

## Synthesis of fluoroacylated 4,5-dihydrofurans and fluoroalkylated tetrahydrofurans by the radical cyclization using manganese(III) acetate. Part II

Mehmet Yilmaz <sup>a,\*</sup>, A. Tarik Pekel <sup>b</sup>

<sup>a</sup> Department of Chemistry, Faculty of Arts and Sciences, Kocaeli University, 41380 Umuttepe, Kocaeli, Turkey

<sup>b</sup> Ankara University, Science Faculty, Department of Chemistry 06100 Tandoğan, Ankara, Turkey

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### ABSTRACT

Manganese(III) acetate-based radical cyclizations of various fluorinated 1,3-dicarbonyl compounds with alkenes produced 3-fluoroacylated 4,5-dihydrofurans and 2-acetyloxy-2-fluoroalkylated tetrahydrofurans in good yields. Mechanism was proposed for the formation of all compounds. The radical cyclization of fluorinated 1,3-dicarbonyls showed to form different cyclized products depending on the structure of alkenes and enol forms of 1,3-dicarbonyls.

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## 1. Introduction

The use of fluorine atom in the synthesis of organic compounds is developing due to their unique physico-chemical and biological properties. Thus, fluorinated organic compounds containing trifluoromethyl have received considerable attention in the medicinal and agricultural chemistry [1]. Many of trifluoromethyl ketones have been found to show enzyme inhibition [2], antimicrobial activity [3] and some trifluoromethyl ketones have been demonstrated as cytotoxic agents against human tumor cell [4].

Traditionally, methods for the synthesis of fluorine containing organic compounds are direct fluorination and fluoroalkylation [5]. One possible approach would be the cyclization of a suitable fluorinated 1,3-dicarbonyl compounds with unsaturated systems mediated by transition metal salts ( $Mn^{+3}$ ,  $Ce^{+4}$ ,  $Ag^+$ , etc.) [6]. These metal salts such as manganese(III) acetate [7] and cerium(IV) ammonium nitrate [8] are very important radical oxidants in the organic synthesis for the construction of carbon–carbon bonds.

Dihydrofurans are significant class of compounds since they show a wide range of biological activities and form the basic structure of many natural compounds [9]. Our research group have

studied the radical cyclization of 1,3-dicarbonyl compounds and 3-oxopropanenitriles with alkenes, alkynes, unsaturated amides and dienes using manganese(III) acetate, resulting the formation of many dihydrofuran derivatives [10]. Recently, we obtained 2,3-dihydro-4*H*-furo[3,2-*c*]chromen-4-ones and 2,3-dihydro-naphtho[2,3-*b*]furan-4,9-diones by the radical cyclization of 4-hydroxycoumarin and 2-hydroxy-1,4-naphthoquinone, respectively [10e]. Previously, we described the synthesis of 3-trifluoroacetyl-4,5-dihydrofurans and 3-[dihydrofuran-2(3*H*)-ylidene]-1,1,1-trifluoroacetones by the treatment of trifluoromethyl-1,3-dicarbonyl compounds with alkenes [10i]. In this paper, we studied radical cyclization of basic and available various tri, and hepta fluorinated 1,3-dicarbonyl compounds **1a–g** with conjugated alkenes **2a–f** using manganese(III) acetate. As a result of these reactions, we obtained fluoroacylated 4,5-dihydrofurans and fluoroalkylated tetrahydrofurans depending on the enol form of 1,3-dicarbonyls and structure of alkenes.

## 2. Results and discussions

All fluorinated-1,3-dicarbonyls **1a–f** are available commercial products and were used in highest purity. The conjugated alkenes **2a–c** were prepared by dehydration from the carbinole formed from Grignard reaction of arylmagnesium bromide and suitable carbonyl compounds. Radical reactions were performed at 1.2:1:2.5 molar ratio (**1:2:Mn(OAc)<sub>3</sub>**) under a nitrogen atmosphere in AcOH. All compounds purified by column chromatography or

\* Corresponding author. Tel.: +90 2623032058; fax: +90 2623032003.  
E-mail address: [mehmet.yilmaz@kocaeli.edu.tr](mailto:mehmet.yilmaz@kocaeli.edu.tr) (M. Yilmaz).

preparative TLC were characterized by IR,  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  NMR, mass spectra and microanalysis.

As seen in Table 1, the radical cyclizations of **1a** and **1b** with **2a** afforded 3-trifluoroacetyl-4,5-dihydrofurans **3a** (72%) and **3b** (95%) in high yields. The compounds of 3-trifluoroacetyl-4,5-dihydrofuran **3c** (34%) and 2-trifluoromethyl-4,5-dihydrofuran **3d** (15%) obtained from the reaction of **1a** with 1-phenyl-1-cyclopentene (**2b**) were differentiated by means of the chemical shifts of carbonyl carbons of these compounds in  $^{13}\text{C}$  NMR spectra. Whereas the carbonyl carbon of **3c** gives quartet ( $^2J_{\text{C}-\text{F}} = 34.8$  Hz) at

177 ppm in  $^{13}\text{C}$  NMR, the carbonyl carbon of compound **3d** gives singlet at 194 ppm. On the other hand, while C-2 carbon of **3d** gives quartet ( $^2J_{\text{C}-\text{F}} = 34.4$  Hz) at 150 ppm, C-2 of **3c** gives singlet at 178 ppm. On the other side, only 3-trifluoroacetyl-4,5-dihydrofurans **3e–g** were isolated from the treatment of **1b–d** with **2b** in good yields. The radical cyclization of 4,4,4-trifluoro-1-thien-2-ylbutane-1,3-dione **1d** with **2c** gave 3-trifluoroacetyl-4,5-dihydrofuran **3h** (83%) in good yield.

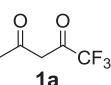
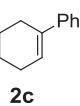
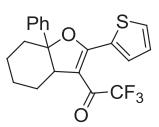
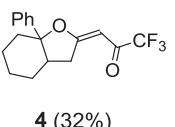
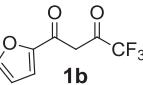
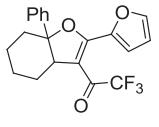
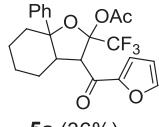
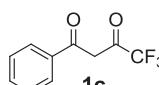
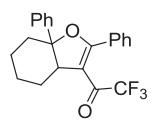
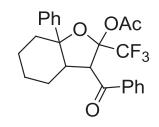
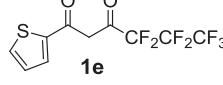
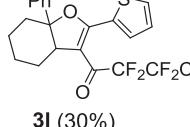
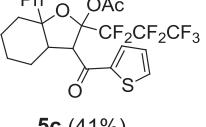
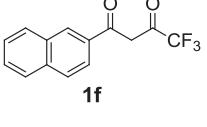
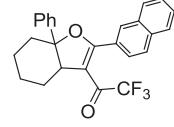
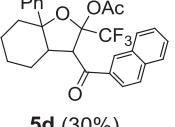
We obtained interesting results from the reactions of **2c** with fluorinated 1,3-dicarbonyl compounds (**1a–c**, **1e**, **1f**) in Table 2.

**Table 1**  
Radical cyclizations of **1a–d** with the alkenes **2a–c**.

Entry	1,3-Dicarbonyl	Alkene	Product	Yield <sup>a</sup> (%)
1				<b>3a</b> , 72
2				<b>3b</b> , 95
3				<b>3c</b> , 34
				<b>3d</b> , 15
4				<b>3e</b> , 57
5				<b>3f</b> , 60
6				<b>3g</b> , 64
7				<b>3h</b> , 83 <b>3i</b> (34%)

<sup>a</sup> Isolated yield based on the amount of the alkene used.

