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Reactivity of Heterodiene Metal Carbonyl Complexes [and Discussion]

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Reactivity of heterodiene metal carbonyl complexes

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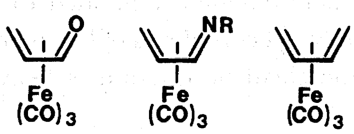
Addition of hard nucleophiles to iron tricarbonyl complexes of α,β-unsaturated ketones and iron tetracarbonyl complexes of α,β-unsaturated esters produces γ-ketocarbonyl compounds. Nucleophilic addition to iron tricarbonyl complexes of α,β-unsaturated imines leads either to pyrrole or β,γ-unsaturated amine formation.

Introduction

The number of investigations into the reactivity and properties of 1-oxadienes and 1-azadienes attached to iron tricarbonyl units, **1**, and **2**, is surprisingly small compared with the number of investigations into the reactivity and properties of hydrocarbon dienes attached to the iron tricarbonyl unit, **3** (figure 1).

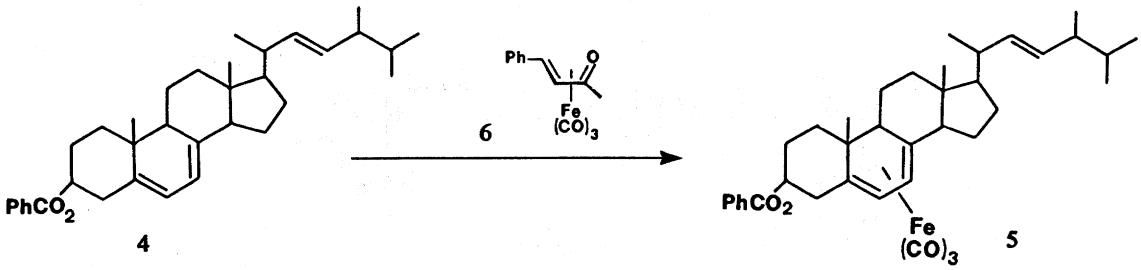


1 2 3

Figure 1

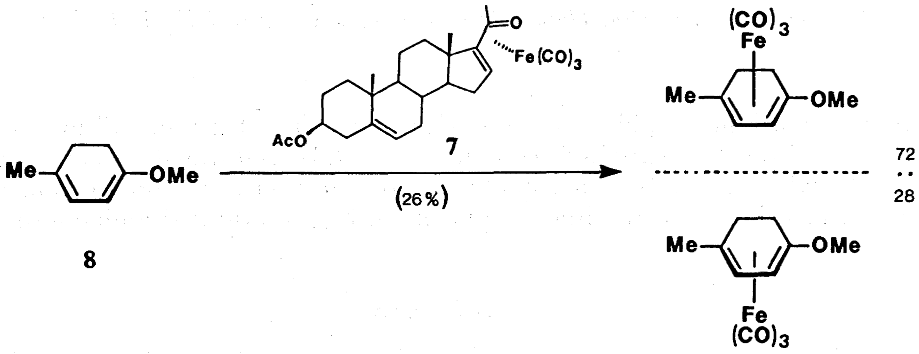
Consequently, our knowledge of heterodiene iron tricarbonyl complex chemistry is much less extensive than our knowledge of homodiene iron tricarbonyl complex chemistry. In view of the synthetic importance of α,β-unsaturated carbonyl and imine compounds, their reactivity after complexation to the iron tricarbonyl unit is worthy of more attention. The salient features of studies undertaken by others, which reveal some of the fundamental chemistry of 1-oxadienes and 1-azadienes attached to the iron tricarbonyl unit, are given below.

Iron tricarbonyl complexes of 1-oxadienes have been shown to be a mild source of the iron tricarbonyl unit (Lewis *et al.* 1972*a*) and this reactivity has been exploited in the synthesis of many iron tricarbonyl complexes of dienes that are heat or light sensitive. For example, ergosteryl benzoate, **4**, was converted into its iron tricarbonyl complex **5** in 65% yield by treatment with (benzylideneacetone)tricarbonyliron(0), **6**, at 90 °C for 20 h. Heating **4** with iron pentacarbonyl, a more traditional source of the iron tricarbonyl unit, required a temperature of 144 °C to give a similar yield (70%) in 20 h (Barton *et al.* 1976) (scheme 1).



