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β-Diketones containing a ferrocenyl group: synthesis, structural aspects, pK_a^1 values, group electronegativities and complexation with rhodium(I)

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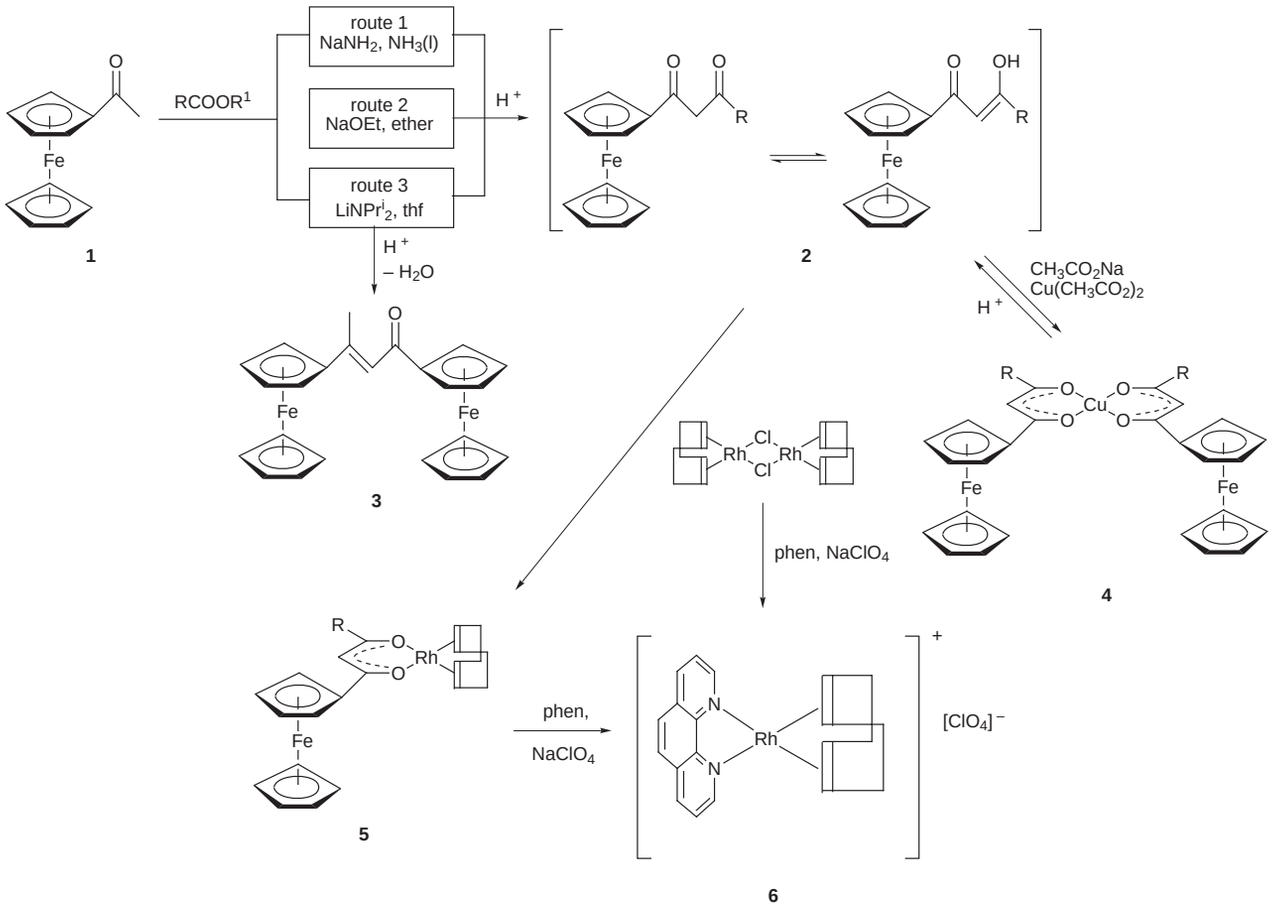
1-Ferrocenyl-4,4,4-trifluorobutane-1,3-dione (ferrocenoyltrifluoroacetone, Hfctfa, pK_a^1 = 6.53 ± 0.03), 4,4,4-trichloro-1-ferrocenylbutane-1,3-dione (trichloroferrocenoylacetone, Hfctca, pK_a^1 = 7.15 ± 0.02), 1-ferrocenylbutane-1,3-dione (ferrocenoylacetone, Hfca, pK_a^1 = 10.01 ± 0.02), 1-ferrocenyl-3-phenylpropane-1,3-dione (benzoylferrocenoylmethane, Hbfcm, pK_a^1 = 10.41 ± 0.02) and 1,3-diferrocenylpropane-1,3-dione (diferrocenoylmethane, Hdfcm, pK_a^1 = 13.1 ± 0.1) were prepared by Claisen condensation of acetylferrocene with an appropriate ester under the influence of sodium amide, sodium ethoxide or lithium diisopropylamide. The group electronegativity of the ferrocenyl group is 1.87 (Gordy scale) as inferred from a linear β-diketone pK_a^1–group electronegativity relationship as well as from a linear methyl ester IR carbonyl stretching frequency–group electronegativity relationship. Complexes [Rh(β-diketone)(cod)] were obtained in yields approaching 80% by treating the β-diketones with $[Rh_2Cl_2(cod)_2]$, while the copper(II) chelates form just as readily. Treatment of all [Rh(β-diketone)(cod)] complexes with 1,10-phenanthroline (phen) and some of its derivatives resulted in substitution of the β-diketone ligand to form $[Rh(cod)(phen)]^+$. The uncomplexed β-diketones are increasingly stable towards the OH^- nucleophile in the order Hdfcm (apparent most unstable) < Hfctfa < Hbfcm < Hfctca < Hfca (most stable). Asymmetric enolisation in the direction furthest from the ferrocenyl group was observed for all β-diketones. This finding is considered to be the result of resonance driving forces rather than inductive electronic effects of substituents on the pseudo-aromatic β-diketone core.

