Electrophilic Activation of Molecular Bromine Mediated by I(III)

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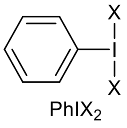
ABSTRACT

In pursuit of a genuine Bromo-λ^3-iodane, it has been found that the combination of Br_2 and electron deficient λ^3-iodanes can result in delivery of both bromine atoms from Br_2 to a range of aryl substrates, some highly deactivated. These brominations occur rapidly in common chlorinated solvents at room temperature and can be obtained with the catalytic activation of commercially available $PhI(OAc)_2$ and $PhI(OTFA)_2$. *para*-NO_2 substituted derivatives are employed to direct bromination towards more deactivated substrates. The mechanism of Br_2 activation is discussed with insights being made, however remains unclear.

INTRODUCTION

Organic hypervalent Iodine(III) compounds (λ^3-iodanes) are useful synthetic compounds which facilitate many different organic and inorganic synthetic processes.[1] Typically, λ^3-iodanes present as T-shaped phenyl substituted species with the general formula of $PhI(L)_2$. The dihalogenated species of $PhIX_2$ (Scheme 1), where X is Cl or F have received extensive attention as safer and easier to handle sources of their elemental counterparts in F_2 and Cl_2.[2]

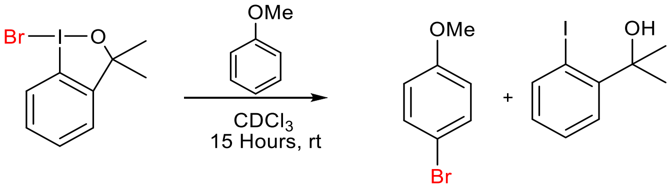


X = Cl, F

Scheme 1. Structure for well-established dihalogenated PhI(III) species.

Though these species are easy to handle, bench stable sources of Cl_2 and F_2, their downside is that they are considered less reactive than their diatomic elemental counterparts. However, we have recently found for $PhICl_2$ in aryl chlorinations the mechanism of action is release of Cl_2 and then chlorination, meaning that $PhICl_2$ is as effective as Cl_2 thermodynamically, but slower acting.[3] Addition of chloride ions was found to effectively catalyze release of Cl_2 from $PhICl_2$ *via* an as-yet undetermined mechanism.[4]

Reports of λ^3-iodoarenes possessing I(III)-Br bonds are exceptionally rare with the closest example of a structurally characterized I(III)-Br species being presented in 2006 by White and co-workers.[5] This species belongs to the compound family of bromoiodinanes first reported by Martin and co-workers in 1979 (Scheme 2).[6] The I(III)-Br bond appears ionic in nature with a bond length of 2.69 Å and its electrophilic bromination activity was limited to electron rich aryl species such as anisole. The reaction between their most reactive analogue and anisole took 15 hours to complete. When anisole is reacted with molecular bromine the reaction only takes 10 minutes at room temperature, demonstrating how unreactive this I-Br compound is in comparison to Br_2 itself.[7]



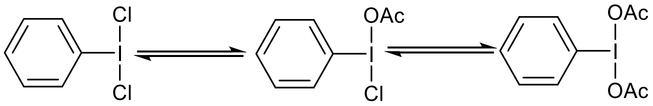
Scheme 2. Electrophilic bromination reactivity observed with anisole by White and co-workers.

$PhIBr_2$ generated from $PhI(OTFA)_2$ and TMS-Br has been recently reported as an intermediate in the bromination of arenes.[8] However, we found conditions that claimed to give $PhIBr_2$ are in fact generating *in situ* molecular bromine, which acts as the brominating agent.[7]

Along with reports of $PhIBr_2$, there have also been reported claims of the mixed PhI(OAc)(Br) species formed *via* reaction of $PhI(OAc)_2$ with HBr, TMS-Br or alkali bromide salts.[9,10] However these conditions were also found to give Br_2 by Evans in 1997 *via* UV-Vis experiments where resultant activity was once again identical to Br_2.[11]

It is common practice for sources of bromide (R_4NBr, HBr, alkali bromides, TMS-Br) to be oxidised with stoichiometric oxidants such as Selectfluor, H_2O_2 and $\lambda^{3/5}$-iodanes as a method to generate *in situ* Br_2 for reactions.[12,13] This is well covered in a recent review by Stevens and co-workers, where the use of $\lambda^{3/5}$-iodanes for this purpose is also described.[13]

Though reports of solutions containing PhI(OAc)(Br) are evidently actually Br_2 and iodobenzene, direct spectroscopic evidence for PhI(OAc)(Cl) has been reported.[11] Though PhI(OAc)(Cl) is observable *via* NMR, it has not been subject to isolation. Inspection of the ^{1}H NMR spectra for PhI(OAc)(Cl) shows that it co-exists in solution with both $PhICl_2$ and $PhI(OAc)_2$ indicating that these compounds exist in equilibrium (Scheme 3).[14]



Scheme 3. Equilibrium observable between $PhI(OAc)_2$, $PhICl_2$ and for PhI(OAc)(Cl).

