Published in final edited form as:

European J Org Chem. 2015 September 1; 2015(27): 5919–5924.

A Mild and General One-Pot Synthesis of Densely Functionalized Diaryliodonium Salts

Dr. Linlin Qin^{[a],†}, Dr. Bao Hu^{[a],[b],†}, Dr. Kiel D. Neumann^[a], Ethan J. Linstad^[a], Katelyenn McCauley^[a], Jordan Veness^[a], Jayson J. Kempinger^[a], and Prof. Dr. Stephen G. DiMagno^[a]

Stephen G. DiMagno: sdimagno1@unl.edu

^[a]Department of Chemistry & Nebraska Center for Materials and Nanoscience, University of Nebraska, Lincoln, Nebraska 68588-0304 (USA), <http://chem.unl.edu/dimagno-group>

^[b]Institute of Industrial Catalysis, College of Chemical Engineering, Zhejiang University of Technology, Hangzhou, Zhejiang 310014 (China)

Abstract

Diaryliodonium salts are powerful and widely used arylating agents in organic chemistry. Here we report a scalable, synthesis of densely functionalized diaryliodonium salts from aryl iodides under mild conditions. This two-step, one-pot process has remarkable functional group tolerance, is compatible with commonly employed acid-labile protective group strategies, avoids heavy metal and transition metal reagents, and provides a direct route to stable precursors to PET imaging agents.

Keywords

iodane synthesis; oxidation; diaryliodonium salts; SelectfluorTM; aryl iodides

Although diaryliodonium salts (diaryl- λ^3 -iodanes) were discovered more than a century ago,^[1] their study is undergoing a renaissance in organic chemistry, where they serve as powerful, and widely applicable, arylation reagents.^[2–5] These compounds arylate a multitude of organic and inorganic nucleophiles to provide functionalized arenes in excellent yields. In particular, the use of diaryliodonium salts as precursors to radiopharmaceuticals is an area of increasingly active research;^[6] Sanford and Scott,^[7] Pike,^[8] Coenen,^[9] DiMagno,^[10] and other groups^[11] have all demonstrated successful conversion of diaryliodonium salt precursors into ¹⁸F-labeled compounds for PET imaging.

Regiospecific methods to synthesize unsymmetrical diaryliodonium salts generally proceed through ArI(III) intermediates, which are generated either by oxidation of an aryl iodide or by addition of an I(III) electrophile to an aromatic compound. The second step involves

Correspondence to: Stephen G. DiMagno, sdimagno1@unl.edu.

[†]These authors contributed equally to this work.

Disclosures

The chemistry reported here is the subject of patent applications (PCT/US 2013/066830, WO 2014/066772) which have been licensed to Ground Fluor Pharmaceuticals, Inc., of Lincoln, NE (GFP). SGD and KDN are shareholders in GFP.

Supporting information for this article is given via a link at the end of the document.

coupling the electrophilic ArIX_2 reagent with a second aryl moiety, either by ligand exchange with an aryl organometallic nucleophile (Ar-B(OH)_2 , ArSnR_3 , ArSiMe_3 , ArZnCl , ArBF_3K), or by electrophilic aromatic substitution of an electron-rich arene.^[2a,12] One-pot oxidation and ligand exchange reactions to synthesize diaryliodonium salts directly from arenes and iodoarenes have also been reported.^[13] These approaches have been reviewed in detail by Merritt and Olofsson (Scheme 1).^[2b] Preparation of the ArIX_2 electrophile typically involves an oxidation under acidic conditions.

Driven by our interest in synthesizing radiofluorinated agents for positron emission tomography (PET) imaging,^[10] we sought a general, one-pot method for preparing diverse diaryliodonium salts directly from the protected parent pharmaceuticals. Important parameters that need to be satisfied for the synthesis of radiopharmaceutical precursors are 1) functional group tolerance, 2) compatibility with commonly employed acid-labile protective group strategies, 3) the avoidance, at every step of the synthesis, of heavy metal reagents that could impact long term stability of the diaryliodonium salts or react with trace ^{18}F -fluoride during labeling procedures, and 4) scalability. These restrictions are actually quite onerous, as is illustrated in Scheme 2 for the retrosynthesis of an unsymmetrical diaryliodonium salt derived from phenylalanine. Path A dictates an extremely mild oxidation process to satisfy restrictions 1 and 2, while path B requires generation an organometallic reagent under weakly basic conditions, and without the assistance of transition metal catalysis, to satisfy restrictions 1 and 3. While multistep workarounds for each of these restrictions may be possible, a direct route involving in situ oxidation of the suitably protected 4-iodophenylalanine followed by treatment with an organometallic reagent is clearly preferred.

