Organic &
Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Check for updates

Cite this: *Org. Biomol. Chem.*, 2020, **18**, 6140

Received 7th July 2020,
Accepted 23rd July 2020

DOI: 10.1039/d0ob01401j

rsc.li/obc

Fluorinations of unsymmetrical diaryliodonium salts containing *ortho*-sidearms; influence of sidearm on selectivity†

Ahmed M. H. Abudken, [a,b] Eric G. Hope,[a] Kuldip Singh[a] and Alison M. Stuart *[a]

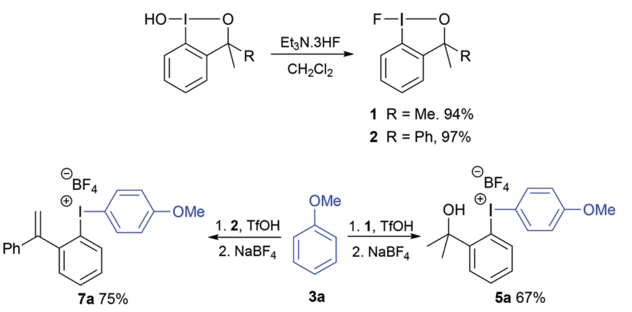
Activated aromatics were reacted with two different fluoroidoane reagents **1** and **2** in the presence of triflic acid to prepare only the *para*-substituted diaryliodonium salts. With fluoroiodane **1** the unsymmetrical diaryliodonium salts contained an *ortho*-propan-2-ol sidearm, whereas the alcohol sidearm was eliminated to form an *ortho*-styrene sidearm in the reaction with fluoroiodane **2**. Only the diaryliodonium salts containing a styrene sidearm were fluorinated successfully to deliver *para*-fluorinated aromatics in good yields.

Introduction

Fluoroaromatics constitute an important class of organic compounds because of their commercial applications in pharmaceuticals, agrochemicals, liquid crystals and positron emission tomography (PET).[1] Fluorine-18 (^{18}F) is the most commonly used radionuclide for PET, mainly due to its half-life of 110 minutes, and this has created a demand for new methods for the late-stage radiofluorination of aromatics. Consequently, the number of synthetic methods available for the preparation of aromatic fluorides has increased dramatically over the last eight years,[2] and the synthesis of aryl carbon–fluorine bonds from fluoride normally requires pre-functionalisation of the aromatic with either boron,[3] tin,[4] *N*-arylsydnone[5] or hypervalent iodine.[6–13]

The fluorination of unsymmetrical diaryliodonium salts was first reported in 1995 by Pike[6] and it has now become a well-established method for the introduction of [^{18}F]fluoride into aromatics.[7] Since fluoride normally attacks the most electron-deficient aromatic ring, an effective strategy for directing fluoride into the desired aryl ring is to use an unsymmetrical aryl(spectator)iodonium salt where the spectator group is an electron-rich aromatic such as 4-methoxyphenyl or 2-thienyl.[6–9] There is also an "*ortho* effect" in these fluorinations which overcomes the electronic effect. If one of the aromatic rings contains an *ortho*-substituent such as methyl, it will direct the fluorination to that ring. Sanford has shown that *ortho*-selectivity can be reversed by using a copper catalysed fluorination of aryl(mesityl)iodonium salts and the reaction is highly selective for fluorination to occur at the less sterically hindered arene, even with highly electron-rich aromatics.[10,11] Recently, she described a two-step procedure involving an S_EAr reaction between activated aromatics, MesI(OH)(OTs) and TMSOTf to generate aryl(mesityl)iodonium triflates which were used *in situ* in a copper-mediated radiofluorination with [^{18}F]KF.[10c] Despite the presence of two *ortho*-methoxy groups, 2,4,6-trimethoxyphenyl was introduced by Chun in 2019 as an excellent new spectator group in the high-temperature radiofluorinations of aryl(2,4,6-trimethoxyphenyl) iodonium triflates where the aryl group was fluorinated with extremely high chemoselectivity.[12] Iodonium ylides, (diacetoxyiodo)arenes and iodoarenes oxidised by *m*-CPBA have also been investigated as precursors to [^{18}F]fluoroarenes.[13]

In 2013 we reported the preparation of the hypervalent iodine(III) reagent **1** from cheap sources of nucleophilic fluoride (Scheme 1) and its application as a new fluorinating reagent for the fluorination of 1,3-diketones, 1,3-ketoesters



Scheme 1 Preparation of fluoroiodane reagents and unsymmetrical diaryliodonium salts.

