Synthesis of trifluoromethylated dihydrofurans by addition of 1,3-dicarbonyl compounds to alkenes promoted by manganese(III) acetate

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DOI: http://dx.doi.org/10.3998/ark.5550190.p007.877

Abstract

Radical addition reaction of trifluoromethyl-1,3-dicarbonyl compounds (**1a-e**) with various alkenes (**2a-f**) was investigated in the presence of manganese(III) acetate. As a result of these reactions trifluoromethyl ketone substituted dihydrofuran and bicyclic enol ether derivatives were obtained. A formation of dihydrofuran's mechanism was proposed for all compounds. Radical addition reactions with 1,1-disubstituted alkenes were obtained in good yields, however with cyclic alkenes were shown poor yields.

Keywords: Manganese(III) acetate, dihydrofuran, oxidative addition, trifluoromethyl compounds

Introduction

The use of organofluorine compounds has been attracted significant attention due to the unique influence of a fluorine substituent on the chemical, physical and physiological properties of these compounds. Thus, organofluorine chemistry impacts many areas of everyday life and technology.[1] These compounds show a large number of industrial uses in lubricants, fire extinguisher agents, surfactants, pharmaceuticals and agrochemicals.[2] Since the fluorine atom is highly reactive and difficult to control, the synthesis of organic fluorine compounds is an ongoing area of research in synthetic organic chemistry.[3]

Traditional methods for the synthesis of organofluorine compounds are direct fluorination [4] and fluoroalkylation.[5] Manganese(III) mediated oxidative radical addition has become a valuable method for the formation of C-C bonds in the last three decades. Since manganese(III) acetate is effective for the formation of C-C bonds within the intramolecular addition to form lactones,[6]

dihydrofurans,[7] furans,[8] and lactams.[9] Another way of obtaining organofluorine compounds is addition of the corresponding fluorinated 1,3-dicarbonyl compounds with unsaturated systems mediated transition metal salts such as Mn^{3+}, Ce^{4+}, Ag^{+} etc.[10] Trifluoromethyl substituted dihydrofuran compounds may be achieved by using this method.

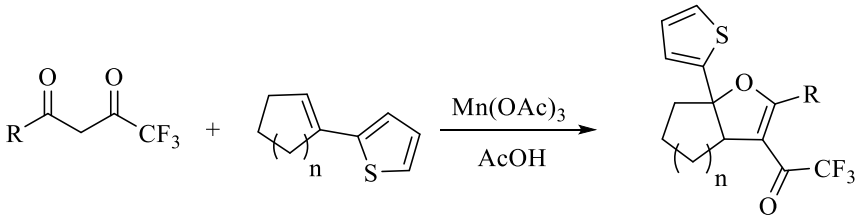
Our research group is focused on radical addition of 1,3-dicarbonyl compounds and 3-oxopropanenitriles as active methylene compounds with unsaturated compounds using manganese(III) acetate and cerium(IV) ammonium nitrate, resulting in the formation of furan and dihydrofuran compounds.[11] Previously, we described the synthesis of 3-trifluoroacetyl-4,5-dihydrofurans and 3-[dihydrofuran-2(*3H*)-ylidene]-1,1,1-trifluoroacetones by the radical addition of 1,3-dicarbonyl compounds with alkenes.[12] Recently, we obtained the fluoroacylated and fluoroalkylated tetrahydrobenzofurans by the treatment of trifluoromethyl-1,3-dicarbonyl compounds with various alkenes.[13]

In this study, we investigate the radical addition reactions of trifluoromethyl-1,3-dicarbonyl compounds (**1a-e**) with various alkenes (**2a-f**) in the presence of manganese(III) acetate resulting in the formation of trifluoromethyl ketone substituted dihydrofuran compounds.

Results and Discussion

The radical addition reactions of 2-thienyl substituted five and six-membered alkenes with triflоromethyl-1,3-dicarbonyl compounds (**2a, 2b**) were used and bicyclic enol ether derivatives were obtained (Table 1).

Table 1. The addition reaction of trifluoromethyl-1,3-dicarbonyl compounds with cyclic alkenes **2a** and **2b**



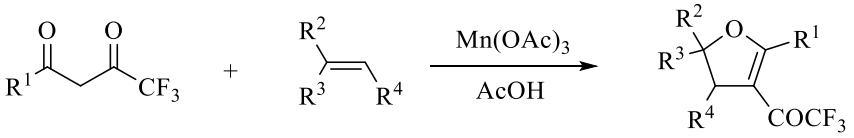
1a-e **2a-b** **3a-e**

Entry	1,3-Dicarbonyl	R	Alkene	n	Yield (%)
1	**1a**	2-Thienyl-	**2a**	2	**3a**, 35
2	**1b**	Phenyl-	**2a**	2	**3b**, 32
3	**1a**	2-Thienyl-	**2b**	1	**3c**, 43
4	**1b**	Phenyl-	**2b**	1	**3d**, 39
5	**1c**	2-Furyl-	**2b**	1	**3e**, 36

