The Reductive Deacylation of the Knoevenagel Condensates by the Use of the Tetracarbonylhydridoferrate(0) Anion. A New Synthetic Route of Ketones from Aldehydes

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The Knoevenagel condensates prepared from 2,4-pentanedione with aldehydes were allowed to react with the tetracarbonylhydridoferrate(0) anion in ethanol to give reductively deacylated monoketones in high yields. However, the exclusive reduction of the α,β-unsaturated double bond of the same condensates was encountered when the reaction was carried out in such a solvent as tetrahydrofuran and acetone. The Knoevenagel condensates, derived from the reaction of ethyl acetoacetate and/or ethyl benzoylacetate with aldehydes, were simply reduced even in ethanol. The reaction mechanism is briefly discussed.

The tetracarbonylhydridoferrate anion $[FeH(CO)_4]^-$ (**1**) is a useful reagent for the dehalogenation of organic halides,[1,2] the reductive alkylation[3,4] and amination[5,6] of carbonyl compounds, the desulfurization of thioketones,[7] and so on. The **1** ferrate is also an effective hydrogenating reagent for α,β-unsaturated carbonyl compounds, giving saturated ones.[8] Conjugated dienes can be converted into monoenes,[9] and the C=N double bond of *N*-benzylideneaniline can also be hydrogenated to give *N*-benzylaniline.[5]

Previously, we briefly reported the reaction of **1** with 3-alkylidene-2,4-pentanedione, **2**, a Knoevenagel condensate.[10] In this reaction, reductively deacetylated products, alkyl methyl ketones, **3**, were obtained in high yields.

This study will deal with the unusual reaction of **1** with 3-alkylidene-2,4-pentanediones, along with several other types of Knoevenagel condensates, **5**, **6**, **7**, and **8**.

Results and Discussion

3-Alkylidene-2,4-pentanediones, prepared from aldehydes and 2,4-pentanedione, such as 3-butylidene-2,4-pentanedione and 3-benzylidene-2,4-pentanedione, were allowed to react with an equimolar amount of **1** for 1 h at room temperature under an argon atmosphere in ethanol. The reaction proceeded rapidly, with a color change from pale yellow to red-brown, giving only the corresponding alkyl methyl ketones, **3**, in high yields (Table 1).

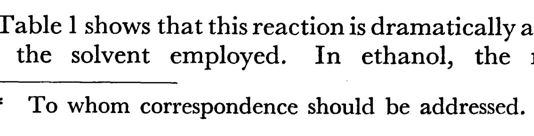

Table 1 shows that this reaction is dramatically affected by the solvent employed. In ethanol, the methyl ketones, **3**, were unexpectedly obtained as products, whereas in tetrahydrofuran or acetone, only the expected reduced products, **4**, were isolated.

The crude condensates, **2**, prepared from 2,4-pentanedione and aldehydes after the removal of the unreacted substrates by distillation, could be converted into **3** smoothly. The results are shown in Table 2.

In the reduction of enamines,[11] Schiff's bases,[12] or α,β-unsaturated carbonyl compounds[12] with **1**, the yields of the products, amines or saturated carbonyl compounds, do not exceed 1.0 mol*** under an argon or nitrogen atmosphere. However, under a carbon monoxide atmosphere, the reaction proceeds with the absorption of carbon monoxide, yielding the products in amounts of about 2—3 mol without forming carbonylated products. In these reactions, it is considered that a major portion of the carbon monoxide absorbed is used to generate the pentacarbonyliron, which is then converted by the base into the ferrate, **1**.

The reaction of **2** (R=Ph) with **1** gave 1.6 mol of 4-phenyl-2-butanone, **3** (R=Ph), even under an argon atmosphere, showing that an active species was reproduced in the course of this reaction. In the reaction in tetrahydrofuran, the yield of 3-benzyl-2,4-pentanedione (**4**, R=Ph) did not exceed 1.0 mol under argon. Now we assume that the carbon monoxide used for the reproduction of pentacarbonyliron might be provided by the eliminated acetyl group.

