

Chemistry of Alkali Metal Tetracarbonylferrates. A Simple Method for Alkylating and Arylating Carbonyl Compounds and Active Methylene Compounds

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Alkylation and arylation of carbonyl compounds and active methylene compounds by means of aldehydes in the presence of potassium tetracarbonylhydridoferrate is described. This reagent reduces benzylideneacetone to benzylacetone under the same conditions. A reaction scheme is suggested. An alternative approach utilizes disodium pentacarbonylchromate to prepare 1,3-diphenylpropan-1-one.

We have previously reported¹ that treating an aldehyde or a ketone containing the partial structure MeCOR or R'CH₂COR (R and R' are H, alkyl, aryl, or part of a ring) with formaldehyde in the presence of potassium tetracarbonylhydridoferrate (I; M = K) (I) in ethanol or water results in reductive methylation of the carbonyl

methoxide in methanol (method A) or pentacarbonyliron with potassium hydroxide in ethanol⁴ (method B). Disodium tetracarbonylferrate can be obtained in an aprotic solvent by stirring pentacarbonyliron and a suspension of sodium amalgam in dry tetrahydrofuran at room temperature under argon⁵ for 2 h (method C).

TABLE I
Reaction of the tetracarbonylhydridoferrate (I) with aldehydes and carbonyl compounds

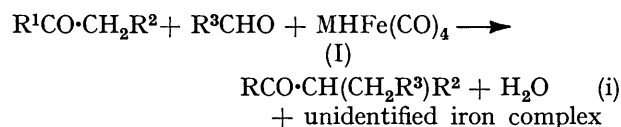
Carbonyl compound	Aldehyde	Product	Yield (%) *
Acetophenone ^a	Acetaldehyde	1-Phenylbutan-1-one	35
Deoxybenzoin ^a	Acetaldehyde	1,2-Diphenylbutan-1-one	37
Butyraldehyde ^b	Butyraldehyde	2-Ethylhexanal	60
Acetone ^b	Benzaldehyde	1-Phenylbutan-3-one	70
Butan-2-one ^b		1-Phenylpentan-3-one	70
Octan-2-one ^b		1-Phenylnonan-3-one	60
Cyclohexanone ^b		2-Benzylcyclohexanone	75
Cyclohexanone ^c		2,6-Dibenzylcyclohexanone	10
Acetophenone ^{b,d}		2,6-Dibenzylcyclohexanone	80
1-Phenylpropan-2-one ^b		1,3-Diphenylpropan-1-one	80, ^b 68 ^d
Acetophenone ^b	<i>p</i> -Chlorobenzaldehyde	1,4-Diphenylbutan-2-one	45
Acetophenone ^b		1,2,5-Triphenylpentan-3-one	8
Acetophenone ^b		3-(<i>p</i> -Chlorophenyl)-1-phenylpropan-1-one	46
Acetophenone ^b		<i>p</i> -Tolualdehyde	1-Phenyl-3-(<i>p</i> -tolyl)propan-1-one
Acetophenone ^b	Isonicotinaldehyde	1-Phenyl-3-(2-pyridyl)propan-1-one	37

* Of pure, isolated compounds.

^a Method A. ^b Method B. ^c Method B with 1 : 2 : 2 carbonyl compound-MHFe(CO)₄-aldehyde ratio. ^d Method C.

compound in high yield. Under similar conditions, using a variety of aldehydes we were able to alkylate primary and secondary amines² and indole.³

During attempts to determine the scope and limitations of these reactions we have examined the reactions between carbonyl compounds and alkyl, aryl, and heterocyclic aldehydes in the presence of the tetracarbonylhydridoferrates (I). These reactions, as described previously, bring about reductive alkylation or arylation of the carbonyl compound [reaction (i)].



M = Na or K

R¹ and R² = H, alkyl, aryl, or part of a ring

R³ = alkyl, aryl, or heteroaryl.

The tetracarbonylhydridoferrates (I) can be prepared directly by refluxing pentacarbonyliron with sodium

¹ G. Cainelli, M. Panunzio, and A. Umani-Ronchi, *Tetrahedron Letters*, 1973, 2491.

² G. Boldrini, M. Panunzio, and A. Umani-Ronchi, *Synthesis*, 1974, 733.

³ G. Boldrini, M. Panunzio, and A. Umani-Ronchi, *J.C.S. Chem. Comm.*, 1974, 359.

In methods A and B alkylation or arylation reactions were carried out by adding dropwise an alcoholic solution of the aldehyde and the carbonyl compound to a solution of the tetracarbonylhydridoferrate (I). In method C, after removal of the excess of amalgam, the disodium tetracarbonylferrate was treated with 1 mol. equiv. of water before adding a solution of aldehyde and carbonyl compound in tetrahydrofuran.