β-Diketone complexes of transition metals have been the subject of many different studies ranging from synthetic,[1] kinetic[2] and structural[3] topics to catalysis[4] and many others.[5] Ferrocene and its derivatives, on the other hand, have been investigated[1,6] equally well, *inter alia* because of their use as colour pigments,[7] high burning rate catalysts[8] in solid fuel, liquid fuel combustion catalysts[9] and smoke suppressant additives.[10] A new field of potential application of both β-diketone complexes of rhodium(I) and derivatives of ferrocene has evolved in recent years with reports that some of these compounds show appreciable antineoplastic activity. Thus it has been shown that, compared to cisplatin $[Pt(NH_3)_2Cl_2]$,[11] certain ferrocenium salts[12] have more favourable 50% lethal dosage (LD_{50}) values, and that [Rh(acac)(cod)] (acac = acetylacetonate) is more effective against Erlich Ascite tumours.[13] Today cisplatin is still one of the most widely used metal-containing chemotherapeutic drugs in the USA, Europe and Japan,[14] but suffers, as do all other chemotherapeutic agents, from many side effects. These include *inter alia* high toxicity to the kidneys and bone marrow,[15] loss of appetite (anorexia),[16] development of drug resistance after continued drug dosage,[17] a high rate of excretion from the body,[18] low aqueous solubility and, perhaps most important of all, inability to distinguish between healthy and cancerous cells.[19] To combat the negative aspects surrounding cisplatin and other chemotherapeutic drugs, new antineoplastic materials are continuously being synthesized and evaluated, new methods of delivering an active drug to a cancerous growth are being developed[20] and combination chemotherapy has been investigated in the hope of finding synergistic effects.[21] Partly because of this, partly because of our kinetic[2] and structural[3] programmes regarding the chemistry of β-diketonato complexes of rhodium(I) and also because of our synthetic program on ferrocene derivatives,[22] we decided to investigate the structural, thermodynamic and chelate-forming properties of various ferrocene-containing β-diketones with Rh^I. Since the ferrocene-containing rhodium(I) chelates obtained are constructed from more than one antineoplastic moiety within the same molecule, they hold the promise of displaying synergistic effects in chemotherapy without the need of administering two or more types of antineoplastic drugs simultaneously to a tumour-bearing mammal.

β-Diketones are normally prepared by Claisen condensation of appropriate carbonyl-containing compounds.[23] The strong electron-donating properties of the ferrocenyl group lower the acidity of the methyl hydrogen atoms of acetylferrocene (**1**) which in turn necessitates the use of strong bases (*i.e.* metal amides or alkoxides) to ensure reasonable yields. Thus Hauser and co-workers[24] synthesized various ferrocene-containing β-diketones, including 1-ferrocenylbutane-1,3-dione (ferrocenoylacetone, Hfca) and 1-ferrocenyl-3-phenylpropane-1,3-dione (benzoylferrocenylmethane, Hbfcm), by using potassium amide as the active base additive in liquid ammonia as solvent. Weinmayr[1b] utilised sodium methoxide as basic initiator to prepare both Hfca and 1-ferrocenyl-4,4,4-trifluorobutane-1,3-dione (ferrocenoyltrifluoroacetone, Hfctfa) in diethyl ether, while Cullen *et al.*[4a] favoured the use of the sterically hindered base lithium diisopropylamide in the preparation of Hfca.

Results and Discussion

Upon utilising sodium amide as basic initiator, Hauser's method[24] resulted in Hfca (**2**, R = CH_3, Scheme 1) in yields not exceeding 22% based on the initial amount of acetylferrocene used. In contrast, 1,3-diferrocenylpropane-1,3-dione (Hdfcm) (**2**, R = ferrocenyl) could only be obtained in trace amounts (*ca.* 5%) *via* this route. By adapting the method of Cullen *et al.*[4a] to a one-pot procedure, we found the $LiNPr^i_2$ route effective for Hfca (38% yield), Hbfcm (**2**, R = phenyl, 28% yield), Hdfcm (30% yield) and 4,4,4-trichloro-1-ferrocenylbutane-1,3-dione (trichloroferrocenoyl acetone, Hfctca) (**2**, R = CCl_3, 16% yield) synthesis provided the added base was never the limiting



Scheme 1 Claisen condensation of acetylferrocene **1** with appropriate esters (R^1 = ethyl or methyl) give the β-diketones Hfctfa (**2**, R = CF_3), Hfctca (**2**, R = CCl_3), Hfca (**2**, R = CH_3), Hbfcm (**2**, R = phenyl) and Hdfcm (**2**, R = ferrocenyl); NMR studies indicated that asymmetric enolisation as shown dominates. Self-aldol condensation of **1** leads to the side product **3**. Copper and rhodium complexation proceed with ease to give **4** and **5** while 1,10-phenanthroline substituted the β-diketone in **5** to exclusively give $[Rh(cod)(phen)]^+$ **6**

reagent (to minimise self aldol condensation of acetylferrocene) and rigorous Schlenk conditions were adhered to. Weinmayr's relatively simple alkoxide method [1b] takes much longer than the more involved amide routes but still results in reasonable yields of Hfca (≈35%) as well as Hfctfa (**2**, R = CF_3; ≈54%). However, we were unsuccessful in obtaining Hfctca and Hbfcm *via* the alkoxide route. 1,3-Diferrocenylbut-2-en-1-one (1-ferrocenoyl-2-ferrocenylpropene) **3**, the dehydrated aldol condensation product [25a] of acetylferrocene, was also isolated from the Hdfcm, Hbfcm and Hfctca reaction mixtures in yields ≤23%. Exhaustive column chromatography of compounds **2** and/or fractional precipitation of the copper complexes **4** followed by free β-diketone generation with 6 mol dm^{-3} HCl (Scheme 1) were needed to separate **2** from **3**. The rhodium(I) complexes, [Rh(β-diketone)(cod)] **5**, were easily prepared in high yield (>75% in dmf from the rhodium(I) dimer $[Rh_2Cl_2(cod)_2]$ but **3** does not react with either Cu^{II} or Rh^{I}. All five complexes of **5** reacted with 1,10-phenanthroline (phen) to generate $[Rh(phen)(cod)]^+$ **6**. The fca is also substituted in **5** (R = CH_3) if it is treated with the 5-nitro-, 4,7-dichloro-, 5,6-dimethyl-, 4,7-dimethyl-, 2,9-dimethyl- and 3,4,7,8-tetramethyl-phenanthroline derivatives to generate the corresponding substituted phenanthroline complex. Confirmation of these reactions, which are the subject of a detailed kinetic study in a forthcoming paper, was obtained by comparing the IR and ^{1}H NMR spectra of the derivatives of **6** so obtained with that of an authentic sample prepared from $[Rh_2Cl_2(cod)_2]$ (Scheme 1).

