High-yielding one-pot synthesis of diaryliodonium triflates from arenes and iodine or aryl iodides†

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Unsymmetric and symmetric diaryliodonium triflates are synthesized from both electron-deficient and electron-rich substrates in a fast, high yielding, and operationally simple protocol employing arenes and aryl iodides or iodine.

Hypervalent iodine compounds have recently received considerable attention as mild, non-toxic and selective reagents in organic synthesis.[1,2] Iodine(III) reagents with two heteroatom ligands, *e.g.* (diacetoxyiodo)benzene and iodosylbenzene, are successfully employed in oxidations of alcohols, alkenes and α-oxidations of carbonyl compounds.[3] The properties of iodine(III) reagents with two carbon ligands resemble those of metals such as Hg, Pb and Pd, allowing for reaction pathways similar to metal-catalyzed reactions while avoiding the drawbacks of cost, toxicity and threshold values in pharmaceutical products.[2] Diaryliodonium salts are the most studied compounds in this class; they are versatile electrophiles in α-arylation of carbonyl compounds[4,5] and metal-catalyzed cross-couplings,[6] and are frequently employed as photoinitiators in polymerizations.[7]

Synthetic routes to diaryliodonium salts typically involve 2–3 steps, with initial oxidation of an aryl iodide to iodine(III) followed by ligand exchange with an arene to obtain the diaryliodonium salt.[8] Preformed inorganic iodine(III) reagents, such as iodosyl fluorosulfate, have been employed to shorten the route.[9] These reagents are, however, not commercially available. Reported reactions with oxidation and ligand exchange in the same pot suffer from narrow substrate scope[10,11] or long reaction times,[11] need excess reagents[12] or employ toxic chromium reagents.[13] In many cases a subsequent anion exchange step is necessary, as the anion influences both the solubility and reactivity of the iodonium salt. Non-nucleophilic anions, such as triflate or tetrafluoroborate, have proven superior to halide anions in many applications.[6,14]

The lack of general and efficient methods for the synthesis of diaryliodonium salts is cumbersome, and clearly limits their scope as environmentally benign reagents in organic chemistry.[15] The development of an operationally simple protocol with broad substrate scope would greatly facilitate the application of these efficient, non-toxic arylation agents. Herein we present our preliminary results on a fast, high-yielding, one-pot synthesis of the title compounds.

An atom efficient and simple one-pot synthesis of diaryliodonium salts would involve treatment of an aryl iodide with a commercially available oxidant in the presence of an arene and a suitable acid, the anion of which would end up in the iodonium salt (eqn. 1).

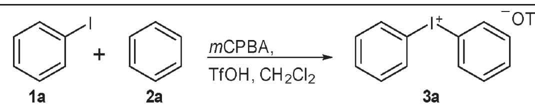
$$\mathrm{Ar^1\text{-}I} + \mathrm{Ar^2\text{-}H} \xrightarrow[\mathrm{HX}]{\text{oxidant}} \mathrm{Ar^1{-}\overset{+}{I}{-}Ar^2}\ \ \mathrm{X^-} \qquad (1)$$

*m*CPBA has recently been reported to oxidize iodobenzene to (diacyloxyiodo)benzene,[16] which encouraged us to investigate whether this oxidant could be employed also in the direct synthesis of iodonium salts. Suitable reaction conditions for the reaction of iodobenzene (**1a**) and benzene (**2a**) with *m*CPBA in organic solvents were thus screened. Boron trifluoride and trifluoromethanesulfonic acid were deemed interesting acids, as they could give rise to iodonium salts with tetrafluoroborate and triflate anions, respectively, without a subsequent anion exchange step. Initial attempts to combine *m*CPBA with boron trifluoride etherate in dichloromethane at room temperature were encouraging, as a diphenyliodonium salt was formed in moderate yield. Due to problems with purification and anion identification, the use of triflic acid instead of $BF_3{\cdot}OEt_2$ was next investigated.

Gratifyingly, the treatment of iodobenzene with *m*CPBA,[17] TfOH and excess benzene in dichloromethane at room temperature resulted in a clean reaction to give iodonium triflate **3a** in 82% isolated yield (Table 1, entry 1). The reaction time could be considerably reduced by increasing the temperature, delivering **3a** in 89% yield after 1 h at 40 °C (entry 3) or in 85% yield after only 10 min at 80 °C (entry 4). In this fast and operationally simple one-pot reaction, **3a** is formed directly from commercially available substrates and can be isolated with a suitable anion in high yield after a simple workup.

