Preparation of *m*-Acylphenol Derivatives by the Reaction of Tricarbonyl(cyclohexadienone)iron Complex and Higher Order Cuprates

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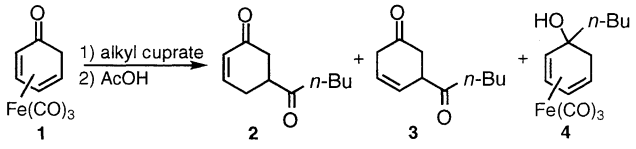
Reaction of tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadien-1-one]iron and higher order cuprates followed by the treatment with acetic anhydride and then with carbon monoxide affords tricarbonyl[(1,2,3,4-η)-1-acetoxy-5-*endo*-acyl-1,3-cyclohexadiene]iron complexes in good yield, which are converted to *meta*-acylphenol derivatives by the oxidation with trimethylamine *N*-oxide.

Direct transformation of phenol derivatives to *meta*-acylphenols has remained unsolved in organic synthesis.[1] In this report, we would like to present a method for the regioselective formation of *meta*-acylphenols[2] by using tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadien-1-one]iron (**1**)[3] as a phenol equivalent.

It has been known that *n*-BuLi and $BrZnCH_2CO_2Et$ add to the carbonyl group in the hexadienone moiety of **1** to afford the corresponding 1,2-addition products such as butylbenzene and ethyl phenylacetate, respectively.[4] We happened to find that treatment of **1** with tritylllithium and then with *t*-butyldimethylsilyl chloride gave a 5-trityl iron complex, tricarbonyl[(1,2,3,4-η)-1-*t*-butyldimethylsilyloxy-5-trityl-1,3-cyclohexadiene]iron, in 74% yield. This finding prompted us to investigate the reaction of **1** with various organometallic reagents with the expectation that regioselective alkylation would be realized at the 5 position of the dienone moiety of the iron complex **1**.

Though simple alkyllithiums afforded 1,2-addition products, *n*-Bu_2CuLi reacted with **1**, and, after quenching the reaction with acetic acid, 5-pentanoyl-2-cyclohexen-1-one (**2**) and 5-pentanoyl-3-cyclohexen-1-one (**3**) were obtained in 44 and 15% yield, respectively, along with 14% of a 1,2-addition product **4**.



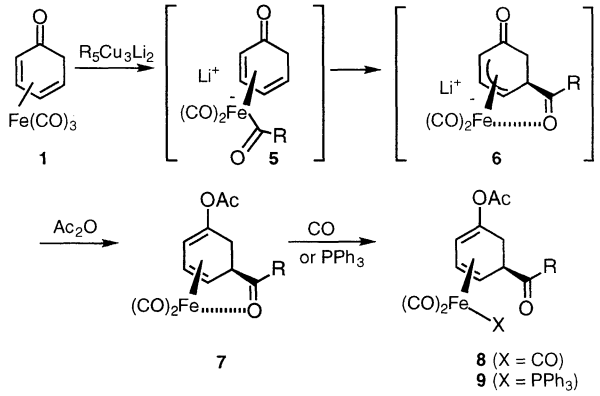
n-Bu_2CuLi	44%	15%	14%
n-$Bu_5Cu_3Li_2$	71%	7%	0%

This result indicates that the cuprate mainly reacts with the coordinated carbon monoxide of the iron complex **1**. The acyl ligand thus generated migrates to the 5-position of the cyclohexadienone moiety. Then, the dicarbonyliron group is cleaved to afford the 5-acylcyclohexadienones **2** and **3** by the treatment with acetic acid.

Acyl anions generated by the reaction of tricarbonyliron complexes of acyclic α,β-unsaturated ketones with alkyllithiums or Grignard reagents are reported to migrate to the β-position to provide 1,4-diketones.[5] In contrast, tricarbonyliron complexes of conjugate dienones react with alkyllithiums or organocuprates-BF_3 to give 1,2-addition products,[6] except the reaction of tricarbonyl[(2,3,4,5-η)-7-methylbicyclo[5.3.0]-2,4,7-decatrien-1-one]iron with Me_2CuLi,[7] in which the acylation reaction proceeds at δ-position of the dienone moiety. Since there has been only this exceptional report on the δ-acylation of dienone moiety, we investigated the conjugated addition reaction of various organometallic reagents to the iron complex **1**.

After screening organocuprate reagents, it was found that a higher order cuprate (*n*-$Bu_5Cu_3Li_2$)[8] generated from 3.5 molar amounts of *n*-BuLi and 2.1 molar amounts of CuI reacted with **1** to give the 5-acyl derivatives **2** and **3** in 71 and 7% yield, respectively, without formation of the 1,2-addition product **4**.

When the reaction of **1** and *s*-$Bu_5Cu_3Li_2$ was quenched with acetic anhydride at -78 °C instead of acetic acid, a thermally unstable and acid sensitive complex **7** (R = *s*-Bu, IR 1639 cm^{-1}) was isolated by the rapid Florisil column chromatography at 0 °C. The unstable complex **7** could be converted to the more stable complex **8**[9] (R = *s*-Bu, IR 1712 cm^{-1}) by bubbling carbon monoxide into the ethereal solution of the complex **7** at room temperature. The complex **8** was also prepared without isolation of the labile complex **7**. That is, **8** was obtained in 97% yield by the treatment of the reaction mixture of **1** and *s*-$Bu_5Cu_3Li_2$ with acetic anhydride and then directly with carbon monoxide. The unstable complex **7** was also converted to a phosphine complex, dicarbonyl[(1,2,3,4-η)-1-acetoxy-5-*endo*-(2-methylbutanoyl)-1,3-cyclohexadiene](triphenylphosphine)iron **9** (R=*s*-Bu, IR 1709 cm^{-1}) by treatment with triphenylphosphine, which was isolated as a crystalline material.



