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Regiospecific syntheses of functionalized diaryliodonium tosylates via [hydroxy(tosyloxy)iido]arenes generated in situ from (diacetoxyiido)arenes

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Abstract

Ready access to ^{18}F -labeled aryl synthons is required for preparing novel radiotracers for molecular imaging with positron emission tomography. Diaryliodonium salts react with cyclotron-produced no-carrier-added [^{18}F]fluoride ion to produce [^{18}F]aryl fluorides. We aimed to prepare functionalized diaryliodonium salts to serve as potential precursors for producing useful ^{18}F -labeled aryl synthons, such as ^{18}F -labeled halomethylbenzenes, benzaldehydes and benzoic acid esters. Such salts were designed to have one functionalized aryl ring, one relatively electron-rich ring, such as 4-methoxyphenyl or 2-thienyl, and a non-fluorine containing weakly nucleophilic anion. Generation of a [hydroxy(tosyloxy)iido]arene from a functionalized (diacetoxyiido)arene in situ followed by treatment with an electron-rich arene, such as anisole or thiophene, or with a functionalized arylstannane gave expedient regiospecific access to a wide range of functionally diverse diaryliodonium tosylates in moderate to high yields (44–98%). The described methodology broadens the scope for producing new functionalized diaryliodonium salts for diverse applications.

INTRODUCTION

Diaryliodonium salts are hypervalent compounds that are classified as diaryl- λ^3 -iodanes.¹ They are of increasing interest in organic synthesis as effective arylating agents.^{2–4} Moreover, diaryliodonium salts have gained particular value for introducing the short-lived positron-emitter fluorine-18 ($t_{1/2} = 109.7$ min) into radiotracers for molecular imaging in animal and human subjects with positron emission tomography (PET).⁵ Uniquely, reactions of diaryliodonium salts with cyclotron-produced [^{18}F]fluoride ion can efficiently introduce fluorine-18 onto electron-rich or electron-deficient aromatic rings at any desired carbon position in a rapid single-step (Scheme 1).^{6–9}

We are further interested to exploit the radiofluorination of diaryliodonium salts for rapid access to functionalized [^{18}F]fluoroarenes that might serve as labeling synthons in the preparation of PET radiotracers. These synthons include ^{18}F -labeled, benzoic acid esters, benzyl halides and benzaldehydes. Several methods exist for the preparation of diaryliodonium salts, and these have recently been categorized and reviewed.³ The vast majority of such methods are applicable to preparing diaryliodonium salts bearing relatively unreactive substituents, such as alkyl, alkoxy or phenyl, and some of these are also known to be suitable for preparing salts with more reactive substituents, such as halo or nitro.

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SUPPORTING INFORMATION ^1H -NMR and ^{13}C -NMR spectra of synthesized compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

However, diaryliodonium salts bearing halomethyl functionality have not been reported. Also the literature precedent on the syntheses of diaryliodonium salts with formyl substituents is sparse,^{10–17} and in some cases has entailed the use of undesirable reagents, such as organomercury compounds^{10,11} or strong acids^{12,13}

Here we report that variously functionalized diaryliodonium tosylates were readily accessed as their tosylates in moderate to high yields by generating a [hydroxy(tosyloxy)iodo]arene (HTIA) from a prepared (diacetoxyiodo)arene in situ for subsequent treatment with either an electron-rich arene or an arylstannane. This convenient methodology, as well as meeting our particular needs, will also be generally useful to others for preparing functionalized diaryliodonium salts for use as reagents or for their other potential applications (e.g., as photoinitiators or bactericides).^{2,3}

We particularly wished to prepare functionalized diaryliodonium salts in which one aryl ring is especially electron-rich, such as a 4-methoxyphenyl or 2-thienyl ring, because such a ring confers high selectivity for radiofluorination at a functionalized partner ring that is relatively less electron-rich.^{6–9,18} Moreover, we wished to avoid salts with strongly nucleophilic or fluorine-containing counterions, for the reasons that nucleophilic anions might compete in subsequent radiofluorination reactions and fluorine-containing anions might undesirably release non-radioactive fluoride ion to dilute the specific radioactivity of the [¹⁸F]fluoride ion.⁵ Therefore, tosylate was considered to be an acceptably benign counterion for our specific purpose.

An attractive approach for the single-step syntheses of diaryliodonium tosylates is treatment of an electron-rich arene¹⁷ or an organometallic reagent, such as an arylsilane,¹⁹ arylboronic acid²⁰ or arylstannane,²¹ with the hypervalent- λ^3 -iodane, [hydroxy(tosyloxy)iodo]benzene,²² especially as the latter is commercially available as Koser's reagent. We considered that the synthetic scope of such useful methods might be expanded for general access to unsymmetrical diaryliodonium salts that would be useful precursors to functionalized [¹⁸F]fluoroarenes as labeling synthons. The use of Koser's reagent restricts the synthesis of diaryliodonium salts to those in which one ring is phenyl. Moreover, highly electron-rich derivatives of Koser's reagent, such as 4-[hydroxy(tosyloxy)iodo]anisole^{23,24} and 2-[hydroxy(tosyloxy)iodo]thiophene²⁵, are unstable, and sometimes violently so²³, when isolated. Therefore, we aimed to explore whether such derivatives might instead be prepared and used safely and effectively in situ.

RESULTS AND DISCUSSION

We were attracted to the use of congeneric (diacetoxyiodo)arenes (λ^3 -iodane diacetates) as starting materials to prepare the required [hydroxyl(tosyloxy)iodo]arenes (HTIAs) as reactive intermediates, since these diacetates are generally found to be stable microcrystalline solids.^{2,26} We envisaged a synthetic approach, in which an iodoarene would first be oxidized to a (diacetoxyiodo)arene with peracetic acid in acetic acid^{27,28} or sodium perborate tetrahydrate in acetic acid²⁷ and in which the isolated diacetate would then be treated with *p*-TsOH·H₂O plus an electron-rich arene or arylstannane. The required (diacetoxyiodo)arenes (**1–13**) were readily obtained, and the outlined approach was rapidly successful in producing a wide range of the targeted functionalized diaryliodonium tosylates, as we now describe.

In the use of this method with electron-rich anisole (Scheme 2), electrophilic substitution by the functionalized HTIA intermediate occurred exclusively at the para position, and gave the target diaryliodonium tosylates in moderate to very high yields (46–90%), as exemplified in twelve examples (**21–32**; Table 1). Thus, this method was effective for introducing

chloromethyl or bromomethyl groups into ortho, meta or para position, methoxycarbonyl or ethoxycarbonyl into meta position, acetyl groups into meta and/or para position, and (diacetoxy)methyl into ortho position. The regioselectivity of the HTIA intermediates for electrophilic substitution at the para position of anisole was remarkable, but also fully consistent with earlier findings. For example, the reagent formed between $\text{PhI}(\text{OAc})_2$ and triflic acid is known to react exclusively at the 4-position of anisole to produce (4-methoxyphenyl)phenyliodonium triflate.²⁹ We further found that the use of highly electron-rich 1,3,5-trimethoxybenzene with 4-chloromethyl(diacetoxyiodo)benzene (Scheme 2) gave the corresponding iodonium salt (**33**) in excellent yield (98%, Table 1).