---

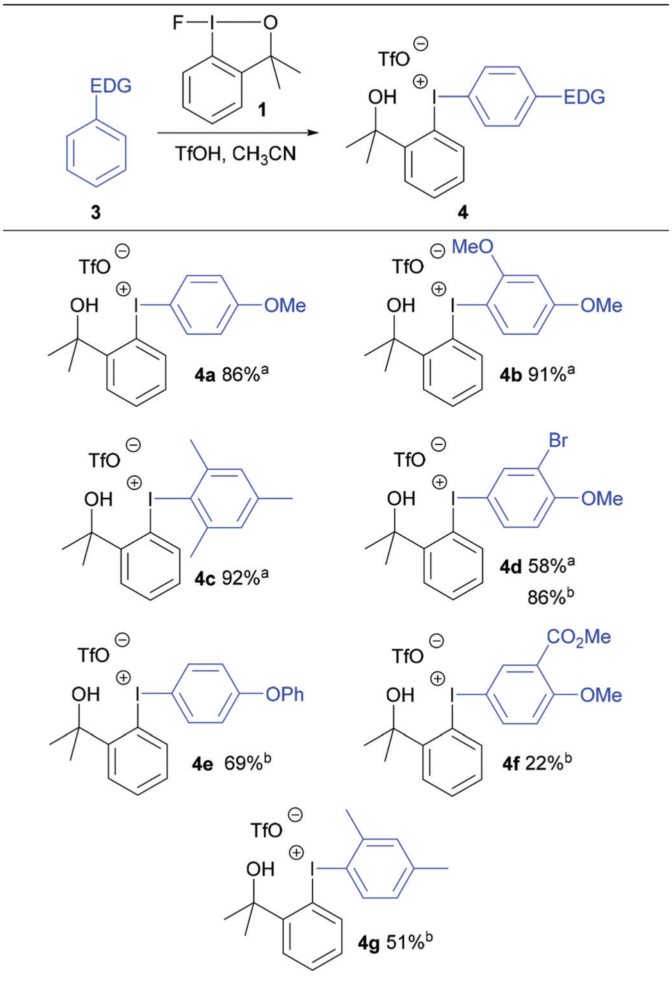
[a] *School of Chemistry, University of Leicester, Leicester, LE1 7RH, UK. E-mail: Alison.Stuart@le.ac.uk*
[b] *College of Pharmacy, Al-Qadisiyah University, Al-Qadisiyah, Iraq*

† Electronic supplementary information (ESI) available: Experimental procedures, NMR spectra. CCDC 2013356–2013360. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob01401j

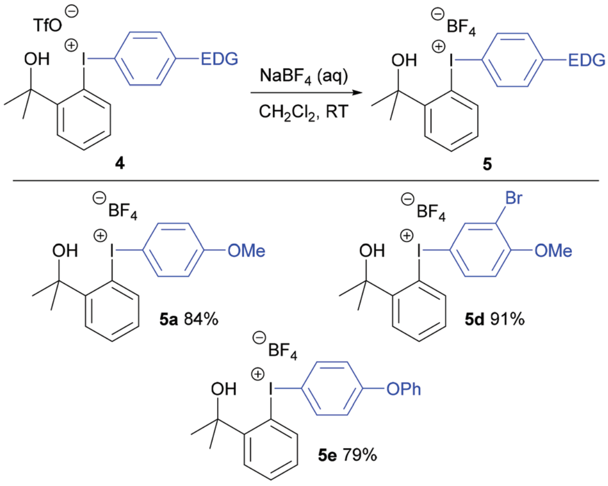
and 1,3-ketoamides.[14a] Since then, the reaction scope of fluoroiodane **1** has extended significantly from the difluorinations of styrenes and cyclopropanes, to intramolecular fluorocyclisations of unsaturated alcohols, amines, amides and carboxylic acids, as well as to radiofluorinations.[14–16] Most of these reactions, however, required a transition metal to activate the fluoroiodane reagent **1** by coordinating to the fluorine atom.[17] We have now established that **1** can be activated by hydrogen bonding to hexafluoroisopropanol and crucially, it removed the need for transition metals.[14d]

We were interested in preparing fluorinated aromatics using fluoroiodane **1** and here, we report the preparation of two new classes of unsymmetrical diaryliodonium salts containing *ortho*-sidearms, **5** and **7**, by a site selective S_EAr reaction between activated aromatics and the fluoroiodane reagents **1** and **2** with triflic acid (Scheme 1). We will also discuss the fluorinations of these unsymmetrical diaryliodonium salts using Sanford's copper catalysed conditions to reverse the "*ortho* effect" and fluorinate selectively the activated aromatics.

Table 1 Preparation of diaryliodonium salts **4** from fluoroiodane reagent **1**



[a] Reaction conditions: Substrate (0.72 mmol), fluoroiodane **1** (1.07 mmol), triflic acid (1.07 mmol) and dry CH_3CN (2 mL) at RT for 1 h. [b] Reaction conditions: Substrate (0.72 mmol), fluoroiodane **1** (1.07 mmol), triflic acid (2.16 mmol) and dry CH_3CN (2 mL) at 0 °C for 2 h.