In 2005, Shreeve^[14] and coworkers reported that iodoarenes could be oxidized smoothly under neutral conditions with 2 eq. of SelectfluorTM (F-TEDA-2BF_4 , Scheme 3), but that the ArIF_2 products formed proved to be too unstable to isolate in good yield. Importantly, they noted that yields of isolated ArI(III) species could be increased significantly in carboxylic acid solvents. Kita^[15] and Ishihara^[16] have also reported preparations of ArI(III) reagents with F-TEDA-2BF_4 under acidic conditions. Guided by these promising results, we reinvestigated the F-TEDA-2BF_4 oxidation of aryl iodides with the aim of developing a protic-acid-free route to stable, yet reactive ArI(III) electrophiles. Our strategy to achieve this goal was simply to replace the proton in acetic or trifluoroacetic acid with a fluorophilic Lewis acid. These efforts led to a direct, one-pot synthesis of unsymmetrical diaryliodonium salts that is centered on oxidation of the “valuable,” densely-functionalized aryl ligand.

Surprisingly, treatment of 4-methoxyiodobenzene **1a** with a mixture of F-TEDA-2BF_4 (1.3 eq.) and trimethylsilyl acetate (TMSOAc , 2.6 eq.) in CD_3CN provided stable 4-methoxyphenyliodonium diacetate **2a** in almost quantitative yield, *along with 2 full equivalents of trimethylsilyl fluoride (TMSF)*. In contrast, when the oxidation was performed under identical conditions, except that the hexafluorophosphate salt of SelectfluorTM (F-TEDA-2PF_6) was employed, an unstable oxidation product formed, which gradually decomposed. In addition, an excess of TMSOAc remained at the end of the reaction. The resemblance of the TEDA-2PF_6 oxidation to Shreeve's “acid-free” $\text{F-TEDA-2BF}_4/\text{CH}_3\text{CN}$ oxidation was striking; these data suggested that the tetrafluoroborate

counterion (BF_4) played a key role in stabilizing the oxidation product by serving as a source of fluoride (Scheme 4).

Support for the proposed mechanism is found in the appearance of new signals, derived from multiple fluoroborate species, in the ^{19}F NMR spectrum of the reaction mixture, and from multiple signals arising from coordinated diazabicyclo[2.2.2]octane in the ^1H NMR spectrum. Addition of tetrabutylammonium tetrafluoroborate (TBABF_4) to oxidations performed with F-TEDA- 2PF_6 proceeded in excellent yields with generation of the full 2 equivalents of TMSF , providing support for the critical role of BF_4 in facilitating formation of **2a**. The proposed mechanism is also consistent with the lower fluoride affinity of BF_3 ($\text{pF} = 8.31$) compared to PF_5 ($\text{pF} = 9.49$)^[17], and suggests that the fluoride affinity of cationic ArIF derivatives is on a par with boron trifluoride, and may be reversible. Additional control experiments in which TMSOAc was combined with F-TEDA- 2BF_4 , with TBABF_4 , or even TBABF_4 in combination with 4-methoxyphenyliodonium diacetate did not generate any TMSF ; these results are consistent with a cationic ArIF species acting as the fluoride transfer agent.

A brief survey of the oxidation conditions (Table 1) showed that a variety of electron-rich and electron-poor arenes could be oxidized smoothly to (diacetoxyiodo)arenes, **2**, at or near room temperature; the electron-poor arenes required slightly more aggressive conditions to complete the oxidation. Reactions performed in CD_3CN and monitored by ^1H NMR spectroscopy indicated that the oxidation proceeded in excellent yield (>90%) in all cases; some losses were associated with the subsequent isolation of the $\text{ArI}(\text{OAc})_2$ products. Importantly, the straightforward preparation of **2g** (Scheme 5) shows that the oxidation occurs under effectively neutral conditions; BOC protecting groups are not cleaved during this process.

