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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 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 arylodonium 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 [¹⁸F]-fluorinated radiotracers in the 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 benzeniodoxole.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., H₂SO₄⁵ or TfOH⁶). 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 (Figure 1). It was also reported that the reaction of IBA with trimethylsilyl

triflate afforded triflyloxybenzeniodoxole **2a**.⁹ However, attempts to isolate triflate **2a** led to the monohydrate (**2a**•H₂O),⁹ whose composition is in agreement with structure **2**.

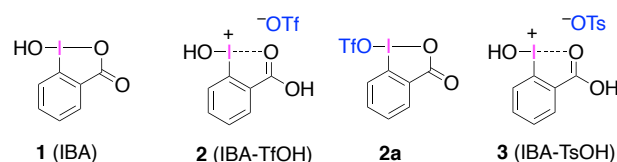


Fig. 1 2-Iodosylbenzoic acid (IBA, **1**) and IBA adducts with sulfonic acids (IBA-TfOH **2**, IBA-TsOH **3**, and triflyloxybenzeniodoxole **2a**).

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•Tf₂O.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/Tf₂O in acetonitrile at room temperature gave the corresponding 1,2,4-oxadiazole **9** in moderate yield. The oxidative dimerization of thiobenzamide **10** using IBA/Tf₂O afforded 3,5-diphenyl-1,2,4-thiadiazole **11** in good isolated yield. All these oxidations proceed under mild conditions similarly to the previously 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 Tf₂O under reaction conditions.

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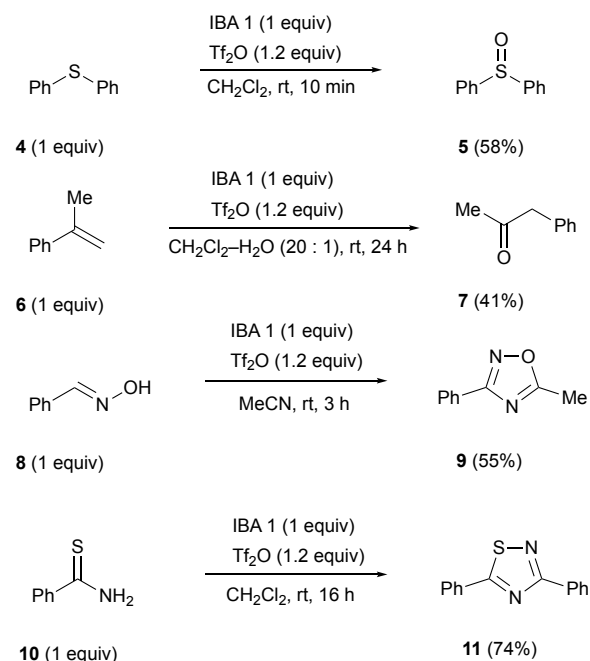
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COMMUNICATION

Journal Name



Scheme 1 Oxidations of organic substrates with IBA/Tf₂O.

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Considering great importance of iodonium salts in academic and industrial research,¹⁻³ we have explored the use of IBA/Tf₂O as a powerful electrophilic reagent for preparation of the corresponding alkenyl- and arylodonium salts.

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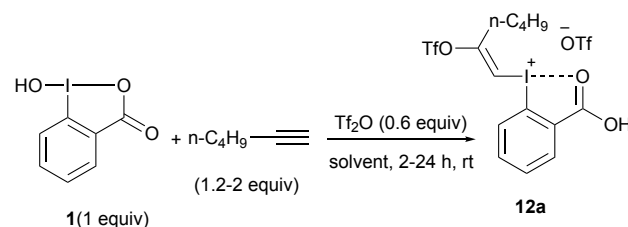
First, we have investigated the preparation of alkenyl derivatives of benziodoxolone by the reaction of IBA/Tf₂O with alkynes. Alkenylbenziodoxolones have attracted significant research interest as efficient reagents for electrophilic alkenylations of various substrates,¹¹ such as alkenylation of sulfur,^{12a,b} 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,13,14} alkynylsilanes,⁷ or alkenylboronic acids.^{12a,e}

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We have found that IBA **1** reacts with alkynes in the presence of Tf₂O at room temperature producing β-trifluorosulfonyloxy alkenylbenziodoxolones **12** as main products (Table 1, entries 1,2). We studied the optimization of reaction conditions using 1-hexyne in the presence of Tf₂O 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, 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 SI for experimental details). Activation of IBA with Tf₂O is required; no reaction of 1-hexyne with IBA occurs in the absence of Tf₂O, or when Ac₂O, (CF₃CO)₂O, Ts₂O, or Ms₂O, and IBA was recovered from the reaction mixture (entries 13-16).