**Table 2**Radical cyclization of fluorinated 1,3-dicarbonyl compounds with **2c**.

Entry	1,3-Dicarbonyl	Alkene	Product and yield <sup>a</sup> (%)
1			 <b>3i</b> (34%)  <b>4</b> (32%)
2			 <b>3j</b> (29%)  <b>5a</b> (36%)
3			 <b>3k</b> (32%)  <b>5b</b> (35%)
4			 <b>3l</b> (30%)  <b>5c</b> (41%)
5			 <b>3m</b> (21%)  <b>5d</b> (30%)

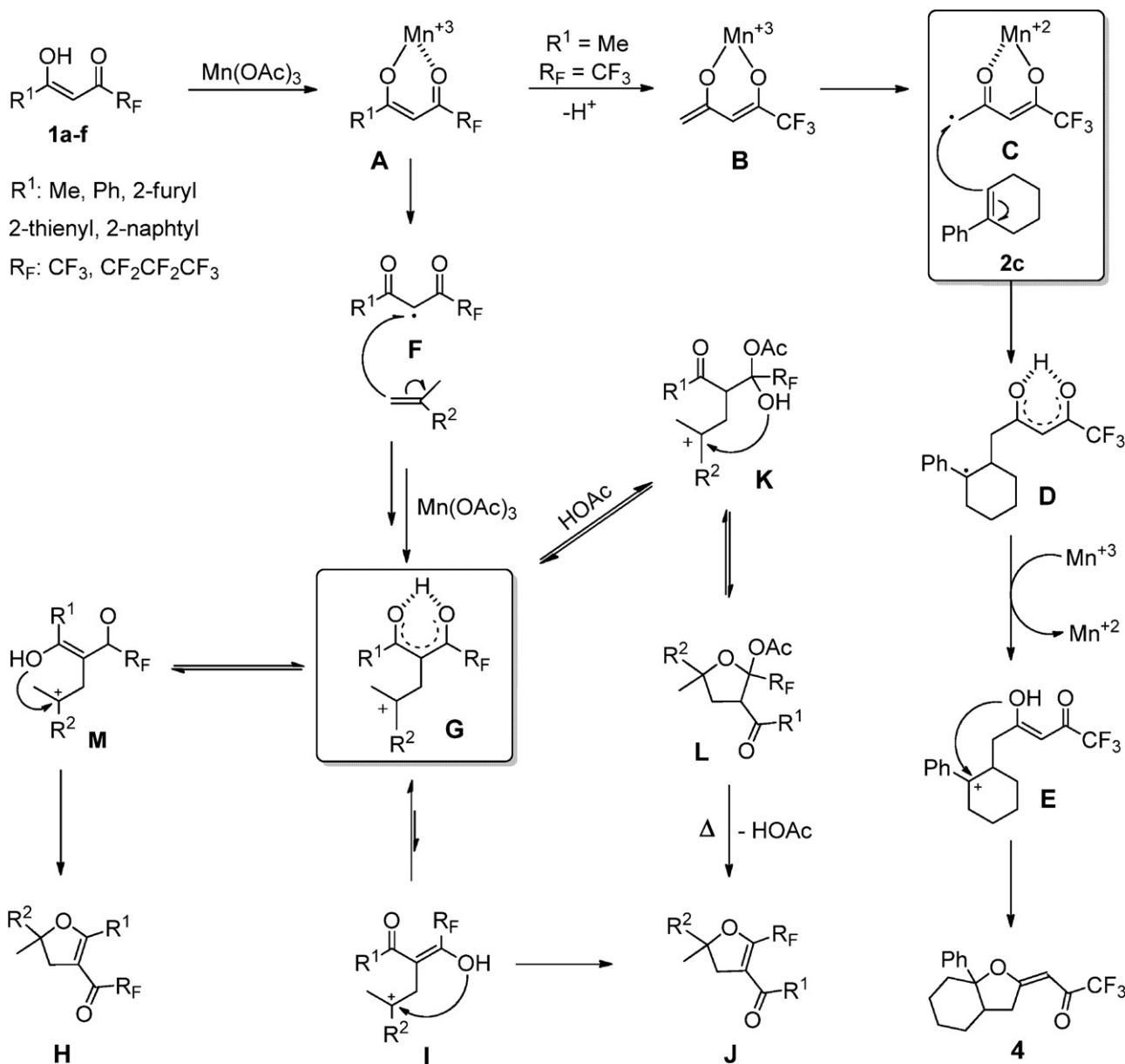
<sup>a</sup> Isolated yield based on the amount of alkene used.

While the reaction of 2,4-pentanedione with **2c** was reported to produce 4,5-dihydrofuran as single product [8b], treatment of **1a** with **2c** formed 3-trifluoroacetyl-4,5-dihydrofuran **3i** and hexahydrobenzofuran-2(3H)-ylidenepropen-2-one **4** (Table 2, entry 1). Since <sup>13</sup>C NMR spectrum of **4** showed a quartet at 181.1 ppm (<sup>2</sup>J<sub>C-F</sub> = 33.8 Hz) for carbonyl carbon, the CF<sub>3</sub> group is adjacent to the carbonyl group. Moreover, COSY spectrum showed that H-3 protons couple with olefinic proton.

3-Fluoroacylated-4,5-dihydrofurans **3j–m** formed by the cyclization of the corresponding enol form of 1,3-dicarbonyls (**1b**, **1c**, **1e**, **1f**) were obtained along with in situ 2-acetyloxy-2-fluoroalkyl-tetrahydrofurans **5a–d** which are HOAc adducts of 2-fluoroalkylated 4,5-dihydrofurans formed by the cyclization of the other enol form of the 1,3-dicarbonyls. Among these compounds, **5c** (dr = 73:27) and **5d** (dr = 80:20) were isolated as diastereomeric mixtures and the ratio was determined by <sup>1</sup>H NMR. Although most of the obtained products have two or more stereocenters, all of the compounds were obtained as one isomer except for **5c** and **5d**.

The mechanism proposed for the formation of all compounds is explained in Scheme 1. According to this mechanism, the

interaction of enol form of the 1,3-dicarbonyl **1a–f** with manganese(III) acetate produces Mn(III)-enolate complex **A**. When the R<sup>1</sup> is methyl group, the elimination of a methyl proton from Mn(III)-enolate complex leads to the formation of Mn(III)-dienolate complex **B**. While Mn<sup>+3</sup> is reduced to Mn<sup>+2</sup>, a terminal radical carbon is formed on this structure. The radical intermediate **D** formed by the addition of an electron from **2c** to the terminal radical is oxidized to carbocation **E** by Mn(OAc)<sub>3</sub> and cyclization of **E** gives the compound **4**. Similarly, a radical-carbon intermediate product **F** is formed while Mn<sup>+3</sup> is reduced to Mn<sup>+2</sup> on the structure **A**. Addition of the radical-carbon to alkene followed oxidation by Mn(OAc)<sub>3</sub> gave intermediate carbocation **G**. Fluoroacylated 4,5-dihydrofurans **H** are formed by the cyclization of carbocation intermediate **M** the enol form of the **G**. 2-Acetyloxy-2-fluoroalkylated tetrahydrofurans **L** are formed via the cyclization of hemiacetalic structure **K** obtained from addition of HOAc to the carbonyl group of **G**. Moreover, fluoroalkylated 4,5-dihydrofurans **J** are formed either by the cyclization of carbocation intermediate **I**, the other enol form of **G**, or a pyrolytic elimination of HOAc from compound **L**.



