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Protecting Group Controlled Remote Regioselective Electrophilic Aromatic Halogenation Reactions

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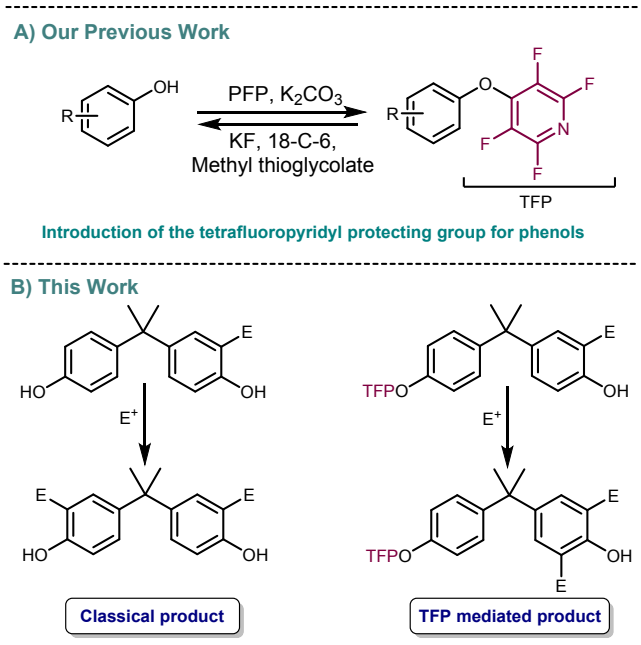
Supporting Information Placeholder

ABSTRACT: Being able to utilise a protecting group to influence remote regiocontrol offers a simple alternative approach to direct late-stage functionalisation of complex organic molecules. However, protecting groups that have the ability to influence reaction regioselectivity remote to their local chemical environment are not widely reported in the literature. Herein, we report the development of remote regioselective electrophilic aromatic substitution (S_EAr) reactions that are enabled via the application of the tetrafluoropyridyl (TFP) phenol protecting group. We demonstrate that through sequential reactions and protection/deprotection of the TFP group, substitution patterns which do not conform to classical S_EAr regioselectivity rules can be readily accessed.

INTRODUCTION

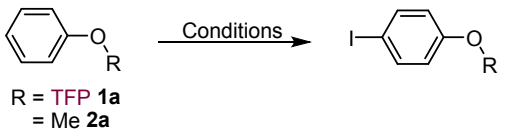
Despite the fact that there has been an impressive increase in the number of reported "*protecting group free*" syntheses of natural products,[1-7] and other complex organic molecules the fact remains that in the majority of cases the use of protecting groups is still required. While the primary role of a protecting group in complex organic synthetic pathways is to mask the reactivity of a particular functionality they are often utilised to also control chemical reactivity or reaction regioselectivity. For example, nitrogen containing protecting groups such as amidines and imines have been used in C-H activation reactions,[8-11] and groups such as *tert*-butyldiphenylsilyl (TBDPS) can be employed to add steric bulky to modulate the accessibility/ reactivity of functional groups in their proximity.[12] In all of the aforementioned synthetic transformations the protecting group used imparts a localised effect and the subsequent reductions, additions, couplings occur near to or adjacent to the protecting group. Conversely, reports of protecting groups being able to influence reaction reactivity or selectively distal from their position have not been widely disclosed in the literature.[13-19] In fact, in order to carry out transformations under remote regiocontrol bespoke directing groups typically need to be installed into the desired substrates and their subsequent removal from the resultant products can require complex synthetic manipulations.[20-23] Having the ability to use a simple protecting group to influence remote regiocontrol would offer an alternative approach to direct late-stage functionalisation methods that typically rely on selective activation of the site of the reaction.[24-26]

As part of a program of work in our laboratory to develop new multi-functional protecting groups we recently reported the use of the tetrafluoropyridyl (TFP) group for the protection of phenols (Scheme 1a).[27] It was found that the TFP protecting group could be readily installed and cleaved from a range of phenol containing compounds. The TFP group was also found to be stable to a wide range of commonly employed reaction conditions.[27] Unlike most of its alternatives the TFP group has somewhat of a unique position as being a phenol protecting group which is highly electron deficient.[28-32] Due to this we envisaged that a TFP protected phenol would be less reactive in electrophilic substitution reactions (S_EAr) compared with either free phenols, alkyl ether protected phenols (e.g. -OMe) or even non-phenolic rings (e.g. benzene). If this was indeed found to be the case, the reactivity difference afforded by TFP protection would provide a straightforward route to differentiate and regioselectively modify a specific ring in systems where multiple aromatic rings were present (Scheme 1b).



Scheme 1. a) Our previous work on the utilisation of TFP moieties as protecting groups for phenols. b) This work, the selective electrophilic aromatic substitution of multi-aromatic systems.

Table 1. Iodination condition screening of TFP aryl ether (**1a**) and anisole (**2a**).



Entry		Conditions	Conv (%)[a]	Yield (%)[b]
1	**1a**	$AgSO_4$ (1.2 equiv.), I_2 (1.2 equiv.), MeOH, 50 °C, 2 h	31	-
2	**1a**	NIS (1.1 equiv.), TFA, rt, 1 h	94	80
3	**1a**	NIS (1.1 equiv.), TFA (0.3 equiv.), MeCN, rt, 1 h	<1	-
4	**1a**	NIS (1.1. equiv), CF_3SO_3H, rt, 1 h	87	-
5	**2a**	$AgSO_4$ (1.2 equiv.), I_2 (1.2 equiv.), MeOH, 50 °C, 2 h	>99	98
6	**2a**	NIS (1.1 equiv.), TFA, rt, 1 h	>99	96
7	**2a**	NIS (1.1 equiv.), TFA (0.3 equiv.), MeCN, rt, 1 h	68	-
8	**2a**	NIS (1.1. equiv), CF_3SO_3H, rt, 1 h[c]	-	-

a) Conversion determined by inspection of ^{1}H NMR spectra. b) Yield following purification by column chromatography. c) A mixture of regioisomeric products was observed, therefore, conversion was not determined.

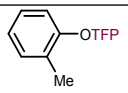
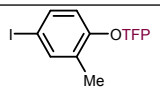
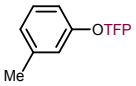
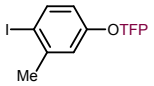
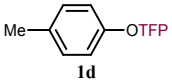
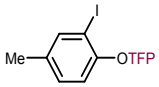
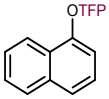
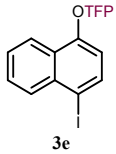
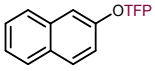
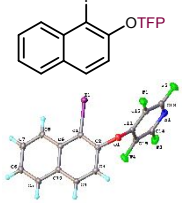
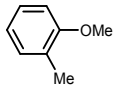
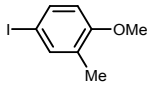
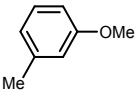
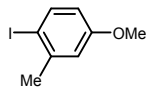
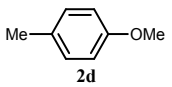
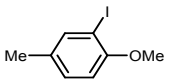
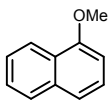
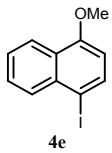
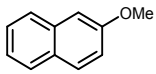
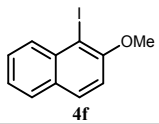
Herein, we detail our investigations into how tetrafluoropyridyl aryl ethers (TFP-ethers) can be utilised to give remote regioselectivity control in electrophilic aromatic substitutions. Our study demonstrates that TFP-ethers can be utilised to allow for efficient access to unsymmetrical biphenols, bisphenols and biaryls.[33] The methodology reported overcomes the statistical product distribution which is a common drawback of the typical approaches used to access such compounds (e.g. cross-coupling).[34]

RESULTS AND DISCUSSION

To begin the study, the electrophilic iodination of TFP-aryl-ether **1a** was carried out under a range of conditions.[35-38] Reaction conversion was monitored using ^{1}H NMR spectroscopy (see ESI, *S2*) and only the *para*-iodo regioisomer was isolated. To compare, the iodination of anisole **2a** was carried out under the same conditions. From this comparative study it was observed that the TFP ether **1a** was significantly less reactive than its methyl ether counterpart **2a** across all of the conditions employed. For example, in the presence of silver sulfate and iodine (Table 1, Entries 1 and 5) the TFP ether **1a** had only reached a conversion of 31% after two hours, while anisole **2a** had been completely consumed to give the iodinated product in the same time period. In order to rationalise these observations computational electron density distribution calculations were carried out (see ESI, *S181*). These showed that the positions which would typically undergo electrophilic aromatic substitution (*ortho*/*para*) were less electron-rich in the TFP phenol **1a** compared to the anisole **2a**, supporting the initial hypothesis and rationalising why a difference in reaction rate was observed.