The halomethyl iodonium tosylates (**21–26**) are potential precursors to ^{18}F fluorobenzyl halides. ^{18}F 4-Fluorobenzyl bromide has already proved to be a useful labeling synthon for producing PET radiotracers⁵, including radiotracers for imaging and cannabinoid subtype 1,³⁰ histamine subtype 3³¹ and delta opioid receptors³². However, the radiosynthesis of this synthon has previously used three steps.³⁰ ^{18}F 3-Fluorobenzyl bromide was recently used to label ^{18}F lapatinib, a potential radiotracer of ERb81/ErbB2 tyrosine kinase.³³ In this case the ^{18}F [(3-bromomethyl)fluorobenzene] was prepared for the first time from an iodonium salt in two radiosynthetic steps. The syntheses of the diaryliodonium salts (**21–26**) allow us to explore whether such ^{18}F fluorobenzyl halides can be prepared more efficiently and simply in a single radiosynthetic step.

We further demonstrated that potential diaryliodonium tosylate precursors to ^{18}F 3-fluorobenzyl bromide that have either 2-thienyl (**34**) or 5-methyl-2-thienyl (**35**) as the electron-rich aryl ring could be prepared similarly from thiophene or 2-methyl-thiophene (Scheme 2) in high and moderate yield (83% and 57%, respectively; Table 1). When the more electron-rich 2-methoxy-thiophene was used as arene, the target diaryliodonium salt (**36**) was formed in high yield (~78%, preceding drying attempt) (Table 1), but proved unstable to drying under vacuum at room temperature. This salt was the only one arising from this study showing instability.

Thiophene was also used as the electron-rich arene to prepare diaryliodonium tosylates bearing a 3-methoxycarbonyl (**37**) or 4-methoxycarbonyl (**38**) substituent on a phenyl ring with a 2-thienyl partner ring in good yields (58% and 83%, respectively; Table 1). The regioselectivity was as expected for attack of an electrophilic agent on thiophene and accords with the report that HTIAs react with thiophene at the 2-position.¹⁷ Although esters of ^{18}F 4-fluorobenzoic acid may be prepared in a single radiosynthetic step by aromatic nucleophilic substitution with ^{18}F fluoride ion in *p*-nitro precursors, radiochemical yields are low.³⁴ Use of a 4-trimethylammonium leaving group improves radiochemical yield.³⁵ However, such aromatic nucleophilic substitution reactions are not expected to be applicable to preparing ^{18}F 3-fluorobenzoic acid esters in acceptable yields.⁵ Ready access to iodonium salts bearing alkoxycarbonyl groups such as **37** and **38** will allow us to explore whether they are superior precursors for the radiosyntheses of ^{18}F 3-fluoro and ^{18}F 4-fluorobenzoic acid esters.

We wished to prepare (4-methoxyphenyl)aryliodonium tosylates bearing electron-withdrawing functional groups, such as formyl, since such salts might serve as useful precursors to ^{18}F fluorobenzaldehydes, which have been demonstrated to be useful labeling agents.³⁶ Although (diacetoxyiodo)arenes and HTIAs may react well and regioselectively with highly electron-rich arenes and heteroarenes they generally show low reactivity towards moderately electron-rich arenes. For example, Koser's reagent fails to react even with benzene or toluene in acetonitrile.¹⁹ By contrast, Koser's reagent reacts readily with organometallic reagents, such as arylstannanes²¹, to produce the corresponding phenylaryliodonium tosylates. Stannylated benzaldehydes proved readily accessible

(Scheme 3). We were therefore able to explore the synthesis of functionalized (4-methoxyphenyl)aryliodonium tosylates through treatment of 4-methoxy-(diacetoxyiodo)benzene with tosic acid followed by a stannylated benzaldehyde. This approach (Scheme 3) gave 3-formylphenyl(4'-methoxyphenyl)iodonium tosylate (**39**), the 4-formyl analog (**40**) and 6-methoxy derivative of **39** (**41**) in moderate yields (44–50%; Table 2). Similarly, use of 2-(diacetoxyiodo)thiophene with a stannylated benzaldehyde (Scheme 4) gave the 3-formylphenyl(2'-thienyl)iodonium tosylate (**43**) and the 6-methoxy analog (**44**) in moderate yields (48%) (Table 2). Clearly, the formyl groups in meta or para position to the tin substituent resisted oxidation in these syntheses. Curiously, in contrast to our success in preparing diaryliodonium tosylates with meta or para formyl groups, all attempts to prepare the ortho-formyl analogs of **39** or **43** failed. The reason is at present unclear, but may be related to the potential for an ortho formyl group to form a stable five-membered benzoiodoxole compound. No ortho formyl diaryliodonium salt has yet been reported. Nonetheless, we envisage that the prepared (2-diacetoxymethyl)diaryliodonium tosylate (**32**) can serve as a precursor to [^{18}F]2-fluorobenzaldehyde in two steps, namely radiofluorination to [^{18}F](2-diacetoxymethyl)fluorobenzene followed by hydrolysis.

We were interested to see how well arylstannanes bearing a less electron-withdrawing substituent might perform in our method of diaryliodonium tosylate synthesis. We found that the iodonium tosylate bearing a 3-acetoxy group (**29**) could be prepared in 79% yield from 3-(tri-*n*-butylstannyl)phenyl acetate and 4-methoxy-(diacetoxyiodo)benzene (Table 2), which is very comparable to the yield achieved from the treatment of 3-acetoxy-(diacetoxyiodo)benzene with anisole (83%, Table 1). Similarly, the iodonium tosylate bearing a 3-methylamido group (**42**) was obtained from the arylstannane in high yield (65%) (Table 2).

In summary, diaryliodonium tosylates having one aryl ring bearing chloromethyl, bromomethyl, ester, aldehyde or amide functionality and another relatively electron-rich ring can be conveniently prepared in moderate to high yields (44–98%) by treating HTIAs, generated in situ, with either electron-rich arenes or organostannanes.

EXPERIMENTAL SECTION

Methods

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded at room temperature. ^1H and ^{13}C chemical shifts are reported in δ units (ppm) downfield relative to the signal for tetramethylsilane. High resolution mass spectra (HRMS) were acquired under electron ionization conditions using a double-focusing high-resolution mass spectrometer. Melting points are uncorrected.

Preparation of (diacetoxyiodo)arenes

(Diacetoxyiodo)arenes (**1–15**) were prepared by oxidation of iodoarenes with either peracetic acid in acetic acid²⁶ or sodium perborate²⁷ in acetic acid, as follows.

3-Chloromethyl-(diacetoxyiodo)benzene (1)—Peracetic acid in acetic acid (32 wt%; 5 mL) was added dropwise to 3-iodobenzyl chloride (2.8 mmol, 0.71 g) at $-10\text{ }^\circ\text{C}$ (ice-salt bath) and the mixture was slowly warmed to rt and stirred overnight (*ca.* 14 h). Consumption of 3-iodobenzyl chloride was monitored by TLC (silica gel, hexane R_f = 0.38). Aqueous acetic acid (10% v/v) was added to the yellow solution. The precipitate was recovered by filtration, washed with water (10 mL) and then diethyl ether (10 mL $\times$ 3), and dried in vacuo for 4 h to give **1** (0.62 g; 59%); mp = 143–144 $^\circ\text{C}$; ^1H -NMR (CDCl_3) δ 8.12 (t, J = 1.6 Hz, 1H), 8.04 (d, J = 8 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 8 Hz, 1H),

4.63 (s, 2H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 140.5, 134.7, 134.6, 131.7, 131.1, 121.4, 44.7, 20.4.

