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Synthesis of dihydrofurans containing trifluoromethyl ketone and heterocycles by radical cyclization of fluorinated 1,3-dicarbonyl compounds with 2-thienyl and 2-furyl substituted alkenes

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ABSTRACT

Manganese(III) acetate based radical cyclization of various fluorinated 1,3-dicarbonyl compounds with 2-thienyl and 2-furyl substituted alkenes produced 3-trifluoroacetyl and 2-trifluoromethyl-dihydrofurans in good yields. The radical cyclizations of 2-methyl-5-[(*E*)-2-phenylvinyl]furan **2b** and 2-[(*E*)-2-phenylvinyl]thiophene **2c** led to the formations of 5-(5-methyl-2-furyl)-4,5-dihydrofuran and 5-(2-thienyl)-4,5-dihydrofuran, respectively. In the reactions of 1,3-dicarbonyls with alkenes, 2-thienyl substituted alkenes formed 4,5-dihydrofurans in higher yields than 2-furyl substituted alkenes.

1. Introduction

Fluorinated organic compounds are very important due to their unique chemical and biological properties. Thus, these compounds have received considerable attention in the medicinal and agricultural chemistry.[1] Many trifluoromethyl ketones have been found to be enzyme inhibitor,[2] antimicrobial activity,[3] and some trifluoromethyl ketones have been demonstrated as cytotoxic agents against human tumor cell.[4]

Dihydrofurans are a significant class of compounds since they show a wide range of biological activities and form the basic structure of many natural compounds.[5] Our research group has been studying the synthesis of dihydrofuran derivatives by the radical cyclization of various 1,3-dicarbonyl compounds and 3-oxopropanenitriles with alkenes, alkynes, unsaturated amides, and dienes.[6] One possible approach for the synthesis of trifluoromethyl ketone containing dihydrofurans would be the cyclization of a suitable fluorinated 1,3-dicarbonyl compound with an unsaturated system mediated by transition metal salts (Mn^{+3}, Ce^{+4}, Ag^{+} etc.). Among these metal salts, manganese(III) acetate,[7] and cerium(IV) ammonium nitrate[7h,8] are widely used as radical oxidants in organic synthesis for the construction of carbon–carbon bonds.

Recently, we have prepared 2,3-dihydro-4*H*-furo[3,2-*c*]chromen-4-ones and 2,3-dihydronaphtho[2,3-*b*]furan-4,9-diones by the radical cyclization of 4-hydroxycoumarin and 2-hydroxy-1,4-naphtoquinone, respectively.[6e] Moreover, we described the synthesis of 3-trifluoroacetyl-4,5-dihydrofurans and 3-[dihydrofurans-2(3*H*)-ylidene]-1,1,1-trifluoroacetones by the treatments of trifluoromethyl-1,3-dicarbonyl compounds with alkenes.[6i] In this paper, it is reported that radical cyclization of several available tri, and hepta fluorinated 1,3-dicarbonyl compounds **1a–f** with 2-thienyl and 2-furyl substituted alkenes **2a–h** using manganese(III) acetate to afford trifluoromethyl ketone containing dihydrofurans and 2-trifluoromethyl-dihydrofurans.

2. Results and discussions

The mechanism proposed for the formation of dihydrofurans is explained in Scheme 1. According to this mechanism, the interaction of enol form **A** of the 1,3-dicarbonyl **1a–f** with manganese(III) acetate produces Mn(III)–enolate complex **B**. While an electron from alkene is added to Mn(III)–enolate complex **B**, Mn^{3+} is reduced to Mn^{2+} and a radical carbon intermediate product **C** is formed via pathway *i*. The structure **C** is oxidized to carbocation **D** with $Mn(OAc)_3$. Cyclization of the carbocation **D** afford 3-trifluoroacetyl-dihydrofuran **E**. Similarly, dihydrofuran **G** can be produced through the cyclization of intermediate carbocation **F** formed by the addition of an electron from alkene to the complex **B**

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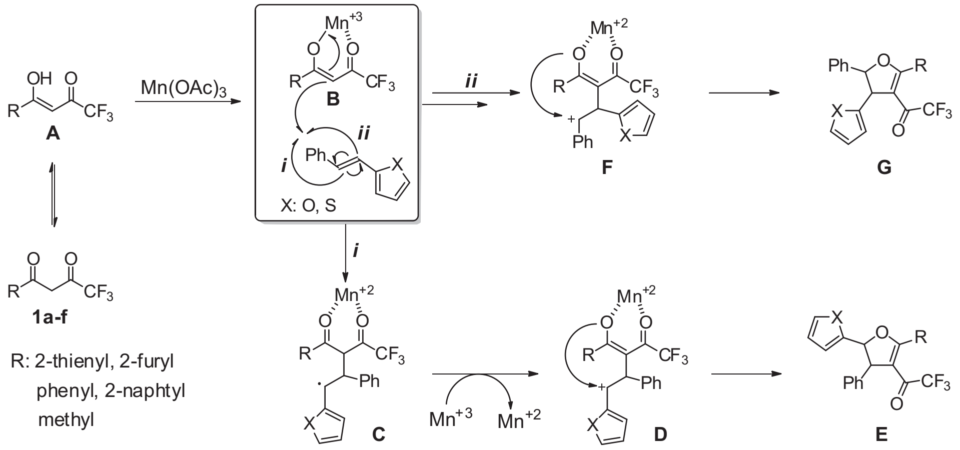


Scheme 1. Mechanism for the formation of dihydrofurans.

by pathway *ii*. Compounds **G** and **E** were differentiated by using HSQC and HMBC spectra. The H5 protons on each of these compounds are observed at lower field than that of H4 protons in the ^{1}H NMR spectra because the H5 protons are adjacent to the ether oxygen, thus the carbon atoms attached to these protons were easily determined by HSQC. Moreover, the HMBC spectra show the C4 carbon correlates with the *ortho*-protons of the phenyl group, thus the Ph group must be attached to the C4 carbon. According to these results, the isolated compound is **E**, produced by the cyclization of carbocation **D** formed by the pathway *i*.

As seen in Table 1, whilst the reactions of 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione **1a** with 2-[(*E*)-2-Phenylvinyl]furan **2a** yielded no product, the reaction of **1a** with 2-methyl-5-[(*E*)-2-phenylvinyl]furan **2b** and 2-[(*E*)-2-phenylvinyl]thiophene **2c** yielded 3-trifluoroacetyl-dihydrofurans **3a** and **3b** in low yields, respectively. Compounds **3a** (dr=88:12) and **3b** (dr=85:15) were isolated as diastereomeric mixtures and the ratio was determined by ^{1}H NMR.

On the other hand, treatment of **1a** and **1b** with 2-isopropenylthiophene (**2d**) gave the corresponding dihydrofuran containing trifluoromethyl ketone in good yields. The radical cyclization of 4,4,4-trifluoro-1-phenylbutane-1,3-dione **1c** and 4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione **1d** with **2d** afforded 3-trifluoroacetyl-dihydrofurans **3e** and **3f** as well as 2-trifluoromethyl-dihydrofurans **4a** and **4b**, formation of these compounds are explained in the Scheme 2.

The radical intermediate **H** formed by the addition of an electron from **2d** to Mn(III)–enolate complex is oxidized to carbocation **I**. While the cyclization of this intermediate gives 3-trifluoroacetyl-4,5-dihydrofurans **K** (**3e**, **3f**), **J** the other enol form of **I** produces 2-trifluoromethyl-4,5-dihydrofurans **L** (**4a**, **4b**). Compounds **K** and **L** were differentiated by the chemical shifts of carbonyl groups and carbons C-2 in ^{13}C NMR spectra. Whereas the carbonyl carbon of compound **K** gives quartet ($^2J_{C-F}=34.5$ Hz) at 175 ppm in ^{13}C NMR, the carbonyl carbon of compound **L** gives singlet at 190 ppm. On the other hand, while C-2 of **K** gives singlet at 172 ppm, C-2 carbon of **L** gives quartet ($^2J_{C-F}=34.4$ Hz) at 150 ppm.

When the radical cyclizations of 2-(1-phenylvinyl)furan (**2e**) and 2-(1-phenylvinyl)thiophene (**2f**) with 1,3-dicarbonyls are compared, it was observed that the reactions of **2f** formed corresponding products in much more higher yields than those of **2e** (Table 2). We previously reported the reaction of **1a** with 1,1-diphenyl ethylene in 78% yield.[6i] We obtained 3-trifluoroacetyl-dihydrofuran in 87% yield from the reaction of **1a** with **2f**. This result demonstrated that the alkene containing thienyl group has higher activity in these radical cyclizations in comparison with the alkenes containing furyl and phenyl group. Additionally, the radical cyclizations of **2f** with the other fluorinated 1,3-dicarbonyl compounds gave dihydrofurans in very good yields. Similarly, while the reactions of 2-[1-(4-methylphenyl)vinyl]thiophene **2g** produced dihydrofurans **3o**–**q** in good yields, the best results were obtained from the reactions of 2-[1-(4-fluorophenyl)vinyl]thiophene (**2h**) with 1,3-dicarbonyls (Table 3).

In conclusion, the radical cyclizations of various fluorinated 1,3-dicarbonyl compounds with 2-thienyl and 2-furyl substituted alkenes mediated by Mn(OAc)$_3$ were performed in this study comparatively. When the radical cyclizations of thienyl and furyl substituted alkenes are compared, thienyl substituted alkenes formed trifluoromethyl ketone containing dihydrofurans in by far higher yields than those of furyl substituted alkenes. This can be explained by that the thienyl group make carbocation intermediate more stable than furyl groups since % aromaticity of thiophene is more than furan.

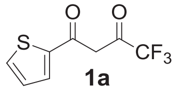
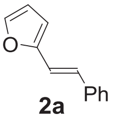
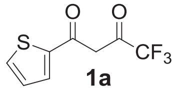
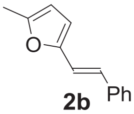
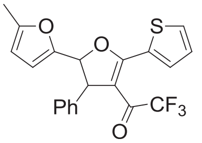
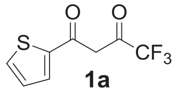
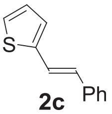
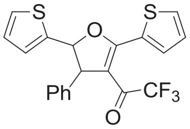
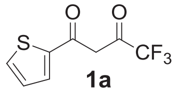
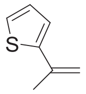
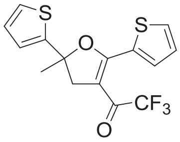
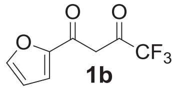
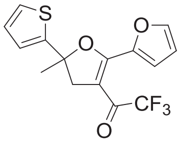
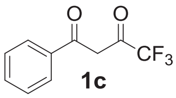
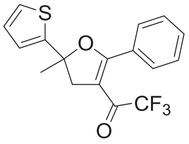
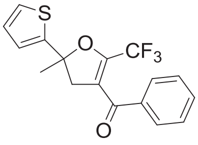
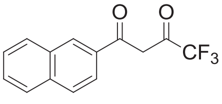
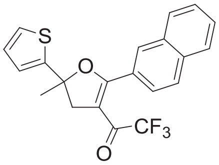
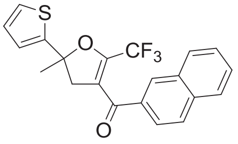
This study shows that radical cyclizations of 1,3-dicarbonyl compounds with alkenes follow mostly the dominant enol form of 1,3-dicarbonyl and in some cases follow both enol forms depending on the structure of 1,3-dicarbonyl. Moreover, this study exhibits heteroaromatic groups on alkene have a significant role in the radical cyclizations. The cyclizations of 1,2-disubstituted alkenes (**2b**, **2c**) occur only on C-1 carbon of the alkenes leading to formations of tetrasubstitued-4,5-dihydrofurans. This study introduces that fluorinated 1,3-dicarbonyl compounds can be used effectively for synthesis of dihydrofurans containing trifluoromethyl and trifluoromethyl ketone in this radical cyclization.

