Synthesis of Biphenyl Iodonium Salts as (Radio)labelling Precursors for Fluoroarenes

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PROCEEDING OF THE SOLUTIONS IN CHEMISTRY 2024, 11–15 NOVEMBER 2024, SVETI MARTIN NA MURI, CROATIA

Abstract: Radiolabelled [18F]fluorobiphenyl moieties are often used for the development of positron emission tomography (PET) tracers in several medicinal fields, including tumor detection, epilepsy, and Alzheimer's disease. Since these electron-rich [18F]fluoroarenes cannot be obtained through traditional S_NAr reactions, other radiolabelling precursors are required. For example, [18F]fluorobiphenyl moieties can be obtained from (biphenyl)(aryl)iodonium salts. These biphenyl iodonium salts are often synthesized from iodobiphenyls or biphenylboronic acids. However, these syntheses require harsh reaction conditions, limiting the scope for oxidation and acid-sensitive biphenyls. As a potential solution, we attempted to synthesize biphenyl iodonium salts from biphenyl and pre-oxidized iodoarenes. However, this approach was found to be unsuccessful. Instead, easily obtained biphenyltrimethylsilanes were found as a promising starting point for the synthesis of biphenyl iodonium salts under mild conditions. The synthesized diaryliodonium salts were successfully used for fluorination reactions, indicating the potential of these precursors in the synthesis of fluoroarenes.

Keywords: radiofluorination, [18F]fluoroarene, biphenyl, diaryliodonium salt, biphenyl iodonium salt.

INTRODUCTION

DIARYLIODONIUM salts are a class of hypervalent iodine(III) species, whose general structure consists of a central iodine(III) atom with two aryl moieties and an anion X⁻ in a T-shaped structure.[1,2] Their electrophilic nature and good leaving group abilities make them a versatile arylating agent for various nucleophiles, including alcohols, amines, amides, thiols, carbonyl compounds and nitroalkanes (Figure 1A).[2–4] This reactivity has also been exploited for the synthesis of radiolabelled [18F]fluoroarenes, using [18F]fluoride as nucleophile (Figure 1B). After the initial discovery by Pike in 1995,[5] several other research groups have further studied the use of diaryliodonium salts as radiofluorination precursors,[6–13] allowing this strategy to be commonly used in fluorine-18 labelling including in the late-stage fluorination of elaborate PET (positron emission tomography) tracers.[14] This is especially useful for the synthesis of electron-rich [18F]fluoroarenes, as their synthesis via more traditional S_NAr methods is not possible.[15–17]

Upon treatment of diaryliodonium salts with nucleophiles, one aryl moiety is transferred to the nucleophile (blue in Figure 1), and the other aryl moiety ends up as aryl iodide waste (green in Figure 1).[2,3] This latter aryl moiety is often referred to as "dummy ligand" if it is incorporated in unsymmetrical diaryliodonium salts in which both aryl moieties are different. Especially in late-stage fluorination approaches, the use of unsymmetrical diaryliodonium salts is beneficial, as this allows for the use of cheaper dummy ligands which greatly diminishes the value of the aryl iodide waste upon fluorination. However, this approach requires good regioselectivity of the reaction. Fortunately, it is known that under metal-free conditions the nucleophile is transferred to the more electron-deficient aryl moiety.[18] As such, unsymmetrical diaryliodonium salts bearing electron-rich dummy ligands, such as the trimethoxybenzene or anisole groups in **1** and **2**, respectively, allow for selective
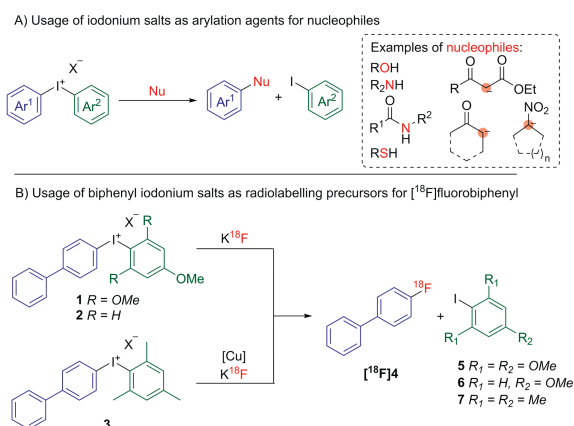
Figure 1. A) Usage of diaryliodonium salts as arylation agents for various nucleophiles. B) Synthesis of [18F]fluoroarene **[18F]4** using diaryliodonium salts **1-3** as radiolabelling precursors. Under metal-free conditions the use of an electron-rich dummy ligand allows for regioselective 18F-fluorination, while bulky mesityl ligands are beneficial in copper-catalyzed approaches.

[18F]fluorination of the partner aryl ligand (Figure 1B).[7,13] Meanwhile, for Cu-catalyzed arylation a bulky dummy ligand, such as the mesityl moiety in **3**, can be used to control the regioselectivity of the oxidative addition to the Cu-catalyst and allow selective [18F]fluorination.[9,19–21]

We got interested in the use of biphenyl iodonium salts (i.e., diaryliodonium salts in which one aryl moiety is a biphenyl group) as radiofluorination precursors for [18F]fluorobiphenyl moieties, given our ongoing research in the synthesis of radioligands targeting GABA transporter 1 and their applications in epilepsy diagnosis.[22–24] Fluorobiphenyl moieties have been recognized as important moieties in potent binders to the GABA transporter,[25] indicating the synthesis of radiofluorinated versions might be a promising approach. Moreover, [18F]fluorobiphenyls have been shown useful in candidate drugs for Alzheimer's disease,[26] monoacylglycerol lipase imaging agents,[27] and orexin receptor-binding PET ligands,[28] and have also been used in research towards radioprobes for tumor detection,[29,30] and in PET imaging agents for translocator protein (TSPO).[31] Given the importance of [18F]fluorobiphenyl moieties for the development of PET tracers in several medicinal fields, we wanted to further study the synthesis of biphenyl iodonium salts as potential radiolabelling precursors.

