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In-situ Generation of Hypervalent Iodine Reagents for the Electrophilic Chlorination of Arenes

Albert Granados, Zhiyu Jia, Marc del Olmo and Adelina Vallribera*

Abstract: Efficient metal-free methods for the electrophilic chlorination of arenes using PIFA and simple chlorine sources are reported. The *in-situ* formation of $PhI(Cl)OCOCF_3$ from PIFA and KCl is proposed, which resulted in chlorinating species for moderate activated arenes. Moreover, the *in-situ* formation of $PhICl_2$ from PIFA and TMSCl resulted in an excellent approach for the chlorination of a great variety of arenes (20 examples) in high yields, even when working at a multigram scale.

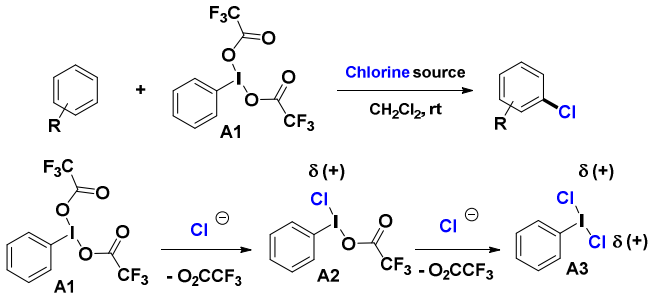
Introduction

Chloroarenes present in many natural products[1] and pharmaceuticals,[2] have been employed as convenient key intermediates in the cross-coupling reactions.[3] The synthesis of chloroarenes has been a staple in the chemical literature, with processes such as the Sandmeyer reaction,[4] the electrophilic aromatic halogenation,[5] and the stoichiometric *ortho*-metalation / chlorination[6] sequence as some of the most popular approaches. As a complement to these classical methods, metal-catalyzed chlorination has also received significant attention,[7] with much efforts focused on transition metal-catalyzed chelation-directed aryl C-H *ortho* activation/chlorination (Ni, Rh, Pd and Ru);[8] and more recently aryl C-H activation/*meta* chlorination (Pd)[8d, 9] and aryl C-H activation *para* chlorination (Fe).[10] However, the requirement of a directing group results in a somewhat limited substrate scope for these methods.

A series of structurally diverse reagents for the direct aromatic chlorination have been employed, including the *N*-chlorosuccinimide,[11] 1,3-dichloro-5,5-dimethyldantoin, SO_2Cl_2, Palau'Chlor®[12] and *N*-chloro-*N*-fluorobenzenesulfonylamine[13].

Regarding the use of mild oxidants, the hypervalent iodine reagents emerged several years ago.[14] They are efficient alternatives to the toxic heavy-metal-based oxidants and expensive organometallic catalysts in many transformations. Iodine (III) species have a three-coordinate T-shaped structure in the solid state, in which two of the iodine substituents contribute in a hypervalent, linear 3-center 4-electron bond. Earlier in 2010,[15a,b] we reported a direct metal-free dehydrogenative coupling between naphthalenic substrates and alkylarenes to form linear arene-capped bis- and quaternaphthalenes under Kita's conditions, using a combination of the hypervalent λ^3-iodo reagent $PhI(O_2CCF_3)_2$ (PIFA) and the BF_3 activator. We also disclosed the transfer of 2-iodoaryl group from PIFA to the α-position of activated ketones.[15c] Kita' s group has demonstrated that PIFA mediates the selective cyanation reaction, using TMSCN and $BF_3.Et_2O$, of a wide range of heteroaromatic compounds.[16a,b] Going back to aryl chlorinations, Kita and collaborators used PIFA and TMSCl for the chlorination of hexylthiophene as unique example.[15c] Chlorination of mesitylene has been carried out with LiCl or NaCl and stoichiometric amounts of Koser's reagent.[17] Huang' s group have described the combination of $PhI(OAc)_2$ (PIDA) and $CuBr_2$ in the C5 halogenation of quinolines.[18a] Rh(III)-catalyzed *ortho*-chlorination of arylpyridines was achieved using PIDA, NaCl and CF_3COOH.[18b] The combination of NaCl and PIDA has been used for the chlorination of indoles.[19] The $PhICl_2$ reagent has also been documented for chlorination of arenes.[20] Moreover 1-chloro-1,2-benziodoxol-3-one has been used for the chlorination of selected arenes.[21] Recently, Solorio-Alvarado[22] group reported the electrophilic *ortho*-chlorination of phenols using the mixture PIFA-$AlCl_3$.