The crystal structure of **5** (R = CH_3) has recently been reported. [3b] Two molecules within the same unit cell were observed, one of which (molecule A) approached very much the extreme case of asymmetric co-ordination with rhodium. As a result, for molecule A, the geometry of the co-ordinated fca is very similar to that found for the asymmetrically enolised free (unco-ordinated) Hfca. [26] The geometry of the fctfa ligand co-ordinated to the Rh^{I} was also recently established. [3c] Structural investigations of fctca-, bfcm- and dfcm-containing rhodium(I) and iridium(I) complexes are currently in progress. Here we use the published [26] crystallographic data of Hfca to explain the observed asymmetric enolisation for all β-diketones in a direction opposite to the aromatic ferrocenyl side group and the following properties of this structure are pertinent. Bell *et al.* [26] found that for Hfca, in the solid state, asymmetric enolisation takes place in the direction away from the aromatic ferrocenyl side group. The dihedral angle of 4.9(2)° between the pseudo-aromatic β-diketone plane and the planar cyclopentadiene ring of the ferrocenyl group attached to the β-diketone skeleton indicates appreciable conjugation between the two groups. The longer bond distance between the β-diketone skeleton and the methyl group, 1.490(8) Å, as compared to β-diketone core/ferrocenyl group distance of 1.468(7) Å, also indicates that the ferrocenyl group conjugates well with the pseudo-aromatic β-diketone core. Regarding the side product **3**, a single crystal structural determination [27] has shown that the ferrocenyl and ferrocenoyl groups are situated *trans* with respect to each other. By comparing the average dihedral angles of the cyclopentadienyl planes of the ferrocenyl and ferrocenoyl groups of **3** linked to plane 1 [consisting of the atoms $COCHC(CH_3)$, Scheme 1], 12.5(3) and 19.3(3)° respectively, one can conclude that, although both ferrocenyl moieties show appreciable conjugation into the planar (sp^2 conjugated) carbon backbone of plane 1, they do so much less effectively than the ferrocenyl group of Hfca conjugating into the β-diketone core. This is expected, for the β-diketone plane is pseudo-aromatic while plane 1 is not.

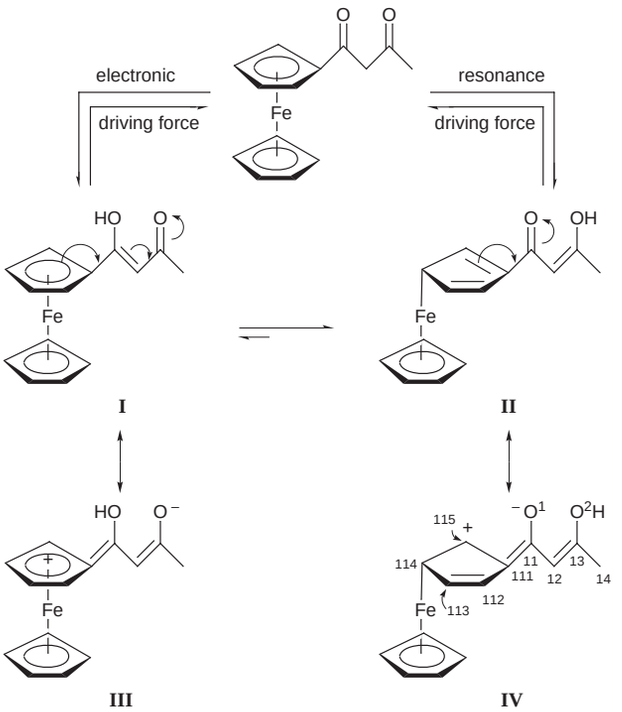
Table 1 pK_a^1 Values and % enol tautomer of various β-diketones. Htfaa = 1,1,1-trifluoroacetylacetone

Compound	pK_a^1 [a]	% Enol [b]	Compound	pK_a^1 [a]	% Enol [b]
Hhfaa	4.35 [c]	100 [c]	Haa	8.95 ± 0.08 [c–e]	91 [d,f]
Htfaa	6.3 [c]	>99	Hfca	10.01 ± 0.02 [d,e]	86 [d,g]
Hbtfa	6.3 [c]	>99	Hdbm	9.35 [c]	>99 [d]
Hfctfa	6.53 ± 0.03 [d,e]	>99	Hbfcm	10.41 ± 0.02 [d,e]	≈95 [d]
Hfctca	7.15 ± 0.02 [d,e]	≈95	Hdfcm	13.1 ± 0.1 [d,e]	>99 [d]
Hba	8.7 [c]	92 [d]			

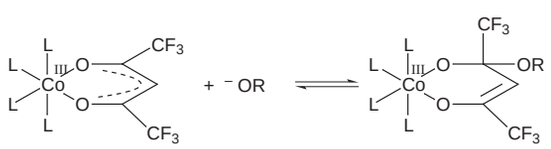
[a] At 21 °C. [b] In $CDCl_3$ at 298 K. [c] Ref. 2(*b*). [d] This work. [e] In water containing 10% acetonitrile, $I = 0.1$ mol dm^{-3} ($NaClO_4$). [f] However, see also ref. 28. [g] However, see also ref. 26.

From a ^{1}H NMR study, by comparing the relative intensities of the CH_2 (keto) and CH (enol) signals, the percentages of enolised tautomers in solution of the prepared and some other β-diketones were established (Table 1). Regarding Hfca, the apparent absence of more than one set of signals for the ferrocenyl substituent as well as the two observed signals for the methyl side group indicate that, as in the solid state, enolisation in solution is predominantly away from the aromatic ferrocenyl group. This result complements that obtained by Bell *et al.*[26] who were unable to predict under their conditions the preferred Hfca enol isomer in solution. It should be noted that, in order to observe the keto isomer in solution, the concentration of the β-diketone solution should be fairly low. High concentrations drive the keto–enol equilibrium towards the enol side[3f] which explains why Bell could not observe the keto isomer in significant quantities. This solution behaviour is also observed[3f] for other β-diketones. Enolisation for Hbfcm, in solution, predominantly took place towards the phenyl group as demonstrated by two distinct sets of ^{1}H NMR signals for the phenyl group *versus* the single set of signals for the ferrocenyl group. In the case of 1-phenylbutane-1,3-dione (benzoylacetone, Hba), the lack of more than one set of phenyl ^{1}H NMR signals and two methyl signals indicate enolisation took place in a direction away from the aromatic phenyl group. Excluding Hdbm (dibenzoylmethane) and Hdfcm, in the case of β-diketones which are >99% enolic (Table 1, these β-diketones have only one ^{1}H NMR active side group, ferrocenyl or phenyl) the relative high field position of the aromatic signals indicates that for Hfctfa, Hfctca and 4,4,4-trifluoro-1-phenylbutane-1,3-dione (Hbtfa) enolisation most likely takes place predominantly away from the aromatic substituent. In order to explain the dominance of the observed enol isomer in each case, two different driving forces that will control the conversion from β-diketone into an enolic isomer may be defined. The first may by labelled an electronic driving force in which the formation of the preferred enol isomer is controlled by the electronegativity of the R and R′ substituents in the β-diketone $RCOCH_2COR'$. When the electronegativity of R is greater than that of R′ the carbon atom of the carbonyl group adjacent to R′ will be less positive in character than the carbon atom of the other carbonyl group. Consequently, from an electronic point of view, the dominant enol isomer should be RCOCH=C(OH)R′. If the documented group electronegativities[29] are correct, from the viewpoint of an electronic driving force as just described, only Hba {group electronegativity of the phenyl group, $\chi_{phenyl} = 2.43$ (apparent) or 3.0 [corrected, see ref. 29(*a*)], while $\chi_{methyl} = 2.30$[29a] or 2.34[29b]} of all the β-diketones just discussed exhibits the expected dominant enol isomer. For all the other mentioned β-diketones having only one aromatic side group one would expect enolisation to take place predominantly in the direction of this aromatic substituent because in each case the electronegativity of the trifluoromethyl[29b] (3.20), trichloromethyl[29b] (2.76) or methyl group is larger than that of the other substituents: either the phenyl or the ferrocenyl group (electronegativity ≈1.87 as per this work). In the case of Hbfcm, which has two aromatic side groups, one would expect, by considering the electronegativities of the ferrocenyl and phenyl groups, enolisation to take place in the direction of the least electronegative ferrocenyl group. This is also in contrast to what was found. Clearly there is a different driving force than the suggested electronic driving force that determines the observed preferred enol configuration in β-diketones where aromatic side groups are present. To explain this observation the existence of a resonance driving force is proposed. The resonance driving force implies that the formation of different canonical forms of a specific isomer will lower the energy of this specific isomer enough to allow it to dominate over the existence of other isomers. Crystallographic studies may be used to support the existence of the resonance driving force as explained for Hfca below. However, the same argument may also, with success, be applied to all the other β-diketones.