The losses associated with purification and isolation of (diacetoxyiodo)arenes made a direct, one-pot diaryliodonium salt synthesis an attractive goal. Potassium (4-methoxyphenyl)trifluoroborate, AnBF_3K , was selected as the nucleophilic coupling partner because 1) anisole has been shown to be an excellent “dummy” directing group for a variety of arylation reactions, and 2) aryl transfer to any trifluoroborane generated during the oxidation step would regenerate the reagent.

Initial NMR-tube scale reactions (dry CD_3CN , iodoarenes **1a–1hh**) indicated that efficient SelectfluorTM oxidation of diverse iodoarenes in the presence of TMSOAc was efficient (>80% yield) and relatively rapid (2 – 48 h) at or near room temperature (See Supporting Information). Upon completion of the oxidation, AnBF_3K , which resulted in no observable reaction; the reaction mixtures were treated with one equivalent of (diacetoxyiodo)arenes are insufficiently electrophilic to engage this aryl nucleophile. Formation of the diaryliodonium salt commenced immediately after the addition of a CD_3CN solution of either trimethylsilyl trifluoroacetate (TMSTFA) or trimethylsilyl triflate (TMSOTf), and was complete within 10 minutes at room temperature. (As we have shown previously, a ligand exchange reaction between iodine and silicon $[\text{ArI}(\text{OAc})_2 + \text{TMSX} \leftrightarrow \text{ArI}(\text{OAc})(\text{X}) + \text{TMSOAc}]$ creates a Lewis acid buffer system that can be used to tune the electrophilicity of the $\text{I}(\text{III})$ center over

a significant range.)^[18] Iodine arylation with AnBF₃K proceeded in excellent yield (> 95%) in all cases.

To demonstrate the practicality of the method, we prepared a relatively large number of unsymmetrical diaryliodonium triflates and hexafluorophosphates (Scheme 6). These compounds, which were selected largely for their potential use as radiosynthesis precursors, featured acid-sensitive (**3(g, h, I, n, t, u, v, aa–ff)**) and base-sensitive (**3(t–y, aa–ee)**) functionality. The larger scale reactions followed the procedure described above for the NMR tube reactions, except that an aqueous work-up, ion-exchange, and recrystallization of the products were performed (see Supporting Information). Significant losses were incurred during the isolation and recrystallization of some of the products, but even quite densely functionalized compounds could be prepared successfully on a multigram scale.

Although most of the reactions reported in Scheme 6 were performed using glove box techniques, the use of rigorously anhydrous conditions and highly purified reagents and solvents are not required. For example, **3t** was synthesized on the benchtop under nitrogen using as received reagents, and the yields were comparable to those obtained under rigorously dry conditions. In fact, the method is robust enough to be transferred to pilot plant facilities; as an example, a cGMP synthesis of a 100 gram lot of **3v**, a diaryliodonium salt precursor to ¹⁸F-6-fluoro-L-DOPA^[10a,10b] was recently completed^[19] by a commercial concern. The reason this system tolerates the presence of adventitious moisture is that the oxidation generates its own acetate buffer if water is present during the course of the reaction. If extremely acid-sensitive functional groups are present in the molecule, additional leeway for the generation of Brønsted acids from water can be gained by adding N-chloromethyldiazabicyclo[2.2.2]octane tetrafluoroborate (CH₂Cl-DABCO) at the beginning of the reaction. This compound, which is also generated in situ during the initial oxidation reaction, is a mild and non-reducing tertiary amine base that can scavenge small amounts of protic acid side products, if desired.

The scalable, heavy-metal-free, one-pot, two step synthesis of diaryliodonium salts described here has a remarkable functional group tolerance, and is compatible with commonly employed acid-labile protective group strategies. Unsymmetrical diaryliodonium salts possessing quite reactive functionalities, including succinimidyl esters and maleimides typically used for bioconjugation, may be synthesized with relative ease from their parent aryl iodides. This improved capability should streamline the development of diaryliodonium salts from complex, pharmaceutically relevant aromatic compounds and expand the scope of potential arylation reagents available for organic synthesis. Moreover, given the increasing importance of diaryliodonium salts as precursors to ¹⁸F-fluorinated radiopharmaceuticals, this simple methodology provides a direct route to stable precursors to PET imaging agents.