After refluxing for 4 h, the mixture was diluted with water and worked up. Table I summarizes the results. The reaction seems to be general for alkyl, alicyclic, and aralkyl ketones and aldehydes as carbonyl components. With regard to the alkylating reagents, the yield is in general higher with aryl aldehydes than with alkyl aldehydes, owing to competing self-condensation of the latter induced by the alkalinity of the medium. The alkylation reaction only occurs if a methylene or a methyl group is present in the position α to the carbonyl group; an α -methine group is unreactive.

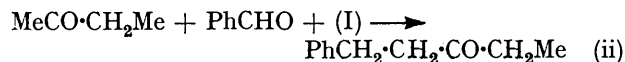
In the case of cyclohexanone, a 1 : 1 : 1 molar ratio of benzaldehyde, the tetracarbonylhydridoferrate, and the

⁴ P. Krumboltz and H. M. A. Stettiner, *J. Amer. Chem. Soc.*, 1949, **71**, 3035; Y. Takegami, Y. Watanabe, T. Mitsudo, H. Masada, *Bull. Chem. Soc. Japan*, 1969, **42**, 202.

⁵ M. P. Cooke, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 6080.

ketone gives predominantly 2-benzylcyclohexanone, whereas 2,6-dibenzylcyclohexanone is formed almost exclusively with a 2 : 2 : 1 ratio of reactants.

The regioselectivity of the reaction seems to depend upon steric factors. Whereas in the reaction with formaldehyde octan-2-one is methylated almost exclusively at the methylene group, in the case of benzaldehyde butan-2-one and octan-2-one give 1-phenylpentan-3-one [reaction (ii)] and 1-phenylnonan-3-one, respectively.



A possible scheme for the α -alkylation is outlined in reactions (iii) and (iv). The initial step probably involves the condensation of the aldehyde and the carbonyl compound, catalysed by the basic medium, to give the

TABLE 2

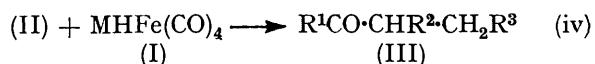
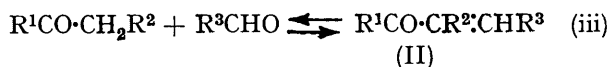
Reaction of the tetracarboxylhydridoferrate (I) with aldehydes and active methylene compounds

Methylene compound	Aldehyde	Product	Yield (%) *
Ethyl malonate ^{a,b}	Formaldehyde ^c	Diethyl methylmalonate	72, ^a 85 ^b
Phenylacetone ^a		2-Phenylpropionitrile	67
Phenylacetone ^a	Benzaldehyde	2,3-Diphenylpropionitrile	75
Ethyl cyanoacetate ^a		Benzylcyanoacetic acid	90
Ethyl acetoacetate ^a		1-Phenylbutan-3-one	50
Ethyl malonate ^a		Diethyl benzylmalonate	40

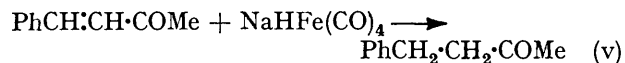
* Of pure, isolated compound.

^a Method B. ^b Method B, with 1 : 3 : 3 active methylene compound-MHFe(CO)₄-aldehyde ratio. ^c Aqueous 40% solution.

intermediate (II), which is irreversibly reduced by the tetracarboxylhydridoferrate (I).



Treatment of benzylideneacetone with the tetracarboxylhydridoferrate (I) under the same conditions as reported affords the expected benzylacetone ⁶ [reaction (v)].



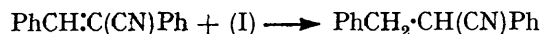
The possibility of utilizing other transition carbonyl-metallates for this alkylation reaction was confirmed by the reaction between acetophenone and benzaldehyde in the presence of sodium pentacarboxylhydridochromate,⁷ which gave 1,3-diphenylpropan-1-one in 62% yield.

The potential utility of the tetracarboxylhydridoferrates (I) for selective reduction in organic synthesis prompted us to investigate the extension of this reaction to active methylene compounds. Treatment of such compounds with formaldehyde or benzaldehyde in the presence of the tetracarboxylhydridoferrate (I) in ethanol gave the corresponding methyl or benzyl derivatives in *ca.* 70% yield (Table 2). Monoalkylated and monoarylated compounds were the exclusive products with all active methylene compounds in-

⁶ R. Noyori, I. Umeda, and T. Ishigami, *J. Org. Chem.*, 1972, **37**, 1542.

vestigated. These results are in line with the mechanism proposed above for alkylation or arylation of carbonyl compounds.

