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Reaction of ferrocenylcarbene complexes of Cr, Mo and W with alkynes: synthesis of ferrocenylcyclobutenones, ferrocenylfurans and ferrocenylketoesters

Metin Zora* and Elif Ünsal Güngör

Department of Chemistry, Middle East Technical University, 06531 Ankara, Turkey

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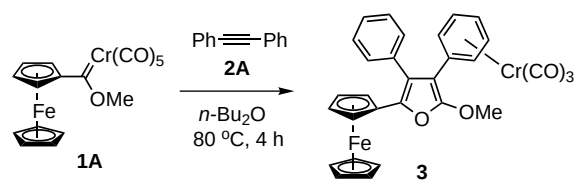
Abstract—Ferrocenylcarbene complexes of Cr, Mo and W react with alkynes to produce cyclobutenones, furans and/or ketoesters. The reaction is quite sensitive to the substituents of the alkyne, regardless of the identity of the metal. Cyclobutenones are formed only in the reactions of diphenylacetylene, a rare occurrence for metal carbene complexes. Ketoesters are secondary reaction products and result from oxidation of furan derivatives during the course of the reaction and/or silica-gel chromatography.

Recently, Fischer type metal carbene complexes have emerged as valuable reagents for organic synthesis.[1] One of the most intensely studied reactions of metal carbene complexes is the coupling of α,β-unsaturated Fischer carbene complexes with alkynes, known as the Dötz reaction.[2] It has been reported that phenols, cyclopentenones, indenes, furans, cyclobutenones, vinylketenes and cyclohexadienones have resulted from these reactions under appropriate conditions.[3] The first product ever isolated from this type of reaction was a phenol derivative,[2,3] which is normally the predominant product of the reaction. 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. Among the numerous Fischer carbene complexes, ferrocenylcarbene complexes of Cr and W have also been described,[4] which represent novel heterobinuclear organometallic compounds consisting of donor–acceptor systems. Complexes having these characteristics are attractive synthetic targets due to their physical and chemical properties.[5] Although many variations of the Dötz reaction are known, the one between ferrocenylcarbene complexes and alkynes has not been investigated in much detail. The only report in this field appears to be referring to the reaction of the ferrocenylcarbene complex of Cr (**1A**) with diphenylacetylene (**2A**) (Scheme 1).[6] The only product reported from this study was the ferrocenylfuran derivative, **3**.[6] Recently, ferrocene derivatives have gained in importance since their oxidized forms such as ferrocenium salts show some antitumor activities.[7] We herein describe a more detailed account of the reaction of ferrocenylcarbene complexes of Cr (**1A**), Mo (**1B**) and W (**1C**) with alkynes (**2**).

The ferrocenylcarbene complexes used in this study were synthesized according to a modified literature procedure.[4] Initially, the reaction of the carbene complex **1A** with diphenylacetylene (**2A**) was examined under a variety of conditions. The best results were obtained in dioxane at 100°C. The results of this study are summarized in Scheme 2 and Table 1.

The reaction of **1A** with a slight excess of **2A** (1.5 equiv.) produced only cyclobutenone **4A** (entry 1),[9] which was not reported previously from this reaction under different conditions.[6] However, the same reaction with an excess of **2A** (2.5 equiv.) afforded two products, cyclobutenone **4A** and furan **5A**,[10] with **4A** the major



Scheme 1.

Keywords: ferrocenylcarbene complexes; ferrocenylcyclobutenones; ferrocenylfurans; ferrocenylketoesters; Dötz reaction; alkynes.

* Corresponding author. Tel.: +90-312-210-3213; fax: +90-312-210-1280; e-mail: zora@metu.edu.tr

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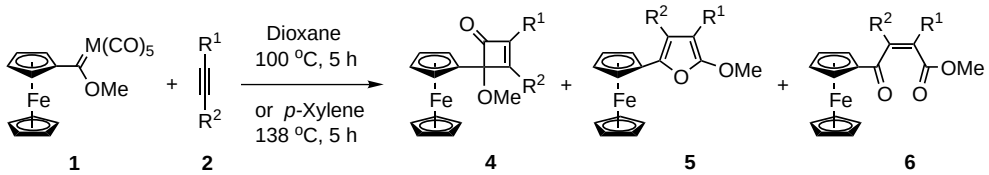

1 2 4 5 6

Scheme 2. Compound **1**: (**A**) M = Cr; (**B**) M = Mo; (**C**) M = W; Compounds **2**, **4**, **5** and **6**: (**A**) $R^1 = R^2 =$ Ph; (**B**) $R^1 =$ Ph, $R^2 =$ Me; (**C**) $R^1 = R^2 = n$-Pr.

