

CHEMISTRY OF ALKALI METAL IRON CARBONYLATES . A NEW METHOD FOR ALKYLATING
ALDEHYDES AND KETONES WITH FORMALDEHYDE

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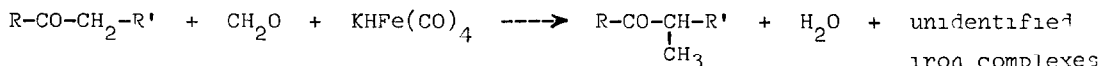
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The d^{10} alkali metal iron carbonyls $M_2Fe(CO)_4$ ($M = Na$ or K), easily obtained by treatment of sodium or potassium hydroxide in protic solvents¹ or of sodium amalgam in tetrahydrofuran² with $Fe(CO)_5$, have been shown to be inexpensive, versatile and selective reagents converting alkyl bromides, iodides, tosylates and acid halogenides into aldehydes, carboxylic acid derivatives and ketones in high yields^{2,3,4}.

A mixture of mono and polynuclear hydrido iron complexes generated in situ from iron pentacarbonyl and a small amount of base in moist solvents selectively and efficiently hydrogenate α, β carbonyl compounds to the corresponding saturated derivatives⁵.

In addition it is also known that potassium tetracarbonylferrate and the corresponding monohydride add to α, β -unsaturated esters giving, after treatment, mainly the corresponding malonates⁶.

We wish now to report that treatment of an aldehyde or a ketone containing the partial structure, CH_3-CO-R or $R'-CH_2-CO-R$ (R and $R' =$ alkyl, aryl or part of a cycle) with formaldehyde in the presence of $KHFe(CO)_4$ in ethanol or water results in the reductive methylation of the carbonyl compound in high yield following the scheme :



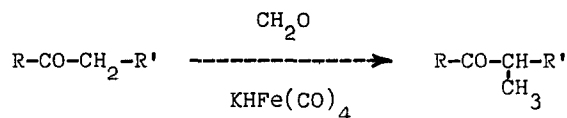
The reaction can be performed either by refluxing a hydro-alcoholic or aqueous solution of $KHFe(CO)_4$ (from one mole of $Fe(CO)_5$ and 3 moles of KOH) with equimolar amounts of the carbonyl compound and formaldehyde for 4-5 hours or merely by warming a solution of one mole of $Fe(CO)_5$, formaldehyde and carbonyl compound

and 3 moles of potassium hydroxide for the same time .

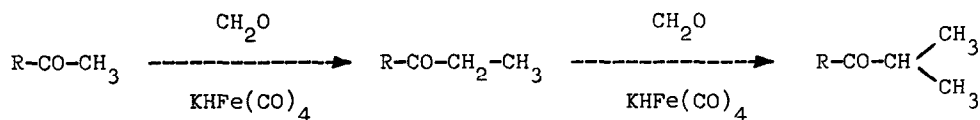
Some results of typical reactions are shown in Table 1 .

Aliphatic alicyclic and aryl aliphatic ketones and aldehydes are readily methylated under these conditions .

The methylation only occurs if a methylene or a methyl group is present in the α position to the carbonyl group, the methine group being unreactive . Carbonyl compounds containing a methylene group are exclusively monomethylated ,



whilst acetophenone gives predominantly a monomethyl derivative if one mole of CH_2O and KFe(CO)_4 per mole of carbonyl compound are employed and almost exclusively the dimethyl derivative with two moles of the reagents .



The regioselectivity of the reaction seems to depend on the relative enolate stability as in the alkylation of ketones . For instance octan-2-one and benzylmethylketone are alkylated almost exclusively at the methylene group⁷.

The conversion of phenylethylketone to phenylisopropylketone illustrates a typical procedure .

To a solution of 1.85 g (33 mmoles) of potassium hydroxide in 100 ml of ethanol 1.5 ml (11 mmoles) of iron carbonyl were added under argon . After refluxing for two hours 0.86 ml (11 mmoles) of a 40% aqueous solution of formaldehyde and 1.34 ml (11 mmoles) of phenylethylketone were added , the reaction mixture refluxed for a further 3 hours , poured into water and extracted with hexane . After drying over anhydrous sodium sulphate the organic layer was evaporated and the residue purified by conventional methods .

A possible reaction mechanism for this novel methylation reaction that accounts for the above mentioned results is given in the following scheme :

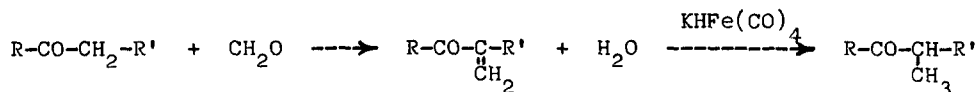
TABLE 1

Reaction between $\text{KHFe}(\text{CO})_4$, CH_2O and carbonyl compounds.

Carbonyl compound	Product	Yield % *
acetophenone ^a	propionophenone (isopropylphenylketone)	70
acetophenone ^b	isopropylphenylketone	20
propionophenone	isopropylphenylketone	90
deoxybenzoin	isopropylphenylketone	85
cyclohexanone ^a	2-phenylpropionophenone	50
cyclohexanone ^b	(2-methylcyclohexanone 2,6-dimethylcyclohexanone)	60
octan-2-one	(nonan-3-one 3-methyl-octan-2-one)	15
benzylmethylketone	3-phenyl-butan-2-one	70
butanal	2-methyl-butanal	5
dodecanal	2-methyl-dodecanal	50
		80
		50
		55

* The yield indicated refers to pure, isolated compounds.

a. Using an 2:1-ketone- CH_2O ratio.b. Using an 1:2-ketone- CH_2O ratio.



Base catalysed condensation of the carbonyl compound with the aldehyde to the corresponding α,β -unsaturated derivatives is followed by an irreversible reductive attack by $KFe(CO)_4$.

Facile reduction of α,β -unsaturated carbonyl compounds by means of $KFe(CO)_4$ to the corresponding saturated derivatives has already been reported in the literature⁵.

In order to enlarge the scope of this reaction and to extend it to other aldehydes further work is being undertaken in our laboratory.

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