In light of the recent advances in the chemistry of hypervalent iodine(III) compounds,[23] applied to the quest for efficient chlorination reactions, herein we report the chlorination of arenes using a system obtained by combining PIFA with various sources of a formal chloride anion under mild conditions (Scheme 1) avoiding the use of Lewis acids. This research project stems from the observation that a charge reversal (*umpolung*) could be achieved for certain anions upon binding to a three-coordinate iodine center. Thus, a chloride anion, upon binding to iodine(III) would acquire an electrophilic character, leading to the same reactivity of a formal Cl^+. The method might thus allow for the use of the readily accessible nucleophilic anions as electrophiles simply by adding a hypervalent iodine reagent **A1** (Scheme 1).



Scheme 1. Aromatic chlorination process and formation of possible key reactive species **A2** and **A3**

Results and Discussion

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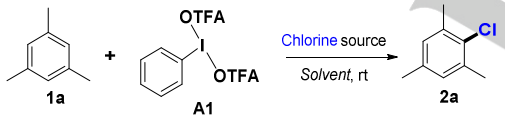
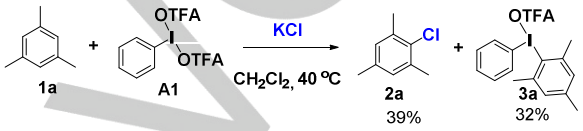
In our first attempt, we planned the use of an inorganic chlorine source, as they are easy handle, safe and very accessible from an economical point of view. We found the work of the group of Karade,[24] in which the chlorination of certain arenes was accomplished by grinding together a 1:1.2:1 mixture of the arene, PIFA and NaCl. The authors mentioned that "the reactions were carried out on a very small scale in an agate pestle and mortar". No more details could be obtained regarding the working scale. In this context, we sought to explore the reaction avoiding grinding chemistry conditions. First, we used 1,3,5-trimethylbenzene, **1a**, as a model, 1.0 equivalent of PIFA and 1.5 equivalents of NaCl in CH_2Cl_2 (Table 1, entry 1). Under these conditions, the chlorinated compound **2a** could be isolated in a 55% yield. A somewhat improved yield (62%) was obtained using potassium chloride (entry 2). The solvent screening determined that the best choice was the dichloromethane; no improvement was achieved in more polar (entries 3-6) or less polar solvents (entries 7-8). Reducing the KCl loading from 1.5 to 1.0 equiv afforded **2a** in a slight lower yield (57%, entry 9); the use of two equivalents does not improve the reactivity to an appreciable extent (entry 10). Performing the reaction at higher temperature (40ºC) reduced the yield of the chlorinated compound to just 39% due to the concomitant formation of the diaryliodonium species **3a** 32% yield (entry 11, for the structure see Scheme 2). The use of 18-crown-6 ether (entry 12) or the employment of the organic salt *n*-Bu_4NCl did not improve the results. Finally, it was noticed that the use of anhydrous solvent and inert atmosphere is crucial to achieve good yields (entries 14-16), since conducting the reaction in open-air conditions led to an intractable reaction mixture.

Table 1. Screening and optimization in the PIFA-inorganic chlorine salt mediated chlorination of mesitylene.



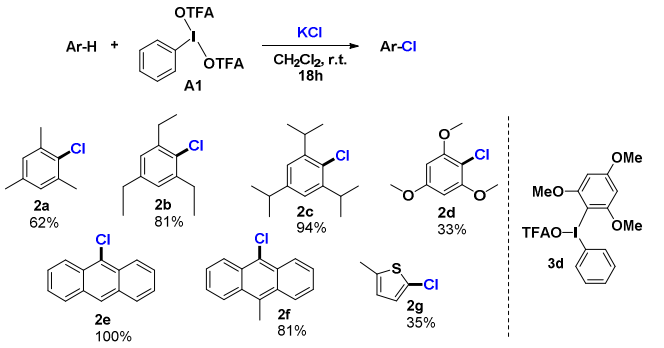
Entry	Chlorine source[a]	Solvent[b]	Yield (%)[c]
1	NaCl	CH_2Cl_2	55
2	KCl	CH_2Cl_2	62
3	KCl	CH_3CN	60
4	KCl	DMF	60
5	KCl	EtOH	20
6	KCl	THF	25
7	KCl	Et_2O	22
8	KCl	Toluene	10
9	KCl[d]	CH_2Cl_2	57
10	KCl[e]	CH_2Cl_2	64
11	KCl[f]	CH_2Cl_2	39
12	KCl[g]	CH_2Cl_2	60
13	*n*-Bu_4NCl	CH_2Cl_2	14
14	KCl	CH_2Cl_2[h]	48
15	KCl	CH_2Cl_2[i]	*n.d.*
16	KCl	CH_2Cl_2[j]	*n.d.*