3. Experimental

3.1. General

Fluorinated 1,3-dicarbonyls **1a**–**f** are available commercial products and used in highest purity. 2-[(*E*)-2-Phenylvinyl]furan **2a**,[9] 2-methyl-5-[(*E*)-2-phenylvinyl]furan **2b**,[10] and 2-[(*E*)-2-phenylvinyl]thiophene **2c**[11] were prepared by the reaction of triphenylphosphoniumbenzyl bromide and suitable aldehyde in NaH/THF. 2-Isopropenylthiophene **2d** was prepared by the reaction of triphenylphosphoniummethyl bromide and 2-acetylthiophene in NaH/THF.[12] The other conjugated alkenes **2e**–**h** were prepared by dehydration from the carbinole formed Grignard reaction of arylmagnesium bromide and suitable carbonyl compounds.[13] All conjugated alkenes were freshly prepared before used in the radical

Table 1
Radical cyclization of fluorinated 1,3-dicarbonyl compounds with **2a**–**d**

Entry	1,3-Dicarbonyl	Alkene	Dihydrofuran	Yield[a] (%)
1	 **1a**	 **2a**	No product	
2	 **1a**	 **2b**		**3a**, 12 dr=88:12
3	 **1a**	 **2c**		**3b**, 17 dr=85:15
4	 **1a**	 **2d**		**3c**, 88
5	 **1b**	**2d**		**3d**, 85
6	 **1c**	**2d**	 **3e** (73%)	 **4a** (15%)
7	 **1d**	**2d**	 **3f** (61%)	 **4b** (11%)

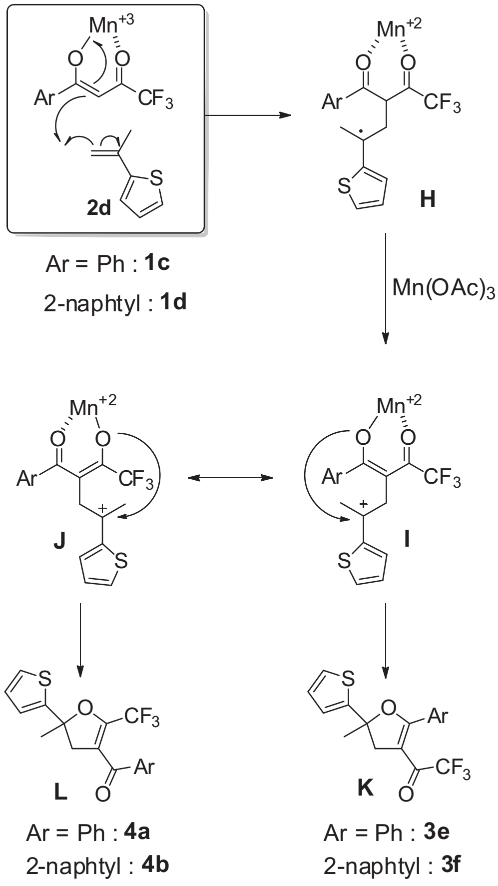
[a] Yield of isolated product based on the alkene.

cyclizations. Radical reactions were performed at 1.2:1:2.5 molar ratio (**1**:**2**:Mn(OAc)$_3$) under nitrogen atmosphere in AcOH. All compounds purified by column chromatography or preparative TLC were characterized by IR, ^{1}H, ^{13}C, ^{19}F NMR, mass spectra and microanalysis.

Melting points were determined on an electrothermal capillary melting point apparatus. IR spectra (KBr disc, CHCl$_3$) were obtained with a Matson 1000 FT-IR in the 400–4000 cm^{-1} range with 4 cm^{-1} resolution. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 MHz and Varian Mercury-400 High performance Digital FT-NMR spectrophotometers. The mass spectra were measured on a Waters 2695 Alliance Micromass ZQ (ESI$^+$) LC/MS spectrophotometer. Elemental analyses were performed on a Leco 932 CHNS-O instrument. Thin layer chromatography (TLC) was performed on Merck aluminum-packed silica gel plates. Purification of the products was performed by column chromatography on silica gel (Merck silica gel 60, 40–63 μm) or preparative TLC on silica gel of Merck (PF$_{254-366\text{nm}}$).

3.2. Synthesis of 2-isopropenylthiophene (2d)[12]

To a solution of methyltriphenylphosphonium bromide (7.50 g, 21 mmol) in anhydrous THF in a three-necked flask fitted with reflux condenser, thermometer, and magnetic stirrer, NaH (0.88 g, 22 mmol, in 60% mineral oil) was added. This mixture was heated at 60 °C for 1 h 2-Acetylthiophene (2.52 g, 20 mmol) was added to this mixture by dropwise, with stirring and cooling in ice, the reaction temperature was maintained between 5 and 10 °C. The temperature was then rapidly taken to reflux for 2 h, and standing overnight at room temperature. After this time, precipitated NaBr was removed by filtering through a funnel with porosity 4. The filtrate was evaporated in vacuum and the residue was extracted with hexane (5×30 mL). The organic phase was dried with Na$_2$SO$_4$ and evaporated. The crude product was purified by column chromatography using hexane as eluent. Yield 63% (1.56 g) as colorless flammable liquid bp 210–212 °C, (lit. bp 60–61 °C, 15 Torr).[12a] δ_H (400 MHz, CDCl$_3$) 7.14 (1H, d, J=5.2 Hz), 7.01 (1H, d, J=3.6 Hz), 6.95



Scheme 2. Mechanism for the formation of **4a** and **4b**.

(1H, dd, J=5.2, 3.6 Hz), 5.37 (1H, s, CH═), 4.96 (1H, s, CH═), 2.14 (3H, s, Me).

3.3. General procedure for 1,1-disubstituted alkenes (2e–h)

To a solution of arylmagnesium bromide obtained from the Grignard reaction of suitable aryl bromide (60 mmol) and magnesium (1.73 g, 72 mmol) in 30 mL dried ether, the ketone was added (50 mmol) by dropwise with cooling and stirring in ice-salt bath. Then the reaction mixture was heated at reflux for 2 h. After this time, the reaction mixture was hydrolyzed with 10% NH_4Cl on ice-salt bath, this mixture standing overnight and extracted with three 50 mL portion of ether. The combined organic phases were neutralized with satd $NaHCO_3$ and dried. Without purification, the crude product in THF was dehydrated with 15% HCl. Upon completion, 20 mL of water was added to the mixture and it was extracted with chloroform (3×50 mL). The combined organic phases were neutralized with satd $NaHCO_3$, dried, and evaporated. The crude product was purified by column chromatography using *n*-hexane as eluent.

*3.3.1. Synthesis of 2-(1-phenylvinyl)furan (**2e**)*[13a]. Yield 75% (6.40 g) as colorless oil (lit. 105–107 °C, 2 Torr).[13a] δ_H (400 MHz, $CDCl_3$) 7.59 (1H, dd, J=7.6, 1.2 Hz), 7.42 (2H, m), 7.36 (3H, m), 6.38 (1H, dd, J=3.6, 2.0 Hz), 6.19 (1H, d, J=3.2 Hz), 5.74 (1H, d, J=1.2 Hz), 5.22 (1H, d, J=1.2 Hz).

*3.3.2. Synthesis of 2-(1-phenylvinyl)thiophene (**2f**)*[13b–e]. Yield 88% (8.20 g) as colorless oil. δ_H (400 MHz, $CDCl_3$) 7.46–7.41 (2H, m), 7.38–7.32 (3H, m), 7.23 (1H, dd, J=4.8, 1.2 Hz), 6.98 (1H, dd, J=4.8, 3.2 Hz), 6.91 (1H, J=3.6, 2.0 Hz), 5.58 (1H, s, H-olefin), 5.24 (1H, s, H-olefin); δ_C (100 MHz, $CDCl_3$) 144.7, 143.3, 141.0, 128.3, 128.2, 128.0, 127.2, 126.5, 125.0, 113.6; δ_C (100 MHz, $CDCl_3$) 154.3, 142.6, 139.8, 139.5, 129.0, 128.5, 128.4, 128.2, 112.3, 111.5, 109.4.

*3.3.3. Synthesis of 2-[1-(4-methylphenyl)vinyl]thiophene (**2g**).* Yield 81% (810 mg) as a white solid mp 114–116 °C. Found: C, 78.18; H, 6.22 $C_{13}H_{12}S$ requires C, 77.95; H, 6.04%; ν_{max} (KBr disc) 3024, 1595 (C═C), 1575, 1020, 783, 748, 692; δ_H (400 MHz, $CDCl_3$) 7.33 (2H, d, J=6.9 Hz), 7.22–7.15 (3H, m), 6.94 (2H, m), 5.54 (1H, s, H-olefin), 5.22 (1H, s, H-olefin), 2.38 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 144.9, 143.2, 138.1, 137.8, 128.8, 128.2, 127.2, 126.3, 124.9, 113.0, 21.2 (Me); LC/MS, *m*/*z* (ESI^+) 201 (MH^+, 100%).

*3.3.4. Synthesis of 2-[1-(4-fluorophenyl)vinyl]thiophene (**2h**).* Yield 77% (785 mg) as colorless oil. Found: C, 70.38; H, 4.32; S, 15.54 $C_{12}H_9FS$ requires C, 70.56; H, 4.44; S, 15.70%; ν_{max} (KBr disc) 3022, 1600, 1500, 1492, 1112, 800, 839, 723; δ_H (400 MHz, $CDCl_3$) 7.40 (2H, dd, J=10.0, 7.6 Hz), 7.23 (1H, dt, J=6.8, 1.2 Hz), 7.03 (2H, m), 6.97 (1H, dd, J=4.8, 1.2 Hz), 6.87 (1H, d, J=4.8 Hz), 5.55 (1H, s), 5.19 (1H, s); δ_C (100 MHz, $CDCl_3$) 164.3, 161.0 (d, $^1J_{C-F}$=294.3 Hz), 144.59, 142.3, 137.0 (d, $^4J_{C-F}$=3.1 Hz), 130.0 (d, $^3J_{C-F}$=9.6 Hz), 127.3, 126.4, 125.2, 114.9 (d, $^2J_{C-F}$=25.9 Hz), 113.6; δ_F (376 MHz, $CDCl_3$) −110 (1F, s); LC/MS, *m*/*z* (ESI^+) 205 (MH^+, 100%).

