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Reactions of dibromotetrafluorobenzene derivatives with sodium phenoxide salts. Competing hydrodebromination and S_NAr processes

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ABSTRACT

1,2- and 1,3-dibromotetrafluorobenzene react with sodium phenoxide derivatives at sites *para* to ring bromine because these positions are activated by fluorine atoms *ortho* and *meta* to the site of nucleophilic substitution. Fluorine *para* to the site of nucleophilic attack is usually deactivating in nucleophilic aromatic substitution processes and this is reflected in the significantly reduced reactivity of 1,4-dibromotetrafluorobenzene which undergoes competing hydrodebromination processes to afford, primarily, 3-bromo-1,2,4,5-tetrafluorobenzene.

1. Introduction

Since the first reported practical syntheses of perfluoroaromatic systems such as hexafluorobenzene were reported [1,2], a 'mirror-image' chemistry involving reactions of these species with various nucleophiles proceeding *via* carbanionic Meisenheimer intermediates has developed [3] and has been reviewed [4]. Solutions to problems of regioselectivity of reactions, functionalisation and a mechanistic rationale for these processes continue to evolve and perfluoroaromatic systems have been used in the synthesis of, for example, polyfluorinated macrocyclic systems [5–9], peptides [10], solid phase organic systems [11], polycyclic derivatives [12–17] and, furthermore, in life-science applications [18].

Surprisingly, corresponding chemistry of perbromofluoroaromatic systems has not been developed to any great extent despite the potential applications of these systems in synthesis because of the presence of synthetically versatile carbon–bromine bonds as well as reactive carbon–fluorine sites for palladium-catalysed and S_NAr type processes respectively. Whilst reactions of bromopentafluorobenzene have been discussed [4], reactions of the three dibromotetrafluorobenzene systems **1**–**3** have not been exploited to any great extent. Indeed, only a very few reactions of **1**–**3** have been reported in the literature and involve reactions of sulfur [19,20] and nitrogen [21,22] nucleophiles for functionalisation and annelation processes.

In this paper, we describe model reactions between various sodium phenoxide salts and **1**–**3** as part of a continuing research programme concerning the synthesis of a range of fluorinated diphenyl ether systems for applications in liquid crystal display technology [23]. From a wider perspective, many diphenyl ethers have useful biological activity and this structural unit is found in many commercially important pharmaceuticals such as liothyronine [24], fenoprofen [25], and liotrix [26] and, given the importance of fluorine atoms in biologically active systems, methodology for the synthesis of fluorinated diphenyl ethers may have other useful applications in medicinal chemistry.

2. Results and discussion

Reactions between **1**–**3** and sodium phenoxide in acetonitrile solution using either conventional or microwave heating are collated in Scheme 1.

Reactions of **1** and **2** proceeded regioselectively to full conversion as assessed by ^{19}F NMR analysis of the crude reaction

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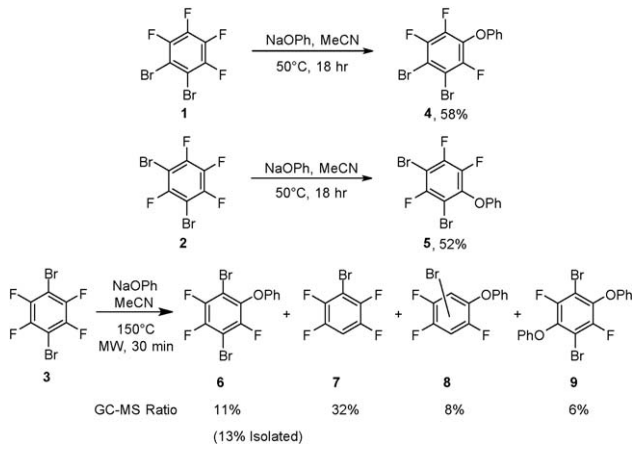


Scheme 1. Reactions of **1**–**3** with sodium phenoxide.

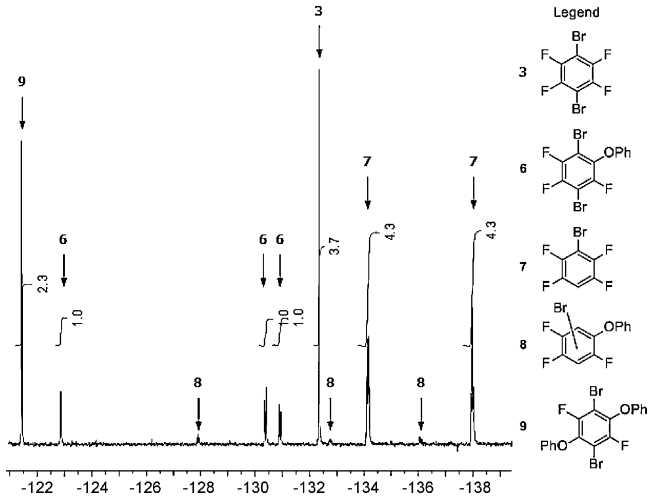


Fig. 2. ^{19}F NMR spectrum of crude reaction mixture between **3** and sodium phenoxide.

mixture and diaryl ethers **4** and **5** were isolated by column chromatography in 58% and 52% yields respectively. The modest yields obtained were due to difficulties in separating the major products from a small number of minor products and some tarry material. The structure of **4** was confirmed by X-ray diffraction (Fig. 1) whilst the structure of **5** was deduced by the observation of three resonances in a 1:1:1 ratio in the ^{19}F NMR spectrum, two of which have a mutual $^{3}J_{FF}$ coupling constant (~20 Hz), whilst the third signal exhibits no such coupling. Substitution at either the 2 or 5 positions of **2** would give rise to a symmetrical product for which the ^{19}F NMR spectra would be expected to consist of only two signals of 2:1 intensity and this is not observed in this case.

Diaryl ethers **4** and **5** arise from displacement of the fluorine atoms that are *para* to ring bromine substituents, consistent with well-established principles [3,4]. For nucleophilic substitution reactions involving related, highly fluorinated aromatic systems, the fluorine atom that has the most activating fluorine atoms *ortho* and *meta* and least deactivating fluorine atoms *para* to the site of nucleophilic attack is displaced preferentially.

In contrast, reaction of **3** gave low yields of the desired diaryl ether derivative **6** and other products **7**–**9** were observed by ^{19}F NMR spectroscopy (Fig. 2) and GC–MS analysis of the crude product mixture. Product **6** was isolated by column chromatography and shows three signals of equal intensity (δ_F −122.8, −130.3, −130.8) consistent with the proposed structure. The highly volatile major product, bromo-1,2,4,5-tetrafluorobenzene **7** was characterised by GC–MS (m/z = 228) and from the presence of two resonances of equal intensity in the ^{19}F NMR spectrum of the crude product mixture which have identical chemical shifts (δ_F −134.1, −137.9 ppm) to that of an authentic commercial sample [27]. The structure of by-product **8** is difficult to identify conclusively but the presence of three signals in equal ratio in the ^{19}F NMR spectrum (δ_F −127.8, −132.7, −136.0) and GC–MS analysis (m/z = 302) are consistent with the proposed molecular formula. Finally, disubstituted product **9** was identified by GC–MS analysis (m/z = 454) and the presence of a single resonance (δ_F −121.4) in the ^{19}F NMR spectrum of the crude product mixture.