**Scheme 1.** Mechanism for the radical cyclizations of fluorinated 1,3-dicarbonyls with alkene.

### 3. Conclusion

In conclusion, the radical cyclizations of various fluorinated 1,3-dicarbonyl compounds with conjugated alkenes mediated by  $Mn(OAc)_3$  were performed in this study. These results show quite different from that of nonfluorinated 1,3-dicarbonyl compounds in many ways. We think that this difference arises from fluorine atoms' changing tautomeric properties of 1,3-dicarbonyl compounds. Enol forms of 1,3-dicarbonyls play an important role in variety of products formed in radical cyclization of alkenes.

This study introduces that fluorinated 1,3-dicarbonyl compounds can be used effectively in the radical cyclizations for synthesis of various fluorinated organic compounds such as fluoroalkylated tetrahydrofurans and fluoroacylated 4,5-dihydrofurans.

## 4. Experimental

#### 4.1. General

Melting points were determined on a electrotermal capillary melting point apparatus. IR spectra (KBr disc,  $\text{CHCl}_3$ ) were obtained with a Matson 1000 FT-IR in the  $400\text{--}4000\text{ cm}^{-1}$  range with  $4\text{ cm}^{-1}$  resolution.  $^1\text{H}$  NMR (400 MHz),  $^{19}\text{F}$  NMR (376 MHz) and  $^{13}\text{C}$  NMR (100 MHz) 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 Agilent 1100 MSD LC/MS (APCI, 100 eV), a Shimadzu GC-17A/GC-MS-QP5000 (EI, 70 eV) and 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 aluminium-packed silica gel plates. Purification of products was performed by column chromatography on silica gel (Merck silica gel 60, 40–63  $\mu$ m) or preparative TLC on silica gel of Merck (PF<sub>254</sub>-366nm). All trifluoromethyl-1,3-dicarbonyl compounds, solvents and reagents were purchased highest purity.

#### 4.2. General procedure for synthesis of 4,5-dihydrodourans and tetrahydrofurans

A solution of manganese(III) acetate dihydrate (5 mmol, 1.35 g) in 20 mL glacial acetic acid was heated under nitrogen atmosphere at 80 °C until it dissolved. After Mn(OAc)<sub>3</sub> dissolved completely, the solution was cooled down to 60 °C. A solution of trifluoromethyl-1,3-dicarbonyl compound (2.5 mmol) and alkene (2 mmol) in 5 mL acetic acid was added to this mixture and the temperature was raised to 80 °C. The reaction was complete when the dark brown colour of the solution disappeared. Acetic acid was evaporated under reduced pressure. Water was added to the residue and extraction was performed with CHCl<sub>3</sub> (3  $\times$  20 mL). The combined organic extracts were neutralized with satd. NaHCO<sub>3</sub> solution, and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated. Crude products were purified by column chromatography or preparative TLC (20 cm  $\times$  20 cm plates, 2 mm thickness) using n-hexane/EtOAc (5:1) as eluent.

#### 4.3. Spectroscopic data of fluoroacylated dihydrofurans and fluoroalkylated tetrahydrofurans

**2,2,2-Trifluoro-1-[2-methyl-5,5-bis(4-methylphenyl)-4,5-dihydrofuran-3-yl]ethanone (3a).** Yield 72% (648 mg) as colourless oil.  $\nu_{\text{max}}$  (KBr disc) 1687 (C=O), 1581 (C=C), 1201 (C-F), 1134 (C-O-C), 906, 816; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.35 (4H, dt,  $J$  = 8.3, 1.9 Hz, arom. H), 7.28 (4H, d,  $J$  = 8.2 Hz, arom. H), 3.87 (2H, s, 4-H), 2.59 (3H, s, CH<sub>3</sub>), 2.46 (6H, s, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  177.7 (q,  $^2J_{\text{C-F}}$  = 35.1 Hz, C=O), 177.4 (C-2), 142.3, 139.1, 130.4, 126.7, 119.3 (q,  $^1J_{\text{C-F}}$  = 290.9 Hz, -CF<sub>3</sub>), 106.6 (C-3), 95.7 (C-5), 42.8 (q,  $^4J_{\text{C-F}}$  = 1.05 Hz, C-4), 21.5, 16.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -77.0 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 360 (M<sup>+</sup>, 23.38), 317 (M<sup>+</sup> -CF<sub>3</sub>CO, 16.05), 291 (M<sup>+</sup>-CF<sub>3</sub>, 13.36), 248 (M<sup>+</sup>-CH<sub>3</sub>CO-CF<sub>3</sub>, 42.61), 220 (M<sup>+</sup>-CF<sub>3</sub>CO-CH<sub>3</sub>CO, 36.75), 202 (M<sup>+</sup>-F<sub>2</sub>-CH<sub>3</sub>CO-C<sub>6</sub>H<sub>5</sub>, 35.32), 91 (PhCH<sub>2</sub><sup>+</sup>, 28.08), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 23.21), 69 (CF<sub>3</sub><sup>+</sup>, 5.25), 43 (CH<sub>3</sub>CO<sup>+</sup>, 100.00). Anal. Calcd for C<sub>21</sub>H<sub>19</sub>F<sub>3</sub>O<sub>2</sub>: C, 69.99; H, 5.31. Found: C, 70.23; H, 5.22.

**2,2,2-Trifluoro-1-[5,5-bis(4-methylphenyl)-4,5-dihydro-2,2-bifuran-3-yl]-ethanone (3b).** Yield 95% (978 mg) as pale yellow oil.  $\nu_{\text{max}}$  (KBr disc) 3028, 2924, 1675 (C=O), 1569 (C=C), 1537, 1219 (C-F), 1180 (C-O-C), 918, 849, 818, 764; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.42 (1H, d,  $J$  = 3.7 Hz), 7.72 (1H, d,  $J$  = 0.9 Hz), 7.38 (4H, d,  $J$  = 8.2 Hz), 7.20 (4H, d,  $J$  = 8.1 Hz), 6.65 (1H, dd,  $J$  = 3.7, 1.6 Hz), 4.00 (2H, s, 4-H), 2.36 (6H, s, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  174.5 (q,  $^2J_{\text{C-F}}$  = 34.3 Hz, C=O), 161.6 (C-2), 147.5, 145.2, 141.5, 138.7, 130.0, 126.4, 123.1, 119.3 (q,  $^1J_{\text{C-F}}$  = 291.4 Hz, -CF<sub>3</sub>), 113.4, 104.2 (C-3), 94.7 (C-5), 42.9 (d,  $^4J_{\text{C-F}}$  = 3.2 Hz, C-4), 21.2 (CH<sub>3</sub>); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -76.8 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 413 (MH<sup>+</sup>, 0.49), 412 (M<sup>+</sup>, 2.29), 343 (M<sup>+</sup>-CF<sub>3</sub>, 1.36), 317 (M<sup>+</sup>-C<sub>5</sub>H<sub>3</sub>O<sub>2</sub>, 20.28), 315 (M<sup>+</sup>-CF<sub>3</sub>, 5.45), 275 (M<sup>+</sup>-CF<sub>3</sub>-C<sub>4</sub>H<sub>3</sub>O, 8.21), 219 (M<sup>+</sup>-CF<sub>3</sub>CO-C<sub>5</sub>H<sub>3</sub>O<sub>2</sub>, 6.61), 178 (M<sup>+</sup>-CF<sub>3</sub>CO-C<sub>5</sub>H<sub>3</sub>O<sub>2</sub>-CH<sub>3</sub>, 11.43), 95 (C<sub>5</sub>H<sub>3</sub>O<sub>2</sub><sup>+</sup>, 100.00), 69 (CF<sub>3</sub><sup>+</sup>, 10.80). Anal. Calcd for C<sub>24</sub>H<sub>19</sub>F<sub>3</sub>O<sub>3</sub>: C, 69.90; H, 4.64. Found: C, 70.06; H, 4.51.

