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Coupling of ferrocenyl chromium carbene complex with cyclobutenediones

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Abstract

The coupling of ferrocenyl chromium carbene complex with cyclobutenediones leads to ferrocenyl-substituted 5-alkylidenefuranones and 4-cyclopentene-1,3-diones, methyl ferrocenoate and acetylferrocene in varying amounts. The scope and limitations of these processes are investigated. In comparison with the phenyl analog, ferrocenyl chromium carbene complex has been found to be less reactive. This is also supported by PM3 calculations. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

After the successful application of the pioneer 'cisplatin', i.e. *cis*-[$PtCl_2(NH_3)_2$], as antitumor agent [1], interest in the use of transition metal complexes in medicine and other biological areas has grown rapidly [2]. Among these derivatives, ferrocenium salts, $Cp_2Fe(III)X$ ($X = PF_6$, $FeCl_4$, 2,4,6-$(NO_2)_3C_6H_2O$, $Cl_3CCO_2 \cdot 2Cl_3CCO_2H$), have proved to be particularly active against a number of tumors [3]. Unsubstituted ferrocene does not display any tumor inhibiting activity even if it is solubilized in water using heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (dmβ-CD) [4], but its oxidized form, i.e. ferrocenium salt, exhibits inhibitory activity [3,4]. Although the excellent solubility of salts in water, caused by their ionic character, proves to be propitious for applications in biological systems, the inhibitory activity of ferrocenium salts is independent of the water solubility. The antitumor effect is related to the oxidation state of the central iron atom, in that only the oxidation state +3 (in ferrocenium cations) exhibits inhibitory effects [4]. Thus, in recent years, considerable interest has been devoted to the synthesis of new ferrocene derivatives since the properly functionalized ferrocene derivatives; particularly their ferrocenium salt forms could be potential antitumor substances [5].

The biological importance of alkylidenefuranones is well known [6]. In particular, alkylidenefuranone derivatives possess antiviral, antibiotic and anticancerous activities. This, together with the finding that ferrocenium salts are active against various animal and human tumors [3,4], suggests that the incorporation of the essential structural features of alkylidenefuranones with a ferrocene moiety could provide compounds with enhanced antitumor activities. Although, since its discovery, ferrocene and its derivatives are among the most thoroughly studied compounds [7], we were surprised that there has been limited study of the ferrocenyl-substituted alkylidenefuranones, particularly, 5-ferrocenyl-methylene-5*H*-furan-2-ones.

Fischer type metal carbene complexes have emerged as valuable reagents for organic synthesis [8]. It has been reported that phenols, cyclopentenones, indenes, furans, furanones, cyclobutenones, vinylketenes and cyclohexadienones have resulted from their reactions under appropriate conditions [9]. An ever-continuing aspect of these studies has been the use of a structurally diverse set of Fischer carbene complexes in these reactions to afford a diverse array of compounds. Although ferrocenylcarbene complexes are known for a long time [10], they have not been utilized extensively in organic synthesis [8b,11]. We have recently reported that the

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ferrocenylcarbene complexes of Cr, Mo and W react with alkynes to produce ferrocenyl-substituted cyclobutenones, furans and/or ketoesters [12]. Our results in that report have shown that, under appropriate conditions with the proper substrates, ferrocenylcarbene complexes can follow the other reactivity patterns of metal carbene complexes, as well. It is known that metal carbene complexes, when treated with cyclobutenediones, afford the corresponding cyclopentenediones and/or alkylidenefuranones via a net insertion of the carbene unit into the C–C bond of the cyclobutenedione [13]. As part of a program to synthesize new ferrocene derivatives, we have investigated the reaction of cyclobutenediones with ferrocenylcarbene complexes, leading to ferrocenyl-substituted 5-alkylidenefuranones and/or 4-cyclopentene-1,3-diones (Scheme 1). These alkylidenefuranones and 4-cyclopentene-1,3-diones are the first examples of these kind, containing a ferrocene moiety. We herein report the preliminary results of this study.

2. Results and discussion

2.1. Synthesis of starting materials

Cyclobutenediones **1** used in this study were synthesized from squaric acid by using well-documented literature procedures [14,15]. Ferrocenylcarbene complex of chromium (**2**) was prepared according to a modified literature procedure [10].