Scheme 1

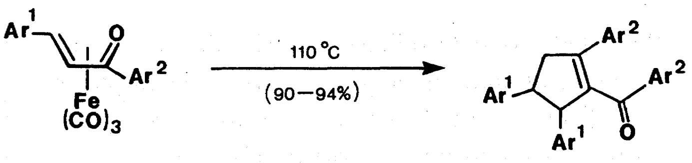
Furthermore, it has been demonstrated that iron tricarbonyl complexes of optically active 1-oxadienes, for example **7**, transfer the iron tricarbonyl unit preferentially to one face of prochiral dienes such as **8**, to produce diene iron tricarbonyl complexes enriched in one enantiomer (Birch *et al.* 1984) (scheme 2).



Scheme 2

This and analogous results are thought to reflect the existence of a reaction intermediate in which both the homodiene and heterodiene are bonded to the iron tricarbonyl unit.

The effect of heat on iron tricarbonyl complexes of benzylideneacetophenone and analogues, **9**, has been shown to lead to the clean production of heavily substituted cyclopentenes, **10** (Otsuji & Ueda 1986) (scheme 3).

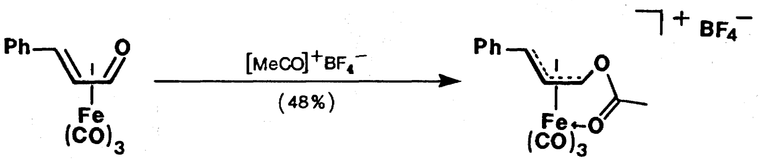


9 10

Scheme 3

The reaction is thought to proceed via electron transfer to the 1-oxadiene ligand thus generating an allylic anion, which, after undergoing a [2+3] cycloaddition with another molecule of **9** and an elimination, gives rise to the cyclopentenes, **10**.

The reactions of iron tricarbonyl complexes of heterodienes with electrophiles have been studied. Acetylation of (cinnamaldehyde)tricarbonyliron(0), **11**, results in reaction at the oxygen atom of the 1-oxadiene and production of the iron allyl species, **12** (Nesmeyanov *et al.* 1974) (scheme 4).



11 12

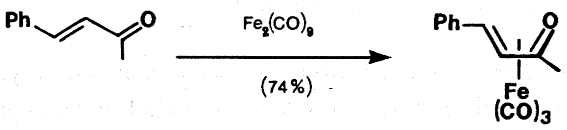
Scheme 4

Protonation of (benzylideneacetone)tricarbonyliron(0), **6**, is thought to occur on the oxygen atom of the 1-oxadiene. Similarly, protonation of (cinnamylideneaniline)tricarbonyliron(0), **13**, occurs reversibly on the nitrogen atom of the 1-azadiene (Lewis *et al.* 1972*b*).

Reactions between (heterodiene)tricarbonyliron(0) complexes and nucleophiles do not appear to have been studied by other workers. As far as we are aware, our studies of the reactivity between (1-oxadiene) and (1-azadiene)tricarbonyliron(0) complexes and nucleophiles, described below, represent the first investigations into this area of chemistry.

NUCLEOPHILIC ATTACK ON (1-OXADIENE)TRICARBONYLIRON(0) COMPLEXES

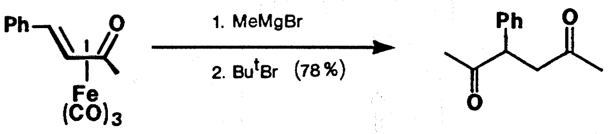
(Benzylideneacetone)tricarbonyliron(0), **6**, an air-stable, red crystalline solid, was prepared from benzylideneacetone and di-iron nonacarbonyl (Lewis *et al.* 1972*b*) (scheme 5). (The yield of **6**, based on benzylideneacetone, was increased from the literature value of 32% to 74% by the use of an excess (3 equivalents) of di-iron nonacarbonyl.)



6

SCHEME 5

Treatment of **6** with methylmagnesium bromide at −78 °C for 7 h followed by addition of ${}^tbutyl$ bromide and work-up gave 3-phenyl-2,5-hexanedione, **14**, in high yield (scheme 6).