The initial reactions were attempted using 4,4,4-trifluoro-1-(2-thienyl)butane-1,3-dione **1a** and 4,4,4-trifluoro-1-phenylbutane-1,3-dione **1b** with 1-(2-thienyl)-1-cyclohexen **2a** and 1-(2-thienyl)-1-cyclopentene **2b**. Trifluoromethyl-1,3-dicarbonyl compounds **1a** and **1b** with six-membered alkene **2a** were subjected to the reaction in the presence of manganese(III) acetate, **3a** (35%) and **3b** (32%) were yielded in poor yields, similarly with five-membered alkene **2b** gave the adduct products **3c** and **3d** in 43% and 39% yields, respectively. Also, the reaction of 2-furyl substituted 1,3-dicarbonyl compound **1c** with **2b** yielded **3e** in 36%. The characterization of the products was performed by ^{1}H- and ^{13}C-NMR spectra. The signals of H-3a protons appeared in the range of 3.59-4.05 ppm with coupling constants of ^{3}J 6.8-9.2 Hz in **3a-e**. Also, an AB system was observed with ^{2}J 13.6-14.8 Hz was found for the diastereotopic H-4 protons of the addition compounds **3c-e**.

In order to obtain highly functionalized dihydrofuran compounds, 1,1-disubstituted alkenes (**2c-f**) were also used with trifluoromethyl-1,3-dicarbonyl compounds (**1a-e**) in the presence of manganese(III) acetate (Table 2).

Table 2. The addition reaction of trifluoromethyl-1,3-dicarbonyl compounds (**1a-e**) with 1,1- and 1,2-disubstituted alkenes (**2c-f**)



