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2-Iodosylbenzoic acid activated by trifluoromethanesulfonic anhydride: efficient oxidant and electrophilic reagent for preparation of iodonium salts†

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2-Iodosylbenzoic acid in the presence of trifluoromethanesulfonic anhydride is an efficient oxidant and electrophilic reagent useful for preparation of the corresponding alkenyl and aryliodonium salts. Compared to the previously reported methods of electrophilic activation of 2-iodosylbenzoic acid, this procedure is compatible with acid-sensitive functional groups, requires mild reaction conditions, and affords products in higher yields.

Organic compounds of polyvalent iodine have found wide application in modern academic and industrial research.[1] In particular, hypervalent iodine(III) and (V) derivatives are widely used as mild and selective oxidants and electrophilic group transfer reagents in organic synthesis.[1,2] Iodonium salts have been utilized as industrial initiators of polymerization,[3] as well as precursors to [^{18}F]-fluorinated radiotracers in Positron Emission Tomography (PET) and biologically active compounds.[1c] 2-Iodosylbenzoic acid (IBA, **1**) is one of the most important iodine(III) reagents commonly used as a mild oxidant and a precursor to the corresponding iodonium salts and other practically important derivatives of benziodoxole.[4] Compared to several other commercially available hypervalent iodine reagents, IBA has higher thermal stability, but much lower electrophilic reactivity. Reactions of IBA usually require activation by a strong protic acid (*e.g.*, H_2SO_4[5] or TfOH[6]). Due to the presence of strong acids in reaction mixtures, reactions of acid-activated IBA are limited exclusively to the non-acid-sensitive substrates. Structures of IBA adducts with sulfonic acids **2**[7] and **3**[8] were confirmed by X-ray analysis (Fig. 1). It was also reported that the reaction of IBA with trimethylsilyl triflate afforded triflyloxybenziodoxole **2a**.[9] However, attempts to isolate triflate **2a** led to the monohydrate (**2a**·H_2O),[9] whose composition is in agreement with structure **2**.

In this communication, we describe the in-situ generation and reactions of a highly electrophilic and nonacidic combination reagent IBA/trifluoromethanesulfonic anhydride. Previously, trifluoromethanesulfonic (triflic) anhydride was used for activation of iodosylbenzene, PhIO, generating highly electrophilic and synthetically useful Zefirov's reagent, PhIO·Tf_2O.[10]

Our initial experiments have demonstrated that in the presence of triflic anhydride, IBA can readily oxidize several organic substrates which are resistant to unactivated IBA (Scheme 1). The oxidation of sulfide **4** selectively afforded sulfoxide **5** in moderate yield. The oxidative rearrangement of α-methyl styrene **6** produced the corresponding product **7**. The reaction of aldoxime **8** with IBA/Tf_2O in acetonitrile at room temperature gave the corresponding 1,2,4-oxadiazole **9** in moderate yield. The oxidative dimerization of thiobenzamide **10** using IBA/Tf_2O afforded 3,5-diphenyl-1,2,4-thiadiazole **11** in good isolated yield. All these oxidations proceed under mild conditions similarly to the previously

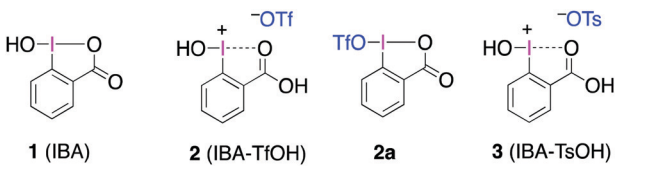

Fig. 1 2-Iodosylbenzoic acid (IBA, **1**) and IBA adducts with sulfonic acids (IBA-TfOH **2**, IBA-TsOH **3**, and triflyloxybenziodoxole **2a**).