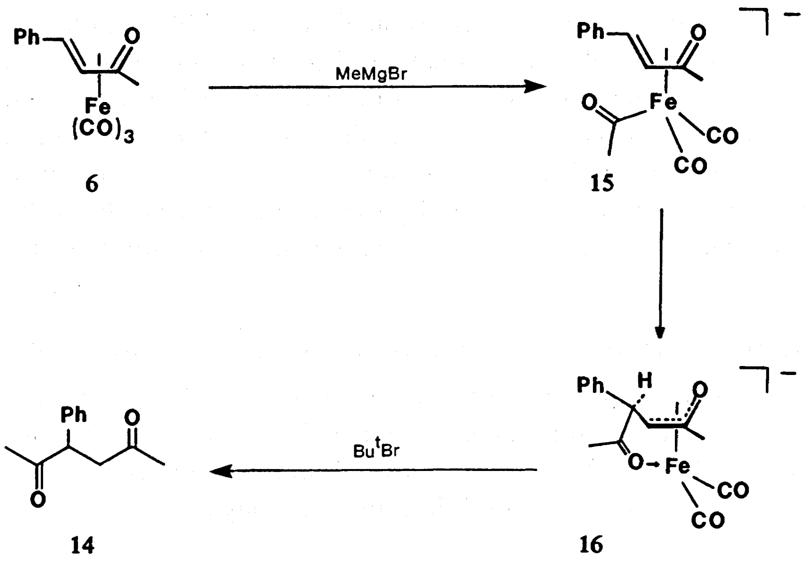
6 **14**

SCHEME 6

A mechanism to account for this reaction is outlined below. Nucleophilic attack on **6** occurs at a metal carbonyl ligand and generates the metal acyl anion **15**. The acyl ligand is subsequently transferred to carbon(4) of the 1-oxadiene ligand to give **16**. Protonation, which may occur either directly at carbon(3) of the oxadiene ligand or indirectly via protonation of the iron atom followed by elimination across the iron–carbon(3) bond, then leads to the reaction product **14** (scheme 7).

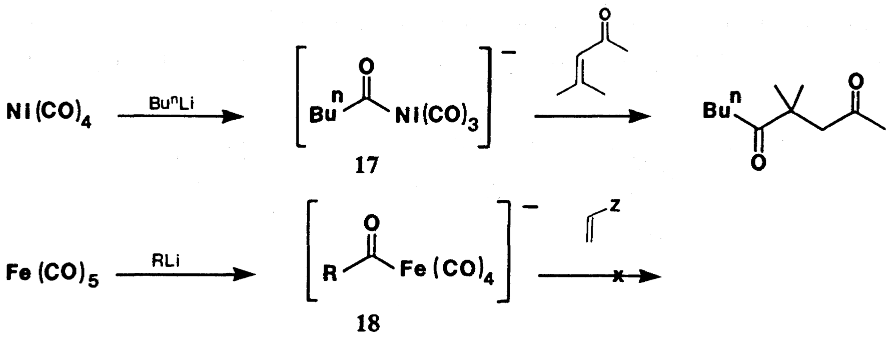
Alkyl-lithium and alkylcuprate reagents also react with (benzylideneacetone)tricarbonyliron(0), **6**, to give 1,4-diketones in good yield and acylation occurs cleanly with a range of alkyl substituents at carbon(2) of the complexed 1-oxadiene. Although acylation does proceed with complexes bearing alkyl substituents at carbon(3) and carbon(4) of the 1-oxadiene, these complexes are more air-sensitive than the complexes bearing a phenyl group on carbon(4) and a hydrogen atom on carbon(3) (Thomas 1987; Thomas *et al.* 1988).

It has been demonstrated that addition of a range of alkyl-lithium reagents to nickel tetracarbonyl produces nickel-acyl anions, e.g. **17**, which can act as acyl donors to Michael



Scheme 7

acceptors and, thus, produce 1,4-dicarbonyl compounds in good yield (Corey & Hegedus 1969). As part of a search for alternatives to the toxic nickel tetracarbonyl in this synthetically useful reaction, it has been reported that saturated iron-acyl anions, e.g. **18**, do not act as acyl donors to Michael acceptors (Cooke & Parlman 1977) (scheme 8).



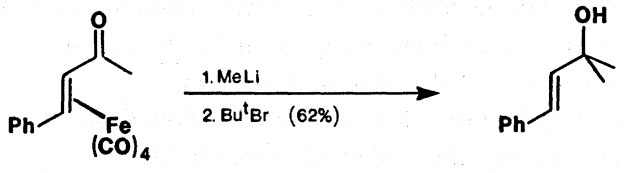
Scheme 8

It was suggested that the lack of reactivity in the iron system is caused by the low lability of the iron carbonyl ligands that prevents the Michael acceptor gaining access to the coordination sphere of the iron through ligand exchange. It was of interest, therefore, to investigate the reactivity between iron tetracarbonyl complexes of Michael acceptors and nucleophiles.