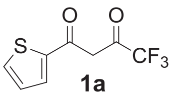
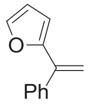
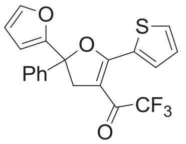
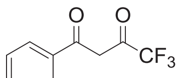
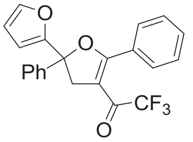
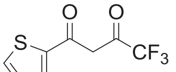
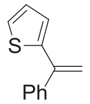
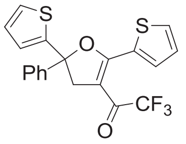
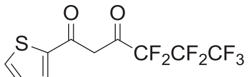
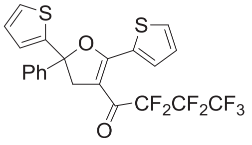
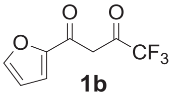
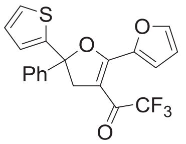
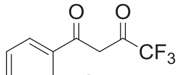
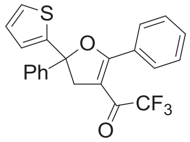
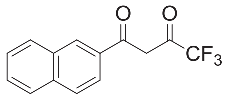
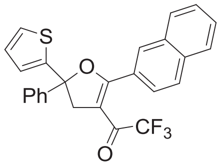
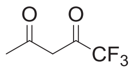
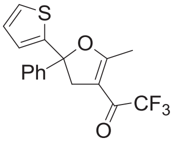
3.4. General procedure for dihydrofurans

A solution of manganese(III) acetate dihydrate (2.5 mmol, 0.67 g) in 10 mL of glacial acetic acid was heated under a nitrogen atmosphere at 80 °C until it dissolved. After $Mn(OAc)_3$ dissolved completely, the solution was cooled down to 60 °C. A solution of trifluoromethyl-1,3-dicarbonyl compound (1.25 mmol) and alkene (1 mmol) in 5 mL of acetic acid was added to this mixture and the temperature was raised to 80–100 °C. The reaction was complete when the dark brown color of the solution disappeared. The acetic acid was evaporated under reduced pressure. 30 mL of water was added to the residue and extraction was performed with $CHCl_3$ (3×20 mL). The combined organic extracts were neutralized with 10 mL of satd $NaHCO_3$ solution, and dried over anhydrous Na_2SO_4 and evaporated. The crude products were purified by column chromatography or preparative TLC (20×20 cm plates, 2 mm thickness) using *n*-hexane/EtOAc (5:1) as eluent.

*3.4.1. 2,2,2-Trifluoro-1-[5′-methyl-3-phenyl-5-(thiophen-2-yl)-2,3-dihydro-2,2′-bifuran-4-yl]ethanone (**3a**).* Yield 12% (48 mg) as yellow oil. Found: C, 62.08; H, 3.43; S, 8.15 $C_{21}H_{15}F_3O_3S$ requires C, 62.37; H, 3.74; S, 7.93%; R_f (20% EtOAc/hexane) 0.46; ν_{max} (KBr disc) 2922, 2853, 1641 (C═O), 1596 (C═C), 1533, 1199 (CF_3), 752, 700; δ_H (300 MHz, $CDCl_3$) 8.43 (1H, dd, J=3.9, 1.2 Hz), 7.65 (1H, dd, J=5.1, 1.2 Hz), 7.29–7.12 (6H, m), 6.28 (1H, d, J=3.3 Hz), 5.90 (1H, dq, J=3.0, 0.9 Hz), 5.38 (1H, d, J=4.2 Hz, H2), 4.85 (1H, dd, J=4.2, $^5J_{H-F}$=1.2 Hz, H3), 2.24 (3H, s, Me); δ_C (75 MHz, $CDCl_3$) 174.2 (q, $^2J_{C-F}$=34.5 Hz, C═O), 166.1 (C5), 152.9, 148.2, 141.2, 134.6, 133.0, 129.5, 127.9, 126.7 (2CH═), 126.6 (2CH═), 125.9, 115.8 (q, $^1J_{C-F}$=290.0 Hz, CF_3), 109.4, 105.5 (C4), 84.7 (C2), 50.7 (q, $^4J_{C-F}$=2.8 Hz, C3), 28.1, 12.7 (Me); δ_F (282 MHz, $CDCl_3$) −84.05 (s, $-CF_3$); LC/MS, *m*/*z* (ESI^+) 405 (MH^+, 100%).

*3.4.2. 2,2,2-Trifluoro-1-[4-phenyl-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3b**).* Yield 17% (69 mg) as a yellow solid mp 58–60 °C. Found: C, 58.95; H, 3.12; S, 15.95 $C_{20}H_{13}F_3O_2S_2$ requires C, 59.10; H, 3.22; S, 15.78%; R_f (20% EtOAc/hexane) 0.43; ν_{max} (KBr disc) 3046, 2951, 1671 (C═O), 1537 (C═C), 1136 (C–O–C), 729, 700; δ_H (400 MHz, $CDCl_3$) 7.36–7.34 (3H, m), 7.25–7.22 (4H, m), 7.15 (1H, dt, J=3.2, 1.2 Hz), 7.03 (1H, dd, J=5.2, 3.6 Hz), 5.77 (1H, d, J=3.6 Hz, H5), 4.84 (1H, dd, J=3.2, $^5J_{H-F}$=1.6 Hz, H4); δ_C (100 MHz, $CDCl_3$) 175.4 (q, $^2J_{C-F}$=35.1 Hz, C═O), 169.1 (C2), 142.0,

Table 2
Radical cyclization of fluorinated 1,3-dicarbonyl compounds with **2e** and **2f**

Entry	1,3-Dicarbonyl	Alkene	Dihydrofuran	Yield[a] (%)
1	 **1a**	 **2e**		**3g**, 36
2	 **1c**	**2e**		**3h**, 33
3	 **1a**	 **2f**		**3i**, 87
4	 **1e**	**2f**		**3j**, 90
5	 **1b**	**2f**		**3k**, 79
6	 **1c**	**2f**		**3l**, 85
7	 **1d**	**2f**		**3m**, 74
8	 **1f**	**2f**		**3n**, 77

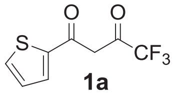
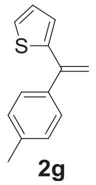
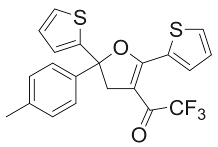
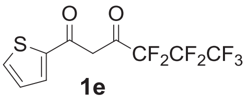
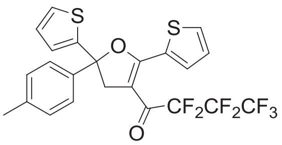
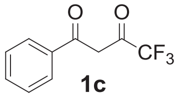
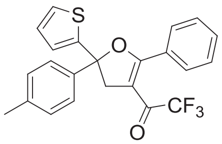
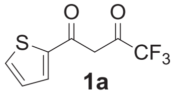
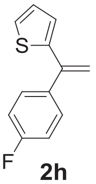
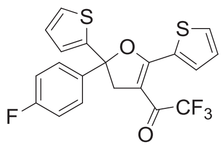
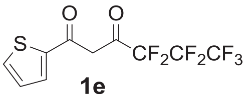
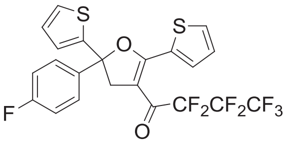
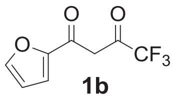
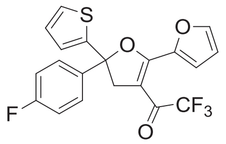
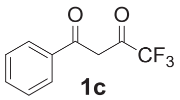
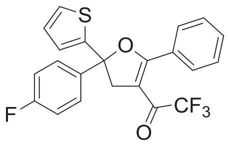
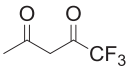
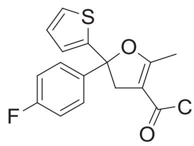
[a] Yield of isolated product based on the alkene.

137.1, 135.8, 134.3, 129.1, 128.3, 128.1, 127.9, 127.8, 126.9 (2CH=), 126.4 (2CH=), 125.8, 117.3 (q, $^1J_{C-F}$=289.6 Hz, CF_3), 107.3 (C3), 88.3 (C5), 55.8 (C4); δ_F (376 MHz, $CDCl_3$) −76.4 (s, CF_3); LC/MS, *m/z* (ESI^+) 407 (MH^+, 100%).

*3.4.3. 2,2,2-Trifluoro-1-[5-methyl-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3c**).* Yield 88% (303 mg) as a light yellow solid mp 75–77 °C. Found: C, 52.02; H, 3.34; S, 18.84 $C_{15}H_{11}F_3O_2S_2$ requires C, 52.32; H, 3.22; S, 18.62%; R_f (20% EtOAc/hexane) 0.50; ν_{max} (KBr disc) 3061, 1670 (C=O), 1538 (C=C), 1136 (C–O–C), 729, 700; δ_H (300 MHz, $CDCl_3$) 8.39 (1H, dd, *J*=3.9, 1.2 Hz), 7.50 (1H, dd, *J*=5.1, 1.2 Hz), 7.10 (1H, dd, *J*=5.1, 1.2 Hz), 7.02 (1H, dd, *J*=5.1, 3.9 Hz), 6.95 (1H, dd, *J*=3.6, 1.2 Hz), 6.83 (1H, dd, *J*=5.1, 3.6 Hz), 3.55 (1H, dd, *J*=15.0, $^5J_{H-F}$=0.9 Hz, Hb-4), 3.34 (1H, dd, *J*=15.0, $^5J_{H-F}$=0.9 Hz, Ha-4), 1.81 (3H, s, Me); δ_C (75 MHz, $CDCl_3$) 174.5 (q, $^2J_{C-F}$=34.6 Hz, C=O), 165.4 (C2), 147.9, 135.6, 134.1, 131.1, 128.1, 127.2, 125.6, 124.0, 117.3 (q, $^1J_{C-F}$=289.6 Hz, CF_3), 103.1 (C3), 88.6 (C5), 44.1 (d, $^4J_{C-F}$=3.3 Hz, C4), 28.8 (Me); δ_F (282 MHz, $CDCl_3$) −76.4 (s, CF_3); LC/MS, *m/z* (ESI^+) 345 (MH^+, 100%).