It should first be noted that crystallographic determinations of the structure of several compounds have indicated that both the ferrocenyl and the phenyl groups conjugate very well with adjacent carbonyl,[27,30a] alkene,[27] aromatic[6,30b] and pseudo-aromatic[26] substituents in free compounds[27,30] and in complexed form.[3] With respect to β-diketones, this conjugation can take place in at least two ways as demonstrated for the two theoretically possible enol forms **I** and **II** of Hfca in Scheme 2. To understand why under our experimental conditions only isomer **II** was observed, implying that the equilibrium between **I** and **II** is shifted very far towards **II**, one may consider the canonical forms **III** and **IV**. The relatively short C11–C111 bond length [1.468(7) Å, see Scheme 2 for atom labelling] compared to the C–C bond length of alkanes [for example[3b] lengths of 1.500–1.552(8) Å observed in the cod fragment of **5**, R = CH_3; bond lengths between the β-diketone pseudo-aromatic core and the carbon atoms of adjacent alkyl groups are usually[3a,b,26,27] around or larger than 1.5 Å] indicates substantial conjugation between the ferrocenyl group and the β-diketone core. Inspection of the bond distances of the cyclopentadienyl ring attached to the β-diketone skeleton[26] indicates bond lengths of 1.435(6) for C111–C112, 1.415(7) for C112–C113, 1.417(7) for C113–C114, 1.426(7) for C114–C115 and 1.420(7) Å for C111–C115 respectively. These bond lengths would fit both canonical forms **III** and **IV**. However, the C–O bond lengths fit only structure **IV**. Bond C13–O2 is long [1.307(7) Å] and typical of an enol structure. In contrast bond C11–O1 [1.287(6) Å] is not short enough for a typical C=O bond [*ca.* 1.206 Å, see for example ref. 3(*d*)]. Indeed, this bond is so long it more closely approaches typical single C–O than double C=O bond lengths, a situation that can only arise if **IV** makes an appreciable contribution to the overall structure of Hfca. Thus, the crystal structure determination of Hfca indicates that zwitterion **IV** arising from isomer **II** dominates over **III** arising from isomer **I**. It should be noted that although the canonical forms indicated in Scheme 2 explain the dominance of isomer **II** over **I** by virtue of the observed ^{1}H NMR and crystallographic data, they by no means imply that other canonical forms and relationships do not also exist. Based on the above arguments, the indications are that with respect to aromatic side groups the driving force which determines which



Scheme 2 Electronic considerations in terms of electronegativity, χ, favour **I** as the enol form of Hfca. However, structure **II** was shown by crystallography and NMR spectroscopy to be dominant. A dihedral angle of 4.9(2)° between the aromatic ferrocenyl group and the pseudo-aromatic β-diketone core implies that energy-lowering canonical forms such as **IV** make a noticeable contribution to the overall existence of Hfca. For clarity the ferrocenyl group in **II** and **IV** is shown in just one canonical form but in both cases the iron atom can be bound to any of the five cyclopentadienyl carbon atoms as indicated in **I**. Likewise, the positive charge of **IV** is also not confined to the single position shown but rather oscillates between C112 and C115 (it cannot be on C111; atom numbers are indicated next to individual atoms) to give rise to four different canonical forms as indicated in **III**. $\chi_{methyl} = 2.34$,[29b] $\chi_{ferrocenyl} = 1.87$



Scheme 3 Reversible hydroxylation (R = H) and methoxylation (R = methyl) for hexafluoroacetylacetone complexes of cobalt(III). L = Ammonia or an amine, see ref. 32(*a*)

enolate is favoured is resonance stabilisation and not electronic factors. Resonance stabilisation favours the formation of intermediates such as **II** and **IV** while electronic factors favour the formation of intermediates resembling **I** and **III**. Since ^{1}H NMR spectroscopy does not distinguish between a ferrocenyl group on the keto side and one on the enol side of the enolic form of Hdfcm [the same applies to the two phenyl groups of 1,3-diphenylpropane-1,3-dione (dibenzoylmethane, Hdbm)] it is assumed that the keto–enol conversion in these two compounds takes place on a timescale much faster than that of NMR.

The increasing tendency towards enolisation of all the β-diketones having only one aromatic side group with stronger acidity in the apparent pK_a^1 range of 4.35–10.01 (Table 1) is expected when the electronegativity of the side groups is considered. The term 'apparent' is used since in this study no attempt was made to partition the experimentally obtained pK_a^1 values between separate pK_a values for the enol and keto tautomers. All the β-diketones with trifluoroacetyl side groups are acidic enough ($pK_a^1 \leqslant 6.53$) to ensure almost complete enolisation (>99% at 298 K). The compounds Hdfcm, Hbfcm and Hdbm differ in structure from all the other β-diketones listed

