HFO-1234yf as a CF3-building block: synthesis of trifluoromethyl-benzophenone derivatives by deoxygenative aromatisation

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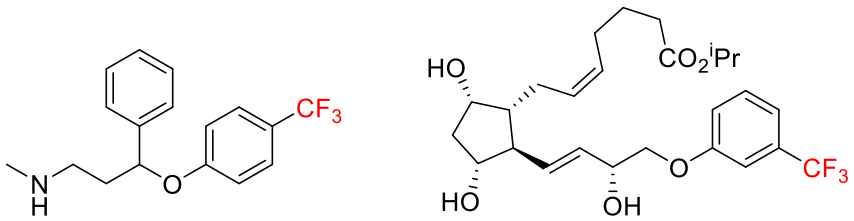
Abstract

Trifluoromethyl ynones derived from the 4th generation refrigerant 2,3,3,3-tetrafluoropropene (HFO-1234yf) undergo rapid Diels-Alder cycloaddition reactions with furans in near quantitative yields. Subsequent deoxygenation of the resulting oxabicyclic adducts leads to formation of *ortho*-trifluoromethylbenzophenones in generally good yields without the need for purification by column chromatography. Complete selectivity for a single regioisomer was observed in all cases. This method provides a new route from an inexpensive feedstock to highly substituted CF_3-aromatic systems that can be difficult to access selectively by established methods.

1. Introduction

Synthesis of organic fluorine-containing compounds, in particularly trifluoromethylated aryl derivatives, continues to be of significant interest due to some unique and valuable chemical and biological properties of these systems (Figure 1).[1] Consequently, there has been significant interest for many years in the synthesis of trifluoromethyl substituted aromatic rings using a wide range of novel processes, most recently including transition metal-catalysed C-H activation reactions and the use of photochemically generated radicals.[2] However, despite their elegance, many of these methods have yet to be applied more broadly on manufacturing scales due, in general, to the relative costs of the reagents and materials involved. The construction of aromatic rings bearing CF_3-groups on the manufacturing scale still usually relies on

the availability of trifluoromethyl-aromatic building blocks derived from the century old Swarts halogen exchange process involving transformation of CCl_3 to CF_3 using anhydrous hydrogen fluoride.[3]



fluoxetine
anti-depressant

travoprost
glaucoma medication

Figure 1. *Example drug molecules containing CF_3-substituted aromatic rings*

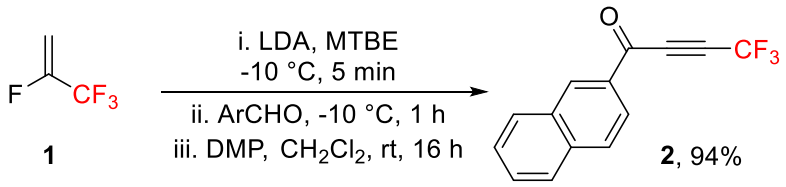
Therefore, new inexpensive, selective methods for the introduction of the CF_3 group onto aromatic rings remain highly desirable. For non-fluorinated systems, construction of the aryl ring from non-benzenoid precursors by various methods allows for the synthesis of highly substituted aryl systems with good regioselectivity, something that may not be possible using the classical approach of functionalising an already trifluoromethylated aromatic substrate.[4] However, whilst there have been several reports concerning cycloaddition reactions of more highly fluorinated systems for the synthesis of fluoroaromatic derivatives,[5] construction of an aryl ring bearing a single CF_3 group selectively using a cycloaddition approach remains relatively rare. Various transition metal-catalysed alkyne [2+2+2] trimerisation reactions using $PhC{\equiv}CF_3$ and $HC{\equiv}CF_3$ have been demonstrated but these only provide access to symmetrical 2,4,6-trisubstituted products.[6] Palladium-catalysed [4+2] cycloaddition of CF_3-enynes with diynes[7] and $TiCl_4$-catalysed [4+2] cycloadditions of CF_3-enones with electron-rich dienes[8] have also been reported, affording 1,3,4,5- and 1,2,3,4,5-substituted CF_3-aromatic derivatives respectively. More recently, an organocatalytic approach to construction of 1,2,3,4-substituted CF_3-benzene systems from trifluoromethyl alkenes and cinnamaldehydes through both [3+3] and [4+2] cycloaddition processes have been described.[9] Of these methods, only the $TiCl_4$-catalysed cycloaddition process described by Langer *et al.*[8] was able to synthesise *ortho*-CF_3 benzophenones but both the diene and dienophile require many steps to prepare.