*3.4.4. 2,2,2-Trifluoro-1-[5-methyl-5-(thiophen-2-yl)-4,5-dihydro-2,2′-bifuran-3-yl]ethanone (**3d**).* Yield 85% (279 mg) as a pale yellow solid mp 88–90 °C. Found: C, 54.96; H, 3.25; S, 9.60 $C_{15}H_{11}F_3O_3S$ requires C, 54.88; H, 3.38; S, 9.77%; R_f (20% EtOAc/

Table 3
Radical cyclization of fluorinated 1,3-dicarbonyl compounds with **2g** and **2h**

Entry	1,3-Dicarbonyl	Alkene	Dihydrofuran	Yield[a] (%)
1	 **1a**	 **2g**		**3o**, 81
2	 **1e**	**2g**		**3p**, 83
3	 **1c**	**2g**		**3q**, 80
4	 **1a**	 **2h**		**3r**, 89
5	 **1e**	**2h**		**3s**, 92
6	 **1b**	**2h**		**3t**, 75
7	 **1c**	**2h**		**3u**, 88
8	 **1f**	**2h**		**3v**, 70

[a] Yield of isolated product based on the alkene.

hexane) 0.45; ν_{max} (KBr disc) 1671 (C═O), 1539 (C═C), 1207 (CF$_3$), 1136 (C–O–C); δ_H (300 MHz, CDCl$_3$) 8.32 (1H, d, J=3.6 Hz), 7.56 (1H, d, J=1.2 Hz), 7.20 (1H, dd, J=5.1, 1.2 Hz), 7.04 (1H, dd, J=3.6, 1.2 Hz), 6.90 (1H, dd, J=5.1, 3.6 Hz), 6.53 (1H, dd, J=3.6, 1.5 Hz), 3.60 (1H, dd, J=14.7, $^5J_{H-F}$=0.6 Hz, Hb-4), 3.37 (1H, dd, J=15.0, $^5J_{H-F}$=0.6 Hz, Ha-4), 1.91 (3H, s, Me); δ_C (75 MHz, CDCl$_3$) 172.4 (q, $^2J_{C-F}$=34.0 Hz, C═O), 159.3 (C2), 146.2, 145.7, 143.0, 125.9, 124.6, 123.1, 121.4, 116.1 (q, $^1J_{C-F}$=289.2 Hz, CF$_3$), 111.7, 102.1 (C3), 87.9 (C5), 42.5 (d, $^4J_{C-F}$=3.3 Hz, C4), 27.5 (Me); δ_F (282 MHz, CDCl$_3$) −84.0 (s, CF$_3$); LC/MS, m/z (ESI$^+$) 329 (MH$^+$, 100%).

*3.4.5. 2,2,2-Trifluoro-1-[5-methyl-2-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3e**).* Yield 73% (247 mg) as yellow oil. Found: C, 60.52; H, 3.56; S, 9.66 $C_{17}H_{13}F_3O_2S$ requires C, 60.35; H, 3.87; S, 9.48%; R_f (20% EtOAc/hexane) 0.55; ν_{max} (KBr disc) 3061, 2965, 2870, 1666 (C═O), 1531 (C═C), 1199 (CF$_3$), 1140 (C–O–C), 731, 700; δ_H (300 MHz, $CDCl_3$) 7.91 (1H, dd, J=6.9, 1.5 Hz), 7.60 (1H, tt, J=7.5, 1.5 Hz), 7.49 (2H, t, J=7.5 Hz), 7.35 (1H, tt, J=5.1, 1.2 Hz), 7.17 (1H, dd, J=3.9, 1.5 Hz), 7.06 (1H, dd, J=5.1, 3.6 Hz), 3.74 (1H, dd, J=14.7, $^5J_{H-F}$=0.9 Hz, Hb-4), 3.51 (1H, dd, J=14.7, $^5J_{H-F}$=0.9 Hz, Ha-4), 2.03 (3H, s, Me); δ_C (75 MHz, $CDCl_3$) 175.6 (q, $^2J_{C-F}$=34.6 Hz, C=O), 172.2 (C2), 147.9, 132.3, 129.9, 129.1, 128.2, 127.2 (2CH=), 125.7 (2CH=), 124.0, 117.2 (q, $^1J_{C-F}$=290.7 Hz, CF_3), 104.6 (C3), 88.8 (C5), 44.3 (d, $^4J_{C-F}$=3.3 Hz, C4), 28.8 (Me); δ_F (282 MHz, $CDCl_3$) −74.2 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 339 (MH^+, 100%).

*3.4.6. 2,2,2-Trifluoro-1-[5-methyl-2-(naphthalen-2-yl)-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3f**).* Yield 61% (237 mg) as yellow oil. Found: C, 65.17; H, 3.80; S, 8.43 $C_{21}H_{15}F_3O_2S$ requires C, 64.94; H, 3.89; S, 8.26%; R_f (20% EtOAc/hexane) 0.50; ν_{max} (KBr disc) 3065, 2967, 2930, 1660 (C=O), 1585 (C=C), 1548, 1197 (CF_3), 1141 (C–O–C), 756, 696; δ_H (300 MHz, $CDCl_3$) 8.38 (1H, s), 7.85–7.71 (4H, m), 7.45 (2H, m), 7.22 (1H, dd, J=5.1, 1.2 Hz), 7.05 (1H, dd, J=3.6, 1.2 Hz), 6.92 (1H, dd, J=4.8, 0.6 Hz), 3.63 (1H, dd, J=14.7, $^5J_{H-F}$=0.9 Hz, Hb-4), 3.42 (1H, dd, J=14.7, $^5J_{H-F}$=0.9 Hz, Ha-4), 1.92 (3H, s, Me); δ_C (75 MHz, $CDCl_3$) 174.5 (q, $^2J_{C-F}$=34.5 Hz, C=O), 172.1 (C2), 147.8, 135.0, 132.3, 131.1, 129.3, 128.2, 127.8, 127.6, 127.0, 126.7, 126.2, 125.6, 125.5, 123.9, 117.0 (q, $^1J_{C-F}$=289.7 Hz, CF_3), 104.7 (C3), 88.6 (C5), 44.3 (q, $^4J_{C-F}$=3.3 Hz, C4), 28.8 (Me); δ_F (282 MHz, $CDCl_3$) −73.7 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 389 (MH^+, 100%).

*3.4.7. 2,2,2-Trifluoro-1-[2-phenyl-5-(thiophen-2-yl)-2,3-dihydro-2,2′-bifuran-4-yl]ethanone (**3g**).* Yield 36% (140 mg) as yellow oil. Found: C, 61.75; H, 3.05; S, 8.42 $C_{20}H_{13}F_3O_3S$ requires C, 61.53; H, 3.36; S, 8.21%; R_f (20% EtOAc/hexane) 0.45; ν_{max} (KBr disc) 2870, 1666 (C=O), 1531 (C=C), 1199 (CF_3), 1140 (C–O–C), 731, 700; δ_H (400 MHz, $CDCl_3$) 8.61 (1H, dd, J=2.4, 1.2 Hz), 7.74 (1H, dd, J=4.0, 1.2 Hz), 7.52–7.40 (6H, m), 7.25 (1H, m), 6.36 (1H, dd, J=3.2, 1.6 Hz), 6.21 (1H, dd, J=5.6, 2.0 Hz), 4.24 (1H, d, J=14.8 Hz, Hb-3), 3.74 (1H, d, J=14.8 Hz, Ha-3); δ_C (100 MHz, $CDCl_3$) 174.5 (q, $^2J_{C-F}$=34.3 Hz, C=O), 164.9 (C5), 153.9, 143.8, 142.0, 141.4, 135.3, 133.8, 128.6, 128.5 (2CH=), 127.9 (2CH=), 125.3, 117.2 (q, $^1J_{C-F}$=289.6 Hz, CF_3), 110.4, 109.9, 103.0 (C4), 88.5 (C2), 41.5 (q, $^4J_{C-F}$=3.0 Hz, C3); δ_F (376 MHz, $CDCl_3$) −74.4 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 391 (MH^+, 100%).

*3.4.8. 1-(2,5-Diphenyl-2,3-dihydro-2,2′-bifuran-4-yl)-2,2,2-trifluoroethanone (**3h**).* Yield 33% (127 mg) as yellow oil. Found: C, 68.51; H, 4.12 $C_{22}H_{15}F_3O_3$ requires C, 68.75; H, 3.93%; R_f (20% EtOAc/hexane) 0.46; ν_{max} (KBr disc) 3030, 2932, 1670 (C=O), 1533 (C=C), 1145 (C–O–C), 756, 700; δ_H (300 MHz, $CDCl_3$) 7.80 (2H, dd, J=7.5, 1.5 Hz), 7.36 (9H, m), 6.25 (1H, dd, J=3.3, 1.2 Hz), 6.08 (1H, dd, J=3.3, 0.9 Hz), 4.09 (1H, d, J=15.0 Hz, Hb-3), 3.62 (1H, d, J=15.0 Hz, Ha-3); δ_C (75 MHz, $CDCl_3$) 175.8 (q, $^2J_{C-F}$=34.4 Hz, C=O), 172.1 (C5), 154.4, 144.1, 141.8, 132.4, 130.0, 129.0, 128.9 (2CH=), 128.8 (2CH=), 128.3 (2CH=), 125.7 (2CH=), 117.2 (q, $^1J_{C-F}$=290.2 Hz, CF_3), 110.7, 110.2, 105.0 (C4), 89.0 (C2), 41.9 (q, $^4J_{C-F}$=3.3 Hz, C3); δ_F (282 MHz, $CDCl_3$) −74.5 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 385 (MH^+, 100%).

*3.4.9. 2,2,2-Trifluoro-1-[5-phenyl-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3i**).* Yield 87% (353 mg) as a pale yellow needle crystal mp 87–89 °C. Found: C, 59.27; H, 3.34; S, 15.54 $C_{20}H_{13}F_3O_2S_2$ requires C, 59.10; H, 3.22; S, 15.78%; R_f (20% EtOAc/hexane) 0.46; ν_{max} (KBr disc) 3028, 1685 (C=O), 1583 (C=C), 1556, 1213 (CF_3), 1138 (C–O–C), 756, 696; δ_H (400 MHz, $CDCl_3$) 8.67 (1H, dd, J=4.0, 0.7 Hz), 7.75 (1H, d, J=5.8 Hz), 7.58 (2H, dd, J=8.6, 1.1 Hz), 7.47–7.40 (3H, m), 7.35 (1H, dd, J=4.9, 0.8 Hz), 7.26 (1H, t, J=4.4 Hz), 7.06 (1H, d, J=3.3 Hz), 7.00 (1H, dd, J=4.8, 3.8 Hz), 4.21 (1H, d, J=14.8 Hz, Hb-4), 4.00 (1H, d, J=14.8 Hz, Ha-4); δ_C (100 MHz, $CDCl_3$) 174.1 (q, $^2J_{C-F}$=36.3 Hz, C=O), 164.8 (C2), 147.4, 143.2, 135.5, 134.1, 130.8, 128.7, 128.5, 128.0, 126.8, 126.6, 126.2 (2CH=), 125.3, 117.2 (q, $^1J_{C-F}$=290.0 Hz, CF_3), 103.2 (C3), 91.2 (C5), 44.6 (q, $^4J_{C-F}$=3.1 Hz, C4); δ_F (376 MHz, $CDCl_3$) −76.4 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 407 (MH^+, 100%).