2.2. Coupling of cyclobutenediones *1* with ferrocenyl chromium carbene complex *2*

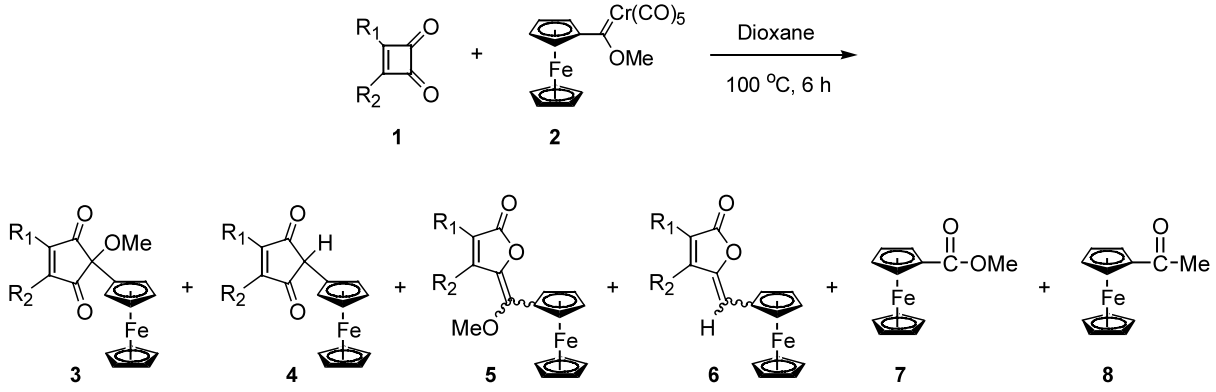
For the coupling reactions, cyclobutenediones **1** were heated to reflux with a slight excess of ferrocenylcarbene complex **2** (1.5 equivalents) in dioxane for 6 h. The results of this study are summarized in Scheme 1 and Table 1.

As indicated in Table 1, the coupling of a variety of cyclobutenediones **1** with ferrocenylcarbene complex **2** led to varying amounts of cyclopentenediones **3** and **4**, alkylidenefuranones **5** and **6**, methyl ferrocenoate (**7**) and acetylferrocene (**8**). Compared with the phenyl analog [13], ferrocenylcarbene complex **2** was noticeably less reactive and afforded the products in lower yields. The reactions carried out at relatively higher temperatures, such as in *p*-xylene at 138 °C, led to complex reaction mixtures and did not improve the yields of the products significantly. Due to low yields, rationalization for the product distribution has not been advanced. Cyclopentenediones and alkylidenefuranones are the expected insertion products of the reactions between Fischer carbene complexes and cyclobutenediones [13]. The mechanism proposed for the formation of cyclopentenediones **3** and **4**, and alkylidenefuranones **5** and **6** is depicted in Scheme 2. CO dissociation from the Fischer carbene complex **2** produces the coordinatively unsaturated Fischer carbene complex **9** [13], which gives oxidative addition into acyl–acyl bond of cyclobutenedione **1** to afford chromacyclopentenedione **10**. Migration of the more electron deficient acyl group in **10** yields chromacyclohexenedione **11**, which affords cyclopentenedione **3** upon reductive elimination (Scheme 2). The formation of deoxygenated cyclopentenedione **4** is a secondary reaction and occurs via a chromium-induced reduction of initially formed cyclopentenedione **3**.