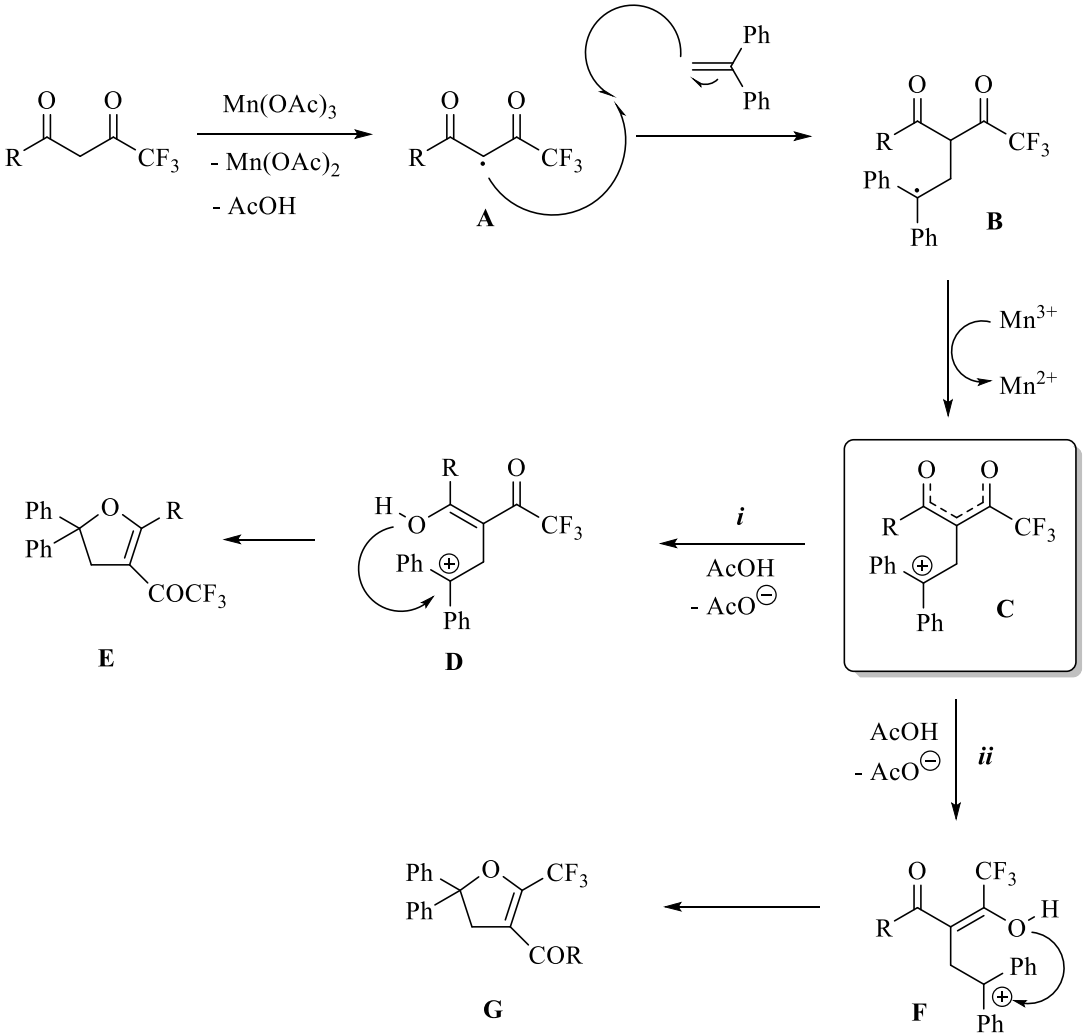
1a-e **2c-f** **3f-o**

Entry	1,3-Dicarbonyl		Alkene				Yield (%)
		R^1		R^2	R^3	R^4	
1	**1a**	2-Thienyl-	**2c**	4-FC_6H_4-	4-FC_6H_4-	H	**3f**, 83
2	**1b**	Ph-	**2c**	4-FC_6H_4-	4-FC_6H_4-	H	**3g**, 78
3	**1c**	2-Furyl-	**2c**	4-FC_6H_4-	4-FC_6H_4-	H	**3h**, 75
4	**1d**	2-Naphthyl-	**2c**	4-FC_6H_4-	4-FC_6H_4-	H	**3i**, 73
5	**1e**	CH_3-	**2c**	4-FC_6H_4-	4-FC_6H_4-	H	**3j**, 63
6	**1c**	2-Furyl-	**2d**	Ph-	Ph-	H	**3k**, 73
7	**1d**	2-Naphthyl-	**2d**	Ph-	Ph-	H	**3l**, 69
8	**1c**	2-Furyl-	**2e**	Ph-	CH_3-	H	**3m**, 37
9	**1d**	2-Naphthyl-	**2e**	Ph-	CH_3-	H	**3n**, 50
10	**1c**	2-Furyl-	**2f**	Ph-	Ph-	C_2H_5-	**3o**, 68

Treatment of **1c** with 4-fluorophenyl bearing alkene **2c** and **2d**, gave the adduct products **3h** and **3k** in 75% and 73% yields, respectively. Similarly, the addition reactions of alkenes **2c** and **2d** with the 2-naphthyl-1,3-dicarbonyl compound **1d** afforded **3i** and **3l** with 73% and 69% yields. On the other hand, when the yields of **3k-n** were compared, **3k** (73%) and **3l** (69%) had

better yields than the ones of **3m** (37%) and **3n** (50%) due to the phenyl group is better stabilizer than methyl. The characterization of the obtained compounds was realized by ^{1}H-NMR spectra. H-4 protons of the **3f-l** are appeared in the range of 3.73-4.06 ppm as singlet. But, an AB system with $^{2}J_{AB}$ 14.4-14.8 Hz was found for the diastereotopic H-4 protons of **3m** and **3n**.

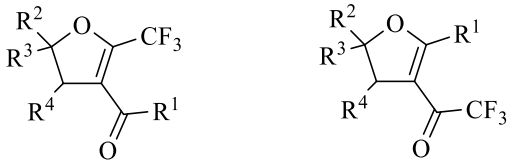
As a result of these reactions, we propose a mechanism depicted in Scheme 1. According to the mechanism, while Mn^{3+} is reduced to Mn^{2+} a C-radical **A** is formed. Then, addition of **A** to alkene forms radical intermediate **B**, meanwhile radical **B** is oxidized to the carbocation **C** by an equivalent amount of manganese(III) acetate. Eventually, addition of **C** can occur with two pathways *i* and *ii*. When the reaction follows pathway *i*, product **E** is formed while with pathway *ii* forms product **G**. Consequently, we only observed **E** and differentiated the compounds **E** and **G** by using ^{13}C-NMR.



Scheme 1. Mechanism for the radical addition reaction of trifluoromethyl-1,3-dicarbonyl compounds with alkenes in the presence of manganese(III) acetate.

According to the reaction mechanism proposed in Scheme 2, it is possible to afford compounds **A** or **B** depended on the addition of 1,3-dicarbonyl compound to alkene resulting in

the substituon of CF_3 group to carbonyl carbon and C2 carbon of dihydrofuran.[11m] But a single product was obtained. So, the exact structure of the compound was determined by ^{13}C-NMR spectra. In the spectrum of **3a**, carbonyl carbon gives a quartet at 174.8 ppm ($^2J_{C\text{-}F}$ 34.3 Hz) while the C2 carbon gives singlet at 166.5 ppm. If CF_3 substituted to C2 carbon, it would appear as quartet at about 150 ppm. The reason of obtaining only single isomer **A** is due to the cyclization of the most stable form of 1,3-dicarbonyl compound[14] (Scheme 1, product **E**). Also, it is observed that carbonyl carbon split into quartet at 173.3-176.5 ppm ($^2J_{C\text{-}F}$ 33.6-35.5 Hz) in all resulting compounds (**3a-o**). This shows that the CF_3 is substituted to carbonyl carbon not C2 on the dihydrofuran.



Scheme 2. Two possible product **A** and **B** after the radical addition of 1,3-dicarbonyl compounds **1a-e** to corresponding alkenes **2a-f**.

Conclusions

In this paper, we easily obtained highly useful intermediates for the pharmaceutically important trifluoromethyl ketone containing dihydrofuran compounds. In addition, a synthetic approach in the presence of manganese(III) acetate with radical addition reaction has been investigated for the synthesis of trifluoromethyl substituted dihydrofuran compounds apart from the fluoroalkylation and direct fluorination to obtain trifluoromethyl ketone compounds.