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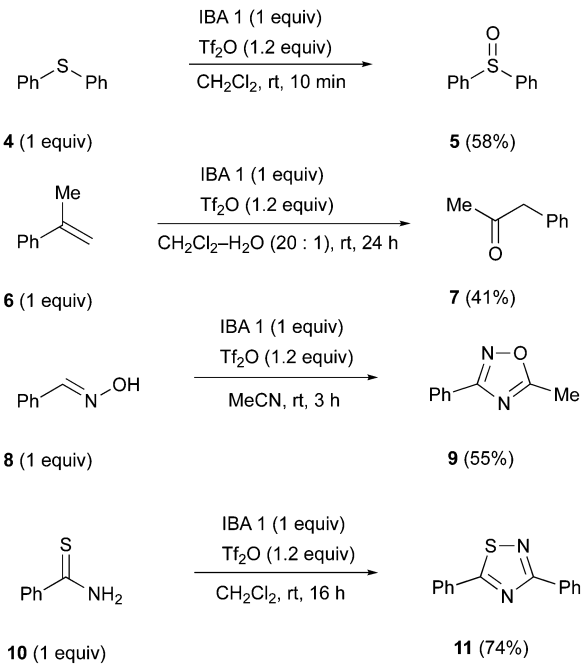


Scheme 1 Oxidations of organic substrates with IBA/Tf_2O.

reported reactions with isolated reagent **2**.[7] Most likely, compound **2** or related electrophilic triflate derivatives (*e.g.*, μ-oxo-type species, ArI(OTf)O(OTf)IAr) represent the actual active species generated in-situ from IBA and Tf_2O under reaction conditions.

Considering great importance of iodonium salts in academic and industrial research,[1–3] we have explored the use of IBA/Tf_2O as a powerful electrophilic reagent for preparation of the corresponding alkenyl- and aryliodonium salts.

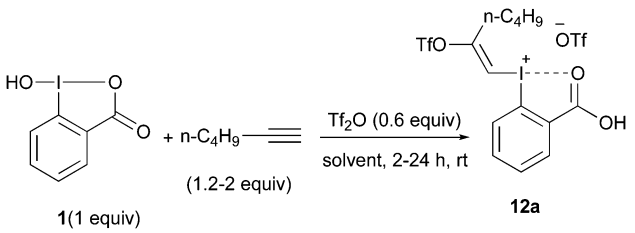
First, we have investigated the preparation of alkenyl derivatives of benziodoxolone by the reaction of IBA/Tf_2O with alkynes. Alkenylbenziodoxolones have attracted significant research interest as efficient reagents for electrophilic alkenylations of various substrates,[11] such as alkenylation of sulfur,[12a,b] oxygen,[12c] phosphine,[12d] or carbon atoms,[12e] and also alkenylation reactions using metal reagents.[12f–k] Several research groups have previously developed general synthetic procedures for the preparation of alkenylbenziodoxolones (or pseudocyclic alkenylbenziodoxolone derivatives) by reactions of activated IBA with alkynes,[12h–14] alkynylsilanes,[7] or alkenylboronic acids.[12a,e]

We have found that IBA **1** reacts with alkynes in the presence of Tf_2O at room temperature producing β-trifluorosulfonyloxy alkenylbenziodoxolones **12** as main products (Table 1, entries 1 and 2). We studied the optimization of reaction conditions using 1-hexyne in the presence of Tf_2O in various solvents (entries 3–9). The results showed that the reaction using dichloromethane gave the desired product **12a** in 93%. In terms of reaction time, we were able to obtain the desired product **12a** in 93% isolated yield at 4–8 hours (entries 10 and 11), but at a shorter reaction time of 2 hours, the product yield was slightly lower (entry 12). Importantly, this procedure works well for the preparation of pure product **12a** in gram scale (entry 11; see ESI,† for experimental details). Activation of IBA with Tf_2O is required; no reaction of 1-hexyne with IBA occurs in the absence of Tf_2O, or with Ac_2O, $(CF_3CO)_2O$, Ts_2O, or Ms_2O, and IBA was recovered from the reaction mixture (entries 13–16).