[a] **1a** (1.7 mmol in 5 mL of CH_2Cl_2), chlorination source (2.5 mmol, 1.5 equiv) and **A1** (1.7 mmol, 1 equiv), rt and Ar atmosphere, overnight. [b] Anhydrous solvent. [c] Isolated yield. [d] 1 equiv. [e] 2 equiv. [f] Reaction done at 40ºC. [g] 1.5 equivalents of 18-crown-6 ether as additive. [h] Wet solvent and argon atmosphere. [i] Dry solvent and open-air reaction. [j] Wet solvent and open-air reaction.



Scheme 2. Reaction of mesitylene using the PIFA-KCl system at 40°C.

Once optimized the chlorination of mesitylene, several aromatic compounds were tested (Scheme 3). All the symmetric tri-substituted arenes were smoothly chlorinated in moderate to excellent yields (**2a-c**, 62-94%). In the case of the most electronically rich 1,3,5-trimethoxybenzene the yield of **2d** was low (33%) due to the formation of the λ^3-diaryliodonium species **3d** (41% yield), as was already observed for **1a**. In fact, the direct reaction between 1,3,5-trimethoxybenzene and PIFA has been previously described in the literature even at room temperature.[25] On the other hand, the more deactivated arenes, such as 1,3,5-tribromobenzene did not reacted under these conditions. Moreover, the chlorination of anthracene and 9-methylanthacene gave excellent yields of the monochlorination products (**2e** 100%; **2f** 81%). However, anthracene-9-carbaldehyde did not react. Thus, the results indicate a clear dependence on the arenes electronic properties, with best results achieved with "moderately" activated substrates, *i. e.* those that are sufficiently π-rich to undergo the chlorination, but not so reactive as to undergo the electrophilic iodination to form a diaryliodonium salt. Regarding the nitrogen-based heterocycles, the reaction was violent and not controlled with pyrrole, 1-methyl-1-*H*-pyrrole and indole, which were oxidized in the presence of PIFA, and in some cases polymerized.[26] In the contrary, 2-methylthiophene gave product **2g** in 35% yield.



Scheme 3. Chlorination of arenes by using the PIFA-KCl system at room temperature. Formation of λ^3-diaryliodonium, **3,** was only observed in the reaction of 1,3,5-trimethoxybenzene

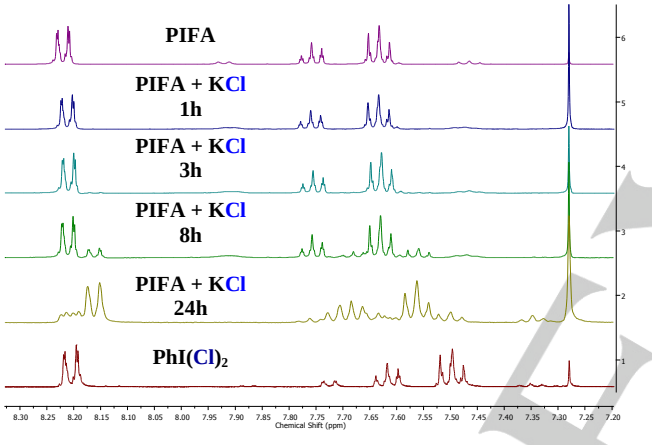
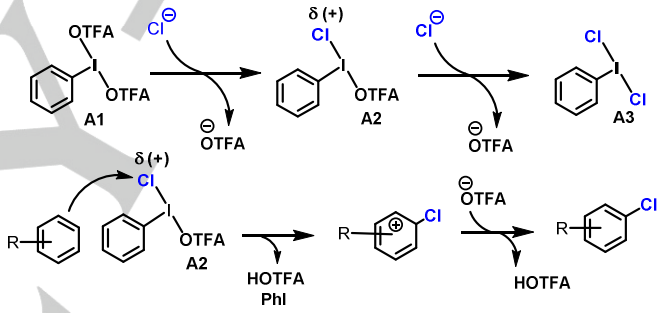


