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Efficient and General One-Pot Synthesis of Diaryliodonium Triflates:

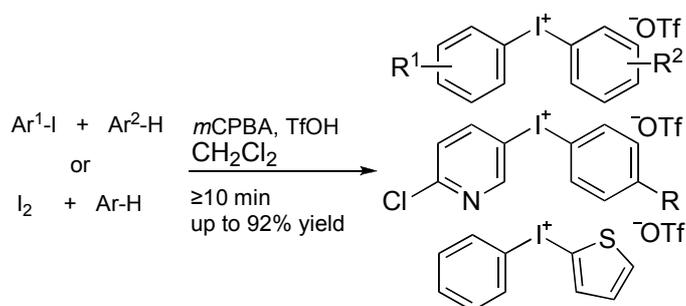
Scope and Limitations

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Abstract:

Symmetric and unsymmetric diaryliodonium triflates have been synthesized from both electron-deficient and electron-rich substrates in a fast, high yielding, and operationally simple one-pot protocol employing arenes and aryl iodides with *m*CPBA and triflic acid. The protocol has been extended to the direct synthesis of symmetric iodonium salts from iodine and arenes, circumventing the need for aryl iodides.



Introduction

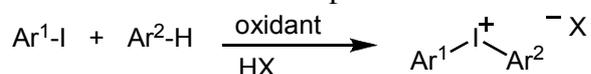
Hypervalent iodine compounds have recently received considerable attention as mild, non-toxic and selective reagents in organic synthesis.^[1, 2] Iodine(V) reagents, such as Dess-Martin periodinane and IBX, are frequently used as mild oxidants of alcohol moieties in total syntheses of natural products. Iodine(III) compounds with two heteroatom ligands, *e.g.* (diacetoxyiodo)benzene and iodosylbenzene, are employed in oxidations of alcohols, alkenes and α -oxidations of carbonyl compounds.^[3] In contrast, iodine(III) reagents with two carbon ligands have properties resembling those of metals such as Hg, Pb and Pd, and can be employed in reaction pathways that are similar to metal-catalyzed reactions.^[2] As the use of transition metals in organic synthesis suffers from drawbacks like cost, toxicity and threshold values in pharmaceutical products, the interest in this type of iodine(III)-mediated reactions has recently increased considerably.^[2]

Diaryl- λ^3 -iodanes, also called diaryliodonium salts, are the most well-known compounds in this class. Due to their highly electron-deficient nature and hyperleaving group ability, they serve as versatile arylating agents with a variety of nucleophiles, *e.g.* in α -arylation of carbonyl compounds.^[4] Their use in copper- and palladium-catalyzed cross-coupling reactions allows milder reaction conditions than in couplings with aryl halides.^[5]

The lack of general, fast and environmentally benign methods for the synthesis of diaryliodonium salts with suitable anions is cumbersome, and clearly limits their scope as reagents in organic chemistry. We have thus developed such a protocol from aryl iodides and arenes; the method was also extended to direct synthesis of diaryliodonium triflates from arenes and iodine.^[6]

Results and discussion

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 (Scheme 1).

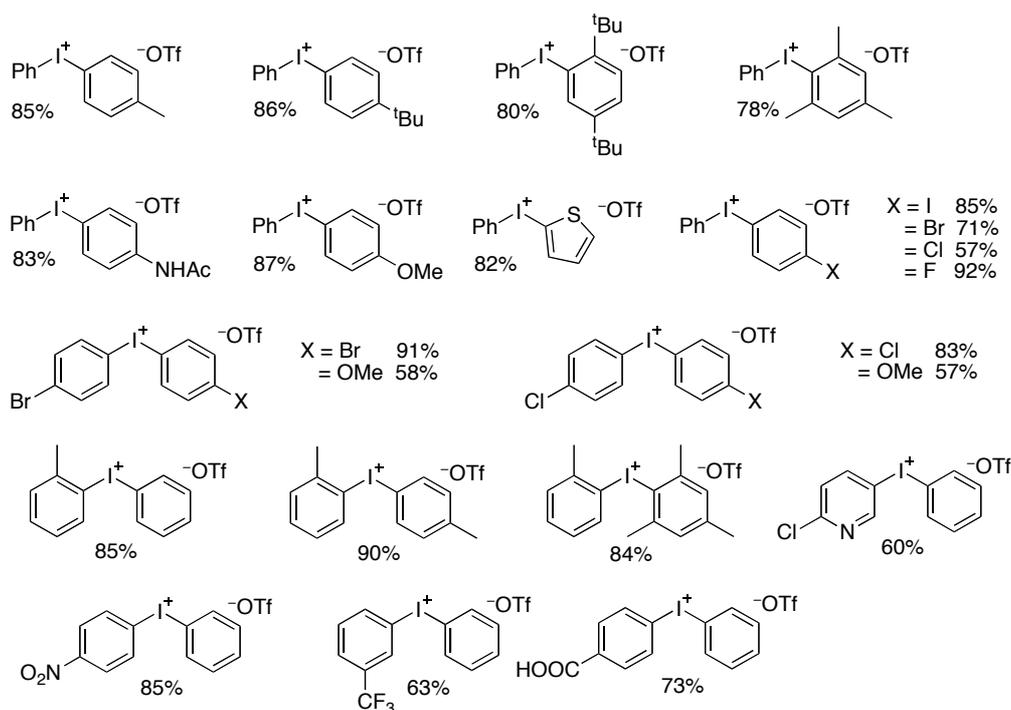


Scheme 1. Desired one-pot synthesis of diaryliodonium salts.