Experimental Section

Typical procedure for the benchtop, one-pot synthesis of a diaryliodonium salt **3t**: Under an atmosphere of dry nitrogen, methyl (*S*)-2-(di-(*tert*-butoxycarbonyl)amino)-3-(4-iodophenyl)propanoate (3.0 mmol, 1.52 g, 1.0 eq.), SelectfluorTM (3.9 mmol, 1.39 g, 1.3 eq.) and 15 mL of dry CH₃CN were introduced to an oven-dried Schlenk flask. A solution of

TMSOAc (7.8 mmol, 1.03 g, 2.6 eq.) in dry CH₃CN (5 mL) was added by syringe dropwise with stirring. This colorless mixture was stirred at room temperature for 24 h; a ¹H NMR spectrum obtained from a withdrawn aliquot confirmed that the oxidation had reached >90% at this time. Solid potassium (4-methoxyphenyl)trifluoroborate (0.64 g, 3.0 mmol, 1.0 equiv.) was added directly to the flask against a flow of nitrogen. Once the added solid was dissolved and a homogeneous mixture was obtained (3 minutes), a solution of TMSOTf (0.67 g, 2.7 mmol, 0.9 eq.) in 10.0 mL of dry CH₃CN was added dropwise by syringe and the yellowish mixture was allowed to stir at room temperature for 10 min. The solvents were removed under reduced pressure and 100 mL of 0.1 M acetate buffer (pH = 5) was added. The mixture was extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were added to a separatory funnel and washed with water (50 mL), and the wash water was extracted further (2 × 50 mL) with CH₂Cl₂. The combined organic extracts were dried over sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The residue was placed under dynamic vacuum to obtain a yellow-tinged foam. This solid was dissolved in 10.0 mL ethyl acetate and added dropwise to a mixture of MTBE and hexane (1:4) to precipitate the diaryliodonium triflate product. The obtained solid was dissolved in 1 mL acetonitrile/water (9: 1 by volume) solution and passed down an Amberlite IRA-400 ion exchange column (triflate counterion). After removal of the solvents under reduced pressure, the purified iodonium triflate product (1.89 g, 83%) of was obtained as a colorless solid. ¹H NMR (CD₃CN, 400 MHz): δ 8.02 (d, *J* = 9.1 Hz, 2 H), 7.96 (d, *J* = 8.4 Hz, 2 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.05 (d, *J* = 9.1 Hz, 2 H), 5.16 (dd, *J*₁ = 10.9 Hz, *J*₂ = 4.8 Hz, 1 H), 3.84 (s 3 H), 3.70 (s, 3 H), 3.43 (dd, *J*₁ = 14.0 Hz, *J*₂ = 4.8 Hz, 1 H), 3.21 (dd, *J*₁ = 14.0 Hz, *J*₂ = 10.9 Hz, 1 H), 1.27 (s, 18 H); ¹³C NMR (CD₃CN, 176 MHz) δ 170.2, 163.4, 151.6, 143.7, 137.8, 134.9, 133.6, 122.0, 120.2, 118.2, 111.6, 101.5, 83.1, 58.6, 55.8, 52.1, 35.3, 27.0; ¹⁹F NMR (CD₃CN, 376 MHz): δ -79.3 (s, 3 F); HRMS: (ESI) calcd. for C₂₇H₃₅INO₇ [M-OTf]⁺ 612.1458; found: 612.1453.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Research reported in this publication was supported by Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health under award number R01 EB015536. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Bao Hu also thanks the National Natural Science Foundation of China (No. 21202148) for support.

References

1. Hartmann C, Meyer V. Ber. 1894; 27:502.
2. Reviews: Bellina F, Rossi R. Tetrahedron. 2009; 65:10269. Merritt EA, Olofsson B. Angew Chem Int Ed. 2009; 48:9052. Yusubov MS, Maskav AV, Zhdankin VV. ARKIVOC. 2011; (i):370. Rousseaux S, Vrancken E, Campagne JM. Angew Chem, Int Ed. 2012; 51:10934. Grushin VV. Chem Soc Rev. 2000; 29:315. Deprez, Nicholas R.; Sanford, Melanie S. Inorg Chem. 2007; 46:1924. [PubMed: 17348723]
- 3.