A mechanistic rationale for the reaction of **3** with phenoxide is given in Scheme 2. In this case, there are no fluorine atoms attached to carbon *para* to ring bromine and so only carbon–fluorine bonds that are deactivated by fluorine atoms *para* are available for nucleophilic substitution processes. Consequently, relatively uncommon bromophilic attack is a competing process in which phenoxide attacks the bromine atom and the electron deficient aromatic ring acts as a good leaving group. Indeed, our observations are consistent with previous examples of bromophilic attack on highly halogenated systems such as reactions of oxygen nucleophiles with hexabromobenzene which give tetrabromobenzene [28]. Subsequent protonation upon workup gives **7**.

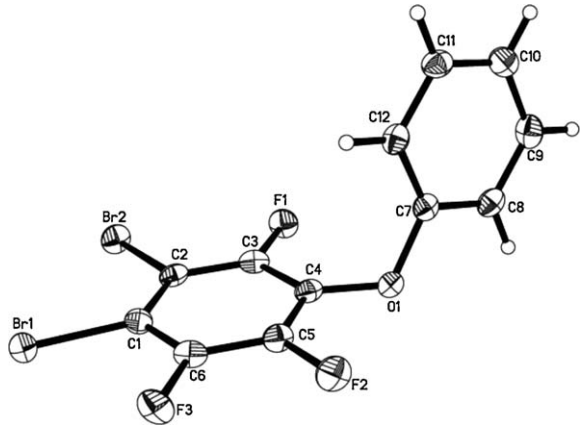
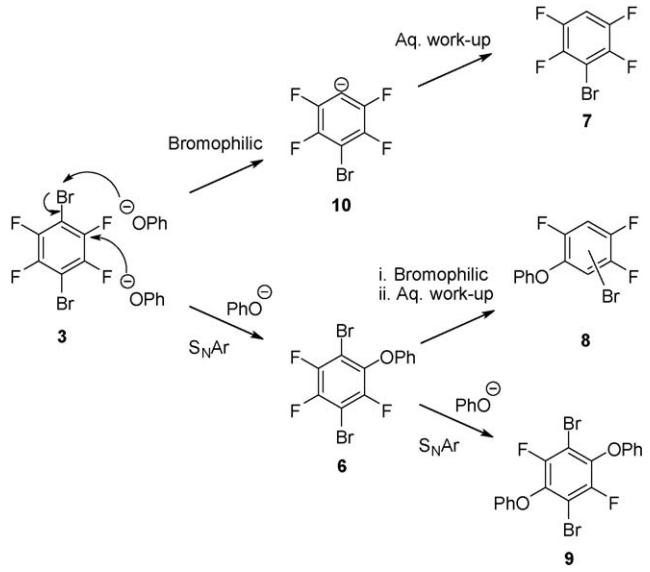
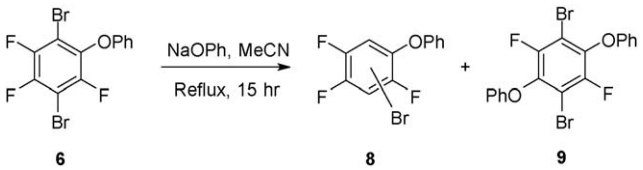


Fig. 1. Molecular structure of **4**.



Scheme 2. Mechanism for the reaction of **3** with sodium phenoxide.



Scheme 3. Reaction of **6** with sodium phenoxide.

8 is formed *via* the reaction of **3** with phenoxide, giving **6**, which may undergo further bromophilic or S_NAr processes to give minor by-products **8** and **9** respectively.

In a separate experiment, a sample of **6** was reacted with sodium phenoxide in acetonitrile solvent to give a mixture of **8** and the disubstituted product **9** (Scheme 3) in approximately equal quantities by ^{19}F NMR analysis, consistent with the mechanism outlined in Scheme 2.

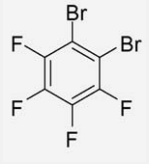
The relative rates of reaction of the dibromotetrafluorobenzenes were established by a competition reaction between a deficiency of sodium phenoxide (10 mol%) with an equimolar mixture of **1**–**3** in THF. The relative reactivities were evaluated by calculating the consumption of each of the three starting materials by ^{19}F NMR spectroscopy of the crude product mixture (Table 1).

It is possible to rationalise the relative reactivities of **1** and **2** by considering the relative activating and deactivating effects of the fluorine atoms attached to the aromatic ring. The site of observed nucleophilic substitution in **1** is activated by one *meta* and two *ortho* fluorine atoms whilst the site of nucleophilic substitution in **2** is activated by one *ortho* fluorine and two *meta* fluorine atoms. Therefore, our kinetic measurements suggest that fluorine *meta* to the site of nucleophilic attack has a greater influence in this system than fluorine *ortho* to the site of attack. This observation is consistent with a reaction profile whereby initial nucleophilic attack exhibits a relatively late transition step in which Meisenheimer intermediate stabilisation is more important than the initial state activation of the electrophile [3]. **3** is the least reactive system since the carbon–fluorine bonds are only activated by one *ortho* and one *meta* fluorine atom and deactivated by one fluorine atom *para* to the site of nucleophilic attack.

Further reactions of **1**–**3** with related alkylated phenoxide derivatives and excess phenoxide are collated in Table 2 and the products observed are consistent with the results discussed above.

Reaction of two equivalents of phenoxide with dibromotetrafluorobenzene systems **1** and **2** affords the respective disubstituted products **10** and **12** in moderate yield with nucleophilic attack occurring preferentially at sites *para* to ring bromine, consistent with the discussion above. The structure of **10** may be assigned by the presence of a single fluorine environment in the ^{19}F NMR spectrum of the purified product whilst the observed C–F coupling constants in the ^{13}C NMR spectrum of **12** are consistent with a 1,4-difluorinated system. Similar reasoning allows for the structural

Table 1
Competition reaction of **1**–**3** with sodium phenoxide.

Electrophile	Relative rate of consumption
	1.0
	2.8
	0.2

assignment of **11** and **13** which can be synthesised from reaction of two equivalents of sodium (4-*n*-pentyl)-phenoxide with **1** and **2** respectively in good yield.

The poor isolated yields of **14**–**16** reflect the low reactivity of starting material **3** and the associated competing bromophilic attack processes as discussed above. The structures of **15a** and **15b** were confirmed by X-ray crystallography (Fig. 3) and analogous structures of **14** and **16** by a comparison of spectral data.

Whilst the molecular geometry of compounds **4**, **15a** and **15b** do not show any unexpected features, the packing of these molecules in crystals is somewhat unusual. In all three crystal structures the molecules are linked together not by the expected stacking $\pi\cdot\pi$ interactions between aromatic rings but by short contacts between the bromine atoms and the aromatic systems of the non-halogenated benzene rings. In all cases the carbon–bromine bond is directed towards one of the carbon–carbon bonds and so the interactions are of "semi-localized" mode according to established classifications [29]. The shortest Br·C distances in these contacts in structures **4**, **15a** and **15b** (3.438, 3.510 and 3.316 Å respectively) correspond well to those reported previously [29] (3.429–3.558 Å). In the structure **4**, pairs of these contacts link molecules in dimers while other Br·Br and C–H·F contacts give rise to a 3D-network. In the structure **15a** the *para*-orientation of bromine atoms results in a different arrangement where the adjacent molecules are linked by pairs of Br·π interactions in chains along the (1 1 0) direction and a similar motif is found in