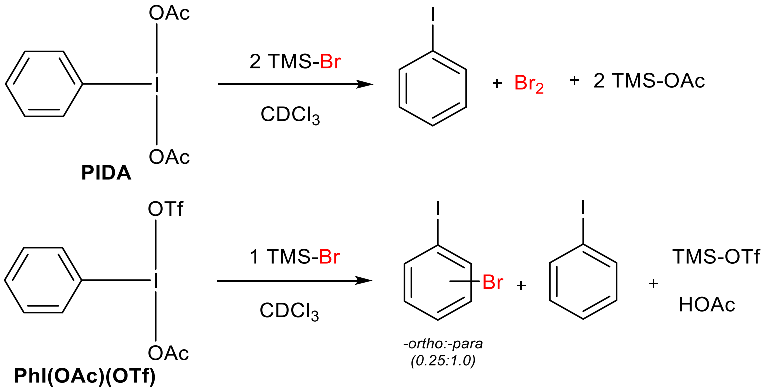
Recently, our group was able to isolate and comprehensively characterise the *p*-nitro substituted compounds NO_2-C_6H_4-I(F)(OTf) and NO_2-C_6H_4-I(Cl)(OTf), the latter of which is a powerful electrophilic chlorinating reagent.[15] These asymmetric species exist discretely in solution, in contrast to PhI(OAc)(Cl),which we attribute to the weak -*trans* influence of -OTf ligands.[16] Ochiai has reported that the axial ligands across the three-centre four-electron (3c-4e) axis in λ^3-iodanes are heavily influenced by -*trans* effects, where λ^3-iodoarenes favour either the mixed combination of a weak and strong donor or the symmetric combination of a moderate donor such as -Cl and -OAc.[17] In other words, the hypervalent 3c-4e axis in I(III) lends itself towards asymmetry when the gap in -*trans* influence is large. The solid-state structures of our recently reported NO_2-C_6H_4-I(F)(OTf) and NO_2-C_6H_4-I(Cl)(OTf) have the shortest I(III)-X bonds reported to date demonstrating the weak -*trans* influence of -OTf.

Though ambitious, a genuine I(III)-Br species may be obtainable as an asymmetric ArIBr(OTf) species where the I(III)-Br bond is reinforced by the weak OTf -*trans* influence. Additionally, with bromine being less electronegative than chlorine we envisioned that the bromine in a Br-I-OTf (3c-4e) bond would be highly electrophilic in character like the chlorine in NO_2-C_6H_4-I(Cl)(OTf). This is desirable for electrophilic bromination applications. In this report, the efforts to access an ArIBr(OTf) species and the highly effective aryl brominating system that was discovered in the process are described.

RESULTS AND DISCUSSION

During our investigations on pyridine bound I(III) Weiss' reagents ($[PhI(Pyr)_2][OTf]_2$),[18] we discovered a more reactive variant by isolating [PhI(4-DMAP)]$[OTf]_2$ having only one pyridine ligand.[19] This was achieved by reaction of $PhI(OAc)_2$ (PIDA) with two equivalents of TMS-OTf and careful addition one equivalent of 4-DMAP. This illustrates that the acetate in PhI(OAc)(OTf) can be displaced on the I(III) centre with TMS reagents in preference to the triflate. Consequently, treatment of PhI(OAc)(OTf) with TMS-Br to exchange with the acetate was the first pathway employed in attempts to access PhIBr(OTf).

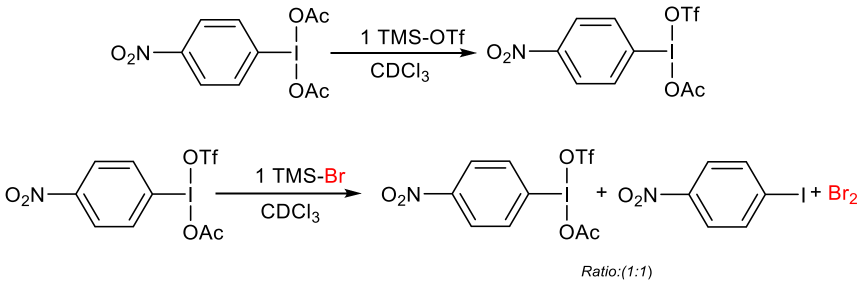
When TMS-Br was added to a solution of PhI(OAc)(OTf) in $CDCl_3$, an orange solution was formed immediately which turned colourless over the course of 15 minutes. The initial hypothesis was that the deep orange colour was the due to the generation of Br_2 like previous reactions of I(III) with TMS-Br,[7] however the rapid dissipation of the colour was unexpected. This led us to suspect whether Br_2 was being generated, because it is not electrophilic enough to react with PhI, the only aryl species in this system, without further activation.[20,21] When Br_2 is generated from the reaction of two equivalents of TMS-Br with $PhI(OAc)_2$, no dissipation of the orange colour is observed, leaving PhI and Br_2 observable and unreacted in solution. In the ^1H NMR spectrum of the PhI(OAc)(OTf)/TMS-Br reaction, the electrophilic bromination products of PhI were observable, with the *-ortho* and *-para* brominated products being present (0.25:1 ratio) alongside residual PhI, along with TMS-OTf and acetic acid (Scheme 4). Though the presence of TMS-OTf initially makes it appear as though TMS-Br exchanged with the triflate on PhI(OAc)(OTf) to directly produce TMS-OTf, our hypothesis is that this reaction transiently produces our target PhIBr(OTf) (which is able to perform electrophilic bromination towards PhI), along with residual PhI and HOTf. HOTf subsequently reacts with TMS-OAc to give HOAc and TMS-OTf, with acetic acid acting as the proton sink over the stronger acid HOTf. In a control reaction between TMS-OAc and one equivalent of HOTf in dry $CDCl_3$, TMS-OTf and HOAc were the only species in the ^1H NMR spectrum, supporting the proposed pathway.