Figure 1. Monitoring of the reaction between KCl and PIFA by ^{1}H NMR in a 360 MHz spectrometer at different times

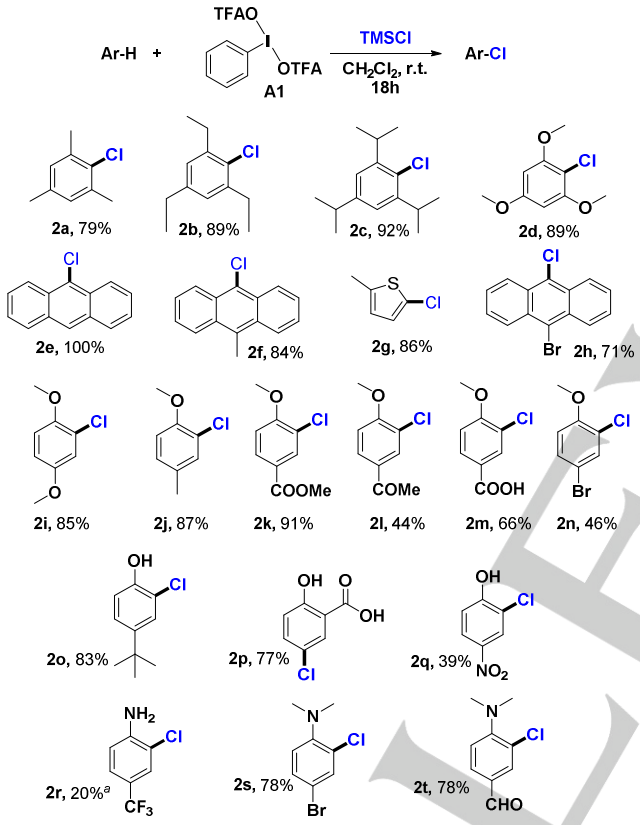
At this stage, we were interested in exploring the mechanism. A possible radical mechanism can be envisaged including cation radicals as reactive intermediates.[27] In fact, when the reaction of 1,3,5-triisopropylbenzene was performed in the presence of TEMPO no monochlorinated product **2c** was obtained and only iodobenzene was detected. However, control experiment by mixing 1 equiv of PIFA and TEMPO led to the total reduction of PIFA to iodobenzene (observed by ^{1}H NMR, see SI) and explained the total suppression of the chlorination process.[28] Then, the evolution of 1:1 mixture of KCl and PIFA was monitored overtime by ^{1}H NMR in $CDCl_3$ (Figure 1). No changes could be appreciated when comparing the spectrum of PIFA alone, **A1**, with the spectra corresponding to its mixture with KCl at 1h or 3h. However, new signals were observed after 8 h consistent with a chemically distinct phenyl group. This set of resonances became predominant after 24 hours. This indicates that PIFA was consumed, leading to the formation of a new species which we tentatively identified as the mixed ligand iodane $PhI(O_2CCF_3)Cl$ (**A2**, Scheme 4). If we compare the ^{1}H NMR spectrum after 24h with the one corresponding to a commercially available sample of $PhICl_2$, it can be seen that only minor amounts of this dichloride are formed. It can be deduced that, upon reaction with KCl, the starting $PhI(O_2CCF_3)_2$ after 24 hours is transformed into an intermediate major specie $PhI(O_2CCF_3)Cl$, **A2**, and a minor $PhICl_2$, **A3**, specie (Scheme 4). So, taking into account that the reaction time is 18 hours for the experiments in Scheme 3, the intermediate **A2** is the plausible chlorinating agent in this reaction. Other possible chlorination pathway could be the direct chlorination of the arenes by Cl_2 generated from the reductive elimination of iodobenzene from **A2** and consequent oxidation of chloride anions by PIFA as proposed by Karade' s group.[23] This possibility was discarded since mixing KCl and PIFA (1.5:1) during 18h, no formation of iodobenzene was detected (neither by ^{1}H NMR or GC, see SI). Thus, we propose the direct reaction with the positively charged chlorine (*umpolung*) of intermediate **A2** through a S_EAr (Scheme 4).



Scheme 4. Sequential ligand exchange from PIFA to $PhICl_2$. *In-situ* generation of $PhI(O_2CCF_3)Cl$ and direct reaction of the arene with **A2**.