*m*CPBA has recently been reported to oxidize iodobenzene to (diacyloxyiodo)-benzenes,^[7] which encouraged us to investigate whether this oxidant could be employed also in the direct synthesis of iodonium salts. Gratefully, initial reactions of iodobenzene and benzene with *m*CPBA^[8] and triflic acid in dichloromethane indeed delivered diphenyliodonium triflate. The optimized conditions, using 1.1 equiv of *m*CPBA and 3 equiv. of TfOH, gave Ph₂I⁺TfO⁻ in 92% isolated yield within 10 min at room temperature.

The optimized protocol was subsequently applied to reactions of various iodoarenes with substituted arenes to yield symmetric and unsymmetric diaryliodonium salts; selected examples are shown in Scheme 2. The reactions were in most cases highly regioselective, yielding substituted salts with high *para*-selectivity. Likewise, the reaction of iodobenzene with thiophene afforded only 2-substituted salt.

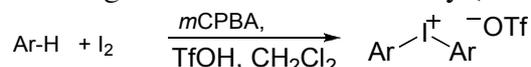
The reaction is insensitive to air and moisture, thus providing a fast and practical method for the synthesis of diaryliodonium salts. A convenient workup and purification procedure was also developed, where the desired salts could be isolated simply by concentrating the reaction mixture followed by precipitation in diethyl ether, delivering the product in high purity without need for an anion exchange step.



Scheme 2. Synthesis of diaryliodonium salts from aryl iodides and substituted arenes.

Direct synthesis from arenes and iodine

Aryl iodides are readily available but often expensive, which would make *in situ* formation of the aryl iodide an appealing extension to our developed synthesis of diaryliodonium salts. Kitamura's group recently showed that (diacetoxyiodo)arenes could be formed directly from arenes and iodine in the presence of an oxidant, presumably with the corresponding aryl iodide as intermediate.^[9] We thus envisioned a one-pot reaction of arenes and molecular iodine with *m*CPBA and TfOH to give iodonium salts directly (Scheme 3).

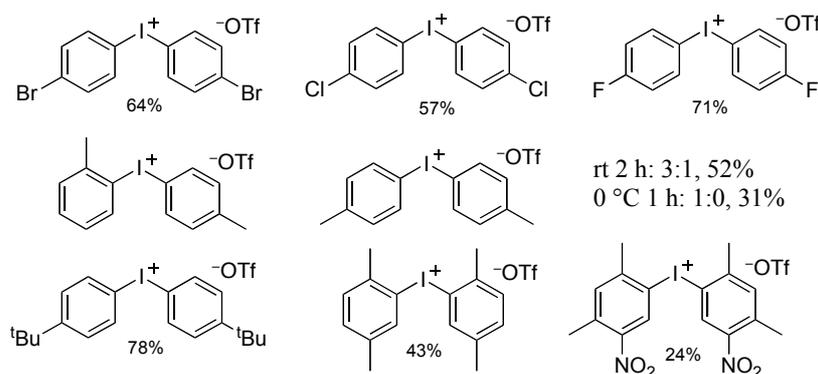


Scheme 3. Synthesis of diaryliodonium salts directly from arenes and iodine.

When benzene and iodine were reacted under our previously optimized conditions with *m*CPBA and TfOH, $\text{Ph}_2\text{I}^+\text{TfO}^-$ was gratefully formed. The use of 4 equivalents of *m*CPBA increased the reactivity, and with 4 equiv. of TfOH the reaction was completed within 10 min at 80 °C, giving $\text{Ph}_2\text{I}^+\text{TfO}^-$ in 78% isolated yield.

This efficient synthesis of diaryliodonium salts was subsequently applied to various arenes (Scheme 4). Aryl halides gave symmetric salts with complete *para*-selectivity. Toluene yielded a regioisomeric mixture of salts with 3:1 regioselectivity favoring *ortho*-iodination. The regioselectivity was higher at lower conversions, and pure *ortho*-salt was obtained after one hour at 0 °C. Other alkyl-substituted arenes gave salts in good to moderate yields with complete regioselectivity.

As this one-pot reaction involves several consecutive steps and many possible sources of byproducts, it is surprising that diaryliodonium salts are easily obtained in moderate to good yields. Another procedure for the direct synthesis of diaryliodonium triflates from iodine was recently published, requiring heating for 72 h and a sequential anion exchange step.^[10]



Scheme 4. Synthesis of salts **3** from molecular iodine and substituted arenes.

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 synthesized from iodobenzene and the corresponding arene, and electron-deficient salts are formed by the reaction of a substituted aryl iodide with an arene. Alkyl-substituted iodonium salts can be formed via both routes in similar yields. The protocol can be extended to the synthesis of iodonium salts directly from iodine and arenes, conveniently circumventing the need for aryl iodides.

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