Benzophenones are common motifs in natural products[10] and are found in various medications, such as ketoprofen,[11] fenofibrate,[12] and raloxifene,[13] as well as being widely used in sunscreens. The benzophenone moiety is also a useful synthetic

handle for further transformations and can be converted to functional groups such as alkenes, oximes, alcohols, cyanohydrins, amines, carbazones, acetals and pinacols. Therefore, CF_3-substituted benzophenones can be useful bioactive compounds in their own right or as precursors to other systems. Previously reported procedures for the synthesis of *ortho*-CF_3 benzophenones have relied on cross-coupling reactions of *ortho*-substituted trifluorotoluene derivatives,[14] Friedel-Crafts-type reactions involving super acid catalysis[15] or trifluoromethylation of *ortho*-aminobenzophenones.[16] However, these methods either lack selectivity for the *ortho* isomer or require directed lithiation procedures to control regioselectivity.

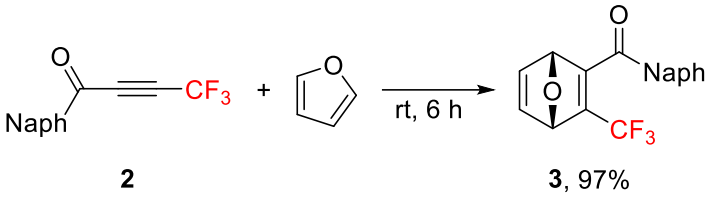
2. Results and discussion

We recently reported the use of trifluoromethyl ynone derivatives, synthesised from the inexpensive and readily available 4th generation refrigerant gas 2,3,3,3-tetrafluoropropene (HFO-1234yf, **1**), as building blocks for the preparation of a wide array of CF_3-substituted systems through reactions with nucleophiles.[17] In this work, we report the use of CF_3-ynones derived from **1** as precursors to polysubstituted CF_3-aryl systems by acting as dienophiles in Diels-Alder [4+2] cycloaddition reactions followed by deoxygenative ring opening of the resulting adduct. Naphthyl trifluoromethyl ynone **2** was chosen as the model starting material for exploring cycloaddition chemistry as it is a crystalline solid that can be prepared from **1** on a multigram scale in excellent yield after simple aqueous workup (Scheme 1).



Scheme 1. *Synthesis of trifluoromethyl ynone **2**; isolated yield given*

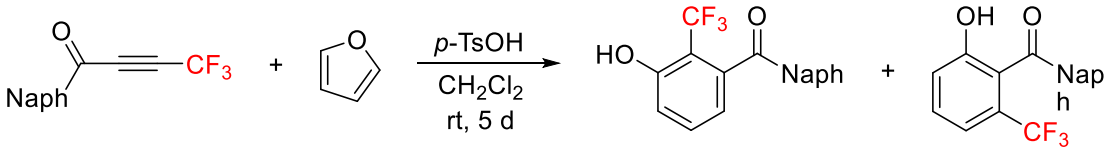
Until now, the cycloaddition reaction of cyclopentadiene with *n*-heptyl trifluoromethyl ynone reported by Hoye *et al.* is the only known example of a Diels-Alder process for ynone substrates of the type RCOC≡CCF_3.[18] Ynone **2** and furan underwent clean Diels-Alder cycloaddition reaction at ambient temperature to form adduct **3** in near quantitative yield (Scheme 2).



2 **3**, 97%

Scheme 2. *Diels-Alder reaction of ynone **2** with furan; isolated yield given*

We envisaged that ring opening of **3** would provide a new route to highly substituted CF_3-phenols. After five days, a mixture of CF_3-ynone **2** and furan in the presence of *p*-TsOH gave two products presumed to be the regioisomeric phenols **4a** and **4b** (Scheme 3), which were observed by NMR spectroscopy and mass spectrometry but could not be separated. The hydrogen atom closest to the more electron withdrawing CF_3 group was assumed to be the most labile and, therefore, **4a** would be the major product but this could not be confirmed unequivocally.



