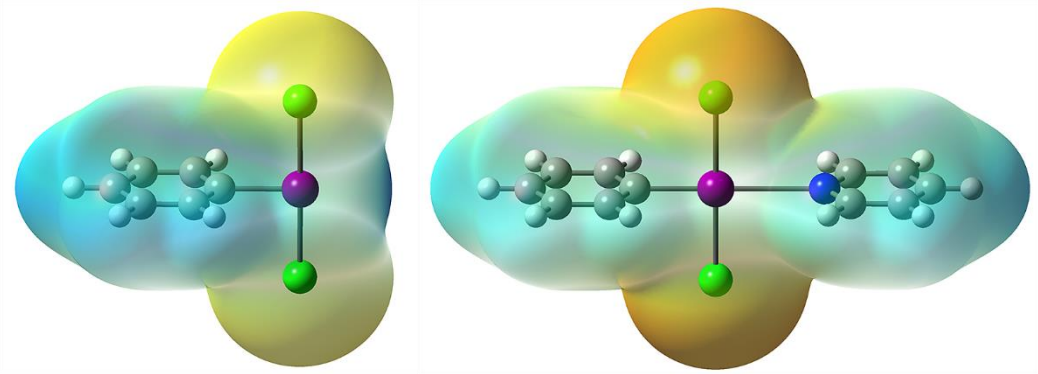

**Figure 3**. Plots of electrostatic potential (ESP) of (a) $PhICl_2$ and (b) $PhICl_2$-Pyr (compound **2**). B3LYP-D3(BJ)/def2-TZVPPD(SMD,acetonitrile) results, isosurface from -6E-2 (dark yellow) to +6E-2 (blue).

It is possible that pyridine might also transiently interact with chlorine along the I-Cl bond axis, however, attempts at optimizing a geometry from a starting point with the pyridine interacting with a chlorine atom resulted in the pyridine dissociating.

The lowest unoccupied MO (LUMO) for $PhICl_2$ is a sigma-symmetric antibonding orbital orientated along the Cl-I-Cl bond axes (Figure 4). The LUMO+1 is found 1.46 eV higher in energy than the LUMO and is also a sigma-symmetric antibonding orbital orientated along the I-C bond axis, which is the orbital the lone pair of the pyridine attacks, despite being higher in energy than the Cl-I-Cl based LUMO.

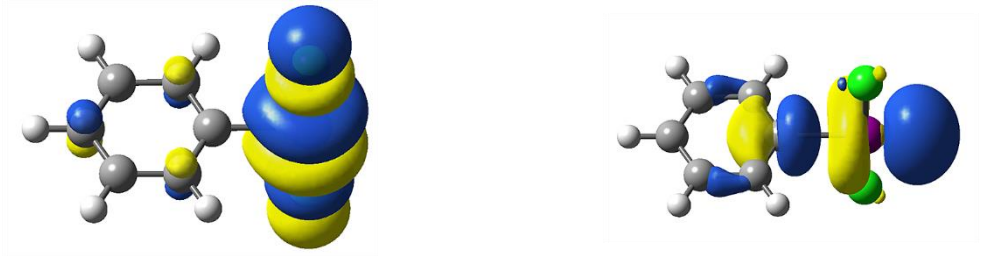

Figure 4. Plots of the LUMO (left) and LUMO +1 (right) for $PhICl_2$.

The calculated electrostatic potential of $PhICl_2$ in Figure 3 clearly shows a more positive sigma hole at the iodine atom than is found at the chlorines, despite the Cl-I-Cl accepting orbital being lower in energy, and consistent with charge density studies described above.

In the pyridine adduct (**2**) the LUMO remains a sigma symmetric antibonding orbital orientated along the Cl-I-Cl bond axis. Relative to $PhICl_2$ the orbital is 0.1 eV higher in energy, which indicates that the adduct should be a poorer electron acceptor than free $PhICl_2$ and a less active source of electrophilic chlorine.

## CONCLUSIONS

We have shown here that pyridine does not displace chloride from $PhICl_2$ and thus a $[PhI(Pyr)(Cl)]^+$ cation is likely not the reactive intermediate in the chemistry described by Murphy and co-workers. Pyridine clearly has an activating role of some kind based on their observations, what this is remains an open question. For $PhICl_2$ the calculated LUMO and the experimentally determined and calculated sigma hole are not aligned, and the nucleophile (pyridine) in this case preferentially interacts with the sigma hole aligned with the LUMO+1, rather than the more accessible sigma symmetric LUMO.

## Acknowledgements

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