In further KOH is added to the reaction solution, **1** may be generated according to Eq. 1.[13] Therefore, we examined the effect of the addition of KOH. The results are shown in Table 3.

$$Fe(CO)_5 + 3KOH \longrightarrow KHFe(CO)_4 + K_2CO_3 + H_2O. \qquad (1)$$

The yield of **3** (R=Ph) increased to about 4 mol at a maximum (Run 15), supporting the above assumption. However, the addition of a large excess of KOH disturbed the reaction (Run 16). In this case, the concentration of the active hydride, **1**, decreases according to

$$KHFe(CO)_4 + KOH \rightleftarrows K_2Fe(CO)_4 + H_2O. \qquad (2)$$

In order to investigate the scope and limitation of this reductive deacylation reaction with **1**, the re-

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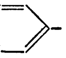
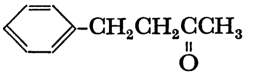
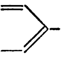
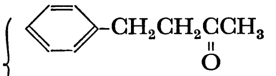
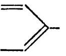
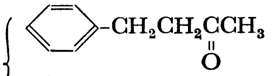
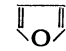
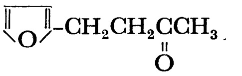
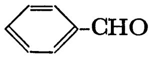
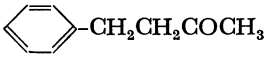
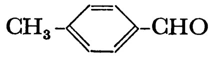
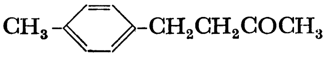
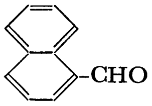
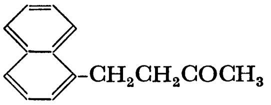
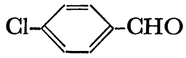
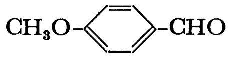
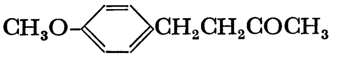
*** 'mol' means mol/mol-ferrate hereafter.

TABLE 1. THE REACTION OF $[FeH(CO)_4]^-$ WITH 3-ALKYLIDENE-2,4-PENTANEDIONE[a]

Run	$\underset{R}{RCH}=C(COCH_3)_2$	Solvent	Product	Yield (%)[b]
1	$CH_3CH_2CH_2$-	EtOH	$CH_3CH_2CH_2CH_2CH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_3$	69 (89)
2	$(CH_3)_2CH$-	EtOH	$(CH_3)_2CHCH_2CH_2\underset{\underset{O}{\|}}{C}CH_3$	60
3	CH_3CH_2-	EtOH	$CH_3CH_2CH_2CH_2\underset{\underset{O}{\|}}{C}CH_3$	71 (92)
4		EtOH		76 (90)
5		THF	 	— 75
6		Acetone	 	trace 65
7		EtOH		82

a) At room temperature for 1 h under an argon atmosphere. b) Isolated yield based on the amount of the condensate. Yields in parentheses were determined by GLPC using internal standards.

TABLE 2. THE SUCCESSIVE REACTION OF A MIXTURE OF ALDEHYDES AND 2,4-PENTANEDIONE WITH $[FeH(CO)_4]^-$ IN ETHANOL[a]

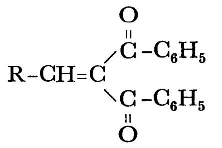
Run	Aldehyde	Product	Yield (%)[b]
8			56
9			54
10			63
11			58
12			47
13	$CH_3CH_2CH_2CHO$	$CH_3CH_2CH_2CH_2CH_2COCH_3$	57

a) At room temperature under an argon atmosphere. b) Isolated yield based on the amount of aldehydes.

TABLE 3. EFFECT OF ADDED KOH IN THE REACTION OF 3-BENZYLIDENE-2,4-PENTANEDIONE WITH $[FeH(CO)_4]^-$ IN ETHANOL[a]

Run	3-Benzylidene-2,4-pentanedione (mmol)	**1** (mmol)	Added KOH (mol/mol-ferrate)	Yield of 4-phenyl-2-butanone (mmol)
14	22	5.5	0	8.0
15	22	5.5	5.5	21.0
16	20	1.0	100	0.7

a) At room temperature for 1 h under an argon atmosphenere.