2 **4a**, 39% **4b**, 30%

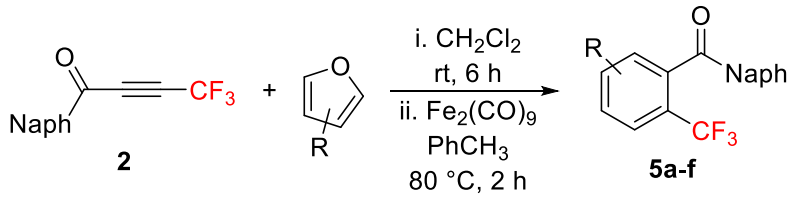
Scheme 3. *p-TsOH catalysed ring opening of Diels-Alder adduct **3**; conversion determined by ^{19}F NMR spectroscopy*

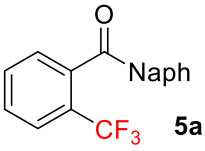
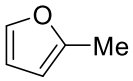
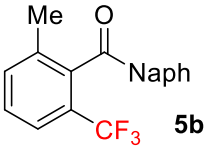
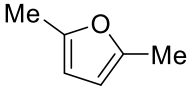
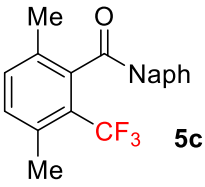
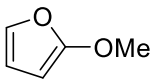
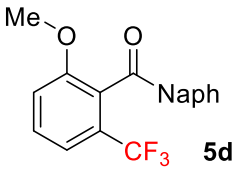
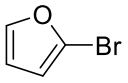
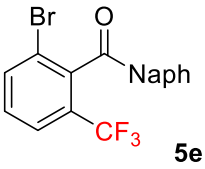
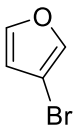
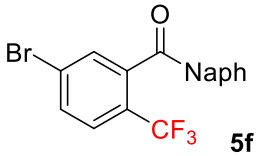
Various other acids and bases (Table 1) were then screened in attempt to develop and more selective and more rapid reaction. Conversion was determined by ^{19}F NMR spectroscopy after overnight reaction at room temperature in an NMR tube. Approximately 10 mg of **3** was used in each case with ~10 mol-% acid or base catalyst in ~0.7 mL CD_3CN. In almost all cases, the result was either a mixture of products that could not be readily separated or no observable reaction at all. A spectroscopically identical mixture was obtained on treating compound **3** with 1.0 M HCl in Et_2O in $CDCl_3$ as with 37% HCl in CD_3CN, demonstrating that the solvent acetonitrile plays a limited, if any, role in the reaction. The reaction of **3** and $BF_3{\cdot}OEt_2$ was also attempted in dry CH_2Cl_2 at 0 °C and was somewhat cleaner but still a complex mixture. The reactions of **3** with NaOH and CF_3CO_2H appeared the most selective and so conducted at higher temperatures in attempt to improve conversion but this led to apparent polymerisation.

Table 1. *Acid and base screening for ring opening of Diels-Alder adduct* ***3***

Acid	% Conversion from 3	Result
$BF_3{\cdot}OEt_2$	38	complex mixture
$FeCl_3$	6	complex mixture
$ZnBr_2$	25	complex mixture
HCl	100	4 products – 3:17:31:49
$AlCl_3$	94	4 products – 6:8:22:58
$TiCl_4$	100	4 products – 3:15:43:38
p-TsOH	0	no reaction
CuOTf	0	no reaction
$La(OTf)_3$	0	no reaction
CF_3CO_2H	5	single product
NaOH	8	single product
Cs_2CO_3	3	single product
KO^tBu	2	single product
K_3PO_4	<1	single product
KF	0	no reaction
DBU	50	complex mixture
DABCO	0	no reaction
Quinuclidine	0	no reaction
BTMG	50	complex mixture

The only conditions we could find for selective ring-opening of adduct **3** was using $Fe_2(CO)_9$ to give a moderate yield of CF_3-benzophenone **5a** via a deoxygenative ring opening,[19] an approach that has been demonstrated in a single example using structurally similar CF_3-ynoates ($CF_3C{\equiv}CO_2Et$) in the total synthesis of a CF_3-analog of natural product salvinorin A.[20] Attempts to use catalytic amounts of metal, such as NH_4ReO_4,[21] were unsuccessful in all cases owing to side reactions of the highly electrophilic CF_3-ynone **2** and so stoichiometric $Fe_2(CO)_9$ was required. Our methodology for the synthesis of CF_3-benzophenone derivatives was expanded to a small range of other commercially available furan substrates with various substitution patterns (Scheme 4). We found the reaction time could be reduced from overnight to just two hours with the product isolated simply by filtration through a short plug of neutral alumina to remove the remaining iron complexes, removing the need for resource-intensive purification procedures such as column chromatography.