Selected recent tandem arylation of diaryliodonium salts, see: Chen J, Chen C, Chen J, Gao H, Qu H. *Synlett*. 2014; 25:2721. Li J, Wang H, Sun J, Yang Y, Liu L. *Org Biomol Chem*. 2014; 12:7904. [PubMed: 25223479] Li P, Cheng G, Zhang H, Xu X, Gao J, Cui X. *J Org Chem*. 2014; 79:8156. [PubMed: 25109616] Li X, Xu J, Zhang P, Gao Y, Wu J, Tang G, Zhao Y. *Synlett*. 2014; 25:2009. Liu F, Yang H, Hu X, Jiang G. *Org Lett*. 2014; 16:6408. [PubMed: 25473728] Pang X, Chen C, Su X, Li M, Wen L. *Org Lett*. 2014; 16:6228. [PubMed: 25420123] Guo W, Li S, Tang L, Li M, Wen L, Chen C. *Org Lett*. 2015; 17:1232. [PubMed: 25719267] Modha SG, Greaney MF. *J Am Chem Soc*. 2015; 137:1416. [PubMed: 25588092] Pang X, Lou Z, Li M, Wen L, Chen C. *Eur J Org Chem*. 2015:3361. Yang Y, Han J, Wu X, Xu S, Wang L. *Tetrahedron Lett*. 2015; 56:3809.

4.

Selected recent examples of transition-metal-catalyzed arylation of diaryliodonium salts, see:

Malmgren J, Nagendiran A, Tai CW, Baekvall JE, Olofsson B. *Chem Eur J*. 2014; 20:13531. [PubMed: 25169833] Prakash M, Muthusamy S, Kesavan V. *J Org Chem*. 2014; 79:7836. [PubMed: 25111372] Bhattacharai B, Tay JH, Nagorny P. *Chem Commun*. 2015; 51:5398. Margraf N, Manolikakes G. *J Org Chem*. 2015; 80:2582. [PubMed: 25650485] Chen J, Chen C, Chen J, Wang G, Qu H. *Chem Commun*. 2015; 51:1356. Moon SY, Koh M, Rathwell K, Jung SH, Kim WS. *Tetrahedron*. 2015; 71:1566. Iyanaga M, Aihara Y, Chatani N. *J Org Chem*. 2014; 79:11933. [PubMed: 25162768] Cahard E, Male HPJ, Tissot M, Gaunt MJ. *J Am Chem Soc*. 2015; 137:7986. [PubMed: 26090564]

5.

Selected recent examples of transition-metal-free arylation of diaryliodonium salts, see: Castro LCM,

Chatani N. *Synthesis*. 2014; 46:2312. Senaweera SM, Weaver JD. *J Org Chem*. 2014; 79:10466. [PubMed: 25271542] Thorat PB, Waghmode NA, Karade NN. *Tetrahedron Lett*. 2014; 55:5718. Wang D, Ge B, Li L, Shan J, Ding Y. *J Org Chem*. 2014; 79:8607. [PubMed: 25171579] Wang D, Yu X, Zhao K, Li L, Ding Y. *Tetrahedron Lett*. 2014; 55:5739. Yang Y, Wu X, Han J, Mao S, Qian X, Wang L. *Eur J Org Chem*. 2014:6854. Chan L, McNally A, Toh QY, Mendoza A, Gaunt MJ. *Chem Sci*. 2015; 6:1277. Riedmueller S, Nachtsheim BJ. *Synlett*. 2015; 26:651. Sundalam SK, Stuart DR. *J Org Chem*. 2015; 80:6456. [PubMed: 26020831] Tinnis F, Stridfeldt E, Lundberg H, Adolfsson H, Olofsson B. *Org Lett*. 2015; 17:2688. [PubMed: 25966029] Mao S, Geng X, Yang Y, Qian X, Wu S, Hanb J, Wang L. *RSC Adv*. 2015; 5:36390.

6.