The structure of **9**[10] was determined by X-ray analysis as shown in Figure 1. In this complex **9**, $Fe(CO)_2PPh_3$ and the acyl moiety orient to *endo* each other. This suggests that the acyl ligand migrates intramolecularly to the dienone moiety from the same side of the iron moiety. By the correlation with the structure of the phosphine complex **9** and their IR spectra, the structures of **8** and **7** were confirmed as tricarbonyl and dicarbonyl-[(1,2,3,4-η)-1-acetoxy-5-*endo*-acyl-1,3-cyclohexadiene]irons, respectively.

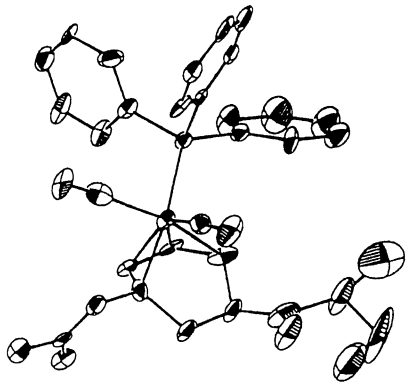
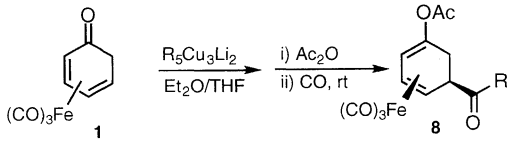


Figure 1.

The results of the reaction of **1** and primary, secondary, and tertiary alkylcuprates are listed in Table 1. Not only acetyl and pentanoyl groups but also 2-methylbutanoyl and pivaloyl groups could be introduced regioselectively, giving the corresponding 5-acyl derivatives **8** in good yield.

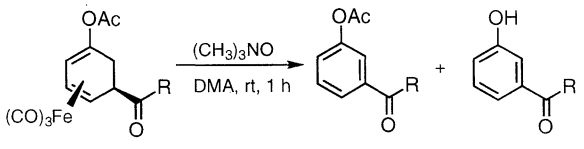
Table1. Reaction of the tricarbonyliron complex **1** with organocuprate[a]



R	Yield / %
Me	68
n-Bu	88
s-Bu	97
t-Bu[b]	91

[a]In all cases, reaction temperature is -78 °C unless otherwise noted. [b]Reaction temperature is 0 °C.

Table 2. Reaction of the tricarbonyliron complex **8** with trimethylamine *N*-oxide



R	Yield / %		
	10	**11**	total (**10** + **11**)
Me	46	25	71
n-Bu	57	25	82
s-Bu	53	14	67
t-Bu	59	16	75

Removal of the iron moiety from the tricarbonyl complexes **8** was accomplished by the oxidation with trimethylamine *N*-oxide[11] in *N,N*-dimethylacetamide (DMA) at room temperature for 1 h. Though the acetyl group was partially cleaved under the reaction conditions, the *meta*-acylphenol derivatives **10** and **11** were obtained in good yield in all cases examined.

Thus, starting from the readily available iron complex of cyclohexadienone **1**, *meta*-acylphenols are prepared in a regioselective manner by the reaction with higher order cuprates.

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9 ^{1}H NMR (500MHz, $CDCl_3$) δ = 0.81 (1.5H, t, J = 7.4 Hz), 0.83 (1.5H, t, 7.5 Hz), 1.01 (1.5H, d, J = 7.0 Hz), 1.03 (1.5H, d, J = 7.0 Hz), 1.31-1.34 (1H, m), 1.60-1.67 (1H, m), 2.02 (3H, s), 2.00-2.12 (1H, m), 2.51-2.54 (2H, m), 2.67-2.69 (1H, m), 3.05-3.25 (1H, m), 5.14 (1H, dd, J = 5.4 and 3.5 Hz), 5.33 (1H, d, J = 3.5 Hz).
10 $C_{33}H_{33}O_5PFe$: Formula weight = 596.44, Monoclinic, $P2_1/c$, a = 16.41(1), b = 10.804(8), c = 17.174(7) Å, β = 98.38(4)°, V = 3012(2) Å^3, Z = 4, No of observations = 3048(I > 3.00σ(I)), D_{calcd} = 1.315 g/cm^3, F(000) = 1248.00, R(Rw) = 0.137(0.112); ^{1}H NMR (500MHz, $CDCl_3$) δ = 0.73 (1.5H, t, J = 7.4 Hz), 0.75 (1.5H, t, J = 7.4 Hz), 0.83 (1.5H, d, J = 6.8 Hz), 0.92 (1.5H, d, J = 6.8 Hz), 1.16-1.23 (2H, m), 1.41-1.55 (1H, m), 2.00-2.06 (1H, m), 2.08 (3H, s), 2.27-3.32 (1H, m), 2.35-2.42 (1H, m), 2.62-2.67 (1H, m), 4.36-4.40 (1H, m), 5.22-5.25 (1H, m), 7.35-7.42 (15H, m).
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