2,3-Diphenylacrylonitrile was reduced to 2,3-diphenylpropionitrile by the tetracarboxylhydridoferrate (I) under the same conditions [reaction (vi)].



EXPERIMENTAL

I.r. spectra were determined with a Hilger-Watts N 9007 Infracord spectrophotometer, n.m.r. spectra with a Perkin-Elmer R1 2B instrument, with tetramethylsilane as internal standard, and mass spectra with a Hitachi-Perkin-Elmer RMU6D (single focus) spectrometer at 70 eV. T.l.c. was performed on silica gel HF₂₅₄ (Merck) and column chromatography on silica gel (0.05–0.02) (Merck), with hexane-ether as solvent.

Pentacarboxyliron was purchased from Schuchardt (Munchen).

General Procedure for Alkylating and Arylating Carbonyl Compounds and Active Methylene Compounds.—Method A. To a stirred solution of sodium methoxide (33 mmol) in methanol (50 ml), pentacarboxyliron (1.5 ml, 11 mmol) was added under argon. The mixture was stirred for 2 h under reflux, then a solution of the aldehyde (11 mmol) and the carbonyl compound or active methylene compound (11 mmol) in methanol (20 ml) was added. The mixture was stirred for a further 4 h, at 40°, poured into ice-water, and extracted with hexane or ether. The extracts were washed with water, dried (Na₂SO₄), and evaporated, and the product was purified by chromatography on silica gel.

Method B. To a stirred solution of potassium hydroxide (1.85 g, 33 mmol) in ethanol (100 ml), pentacarboxyliron (1.5 ml, 11 mmol) was added under argon. The mixture was stirred for 2 h under reflux, then a solution of the aldehyde (11 mmol) and the carbonyl compound or active methylene compound (11 mmol) in ethanol (20 ml) was added dropwise under argon. The mixture was refluxed for a further 5 h, poured into water and extracted with ether. After drying (Na₂SO₄) the organic layer was evaporated and the residue purified by conventional methods.

Method C. To a stirred suspension of sodium amalgam in dry tetrahydrofuran (50 ml) [from mercury (100 g) and sodium (0.76 g, 33 mmol)], pentacarboxyliron (1.5 ml, 11 mmol) was added dropwise under argon. The mixture was stirred for 2 h at room temperature, and the excess of amalgam was removed through a side arm. The suspension containing the disodium tetracarboxylferrate was treated with water (0.2 ml, 11 mmol), followed by the aldehyde

⁷ H. E. Podall, H. B. Prestridge, and H. Shapiro, *J. Amer. Chem. Soc.*, 1961, **83**, 2057.

(1.1 ml, 11 mmol) and the carbonyl compound (11 mmol) in tetrahydrofuran (20 ml). The mixture was refluxed for 3 h, poured into ice-water, and extracted with ether. After drying (Na_2SO_4), the product was purified by chromatography on silica gel.

1-Phenyl-3-(2-pyridyl)propan-1-one, prepared by method B (37%) had m.p. 62° (from hexane-benzene) δ (CCl_4) 3.1 (q, $\text{CH}_2\text{-CH}_2$) and 7-8.6 (aromatic), m/e 211 (M^+) (Found: C, 79.3; H, 6.2; N, 6.8. $\text{C}_{14}\text{H}_{13}\text{NO}$ requires C, 79.6; H, 6.2; N, 6.6%).

Conversion of Benzylideneacetone into Benzylacetone.—To a suspension of potassium tetracarbonylhydridoferrate (11 mmol) prepared in ethanol (method B), benzylideneacetone (11 mmol) in ethanol (10 ml) was added. The mixture was refluxed for 2 h and worked up. Benzylacetone was isolated in 85% yield.

Reaction of Disodium Pentacarbonylchromate with Benz-

aldehyde and Acetophone.—To a stirred suspension of sodium amalgam in dry tetrahydrofuran (50 ml) [from mercury (100 g) and sodium (0.76 g)], hexacarbonylchromium (2.2 g, 11 mmol) was added in one portion under argon. The mixture was stirred and refluxed for 5 h, and the excess of amalgam was removed through a side arm. The suspension containing the pentacarbonylchromate was treated with water (0.2 ml, 11 mmol), followed by benzaldehyde (1.1 ml, 11 mmol) and acetophenone (11 mmol) in tetrahydrofuran (20 ml). The mixture was refluxed for 3 h, poured into ice-water, and extracted with ether. After drying (Na_2SO_4), the product was purified by chromatography on silica gel; 1,3-diphenylpropan-1-one was isolated in 62% yield.

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