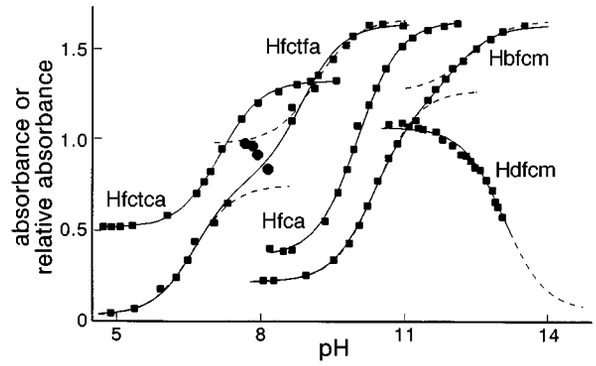


Fig. 1 Absorbance dependence on pH of Hfctfa (0.1266 mmol dm^{-3}, 320 nm), Hfctca (0.1044 mmol dm^{-3}, 330 nm), Hfca (0.1059 mmol dm^{-3}, 326 nm), Hbfcm (0.0639 mmol dm^{-3}, 360 nm) and Hdfcm (9.230 mmol dm^{-3}, 420 nm) at 21 °C. The absorbance indicated for Hfctfa is exact, but those for all the other β-diketones were adjusted to a relative value in order to show all curves on the same axis system. Only ■ data were used in the fitting program. For Hfctfa, the points shown as ● (at pH close to 8; not included in the data set used for the pK_a^1 fitting) indicate an OH^- consumption to form a new compound speculated to be a hydroxylated species similar to that formed by hexafluoroacetylacetone (see Scheme 3). Solvent: water containing 10% acetonitrile, $I = 0.100$ mol dm^{-3} ($NaClO_4$)

in Table 1 by having two aromatic substituents per molecule. Hence resonance stabilisation of Hdbm, Hbfcm and Hdfcm, as just explained for Hfca, will increase greatly and account for the observed seemingly unusual high percentage of enolisation in these three compounds. The newly determined pK_a^1 values of the β-diketones cited in Table 1 were obtained from a least-squares fit of UV absorbance/pH data using equation (1)[31a]

$$A_T = \frac{A_{HA}10^{-pH} + A_A10^{-pK_a^1}}{10^{-pH} + 10^{-pK_a^1}} \quad (1)$$

(Fig. 1, single pK_a^1) or (2)[31b] (Fig. 1, two pK_a^1 values) with A_T = total absorbance, A_{HA} the absorbance of the β-diketone in the protonated form, and A_A the absorbance of the deprotonated (basic) form. In equation (2), pK_{a2}^1 represents the appar-

$$A_T = \frac{A_{HA}(10^{-pH})^2 + A_A(10^{-pK_a^1})(10^{-pH}) + A_F(10^{-pK_a^1})(10^{-pK_{a2}^1})}{(10^{-pH})^2 + (10^{-pH})(10^{-pK_a^1}) + (10^{-pK_a^1})(10^{-pK_{a2}^1})} \quad (2)$$

ent pK_a^1, or more likely the pH dependent formation constant of an *in situ* formed, possibly hydroxylated species (compare Scheme 3) with final absorption A_F, specifically in the case of Hfctfa and Hbfcm. Whether pH/absorbance data for Hfctfa and Hbfcm were fitted by equation (1) (separate, single pK_a^1 fits for each pK_a^1) or (2) (a single fit to determine both pK_a^1 values simultaneously) made essentially no difference to the obtained pK_a^1 values. The reason for pK_{a2}^1 for Hfctfa and Hbfcm is still unknown, but it is possible that reversible hydroxylation, similar to that observed for 1,1,1,5,5,5,-hexafluoroacetylacetone (Hhfaa)[32a] (Scheme 3) may take place. This subject is now under further investigation. The electronic spectra of compounds **2**, **5** and **6** (R = CH_3) are shown in Fig. 2, while peak absorption coefficients are in Table 2. The basic forms of **2** become progressively more stable towards alkaline solutions in the order Hdfcm (most unstable) < Hfctfa < Hbfcm < Hfctca < Hfca (most stable). The general instability of all β-diketones towards aqueous alkali media (cleavage at the methine position takes place[33a]) is probably the major reason for Hdfcm's alkaline instability. Since the β-diketones were not all well soluble in pure or basic water, water–acetonitrile mixtures were used as solvent. We have found that such mixtures have much less influence on β-diketone pK_a^1 determinations than[32b] do 1,4-dioxane, methanol, ethanol or propan-2-ol. The effect of the amount of acetonitrile or 1,4-dioxane in the solvent medium

Table 2 Peak molar absorption coefficients, ε, at the corresponding wavelength, λ_{max}, of free (in water containing 10% acetonitrile) and rhodium(I) complexed β-diketones (in methanol)

	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})			
Compound	protonated	unprotonated	Compound	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})
Hfctfa	469 (1130)	324 (6170)	[Rh(fctfa)(cod)]	472 (1900)
Hfctca	345 (6750)	335 (12 170)	[Rh(fctca)(cod)]	495 (2360)
Hfca	473 (1010)	330 (24 420)	[Rh(fca)(cod)]	335 (8530)
Hbfcm	375 (10 320)	345 (18 270)	[Rh(bfcm)(cod)]	475 (2380)
Hdfcm	344 (11 360)	369 (3130)	[Rh(dfcm)(cod)]	470 (1570)

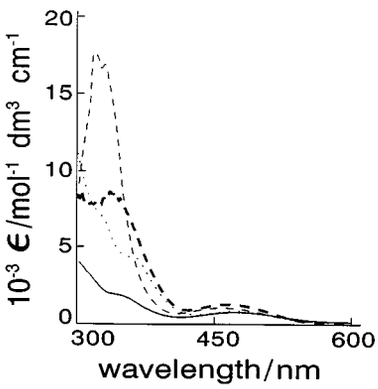


Fig. 2 The UV spectra of Hfca, both in acidic (——, pH 2.0) and basic (– – –, pH 13.0) form, recorded in water, superimposed on the spectra of [Rh(fca)(cod)] (— — —) and [Rh(cod)(phen)]$^+$ (·····) in methanol

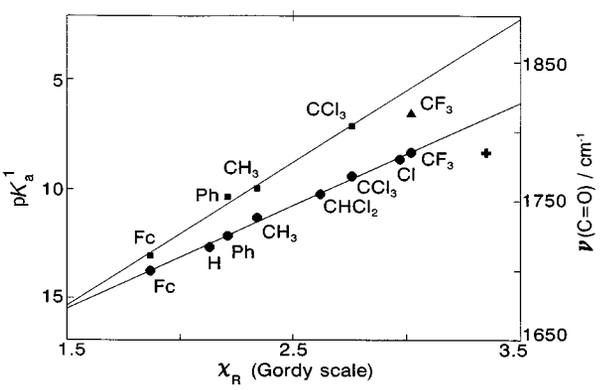


Fig. 3 Linear relationships observed between group electronegativities, χ_R, and pK_a^1 values of β-diketones of the type FcCOCH$_2$COR, Fc = ferrocenyl (upper) as well as carbonyl stretching frequencies, ν(C=O) (lower), of methyl esters of the type RCOOMe; R is indicated on each plot. For R = CF$_3$ the ethyl ester was used. Points marked as ▲ (this study) and + (from ref. 29) were not used in the fitting

was tested using Hfca and Hfctfa as references. The pK_a^1 of Hfca in water and water containing 10% acetonitrile were 9.96 and 10.01 respectively. For Hfctfa the pK_a^1 was 6.53 in water containing 10% acetonitrile, 6.9 in water containing 5% aqueous 1,4-dioxane and 7.0 in 50% aqueous acetonitrile [at 21 °C and I = 0.1 mol dm^{-3} ($NaClO_4$)].

