Synthesis of furan-substituted dihydrofuran compounds by radical-cyclization reactions mediated by manganese(III) acetate

Mehmet Yılmaz,[a] Emre Biçer,[b]* Aslı Ustalar,[a] and A. Tarık Pekel[b]

[a]Department of Chemistry, Faculty of Arts and Sciences, Kocaeli University, 41380 Umuttepe/Kocaeli, Turkey
[b]Department of Chemistry, Faculty of Science, Ankara University, 06100, Tandoğan/Ankara, Turkey
E-mail: bicer_emre@yahoo.com

DOI: http://dx.doi.org/10.3998/ark.5550190.p008.482

Abstract

In this study, novel furan substituted dihydrofuran compounds were synthesized by the radical addition of 1,3-dicarbonyl compounds to 1,1- and 1,2-disubstituted alkenes using manganese(III) acetate in HOAc. It is observed that 1,1-disubstituted alkenes gave better yields whereas 1,2-disubstituted alkenes gave moderate yields. Besides, 1,2-disubstituted alkenes gave us *cis*-isomers whereas trifluoromethylated 1,3-dicarbonyl compounds with 1,2-disubstituted alkenes gave us *trans*-isomers of dihydrofuran determined by NOSY spectra.

Keywords: 4,5-Dihydrofuran, manganese(III) acetate, cyclization, furan substituted

Introduction

During the past decades manganese(III) acetate is used as one-electron oxidant for the formation of C-C bonds in free-radical chemistry.[1] Radical precursors such as carboxylic acids, malonates, ketones, 1,3-diketones, and β-keto esters treated with manganese(III) acetate undergo inter- and intramolecular cyclization for the formation of furans,[2] dihydrofurans,[3] lactones,[4] and lactams.[5] In addition, manganese(III) acetate-promoted addition reactions have been applied to the synthesis of natural products, such as pheromones.[6]

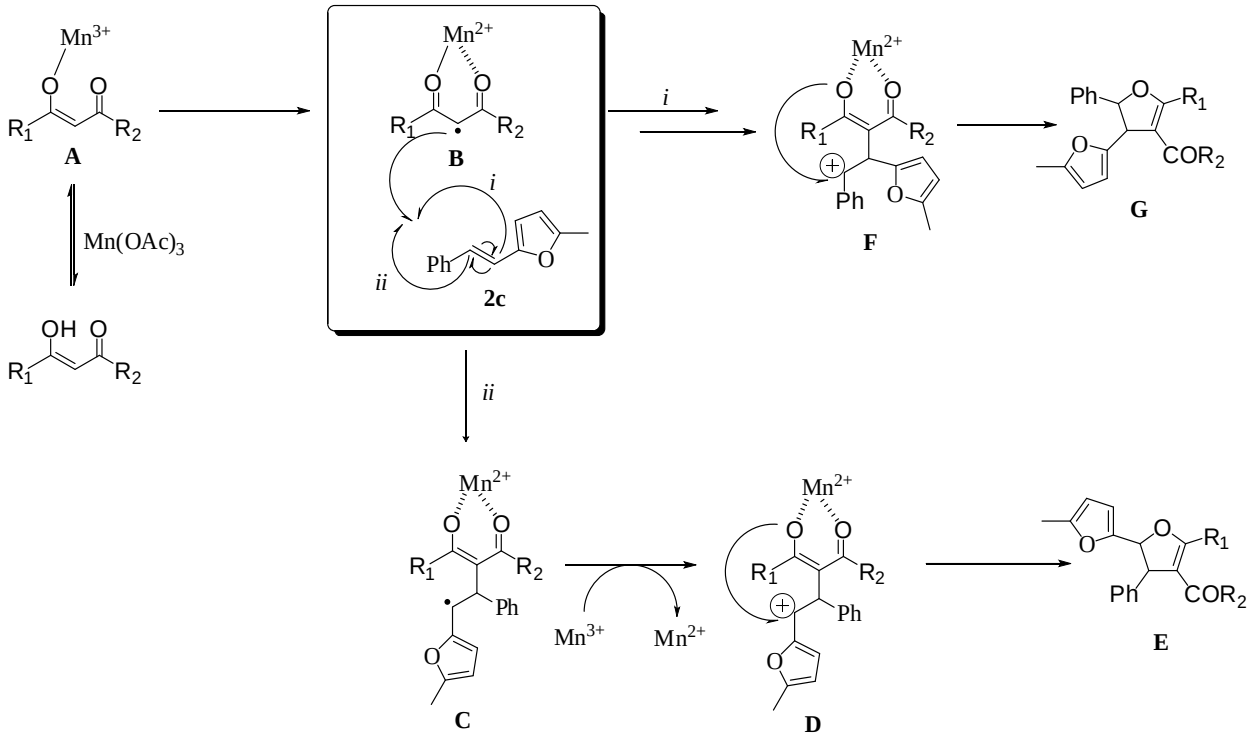
Previously, we have reported the formation of furan[7] and dihydrofuran[8-10] derivatives resulting in the radical additions with alkenes and alkynes. 4-Hydrocoumarins, 2-hydroxy-1,4-naphtoquinones [11] and 3-oxopropanenitriles[12] have been used as enolizable compounds. Also, 3-cyanodihydrofurans synthesized by our group has shown anti-bacterial and anti-fungal activities.[13]

In this study, aiming the synthesis of the 2-furyl substituted dihydrofuran compounds (**3a-e**, **4a-d, 5a-d**) was used as 1,1- and 1,2-disubstituted alkenes with 1,3-dicarbonyl compounds

mediated by manganese(III) acetate in HOAc at 60 ºC. As a result of the radical addition reactions, we obtained the 2-furyl substituted 4,5-dihydrofuran compounds with modest to high yields. Besides, an investigation of the configuration determination was studied in the resulting dihydrofurans.