**2,2,2-Trifluoro-1-(2-methyl-6a-phenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-3-yl)ethanone (3c).** Yield 34% (252 mg) as colourless oil.  $\nu_{\text{max}}$  (KBr disc) 2963, 2872, 1679 (C=O), 1571 (C=C), 1199 (C-F), 1140 (C-O-C), 762, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.33–7.22 (5H, m), 3.72 (1H, d,  $J$  = 8.4 Hz, 3a-H), 2.33 (3H, s, CH<sub>3</sub>), 2.30 (1H, dd,  $J$  = 13.9, 5.9 Hz), 1.98 (1H, dd,  $J$  = 13.8, 6.2 Hz), 1.84 (2H, m), 1.64 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  178.6 (C-2), 177.9 (q,  $^2J_{\text{C-F}}$  = 34.8 Hz, C=O), 144.1, 129.6, 128.7, 125.4, 117.8 (q,  $^1J_{\text{C-F}}$

$=$  290.9 Hz, -CF<sub>3</sub>), 112.0 (C-3), 103.6 (C-6a), 53.7 (CH<sub>3</sub>), 42.8 (C-6), 36.4 (C-3a), 25.1 (C-4), 16.4 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -66.3 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 297 (MH<sup>+</sup>, 20.98), 296 (M<sup>+</sup>, 50.35), 281 (M<sup>+</sup>-CH<sub>3</sub>, 1.78), 278 (MH<sup>+</sup>-F, 7.21), 227 (M<sup>+</sup>-CF<sub>3</sub>, 13.29), 199 (M<sup>+</sup>-CF<sub>3</sub>CO, 6.38), 105 (PhCO<sup>+</sup>, 43.71), 91 (PhCH<sub>2</sub><sup>+</sup>, 12.94), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 35.84), 69 (CF<sub>3</sub><sup>+</sup>, 13.99), 43 (CH<sub>3</sub>CO<sup>+</sup>, 100.00). Anal. Calcd for C<sub>16</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: C, 64.86; H, 5.10. Found: C, 64.75; H, 5.21.

**1-[2-(Trifluoromethyl)-6a-phenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-3-yl]ethanone (3d).** Yield 15% (111 mg) as colourless oil.  $\nu_{\text{max}}$  (KBr disc) 2961, 2872, 1656 (C=O), 1581 (C=C), 1148 (C-F), 1151 (C-O-C), 760, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.37 (5H, m, arom. H), 3.84 (1H, dt,  $J$  = 8.8,  $^5J_{\text{H-F}}$  = 1.9 Hz, 3a-H), 2.44 (1H, dd,  $J$  = 14.0, 5.9 Hz), 2.35 (3H, s, CH<sub>3</sub>), 2.01 (2H, m), 1.95 (2H, m), 1.80 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  194.6 (C=O), 150.0 (q,  $^2J_{\text{C-F}}$  = 34.4 Hz, C-2), 144.0, 129.8, 129.0, 125.1, 121.6 (C-3), 119.5 (q,  $^1J_{\text{C-F}}$  = 273.8 Hz, -CF<sub>3</sub>), 101.8 (C-6a), 57.5 (CH<sub>3</sub>), 44.1 (C-6), 30.3 (q,  $^4J_{\text{C-F}}$  = 3.5 Hz, C-3a), 35.0 (C-4), 25.4 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -63.5 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 297 (MH<sup>+</sup>, 3.78), 296 (M<sup>+</sup>, 16.35), 278 (MH<sup>+</sup>-F, 13.17), 227 (M<sup>+</sup>-CF<sub>3</sub>, 32.52), 199 (M<sup>+</sup>-CF<sub>3</sub>CO, 26.67), 185 (MH<sup>+</sup>-CF<sub>3</sub>CO-CH<sub>3</sub>, 33.03), 142 (M<sup>+</sup>-CF<sub>3</sub>CO-C<sub>3</sub>H<sub>5</sub>O, 25.07), 91 (PhCH<sub>2</sub><sup>+</sup>, 21.78), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 35.29), 43 (CH<sub>3</sub>CO<sup>+</sup>, 100.00). Anal. Calcd for C<sub>16</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: C, 64.86; H, 5.10. Found: C, 64.73; H, 5.32.

**2,2,2-Trifluoro-1-[2-(2-furyl)-6a-phenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-3-yl]ethanone (3e).** Yield 57% (496 mg) as yellow oil.  $\nu_{\text{max}}$  (KBr disc) 3027, 2925, 1711 (C=O), 1698 (C=C), 1592, 1221 (C-F), 926 (C-O-C), 749, 693; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.36 (1H, d,  $J$  = 3.6 Hz), 7.69 (1H, dd,  $J$  = 1.6, 0.8 Hz), 7.48 (2H, d,  $J$  = 8.0 Hz), 7.39 (2H, t,  $J$  = 7.2 Hz), 7.32 (1H, tt,  $J$  = 7.6, 1.2 Hz), 6.63 (1H, dd,  $J$  = 4.0, 1.6 Hz), 3.97 (1H, d,  $J$  = 8.8 Hz, 4-H), 2.55 (1H, dd,  $J$  = 14.4, 6.0 Hz, 6a-H), 2.27–2.15 (2H, m), 2.03–1.94 (2H, m), 1.84 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  174.4 (q,  $^2J_{\text{C-F}}$  = 34.3 Hz, C=O), 161.8 (C-2), 146.8, 144.3, 142.7, 128.8, 128.2, 124.6, 122.4, 121.8–113.1 (q,  $^1J_{\text{C-F}}$  = 289.6 Hz, -CF<sub>3</sub>), 112.8, 109.4 (C-3), 102.5 (C-6a), 53.6, 42.1, 36.9, 25.0; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -74.6 (s, CF<sub>3</sub>); LC-MS (ESI<sup>+</sup>), m/z (%): 349 (MH<sup>+</sup>, 100%). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>: C, 65.52; H, 4.34. Found: C, 65.65; H, 4.52.

**2,2,2-Trifluoro-1-(2,6a-diphenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-3-yl)ethanone (3f).** Yield 60% (537 mg) as colourless oil.  $\nu_{\text{max}}$  (KBr disc) 2963, 2870, 1681 (C=O), 1583 (C=C), 1205 (C-F), 1140 (C-O-C), 760, 696; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.81 (2H, dt,  $J$  = 7.3, 1.3 Hz), 7.55–7.37 (8H, m, arom. H), 4.01 (1H, d,  $J$  = 8.6 Hz, 3a-H), 2.51 (1H, dd,  $J$  = 13.9, 5.8 Hz), 2.27–2.15 (2H, m), 2.11 (1H, m), 2.01 (1H, m), 1.88 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  177.1 (q,  $^2J_{\text{C-F}}$  = 34.7 Hz, C=O), 174.3 (C-2), 143.6, 132.6, 130.4, 130.0, 129.5, 128.8, 128.7, 125.1, 118.9 (q,  $^1J_{\text{C-F}}$  = 291.7 Hz, -CF<sub>3</sub>), 111.2, 102.3 (C-3), 54.3 (C-3a), 42.4 (C-6), 36.4 (C-4), 24.8 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -75.3 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 359 (MH<sup>+</sup>, 4.31), 358 (M<sup>+</sup>, 15.99), 289 (M<sup>+</sup>-CF<sub>3</sub>, 7.72), 261 (M<sup>+</sup>-CF<sub>3</sub>CO, 2.99), 184 (M<sup>+</sup>-CF<sub>3</sub>CO-PhCO, 1.18), 105 (PhCO<sup>+</sup>, 100.00), 91 (PhCH<sub>2</sub><sup>+</sup>, 7.85), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 67.12), 69 (CF<sub>3</sub><sup>+</sup>, 5.60). Anal. Calcd for C<sub>21</sub>H<sub>17</sub>F<sub>3</sub>O<sub>2</sub>: C, 70.38; H, 4.78. Found: C, 70.72; H, 4.63.