Table 1 Optimization of the reaction of IBA/Tf₂O with 1-hexyne



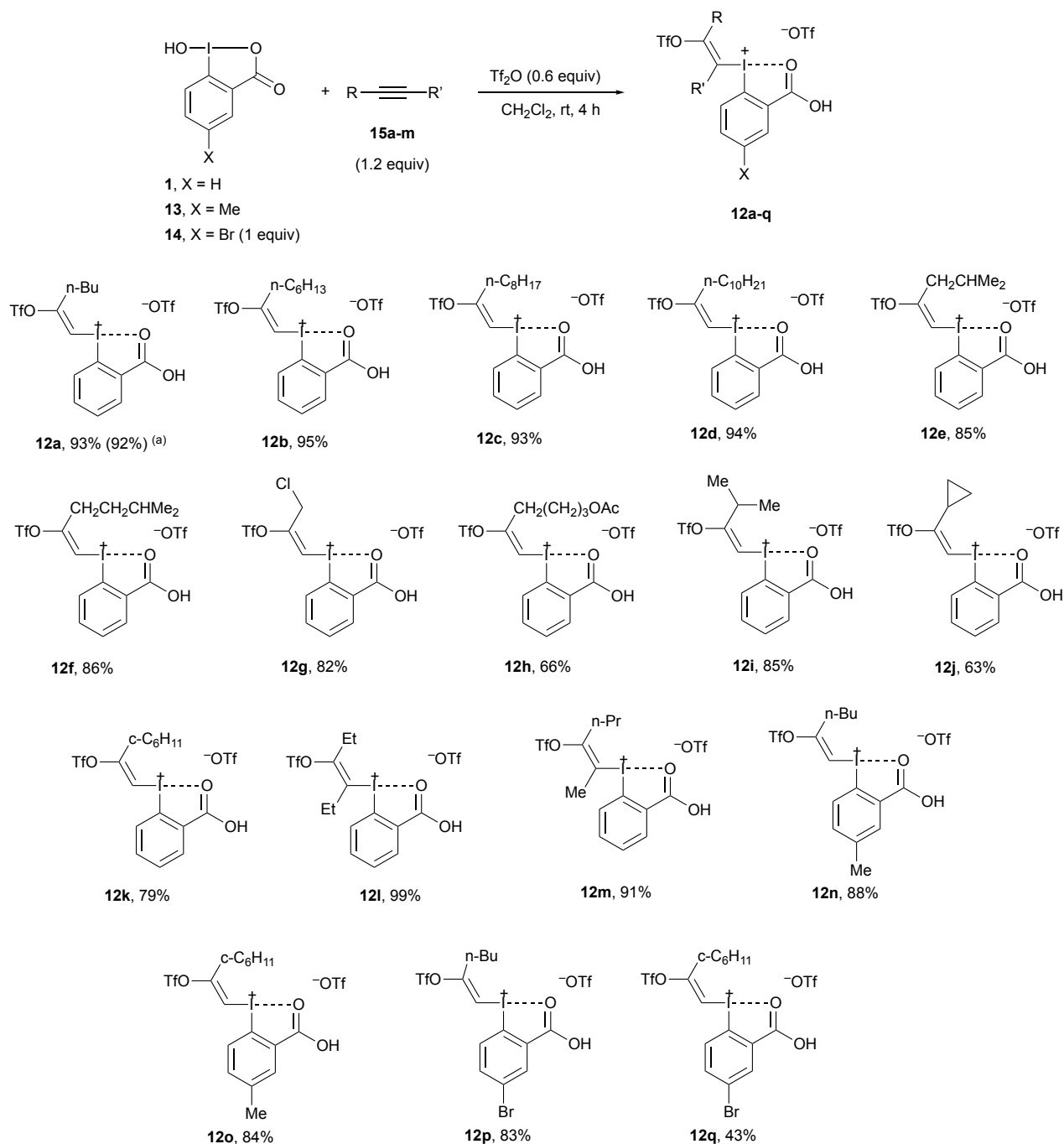
Entry	1-Hexyne (equiv)	Solvent	Time (h)	Yields (a)
1	2	CH ₂ Cl ₂	24	90
2	1.5	CH ₂ Cl ₂	24	90
3	1.2	CH ₂ Cl ₂	24	93
4	1.2	CHCl ₃	24	87
5	1.2	ClCH ₂ CH ₂ Cl	24	92
6	1.2	Heptane	24	74
7	1.2	AcOEt	24	93
8	1.2	THF	24	9
9	1.2	MeCN	24	72
10	1.2	CH ₂ Cl ₂	8	93
11	1.2	CH ₂ Cl ₂	4	93 (92) ^(b)
12	1.2	CH ₂ Cl ₂	2	91
13 ^(c)	1.2	CH ₂ Cl ₂	24	0
14 ^(d)	1.2	CH ₂ Cl ₂	24	0
15 ^(e)	1.2	CH ₂ Cl ₂	24	0
16 ^(f)	1.2	CH ₂ Cl ₂	24	0

