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

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**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]

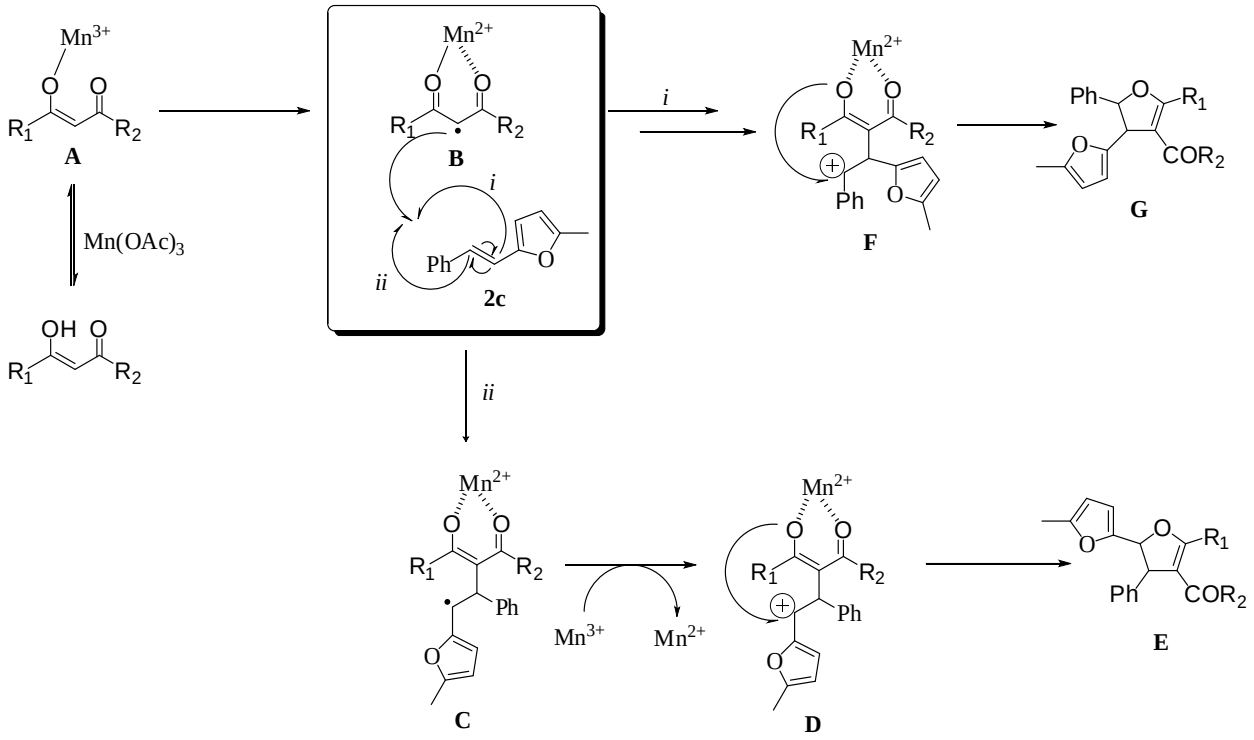
In this study, aiming the synthesis of the 2-furyl substituted dihydrofuran compounds (**3a-e**, **4a-d, 5a-d**) was used as 1,1- and 1,2-disubstituted alkenes with 1,3-dicarbonyl compounds

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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

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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.