Most literature methods for the preparation of biphenyl iodonium salts start either from iodobiphenyl **8** [7,13,32–41] or biphenylboronic acid **12**[42–46] (Figure 2A). However, this approach could be met with difficulties when applied to the synthesis of more substituted biphenyl iodonium salts, thereby limiting the potential application of these radiolabelling precursors in the late-stage fluorination
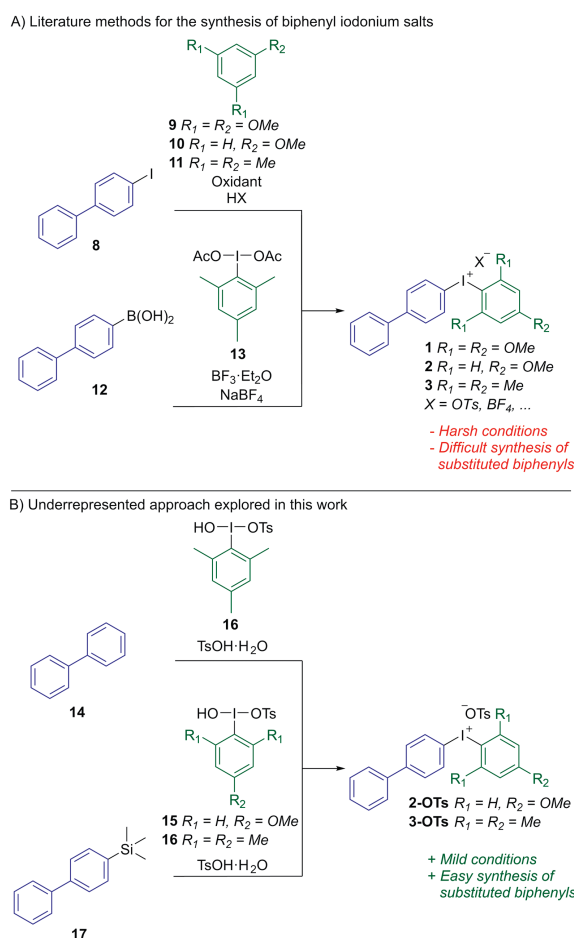
Figure 2. A) Literature methods for the synthesis of biphenyl iodonium salts starting from iodobiphenyl **8** or biphenyl-boronic acid **12**; B) Synthesis of biphenyl iodonium salts starting from biphenyl **14** and 4-(trimethylsilyl)biphenyl **17** which is the focus of this research.

of PET tracers. Firstly, the synthesis of the iodobiphenyl or biphenyl boronic acid starting materials may be rather challenging for more substituted biphenyls, especially considering the fact that biphenyl groups are often constructed via Suzuki cross-coupling reactions, in which both iodine and boronic acid moieties are reactive. Moreover, these literature methods require quite harsh conditions, requiring all substituents in iodobiphenyl starting materials to be stable in oxidative conditions, and requiring more elaborate biphenylboronic acids to be stable in the presence of the strong Lewis acid BF$_3$·Et$_2$O.

A potential solution to these problems would be to start from biphenyl **14** and have the iodine on the dummy ligand (Figure 2B). Since this approach requires no halide or boronic acid handle on the biphenyl group, the biphenyl moiety can be easily constructed through a Suzuki cross-coupling reaction. Moreover, the possibility of using pre-

oxidized dummy ligands allows for a synthesis in relatively mild conditions with no problems for oxidation-sensitive groups. However, this synthesis starting from biphenyl **14** is very underrepresented in literature, with only one example being performed by the Olofsson group.[47] Therefore, in this paper we further investigate the synthesis of biphenyl iodonium salt **3-OTs** starting from biphenyl. We compare this method with the more frequently employed synthetic methods based on iodobiphenyl or biphenyl-boronic acid precursors. Finally, we elaborate on the use of trimethylsilyl substituted biphenyl **17** as precursor for the synthesis of biphenyl iodonium salts **2-OTs** and **3-OTs** (Figure 2B). This research may provide a useful guide for those who are interested in the synthesis of biphenyl iodonium salts for various applications.

MATERIALS AND METHODS

General Methods

The reagents were bought from commercial suppliers and used as received, unless noted otherwise. *m*-CPBA was dried under vacuum and iodometrically titrated to determine the concentration of active oxidizing agent.[48] Moisture and air sensitive reactions were carried out under nitrogen environment using standard Schlenk-techniques. Thin layer chromatography was performed using TLC Silica gel 60 F_{254} TLC plates (Merck) and visualized using UV-light (254 nm). Flash column chromatography was performed using a Biotage Isolera One Flash Chromatograph and pre-packed silica cartridges (Biotage Sfär Silica D Duo 60 μm). Melting points were determined using a Stuart SMP10 melting point apparatus.

NMR measurements were carried out using a JEOL 400YH 400 MHz NMR spectrometer. Chemical shift values are reported in ppm and referenced to the residual solvent signal.[49] Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration.

GC-MS measurements were performed using a Shimadzu GCMS-QP2020 NX gas chromatograph-mass spectrometer. Samples were prepared as 1 mg mL^{-1} solutions in chloroform, after which 1 μL of the solution was injected using split injection with a split ratio of –1.0 and an injector temperature of 250 °C. A pressure-controlled (120.0 kPa) helium flow rate of 2.04 mL min^{-1} was used for chromatographic separation on a SLB 5MS column with a 30 m length, a 0.25 mm inner diameter, and a 0.25 μm film thickness. The temperature program of the column oven consisted of four stages; 50 °C was held for one minute, then ramped to 200 °C at a rate of 40 °C min^{-1}, followed by ramping to 300 °C at a rate of 15 °C min^{-1}, after which the latter temperature was held for four minutes to give a total

run time of 15.42 min. MS data was measured using quadrupole mass analyzer after electron-impact ionization at 70 eV with an ion source temperature of 250 °C. The MS range was analyzed from 35 to 750 *m/z* with a scan speed of 5000 amu/s and a solvent delay of 2 min. For the fluorination trials a longer GC-MS method was used, in which the temperature of the column oven was held at 50 °C for one minute, then ramped to 300 °C at a rate of 5 °C min^{-1}, after which the latter temperature was held for four minutes to give a total run time of 55.00 min. Other parameters were the same as stated above.

SYNTHESIS OF BIPHENYL-4-YL(2,4,6-TRIMETHOXYPHENYL)IODONIUM TOSYLATE (1-OTs)

*Method A (starting from iodobiphenyl **8** and trimethoxybenzene **9**):* The diaryliodonium salt was prepared according to a procedure by Stuart and co-workers.[32] A round-bottomed flask was charged with 4-iodobiphenyl (**8**) (0.14 g, 0.50 mmol, 1.0 equiv.) and MeCN (2 mL), after which TsOH · H$_2$O (96 mg, 0.51 mmol, 1.0 equiv.) and *m*-CPBA (96 mg, 0.51 mmol, 91 %, 1.0 equiv.) were added. After attaching a reflux condenser, the reaction was lowered into a pre-heated oil bath and stirred at 77 °C for 30 minutes. Then, the reflux condenser was removed to add 1,3,5-trimethoxybenzene (**9**) (85 mg, 0.51 mmol, 1.0 equiv.) and stirring was continued at 77 °C for 5 minutes. The reaction was concentrated *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in a light brown powder (0.15 g, 0.23 mmol, 47 %). mp: 143–144 °C (lit: 162–164 °C); ^{1}H NMR (DMSO-d$_6$, 400 MHz) *δ*: 7.98 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.66 (d, *J* = 7.4 Hz, 2H), 7.53–7.38 (m, 5H), 7.10 (d, *J* = 7.7 Hz, 2H), 6.48 (s, 2H), 3.97 (s, 6H), 3.87 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (DMSO-d$_6$, 101 MHz) δ: 166.2, 159.5, 145.8, 143.2, 138.2, 137.6, 134.9, 129.7, 129.2, 128.6, 128.1, 127.0, 125.5, 114.6, 92.1, 87.1, 57.4, 56.2, 20.8. Analytical data are in accordance with literature.[7,32]