**2,2,2-Trifluoro-1-(6a-phenyl-2-thien-2yl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-3-yl)ethanone (3g).** Yield 64% (582 mg) as a yellow solid, m.p. 95–96 °C (Hexane/EtOAc).  $\nu_{\text{max}}$  (KBr disc) 1660 (C=O), 1531 (C=C), 1199 (C-F), 1140 (C-O-C), 731, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.65 (1H, dd,  $J$  = 4.0, 1.2 Hz), 7.79 (1H, dd,  $J$  = 5.1, 1.2 Hz), 7.53 (2H, dt,  $J$  = 7.1, 1.6 Hz), 7.46 (2H, td,  $J$  = 6.2, 1.5 Hz), 7.42 (1H, tt,  $J$  = 7.2, 1.4 Hz), 7.31 (1H, dd,  $J$  = 5.0, 4.0 Hz), 4.06 (1H, d,  $J$  = 8.9 Hz, 3a-H), 2.58 (1H, dd,  $J$  = 13.9, 5.8 Hz), 2.26 (1H, m), 2.35 (1H, m), 2.07 (2H, m), 1.92 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  176.3 (q,  $^2J_{\text{C-F}}$  = 34.2 Hz, C=O), 167.9 (C-2), 143.9, 136.4, 134.8, 132.0, 129.9, 129.1, 129.0, 125.4, 119.8 (q,  $^1J_{\text{C-F}}$  = 291.6 Hz, -CF<sub>3</sub>), 109.9 (C-3), 102.6 (C-6a), 54.5 (d,  $^4J_{\text{C-F}}$  = 2.3 Hz, C-3a), 42.6 (C-6), 37.4 (C-4), 25.4 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  -74.2 (s, CF<sub>3</sub>); GC-MS (EI, 70 eV), m/z (%): 364 (M<sup>+</sup>, 28.67), 326

(M<sup>+</sup>–F<sub>2</sub>, 21.84), 295 (M<sup>+</sup>–CF<sub>3</sub>, 18.69), 258 (M<sup>+</sup>–PhCO, 20.63), 252 (M<sup>+</sup>–CF<sub>3</sub>–C<sub>3</sub>H<sub>5</sub>–C<sub>5</sub>H<sub>3</sub>OS, 33.67), 111 (C<sub>5</sub>H<sub>3</sub>OS<sup>+</sup>, 100.00), 105 (PhCO<sup>+</sup>, 39.0), 83 (C<sub>4</sub>H<sub>3</sub>S<sup>+</sup>, 14.92). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>F<sub>3</sub>O<sub>2</sub>S: C, 62.63; H, 4.15; S, 8.80. Found: C, 62.82; H, 4.08; S, 8.64.

2,2,2-Trifluoro-1-(7a-phenyl-2-thien-2-yl-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl)ethanone (**3h**). Yield 83% (784 mg) as a yellow solid, m.p. 105–107 °C (Hexane/EtOAc).  $\nu_{\text{max}}$  (KBr disc) 1664 (C=O), 1531 (C=C), 1203 (C–O–C), 1138 (C–F), 758, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.67 (1H, dd, *J* = 4.0, 1.1 Hz), 7.76 (1H, dd, *J* = 5.0, 1.1 Hz), 7.47 (2H, dt, *J* = 7.3, 1.5 Hz), 7.37 (2H, td, *J* = 7.0, 1.9 Hz), 7.28 (3H, m), 3.64 (1H, t, *J* = 7.2 Hz, 3a-H), 2.45 (1H, dd, *J* = 12.6, 4.2 Hz), 2.38 (1H, t, *J* = 10.8 Hz), 1.68 (2H, m), 1.82 (3H, m), 1.42 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  175.8 (q, <sup>2</sup>J<sub>C–F</sub> = 34.5 Hz, C=O), 167.9 (C-2), 146.4, 136.5, 135.0, 133.0, 129.2, 128.7, 128.2, 125.1, 119.8 (q, <sup>1</sup>J<sub>C–F</sub> = 291.4 Hz, –CF<sub>3</sub>), 113.9 (C-3), 93.2 (C-7a), 45.6 (C-3a), 36.8 (C-7), 31.7 (C-4), 22.4 (C-6), 21.9 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –74.0 (s, CF<sub>3</sub>); GC–MS (EI, 70 eV), *m/z* (%): 379 (MH<sup>+</sup>, 2.25), 378 (M<sup>+</sup>, 32.96), 309 (M<sup>+</sup>–CF<sub>3</sub>, 21.77), 266 (M<sup>+</sup>–CF<sub>3</sub>–C<sub>3</sub>H<sub>7</sub>, 10.73), 198 (M<sup>+</sup>–CF<sub>3</sub>–C<sub>5</sub>H<sub>3</sub>OS, 13.67), 111 (C<sub>5</sub>H<sub>3</sub>OS<sup>+</sup>, 53.07), 110 (C<sub>5</sub>H<sub>2</sub>OS<sup>+</sup>, 100.00), 105 (PhCO<sup>+</sup>, 16.45), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 41.23), 69 (CF<sub>3</sub><sup>+</sup>, 16.34). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>F<sub>3</sub>O<sub>2</sub>S: C, 63.48, H 4.53, S 8.47. Found: C 63.35, H 4.48, S 8.36.

2,2,2-Trifluoro-1-(2-methyl-7a-phenyl-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl)ethanone (**3i**). Yield 34% (264 mg) as colourless oil.  $\nu_{\text{max}}$  (KBr disc) 2937, 2864, 1662 (C=O), 1589 (C=C), 1540, 1253 (C–F), 1171 (C–O–C), 766, 694; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.35 (4H, m), 7.31 (1H, t, *J* = 4.2 Hz), 3.48 (1H, t, *J* = 6.7 Hz, 3a-H), 2.44 (3H, s, CH<sub>3</sub>), 2.21 (2H, m), 1.85 (1H, m), 1.71 (2H, m), 1.55 (1H, m), 1.42 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  178.4 (C-2), 177.7 (q, <sup>2</sup>J<sub>C–F</sub> = 35.1 Hz, C=O), 146.9, 129.5, 128.7, 126.7, 125.1, 119.2 (q, <sup>1</sup>J<sub>C–F</sub> = 290.7 Hz, –CF<sub>3</sub>), 115.3, 94.1 (C-7a), 45.7 (C-3a), 35.7 (C-7), 29.4 (C-4), 20.6 (C-6), 16.8 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –76.5 (s, CF<sub>3</sub>); GC–MS (EI, 70 eV), *m/z* (%): 311 (MH<sup>+</sup>, 2.28), 310 (M<sup>+</sup>, 2.31), 267 (M<sup>+</sup>–CH<sub>3</sub>CO, 5.72), 213 (M<sup>+</sup>–CF<sub>3</sub>CO, 3.80), 199 (MH<sup>+</sup>–CH<sub>3</sub>, –CF<sub>3</sub>CO<sup>+</sup>, 8.41), 91 (PhCH<sub>2</sub><sup>+</sup>, 19.86), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 10.92), 69 (CF<sub>3</sub><sup>+</sup>, 10.81), 43 (CH<sub>3</sub>CO<sup>+</sup>, 100.00). Anal. Calcd for C<sub>17</sub>H<sub>17</sub>F<sub>3</sub>O<sub>2</sub>: C, 65.80; H, 5.52. Found: C, 65.82; H 5.38.