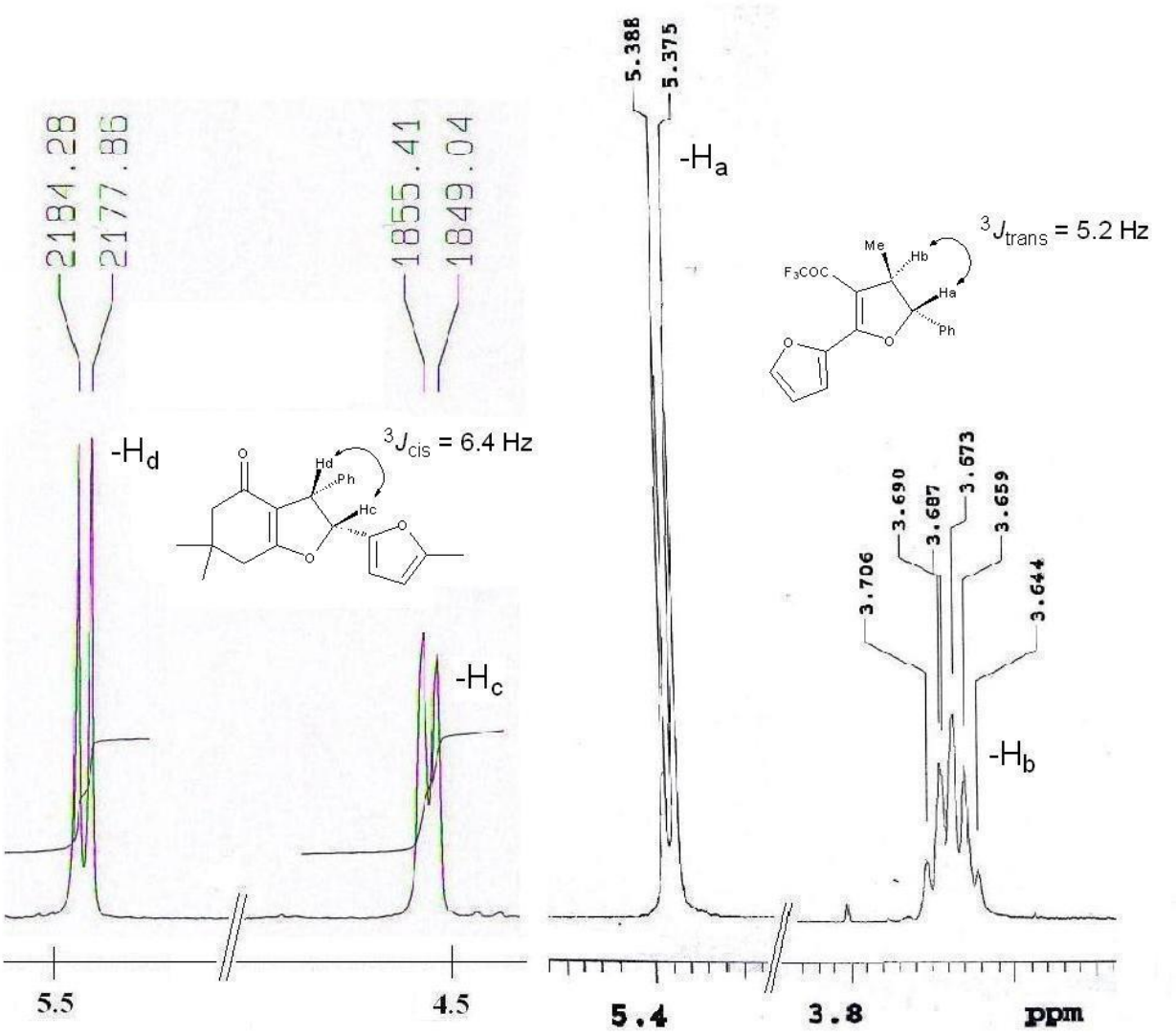
Within this study, 1,1-disubstituted alkene **2a** was used in the radical addition reactions with various 1,3-dicarbonyl compounds. It is determined that the product yields are higher than the ones of **2b**. **3c** was yielded in 80% with the radical cyclization reaction of **1c** with **2a**. However, 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 $\delta$ = 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.

