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The Carbonylation of α-Haloacetophenones and Benzyl Halides by Disodium Tetracarbonylferrate

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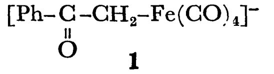
Synopsis. α-Haloacetophenones and benzyl chlorides can be converted into derivatives of β-keto acid and phenylacetic acid respectively by two succesive reactions, with $Na_2Fe(CO)_4$ and then with nitrobenzenes or iodine-ethanol as the oxidizing reagents.

Tetracarbonylferrate, such as potassium tetracarbonylhydridoferrate and disodium tetracarbonylferrate, are excellent reagents for the carbonylation of alkyl halides.[1)] These reactions involve acylcarbonylferrates as the key intermediates, from which the corresponding carbonylated products, such as aldehydes, ketones, and acid derivatives are derived.[2)] The reaction of the ferrates with α-haloacetophenones and benzyl chloride, however, has been shown to give only alkyl complexes, β-oxoalkyl- (**1**)[3)] and benzyltetracarbonylferrate (**2**).[1b)] An attempt to prepare the corresponding acyl complexes from **1** and **2** in the manner described in the literature[1b)] has been unsuccessful. **1** and **2** give acetophenone and toluene respectively upon protonation. **1** shows specific behavior in the reaction with acyl halides. The treatment of **1** with acyl halides and then with acetic acid gives enol esters.[3)] Acyl- and carbamoyltetracarbonylferrates are excellent reagents for the reductive acylation and carbamoylation of nitro compounds into amides and ureas respectively.[2d,4)]



$[Ph\text{-}\overset{}{\underset{\underset{O}{\|}}{C}}\text{-}CH_2\text{-}Fe(CO)_4]^-$ **1**

$[Ph\text{-}CH_2\text{-}Fe(CO)_4]^-$ **2**

$$[RCOFe(CO)_4]^- + ArNO_2 \longrightarrow RCONHAr$$

The present study will deal with the transformation of **1** and **2** into β-keto acid derivatives and phenylacetic acid derivatives respectively by the treatment of **1** and **2** with nitrobenzenes and iodine-ethanol as oxidizing reagents.

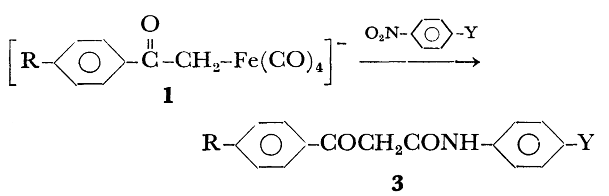
Results and Discussion

Derivatives of tetracarbonylferrates are powerful reducing reagents for the reduction of nitro compounds, giving amines, amides, and ureas. The alkyl complexes, **1** and **2**, also have a great reactivity for nitrobenzene, nitrotoluene, and *p*-chloronitrobenzene. The nitro compounds react smoothly with **1** and **2** at room temperature, with the evolution of gas. The reaction is completed in less than 30 min. The major products are β-keto amides (**3**) and phenylacetamides (**4**) from **1** and **2** respectively. The treatment of **2a** with iodine-ethanol gives ethyl phenylacetate. The results are summarized in Table 1.

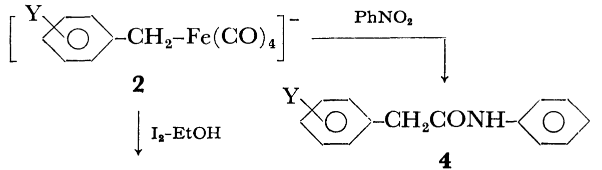
TABLE 1. THE CARBONYLATION OF α-HALOACETOPHENONES AND BENZYL CHLORIDES WITH DISODIUM TETRACARBONYLFERRATE

Run	Halide	Oxidizing agent	Product (Yield % per halide)
1	α-Chloro-acetophenone	Nitrobenzene	**3a** (44) and *N*-Phenacyl-aniline (trace)
2	α-Chloro-acetophenone	*p*-Nitrotoluene	**3b** (22)
3	α-Chloro-acetophenone	*p*-Chloro-nitrobenzene	**3c** (11)
4	α-Bromo-*p*-phenyl-acetophenone	Nitrobenzene	**3d** (50) and 4-Acetylbiphenyl (50)
5	Benzyl chloride	Nitrobenzene	**4a** (35)
6	*p*-Chlorobenzyl chloride	Nitrobenzene	**4b** (24)
7	*o*-Chlorobenzyl chloride	Nitrobenzene	**4c** (16)
8	Benzyl chloride	Iodine-ethanol	Ethyl phenyl-acetate (38)

These results indicate that α-haloacetophenones and benzyl halides can be transformed into carbonylated derivatives by a two-step procedure, a reaction with the ferrate and then with an oxidizing agent. *N*-Phenacylaniline, an expected products from **1a**, was obtained, but in only a poor yield. Although the reaction mechanism is not clear, the alkyl groups of **1** and **2** appear to be transformed into the corresponding acyl types through the reaction. With the reaction of iodine, an oxidative addition of iodine to the alkyl ferrate(0) seems to be the first step; the coordination of iodine may cause an alkyl migration to one of the coordinated carbon mon-



a: R=H, Y=H **c**: R=H, Y=Cl
b: R=H, Y=Me **d**: R=Ph, Y=H



$PhCH_2COOEt$
Y=H

a: Y=H
b: Y=*p*-Cl
c: Y=*o*-Cl

oxides to give an acyl iron(II) complex such as [RCOFe$(CO)_3I_2$], from which an acyl iodide may be formed. The cleavage of acylcarbonylmetal complexes with iodine and bromine has already been reported in manganese and cobalt series.[5)] The reaction of nitrobenzenes also seems to involve an oxidizing step to iron(II) complexes, which may be favorable for the formation of acyl complexes.[6)] Thus, the reduction of nitrobenzenes with the ferrate, **1** and **2**, is completed by *N*-acylation.

