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LETTERS

Radical additions to tricarbonyl[(1-4-η)-2-methoxy-5-methylenecyclohexa-1,3-diene]iron

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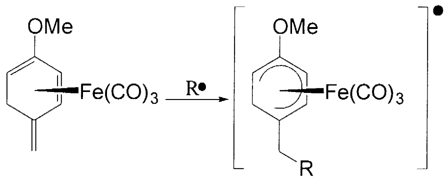
Abstract

Tricarbonyl[(1-4-η)-2-methoxy-5-methylenecyclohexa-1,3-diene]iron was found to undergo facile radical addition regioselectively at the exocyclic methylene group to yield aromatized product upon demetalation.

Tricarbonyl[(1-4-η)-2-methoxy-5-methylenecyclohexa-1,3-diene]iron **1** has proven to be a valuable intermediate in organic synthesis.[1,2] The chemistry has centered on the ability of complex **1** to form a stable cyclohexadienyliron cationic intermediate upon reaction with electrophiles. This has resulted in the successful 1,3-dipolar cycloaddition[1] and sequential electrophilic–nucleophilic addition[2] to complex **1**. Although the cyclohexadienyliron cationic intermediate is stable and widely used in the synthesis of natural products,[3] the existence of the cyclohexadienyliron radical as a transient intermediate has also been implicated[4] but not widely explored. In the last decade, the formation of a carbon–carbon bond using free radicals has become an important tool for synthetic chemists. Consequently, we investigated the possibilities of radical addition to tricarbonyl[(1-4-η)-2-methoxy-5-methylenecyclohexa-1,3-diene]iron in a controlled manner. The success of free radical addition to tricarbonyl[(1-4-η)-2-methoxy-5-methylenecyclohexa-1,3-diene]iron will add a new dimension to the repertoire of synthetic methodology available at present.



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The starting triene complex **1** was prepared in nearly quantitative yield. This complex is unstable and sensitive to oxidative decomplexation. Our initial study centered on radicals that can be produced photolytically or thermally by a cleaving disulfide and C–halogen bond. When complex **1** was treated with phenylthiyl radical ($PhS^{\cdot}$) generated from the photolysis of diphenyl disulfide,[5] 4-methoxybenzylphenylsulfide **2** was furnished in 75% yield (Table 1). This presumably arises via a regioselective radical addition to the exocyclic double bond to generate a transient radical intermediate that demetalated and aromatized, respectively. We next turned our attention to the radical addition of carbon tetrabromide[6] (CBr_4, $h\nu$) and carbon tetrachloride (CCl_4, $h\nu$) to complex **1** and this gave 1-methoxy-4-(2,2,2-tribromoethyl)benzene **3** and 1-methoxy-4-(2,2,2-trichloroethyl)benzene **4**, respectively. In all of these cases, demetalation and aromatization followed the additions of radical.

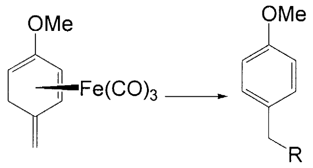
To further explore the scope of this methodology, we next examined the reactions of a carbon radical generated by a reductive process. The allyl radical was produced by the reaction of allyl bromide with tributyltin hydride and this gave 1(4-methoxyphenyl)-2-propene **5**. Even though the radical was generated under reductive conditions, demetalation was not prevented. Also in our investigation on the Diels–Alder reaction of complex **1** with *o*-xylylene (*o*-xylylene dibromide/activated zinc),[7,8] this did not produce the anticipated cycloadduct, but instead gave 1-(4-methoxyphenetyl)-2-methylbenzene **6**. The reaction of aryl- and alkylhalide with activated zinc to give organozinc is well documented, but recently it has been reported that they can also exist as a radical type during reaction.[9a–c] Treatment of complex **1** with benzyl and propyl bromide in the presence of activated zinc again produced the anticipated 1-(4-methoxyphenyl)-2-phenylethane **7** and 1-isobutyl-4-methoxybenzene **8**, respectively. Attempts to carry out carbanion addition to the exocyclic double bond in complex **1** using the Grignard reagent or organolithium were unsuccessful.