Then we studied the use of TMSCl reagent as chlorine source (Scheme 1). As a first trial, we performed the reaction of the most activated arene of the series, 1,3,5-trimethoxybenzene, with TMSCl (2.0 equiv.) and PIFA (1 equiv.) under argon atmosphere. Gratifyingly, we isolated **2d** in an 89% yield improving in a great extend the result achieved with KCl (33% yield) (Scheme 3). Moreover, the reaction was carried out at room temperature and, more remarkably, it was over after 20 minutes. Addition of hexane gives rise to the precipitation of the compound that can be isolated from iodobenzene by filtration. This working up was used for all the solid chloroarenes. The same conditions applied to 1,3,5-trialkylsubstitutes arenes (Scheme 5), afforded the desired compounds **2a-c** in excellent yields (79-92%). Compounds **2e**, **2f** and **2h** were obtained by chlorination of anthracene, methylanthracene and bromoanthracene in 100, 84 and 71% yield, respectively. Unfortunately, the very electronically poor 1,3,5-tribromobenzene, 1,3,5-tris(bromomethyl)benzene and anthracene-9-carbaldehyde did not react even at reflux conditions. The treatment of 1-methyl-1*H*-pyrrole gave complex

mixtures whereas 2-methylthiophene gave **2g** in a high 86% yield. We also studied some anisole derivatives, compounds **2i-k** were obtained in excellent yields, conversely, when electron-withdrawing groups are present *para* to the OMe substituent, the yield diminishes (**2l-n**, 41-46%) except for **2k**. The same behavior is observed for substituted phenols (**2o** vs **2q**), although salicylic acid was chlorinated smoothly in 77% yield. The method is also applicable to unsubstituted and *N*,*N*-disubstituted anilines. In the case of **2r**, the yield was lower due to the presence of the strongly electron-withdrawing CF_3 group. This behavior is characteristic of an electrophilic aromatic substitution mechanism. The method is tolerant with functional groups sensitive to oxidative processes as $–NH_2$ and –CHO.



Scheme 5. Scope for the chlorination of arenes by using the PIFA-TMSCl system. All reactions were done by using 1.0 equiv. of PIFA and 2.0 equiv. of TMSCl at room temperature. [a]Yield measured by ^{1}H NMR.

To cast some light about the true chlorinating species in this mechanism, we analyzed by ^{1}H NMR the mixture between PIFA and TMSCl (Figure 2). This experiment allowed as to discover the exchange of both OTFA groups in PIFA by two chlorine atoms, generating *in-situ* the $PhI(Cl)_2$ (**A3**) compound. Chloride anion from TMSCl, upon binding to iodine(III) acquires an electrophilic character (*umpolung*). Formation of **A2** could not be observed. We propose a previous activation of PIFA through the coordination of the oxygen atom of OTFA groups with the trimethylsilyl group before nucleophilic chloride substitution takes place (Scheme 6). Additionally, we isolated **A3** simply mixing PIFA and TMSCl in dry dichloromethane at room temperature in 5 minutes (93% yield). However, we observed that compound **A3** decomposed at room temperature and although it's commercially available results a very expensive reagent. Thus, it is really useful to prepare this reagent *in–situ*. With these results in hand, we assume that the $PhI(Cl)_2$ is responsible of the chlorination process following an electrophilic aromatic substitution and we propose the mechanism shown in Scheme 6.

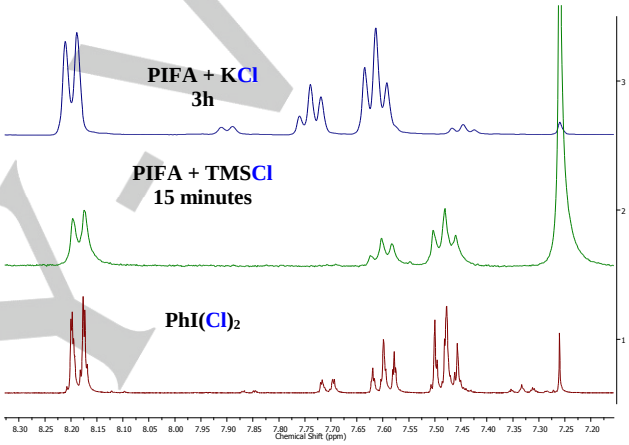
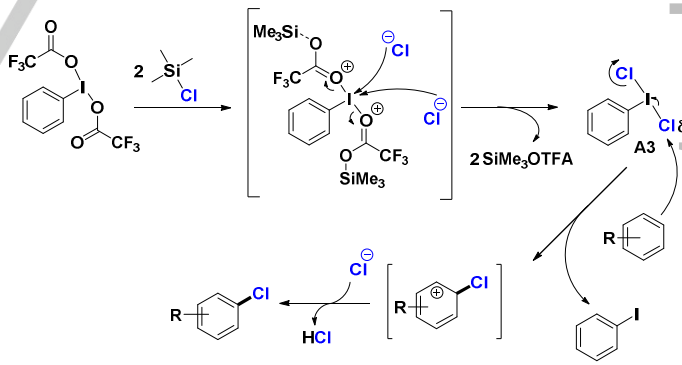