Experimental

Materials. The tetrahydrofuran was distilled over $LiAlH_4$ prior to use. The disodium tetracarbonylferrate was prepared according to the method described an earlier article.[1b)] The benzyl chloride, *o*- and *p*-chlorobenzyl chloride, α-chloroacetophenone, α-bromo-*p*-phenylacetophenone, and nitrobenzenes were all commercial products. The nitrobenzenes were dried over a molecular sieve (3A) and distilled before use.

General Reaction Procedure. To the ferrate (11 mmol) in tetrahydrofuran (40 ml), were added an α-haloacetophenone or benzyl chloride (11 mmol) solution in tetrahydrofuran (10 ml); the reaction mixture was then stirred under an argon atmosphere at room temperature for 30 min. To this solution, an oxidizing agent, such as a nitrobenzene (11 mmol) solution in tetrahydrofuran (10 ml) or an iodine-saturated solution in ethanol (30 ml), was added drop by drop, and then the mixture was stirred for about 1 h until the evolution of gas ceased.

Analyses. The ethyl phenylacetate was analyzed by GLC using a column (3 mmϕ, 3 m) packed with Apiezone Grease L (10%) on Neopak 1A. The other products were isolated by chromatography and analyzed by means of IR, PMR, and elemental analysis. The IR spectra were recorded on a 215 Hitachi spectrometer. The ^1H NMR spectra were taken on a JEOL-PM-60 spectrometer. All the chemical shifts are given in δ values relative to a Me_4Si standard. All the melting points were taken on a Yanagimoto apparatus and are uncorrected. All the products (**3** and **4**) are known compounds and were identified by means of their IR and PMR spectra. The elemental analyses of the products gave satisfactory results.

Benzoylacetanilide (3a). The filtered and concentrated reaction mixture was chromatographed on a 2×30 cm florisil column. The elution of the chromatogram with benzene gave brown crystals: Found: C, 79.53; H, 5.90; N, 6.35; O, 8.22%. Calcd for $C_{14}H_{13}NO$: C, 79.62; H, 6.16; N, 6.64; O, 7.58%. This compound appeared to be *N*-phenacylaniline, but its yield was not big enough for further analysis. Further elution of the chromatogram with ether gave colored crystals (**3a**; yield, 44%), which was later recrystallized from ethanol/petroleum ether. The IR and PMR spectra of the crystals were identical with those of an authentic benzoylacetanilide (Aldrich). Mp, 107.5—108.5 °C.

N-*(*p-*Tolyl)benzoylacetamide (3b).* Chromatography on a 2×30 cm florisil column, using methanol as an eluant, gave crystals (**3b**; yield, 22%), which were later recrystallized from ethanol. Mp, 142.0—143.0 °C. IR (KBr): ν(NH) 3300(m), ν(COAr) 1690(s), ν(CONH) 1640(s) cm^{-1}. PMR (d^6 DMSO): δ 2.3 (s, 3H), 4.1 (s, 2H), 7.0—8.2 (m, 9H), 10.1 (s, 1H) ppm.

N-*(*p-*Chlorophenyl)benzoylacetamide (3c).* Chromatography on a 2×30 cm silica gel column, using ether as an eluant, gave crystals (**3c**; yield, 11%). Mp, 163.0—164.0 °C. IR (KBr): ν(NH) 3300(w), ν(CO) 1690(s) and 1660(s) cm^{-1}. PMR (d^6 DMSO): δ 4.2 (s, 2H), 7.2—8.1 (m, 9H) ppm.

*(*p-*Phenylbenzoyl)acetanilide (3d).* Chromatography on a 2×30 cm silica gel using dichloromethane gave yellow crystals (4-acetylbiphenyl; yield, 50%), identified by means of the IR and PMR spectra using an authentic sample. The further elution of the chromatogram with ethanol gave crystals (**3d**; yield, 50%), later recrystallized from chloroform. Mp, 181.0—184.0 °C. IR(KBr): ν(NH) 3300(m), ν(CO) 1690(s) and 1660(s) cm^{-1}. PMR (d^6 DMSO): δ 4.2 (s, 2H), 6.7—8.3 (m, 14H), 10.2 (s, 1H) ppm.

Phenylacetanilide (4a). The filtered and concentrated reaction mixture was extracted with ethanol to give crystals (**4a**; yield, 35%). Mp, 116.5—117.5 °C. IR (KBr): ν(NH), 3300(m), ν(CO) 1655(s) cm^{-1}. PMR ($CDCl_3$): δ 3.7 (s, 2H), 6.8—7.9 (m, 10H) ppm.

*(*p-*Chlorophenyl)acetanilide (4b).* Chromatography on a 2×30 cm silica gel column, using ether and ethanol as eluants, gave crystals (**4b**; yield, 24%). Mp, 169.5—171.5 °C. IR (KBr): ν(NH) 3300(m), ν(CO) 1660(s) cm^{-1}. PMR ($CDCl_3$): δ 3.7 (s, 2H), 6.8—7.7 (m, 9H), 10.1 (s, 1H) ppm.

*(*o-*Chlorophenyl)acetanilide (4c).* Chromatography on a 2×30 cm silica gel column, using dichloromethane and ether as eluants, gave crystals (**4c**; yield, 16%), which were then recrystallized from ethanol. Mp, 138.0—141.0 °C. IR (KBr): ν(NH) 3300(m), ν(CO) 1660(s) cm^{-1}. PMR ($CDCl_3$): δ 3.9 (s, 2H), 6.8—7.8 (m, 9H), 10.1 (s, 1H) ppm.

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