One-Step Synthesis of 1,4-Diketones by Nucleophilic Reaction to Tricarbonyl Complexes of α,β-Unsaturated Ketones

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Synopsis. Tricarbonyliron complexes of 3-buten-2-one, 3-penten-2-one, and 4-phenyl-3-buten-2-one reacted with organolithium and Grignard reagents to afford 1,4-diketones in one step, some of the products are amenable to convertion to natural products.

Much attention has been devoted in recent years to the chemistry of iron carbonyl complexes of dienes and polyenes.[1] Recently, the reaction of tricarbonyl-(4-phenyl-3-buten-2-one)iron and its derivatives with organolithium and Grignard reagents to give the corresponding 1,4-diketones has been reported.[2] This has prompted us to report our similar results and their application to the synthesis of some natural products.[3]

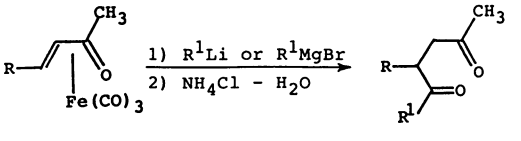
(3-Buten-2-one)tricarbonyliron (**1**)[4] was reacted with 2.5 molar equivalents of butyllithium in THF at −78 °C for 25 min. The reaction mixture was quenched with diluted H_2SO_4 or with saturated NH_4Cl aqueous solution to give 2,5-nonanedione **2** (R^1=*n*-Bu) in 62% yield. The reaction of **1** with *t*-BuLi and PhLi afforded the corresponding 1,4-diketones in 29% and 75% yields, respectively.

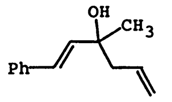
The similar reaction of (3-penten-2-one)tricarbonyliron (**3**)[5] and tricarbonyl(4-phenyl-3-buten-2-one)iron (**5**)[6] with organolithium and Grignard reagents also yielded the corresponding 1,4-diketones **4** and **5**, respectively; the results are shown in Table 1. The reaction of **5** with allylmagnesium bromide, however, afforded a 1,2-addition product **7** in 80% yield.

The structures of these products were determined by spectroscopic analyses or by the comparison of their ^{1}H NMR and/or IR spectra with those of authentic samples.

As has already been reported,[2] the reactions probably proceed by acyl transfer from a metal acyl intermediate to the, α,β-unsaturated ketone followed by protonation. Therefore, we attempted a quenching of a reaction mixture of **1** and *n*-BuLi with excess MeI instead of NH_4Cl aqueous solution, however, no methylated product could be obtained, only **2** (R^1=*n*-Bu) was produced.

The reaction of **1** with hexyl- and *p*-methylbenzylmagnesium bromide afforded the corresponding 1,4-diketones **8** and **9** in 82% and 19% yields, respectively, as shown in Table 1. The compound **8** was then





1 R = H 2 R = H 7

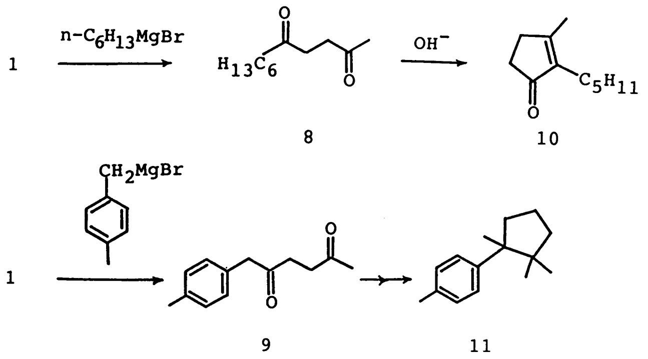
3 R = CH_3 4 R = CH_3

5 R = Ph 6 R = Ph

Table 1. Synthesis of 1,4-Diketones (in THF, −78 °C)