Table 1. Reaction of ferrocenylcarbene complexes **1** with alkynes **2**[a]

Entry	Reacting partners	Equiv. of alkyne **2**	Products (% yield)[b]
1	**1A**+**2A**	1.5	**4A** (38)
2	**1A**+**2A**	2.5	**4A** (43)+**5A** (20)
3	**1A**+**2B**	1.5	**5B** (13)
4	**1A**+**2B**	2.5	**5B** (29)+**6B** (10)
5	**1A**+**2C**	1.5	**6C** (15)
6	**1A**+**2C**	2.5	**5C** (18)+**6C** (21)
7	**1B**+**2A**	1.5	**4A** (27)
8	**1B**+**2A**	2.5	**4A** (37)
9	**1B**+**2B**	2.5	**5B** (40)+**6B** (19)
10	**1B**+**2C**	2.5	**5C** (10)+**6C** (17)
11	**1C**+**2A**	2.5	**4A** (34)+**5A** (30)

[a] All reactions were carried out in dioxane at 100°C, except the one in entry 11 which was conducted in *p*-xylene at 138°C. For a representative procedure, see Ref. 8.
[b] Isolated yields.

product of the reaction (entry 2). The reaction between the carbene complex **1A** and 1-phenylpropyne (**2B**) yielded only the furan derivative **5B** (entry 3). The same reaction with excess **2B** (2.5 equiv.) led to the formation of furan **5B** and ketoester **6B** (entry 4). Similarly, the reaction of the carbene complex **1A** with 4-octyne (**2C**) gave furan **5C** and/or ketoester **6C** depending upon the equivalents of **2C** used (entries 5 and 6). Interestingly, in the reactions with 1-phenylpropyne (**2B**) and 4-octyne (**2C**) (entries 3–6), cyclobutenones were not observed. Moreover, in these reactions, ketoesters were obtained along with furan derivatives. The formation of ketoesters may not actually represent a different reaction pathway, since their formation is a secondary reaction process and occurs via oxidation of furan derivatives during the course of the reaction, as evidenced by the NMR and IR spectra of the crude products, and/or during the chromatographic purification on silica gel. The oxidation of furans to ketoesters can be diminished if the silica gel is pretreated with triethylamine. Secondary oxidation processes have often been observed in the reactions of carbene complexes.[11] Ferrocenylfurans **5B** and **5C** are stable enough for characterization by ^{1}H and ^{13}C NMR but slowly furnish the corresponding ketoesters **6B** and **6C** on exposure to air. It should be noted that, compared with **5B** and its oxidation product **6B**, the proportion of oxidized compound **6C** increased at the expense of compound **5C**, presumably due to the relative instability of **5C**. However, the ferrocenylfuran **5A** was quite stable since no ketoester resulted from this compound during silica-gel chromatography. As shown by previous investigators,[11] the substitution pattern of 2-methoxyfuran derivatives is important with regard to their stability.

Since molybdenum carbene complexes typically display greater reactivity than either chromium or tungsten carbene complexes,[12] the ferrocenylmolybdenum carbene complex **1B** was prepared for the first time and its reactions with alkynes examined.[13] The reaction of the carbene complex **1B** with diphenylacetylene (**2A**) afforded only cyclobutenone **4A** (entries 7 and 8), as in the case of the reaction between chromium carbene complex **1A** and **2A**. However, as noted in entry 9, the reaction of carbene complex **1B** with **2B** led to a mixture of the furan **5B** and ketoester **6B**, without the formation of any cyclobutenone. A similar trend was observed in the reaction of **1B** with **2C**, where furan **5C** and ketoester **6C** were obtained (entry 10). The tungsten carbene complex **1C** was noticeably less reactive and its reaction with alkynes required high reaction temperatures. For instance, the reaction of carbene complex **1A** with **2A** in dioxane at 100°C did not produce any product. However, the same reaction in *p*-xylene at 138°C yielded a mixture of cyclobutenone **4A** and furan **5A** (entry 11).

As can be seen from the Table 1, the use of excess alkyne, such as 2.5 equiv., clearly increases the yields of the products. The use of excess alkyne increases the number of products as well. It should be pointed out that the overall reaction appears to be sensitive to the substitution pattern of the alkyne since, for instance, cyclobutenones have been observed only in reactions of diphenylacetylene (**2A**), regardless of the identity of the metal in the carbene complex. Moreover, when formed, cyclobutenones are the single or the major product of these reactions. The formation of cyclobutenones from the reactions of carbene complexes with alkynes has been known for some time but they are rarely the major products from these reactions.[9,11a]

In summary, we have investigated the reactions of ferrocenylcarbene complexes of Cr (**1A**), Mo (**1B**) and W (**1C**) with alkynes, producing cyclobutenones, furans and/or ketoesters. Although no benzannulation products other than furan derivatives have been observed in these reactions, our studies have shown that, under appropriate conditions, ferrocenylcarbene complexes can follow the reactivity patterns of other carbene complexes to afford a diverse array of ferrocenyl compounds. We are continuing to explore the further reactivity of ferrocenylcarbene complexes **1A**–**C**.