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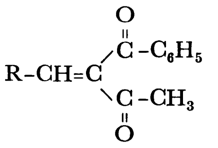

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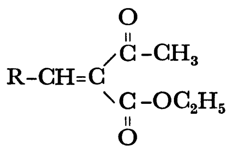

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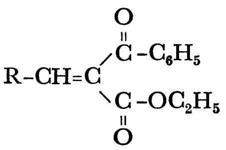
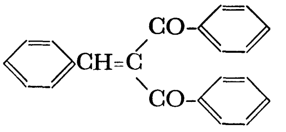
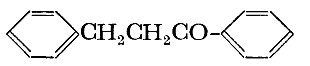
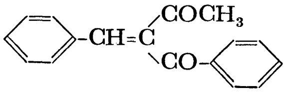
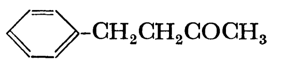
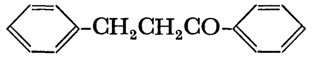
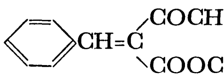
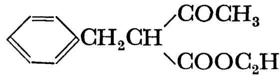
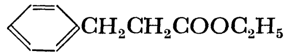
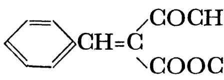
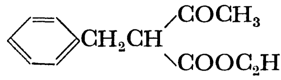
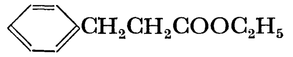
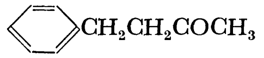
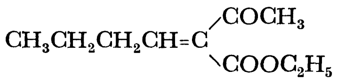
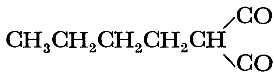
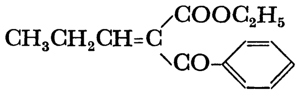
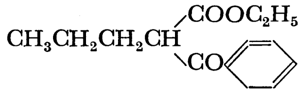


8

action of the other Knoevenagel condensates, **5**, **6**, **7**, and **8**, with **1** was attempted. The results are shown in Table 4.

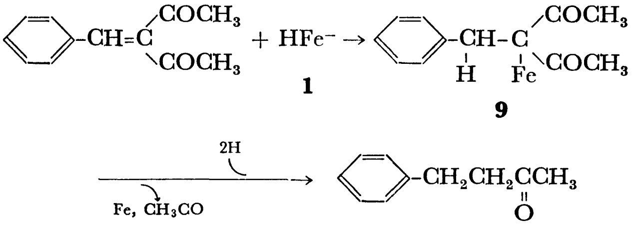
2-Benzylidene-1,3-diphenyl-1,3-propanedione, **5**, gave 1,3-diphenyl-1-propanone exclusively. The reaction of **6** with **1** afforded 4-phenyl-2-butanone (17%) and 1,3-diphenyl-1-propanone (69%) respectively. This shows that the acetyl group is more releasable than the

Table 4. The reaction of several Knoevenagel condensates with $[FeH(CO)_4]^-$ in ethanol

Run	Knoevenagel condensate	Reaction conditions		Product	Yield (%)
		Temp (°C)	Time (h)		
17		r. t.	2		80
18		r. t.	2		17
					69
19		r. t.	17		90
					< 1
20		80	5		40
					< 1
					39
21	 $CH_3CH_2CH_2CH{=}C\begin{smallmatrix}COCH_3\\COOC_2H_5\end{smallmatrix}$	r. t.	24	 $CH_3CH_2CH_2CH_2CH\begin{smallmatrix}COCH_3\\COOC_2H_5\end{smallmatrix}$	70
				$CH_3CH_2CH_2CH_2CH_2COOC_2H_5$	6
				$CH_3CH_2CH_2CH_2CH_2COCH_3$	< 1
22		r. t.	18		70

benzoyl group under these reaction conditions. However, the reaction of the **7** condensates with **1** in ethanol gave simply reduced compounds, along with a trace of deacetylated compounds, at room temperature. However, at higher temperatures, 4-phenyl-2-butanone was obtained in a 39% yield. The condensate of ethyl benzoylacetate and propionaldehyde (**8**, R=Et) gave similar results.