In an attempt to use the obtained pK_a^1 values of compounds **2** to determine the group electronegativity of the ferrocenyl group, χ_{Fc}, from known χ_R values (Gordy scale[29b]) for the other R substituents on the β-diketones an inconsistency was observed for the published χ_{Ph} value. Using literature values[29] for group electronegativities it would not fit on the straight line generated by the fit of pK_a^1 and χ_R (R = Ph, CH$_3$ or CCl$_3$). Utilising the stretching frequency of the carbonyl group [ν(C=O)] of the methyl esters of the indicated compounds (Fig. 3) the effective or apparent χ_{Ph} was redetermined as 2.21 by extrapolation of the linear relationship between χ_R and $\nu(C{=}O)_R$ while χ_{Fc} and χ_{CF_3} were found to be 1.87 and 3.01 respectively. The obtained effective CF$_3$ group electronegativity stands in contrast to literature values[29] of 3.2 and 3.35. The scattering of CF$_3$ group electronegativities is the direct result of the uncertainty in the structure observed for trifluoroacetyl-containing molecules and is *inter alia* also echoed in reported pK_a^1 values of 4.35–5.3 for hexafluoroacetylacetone.[32a] The newly obtained χ_{Ph} fitted the linear plot of pK_a *versus* χ_R, R = CCl$_3$, CH$_3$ or phenyl, very well (Fig. 3). Extrapolation of this line also resulted in an apparent χ_{Fc} value of 1.87 which is mutually consistent with the value derived from the ν(C=O) *vs.* group electronegativity relationship. A polarographically determined χ_{Fc} value of 2.08 reported elsewhere[33b] is in close agreement with the above mentioned results. Once again the value obtained for the CF$_3$ group did not fit the trend set by the other R groups for reasons adequately described above.

Experimental

Materials

Ferrocene (Strem), *n*-butyllithium and other solid reagents (Merck) were used without further purification. Liquid reactants and solvents were distilled prior to use; water was double distilled. Diethyl ether and thf were dried by refluxing under nitrogen over sodium wire and distilled directly before use. Flash chromatography was performed on Kieselgel 60 (Merck, grain size 0.063–0.2 mm, eluent ether–hexane 2:3 by volume) or, if stated eluent 2, Sephadex LH-20 (Pharmacia, hexane–ethanol 6:1 by volume) utilising an overpressure that never exceeded 100 Torr (1 Torr = 1 mmHg = 133.32 Pa).

Acid dissociation constant determinations and spectroscopy

Proton NMR spectra at 298 K were recorded either on a Bruker AM-300 or WP-80 instrument, with chemical shifts presented as δ values referenced to $SiMe_4$ at 0.00 ppm. Electronic spectra were recorded on a Hitachi Model 150-20 and IR spectra (KBr pellets unless otherwise stated) on a Hitachi Model 270-50 instrument. The pK_a^1 values were determined by measuring the absorbance at different pH during an acid–base titration in water or acetonitrile–water mixtures, 1:9 by volume, I = 0.100 mol dm^{-3} ($NaClO_4$) at 21.0 °C. β-Diketone concentrations were where possible less than 0.2 mmol dm^{-3} and are indicated in Fig. 1. A linear response by the pH meter (Orion model SA 720), fitted with a glass electrode, was ensured by calibration with commercial buffers (Sigma) at pH = −log α_H = 4.01, 7.00 and 12.00 respectively, α_H = activity of H$^+$. A test pK_a^1 determination was then performed by titrating the well characterised compound acetylacetone with sodium hydroxide. A least squares fit of the obtained UV absorbance/pH data for this titration using equation (1), utilising the fitting program MINSQ,[33c] resulted in a pK_a^1 of 8.95 ± 0.08 in water. This was within experimental error the same as the best available published pK_a^1 for acetylacetone in water (8.878 ± 0.005 when I = 1 mol dm^{-3} and 8.98 when I = 0.0172 mol dm^{-3}).[32b] It was therefore concluded that the electrode was calibrated to measure hydrogen ion concentration under the conditions used. It is not expected that the electrode would behave differently for

any of the other pK_a^1 determinations because only pK_a^1 values of a series of β-diketones were determined. For Hfca, titration was performed with $HClO_4$ from high pH, adjusted with NaOH, to low pH since compound **2** (R = CH_3) would not dissolve in non-alkaline water. Owing to the slow rate of dissolving OH-unstable Hdfcm and Hfctca, solutions of these β-diketones in acetonitrile were treated with aqueous NaOH to a final mixed solvent constitution of 90% water and a pH high enough to ensure that the β-diketones were fully in the deprotonated form, before titrations commenced. The influence of acetonitrile on the pK_a^1 determination was studied by repeating the determination for Hfca in water containing 10% acetonitrile. The obtained pK_a^1 was within 99.5% of the value obtained in pure water. The influence of 1,4-dioxane was much more pronounced. Water containing only 5% 1,4-dioxane caused a pK_a^1 drift for Hfctfa of more than 7%. Acetonitrile induced a drift this large in the pK_a^1 of Hfctfa only when the mixed solvent contained 50% acetonitrile (see text). It was best to determine the pK_a^1 of Hfctfa and Hbfcm by titration from low to high pH due to an unknown, but apparently semi-reversible, side reaction taking place on the basic side of the pK_a of the ligand. Therefore Hfctfa and Hbfcm were first dissolved in acetonitrile followed by addition of water and $HClO_4$ to a final mixed solvent constitution of 10% acetonitrile, pH 3.5 before finally titrating with NaOH.

Atomic absorption iron analysis

Samples were prepared by heating ferrocenyl-containing compound (10–30 mg) with 27.5% nitric acid (0.8 cm^3) and water (1 cm^3) to gentle simmering. The colour changed from blue to orange-yellow. After 10 min, water (5 cm^3) was added and the new solution again heated to gentle simmering for 30 min. The cooled solution was diluted to 10 cm^3 in a volumetric flask and the iron content (between 5 and 15 ppm) of the solution determined against standard iron(III) solutions of concentration 5, 10 and 15 ppm on a Varian SpectrAA-300 atomic absorption spectrophotometer fitted with coprocessor. A blank (10 cm^3 55% HNO_3 diluted to 250 cm^3) correction was made.