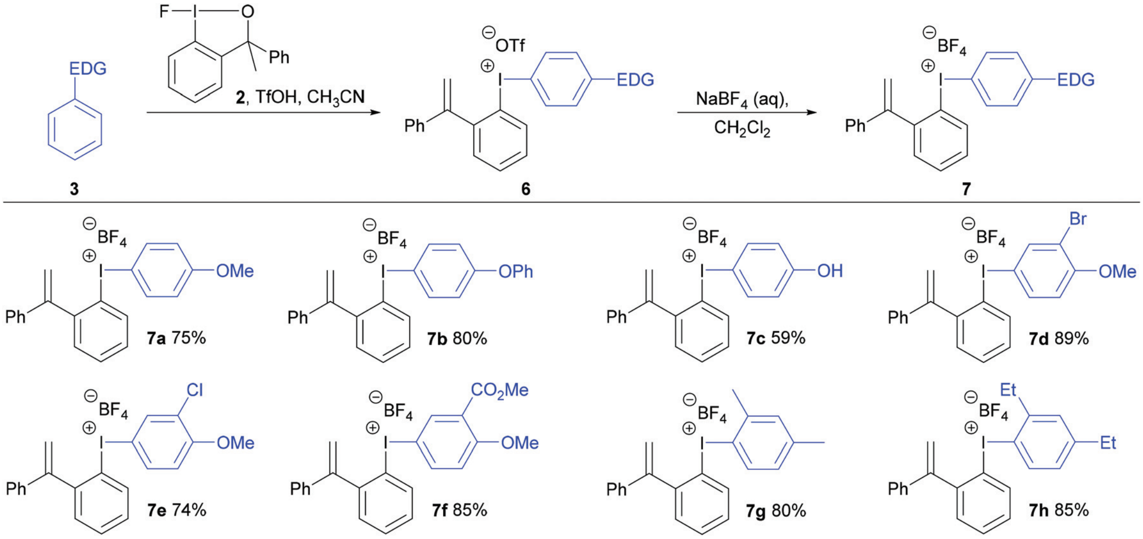
Scheme 2 Metathesis reactions using $NaBF_4$ (aq).

Results and discussion

Initially, anisole was reacted with fluoroiodane **1** and 1.5 equivalents of triflic acid in acetonitrile at room temperature to form exclusively the *para*-substituted diaryliodonium triflate **4a** in 86% yield in just 1 hour at room temperature (Table 1). 1,3-Dimethoxybenzene and mesitylene were reacted with fluoroiodane **1** and triflic acid to form the diaryliodonium salts **4b** and **4c** in 91–92% yield. When the same reaction conditions were applied to the less activated aromatic, 2-bromoanisole, the diaryliodonium salt **4d** was obtained in a moderate 58% yield. After further optimisation (see Table S3 in ESI†), the yield increased to 86% when 2-bromoanisole was reacted with fluoroiodane **1** and 3 equivalents of triflic acid in acetonitrile at 0 °C for 2 hours. The optimised protocol was applied to other less activated aromatics such as diphenyl ether, methyl-2-methoxybenzoate and *m*-xylene to form the unsymmetrical diaryliodonium salts **4e**, **4f** and **4g** in moderate to good yields (22–69%). All the diaryliodonium triflates were obtained as stable, white powders which were purified simply by washing with hexane and diethyl ether.

The triflate counteranions in the unsymmetrical diaryliodonium salts **4** were exchanged easily by stirring the salt in dichloromethane with aqueous sodium tetrafluoroborate at room temperature for 18 hours (Scheme 2). This simple procedure delivered the diaryliodonium tetrafluoroborates **5** in good yields (79–91%).

A new analogue of the fluoroiodane reagent **1**, where one of the methyl groups was replaced by a phenyl group, was then prepared by a five-step synthesis (see ESI†). The phenyl group was introduced to encourage the alcohol sidearm in the diaryliodonium salts to eliminate and form an alkene in conjugation with two aromatic rings under the strong acidic conditions used in their synthesis. Hence, a new class of unsymmetrical



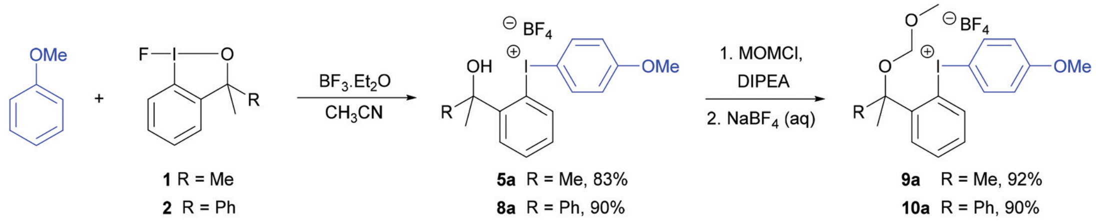
Scheme 3 Preparation of diaryliodonium salts **7** from fluoroiodane reagent **2** and the overall yields for the two steps are reported.