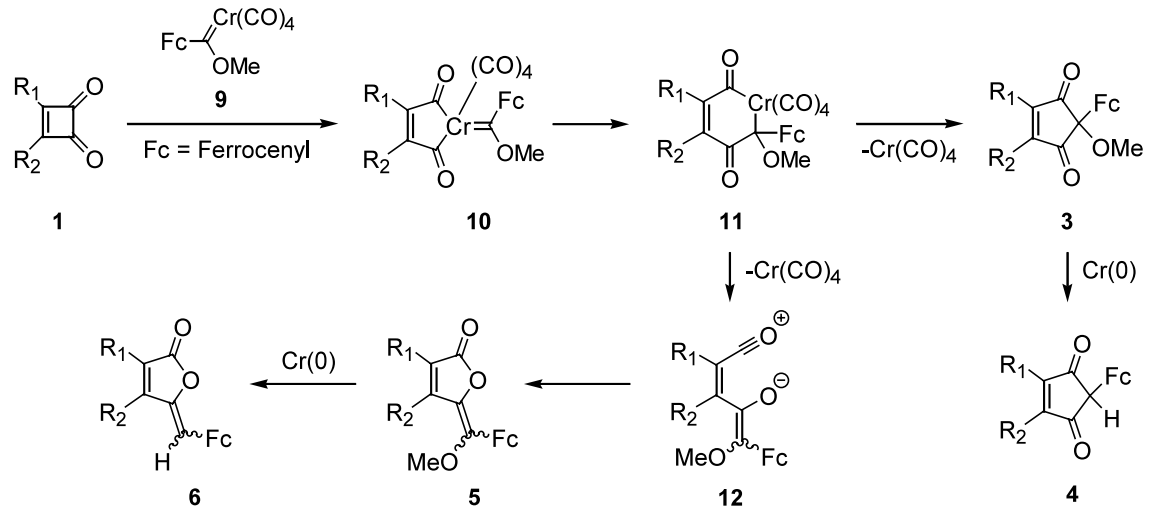
Table 1
Coupling of cyclobutenediones **1** with ferrocenylcarbene complex **2** [a]

Entry	R_1	R_2	Cyclobutenedione	Products (% yield) [b]
1	Me	*i*-PrO	**1A**	**3A** (14)+**4A** (6)+**5A** [c] (8)+**8** (15)
2	Ph	*i*-PrO	**1B**	**5B** [c] (8)+**7** (12)
3	Me	Me	**1C**	**5C** (9)+**7** (18)+**8** (9)
4	Ph	Ph	**1D**	**5D** (8)+**6D** (11)
5	*i*-PrO	*i*-PrO	**1E**	**5E** [c] (5)

[a] All reactions were carried out in dioxane at 100 °C.
[b] Isolated yields.
[c] Configuration of exocyclic double bond was assigned as *E*.



Scheme 1. Compounds **1**, **3**–**6**: (A) $R_1 = Me$, $R_2 = i$-PrO; (B) $R_1 = Ph$, $R_2 = i$-PrO; (C) $R_1 = R_2 = Me$; (D) $R_1 = R_2 = Ph$; (E) $R_1 = R_2 = i$-PrO.



Scheme 2.

Secondary deoxygenation processes have often been observed in the reactions of chromium carbene complexes [13,16]. In all reactions of Table 1, alkylidenefuranones **5** were observed, which is consistent with the findings of Herndon and coworkers [13] using phenyl chromium carbene complex. Although the interconversion of cyclopentenediones and alkylidenefuranones is well known [17], alkylidenefuranone **5** is the primary product of the coupling reactions and does not result from the rearrangement of initially formed cyclopentenedione **3** under the reaction conditions. Cyclopentenedione, such as **3** with a phenyl instead of a ferrocenyl group, does not convert into corresponding alkylidenefuranone when heated to 100 °C in dioxane, in the absence or presence of chromium hexacarbonyl, or when it is additive in the coupling reaction of other carbene complexes, as shown before [13]. As illustrated in Scheme 2, elimination of chromium gives enolate-acylium intermediate **12**, which undergoes intramolecular *O*-acylation to afford alkylidenefuranone **5** [13]. Deoxygenated alkylidenefuranone **6** results from the reduction of initially formed **5** by chromium byproducts during the course of the reaction, as in the formation of cyclopentenediones **4** from **3** [13]. Although such a reduction was not previously reported from similar studies [13], treatment of alkylidenefuranone **5A** with chromium hexacarbonyl in refluxing dioxane led to a slow reduction to **6A**.