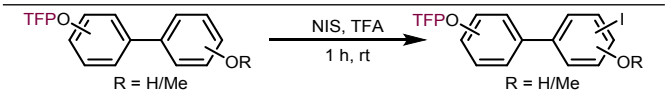
To probe the substrate scope for iodination, a comparative study between a range of substituted TFP-phenols and methyl-protected phenols was undertaken. We selected methyl- substituted compounds **1b-d** to study the regioselectivity of the reactions. To investigate the differences in reactivity between the various substrates, two sets of reaction conditions were chosen, one in which both OTFP and OMe compounds reacted rapidly (NIS, TFA, rt, 1h) and one in which the OTFP was significantly less reactive than OMe ($AgSO_4$, I_2, MeOH, 50 °C, 2 h). As with the previous study, conversion of the reactions was measured using ^{1}H NMR spectroscopy and selected reaction products were isolated to determine the regiochemistry (see ESI, *S13 – S56*).

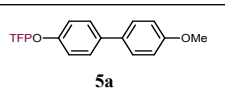
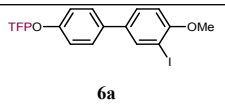
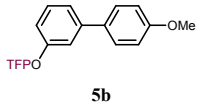
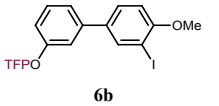
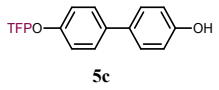
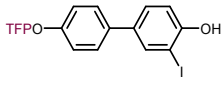
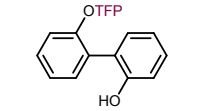
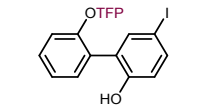
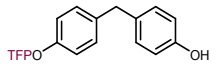
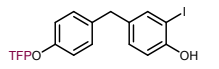
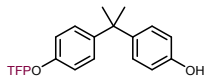
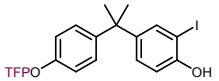
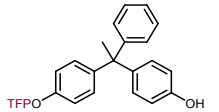
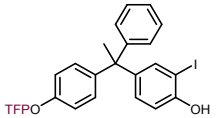
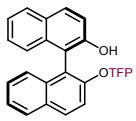
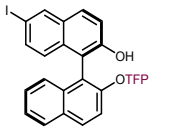
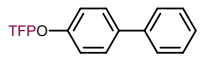
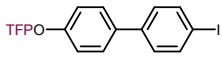
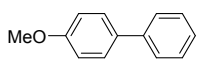
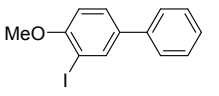
Table 2. Comparison of reactivity and regioselectivity between substituted OMe- and OTFP-containing compounds.

Entry	Starting Material	Major Product	Conv/ Yield (%)
1	 **1b**	 **3b**	**A** 81/68 **B** 7/-
2	 **1c**	 **3c**	**A** 94/74 **B** 15/-
3	 **1d**	 **3d**	**A** 79/65 **B** <1/-
4	 **1e**	 **3e**	**A** >99/91 **B** 25/-[a]
5	 **1f**	 **3f**	**A** 78/62 **B** 17/-
6	 **2b**	 **4b**	**A** >99/62 **B** >99/68
7	 **2c**	 **4c**	**A** >99/64 **B** >99/78
8	 **2d**	 **4d**	**A** >99/64 **B** >99/81
9	 **2e**	 **4e**	**A** -/-[b] **B** >99/77
10	 **2f**	 **4f**	**A** >99/59 **B** >99/63

a) A mixture of two regioisomeric products were observed in the crude ^{1}H NMR spectra of the reaction mixture, but the major component was unreacted SM. b) A complex mixture was observed in the crude ^{1}H NMR spectra of the reaction mixture.

Table 3. Scope of selective iodination reaction.



Entry	Starting Material	Major Product[a]	Yield (%)[b]
1	 **5a**	 **6a**	93
2	 **5b**	 **6b**	96
3	 **5c**	 **6c**	87
4	 **5d**	 **6d**	84
5	 **5e**	 **6e**	80
6	 **5f**	 **6f**	68
7	 **5g**	 **6g**	58
8	 **5h**	 **6h**	88
9	 **5i**	 **6i**	87
10	 **5j**	 **6j**	63

a) Regiochemistry of product determined by 2D NMR analysis. b) Isolated yield following flash column chromatography.

Across the series, it was observed that under silver sulfate-mediated conditions all OMe derivatives (**2b-f**) were significantly more reactive than their OTFP (**1b-f**) counterparts. For example, in the cases of 4-methyl compounds **1d** and **2d** where complete quantitative conversion to the iodo compound was seen for the OMe derivative (**2d**) no conversion was obtained for the OTFP compound (**1d**) (Table 2, Entries 3 and 8). It was observed that the regiochemical outcomes of the iodination reactions were the same regardless of which protecting group was employed. This result is not unexpected given the previously calculated electron density distribution profiles for **1a** and **2a** (see ESI, *S181*).