2,2,2-Trifluoro-1-[2-(2-furyl)-7a-phenyl-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl]ethanone (**3j**). Yield 29% (263 mg) as pale yellow oil.  $\nu_{\text{max}}$  (KBr disc) 2940, 2862, 1668 (C=O), 1569 (C=C), 1529, 1263 (C–F), 1201 (C–O–C), 918, 762, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.32 (1H, d, *J* = 3.7 Hz), 7.76 (1H, t, *J* = 1.1 Hz), 7.47 (1H, dd, *J* = 7.6, 1.3 Hz), 7.34 (1H, t, *J* = 7.8 Hz), 7.47 (1H, dd, *J* = 5.6, 2.2 Hz), 7.34 (1H, t, *J* = 7.8 Hz), 7.27 (1H, tt, *J* = 5.6, 2.2 Hz), 6.66 (1H, dd, *J* = 3.7, 1.7 Hz), 3.58 (1H, t, *J* = 7.7 Hz, 3a-H), 2.47 (1H, d, *J* = 13.5 Hz, 4-H), 2.32 (1H, m, 4-H), 1.88 (1H, m), 1.80 (2H, m), 1.63 (1H, m), 1.41 (2H, t, *J* = 9.2 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  174.2 (q, <sup>2</sup>J<sub>C–F</sub> = 34.3 Hz, C=O), 162.5 (C-2), 147.7, 145.8, 128.9, 128.3, 126.4, 124.9, 123.1, 119.4 (q, <sup>1</sup>J<sub>C–F</sub> = 291.3 Hz, –CF<sub>3</sub>), 113.8, 113.4 (C-3), 93.5 (C-7a), 45.2 (d, <sup>4</sup>J<sub>C–F</sub> = 1.8 Hz, C-3a), 36.4 (C-7), 31.2 (C-4), 22.0 (C-6), 21.5 (C-5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –74.3 (s, CF<sub>3</sub>); GC–MS (EI, 70 eV), *m/z* (%): 363 (MH<sup>+</sup>, 12.05), 362 (M<sup>+</sup>, 28.49), 344 (M<sup>+</sup>–H<sub>2</sub>O, 14.53), 293 (M<sup>+</sup>–CF<sub>3</sub>, 23.06), 265 (M<sup>+</sup>–CF<sub>3</sub>CO, 24.62), 262 (M<sup>+</sup>–C<sub>5</sub>H<sub>3</sub>O<sub>2</sub>, 34.60), 105 (PhCO<sup>+</sup>, 21.74), 95 (C<sub>5</sub>H<sub>3</sub>O<sub>2</sub><sup>+</sup>, 100.00), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 29.00), 69 (CF<sub>3</sub><sup>+</sup>, 38.03), 55 (C<sub>4</sub>H<sub>7</sub><sup>+</sup>, 14.98). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>F<sub>3</sub>O<sub>3</sub>: C, 66.29; H, 4.73. Found: C, 66.36; H, 4.92.

1-(2,7a-Diphenyl-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl)-2,2,2-trifluoroethanone (**3k**). Yield 32% (298 mg) as pale yellow oil.  $\nu_{\text{max}}$  (KBr disc) 3055, 2930, 2861, 1681 (C=O), 1589 (C=C), 1199 (C–F), 1143 (C–O–C), 758, 694; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.76 (2H, td, *J* = 7.2, 1.4 Hz), 7.47–7.22 (8H, m), 3.57 (1H, t, *J* = 7.2 Hz, 3a-H), 2.29 (2H, m), 1.78 (1H, m), 1.66 (2H, m), 1.52 (2H, m), 1.45 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  175.9 (q, <sup>2</sup>J<sub>C–F</sub> = 34.5 Hz, C=O), 173.0 (C-2), 145.0, 132.1, 129.8, 128.4, 128.0, 127.7, 126.5, 124.2, 118.2 (q, <sup>1</sup>J<sub>C–F</sub> = 289.5 Hz, –CF<sub>3</sub>), 111.3 (C-3), 92.3 (C-7a), 45.7 (C-3a), 35.6 (C-7), 29.7 (C-4), 20.8 (C-6), 20.7 (C-

5); <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –74.0 (s, CF<sub>3</sub>); GC–MS (EI, 70 eV), *m/z* (%): 373 (MH<sup>+</sup>, 9.31), 372 (M<sup>+</sup>, 23.39), 354 (MH<sup>+</sup>–F, 23.53), 303 (M<sup>+</sup>–CF<sub>3</sub>, 19.80), 267 (M<sup>+</sup>–PhCO<sup>+</sup>, 100.00), 91 (PhCH<sub>2</sub><sup>+</sup>, 13.53), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 40.39), 69 (CF<sub>3</sub><sup>+</sup>, 24.90). Anal. Calcd for C<sub>22</sub>H<sub>19</sub>F<sub>3</sub>O<sub>2</sub>: C, 70.96; H 5.14. Found: C, 71.25; H, 5.06.

2,2,3,4,4,4-Heptafluoro-1-[7a-phenyl-2-(2-thienyl)-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl]butan-1-one (**3l**). Yield 30% (359 mg) as pale yellow oil.  $\nu_{\text{max}}$  (KBr disc) 3027, 2978, 1691 (C=O), 1643 (C=C), 1235 (C–F), 966 (C–O–C), 748, 693; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.62 (1H, dd, *J* = 4.0, 1.2 Hz), 7.72 (1H, dd, *J* = 5.2, 1.2 Hz), 7.41 (2H, d, *J* = 7.2 Hz), 7.29 (2H, t, *J* = 7.2 Hz), 7.23 (2H, m), 3.59 (1H, m, 3a-H), 2.41 (1H, dt, *J* = 15.2, 2.0 Hz), 2.31 (1H, m), 1.85 (1H, m), 1.75 (2H, m), 1.59 (1H, m), 1.38 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  176.9 (t, <sup>2</sup>J<sub>C–F</sub> = 25.1 Hz, C=O), 167.4 (C-2), 142.2, 135.8, 134.3, 132.1, 128.5, 128.2, 127.7, 124.2, 122.0–113.3 (qt, <sup>1</sup>J<sub>C–F</sub> = 286.5, <sup>2</sup>J<sub>C–F</sub> = 34.2 Hz, –CF<sub>2</sub>–CF<sub>2</sub>–CF<sub>3</sub>), 114.3 (d, <sup>3</sup>J<sub>C–F</sub> = 3.0 Hz, C-3), 113.0–107.7 (tt, <sup>1</sup>J<sub>C–F</sub> = 266.7, <sup>2</sup>J<sub>C–F</sub> = 31.2 Hz, –CF<sub>2</sub>–CF<sub>2</sub>–CF<sub>3</sub>), 111.5–106.2 (tqt, <sup>1</sup>J<sub>C–F</sub> = 265.2, <sup>2</sup>J<sub>C–F</sub> = 38.9 Hz, <sup>3</sup>J<sub>C–F</sub> = not determined –CF<sub>2</sub>–CF<sub>2</sub>–CF<sub>3</sub>), 92.2, 45.5 (d, <sup>4</sup>J<sub>C–F</sub> = 6.1 Hz, C-4), 36.1, 31.6, 21.9, 21.4; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –80.8 (t, <sup>3</sup>J<sub>F–F</sub> = 9.4 Hz, 2 F, –CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub>), –126.4 (m, 2 F, –CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub>), –126.6 (t, <sup>3</sup>J<sub>F–F</sub> = 52.6 Hz, 2 F, –CF<sub>2</sub>CF<sub>2</sub>CF<sub>3</sub>); LC–MS (ESI<sup>+</sup>), *m/z* (%): 479 (MH<sup>+</sup>, 100%). Anal. Calcd for C<sub>22</sub>H<sub>17</sub>F<sub>7</sub>O<sub>2</sub>S: C, 55.23; H, 3.58; S, 6.70. Found: C, 55.05; H, 3.32; S, 6.77.