Treatment of (benzylideneacetone)tetracarbonyliron(0) **19**, with methyl-lithium resulted in direct attack on the unprotected carbonyl group of the benzylideneacetone ligand to give the alcohol **20** as the major product (scheme 9).

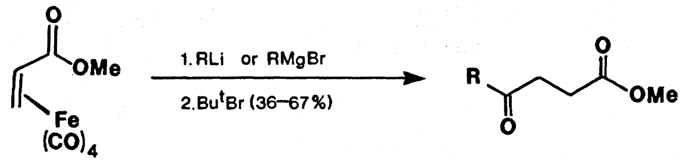
Methyl acrylate (less electrophilic carbonyl group) was subsequently complexed to the iron tetracarbonyl unit, **21**, and addition of a range of hard nucleophiles to **21** gave γ-ketoesters in fair to good yield (Thomas & Rakshit 1987) (scheme 10).

Extension of this reactivity to generate γ-ketoesters containing optically active centres is currently being examined.



19 20

SCHEME 9

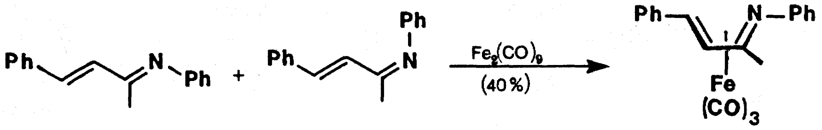


21

SCHEME 10

NUCLEOPHILIC ATTACK ON (1-AZADIENE)TRICARBONYLIRON(0) COMPLEXES

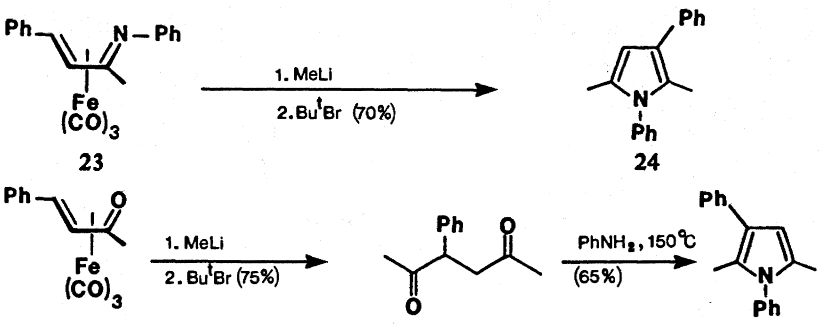
Condensation of aniline with benzylideneacetone under zinc chloride catalysis produces a mixture of stereoisomeric imines, **22**. Heating this mixture with di-iron nonacarbonyl gave the iron complex of the E_{CN} isomer, **23** (scheme 11). There was no evidence for the formation of the Z_{CN} isomer complex, which is presumably caused by a strong interaction between an *ortho* hydrogen of the *N*-phenyl group and the carbon(4) hydrogen.



22 23

SCHEME 11

Addition of methyl-lithium to **23** followed by protonation and work-up gave the novel pyrrole **24** as the major product. This identification was confirmed by an independent synthesis of **24** from **6** (Thomas & Danks 1988) (scheme 12).



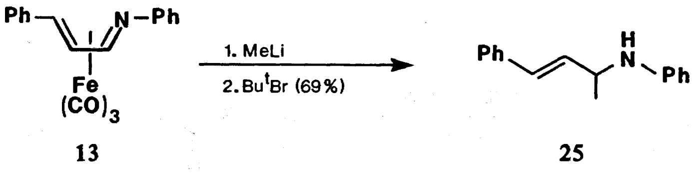
23 24

6 24

SCHEME 12

The low temperature used in the formation of **24** from complex **23** strongly suggests that the iron moiety not only acts as a carbonylating agent in the reaction, but also is intimately involved in the ring-closure step of the pyrrole formation.