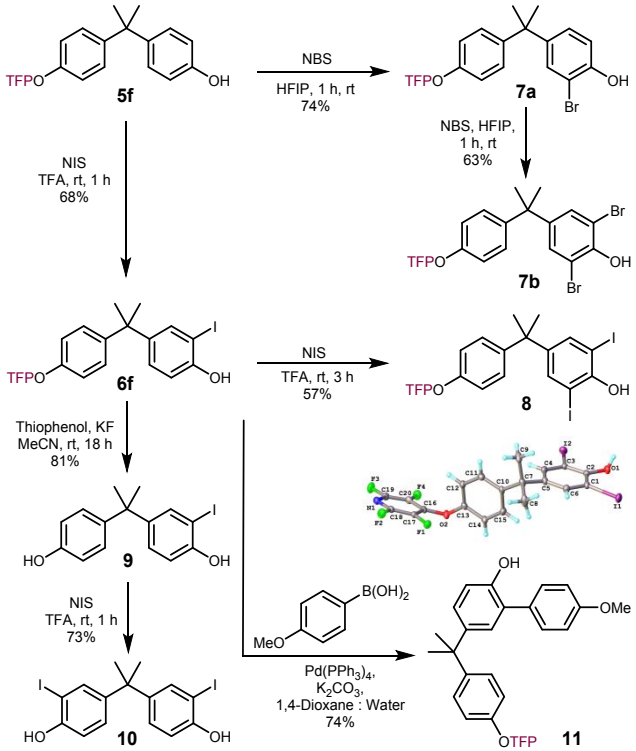
After it had been confirmed that a range of TFP-protected phenols could undergo iodination, a competition experiment utilising a compound containing two phenol rings, one protected with a TFP group and one with a methylated phenolic oxygen, was undertaken. The orthogonally protected biphenol **5a** was synthesized in one step. **5a** was then exposed to iodination conditions (TFA, NIS, rt, 1h), which were shown to readily iodinate both OMe and OTFP substrates. From the ^{1}H NMR spectrum obtained it was clear that mono-substitution had occurred and that one regioisomer **6a** (>95%) had formed (Table 3, Entry 1). **6a** was purified and its regiochemistry confirmed by 2D NMR (see ESI, *S84 – S87*). As hypothesised iodination had only occurred on one of the aromatic rings and *ortho* to the methoxy group (Table 3, Entry 1). This demonstrated that even under conditions in which both OTFP and OMe aryl rings *could* undergo electrophilic aromatic substitution, the reaction occurred selectively on the OMe-substituted ring. When the OTFP group was moved to the *meta* position relative to the central C-C biaryl bond (**5b**) iodination still occurred selectively only on the OMe-substituted ring (**6b**) (Table 3, Entry 2). It was also found that in a competition experiment, between an OTFP-protected phenol ring and a free phenolic ring, substitution occurs selectively on the free phenolic ring (Table 3, Entries 3 and 4). Substitution occurred *ortho* to the oxygen in the case of compound **5c** and *para* to the oxygen in compound **5d** (Table 3, Entries 3 and 4). We also studied iodination of bis-phenols, where the two phenolic rings are not directly attached to each other.[39-42] This is an important class of compounds, especially in the polymer arena (e.g. bis-phenol A (BPA)).[43-45] A series of bis-phenol TFP derivatives were synthesised (**5e-g**) and subsequently iodinated to give the mono-iodinated products (Table 3, Entries 5-7). As previously seen for the biphenol systems regioselective substitution occurred adjacent to the phenolic oxygen to give **6e-g**. The structures of **6e-g** were confirmed by 2D NMR correlations (see ESI, *S109 – S127*). It is worth noting that when unprotected BPA was exposed to the same iodination reaction conditions (NIS, TFA, rt) an inseparable mixture of mono- and di-iodinated products in addition to unfunctionalised BPA was generated (see ESI, *S179 – S180*). We were also able to selectively modify a TFP-protected BINOL (**5h**) to regioselectively generate **6h** (Table 3, Entry 8). To complete our study we wanted to probe the reactivity difference between a TFP-phenolic ring and an unmodified phenyl ring. To do this test substrate **5i** was synthesised in one step from 4-phenylphenol as previously reported. Iodination of **5i** resulted in the regioselective formation of compound **6i** in 87% yield (Table 3, Entry 9). **6i** would not be the expected regioisomer if the iodination reaction was carried out in the absence of the TFP protecting group or on the OMe protected system. Importantly, the formation of **6i** demonstrates that TFP protection offers a route to selectively modify phenyl rings in the presence of phenols which is currently challenging to do given the electronic make up of these two aromatic systems. In order to lend further evidence to a methyl substituted phenyl ring being more activated that an OTFP ether we conducted a competition experiment, We took a mixture of TFP-ether **1a** (1 equiv.) and toluene (1 equiv.) and exposed them to iodination conditions (TFA, NIS (1 equiv.)). Following the reaction we measured the product distribution by ^{1}H NMR (see ESI *S176*).It was clear that **1a** had not reacted and instead 4-iodotoluene was generated as the major product. To confirm this we spiked our NMR sample of our reaction mixture

with 4-iodotoluene, clear overlap of the signals confirmed our original spectral assignment (see ESI *S177*). We also conducted the iodination of compound 5j, the OMe analogue of 5i, this reaction gave compound 6j with substitution occurring *ortho* to the OMe group in 63% yield. This further demonstrated that the installation of the OTFP group allows access to substitution patterns which require selective modification away from the most electron rich ring.

Having established the ability of the TFP group to clearly control the regioselectivity of S_EAr reactions we looked to use the methodology to sequentially add multiple electrophiles in a controlled and regioselectively manner. A second iodination reaction was carried out on compound **6f**. The second iodine was added selectively onto the same ring as the first, *ortho* to the free phenolic oxygen, giving di-iodo compound **8** in 57% yield (Scheme 2).

The regiochemistry of **8** was confirmed by obtaining a crystal structure and further evidenced by 2D NMR spectra (see ESI, *S158 – S163*).[46] This result showed that even when an aromatic ring already contained a deactivating group like iodine it was still more reactive in S_EAr reactions than the TFP-protected phenol ring. This is the first example, to the best of our knowledge, of the synthesis of an unsymmetrical bis-phenol system in which two electrophiles have been added selectively and sequentially to the same phenolic ring. Removal of the TFP group from **5f** and then subsequent iodination, allowed us to selectively install a single iodine on to each of the phenolic rings giving **10** in 73% yield (Scheme 2). The synthesis of **8** and **10** clearly demonstrated the application of the TFP protecting group as a useful tool to control the regiochemical outcome of S_EAr reactions in more complex systems. In addition the synthesis of **8** highlights that the TFP approach allows access to substitution patterns which do not conform to classical S_EAr regioselectivity rules for multi-aryl systems.

Scheme 2. TFP regiocontrolled synthesis of unsymmetric aryl systems.



In addition aryl species, **5f** and **6f** were further modified (Scheme 2). By exposing the mono-iodo-TFP-bisphenol A derivative **6f** to Suzuki-Miyaura cross-coupling conditions, the tri-aryl compound **11,** with one free phenolic oxygen and two orthogonally protected phenolic oxygens, was produced in 74% yield (Scheme 2). The TFP group could be easily removed from compound **5f** using a modified version of our previously reported conditions[7] to give mono-iodo-bisphenol A **9** in 81% yield (Scheme 2). Other electrophiles could also be employed, for example, bromination of compound **5f** occurred smoothly to give a single regioisomeric product **7a** in 74% yield (Scheme 2), consistent with the regioselecitivity observed for iodination. We then brominated compound **7a** again under the same previous conditions to give us the di-bromo compound **7b**. The regiochemistry of this compound was found to be analogous to that of the di-iodo compound **8**.

CONCLUSIONS

In conclusion, we have demonstrated that through installation of a tetrafluoropyridyl (TFP) moiety on a phenolic ring, the aromatic system's reactivity towards electrophilic aromatic substitutions can be significantly reduced. The methodology reported allows for precise and remote regiocontrol of S_EAr reactions without the requirement for a bespoke directing group. The TFP group can perform dual functions, acting as both a protecting and a directing group which can give, substitution patterns which do not conform to classical regioselectivity rules for multi-aryl systems. The simplicity of the TFP protecting group approach to control remote regioselectivity in electrophilic aromatic substitutions makes it highly amenable to a wide range of areas within the broad field of synthetic chemistry.

EXPERIMENTAL SECTION

General Methods. All starting materials and reagents were bought from commercial sources and used as received. All reference anisoles and methoxynaphthols were purchased from Fluorochem UK and their NMR spectra recorded as received. All reactions apart from where noted were carried out in air using non-dried solvents or reagents. All flash column chromatography was carried out using silica purchased from Sigma Aldrich using the solvent system noted. ^{1}H NMR spectra were recorded at 400, 600 and 700 MHz using Bruker Avance III, Varian VNMRS-600 and Varian VNMRS-700 spectrometers. ^{13}C NMR spectra were recorded at 101, 151 and 176 MHz using Bruker Avance III, Varian VNMRS-600 and Varian VNMRS-700 spectrometers. ^{19}F NMR spectra were recorded at 376 MHz using a Bruker Avance III spectrometer. In cases where it was required 2D NMR techniques were used to confirm compound identity. Chemical shifts are reported in ppm and are referenced to residual solvent peaks; $CHCl_3$ (^{1}H 7.26 ppm, ^{13}C 77.0 ppm) and CH_3CN (^{1}H 1.96 ppm, ^{13}C 118.3). Mass spectra were collected on a Waters TQD mass spectrometer and accurate mass spectra were collected on a Waters LCT Premier XE mass spectrometer using a QTOF mass analyser. Infrared absorption spectra were recorded using a Perkin Elmer Frontier FTIR spectrometer fitted with an ATR attachment. Melting points were carried out in triplicate and an average of the values taken and reported as a range using a Stuart SMP10 melting point apparatus. Melting points were carried out directly on material purified by flash column chromatography

General Procedures

General Procedure for the Synthesis of Tetrafluoropyridyl Ethers. To a stirred solution of phenol (1 equiv.) in acetonitrile (20 mL) was added pentafluoropyridine (1.05 equiv.) and potassium

carbonate (1.05 equiv.). The reaction mixture was stirred at room temperature for 16 h. After this time the reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (100% hexane to 25% EtOAc/75% hexane).