furan	product	% isolated yield
	 **5a**	42%
	 **5b**	69%
	 **5c**	61%
	 **5d**	74%
	 **5e**	89%
	 **5f**	78%

Scheme 4. *Substrate scope for deoxygenative aromatisation reactions;* [a]*isolated yield*

Less electron-rich dienes, such as ethyl 2-furoate or 3-furoate and a variety of oxazoles, proved unreactive towards cycloaddition, even at elevated temperatures. However, brominated furans were well tolerated (**5e** and **5f**), providing a potentially useful functional intermediate for further synthetic transformations. In contrast to reports of reactions between 2-methoxyfuran and hexafluorobutyne which led directly to an aromatic derivative,[22] 2-methoxyfuran did not give an intermediate that rapidly

ring opened following cycloaddition with **2** but instead required deoxygenative aromatisation to give **5d** as for all other substrates. In all cases, the products were obtained as oily solids. Whilst compounds **5a**-**f** may be expected to be crystalline due to their high molecular weight and π-stacking interactions, the presence of an *ortho*-CF_3 group may diminish these interactions and prevent crystallisation.

Complete regioselectivity was observed in each case for the isomers shown, with the structure determined by ^{1}H-^{1}H NOE spectroscopy. For example, in **5b** there was a correlation between the hydrogen atoms of the methyl group and those on the naphthyl ring. This indicates spatial proximity between these hydrogen atoms and, therefore, that the sole regioisomer formed is that shown in Figure 2 as the other possible isomer would not give rise to this correlation.

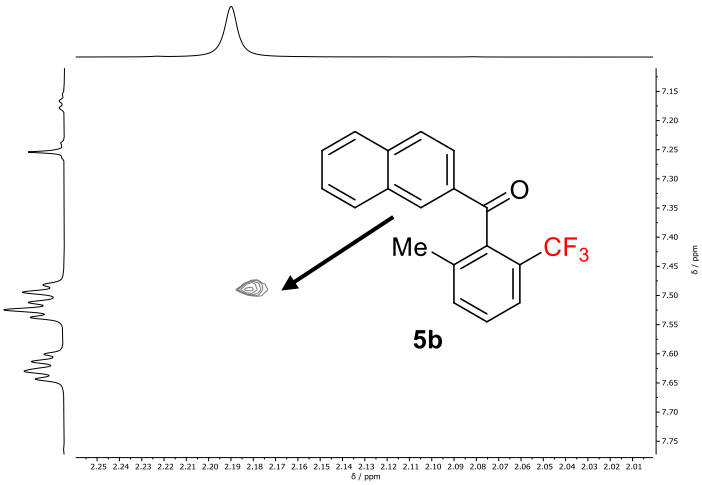


Figure 2. *^{1}H-^{1}H NOESY for **5b** used to determine regioselectivity*

3. Conclusions

In conclusion, we have demonstrated that polysubstituted *ortho*-CF_3 benzophenones can be synthesised in good yields with complete regioselectivity from trifluoromethyl ynones, which can in turn be readily derived from the inexpensive refrigerant gas HFO-1234yf. Quantitative conversion of the initial regioselective Diels-Alder reaction was followed by an efficient iron-mediated deoxygenation process which tolerated various useful functional groups. By altering the substituent of the RCOC≡CCF_3 dienophile or the substituents on the furan diene, various degrees of complexity could be introduced to the system with complete regioselectivity for a single product. Whilst the use of a stoichiometric transition metal complex may preclude its use on a manufacturing scale,

this methodology presents a useful route to access highly substituted *ortho*-CF_3 benzophenones on the laboratory scale and their derivatives more easily for use in, for example, medicinal chemistry discovery programmes.