Syntheses

Acetylferrocene 1. This was prepared (in 81% yield) by treating ferrocene with acetic anhydride according to a published procedure[6b] with care being taken to maintain the internal temperature[34] of the reaction mixture between 100 and 105 °C. Recrystallisation from hexane gave a sufficiently pure product for β-diketone syntheses.

Methyl ferrocenoate. Ferrocenoic acid was prepared *via* the lithium intermediate as described elsewhere[35] and esterified by refluxing it (1.6 g, 7 mmol) in methanol (100 cm^3) in the presence of concentrated H_2SO_4 (0.04 cm^3) under nitrogen for 48 h. The resulting liquid was poured onto ice (150 g) and extracted with ether (3 × 100 cm^3). The combined ether extracts were washed with water, 5% aqueous $NaHCO_3$ and again water to afford, after removal of the dried ($NaSO_4$) solvent, the ester (1.19 g, 70%), m.p. 70 °C (lit.,[36] 70 °C); δ_H(80 MHz, $CDCl_3$) 3.78 (3 H, s, CH_3), 4.17 (5 H, s, C_5H_5), 4.35 (2 H, t, C_5H_4) and 4.76 (2 H, t, C_5H_4).

β-Diketones 2. Only one representative example is provided for each of the three methods.

Hdfcm (**2**, R = *ferrocenyl*), *sodamide method*. Solid acetylferrocene **1** (0.456 g, 2 mmol) was slowly added during 30 min with vigorous stirring to a suspension of $NaNH_2$ (0.215 g, 5.5 mmol) in distilled[37] ammonia (15 cm^3). The resulting yellow suspension was stirred for 15 min before freshly prepared dry methyl ferrocenoate (0.976 g, 4 mmol) dissolved in dry ether (10 cm^3) was added dropwise. After stirring the cooled red suspension for 1 h, dry ether (3 cm^3) was carefully added followed by slowly heating the mixture to 40 °C to remove all NH_3(l). The resulting suspension was refluxed for 15 min, the residue filtered off, washed with ether (4 × 5 cm^3) and dissolved without delay in warm (60 °C) water. By adjusting the pH to 2 (HCl) a red-brown precipitate was obtained which was extracted with ether (3 × 5 cm^3), washed with water (10 cm^3) and dried ($MgSO_4$). Removal of the solvent followed by flash chromatography (R_f = 0.58) afforded Hdfcm (0.061 g, 7%) as deep red needles after solvent removal, m.p. 157 °C (Found: Fe, 25.2. $C_{23}H_{20}Fe_2O_2$ requires 25.38%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1640 and 1710 (C=O); δ_H(300 MHz, $CDCl_3$) 4.19 (10 H, s, 2 × C_5H_5), 4.49 (4 H, t, 2 × C_5H_4), 4.82 (4 H, t, 2 × C_5H_4) and 5.96 (1 H, s, enol CH).

Hfctfa (**2**, R = CF_3), *sodium ethoxide method*, *an adaptation of a published procedure*.[1] A suspension of solid sodium ethoxide[38] (3.4 g, 50 mmol) in an ether solution (40 cm^3) of acetylferrocene (5.47 g, 24 mmol) was stirred for 15 min before ethyl trifluoroacetate (6.82 g, 48 mmol), prepared, purified and dried in the same way as described for ethyl acetate,[39] was slowly added. The resulting orange-red precipitate was filtered off after 12 h of stirring, washed with dry ether and dissolved in lukewarm (50–60 °C) water. The aqueous solution was filtered *without delay*, the pH immediately lowered to 2 with HCl and extracted with ether (3 × 100 cm^3). Washing of the ether extract with water (3 × 100 cm^3), followed by drying ($NaSO_4$) and solvent removal under pressure, afforded solid Hfctfa (4.22 g, 54%); m.p. 102 °C (lit.,[1] 102 °C). Flash column chromatography (R_f = 0.48) afforded spectroscopically pure Hfctfa (Found: Fe, 17.3. $C_{14}H_{14}F_3FeO_2$ requires 17.23%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1620 (C=O); δ_H(80 MHz, $CDCl_3$) 4.20 (5 H, s, C_5H_5), 4.65 (2 H, t, C_5H_4), 4.85 (2 H, t, C_5H_4) and 6.07 (1 H, s, CH).

Hbfcm (**2**, R = *phenyl*), *lithium diisopropylamide method*. Rigorous Schlenk conditions were adhered to. A light yellow solution of $LiNPr^i_2$ was prepared by adding *n*-butyllithium (4.21 cm^3 of a 1.6 mol dm^{-3} solution in hexane) to an ice-cooled solution of freshly distilled diisopropylamine (0.73 g, 7.2 mmol) in thf (15 cm^3). This was added to a solution of acetylferrocene (1.46 g, 6.4 mmol) in thf (10 cm^3) and stirred at room temperature for 20 min before methyl benzoate (0.81 g, 6 mmol) dissolved in thf (10 cm^3) was added. Stirring of the resulting reaction mixture continued for 4 h before it was shaken with HCl (50 cm^3, 1 mol dm^{-3}) and immediately extracted with ether (5 × 80 cm^3). The combined ether extracts were thoroughly washed with water, dried ($MgSO_4$) and evaporated to dryness under reduced pressure. Flash chromatography of the residue (R_f = 0.58) afforded Hbfcm (0.56 g, 28%), m.p. 107 °C (lit.,[24] 106 °C) (Found: Fe, 16.6. $C_{19}H_{16}FeO_2$ requires 16.81%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1640 and 1710 (C=O); δ_H(300 MHz, $CDCl_3$) 3.91 (0.1 H, s, keto CH_2), 4.20 (5 H, s, C_5H_5), 4.54 (2 H, t, C_5H_4), 4.88 (2 H, t, C_5H_4), 6.48 (0.95 H, s, enol CH), 7.41–7.51 and 7.88–8.11 (5 H, m, C_6H_5). Compound **3** was isolated from the reaction mixture in yields up to 20%, R_f = 0.54, m.p. 116 °C (Found: Fe, 26.1. $C_{24}H_{22}Fe_2O$ requires 26.21%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1630 (C=O); δ_H[300 MHz, $(CD_3)_2CO$] 2.55 (3 H, d, CH_3), 4.19 (5 H, s, C_5H_5 on the alkenyl side), 4.22 (5 H, s, C_5H_5 of ferrocenoyl), 4.46 (2 H, t, C_5H_4 on the alkenyl side), 4.57 (2 H, t, C_5H_4 of ferrocenoyl), 4.79 (2 H, t, C_5H_4 on the alkenyl side), 4.88 (2 H, t, C_5H_4 of ferrocenoyl) and 6.89 (1 H, q, CH).