General Procedure for Suzuki-Miyaura Cross-Coupling. A solution of tetrafluoropyridyl-iodo-phenol (1 equiv.) and corresponding boronic acid were dissolved in 1,4-dioxane (10 mL) and the solution degassed by bubbling nitrogen for 1 h. At the same time a solution of K_2CO_3 (3 equiv.) in water was also degassed by bubbling nitrogen for 1 h. After this time, $Pd(PPh_3)_4$ (5 mol%) was added to the dioxane solution and the resulting mixture degassed for a further 10 min. The K_2CO_3 water solution was then transferred *via* syringe to the dioxane solution and the resulting mixture was heated at reflux for 12 h. The reaction mixture was then cooled and concentrated under reduced pressure. The resulting residue was taken up in EtOAc (50 mL) and washed with H_2O (25 mL), the organic layer was dried over $MgSO_4$, filtered and concentrated. The recovered residue was then subjected to flash column chromatography (100% hexane to 20% EtOAc/80% hexane).

General Procedure for Iodination Using Conditions A. To a stirred solution of TFP ether or methoxy ether (1 equiv.) in TFA (2 mL) was added NIS (1.1 equiv) and the resulting solution stirred for 1h at rt. After this time the reaction mixture was concentrated under reduced pressure. The resulting residue was taken up in EtOAc (30 mL) and washed with 1M sodium thiosulfate solution. The organic fraction was then dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography.

General Procedure for Iodination Using Conditions B. A solution of $AgSO_4$ (1.2 equiv.) and iodine (1.2 equiv.) was stirred in MeOH (10 mL) at 50 °C for 10 min. After this time the TFP ether or methoxy ether (1 equiv.) was added and the resulting solution stirred at 50 °C for 2 h. Following this the reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography.

2,3,5,6-tetrafluoro-4-phenoxypyridine (1a) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 10.6 mmol of the corresponding phenol as a clear oil (2.52 g) in 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H), 7.28 – 7.22 (m, 1H), 7.09 (appd, *J* = 8.1 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -154.2 – -154.4 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 155.8, 145.0 – 144.7 (m), 144.5 – 144.3 (m), 143.6 – 143.3 (m), 137.0 – 136.8 (m), 135.5 – 135.3 (m), 130.0, 125.1, 116.6; IR ν_{max} (ATR)/cm^{-1} 1641, 1591, 1469, 1192, 1068, 971, 741, 687; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{11}H_4NOF_4^-$ = 242.0229 found = 242.0218.

2,3,5,6-tetrafluoro-4-(naphthalen-1-yloxy)pyridine (1e) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 3.47 mmol of the corresponding naphthol as a cream coloured solid (0.979 g) in 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.23 (m, 1H), 7.98 – 7.91 (m, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.45 – 7.38 (m, 1H), 6.92 (dd, *J* = 7.6, 0.9 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.3 – -88.6 (m, 2F), -154.3 – -154.5 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 151.8, 145.0 – 144.7 (m), 143.6 – 143.4 (m), 137.0 – 136.8 (m), 135.5 – 135.3 (m), 134.8, 127.9, 127.2, 126.8, 125.2, 125.1, 125.0, 121.1, 110.2; IR ν_{max} (ATR)/cm^{-1} 1642, 1498, 1476, 1388, 1092, 967, 766, 560; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{15}H_6NOF_4^-$ = 292.0386 found = 292.0369; MP 81-83 °C.

2,3,5,6-tetrafluoro-4-(naphthalen-2-yloxy)pyridine (1f) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 3.47 mmol of the corresponding naphthol as a white crystalline solid (0.987 g) in 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.87 (m, 2H), 7.78 (appd, *J* = 8.1 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.39 – 7.32 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.3 – -88.5 (m, 2F), -154.0 – -154.2 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.5, 145.0 – 144.8 (m), 144.5 – 144.3 (m), 143.7 – 143.4 (m), 137.2 – 136.9 (m), 135.7 – 135.4 (m), 133.7, 130.9, 130.5, 127.9, 127.3, 127.2, 125.7, 117.2, 112.2; IR ν_{max} (ATR)/cm^{-1} 1647, 1628, 1480, 1208, 1153, 1124, 1061, 976, 817, 747, 472; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{15}H_6NOF_4^-$ = 292.0386 found = 292.0376; MP 94-95 °C.

2,3,5,6-tetrafluoro-4-(4-iodophenoxy)pyridine **(product Table 1)** Iodination was carried out as detailed in the general procedure A from 0.82 mmol of the corresponding tetrafluoropyridyl phenol as a white crystalline solid (0.242 g) in 80% yield. Characterisation was consistent with our previously reported literature values.[27] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.9 – -88.1 (m, 2F), -153.9 – -154.1 (m, 2F); IR ν_{max} (ATR)/cm$^-$ 1645, 1460, 1198, 1072, 970, 807, 485.

2,3,5,6-tetrafluoro-4-(4-iodo-2-methylphenoxy)pyridine (3b) Iodination was carried out as detailed in the general procedure A from 0.39 mmol of the corresponding tetrafluoropyridyl phenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a white crystalline solid (0.101 g) in 68% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 1H), 7.48 – 7.43 (m, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 2.32 (s, 3H, CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.1 – -88.5 (m, 2F), -155.2 – -155.4 (m, 2F); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 154.3, 145.1 – 144.8 (m), 144.6 – 144.3 (m), 143.5 – 143.2 (m), 140.4, 136.8 – 136.5 (m), 136.1, 135.1 – 134.8 (m), 130.6, 117.5, 88.8, 15.6; IR ν_{max} (ATR)/cm^{-1} 2927, 1641, 1471, 1222, 1170, 1121, 1064, 971; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{12}H_5NOF_4I^-$ = 381.9352 found = 381.9352; MP 69-70 °C.

2,3,5,6-tetrafluoro-4-(4-iodo-3-methylphenoxy)pyridine (3c) Iodination was carried out as detailed in the general procedure A from 0.39 mmol of the corresponding tetrafluoropyridyl phenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear colourless oil (0.111 g) in 74% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6 Hz, 1H), 6.95 (d, *J* = 3.1 Hz, 1H), 6.61 (dd, *J* = 8.6, 3.1 Hz, 1H), 2.42 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.1 – -88.3 (m, 2F), -154.0 – -154.2 (m, 2F); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.0, 145.1 – 144.8 (m), 144.1 – 143.8 (m), 143.7, 143.5 – 143.2 (m), 140.0, 137.1 – 136.8 (m), 135.4 – 135.1 (m), 117.9, 115.7, 95.3, 28.2; IR ν_{max} (ATR)/cm^{-1} 2925,1642, 1466, 1222, 1158, 1072, 1015, 972; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{12}H_5NOF_4I^-$ = 381.9352 found = 381.9357.

2,3,5,6-tetrafluoro-4-(2-iodo-4-methylphenoxy)pyridine (3d) Iodination was carried out as detailed in the general procedure A from 0.39 mmol of the corresponding tetrafluoropyridyl phenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear colourless oil (0.097 g) in 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.70 (m, 1H), 7.18 – 7.13 (m, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 2.36 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -155.2 – -155.4 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.1, 145.0 – 144.8 (m), 144.6 – 144.4 (m), 143.6 – 143.3 (m), 140.4, 137.4, 136.3 – 135.9 (m), 134.9 – 134.5 (m), 130.4, 117.1, 86.0, 20.3; IR ν_{max} (ATR)/cm^{-1} 2926, 1640, 1477, 1218, 1203, 1071, 972; HRMS (ESI$^-$) calcd for $[M\text{-}H]^-$ $C_{12}H_5NOF_4I^-$ = 381.9352 found = 381.9354.