*Method B (starting from iodobiphenyl **8** and trimethoxybenzene **9**):* The diaryliodonium salt was prepared according to a procedure by Chun and co-workers.[7] A round-bottomed flask was charged with 4-iodobiphenyl (**8**) (0.14 g, 0.50 mmol, 1.0 equiv.), *m*-CPBA (0.11 g, 0.58 mmol, 91%, 1.2 equiv.), TsOH · H$_2$O (0.11 g, 0.55 mmol, 1.1 equiv.) and DCM (4 mL), after which the mixture was stirred at room temperature for 4 h. Then, 1,3,5-trimethoxybenzene (**9**) (0.13 g, 0.75 mmol, 1.5 equiv.) was added to the mixture, after which the mixture was stirred at room temperature for 0.5 h. The solvent was removed *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in a white powder (0.28 g, 0.45 mmol, 89 %). mp: 167–170 °C (lit: 162–164 °C); ^{1}H NMR (DMSO-d$_6$,

400 MHz) δ: 7.98 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 7.4 Hz, 2H), 7.53 – 7.38 (m, 5H), 7.10 (d, J = 7.7 Hz, 2H), 6.48 (s, 2H), 3.97 (s, 6H), 3.87 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (DMSO-d$_6$, 101 MHz) δ: 166.5, 159.7, 146.0, 143.4, 138.4, 137.8, 135.2, 129.9, 129.4, 128.8, 128.3, 127.2, 125.7, 114.8, 92.3, 87.3, 57.6, 56.4, 21.0. Analytical data are in accordance with literature.[7,32]

SYNTHESIS OF BIPHENYL-4-YL(4-METHOXYPHENYL)IODONIUM TOSYLATE (2-OTs)

Koser intermediate **15** (0.10 g, 0.24 mmol, 1.0 equiv.), 4-(trimethylsilyl)biphenyl (**17**) (54 mg, 0.24 mmol, 1.0 equiv.), and TsOH · H$_2$O (45 mg, 0.24 mmol, 1.0 equiv.) were introduced into a pressure vial, which was used instead of a round-bottomed flask equipped with condenser because of the small solvent volume. MeCN (0.66 mL) was added, after which the pressure vial was capped and the reaction mixture was stirred at 77 °C for 4 h. Afterwards, the solvent was removed *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in an off-white powder (36 mg, 64 µmol, 27 %). mp = 154–155 °C (lit: 178–181 °C); ^{1}H NMR (CD$_3$OD, 400 MHz) δ: 8.16 (d, J = 8.2 Hz, 2H), 8.10 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 7.9 Hz, 2H), 7.68 (d, J = 7.7 Hz, 2H), 7.60 (d, J = 7.3 Hz, 2H), 7.43 (dt, J = 17.3, 7.0 Hz, 3H), 7.19 (d, J = 7.7 Hz, 2H), 7.04 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (CD$_3$OD, 101 MHz) δ: 163.8, 145.9, 142.9, 141.0, 139.3, 137.9, 135.9, 130.7, 129.6, 129.2, 127.6, 126.3, 118.2, 114.2, 104.1, 55.7, 20.7. Analytical data are in accordance with literature.[13]

SYNTHESIS OF BIPHENYL-4-YL(MESITYL)IODONIUM TOSYLATE (3-OTs)

Route A (starting from iodomesitylene 7 and biphenyl 14): m-CPBA (56 mg, 0.25 mmol, 77 %, 1.0 equiv.), iodomesitylene (**7**) (62 mg, 0.25 mmol, 1.0 equiv.), and biphenyl (**14**) (39 mg, 0.25 mmol, 1.0 equiv.) were dissolved in CH$_2$Cl$_2$/TFE (1 : 1, 1.3 mL). Subsequently, TsOH · H$_2$O (48 mg, 0.25 mmol, 1.0 equiv.) was added in one portion and the mixture was stirred for 6 or 16 hours (see Table 1) at rt. The solvent was removed *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in small amounts of discolored/black solid (see Table 1).

Route B (starting from Koser intermediate 16 and biphenyl 14): Koser intermediate **16** (0.10 g, 0.23 mmol, 1.0 equiv.) was dissolved in solvent (Table 2), followed by the addition of biphenyl (**14**) (42 mg, 0.27 mmol, 1.2 equiv.) and (if applicable) the additive TsOH · H$_2$O (46 mg, 0.24 mmol, 1.1 equiv., see Table 2) was added. After stirring for 16 h at rt, the solvent was removed *in vacuo* and the crude product

was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in small amounts of discolored/black solid (see Table 2).

Route C (starting from iodobiphenyl 8 and mesitylene 11): The diaryliodonium salt was prepared according to a procedure by Olofsson and co-workers.[47] m-CPBA (56 mg, 0.25 mmol, 77 %, 1.0 equiv.), 4-iodobiphenyl (**8**) (70 mg, 0.25 mmol, 1.0 equiv.), and mesitylene (**11**) (35 µL, 0.25 mmol, 1.0 equiv.) were dissolved in DCM/TFE (1 : 1, 1.25 mL). Subsequently, TsOH · H$_2$O (48 mg, 0.25 mmol, 1.0 equiv.) was added in one portion and the mixture was stirred for at rt for 16 h. Afterwards, the solvent was removed *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in a white powder (67 mg, 0.12 mmol, 47 %). mp = 175–176 °C (lit: 184–186 °C); ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 8.00 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 7.5 Hz, 2H), 7.49-7.34 (m, 5H), 7.19 (s, 2H), 7.06 (d, J = 7.8 Hz, 2H), 2.59 (s, 6H), 2.26 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (DMSO-d$_6$, 101 MHz) δ: 146.2, 143.9, 143.7, 142.2, 138.6, 138.2, 135.6, 130.4, 130.3, 129.7, 129.2, 128.6, 127.5, 126.0, 123.2, 113.5, 26.9, 21.3, 21.1. Analytical data are in accordance with literature.[46]