4. Experimental

4.1. General Information

2,3,3,3-Tetrafluoropropene, (HFO-1234yf, **1**), was purchased from Apollo Scientific in 100 g cylinders. 1-(2'-Naphthyl)-4,4,4-trifluorobut-2-yn-1-one (**2**) was prepared from 2,3,3,3,-tetrafluoropropene (**1**) and 2-naphthaldehyde via the method we have previously described.[17] All other chemicals were purchased from Acros Organics, Fisher Scientific, Fluorochem or Sigma Aldrich and were used without any further purification. 'Alumina' refers to activated, neutral, Brockmann I aluminium oxide purchased from SigmaAldrich. Glassware was oven-dried prior to use but no other precautions were taken to exclude air or moisture unless otherwise stated. Thin layer chromatography was carried out using Macherey-Nagel™ standard SIL G silica layers (5-17 μm with fluorescence indicator UV_{254}, compounds visualised under UV light) on Polygram™ polyester sheets purchased from Fisher Scientific.

Hydrogen, carbon and fluorine nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 400 Ultrashield (^{1}H NMR at 400 MHz; ^{13}C NMR at 101 MHz; ^{19}F NMR at 376 MHz) spectrometer with residual solvent peaks as the internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.2 ppm) or relative to an external standard (^{19}F NMR, $CFCl_3$ at 0.00 ppm). NMR spectroscopic data are reported as follows: chemical shift (ppm), integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant(s) (Hz), assignment. NMR assignments were made using COSY, DEPT-135, HSQC and HMBC experiments where appropriate and spectra were analysed using MestReNova software.

Low resolution LC-MS data was recorded on a Waters Ltd TQD mass spectrometer equipped with Acquity UPLC BEH C18 1.7 μm column (2.1 mm x 50 mm). Gas chromatography mass spectra (GC-MS) data were recorded on a Shimadzu QP2010-Ultra equipped with a Rxi-17Sil MS column (0.15 μm x 10 m x 0.15 mm) under electron ionisation (EI) conditions at 70 eV using a helium carrier gas. Accurate mass analysis

was achieved with a Waters Ltd QtoF Premier mass spectrometer equipped with an accurate solids analysis probe (ASAP) or a Waters Ltd LCT Premier XE mass spectrometer equipped with Acquity UPLC and ASAP.

4.2. Isolation of ynone-furan cycloadduct

Compound 3: Compound **2** (0.557 g, 2.24 mmol) and furan (10 mL) were stirred at room temperature for 6 hours then concentrated *in vacuo* to give (3-trifluoromethyl-7-*oxa*-norborna-2,5-dien-2-yl)-(2'-naphthyl) ketone, **3** (0.688 g, 97%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 5.67 (1H, q, $^4J_{HF}$ 1.1, C(4)H), 5.82 (1H, t, $^3J_{HH}$ 1.8, C(7)H), 7.26 (1H, m, C(5)H), 7.45 (1H, dd, $^3J_{HH}$ 5.3, $^3J_{HH}$ 1.8, C(6)H), 7.62 (2H, m, C(3'/4')H), 7.95 (4H, m, (C6'-9')H), 8.36 (1H, s, C(1')H). δ_F (376 MHz; $CDCl_3$) −62.48 (d, $^4J_{HF}$ 1.1). δ_C (101 MHz; $CDCl_3$) 84.0 (q, $^3J_{CF}$ 2.2, C4), 86.9 (s, C7), 122.1 (q, $^1J_{CF}$ 268.9, CF_3), 127.3 (s, Ar), 128.1 (s, Ar), 129.1 (s, Ar), 129.5 (s, Ar), 130.0 (s, Ar), 132.5 (s, Ar), 132.6 (s, Ar), 133.4 (s, Ar), 136.4 (s, Ar), 142.1 (s, Ar), 143.8 (s, Ar), 145.6 (q, $^2J_{CF}$ 36.5, C3), 156.5 (q, $^3J_{CF}$ 4.8, C2), 191.5 (s, C1). HRMS (ESI+) *m/z* calc. for $C_{18}H_{11}O_2F_3$ $[M+H]^+$ 317.0789; found 317.0781.

4.3. Deoxygenative ring opening

General procedure: Compound **2** (1 eq.) and the diene (1 eq.) were dissolved in CH_2Cl_2 and stirred at room temperature for 6 hours. The resulting solution was then concentrated *in vacuo* then the residue dissolved in toluene. Diironnonacarbonyl (2 eq.) was added and heated to 80 °C for 2 hours before being allowed to cool to room temperature. The reaction mixture was filtered through a plug of alumina, which was washed with toluene and the combined washings concentrated *in vacuo* to give the benzophenone product without further purification unless otherwise specified.