A tentative mechanism of the reductive deacylation reactions of 3-benzylidene-2,4-pentanedione with **1** is illustrated in Scheme 1. First, **1** attacks an olefinic double bond of **2** to give a complex, **9**. It has been reported that the iron atom is attached to the α-carbon of the olefinic bond in the reduction of α,β-unsaturated carbonyl compounds[8] and the hydroacylation of α,β-unsaturated carboxylic esters.[14] The elimination of carbonyliron and acetyl groups, followed with the abstraction of the proton from the solvent, would then give **3**. Some of the products obtained by the elimination of acyl and carbonyliron groups are assumed to be exist as acylcarbonylferrates ($[RCOFe(CO)_4]^-$), which are then protonated to give aldehydes.[15,16] In the reaction of **1** with 2-benzylidenebenzoylacetone, about 10% of the benzaldehyde was detected in the reaction mixture by GLPC, a finding which would support the formation of acylcarbonylferrate.



($HFe^- = [FeH(CO)_4]^-$)

Scheme 1.

Experimental

All the melting points and boiling points are uncorrected. The acetylacetone, dibenzoylmethane, benzoylacetone, ethyl acetoacetate, ethyl benzoylacetate, and aldehydes were all commercial products. The benzene, tetrahydrofuran, and piperidine were obtained from commercial sources and were dehydrated and distilled before use. The pentacarbonyliron was also a commercial product and was used without purification.

3-Alkylidene-2,4-pentanedione. General procedure was as follows. After an equimolar mixture of 2,4-pentanedione and an aldehyde had been cooled in an ice-bath, 0.4—0.5 mol% of piperidine was added, drop by drop; thereafter the mixture was stirred for 5 h at 0 °C and then at room temperature for 5 h. The reaction mixture was then subjected to fractional distillation. The yields were 60—75% in all cases. The analytical data were as follows. 3-Propylidene-2,4-pentanedione; bp 81—89 °C/14.5 mmHg. Found: C, 68.64; H, 8.80%. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.90%. 3-Butylidene-2,4-pentanedione; bp 104—109 °C/13 mmHg. 3-Benzylidene-2,4-pentanedione; bp 108 °C/0.09 mmHg.

Found: C, 76.30; H, 6.61%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43%. 3-Furfurylidene-2,4-pentanedione; bp 116 °C/0.8 mmHg (lit,[17] bp 128—129 °C/4 mmHg). 3-Isobutylidene-2,4-pentanedione; bp 89—93 °C/14 mmHg. These compounds gave satisfactory IR and NMR spectroscopic data.

Other Knoevenagel Condensates. The condensates of aldehydes with ethyl acetoacetate or ethyl benzoylacetate were prepared according to a method similar to that used for 3-alkylidene-2,4-pentanediones. Ethyl 2-acetyl-2-hexenoate; bp 100—109 °C/15 mmHg. Found: C, 65.17; H, 8.67%. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76%. Ethyl 2-acetyl-3-phenyl-2-propenoate; bp 110—114 °C/0.2 mmHg. Found: C, 71.58; H, 6.51%. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47%. Ethyl 2-benzoyl-2-pentenoate; bp 108—109 °C/0.38 mmHg. Found: C, 72.35; H, 6.69%. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94%. Satisfactory IR and NMR data were obtained for these compounds. The 2-benzylidenedibenzoylmethane and 2-benzylidenebenzoylacetone were prepared according to the methods described in the literature.[18]