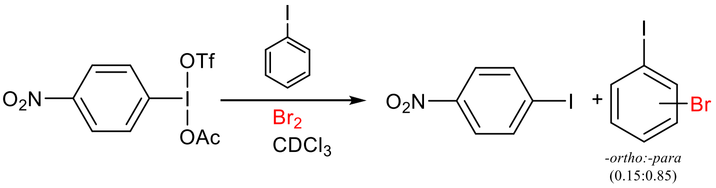
Scheme 4. Divergent reactivity of PIDA (top) and PhI(OAc)(OTf) (bottom) when treated with TMS-Br.

With the bromination of PhI from the reaction between PhI(OAc)(OTf)/TMS-Br being complete in less than 5 minutes, the active brominating species in this reaction is apparently substantially more electrophilic than molecular bromine as Br_2 does not brominate PhI. Our previous work with ArICl(OTf) has shown that upon generation PhICl(OTf) immediately undergoes self-chlorination, whereas in NO_2-C_6H_4-ICl(OTf), this decomposition pathway is suppressed, making it isolable and have its chemistry explored.[15] Thus our target became NO_2-C_6H_4-IBr(OTf).

We first sought to synthesise NO_2-C_6H_4-I(OAc)(OTf) for subsequent treatment with TMS-Br. This compound was easily generated *via* reaction of NO_2-C_6H_4-I(OAc)$_2$ with TMS-OTf (Scheme 5). NO_2-C_6H_4-I(OAc)(OTf) was treated with one equivalent of TMS-Br in $CDCl_3$ resulting in an orange solution. ^{1}H NMR analysis revealed the presence of NO_2-C_6H_4-I(OAc)(OTf) and the I(I) species NO_2-C_6H_4-I in a 1:1 ratio (Scheme 5). The presence of NO_2-C_6H_4-I and the orange colour in the solution led us to conclude that the reaction produced Br_2. This has been observed with other I(III) species when exposed to bromide sources.[7] PhI was subsequently added to this same solution, and the orange colour dissipated within 15 minutes. ^{1}H NMR analysis confirmed bromination of PhI as well as complete conversion of NO_2-C_6H_4-I(OAc)(OTf) to NO_2-C_6H_4-I (Scheme 6). While no new I(III) species was observed, an electrophilic brominating species of some kind was being formed as PhI does not react with Br_2 on its own. We then sought to further investigate the nature of this new system and test it against other deactivated aryl substrates.



Scheme 5. Synthesis of NO_2-C_6H_4-I(OAc)(OTf) (top) and its subsequent treatment with TMS-Br (bottom).



Scheme 6. Observed bromination of PhI using NO_2-PhI(OAc)(OTf) and Br_2.

It seems most likely that NO_2-C_6H_4-I(OAc)(OTf) is activating Br_2 in some way. To increase our understanding of the system, an analogue that would possess a higher oxidative potential[22] in NO_2-C_6H_4-I(OTFA)(OTf), where OTFA = trifluoroacetate, was targeted. We hypothesised that it would help elucidate the nature of Br_2 activation if NO_2-C_6H_4-I(OTFA)(OTf) displayed a higher level of Br_2 activation than NO_2-C_6H_4-I(OAc)(OTf), as an ArI(III) species with cationic $[ArI(OTFA)]^+$ character would be expected to be a stronger Lewis acid and oxidant than one with $[ArI(OAc)]^+$.[23,24] To access the new target, NO_2-C_6H_4-$I(OTFA)_2$ was reacted with TMS-OTf. The ^1H NMR spectrum of the reaction mixture showed a single aromatic environment which we attributed to NO_2-C_6H_4-I(OTFA)(OTf). The aryl proton signals were downfield from NO_2-C_6H_4-I(OAc)(OTf), indicative of a more electron poor ring, translating into a more oxidizing I(III) centre.[24,25]. Single crystals suitable for X-ray crystallography were grown *via* vapour diffusion ($CHCl_3$:pentane) to confirm the compound's identity (Figure 1).

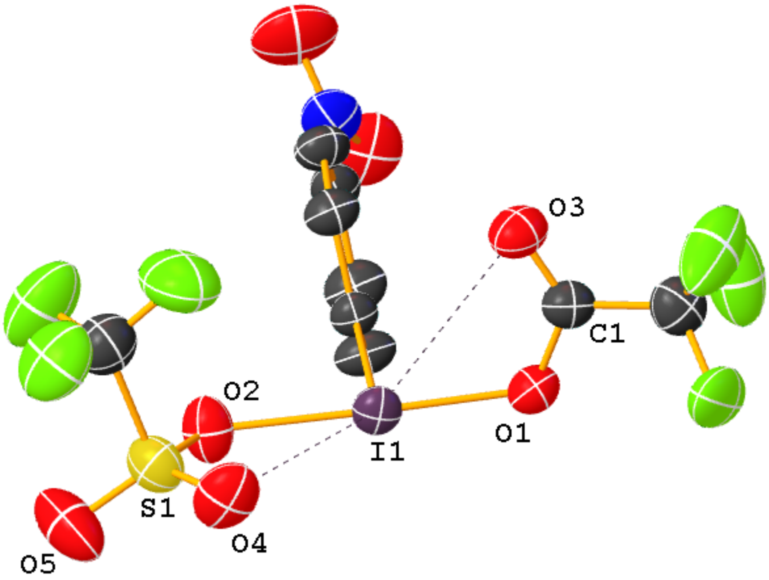
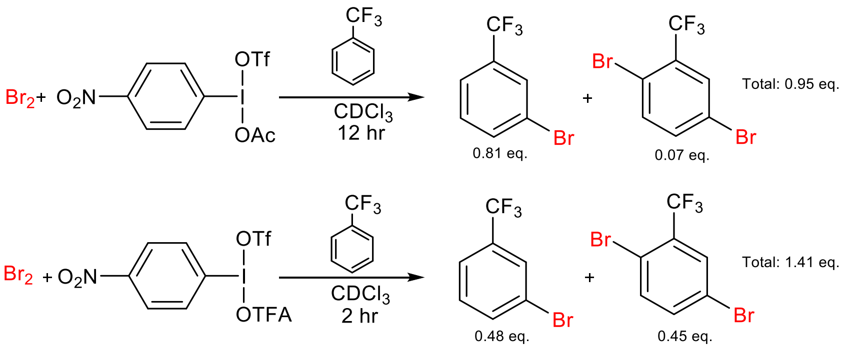