Compound 5a: Compound **3** (0.459 g, 1.45 mmol) and diiron nonacarbonyl (1.509 g, 4.15 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-phenyl]-methanone, **5a** (0.187 g, 43%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 7.47 (1H, m), 7.53 (1H, m), 7.62 (1H, m), 7.67 (2H, m), 7.88 (4H, m), 8.03 (1H, m), 8.11 (1H, m). δ_F (376 MHz; $CDCl_3$) −57.94 (s). δ_C (101 MHz; $CDCl_3$) 123.8 (d, $^1J_{CF}$ 274.0), 124.8 (s, Ar), 126.9 (q, $^3J_{CF}$ 4.6), 127.1 (s, Ar), 128.0 (s, Ar), 128.4 (s, Ar), 128.5 (d, $^2J_{CF}$ 32.3), 128.7 (s, Ar), 129.2 (s, Ar),

129.9 (s, Ar), 130.0 (s, Ar), 131.6 (s, Ar), 132.4 (s, Ar), 133.4 (s, Ar), 134.0 (s, Ar), 136.1 (s, Ar), 138.6 (s, Ar), 195.7 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $[M+H]^+$ $C_{18}H_{11}F_3O$ 301.0840; found 301.0831.

Compound 5b: Compound **2** (0.086 g, 0.35 mmol), 2-methylfuran (0.0031 mL, 0.35 mmol) and diiron nonacarbonyl (0.247 g, 0.679 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-6-(methyl)-phenyl]-methanone, **5b** (0.075 g, 69%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 2.19 (3H, s, Me), 7.53 (3H, m, ArH), 7.63 (2H, m, ArH), 7.90 (3H, m, ArH), 7.99 (1H, m, ArH), 8.11 (1H, s, C(3')H). δ_F (376 MHz; $CDCl_3$) −57.64 (s). δ_C (101 MHz; $CDCl_3$) 19.6 (s, Me), 124.0 (q, $^1J_{CF}$ 274.3, CF_3), 124.1 (d, $^3J_{CF}$ 4.8, C1/3), 124.2 (s, Ar), 127.0 (s, Ar), 128.0 (q, $^2J_{CF}$ 31.6, C2), 128.0 (s, Ar), 129.0 (s, Ar), 129.1 (s, Ar), 129.2 (s, Ar), 129.3 (s, Ar), 130.0 (s, Ar), 132.4 (s, Ar), 132.6 (s, Ar), 134.1 (s, Ar), 134.3 (s, Ar), 136.2 (d, $^3J_{CF}$ 3.2, C1/3), 138.0 (q, $^4J_{CF}$ 2.1, C4-6), 196.9 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $C_{19}H_{13}OF_3$ $[M+H]^+$ 315.0997; found 315.0994.

Compound 5c: Compound **2** (0.033 g, 0.14 mmol), 2,5-dimethylfuran (0.015 mL, 0.14 mmol) and diiron nonacarbonyl (0.098 g, 2.7 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-3,6-(dimethyl)-phenyl]-methanone, **5c** (0.027 g, 61%), as a yellow solid, m.p. °C. δ_H (400 MHz; $CDCl_3$) 2.12 (3H, s, Me), 2.56 (3H, s, Me), 7.34 (2H, m, Ar), 7.57 (2H, m, Ar), 7.95 (5H, m, Ar). δ_F (376 MHz; $CDCl_3$) −54.63 (s). δ_C (101 MHz; $CDCl_3$) 19.3 (s, Me), 20.1 (s, Me), 123.3 (q, $^2J_{CF}$ 31.9, C2), 124.1 (s, Ar), 126.2 (q, $^1J_{CF}$ 274.1, CF_3) 127.0 (s, Ar), 128.0 (s, Ar), 129.0 (s, Ar), 129.9 (s, Ar), 131.9 (s, Ar), 132.7 (s, Ar), 132.7 (s, Ar), 133.1 (s, Ar), 133.7 (s, Ar), 134.4 (s, Ar), 135.4 (s, Ar), 135.4 (s, Ar), 136.1 (s, Ar), 138.4 (s, Ar), 197.4 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $C_{20}H_{15}OF_3$ $[M+H]^+$ 329.1153; found 329.1159.