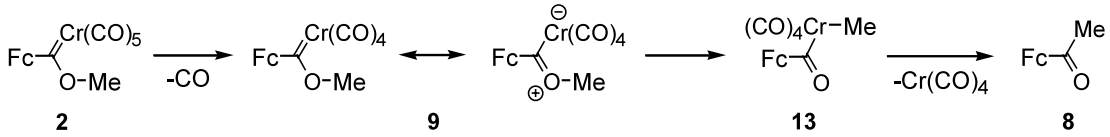
Formation of ester **7** in some reactions (entries 2 and 3) can be attributed to the oxidation of ferrocenylcarbene complex **2** by means of low-valent chromium species generated during the reaction [18,19]. Although metal carbene complexes can be oxidized efficiently to corresponding esters by using a variety of reagents [19], Fischer carbene complexes thermally decompose slowly in refluxing solvents such as dioxane to produce esters.

Interestingly, from some reactions (entries 1 and 3), acetylferrocene (**8**) was isolated [20]. Formation of ketones from reactions of Fischer carbene complexes is very rare and has only few precedents [21,22]. The mechanism proposed for the formation of **8** is outlined in Scheme 3. Following CO dissociation from carbene complex **2**, the resulting coordinatively unsaturated carbene complex **9** experiences a 1,3-methyl shift to afford complex **13**, which gives acetylferrocene (**8**) upon reductive elimination. A similar mechanism was previously proposed by Sarkar for the ketone formation from thermolysis of Fischer carbene complexes [21a,21b].

2.3. Structural assignments of alkylidenefuranones

The indicated regiochemistry of alkylidenefuranones **5A** and **5B** has been assigned on the basis of comparison of ^{13}C-NMR spectra in similar systems [13,23]. In a 4-alkoxyfuranone, i.e. **5A**,**B**, the β-carbonyl carbon is unusually downfield while α-carbonyl carbon is upfield. However, in a 3-alkoxyfuranone, i.e. **5A**,**B** if R_1 and R_2 are reversed, considerably less polarization is observed. In **5A** and **5B**, α-carbonyl carbons appear at δ 146.9 and 149.1, respectively, and β-carbonyl carbons at δ 162.4 and 162.2, which are more consistent with the indicated 4-alkoxyfuranone structures.

Configurational assignment of γ,δ-unsaturated double bond in alkylidenefuranones **5A**,**B**,**E** has been based primarily on the severe chemical shift differences of the isopropyl methyls and methines in the ^{1}H-NMR spectra. In similar compounds, i.e. **5A**,**B** if Fc is replaced by Ph, the chemical shift of the isopropyl methyls in the *Z* isomers is below δ 0.90, while the same protons in the *E* isomers occur at δ 1.40–1.42 [13]. Similarly, the isopropyl methines of those compounds appear at δ 4.39–4.51 in the *Z* isomers and δ 4.83–4.88 in the *E*



2 9 13 8

Scheme 3.

isomers. This large effect has been attributed to strong anisotropic interaction of the aromatic rings and the isopropoxy groups [13]. In the light of these observations and with the expectation of similar anisotropic interaction between ferrocenyl and isopropoxy groups, the configuration of γ,δ-unsaturated double bond in alkylidenefuranones **5A**,**B**,**E** has been assigned as *E* since the isopropyl methyls appear at δ 1.19–1.41, while the isopropyl methines at δ 4.57–5.26. Similar configurational assignment could not be made for furanones **5C**,**D** and **6D** due to the absence of such isopropoxy groups. It should be noted that the methoxy groups in **5C**,**D** could not be utilized for assignment purposes since they resonate in a narrow chemical shift range.

2.4. Reactivity of ferrocenyl chromium carbene complex 2

More insight into the reactivity of ferrocenylcarbene complex **2** can be achieved by means of isodesmic Eq. (1). The reaction energies of isodesmic equations have been successfully used for the estimation of relative reactivities (or stabilities) of compounds [24]. The reaction enthalpy of Eq. (1) was calculated at the semi-emprical PM3 level [25] using PC SPARTAN PRO program [26].

$$(CO)_5Cr{=}\underset{\mathbf{2}}{C(Fc)}(OCH_3) + Ph{-}CH{=}CH_2 \rightarrow (CO)_5Cr{=}\underset{\mathbf{13}}{C(Ph)}(OCH_3) + Fc{-}CH{=}CH_2 \quad (1)$$

$$\Delta H = 4.9 \text{ kcal mol}^{-1}$$

ΔH value for isodesmic reaction of Eq. (1) has been found to be positive. In the light of this result, ferrocenyl group stabilizes the carbene complex more compared to the phenyl group. Thus, in practice, ferrocenylcarbene complex **2** is expected to be more stable and less reactive, which is consistent with the experimental results. The relative stability of carbene complex **2** is attributed to the π-donor ability of cyclopentadienyl moiety to stabilize the electropositive carbene carbon.