(a) Isolated yields. (b) Large scale reaction. (c) Using Ac₂O instead of Tf₂O. (d) Using (CF₃CO)₂O instead of Tf₂O. (e) Using Ts₂O instead of Tf₂O. (f) Using Ms₂O instead of Tf₂O.

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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 **12 a-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**).

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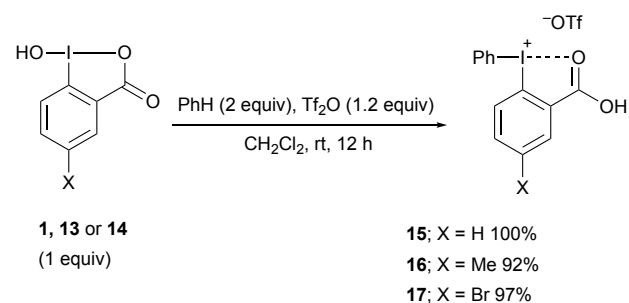


Scheme 2 Preparation of pseudocyclic alkenylbenziodoxolone derivatives **12** from alkyne **15** and IBA/ Tf_2O . (a) Large scale reaction.

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 .¹⁶



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

Conclusions

2-Iodosylbenzoic acid in the presence of trifluoromethanesulfonyl anhydride is an efficient oxidant and electrophilic reagent useful for preparation of the corresponding alkenyl and aryl-iodonium 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.