Complex	Reagent	Reaction time/min	Product (yield/%[a])
1	*n*-BuLi	25	**2** R^1=*n*-Bu[b] (62)
1	*t*-BuLi	40	**2** R^1=*t*-Bu[c] (29)
1	*n*-C_6H_{13}MgBr	20	**8** (**2** R^1=*n*-C_6H_{13}[d]) (82)
1	PhLi	25	**2** R^1=Ph[b] (75)
1	*p*-$MeC_6H_4CH_2$MgBr	65	**9** (**2** R^1=*p*-$MeC_6H_4CH_2$[e]) (19)
3	*n*-BuLi	10	**4** R_1=*n*-Bu[f] (53)
3	*t*-BuLi	10	**4** R^1=*t*-Bu[d] (32)
3	PhLi	10	**4** R_1=Ph[d] (29)
5	*n*-BuLi	60	**6** R_1=*n*-Bu[d] (61)
5	*s*-BuLi	20	**6** R^1=*s*-Bu (45)[g]
5	*t*-BuLi	110	**6** R^1=*t*-Bu[c] (17)
5	PhLi	60	**6** R^1=Ph[f] (19)
5	CH_2=CHMgBr	80	**6** R^1=CH=CH_2 (64)

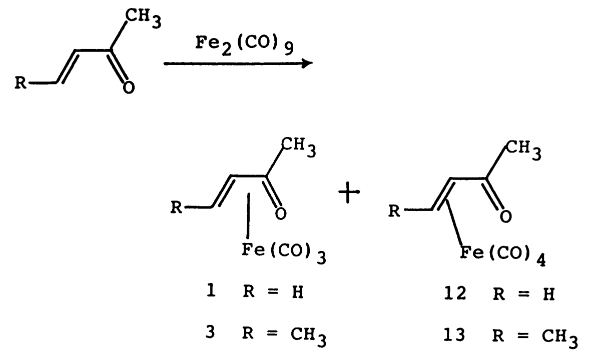
a) Isolated yield. b) Ref. 7. c) Ref. 8. d) Ref. 9. e) Ref. 10. f) Ref. 11. g) Contaminated with an unidentified product.



transformed by cyclization in basic medium conditions to dihydrojasmone **10**.[9] The compound **9** was reported to be converted to cuparene **11**.[10]

Thus it is found that this one-step synthesis of 1,4-diketones by nucleophilic reaction to tricarbonyliron complexes of α,β-unsaturated ketones will be widely useful to natural product syntheses. However, from these limited examples, we can not conclude which of the two reagents, alkyllithium and Grignard reagent, is the better in this 1,4-diketone synthesis.

In the course of the synthesis of **1** and **3** by the reaction of 3-buten-2-one and 3-penten-2-one with $Fe_2(CO)_9$ in benzene, we isolated new complexes [3-4-η-(3-buten-2-one)]tetracarbonyliron (**12**) and [3-4-η-(3-penten-2-one)]tetracarbonyliron (**13**) as orange oils along with tricarbonyl complexes **1** and **3**, respectively. The yield of **12** was dependent on the reaction temperature, thus, **1** and **12** were obtained in 7% and 47% yields, respectively at 60 °C and in 53% and 3% yields at 80 °C. Furthermore, **12** was gradually changed to **1** by heating in benzene. The structures of **12** and **13** were determined by the above fact as well as the analyses of ^{1}H NMR, IR and/or mass spectra (see Experimental).



Experimntal

General. The IR spectra were obtained with a Hitachi 260-50 spectrophotometer, ^{1}H NMR spectra were recorded with JEOL JNM-270 (270 MHz) or JNM-H60 (60 MHz) spectrometer in $CDCl_3$ solutions, and mass spectra were measured with JEOL JMS D-200 spectrometer.

Syntheses of (3-Buten-2-one)tricarbonyliron (1) and [3-4-η-(3-Buten-2-one)]tetracarbonyliron (12). A solution of 3-buten-2-one (0.41 ml, 5.0 mmol) and $Fe_2(CO)_9$ (2.728 g, 7.5 mmol) in anhydrous benzene (25 ml) was heated at 80 °C overnight. The precipitate was filtered off, solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (45 g) using benzene as eluent to give complexes **1** (554 mg, 53% yield) and **12** (40 mg, 3% yield) as orange oils.