In the next step, we have utilized our optimized procedure for the preparation of pseudocyclic alkenylbenziodoxolones **12** from a broad range of alkynes **15**, IBA **1**, and also from substituted iodosylbenzoic acids **13** and **14** (Scheme 2). In general, the reactions of alkynes **15** with primary alkyl group gave the corresponding products **12a-f,n** in highest isolated yields (85–95%). Most notably, this mild procedure worked for the preparation of products **12h** and **12j** with sensitive ester and cyclopropyl substituents. Compared to the previously reported procedure using IBA/HOTf,[7,14] the new procedure gives generally higher yields of products **12** (for example, 13% better isolated yield for product **12a**).

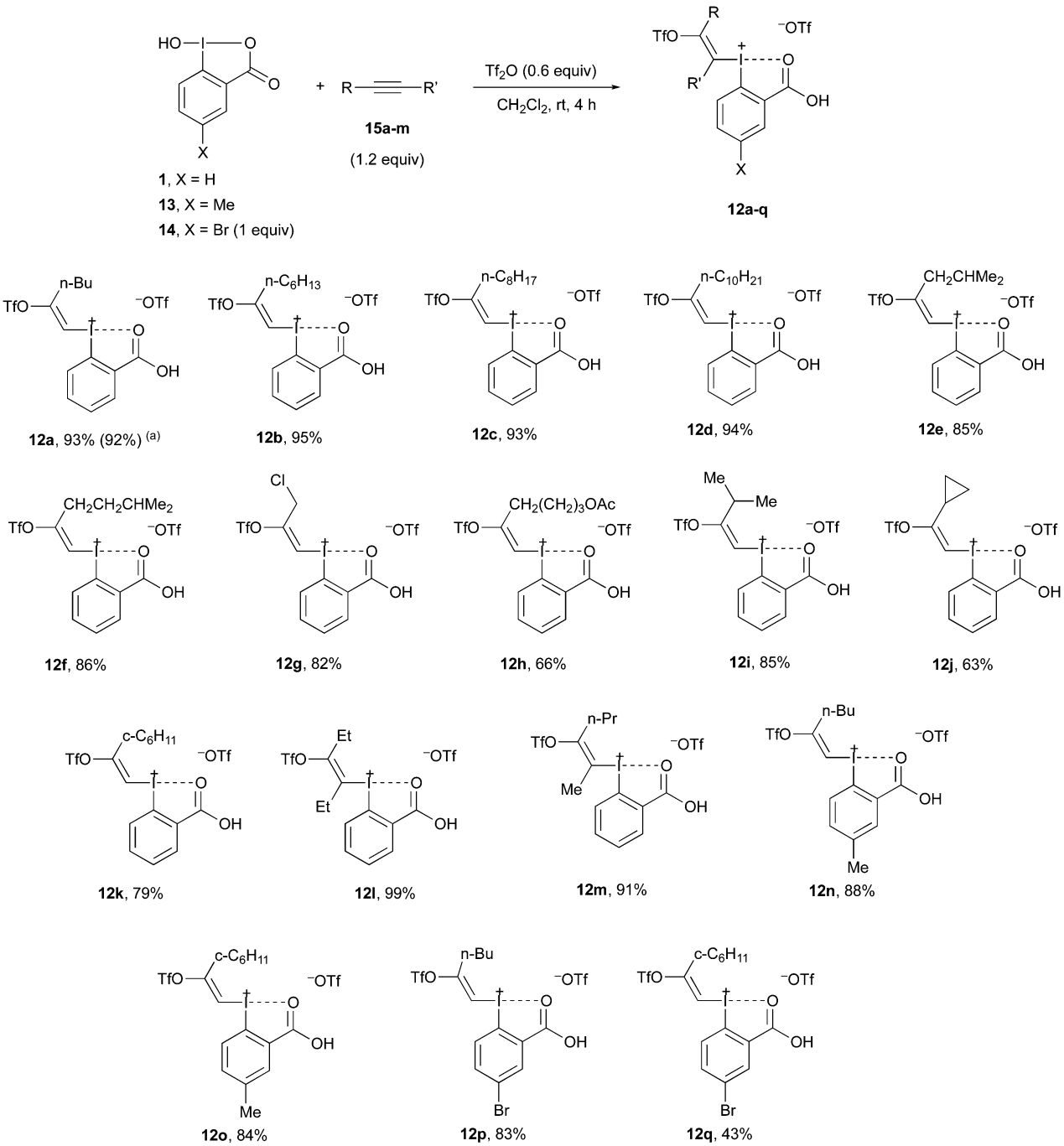
Finally, our new procedure works especially well for the efficient preparation of important phenyl benziodoxole derivatives **15–17** from iodosylbenzoic acids **1**, **13** or **14**, benzene, and Tf_2O in almost quantitative yields. A common benzyne precursor, phenylbenziodoxole,[15] can be easily obtained from iodonium salt **15** by simple treatment with $NaHCO_3$ (Scheme 3).[16]