Results and Discussion

In our previous studies, we published radical addition reactions of 1,1- and 1,2-disubstituted alkenes with various 1,3-dicarbonyl compounds. It is observed that a single carbocation center is formed with 1,1-disubstituted alkenes while two possible carbocation centers are formed with 1,2-disubstituted alkenes.[14,15]



Scheme 1. Reaction mechanism for the formation of 2- furyl substituted 4,5-dihydrofurans.

Reaction mechanism proposed for radical addition reactions was depicted in Scheme 1. According to the mechanism, interaction of $Mn(OAc)_3$ with 1,3-dicarbonyl compounds result in a manganese(III)-enolato complex **A**. An α-carbon radical **B** is formed while Mn^{3+} is reduced to Mn^{2+}. Addition of **B** to the alkene **2c** may be achieved in two pathways (*i* and *ii*). If the reaction follows pathway *i*, radical intermediate **F** is generated and final product **G** is obtained. On the other hand, if the pathway *ii* occurs, radical intermediate **C** is generated, which then oxidizes to carbocation **D** with an equivalent manganese(III) acetate. Thereafter the intramolecular ring

closure dihydrofuran **E** is obtained. Moreover, there are two possible carbocations can be formed depending on the addition to alkene. This resulted in the formation of products **E** and **G**. However, only 4,5-dihydrofuran product **E** was isolated. The other cyclization product has not been observed. Differentiation of products **E** and **G** was clarified by ^{1}H-NMR and HMBC as described in literature.[16]

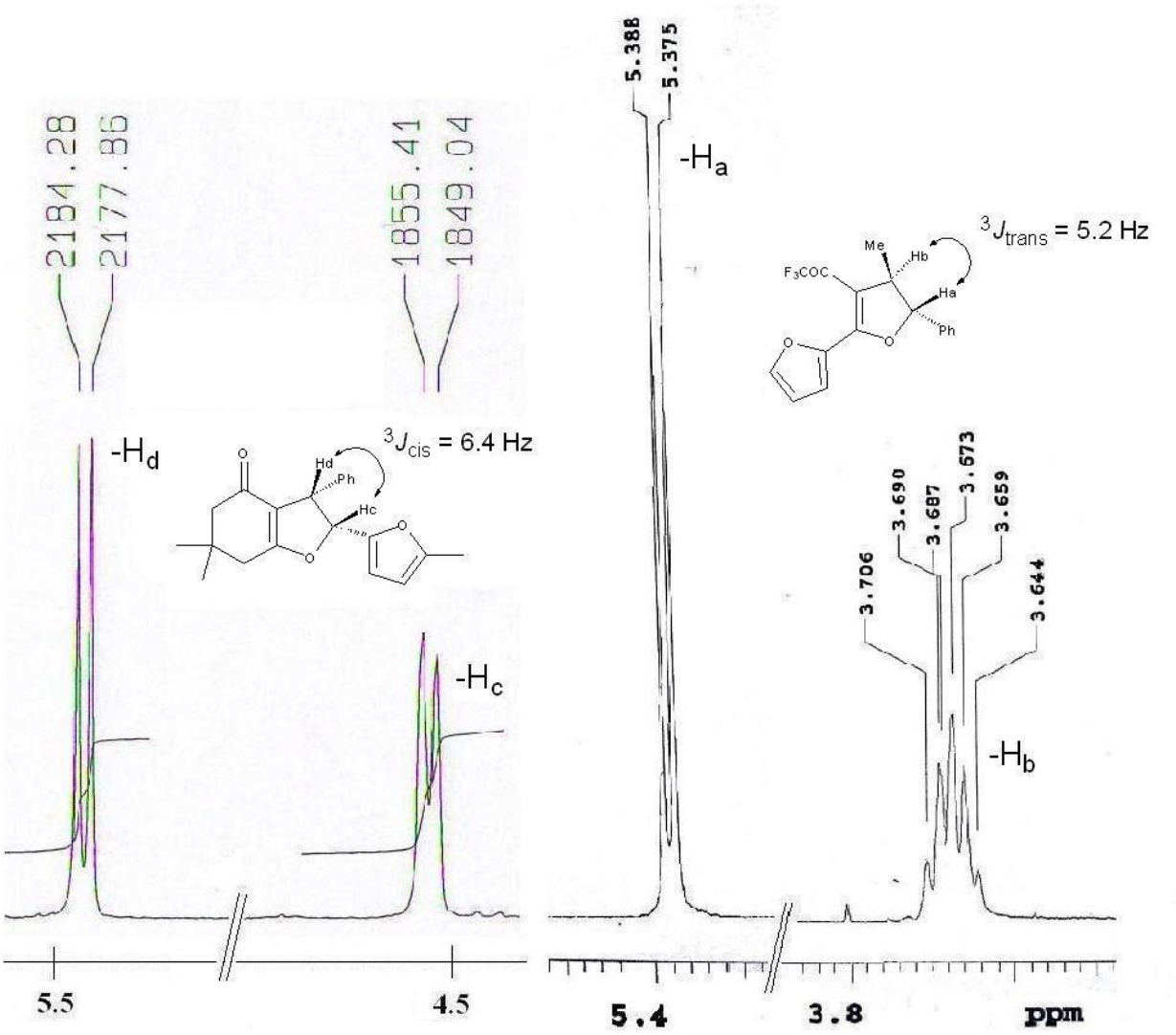
2-Furyl moeity in the dihydrofuran (**4b**) resulting from the reaction of 1,3-dicarbonyl compound **1c** with 1,2-disubstituted alkene **2b** may be substituted on dihydrofuran's 2- or 3-position. The determination of the product formed was detected by using HMBC. Accordingly, due to C-3 carbon atom correlates with the *ortho*-H atoms of the phenyl group, this indicates that phenyl group is attached to C-3 and thus the 2-furyl group is attached to the C-5 atom of the dihydrofuran.