*3.4.10. 2,2,3,3,4,4,4-Heptafluoro-1-[5-phenyl-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]butan-1-one (**3j**).* Yield 90% (455 mg) as a pale yellow solid mp 79–81 °C. Found: C, 52.49; H, 2.27; S, 12.86 $C_{22}H_{13}F_7O_2S_2$ requires C, 52.17; H, 2.59; S, 12.66%; R_f (20% EtOAc/hexane) 0.47; ν_{max} (KBr disc) 3046, 1672 (C=O), 1537, 1215, 729, 700; δ_H (400 MHz, $CDCl_3$) 8.56 (1H, d, J=4.0 Hz), 7.66 (1H, d, J=5.2 Hz), 7.49 (2H, d, J=7.6 Hz), 7.38 (2H, t, J=7.2 Hz), 7.26 (1H, dt, J=5.2, 1.2 Hz), 7.18 (1H, t, J=4.4 Hz), 6.98 (1H, dt, J=3.6, 1.2 Hz), 6.92 (1H, tt, J=4.4, 1.2 Hz), 4.17 (1H, d, J=15.2 Hz, Hb-4), 3.94 (1H, d, J=15.2 Hz, Ha-4); δ_C (100 MHz, $CDCl_3$) 176.9 (t, $^2J_{C-F}$=25.1 Hz, C=O), 165.7 (C2), 147.5, 143.3, 135.9, 134.4, 131.0, 128.9, 128.6, 128.2, 127.0, 126.8, 126.4 (2CH=), 125.5, 118.0 (qt, $^1J_{C-F}$=286.5, $^2J_{C-F}$=33.5 Hz, $-CF_2CF_2\mathit{CF}_3$), 110.5 (tt, $^1J_{C-F}$=266.7, $^2J_{C-F}$=31.2 Hz, $-CF_2CF_2CF_3$), 109.2 (tqt, $^1J_{C-F}$=264.4, $^2J_{C-F}$=38.1, $^2J_{C-F}$=31.2 Hz, $-CF_2\mathit{CF}_2CF_3$), 105.1 (C3), 91.4 (t, $^5J_{C-F}$=2.3 Hz, C5), 44.8 (t, $^4J_{C-F}$=6.9 Hz, C4); δ_F (376 MHz, $CDCl_3$) −126.4 (2F, s, $-\mathit{CF}_2CF_2CF_3$), −118.0 (2F, dq, J_{F-F}=53.0, 9.0 Hz, $-CF_2\mathit{CF}_2CF_3$), −80.6 (3F, t, $^3J_{F-F}$=9.0 Hz, $-CF_2CF_2\mathit{CF}_3$); LC/MS, *m*/*z* (ESI^+) 507 (MH^+, 100%).

*3.4.11. 2,2,2-Trifluoro-1-[5-phenyl-5-(thiophen-2-yl)-4,5-dihydro-2,2′-bifuran-3-yl]ethanone (**3k**).* Yield 65% (254 mg) as yellow oil. Found: C, 61.64; H, 3.54; S, 8.04 $C_{20}H_{13}F_3O_3S$ requires C, 61.53; H, 3.36; S, 8.21%; R_f (20% EtOAc/hexane) 0.43; ν_{max} (KBr disc) 3028, 2922, 1685 (C=O), 1585, 1556 (C=C), 1209 (CF_3), 1136 (C–O–C), 758, 692; δ_H (400 MHz, $CDCl_3$) 8.43 (1H, d, J=3.6 Hz), 7.71 (1H, t, J=0.8 Hz), 7.56 (2H, dd, J=8.0, 1.6 Hz), 7.45–7.38 (4H, m), 7.33 (1H, dd, J=4.8, 1.2 Hz), 7.01 (1H, dd, J=4.0, 1.6 Hz), 6.97 (1H, t, J=3.6 Hz), 6.64 (1H, dd, J=3.6, 1.6 Hz), 4.17 (1H, d, J=15.2 Hz, Hb-4), 3.95 (1H, d, J=15.2 Hz, Ha-4); δ_C (100 MHz, $CDCl_3$) 174.3 (q, $^2J_{C-F}$=34.6 Hz, C=O), 160.3 (C2), 147.3, 147.1, 144.3, 143.2, 128.8, 128.7, 127.0, 126.9, 126.8 (2CH=), 125.6, 122.9, 117.4 (q, $^1J_{C-F}$=288.8 Hz, CF_3), 113.2, 103.6 (C3), 91.9 (C5), 44.5 (d, $^4J_{C-F}$=3.0 Hz, C4); δ_F (376 MHz, $CDCl_3$) −76.2 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 391 (MH^+, 100%).

*3.4.12. 1-[2,5-Diphenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]-2,2,2-trifluoroethanone (**3l**).* Yield 85% (340 mg) as a colorless cubic crystal mp 103–105 °C. Found: C, 66.13; H, 3.58; S, 8.21 $C_{22}H_{15}F_3O_2S$ requires C, 65.99; H, 3.78; S, 8.01%; R_f (20% EtOAc/hexane) 0.48; ν_{max} (KBr disc) 3059, 2963, 2870, 1681 (C=O), 1583 (C=C), 1550, 1490, 1448, 1269, 1205 (CF_3), 1140 (C–O–C), 883, 760, 696; δ_H (400 MHz, $CDCl_3$) 7.97 (2H, dd, J=8.5, 1.2 Hz), 7.59 (2H, d, J=7.4 Hz), 7.51–7.408 (6H, m), 7.37 (1H, dd, J=4.9, 0.9 Hz), 7.06 (1H, dd, J=3.6, 1.0 Hz), 7.03 (1H, t, J=4.8 Hz), 4.20 (1H, d, J=14.8 Hz, Hb-4), 4.00 (1H, d, J=14.8 Hz, Ha-4); δ_C (100 MHz, $CDCl_3$) 175.3 (q, $^2J_{C-F}$=34.6 Hz, C=O), 171.6 (C2), 147.7, 143.3, 132.2, 129.8, 128.8 (2CH=), 128.7, 128.4, 128.1, 126.8 (2CH=), 126.6 (2CH=), 126.1 (2CH=), 125.4, 116.8 (q, $^1J_{C-F}$=291.4 Hz, CF_3), 104.9 (C3), 91.4 (C5), 44.8 (d, $^4J_{C-F}$=3.5 Hz, C4); δ_F (376 MHz, $CDCl_3$) −76.4 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 401 (MH^+, 100%).

*3.4.13. 2,2,2-Trifluoro-1-[2-(naphthalen-2-yl)-5-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3m**).* Yield 74% (333 mg) as yellow oil. Found: C, 69.02; H, 3.58; S, 7.01 $C_{26}H_{17}F_3O_2S$ requires C, 69.32; H, 3.80; S, 7.12%; R_f (20% EtOAc/hexane) 0.48; ν_{max} (KBr disc) 3055, 2930, 2861, 1681 (C=O), 1589 (C=C), 1544, 1448, 1276, 1199 (CF_3), 1143 (C–O–C), 758, 694; δ_H (400 MHz, $CDCl_3$) 8.53 (1H, s), 7.91–7.80 (4H, m), 7.54–7.49 (4H, m), 7.38 (2H, t, J=7.6 Hz), 7.33 (1H, d, J=7.6 Hz), 7.28 (1H, d, J=5.2 Hz), 6.98 (1H, d, J=3.6 Hz), 6.94 (1H, t, J=4.0 Hz), 4.15 (1H, d, J=14.8 Hz, Hb-4), 3.95 (1H, d, J=14.8 Hz, Ha-4); δ_C (100 MHz, $CDCl_3$) 175.3 (q, $^2J_{C-F}$=34.3 Hz, C=O), 171.9 (C2), 147.9, 143.6, 135.4, 132.5, 131.5 (2CH=), 129.5 (2CH=), 128.9, 128.7, 128.5, 128.0, 127.9, 127.0, 126.9, 126.8, 126.3 (2CH=), 125.9, 125.7, 117.2 (q,

$^{1}J_{\mathrm{C-F}}$=290.3 Hz, CF_3), 105.0 (C3), 91.7 (C5), 45.2 (C4); δ_{F} (376 MHz, $CDCl_3$) −74.0 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 451 (MH^+, 100%).

*3.4.14. 2,2,2-Trifluoro-1-[2-methyl-5-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3n**).* Yield 77% (260 mg) as yellow oil. Found: C, 60.15; H, 4.02; S, 9.29 $C_{17}H_{13}F_3O_2S$ requires C, 60.35; H, 3.87; S, 9.48%; R_f (20% EtOAc/hexane) 0.52; $\nu_{\max}$ (KBr disc) 3062, 1685 (C=O), 1583, 1556 (C=C), 1213 (CF_3), 1137 (C–O–C), 875, 755, 696; δ_{H} (400 MHz, $CDCl_3$) 7.47–7.37 (5H, m), 7.31 (1H, dd, *J*=4.8, 1.2 Hz), 6.96 (2H, m), 3.95 (1H, d, *J*=14.4 Hz, Hb-4), 3.71 (1H, d, *J*=14.4 Hz, Ha-4), 2.49 (3H, s, Me); δ_{C} (100 MHz, $CDCl_3$) 176.2 (q, $^{2}J_{\mathrm{C-F}}$=35.0 Hz, C=O), 175.7 (C2), 147.7, 143.4, 128.6, 128.4, 126.7, 126.5, 126.0 (2CH=), 125.2, 116.7 (q, $^{1}J_{\mathrm{C-F}}$=288.8 Hz, CF_3), 105.5 (C3), 92.2 (C5), 43.7 (C4), 15.9 (Me); δ_{F} (376 MHz, $CDCl_3$) −74.8 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 339 (MH^+, 100%).