Table 1 Optimization of the reaction of IBA/Tf_2O with 1-hexyne



Entry	1-Hexyne (equiv.)	Solvent	Time (h)	Yields[a]
1	2	CH_2Cl_2	24	90
2	1.5	CH_2Cl_2	24	90
3	1.2	CH_2Cl_2	24	93
4	1.2	$CHCl_3$	24	87
5	1.2	$ClCH_2CH_2Cl$	24	92
6	1.2	Heptane	24	74
7	1.2	AcOEt	24	93
8	1.2	THF	24	9
9	1.2	MeCN	24	72
10	1.2	CH_2Cl_2	8	93
11	1.2	CH_2Cl_2	4	93 (92)[b]
12	1.2	CH_2Cl_2	2	91
13[c]	1.2	CH_2Cl_2	24	0
14[d]	1.2	CH_2Cl_2	24	0
15[e]	1.2	CH_2Cl_2	24	0
16[f]	1.2	CH_2Cl_2	24	0

[a] Isolated yields. [b] Large scale reaction. [c] Using Ac_2O instead of Tf_2O. [d] Using $(CF_3CO)_2O$ instead of Tf_2O. [e] Using Ts_2O instead of Tf_2O. [f] Using Ms_2O instead of Tf_2O.



Scheme 2 Preparation of pseudocyclic alkenylbenziodoxolone derivatives **12** from alkynes **15** and IBA/Tf_2O. (a) Large scale reaction.

Conclusions

2-Iodosylbenzoic acid in the presence of trifluoromethanesulfonic anhydride is an efficient oxidant and electrophilic reagent useful for preparation of the corresponding alkenyl and aryliodonium salts. Compared to the previously reported methods of electrophilic activation of IBA, our procedure is compatible with acid-sensitive functional groups, requires mild reaction conditions, and affords products in higher yields.

Conflicts of interest

There are no conflicts to declare.

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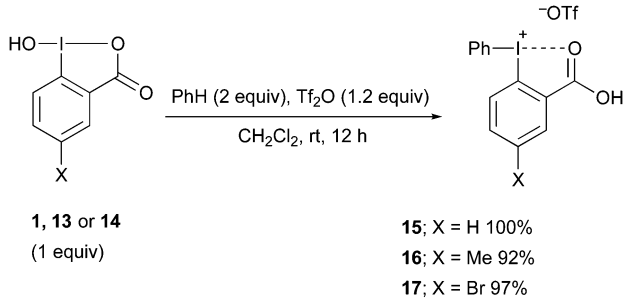

Scheme 3 Preparation of phenyl benziodoxole derivatives **15–17** from iodosylbenzoic acids **1**, **13** or **14**, benzene, and Tf_2O.

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