(a) For reviews of radiochemistry with diaryliodonium salt, see: Yusubov MS, Yu Svitich D, Larkina MS, Zhdankin VV. *ARKIVOC*. 2013; (i):364. Kovac M, Mavel S, Anderluh M. *Curr Org Chem*. 2013; 17:2921. Cai L, Lu S, Pike VW. *Eur J Org Chem*. 2008:2853.

7. a) Ichiishi N, Brooks AF, Topczewski JJ, Rodnick ME, Sanford MS, Scott PJH. *Org Lett*. 2014; 16:3224. [PubMed: 24890658] b) Ichiishi N, Canty AJ, Yates BF, Sanford MS. *Organometallics*. 2014; 33:5525. [PubMed: 25328272]

8. a) Pike VW, Aigbirio FI. *J Chem Soc Chem Commun*. 1995:2215. b) Shah A, Pike VW, Widdowson DA. *J Chem Soc Perkin Trans*. 1998; 1:2043. c) Chun J-H, Pike VW. *Eur J Org Chem*. 2012:4541. d) Chun JH, Pike VW. *Chem Commun*. 2012; 48:9921. e) Chun J-H, Pike VW. *Org Biomol Chem*. 2013; 11:6300. [PubMed: 23942997] f) J.-H. Chun, S. Lu.; V. W. Pike, *Eur. J. Org. Chem*. 2011, 4439; g) Chun J-H, Lu S, Lee Y-S, Pike VW. *J Org Chem*. 2010; 75:3332. [PubMed: 20361793]

9. a) Ross TL, Ermert J, Hocke C, Coenen HH. *J Am Chem Soc*. 2007; 129:8018. [PubMed: 17536798] b) Helfer A, Meleán JC, Ermert J, Infantino A, Coenen HH. *Appl Radiat Isot*. 2013; 82:264. [PubMed: 24100001] c) Ross TL, Ermert J, Coenen HH. *Molecules*. 2011; 16:7621. [PubMed: 21900864]