Figure 1. Solid state structure of NO_2-C_6H_4-I(OTFA)(OTf). Ellipsoids are depicted at the 50% probability level. Selected bond distances (Å): I(1)-O(1) 2.088(4), I(1)-O(2) 2.247(4)

Both NO_2-C_6H_4-I(OTFA)(OTf) and NO_2-C_6H_4-I(OAc)(OTf) were reacted with a modest range of deactivated aryl substrates in the presence of Br_2 to compare the rates of electrophilic bromination for each system. Monitoring of these reactions with ^{1}H NMR revealed that NO_2-C_6H_4-I(OTFA)(OTf)/Br_2 was indeed a faster brominating system. This is best illustrated by the reaction of both systems with benzotrifluoride, where the NO_2-C_6H_4-I(OTFA)(OTf)/Br_2 system was observed to complete in two hours and the NO_2-C_6H_4-I(OAc)(OTf)/Br_2 system required over 12 hours to reach completion. A substantially larger amount of dibrominated benzotrifluoride was also observed in reaction with NO_2-C_6H_4-I(OTFA)(OTf) (Scheme 7). Though the mechanism of Br_2 activation or source of electrophilic bromine remained unclear, I(III) was converted to I(I) in these reactions indicating an oxidative process. Despite only one equivalent of Br_2 and I(III) reagent being added to these initial screens, summation of the brominated product integrations in ratio to NO_2-C_6H_4-I revealed that bromination was occurring well above one turnover based on Br_2. When Br_2 is used alone in EAS, quantitative yields are in ratio of one bromination per molecule of Br_2 with formation of one equivalent of HBr. These I(III) reagents are not only activating Br_2 towards aryl bromination in some way, but the generated HBr also appears to be reoxidized and introduced into the product.

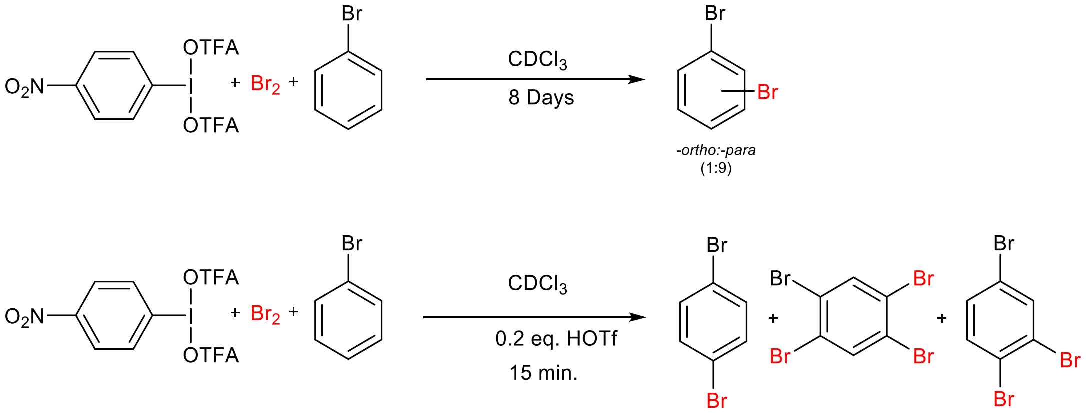


Scheme 7. Comparison of brominating activity observed between NO_2-C_6H_4-I(OAc)(OTf) and NO_2-C_6H_4-I(OTFA)(OTf) against benzotrifluoride in the presence of Br_2.

This result led us to investigate how our recently reported NO_2-C_6H_4-I(OTf)$_2$,[26] an even more electron poor I(III) complex, would perform. Reaction of Br_2 and NO_2-C_6H_4-I(OTf)$_2$ in $CDCl_3$ resulted in formation of brominated *p*-NO_2-PhI at the meta position. When NO_2-C_6H_4-I(OTFA)(OTf) is treated with Br_2 only a small amount of bromination of NO_2-PhI is observed after several hours, with no bromination observed in the case of NO_2-C_6H_4-I(OAc)(OTf) under the same conditions. These observations suggest as the I(III) centre becomes more electron deficient it renders Br_2 more reactive towards aryl brominations. Use of NO_2-C_6H_4-I(OTf)$_2$ gives the most powerful brominating system considered here, however self bromination and previously reported propensity towards aryl iodonium salt formation could interfere with aryl brominations.[26] The NO_2-C_6H_4-I(OTFA)(OTf)/Br_2 system only self brominates sluggishly and its brominating ability is sufficient to brominate all substrates more activated than NO_2-PhI, which is the current limiting factor for substrate scope. Considering this, NO_2-C_6H_4-I(OTFA)(OTf) was selected as the most appropriate I(III) species to carry into further optimization.