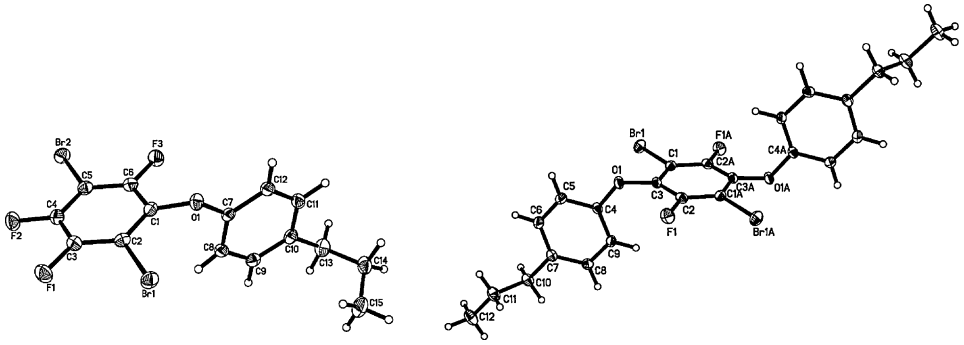
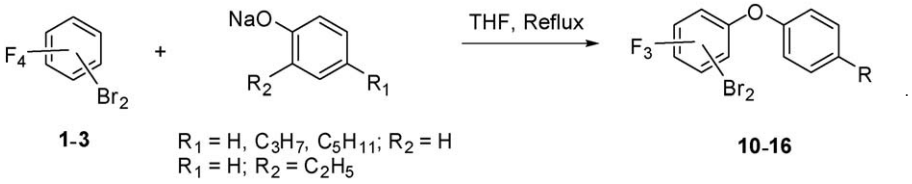


Fig. 3. Molecular structures of **15a** and **15b**.

Table 2
Reactions of **1**–**3** with phenoxide derivatives.



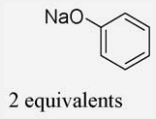
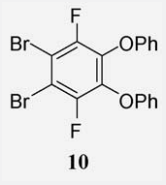
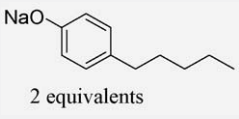
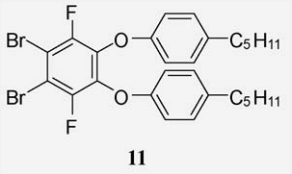
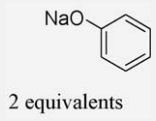
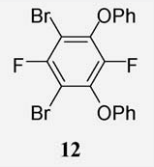
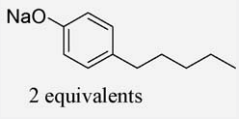
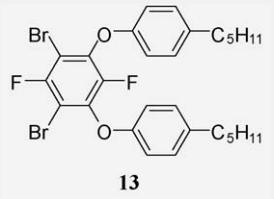
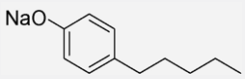
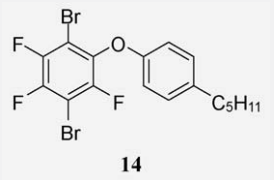
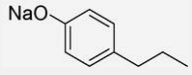
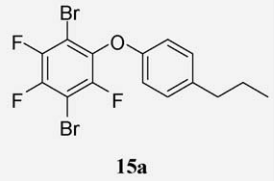
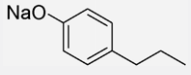
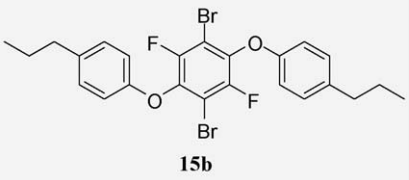
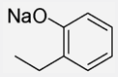
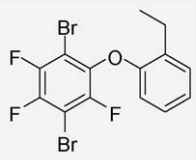
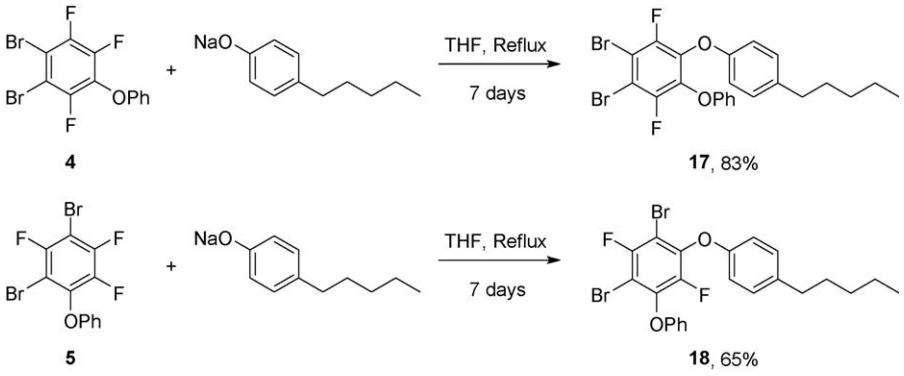
Electrophile	Nucleophile	Product	Isolated yield/%
1	 2 equivalents	 **10**	57
1	 2 equivalents	 **11**	64
2	 2 equivalents	 **12**	56
2	 2 equivalents	 **13**	70
3		 **14**	4
3		 **15a**	6
3		 **15b**	10[a]

Table 2 (*Continued*)

Electrophile	Nucleophile	Product	Isolated yield/%
3		 **16**	4

[a] Isolated from the reaction of **3** with one equivalent of sodium 4-propylphenoxide.



Scheme 4. Synthesis of disubstituted derivatives **17** and **18**.

structure **15b**. Another unusual feature of structure **15b** is a very close contact between C($C_6F_2Br_2$)–O ether bonds of molecules in neighboring anti-parallel chains where the O·O and O·C distances are equal to 2.884 and 2.996 Å.

Biphenyl ether derivatives **4** and **5** react with sodium 4-*n*-pentylphenoxide to give the disubstituted systems **17** and **18** respectively (Scheme 4). Structural assignments of **17** and **18** are based on the symmetrical analogues **10** and **12** and, indeed, the chemical shifts of each of the fluorine environments in the respective NMR spectra are consistent with the proposed structures.

3. Conclusions

1,2- and 1,3-Dibromotetrafluorobenzene react with phenoxide nucleophiles to afford novel functionalised biphenyl ethers with high regioselectivity and the observed sites of nucleophilic substitution can be readily explained by a consideration of the relative activating effects of the fluorine atoms present on the aromatic ring. 1,4-Dibromotetrafluorobenzene is the least reactive electrophile of the dibromotetrafluorobenzene series because nucleophilic substitution occurs at sites that are deactivated by *para* fluorine. In this case, hydrodebromination processes compete with nucleophilic substitution to afford 3-bromo-1,2,4,5-tetrafluorobenzene and a number of minor products. Finally, the diaryl ether products, 1,2-dibromo-3,5,6-trifluoro-4-phenoxybenzene **4** and 1,3-dibromo-2,4,5-trifluoro-6-phenoxybenzene **5**, are sufficiently electrophilic to react with another equivalent of an alkylated phenoxide derivative and form a number of triphenyl diethers, with the second substitution occurring preferentially at the unsubstituted site *para* to ring bromine.