10. a) Kuik W, Kema IP, Brouwers Adrienne H, Zijlma R, Neumann KD, Dierckx RAJO, DiMagno SG, Elsinga PH. *J Nucl Med.* 2015; 56:106. [PubMed: 25500826] b) Neumann KD, Qin L, Vavere AL, Snyder SE, DiMagno SG. *J Nucl Med.* 2012; 53:21P. [PubMed: 22213820] c) Neumann K, Glaspy K, Vavere A, Snyder SE, DiMagno SG. *J Nucl Med.* 2013; 54:223P.d) Neumann KD, Vavere AL, Snyder SE, DiMagno SG. *J Labelled Compd Radiopharm.* 2011; 54:S492.
11. a) Moon BS, Kil HS, Park JH, Kim JS, Park J, Chi DY, Lee BC, Kim SE. *Org Biomol Chem.* 2011; 9:8346. [PubMed: 22057475] b) Chun J, Telu S, Lu S, Pike VW. *Org Biomol Chem.* 2013; 11:5094. [PubMed: 23804017] c) R. Edwards, A. D. Westwell, S. Daniels, T. Wirth, *Eur. J. Org. Chem.* 2015, 625; d) Zlatopolskiy BD, Zischler J, Krapf P, Zarrad F, Urusova EA, Kordys E, Endepols H, Neumaier B. *Chem Eur J.* 2015; 21:5972. [PubMed: 25708748] e) Jang KS, Jung Y-W, Gu G, Koeppe RA, Sherman PS, Quesada CA, Raffel DM. *J Med Chem.* 2013; 56:7312. [PubMed: 23965035] f) Carroll MA, Nairne J, Woodcraft JL. *J Labelled Compd Radiopharm.* 2007; 50:452.
12. a) Shah A, Pike VW, Widdowson DA. *J Chem Soc, Perkin Trans.* 1997; 1:2463.b) Kitamura T, Matsuyuki J, Taniguchi H. *Synthesis.* 1994:147.c) Kitamura T, Matsuyuki J, Nagata K, Furuki R, Taniguchi H. *Synthesis.* 1992:945.d) Carroll MA, Pike VW, Widdowson DA. *Tetrahedron Lett.* 2000; 41:5393.e) Zhdankin VV, Scheuller MC, Stang PJ. *Tetrahedron Lett.* 1993; 34:6853.f) Stang PJ, Zhdankin VV, Tykwinski R. *Tetrahedron Lett.* 1992; 33:1419.g) Pike VW, Butt F, Shah A, Widdowson DA. *J Chem Soc, Perkin Trans.* 1999; 1:245.h) G. F. Koser, R. H. Wettach, C. S. Smith, *J. Org. Chem.* 1980, 45, 1543; i) Stang PJ, Zhdankin VV, Tykwinski R, Zefirov NS. *Tetrahedron Lett.* 1991; 32:7497.j) Ochiai M, Toyonari M, Nagaoka T, Chen DW, Kida M. *Tetrahedron Lett.* 1997; 38:6709.k) Kitamura T, Kotani M, Fujiwara Y. *Tetrahedron Lett.* 1996; 37:3721.
13. a) Iwama T, Birman VB, Kozmin SA, Rawal VH. *Org Lett.* 1999; 1:673. [PubMed: 10823199] b) Hossain MD, Kitamura T. *Tetrahedron.* 2006; 62:6955.c) Hossain MD, Kitamura T. *J Org Chem.* 2006; 71:9903. [PubMed: 17168620] d) A. Kryski, L. Skulski, *Molecules* 2001, 6, 875; e) P. Kazmierczak, L. Skulski, *Synthesis* 1995, 1027; f) M. Bielawski, B. Olofsson, *Chem. Commun.* 2007, 2521; g) M. Bielawski, M. Zhu, B. Olofsson, *Adv. Synth. Catal.* 2007, 349, 2610; h) Bielawski M, Aili D, Olofsson B. *J Org Chem.* 2008; 73:4602. [PubMed: 18505294] i) Zhu M, Jalalian N, Olofsson B. *Synlett.* 2008:592.j) Merritt EA, Malmgren J, Klinke FJ, Olofsson B. *Synlett.* 2009:2277.
14. Ye C, Twamley B, Shreeve JM. *Org Lett.* 2005; 7:3961. [PubMed: 16119942]
15. Dohi T, Maruyama A, Takenaga N, Senami K, Minamitsuji Y, Fujioka H, Caemmerer SB, Kita Y. *Angew Chem Int Ed.* 2008; 47:3787.
16. a) Uyanik M, Yasui T, Ishihara K. *Tetrahedron.* 2010; 66:5841.b) Uyanik M, Yasui T, Ishihara K. *Angew Chem Int Ed.* 2010; 49:2175.c) Uyanik M, Yasui T, Ishihara K. *Angew Chem Int Ed.* 2013; 52:9215.
17. Christe KO, Dixon DA, McLemore D, Wilson WW, Sheehy JA, Boatz JA. *J Fluorine Chem.* 2000; 101:151.
18. Hu B, Miller WH, Neumann KD, Linstad EJ, DiMagno SG. *Chem Eur J.* 2015; 21:6394. [PubMed: 25757054]
19. Ground Fluor Pharmaceuticals, Inc. Lincoln, NE.

Scheme 1. Synthetic strategies for preparing diaryliodonium salts.^[2b]

Scheme 2.

Retrosynthesis of an unsymmetrical diaryliodonium salt derived from phenylalanine.

Scheme 3.

Preparation of ArI(III) reagents with F-TEDA-2BF_4 from iodoarenes.

Scheme 4.

A proposed mechanism for the oxidative diacetoxylation of iodoarenes in the presence of F-TEDA·2BF₄ and TMSOAc.

Scheme 5.

Synthesis of (diacetoxyiodo)arene **2g** from iodoarene **1g**.

Scheme 6.

Diaryliodonium salts prepared using the reported method.

Table 1

Preparation of (diacetoxiodo)arenes **2** from iodoarenes **1**.^[a]

Entry	ArI	R	T [°C]	t [h]	Prod.	Yield [%] ^[b]
1	1a	4-OMe	23	3	2a	70
2	1b	2-OMe	23	3	2b	65
3	1c	3-CF ₃	23	8	2c	80
4	1d	3-CN	23	8	2d	70
5	1e	3,5-CO ₂ Me	50	22	2e	93
6	1f	4-NO ₂	50	33	2f	85

^[a] Reaction conditions: 0.50 mmol scale, 6.0 mL of CH₃CN, N₂. For details of operations, see Supporting Information.^[b] Isolated yields.