The following compounds **2–13** were prepared likewise. In syntheses where addition of aqueous acetic acid gave no precipitate, the yellow solution was extracted with dichloromethane. The organic layers were then dried over MgSO_4 and evaporated to give a yellow oil which solidified when triturated with diethyl ether.

2-Chloromethyl-(diacetoxyiodo)benzene (2)—White solid (84%); mp = 151–152 °C; ^1H -NMR (CDCl_3) δ 8.25 (dd, J = 0.8, 8 Hz, 1H), 8.04 (dd, J = 1.6, 7.6 Hz, 1H), 7.66 (dt, J = 1.2, 7.6 Hz, 1H), 7.42 (dt, J = 1.6, 7.6 Hz, 1H), 4.89 (s, 2H), 1.99 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 138.8, 137.7, 133.0, 130.9, 125.1, 47.8, 20.3.

4-Chloromethyl-(diacetoxyiodo)benzene (3)—White solid (52%); mp = 142–145 °C; ^1H -NMR (CDCl_3): δ 8.09 (d, J = 6.8 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 4.62 (s, 2H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 141.3, 135.3, 130.9, 120.9, 44.8, 20.4.

2-Bromomethyl-(diacetoxyiodo)benzene (4)—White solid (45%); mp = 113–115 °C; ^1H -NMR (CDCl_3) δ 8.23 (d, J = 6.4 Hz, 1H), 7.75 (dd, J = 2, 8.4 Hz, 1H), 7.63 (dt, J = 2, 7.6 Hz, 1H), 7.39 (dt, J = 2.8, 8.8 Hz, 1H), 4.78 (s, 2H), 2.00 (s, 6H); ^{13}C -NMR (CDCl_3) δ 175.9, 138.6, 137.3, 132.5, 132.4, 130.8, 130.3, 124.8, 33.8, 19.7.

3-Bromomethyl-(diacetoxyiodo)benzene (5)—White solid (73%); mp = 130–132 °C; ^1H -NMR (CDCl_3) δ 8.11 (t, J = 1.6 Hz, 1H), 8.01 (dt, J = 1.2, 8 Hz, 1H), 7.62 (dt, J = 1.2, 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 140.8, 135.1, 134.6, 132.3, 131.2, 121.3, 31.3, 20.4.

4-Bromomethyl-(diacetoxyiodo)benzene (6)—Pale yellow solid (42%); mp = 131–133 °C; ^1H -NMR (CDCl_3) δ 8.06 (dd, J = 2, 6.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 4.49 (s, 2H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 141.7, 138.0, 135.4, 131.5, 130.8, 120.8, 31.4, 20.4.

3-Methoxycarbonyl-(diacetoxyiodo)benzene (7)—Pale yellow solid (30%); mp = 163–165 °C; ^1H -NMR (CDCl_3) δ 8.75 (t, J = 1.6 Hz, 1H), 8.28–8.25 (m, 2H), 7.59 (t, J = 8 Hz, 1H), 3.97 (s, 3H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 165.0, 138.9, 136.1, 132.6, 130.8, 123.1, 121.2, 52.3, 20.3.

3-Ethoxycarbonyl-(diacetoxyiodo)benzene (8)—White solid (19%); mp = 113–115 °C; ^1H -NMR (CDCl_3) δ 8.74 (t, J = 1.6 Hz, 1H), 8.26 (dd, J = 1.6, 8 Hz, 2H), 7.58 (t, J = 8 Hz, 1H), 4.42 (q, J = 7.2, 2H), 2.02 (s, 6H), 1.43 (t, J = 6.8 Hz, 3H); ^{13}C -NMR (CDCl_3) δ 176.6, 164.5, 138.9, 136.0, 133.2, 132.6, 130.8, 121.1, 61.9, 20.4, 14.3.

3-Acetoxy-(diacetoxyiodo)benzene (9)—White solid (51%); mp = 121–123 °C; ^1H -NMR (CDCl_3) δ 7.95–7.92 (m, 1H), 7.89 (t, J = 2 Hz, 1H), 7.52 (t, J = 8 Hz, 1H), 7.36–7.33 (m, 1H), 2.34 (s, 3H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 168.5, 151.3, 132.0, 131.3, 128.3, 125.3, 120.5, 21.0, 20.4.

4-Acetoxy-(diacetoxyiodo)benzene (10)—White solid (49%); mp = 153–155 °C; ^1H -NMR (CDCl_3): δ 8.09 (dd, J = 2.4, 7.2 Hz, 2H), 7.23 (dd, J = 2, 8.8 Hz, 2H), 2.34 (s, 3H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 168.6, 153.4, 136.5, 124.4, 117.3, 21.1, 20.4.

3,4-Diacetoxy-(diacetoxyiodo)benzene (11)—Pale yellow solid (47%); mp = 140–142 °C; ^1H -NMR (CDCl_3) δ 7.97–7.93 (m, 2H), 7.34 (d, J = 8.4 Hz, 1H), 2.33 (s, 6H), 2.02

(s, 6H); ^{13}C -NMR (CDCl_3) δ 176.6, 167.4, 167.3, 144.9, 143.1, 133.1, 130.4, 125.6, 116.2, 20.6, 20.5, 20.3.

4-Methoxycarbonyl-(diacetoxyiodo)benzene (12)—Pale yellow solid (19%); mp = 136–138 °C (lit.³⁷ mp = 150.0–153.3 °C); ^1H -NMR (CDCl_3) δ 8.17–8.12 (m, 4H), 3.97 (s, 3H), 2.02 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 165.5, 134.9, 133.1, 131.8, 125.7, 52.7, 20.4.

2-(Diacetoxymethyl)-(diacetoxyiodo)benzene (13)—White solid (43%); mp = 140–143 °C; ^1H -NMR (CDCl_3) δ 8.32 (d, J = 7.6 Hz, 1H), 7.85 (s, 1H), 7.79 (dd, J = 1.2, 7.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.51 (dt, J = 1.6, 7.6 Hz, 1H), 2.13 (s, 6H), 1.98 (s, 6H); ^{13}C -NMR (CDCl_3) δ 176.5, 168.3, 168.1, 138.5, 136.4, 132.5, 132.3, 130.0, 121.5, 91.1, 20.6, 20.2.