diaryliodonium salts containing an *ortho*-styrene sidearm was prepared by reacting a series of activated aromatics with fluoroiodane **2** and triflic acid in acetonitrile at 0 °C for 2 hours. After stirring the diaryliodonium triflates **6** in dichloromethane with an aqueous solution of sodium tetrafluoroborate, the diaryliodonium tetrafluoroborates **7a** to **7h** were produced in good yields (74–89%) over the two steps (Scheme 3). The reaction worked particularly well with less activated aromatics such as diphenyl ether, methyl-2-methoxybenzoate and *m*-xylene delivering the diaryliodonium triflates **6b**, **6f** and **6g** in better yields (85%, 90% and 89% respectively) than the same reactions with fluoroiodane **1** where the salts, **4e**, **4f** and **4g**, were obtained in 69%, 22% and 51% yields respectively. In the reaction between benzyl phenyl ether and fluoroiodane **2**, the benzyl protecting group was removed under the strong acidic conditions producing the *p*-phenol salt **6c** and subsequently **7c** in 59% overall yield after anion exchange. Interestingly, the first general procedure for preparing *para*-hydroxy substituted diaryliodonium salts was only reported in 2018 by Zhdankin using Koser's reagent, triisopropylsiloxyarenes and triflic acid to deprotect the aryl silyl ethers.[18] Some arenes, however, were incompatible with the reaction (Scheme 3) including 1,3-dimethoxybenzene, 1,2-dimethoxybenzene, 1-methoxy-2-methylbenzene, acetanilide and *N*-methylindole.

The diaryliodonium tetrafluoroborate **5a** was also prepared in one-step by the direct reaction between anisole, fluoroiodane reagent **1** and the Lewis acid, boron trifluoride (Scheme 4). Unfortunately, this reaction did not work with less activated aromatics such as 2-bromoanisole. When anisole was reacted with fluoroiodane reagent **2** and boron trifluoride, the alcohol sidearm did not undergo elimination and the diaryliodonium tetrafluoroborate **8a** containing a 1-phenylethan-1-ol sidearm was formed in 90% yield. Before attempting to fluorinate these unsymmetrical diaryliodonium salts, the free hydroxy groups in **5a** and **8a** were protected with MOMCl (Scheme 4). An excess of both MOMCl and *N*,*N*-diisopropylethylamine (Hunig's base) were used to ensure complete conversion to products **9a** and **10a** which were isolated in excellent yields after stirring the crude products with an aqueous solution of sodium tetrafluoroborate. The last step was essential because without it, some of the salt was obtained with a chloride counteranion which affected the subsequent fluorinations.

Solid-state structures

The solid-state structures of **5a** containing a propan-2-ol sidearm and **8a** containing a 1-phenylethan-1-ol sidearm are shown in Fig. 1 and 2. The I(1)–C(1) (2.132(3) and 2.134(3) Å) and I(1)–C(10)/C(15) (2.087(3) and 2.088(3) Å) bond lengths are practically identical for the two diaryliodonium salts. The dis-



Scheme 4 Preparation of diaryliodonium tetrafluoroborates, **5a** and **8a**, and protection of alcohol sidearm.

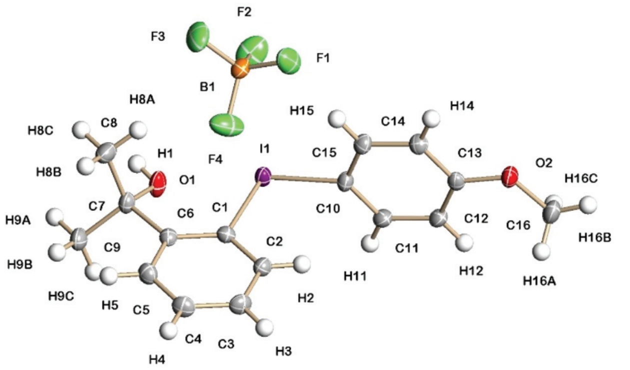


Fig. 1 Molecular structure of **5a** containing a propan-2-ol sidearm and showing 50% displacement ellipsoids. Selected bond lengths and angles: I(1)–C(1) 2.132(3) Å; I(1)–C(10) 2.087(3) Å; I(1)···O(1) 2.576(2) Å; C(10)–I(1)–C(1) 98.35(10)°; O(1)···I(1)–C(10) 169.24(8)°.

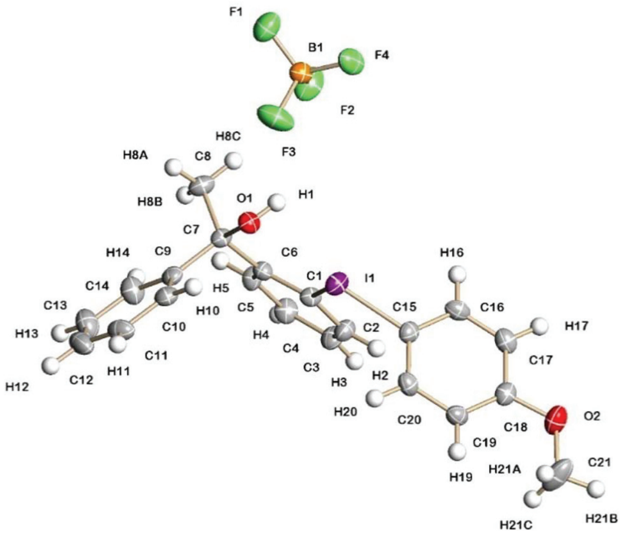


Fig. 2 Molecular structure of **8a** containing a 1-phenylethan-1-ol sidearm and showing 50% displacement ellipsoids. Selected bond lengths and angles: I(1)–C(1) 2.134(3) Å; I(1)–C(15) 2.088(3) Å; I(1)···O(1) 2.589(2) Å; C(15)–I(1)–C(1) 97.12(11)°; O(1)···I(1)–C(15) 168.84(8)°.