Route D (starting from Koser intermediate 16 and 4-(trimethylsilyl)biphenyl 17): Koser intermediate **16** (0.10 g, 0.23 mmol, 1.0 equiv.), 4-(trimethylsilyl)biphenyl (**17**) (52 mg, 0.23 mmol, 1.0 equiv.), and TsOH · H$_2$O (44 mg, 0.23 mmol, 1.0 equiv.) were introduced into a pressure vial, which was used instead of a round-bottomed flask equipped with condenser because of the small solvent volume. MeCN (0.66 mL) was added, after which the pressure vial was capped and the reaction mixture was stirred at 77 °C for 4 h. Afterwards, the solvent was removed *in vacuo* and the crude product was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in an off-white powder (0.10 g, 0.18 mmol, 79 %). mp = 171–172 °C (lit: 184–186 °C); ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 8.03 (d, J = 8.6 Hz, 2H), 7.77 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 7.0 Hz, 2H), 7.56-7.37 (m, 5H), 7.22 (s, 2H), 7.10 (d, J = 7.8 Hz, 2H), 2.62 (s, 6H), 2.29 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (DMSO-d$_6$, 101 MHz) δ: 145.7, 143.4, 143.1, 141.6, 138.1, 137.6, 135.0, 129.9, 129.8, 129.2, 128.7, 128.1, 127.0, 125.5, 122.7, 113.0, 26.4, 20.8, 20.5. Analytical data are in accordance with literature.[46]

SYNTHESIS OF BIPHENYL-4-YL(MESITYL)IODONIUM TETRAFLUOROBORATE (3-BF$_4$)

The diaryliodonium salt was prepared according to a procedure by Sanford and co-workers.[43] Biphenyl-4-boronic acid (**12**) (0.10 g, 0.51 mmol, 1.0 equiv.) was dissolved in DCM

(6.7 mL) in an oven-dried round-bottomed flask equipped with CaCl$_2$ drying tube. The mixture was cooled to 0 °C, BF$_3$·Et$_2$O (70 μL, 0.56 mmol, 1.1 equiv.) was added, and the mixture was stirred for 10 minutes at 0 °C. Afterwards, a solution of diacetoxyiodo reagent **13** (0.19 g, 0.53 mmol, 1.1 equiv.) in DCM (1.6 mL) was added and the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched by the addition of sat. aq. NaBF$_4$ (10 mL). After 30 minutes of vigorous stirring, the product was extracted with DCM (3 × 15 mL). The combined organic layers were dried over anhydrous MgSO$_4$ and evaporated *in vacuo*, after which the crude product was triturated in Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in a white powder (0.19 g, 0.38 mmol, 76 %). mp = 201–202 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.04 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 7.3 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.23 (s, 2H), 2.64 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 143.4, 143.1, 141.6, 138.1, 135.0, 129.9, 129.8, 129.2, 128.7, 127.0, 122.8, 113.1, 26.4, 20.5; ^{19}F NMR (DMSO-d_6, 376 MHz) δ: -148.04 (s, 0.8 F), -148.10 (q, J = 1.0 Hz, 3.2 F). Analytical data are in accordance with literature.[43] The observed splitting in ^{19}F NMR is due to the ^{11}B/^{10}B isotope effects.

SYNTHESIS OF IODOMESITYLENE DIACETATE (13)

Iodomesitylene diacetate (**13**) was synthesized according to a literature procedure developed by Mo and co-workers.[50] To a round-bottomed flask equipped with a stirring bar, sodium periodate (2.1 g, 10 mmol, 1.0 equiv.), sodium acetate (1.6 g, 20 mmol 2.0 equiv.), and acetic acid (17 mL) were added. Subsequently, acetic anhydride (1.5 mL, 16 mmol. 1.6 equiv.) and iodomesitylene (**7**) (2.5 g, 10 mmol, 1.0 equiv.) were added. The reaction mixture was then refluxed at 120 °C for 2 h. After this time the reaction was quenched by the addition of water (50 mL). The product was extracted with DCM (3 x 25 mL), and the combined organic layers were washed with brine (50 mL), dried over anhydrous MgSO$_4$, and evaporated *in vacuo*. The crude residue was triturated with petroleum ether and stirred for 1 h. The diacetoxyiodo reagent was then isolated *via* vacuum filtration and washed with petroleum ether, resulting in a white powder (2.4 g, 6.5 mmol, 65 %). mp = 165–167 °C (lit: 160–163 °C); ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 7.10 (s, 2H), 2.70 (s, 6H), 2.35 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (CDCl$_3$, 101 MHz) δ: 176.6, 143.3, 141.5, 129.7, 129.1, 26.9, 21.3, 20.5. Analytical data are in accordance with literature.[51,52]

SYNTHESIS OF HYDROXY(TOSYLOXY)IODO-4-METHOXYBENZENE (15)

Hydroxy(tosyloxy)iodo-4-methoxybenzene (**15**) was synthesized according to a literature procedure developed by

Wirth and co-workers.[53] 4-Iodoanisole (**6**) (0.50 g, 2.1 mmol, 1.0 equiv.) was dissolved in DCM (3.0 mL), after which *m*-CPBA (0.41 g, 2.1 mmol, 91 %, 1.0 equiv.) and TsOH · H$_2$O (0.41 g, 2.1 mmol, 1.0 equiv.) were added. The reaction mixture was stirred at room temperature for 30 minutes, after which the product was triturated with Et$_2$O and stirred for 10 minutes. The product was isolated *via* vacuum filtration, washed with Et$_2$O, and briefly (2 minutes) dried *in vacuo* to yield the product as an off-white powder (0.73 g, 1.7 mmol, 81 %). While the compound is relatively stable in solution, it degrades within 20 minutes when isolated as a solid (see Supplementary Figures S29-32).[54,55] Therefore, the product was immediately used in the next step after isolation. mp = decomposition at rt; ^{1}H NMR (CD$_3$OD, 400 MHz) δ: 8.30–8.21 (m, 2H), 7.66 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.17–7.11 (m, 2H), 3.91 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (CD$_3$OD, 101 MHz) δ: 165.5, 143.1, 141.8, 140.2, 129.8, 126.9, 118.3, 111.6, 56.5, 21.3. Analytical data are in accordance with literature.[53,54]

SYNTHESIS OF HYDROXY(TOSYLOXY)IODOMESITYLENE (16)