2-(Diacetoxyiodo)thiophene (14)—Sodium perborate tetrahydrate (7.69 g, 50 mmol) was added portion-wise over 30 min to a solution of 2-iodothiophene (1.05 g, 5 mmol) in acetic acid (50 mL). The temperature was raised to 50 °C and the mixture stirred at this temperature overnight (*ca.* 14 h). The resulting solid was filtered off and the filtrate was concentrated *in vacuo*. The product was extracted with dichloromethane (30 mL $\times$ 3) and washed with water (100 mL $\times$ 2). The organic layers were dried over MgSO_4 and concentrated to a pale yellow oil. Trituration of this oil with Et_2O gave solids that were filtered off, washed with Et_2O , and dried under vacuum to give **14** as a white solid (0.58 g, 35%); mp = 115–118 °C (lit.³⁸ mp = 120–122 °C; lit.³⁹ mp = 112–119 °C). ^1H -NMR (CDCl_3) δ 7.78 (dd, J = 1.2, 3.6 Hz, 1H), 7.64 (dd, J = 1.2, 5.2 Hz, 1H), 7.15–7.13 (m, 1H), 2.02 (s, 6H); ^{13}C NMR (CDCl_3) δ 177.0, 139.1, 134.9, 128.7, 106.3, 20.4.

4-Methoxy-(diacetoxyiodo)benzene (15).²⁸—This compound was prepared in the same manner as **N** and obtained as a white solid (34%); mp = 85–88 °C (lit.⁴⁰ mp = 88–90 °C); ^1H -NMR (CDCl_3) δ 8.01 (d, J = 9.2 Hz, 2H), 6.97 (d, J = 9.2 Hz, 2H), 3.87 (s, 3H), 2.00 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.34, 162.2, 137.1, 116.6, 111.7, 55.6, 20.4.

Preparation of arylstannanes

Arylstannanes (**16–20**) were prepared from iodoarenes by treatment with either hexamethylditin⁴¹ or hexa-*n*-butylditin⁴² over palladium catalyst, as follows.

N-Methyl-3-(trimethylstannyl)benzamide (16)—3-Iodo-*N*-methylbenzamide (0.73 g, 2.8 mmol) bis(trimethylditin) (1.00 g, 3.1 mmol) and $\text{Pd}(\text{PPh}_3)_4$ catalyst (0.068 g, 0.05 mmol) were added to toluene (20 mL) under argon. This mixture was refluxed overnight and the precipitate then filtered off. The filtrate was concentrated *in vacuo* and the remaining crude oil was purified with column chromatography (silica gel, 50% EtOAc/hexane) to give **16** (R_f = 0.35) as a white solid (0.39 g, 44%); mp = 91–92 °C; ^1H NMR (CDCl_3) δ 7.88 (d, J = 1.2 Hz, 1H), 7.67–7.65 (m, 1H), 7.62–7.60 (m, 1H), 7.38 (t, J = 7.2 Hz, 1H), 6.14 (s, br, 1H), 3.02 (d, J = 4.8 Hz, 3H), 0.31 (s, 9H); ^{13}C NMR (CDCl_3) δ 168.8, 143.2, 138.8, 134.1, 128.0, 126.5, 26.9, –7.77.

4-Tri-*n*-butylstannylbenzaldehyde (17)—Bis(tri-*n*-butylditin) (2.61 g, 4.5 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (0.084 g, 0.07 mmol) were added to a solution of 4-iodobenzaldehyde (1.03 g, 4.4 mmol) in 1,4-dioxane (20 mL) under argon. This mixture was refluxed for 8 h. The resulting dark precipitate was filtered off on a Celite pad and the filtrate was concentrated *in vacuo*. Column chromatography (silica gel; 5% EtOAc/hexane) of the crude oil gave **17** (R_f = 0.43) as a colorless oil (1.10 g, 63%); ^1H NMR (CDCl_3) δ 9.99 (s, 1H), 7.81–7.77 (m, 2H), 7.67–7.60 (m, 2H), 1.57–1.51 (m, 6H), 1.36–1.31 (m, 6H), 1.13–1.09 (m, 6H), 0.89 (t, J = 7.6 Hz,

9H); ^{13}C NMR (CDCl_3) δ 192.7, 152.5, 136.9, 135.9, 128.4, 29.0, 27.3, 13.6, 9.7. Spectroscopic data correspond to reported data.⁴³

3-Tri-*n*-butylstannylbenzaldehyde (18)—This was prepared as described for **17**. Colorless oil (61%); ^1H NMR (CDCl_3): δ 10.02 (s, 1H), 8.02–7.92 (m, 1H), 7.81–7.77 (m, 1H), 7.74–7.72 (m, 1H), 7.51–7.75 (m, 1H), 1.57–1.51 (m, 6H), 1.37–1.31 (m, 6H), 1.13–1.09 (m, 6H), 0.89 (t, $J = 7.2$ Hz, 9H); ^{13}C NMR (CDCl_3) δ 193.1, 143.5, 142.5, 137.6, 135.5, 129.4, 128.3, 29.0, 27.3, 13.6, 9.6. Spectroscopic data correspond to reported data.⁴⁴

4-Methoxy-3-(tri-*n*-butylstannyl)benzaldehyde (19)—Bis(tributyliditin) (1.94 g, 3.3 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (0.034 g, 0.03 mmol) were added to a solution of 3-iodo-4-methoxybenzaldehyde (0.79 g, 3.0 mmol) in toluene (20 mL) at rt under argon. This mixture was refluxed overnight. The resulting dark precipitate was removed by filtration on Celite pad and the filtrate toluene solution was concentrated *in vacuo*. Column chromatography (silica gel; 20% EtOAc/hexane) of the crude oil gave **19** ($R_f = 0.5$) as a pale yellow oil (1.12 g, 87%); ^1H NMR (CDCl_3) δ 9.89 (s, 1H), 7.90 (d, $J = 2$ Hz, 1H), 7.83 (dd, $J = 2.4, 8.8$ Hz, 1H), 6.90 (dd, $J = 6.8, 15.2$ Hz, 1H), 3.86 (s, 3H), 1.55–1.50 (m, 6H), 1.36–1.30 (m, 6H), 1.11–1.07 (m, 6H), 0.89 (t, $J = 7.2$ Hz, 9H); ^{13}C NMR (CDCl_3) δ 191.1, 168.6, 138.8, 133.2, 131.7, 130.1, 108.7, 55.4, 29.0, 27.2, 13.4, 9.8.

3-(Tri-*n*-butylstannyl)phenyl acetate (20)—This was prepared as described for **19**. Colorless oil (60%); ^1H NMR (CDCl_3) δ 7.35–7.29 (m, 2H), 7.14 (d, $J = 2.4$ Hz, 1H), 7.02–6.99 (m, 1H), 2.29 (s, 3H), 1.57–1.49 (m, 6H), 1.37–1.30 (m, 6H), 1.08–1.04 (m, 6H), 0.88 (t, $J = 7.6$ Hz, 9H); ^{13}C NMR (CDCl_3) δ 169.5, 150.3, 143.9, 133.8, 128.7, 121.1, 28.9, 27.3, 21.2, 13.6, 9.6.

