



# Synthesis of ferrocene substituted dihydrofuran derivatives via manganese(III) acetate mediated radical addition-cyclization reactions



Hakan Aslan <sup>a,\*</sup>, Atilla Öktemer <sup>a</sup>, Hakan Dal <sup>b</sup>, Tuncer Hökelek <sup>c</sup>

<sup>a</sup> Department of Chemistry, Ankara University, 06100 Tandogan, Ankara, Turkey

<sup>b</sup> Department of Chemistry, Anadolu University, 26470 Yenibağlar, Eskişehir, Turkey

<sup>c</sup> Department of Physics, Hacettepe University, 06800 Beytepe, Ankara, Turkey

## ARTICLE INFO

### Article history:

Received 10 August 2017

Received in revised form

20 October 2017

Accepted 6 November 2017

Available online 8 November 2017

### Keywords:

Manganese(III) acetate

Ferrocene

Trans-dihydrofuran

Allylidene derivatives

Benzofuran

## ABSTRACT

In this study, the manganese(III) acetate mediated radical addition-cyclization reactions of ferrocene substituted alkenes and active methylene compounds were carried out. The regio- and stereoselective radical cyclization reactions of (E)-styrylferrocene (**1a**) and active methylene compounds (**2a-g**) gave *trans*-5-ferrocenyl-4-phenyl-4,5-dihydrofuran compounds as the sole products. The reactions of 1-ferrocenyl-1-aryl(heteroaryl)ethenes (**1b-e**) and active methylene compounds (**2a-f**) via Mn(OAc)<sub>3</sub> led to furan and benzofuran derivatives (**10-33**) in mid-good yields (up to 75%). Surprisingly, ferrocene substituted allylidene derivatives were obtained from the Mn(OAc)<sub>3</sub> mediated reactions of 1-aryl-1-ferrocenylethene (**1b-d**) and 1,3-dimethylbarbituric acid (**2g**). The uses of ferrocene substituted alkenes in manganese(III) acetate mediated radical reactions is the first example in this field as far as we know.

© 2017 Elsevier Ltd. All rights reserved.

## 1. Introduction

Ferrocene has attracted much attention due to it having both organic and inorganic properties, high thermal stability, good solubility in organic solvents, easy synthesis,<sup>1</sup> and reversible redox properties.<sup>2</sup> Ferrocene derivatives are used as homogeneous catalysts,<sup>3</sup> chemosensors,<sup>4</sup> asymmetric ligands,<sup>5</sup> non-linear optical materials,<sup>6</sup> conductive polymers,<sup>7</sup> liquid crystals<sup>8</sup> and biosensors.<sup>9</sup> In addition, ferrocene compounds<sup>10</sup> and ferrocenium salts<sup>10c,11</sup> have strong antitumor activities.

Furan and benzofuran derivatives form the basic structure of many natural compounds and show a wide range of biological activities.<sup>12</sup> In addition, these compounds are used as substrates for the synthesis of many polyfunctional organic compounds.<sup>13</sup>

There are only a few studies that include both ferrocene and furan groups. These studies are concentrated on synthesis of ferrocenylfurans,<sup>14</sup> furan and ferrocene containing conjugates and their electrochemical behaviour,<sup>15</sup> applications of nonlinear optical materials,<sup>6</sup> and cytotoxic investigations of ferrocenylfurans.<sup>16</sup>

Furan compounds can easily be prepared by the oxidative cyclization reaction of an active methylene compound and an

unsaturated system mediated by transition metal salts (Mn<sup>3+</sup>,<sup>17</sup> Ce<sup>4+</sup>,<sup>18</sup> Cu<sup>2+</sup>,<sup>19</sup>). Manganese(III) acetate has introduced differences in the field of free radical chemistry, due to its selectivity, specificity, mild and efficient reaction conditions.<sup>20</sup>

The first study of the Mn(OAc)<sub>3</sub> mediated oxidation reactions of ferrocene compounds was made in 1976.<sup>21</sup> It was reported that diferrocenylmethane derivatives were obtained by the oxidation and aromatic electrophilic substitution reactions of methylferrocene without the presence of any cyclization product. Following this study, we have not been able to find any research dealing with Mn(OAc)<sub>3</sub> mediated reactions of ferrocene compounds until the present.

