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ORGANOIRON COMPLEXES IN ORGANIC SYNTHESIS. A FACILE TMS MEDIATED DECARBOXYLATION OF ORGANOIRON COMPLEXES

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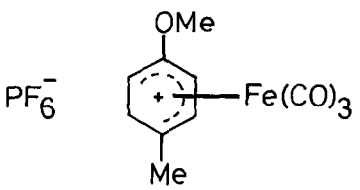
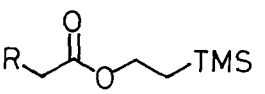
Abstract: The adducts of TMS-ethanol keto esters and cyclohexadienyl-$Fe(CO)_3$ salts are readily decarboxylated on treatment with fluoride ion in good yield.

The application of organoiron chemistry for the synthesis of natural products is currently receiving much attention.[1] The organoiron complex (1) and related compounds have been used as starting materials for the synthesis of steroids,[2] alkaloids[3] and terpenes.[4]

The methodology exploited in these examples takes advantage of the ability of the complex (1) to react with keto-esters giving rise to carbon-carbon bond formation. Harder nucleophiles such as ketone enolates are unsatisfactory owing to O-alkylation or deprotonation of the complex.[5] Hence, when mono-ketone adducts are required, they have, in the past, been prepared *via* decarboxylation of the corresponding keto-ester adducts. However, since the decarboxylation of an iron-complex is often a low yielding step, there is considerable attraction to finding methods of overcoming this problem.[6]



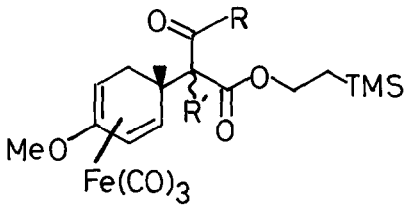
(1)

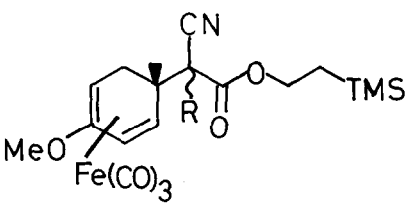


(2) R = MeCO
(3) R = PhCO
(4) R = CN

Previously, methyl keto-esters have been used, necessitating very forcing conditions such as tetrabutylammonium acetate in hot hexamethylphosphorictriamide[7] to effect decarboxylation.

In a search for milder conditions the trimethylsilyl ethanol keto-esters (2)[8] and (3)[9] were prepared. (Esters of this kind are known to decarboxylate readily on treatment with fluoride ion.[10])

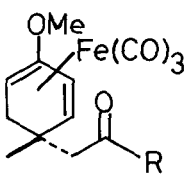


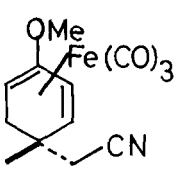


(5) R = Me, R' = α-H
(6) R = Me, R' = β-H
(7) R = Ph, R' = α-H
(8) R = Ph, R' = β-H

(9) R = α-H
(10) R = β-H

Preparation of the sodium enolate of the keto ester (2) and subsequent addition to (1) under standard conditions gave the required adduct as a mixture of diastereoisomers (5) and (6) in 53% yield.[11] Likewise, the keto-ester (3) gave (7) and (8) in 80% yield.[11] As anticipated, on treatment with tetrabutyl ammonium fluoride in tetrahydrofuran at room temperature, adducts (5 and 6) or (7 and 8) were efficiently decarboxylated giving rise to the ketones (11) and (12) in 87% and 90% yield[11] respectively.





(11) R = Me
(12) R = Ph

(13)

In addition to keto-esters, cyanoacetic esters[12] have also been used as nucleophiles, adding readily to salts such as (1). To explore the possibility of obtaining what would effectively be an adduct of acetonitrile, by the decarboxylation of a cyanoacetic acid adduct, the ester (4) was prepared.[13] Addition of the sodium salt of (4) to the salt (1) under the usual conditions then gave the diastereoisomers (9) and (10) in 75% yield.[11] However, treatment of this mixture with tetrabutylammonium fluoride under the above conditions at room temperature gave no reaction. On reflux, decarboxylation did occur to

give (13) but only in the moderate yield[11] of 40%.

In conclusion, we show that the very mild conditions required to effect decarboxylation of the TMS-esters and the ready availability of keto-acids[14] represent a significant improvement on existing methods and further increase the importance of organoiron chemistry.

The application of this method for the preparation of novel steroidal compounds is currently being investigated.

Typical Procedure:

To a stirred suspension of sodium hydride (from 200mg 50% dispersion in mineral oil, washed with dry pentane) in dry tetrahydrofuran (10ml) at 0°C under nitrogen, was added a solution of the keto-ester (2) (640mg) in dry tetrahydrofuran (10ml). After stirring for 0.5h the vessel was briefly opened with back flushing of nitrogen whilst the salt (1) (1.5g) was added in one portion. Stirring was continued for 0.5h during which the reactants were allowed to warm to room temperature. The resulting yellow solution was poured into ether (50ml) and washed successively with aqueous sodium hydrogen carbonate and water. The ether layer was dried ($MgSO_4$) and evaporated under reduced pressure to give, after purification by flash column chromatography (3% ethyl acetate/benzene), the mixture of diastereoisomers (5) and (6) (900mg,53%).

To a solution of the above diastereoisomers (5) and (6) (100mg) in dry tetrahydrofuran (10ml) under nitrogen was added a solution of tetra-n-butylammonium fluoride in tetrahydrofuran (0.22ml,1M). The resulting mixture was stirred at room temperature for 30 min then the solvent removed under reduced pressure on a cold water bath. The residue was dissolved in ether (25ml) and washed with brine. Evaporation of the solvent and purification by flash column chromatography (20% ethyl acetate/benzene) gave (11) (60mg,87%).

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