*3.4.15. 2,2,2-Trifluoro-1-[5-(4-methylphenyl)-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3o**).* Yield 81% (340 mg) as yellow solid mp 90–92 °C. Found: C, 60.22; H, 3.95; S, 15.29 $C_{21}H_{15}F_3O_2S_2$ requires C, 59.99; H, 3.60; S, 15.25%; R_f (20% EtOAc/hexane) 0.46; $\nu_{\max}$ (KBr disc) 3028, 2924, 1687 (C=O), 1581 (C=C), 1323, 1201 (CF_3), 1134 (C–O–C), 906, 816, 691; δ_{H} (400 MHz, $CDCl_3$) 8.58 (1H, dd, *J*=4.4, 1.2 Hz), 7.67 (1H, dd, *J*=5.2, 1.2 Hz), 7.39 (2H, d, *J*=8.4 Hz), 7.27 (1H, dd, *J*=4.8, 1.6 Hz), 7.19 (1H, d, *J*=0.8 Hz), 7.20 (2H, d, *J*=8.4 Hz), 6.98 (1H, dd, *J*=3.2, 1.2 Hz), 6.93 (1H, dd, *J*=4.8, 3.6 Hz), 4.10 (1H, d, *J*=15.2 Hz, Hb-4), 3.90 (1H, d, *J*=15.2 Hz, Ha-4), 2.35 (3H, s, Me); δ_{C} (100 MHz, $CDCl_3$) 174.4 (q, $^{2}J_{\mathrm{C-F}}$=34.3 Hz, C=O), 165.1 (C2), 147.8, 140.5, 138.6, 135.7, 134.2, 131.1, 129.5, 128.2, 126.9, 126.7, 126.3 (2CH=), 125.5, 117.5 (q, $^{1}J_{\mathrm{C-F}}$=289.5 Hz, CF_3), 103.4 (C3), 91.4 (C5), 44.8 (d, $^{4}J_{\mathrm{C-F}}$=3.1 Hz C4), 21.4 (Me); δ_{F} (376 MHz, $CDCl_3$) −77.5 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 421 (MH^+, 100%).

*3.4.16. 2,2,3,3,4,4,4-Heptafluoro-1-[5-(4-methylphenyl)-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]butan-1-one (**3p**).* Yield 83% (432 mg) as a yellow solid mp 87–89 °C. Found: C, 52.92; H, 2.83; S, 12.12 $C_{23}H_{15}F_7O_2S_2$ requires C, 53.07; H, 2.90; S, 12.32%; R_f (20% EtOAc/hexane) 0.5; $\nu_{\max}$ (KBr disc) 1671 (C=O), 1539, 1206, 1136, 732; δ_{H} (400 MHz, $CDCl_3$) 8.55 (1H, dd, *J*=3.6, 1.2 Hz), 7.65 (1H, dd, *J*=5.2, 1.2 Hz), 7.38 (2H, d, *J*=8.0 Hz), 7.26 (1H, dd, *J*=5.2, 1.6 Hz), 7.19 (2H, d, *J*=8.0 Hz), 7.18 (1H, d, *J*=9.2 Hz), 6.97 (1H, dd, *J*=3.6, 1.2 Hz), 6.93 (1H, dd, *J*=5.2, 3.6 Hz), 4.14 (1H, dt, *J*=14.8, $^{5}J_{\mathrm{H-F}}$=2.0 Hz, Hb-4), 3.93 (1H, dt, *J*=14.8, $^{5}J_{\mathrm{H-F}}$=0.8 Hz, Ha-4), 2.34 (3H, s, Me); δ_{C} (100 MHz, $CDCl_3$) 176.6 (t, $^{2}J_{\mathrm{C-F}}$=25.1 Hz, C=O), 165.5 (C2), 147.5, 140.2, 138.3, 135.6, 134.1, 130.9, 129.3, 127.9, 126.7, 126.5, 126.0 (2CH=), 125.3, 117.7 (qt, $^{1}J_{\mathrm{C-F}}$=286.5, $^{2}J_{\mathrm{C-F}}$=33.6 Hz, $-CF_2CF_2CF_3$), 110.4 (tt, $^{1}J_{\mathrm{C-F}}$=266.7, $^{2}J_{\mathrm{C-F}}$=31.3 Hz, $-CF_2CF_2CF_3$), 108.9 (tqt, $^{1}J_{\mathrm{C-F}}$=265.2, $^{2}J_{\mathrm{C-F}}$=38.1, $^{2}J_{\mathrm{C-F}}$=31.3 Hz, $-CF_2CF_2CF_3$), 104.9 (C3), 91.2 (t, $^{5}J_{\mathrm{C-F}}$=2.3 Hz, C5), 44.6 (t, $^{4}J_{\mathrm{C-F}}$=6.1 Hz, C4), 21.1 (Me); δ_{F} (376 MHz, $CDCl_3$) −126.4 (2F, s, $-CF_2CF_2CF_3$), −118.0 (2F, dq, $J_{\mathrm{F-F}}$=53.0, 9.2 Hz, $-CF_2CF_2CF_3$), −80.6 (3F, t, $^{3}J_{\mathrm{F-F}}$=9.2 Hz, $-CF_2CF_2CF_3$); LC/MS, *m*/*z* (ESI^+) 521 (MH^+, 100%).

*3.4.17. 2,2,2-Trifluoro-1-[5-(4-methylphenyl)-2-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3q**).* Yield 80% (331 mg) as yellow oil. Found: C, 66.60; H, 4.22; S, 7.56 $C_{23}H_{17}F_3O_2S$ requires C, 66.66; H, 4.13; S, 7.74%; R_f (20% EtOAc/hexane) 0.48; $\nu_{\max}$ (KBr disc) 3028, 2924, 1675 (C=O), 1569 (C=C), 1537, 1219 (CF_3), 1180 (C–O–C), 918, 849, 818, 764; δ_{H} (400 MHz, $CDCl_3$) 7.89 (2H, dd, *J*=7.2, 1.6 Hz), 7.52 (1H, t, *J*=7.6 Hz), 7.44 (2H, t, *J*=7.6 Hz), 7.38 (2H, d, *J*=8.4 Hz), 7.30 (1H, dd, *J*=5.2, 1.6 Hz), 7.20 (2H, d, *J*=8.4 Hz), 6.96 (2H, m), 4.07 (1H, d, *J*=15.2 Hz, Hb-4), 3.89 (1H, d, *J*=15.2 Hz, Ha-4), 2.36 (3H, s, Me); δ_{C} (100 MHz, $CDCl_3$) 175. 2 (q, *J*=34.3 Hz, C=O), 171.8 (C2), 148.0, 140.6, 138.5, 132.4, 130.0, 129.5, 129.0, 128.2 (2CH=), 126.9 (2CH=), 126.7, 126.2 (2CH=), 125.5 (2CH=), 117.0 (q, *J*=288.9 Hz, CF_3), 105.1 (C3), 91.6 (C5), 44.9 (C4), 21.3 (Me); δ_{F} (376 MHz, $CDCl_3$) −7.4 (s, CF_3); LC/MS, *m*/*z* (ESI^+) 415 (MH^+, 100%).

*3.4.18. 2,2,2-Trifluoro-1-[5-(4-fluorophenyl)-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3r**).* Yield 89% (377 mg) as yellow solid mp 82–84 °C. Found: C, 56.45; H, 2.98; S, 15.35 $C_{20}H_{12}F_4O_2S_2$ requires C, 56.60; H, 2.85; S, 15.11%; R_f (20% EtOAc/hexane) 0.43; $\nu_{\max}$ (KBr disc) 2940, 2862, 1668 (C=O), 1569 (C=C), 1529, 1477, 1263 (CF_3), 1201 (C–O–C), 918, 850, 762, 700; δ_{H} (400 MHz, $CDCl_3$) 8.48 (1H, dd, *J*=4.0, 1.2 Hz), 7.58 (1H, dd, *J*=4.8, 1.2 Hz), 7.37 (2H, m), 7.20 (1H, dd, *J*=4.8, 1.2 Hz), 7.10 (1H, t, *J*=4.4 Hz), 6.97 (1H, dd, *J*=9.2, 2.0 Hz), 6.85 (1H, t, *J*=4.0 Hz), 4.02 (1H, d, *J*=15.2 Hz, Hb-4), 3.76 (1H, d, *J*=15.2 Hz, Ha-4); δ_{C} (100 MHz, $CDCl_3$) 174.6 (q, $^{2}J_{\mathrm{C-F}}$=34.3 Hz, C=O), 164.9 (C2), 163.0 (d, $^{1}J_{\mathrm{C-F}}$=246.1 Hz, C_{ipso}), 139.2 (d, $^{4}J_{\mathrm{C-F}}$=3.1 Hz), 135.7, 134.4, 130.8, 128.2, 127.5, 127.5 (d, $^{3}J_{\mathrm{C-F}}$=8.4 Hz), 127.0, 126.9, 126.4 (2CH=), 117.3 (q, $^{1}J_{\mathrm{C-F}}$=288.8 Hz, CF_3), 115.7 (d, $^{2}J_{\mathrm{C-F}}$=21.4 Hz), 103.2 (C3), 90.9 (C5), 44.8 (d, $^{4}J_{\mathrm{C-F}}$=3.8 Hz, C4); δ_{F} (376 MHz, $CDCl_3$) −110 (1F, m, arom.CF), −74.3 (3F, s, CF_3); LC/MS, *m*/*z* (ESI^+) 425 (MH^+, 100%).

*3.4.19. 2,2,3,3,4,4,4-Heptafluoro-1-[5-(4-fluorophenyl)-2,5-di(thiophen-2-yl)-4,5-dihydrofuran-3-yl]butan-1-one (**3s**).* Yield 92% (482 mg) as yellow solid mp 64–66 °C. Found: C, 50.21; H, 2.15; S, 12.44 $C_{22}H_{12}F_8O_2S_2$ requires C, 50.38; H, 2.31; S, 12.23%; R_f (20% EtOAc/hexane) 0.48; $\nu_{\max}$ (KBr disc) 3031, 672 (C=O), 1538, 1209, 729; δ_{H} (400 MHz, $CDCl_3$) 8.56 (1H, dd, *J*=3.6, 1.2 Hz), 7.67 (1H, dd, *J*=4.8, 1.2 Hz), 7.46 (2H, dd, *J*=8.8, 1.2 Hz), 7.30 (1H, dd, *J*=5.2, 1.2 Hz), 7.19 (1H, t, *J*=4.8 Hz), 7.07 (2H, t, *J*=8.8 Hz), 6.98 (1H, dd, *J*=3.2, 1.2 Hz), 6.95 (1H, t, *J*=3.2 Hz), 4.16 (1H, d, *J*=14.8 Hz, Hb-4), 3.91 (1H, dt, *J*=14.8 Ha-4); δ_{C} (100 MHz, $CDCl_3$) 176.6 (t, $^{2}J_{\mathrm{C-F}}$=25.1 Hz, C=O), 165.3 (C2), 162.6 (d, $^{1}J_{\mathrm{C-F}}$=246.9 Hz, C_{ipso}), 147.0, 139.0 (d, $^{4}J_{\mathrm{C-F}}$=3.0 Hz), 135.7, 134.3, 130.7, 128.0, 127.0 (d, $^{3}J_{\mathrm{C-F}}$=7.7 Hz), 126.8, 126.7, 126.2 (2CH=), 115.6 (d, $^{2}J_{\mathrm{C-F}}$=21.4 Hz), 117.7 (qt, $^{1}J_{\mathrm{C-F}}$=286.6, $^{2}J_{\mathrm{C-F}}$=33.5 Hz, $-CF_2CF_2CF_3$), 110.3 (tt, $^{1}J_{\mathrm{C-F}}$=266.0, $^{2}J_{\mathrm{C-F}}$=31.2 Hz, $-CF_2CF_2CF_3$), 108.9 (tqt, $^{1}J_{\mathrm{C-F}}$=264.0, $^{2}J_{\mathrm{C-F}}$=38.1, $^{2}J_{\mathrm{C-F}}$=31.2 Hz, $-CF_2CF_2CF_3$), 104.7 (C3), 90.7 (t, $^{5}J_{\mathrm{C-F}}$=2.1 Hz, C5), 44.7 (t, $^{4}J_{\mathrm{C-F}}$=6.9 Hz, C4); δ_{F} (376 MHz, $CDCl_3$) −126.5 (s, $-CF_2CF_2CF_3$), −118.0 (dq, $J_{\mathrm{F-F}}$=43.6, 9.4 Hz, $-CF_2CF_2CF_3$), −113.7 (1F, m, arom. C–F), −80.6 (3F, t, $^{3}J_{\mathrm{F-F}}$=9.4 Hz, $-CF_2CF_2CF_3$); LC/MS, *m*/*z* (ESI^+) 525 (MH^+, 100%).