CATALYTIC GENERATION OF NO_2-PhI(OTFA)(OTf) FOR Br_2 ACTIVATION

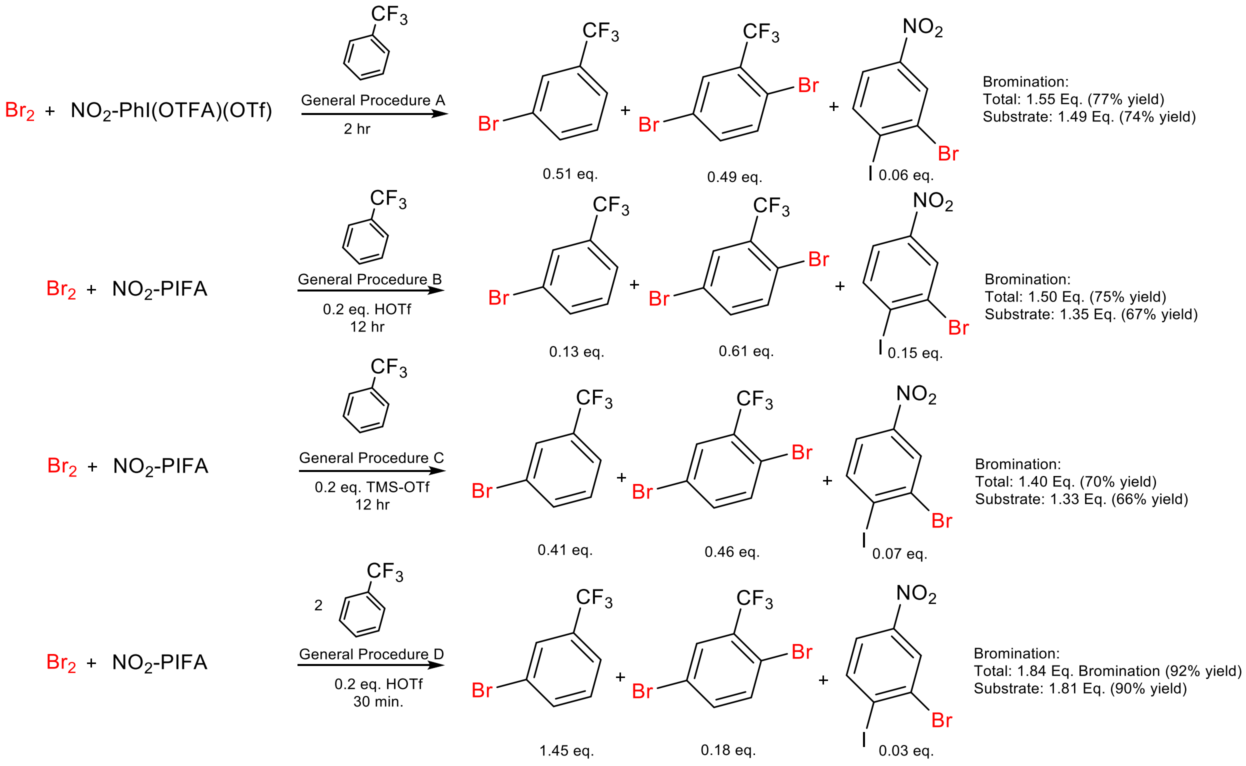
We have recently demonstrated the activation of NO_2-$C_6H_4ICl_2$ for electrophilic chlorination with catalytic loadings of HOTf, generating NO_2-C_6H_4ICl(OTf) *in situ*.[15] To determine whether we could produce a brominating system that utilises the activity of NO_2-C_6H_4-I(OTFA)(OTf) in a more economical manner, we investigated whether treatment of NO_2-C_6H_4-I(OTFA)$_2$ with catalytic loadings of HOTf or TMS-OTf would produce similar reactivity to NO_2-C_6H_4-I(OTFA)(OTf) when in solution with Br_2 and an aryl substrate. To test this, two reactions were charged with NO_2-C_6H_4-I(OTFA)$_2$, bromobenzene and Br_2 in $CDCl_3$. One solution was treated with a 20% loading of HOTf. In the acid-free reaction, the bromobenzene was consumed over the course of 8 days to give the *-para* and *-ortho* bromination products in a respective 9:1 ratio. Though the rate of this reaction was sluggish, Br_2 is not electrophilic enough to brominate bromobenzene without activation, showing that NO_2-C_6H_4-I(OTFA)$_2$ has a mild activating effect on Br_2.[20,21] In the HOTf treated solution the solution rapidly turned colourless. ^{1}H NMR analysis exhibited that the reaction had proceeded to completion within 15 minutes. Di- and tri-brominated products were identified alongside *p*-dibromobenzene (Scheme 8). Bromination turnovers >1 per Br_2 were observed in the HOTf system, consistent with the previous observations. When we substituted HOTf for 0.2 equivalents of TMS-OTf, comparable reactivity was observed demonstrating that both HOTf and TMS-OTf can be introduced to NO_2-C_6H_4-I(OTFA)$_2$ at catalytic loadings to form a system using Br_2 that can rapidly brominate deactivated aromatic systems with a bromination turnover >1 per Br_2 molecule.