3. Conclusion

In summary, we have investigated the reaction of ferrocenylcarbene complex of chromium with cyclobutenediones, producing 4-cyclopentene-1,3-diones, 5-alkylidenefuranones, methyl ferocenoate and acetylferrocene. In the coupling reactions studied, as supported with the PM3 calculations, ferrocenyl chromium carbene complex has been found to be less reactive than the phenyl chromium carbene complex and afforded products in lower yields. Acetylferrocene results from the intramolecular rearrangement of carbene complex itself, a rare occurrence for metal carbene complexes. We are continuing to improve the yields of products, as well as to explore the further reactivity of ferrocenylcarbene complexes.

4. Experimental

4.1. General consideration

Nuclear magnetic resonance (^{1}H and ^{13}C) spectra were recorded on a Bruker AM 400 spectrometer (400.1 MHz for ^{1}H and 100.6 for ^{13}C). Chemical shifts are reported in parts per million (δ) downfield from an internal Me_4Si reference. Coupling constants (*J* values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). DEPT ^{13}C-NMR information is given in parenthesis as C, CH, CH_2 and CH_3. IR spectra were recorded on a Perkin–Elmer 1600 Series FT-IR spectrometer. Band positions are reported in reciprocal centimetres (cm^{-1}). Band intensities are reported relative to the most intense band and are listed as: br (broad), vs (very strong), s (strong), m (medium), w (weak), vw (very weak). Mass spectra (MS) were obtained on a Micromass UK Platform-II spectrometer using electron impact (EI); *m*/*e* values are reported, followed by the relative intensity in parenthesis. High resolution mass spectra (HRMS) were obtained on a VG ZabSpec spectrometer with double focusing magnetic sector using EI. Flash column chromatography was performed using thick-walled glass columns and 'flash grade' silica gel (Merck 230-400 mesh). Routine thin layer chromatography (TLC) was affected by using precoated 0.25 mm silica gel plates purchased from Merck. The relative proportion of solvents in mixed chromatography solvents refers to the volume–volume ratio.

Chromium hexacarbonyl was purchased from Strem Company and ferrocene from Aldrich Chemical Company and they were used as received. Diethyl ether, THF and dioxane were distilled from Na-benzophenone ketyl prior to use. All reactions were performed in an inert

atmosphere created by slight positive pressure (ca. 0.1 psi) of Ar. The preparation of ferrocenylcarbene complex **2** was accomplished according to the modification of Connor's procedure [10], as given below.

4.2. Pentacarbonyl[(ferrocenyl)methoxymethylene]chromium (**2**)

To a solution of ferrocene (3.00 g, 16.10 mmol) in Et_2O (50 ml) at 0 °C under Ar was added via syringe *tert*-butyllithium (9.5 ml of a 1.7 M of C_6H_{12}–ether solution, 16.10 mmol) over a period of 20 min. The resulting solution was stirred for 2 h at this temperature and transferred via cannula to a suspension of chromium hexacarbonyl (2.96 g, 13.40 mmol) in Et_2O (50 ml) at 0 °C under Ar. The mixture was stirred for 2 h at 0 °C and methyl trifluoromethanesulfonate (2.0 ml, 20.16 mmol) was added. After stirring at room temperature (r.t.) for 20 min, the mixture was poured into saturated aq. $NaHCO_3$ solution in a separatory funnel, and then extracted with C_6H_{14} (3 × 150 ml). Combined C_6H_{14} layers were washed with water and saturated aq. NaCl solution, respectively. After drying over Na_2SO_4, the solvent was removed on a rotary evaporator. The crude oil obtained was purified by flash chromatography on silica gel using C_6H_{14} as the eluent. The dark brown fraction ($R_f = 0.37$ in C_6H_{14}) was collected to give carbene complex **2** (4.05 g, 72%). ^{1}H-NMR ($CDCl_3$): δ 4.99 (s, 2H), 4.79 (s, 2H), 4.69 (s, 3H), 4.25 (s, 5H); IR (CH_2Cl_2): 2054 (vw), 1933 (vs), 1272 (vs), 1269 (vs), 1264 (vs), 1223 (vw), 980 (vw), 783 (vw), 752 (vs), 743 (vs), 709 (vs), 508 (m) cm^{-1}. The spectral data are in agreement with those reported previously for this compound [10].