2,2,2-Trifluoro-1-[7a-phenyl-2-(2-naphthyl)-3a,4,5,6,7,7a-hexahydro-1-benzofuran-3-yl]ethanone (**3m**). Yield 21% (222 mg) as yellow oil.  $\nu_{\text{max}}$  (KBr disc) 2962, 1692 (C=O), 1644 (C=C), 1078 (C–F), 1146 (C–O–C), 786, 692; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.48 (1H, s), 7.90 (1H, dd, *J* = 7.6, 1.2 Hz), 7.86 (2H, s), 7.85 (1H, dd, *J* = 7.6, 0.8 Hz), 7.58–7.50 (4H, m), 7.37 (2H, t, *J* = 7.2 Hz), 7.27 (1H, tt, *J* = 7.2, 1.2 Hz), 3.67 (1H, t, *J* = 7.2 Hz, 3a-H), 2.37 (2H, m), 1.91–1.83 (1H, m), 1.77–1.71 (2H, m), 1.65–1.54 (2H, m), 1.44 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  175.7 (q, <sup>2</sup>J<sub>C–F</sub> = 34.3 Hz, C=O), 173.0 (C-2), 145.1, 135.0, 132.3, 131.2, 129.0, 128.4, 128.1, 127.8, 127.7, 126.9, 126.7, 125.7, 124.3, 121.2–112.5 (q, <sup>1</sup>J<sub>C–F</sub> = 289.0 Hz, –CF<sub>3</sub>), 114.2 (C-3), 92.4 (C-7a), 45.9, 35.6, 29.8, 20.9, 20.7; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –73.8 (s, CF<sub>3</sub>); LC–MS (ESI<sup>+</sup>), *m/z* (%): 423 (MH<sup>+</sup>, 100%). Anal. Calcd for C<sub>26</sub>H<sub>21</sub>F<sub>3</sub>O<sub>2</sub>: C, 73.92; H 5.01. Found: C, 73.75; H, 4.82.

(3E)-1,1,1-Trifluoro-3-(7a-phenylhexahydro-1-benzofuran-2(3H)-ylidene)acetone (**4**). Yield 32% (248 mg) as colourless oily solid.  $\nu_{\text{max}}$  (KBr disc) 2936, 2861, 1695 (C=O), 1591 (C=C), 1195 (C–F), 1147 (C–O–C), 758, 700; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.40–7.29 (5H, m), 6.23 (1H, d, *J* = 0.6 Hz, H<sub>olef</sub>), 3.16 (1H, dd, *J* = 18.6, 0.7 Hz, 3-Ha), 2.84 (1H, ddd, *J* = 18.6, 6.4, 1.7 Hz, 3-Hb), 2.68 (1H, m, 3a-H), 2.22 (1H, tt, *J* = 15.3, 5.2 Hz), 1.92 (2H, m), 1.76 (1H, m), 1.67 (1H, m), 1.51 (1H, m), 1.45 (1H, m, 5-H), 1.25 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  186.1 (C-2), 181.1 (q, <sup>2</sup>J<sub>C–F</sub> = 33.8 Hz, C=O), 144.8, 129.7, 129.1, 125.6, 117.8 (q, <sup>1</sup>J<sub>C–F</sub> = 291.4 Hz, –CF<sub>3</sub>), 94.11 (C-7), 94.0 (C-3), 40.8 (C-6), 40.7 (C-5), 37.0, 28.9, 23.4, 21.9; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  –78.7 (s, CF<sub>3</sub>); GC–MS (EI, 70 eV), *m/z* (%): 311 (MH<sup>+</sup>, 10.51), 310 (M<sup>+</sup>, 24.99), 241 (M<sup>+</sup>–CF<sub>3</sub>, 11.83), 170 (M<sup>+</sup>–CF<sub>3</sub>CO–C<sub>3</sub>H<sub>7</sub>, 14.23), 156 (M<sup>+</sup>–CF<sub>3</sub>CO–C<sub>3</sub>H<sub>5</sub>O, 100.00), 91 (PhCH<sub>2</sub><sup>+</sup>, 69.37), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 29.21), 69 (CF<sub>3</sub><sup>+</sup>, 47.12). Anal. Calcd for C<sub>17</sub>H<sub>17</sub>F<sub>3</sub>O<sub>2</sub>: C, 65.80; H, 5.52. Found: C, 65.75; H, 5.41.

3-(2-Furoyl)-2-(trifluoromethyl)-7a-phenyl-octahydro-1-benzofuran-2-yl acetate (**5a**). Yield 36% (380 mg) as a colourless solid, m.p. 156–158 °C (Hexane/EtOAc).  $\nu_{\text{max}}$  (KBr disc) 2938, 2864, 1762 (C=O), 1679 (C=O), 1190 (C–F), 1088 (C–O–C), 764, 701; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.61 (1H, d, *J* = 6.4 Hz), 7.56 (2H, d, *J* = 7.2 Hz), 7.36 (2H, t, *J* = 7.3 Hz), 7.30 (2H, m), 6.61 (1H, t, *J* = 5.8 Hz), 5.51 (1H, d, *J* = 13.2 Hz, 3-H), 3.63 (1H, dd, *J* = 13.2, 6.0 Hz, 3a-H), 2.66 (1H, td, *J* = 13.6, 3.2 Hz), 2.25 (3H, s, CH<sub>3</sub>), 2.18 (1H, dt, *J* = 13.4, 3.8 Hz), 1.88 (1H, m), 1.70 (2H, m), 1.58 (1H, m), 1.22 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  182.5 (C=O), 168.7 (C=O), 153.8, 146.9, 144.6, 128.3, 127.6, 125.7, 122.8 (q, <sup>1</sup>J<sub>C–F</sub> = 287.2 Hz, –CF<sub>3</sub>), 117.9, 113.2, 105.6 (q, <sup>2</sup>J<sub>C–F</sub> = 34.2 Hz, C-2), 88.2 (C-7a), 52.5, 42.9 (C-7), 36.6 (C-

4), 25.4, 22.7 (C-6), 20.4 (C-5);  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  –78.0 (s,  $\text{CF}_3$ ); GC-MS (APCI, 100 eV),  $m/z$  (%): 422 ( $\text{M}^+$ , 21.05), 421 ( $\text{M}^+ - \text{H}$ , 13.62), 379 ( $\text{M}^+ - \text{CH}_3\text{CO}$ , 34.13), 362 ( $\text{M}^+ - \text{CH}_3\text{CO}_2\text{H}$ , 100.00), 355 ( $\text{M}^+ - \text{C}_4\text{H}_3\text{O}$ , 9.20), 309 ( $\text{M}^+ - \text{CF}_3 - \text{CO}_2$ , 62.82), 266 ( $\text{M}^+ - \text{C}_4\text{H}_3\text{F}_3\text{O}_3$ , 23.30), 157 ( $\text{C}_4\text{H}_3\text{F}_3\text{O}_3^+$ , 95.15), 95 ( $\text{C}_5\text{H}_3\text{O}_2^+$ , 4.30), 91 ( $\text{PhCH}_2^+$ , 29.85), 69 ( $\text{CF}_3^+$ , 9.13). Anal. Calcd for  $\text{C}_{22}\text{H}_{21}\text{F}_3\text{O}_5$ : C, 62.56; H 5.01. Found: C, 62.72; H, 4.93.