Hydroxy(tosyloxy)iodomesitylene (**16**) was synthesized according to a literature procedure developed by Stuart and co-workers.[56] To a round bottom flask equipped with a stirring bar, iodomesitylene (**1**) (0.71 g, 2.9 mmol, 1.0 equiv.), MeCN (3.0 mL) and TsOH · H$_2$O (0.55 g, 2.9 mmol, 1.0 equiv.) were added. Subsequently, *m*-CPBA (0.65 g, 2.9 mmol, 77 %, 1.0 equiv.) was added in one portion at room temperature. Afterwards, the reaction mixture was stirred at 77 °C for 40 min. After this time the reaction mixture was allowed to gradually reach room temperature. The crude residue was triturated with Et$_2$O and stirred for 1 h. The product was isolated *via* vacuum filtration and washed with Et$_2$O, resulting in a white powder (0.99 g, 2.3 mmol, 79 %). mp = 102–103 °C (lit: 104–105 °C); ^{1}H NMR (CD$_3$OD, 400 MHz) δ: 7.59 (d, J = 5.1 Hz, 2H), 7.26 (s, 2H), 7.19 (d, J = 8.6 Hz, 2H), 2.71 (s, 6H), 2.40 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (CD$_3$OD, 101 MHz) δ: 147.3, 144.1, 142.8, 141.9, 130.5, 129.8, 126.9, 26.7, 21.3, 21.3. Analytical data are in accordance with literature.[54,56]

SYNTHESIS OF 4-(TRIMETHYLSILYL)BIPHENYL (17)

4-(Trimethylsilyl)biphenyl (**17**) was synthesized according to a modified literature procedure developed by Kuninobu and co-workers.[57] 4-(Trimethylsilyl)phenyl)boronic acid (0.58 g, 3.0 mmol, 1.0 equiv.), K$_2$CO$_3$ (1.2 g, 9.0 mmol, 3.0 equiv.), and Pd(PPh$_3$)$_4$ (35 mg, 30 μmol, 1.0 mol%) were introduced into an oven-dried Schlenk flask. Afterwards, a mixture of degassed toluene/MeOH/H$_2$O (9 : 1 : 5, 9.0 mL) was added followed by bromobenzene (0.32 mL, 3.0 mmol, 1.0 equiv.). The reaction mixture was stirred at reflux overnight under nitrogen. After cooling to room

temperature, water (10 mL) was added and the product was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and evaporated *in vacuo* to give the crude product. The crude product was purified using flash column chromatography (17 bar, 80 mL min⁻¹) eluting with heptane to give the title product **17** as a white solid (0.60 g, 2.7 mmol, 89 %). R_f (heptane) = 0.46; mp = 51–52 °C (lit: 51–52 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.66–7.59 (m, 6H), 7.49–7.43 (m, 2H), 7.39–7.34 (m, 1H), 0.33 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ: 141.8, 141.3, 139.4, 134.0, 128.9, 127.5, 127.3, 126.7, -0.9; MS (EI) *m/z* (%): 226.2 (22), 212.1 (17), 211.1 (100), 195.1 (8), 181.1 (6),165.1 (15), 152.1 (13), calcd for $C_{15}H_{18}Si^+$ = 226.1. Analytical data are in accordance with literature.[58,59]

SYNTHESIS OF 4-FLUOROBIPHENYL (4) USING THE SYNTHESIZED DIARYLIODONIUM SALTS

*Method A (starting from **3-OTs**):* Fluorination of mesityl iodonium salt **3-OTs** was performed according to a literature procedure developed by Sanford and co-workers.[43] Diaryliodonium salt **3-OTs** (29 mg, 50 μmol, 1.0 equiv.), KF (3.2 mg, 55 μmol, 1.1 equiv.), 18-crown-6 (5.3 mg, 20 μmol, 0.40 equiv.), and Cu(OTf)₂ (3.6 mg, 10 μmol, 0.20 equiv.) were added to a pressure vial. Anhydrous DMF (0.50 mL) was added, after which the pressure vial was capped. The reaction mixture was thoroughly mixed using a vortex shaker, after which it was stirred at 60 °C for 16 hours. After cooling to room temperature, presence of the desired product 4-fluorobiphenyl (**4**) was determined by GC-MS and ¹⁹F NMR. For GC-MS analysis, 62 μL of the crude reaction mixture was transferred to a vial, after which the volatiles were evaporated *in vacuo* and the residue was redissolved in CHCl₃ (1.5 mL). For ¹⁹F NMR analysis, 0.40 mL of the crude reaction mixture and 0.10 mL CDCl₃ were added to an NMR tube, after which ¹⁹F NMR was measured. 1-Fluoro-2-nitrobenzene (2.6 μL, 25 μmol, 0.50 equiv.) was then added as internal standard in order to determine the conversion (23 %) by ¹⁹F NMR. Lastly, in order to verify product formation, the NMR sample was spiked with commercial 4-fluorobiphenyl (**4**) (approx. 3.0 mg). ¹⁹F NMR (376 MHz, DMF/CDCl₃ 4:1) δ: -117.34–117.45 (m); MS (EI) *m/z* (%): 172.2 (100), 171.2 (50), 146.2 (28), 133.2 (15), 85.1 (29), calcd for $C_{12}H_9F^+$ = 172.1. Analytical data are in accordance with literature.[43,60,61]

*Method B (starting from **3-OTs**):* Mesityl diaryliodonium salt **3-OTs** (17 mg, 30 μmol, 1.0 equiv.), KF (1.9 mg, 33 μmol, 1.1 equiv.), Kryptofix 222 (11 mg, 30 μmol, 1.0 equiv.), and (MeCN)₄CuOTf (11 mg, 30 μmol, 1.0 equiv.) were added to a V-vial. Anhydrous DMF (0.50 mL) was added, after which the vial was sealed with a PTFE/Silicone septum cap. The reaction mixture was thoroughly mixed using a vortex shaker, after which it was stirred at 85 °C for 20 minutes. After cooling to room temperature, presence of the desired product 4-fluorobiphenyl (**4**) was determined by GC-MS and ¹⁹F NMR, according to the procedure in Method A using 0.10 mL crude reaction mixture for GC-MS analysis and 1.6 μL (15 μmol, 0.50 equiv.) 1-fluoro-2-nitrobenzene as internal standard for ¹⁹F NMR. Conversion was determined to be 13 % using ¹⁹F NMR. Analytical data are in accordance with the ones reported for Method A.
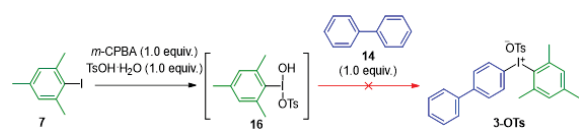
*Method C (starting from **2-OTs**):* Anisyl diaryliodonium salt **2-OTs** (17 mg, 30 μmol, 1.0 equiv.), KF (1.9 mg, 33 μmol, 1.1 equiv.), and Kryptofix 222 (11 mg, 30 μmol, 1.0 equiv.) were added to a V-vial. Anhydrous DMF (0.50 mL) was added, after which the vial was sealed with a PTFE/Silicone septum cap. The reaction mixture was thoroughly mixed using a vortex shaker, after which it was stirred at 150 °C for 20 minutes. After cooling to room temperature, presence of the desired product 4-fluorobiphenyl (**4**) was determined by GC-MS and ¹⁹F NMR, according to the procedure in Method A using 0.10 mL crude reaction mixture for GC-MS analysis and 1.6 μL (15 μmol, 0.50 equiv.) 1-fluoro-2-nitrobenzene as internal standard for ¹⁹F NMR. Conversion was determined to be 19 % using ¹⁹F NMR. Analytical data are in accordance with the ones reported for Method A.