Within this study, 1,1-disubstituted alkene **2a** was used in the radical addition reactions with various 1,3-dicarbonyl compounds. It is determined that the product yields are higher than the ones of **2b**. **3c** was yielded in 80% with the radical cyclization reaction of **1c** with **2a**. However, the radical cyclization with another cyclic 1,3-dicarbonyl compound **1d** yielded **3d** in 57%. The ^{1}H-NMR spectra of the products showed that the H-4 protons in **3a-b** and H-3 protons in **3c-e** were diastereotopic with the chemical shifts of δ = 3.2 - 3.8 ppm. Also, an AB system with $^{2}J_{AB}$ = 14.4 - 14.8 Hz was found for H-4 protons in **3a** and **3b**. The AB system was further split into a quartet by a coupling of ^{5}J = 1.5 - 2.0 Hz with the protons of methyl group substituted to C-2 carbon. Similarly, H-3 protons split into a dublet by a ^{5}J = 2.0 Hz with the H-7 in **3c-e**.

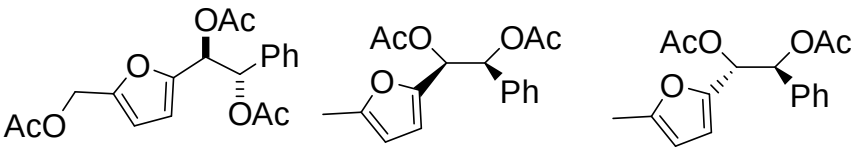
Treatment of **1b** with **2c** gave us a mixture of *cis*- and *trans*-isomers. These isomers were identified by ^{1}H-NMR spectrum, namely H-4 proton of **4a** resonates with H-5 proton with $^{3}J_{trans}$ = 5.5 Hz, whereas other isomer resonated with $^{3}J_{cis}$ = 6.5 Hz. The amount of the isomers were 1:1 which was calculated from ^{1}H-NMR spectrum. However, interestingly, the cyclization reaction of **1c** with **2b** gave us **4b** as a sole isomer which is in *cis*-configuration due to vicinal constant coupling $^{3}J_{cis}$ = 6.4 Hz between H-2 and H-3 protons. Similarly, the cyclization reaction of **1d** and **1e** gave use **4c** and **4d** in *cis*-configuration in 42% and 60% yields, respectively. Thus, this result is considered from the hindered structure of the cyclohexenone. As a result of the rotational barrier, *cis*-isomer is obtained. The configuration of the compounds **4b-d** and were identified by using ^{1}H-NMR and NOSY. Thus, discussions about the configuration of 2-furyl and phenyl moeities directed us to understand the configuration of the compounds. In the NOSY spectum of **4b**, it is definitely clear that the phenyl and 2-furyl moeities are in *cis*-configuration, because of the fact that strong correlation of H-2 and H-3 is clearly seen in the spectrum. Also, coupling constants of H-2 and H-3 were found in ^{3}J = 6.4 Hz which is in *cis*-configuration belonging to **4b-d**. Furthermore, H-3 protons gave a dublet by a ^{5}J = 1.6 Hz with the H-7 (Scheme 2). In addition, H-2 protons of **4b-d** were observed at lower field than that of H-3 protons, due to H-2 protons are next to the ether oxygen.

Additionally, acetylation of alkene was observed as a side product in the cyclization reactions of **2b**. The cyclization reactions of alkene **2b** gave us acetoxy substituted alkene **6** as well as 1,2-

acetoxy substituted alkenes in both *syn*- and *anti*- products as a mixture in 1:5 ratio (**7** and **8**) (Scheme 3).



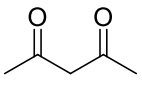
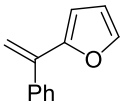
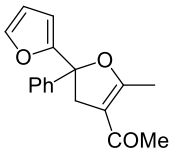
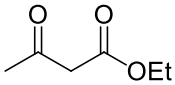
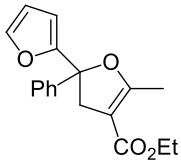
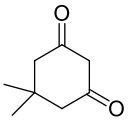
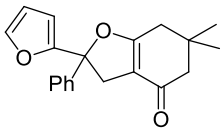
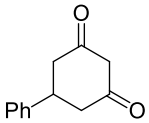
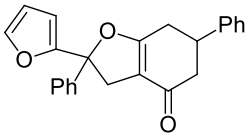
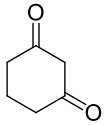
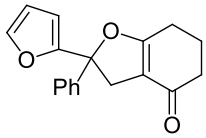
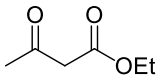
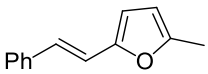
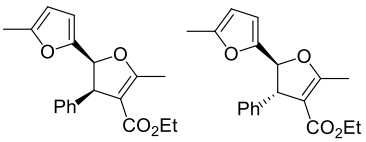
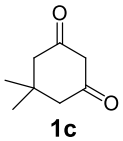
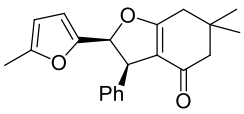
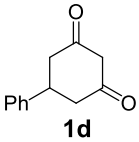
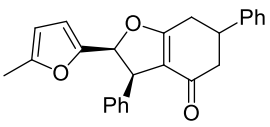
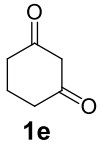
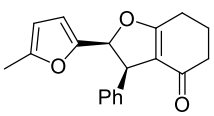
Scheme 2. Part of NMR spectra of the compounds **4b** and **5b.**



6 **7** **8**

Scheme 3. Side-products were obtained by the reaction of **2b** with 1,3-dicarbonyl compounds.