Figure 2. Monitoring of the reaction between TMSCl and PIFA by ^{1}H NMR on a 360 MHz spectrometer



Scheme 6. Proposed mechanism for the electrophilic aromatic chlorination of arenes by the PIFA-TMSCl system.

This methodology was successful applied in multigram reactions. For example, the chlorination of 10 g of 1,3,5-trimethoxybenzene afforded **2d** in 82% yield (9,90 g). Similarly, the 4-chloro salicylic acid **2p**, a useful intermediate in the agrochemicals and medicinal chemistry synthesis,[29] was obtained on a 6 g scale in a 77% yield.

Conclusions

In summary, we have developed two procedures for the chlorination of arenes based on the discovery that using PIFA with two different chloride sources distinct I(III)-based reactive intermediates are obtained. Our first protocol takes place under very mild conditions, using mixtures of KCl and PIFA, yielding in good to excellent yields the monochlorination of weakly activated arenes. In this case formation of $PhI(O_2CCF_3)Cl$ as reactive species is proposed. On the other hand, using TMSCl as chlorinating agent, we can extent the scope of the arene substrates, presumably due to the full *in-situ* generation of $PhI(Cl)_2$. Once the intermediate is formed, the next step proceeds via an electrophilic aromatic substitution. This methodology using PIFA and TMSCl was applied in the electrophilic chlorination of a great number of substrates (20 examples) and proceeds readily on multigram scale. Best yields were achieved for electronic rich or moderately rich aromatic substrates.

Experimental Section

General Information. All reagents were purchased from Sigma-Aldrich or Fluorochem and were used as received, without further purification. Solvents were previously distilled prior use using known procedures. ^1H and ^{13}C NMR spectra were recorded with a Bruker DXP-250 MHz NMR Spectrometer with $CDCl_3$ as the solvent. ^1H shifts were referenced to $CDCl_3$ at 7.26 ppm. ^{13}C shifts were referenced to $CDCl_3$ at 77 ppm. Infrared spectroscopy measurements were carried out using the Total Attenuated Reflectance (ATR) technique, on a Perkin Elmer HART spectrum, with a ZeSe flat plate accessory of 60º.

General procedure for the chlorination using KCl

In a multi-reaction tube 2 mmol of PIFA (842 mg, 1 equiv.) were dissolved in dry CH_2Cl_2 under argon atmosphere. Next, 220 mg of KCl (4 mmol, 1.5 equiv.) were added to the solution and led stirred for 10 minutes. Then, the corresponding arene was added in one portion (2 mmol) allowing the reaction to proceed at room temperature overnight. When the reaction was over, the solution was poured into water and extractions with CH_2Cl_2 were performed. The organics were evaporated, and the crude was well dried under high vacuum yielding the chlorinated arene.

General procedure for the chlorination using TMSCl

In a multi-reaction tube 1.8 mmol of PIFA (720 mg, 1 equiv.) were dissolved in 12 mL of dry CH_2Cl_2 under argon atmosphere. Next, 0.34 mL of TMSCl (3.3 mmol, 2.0 equiv.) were added to the solution and led stirred for 10 minutes. The clear solution turned yellowish. Then, the corresponding arene was added in one portion (1.7 mmol) allowing the reaction to proceed at room temperature. When the reaction was over, the solution was poured into water and extractions with CH_2Cl_2 were performed. The organics were evaporated, and the crude was well dried under high vacuum yielding the desired chloroarene.

2-Chloro-1,3,5-trimethylbenzene **2a**.[30] Yellow oil; ^1H NMR (360 MHz, $CDCl_3$) δ 1.24–1.28 (9H, m), 2.59 (2H, q, *J* = 7.5 Hz), 2.75 (4H, q, *J* = 7.5 Hz), 6.95 ppm (2H, s); isolated yield: 305 mg (79%) from 300 mg of **1a**.