Compound 5d: Compound **2** (0.073 g, 0.294 mmol), 2-methoxyfuran (0.027 mL, 0.294 mmol) and diiron nonacarbonyl (0.239 g, 0.657 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-6-methoxyphenyl]-methanone, **5d** (0.072 g, 74%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 3.72 (3H, s, OMe), 7.20 (1H, m, C(2'-5')H), 7.39 (1H, m, C(2'-5')H), 7.52 (1H, m, C(2'-5')H), 7.59 (2H, m, C(3'/4')H), 7.89 (3H, m, C(6'-9')H), 7.99 (1H, m, C(6'-9')H), 8.16 (1H, m, C(1')H). δ_F (376 MHz; $CDCl_3$) −58.05 (s). δ_C (101 MHz; $CDCl_3$) 56.3 (s, OMe), 114.7 (s, Ar), 118.4 (q, $^3J_{CF}$ 4.7, C1), 123.6 (q, $^1J_{CF}$ 274.4, CF_3), 124.4 (s, Ar), 126.8 (s, Ar), 127.9 (s, Ar), 128.0 (s, Ar), 128.6 (s, Ar), 128.8 (s, Ar), 129.3 (q, $^2J_{CF}$ 32.2, C2), 129.9 (s, Ar), 130.8 (s, Ar), 132.1 (s, Ar), 132.6 (s, Ar), 134.6 (s, Ar),

136.1 (s, Ar), 157.3 (s, C6), 194.5 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $C_{19}H_{13}F_3O_2$ $[M+H]^+$ 331.0946; found 331.0943.

Compound 5e: Compound **2** (0.076 g, 0.031 mmol), 2-bromofuran (0.045 mL, 0.031 mmol) and diiron nonacarbonyl (0.220 g, 0.062 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-phenyl]-methanone, **5e** (0.104 g, 89%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 7.23 (1H, m, Ar), 7.37 (1H, m, Ar), 7.64 (3H, m, Ar), 7.94 (2H, m, Ar), 8.02 (2H, m, Ar), 8.37 (1H, m, Ar). δ_F (376 MHz; $CDCl_3$) −63.41 (s). δ_C (101 MHz; $CDCl_3$) 119.3 (q, $^3J_{CF}$ 4.7, C1), 121.1 (s, Ar), 123.8 (q, $^1J_{CF}$ 274.4, CF_3), 124.4 (s, Ar), 125.8 (s, Ar), 127.1 (s, Ar), 128.1 (s, Ar), 128.3 (q, $^2J_{CF}$ 32.4, C2), 129.1 (s, Ar), 129.3 (s, Ar), 130.1 (s, Ar), 130.7 (s, Ar), 131.3 (s, Ar), 132.7 (s, Ar), 136.3 (s, Ar), 136.8 (s, Ar), 172.3 (s, C6), 193.4 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $C_{18}H_{10}BrF_3O$ $[M+H]^+$ 378.9945; found 378.9954.

Compound 5f: Compound **2** (0.171 g, 0.689 mmol), 3-bromofuran (0.061 mL, 0.69 mmol) and diiron nonacarbonyl (0.664 g, 0.183 mmol) gave naphthalen-2-yl-[2-(trifluoromethyl)-5-bromophenyl]-methanone, **5f** (0.204 g, 78%), as a yellow oil. δ_H (400 MHz; $CDCl_3$) 7.53 (2H, m, Ar), 7.63 (1H m, Ar), 7.79 (1H, m, Ar), 7.92 (5H, m, Ar), 8.12 (1H, m, Ar). δ_F (376 MHz; $CDCl_3$) −58.07 (s). δ_C (101 MHz; $CDCl_3$) 119.3 (q, $^3J_{CF}$ 4.6, C1), 121.0 (s, Ar), 123.7 (q, $^1J_{CF}$ 274.2, CF_3), 124.4 (s, Ar), 125.7 (s, Ar), 127.1 (s, Ar), 128.1 (s, Ar), 128.3 (q, $^2J_{CF}$ 32.3, C2), 129.0 (s, Ar), 129.3 (s, Ar), 130.0 (s, Ar), 130.7 (s, Ar), 131.2 (s, Ar), 132.6 (s, Ar), 136.3 (s, Ar), 136.7 (s, Ar), 172.2 (s, C5), 193.3 (s, C=O). HRMS (ESI+) *m*/*z* calc. for $C_{18}H_{10}BrF_3O$ $[M+H]^+$ 378.9945; found 378.9960.

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References and Notes

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