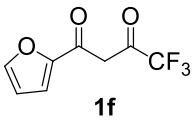
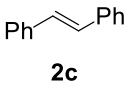
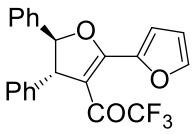
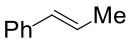
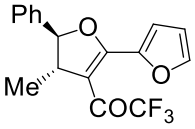
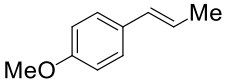
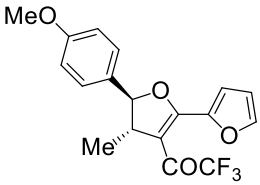
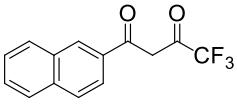
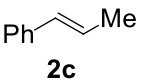
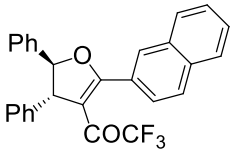
Table 1. Radical cyclization reaction of 1,3-dicarbonyls with 2-furyl substituted alkenes

Entry	1,3-Dicarbonyl	Alkene	Product		Yield (%)
1	 **1a**	 **2a**		**3a**	56
2	 **1b**	**2a**		**3b**	67
3	 **1c**	**2a**		**3c**	80
4	 **1d**	**2a**		**3d**	57
5	 **1e**	**2a**		**3e**	60
6	 **1b**	 **2b**		**4a**	15
7	 **1c**	**2b**		**4b**	64
8	 **1d**	**2b**		**4c**	42
9	 **1e**	**2b**		**4d**	60

Finally, a comparison of 1,1-disubstituted alkene **2a** with 1,2-disubstituted **2b** with the reaction of **1c** in terms of the yields, better yields were observed with 1,1-disubstituted alkene **2a** because of the intermediate carbocation stability.

On the other hand, these results led us to deal with configuration change. Thus, trifluoromethyl substituted 1,3-dicarbonyl compounds **1f** and **1g** with 1,2-disubstituted alkenes **2c-d** were employed in the radical cyclization reactions in the presence of manganese(III) acetate (Table 2). It has been reported by Antonioletti *et.al.* that the vicinal coupling constants of methine protons appear J_{cis} = 6 -12 Hz in *cis*-configuration of dihydrofurans, whereas J_{trans} = 3-6 Hz in *trans*-configuration.[17-19] Surprisingly, we observed that the H-4 and H-5 protons are in *trans*-configuration in terms of the coupling constants of the compounds **5a-d**. We observed lower coupling constants ranging from 2.4 Hz to 5.2 Hz which are less than that of the *cis*-isomers of **4a-d**. A part of NMR spectrum belonging to H-4 and H-5 protons of **5b** was shown in Scheme 2. Thus, the lower coupling constants indicate us that the compounds **5a-d** are in *trans*-configuration.

Table 2. Radical cyclization reaction of 1,3-dicarbonyls with 1,2-disubstituted alkenes

Entry	1,3-Dicarbonyl	Alkene	Product		Yield (%)
1	 **1f**	 **2c**		**5a**	18
2	**1f**	 **2d**		**5b**	40
3	**1f**	 **2d**		**5c**	28
4	 **1g**	 **2c**		**5d**	21

Conclusions

Consequently, radical addition reactions of 1,3-dicarbonyl compounds with 1,1- and 1,2-disubstituted alkenes were investigated in this study in the presence of manganese(III) acetate, it

is observed that the highest yields were observed with 1,1-disubstituted alkene **2a**. However, *syn*- and *anti*- products mixture and acetoxy substituted alkene products obtained from the reaction of **2b** with ethylacetoacetate (**1b)**. Thus, due to the strained structure of the cyclic 1,3-carbonyl compounds **1c-e**, only one *cis*-isomers of the products was obtained in the radical cyclization reaction of **2b**. On the other hand, on the contrary to the results with the reactions of alkene **2b**, *trans*-isomers were obtained in the reaction of trifluoromethylated-1,3-dicarbonyl compounds with various 1,2-disubstituted alkenes (**2c** and **2d**).

Experimental Section

General. Acetylacetone (**1a**), ethyl acetoacetate (**1b**), dimedone (**1c**), 5-phenyl-1,3-cyclohexanedione (**1d**), 1,3-cyclohexanedione (**1e**) 4,4,4-trifluoro-1-(2-furyl)butane-1,3-dione (**1f**), and 4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione (**1g**) are commercially available products and all were used as 1,3-dicarbonyl compounds. 2-(1-Phenylvinyl)furan (**2a**), 2-methyl-5-[(*E*)-2-phenylvinyl]furan (**2b**)**,** *trans*-stilbene (**2c**), (*E*)-1-propenylbenzene (**2d**), and 1-methoxy-4-[(1*E*)-1-propenyl]benzene (**2e**) were prepared as described in the literature.[10, 20-24] Manganese(III) acetate dihydrate (98%) was prepared using an electrochemical method according to the literature.[25] All compounds were purified through column chromatography or preparative TLC and characterized by IR, ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR, HMBC, NOSY, LC/MS, and microanalysis.