2-Chloro-1,3,5-triethylbenzene **2b**.[31] Colorless oil; ^1H NMR (360 MHz, $CDCl_3$) δ 1.24–1.28 (9H, m), 2.59 (2H, q, *J* = 7.5 Hz), 2.75 (4H, q, *J* = 7.5 Hz), 6.95 (2H, s); isolated yield: 324 mg (89%) from 300 mg of **1b**.

2-Chloro-1,3,5-triisopropylbenzene **2c**.[32] Yellow oil; ^1H NMR (360 MHz, $CDCl_3$) δ 1.35 (18H, m), 2.97 (1H, sept, *J* = 6.9 Hz), 3.58 (2H, sept, *J* = 6.9 Hz), 6.10 (2H, s); isolated yield: 322 mg (92%) from 300 mg of **1c**.

2-Chloro-1,3,5-trimethoxybenzene **2d**.[33] Yellowish solid, Mp = 92-93 ºC; ^1H NMR (360 MHz, $CDCl_3$) δ 3.83 (3H, s), 3.90 (6H, s), 6.20 (2H, s), isolated yield: 536 mg (89%) from 500 mg of **1d**.

9-Chloroanthracene **2e**.[31] Green solid, Mp = 49.5-51 ºC; ^1H NMR (360 MHz, $CDCl_3$) δ 7.51-7.61 (4H, m), 7.88 (2H, d), 8.08 (2H, d), 8.48 (1H, s); isolated yield: 245 mg (100%) from 200 mg of **1e**.

9-Chloro-10-methylanthracene **2f**.[33] Tan solid, Mp = 175-177 ºC; ^1H NMR (360 MHz, $CDCl_3$) δ 3.11 (3H, s), 7.55-7.64 (4H, m), 8.31-8.34 (2H, d), 8.55-8.59 (2H, d); isolated yield: 198 mg (84%) from 200 mg of **1f**.

2-Chloro-5-methylthiophene **2g**.[34] Oil; ^1H NMR (360 MHz, $CDCl_3$) δ 2.30 (3H, s), 6.40-6.42 (1H, m), 6.58 (1H, d); isolated yield: 406 mg (86%) from 350 mg of **1g**.

9-Bromo-10-chloroanthracene **2h**.[35] Yellow solid, Mp = 201-203ºC; ^1H NMR (360 MHz, $CDCl_3$) δ 7.63 (4H, m), 8.60 (4H, m); isolated yield: 161 mg (71%) from 200 mg of **1h**..

2-Chloro-1,4-dimethoxybenzene **2i**.[24] Yellow oil; ^1H NMR (360 MHz, $CDCl_3$) δ 3.77 (3H, s), 3.86 (3H, s), 6.80 (2H, m), 6.99 (1H, d, *J* = 3.0 Hz); isolated yield: 425 mg (85%) from 400 mg of **1h**.

2-Chloro-1-methoxy-4-methylbenzene **2j**.[36] Colorless oil; ^1H NMR (360 MHz, $CDCl_3$) δ 2.27 (3H, s), 3.87 (3H, s), 6.82 (1H, d, *J* = 8.4 Hz), 7.00 (1 H, dd, *J* = 8.4 Hz, *J* =2.6 Hz), 7.18 ppm (1H, d, *J* = 2.6 Hz); isolated yield: 167 mg (87%) from 150 mg of **1j**.

Methyl 3-chloro-4-methoxybenzoate **2k**.[5c] White solid, Mp = 88-90ºC; ^1H NMR (360 MHz, $CDCl_3$) δ 3.91 (3H, s), 3.98 (3H, s), 6.97 (1H, d, *J* = 8.6 Hz), 7.96 (1H, dd, *J* = 8.6 Hz, *J* = 2.0 Hz), 8.08 (1H, d, *J* = 2.0 Hz); isolated yield: 395 mg (91%) from 360 mg of **1k**.

3-Chloro-4-methoxyacetophenone **2l**.[5c] Tan solid; Mp = 73-75 ºC; ^1H NMR (250 MHz, $CDCl_3$) δ 2.58 (3H, s), 4.00 (3H, s), 6.99 (1H, d, *J* = 7.6 Hz), 7.90 (1H, dd, *J* = 7.6 Hz, *J* = 2.0 Hz), 8.01 (1H, d, *J* = 2.0 Hz); isolated yield: 162 mg (44%) from 300 mg of **1l**.