2,3,5,6-tetrafluoro-4-[(4-iodonaphthalen-1-yl)oxy]pyridine (3e) Iodination was carried out as detailed in the general procedure A from 0.34 mmol of the corresponding tetrafluoropyridyl naphthol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a white crystalline solid (0.129 g) in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.23 (m, 1H), 8.18 – 8.14 (m, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.65 (m, 2H), 6.67 (d, *J* = 8.1 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.7 – -88.0 (m, 2F), -153.8 – -154.1 (m, 2F); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.6, 145.7 – 145.2 (m), 144.5 – 144.1 (m), 143.2 – 142.8 (m), 137.8 – 137.2 (m), 136.1, 135.3, 135.1 – 134.6 (m), 132.5, 129.1, 127.7, 125.7, 121.8, 111.1, 94.4; IR ν_{max} (ATR)/cm^{-1} 1641, 1594, 1473, 1085, 962, 761, 580; HRMS (ESI$^-$) Calculated for $[M-H]^-$ $C_{15}H_5NOF_4I^-$ = 417.9352 found = 417.9363; MP 78-79 °C.

2,3,5,6-tetrafluoro-4-[(1-iodonaphthalen-2-yl)oxy]pyridine (3f) Iodination was carried out as detailed in the general procedure A with the following modification. Following flash column chromatography (100% hexane to 20% EtOAc/80% hexane) the recovered solid was recrystallised from hexane. The reaction was carried out on 0.68 mmol of the corresponding tetrafluoropyridyl phenol this gave the product as a white crystalline solid in a 62% (0.174 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.21 (m, 1H), 7.90 – 7.83 (m, 2H), 7.71 – 7.65 (m, 1H), 7.61 – 7.54 (m, 1H), 7.18 (d, *J* = 8.9 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.4 – -88.6 (m), -155.2 – -155.4 (m); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.6, 145.7 – 145.2 (m), 144.5 – 144.0 (m), 143.3 – 142.8 (m), 137.7 – 137.3 (m), 136.1, 135.3, 135.1 – 134.6 (m), 132.5, 129.1, 127.7, 125.7, 121.8, 111.1, 94.4; IR ν_{max} (ATR)/cm^{-1} 1642, 1473, 1203, 984, 961, 815, 762, 521; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{15}H_5NOF_4I^-$ = 417.9352 found = 417.9363; MP 121-123 °C.

1-iodo-4-methoxybenzene **(product Table 1)** Iodination was carried out as detailed in the general procedures (A/B) from 1.85 mmol of the corresponding anisole as a white solid with the following yields (A 0.419 g, 96%) (B 0.423 g, 98%). All characterisation data were consistent with previously reported literature values.[47] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 3.0 Hz, 1H), 6.51 (dd, *J* = 8.6, 3.0 Hz, 1H), 3.80 (s, 3H), 2.42 (s, 3H);^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 142.4, 139.3, 115.9, 113.4, 89.7, 55.3, 28.3; IR ν_{max} (ATR)/cm^{-1} 2933, 2836, 1598, 1568, 1471, 1236, 1167, 1011, 1045, 797, 589, 440.

4-iodo-1-methoxy-2-methylbenzene (4b) Iodination was carried out as detailed in the general procedures (A/B) from A = 1.64 mmol B = 0.82 mmol of the corresponding methoxy phenol as a white solid (A 0.251 g, 62%) (B 0.135 g, 68%). All characterisation data were consistent with previously reported literature values.[48] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H,), 6.61 (d, *J* = 8.3 Hz, 1H), 3.82 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.7, 138.98, 135.5, 129.5, 112.2, 82.5, 55.4, 15.9; IR ν_{max} (ATR)/cm^{-1} 2971, 2837, 1486, 1476, 1242, 1027, 805, 614.

1-iodo-4-methoxy-2-methylbenzene (4c) Iodination was carried out as detailed in the general procedures (A/B) from A = 1.64 mmol B = 0.85 mmol of the corresponding methoxy phenol as a clear colourless oil (A 0.257 g, 64%) (B 0.157 g, 78%). All characterisation data were consistent with previously reported literature values.[48] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 3.0 Hz, 1H), 6.51 (dd, *J* = 8.6, 3.0 Hz, 1H), 3.80 (s, 3H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 142.4, 139.3, 115.9, 113.4, 89.7, 55.3, 28.3; IR ν_{max} (ATR)/cm^{-1} 2933, 2836, 1598, 1568, 1471, 1236, 1167, 1011, 1045, 797, 589, 440.

2-iodo-1-methoxy-4-methylbenzene (4d) Iodination was carried out as detailed in the general procedures (A/B) from A = 1.64 mmol B = 0.85 mmol of the corresponding methoxy phenol as a clear colourless oil (A 0.260 g, 64%) (B 0.165 g, 81%). All characterisation data were consistent with previously reported literature values.[47] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H), 7.14 – 7.10 (m, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 3.87 (s, 3H), 2.28 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.1, 139.8, 132.0, 130.0, 110.8, 85.8, 56.5, 20.0; IR ν_{max} (ATR)/cm^{-1} 2920, 2836, 1489, 1276, 1248, 1049, 1019, 802, 730, 548.

1-iodo-4-methoxynaphthalene (4e) Iodination was carried out as detailed in the general procedure B from 0.64 mmol of the corresponding methoxynaphthalene as a brown oil (0.138 g) in 77% yield. All characterisation data were consistent with previously reported literature values.[49] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (appd, *J* = 9.1 Hz, 1H), 8.07 (appd, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.63 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.55 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 6.60 (d, *J* = 8.2 Hz, 1H), 4.00 (s, 3H);^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.3, 136.9, 134.7, 131.8, 128.2, 126.7, 126.0, 122.5, 105.6, 88.2, 55.7; IR ν_{max} (ATR)/cm^{-1} 2932, 2836, 1586, 1417, 1366, 1258, 1240, 1084, 805, 755, 616.

1-iodo-2-methoxynaphthalene (4f) Iodination was carried out as detailed in the general procedures (A/B) from A = 1.26 mmol B = 0.64 mmol of the corresponding methoxynaphthalene as a cream coloured solid (A 0.214 g, 59%) (B 0.131 g, 63%). All characterisation data were consistent with previously reported literature values.[49] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.80 – 7.74 (m, 1H, Ar*H*), 7.57 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H), 7.24 (d, *J* = 8.9 Hz, 1H), 4.05 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.65, 135.65, 131.20, 130.39, 129.92, 128.21, 128.14, 124.37, 112.95, 87.72, 57.26; IR ν_{max} (ATR)/cm^{-1} 3007, 2970, 1618, 1264, 1059, 1022, 887, 801, 743, 512.

2,3,5,6-tetrafluoro-4-({4'-methoxy-[1,1'-biphenyl]-4-yl}oxy)pyridine (5a) The title compound was synthesised according to the general procedure for the for Suzuki-Miyaura cross-coupling from 0.27 mmol of the corresponding tetrafluoropyridyl phenol iodide as a white crystalline solid (0.090 g) in 96% yield.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.9 Hz, 2H), 7.52 (d, *J* = 8.9 Hz, 2H), 7.13 (d, *J* = 8.9 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.5 – -88.7 (m, 2F), -154.1 – -154.3 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.3, 154.8, 145.0 – 144.7 (m), 144.6 – 144.4 (m), 143.6 – 143.4 (m), 138.1, 137.0 – 136.8 (m), 135.6 – 135.3 (m), 132.4, 128.2, 128.0, 117.0, 114.3, 55.3; IR ν_{max} (ATR)/cm^{-1} 2972, 1642, 1600, 1478, 1067, 968, 813; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{18}H_{10}NO_2F_4^-$ = 348.0648 found = 348.0646; MP 156-157 °C.

2,3,5,6-tetrafluoro-4-({4'-methoxy-[1,1'-biphenyl]-3-yl}oxy)pyridine (5b) The title compound was synthesised according to the general procedure for the for Suzuki-Miyaura cross-coupling from 0.27 mmol of the corresponding tetrafluoropyridyl phenol iodide as a white crystalline solid (0.085 g) in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.9 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.28 – 7.23 (m, 1H), 7.06 – 6.96 (m, 3H), 3.88 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.4 – -88.6 (m, 2F), -154.0 – -154.2 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.7, 156.2, 145.0 – 144.8 (m), 144.5 – 144.3 (m), 143.6 – 143.4 (m), 143.3, 137.1 – 136.1 (m), 135.6 – 135.3 (m), 132.2, 130.2, 128.2, 123.5, 115.0, 114.5, 114.3, 55.4; IR ν_{max} (ATR)/cm^{-1} 3034, 2844, 1603, 1581, 1462, 1282, 966, 837, 782; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{18}H_{10}NO_2F_4^-$ = 348.0648 found = 348.0631; MP 98-100 °C.