*3.4.20. 2,2,2-Trifluoro-1-[5-(4-fluorophenyl)-5-(thiophen-2-yl)-4,5-dihydro-2,2′-bifuran-3-yl]ethanone (**3t**).* Yield 75% (306 mg) as yellow oil. Found: C, 58.56; H, 3.14; S, 7.67 $C_{20}H_{12}F_4O_3S$ requires C, 58.82; H, 2.96; S, 7.85%; R_f (20% EtOAc/hexane) 0.41; $\nu_{\max}$ (KBr disc) 3028, 2922, 1685 (C=O), 1585, 1556 (C=C), 1209 (CF_3), 1136 (C–O–C), 758, 702; δ_{H} (400 MHz, $CDCl_3$) 8.42 (1H, d, *J*=3.6 Hz), 7.70 (1H, d, *J*=1.2 Hz), 7.53 (2H, dd, *J*=6.8, 3.2 Hz), 7.33 (1H, dd, *J*=4.8, 1.2 Hz), 7.12 (2H, t, *J*=8.4 Hz), 7.01–6.96 (2H, m), 6.64 (1H, dd, *J*=3.6, 2.0 Hz), 4.14 (1H, d, *J*=15.2 Hz, Hb-4), 3.88 (1H, d, *J*=15.2 Hz, Ha-4); δ_{C} (100 MHz, $CDCl_3$) 173.5 (q, $^{2}J_{\mathrm{C-F}}$=34.3 Hz, C=O), 162.6 (d, $^{1}J_{\mathrm{C-F}}$=246.9 Hz, C_{ipso}), 160.0 (C2), 146.9, 146.8 (2CH=), 144.0, 138.9 (d, $^{4}J_{\mathrm{C-F}}$=3.0 Hz), 127.3 (d, $^{3}J_{\mathrm{C-F}}$=8.4 Hz, 2CH=), 126.8, 126.5, 122.7, 116.7 (q, $^{1}J_{\mathrm{C-F}}$=287.0 Hz, CF_3), 115.5 (d, $^{2}J_{\mathrm{C-F}}$=21.3 Hz, 2CH=), 112.8, 103.2 (C3), 91.2 (C5), 44.3 (q, $^{4}J_{\mathrm{C-F}}$=3.1 Hz, C4); δ_{F} (376 MHz, $CDCl_3$) −110 (1F, m, arom.CF), −74.4 (3F, s, CF_3); LC/MS, *m*/*z* (ESI^+) 409 (MH^+, 100%).

*3.4.21. 2,2,2-Trifluoro-1-[5-(4-fluorophenyl)-2-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3u**).* Yield 88% (368 mg) as yellow oil. Found: C, 62.86; H, 3.49; S, 7.43 $C_{22}H_{14}F_4O_2S$ requires C, 63.15; H, 3.37; S, 7.66%; R_f (20% EtOAc/hexane) 0.44; $\nu_{\max}$ (KBr disc) 3063, 2980, 1685 (C=O), 1575 (C=C), 1199 (CF_3), 1138 (C–O–C), 904, 764, 700; δ_{H} (400 MHz, $CDCl_3$) 7.92 (2H, dd, *J*=8.8, 1.2 Hz), 7.55 (1H, t, *J*=7.6 Hz), 7.50–7.45 (4H, m), 7.35 (1H, dd, *J*=4.8, 2.0 Hz), 7.11 (2H, t, *J*=8.8 Hz), 7.00 (2H, m), 4.13 (1H, d, *J*=14.8 Hz, Hb-4), 3.89 (1H, d, *J*=14.8 Hz, Ha-4); δ_{C} (100 MHz, $CDCl_3$) 175.0 (q, $^{2}J_{\mathrm{C-F}}$=35.4 Hz, C=O), 171.4 (C2), 162.6 (d, $^{1}J_{\mathrm{C-F}}$=246.2 Hz, C_{ipso}), 139.1 (d, $^{4}J_{\mathrm{C-F}}$=3.0 Hz), 132.2, 129.7, 128.7, 128.6, 128.0, 127.3 (d,

$^{3}J_{\mathrm{C-F}}=8.4$ Hz, 2CH=), 126.8 (2CH=), 126.6, 126.0 (2CH=), 116.8 (q, $^{1}J_{\mathrm{C-F}}=290.3$ Hz, CF$_3$), 115.5 (d, $^{2}J_{\mathrm{C-F}}=21.4$ Hz, 2CH=), 104.8 (C3), 90.9 (C5), 44.8 (q, $^{4}J_{\mathrm{C-F}}=3.9$ Hz, C4); δ_{F} (376 MHz, CDCl$_3$) −115.1 (1F, m, arom.CF), −77.1 (3F, s, CF$_3$); LC/MS, m/z (ESI$^+$) 419 (MH$^+$, 100%).

*3.4.22. 2,2,2-Trifluoro-1-[5-(4-fluorophenyl)-2-methyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (**3v**).* Yield 70% (249 mg) as colorless oil. Found: C, 57.55; H, 3.45; S, 9.24 $C_{17}H_{12}F_4O_2S$ requires C, 57.30; H, 3.39; S, 9.00%; R_f (20% EtOAc/hexane) 0.51; $\nu_{\max}$ (KBr disc) 3053, 2934, 1679 (C=O), 1571 (C=C), 1330, 1195 (CF$_3$), 1145 (C–O–C), 985, 906, 746, 702; δ_{H} (400 MHz, CDCl$_3$) 7.41 (2H, dd, J=9.2, 5.2 Hz), 7.31 (1H, dd, J=5.2, 1.2 Hz), 7.08 (2H, t, J=8.4 Hz), 6.97 (1H, dd, J=6.0, 4.8 Hz), 6.90 (1H, dd, J=3.2, 1.2 Hz), 3.91 (1H, d, J=14.8 Hz, Hb-4), 3.65 (1H, d, J=14.8 Hz, Ha-4), 2.46 (3H, s, Me); δ_{C} (100 MHz, CDCl$_3$) 176.2 (q, $^{2}J_{\mathrm{C-F}}=35.0$ Hz, C=O), 175.4 (C2), 162.5 (d, $^{1}J_{\mathrm{C-F}}=246.0$ Hz, C_{ipso}), 147.5, 139.3, 127.2 (d, $^{3}J_{\mathrm{C-F}}=8.4$ Hz, 2CH=), 126.8, 126.6, 126.0, 116.6 (q, $^{1}J_{\mathrm{C-F}}=289.6$ Hz, CF$_3$), 115.4 (d, $^{2}J_{\mathrm{C-F}}=21.3$ Hz, 2CH=), 105.4 (C3), 91.7 (C5), 43.8 (C4), 15.9 (Me); δ_{F} (376 MHz, CDCl$_3$) −112.6 (1F, m, arom.CF), −77.0 (3F, s, CF$_3$); LC/MS, m/z (ESI$^+$) 357 (MH$^+$, 100%).

*3.4.23. [5-Methyl-5-(thiophen-2-yl)-2-(trifluoromethyl)-4,5-dihydrofuran-3-yl](phenyl)methanone (**4a**).* Yield 15% (51 mg) as yellow oil. Found: C, 60.66; H, 3.54; S, 9.24 $C_{17}H_{13}F_3O_2S$ requires C, 60.35; H, 3.87; S, 9.48%; R_f (20% EtOAc/hexane) 0.35; $\nu_{\max}$ (KBr disc) 3073, 2936, 2861, 1664 (C=O), 1531 (C=C), 1203 (CF$_3$), 1138 (C–O–C), 758, 700; δ_{H} (400 MHz, CDCl$_3$) 7.81 (2H, dd, J=8.0, 1.6 Hz), 7.59 (1H, tt, J=7.6, 1.6 Hz), 7.46 (2H, t, J=7.6 Hz), 7.32 (1H, dd, J=5.2, 1.6 Hz), 7.10 (1H, dd, J=4.0, 1.6 Hz), 7.02 (1H, dd, J=4.8, 4.0 Hz), 3.55 (1H, dq, J=16.0, $^{5}J_{\mathrm{H-F}}=2.8$ Hz, Hb-4), 3.40 (1H, dq, J=16.0, $^{5}J_{\mathrm{H-F}}=2.8$ Hz, Ha-4), 1.97 (3H, s, Me); δ_{C} (100 MHz, CDCl$_3$) 192.2 (C=O), 158.6 (q, $^{2}J_{\mathrm{C-F}}=34.4$ Hz, C2), 147.9, 137.9, 133.8, 129.0 (2CH=), 128.8, 127.2, 125.6 (2CH=), 123.9, 117.1 (q, $^{1}J_{\mathrm{C-F}}=290.1$ Hz, CF$_3$), 106.3 (C3), 88.5 (C5), 48.4 (C4), 28.9 (Me); δ_{F} (376 MHz, CDCl$_3$) −74.0 (s, CF$_3$); LC/MS, m/z (ESI$^+$) 339 (MH$^+$, 100%).

*3.4.24. 5-Methyl-3-(naphthalen-2-ylcarbonyl)-5-(thiophen-2-yl)-2-(trifluoromethyl)tetrahydrofuran-2-yl acetate (**4b**).* Yield 11% (43 mg) as yellow oil. Found: C, 64.76; H, 3.67; S, 8.53 $C_{21}H_{15}F_3O_2S$ requires C, 64.94; H, 3.89; S, 8.26%; R_f (20% EtOAc/hexane) 0.40; $\nu_{\max}$ (KBr disc) 3061, 2976, 1683 (C=O), 1583 (C=C), 1554, 1211 (CF$_3$), 1138 (C–O–C), 758, 696; δ_{H} (400 MHz, CDCl$_3$) 8.27 (1H, s), 7.91–7.87 (4H, m), 7.62 (1H, td, J=6.8, 1.6 Hz), 7.56 (1H, td, J=6.8, 1.6 Hz), 7.36 (1H, dd, J=4.8, 1.2 Hz), 7.14 (1H, dd, J=3.6, 1.2 Hz), 7.05 (1H, dd, J=5.2, 3.6 Hz), 3.57 (1H, dq, J=16.0, $^{5}J_{\mathrm{H-F}}=2.1$ Hz, Hb-4), 3.46 (1H, dq, J=16.0, $^{5}J_{\mathrm{H-F}}=2.1$ Hz, Ha-4), 2.01 (3H, s, Me); δ_{C} (100 MHz, CDCl$_3$) 190.8 (C=O), 148.1, 144.4 (q, $^{2}J_{\mathrm{C-F}}=38.8$ Hz, C2), 136.0, 135.2, 132.5, 131.6, 129.9, 129.1, 128.9, 128.1, 127.2, 127.1, 125.6, 124.2, 123.9, 115.9 (q, $^{1}J_{\mathrm{C-F}}=288.4$ Hz, CF$_3$), 103.3 (C3), 88.6 (C5), 48.6 (C4), 28.9 (Me); δ_{F} (376 MHz, CDCl$_3$) −76.4 (s, CF$_3$); LC/MS, m/z (ESI$^+$) 389 (MH$^+$, 100%).