Experimental Section

General. 4,4,4-Trifluoro-1-(2-thienyl)butane-1,3-dione **1a**, 4,4,4-trifluoro-1-phenylbutane-1,3-dione **1b**, 4,4,4-trifluoro-1-(2-furyl)butane-1,3-dione **1c**, 4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione **1d**, and 1,1,1-trifluoropentane-2,4-dione **1e** were purchased from Sigma-Aldrich and all were used as 1,3-dicarbonyl compounds. 1-(2-Thienyl)-1-cyclohexene **2a**, 1-(2-thienyl)-1-cyclopentene **2b**, 4,4'-(ethane-1,1-diyl)bis(fluorobenzene) **2c**, ethene-1,1-diyldibenzene **2d**, 1,1-diphenyl-1-butene **2f** were prepared as described in the literature[15] and prop-1-en-2-ylbenzene **2e** were purchased from Sigma-Aldrich. All conjugated alkenes were freshly prepared before using in the radical additions. Manganese(III) acetate dihydrate (98%) was prepared using an electrochemical method according to the literature.[16]

Melting points were determined using a Gallenkamp capillary melting point apparatus. IR spectra (KBr disc, $CHCl_3$) were obtained with a Matson 1000 FTIR spectrometer in the 400-4000 cm^{-1} range with 4 cm^{-1} resolution.^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), and ^{19}F-NMR (376 MHz) spectra were recorded on a Bruker DPX-400 MHz High Performance Digital FT-NMR spectrometer in $CDCl_3$ using TMS as internal standard. The mass spectra were measured on a Waters 2695 Alliance HPLC waters micromass 2Q (ESI method) and Micromass UK Platform II (EIMS method) spectrophotometers. Element analyses were performed on a Leco 932 CHNS-O instrument. Thin layer chromatography (TLC) was performed using Merck aluminium-packed silica gel plates. Purification of products was performed by column chromatography on silica gel (Merck silica gel 60, 40-60 μm) or preparative TLC on silica gel of Merck ($PF_{254-366}$ nm).

General procedure for the synthesis of dihydrofurans (3a-o). Manganese(III) acetate dihydrate (0.83 g, 3 mmol) in 20 mL of glacial acetic acid was heated under nitrogen atmosphere to 80 °C until it dissolved. After the solution cooled down to 60 °C, a solution of 1,3-dicarbonyl compound (2 mmol) and alkene (1 mmol) in 5 mL acetic acid was added to this mixture. The reaction was completed when the initial dark brown color of the solution disappeared. Water (20 mL) was added to this solution and extracted with $CHCl_3$ (3x20 mL). The combined organic phases were neutralized with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4 and evaporated. The crude products were purified by column chromatography on silica gel or preparative TLC using n-hexane/EtOAc as eluent.

1-(2,7a-Di(2-thienyl)-3a,4,5,6,7,7a-hexahydrobenzofuran-3-yl)-2,2,2-trifluoroethanone (3a). Yellow oil, 35%, 134 mg. IR (KBr disc, cm^{-1}): 1664 (C=O), 1531 (C=C), 1203, 1138 (C-F), 758, 700. ^{1}H NMR (400 MHz, $CDCl_3$), δ_H: 8.51 (1H, dd, *J* 3.6 and 1.2 Hz), 7.69 (1H, dd, *J* 4.4 and 1.2 Hz), 7.19 (1H, td, *J* 4.4 and 1.2 Hz), 7.16 (1H, dd, *J* 5.2 and 1.2 Hz), 7.04 (1H, dd, *J* 3.6 and 1.2 Hz), 6.90 (1H, dd, *J* 5.2 and 3.6 Hz), 3.59 (1H, t, *J* 6.8 Hz, H3a), 2.60 (1H, d, *J* 15.2 Hz, H4a), 2.26 – 2.30 (1H, m, H4b), 1.91 – 1.99 (1H, m), 1.71 – 1.78 (2H, m), 1.56 – 1.65 (1H, m), 1.33 – 1.40 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 174.8 (q, $^2J_{C-F}$ 34.3 Hz, C=O), 166.5 (C2), 149.6, 135.7, 134.2, 131.9, 128.1, 126.7, 124.4, 123.3, 121.9 (q, $^1J_{C-F}$ 289.5 Hz, CF_3), 113.2 (C3), 90.7, 46.3, 36.6, 31.2, 21.8, 21.4. *m/z* (ESI^+): 385.36 (MH^+, 100%). Anal. Calcd. for $C_{18}H_{15}F_3O_2S_2$ (384.44): C, 56.24; H, 3.93; S, 16.68%. Found: C, 56.13; H, 3.85; S, 16.59%.