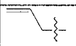
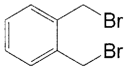
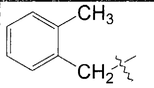
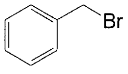
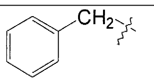
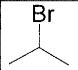
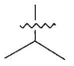
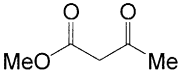
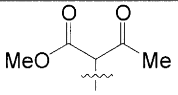
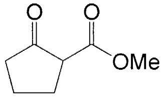
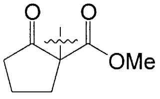
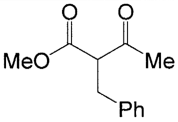
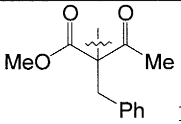
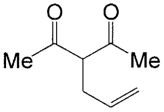
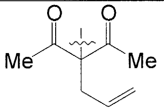
Our attention next turned to the generation of radicals using oxidative process. Metal oxidants are reagents commonly employed for the demetalation of organoiron complexes. But on the other hand, oxidative cyclization of the cyclohexadienyliron complex has been carried out successfully using thallium(III) trifluoroacetate,[10] iron(III) chloride,[11] and manganese dioxide[12] without demetalation. Thus, we chose to study the manganese(III) acetate-promoted intermolecular addition of an α-oxo- or α,α-dioxoalkyl radical[13] to complex **1**. Furthermore, the ambiphilic and electrophilic nature of these radicals will be typically matching for the electron rich exocyclic bond. A manganese(III)-promoted reaction of complex **1** with methyl acetoacetate gave the corresponding methyl 2-(4-methoxybenzyl)-3-oxobutanoate **9**. No further intramolecular tandem annulation of the intermediate to give spiro-dihydrofuran was obtained. Using the same protocol, methyl 2-oxo-cyclopentanecarboxylate was found to give methyl 1-(4-methoxybenzyl)-2-oxo-cyclopentanecarboxylate **10**. In each of these cases, the lability of the radical intermediate was observed. We hoped to utilize an alkene-tethered β-keto ester or β-diketone to act as an intramolecular trap for the labile radical intermediate. Thus, we synthesized methyl-2-benzyl-3-oxobutanoate ($CH_3COCH_2COOCH_3/^{t}BuOK/Bz\text{-}Br$) and 3-allyl-2,4-pentanedione ($CH_3COCH_2CO\text{–}CH_3/^{t}BuOK/allyl\text{-}Br$). These were again subjected to the Mn(III)-promoted oxidative addition to complex **1** leading to the formation of methyl 2-benzyl-2-(4-methoxybenzyl)-3-oxobutanoate **11** and 3-allyl-3-(4-methoxybenzyl)-2,4-pentane-dione **12**, respectively. The attempted intramolecular trapping of the transient radical was unsuccessful.

It is perhaps noteworthy that the sequence described here is the first successful intermolecular radical addition to complex **1**. This can be used for the introduction of a 4-methoxybenzyl functional group, promoted by a radical addition reaction. We are currently investigating the reaction in greater detail, to further delineate the intramolecular cyclization of the transient radical intermediate.

General procedure for photolytical reactions: To a solution of complex **1** (1 mmol) in C_6H_6 under nitrogen was added PhS–SPh (1.1 mmol) (or CBr_4 (1.1 mmol) or neat CCl_4 without C_6H_6). The reaction