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References and notes

1. (a) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, 2006; (b) Kirisch, P. *Modern Fluoroorganic Chemistry*; Wiley-VCD: Weinheim, Germany, 2004; (c) Filler, R.; Kobayashi, Y.; Yagupolskii, L. M. *Organofluorine Compounds in Medical Chemistry and Biochemistry Applications*; Elsevier: Amsterdam, 1993; (d) Hiyama, T. *Organofluorine Compounds. Chemistry and Application*; Springer: Berlin, 2000; (e) Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell: Oxford, 2004; (f) Isanbor, C.; O'Hagan, D. *J. Fluorine Chem.* **2006**, *127*, 303–319; (g) Ismail, F. M. D. *J. Fluorine Chem.* **2002**, *118*, 27–33.
2. (a) Tozer, M. J.; Herpin, T. F. *Tetrahedron* **1996**, *52*, 8619–8683; (b) Altenburger, J. M.; Schirlin, D. *Tetrahedron Lett.* **1991**, *32*, 7255–7258; (c) Brady, K.; Wei, A. Z.; Ringe, D.; Abeles, R. H. *Biochemistry* **1990**, *29*, 7600–7607; (d) Tanaka, T.; Kawase, M.; Tani, S. *Life Sci.* **2003**, *73*, 2985–2990; (e) Spengler, G.; Molnar, A.; Klausz, G.; Mandi, Y.; Kawase, M.; Motohashi, N.; Molnar, J. *Int. J. Antimicrob. Agents* **2004**, *23*, 631–633; (f) Frey, R. R.; Wada, C. K.; Garland, R. B.; Curtin, M. L.; Michaelides, M. R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3443–3447.
3. (a) Kawase, M.; Harada, H.; Saito, S.; Cui, J.; Tani, S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 193–194; (b) Kawase, M.; Motohashi, N.; Sakagami, H.; Kanamoto, T.; Nakashima, H.; Ferenczy, L.; Wolfard, K.; Miskolci, C.; Molnár, J. *Int. J. Antimicrob. Agents* **2001**, *18*, 161–165; (c) Molnár, A.; Wolfart, K.; Kawase, M.; Motohashi, N.; Molnár, J. *In Vivo* **2004**, *18*, 505–507.
4. Kawase, M.; Sakagami, H.; Kusama, K.; Motohashi, N.; Saito, S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3113–3118.
5. (a) Dean, F. M. *Advences in Heterocyclic Chemistry*; Academic: New York, NY, 1982; Vol. 30; 167–238; (b) Dean, F. M.; Sargent, M. V. *Comprehensive Heterocyclic Chemistry*; Pergamon: New York, NY, 1984; Vol. 4, Part 3, 531–598; (c) Elbe, H.-L.; Kunisch, F.; Bielefeldt, D.; Tiemann, R.; Stenzel, K.; Dutzmann, S.; Kugler, M.; Schrage, H. U.S. Patent 6,107,336, Aug. 22, 2000. (d) Logoglu, E.; Yılmaz, M.; Katircioglu, H.; Yakut, M.; Mercan, S. *Med. Chem. Res.* **2010**, *19*, 490–497; (e) Miski, M.; Jakupovic, J. *Phytochemistry* **1990**, *29*, 1995–1998; (f) Zdero, C.; Bohlman, F.; King, R. M.; Robinson, H. *Phytochemistry* **1986**, *25*, 509–516; (g) Hofman, G.; Jhonson, R. K. *J. Nat. Prod.* **1993**, *56*, 1500–1505.
6. (a) Alagoz, O.; Yılmaz, M.; Pekel, A. T. *Synth. Commun.* **2006**, *36*, 1005–1013; (b) Yılmaz, M.; Pekel, A. T. *Synth. Commun.* **2001**, *31*, 3871–3876; (c) Yılmaz, M.; Pekel, A. T. *Synth. Commun.* **2001**, *31*, 2189–2194; (d) Yılmaz, M.; Bicer, E.; Pekel, A. T. *Turk. J. Chem.* **2005**, *29*, 579–587; (e) Yılmaz, M.; Yakut, M.; Pekel, A. T. *Synth. Commun.* **2008**, *38*, 914–927; (f) Yılmaz, M.; Uzunalioglu, N.; Pekel, A. T. *Tetrahedron* **2005**, *61*, 8860–8867; (g) Burgaz, E. V.; Yilmaz, M.; Pekel, A. T.; Oktemer, A. *Tetrahedron* **2007**, *63*, 7229–7239; (h) Yılmaz, M.; Uzunalioglu, N.; Yakut, M.; Pekel, A. T. *Turk. J. Chem.* **2008**, *32*, 411–422; (i) Yılmaz, M.; Pekel, A. T. *J. Fluorine Chem.* **2005**, *126*, 401–406.
7. (a) Citterio, A.; Santi, R.; Fiorani, T.; Strologo, S. *J. Org. Chem.* **1989**, *54*, 2703–2712; (b) Citterio, A.; Fancelli, D.; Finzi, C.; Pesce, L. *J. Org. Chem.* **1989**, *54*, 2713–2718; (c) Mellor, J. M.; Mohammed, S. *Tetrahedron Lett.* **1991**, *32*, 7111–7114; (d) Mellor, J. M.; Mohammed, S. *Tetrahedron* **1993**, *49*, 7547–7556; (e) Nishino, H.; Hguyen, V.; Yoshinaga, S.; Kurosawa, K. *J. Org. Chem.* **1996**, *61*, 8264–8271; (f) Garzino, F.; Méou, A.; Brun, P. *Tetrahedron Lett.* **2000**, *41*, 9803–9807; (g) Gregory, B.; Parsons, A. F.; Thomas, C. B. *Tetrahedron Lett.* **2000**, *41*, 7751–7755; (h) Kajikawa, S.; Nishino, H.; Kurosawa, K. *Heterocycles* **2001**, *54*, 171–183; (i) Gregory, B.; Parsons, A. F.; Thomas, C. B. *Tetrahedron* **2001**, *57*, 4719–4728; (j) Melikyan, G. G. *Synthesis* **1993**, 833–850; (k) Igbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519–564; (l) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339–363; (m) Wang, G.-W.; Dong, Y.-W.; Wu, P.; Yuan, T.-T.; Shen, Y.-B. *J. Org. Chem.* **2008**, *73*, 7088–7095; (n) Pan, X.-Q.; Zou, J.-P.; Zhang, W. *Mol Diversity* **2009**, *13*, 421–438; (o) Demir, A. S.; Emrullahoglu, M. *Curr. Org. Synth.* **2007**, *4*, 223–237; (p) Yilmaz, E. V. B.; Yilmaz, M.; Oktemer, A. *ARKIVOC* **2011**, *ii*, 363–376.
8. (a) Baciocchi, E.; Ruzziconi, R. *Synth. Commun.* **1988**, *18*, 1841–1846; (b) Nair, V.; Mathew, J.; Radhakrishnan, K. V. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1487–1492; (c) Kobayashi, K.; Sakashita, K.; Akamatsu, H.; Tanaka, K.; Uchida, M.; Uneda, T.; Kitamura, T.; Morikawa, O.; Konishi, H. *Heterocycles* **1999**, *51*, 2881–2892; (d) Lee, Y. R.; Kim, B. S.; Kim, D. H. *Tetrahedron* **2000**, *56*, 8845–8853; (e) Nair, V.; Treesa, P. M.; Maliakal, D.; Rath, N. P. *Tetrahedron* **2001**, *57*, 7705–7710; (f) Tseng, C.-H.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2002**, *58*, 7625–7633; (g) Liao, Y.-J.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2003**, *59*, 3511–3520; (h) Kobayashi, K.; Nagase, K.; Morikawa, O.; Konishi, H. *Heterocycles* **2003**, *60*, 939–946; (i) Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2004**, *60*, 1841–1847; (j) Nair, V.; Deepthi, A. *Chem. Rev. C* **2007**, *107*, 1862–1891; (k) Nair, V.; Mohanan, K.; Suja, T. D.; Suresh, E. *Tetrahedron Lett.* **2006**, *47*, 2803–2806; (l) Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem.* **2008**, *73*, 6835–6837.
9. (a) Manfredinia, S.; Guarneria, M.; Simonia, D.; Granab, E.; Bosellib, C.; Zontab, F.; Ferianic, A.; Gaviraghic, G.; Tosonc, G. *Eur. J. Med. Chem.* **1994**, *29*, 153–161; (b) Ward, W. J., Jr.; McEwen, W. E. *J. Org. Chem.* **1990**, *55*, 493–500; (c) Baker, R.; Sims, R. J. *Synthesis* **1981**, *117*.
10. (a) Hajos, Z. G.; Wachter, M. P.; Werblood, H. M. *Synth. Commun.* **1989**, *19*, 3295–3300; (b) Karminski-Zamola, G.; Jakopčić, K. *J. Heterocycl. Chem.* **1981**, *18*, 193–196.
11. (a) Fry, A. J.; Allukian, M.; Williams, A. D. *Tetrahedron* **2002**, *58*, 4411–4416; (b) Maccarone, E.; Mamo, A.; Perrini, G.; Torre, M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 324–326.
12. (a) Lozac'h, N.; Teste, J. *C. R. Chim.* **1952**, *234*, 1891–1893; (b) Skuballa, W.; Schillinger, E.; Stürzebecher, C.-S.; Vorbrüggen, H. *J. Med. Chem.* **1986**, *29*, 315–317.
13. (a) See for **2e**; Luo, F.-T.; Fwub, S.-L.; Huang, W.-S. *Tetrahedron Lett.* **1992**, *45*, 6839–6840; (b) See for **2f**; Sperber, N.; Papa, D.; Schwenk, E.; Sherlock, M. *J. Am. Chem. Soc.* **1949**, *71*, 887–889; (c) Maruyama, K.; Otsuki, T.; Mitsui, K.; Tojo, M. *J. Heterocycl. Chem.* **1980**, *17*, 695–700; (d) Berthiol, F.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2003**, *6*, 1091–1096; (e) Itami, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 11577–11585.