Melting points were determined using a Gallenkamp capillary melting point apparatus. IR spectra (KBr disc) were obtained with a Matson 1000 FTIR spectrometer in the 400-4000 cm^{-1} range with 4cm^{-1} resolution. ^{1}H-NMR, ^{13}C-NMR and ^{19}F-NMR spectra were recorded on a Bruker DPX-400 MHz High Performance Digital FT-NMR spectrometer. The mass spectra were measured on a Micromass UK Platform II spectrophotometer. Element analyses were performed on a Leco 932 CHNS-O instrument.

General procedure for the synthesis of dihydrofurans. Manganese(III) acetate dihydrate (0.83 g, 3 mmol) in 20 mL of glacial HOAc was heated under nitrogen atmosphere to 80 ºC until it dissolved. Thereafter the solution was cooled to 60 ºC, a solution of 1,3-dicarbonyl compound (2 mmol) and alkene (1 mmol) in 5 mL HOAc was added to this mixture. The reaction was completed when the initial dark brown color of the solution had changed to red. H_2O (20 mL) was added and the mixture extracted with $CHCl_3$ (3x20 mL). The combined organic phases were neutralized with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4 and then evaporated. Crude products were purified by column chromatography on silica gel or preparative TLC using *n*-hexane/EtOAc as eluent.

1-(5-(2-Furyl)-2-methyl-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (3a). Yellow oil, 56%, 150 mg. FT-IR (KBr disc, cm^{-1}): 3061, 2925, 2867, 1674 (C=O), 1604 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.35 – 7.44 (6H, m), 6.34 (1H, dd, *J* 3.3, 1.8 Hz), 6.22 (1H, d, *J* 3.3 Hz), 3.87 (1H,

dd, *J* 14.4, 1.5 Hz, H4b), 3.37 (1H, dd, *J* 14.4, 1.5 Hz, H4a), 2.39 (3H, d, *J* 1.5 Hz), 2.25 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 193.99 (C=O), 165.52, 155.09, 143.23, 142.75, 128.25, 127.87, 125.16, 111.82, 110.14, 108.75, 86.75, 77.20, 43.04, 29.32, 14.93. *m/z* (%): 268 (21.9, M^+), 250 (3.9, M^+ - H_2O), 225 (14.1, M^+ - C_2H_3O), 77 (13.4, $C_6H_5^+$), 43 (100.0, $C_2H_3O^+$). Anal. Calcd. for $C_{17}H_{16}O_3$ (268.31): C, 76.10; H, 6.01%. Found: C, 76.24; H, 6.19%.

Ethyl 5-(2-furyl)-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate (3b). Yellow oil, 67%, 200 mg. FT-IR (KBr disc, cm^{-1}): 3119, 3060, 2979, 2932, 1699 (C=C), 1653 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H:7.34 – 7.44 (6H, m), 6.34 (1H, dd, *J* 3.3, 1.8 Hz), 6.15 (1H, dd, *J* 3.3, 0.7 Hz), 4.20 (2H, q, *J* 7.1 Hz), 3.83 (1H, dq, *J* 14.6, 1.5 Hz, H4b), 3.32 (1H, dq, *J* 14.6, 1.5, H4a), 2.34 (3H, t, *J* 1.6 Hz), 1.30 (3H, t, *J* 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 166.3 (C=O), 166.0 (C=C), 155.6, 143.5, 143.3, 128.5, 128.1, 125.5, 110.4, 108.9, 101.8 (C=C), 87.1 (C-O), 59.9, 42.7, 14.7, 14.4. *m/z* (%): 298 (1.8, M^+), 280 (0.3, M^+ - H_2O), 252 (13.4, M^+ - C_2H_5OH), 224 (2.9, M^+ - $C_3H_6O_2$), 128 (5.0, $C_5H_8O_3^+$), 77 (9.5, $C_6H_5^+$). Anal. Calcd. for $C_{18}H_{18}O_4$ (298.33): C, 72.47; H, 6.08%. Found: C, 72.31; H, 6.24%.

2-(2-Furyl)-6,6-dimethyl-2-phenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (3c). Yellow oil, 80%, 227 mg. FT-IR (KBr disc, cm^{-1}): 3056, 2954, 2890, 1633 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.40 – 7.42 (1H, m), 7.35 – 7.39 (5H, m), 6.32 (1H, dd, *J* 3.6, 1.6 Hz), 6.14 (1H, dd, *J* 3.6, 0.8 Hz), 3.72 (1H, dt, *J* 14.8, 2.0 Hz, Hb-3), 3.24 (1H, dt, *J* 14.8, 2.0 Hz, Ha-3), 2.43 (2H, t, *J* 2.0 Hz, H-7), 2.26 (2H, d, *J* 3.6 Hz, H-5), 1.14 (3H, s), 1.12 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 194.58 (C=O), 174.29 (C=C), 154.72, 143.48, 142.24, 128.29, 127.99, 125.20, 111.09, 110.14, 109.09 (C=C), 90.59 (C-O), 50.84, 38.71, 37.67, 34.17, 28.61, 28.54. *m/z* (%): 310 (42.1, MH_2^+), 309 (100.0, MH^+), 291 (3.5, M^+ - H_2O). Anal. Calcd. for $C_{20}H_{20}O_3$ (308.37): C, 77.90; H, 6.54%. Found: C, 77.63; H, 6.61%.