4. Experimental

4.1. General

All starting materials were obtained commercially. All solvents were dried using literature procedures. NMR spectra were recorded in deuterochloroform, unless otherwise stated. ^{1}H, ^{13}C, ^{19}F, HSQC, COSY and HMBC NMR spectra were recorded on Varian-500 and Varian-700 spectrometers in the solvent stated. The ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (the peak integration, s = singlet, d = doublet, m = multiplet, bs = broad singlet), *J* coupling constant (Hz). Elemental analyses were conducted on an Exeter Analytical Inc CE-440 elemental analyser. All infra-red spectra were recorded using a FT-IR Perkin Elmer Spectrum RX1 machine. Mass spectra were recorded on a Thermo-Finnigan Trace instrument coupled with a Hewlett Packard 5890 series II Gas Chromatograph. Melting points were measured using a Gallenkamp melting point apparatus recorded at atmospheric pressure and are uncorrected. The progress of reactions was monitored by ^{19}F NMR spectroscopy. Column chromatography was carried out on silica gel (Fluorochem).

4.2. Reactions of dibromotetrafluorobenzene systems 1–3 with nucleophiles

4.2.1. 1,2-Dibromo-3,4,6-trifluoro-5-phenoxybenzene 4

Sodium phenoxide (0.67 g, 5.8 mmol) was added to 1,2-dibromo-3,4,5,6-tetrafluorobenzene (1.61 g, 5.2 mmol) in anhydrous acetonitrile (160 mL) under an atmosphere of dry argon and heated to reflux for 15 h, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane as the eluent afforded *1,2-dibromo-3,5,6-trifluoro-4-phenoxybenzene* 4 (1.16 g, 58%) as a white solid; m.p. 69–70 °C (Found C, 37.7; H, 1.3. $C_{12}H_5OBr_2F_3$ requires: C, 37.7; H, 1.32); δ_H 6.95 (2H, dm, $^{3}J_{HH}$ 8.5, H_{ortho}), 7.13 (1H, tt, $^{3}J_{HH}$ 7.5, $^{4}J_{HH}$ 1.0, H_{para}), 7.34 (2H, ddm, $^{3}J_{HH}$ 8.5, $^{3}J_{HH}$ 7.5, H_{meta}); δ_C 109.0 (dd, $^{2}J_{CF}$ 22.5, $^{3}J_{CF}$ 4.8, C-2), 110.0 (d, $^{2}J_{CF}$ 20.6, C-1), 115.8 (s, C_{ortho}), 124.1 (s, C_{para}), 130.1 (s, C_{meta}), 133.0 (ddd, $^{2}J_{CF}$ 17.6, $^{2}J_{CF}$ 12.6, $^{3}J_{CF}$ 2.5, C-5), 144.8 (ddd, $^{1}J_{CF}$ 257, $^{2}J_{CF}$ 16.1, $^{4}J_{CF}$ 4.6, C-3), 146.4 (ddd, $^{1}J_{CF}$ 249, $^{2}J_{CF}$ 12.7, $^{3}J_{CF}$ 4.4, C-4), 150.5 (ddd, $^{1}J_{CF}$ 250, $^{3}J_{CF}$ 3.5, $^{4}J_{CF}$ 3.5, C-6), 157.2

(s, C_{ipso}); δ_F −116.8 (1F, dd, $^4J_{FF}$ 3.0, $^5J_{FF}$ 9.0, F-6), −125.5 (1F, dd, $^3J_{FF}$ 21.5, $^5J_{FF}$ 9.0, F-3), −146.2 (1F, d, $^3J_{FF}$ 21.5, $^4J_{FF}$ 3.0, F-4); *m*/*z* (EI^+) 384 ($[M]^+$, 10), 382 ($[M]^+$, 18), 380 ($[M]^+$, 9), 222 (12), 77 (100), 51 (48).

4.2.2. 1,3-Dibromo-2,4,5-trifluoro-6-phenoxybenzene 5

Sodium phenoxide (0.67 g, 5.8 mmol) was added to 1,3-dibromo-2,4,5,6-tetrafluorobenzene (1.61 g, 5.2 mmol) in anhydrous acetonitrile (160 mL) under an atmosphere of dry argon. The mixture was refluxed for 15 h, cooled, poured on to water (100 mL) and extracted with dichloromethane (3 × 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane as the eluent afforded *1,3-dibromo-2,4,5-trifluoro-6-phenoxybenzene* 5 (0.87 g, 44%) as a white solid; m.p. 74–75 °C (Found C, 37.8; H, 1.3. $C_{12}H_5OBr_2F_3$ requires: C, 37.7; H, 1.3%); δ_H 6.91 (2H, dm, $^3J_{HH}$ 8.0, H_{ortho}), 7.13 (1H, tm, $^3J_{HH}$ 7.5, H_{para}), 7.34 (2H, tm, $^3J_{HH}$ 8.0, H_{meta}); δ_C 96.2 (dd, $^2J_{CF}$ 27.8, $^2J_{CF}$ 22.1, C-3), 102.2 (dd, $^2J_{CF}$ 25.1, $^3J_{CF}$ 4.7, C-1), 115.6 (s, C_{ortho}), 123.9 (s, C_{para}), 140.0 (s, C_{meta}), 141.8 (td, $^2J_{CF}$ 11.9, $^3J_{CF}$ 3.5, C-6), 142.4 (ddd, $^1J_{CF}$ 256, $^2J_{CF}$ 15.2, $^3J_{CF}$ 4.9, C-4), 148.7 (ddd, $^1J_{CF}$ 251, $^2J_{CF}$ 13.1, $^4J_{CF}$ 5.5, C-5), 153.2 (ddd, $^1J_{CF}$ 245, $^3J_{CF}$ 4.3, $^4J_{CF}$ 4.3, C-2), 156.8 (s, C_{ipso}); δ_F −101.5 (1F, d, $^5J_{FF}$ 9.0, F-2), −126.3 (1F, d, $^3J_{FF}$ 21.5, F-4), −121.9 (1F, dd, $^3J_{FF}$ 21.5, $^5J_{FF}$ 9.0, F-5); *m*/*z* (EI^+) 384 ($[M]^+$, 48), 382 ($[M]^+$, 64), 380 ($[M]^+$, 53), 222 (100), 77 (67), 51 (42).

4.2.3. 1,4-Dibromo-2,3,5-trifluoro-6-phenoxybenzene 6

Sodium phenoxide (3.33 g, 29 mmol) was added to 1,4-dibromo-2,3,5,6-tetrafluorobenzene (8.12 g, 26 mmol) in anhydrous acetonitrile (160 mL) under an atmosphere of dry argon. The mixture was refluxed for 15 h, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane as the eluent afforded *1,4-dibromo-2,3,5-trifluoro-6-phenoxybenzene* 6 (1.72 g, 17%) as a white solid; m.p. 109–111 °C (Found: C, 37.7; H, 1.3. $C_{12}H_5OBr_2F_3$ requires: C, 37.7; H, 1.3%); δ_H 6.87 (2H, d, $^3J_{HH}$ 8.7, H_{ortho}), 7.10 (1H, t, $^3J_{HH}$ 7.3, H_{para}), 7.32 (2H, ddm, $^3J_{HH}$ 8.7, $^3J_{HH}$ 7.3, H_{meta}); δ_C 99.5 (tm, $^2J_{CF}$ 23.3, C-4), 107.2 (dm, $^2J_{CF}$ 19.7, C-1), 115.4 (s, C_{ortho}), 123.7 (s, C_{para}), 130.1 (s, C_{meta}), 138.0 (ddd, $^2J_{CF}$ 16.7, $^3J_{CF}$ 4.9, $^4J_{CF}$ 1.4, C-6), 145.8 (ddd, $^1J_{CF}$ 250, $^2J_{CF}$ 15.3, $^3J_{CF}$ 4.8, C-3), 146.2 (ddd, $^1J_{CF}$ 251, $^2J_{CF}$ 16.1, $^4J_{CF}$ 3.7, C-4), 150.2 (ddd, $^1J_{CF}$ 251, $^3J_{CF}$ 3.4, $^4J_{CF}$ 3.4, C-5); δ_F −121.9 (1F, d, $^5J_{FF}$ 9.4, F-5), −129.7 (1F, d, $^3J_{FF}$ 23.1, F-3), −130.3 (1F, dd, $^3J_{FF}$ 23.1, $^5J_{FF}$ 9.4, F-2); *m*/*z* (EI^+) 384 ($[M]^+$, 47), 382 ($[M]^+$, 61), 380 ($[M]^+$, 51), 222 (98), 77 (100).