Synthesis of functionalized diaryliodonium salts by treating HTIAs with electron-rich arenes

2-Chloromethylphenyl(4'-methoxyphenyl)iodonium tosylate (21)—*p*-TsOH·H₂O (0.15 g, 0.8 mmol) was added to a suspension of 2-chloromethyl-(diacetoxiodo)benzene (0.31 g, 0.8 mmol) in MeCN (2 mL), giving an intense yellow solution, which was immediately diluted with chloroform (20 mL). Anisole (0.22 g, 2 mmol) was added and the resultant pale yellow solution was then refluxed for 4 h. The consumption of HTIA was monitored with KI-starch paper. Solvent was then removed under reduced pressure and the yellow oily residue was triturated with Et₂O (30 mL). Precipitate was filtered off, washed with Et₂O, dried under vacuum for 4 h, and recrystallized from MeOH/Et₂O to give **21** as a white solid (0.38 g, 83%). mp = 172–174 °C; ^1H -NMR ($\text{MeOD}-d_4$) δ 8.33 (d, $J = 8.4$ Hz, 1H), 8.11 (d, $J = 8.8$ Hz, 2H), 7.77–7.67 (m, 4H), 7.45 (t, $J = 8.4$ Hz, 1H), 7.21 (d, $J = 8.8$ Hz, 2H), 7.05 (d, $J = 8.8$ Hz, 2H), 4.98 (s, 2H), 3.84 (s, 3H), 2.36 (s, 3H); ^{13}C -NMR ($\text{MeOD}-d_4$) δ 164.7, 143.7, 141.8, 141.2, 139.1, 138.6, 134.9, 133.5, 133.4, 129.9, 127.1, 120.2, 119.0, 104.7, 56.5, 21.5; HRMS [$\text{M}-\text{OTs}$]⁺ Calc'd. for C₁₄H₁₃OCII: 358.9700, Found: 358.9697.

The following compounds (**22**–**38**) were prepared likewise from the appropriate functionalized HTIA and an electron-rich arene (anisole, 1,3,5-trimethoxybenzene, thiophene, 2-methyl thiophene or 2-methoxythiophene).

3-Chloromethylphenyl(4'-methoxyphenyl)iodonium tosylate (22)—Yield: 84%. mp = 170–171 °C; ^1H -NMR (CDCl_3) δ 8.00 (s, 1H), 7.89 (dd, $J = 2, 7.2$ Hz, 2H), 7.82 (d, $J = 8$ Hz, 1H), 7.51 (d, $J = 8$ Hz, 3H), 7.31 (t, $J = 8$ Hz, 1H), 7.04 (d, $J = 8$ Hz, 2H), 6.84 (dd, $J = 2, 7.2$ Hz, 2H), 4.46 (s, 2H), 3.80 (s, 3H), 2.32 (s, 3H); ^{13}C -NMR (CDCl_3) δ 162.5,

142.4, 141.2, 139.6, 137.5, 134.3, 134.1, 131.7, 131.5, 128.5, 126.0, 117.6, 115.7, 103.6, 55.6, 44.5, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₄H₁₃OClI: 358.9700, Found: 358.9694.

4-Chloromethylphenyl(4'-methoxyphenyl)iodonium tosylate (23)—Yield 90%. mp = 191–193 °C; ¹H-NMR (MeOD-*d*₄) δ 8.09 (t, *J* = 8 Hz, 4H), 7.69 (d, *J* = 8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.67 (s, 2H), 3.84 (s, 3H), 2.36 (s, 3H); ¹³C-NMR (MeOD-*d*₄) δ 164.7, 144.3, 143.7, 141.8, 138.8, 136.5, 133.2, 130.0, 127.1, 119.0, 115.9, 104.8, 56.5, 45.5, 21.5; HRMS [M-OTs]⁺ Calc'd. for C₁₄H₁₃OClI: 358.9700, Found: 358.9700.

2-Bromomethylphenyl(4'-methoxyphenyl)iodonium tosylate (24)—Yield 46%. mp = 135–137 °C; ¹H-NMR (MeOD-*d*₄): δ 8.30 (d, *J* = 7.6 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 2H), 7.77 (dd, *J* = 2, 7.6 Hz, 1H), 7.70–7.65 (m, 3H), 7.42 (dt, *J* = 2.4, 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 4.89 (s, 2H), 3.85 (s, 3H), 2.37 (s, 3H); ¹³C-NMR (MeOD-*d*₄): δ 164.8, 143.7, 141.8, 141.7, 139.1, 138.7, 134.9, 133.5, 133.4, 130.0, 127.1, 120.2, 119.0, 104.6, 56.5, 35.3, 21.5; HRMS [M-OTs]⁺ Calc'd. for C₁₄H₁₃OBrI: 402.9195, Found: 402.9195.

3-Bromomethylphenyl(4'-methoxyphenyl)iodonium tosylate (25)—Yield 78%. mp = 171–173 °C; ¹H-NMR (CDCl₃) δ 8.00 (s, 1H), 7.89 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 1H), 7.51 (t, *J* = 8.4 Hz, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 8 Hz, 2H), 6.85 (d, *J* = 9.2 Hz, 2H), 4.35 (s, 2H), 3.81 (s, 3H), 2.32 (s, 3H); ¹³C-NMR (CDCl₃) δ 162.5, 142.6, 141.5, 139.4, 137.5, 134.7, 134.0, 132.8, 131.7, 128.5, 126.0, 117.6, 115.8, 103.6, 55.6, 31.2, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₄H₁₃OBrI: 402.9195, Found: 402.9192.

4-Bromomethylphenyl(4'-methoxyphenyl)iodonium tosylate (26)—Yield 81%. mp = 139–141 °C; ¹H-NMR (CDCl₃) δ 7.88 (t, *J* = 7.2 Hz, 4H), 7.48 (d, *J* = 8 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 4.38 (s, 2H), 3.79 (s, 3H), 2.31 (s, 3H); ¹³C-NMR (CDCl₃) δ 162.4, 142.4, 141.4, 139.4, 137.5, 135.0, 131.9, 128.5, 126.0, 117.5, 115.2, 103.8, 55.6, 31.3, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₄H₁₃OBrI: 402.9195, Found: 402.9199.

[3-(Methoxycarbonyl)phenyl](4'-methoxyphenyl)iodonium tosylate (27)—Yield 63%. mp = 155–157 °C; ¹H-NMR (MeOD-*d*₄) δ 8.71 (s, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.25 (d, *J* = 7.2 Hz, 1H), 8.12 (d, *J* = 10 Hz, 2H), 7.68 (d, *J* = 5.6 Hz, 2H), 7.62 (t, *J* = 6 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.06 (d, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.83 (s, 3H), 2.35 (s, 3H); ¹³C-NMR (MeOD-*d*₄) δ 166.2, 164.8, 143.7, 141.8, 140.2, 138.9, 136.7, 134.9, 134.1, 133.3, 129.9, 127.1, 119.1, 116.7, 104.8, 56.5, 53.4, 21.4; HRMS [M-OTs]⁺ Calc'd. for C₁₅H₁₄O₃I: 368.9988, Found: 368.9984.

3-(Ethoxycarbonyl)phenyl(4'-methoxyphenyl)iodonium tosylate (28)—Yield 69%. mp = 173–175 °C; ¹H-NMR (CDCl₃) δ 8.44 (s, 1H), 8.22 (d, *J* = 8 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8 Hz, 2H), 7.42 (t, *J* = 8 Hz, 1H), 7.02 (d, *J* = 8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 2.31 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H); ¹³C-NMR (CDCl₃) δ 164.3, 162.6, 142.4, 139.6, 138.8, 137.4, 135.1, 133.6, 132.3, 131.4, 128.5, 126.0, 117.6, 115.9, 104.0, 61.8, 55.6, 21.3, 14.2; HRMS [M-OTs]⁺ Calc'd. for C₁₆H₁₆O₃I: 383.0144, Found: 383.0133.