RESULTS AND DISCUSSION

In order to study the possibility of obtaining biphenyl iodonium salts from biphenyl, initial experiments were conducted using iodomesitylene (**5**) and biphenyl (**14**) according to the method developed by Olofsson and co-workers (Table 1).[47] In this one-step approach Koser intermediate **16** is generated *in situ* from iodomesitylene (**5**), *m*-CPBA, and TsOH, after which a dehydrative condensation can yield diaryliodonium salt **3-OTs**. Since the use of fluoroalcohol media is known to be beneficial for the dehydrative condensation of arenes with iodine(III) compounds,[62] the synthesis of **3-OTs** was attempted using a mixture of DCM/TFE (1/1).

Unfortunately, this method did not work in our hands and the reactions resulted in complex reaction mixtures from which no iodine(III) product could be isolated after trituration (Table 1, Entry 1, 2). This outcome might be associated with the fact that the synthesis of diaryliodonium salts with electron-rich arenes, such as biphenyls, naphtalenes and diaryl ethers, may result in competing arene oxidation.[63] Therefore, it was investigated whether delayed addition of biphenyl could mitigate potential side-reactions arising from early oxidation of biphenyl, but unfortunately this did not solve the problem and the same outcome as before was achieved (Table 1, Entry 3).

After the unsuccessful outcomes in the one-step

Table 1. Optimization for the reaction between biphenyl (**14**) and iodomesitylene (**7**).

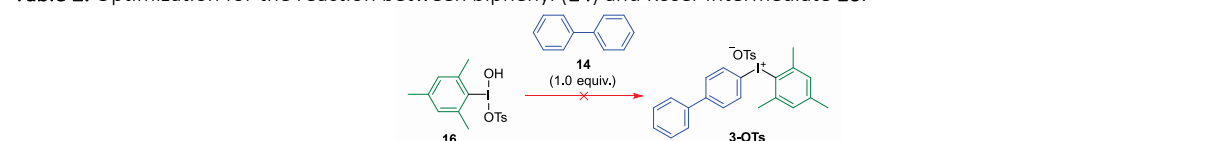| Entry	Solvent	Conc. **7** / mol L⁻¹	Temp. / °C	Time / h	Yield / %	Comment
1	50% TFE in DCM	0.2	25	16	NR	
2	50% TFE in DCM	0.2	25	6	NR	
3	50% TFE in DCM	0.2	25	6	NR	Biphenyl **14** added after 1 h

NR – no reaction

pathway according to literature procedure using biphenyl (**14**) and iodomesitylene (**5**),[47] a two-step pathway using Koser intermediate **16** was evaluated (Table 2), as the use of this pre-oxidized iodine(III) intermediate might give more control over the reaction and prevent side-reactions. Moreover, the possibility of using pre-oxidized dummy ligands allows for a synthesis in relatively mild conditions that can be translated more easily to more complicated biphenyls as it does not give problems for oxidation-sensitive groups.

Recognizing the enhanced efficiency of dehydrative condensation of arenes with iodine(III) compounds in fluoroalcohol media,[62] it was decided to evaluate the efficacy of the synthesis of **3-OTs** in various DCM-TFE mixtures (Table 2). Solvent mixture containing up to 10 %

TFE in DCM (Table 2, Entry 1, 2) were found to be insufficient to initiate the electrophilic aromatic substitution (EAS) reaction, leaving unreacted **16** after trituration in ether (according to ¹H NMR analysis). On the other hand, solvent mixtures containing at least 25 % TFE in DCM (Table 2, Entry 3–5) resulted in complex reaction pathways from which no iodine(III) product could be isolated after trituration.

Given the unsuccessful results for the direct dehydrative approach, an alternative procedure was attempted employing the use of acid additives. Using TsOH in MeCN (Table 2, Entry 6),[46] the reaction yielded a black solid in small quantities instead of the desired off-white solid (Supplementary Figure S1). This outcome can be attributed to the previously mentioned competing arene oxidations.[63] Although the synthesized diaryliodonium salt provided a clean ¹H NMR spectrum, it is known that discolored diaryliodonium salts often tend to display lower productivity in arylations.[63] As this is undesired for the radiofluorination, several attempts were performed to minimize the competing arene oxidation. Unfortunately, neither slower addition of biphenyl (Table 2, Entry 7), change in concentration (Table 2, Entry 8), or change of solvent (Table 2, Entry 9) proved effective and all yielded small amounts of discolored diaryliodonium salts as product.

Due to the unsuccessful results for the synthesis of biphenyl iodonium salt **3-OTs** starting from biphenyl (**14**), it was recognized that an iodine group or metalloid handle on the biphenyl would be required to avoid competing arene oxidation reactions and prevent the formation of less reactive discolored diaryliodonium salts. Despite the fact these metalloid or iodide based methods have considerable

Table 2. Optimization for the reaction between biphenyl (**14**) and Koser intermediate **16**.