4.2.4. (4,5-Dibromo-3,6-difluoro-1,2-phenylene)bis(oxy)dibenzene 10

Sodium hydride (0.07 g, 1.8 mmol, 60% (*w*/*w*) in mineral oil) was washed three times with dry hexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was removed and replaced with dry THF (15 mL). Phenol (0.17 g, 1.8 mmol) was dissolved in dry THF (15 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped, 1,2-dibromo-3,4,5,6-tetrafluorobenzene (0.24 g, 0.8 mmol) was added and the reaction heated to reflux for 5 days. The mixture was cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane as the eluent afforded (*4,5-dibromo-3,6-difluoro-1,2-phenylene*)*bis*(*oxy*)*dibenzene* 10 (0.20 g, 57%) as a white solid; m.p. 89–90 °C (Found: C, 47.6; H, 2.3. $C_{18}H_{10}O_2Br_2F_2$ requires: C, 47.4; H, 2.2%); ν_{max} 1582, 1485, 1436, 1251, 1195, 1158, 1022 cm^{-1}; δ_H 6.79 (2H, m, $^3J_{HH}$ 8.7, $^4J_{HH}$ 0.9, H_{ortho}), 7.03 (1H, m, $^3J_{HH}$ 7.4, $^4J_{HH}$ 0.9, H_{para}), 7.22 (2H, m, $^3J_{HH}$ 8.7, $^3J_{HH}$ 7.4, H_{meta}); δ_C 110.0 (dd, $^2J_{CF}$ 17.3, $^3J_{CF}$ 5.9, C-4), 115.9 (s, C_{ortho}), 123.7 (s, C_{para}), 129.8 (s, C_{meta}), 137.6 (dd, $^2J_{CF}$ 14.0, $^3J_{CF}$ 4.2, C-1), 150.9 (dd, $^1J_{CF}$ 250, $^4J_{CF}$ 4.3, C-3), 157.1 (s, C_{ipso}); δ_F −117.4 (s); *m*/*z* (EI^+) 458 ($[M]^+$, 12), 456 ($[M]^+$, 24), 454 ($[M]^+$, 12), 282 (25), 77 (100), 51 (34).

4.2.5. 4,4′-(4,5-Dibromo-3,6-difluoro-1,2-phenylene)bis(oxy)bis(pentylbenzene) 11

Sodium hydride (0.14 g, 3.5 mmol, 60% (*w*/*w*) in mineral oil) was washed three times with dry hexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was removed and replaced with dry THF (15 mL). 4-*n*-Pentylphenol (0.57 g, 3.5 mmol) was dissolved in dry THF (15 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped, 1,2-dibromo-3,4,5,6-tetrafluorobenzene (0.5 g, 1.6 mmol) was added and the reaction heated to reflux for 4 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane:DCM (19:1) as the eluent afforded *4,4′-(4,5-dibromo-3,6-difluoro-1,2-phenylene)bis*(*oxy*)*bis*(*pentylbenzene*) 11 (0.61 g, 64%) as a colourless liquid; (Found C, 56.2; H, 5.1. $C_{28}H_{30}O_2Br_2F_2$ requires: C, 56.4; H, 5.1%); δ_H 0.87 (3H, t, $^3J_{HH}$ 7.0, CH_3), 1.23–1.35 (4H, m, CH_2), 1.54 (2H, m, CH_2), 2.53 (2H, tm, $^3J_{HH}$ 7.8, $ArCH_2$), 6.70 (2H, AX, $^3J_{AX}$ 8.3, H_{meta}), 7.01 (2H, AX, $^3J_{AX}$ 8.3, H_{ortho}); δ_C 14.3 (s, CH_3), 22.7 (s, CH_2CH_3), 31.5 (s, CH_2), 31.7 (s, CH_2), 35.3 (s, $ArCH_2$), 109.6 (dt, $^2J_{CF}$ 9.8, $^3J_{CF}$ 4.0, C-4), 115.8 (s, C_{meta}), 129.5 (s, C_{ortho}), 138.0 (dd, $^2J_{CF}$ 13.5, $^3J_{CF}$ 3.8, C-1), 138.2 (s, *C*–CH_2), 150.9 (dd, $^1J_{CF}$ 250, $^4J_{CF}$ 4.3, C-3), 155.3 (s, C–O); δ_F −117.6 (s); *m*/*z* (EI^+) 598 ($[M]^+$, 28), 596 ($[M]^+$, 48), 594 ($[M]^+$, 27), 483 (100).

4.2.6. (4,6-Dibromo-2,5-difluoro-1,3-phenylene)bis(oxy)dibenzene 12

Sodium hydride (0.07 g, 1.8 mmol, 60% (*w*/*w*) in mineral oil) was washed three times with dry hexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was replaced with dry THF (15 mL). Phenol (0.16 g, 1.7 mmol) was dissolved in dry THF (15 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped, 1,3-dibromo-2,4,5,6-tetrafluorobenzene (0.26 g, 0.84 mmol) was added and the reaction heated to reflux for 2 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent revaporated. Column chromatography of the residue on silica gel with hexane:ethyl acetate (14:1) as the eluent afforded (*4,6-dibromo-2,5-difluoro-1,3-phenylene*)*bis*(*oxy*)*dibenzene* 12 (0.21 g, 56%) as a white solid; m.p. 123 °C (Found C, 47.5; H, 2.2. $C_{18}H_{10}O_2Br_2F_2$ requires: C, 47.4; H, 2.2%); ν_{max} 1530, 1489, 1454, 1424, 1203, 1166, 1076 cm^{-1}; δ_H 6.89 (4H, m, H_{ortho}), 7.08 (2H, m, H_{para}), 7.30 (4H, m, H_{meta}); δ_C 103.4 (d, $^2J_{CF}$ 25.0, C-4), 115.5 (s, C_{ortho}), 123.7 (s, C_{para}), 130.0 (s, C_{meta}), 141.8 (dd, $^2J_{CF}$ 13.0, $^3J_{CF}$ 4.0, C-1), 147.0 (dd, $^1J_{CF}$ 257, $^4J_{CF}$ 4.4, C-2), 153.7 (dd, $^1J_{CF}$ 245, $^4J_{CF}$ 4.0, C-5), 156.9 (s, C_{ipso}); δ_F −100.4 (1F, d, $^5J_{FF}$ 10.1, F-5), −140.4 (1F, d, $^5J_{FF}$ 10.1, F-2); *m*/*z* (EI^+): 458 ($[M]^+$, 8), 456 ($[M]^+$, 15), 454 ($[M]^+$, 8), 282 (16), 77 (100), 51 (42).