Scheme 8. Observed reactivity of NO_2-C_6H_4-I(OTFA)$_2$/Br_2 against bromobenzene with and without HOTf.

To assess bromination rates between different activation systems, benzotrifluoride was employed as a model deactivated aryl substrate. As can be seen in Scheme 11, we compared activity of NO_2-C_6H_4-I(OTFA)(OTf) (Procedure A) against the catalytic activation of NO_2-C_6H_4-I(OTFA)$_2$ with HOTf (Procedure B) and TMS-OTf (Procedure C). HOTf was found to be a more effective activator than TMS-OTf, while also being more atom efficient. With previous reactions demonstrating that two brominations occur per equivalent of Br_2 and I(III), we also screened NO_2-C_6H_4-I(OTFA)$_2$ /0.2 HOTf against two equivalents of substrate (General procedure D). A small reaction rate increase was expected here due to increased substrate concentration. However, we did not expect such a significant reduction in reaction time, which was reduced to 30 minutes for complete consumption of I(III) to be observed. Reactions using HOTf rather than TMS-OTf had higher yields of bromination. Acidic systems are well established to enhance the rates of electrophilic halogenation.[13] Using HOTf as the activator introduces exogenous protons to enhance reactivity, where a TMS-OTf activated system only contains the protons produced through EAS.

General procedure D (Scheme 9) appears to be the most appropriate system for obtaining high-yield and rapid brominations against deactivated substrates (and is performable outside the glovebox with sufficiently dried solvent). This system was tested against a range of deactivated substrates with varying activation levels and functionalities. Rapid, high yielding brominations were observed (Scheme 10). In the more deactivated substrates, observed yields and selectivity for monobromination reduced as expected. Reactions depicted in Scheme 10 were limited to two equivalents of substrate, as previously mentioned, an increase in substrate past two equivalents would increase selectivity towards monobromination by virtue of collisional frequency with the target substrate.



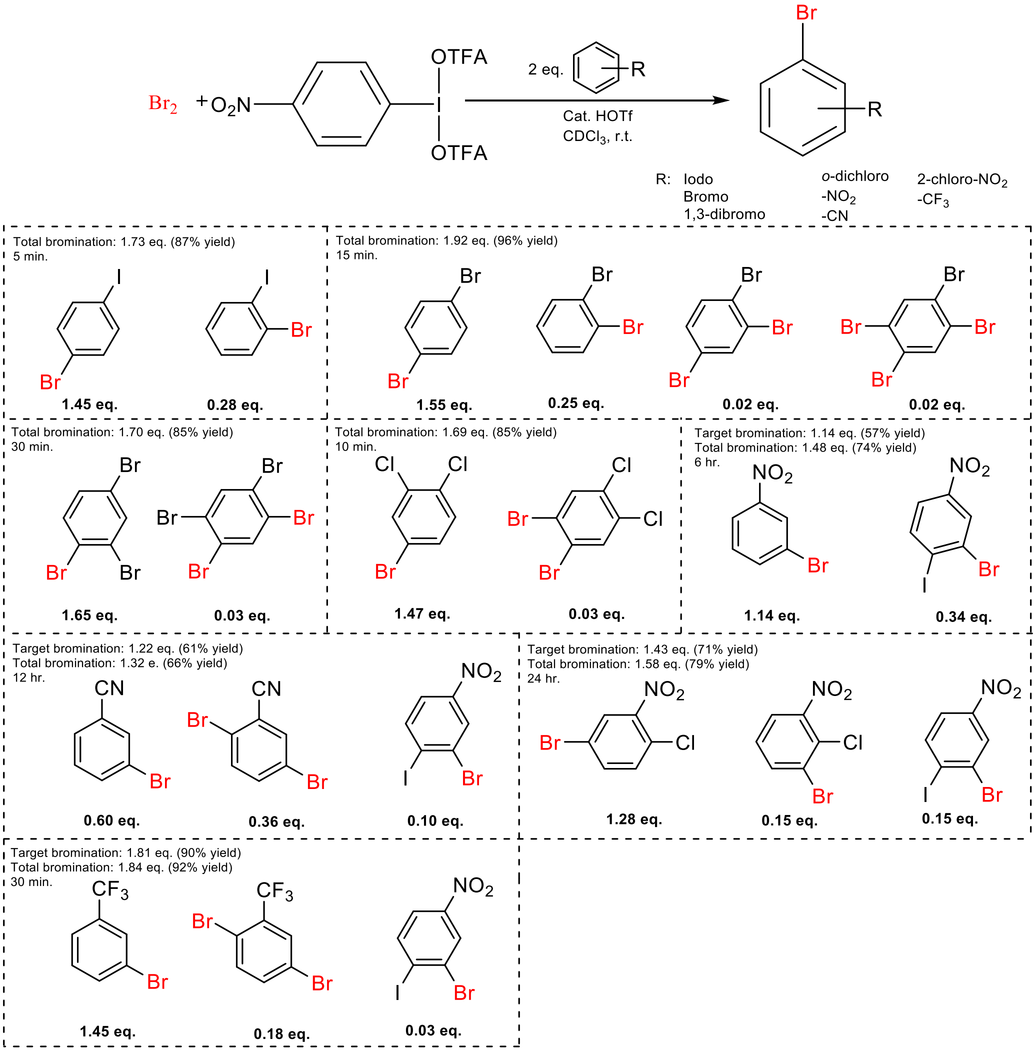
Bromination:
Total: 1.55 Eq. (77% yield)
Substrate: 1.49 Eq. (74% yield)