Entry	Solvent	Conc. **16** / mol L⁻¹	Temp. / °C	Time / h	Additive	Yield / %	Comment
1	DCM	0.2	25	o.n.	-	NR	Only unreacted **16** obtained
2	10% TFE in DCM	0.2	25	o.n.	-	NR	Only unreacted **16** obtained
3	25% TFE in DCM	0.2	25	o.n.	-	NR	Complex mixture
4	50% TFE in DCM	0.2	25	o.n.	-	NR	Complex mixture
5	TFE	0.2	25	o.n.	-	NR	Complex mixture
6	MeCN	0.2	25	o.n.	TsOH · H₂O	22	Discolored product
7	MeCN	0.2	25	o.n.	TsOH · H₂O	17	Biphenyl **14** added over 30 min, discolored product
8	MeCN	0.4	25	o.n.	TsOH · H₂O	9	Discolored product
9	DCM	0.2	25	o.n.	TsOH · H₂O	11	Discolored product

o.n. – overnight; NR – no reaction.
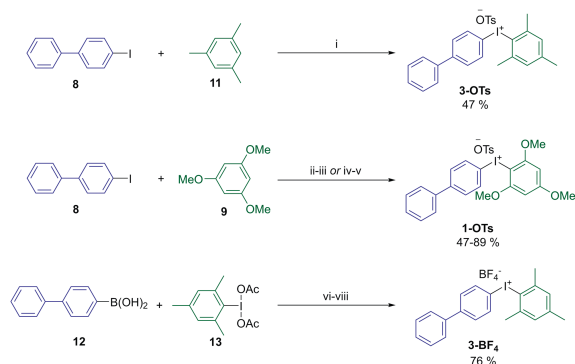
Scheme 1. Synthesis of biphenyl iodonium salts **1** and **3** starting from iodobiphenyl **8** and biphenylboronic acid **12**. Reagents and conditions: i) **8** (1.0 equiv.), **11** (1.0 equiv.), *m*-CPBA (1.0 equiv.), TsOH · H$_2$O (1.0 equiv.) DCM/TFE (1/1), rt, 16 h, 47 %; ii) **8** (1.0 equiv.), *m*-CPBA (1.0 equiv.), TsOH · H$_2$O (1.0 equiv.), MeCN, 77 °C, 30 min, iii) **9** (1.0 equiv.), 77 °C, 5 min, 47 %; iv) **8** (1.0 equiv.), *m*-CPBA (1.2 equiv.), TsOH · H$_2$O (1.1 equiv.), DCM, rt, 4 h, v) **9** (1.5 equiv.), rt, 30 min, 89 %; vi) **12** (1.0 equiv.), BF$_3$·Et$_2$O (1.1 equiv.), DCM, 0 °C, 10 min, vii) **13** (1.1 equiv.), DCM, 2 h, rt, viii) Sat. aq. NaBF$_4$, 76 %.

downsides (*vide supra*), we decided to investigate them in more detail. Therefore, diaryliodonium salts **1** and **3** were synthesized from iodophenyl (**8**) and biphenylboronic acid (**12**) according to literature procedures (Scheme 1).[47] To our delight, the one-pot synthesis using iodobiphenyl (**8**) and mesitylene (**11**) in TFE/DCM (1/1) cleanly afforded the desired product **3-OTs** as an off-white solid in moderate yield. Moreover, it was found that diaryliodonium salt **1-OTs** could be obtained when trimethoxybenzene (**9**) was

used as dummy ligand. For this product it was found that in our hands a synthesis in MeCN at reflux temperature gave a light brown product,[32] but a cleaner product could be obtained in higher yields when using DCM at room temperature.[7] Besides the synthesis starting from iodobiphenyl, the mesityl diaryliodonium salt **3-BF$_4$** was also obtained from biphenylboronic acid (**12**) and diacetoxyiodo reagent **13**, providing a means to access diaryliodonium salts with oxidation-sensitive groups on the biphenyl ligand.

However, both biphenyl starting materials **8** and **12** can be difficult to synthesize, especially for more substituted biphenyls, as the iodine and boronic groups are both reactive in Suzuki reactions (*vide supra*). Therefore, we aimed to find a different metalloid handle that does not show cross-reactivity with Suzuki reactions and can thus allow for easy access to more substituted biphenyl diaryliodonium salts. Fortunately, aryltrimetylsilanes are known to react with pre-oxidized iodoarenes to form diaryliodonium salts and were therefore employed for the synthesis of biphenyl iodonium salts (Table 3).[64,65]

To that end, 4-(trimethylsilyl)biphenyl (**17**) was synthesized from bromobenzene and 4-(trimethylsilyl)-phenylboronic acid under Suzuki cross-coupling conditions (see Materials and Methods). Treatment of **17** with Koser intermediate **16** in DCM at room temperature did not afford any diaryliodonium salt **3-OTs**, and only a small amount of unreacted Koser intermediate **16** was obtained after trituration in ether (Table 3, Entry 1). Increasing the temperature and performing the reaction in MeCN at 77 °C allowed for the reaction to proceed and afforded the product **3-OTs** (Table 3, Entry 2). However, the reaction did not go to completion and a mixture of product and starting

Table 3. Optimization for the reaction between 4-(trimethylsilyl)biphenyl (**17**) and Koser intermediates **15** and **16**.
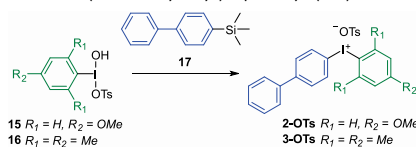
| Entry	SM / Prod	Solvent	Conc. **16** / mol L^{-1}	Temp. / °C	Time / h	Additive	Yield / %	Comment
1	**16 / 3-OTs**	DCM	0.12	25	16		NR	Unreacted **16** was obtained
2	**16 / 3-OTs**	MeCN	0.12	77	4		23	Mixture of **3-OTs** and **16** (2 : 3)
3	**16 / 3-OTs**	MeCN	0.24	77	4		52	Pure **3-OTs** was obtained
4	**16 / 3-OTs**	MeCN	0.36	77	4		56	Pure **3-OTs** was obtained
5	**16 / 3-OTs**	MeCN	0.36	77	4	TsOH · H$_2$O	79	Pure **3-OTs** was obtained
6	**15 / 2-OTs**	MeCN	0.36	77	4	TsOH · H$_2$O	27	Pure **2-OTs** was obtained
7	**15 / 2-OTs**	DCM	0.36	25	16		ND	Mixture of **2-OTs** and **15**
8	**15 / 2-OTs**	DCM	0.36	25	16	TsOH · H$_2$O	24	Pure **2-OTs** was obtained

SM = Starting material; Prod = product; NR = No reaction; ND = Not determined (due to partial degradation of **15**, it was not possible to precisely determine the fraction of product **2-OTs** in the mixture)

material **16** was obtained. Fortunately, increasing the concentration solved this problem, and pure product **3-OTs** could be obtained in good yields (Table 3, Entry 3). While a further increase in concentration afforded a slight increase in yield (Table 3, Entry 4), the use of TsOH · H$_2$O as an acid additive was found to be effective and produced the product **3-OTs** in a good 79 % yield (Table 3, Entry 5), which is comparable to procedures starting from iodobiphenyls or biphenylboronic acids in both this research (Scheme 1) and literature.[7,32,43,46]