4.2.7. 4,4′-(4,6-Dibromo-2,5-difluoro-1,3-phenylene)bis(oxy)bis(pentylbenzene) 13

Sodium hydride (0.16 g, 4 mmol, 60% (*w*/*w*) in mineral oil) was washed three times with dryhexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was removed and replaced with dry THF

(15 mL). 4-Pentylphenol (0.59 g, 3.6 mmol) was dissolved in dry THF (15 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped, 1,3-dibromo-2,4,5,6-tetrafluorobenzene (0.53 g, 1.7 mmol) was added and the reaction heated to reflux for 4 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography of the residue on silica gel with hexane:DCM (10:1) as the eluent afforded *4,4′-(4,6-dibromo-2,5-difluoro-1,3-phenylene)bis(oxy)bis(pentylbenzene*) 13 (0.72 g, 70%) as a white solid; m.p. 99–101 °C (Found C, 56.4; H, 5.1. $C_{28}H_{30}O_2Br_2F_2$ requires: C, 56.4; H, 5.05%); ν_{max} 2921, 2851, 1590, 1501, 1455, 1425, 1206, 1165, 1072 cm^{-1}; δ_H 0.86 (6H, t, $^3J_{HH}$ 7.1, CH_3), 1.23–1.34 (8H, m, CH_2), 1.56 (4H, m, CH_2), 2.53 (4H, t, $^3J_{HH}$ 7.8, $ArCH_2$), 6.78 (4H, AX, $^3J_{AX}$ 8.6, H_{ortho}), 7.07 (4H, AX, $^3J_{AX}$ 8.6, H_{meta}); δ_C 14.2 (s, CH_3), 22.7 (s, CH_2), 31.4 (s, CH_2), 31.7 (s, CH_2), 35.3 (s, CH_2), 103.2 (d, $^2J_{CF}$ 24.9, C-4), 115.3 (s, C_{ortho}), 129.7 (s, C_{para}), 138.3 (s, C_{meta}), 142.0 (dd, $^2J_{CF}$ 13.3, $^3J_{CF}$ 3.7, C-1), 147.1 (dd, $^1J_{CF}$ 256, $^4J_{CF}$ 3.9, C-2), 153.6 (dd, $^1J_{CF}$ 245, $^4J_{CF}$ 4.1, C-5), 155.0 (s, C_{ipso}); δ_F −100.7 (1F, d, $^5J_{FF}$ 10.0, F-5), −140.4 (1F, d, $^5J_{FF}$ 10.0, F-2); *m/z* (EI^+) 598 ($[M]^+$, 29), 596 ($[M]^+$, 54), 594 ($[M]^+$, 27), 483 (100), 297 (44), 77 (16).

4.2.8. 1,4-Dibromo-2,3,5-trifluoro-6-(4-pentylphenoxy)benzene **14**

Sodium metal (0.3 g, 13 mmol) was added to a solution of 4-pentylphenol (1.73 g, 10 mmol) in dry THF (30 mL) under an inert argon atmosphere which was maintained throughout the experiment. After all of the sodium had reacted, 1,4-dibromo-2,3,5,6-tetrafluorobenzene (3.08 g, 10.0 mmol) was added and the mixture heated to reflux for 20 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered, solvent evaporated and the resulting solid purified by recrystallisation from ethanol and water. Further column chromatography on silica gel with hexane:DCM (9:1) as the eluent afforded *1,4-dibromo-2,3,5-trifluoro-6-(4-pentylphenoxy)benzene* 14 (0.20 g, 4%,) as a white solid; m.p. 69–71 °C (Found C, 45.4; H, 3.4. $C_{17}H_{15}OBr_2F_3$ requires: C, 45.2; H, 3.3%); δ_H 0.90 (3H, t, $^3J_{HH}$ 6.8, CH_3), 1.33 (4H, m, CH_2), 1.60 (2H, tt, $^3J_{HH}$ 7.9, $^3J_{HH}$ 7.3, CH_2), 2.57 (2H, t, $^3J_{HH}$ 7.9, $ArCH_2$), 6.80 (2H, AX, $^3J_{AX}$ 8.6, H_{ortho}), 7.12 (2H, AX, $^3J_{AX}$ 8.6, H_{meta}); δ_C 14.3 (s, CH_3), 22.8 (s, CH_2), 31.5 (s, C-12), 31.7 (s, CH_2), 35.3 (s, $ArCH_2$), 99.5 (dd, $^2J_{CF}$ 23.6, $^2J_{CF}$ 23.6, C-4), 107.2 (d, $^2J_{CF}$ 21.3, C-1), 115.3 (s, C_{ortho}), 129.8 (s, C_{meta}), 138.3 (m, C-6), 138.4 (s, C–CH_2), 145.7 (ddd, $^1J_{CF}$ 245, $^2J_{CF}$ 14.7, $^3J_{CF}$ 4.4, C-3), 146.5 (ddd, $^1J_{CF}$ 247, $^2J_{CF}$ 13.9, $^4J_{CF}$ 2.9, C-2), 150.3 (ddd, $^1J_{CF}$ 252, $^3J_{CF}$ 4.0, $^4J_{CF}$ 4.0, C-5), 155.1 (s, C–O); δ_F −122.0 (dd, $^4J_{FF}$ 2.3, $^5J_{FF}$ 11.6, F-5), −130.0 (dd, $^3J_{FF}$ 20.6, $^4J_{FF}$ 2.3, F-3), −130.5 (dd, $^3J_{FF}$ 22.7, $^5J_{FF}$ 11.6, F-2); *m/z* (EI^+) 454 ($[M]^+$, 28), 452 ($[M]^+$, 55), 450 ($[M]^+$, 28), 395 (100).

4.2.9. 1,4-Dibromo-2,3,5-trifluoro-6-(4-propylphenoxy)benzene **15a** *and 4,4′-(2,5-dibromo-3,6-difluoro-1,4-phenylene)bis(oxy)bis(propylbenzene)* **15b**