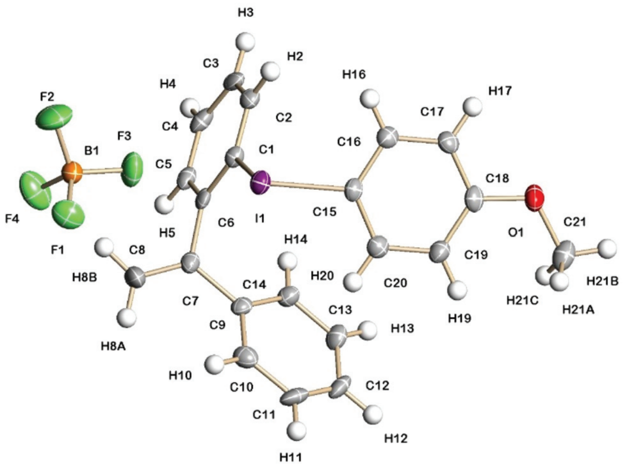


Fig. 3 Molecular structure of **7a** containing an *o*-styrene sidearm and showing 50% displacement ellipsoids. Selected bond lengths and angles: I(1)–C(1) 2.118(4) Å; I(1)–C(15) 2.099(4) Å; I(1)···F(3) 3.023(3) Å; C(15)–I(1)–C(1) 95.26(14)°; F(3)···I(1)–C(15) 171.38(13)°.

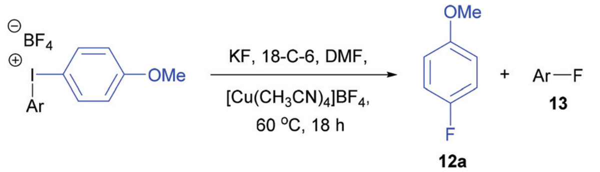
tinct C(15)/C(10)–I(1)–C(1) bond angles are typical for the pseudo T-shape of diaryliodonium salts and range from 97.1(1) to 98.4(1)°. In both solid-state structures there is a strong intramolecular interaction between I(1) and O(1) (2.576(2) and 2.589(2) Å) with an O(1)···I(1)–C(10) bond angle of 169°.

Fig. 3 shows the solid-state structure of **7a** containing an *o*-styrene sidearm and the X-ray crystal structures of the related triflate **6a** and tosylate **11a** that both contain the same *o*-styrene sidearm are presented in the ESI.† In this series of diaryliodonium salts, the I(1)–C(1) bond lengths (2.102(3)–2.118(4) Å) are very similar to the I(1)–C(15) bond lengths (2.094(3)–2.100(4) Å) and the C(15)–I(1)–C(1) bond angles range from 92.8(1) to 98.0(1)°. The C(7)–C(8) bond lengths are 1.314(5)–1.331(5) Å which is typical for an alkene C=C bond length (1.322 Å)[19] and the bond angles around C(7) are normal for an sp^2 hybridised carbon atom. There is secondary bonding between the iodine and the oxygen atoms of the tosylate and triflate counteranions in **11a** and **6a** respectively. There are two intramolecular interactions in **11a**, I(1)···O(4) = 2.721(3) Å and I(1A)···O(2) = 2.850(3) Å, as well as two intermolecular interactions, I(1)···O(2A) = 2.805(3) Å and I(1A)···O(3A) = 2.859(3) Å. The intramolecular and intermolecular interactions in **6a** are slightly weaker with the triflate anion, I(1)···O(3) = 2.930(2) Å and I(1)···O(4) = 3.094(3) Å respectively. An intramolecular interaction (3.023(3) Å) between F(3) of the tetrafluoroborate counteranion and I(1) is also present in **7a**.

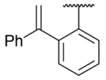
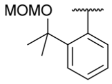
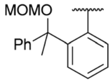
Fluorinations