3-Acetoxyphenyl(4'-methoxyphenyl)iodonium tosylate (29)—Yield 88%; mp = 149–150 °C; ¹H-NMR (MeOD-*d*₄) δ 8.08 (dd, *J* = 3.2, 9.2 Hz, 2H), 8.00–7.96 (m, 2H), 7.69 (dd, *J* = 0.8, 8 Hz, 2H), 7.54 (t, *J* = 8 Hz, 1H), 7.43–7.40 (m, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.08–7.05 (m, 2H), 3.85 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H); ¹³C-NMR (MeOD-*d*₄) δ 170.4,

164.7, 153.5, 143.8, 141.8, 138.8, 133.7, 133.3, 130.0, 129.7, 127.3, 127.1, 119.4, 115.6, 104.8, 56.5, 21.5, 20.9; HRMS [M-OTs]⁺ Calc'd. for C₁₅H₁₄O₃I: 368.9988, Found: 368.9986.

4-Acetoxyphenyl(4'-methoxyphenyl)iodonium tosylate (30)—Yield 88%. mp, 157–159 °C; ¹H-NMR (CDCl₃) δ 7.94 (dd, *J* = 2, 7.2 Hz, 2H), 7.88 (dd, *J* = 2, 7.2 Hz, 2H), 7.94 (dd, *J* = 1.6, 4.8 Hz, 2H), 7.05–7.00 (m, 4H), 6.80 (dd, *J* = 2, 9.2 Hz, 2H), 3.78 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H); ¹³C-NMR (CDCl₃) δ 168.5, 162.3, 152.9, 142.5, 139.3, 137.5, 136.1, 128.5, 126.0, 124.8, 117.4, 111.4, 104.3, 55.5, 21.2, 21.1; HRMS [M-OTs]⁺ Calc'd. for C₁₅H₁₄O₃I: 368.9988, Found: 368.9986.

3, 4-Diacetoxyphenyl(4'-methoxyphenyl)iodonium tosylate (31)—Yield 86%. mp, 155–156 °C; ¹H-NMR (CDCl₃) δ 7.91–7.88 (m, 3H), 7.83 (dd, *J* = 2, 8.8 Hz, 1H), 7.41 (d, *J* = 8 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 7.6 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 3.75 (s, 3H), 2.29 (s, 3H), 2.26 (s, 3H), 2.22 (s, 3H); ¹³C-NMR (CDCl₃) δ 167.5, 167.4, 162.4, 144.9, 143.3, 142.3, 139.4, 137.7, 133.1, 130.2, 128.5, 126.1, 126.0, 117.4, 110.6, 104.4, 55.6, 21.3, 20.6, 20.5; HRMS [M-OTs]⁺ Calc'd. for C₁₇H₁₆O₅I: 427.0043, Found: 427.0044.

[2-(Diacetoxymethyl)phenyl](4'-methoxyphenyl)iodonium tosylate (32)—Yield 77%. mp, 150–153 °C; ¹H-NMR (MeOD-*d*₄) δ 8.28 (dd, *J* = 0.8, 8 Hz, 1H), 8.07 (dd, *J* = 2, 7.2 Hz, 2H), 7.86–7.84 (m, 2H), 7.77 (dt, *J* = 0.8, 7.6 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.56 (dt, *J* = 1.6, 8 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 9.2 Hz, 2H), 3.84 (s, 3H), 2.36 (s, 3H), 2.12 (s, 6H); ¹³C-NMR (MeOD-*d*₄) δ 170.3, 164.8, 143.8, 141.8, 138.7, 138.6, 138.3, 135.9, 134.6, 131.9, 129.9, 127.1, 119.1, 116.7, 104.7, 92.7, 56.6, 21.5, 20.7; HRMS [M-OTs]⁺ Calc'd. for C₁₈H₁₈O₅I: 441.0199, Found: 441.0192.

4-Chloromethylphenyl(2',4',6'-trimethoxyphenyl)iodonium tosylate (33)—Yield 98%. mp = 185–187 °C; ¹H-NMR (MeOD-*d*₄) δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8 Hz, 2H), 6.41 (s, 2H), 4.65 (s, 2H), 3.97 (s, 6H), 3.89 (s, 3H), 2.36 (s, 3H); ¹³C-NMR (MeOD-*d*₄) δ 169.0, 161.6, 143.9, 143.8, 141.8, 136.3, 132.9, 129.9, 127.1, 115.3, 93.1, 86.4, 57.9, 56.8, 45.6, 21.5; HRMS [M-OTs]⁺ Calc'd. for C₁₆H₁₇O₃ClI: 418.9911, Found: 418.9906.

3-Bromomethylphenyl(2'-thienyl)iodonium tosylate (34)—Yield 83%. mp = 138–140 °C; ¹H-NMR (CDCl₃) δ 8.01 (t, *J* = 1.6 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.81 (dd, *J* = 1.2, 4 Hz, 1H), 7.58 (dd, *J* = 0.8, 5.2 Hz, 1H), 7.50–7.47 (m, 3H), 7.29 (t, *J* = 8 Hz, 1H), 7.07–7.02 (m, 3H), 4.33 (s, 2H), 2.32 (s, 3H); ¹³C-NMR (CDCl₃) δ 142.1, 141.5, 140.7, 139.7, 136.2, 134.3, 133.6, 132.1, 131.7, 129.6, 128.6, 125.9, 118.7, 99.2, 31.2, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₁H₉SBrl: 378.8653, Found: 378.8651.

3-Bromomethylphenyl(5'-methyl-2'-thienyl)iodonium tosylate (35)—Yield 57%. mp = 163–165 °C; ¹H-NMR (CDCl₃) δ 8.00 (t, *J* = 1.6 Hz, 1H), 7.82 (dq, *J* = 0.8, 8.4 Hz, 1H), 7.61 (d, *J* = 4 Hz, 1H), 7.53 (dd, *J* = 2, 6.4 Hz, 2H), 7.49 (d, *J* = 8 Hz, 1H), 7.30 (t, *J* = 8 Hz, 1H), 7.07 (dd, *J* = 0.4, 8 Hz, 2H), 6.71–6.70 (m, 1H), 4.34 (s, 2H), 2.57 (s, 3H), 2.33 (s, 3H); ¹³C-NMR (CDCl₃) δ 152.4, 142.2, 141.5, 141.4, 139.7, 134.0, 133.3, 132.1, 131.7, 128.6, 128.2, 126.0, 118.8, 94.6, 31.2, 21.3, 15.5; HRMS [M-OTs]⁺ Calc'd. for C₁₂H₁₁SBrl: 392.8810, Found: 392.8807.