Sodium metal (0.3 g, 13 mmol) was added to a solution of 4-*n*-propylphenol (1.43 g, 10.5 mmol) in dry THF (30 mL) under an inert argon atmosphere which was maintained throughout the experiment. After all of the sodium had reacted, 1,4-dibromo-2,3,5,6-tetrafluorobenzene (3.10 g, 10.1 mmol) was added and the reaction mixture was heated to reflux for 20 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered, solvent evaporated and the resulting solid purified by recrystallisation from ethanol and water. Column chromatography on silica gel with hexane:DCM (9:1) as the eluent afforded *1,4-dibromo-2,3,5-trifluoro-6-(4-propylphenoxy)benzene* **15a** (0.26 g, 6%,) as a white solid; m.p. 58–60 °C (Found C, 42.5; H, 2.6. $C_{15}H_{11}OBr_2F_3$ requires: C, 42.5; H, 2.6%); δ_H 0.95 (3H, t, $^3J_{HH}$ 7.3, CH_3), 1.63 (2H, tt, $^3J_{HH}$ 7.5, $^3J_{HH}$ 7.3, CH_2), 2.56 (2H, t, $^3J_{HH}$ 7.5, $ArCH_2$), 6.80 (2H, AX, $^3J_{AX}$ 8.5, H_{ortho}), 7.12 (2H, AX, $^3J_{AX}$ 8.5, H_{meta}); δ_C 14.0 (s, CH_3), 24.9 (s, CH_2), 37.4 (s, $ArCH_2$), 99.5 (dd, $^2J_{CF}$ 22.8, $^2J_{CF}$ 22.8, C-4), 107.2 (d, $^2J_{CF}$ 20.7, C-1), 115.3 (s, C_{ortho}), 129.9 (s, C_{meta}), 138.3 (ddd, $^2J_{CF}$ 16.1, $^3J_{CF}$ 5.8, $^4J_{CF}$ 2.9, C-6), 138.9 (s, *C*–CH_2), 145.7 (ddd, $^1J_{CF}$ 248, $^2J_{CF}$ 14.7, $^3J_{CF}$ 4.5, C-3), 146.1 (ddd, $^1J_{CF}$ 249, $^2J_{CF}$ 13.5, $^4J_{CF}$ 2.9, C-2), 150.2 (ddd, $^1J_{CF}$ 251, $^3J_{CF}$ 3.4, $^4J_{CF}$ 3.4, C-5), 155.1 (s, C–O); δ_F −122.0 (dd, $^4J_{FF}$ 3.2, $^5J_{FF}$ 10.7, F-5), −130.0 (dd, $^3J_{FF}$ 20.7, $^4J_{FF}$ 3.2, F-3), −130.5 (dd, $^3J_{FF}$ 20.7, $^5J_{FF}$ 10.7, F-2); *m/z* (EI^+) 426 ($[M]^+$, 28), 424 ($[M]^+$, 44), 422 ($[M]^+$, 23), 395 (100); and, *4,4′-(2,5-dibromo-3,6-difluoro-1,4-phenylene)bis(oxy)bis(propylbenzene* 15b (0.29 g, 10%) as a white solid; m.p. 117–119 °C (Found C, 53.3; H, 4.1. $C_{24}H_{22}O_2Br_2F_2$ requires: C, 53.4; H, 4.1%); δ_H 0.96 (3H, t, $^3J_{HH}$ 7.3, CH_3), 1.64 (2H, m, CH_2), 2.58 (2H, t, $^3J_{HH}$ 7.7, $ArCH_2$), 6.85 (2H, m, H_{ortho}), 7.15 (2H, m, H_{meta}); δ_C 14.0 (s, CH_3), 24.9 (s, CH_2), 37.5 (s, $ArCH_2$), 107.0 (dd, $^2J_{CF}$ 15.5, $^3J_{CF}$ 7.3, C-2), 115.4 (s, C_{ortho}), 129.9 (s, C_{meta}), 138.5 (s, C–CH_2), 139.2 (dd, $^2J_{CF}$ 13.9, $^3J_{CF}$ 4.6, C-1), 150.7 (dd, $^1J_{CF}$ 251, $^4J_{CF}$ 4.4, C-3), 155.3 (s, C–O); δ_F −120.8 (s); *m/z* (EI^+) 542 ($[M]^+$, 24), 540 ($[M]^+$, 48), 538 ($[M]^+$, 51), 90 (100).

4.2.10. 1,4-Dibromo-2,3,5-trifluoro-6-(2-propylphenoxy)benzene **16**

Sodium metal (0.3 g, 13 mmol) was added to a solution of 2-propylphenol (1.43 g, 10.5 mmol) in dry THF (30 mL) under an inert argon atmosphere which was maintained throughout the experiment. After all of the sodium had reacted, 1,4-dibromo-2,3,5,6-tetrafluorobenzene (3.02 g, 9.8 mmol) was added to the mixture which was heated to reflux for 20 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered, solvent evaporated and the resulting solid purified by recrystallisation from ethanol and water. Column chromatography on silica gel with hexane:DCM (4:1) as the eluent afforded *1,4-dibromo-2,3,5-trifluoro-6-(2-propylphenoxy)benzene* 16 (0.17 g, 4%) as a white solid; m.p. 56–58 °C (Found C, 42.3; H, 2.6. $C_{15}H_{11}OBr_2F_3$ requires: C, 42.5; H, 2.6%); δ_H 1.01 (3H, t, $^3J_{HH}$ 7.4, CH_3), 1.75 (2H, dm, $^3J_{HH}$ 7.4, CH_2), 2.79 (2H, t, $^3J_{HH}$ 7.7, $ArCH_2$), 6.38 (1H, d, $^3J_{HH}$ 8.0, ArH), 7.04 (2H, m, ArH), 7.25 (1H, d, $^3J_{HH}$ 6.2, ArH); δ_C 14.3 (s, CH_3), 23.3 (s, CH_2), 32.5 (s, $ArCH_2$), 99.6 (ddd, $^2J_{CF}$ 23.8, $^2J_{CF}$ 23.8, $^3J_{CF}$ 1.9, C-4), 107.2 (dd, $^2J_{CF}$ 19.8, $^3J_{CF}$ 1.8, C-1), 112.6 (s, ArC), 123.5 (s, ArC), 127.1 (s, ArC), 131.2 (s, *C*–CH_2), 131.4 (s, ArC), 138.2 (ddd, $^2J_{CF}$ 11.5, $^3J_{CF}$ 4.1, $^4J_{CF}$ 2.7, C-6), 145.9 (ddd, $^1J_{CF}$ 246, $^2J_{CF}$ 12.3, $^3J_{CF}$ 3.5, C-3), 146.1 (ddd, $^1J_{CF}$ 255, $^2J_{CF}$ 21.3, $^4J_{CF}$ 2.1, C-2), 150.2 (ddd, $^1J_{CF}$ 249, $^3J_{CF}$ 3.5, $^4J_{CF}$ 3.5, C-5), 155.0 (s, C–O); δ_F −122.2 (d, $^4J_{FF}$ 9.5, F-5), −130.1 (d, $^3J_{FF}$ 23.2, F-3), −130.4 (dd, $^3J_{FF}$ 23.6, $^5J_{FF}$ 9.5, F-2); *m/z* (EI^+) 426 ($[M]^+$, 28), 424 ($[M]^+$, 46), 422 ($[M]^+$, 24), 395 (20), 315 (100).

4.2.11. 1,2-Dibromo-3,6-difluoro-4-(4-pentylphenoxy)-5-phenoxybenzene **17**

Sodium hydride (0.025 g, 0.63 mmol, 60% (*w/w*) in mineral oil) was washed three times with dry hexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was removed and replaced with dry THF (15 mL). 4-Pentylphenol (0.10 g, 0.63 mmol) was dissolved in dry THF (10 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped, a solution of 1,2-dibromo-3,4,6-trifluoro-5-phenoxybenzene (0.22 g, 0.57 mmol) in dry THF (15 mL) was added and the reaction mixture heated to reflux for 7 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography on silica gel with hexane:DCM (5:1) as the eluent afforded *1,2-dibromo-3,6-difluoro-4-(4-pentylphenoxy)-5-phenoxybenzene* 17 (0.25 g, 83%) as a colourless oil;