*Preparation of Tetracarbonylhydridoferrate (**1**).* All the reactions were carried out in a 200-ml, three-necked flask equipped with a buret and a magnetic stirrer under an argon atmosphere. **1** in ethanol was prepared according to the method described in a previous paper.[19] **1** in tetrahydrofuran was prepared as follows. To a stirred suspension of the sodium amalgam in dry tetrahydrofuran (50 ml) prepared from mercury (100 g) and sodium (0.70 g), pentacarbonyliron (1.5 ml, 11 mmol) was added, drop by drop, under argon. The mixture was then stirred for 2 h at room temperature, and the excess of the amalgam was removed through a side arm. The suspension containing the dianion, disodium tetracarbonylferrate(−II) ($Na_2Fe(CO)_4$), was treated with acetic acid (11 mmol).[20] **1** in acetone was prepared by adding 1.5 ml (11 mmol) of $Fe(CO)_5$ to a mixture of acetone (30 ml) and a 10-M KOH aqueous solution (3 ml).

*Reaction of the Knoevenagel Condensates with **1**.* The reaction of 3-benzylidene-2,4-pentanedione with **1** illustrates a typical procedure. To an ethanol solution (33 ml) of **1** (11 mmol), an ethanol solution of 3-benzylidene-2,4-pentanedione (11 mmol) was added, after which the reaction mixture was stirred for 1 h at room temperature under argon. After the solvent had then been evaporated, the residue was extracted with diethyl ether and the ether layer was washed twice with water and dried over sodium sulfate. The solvent was removed *in vacuo*, and the liquid remaining was then subjected to fractional distillation. The product was identified as 4-phenyl-2-butanone by IR, NMR, and GLPC using an authentic sample; bp 106 °C/12.5 mmHg. Yield, 76% (GLPC yield, 90%). The analytical data of some of the other results were as follows. 4-(2-Furyl)-2-butanone; bp 76—77 °C/13 mmHg. Found: C, 69.29; H, 7.23%. Calcd for $C_8H_{10}O_2$: C, 69.54; H, 7.30%. 3-Benzyl-2,4-pentanedione; bp 95—97 °C/0.25 mmHg (lit,[21] bp 115—118 °C/4 mmHg). Found: C, 75.87; H, 7.46%. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%. Ethyl 2-acetyl-3-phenylpropionate; bp 85 °C/0.06 mmHg. Found: C, 71.51; H, 7.53%. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32%.

*The Successive Reaction of the Mixtures of Aldehydes and 2,4-Pentanedione with **1**.* The synthesis of 4-(*p*-tolyl)-2-butanone from *p*-tolualdehyde illustrates a typical procedure. After a mixture of *p*-tolualdehyde (11 mmol) and 2,4-pentanedione had been cooled in an ice-bath, 0.05 mmol of piperidine was added, drop by drop, by the use of a micro syringe, after which the mixture was stirred for 5 h at 0 °C and then at room temperature for 5 h. The reaction mixture was then evaporated, and the residual liquid was added to the ethanol solution of **1** (11 mmol). The mixture was stirred for 1 h at room temperature under argon. After the solvent had been evaporated, the residue was extracted with diethyl ether, and the ether layer was washed twice with water and dried over sodium sulfate. The solvent was evaporated, and the liquid remaining was subjected to fractional distillation. The product was identified as 4-(*p*-tolyl)-2-butanone by IR, NMR, and elemental analysis; bp 69 °C/0.6 mmHg; yield, 54%. Found: C, 81.36; H, 8.84%. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70%. The analytical data of the other results were as follows. 4-(α-Naphthyl)-2-butanone; bp 100—102 °C/0.15 mmHg. Found: C, 84.83; H, 7.10%. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12%. 4-(*p*-Methoxyphenyl)-2-butanone; bp 100—103 °C/0.23 mmHg. 4-(*p*-Chlorophenyl)-2-butanone; bp 89—90 °C/0.26 mmHg. Found: C, 65.55; H, 6.25%. Calcd for $C_{10}H_{11}ClO$: C, 65.76; H, 6.07%. Satisfactory IR and NMR data were obtained for these compounds.

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