**3-Benzoyl-2-(trifluoromethyl)-7a-phenyl-octahydro-1-benzofuran-2-yl acetate (5b).** Yield 35% (378 mg) as a colourless solid, m.p. 130–132 °C (Hexane/EtOAc).  $\nu_{\text{max}}$  (KBr disc) 2934, 2864, 1762 (C=O), 1685 (C=O), 1596 (C=C), 1203 (C–F), 1186 (C–O–C), 762, 696;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.94 (2H, dd,  $J$  = 8.4, 1.2 Hz), 7.62 (1H, tt,  $J$  = 7.6, 1.2 Hz), 7.60 (2H, dt,  $J$  = 6.8, 1.6 Hz), 7.52 (2H, t,  $J$  = 7.6 Hz), 7.37 (2H, td,  $J$  = 8.0, 0.8 Hz), 7.29 (1H, tt,  $J$  = 7.2, 1.2 Hz), 5.63 (1H, d,  $J$  = 12.8 Hz, 3-H), 3.65 (1H, dd,  $J$  = 12.8, 5.8 Hz, 3a-H), 2.65 (1H, td,  $J$  = 13.2, 3.6 Hz, 4-H), 2.15 (3H, s,  $-\text{CH}_3$ ), 2.20 (1H, m), 1.76 (2H, m), 1.92 (1H, m), 1.65 (2H, m), 1.52 (1H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  194.7 (C=O), 168.8 (C=O), 144.5, 138.3, 133.9, 128.4, 128.2, 127.7, 125.8, 122.0 (q,  $^1\text{J}_{\text{C}-\text{F}}$  = 287.2 Hz,  $-\text{CF}_3$ ), 116.0 (q,  $^2\text{J}_{\text{C}-\text{F}}$  = 34.2 Hz, C-2), 88.3 (C-7a), 52.3 ( $\text{CH}_3$ ), 44.5, 43.2, 36.6, 25.4, 22.2, 20.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  –73.6 (s,  $\text{CF}_3$ ); GC-MS (APCI, 100 eV),  $m/z$  (%): 432 ( $\text{M}^+$ , 1.71), 431 ( $\text{M}^+ - \text{H}$ , 13.20), 389 ( $\text{M}^+ - \text{CH}_3\text{CO}$ , 11.12), 373 ( $\text{M}^+ - \text{CH}_3\text{CO}_2$ , 26.00), 371 ( $\text{M}^+ - \text{CH}_3\text{CO}_2\text{H}$ , 100.00), 355 ( $\text{M}^+ - \text{C}_6\text{H}_5$ , 29.81), 335 ( $\text{M}^+ - \text{CF}_3\text{CO}$ , 17.23), 277 ( $\text{MH}^+ - \text{C}_4\text{H}_3\text{F}_3\text{O}_3$ , 28.41), 157 ( $\text{C}_4\text{H}_4\text{F}_3\text{O}_3^+$ , 73.30), 105 ( $\text{PhCO}^+$ , 55.20), 91 ( $\text{PhCH}_2^+$ , 24.90), 77 ( $\text{C}_6\text{H}_5^+$ , 11.42). Anal. Calcd for  $\text{C}_{24}\text{H}_{23}\text{F}_3\text{O}_4$ : C, 66.66; H, 5.36. Found: C, 66.82; H, 5.14.

**2-(Heptafluoropropyl)-7a-phenyl-3-(2-thienylcarbonyl)octahydro-1-benzofuran-2-yl acetate (5c).** Yield 41% (441 mg) as yellow oil.  $\nu_{\text{max}}$  (KBr disc) 2975, 2926, 1714 (C=O), 1650 (C=O), 1240 (C–F), 934 (C–O–C), 749, 693;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.70 (1H, m), 7.50 (2H, dd,  $J$  = 7.2, 1.6 Hz), 7.35 (2H, t,  $J$  = 6.4 Hz), 7.28 (t,  $J$  = 6.8 Hz), 7.17 (dd,  $J$  = 4.8, 4.0 Hz), 5.68 (1H, d,  $J$  = 13.2 Hz, 3-H), 3.79 (1H, dd,  $J$  = 13.2, 6.4 Hz, 3a-H), 2.78 (1H, td,  $J$  = 14.0, 4.0 Hz, 7-H), 2.19 (3H, s,  $\text{CH}_3$ ), 2.07 (1H, m), 1.95 (1H, m), 1.80 (1H, m), 1.64 (2H, m), 1.49 (1H, m), 1.14 (1H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.3 (C=O), 169.2 (C=O), 145.9, 144.8, 135.1, 132.0, 128.5, 128.0, 127.5, 125.8, coupling constants of  $\text{CF}_2\text{CF}_2\text{CF}_3$  are not determined, 108.2 (t,  $^2\text{J}_{\text{C}-\text{F}}$  = 34.6 Hz, C-2), 89.4, 54.2, 42.7 (d,  $^3\text{J}_{\text{C}-\text{F}}$  = 5.3 Hz, C-3), 37.2, 25.8, 22.9, 22.5, 20.7;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  –80.6 (t,  $J$  = 9.4 Hz,  $\text{CF}_2\text{CF}_2\text{CF}_3$ ), –118.0 (q,  $J$  = 9.3 Hz,  $\text{CF}_2\text{CF}_2\text{CF}_3$ ), –126.7 (t,  $J$  = not determined  $\text{CF}_2\text{CF}_2\text{CF}_3$ ); LC-MS (ESI $^+$ ),  $m/z$  (%): 538 ( $\text{MH}^+ - \text{HOAc}$ , 100%). Anal. Calcd for  $\text{C}_{24}\text{H}_{21}\text{F}_7\text{O}_4\text{S}$ : C, 53.53; H, 3.93; S, 5.95. Found: C, 53.47; H, 4.04; S, 5.87.

**2-(Trifluoromethyl)-3-(2-naphthoyl)-7a-phenyl-octahydro-1-benzofuran-2-yl acetate (5d).** Yield 30% (290 mg) as yellow oil.  $\nu_{\text{max}}$  (KBr disc) 3026, 2959, 1718 (C=O), 1633 (C=O), 1026, 761, 697;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.46 (1H, s), 8.03 (1H, d,  $J$  = 8.8 Hz), 7.98–7.89 (3H, m), 7.63–7.57 (4H, m), 7.37 (2H, t,  $J$  = 7.2 Hz), 7.29 (1H, tt,  $J$  = 7.2, 1.2 Hz), 5.82 (1H, d,  $J$  = 12.8 Hz, 3-H), 3.77 (1H, dd,  $J$  = 12.8, 5.6 Hz, 3a-H), 2.72 (1H, td,  $J$  = 13.6, 4.0 Hz), 2.23 (1H, m), 2.13 (3H, s,  $\text{CH}_3$ ), 1.79 (2H, m), 1.69–1.56 (2H, m), 1.25 (2H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  194.2 (C=O), 168.6 (C=O), 144.2, 136.0, 135.8, 132.3, 130.1, 128.7, 128.6, 128.5, 128.0, 127.9, 127.7, 126.3, 126.1, 124.1, 122.3 (q,  $^1\text{J}_{\text{C}-\text{F}}$  = 286.3 Hz,  $-\text{CF}_3$ ), 106 (q,  $^2\text{J}_{\text{C}-\text{F}}$  = 34.4 Hz, C-2), 88.2, 52.1, 42.5, 36.3, 24.7, 22.2, 20.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ):  $\delta$  –76.4 (s, 3F); LC-MS (ESI $^+$ ),  $m/z$  (%): 482 ( $\text{MH}^+ - \text{HOAc}$ , 100%). Anal. Calcd for  $\text{C}_{28}\text{H}_{25}\text{F}_3\text{O}_4$ : C, 69.70; H, 5.52. Found: C, 69.85; H, 5.67.

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