Acknowledgements

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Notes and references

- For recent books, see: (a) B. Olofsson, I. Marek and Z. Rappoport, eds., *Patai's Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds*, Wiley, Chichester (UK), 2019. (b) T. Wirth, ed., *Hypervalent Iodine Chemistry: Modern Developments in Organic Synthesis*. *Top. Curr. Chem.* **373**, Springer, 2016. (c) V. V. Zhdankin, *Hypervalent Iodine Chemistry: Preparation, Structure, and Synthetic Applications of Polyvalent Iodine Compounds*, Wiley, Chichester (UK), 2013.
- Recent reviews: (a) D. P. Hari, P. Caramenti and J. Waser, *Acc. Chem. Res.*, 2018, **51**, 3212-3225. (b) A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328-3435. (c) J. Charpentier, N. Fruh and A. Togni, *Chem. Rev.*, 2015, **115**, 650-682. (d) V. V. Zhdankin, *ARKIVOC*, 2020, (**iv**), 1-11. (e) D. P. Hari, P. Caramenti and J. Waser, *Acc. Chem. Res.*, 2018, **51**, 3212-3225. (f) J. Waser, *Synlett*, 2016, **27**, 2761-2773. (g) Y. Li, D. P. Hari, M. V. Vita and J. Waser, *Angew. Chem., Int. Ed.*, 2016, **55**, 4436-4454. (h) X. Huang and J. T. Groves, *ACS Catal.*, 2016, **6**, 751-759. (i) X. Wang and A. Studer, *Acc. Chem. Res.*, 2017, **50**, 1712-1724. (j) M. S. Yusubov, P. Postnikov, A. Yoshimura and V. V. Zhdankin, *Synlett*, 2020, **31**, 315-326. (k) A. Olding and C. C. Ho, *Aust. J. Chem.*, 2019, **72**, 646-648.
- A. Vaish and N. V. Tsarevsky, eds., *Hypervalent Iodine Compounds in Polymer Science and Technology*, John Wiley & Sons, Inc., 2018.
- 1-Hydroxy-1,2-Benziodoxol-3(1H)-One. V. V. Zhdankin in: *Encyclopedia of Reagents for Organic Synthesis*. Fuchs, P.L. Ed., John Wiley & Sons, Ltd., Chichester, England, **2020**.
- H. E. Folsom and J. Castrillon, *Synth. Commun.*, 1992, **22**, 1799-1806.
- A. Yoshimura, K. C. Nguyen, S. C. Klaseen, P. S. Postnikov, M. S. Yusubov, A. Saito, V. N. Nemykin and V. V. Zhdankin, *Asian J. Org. Chem.*, 2016, **5**, 1128-1133.
- A. Yoshimura, K. C. Nguyen, S. C. Klaseen, A. Saito, V. N. Nemykin and V. V. Zhdankin, *Chem. Commun.*, 2015, **51**, 7835-7838.
- A. Yoshimura, S. C. Klaseen, M. T. Shea, K. C. Nguyen, G. T. Rohde, A. Saito, P. S. Postnikov, M. S. Yusubov, V. N. Nemykin and V. V. Zhdankin, *Chem. - Eur. J.*, 2017, **23**, 691-695.
- V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz and A. J. Simonsen, *J. Org. Chem.*, 1996, **61**, 6547-6551.
- M. S. Yusubov and V. V. Zhdankin, *Mendeleev Commun.*, 2021, **31**, 282-287.
- For a review on synthetic applications of alkenylbenziodoxoles, see: N. Declas, G. Pisella and J. Waser, *Helv. Chim. Acta*, 2020, **103**, e2000191.
- (a) L. Castoldi, E. M. Di Tommaso, M. Reitti, B. Graefen and B. Olofsson, *Angew. Chem., Int. Ed.*, 2020, **59**, 15512-15516. (b) B. Liu, J. V. Alegre-Requena, R. S. Paton and G. M. Miyake, *Chem. - Eur. J.*, 2020, **26**, 2386-2394. (c) N. Declas and J. Waser, *Angew. Chem., Int. Ed.*, 2020, **59**, 18256-18260. (d) L. Castoldi, A. A. Rajkiewicz and B. Olofsson, *Chem. Commun.*, 2020, **56**, 14389-14392. (e) E. Stridfeldt, A. Seemann, M. J. Bouma, C. Dey, A. Ertan and B. Olofsson, *Chem. - Eur. J.*, 2016, **22**, 16066-16070. Representative reaction using metal reagents: (f) G. Pisella, A. Gagnebin and J. Waser, *Org. Lett.*, 2020, **22**, 3884-3889. (g) J. Wu, X. Deng and N. Yoshikai, *Chem. - Eur. J.*, 2019, **25**, 7839-7842. (h) J. Wu, K. Xu, H. Hirao and N. Yoshikai, *Chem. - Eur. J.*, 2017, **23**, 1521-1525. (i) A. Boelke, L. D. Caspers and B. J. Nachtsheim, *Org. Lett.*, 2017, **19**, 5344-5347. (j) W. Ding, J. Chai, C. Wang, J. Wu and N. Yoshikai, *J. Am. Chem. Soc.*, 2020, **142**, 8619-8624. (k) P. Caramenti, N. Declas, R. Tessier, M. D. Wodrich and J. Waser, *Chem. Sci.*, 2019, **10**, 3223-3230.
- (a) R. A. Laskar, W. Ding and N. Yoshikai, *Org. Lett.*, 2021, **23**, 1113-1117. (b) B. Wu, J. Wu and N. Yoshikai, *Chem. - Asian J.*, 2017, **12**, 3123-3127.
- A. Yoshimura, C. D. Huss, M. Liebl, G. T. Rohde, S. M. Larson, G. B. Frahm, M. W. Luedtke, T. J. Schumacher, Z. S. Gardner, V. V. Zhdankin, P. S. Postnikov, M. S. Yusubov, T. Kitamura and A. Saito, *Adv. Synth. Catal.*, 2021, **363**, 3365-3371.
- L. F. Fieser and M. J. Haddadin, *Org. Synth.*, 1966, **46**, 107-112.
- A. Yoshimura, S. M. Larson, G. B. Frahm, C. D. Huss, G. T. Rohde, V. N. Nemykin, M. S. Yusubov, A. Saito and V. V. Zhdankin, *ARKIVOC*, 2020, (**iv**), 35-49.