4'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-biphenyl]-4-ol (5c) The title compound was synthesised according to the general procedure for the for Suzuki-Miyaura cross-coupling from 1.08 mmol of the corresponding tetrafluoropyridyl phenol iodide as a white crystalline solid (0.355 g) in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 9.0 Hz, 2H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 4.80 (brs, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.5 – -88.7 (m, 2F), -154.1 – -154.3 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 155.3, 154.8, 138.0, 132.7, 128.3, 128.2, 117.0, 115.8. Note: Quaternary fluoropyridyl carbons were not observed; IR ν_{max} (ATR)/cm^{-1} 3378, 1642, 1599, 1459, 1202, 1167, 968, 822, 510; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{17}H_8NO_2F_4^-$ = 334.0491 found = 334.0485; MP 125-127 °C.

2'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-biphenyl]-2-ol (5d) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 1.07 mmol of the corresponding biphenol as a clear oil (0.199 g) in 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.36 (m, 3H), 7.29 – 7.18 (m, 3H), 7.00 – 6.89 (m, 2H), 5.00 (brs, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.4 – -89.6 (m, 2F), -155.0 – -155.3 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.4, 152.8, 144.7 – 144.4 (m), 143.3 – 143.0 (m), 136.1 – 135.8 (m), 134.7 – 134.3 (m), 132.4, 130.8, 130.1, 130.0, 127.3, 126.2, 122.6, 120.8, 118.1, 115.9; IR ν_{max} (ATR)/cm^{-1} 3448, 1642, 1471, 1187, 1067, 974, 752; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{17}H_8NO_2F_4^-$ = 334.0491 found = 334.0500.

4-({4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}methyl)phenol (5e) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 5.0 mmol of bis(4-hydroxyphenyl)methane with the following modification. In order to prevent two TFP groups from being added, the equivalents of pentafluoropyridine and potassium carbonate were decreased to 0.9 equiv. The compound was purified using flash column chromatography (100% hexane to 100% toluene). This gave the product as a colourless oil (0.792 g) in 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.71 (brs, 1H), 3.93 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.7 – -88.9 (m, 2F), -154.3 – -154.5 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 154.2, 154.0, 145.0 – 144.7 (m), 144.8 – 144.5 (m), 143.6 – 143.3 (m), 138.6, 137.0 – 136.7 (m), 135.5 – 135.2 (m), 132.8, 130.2, 130.0, 116.7, 115.4, 40.2; IR ν_{max} (ATR)/cm^{-1} 3363, 1642, 1497, 1193, 1133, 1068, 972, 815; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{18}H_{10}NO_2F_4$ = 348.0648 found = 348.0661.

4-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl) phenol (5f) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 4.38 mmol of the corresponding BPA with the following modification. In order to prevent two TFP groups from being added, the equivalents of pentafluoropyridine and potassium carbonate were decreased to 0.9 equiv. The compound was purified using flash column chromatography using a mixture of hexane and toluene 2:1. This gave the product as a colourless oil (0.704 g) in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.9 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 4.89 (br s, 1H), 1.68 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.7 – -88.9 (m, 2F), -154.2 – -154.4 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.7, 153.4, 148.0, 145.0 – 144.7 (m), 144.7 – 144.5 (m), 143.6 – 143.3 (m), 142.5, 137.0 – 136.8 (m), 135.6 – 135.3 (m), 128.3, 127.9, 116.1, 114.8, 42.0, 30.9; IR ν_{max} (ATR)/cm^{-1} 3352, 1641, 1497, 1202, 1170, 1066, 972, 830, 554; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{20}H_{14}NO_2F_4^-$ = 376.0961 found = 376.0938.

4-(1-phenyl-1-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}ethyl)phenol (5g) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 3.44 mmol of the corresponding bisphenol with the following modification. In order to prevent two TFP groups from being added, the equivalents of pentafluoropyridine and potassium carbonate were decreased to 0.9 equiv. The compound was purified using flash column chromatography (100% hexane to 100% toluene). This gave the product as a colourless oil (0.718 g) in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 3H), 7.27 – 7.21 (m, 1H), 7.10 (appt, *J* = 7.4 Hz, 4H), 6.96 (d, *J* = 8.6 Hz, 4H), 6.77 (d, *J* = 8.6 Hz, 2H), 4.82 (brs, 1H), 2.17 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -154.1 – -154.3 (m, 2F); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.9, 153.8, 148.9, 146.4, 143.0 – 142.7 (m), 141.0, 137.6 – 137.2 (m), 135.1 – 134.6 (m), 130.3, 129.9, 128.5, 128.0, 126.2, 115.9, 114.8, 51.5, 30.7. Note: Two quaternary fluoropyridyl carbons were not observed; IR ν_{max} (ATR)/cm^{-1}3367, 2982, 1642, 1598, 1470, 1204, 1171, 972, 829, 701; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{25}H_{16}NO_2F_4^-$ = 438.1117 found = 438.1102.

[R]-2'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-binaphthalene]-2-ol (5h) The title compound was synthesised according to the general procedure for the synthesis of tetrafluoropyridyl ethers from 1.75 mmol of the corresponding BINOL with the following modification. In order to prevent two TFP groups from being added, the equivalents of pentafluoropyridine were decreased to 0.9 equiv. The compound was purified using flash column chromatography using a mixture of hexane and toluene 2:1. This gave the product as a clear oil (0.485 g) in 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.47 – 7.32 (m, 3H), 7.31 – 7.22 (m, 2H), 7.03 (d, *J* = 8.4 Hz, 1H), 4.90 (s, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -90.1 – -90.4 (m, 2F), -154.3 – -154.6 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 152.8, 151.8, 144.8 – 144.5 (m), 144.2 – 143.8 (m), 142.8 – 142.5 (m), 135.9 – 135.4 (m), 134.4 – 134.0 (m), 133.5, 132.9, 131.8, 131.6, 131.0, 129.0, 128.6, 128.5, 128.2, 128.1, 128.1, 127.0, 126.5, 125.6, 125.3, 119.1, 118.9, 117.3, 112.1; IR ν_{max} (ATR)/cm^{-1} 3524, 1641, 1474, 1203, 1081, 972, 815, 729; HRMS (ESI$^-$) calcd for [M-H]$^-$ $C_{25}H_{12}NO_2F_4^-$ = 434.0804 found = 434.0787.

2,3,5,6-tetrafluoro-4-({3'-iodo-4'-methoxy-[1,1'-biphenyl]-4-yl}oxy)pyridine (6a) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.14 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a cream coloured solid (0.065 g) in 93% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.97 (d, *J* = 2.3 Hz, 1H), 7.52 – 7.47 (m, 3H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 1H), 3.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.3 – -88.6 (m, 2F), -154.0 – -154.2 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 157.8, 155.1, 145.0 – 144.8 (m), 144.5 – 144.2 (m), 143.6 – 143.4 (m), 137.9, 137.1 – 136.8 (m), 136.6, 135.5 – 135.3 (m), 134.4, 128.3, 128.0, 117.0, 111.0, 86.5, 56.5; IR ν_{max} (ATR)/cm^{-1} 2840, 1643, 1595, 1477, 1272, 1207, 1072, 977, 804; HRMS (ESI$^+$) calcd for [M]$^+$ $C_{18}H_{10}NO_2F_4I^+$ = 474.9692 found = 474.9674 MP 93-95 °C.