2,2,2-Trifluoro-1-(2-phenyl-7a-(2-thienyl)-3a,4,5,6,7,7a-hexahydrobenzofuran-3-yl)ethanone (3b). Yellow oil, 32%, 120 mg. IR (KBr disc, cm^{-1}): 3055, 2930, 2861, 1681 (C=O), 1589 (C=C), 1199 (C-F), 1143, 758, 694. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.78 (2H, dt, *J* 7.2 and 1.6 Hz), 7.51 (1H, tt, *J* 7.2 and 1.6 Hz), 7.42 (2H, tt, *J* 7.2 and 1.6 Hz), 7.24 (1H, dd, *J* 4.8 and 1.2 Hz), 7.08 (1H, dd, *J* 3.6 and 1.2 Hz), 6.96 (1H, dd, *J* 5.2 and 4.0 Hz), 3.63 (1H, td, *J* 8.0 and 7.2 Hz, H3a), 2.54 (1H, d, *J* 14.8 Hz, H4a), 2.27 – 2.31 (1H, m, H4b), 1.97 – 2.05 (1H, m), 1.39 – 1.75 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.7 (q, $^2J_{C-F}$ 35.1 Hz, C=O), 162.7(C2), 148.8, 132.1, 130.0, 127.9, 127.6, 126.6, 124.5, 123.5, 115.3 (q, $^1J_{C-F}$ 289.5 Hz, CF_3), 114.3 (C3), 90.5, 47.1, 35.5, 29.6, 20.8, 20.7. ^{19}F NMR (376 MHz, $CFCl_3$) δ_F: - 73.9 (s, CF_3).

m/z (ESI$^+$): 379.4 (MH$^+$, 100%). Anal. Calcd. for $C_{20}H_{17}F_3O_2S$ (378.41): C, 63.48; H, 4.53; S, 8.47%. Found: C, 63.35; H, 4.42; S, 8.36%.

1-(2,6a-Di(2-thienyl)-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*])-2,2,2-trifluoroethanone (3c). Yellow oil, 43%, 159 mg. IR (KBr disc, cm^{-1}): 1660 (C=O), 1531 (C=C), 1199 (C-F), 1140, 731, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.40 (1H, dd, *J* 3.6 and 1.2 Hz), 7.60 (1H, dd, *J* 5.2 and 1.2 Hz), 7.20 (1H, tt, *J* 4.8 and 1.2 Hz), 7.10 (1H, td, *J* 4.8 and 1.2 Hz), 6.99 (1H, dt, *J* 4.0 and 1.2 Hz), 6.91 (1H, tt, *J* 5.2 and 1.6 Hz), 3.96 (1H, d, *J* 8.8 Hz, H3a), 2.53 (1H, dd, *J* 13.6 and 5.2 Hz), 2.11 – 2.22 (2H, m), 1.71 – 1.90 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 174.9 (q, $^2J_{C\text{-}F}$ 34.3 Hz, C=O), 166.2 (C2), 146.0, 135.6, 133.9, 130.9, 128.0, 127.2, 125.6, 123.7, 113.2 (q, $^1J_{C\text{-}F}$ 289.5 Hz), 108.8 (C3), 99.3, 54.1, 41.5, 36.5, 24.8. *m/z* (ESI$^+$): 370.95 (MH$^+$, 100%). Anal. Calcd. for $C_{17}H_{13}F_3O_2S_2$ (370.41): C, 55.12; H, 3.54; S, 17.31%. Found: C, 55.05; H, 3.48; S, 17.27%.

2,2,2-Trifluoro-1-(2-phenyl-6a-(2-thienyl)-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*]furan-3-yl)ethanone (3d). Yellow oil, 39%, 141 mg. IR (KBr disc, cm^{-1}): 2963, 2870, 1681 (C=O), 1583 (C=C), 1205 (C-F), 1140, 760, 696. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.68 (2H, dd, *J* 8.0 and 1.2 Hz), 7.42 (1H, tt, *J* 7.6 and 1.6 Hz), 7.33 (2H, tt, *J* 8.0 and 1.6 Hz), 7.22 (1H, dd, *J* 5.2 and 1.2 Hz), 7.02 (1H, dd, *J* 4.0 and 1.2 Hz), 6.93 (1H, dd, *J* 5.2 and 3.6 Hz), 3.92 (1H, d, *J* 8.8 Hz, H4), 2.48 (1H, dd, *J* 13.6 and 5.6 Hz), 2.09 – 2.21 (2H, m), 1.72 – 1.94 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 176.1 (q, $^2J_{C\text{-}F}$ 35.1 Hz, C=O), 173.0 (C2), 146.0, 132.1, 130.0, 129.3, 128.1, 127.3, 125.7, 123.7, 112.7 (q, $^1J_{C\text{-}F}$ 290.3 Hz, CF_3), 110.5 (C3), 99.5, 54.6, 41.5, 36.0, 24.8. *m/z* (ESI$^+$): 364.99 (MH$^+$, 100%). Anal. Calcd. for $C_{19}H_{15}F_3O_2S$ (364.38): C, 62.63; H, 4.15; S, 8.80%. Found: C, 62.55; H, 4.01; S, 8.69%.