To determine the generality of this novel one-pot reaction, it was applied to the synthesis of various diaryliodonium salts **3** from aryl iodides **1** and arenes **2** (Table 2). Most previous protocols have been restricted to the synthesis of either electron-rich or

Table 1 Temperature influence on the synthesis of **3a**[a]



Entry	**2a** (equiv.)	TfOH (equiv.)	T (°C)	Time	Yield (%)[b]
1	5	2	rt	21 h	82
2	2	3	rt	21 h	89
3	2	3	40	1 h	89
4	1.1	3	80	10 min	85

[a] Reaction conditions: **1a** (0.23 mmol), **2a** and *m*CPBA (0.25 mmol) were dissolved in CH_2Cl_2 (2 mL), TfOH was added at rt and the reaction was stirred at the indicated temperature for the indicated time in a sealed tube. [b] Isolated yield.

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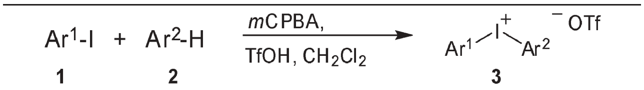
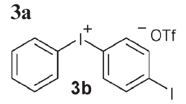
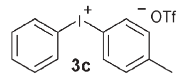
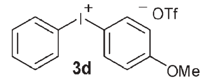
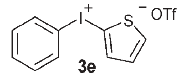
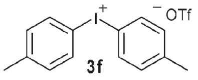
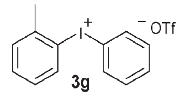
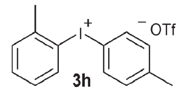
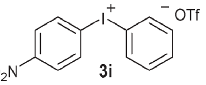
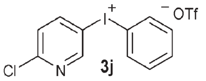
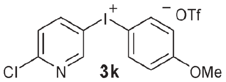
† Electronic supplementary information (ESI) available: Synthetic procedures, analytical data and NMR spectra for salts **3**. See DOI: 10.1039/b701864a

Table 2 Synthesis of substituted diaryliodonium salts **3**[a]



Entry	**1** (Ar^1I)	**2** (Ar^2H)	Salt **3**[b]	Yield (%)[c]
1[d]	**1a** (PhI)	**2a** (PhH)	**3a**	85
2	**1a** (PhI)	**2b** (PhI)	 **3b**	85
3	**1a** (PhI)	**2c** (PhMe)	 **3c**	85
4	**1a** (PhI)	**2d** (PhOMe)	 **3d**	87
5	**1a** (PhI)	**2e** (thiophene)	 **3e**	82
6[d]	**1b** (4-MePhI)	**2a** (PhH)	**3c**	71
7	**1b** (4-MePhI)	**2c** (PhMe)	 **3f**	52
8	**1c** (2-MePhI)	**2a** (PhH)	 **3g**	85
9	**1c** (2-MePhI)	**2c** (PhMe)	 **3h**	87
10	**1d** (4-NO_2PhI)	**2a** (PhH)	 **3i**	85
11[d]	**1e** (2-chloro-5-iodopyridine)	**2a** (PhH)	 **3j**	60
12[d]	**1e** (2-chloro-5-iodopyridine)	**2d** (PhOMe)	 **3k**	53

[a] Reaction conditions: **1** (1.0 equiv.), **2** (1.1 equiv.), *m*CPBA (1.1 equiv.) and TfOH (2.0 equiv.) in CH_2Cl_2, see Table 1 and ESI for details. [b] Formed with complete regioselectivity. [c] Isolated yield. [d] 3.0 equiv. of TfOH were used.

electron-deficient iodonium salts, as the reactivity of the arenes varies dramatically with the electronic properties.[8] Aryl iodides **1** and arenes **2** were thus selected to investigate the formation of both electron-rich and electron-deficient salts, including heteroaryl salts.

The use of iodobenzene both as aryl iodide (**1a**) and arene (**2b**) yielded 4-iodophenyl(phenyl)iodonium triflate (**3b**) as a single regioisomer (entry 2). Likewise, the reaction of **1a** with toluene (**2c**) was smooth, and unsymmetrical salt **3c** could be isolated in good yield (entry 3). The electron-rich arenes anisole (**2d**) and thiophene (**2e**) were, as expected, very reactive under the standard conditions. By decreasing the temperature to −78 °C, salts **3d** and **3e** could be obtained in excellent yields (entries 4, 5). Heteroaryl salt **3e** has previously been synthesized in several steps *via* the corresponding stannane,[18] which further illuminates the efficiency and environmental friendliness of our procedure.

Unsymmetrical salt **3c** could also be formed by the reaction of 4-iodotoluene (**1b**) with benzene, as shown in entry 6. Aryl iodide **1b** was also employed to form the symmetrically substituted bis(4-methylphenyl)iodonium salt **3f** (entry 7). The reason for the moderate yield of **3f** is unclear, as 2-iodotoluene (**1c**) delivered salts **3g** and **3h** in high yields upon reaction with benzene and toluene, respectively (entries 8, 9).

Generally, the synthesis of electron-rich salts was easier from iodobenzene and a substituted arene than from the "reverse" reaction of a substituted aryl iodide with benzene (compare entries 3 and 6). 4-Iodoanisole and 2-iodothiophene both participated in the reaction with benzene, but unidentified byproducts were formed.