4.3. General procedure for the reaction of ferrocenyl carbene complex **2** with cyclobutenediones **1** (Table 1)

A solution of carbene complex **2** (1.00 mmol) and cyclobutenedione **1** (1.50 mmol) in dioxane (10.00 ml) was heated to reflux under Ar for a period of 6 h. The mixture was allowed to cool to r.t. and the solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel using 19:1 C_6H_{14}–EtOAc followed by 9:1 C_6H_{14}–EtOAc as the eluent. The products indicated in Table 1 were isolated.

4.4. Spectral data for products

4.4.1. 2-Ferrocenyl-4-isopropoxy-2-methoxy-5-methyl-4-cyclopentene-1,3-dione (**3A**)

Dark red oil, $R_f = 0.42$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 5.66 (septet, 1H, $J = 6.1$ Hz), 4.73 (s, 1H), 4.32 (s, 1H), 4.13 (s, 3H), 4.11 (s, 1H), 4.02 (s, 1H), 3.74 (s, 5H), 1.80 (s, 3H), 1.43 (d, 3H, $J = 6.1$ Hz), 1.35 (d, 3H, $J = 6.1$ Hz); ^{13}C-NMR ($CDCl_3$): δ 197.7 (C), 192.5 (C), 166.1 (C), 132.8 (C), 78.5 (C), 75.5 (CH), 71.6 (CH), 70.5 (CH), 70.1 (CH), 68.8 (CH), 57.6 (C), 51.9 (CH_3), 23.9 (CH_3), 23.7 (CH_3), 7.0 (CH_3); IR (CH_2Cl_2): 3097 (vw), 2954 (w), 1709 (vs), 1624 (m), 1463 (m), 1387 (m), 1326 (m), 1275 (vs), 1190 (w), 1143 (s), 1104 (m), 825 (m) cm^{-1}; MS (EI): 382 ($[M]^+$, 100), 340 (64), 325 (28), 311 (17), 296 (11), 258 (17), 244 (46), 230 (13), 213 (26), 185 (16), 159 (12), 129 (14), 121 (20); HRMS (EI): Calc. for $C_{20}H_{22}{}^{56}FeO_4$: 382.0867. Found: 382.0879.

4.4.2. 2-Ferrocenyl-4-isopropoxy-5-methyl-4-cyclopentene-1,3-dione (**4A**)

Dark red oil, $R_f = 0.33$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 5.45 (septet, 1H, $J = 6.1$ Hz), 4.07 (s, 3H), 4.00 (s, 1H), 3.93 (s, 1H), 3.76 (s, 5H), 1.83 (s, 3H), 1.32 (d, 3H, $J = 6.1$ Hz), 1.30 (d, 3H, $J = 6.1$ Hz); ^{13}C-NMR ($CDCl_3$): δ 195.6 (C), 194.2 (C), 164.2 (C), 135.4 (C), 77.8 (C), 75.0 (CH), 71.5 (CH), 70.6 (CH), 69.2 (CH), 69.1 (CH), 68.6 (CH), 23.7 (CH_3), 7.4 (CH_3); IR (CH_2Cl_2): 3096 (vw), 2979 (w), 2871 (w), 1689 (vs), 1628 (s), 1448 (vw), 1388 (s), 1326 (s), 1152 (m), 1104 (s) cm^{-1}; MS (EI): 352 ($[M]^+$, 100), 351 (75), 311 (18), 310 (94), 309 (97), 243 (47), 226 (32), 224 (23), 199 (10), 159 (13), 121 (36), 115 (12); HRMS (EI): Calc. for $C_{19}H_{20}{}^{56}FeO_3$: 352.0761. Found: 352.0745.