Initially, the unsymmetrical diaryliodonium salts **7a**, **9a** and **10a** were reacted with potassium fluoride (1.1 equivalent) and 18-crown-6 (0.4 equivalent) in DMF at 60 °C for 18 hours both with and without $[Cu(MeCN)_4]BF_4$ (0.2 equivalent), as reported by Sanford in the fluorination of aryl(mesityl)iodonium salts (Table 2).[10a] Without the copper catalyst the *ortho*-effect dominated in the fluorination of **7a** (entry 1) and the aryl group containing the *ortho*-styrene sidearm was fluorinated producing 1-fluoro-2-(1-phenylvinyl)benzene **13a** in 53% yield with byproduct 4-iodoanisole formed in 72% yield. However, the *ortho*-effect was reversed in the copper-catalysed fluorination and the desired product, 4-fluoroanisole **12a**, was delivered in a moderate 39% yield (entry 2). Surprisingly, when the unsymmetrical salts, **9a** and **10a**, were fluorinated in the absence of copper, there was very little fluorination but there was still a strong *ortho*-effect with 4-iodoanisole being obtained in 79% and 85% yield respectively (entries 3 and 5). Under the copper-catalysed conditions (entries 4 and 6) fluorination was observed, but the *ortho*-effect was not reversed and the aryl groups containing the *ortho*-sidearms were fluorinated in 74 and 65% yields respectively. Presumably, the presence of the oxygen atoms in the sidearms of **9a** and **10a**, which had strong

Table 2 Preliminary fluorinations of unsymmetrical diaryliodonium salts **7a**, **9a** and **10a**



12a **13**

Entry	Substrate	Ar group	[Cu] (equiv.)	12a[a] (%)	13[a] (%)
1	**7a**		0	0	53
2	**7a**		0.2	39	7
3	**9a**		0	0	8
4	**9a**		0.2	0	74
5	**10a**		0	0	6
6	**10a**		0.2	0	65

[a] Determined by GC and ^{19}F NMR spectroscopy with internal standards.

interactions with the iodine atom in the solid-state structures, were affecting the selectivity of these fluorinations.

The fluorination of **7a** was optimised by screening the reaction conditions, different solvents, copper catalysts and fluorinating reagents (see ESI† for full details). Increasing the reaction temperature to 80 °C in entry 1 (Table 3) improved both the yield of 4-fluoroanisole **12a** to 45% and the selectivity of the reaction to 90 : 10. Since the use of TEMPO has proved beneficial for the fluorinations of some diaryliodonium salts,[7] 1 equivalent of TEMPO was used in entry 2 but it had no effect on the reaction. Both [Cu(MeCN)$_4$]OTf and Cu(OTf)$_2$ were good catalysts with Cu(OTf)$_2$ providing 4-fluoroanisole in 60% yield. The yield improved to 65% and the selectivity increased to 92 : 8 by reducing the reaction time to 4 hours in entry 5. The uncatalysed reaction in entry 6 proceeded in an excellent 80% yield but with the opposite selectivity (1 : 99). Finally, the effects of changing the counteranion from tetrafluoroborate **7a** to triflate **6a** (entry 7) and tosylate **11a** (entry 8) were investigated under the optimised reaction conditions but only low yields of 4-fluoroanisole **12a** were obtained.

Having established optimum conditions, each of the diaryliodonium tetrafluoroborates, **7a** to **7h**, were fluorinated using potassium fluoride and 20 mol% Cu(OTf)$_2$ in DMF at 80 °C for 4 h (Table 4). The salts, **7a** and **7b**, produced the desired *p*-fluorinated aromatics, **12a** and **12b**, in good yields (61–65%) with excellent selectivities (91 : 9). However, *p*-fluorophenol **12c** was only obtained in a low 20% yield in the fluorination of **7c** but this was probably due to the free hydroxy group in the salt.[20] In the copper-catalysed fluorinations of **7d** to **7f**, the fluorinated aromatics **12d** to **12f** were produced in good (66%) to excellent (82%–87%) yields and with high selectivities (93 : 7). As expected, the selectivity dropped to 75 : 25 in the fluorination of **7g** because of the presence of the *ortho*-methyl

Table 3 Optimisation of fluorination conditions

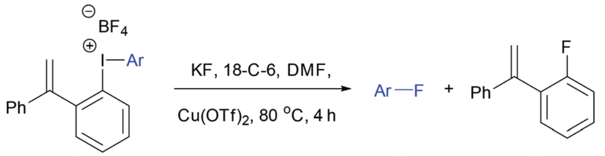
6a X = TfO
7a X = BF$_4$
11a X = TsO

12a **13a**

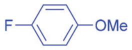
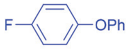
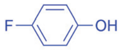
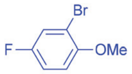
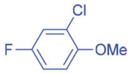
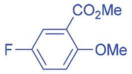
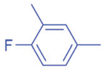
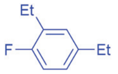
Entry	Substrate	Cu catalyst	Time (h)	12a[a] (%)	13a[a] (%)	12a : 13a
1	**7a**	[Cu(MeCN)$_4$]BF$_4$	18	45	5	90 : 10
2[b]	**7a**	[Cu(MeCN)$_4$]BF$_4$	18	43	5	90 : 10
3	**7a**	[Cu(MeCN)$_4$]OTf	18	50	7	88 : 12
4	**7a**	Cu(OTf)$_2$	18	60	9	87 : 13
5	**7a**	Cu(OTf)$_2$	4	65	6	92 : 8
6	**7a**	No catalyst	4	1	80	1 : 99
7	**6a**	Cu(OTf)$_2$	4	34	1	97 : 3
8	**11a**	Cu(OTf)$_2$	4	13	1	93 : 7

[a] Determined by GC with an internal standard. [b] 1 Equivalent of TEMPO in the dark.