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8. **Representative procedure for the reaction of ferrocenylcarbene complexes with alkynes**: The reaction of ferrocenylcarbene complex **1A** with **2A** (Table 1, Entry B). A solution of carbene complex **1A** (210 mg, 0.50 mmol) and diphenylacetylene (**2A**) (223 mg, 1.25 mmol) in dioxane (10 mL) was heated to reflux under argon for a period of 5 h. The mixture was allowed to cool to room temperature and the solvent was removed on a rotary evaporator. Final purification was achieved by flash chromatography on silica gel using 19:1 hexane/ethyl acetate followed by 9:1 hexane/ethyl acetate as the eluent. Two fractions were isolated. The first fraction (R_f=0.46 in 9:1 hexane/ethyl acetate) was assigned as ferrocenylfuran **5A** (43 mg, 20%). The second fraction (R_f=0.36 in 9:1 hexane/ethyl acetate) was identified as ferrocenylcyclobutenone **4A** (93 mg, 43%).
Spectral data for 4A: ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.86 (pseudo d, 4H, J=8.1 Hz), 4.44 (m, 6H), 4.56 (s, 1H), 4.21 (s, 1H), 4.14 (s, 5H), 4.10 (s, 1H), 3.95 (s, 1H), 3.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 191.0 (C), 169.7 (C), 145.5 (C), 131.7 (CH), 131.2 (C), 129.7 (CH), 129.0 (CH), 128.9 (CH), 128.4 (CH), 128.0 (CH), 98.7 (C), 85.7 (C), 77.2 (C), 69.3 (CH), 68.1 (CH), 68.0 (CH), 67.9 (CH), 66.6 (CH), 53.2 (CH_3); IR (CH_2Cl_2): 3065 (vw), 2931 (vw), 1750 (vs), 1444 (vw), 1346 (m), 1195 (vw), 1144 (vw), 1097 (w), 909 (m) cm^{-1}. MS (EI): 434 (M^+, 100), 419 (89), 403 (16), 391 (13), 375 (23), 368 (34), 311 (23), 286 (17), 254 (55), 241 (35), 213 (30), 185 (25), 178 (16), 165 (12), 129 (21), 121 (32); HRMS: calcd for $C_{27}H_{22}{}^{56}FeO_2$ 434.0969, found 434.0983.
Spectral data for 5A: ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.38–7.06 (m, 10H), 4.27 (s, 2H), 4.12 (s, 2H), 4.08 (s, 5H), 4.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 155.4 (C), 139.8 (C), 134.3 (C), 132.1 (C), 130.8 (CH), 128.8 (CH), 128.7 (CH), 128.3 (CH), 127.6 (CH), 126.0 (CH), 121.6 (C), 102.3 (C), 76.8 (C), 69.6 (CH), 68.4 (CH), 66.1 (CH), 59.4 (CH_3); IR (CH_2Cl_2): 3065 (m), 3036 (m), 2978 (s), 1635 (vs), 1597 (vs), 1457 (s), 1395 (s), 1374 (m), 1316 (m), 1268 (vs) cm^{-1}. MS (EI): 434 (M^+, 100), 419 (95), 353 (12), 252 (20), 241 (15), 213 (45), 185 (44), 129 (34), 121 (29), 83 (34); HRMS: calcd for $C_{27}H_{22}{}^{56}FeO_2$ 434.0969, found 434.0954.
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13. **Spectral data for ferrocenylmolybdenum carbene complex 1B**: ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 4.99 (s, 2H), 4.83 (s, 2H), 4.59 (s, 3H), 4.26 (s, 5H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 323.7 (C), 213.1 (C), 206.9 (C), 93.7 (C), 75.5 (CH), 73.2 (CH), 71.0 (CH), 68.0 (CH_3); IR (CH_2Cl_2): 2063 (m), 1936 (vs), 1275 (m) cm^{-1}. MS (EI): 466 (M^+, 61), 410 (24), 382 (58), 354 (91), 326 (64), 296 (25), 283 (100), 255 (23), 244 (64), 213 (16), 186 (17), 152 (17), 122 (27); HRMS: calcd for $C_{17}H_{12}{}^{56}Fe^{98}MoO_6$ 465.9037, found 465.9038.