2,2,2-Trifluoro-1-(2-(2-furyl)-6a-(2-thienyl)-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*]furan-3-yl)ethanone (3e). Yellow oil, 36%, 127 mg. IR (KBr disc, cm^{-1}): 3027, 2925, 1711 (C=O), 1698 (C=C), 1592, 1221 (C-F), 926, 749, 693. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.35 (1H, d, *J* 4.0 Hz), 7.65 (1H, d, *J* 0.8 Hz), 7.29 (1H, dd, *J* 5.2 and 0.8 Hz), 7.11 (1H, dd, *J* 3.6 and 0.8 Hz), 6.98 (1H, dd, *J* 5.2 and 4.0 Hz), 6.61 (1H, dd, *J* 3.6 and 1.6 Hz), 4.05 (1H, d, *J* 9.2 Hz, H3a), 2.68 (1H, dd, *J* 13.6 and 5.6 Hz), 2.21 – 2.32 (2H, m), 1.82 – 1.98 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 174.2 (q, $^2J_{C\text{-}F}$ 34.3 Hz, C=O), 161.3 (C2), 146.9, 145.5, 144.2, 127.2, 125.8, 124.2, 122.6, 121.8 (q, $^1J_{C\text{-}F}$ 289.5 Hz, CF_3), 112.8, 109.3 (C3), 99.9, 53.7, 41.3, 36.4, 24.7. *m/z* (ESI$^+$): 355 (MH$^+$, 100%). Anal. Calcd. for $C_{17}H_{13}F_3O_3S$ (354.34): C, 57.62; H, 3.70; S, 9.05%. Found: C, 57.51; H, 3.59; S, 8.98%.

1-(5,5-Bis(4-fluorophenyl)-2-(2-thienyl)-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3f). Yellow oil, 83%, 361 mg. IR (KBr disc, cm^{-1}): 2940, 2862, 1668 (C=O), 1569 (C=C), 1529, 1477, 1263 (C-F), 1201, 918, 850, 762, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.66 (1H, dd, *J* 4.0 and 1.1 Hz), 7.77 (1H, dd, *J* 5.0 and 1.1 Hz), 7.40 – 7.45 (4H, m), 7.28 (1H, d, *J* 5.0 Hz), 7.06 – 7.12 (4H, m), 3.99 (2H, s, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.4 (q, $^2J_{C\text{-}F}$ 34.6 Hz, C=O), 165.8 (C2), 164.7, 162.2, 139.9, 136.2, 134.8, 131.5, 129.6, 129.0, 128.3, 127.6, 119.3 (q, $^1J_{C\text{-}F}$ 284 Hz, CF_3), 117.6, 117.1, 116.8, 116.5, 115.6, 115.4, 103.7 (C3), 93.1 (C5), 43.5 (C4). Anal.

Calcd. for $C_{22}H_{13}F_5O_2S$ (436.39): C, 60.55; H, 3.00; S, 7.35%. Found: C, 60.44; H, 2.93; S, 7.27%.

1-(5,5-Bis(4-fluorophenyl)-2-phenyl-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3g). Yellow oil, 78%, 335 mg. IR (KBr disc, cm^{-1}): 3063, 2980, 1685 (C=O), 1575 (C=C), 1199 (C-F), 1138, 904, 764, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.67 (2H, dd, *J* 7.2 and 1.3 Hz), 7.31 – 7.35 (1H, m), 7.23 – 7.27 (2H, m), 7.16 – 7.21 (4H, m), 6.83 – 6.89 (4H, m), 3.73 (2H, s, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.2 (q, $^2J_{C\text{-}F}$ 35.05 Hz, C=O), 163.7, 163.6, 161.2 (C2), 139.3, 133.1, 131.5, 130.4, 129.4, 128.9, 128.8, 128.6, 128.3, 128.1, 127.8, 127.4, 127.3, 126.8, 121.1 (q, $^1J_{C\text{-}F}$ 291.7 Hz, CF_3), 116.7, 116.6, 104.8 (C3), 92.7 (C5), 44.7 (C4). ^{19}F-NMR (376 MHz, $CFCl_3$) δ_F: -75.92 (s, CF_3), -113.00 (s, C-F). Anal. Calcd. for $C_{24}H_{15}F_5O_2$ (430.37): C, 66.98; H, 3.51%. Found: C, 66.86; H, 3.44%.

1-(5,5-Bis(4-fluorophenyl)-2-(2-furyl)-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3h). Pale yellow oil, 75%, 315 mg. IR (KBr disc, cm^{-1}): 3028, 2922, 1685 (C=O), 1585, 1556 (C=C), 1209 (C-F), 1136, 758, 702. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.42 (1H, d, *J* 3.7 Hz), 7.74 (1H, d, *J* 1.3 Hz), 7.47 (4H, dd, *J* 7.0 and 2.1 Hz), 7.12 (4H, t, *J* 8.6 Hz), 6.68 (1H, dd, *J* 3.7 and 1.7 Hz), 3.96 (2H, s, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 173.4 (q, $^2J_{C\text{-}F}$ 35.5 Hz, C=O), 163.7 (C2), 161.2, 160.1, 146.8, 143.9, 139.1, 139.0, 127.6, 122.6, 118.5 (q, $^1J_{C\text{-}F}$ 290.3 Hz, CF_3), 115.7, 115.6, 115.3, 112.8, 103.3 (C3), 93.1 (C5), 42.8 (C4). ^{19}F NMR (376 MHz, $CFCl_3$) δ_F: -76.05 (s, CF_3), -113.52 (s, C-F). Anal. Calcd. for $C_{22}H_{13}F_5O_3$ (420.33): C, 62.86; H, 3.12%. Found: C, 62.79; H, 3.01%.