When the same reaction was carried out at 60 °C, **1** and **12** were obtained in 7% and 47% yields, respectively.

1:[4] IR (neat), 2080, 2010, 1990 cm^{-1}; MS m/z 210 (M^+), 182, 154; ^{1}H NMR ($CDCl_3$) δ=1.36 (d, d, J=2, 12 Hz, H-4(Z)), 2.07 (d, d, J=2, 7 Hz, H-4(E)), 2.48 (s, CH_3), 5.54 (d, d, J=7, 12 Hz, H-3).

12: IR (neat), 2110, 2030, 1960 cm^{-1}; MS m/z 238 (M^+), 210, 182, 154; ^{1}H NMR ($CDCl_3$) δ=2.35 (s, CH_3), 2.56 (d, d, J=2, 7 Hz, H-4(E)), 2.98 (d, d, J=2, 12 Hz, H-4(Z)), 3.53 (d, d, J=7, 12 Hz, H-3).

The patterns of the C=O stretching region in the IR spectra of **1** and **12** are very similar to those of tricarbonyliron and tetracarbonyliron complexes of styrene, respectively.[12]

Similarly, complexes **3** and **13** were obtained by the reaction of 3-penten-2-one and $Fe_2(CO)_9$ as orange oils.

3:[5] IR (neat), 2065, 1990, 1972 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.52 (d, J=6 Hz, CH_3), 1.9—2.4 (m, H-4), 2.48 (s, CH_3), 5.47 (d, J=9 Hz, H-3).

13: unstable orange oil; IR (neat), 2105, 2030, 1980 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.81 (d, J=6 Hz, CH_3), 2.33 (s, CH_3), 3.5—4.2 (m, 2H).

General Procedure of the Reaction of Complexes with Organolithium and Grignard Reagents. The general procedure will be illustrated below by using the reactions of (3-buten-2-one)tricarbonyliron (**1**) and n-BuLi, and tricarbonyl(4-phenyl-3-buten-2-one)iron (**5**) and vinylmagnesium bromide as example.

A stirred solution of **1** (106.6 mg, 0.5 mmol) in anhydrous THF (2 ml) was cooled at −78 °C under N_2 atmosphere and was added dropwise 2.34 M hexane solution (1 M=1 mol dm^{-3}) of n-BuLi (0.54 ml, 1.25 mmol). After 25 min, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl (5 ml), extracted with CH_2Cl_2 three times, the extract was dried over anhydrous Na_2SO_4, the solvent was removed, and the residue was purified by preparative TLC on silica gel using a mixture of hexane and AcOEt (3:1) as eluent to give 2,5-nonanedione 2 (R^1=n-Bu) (49.1 mg, 62% yield) as colorless oil.

A stirred solution of **5** (143.1 mg, 0.5 mmol) in anhydrous THF (2 ml) was cooled at −78 °C under N_2 atmosphere and was added dropwise 0.9 M ethereal solution of vinylmagnesium bromide (1.5 ml, 1.25 mmol). After 80 min, the reaction mixture was quenched with saturated NH_4Cl (5 ml) and extracted with CH_2Cl_2. The extract was dried over anhydrous Na_2SO_4, the solvent removed, and the residue purified by preparative TLC using a mixture of hexane and AcOEt (5: 1) to give 4-phenyl-1-heptene-3,6-dione (**6**) (R^1=CH=CH_2) (66.7 mg, 64% yield) as colorless oil.

IR (neat), 1708, 1675 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.15 (s, CH_3), 2.63 (1H, d, d, J=4, 19 Hz, H-5), 3.58 (1H, d, d, J=11 19 Hz, H-5), 4.46 (d, d, J=4, 11 Hz, H-4), 5.68 (d, d, J=3, 10 Hz, H-2), 6.23—6.42 (2H, m, H-1), 7.10—7.40 (m, Ph).

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