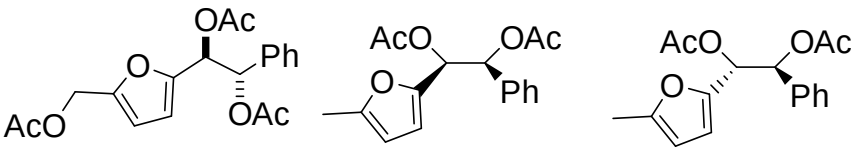
Additionally, acetylation of alkene was observed as a side product in the cyclization reactions of **2b**. The cyclization reactions of alkene **2b** gave us acetoxy substituted alkene **6** as well as 1,2-

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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.**

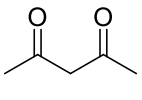
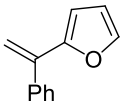
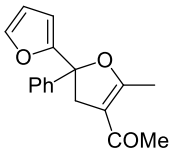
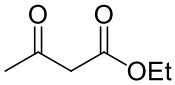
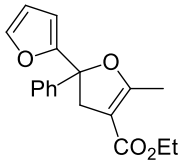
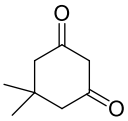
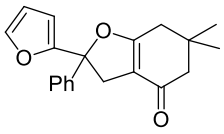
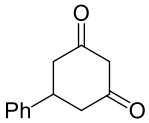
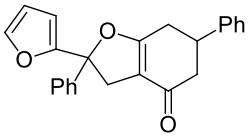
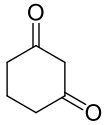
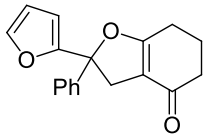
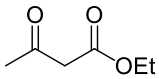
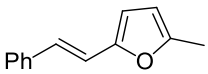
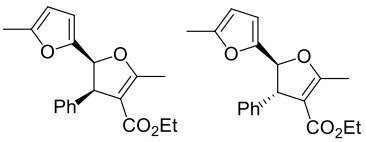
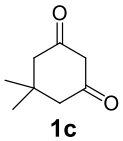
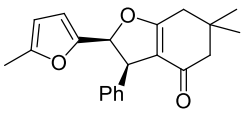
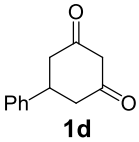
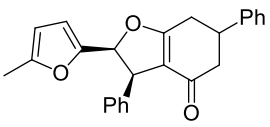
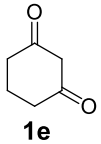
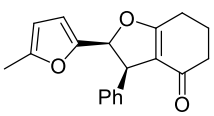



**6** **7** **8**

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

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

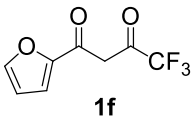
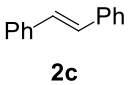
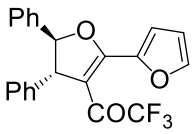
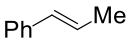
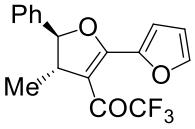
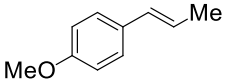
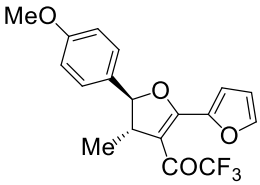
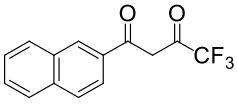
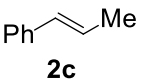
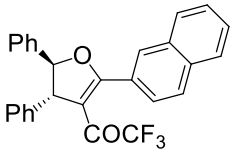
| Entry | 1,3-Dicarbonyl | Alkene | Product | | Yield (%) |
|---|---|---|---|---|---|
| 1 |  **1a** |  **2a** |  | **3a** | 56 |
| 2 |  **1b** | **2a** |  | **3b** | 67 |
| 3 |  **1c** | **2a** |  | **3c** | 80 |
| 4 |  **1d** | **2a** |  | **3d** | 57 |
| 5 |  **1e** | **2a** |  | **3e** | 60 |
| 6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


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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

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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 4$cm^{-1}$ 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, $CDCl_3$) $\delta_H$: 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,

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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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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%.

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**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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 175.7 (q, $^2J_{C-F}$ 34.3 Hz,

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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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CFCl_3$) $\delta_F$: -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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_C$: 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, $CDCl_3$) $\delta_H$: 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, $CDCl_3$) $\delta_H$: 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

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(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, $CDCl_3$) $\delta_C$: 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%.

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