Hfctca. The $LiNPr^i_2$ method resulted in Hfctca (m.p. 52 °C, 16% yield). It took several days to solidify after solvent removal. Eluent 2 was used to prevent acid induced degradation of Hfctca during chromatography (Found: Fe, 14.8. $C_{14}H_{11}Cl_3FeO_2$ requires 14.95%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1620 (C=O); δ_H(300 MHz, $CDCl_3$) 4.14 (0.1 H, s, keto CH_2), 4.22 (5 H, s, C_5H_5), 4.62 (2 H, t, C_5H_4), 4.86 (2 H, t, C_5H_4) and 6.35 (0.95 H, s, enol CH).

Characterisation data for Hfca (Found: Fe, 20.6. $C_{14}H_{14}FeO_2$ requires 20.68%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 1620 (C=O); δ_H(80 MHz,

$CDCl_3$) 2.02 (2.64 H, s, enol CH_3), 2.27 (0.36 H, s, keto CH_3), 3.80 (0.24 H, s, keto CH_2), 4.12 (5 H, s, C_5H_5), 4.46 (2 H, t, C_5H_4), 4.74 (2 H, t, C_5H_4) and 5.69 (0.86 H, s, enol CH).

Copper(II) complexes 4. Crude compounds **2** could be purified with good effect *via* copper(II) complexation. The general procedure was as follows: to a solution of crude solid β-diketone (up to 30 mmol) in acetone (20 cm^3) was added copper(II) acetate (10.7 g, 54 mmol, super saturated) and sodium acetate (2.2 g, 2.7 mmol) dissolved in water (120 cm^3). The precipitate **4** that formed was filtered off after 45 min of stirring at room temperature, thoroughly washed with water and dissolved in chloroform (80 cm^3). Liberation of the free β-diketone was accomplished by shaking the chloroform solution of **4** with an equal volume of HCl (6 mol dm^{-3}), washing with water and evaporating to dryness under reduced pressure.

Di-μ-chloro-bis(η-cycloocta-1,5-diene)dirhodium(I). The complex was prepared according to a published procedure.[40] δ_H(300 MHz, $CDCl_3$) 1.30 (4 H, m, half of $4CH_2$), 2.08 (4 H, m, half of $4CH_2$) and 4.42 (4 H, m, 4CH).

[Rh(β-diketone)(cod)] complexes 5. The general procedure was as follows. To a stirred yellow, near saturated solution of $[Rh_2Cl_2(cod)_2]$ (0.5 g, 1 mmol) in dmf (6 cm^3) was added solid β-diketone **2** (2 mmol). After 5 min of stirring the crude product **5** was precipitated with an excess of water, filtered off and dissolved in ether. The ether solution was washed with water, dried ($MgSO_4$) and evaporated to dryness. Flash column chromatography gave **5** spectroscopically pure in high yield.

[Rh(fctfa)(cod)]. $R_f = 0.73$; 87% yield. δ_H(300 MHz, $CDCl_3$) 1.84 (4 H, m, half of aliphatic C_8H_{12} protons), 2.49 (m, 4 H, other half of aliphatic C_8H_{12} protons), 4.18 (m, 9 H, four olefinic protons of C_8H_{12} and 5 H of C_5H_5), 4.45 (2 H, t, C_5H_4), 4.70 (2 H, t, C_5H_4) and 5.93 (1 H, s, CH).

[Rh(fctca)(cod)]. $R_f = 0.73$; 57% yield. δ_H(300 MHz, $CDCl_3$) 1.84 (4 H, m, half of aliphatic C_8H_{12} protons), 2.49 (4 H, m, other half of aliphatic C_8H_{12} protons), 4.18 (9 H, m, 4 olefinic protons of C_8H_{12} and 5 H of C_5H_5), 4.43 (2 H, t, C_5H_4), 4.68 (2 H, t, C_5H_4) and 6.39 (1 H, s, CH).

[Rh(fca)(cod)]. $R_f = 0.79$; 73% yield. δ_H(300 MHz, $CDCl_3$) 1.75 (4 H, m, half of aliphatic C_8H_{12} protons), 2.09 (3 H, s, CH_3), 2.38 (4 H, m, half of aliphatic C_8H_{12} protons), 4.08 (5 H, s, C_5H_5), 4.18 (2 H, t, C_5H_4), 4.45 (4 H, m, olefinic protons of C_8H_{12}), 4.73 (2 H, t, C_5H_4) and 5.80 (1 H, s, CH).

[Rh(bfcm)(cod)]. $R_f = 0.78$; 77% yield. δ_H(300 MHz, $CDCl_3$) 1.84 (4 H, m, half of aliphatic C_8H_{12} protons), 2.49 (4 H, m, other half of aliphatic C_8H_{12} protons), 4.17 (9 H, m, 4 olefinic protons of C_8H_{12} and 5 H of C_5H_5), 4.35 (2 H, t, C_5H_4), 4.70 (2 H, t, C_5H_4), 6.25 (1 H, s, CH), 7.37 (3 H, m, C_6H_5) and 7.78 (2 H, m, C_6H_5).

[Rh(dfcm)(cod)]. $R_f = 0.84$; 79% yield. δ_H(300 MHz, $CDCl_3$) 1.86 (4 H, m, half of aliphatic C_8H_{12} protons), 2.51 (4 H, m, other half of aliphatic C_8H_{12} protons), 4.10 (4 H, m, olefinic protons of C_8H_{12}), 4.15 (10 H, s, $2C_5H_5$), 4.33 (4 H, t, half of $2C_5H_4$), 4.67 (4 H, m, half of $2C_5H_4$) and 5.92 (1 H, s, CH).

[Rh(cod)(phen)][ClO_4] 6. *Method* 1, *by treating* $[Rh_2Cl_2(cod)_2]$ *with phen*. The product obtained in each reaction according to method 2 was the same (as judged by IR and ^1H NMR spectroscopy) as that obtained by allowing compounds $[Rh_2Cl_2(cod)_2]$ and **5** to react with phen according to a literature procedure[2b,40] to obtain **6**. δ_H[300 MHz, $(CD_3)_2SO$] 2.15 (4 H, m, half of aliphatic C_8H_{12} protons), 2.56 (4 H, m, other half of aliphatic C_8H_{12} protons), 4.78 (4 H, m, olefinic protons of C_8H_{12}), 8.03 (2 H, dd, $C_{12}H_8N_2$), 8.22 (2 H, s, $C_{12}H_8N_2$), 8.43 (2 H, dd, $C_{12}H_8N_2$) and 8.89 (2 H, dd, $C_{12}H_8N_2$).

Method 2, *by treating compound* **5** *with phen*. Equimolar amounts of the β-diketonate **5** and phen, each dissolved in the minimum of acetone, were mixed. Addition of an excess of a saturated solution of $NaClO_4$ in acetone, precipitated **6** in *ca.* 64% yield.

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