2-(2-Furyl)-2,6-diphenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (3d). Yellow oil, 57%, 203 mg. FT-IR (KBr disc, cm^{-1}): 3056, 3023, 2921, 2882, 1630 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ_H: 7.30 – 7.42 (13H, m), 3.65 (2H, s, H-3), 3.51 – 3.55 (1H, m), 2.82 – 2.94 (2H, m), 2.67 (2H, d, *J* 8.3 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 193.81 (C=O), 174.55 (C=C), 154.60, 143.63, 142.54, 128.81, 128.40, 127.11, 126.73, 125.37, 125.28, 112.66, 112.56 110.32, 110.26, 109.57, 109.28 (C=C), 90.88 (C-O), 43.82, 40.32, 38.79, 31.16. *m/z* (%): 358 (25.0, MH_2^+), 357 (100.0, MH^+). Anal. Calcd. for $C_{24}H_{20}O_3$ (356.41) C, 80.88; H, 5.66%. Found: C, 80.63; H, 5.72%.

2-(2-Furyl)-2-phenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (3e). Yellow oil, 60%, 168 mg. FT-IR (KBr disc, cm^{-1}): 3028, 2964, 2926, 1635 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.42 (1H, dd, *J* 2.0, 1.0 Hz), 7.37 – 7.39 (4H, m), 7.30 – 7.36 (1H, m), 6.32 (1H, dd, *J* 3.5, 2.0 Hz), 6.14 (1H, d, *J* 3.5 Hz), 3.73 (1H, dt, *J* 15.0, 2.0 Hz, H-3a), 3.24 (1H, dt, *J* 15.0, 2.0 Hz, H-3b), 2.55 – 2.58 (2H, m), 2.32 – 2.43 (2H, m), 2.05 – 2.13 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 195.41 (C=O), 175.38 (C=C), 154.79, 143.63, 142.37, 128.42, 128.13, 125.34, 112.68, 110.29, 109.29 (C=C), 90.42 (C-O), 38.94, 36.46, 23.91, 21.70. *m/z* (ESI^+): 281 (MH^+, 100%). Anal. Calcd. for $C_{18}H_{16}O_3$ (280.32): C, 77.12; H, 5.75%. Found: C, 77.43; H, 5.79%.

Ethyl 5-(2-furyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-carboxylate (4a). Yellow oil, 15%, 47 mg. FT-IR (KBr disc, cm^{-1}): 3137, 3043, 2921, 1678 (C=C), 1655. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.40 – 7.20 (14H, m), 6.28 (1H, d, *J* 3.0 Hz), 5.95 (1H, d, *J* 3.0 Hz), 5.41 (1H, d, *J* 6.0 Hz), 5.28 (1H, d, *J* 7.0 Hz), 4.54 (1H, d, *J* 6.5 Hz), 4.25 (1H, d, *J* 5.5 Hz), 4.07 – 4.01 (2H, m), 4.0 – 3.92 (2H, m), 2.45 (3H, s), 2.35 (3H, s), 2.31 (3H, s), 1.57 (3H, s), 1.04 (3H, t, *J* 7.0 Hz), 1.02 (3H, t, *J* 7.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C: 193.9 (C=O), 165.2, 155.1, 143.2, 142.7, 128.3, 127.9, 125.2, 111.8, 110.1, 108.7, 86.7, 43.0, 29.3, 14.9. *m/z* (ESI^+): 313 (MH^+, 100%). Anal. Calcd. for $C_{19}H_{20}O_4$ (312.36): C, 73.06; H, 6.45%. Found. C, 72.99; H, 6.57%.

6,6-Dimethyl-2-(5-methyl-2-furyl)-3-phenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (4b). Yellow oil, 64%, 206 mg. FT-IR (KBr disc, cm^{-1}): 3030, 2959, 2938, 1637 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.19 – 7.34 (5H, m), 6.35 (1H, d, *J* 3.1 Hz), 6.00 (1H, dd, *J* 3.1, 0.8 Hz), 5.45 (1H, d, *J* 6.4 Hz, H-2), 4.63 (1H, d, *J* 6.4, 1.6 Hz, H-3), 2.47 (2H, s), 2.33 (2H, s), 2.31 (3H, s), 1.22 (3H, s), 1.17 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 194.4 (C=O), 176.2 (C-7a), 154.2, 149.6, 141.9, 139.5, 132.1, 128.9, 127.4, 114.9 (C-3a), 110.7, 106.8, 94.1, 88.0 (C-2), 51.4, 49.6, 38.3, 29.9, 13.9. *m/z* (%): 323 (2.2, MH^+), 322 (9.7, M^+), 279 (7.4, M^+ - C_3H_7), 265 (2.6, M^+ - C_4H_9), 241 (4.0, M^+ - C_5H_5O), 109 (3.4, $C_6H_5O_2^+$), 95 (11.1, $C_6H_7O^+$), 91 (6.0, $C_7H_7^+$), 43 (100.0, $C_3H_7^+$). Anal. Calcd. for $C_{21}H_{22}O_3$ (322.40): C, 78.23; H, 6.88%. Found: C, 78.53; H, 6.72%.