3-Bromomethylphenyl(5'-methoxy-2'-thienyl)iodonium tosylate (36)—Yield 78%. mp = 58–59 °C. ¹H-NMR (CDCl₃) δ 7.97 (t, *J* = 2 Hz, 1H), 7.81 (dd, *J* = 1.2, 8 Hz, 1H), 7.64 (dd, *J* = 1.6, 8 Hz, 2H), 7.55–7.51 (m, 2H), 7.35 (t, *J* = 8 Hz, 1H), 7.12 (d, *J* = 8

Hz, 2H), 6.22 (d, $J = 4.4$ Hz, 1H), 4.37 (s, 2H), 3.95 (s, 3H), 2.34 (s, 3H); ^{13}C -NMR (CDCl_3) δ 176.0, 142.3, 141.8, 141.6, 139.8, 133.3, 132.5, 132.2, 131.9, 128.7, 126.0, 119.1, 107.2, 61.0, 31.1, 21.3. This compound decomposed to a black tar during drying under vacuum at room temperature.

[3-(Methoxycarbonyl)phenyl](2'-thienyl)iodonium tosylate (37)—Yield 58%. mp = 140–141 °C; ^1H -NMR ($\text{MeOD}-d_4$) δ 8.76 (s, 1H), 8.37 (d, $J = 7.2$ Hz, 1H), 8.26 (d, $J = 7.6$ Hz, 1H), 8.05 (d, $J = 2.8$ Hz, 1H), 7.90 (d, $J = 5.6$ Hz, 1H), 7.69–7.62 (m, 3H), 7.22–7.17 (m, 3H), 3.94 (s, 3H), 2.36 (s, 3H); ^{13}C -NMR ($\text{MeOD}-d_4$) δ 166.1, 143.7, 142.7, 141.8, 139.9, 139.1, 136.5, 134.9, 134.3, 133.4, 131.1, 130.0, 127.1, 119.1, 99.3, 53.5, 21.5; HRMS $[\text{M}-\text{OTs}]^+$ Calc'd. for $\text{C}_{12}\text{H}_{10}\text{O}_2\text{SI}$: 344.9446, Found: 344.9447.

[4-(Methoxycarbonyl)phenyl](2'-thienyl)iodonium tosylate (38)—Yield 83%. mp = 188–190 °C; ^1H -NMR ($\text{MeOD}-d_4$) δ 8.26 (dd, $J = 2, 7.2$ Hz, 2H), 8.32 (dd, $J = 1.6, 6.8$ Hz, 2H), 8.05 (dd, $J = 1.2, 3.6$ Hz, 1H), 7.92 (dd, $J = 1.2, 5.2$ Hz, 1H), 7.69 (d, $J = 5.6$ Hz, 2H), 7.23–7.18 (m, 3H), 3.92 (s, 3H), 2.36 (s, 3H); ^{13}C -NMR ($\text{MeOD}-d_4$) δ 166.8, 143.7, 142.8, 141.8, 139.2, 136.0, 135.2, 133.7, 131.1, 130.0, 127.1, 123.4, 99.1, 53.4, 21.5; HRMS $[\text{M}-\text{OTs}]^+$ Calc'd. for $\text{C}_{12}\text{H}_{10}\text{O}_2\text{SI}$: 344.9446, Found: 344.9442.

Syntheses of functionalized diaryliodonium salts through reaction of the HTIA from 4-methoxy-(diacetoxyiodo)benzene with functionalized arylstannanes

3-Formylphenyl(4'-methoxyphenyl)iodonium tosylate (39)— p -TsOH·H₂O (0.10 g, 0.53 mmol) was added to a suspension of 4-methoxy-(diacetoxyiodo)benzene (0.19 g, 0.53 mmol) in MeCN (2 mL) while cooling this mixture to 0 °C. The resultant yellow solution was diluted with chloroform (15 mL). 3-Formyl-3-(tri-*n*-butylstannyl)benzaldehyde (0.21 g, 0.52 mmol) in chloroform (5 mL) was added in portions and the mixture gradually heated to reflux for 2 h. The consumption of organotin compound was monitored by TLC (silica gel, 5% EtOAc/hexane; $R_f = 0.4$) and disappearance of HTIA was confirmed with KI-starch paper. The reaction mixture was then cooled to rt and solvent was removed *in vacuo* to give a pale yellow oil which was triturated with Et₂O. Solid was filtered off, washed with Et₂O, and dried under vacuum to give **39** as a white solid. Yield 44%. mp = 156–159 °C; ^1H -NMR (CDCl_3) δ 9.81 (s, 1H), 8.41 (s, 1H), 8.22 (d, $J = 8$ Hz, 1H), 7.94–7.90 (m, 3H), 7.47–7.40 (m, 3H), 6.98 (d, $J = 8$ Hz, 2H), 6.81 (d, $J = 9.2$ Hz, 2H), 3.78 (s, 3H), 2.29 (s, 3H); ^{13}C -NMR (CDCl_3) δ 189.9, 162.5, 142.2, 140.0, 139.7, 138.5, 137.7, 136.0, 131.8, 131.2, 128.5, 125.9, 117.51, 116.9, 104.1, 55.6, 21.2; HRMS $[\text{M}-\text{OTs}]^+$ Calc'd. for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{I}$: 338.9882, Found: 338.9880.

The following compounds (**40–44**) were prepared similarly.

4-Formylphenyl(4'-methoxyphenyl)iodonium tosylate (40)—Yield 52%. mp = 184–187 °C; ^1H -NMR (CDCl_3) δ 9.93 (s, 1H), 8.10 (d, $J = 8.4$ Hz, 2H), 7.90 (d, $J = 9.2$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 2H), 7.41 (d, $J = 8$ Hz, 2H), 6.99 (d, $J = 8$ Hz, 2H), 6.81 (d, $J = 9.2$ Hz, 2H), 3.78 (s, 3H), 2.29 (s, 3H); ^{13}C -NMR (CDCl_3) δ 190.7, 162.5, 142.1, 139.7, 137.8, 137.6, 135.2, 131.6, 128.5, 125.9, 122.2, 117.5, 104.1, 55.6, 21.3; HRMS $[\text{M}-\text{OTs}]^+$ Calc'd. for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{I}$: 338.9882, Found: 338.9878.

3-Formyl-6-methoxyphenyl(4'-methoxyphenyl)iodonium tosylate (41)—Yield 50%. mp = 185–187 °C; ^1H -NMR (CDCl_3) δ 9.77 (s, 1H), 8.16 (d, $J = 2$ Hz, 1H), 7.99 (dd, $J = 1.6, 8.4$ Hz, 1H), 7.91 (dd, $J = 2, 6.8$ Hz, 2H), 7.51 (d, $J = 2$ Hz, 2H), 7.10–7.03 (m, 3H), 6.87 (dd, $J = 2, 6.8$ Hz, 2H), 4.02 (s, 3H), 3.82 (s, 3H), 2.31 (s, 3H); ^{13}C -NMR (CDCl_3) δ 188.4, 162.7, 160.8, 142.4, 139.6, 137.8, 136.8, 135.3, 132.2, 128.5, 126.0, 117.7, 112.2,

106.6, 102.1, 57.6, 55.6, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₅H₁₄O₃I: 368.9988, Found: 368.9982.