Bromination:
Total: 1.50 Eq. (75% yield)
Substrate: 1.35 Eq. (67% yield)

Bromination:
Total: 1.40 Eq. (70% yield)
Substrate: 1.33 Eq. (66% yield)

Bromination:
Total: 1.84 Eq. Bromination (92% yield)
Substrate: 1.81 Eq. (90% yield)

Scheme 9. Observed products when benzotrifluoride was treated with general procedures A, B, C & D.

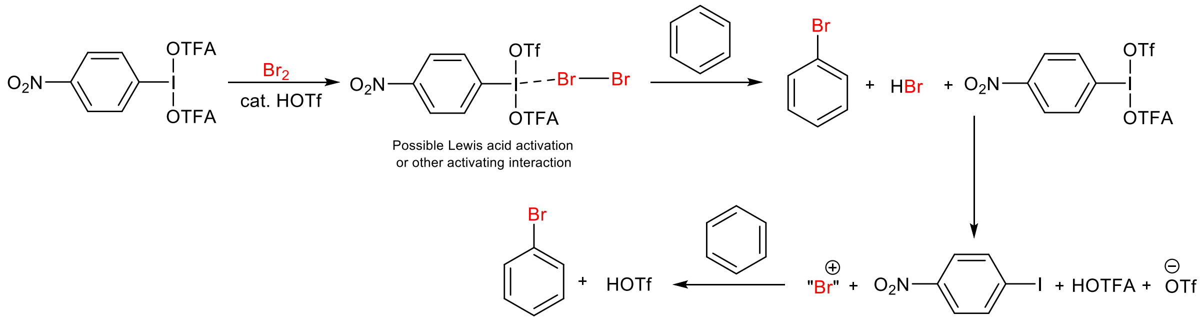


Scheme 10. Brominations of deactivated aryl substrates under general procedure D; 1 eq. NO_2-C_6H_4-I$(OTFA)_2$, 1 eq. Br_2, 0.2 HOTf, 2 eq. substrate. Ratios and effective brominations determined *via* ^{1}H NMR spectroscopy using NO_2-PhI as an internal standard.

I(III) reagents have been previously shown to catalyse electrophilic halogenations, but not to this extent. McNelis has demonstrated the utilisation of Koser's reagent PhI(OH)(OTs) to activate molecular I_2 stoichiometrically and NBS catalytically as a Lewis acidic activation source for the halogenation of activated aryl substrates.[27-29]

MECHANISM

To reiterate the nature of this system as determined throughout our experiments: Molecular bromine in combination with I(III) are conditional for these halogenations to take place, brominations do not proceed if two equivalents of TMS-Br are added to I(III), resulting in reduction to I(I) and Br_2 elimination. Protic conditions are not conditional. Water quenches the reactivity of these systems and finally, up to two brominations occur per Br_2.



Possible Lewis acid activation or other activating interaction

Scheme 10. Possible process for catalytically mediated activation and recyclization of Br_2 for electrophilic bromination of deactivated aryl substrates.

We can conclude that bromination does not occur *via* initial generation of a stoichiometric source of Br^+ such as I(III)-Br, Br-OTf or a form of Br^+ ion, as a pathway of this nature would immediately consume I(III) in a 1:1 ratio. Br_2 is considered to remain intact until electrophilic bromination occurs as colour of Br_2 is not observed to dissipate and exposure of I(III) to Br_2 does not result in generation of I(I) as monitored by ^1H NMR. We surmised that the initial activation of Br_2 could be *via* the I(III) acting as a Lewis acid. In the ^1H NMR spectrum of NO_2-C_6H_4-$I(OTf)_2$/Br_2 a new I(III) associated peak at 8.29 ppm is observed, which is ~0.30 ppm upfield from NO_2-C_6H_4-$I(OTf)_2$ indicating increased electron density on the iodine centre from NO_2-C_6H_4-$I(OTf)_2$ but ~0.36 ppm downfield from NO_2-PhI suggesting the iodine centre is still in a higher oxidation state. NO_2-C_6H_4-$I(OTf)_2$ is still present as a discrete species in this solution. The ratio of this new species and NO_2-C_6H_4-$I(OTf)_2$ is nearly exactly 1:1. In ^{19}F NMR, only two peaks present at a nearly 1:1 ratio; one at -75.3 ppm concordant with NO_2-C_6H_4-$I(OTf)_2$ and a new peak at -76.8 ppm, indicating increased electron density at the triflate but not to the point of fully ionized triflate at -79 ppm. With only two discrete environments present in ^{19}F NMR (in the ratio of ^1H environments) we consider formation of a Lewis adduct where an OTf is displaced by Br_2 to produce an axial $[OTf\text{-}I\text{-}Br_2]^+$ motif unlikely, as one would expect two new ^{19}F NMR shifts if a symmetrical OTf-I-OTf motif was not present in the new species. This new species could arise from Br_2 interacting with iodine along the C-I bond axis, with iodine acting as a Lewis acid. Unfortunately attempts to obtain a crystal structure possessing an adduct of Br_2 with I(III) were unsuccessful. Only one Br_2 adduct has been structurally determined to date.[30]

This Lewis acid activated Br_2 undergoes electrophilic aromatic substitution, generating an aryl bromide and HBr. The bromide in HBr could then be oxidized by the I(III) to an activated electrophilic bromine source, which can then undergo electrophilic aromatic substitution and HOTf generation. While this mechanism is speculative it does account for the NMR observations of a solution of $NO_2\text{-}C_6H_4\text{-}I(OTf)_2/Br_2$, the requirement for only a catalytic loading of HOTf and the 2 brominations per equivalent of Br_2 and I(III).