Electron-deficient iodonium salts were, on the other hand, best made from the corresponding electron-deficient aryl iodide with benzene as the arene. This is exemplified by the reaction of iodo-4-nitrobenzene (**1d**) with benzene, which delivered salt **3i** in 85% yield (entry 10). The reverse reaction with iodobenzene and nitrobenzene was sluggish and gave salt **3b** as a byproduct, the result of competing reaction pathways of **1a** between oxidation and reaction with the formed iodine(III) intermediate.

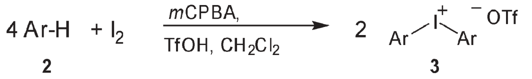
The generality of the developed protocol is especially evident from the successful reaction of 2-chloro-5-iodopyridine (**1e**) with benzene or anisole to give salts **3j** and **3k**, respectively (entries 11, 12). Iodonium salts containing this aryl moiety have recently been used in an efficient total synthesis of (−)-epibatidine.[4] Pyridyl iodonium salts have previously been inaccessible by acidic routes, and salt **3j** was formerly obtained by a basic, atom-inefficient two-step procedure[19] in moderate yield, which was still inadequate for the preparation of salt **3k**.[20] The formation of iodonium salts **3** from substituted arenes **2** was in all cases highly regioselective, yielding salts **3b–d,f,h,k** with complete *para*-selectivity. Likewise, the reaction of **1a** with thiophene (**2e**) afforded only 2-substituted **3e**.

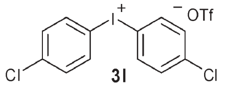
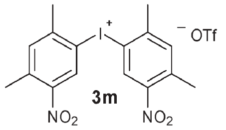
Having succeeded in the direct synthesis of diaryliodonium salts from aryl iodides, we looked into possible extensions of this reaction. As aryl iodides are readily available but often expensive, we argued that it might be possible to form the aryl iodide *in situ*.[21] Hence, the reaction of benzene (**2a**) and iodine with *m*CPBA and TfOH was studied, and indeed delivered iodonium salt **3a** in high yield in only 10 min at 80 °C or 22 hours at room temperature (Table 3, entries 1, 2).

This efficient synthesis of diaryliodonium salts was subsequently applied to other arenes. Toluene (**2c**) yielded a mixture of salts **3h** and **3f** with 3 : 1 regioselectivity favouring *ortho*-iodination (entry 3). The regioselectivity was higher at lower conversions, and pure **3h** was obtained after one hour at 0 °C (entry 4). Chlorobenzene (**2f**) gave symmetric salt **3l** with complete *para*-selectivity (entry 5). Even highly functionalized, deactivated arene **2g** participated in the reaction to give salt **3m** (entry 6). As this one-pot reaction involves several consecutive steps and many possible sources of byproducts, it is surprising that salts **3** are easily isolated in moderate to good yields.

In conclusion, a facile, direct synthesis of diaryliodonium triflates from the corresponding aryl iodide and arene has been realized. The method is fast, high yielding, operationally simple and has a large substrate scope. Electron-rich salts are conveniently

Table 3 Direct synthesis of salts **3** from arenes and iodine[a]



Entry	**2** (ArH)	*T* (°C)	Time	Salt **3**[b]	Yield (%)[c]
1	**2a** (PhH)	80	10 min	**3a**	78
2	**2a** (PhH)	rt	22 h	**3a**	81
3	**2c** (PhMe)	rt	2 h	**3h** : **3f** ratio 3 : 1	52
4	**2c** (PhMe)	0	1 h	**3h**	31
5	**2f** (PhCl)	rt	21 h	 **3l**	57
6	**2g** (4-nitro-*m*-xylene)	rt	19 h	 **3m**	24

[a] Reaction conditions: I_2 (1.0 equiv.), **2** (4–10 equiv.), *m*CPBA (4 equiv.) and TfOH (4 equiv.) in CH_2Cl_2, see ESI for details. [b] Formed with complete regioselectivity apart from entry 3. [c] Isolated yield.

synthesized from iodobenzene and the corresponding arene, and electron-deficient salts are formed by the reaction of a substituted aryl iodide with benzene. The protocol can be extended to the synthesis of iodonium salts directly from iodine and arenes, conveniently circumventing the need for aryl iodides. A thorough investigation of the scope and limitations of these reactions is underway, and will be reported separately.

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21 The oxidation of iodine and arenes to aryl iodides or (diacetoxyiodo)-benzene is known; see M. D. Hossain and T. Kitamura, *Tetrahedron Lett.*, 2006, **47**, 7889–7891 and references therein. After the completion of this work Kitamura reported a procedure for the direct synthesis of diaryliodonium salts from iodine, requiring heating at 40 °C for 72 h and a sequential anion exchange step (12 h), see ref. 11.