2-(5-methyl-2-furyl)-3,6-diphenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (4c). Yellow oil, 42%, 156 mg. FT-IR (KBr disc, cm^{-1}): 3050, 2961, 2919, 1641 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.20 – 7.39 (10H, m), 6.35 (1H, d, *J* 3.2 Hz), 5.98 (1H, dd, *J* 3.2, 0.8 Hz), 5.48 (1H, d, *J* 6.4 Hz, H-2), 4.65 (1H, dd, *J* 6.4, 1.6 Hz, H-3), 3.53 – 3.57 (1H, m, H-6), 2.72 – 2.88 (2H, m), 2.64 – 2.66 (2H, m), 2.33 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_H: 193.2 (C=O), 176.4 (C-7a), 154.3, 149.5, 142.8, 141.8, 129.1, 129.0, 127.4, 127.0, 116.4, 110.9, 106.8 (C-3a), 88.2 (C-2), 49.5, 44.5, 40.6, 32.0, 13.9. *m/z* (%): 372 (30.0, MH_2^+), 371 (100.0, MH^+), 289 (20.0, M^+ - C_5H_5O). Anal. Calcd. for $C_{25}H_{22}O_3$ (370.44): C, 81.06; H, 5.99%. Found: C, 81.19; H, 5.90%.

2-(5-methyl-2-furyl)-3-phenyl-2,3,6,7-tetrahydrobenzofuran-4(*5H*)-one (4d). Yellow oil, 60%, 177 mg. FT-IR (KBr disc, cm^{-1}): 3123, 2979, 2924, 1698 (C=C), 1648 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.10 – 7.24 (5H, m), 6.27 (1H, d, *J* 3.2 Hz), 5.90 (1H, dd, *J* 3.2, 0.8 Hz), 5.33 (1H, d, *J* 6.4 Hz, H-2), 4.55 (1H, d, *J* 6.4, 1.6 Hz, H-3), 2.46 – 2.55 (2H, m), 2.30 – 2.35 (2H, m), 2.23 (3H, s), 2.03 – 2.09 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 194.60 (C=O), 176.81 (C=C), 153.97, 149.28, 141.53, 128.72, 127.13, 127.09, 116.00, 110.59, 106.56 (C=C), 87.47 (C-O), 49.37, 36.88, 24.26, 21.74, 13.68. *m/z* (%): 295 (100.0, MH^+), 213 (45.1, M^+ - C_5H_5O), 99 (5.1, $C_5H_7O_2^+$), 83 (13.2, $C_5H_7O^+$). Anal. Calcd. for $C_{19}H_{18}O_3$ (294.34): C, 77.53; H, 6.16%. Found: C, 77.43; H, 6.29%.

2,2,2-Trifluoro-1-(2-(2-furyl)-4,5-diphenyl-4,5-dihydrofuran-3-yl)ethanone (5a). Yellow oil, 18%, 69 mg. FT-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: 8.39 (1H, dd, *J* 3.6, 0.8 Hz), 7.73 (1H, dd, *J* 1.6, 0.8 Hz), 7.30 – 7.40 (7H, m), 7.22 – 7.26 (3H, m), 6.70 (1H, dd, *J* 4.0, 1.6 Hz), 5.61 (1H, d, *J* 4.0 Hz, H-5), 4.71 (1H, dd, *J* 4.0, 1.2 Hz, H-4). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.7 (q, $^2J_{C-F}$ 34.3 Hz,

C=O), 162.1 (C-2), 147.2, 144.0, 142.9, 139.8, 129.4, 129.3, 129.2, 127.3, 125.4, 122.7, 118.3 (q, $^{1}J_{C\text{-}F}$ 285.0 Hz, CF_3), 113.0, 108.1 (C-3), 93.4 (C-5), 56.3 (C-4). *m/z* (%): 384 (5.9, M^+), 366 (1.2, M^+ - H_2O), 315 (2.9, M^+ - CF_3), 91 (7.4, $C_6H_5CH_2^+$), 77 (15.5, $C_6H_5^+$). Anal. Calcd. for $C_{22}H_{15}F_3O_3$ (384.35): C, 68.75; H, 3.93%. Found: C, 68.62; H, 3.82%.

2,2,2-Trifluoro-1-(2-(2-furyl)-4-methyl-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (5b). Yellow oil, 40%, 129 mg, FT-IR (KBr disc, cm^{-1}): 1658 (C=O), 1529 (C=C), 1176, 727, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.25 (1H, dd, *J* 3.6, 1.2 Hz), 7.68 (1H, dd, *J* 6.0, 1.6 Hz), 7.25 – 7.44 (5H, m), 6.63 (1H, dd, *J* 3.6, 1.6 Hz), 5.41 (1H, d, *J* 2.4 Hz, H-5), 3.66 (1H, quintet, *J* 5.2 Hz, H-4), 1.48 (3H, d, *J* 6.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 175.5 (q, $^{2}J_{C\text{-}F}$ 35.5 Hz, C=O) 161.1 (C-2), 146.8, 144.2, 139.3, 128.9, 128.8, 126.1, 125.3, 122.1, 118.5 (q, $^{1}J_{C\text{-}F}$ 289.6, CF_3), 112.7, 111.4, 110.2 (C-3), 92.1 (C-5), 44.6 (C-4), 22.1 (CH_3). ^{19}F-NMR (376 MHz, $CFCl_3$) δ_F: -74.09 (s, CF_3). *m/z* (%): 322 (9.3, M^+), 307 (3.6, M^+ - CH_3), 253 (8.6, M^+ - CF_3), 210 (9.2, M^+ - CF_3CO - CH_3), 91 (23.7, $C_6H_5CH_2^+$), 77 (22.4, $C_6H_5^+$). Anal. Calcd. for $C_{17}H_{13}F_3O_3$ (322.28): C, 63.36; H, 4.07%. Found: C, 63.27; H, 3.98%.