2,3,5,6-tetrafluoro-4-({3'-iodo-4'-methoxy-[1,1'-biphenyl]-3-yl}oxy)pyridine (6b) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.23 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear oil (0.109 g) in 96% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.97 (d, *J* = 2.3 Hz, 1H),

7.49 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.37 – 7.34 (m, 1H), 7.21 (t, *J* = 2.1 Hz, 1H), 6.98 – 6.96 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.3 – -88.5 (m, 2F), -154.0 – -154.2 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 158.1, 156.2, 145.0 – 144.7 (m), 144.4 – 144.2 (m), 143.6 – 143.4 (m), 141.7, 138.0, 137.0 – 136.8 (m), 135.5 – 135.3 (m), 134.2, 130.3, 128.2, 123.6, 115.2, 115.0, 111.0, 86.5, 56.5; IR ν_{max} (ATR)/cm^{-1} 2934, 2842, 1642, 1469, 1270, 1250, 1164, 1070, 972, 692; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{18}H_9NO_2F_4I^-$ = 473.9614 found = 473.9637; MP 86-87 °C.

3-iodo-4'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-biphenyl]-4-ol (6c) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.17 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear oil (0.068 g) in 87% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.2 Hz, 1H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.43 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 5.35 (brs, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.3 – -88.5 (m, 2F), -154.0 – -154.2 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 155.1, 154.5, 145.0 – 144.8 (m), 144.4 – 144.2 (m), 143.6 – 143.4 (m), 137.0 – 136.7 (m), 136.6, 136.5, 135.5 – 135.3 (m), 134.5, 117.1, 115.3, 86.2; IR ν_{max} (ATR)/cm^{-1} 3444, 1647, 1475, 1215, 1164, 1075, 971, 816, 513; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{17}H_7NO_2F_4I^-$ = 459.9458 found = 459.9472; MP 113-115 °C.

5-iodo-2'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-biphenyl]-2-ol (6d) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.31 mmol of the corresponding tetrafluoropyridyl bisphenol as a clear oil (0.119 g) in 84% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.53 – 7.49 (m, 2H), 7.47 – 7.43 (m, 1H), 7.39 – 7.37 (m, 1H), 7.37 – 7.32 (m, 1H), 7.10 (d, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 9.1 Hz, 1H), 5.04 (brs, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -154.6 – -154.9 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 153.2, 152.9, 144.9 – 144.5 (m), 144.4 – 144.1 (m), 143.5 – 143.1 (m), 139.1, 138.7, 136.3 – 136.0 (m), 134.9 – 134.5 (m), 132.3, 130.5, 126.2, 125.7, 125.3, 118.2, 117.5, 82.4; IR ν_{max} (ATR)/cm^{-1} 3672, 1651, 1474, 1271, 1184, 1042, 983, 873, 759, 741, 615; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{17}H_7NO_2F_4I^-$ = 459.9458 found = 459.9451; MP 109-111 °C.

2-iodo-4-({4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}methyl)phenol (6e) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.44 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 100% toluene) to give the product as a clear oil (0.167 g) in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.1 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.07 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.31 (brs, 1H), 3.91 (s, 2H); ^{19}F NMR (376 MHz, C DCl$_3$) δ -88.6 – -88.8 (m, 2F), -154.2 – -154.4 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 154.3, 153.4, 145.0 – 144.7 (m), 144.7 – 144.4 (m), 143.6 – 143.4 (m), 138.2, 137.8, 137.0 – 136.8 (m), 135.5 – 135.3 (m), 134.8, 130.7, 130.3, 116.8, 115.1, 85.8, 39.6; IR ν_{max} (ATR)/cm^{-1} 3489, 1641, 1468, 1194, 1068, 971, 815; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{18}H_9NO_2F_4I^-$ = 473.9614 found = 473.9595.

2-iodo-4-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl)phenol (6f) The title compound was synthesised according to the general procedure for iodination using conditions A from 1.86 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a cream coloured solid (0.615 g) in 68% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.3 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.03 (dd, *J* = 8.5 Hz, 2.3 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 1H), 5.17 (brs, 1H), 1.62 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -154.1 – -154.4 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 153.8, 152.9, 147.2, 145.0 – 144.7 (m), 144.7 – 144.4 (m), 143.6 – 143.3 (m), 137.1 – 136.7 (m), 136.0, 135.6 – 135.2 (m), 129.0, 128.2, 116.2, 114.6, 85.6, 41.9, 30.9; IR ν_{max} (ATR)/cm^{-1} 1644, 1501, 1484, 1224, 1175, 1126, 1070, 979; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{20}H_{13}NO_2F_4I^-$ = 501.9927 found = 501.9909; MP 87-89 °C.

2-iodo-4-(1-phenyl-1-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}ethyl)phenol (6g) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.68 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear oil (0.223 g) in 58% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.2 Hz, 1H), 7.28 (appt, *J* = 7.7 Hz, 2H), 7.22 (appt, *J* = 7.3 Hz, 1H), 7.09 – 7.04 (m, 4H), 6.97 – 6.91 (m, 3H), 6.88 (d, *J* = 8.5 Hz, 1H), 5.24 (brs, 1H), 2.12 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.5 – -88.7 (m, 2F), -154.1 – -154.3 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 154.0, 153.1, 148.2, 145.8, 145.0 – 144.7 (m), 144.5 – 144.3 (m), 143.6 – 143.4 (m), 143.0, 137.9, 137.0 – 136.8 (m), 135.5 – 135.3 (m), 130.8, 130.2, 128.4, 128.1, 126.4, 116.1, 114.3, 85.6, 51.3, 30.7; IR ν_{max} (ATR)/cm^{-1} 3484, 1641, 1470, 1205, 1171, 1071, 972, 700; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{25}H_{15}NO_2F_4I^-$ = 564.0084 found = 564.0082.

6-iodo-2'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]-[1,1'-binaphthalene]-2-ol (6h) The title compound was synthesised according to the general procedure for iodination using conditions A from 1.15 mmol of the corresponding tetrafluoropyridyl bisphenol and purified by flash column chromatography (100% hexane to 20% EtOAc/80% hexane) to give the product as a clear oil (0.570 g) in 88% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.17 (d, *J* = 1.8 Hz, 1H), 8.10 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.47 (dd, *J* = 8.9 Hz, 1.7 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.77 (d, *J* = 8.9 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -89.5 – -89.7 (m, 2F), -154.4 – -154.6 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 152.6, 152.1, 136.7, 135.4, 133.3, 131.9, 131.9, 131.7, 130.4, 129.9, 128.6, 128.3, 126.6, 125.8, 125.3, 118.3, 118.3, 118.2, 112.5, 88.7. Note: Quaternary fluoropyridyl carbons were not observed; IR ν_{max} (ATR)/cm^{-1} 1640, 1583, 1477, 1204, 974, 819, 736; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{25}H_{11}NO_2F_4I^-$ = 559.9771 found = 559.9771.

2,3,5,6-tetrafluoro-4-({4'-iodo-[1,1'-biphenyl]-4-yl}oxy)pyridine (6i) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.21 mmol of the corresponding tetrafluoropyridyl ether with the following modification. A catalytic amount of acetonitrile was added to the reaction mixture to solubilise the starting material. The product was purified by flash column chromatography (100% hexane to 10% EtOAc/90% hexane). This gave the title compound as a white solid (0.081 g) in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.5, 2H), 7.58 (d, *J* = 8.9, 2H), 7.32 (d, *J* = 8.5, 2H), 7.15 (d, *J* = 8.9, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.2 – -88.4 (m, 2F), -153.9 – -154.1 (m, 2F); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 155.5, 145.0 – 144.8 (m), 144.3 – 144.1 (m), 143.6 – 143.4 (m), 139.3, 138.0, 137.2, 137.1 – 136.8 (m), 135.6 – 135.3 (m), 128.8, 128.5, 117.1, 93.3; IR ν_{max} (ATR)/cm^{-1} 1641, 1493, 1472, 1168, 1064, 969, 809, 762; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{17}H_7NOF_4I^-$ = 443.9509 found = 443.9514; MP 109-110 °C.