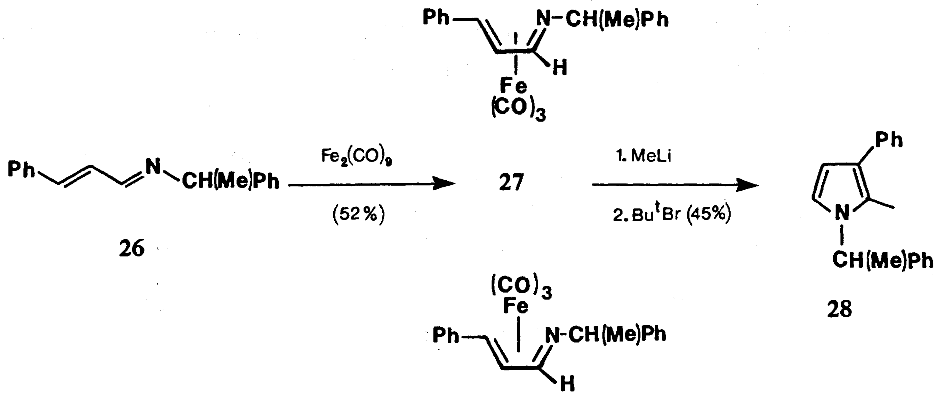
Nucleophilic attack on (cinnamylideneaniline)tricarbonyliron(0) **13**, occurs directly at carbon(2) of the azadiene to give the amine **25** (scheme 13).



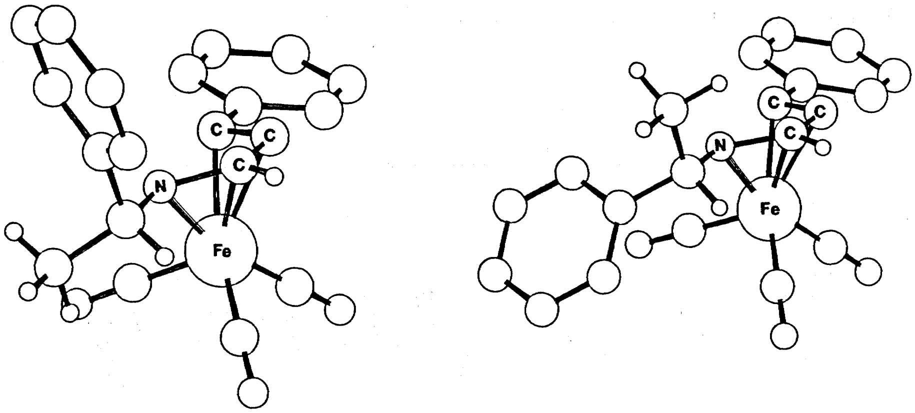
SCHEME 13

Experiments to determine whether or not attack occurs while the 1-azadiene is still attached to the metal are in progress.

Condensation of cinnamaldehyde with (*S*)-α-methylbenzylamine produces a 1-azadiene **26**, which complexes to the iron tricarbonyl unit to give a 1:1 mixture of diastereoisomers **27**. Treatment of the diastereoisomeric mixture **27** with methyl-lithium gave the pyrrole **28** as the major product (scheme 14).



SCHEME 14



27a **27b**

FIGURE 2

Molecular modelling of the diastereoisomeric forms of **27** using Chem-X (Chemical Design Ltd, Oxford, U.K.) revealed the most stable conformation of each diastereoisomer, **27a** and **27b** (figure 2). (The results obtained from the molecular modelling were in excellent agreement with results obtained from NOE (nuclear Overhauser effect) difference spectroscopy.)

These models suggest that the approach of a nucleophile to carbon(2) of the 1-azadiene is impeded by either the phenyl or methyl group on the α-methylbenzylamine moiety. Nucleophilic attack is thus directed towards a metal carbonyl ligand and subsequent pyrrole formation.

CONCLUSIONS

The reactions of nucleophiles with heterodiene iron tricarbonyl complexes, a neglected area of chemistry, have been the subject of preliminary investigations. The results of these investigations, together with the stereochemical properties of heterodiene iron tricarbonyl complexes, suggest that these transition metal complexes have considerable potential in organic synthesis.

We thank Dr B. K. Blackburn (Oxford, U.K.) for the molecular modelling studies of compound **27**.

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Discussion

B. T. GOLDING (*Department of Organic Chemistry, University of Newcastle upon Tyne, U.K.*). Has Dr Thomas observed hydration at the C=N in her (α,β-unsaturated imine) iron(tricarbonyl) complexes?

SUSAN E. THOMAS. The complexed imine functionality does not appear to be susceptible to hydration under the conditions used in our reactions and work-ups. We have not, however, performed experiments specifically designed to investigate hydration.