(Found C, 52.6; H, 3.7. $C_{23}H_{20}O_2Br_2F_2$ requires: C, 52.5; H, 3.8%); δ_H 0.87 (3H, t, $^3J_{HH}$ 7.2, CH_3), 1.23–1.35 (4H, m, CH_2), 1.54 (2H, m, CH_2), 2.51 (2H, t, $^3J_{HH}$ 7.8, $ArCH_2$), 6.71 (2H, m, ArH), 6.79 (2H, m, ArH), 7.01 (2H, ArH), 7.03 (1H, m, ArH), 7.22 (2H, m, ArH); δ_C 14.3 (s, CH_3), 22.7 (s, CH_2), 31.5 (s, CH_2), 31.6 (s, CH_2), 35.3 (s, $ArCH_2$), 109.7 (d, $^2J_{CF}$ 22.1, C–Br), 109.9 (d, $^2J_{CF}$ 22.1, C–Br), 115.8 (s, Ar), 115.9 (s, Ar), 123.6 (s, Ar), 129.5 (s, Ar), 129.7 (s, Ar), 137.5 (dd, $^2J_{CF}$ 15.6, $^3J_{CF}$ 3.5, C–Ar), 138.0 (dd, $^2J_{CF}$ 15.5, $^3J_{CF}$ 3.5, C–Ar), 138.3 (s, Ar), 150.9 (dd, $^1J_{CF}$ 251, $^4J_{CF}$ 5.1, C–F), 151.0 (dd, $^1J_{CF}$ 250, $^4J_{CF}$ 4.3, C–F), 155.3 (s, C–O), 157.2 (s, C–O); δ_F −117.4 (1F, d, $^5J_{FF}$ 9.8, ArF), −117.5 (1F, d, $^5J_{FF}$ 9.8, ArF); m/z (EI$^+$) 528 ([M]$^+$, 10), 526 ([M]$^+$, 21), 524 ([M]$^+$, 11), 471 (45), 469 (100), 467 (51).

4.2.12. 1,3-Dibromo-2,5-difluoro-4-(4-pentylphenoxy)-6-phenoxybenzene **18**

Sodium hydride (0.05 g, 1.33 mmol, 60% (w/w) in mineral oil) was washed three times with dry hexane (10 mL) under an atmosphere of dry argon which was maintained throughout the experiment. The hexane/oil solution was removed and replaced with dry THF (15 mL). 4-Pentylphenol (0.19 g, 1.2 mmol) was dissolved in dry THF (10 mL) and carefully added, with stirring, to the sodium hydride and THF mixture. After the evolution of hydrogen gas had stopped a solution of 1,3-dibromo-2,4,5-trifluoro-6-phenoxybenzene (0.40 g, 1.04 mmol) in dry THF (15 mL) was added and the reaction mixture heated to reflux for 7 days, cooled, poured on to water (100 mL) and extracted with dichloromethane (3× 50 mL). The combined extracts were washed with water (100 mL), dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography on silica gel with hexane:DCM (5:1) as the eluent afforded *1,3-dibromo-2,5-difluoro-4-(4-pentylphenoxy)-6-phenoxybenzene* 18 (0.36 g, 65%) as a white solid; m.p. 53 °C (Found: C, 52.8; H, 3.9. $C_{23}H_{20}O_2Br_2F_2$ requires: C, 52.5; H, 3.8%); ν_{max} 2931, 2859, 1590, 1504, 1459, 1422, 1199, 1077 cm^{-1}; δ_H 0.87 (3H, t, $^3J_{HH}$ 7.1, CH_3), 1.25–1.34 (4H, m, CH_2), 1.56 (2H, m, CH_2), 2.53 (2H, t, $^3J_{HH}$ 7.8, $ArCH_2$), 6.79 (2H, m, ArH), 6.88 (2H, m, ArH), 7.06–7.09 (3H, m, ArH), 7.29 (2H, m, ArH); δ_C 14.2 (s, CH_3), 22.7 (s, CH_2), 31.4 (s, CH_2), 31.7 (s, $ArCH_2$), 35.3 (s, $ArCH_2$), 103.2 (d, $^2J_{CF}$ 25.2, C-3), 103.5 (d, $^2J_{CF}$ 24.4, C-1), 115.3 (s, Ar), 115.5 (s, Ar), 123.7 (s, Ar), 129.8 (s, Ar), 130.0 (s, Ar), 138.3 (s, Ar), 141.7 (dd, $^2J_{CF}$ 13.7, $^3J_{CF}$ 3.7, C–O), 142.1 (dd, $^2J_{CF}$ 13.1, $^3J_{CF}$ 4.5, C–O), 147.1 (dd, $^1J_{CF}$ 257, $^4J_{CF}$ 4.3, C-2), 153.6 (dd, $^1J_{CF}$ 245, $^4J_{CF}$ 3.8, C-5), 155.0 (s, C–O), 156.9 (s, C–O); δ_F −100.52 (1F, d, $^5J_{FF}$ 10.1, F-2), −140.4 (1F, d, $^5J_{FF}$ 10.1, F-5); m/z (EI$^+$) 528 ([M]$^+$, 18), 526 ([M]$^+$, 34), 524 ([M]$^+$, 16), 471 (42), 469 (88), 77 (100), 51 (41).

4.3. X-ray crystallography

Single crystal X-ray data for compounds **4**, **15a** and **15b** were collected on a Bruker SMART-CCD 6000 diffractometer equipped with Cryostream (Oxford Cryosystem) cooling device at 120.0 K using graphite monochromated Mo Kα radiation (λ = 0.71073 Å). All structures were solved by direct method and refined by full-matrix least squares on F^2 for all data using SHELXTL and Olex2 software. All non-hydrogen atoms were refined with anisotropic displacement parameters, H-atoms were located on the difference map and refined isotropically in the structures **15a** and **15b**, in structure **4** hydrogen atoms were put in calculated positions and refined in riding mode. Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 761666–761668.

4.3.1. Crystal data for 4

$C_{12}H_5OF_3Br_2$, M = 381.98, monoclinic, space group $P2_1/c$, a = 10.3435(2), b = 5.0841(1), c = 19.3488(4) Å, β = 93.27(1)°, U = 1159.71(4) Å^3, F(0 0 0) = 728, Z = 4, D_c = 2.188 mg m^{-3}, μ = 7.01 mm^{-1}. 15,689 reflections were collected yielding 3379 unique data (R_{merg} = 0.053). Final $wR_2(F^2) = 0.0656$ for all data (163 refined parameters), conventional $R(F)$ = 0.0273 for 2611 reflections with $I \geq 2\sigma$, GOF = 0.961.

4.3.2. Crystal data for 15a

$C_{15}H_{11}OF_3Br_2$, M = 424.06, triclinic, space group P-1, a = 5.2846(2), b = 11.6877(4), c = 12.1611(4) Å, α = 79.08(1), β = 81.76(1), γ = 83.89(1)°, U = 727.48(8) Å^3, F(0 0 0) = 412, Z = 2, D_c = 1.936 mg m^{-3}, μ = 5.60 mm^{-1}. 7940 reflections were collected yielding 4351 unique data (R_{merg} = 0.018). Final $wR_2(F^2) = 0.0669$ for all data (234 refined parameters), conventional $R(F)$ = 0.0238 for 3800 reflections with $I \geq 2\sigma$, GOF = 1.032.

4.3.3. Crystal data for 15b

$C_{24}H_{22}O_2F_2Br_2$, M = 540.24, monoclinic, space group $C2/c$, a = 24.6912(9), b = 5.7125(2), c = 18.2830(7) Å, β = 122.68(1)°, U = 2170.5(1) Å^3, F(0 0 0) = 1080, Z = 4, D_c = 1.653 mg m^{-3}, μ = 3.77 mm^{-1}. 11,797 reflections were collected yielding 3454 unique data (R_{merg} = 0.028). Final $wR_2(F^2) = 0.0608$ for all data (180 refined parameters), conventional $R(F)$ = 0.0251 for 2811 reflections with $I \geq 2\sigma$, GOF = 1.038.

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