Besides the synthesis of mesityl iodonium salt **3-OTs**, 4-(trimethylsilyl)biphenyl (**17**) was also used for the synthesis of diaryliodonium salts with electron rich dummy ligands to allow copper-free arylations. While trimethoxyphenyl iodonium salt **1-OTs** cannot be obtained through this method because the synthesis of the required Koser intermediate by oxidation of iodotrimethoxybenzene **5** is known to lead to complete decomposition of the starting material,[66] anisyl iodonium salt **2-OTs** could be obtained in moderate yields. To that end, 4-iodoanisole (**6**) was oxidized to give Koser intermediate **15** (see Materials and Methods). Due to the instability of this pre-oxidized reagent upon storage (see Supplementary Figures S29–32),[54,55] the Koser intermediate was immediately used for the synthesis of biphenyl iodonium salt **2-OTs**. Under the previously optimized conditions, a moderate 27 % yield was obtained (Table 3, Entry 6). Given the reactivity of the electron-rich Koser intermediate **15**, it was then evaluated whether milder conditions in DCM at room temperature could increase the yield. While this attempt (Table 3, Entry 7) resulted in a mixture between (partially decomposed) starting material **15** and product **2-OTs**, the addition of TsOH · H$_2$O as an acid additive solved this problem and afforded pure product in a similar 24 % yield (Table 3, Entry 8). These positive results indicate that biphenyltrimethylsilanes can be used as an alternative starting material for biphenyl iodonium salts with both bulky and electron-rich dummy ligands. Moreover, the use of pre-oxidized dummy ligands and the mild reaction conditions of this reaction indicate that biphenyltrimethylsilanes could be a promising starting point for the synthesis of more substituted biphenyl iodonium salts as well.

In order to show the usability of the synthesized diaryliodonium salts in fluorination reactions, several trial fluorinations were performed using biphenyl iodonium salts **2-OTs** and **3-OTs** (Scheme 2). First, mesityl iodonium salt **3-OTs** was used in the copper-catalysed fluorination procedure developed by Sanford and co-workers,[43] obtaining a 23 % conversion to the desired product **4** (determined by ^{19}F NMR). In an attempt to emulate radiofluorination conditions, in which a short reaction time is required due to the decay of the fluorine-18, a trial was performed over 20 minutes at a slightly higher temperature
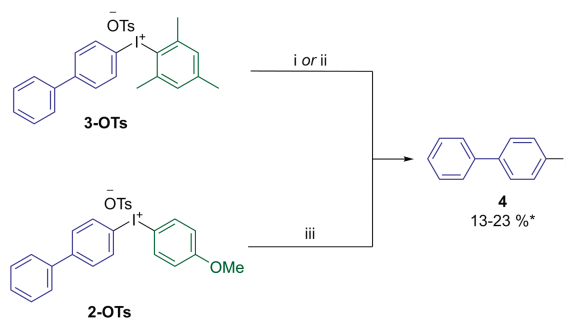
Scheme 2. Fluorination trials with biphenyl iodonium salts **2-OTs** and **3-OTs**. Reagents and conditions: i) **3-OTs** (1.0 equiv.), KF (1.1 equiv.), 18-crown-6 (0.40 equiv.), Cu(OTf)$_2$ (0.20 equiv.) DMF, 60 °C, 16 h, 23 %*; ii) **3-OTs** (1.0 equiv.), KF (1.1 equiv.), K222 (1.0 equiv.), (MeCN)$_4$CuOTf (1.0 equiv.) DMF, 85 °C, 20 min, 13 %*; iii) **2-OTs** (1.0 equiv.), KF (1.1 equiv.), K222 (1.0 equiv.), DMF, 150 °C, 20 min, 19 %*. *Conversion determined by ^{19}F NMR.

(85 °C) using the often-used complexing agent K222[14] and copper(I) catalyst (MeCN)$_4$CuOTf, which was also used in the radiofluorination of (biphenyl)(mesityl)iodonium salt **3-BF$_4$** in literature.[9] In this case, 4-fluorobiphenyl **4** was formed in a 13 % conversion, indicating that fluorination of **3-OTs** is also possible in short time. Copper-free fluorination of anisyl diaryliodonium salt **2-OTs** was also attempted, but only led to trace amounts of **4** at 85 °C. Instead, a higher temperature (150 °C) was required to obtain 4-fluorobiphenyl (**4**) in a 19 % conversion, in similar conditions to the copper-free radiofluorination of compound **2-OTs** in literature.[13]

CONCLUSION

As a means to provide easy access to biphenyl iodonium salts and allow for a broader application of biphenyl iodonium salts in the late-stage fluorination of PET tracers, the synthesis of biphenyl iodonium salts starting from biphenyl (**14**) and pre-oxidized dummy ligand **16** was investigated. Unfortunately, this approach was found to be unsuccessful and only small amounts of less reactive discolored product could be obtained. Therefore, it was recognized that an iodine group or metalloid handle on the biphenyl would be required to avoid competing arene oxidation reactions and allow for effective synthesis of biphenyl iodonium salts.

As such, biphenyl iodonium salts **1** and **3** were synthesized from iodophenyl (**8**) and biphenylboronic acid (**12**) according to literature procedures.[7,32,43,47] However, as both iodine and boronic groups are reactive in Suzuki reactions, synthesis of iodobiphenyl or biphenylboronic acids may be troublesome for more substituted biphenyls.

Moreover, milder reaction conditions without the use of oxidants or $BF_3 \cdot Et_2O$ would be beneficial to access more substituted biphenyl iodonium salts.

Therefore, we employed trimethylsilane as a different metalloid handle that does not show cross-reactivity with Suzuki reactions and allows for the synthesis of diaryliodonium salts in mild conditions. Treatment of 4-(trimethylsilyl)biphenyl (**17**) with Koser intermediates **15** and **16** in MeCN at 77 °C allowed easy access to biphenyliodonium salts **2-OTs** and **3-OTs** in moderate to good yields. The synthesized diaryliodonium salts were then used in fluorination trials, in which conversion to 4-fluorobiphenyl (**4**) was obtained in both copper-catalysed and copper-free reaction conditions.

The showcased fluorination examples combined with the mild reaction conditions and use of pre-oxidized dummy ligands during the diaryliodonium salts synthesis indicate that biphenyltrimethylsilanes could be a promising starting point for the synthesis of more substituted biphenyl iodonium salts and may allow for a wider use of these radiofluorination precursors in the synthesis of PET tracers or other applications like arylations of nucleophiles with biphenyl groups.

Supplementary Information. Supporting information to the paper is attached to the electronic version of the article at: https://doi.org/10.5562/cca4165.

PDF files with attached documents are best viewed with Adobe Acrobat Reader which is free and can be downloaded from Adobe's web site.

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