Table 4 Fluorinations of unsymmetrical diaryliodonium salts



9 **12** **13a**

Entry	Substrate	Product	12[a] (%)	13a[a] (%)	12 : 13a
1	**7a**	 **12a**	65	6	92 : 8
2	**7b**	 **12b**	61	6	91 : 9
3	**7c**	 **12c**	20	0	100 : 0
4	**7d**	 **12d**	87	6	94 : 6
5	**7e**	 **12e**	66	5	93 : 7
6	**7f**	 **12f**	82	7	92 : 8
7	**7g**	 **12g**	63	21	75 : 25
8	**7h**	 **12h**	23	26	47 : 53

[a] Determined by ^{19}F NMR spectroscopy with an internal standard.

group in the activated aromatic, but 2,4-dimethylfluorobenzene **12g** was still formed in a good 63% yield. The selectivity was reduced further to 47 : 53 in the fluorination of **7h** due to the bigger ethyl substituent in the *ortho*-position and the desired fluorinated aromatic **12h** was only obtained in a low 23% yield.

Conclusions

In summary, this paper describes a convenient synthesis of *para*-fluorinated aromatics from activated aromatics and fluoroiodane reagent **2**. Initially, two new classes of unsymmetrical diaryliodonium salts containing *ortho*-sidearms were prepared by a site selective S_EAr reaction between activated aromatics and two different fluoroiodane reagents **1** and **2** with triflic acid. With fluoroiodane **1** the unsymmetrical diaryliodonium salts contained an *ortho*-propan-2-ol sidearm, whereas the alcohol sidearm was eliminated to form an *ortho*-styrene sidearm in the reaction with fluoroiodane **2**. After counteranion exchange, only the diaryliodonium tetrafluoroborates containing a styrene sidearm **7** reacted selectively with potassium fluoride under copper-catalysed conditions to form *para*-fluorinated aromatics **12** in good yields (61–87%).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

AMHA would like to thank The Higher Committee for Education Development in Iraq (HCED) and the University of Al-Qadisiyah for the PhD scholarship.

Notes and references

1 (*a*) Y. Zhou, J. Wang, Z. Gu, S. Wang, W. Zhu, J. L. Acena, V. A. Soloshonok, K. Izawa and H. Liu, *Chem. Rev.*, 2016, **116**, 422; (*b*) J. Wang, M. Sanchez-Rosello, J. L. Acena, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.*, 2014, **114**, 2432; (*c*) P. Jeschke, *ChemBioChem*, 2004, **5**, 570; (*d*) P. Kirsch, *J. Fluorine Chem.*, 2015, **177**, 29; (*e*) M. Bremer, P. Kirsch, M. Klasen-Memmer and K. Tarumi, *Angew. Chem., Int. Ed.*, 2013, **52**, 8880; (*f*) S. Preshlock, M. Tredwell and V. Gouverneur, *Chem. Rev.*, 2016, **116**, 719; (*g*) X. Deng, J. Rong, L. Wang, N. Vasdev, L. Zhung, L. Josephson and S. H. Liang, *Angew. Chem., Int. Ed.*, 2019, **58**, 2580.

2 M. G. Campbell and T. Ritter, *Chem. Rev.*, 2015, **115**, 612.

3 (*a*) Y. Ye, S. D. Schimler, P. S. Hanley and M. S. Sanford, *J. Am. Chem. Soc.*, 2013, **135**, 16292; (*b*) M. Tredwell, S. M. Preshlock, N. J. Taylor, S. Gruber, M. Huiban, J. Passchier, J. Mercier, C. Génicot and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2014, **53**, 7751; (*c*) A. V. Mossine, A. F. Brooks, K. J. Makaravage, J. M. Miller, N. Ichiisi, M. S. Sanford and P. J. H. Scott, *Org. Lett.*, 2015, **17**, 5780.

4 K. J. Makaravage, A. F. Brooks, A. V. Mossine, M. S. Sanford and P. J. H. Scott, *Org. Lett.*, 2016, **18**, 5440.

5 (*a*) M. K. Narayanam, G. Ma, P. A. Champagne, K. N. Houk and J. M. Murphy, *Angew. Chem., Int. Ed.*, 2017, **56**, 13006; (*b*) M. K. Narayanam, G. Ma, P. A. Champagne, K. N. Houk and J. M. Murphy, *Synlett*, 2018, **29**, 1131.

6 (*a*) V. W. Pike and F. I. Aigbirhio, *J. Chem. Soc., Chem. Commun.*, 1995, 2215; (*b*) V. W. Pike and F. I. Aigbirhio, *J. Labelled Compd. Radiopharm.*, 1995, **37**, 120.

7 (*a*) V. W. Pike, *J. Labelled Compd. Radiopharm.*, 2018, **61**, 196; (*b*) M. S. Yusubov, D. Y. Svitich, M. S. Larkina and V. V. Zhdankin, *ARKIVOC*, 2013, **7**(i), 364.