4.4.3. 4-Isopropoxy-5-((ferrocenyl)(methoxy)methylene)-3-methyl-2(5H)-furanone (**5A**)

Dark red oil, $R_f = 0.20$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 4.80 (m, 1H), 4.78 (s, 2H), 4.43 (s, 2H), 4.10 (s, 5H), 3.72 (s, 3H), 1.90 (s, 3H), 1.34 (d, 6H, $J = 6.0$ Hz); ^{13}C-NMR ($CDCl_3$): δ 170.7 (C), 162.4 (C), 146.9 (C), 135.8 (C), 102.2 (C), 77.1 (C), 75.2 (CH), 71.0 (CH), 70.5 (CH), 69.2 (CH), 63.6 (CH_3), 23.0 (CH_3), 9.3 (CH_3); IR (CH_2Cl_2): 2981 (w), 2933 (w), 1739 (vs), 1621 (s), 1515 (m), 1456 (m), 1405 (m), 1265 (m), 1188 (m), 1146 (w), 1104 (w) cm^{-1}; MS (EI): 382 ($[M]^+$, 100), 340 (30), 325 (7), 309 (7), 275 (5), 243 (8), 224 (16), 213 (19), 185 (11), 129 (10), 121 (8); HRMS (EI): Calc. for $C_{20}H_{22}{}^{56}FeO_4$: 382.0867. Found: 382.0864.

4.4.4. 4-Isopropoxy-5-((ferrocenyl)(methoxy)methylene)-3-phenyl-2(5H)-furanone (**5B**)

Dark red oil, $R_f = 0.32$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 7.73 (m, 2H), 7.35 (m, 2H), 7.26 (m, 1H), 4.87 (t, 2H, $J = 1.8$ Hz), 4.57 (septet, 1H, $J = 6.1$ Hz), 4.41 (t, 2H, $J = 1.8$ Hz), 4.14 (s, 5H), 3.81 (s, 3H), 1.19 (d, 6H, $J = 6.1$ Hz); ^{13}C-NMR ($CDCl_3$): δ 168.3 (C), 162.2 (C), 149.1 (C), 135.8 (C), 130.8 (C), 129.2 (CH), 128.7 (CH), 128.4 (CH), 109.0 (C), 77.6 (CH), 76.5 (C), 71.3 (CH), 70.7 (CH), 70.5 (CH), 69.4 (CH), 63.9 (CH_3), 22.6 (CH_3), 22.6 (CH_3); IR (CH_2Cl_2): 3054 (vw), 2979 (w), 2934 (w), 1739 (vs), 1616 (s), 1541 (vw),

1493 (w), 1457 (w), 1404 (m), 1320 (w), 1137 (m), 1099 (w), 1052 (w) cm^{-1}; MS (EI): 444 ($[M]^+$, 100), 403 (10), 402 (37), 382 (6), 352 (7), 305 (10), 286 (16), 213 (21), 185 (15), 129 (11), 121 (9); HRMS (EI): Calc. for $C_{25}H_{24}{}^{56}FeO_4$: 444.1024. Found: 444.1036.

4.4.5. 5-((Ferrocenyl)(methoxy)methylene)-3,4-dimethyl-2(5H)-furanone (**5C**)

Dark red oil, $R_f = 0.21$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 4.86 (s, 2H), 4.44 (s, 2H), 4.18 (s, 5H), 3.77 (s, 3H), 2.30 (s, 3H), 1.91 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ 171.0 (C), 147.3 (C), 147.0 (C), 141.1 (C), 121.8 (C), 76.3 (C), 70.7 (CH), 70.5 (CH), 69.4 (CH), 62.4 (CH_3), 12.8 (CH_3), 9.0 (CH_3); IR (CH_2Cl_2): 2935 (w), 1740 (vs), 1612 (m), 1454 (w), 1269 (w), 1195 (w), 1142 (w), 1113 (w), 1054 (m) cm^{-1}; MS (EI): 338 ($[M]^+$, 100), 323 (15), 295 (20), 243 (5), 213 (19), 185 (15), 129 (10), 121 (11); HRMS (EI): Calc. for $C_{18}H_{18}{}^{56}FeO_3$: 338.0605. Found: 338.0602.