2,2,2-Trifluoro-1-(2-(2-furyl)-5-(4-methoxyphenyl)-4-methyl-4,5-dihydrofuran-3-yl)ethanone (5c). Yellow oil, 28%, 99 mg. FT-IR (KBr disc, cm^{-1}): 2922, 1671 (C=O), 1539 (C=C), 1207, 1136 (C-F), 729. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.24 (1H, d, *J* 3.6 Hz), 7.65 (1H, d, *J* 1.6 Hz), 7.30 (2H, d, *J* 9.2 Hz), 6.91 (2H, dd, *J* 6.4, 2.0 Hz), 6.62 (1H, dd, *J* 3.6, 1.2 Hz), 5.34 (1H, d, *J* 3.6 Hz, H-5), 3.80 (3H, s), 3.63 – 3.64 (1H, m, H-4), 1.45 (3H, d, *J* 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 172.3 (q, $^{2}J_{C\text{-}F}$ 32.3 Hz, C=O), 160.0 (C-2), 146.2, 143.5, 140.2, 129.3, 125.4, 125.3, 118.7 (q, $^{1}J_{C\text{-}F}$ 280.3 Hz, CF_3), 116.3, 112.9, 111.1, 110.7 (C-3), 90.3 (C-5), 48.5 (C-4), 27.6, 15.2. *m/z* (ESI^+): 353 (MH^+ , 100%). Anal. Calcd. for $C_{18}H_{15}F_3O_4$ (352.30): C, 61.37; H, 4.29%. Found: C, 61.28; H, 4.17%.

2,2,2-Trifluoro-1-(4-methyl-2-(2-naphthyl)-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (5d). Yellow oil, 21%, 93 mg. FT-IR (KBr disc, cm^{-1}): 3029, 2954, 1623 (C=O), 1600 (C=C), 1203, 748, 688. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 8.40 (1H, s), 7.93 (1H, d, *J* 8.0 Hz), 7.88 (2H, t, *J* 4.0 Hz), 7.80 (1H, dd, *J* 8.8, 2.0 Hz), 7.59 (1H, td, *J* 7.6, 1.6 Hz), 7.55 (1H, td, *J* 6.8, 1.2 Hz), 7.37 – 7.43 (5H, m), 5.39 (1H, d, *J* 5.2 Hz, H-5), 3.71 (1H, quintet, *J* 5.6 Hz, H-4), 1.53 (3H, d, *J* 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 171.8 (q, $^{2}J_{C\text{-}F}$ 31.8 Hz, C=O), 163.7 (C-2), 137.4, 132.6, 130.1, 128.7, 128.3, 128.1, 128.0, 127.9, 126.9, 126.2, 125.8, 125.3, 124.2, 121.3, 117.1 (q, $^{1}J_{C\text{-}F}$ 282.1 Hz, CF_3), 103.2 (C-3), 99.3 (C-5), 52.3 (C-4). *m/z* (ESI^+): 383 (MH^+ , 100%). Anal. Calcd. for $C_{28}H_{19}F_3O_2$ (444.44): C, 72.24; H, 4.48%. Found: C, 72.13; H, 4.41%.

1-(5-(acetoxymethyl)furan-2-yl)-2-phenylethane-1,2-diyl diacetate (6). Pale yellow oil, 16%, 58 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.21 – 7.40 (5H, m), 6.40 (1H, d *J* 3.0 Hz), 6.37 (1H, d, *J* 3.0 Hz), 5.28 (1H, d, *J* 6.5 Hz), 5.06 (2H, s), 4.60 (1H, d, *J* 6.5 Hz), 2.39 (3H, s), 2.10 (3H, s), 1.95 (3H, s). Anal. Calcd. for $C_{19}H_{20}O_7$ (360.36): C, 63.33; H, 5.59%. Found: C, 63.21; H 5.68%.

1-(5-methylfuran-2-yl)-2-phenylethane-1,2-diyl diacetate (7 and 8 mixture, 1:5). Pale yellow oil, 25%, 76 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.23 – 7.30 (10H, m), 6.30 (1H, d, *J* 8.5 Hz), 6.13 (1H, d, *J* 8.5 Hz), 6.10 (1H, d, *J* 3.0 Hz), 5.98 (2H, d, *J* 3.0 Hz), 5.79 (1H, d, *J* 3.0 Hz), 5.25

(1H, d, *J* 7.0 Hz), 4.64 (1H, d, *J* 7.0 Hz), 2.40 (3H, s), 2.35 (3H, s), 2.26 (3H, s), 2.12 (3H, s), 2.10 (3H, s), 1.96 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 169.8, 169.7, 152.7, 149.6, 146.7, 142.7, 136.3, 129.0, 128.4, 128.2, 127.4, 127.3, 127.2, 111.4, 110.1, 106.5, 106.2, 85.1, 70.2, 53.5, 29.6, 21.10, 20.9, 15.1, 13.6, 13.5. Anal. Calcd. for $C_{17}H_{18}O_5$ (302.32): C, 67.54; H, 6.00%. Found: C, 67.41; H 5.88%.

Acknowledgements

The authors are grateful to Kocaeli University Science Research Foundation (2010/57, 2012/28, 2012/77 and 2012/84) for financial support. Also, the author Dr. Emre Biçer thanks to Mrs. Hilal Biçer for her encouragement and endless support during typing this paper.

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