[3-(Methylcarbamoyl)phenyl](4'-methoxyphenyl)iodonium tosylate (42)—Yield 65%. mp = 172–173 °C; ¹H-NMR (MeOD-*d*₄) δ 8.53 (t, *J* = 1.6 Hz, 1H), 8.24 (dq, *J* = 0.8, 8 Hz, 1H), 8.10 (dd, *J* = 2, 7.6 Hz, 2H), 8.04 (dq, *J* = 1.2, 8 Hz, 1H), 7.68 (dd, *J* = 1.6, 8 Hz, 2H), 7.59 (t, *J* = 8 Hz, 1H), 7.21 (d, *J* = 8 Hz, 2H), 7.06 (dd, *J* = 3.2, 10.4 Hz, 2H), 3.84 (s, 3H), 2.91 (s, 3H), 2.36 (s, 3H); ¹³C-NMR (MeOD-*d*₄) δ 167.9, 164.8, 143.7, 141.8, 139.2, 138.9, 138.6, 135.1, 133.2, 131.7, 130.0, 127.1, 119.1, 116.8, 104.7, 56.5, 27.2, 21.5; HRMS [M-OTs]⁺ Calc'd. for C₁₅H₁₅NO₂I: 368.0148, Found: 368.0150.

3-Formylphenyl(2'-thienyl)iodonium tosylate (43)—Yield 48%. mp = 153–156 °C; ¹H-NMR (CDCl₃) δ 9.82 (s, 1H), 8.40 (t, *J* = 1.6 Hz, 1H), 8.25 (dq, *J* = 1.2, 8 Hz, 1H), 7.94 (dt, *J* = 1.2, 7.6, 1H), 7.86 (dd, *J* = 1.2, 4 Hz, 1H), 7.58 (dd, *J* = 1.2, 5.2 Hz, 1H), 7.49 (t, *J* = 4.8 Hz, 1H), 7.43 (d, *J* = 8 Hz, 2H), 7.04–7.02 (m, 3H), 2.32 (s, 3H); ¹³C-NMR (CDCl₃) δ 189.5, 141.1, 140.2, 139.4, 138.6, 136.5, 135.3, 132.0, 131.6, 131.5, 129.8, 128.7, 125.9, 119.5, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₁H₈O₂SI: 314.9341, Found: 314.9340.

3-Formyl-6-methoxyphenyl(2'-thienyl)iodonium tosylate (44)—Yield 48%; mp = 178–179 °C; ¹H-NMR (CDCl₃) δ 9.73 (s, 1H), 7.97 (dd, *J* = 2, 8.4 Hz, 1H), 7.76 (dd, *J* = 1.2, 4 Hz, 1H), 7.51 (dd, *J* = 1.2, 5.2 Hz, 1H), 7.41 (dd, *J* = 1.6, 8.4 Hz, 2H), 7.06–7.01 (m, 3H), 6.97 (dd, *J* = 3.6, 5.2 Hz, 1H), 4.02 (s, 3H), 2.31 (s, 3H); ¹³C-NMR (CDCl₃) δ 188.4, 160.6, 142.1, 140.4, 139.7, 138.9, 135.5, 135.0, 131.8, 129.2, 128.5, 125.9, 112.2, 110.2, 98.5, 57.4, 21.3; HRMS [M-OTs]⁺ Calc'd. for C₁₂H₁₀O₂SI: 344.9446, Found: 344.9441.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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R^1 = electron-withdrawing or
electron-donating group

Ar = a relatively electron-deficient aryl group *e.g.*,
4-methoxyphenyl or 2-thienyl

Scheme 1.

General utility of diaryliodonium salts for preparing [^{18}F]fluoroarenes from cyclotron-produced [^{18}F]fluoride ion.

Scheme 2.

Synthesis of diaryliodonium tosylates via the generation of HTIAs in situ followed by treatment with an electron-rich arene. Reagents and conditions: i) sodium perborate in MeCO₂H or peracetic acid in MeCO₂H; ii) *p*-TsOH·H₂O, MeCN/CHCl₃, reflux; iii) reflux.

Scheme 3.

Synthesis of functionalized diaryliodonium tosylates by treating 4-[hydroxy(tosyloxy)iodo]anisole, generated in situ, with arylstannanes. Reagents and conditions: i) sodium perborate in MeCO_2H ; ii) $p\text{-TsOH}\cdot\text{H}_2\text{O}$, MeCN , reflux; iii) R_6Sn_2 , $\text{Pd}(\text{PPh}_3)_4$, 1,4-dioxane, reflux; iv) CHCl_3 , reflux ($\text{R} = \text{Me}$ for **29** and $\text{R} = n\text{-Bu}$ for **39–42**).

Scheme 4.

Synthesis of 2-thienylaryliodonium salts bearing an aldehyde group on the non-thienyl ring. Reagents and conditions: i) sodium perborate in MeCO₂H, 50 °C; overnight; ii) *p*-TsOH·H₂O, MeCN, reflux; iii) CHCl₃, reflux.

Table 1

Yields of Substituted Diaryliodonium Tosylates ($\text{ArI}^+4\text{-MeOC}_6\text{H}_4\text{OTs}^-$) from (Diacetoxy)iodoarenes ($\text{R}^1\text{R}^2\text{ArI}(\text{OAc})_2$) and Electron-Rich Arenes.

Entry	(Diacetoxyiodo)arene		Electron-rich arene	Product	Yield (%)
	R^1	R^2			
1	2- CH_2Cl	H	Anisole		83
2	3- CH_2Cl	H	Anisole		84
3	4- CH_2Cl	H	Anisole		90
4	2- CH_2Br	H	Anisole		46
5	3- CH_2Br	H	Anisole		78
6	4- CH_2Br	H	Anisole		81
7	3-MeOCO	H	Anisole		63
8	3-EiOCO	H	Anisole		69
9	3-AcO	H	Anisole		88
10	4-AcO	H	Anisole		88
11	3-AcO	4-AcO	Anisole		86
12	2- $\text{CH}(\text{OAc})_2$	H	Anisole		77

Entry	(Diaceoxyiodo)arene		Electron-rich arene	Product	Yield (%)
	R ¹	R ²			
13	4-CH ₂ Cl	H	1,3,5-Trimethoxybenzene		98
14	3-CH ₂ Br	H	Thiophene		83
15	3-CH ₂ Br	H	2-Methylthiophene		57
16	3-CH ₂ Br	H	2-Methoxythiophene		~78
17	3-MeOCO	H	Thiophene		58
18	4-MeOCO	H	Thiophene		83

Table 2

Yields of Substituted Diaryliodonium Tosylates from a (Diacetoxyiodo)arene Treated with a Substituted Arylstannane.

Entry	R ¹	R ²	R ³	(Diacetoxyiodo)arene	Product	Yield (%)
1	3-OAc	H	Me	4-MeOC ₆ H ₄ I(OAc) ₂		79
2	3-CHO	H	Bu	4-MeOC ₆ H ₄ I(OAc) ₂		44
3	4-CHO	H	Bu	4-MeOC ₆ H ₄ I(OAc) ₂		52
4	3-CHO	6-MeO	Bu	4-MeOC ₆ H ₄ I(OAc) ₂		50
5	3-MeNHCO	H	Bu	4-MeOC ₆ H ₄ I(OAc) ₂		65
6	3-CHO	H	Bu	2-Thienyliodo(OAc) ₂		48
7	3-CHO	6-MeO	Bu	2-Thienyliodo(OAc) ₂		48