3-Chloro-4-methoxybenzoic acid **2m**.[10] Brown solid; Mp = 55-57 ºC; ^1H NMR (250 MHz, $CDCl_3$) δ 3.65 (3H, s), 6.73 (1H, d, *J* = 7.8 Hz), 7.65 (1H, dd, *J* = 7.8 Hz, *J* = 1.8 Hz), 7.72 (1H, d, *J* = 1.8 Hz); isolated yield: 162 mg (66%) from 200 mg of **1m**.

4-Bromo-2-chloro-1-methoxybenzene **2n**.[37] Yellow solid; Mp = 68-70 ºC; ^1H NMR (250 MHz, $CDCl_3$) δ 4.00 (3H, s), 7.02 (1H, d, *J* = 7.4 Hz), 8.04 (1H, dd, *J* = 7.4 Hz, *J* = 1.9 Hz), 8.15 (1H, d, *J* = 1.9 Hz); isolated yield: 109 mg (46%) from 200 mg of **1n**.

4-*(Tert*-butyl)-2-chlorophenol **2o**.[38] Colorless oil; ^1H NMR (360 MHz, $CDCl_3$) δ 1.32 (9H, s), 6.52 (2H, broad singlet), 6.81 (1H, dd, *J* = 7.2 Hz, *J* = 1.8 Hz), 7.00 (1H, d, *J* = 8.4 Hz); isolated yield: 347 mg (83%) from 340 mg of **1o**.

5-Chloro-2-hydroxybenzoic acid **2p**.[39] Tan solid, Mp = 168-170ºC;. ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.01 (1H, d, *J* = 8.6 Hz), 7.50 (1H, dd, *J* = 8.6 Hz, *J* = 2.0 Hz), 7.92 (1H, d, *J* = 2.0 Hz); isolated yield: 5.67 g (77%) from 6.00 g of **1p**.

2-Chloro-4-nitrophenol **2q**.[10] White off solid, Mp = 106-108 ºC; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.22 (1H, s), 7.16 (1H, d, *J* = 8.1 Hz), 8.16 (1H, dd, *J* = 8.1 Hz, *J* = 2.0 Hz), 8.32 (1H, d, *J* = 2.0 Hz); isolated yield: 61 mg (39%) from 125 mg of **1q**.

2-Chloro-4-(trifluoromethyl)aniline **2r**.[40] ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.26 (2H, bs), 6.78 (1H, d, *J* = 8.2 Hz), 7.29 (1H, d, *J* = 8.2 Hz), 7.53 (1H, s).

4-Bromo-2-chloro-N,N-dimethylaniline **2s**.[41] Tan solid, Mp. = 110-112 ºC; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.81 (6H, s), 6.94 (1H, d, *J* = 7.2 Hz), 7.33 (1H, dd, *J* = 7.2 Hz, *J* = 2.0 Hz), 7.51 (1H, d, *J* = 2.0 Hz); isolated yield: 228 mg (78%) from 250 mg of **1s**.

3-Chloro-4-(dimethylamino)benzaldehyde **2t**.[42] Tan solid, Mp = 72-73 ºC; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.98 (6H, s), 7.08 (1H, d, *J* = 9.8 Hz), 6.70 (1H, dd, *J* = 9.8 Hz, *J* = 3.6 Hz), 7.85 (1H, d, *J* = 3.6 Hz), 9.82 (1H, s); isolated yield: 480 mg (78%) from 500 mg of **1t**.

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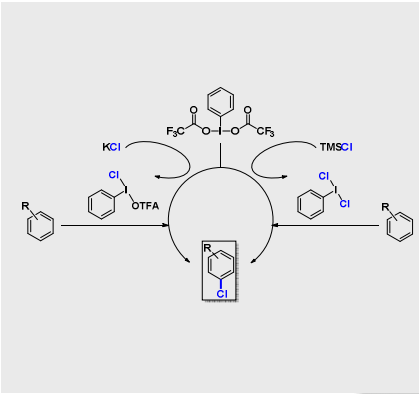
Efficient metal-free methods for the electrophilic chlorination of arenes using PIFA and simple chlorine sources are reported. The *in-situ* formation of different I(III)-based species such as $PhI(OCOCF_3)Cl$ and $PhICl_2$ are proposed as chlorinating agents when using the combination of PIFA-KCl and PIFA-TMSCl respectively.



Aromatic chlorination*

*Albert Granados, Zhiyu Jia, Marc del Olmo and Adelina Vallribera**

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***In-situ* Generation of Hypervalent Iodine Reagents for the Electrophilic Chlorination of Arenes**

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