CONSIDERATIONS TOWARDS OTHER I(III) MEDIATED BROMINATIONS

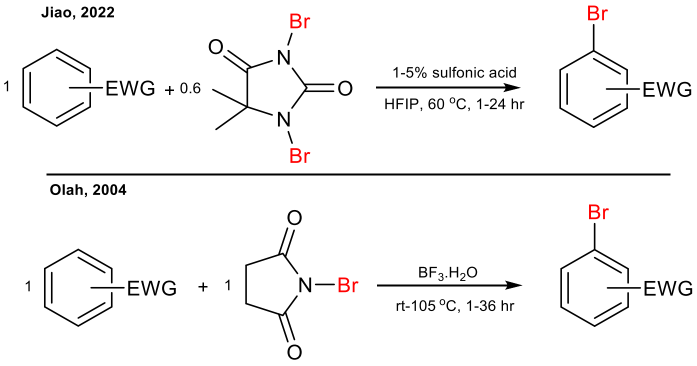
λ^3-Iodanes are considered a green alternative for organic chemistry applications and have been described as underutilized in industrial applications.[31,32] $PhI(OAc)_2$ and $PhI(OTFA)_2$ have both been used as a method for the generation of *in situ* Br_2 using bromide sources for the electrophilic bromination, where equivalency of bromide often varied between one and two equivalents; in all cases with these reagents the aryl bromination substrates were electron rich and activated.[9,33,11,34,8,10,35,31,36,7,37-39] Often when one equivalent of bromide source was used, the quantitative delivery of the bromide source to aryl substrate is justified by unobserved intermediates such as PhIBr(OAc),[9,40] Br-OAc,[10,35,36,39] or their -OTFA alternatives[37,39] as stoichiometric “Br^+” sources without the provision of substantial evidence. As mentioned in the introduction, our group has found the active species in these systems to simply be Br_2

through a combination of theoretical and experimental methods.[7] Considering that Br_2 only delivers one atom of bromine in substitution reactions it is reasonable to suggest that bromine in these systems is simply being regenerated by the remaining I(III) and HBr produced through EAS to deliver close to quantitative Br^+ in the same way we have observed in this investigation. Ironically because we have observed that an analogue of $PhI(OTFA)_2$ activates Br_2 (Scheme 8), substitution of two equivalents of bromide for one in these systems would not only be more economical but may also display faster reaction times through this activation.[8]

Searching the literature revealed one other case of Br_2 being utilised directly in combination with I(III), where Cheng and co-workers reported the reaction of 0.5 Br_2/0.5 PIDA/1 substrate.[33]

Another pathway one might consider for the source of Br^+ in these systems is the formation of BrOTf, however a report by Langlois and co-workers purporting BrOTf generation reported a bromination of toluene taking 18 hours which is incomparable to our presented system.[41]

Looking at other systems for the bromination of highly deactivated substrates, Jiao and co-workers have recently reported the bromination of deactivated aryl substrates with catalytic sulfonic acids and DMDMH (Scheme 11).[42] This system generates electrophilic bromine by a synergistic effect of HFIP as the solvent and sulfonic acid. Products obtained this system were at similar deactivation levels to ours but conditional on HFIP being solvent where ours is performed in simple chlorinated solvent. Reaction times in this report are longer, with benzotrifluoride taking 24 hours to proceed to obtain 89% bromination, general procedure D in our system obtains a similar yield in 30 minutes (Scheme 6.12).



Scheme 11. Brominating systems reported by Jiao and Olah.

NBS has also been activated towards powerful bromination in media such as H_2SO_4,[43] or $BF_3.H_2O$ (Scheme 11).[44] Both systems required heating and extended reaction periods for bromination of more deactivated substrates. The $BF_3.H_2O$ system was also found to be incompatible with trifluorobenzenes due to the transformation of $-CF_3$ into a -COOH functionality.

CONCLUSION

To summarise, in the pursuit of an ArIBr(OTf) species we have identified an electrophilic brominating system that not only turbocharges molecular bromine, but also efficiently recycles it to halve the amount of bromine required in ratio to substrate. We have found an optimal activating species in NO_2-C_6H_4-I(OTFA)(OTf), a powerful novel λ^3-iodoane which can be generated catalytically *via* two methods, and even under bench conditions with HOTf. Having optimised a system for bromination, here we demonstrate the propensity of this system against a range of highly deactivated substrates and discuss insights mechanism of bromine activation. The mechanism of activation currently remains unclear. This system is powerful towards bromination of aryl substrates under mild conditions. Favourable characteristics of this system include that it can be performed outside the glovebox with sufficiently dry solvent, is metal free, does not require heating, is rapid, and utilises bromine quantitatively.

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