In this study, manganese(III) acetate mediated oxidative cyclization reactions of ferrocene substituted alkene and active methylene compounds have been carried out. As a result, ferrocene substituted dihydrofuran, benzofuran and pyrimidine derivatives with the potential of showing biological activity were obtained. The use of ferrocene substituted alkenes in manganese(III) acetate mediated radical reactions is the first example in this field as far as we know.

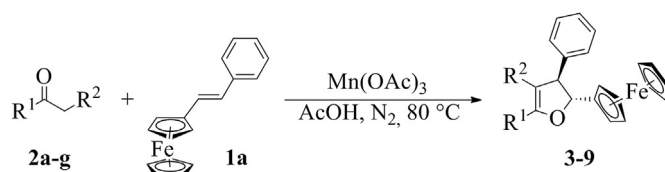
## 2. Results and discussion

Initially, the reactions of (E)-styrylferrocene (**1a**) and active methylene compounds (**2a-g**) via Mn(OAc)<sub>3</sub> were studied.

\* Corresponding author.

E-mail address: [haslan@science.ankara.edu.tr](mailto:haslan@science.ankara.edu.tr) (H. Aslan).

**Table 1**  
Products of the oxidative cyclization reactions of **1a** with **2a-g** via Mn(OAc)<sub>3</sub>.<sup>a</sup>



Entry	Active Methylene	Time (min)	Product		Yield, % <sup>b</sup>
			R <sup>1</sup>	R <sup>2</sup>	
1	<b>2a</b>	20	CH <sub>3</sub>	COCH <sub>3</sub>	10 ( <b>3</b> )
2	<b>2b</b>	25	CH <sub>3</sub>	COEt	30 ( <b>4</b> )
3	<b>2c</b>	14		CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> CO	50 ( <b>5</b> )
4	<b>2d</b>	20		CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CO	28 ( <b>6</b> )
5	<b>2e</b>	27	C <sub>6</sub> H <sub>5</sub>	CN	24 ( <b>7</b> )
6	<b>2f</b>	32	Thien-2-yl	CN	25 ( <b>8</b> )
7	<b>2g</b>	22		N(CH <sub>3</sub> )CON(CH <sub>3</sub> )CO	15 ( <b>9</b> )

<sup>a</sup> All the reactions were carried out in a 1: 2: 3 molar ratio of alkene (**1a**), active methylene (**2a-g**) and Mn(OAc)<sub>3</sub> in AcOH at 80 °C.

<sup>b</sup> Isolated yield based on alkene.

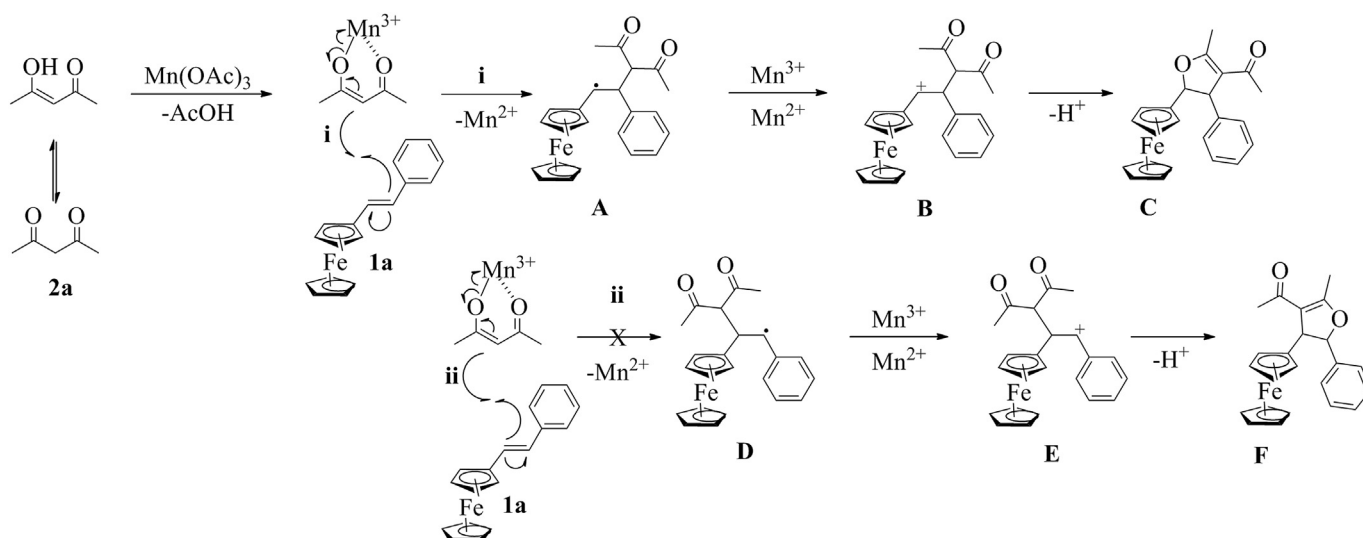
Although two regioisomers and two stereoisomers may form in these reactions, *trans*-5-ferrocenyl-4-phenyl-dihydrofuran compounds (**3–9**) were obtained as the sole product (Table 1).