4.4.6. 5-((Ferrocenyl)(methoxy)methylene)-3,4-diphenyl-2(5H)-furanone (**5D**)

Dark red oil, $R_f = 0.33$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 7.37–7.22 (m, 6H), 7.20–7.10 (m, 4H), 4.86 (s, 2H), 4.45 (s, 2H), 4.18 (s, 5H), 3.05 (s, 3H); ^{13}C-NMR (C_3H_6O-d_6): δ 168.5 (C), 151.0 (C), 149.7 (C), 140.0 (C), 134.1 (C), 131.6 (C), 130.0 (CH), 129.8 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 123.7 (C), 77.1 (C), 71.8 (CH), 71.0 (CH), 70.0 (C), 63.0 (CH_3); IR (CH_2Cl_2): 2956 (vs), 2928 (vs), 2865 (s), 1738 (s), 1646 (w), 1601 (vw), 1458 (m), 1377 (w), 1254 (w), 1133 (vw) cm^{-1}; MS (EI): 462 ($[M]^+$, 100), 460(6), 419 (4), 367 (10), 213 (22), 185 (11), 129 (7), 121 (6); HRMS (EI): Calc. for $C_{28}H_{22}{}^{56}FeO_3$: 462.0918. Found: 462.0909.

4.4.7. 3,4-Diisopropoxy-5-((ferrocenyl)(methoxy)methylene)-2(5H)-furanone (**5E**)

Dark red oil, $R_f = 0.32$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 5.26 (septet, 1H, $J = 6$ Hz), 4.98 (septet, 1H, $J = 6.0$ Hz), 4.87 (s, 2H), 4.44 (s, 2H), 4.21 (s, 5H), 3.79 (s, 3H), 1.41 (d, 6H, $J = 6.0$ Hz), 1.33 (d, 6H, $J = 6.0$ Hz); ^{13}C-NMR ($CDCl_3$): δ 164.8 (C), 150.2 (C), 147.0 (C), 133.7 (C), 122.3 (C), 77.6 (CH), 74.6 (CH), 74.0 (CH), 70.6 (CH), 70.3 (CH), 70.1 (CH), 63.4 (CH_3), 23.0 (CH_3), 22.9 (CH_3); IR (CH_2Cl_2): 3097 (w), 2980 (m), 2935 (w), 1742 (vs), 1623 (s), 1462 (m), 1381 (m), 1275 (s), 1116 (s), 1051 (m) cm^{-1}; MS (EI): 426 ($[M]^+$, 100), 384 (18), 342 (19), 313 (20), 299 (7), 285 (6), 257 (6), 226 (7), 213 (10), 186 (10), 163 (6), 129 (8), 121 (10); HRMS (EI): Calc. for $C_{22}H_{26}{}^{56}FeO_5$: 426.1129. Found: 426.1116.

4.4.8. 5-(Ferrocenylmethylene)-3,4-diphenyl-2(5H)-furanone (**6D**)

Dark red oil, $R_f = 0.39$ in 9:1 C_6H_{14}–EtOAc: ^{1}H-NMR ($CDCl_3$): δ 7.40 (m, 3H), 7.36 (m, 2H), 7.26 (m, 2H), 7.19 (m, 3H), 5.80 (s, 1H), 4.73 (s, 2H), 4.40 (s, 2H), 4.10 (s, 5H); ^{13}C-NMR ($CDCl_3$): δ 169.3 (C), 149.5 (C), 146.8 (C), 131.3 (C), 130.3 (C), 129.8 (CH), 129.5 (CH), 129.4 (CH), 129.4 (CH), 128.7 (CH), 128.7 (CH), 123.4 (C), 115.5 (CH), 77.6 (C), 71.6 (CH), 71.2 (CH), 70.2 (CH); IR (CH_2Cl_2): 3054 (w), 2928 (w), 1745 (vs), 1645 (m), 1456 (w), 1266 (w) cm^{-1}; MS (EI): 432 ($[M]^+$, 100), 430 (6), 367 (5), 310 (3), 253 (4), 252 (3), 121 (4); HRMS (EI): Calc. for $C_{27}H_{20}{}^{56}FeO_2$: 432.0813. Found: 432.0829.

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