3-iodo-4-methoxy-1,1'-biphenyl (6j) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.54 mmol from 4-methoxybiphenyl and purified by flash column chromatography (100% hexane to 10% EtOAc/90% hexane) to give the product as a white solid (0.105 g) in 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 2.3 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.45 (appt, *J* = 7.6 Hz, 2H), 7.36 (appt, *J* = 7.3 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 3.95 (s, 3H); ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 157.6, 139.3, 138.0, 135.8, 128.8, 128.1, 127.1, 126.7, 111.0, 86.4, 56.5; IR ν_{max} (ATR)/cm^{-1} 2933, 2834, 1595, 1480, 1282, 1250, 1054, 1016, 813, 760; HRMS (ESI$^+$) calcd for $[M]^+$ $C_{13}H_{11}OI^-$ = 309.9855 found = 309.9856; MP 86-87 °C.

2-bromo-4-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl)phenol (7a) To a solution of compound 5f (0.200 g, 0.53 mmol) in hexafluoroisopropanol (2 mL) was added NBS (0.095 g, 0.53 mmol) and the resulting reaction mixture was stirred at rt for 1 h. The reaction mixture was then concentrated under reduced pressure and the recovered residue was purified directly with flash column chromatography (100% hexane to 100% toluene). This gave the desired compound as a colourless oil (0.179 g) in 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.3 Hz, 1H), 7.24 (d, *J* = 8.9 Hz, 1H), 7.06 (dd, *J* = 8.5 Hz, 2.3 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 1H), 5.43 (brs, 1H), 1.67 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.6 – -88.8 (m, 2F), -154.2 – -154.3 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.8, 150.3, 147.2, 145.0 – 144.7 (m), 144.6 – 144.4 (m), 144.1, 143.6 – 143.4 (m), 137.0 – 136.8 (m), 135.6 – 135.3 (m), 129.9, 128.2, 127.8, 116.2, 115.7, 109.9, 42.1, 30.9; IR ν_{max} (ATR)/cm^{-1} 3516, 2971, 1641, 1465, 1203, 1171, 1065, 973, 825; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{20}H_{13}NO_2F_4Br^-$ = 454.0066 found = 454.0071.

2,6-dibromo-4-(2-{4-[(2,3,5,6-tetramethylpyridin-4-yl)oxy]phenyl}propan-2-yl)phenol (7b) To a solution of compound 7 (0.050 g, 0.12 mmol) in hexafluoroisopropanol (2 mL) was added NBS (0.021 g, 0.12 mmol) and the resulting mixture was stirred at rt for 1 h. The reaction mixture was then concentrated under reduced pressure and the recovered residue was purified directly with flash column chromatography (100% hexane to 100% toluene). This gave the desired compound as a white solid (0.040 g) in 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.80 (brs, 1H), 1.66 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.47 – -88.69 (m, 2F), -154.07 – -154.26 (m, 2F); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 154.0, 147.4, 146.4, 145.0, 144.6 – 144.4 (m), 143.4 – 143.2 (m), 137.2 – 136.9 (m), 135.4 – 135.2 (m), 130.4, 128.2, 116.4, 109.6, 42.1, 30.8. Note: One quaternary fluoropyridyl carbon was not observed; IR ν_{max} (ATR)/cm^{-1} 3500, 2870, 1641, 1499, 1474, 1205, 1173, 1069; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{20}H_{12}Br_2F_4NO_2^-$= 531.9171 found = 531.9171; MP 115-117 °C.

2,6-diiodo-4-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl)phenol (8) To a solution of compound 6f (0.600 g 1.19 mmol) in TFA (1mL) was added NIS (0.295 g, 1.31 mmol) and the resulting reaction mixture stirred at room temperature for 3 h. After this time the reaction mixture was concentrated under reduced pressure and then directly to flash column chromatography (100% hexane to 100% toluene). This gave the target compound **8** as a colourless crystalline solid (0.425 g) in a 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 2H), 7.22 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 5.66 (brs, 1H), 1.64 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.5 – -88.7 (m, 2F), -154.1 – -154.3 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 153.9, 151.7, 146.5, 146.4, 145.0 – 144.7 (m), 144.6 – 144.4 (m), 143.6 – 143.4 (m), 137.6, 137.0 – 136.8 (m), 135.5 – 135.3 (m), 128.2, 116.4, 82.1, 41.8, 30.8; IR ν_{max} (ATR)/cm^{-1} 1643, 1591, 1489, 1248, 1076, 740; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{20}H_{12}NO_2F_4I_2^-$ = 627.8894 found = 627.8912; MP 141-143 °C.

4-[2-(4-hydroxyphenyl)propan-2-yl]-2-iodophenol (9) To a solution of 2-iodo-4-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl)phenol (0.230 g, 0.46 mmol) in MeCN (10 mL) was added potassium fluoride (0.053 g, 0.92 mmol) and thiophenol (0.152 g, 1.38 mmol) and the resulting reaction mixture stirred at rt for 18 h. After this time the reaction mixture was concentrated under reduced pressure and the recovered residue purified directly by flash column chromatography (100% hexane to 25% EtOAc/75% hexane). This gave the title product as a clear oil (0.132 g) in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 2.3 Hz, 1H), 7.11 – 7.06 (m, 3H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 5.37 (brs, 1H), 1.63 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.5, 152.6, 145.4, 142.5, 136.1, 129.1, 127.9, 114.9, 114.5, 85.5, 41.6, 31.0; IR ν_{max} (ATR)/cm^{-1} 3248, 1644, 1595, 1511, 1500, 1489, 1224, 1177, 820, 560; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{15}H_{14}O_2I^-$ = 353.0039 found = 353.0041.

4-[2-(4-hydroxy-3-iodophenyl)propan-2-yl]-2-iodophenol (10) The title compound was synthesised according to the general procedure for iodination using conditions A from 0.40 mmol of the corresponding mono-iodo-BPA this gave the desired product as a clear oil (0.141 g) in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.3 Hz, 2H), 7.06 (dd, *J* = 8.5 Hz, 2.3 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.24 (brs, 2H), 1.61 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.9, 144.6, 136.0, 129.0, 114.7, 85.6, 41.5, 31.0; IR ν_{max} (ATR)/cm^{-1} 3478, 2966, 1645, 1489, 1226, 1165, 1077, 1018, 979; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{15}H_{13}O_2I_2^-$ = 478.9005 found = 478.9018.

Synthesis of 4'-methoxy-5-(2-{4-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]phenyl}propan-2-yl)-[1,1'-biphenyl]-2-ol (11) The title compound was synthesised according to the general procedure for the for Suzuki-Miyaura cross-coupling from 0.54 mmol of the corresponding tetrafluoropyridyl phenol iodide. The compound was purified using flash column chromatography (100% hexane to 100% toluene) to give the product as a brown oil (0.192 g) in 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.11 – 7.06 (m, 3H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 1H), 5.10 (brs, 1H), 3.88 (s, 3H), 1.70 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -88.7 – -88.9 (m, 2F), -154.2 – -154.5 (m, 2F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.3, 153.7, 150.5, 148.0, 142.5, 130.2, 129.4, 128.5, 128.3, 127.2, 127.1, 116.2, 115.2, 114.7, 55.4, 42.1, 31.0; IR ν_{max} (ATR)/cm^{-1} 2966, 1642, 1603, 1475, 1202, 1170, 1066, 975, 832; HRMS (ESI$^-$) calcd for $[M-H]^-$ $C_{27}H_{20}NO_3F_4^-$ = 482.1379 found = 482.1368.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of ^{1}H, ^{19}F and ^{13}C NMR spectra for synthesized compounds, NMR data for reaction screening, computational data, X-ray analysis of **3f** and **8** (PDF)

X-ray crystal data of **3f** and **8** (CIF)

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Notes

The authors declare no competing financial interests.

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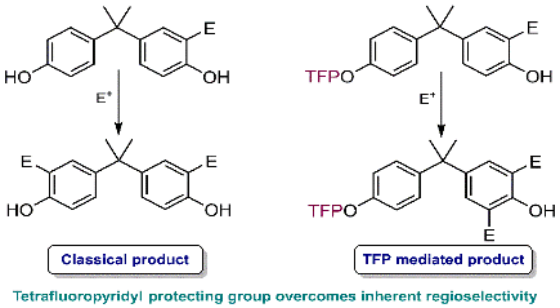

Tetrafluoropyridyl protecting group overcomes inherent regioselectivity