1-(5,5-Bis(4-fluorophenyl)-2-(2-naphthyl)-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3i). Pale yellow oil, 73%, 350 mg. IR (KBr disc, cm^{-1}): 3055, 2930, 2861, 1681 (C=O), 1589 (C=C), 1544, 1448, 1276, 1199 (C-F), 1143, 758, 694. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.58 (1H, s), 7.99 (1H, d, *J* 7.8 Hz), 7.83 – 7.92 (3H, m), 7.64 (1H, td, *J* 7.0 and 1.6 Hz), 7.59 (1H, td, *J* 7.0 and 1.6 Hz), 7.45 – 7.50 (4H, m), 7.09 – 7.15 (4H, m), 4.05 (2H, s, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.4 (q, $^2J_{C\text{-}F}$ 34.3 Hz, C=O), 163.9 (C2), 161.5, 139.7, 135.3, 132.8, 132.7, 131.5, 131.4, 129.5, 128.6, 128.0, 127.9, 127.8, 127.0, 126.1, 125.7, 118.6 (q, $^1J_{C\text{-}F}$ 290.3 Hz, CF_3), 116.0, 115.9, 115.8, 115.7, 105.2 (C3), 93.0 (C5), 43.7 (C4). ^{19}F NMR (376 MHz, $CFCl_3$) δ_F: -76.198 (s, CF_3), -113.8 (s, C-F). Anal. Calcd. for $C_{28}H_{17}F_5O_2$ (480.43): C, 70.00; H, 3.57%. Found: C, 69.95; H, 3.49%.

1-(5,5-Bis(4-fluorophenyl)-2-methyl-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3j). Pale yellow oil, 63%, 231 mg. IR (KBr disc, cm^{-1}): 3063, 2980, 1685 (C=O), 1575 (C=C), 1199 (C-F), 1138, 904, 764, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.37 (4H, dd, *J* 8.8 and 2.1 Hz), 7.07 (4H, dd, *J* 8.7 and 2.1 Hz), 3.81 (2H, s, H4), 2.52 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 176.5 (q, $^2J_{C\text{-}F}$ 34.9 Hz, C=O), 175.7 (C2), 163.6, 161.2, 139.8, 139.6, 139.5, 139.2, 127.9, 127.8, 127.7, 127.5, 121.0 (q, $^1J_{C\text{-}F}$ 289.5 Hz, CF_3), 105.5 (C4), 93.7 (C5), 42.4 (C4), 15.7 (CH_3). Anal. Calcd. for $C_{19}H_{13}F_5O_2$ (368.30): C, 61.96; H, 3.56%. Found: C, 61.85; H, 3.48%.

2,2,2-Trifluoro-1-(2-(2-furyl)-5,5-diphenyl-4,5-dihydrofuran-3-yl)ethanone (3k). Yellow oil, 73%, 280 mg. IR (KBr disc, cm^{-1}): 3028, 2922, 1685 (C=O), 1585, 1556 (C=C), 1209 (C-F), 1136, 758, 692. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.41 (1H, d, *J* 4.0 Hz), 7.72 (1H, d, *J* 1.6 Hz),

7.29 – 7.49 (10H, m), 6.65 (1H, dd, *J* 3.2 and 1.6 Hz), 4.01 (2H, s, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 173.8 (q, $^2J_{C-F}$ 34.3 Hz, C=O), 160.5 (C2), 146.7, 144.2, 143.5, 128.6, 128.1, 125.7, 122.4, 118.6, (q, $^1J_{C-F}$ 289.6 Hz, CF_3) 112.7, 103.5 (C3), 93.9 (C5), 43.2 (C4). *m/z* (%): 384 (6.35, M^+), 366 (4.68, M^+ - H_2O), 355 (0.22, M^+ - C_2H_5), 315 (3.59, M^+ - CF_3), 287 (5.31, M^+ - CF_3CO), 77 (32.23, $C_6H_5^+$). Anal. Calcd. for $C_{22}H_{15}F_3O_3$ (384.35): C, 68.75; H, 3.93%. Found: C, 68.67; H, 3.84%.

2,2,2-Trifluoro-1-(2-naphthyl)-5,5-diphenyl-4,5-dihydrofuran-3-yl)ethanone (3l). Yellow oil, 69%, 306 mg. IR (KBr disc, cm^{-1}): 3055, 2930, 2861, 1681 (C=O), 1589 (C=C), 1544, 1448, 1276, 1199 (C-F), 1143, 758, 694. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.56 (1H, s), 7.78 – 7.94 (6H, m), 7.29 – 7.54 (6H, m), 7.29 – 7.40 (5H, m), 4.06 (2H, m, H4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.5 (q, $^2J_{C-F}$ 34.3 Hz, C=O), 171.9 (C2), 143.8, 137.6, 135.0, 132.4, 132.3, 131.1, 130.0, 129.2, 128.7, 128.3, 128.2, 128.1, 127.7, 127.6, 126.6, 121.3 (q, $^1J_{C-F}$ 289.6 Hz, CF_3), 105.1 (C3), 93.6 (C5), 43.3 (C4). ^{19}F NMR (376 MHz, $CFCl_3$) δ_F: -76.148 (s, CF_3). *m/z* (ESI^+): 445 (MH^+, 100%). Anal. Calcd. for $C_{28}H_{19}F_3O_2$ (444.44): C, 75.67; H, 4.31%. Found: C, 75.61; H, 4.28%.