8 (*a*) T. L. Ross, J. Ermert and H. H. Coenen, *J. Labelled Compd. Radiopharm.*, 2005, **48**(Suppl. 1), S153; (*b*) T. L. Ross, J. Ermert, C. Hocke and H. H. Coenen, *J. Am. Chem. Soc.*, 2007, **129**, 8018; (*c*) M. A. Carroll, C. Jones and S.-L. Tang, *J. Labelled Compd. Radiopharm.*, 2007, **50**, 450.

9 V. W. Pike and J.-H. Chun, *Org. Biomol. Chem.*, 2013, **11**, 6300.

10 (*a*) N. Ichiishi, A. J. Canty, B. F. Yates and M. S. Sanford, *Org. Lett.*, 2013, **15**, 5134; (*b*) N. Ichiishi, A. F. Brooks, J. J. Topczewski, M. E. Rodnick, M. S. Sanford and P. J. H. Scott, *Org. Lett.*, 2014, **16**, 3224; (*c*) M. S. McCammant, S. Thompson, A. F. Brooks, S. W. Krska, P. J. H. Scott and M. S. Sanford, *Org. Lett.*, 2017, **19**, 3939.

11 (*a*) A. Yamaguchi, H. Hanaoka, T. Higuchi and Y. Tsushima, *J. Nucl. Med.*, 2018, **59**, 815; (*b*) A. Yamaguchi, H. Hanaoka, T. Higuchi and Y. Tsushima, *J. Labelled Compd. Radiopharm.*, 2020, **63**, 368.

12 Y.-D. Kwon, J. Son and J.-H. Chun, *J. Org. Chem.*, 2019, **84**, 3678.

13 (*a*) B. H. Rotstein, N. A. Stephenson, N. Vasdev and S. H. Liang, *Nat. Commun.*, 2014, **5**, 4365; (*b*) J. Cardinale, J. Ermert, S. Humpert and H. H. Coenen, *RSC Adv.*, 2014, **4**, 17293; (*c*) M. B. Haskali, S. Telu, Y.-S. Lee, C. L. Morse, S. Lu and V. W. Pike, *J. Org. Chem.*, 2016, **81**, 297; (*d*) Y.-D. Kwon, J. Son and J.-H. Chun, *Org. Lett.*, 2018, **20**, 7902.

14 (*a*) G. C. Geary, E. G. Hope, K. Singh and A. M. Stuart, *Chem. Commun.*, 2013, **49**, 9263; (*b*) G. C. Geary, E. G. Hope, K. Singh and A. M. Stuart, *RSC Adv.*, 2015, **5**, 16501; (*c*) G. C. Geary, E. G. Hope and A. M. Stuart, *Angew. Chem., Int. Ed.*, 2015, **54**, 14911; (*d*) H. Minhas, W. Riley, A. M. Stuart and M. Urbonaite, *Org. Biomol. Chem.*, 2018, **16**, 7170.

15 (*a*) N. O. Ilchenko, B. O. A. Tasch and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2014, **53**, 12897; (*b*) W. Yuan and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2015, **54**, 8533; (*c*) W. Yuan, L. Eriksson and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2016, **55**, 8410; (*d*) N. O. Ilchenko, M. Heberg and K. J. Szabó, *Chem. Sci.*, 2017, **8**, 1056; (*e*) A. Ulmer, C. Brunner, A. M. Arnold, A. Poething and T. Gulder, *Chem.*

– *Eur. J.*, 2016, **22**, 3660; (*f*) C. Brunner, A. Andries-Ulmer, G. M. Kiefl and T. Gulder, *Eur. J. Org. Chem.*, 2018, 2615.

16 (*a*) B. Yang, K. Chansaenpak, H. Wu, L. Zhu, M. Wang, Z. Li and H. Lu, *Chem. Commun.*, 2017, **53**, 3497; (*b*) M. A. Cortés González, P. Nordeman, A. Bermejo Gómez, D. N. Meyer, G. Antoni, M. Schou and K. J. Szabó, *Chem. Commun.*, 2018, **54**, 4286.

17 (*a*) T. Yan, B. Zhou, X.-S. Xue and J.-P. Cheng, *J. Org. Chem.*, 2016, **81**, 9006; (*b*) B. Zhou, T. Yan, X.-S. Xue and J.-P. Cheng, *Org. Lett.*, 2016, **18**, 6128; (*c*) J. Zhang, K. J. Szabó and F. Himo, *ACS Catal.*, 2017, **7**, 1093.

18 A. Yoshimura, M. T. Shea, O. Guselnikova, P. S. Postnikov, G. T. Rohde, A. Saito, M. S. Yusubov, V. N. Nemykin and V. V. Zhdankin, *Chem. Commun.*, 2018, **54**, 10363.

19 L. Wang, Z. Jian, C. G. Daniliuc, G. Kehr and G. Erker, *Dalton Trans.*, 2018, **47**, 10853.

20 When the fluorination of **7c** was attempted under the same reaction conditions, but without the copper catalyst, there was no evidence of any fluorination at all.