The proposed mechanism of these reactions is shown in Scheme 1. The *trans*-5-ferrocenyl-4-phenyl-dihydrofuran compounds (**3–9**) are probably formed by following the commonly accepted route.<sup>22</sup> According to this mechanism, a Mn(III)-enolate complex is formed through the interaction of Mn(OAc)<sub>3</sub> and the enol form of the active methylene compound. Interaction of the Mn(III)-enolate complex and alkene (**1a**) affords a radical carbon intermediate (**A**) via pathway **i**. **A** is then oxidized by Mn(OAc)<sub>3</sub> to form a carbocation (**B**). 5-Ferrocenyl-4-phenyl-dihydrofuran (**C**) is produced through the cyclization of **B**. Similarly, the radical carbon intermediate (**D**), carbocation (**E**) and 4-ferrocenyl-5-phenyl-dihydrofuran (**F**) can also be attained respectively via pathway **ii**. Only one product with the skeletal structure of compound **C** was obtained from the related reactions (see Fig. 1).

The structure of the product was identified using HSQC, HMBC and NOESY spectra. Due to being adjacent to the oxygen atom, H5 and C5 resonate at a lower field than H4 and C4, respectively. The

H4-H5 protons and C4-C5 carbons were determined using HSQC spectra. HMBC spectra show that H5 correlates with the ortho-carbons of the ferrocenyl group, and doesn't correlate with ortho-carbons of the phenyl group. Similarly, H4 correlates with the ortho-carbons of the phenyl group, and doesn't correlate with ortho-carbons of the ferrocenyl group. These results prove that the ferrocenyl group is attached to the C5 carbon and the obtained product is **C** by pathway **i**. As the ferrocenyl group possesses considerably more electron donating properties than the phenyl group,<sup>23</sup> **A** and **B** are more stable than **D** and **E**, respectively. For this reason, reaction path **ii** doesn't proceed to form **F**. Moreover, in the NOESY spectra of products **3–9**, there is either no correlation or weak correlation between the H4 and H5 protons which shows that these protons are in the *trans* configuration. To ensure that the product (**3–9**) structures are in the *trans* configuration, the structure of one of these compounds (**8**) was confirmed by X-ray crystallography.<sup>24</sup> It can clearly be seen from the ORTEP view that **8** is a *trans*-dihydrofuran (Fig. 2).

Mn(OAc)<sub>3</sub> mediated reactions of 1-ferrocenyl-1-aryl(heteroaryl) ethenes (**1b-e**) and active methylene compounds (**2a-f**) lead to the



**Scheme 1.** Proposed mechanism for the formation of ferrocenyl substituted dihydrofurans.

Download English Version:

<https://daneshyari.com/en/article/7828068>

Download Persian Version:

<https://daneshyari.com/article/7828068>

[Daneshyari.com](https://daneshyari.com)