Table 1
Products of radical addition to complex **1**



Reagents	Conditions	Products	Yield (%)
PhS-SPh	hν, C_6H_6, Δ, 8hr	PhS- **2**[14]	75
CBr_4	hν, C_6H_6, 8hr	Br_3C- **3**[15]	45
CCl_4	hν, CCl_4, Δ, 8hr	Cl_3C- **4**	91
	*n*-Bu_3SnH, Δ, AIBN, 8hr	 **5**[16]	39
	Zn, THF, Δ, 4hr	 **6**	83
	Zn, THF, Δ, 4hr	 **7**[17]	71
	Zn, THF, Δ, 6hr	 **8**[18]	35
	$Mn(OAc)_3$, C_6H_6, r.t, 24hr	 **9**	41
	$Mn(OAc)_3$, C_6H_6, r.t, 24hr	 **10**	45
	$Mn(OAc)_3$, C_6H_6, r.t, 24hr	 **11**	70
	$Mn(OAc)_3$, C_6H_6, r.t, 24hr	 **12**	35

mixture was refluxed and exposed to a 100 watt light bulb for 10 h. The resulting mixture was poured into a brine solution and the organic layer separated, dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by column chromatography on silica gel (hexane:ethyl acetate, 20:1) gave **2**: ^1H NMR ($CDCl_3$, 200 MHz) δ 3.82 (s, 3H), 3.86 (s, 2H), 6.90 (d, 2H, J=8.7 Hz), 7.36 (d, 2H, J=8.7 Hz). Anal. calcd for $C_9H_9OCl_3$: C, 45.13; H, 3.79. Found: C, 45.05; H, 3.75. Similar conditions were used to purify **3** and **4**.

General procedure for the reaction of halogenated compounds in the presence of zinc: To a solution of complex **1** (1 mmol) in THF under nitrogen was added zinc (3 mmol), followed by the halogenated compound (1.1 mmol). The reaction was stirred for 5 h and the reaction mixture was filtered with Celite. The THF was evaporated in vacuo, water was added and extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by column chromatography on silica gel (hexane:ethyl acetate, 4:1) gave **6**: mp 54–56°C. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.29 (s, 3H), 2.85 (m, 4H), 3.78 (s, 3H), 6.84 (d, 2H, J=8.7 Hz), 7.03–7.20 (m, 6H). Anal. calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.58; H, 7.84 (compound **7** purified with hexane:ethyl acetate, 5:1).

General procedure for the manganese(III)-promoted radical reaction: To a solution of the ketoester or diketone (1.1 mmol) in benzene under nitrogen was added Mn(III)OAc_3. A solution of complex **1** (1 mmol) in benzene was added slowly and the solution was stirred at room temperature until all the complex has been consumed (10–15 h). A solution of Na_2SO_3 was then added, and the mixture filtered with Celite and washed well with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by column chromatography on silica gel (hexane:ethyl acetate, 4:1) gave **9**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.17 (s, 3H), 2.98 (d, 2H, J=8.8 Hz), 3.52 (t, 1H, J=4.4 Hz), 3.57 (s, 3H), 3.65 (s, 3H), 6.69 (d, 2H, J=8.4 Hz), 6.97 (d, 2H, J=8.4 Hz). Anal. calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.92; H, 6.65. Compound **10** (hexane:ethyl acetate, 4:1): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.95 (m, 4H), 2.40 (m, 2H), 3.10 (q, 2H, J=2.4 Hz), 3.72 (s, 3H), 3.78 (s, 3H), 6.79 (d, 2H, J=8.4 Hz), 7.04 (d, 2H, J=8.4 Hz). Anal. calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.42; H, 6.97. Compound **11** (hexane:ethyl acetate, 5:1): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.93 (s, 3H), 3.19 (close s, 4H), 3.65 (s, 3H), 3.76 (s, 3H), 7.07–7.26 (m, 9H). Anal. calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.15; H, 6.46. Compound **12** (hexane:ethyl acetate, 3:1): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.10 (s, 6H), 2.60 (d, 2H, J=7.2 Hz), 3.17 (s, 2H), 3.77 (s, 3H), 5.03 (d, 1H, J=15.8 Hz), 5.18 (d, 1H, J=15.8 Hz), 5.54 (m, 1H), 6.79 (d, 2H, J=8.7 Hz), 6.96 (d, 2H, J=8.7 Hz). HRMS calcd. for $C_{16}H_{20}O_3$ (M^+): 259.3310. Found: 259.2754.

Acknowledgements

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