2,2,2-Trifluoro-1-(2-(2-furyl)-5-methyl-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (3m). Yellow oil, 37%, 119 mg. IR (KBr disc, cm^{-1}): 1671 (C=O), 1539 (C=C), 1207 (C-F), 1136. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.43 (1H, d, *J* 3.6 Hz), 7.70 (1H, d, *J* 1.2 Hz), 7.26 – 7.47 (5H, m), 6.40 (1H, dd, *J* 3.6 and 1.2 Hz), 3.66 (1H, d, *J* 14.8 Hz, H4a), 3.50 (1H, d, *J* 14.8 Hz, H4b), 1.87 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 173.3 (q, $^2J_{C-F}$ 34.3 Hz, C=O), 161.0 (C2), 146.8, 144.9, 144.6, 128.9, 128.1, 124.4, 122.4, 118.8 (d, $^1J_{C-F}$ 289.6 Hz, CF_3), 112.9, 103.5 (C3), 91.4 (C5), 43.4 (C4), 29.3 (CH_3). *m/z* (%): 322 (M^+, 10.30), 304 (M^+ - H_2O, 5.45), 253 (M^+ - CF_3, 4.06), 91 ($C_6H_5CH_2^+$, 13.05), 77 ($C_6H_5^+$, 52.06). Anal. Calcd. for $C_{17}H_{13}F_3O_3$ (322.28): C, 63.36; H, 4.07%. Found: C, 63.25; H, 4.00%.

2,2,2-Trifluoro-1-(5-methyl-2-(2-naphthyl)-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (3n). Pale yellow oil, 50%, 191 mg. IR (KBr disc, cm^{-1}): 3065, 2967, 2930, 1660 (C=O), 1585 (C=C), 1548, 1197 (C-F), 1141, 756, 696. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.53 (1H, s), 7.96 (2H, d, *J* 8.0 Hz), 7.89 (2H, dd, *J* 7.2 and 2.0 Hz), 7.59 (1H, td, *J* 8.0 and 1.6 Hz), 7.56 (1H, td, *J* 8.4 and 1.6 Hz), 7.34 – 7.49 (5H, m), 3.63 (1H, dd, *J* 14.4 and 1.2 Hz, H4a), 3.52 (1H, dd, *J* 14.4 and 1.2 Hz, H4b), 1.90 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.5 (q, $^2J_{C-F}$ 33.6 Hz, C=O), 172.6 (C2), 144.9, 135.0, 132.3, 130.9, 129.3, 128.8, 128.2, 127.9, 127.7, 127.6, 126.7, 125.6, 124.2, 118.5 (q, $^1J_{C-F}$ 289.5 Hz, CF_3) 104.7 (C3), 90.8 (C5), 43.8 (C4), 29.2 (CH_3). ^{19}F NMR (376 MHz, $CFCl_3$) δ_F: -76.342 (s, CF_3). *m/z* (ESI^+): 383 (MH^+ , 100%). Anal. Calcd. for $C_{23}H_{17}F_3O_2$ (382.38): C, 72.24; H, 4.48%. Found: C, 72.15; H, 4.41%.

1-(4-Ethyl-2-(2-furyl)-5,5-diphenyl-4,5-dihydrofuran-3-yl)-2,2,2-trifluoroethanone (3o). Dark yellow oil, 68%, 280 mg. IR (KBr disc, cm^{-1}): 3059, 2965, 2930, 1646 (C=O), 1606 (C=C), 1211, 1134 (C-F). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.21 (1H, d, *J* 4.0 Hz), 7.71 (1H, d, *J* 1.6 Hz), 7.65 (2H, d, *J* 7.6 Hz), 7.46 (2H, d, *J* 7.6 Hz), 7.26 – 7.35 (6H, m), 6.62 (1H, d, *J* 3.2 Hz), 4.15 (1H, t, *J* 5.6 Hz, H4), 1.44 – 1.62 (2H, m), 0.54 (3H, t, *J* 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 174.1 (q, $^2J_{C-F}$ 35.1 Hz, C=O), 159.6 (C2), 146.8, 144.6, 143.6, 139.5, 128.4, 128.1, 127.6,

126.5, 125.9, 122.2, 118.6 (q, $^{1}J_{C\text{-}F}$ 289.5 Hz, CF_3), 112.8, 112.6, 111.3 (C3), 97.1 (C5), 49.0 (C4), 25.4, 10.3. *m/z* (ESI^+): 413 (MH^+ , 100%). Anal. Calcd. for $C_{24}H_{19}F_3O_3$ (412.40): C, 69.90; H, 4.64%. Found: C, 69.82; H, 4.57%.

Acknowledgements

The authors are grateful to Kocaeli University BAP (2008/28, 2010/57 and 2012/28) Science Research Foundations for financial support. The author Emre Biçer would like to thank to Mrs. Hilal Biçer for her encouragement, support and endless patience and help for evaluation of NMR data during the typing of this paper.

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